

Swiss eHealth Summit, 9/15/2015, Bern

Predicting Diagnoses with Drug Orders, Routes and Doses

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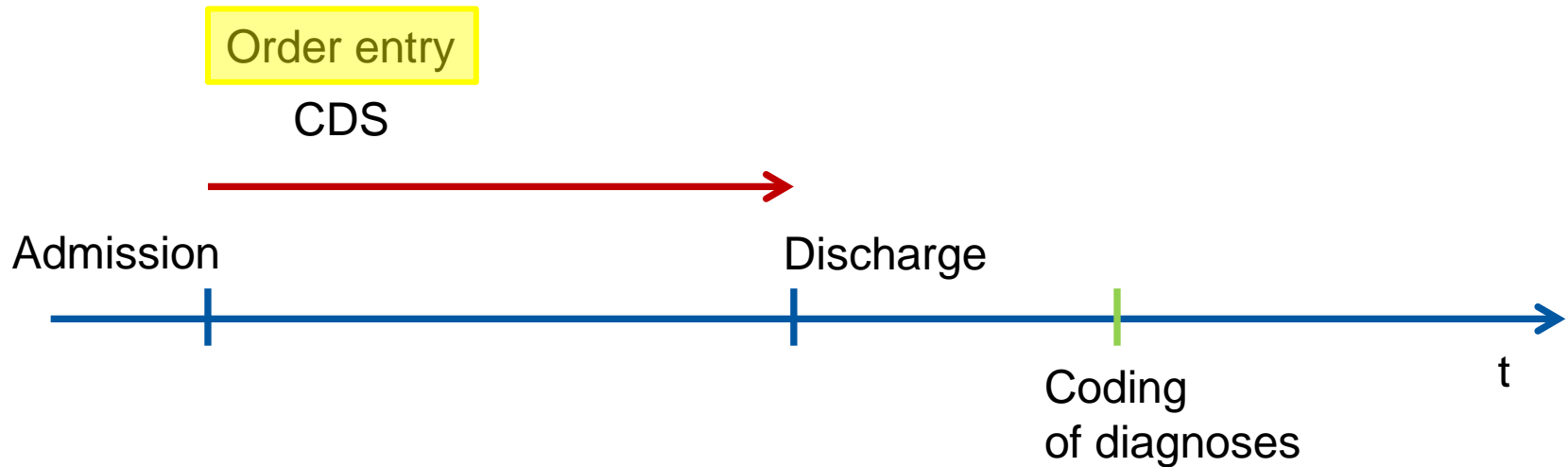


BRIGHAM AND
WOMEN'S HOSPITAL



HARVARD
MEDICAL SCHOOL

Hospitalization & Coding of Diagnoses



Add Diagnosis

The drug **levothyroxine** ordered for **TENTHFLOOR, PHARMI** is typically used for the treatment of hypothyroidism or the suppression of benign or malignant thyroid tissue. No such problem appears on the patient's problem list as an ICD-9 code. Please check the box below to place the correct problem on the patient's problem list.

To cancel this order, click 'Cancel Order.'
To ignore this alert and place the order without entering a diagnosis, click 'Ignore Alert.'

Alert Action

Cancel

Ignore Alert

Add Diagnosis

Add Problem(s) for:

- GOITER, SPECIFIED AS SIMPLE
- MALIGNANT NEOPLASM OF THYROID GLAND
- NONTOXIC MULTINODULAR GOITER
- NONTOXIC UNINODULAR GOITER
- UNSPECIFIED HYPOTHYROIDISM

OK

Fig. 1 – Example of a medication-diagnosis link alert. The alert is for an order for levothyroxine in a test patient.

Int J Med Inform. 2010 May;79(5):332-8.

Table 1

Top 50 medication-problem associations under chi square.

Medication	Problem
Cyclosporine micro (Neoral)	Cardiac transplant
Ritonavir	HIV/AIDS ^b
Tenofovir/emtricitabine ^a	HIV/AIDS ^b
Multivitamin (vitamins A, D, E, K)	Cystic fibrosis
Atazanavir	HIV/AIDS ^b
Efavirenz/emtricitabine/tenofovir ^a	HIV/AIDS ^b
Efavirenz/emtricitabine/tenofovir ^a	HIV positive
Ritonavir	HIV positive
Cyclosporine micro (Neoral)	Stress test
Tenofovir/emtricitabine ^a	HIV positive
Atazanavir	HIV positive
Dornase alfa	Cystic fibrosis
Hydroxyurea (non-oncology dose)	Sickle cell anemia

J Biomed Inform. 2010 Dec;43(6):891-901.



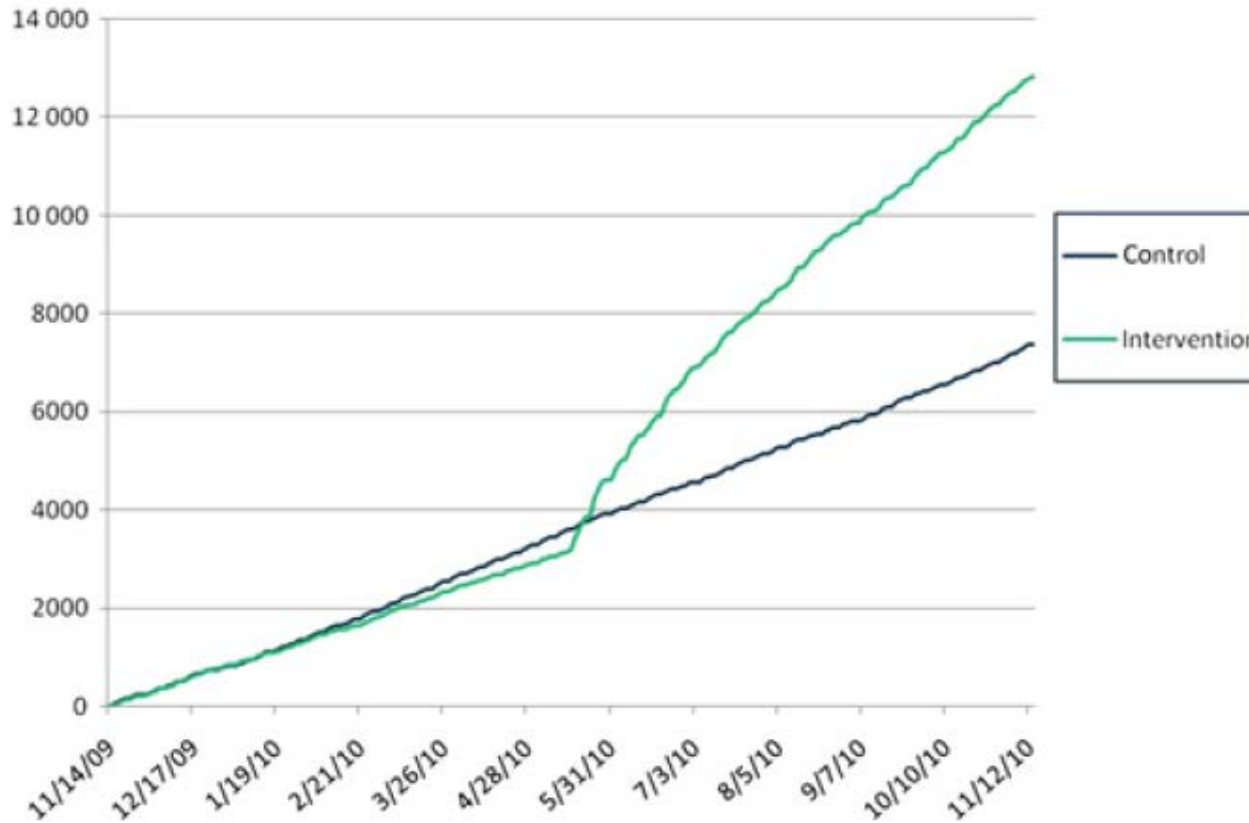


Figure 3 Cumulative number of study problems added during pre-intervention and intervention periods.

J Am Med Inform Assoc. 2012 Jul-Aug;19(4):555-61.

Contingency Table

		Diagnosis	
		present ICD-9 code added to the hospitalization	not present no such ICD-9 code added to the hospitalization
Medication	present medication order entered during hospitalization	TP	FP
	not present no such order entered during hospitalization	FN	TN

Possible combination (1 out of 258,346): levothyroxine and hypothyroidism.



Table 1: Top ten predictions (single listing of diagnoses) out of 258,346 drug-diagnosis combinations, ordered by χ^2 descending.

	Drug	Diagnosis	PPV [%]	Sensitivity [%]	Specificity [%]	χ^2 statistic
1.	Oxytocin	Outcome of delivery, single liveborn	93.5	90.8	99.0	45604.6
4.	Coagulation factor VIII	Congenital factor VIII disorder	93.1	67.5	100.0 ‡	34613.7
5.	Levothyroxine sodium	Unspecified acquired hypothyroidism	70.9	90.2	96.6	33425.4
6.	Palifermin	E946.8	66.7	88.9	100.0 ‡	32645.3
9.	Levodopa and decarboxylase inhibitor	Paralysis agitans	70.2	74.0	99.9	28506.1
10.	Dornase alfa (desoxyribonuclease)	Cystic fibrosis with pulmonary manifestations	63.6	78.5	99.8	27412.1
11.	Allergic reaction desensitization kit	Need for desensitization to allergens	59.8	75.3	99.9	24762.5
13.	Eculizumab	Hemolytic-uremic syndrome	71.4	62.5	100.0 ‡	24592.7
14.	Nimodipine	Subarachnoid hemorrhage	78.7	56.7	100.0 ‡	24549.7
15.	Erythropoietin	End stage renal disease	87.9	49.5	99.9	23626.6

E946.8: 'Other agents primarily affecting skin and mucous membrane causing adverse effects in therapeutic use'

PPV: positive predictive value

‡ actual value is slightly below 100%

Table 2. Top ten predictions (single listing of diagnoses) out of 310,102 drug and route-diagnosis combinations, ordered by χ^2 descending.

	Drug	Route	Diagnosis	PPV [%]	Sensitivity [%]	Specificity [%]	χ^2 statistic
1.	Oxytocin	IV	Outcome of delivery, single liveborn	93.5	89.8	99.1	45015.7
4.	Coagulation factor VIII	IV	Congenital factor VIII disorder	93.1	67.5	100.0 ‡	34613.7
5.	Levothyroxine sodium	PO	Unspecified acquired hypothyroidism	71.1	88.5	96.7	32853.0
6.	Palifermin	IV BOLUS	E946.8	66.7	88.9	100.0 ‡	32645.3
9.	Levodopa and decarboxylase inhibitor	PO	Paralysis agitans	70.6	73.6	99.9	28524.7
11.	Eculizumab	IV BOLUS	Hemolytic-uremic syndrome	71.4	62.5	100.0 ‡	24592.7
12.	Nimodipine	PO	Subarachnoid hemorrhage	79.5	55.8	100.0 ‡	24374.9
13.	Erythropoietin	IV BOLUS	End stage renal disease	91.5	48.4	99.9	24069.7
14.	Vancomycin	PO	Intestinal infection due to Clostridium difficile	60.9	69.5	99.6	23107.4
15.	Tobramycin	IV	Cystic fibrosis with pulmonary manifestations	78.1	52.9	99.9	22700.6

E946.8: 'Other agents primarily affecting skin and mucous membrane causing adverse effects in therapeutic use'

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Table 3. Comparison of drugs with and without route information predicting diagnoses; top ten (single listing of diagnoses) out of 310,102 compared prediction pairs, ordered by χ^2 gain descending.

	Drug	PPV [%]	Sensitivity [%]	Specificity [%]	By including this route	PPV [%]	Sensitivity [%]	Specificity [%]	Associated diagnosis	χ^2 statistic gain by including route
1.	Vancomycin	3.6	82.5	80.9	PO	60.9	69.5	99.6	Intestinal infection due to Clostridium difficile	21920.2
2.	Acetylcysteine	1.5	77.8	98.4	IV	28.3	72.2	99.9	Poisoning by aromatic analgesics, not elsewhere classified	10587.0
3.	Sodium chloride	2.7	73.1	89.2	INH	49.7	36.8	99.8	Cystic fibrosis with pulmonary manifestations	9100.0
4.	Epinephrine	5.8	54.6	98.4	IM	36.0	51.5	99.8	Need for desensitization to allergens	8497.0
5.	Cromoglicic acid	25.0	54.5	100.0 ‡	PO	50.0	54.5	100.0 ‡	Congenital pigmentary anomalies of skin	7514.5
6.	Rufinamide	60.0	33.3	100.0 ‡	GTUBE or JTUBE	100.0	33.3	100.0	Congenital quadriplegia	7348.4
7.	Nalbuphine	56.6	41.7	95.2	IV	89.2	37.6	99.3	Outcome of delivery, single liveborn	6607.1
8.	Paracetamol	4.2	93.7	27.2	PR	28.6	50.8	95.7	Acute posthemorrhagic anemia	6490.2
9.	Ondansetron	3.0	93.9	51.9	PO	16.9	84.6	93.5	Encounter for antineoplastic chemotherapy	6459.0
11.	Acetylcysteine	0.7	85.7	98.4	IV	13.0	85.7	99.9	Accidental poisoning by aromatic analgesics, not elsewhere classified	5847.7

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Table 4. Top ten predictions (single listing of diagnoses) out of 351,266 drug, route and dose-diagnosis combinations, ordered by χ^2 descending.

	Drug	Route	Unit	Dose	Diagnosis	PPV [%]	Sensitivity [%]	Specificity [%]	χ^2 statistic
1.	Diphenhydramine	PO	MG	High	Outcome of delivery, single liveborn	89.2	92.2	98.3	43882.5
4.	Palifermin	IV BOLUS		High	E946.8	75.0	66.7	100.0 ‡	27544.0
5.	Coagulation factor VIII	IV	UNITS	Low	Congenital factor VIII disorder	95.2	50.0	100.0 ‡	26224.8
6.	Nimodipine	PO	MG	High	Subarachnoid hemorrhage	81.7	55.8	100.0 ‡	25063.8
7.	Levothyroxine sodium	PO	MCG	Low	Unspecified acquired hypothyroidism	77.6	60.2	98.4	23871.9
8.	Multienzymes (lipase, protease etc.)	PO	TAB	High	Cystic fibrosis with pulmonary manifestations	55.3	74.9	99.8	22698.7
10.	Levodopa and decarboxylase inhibitor	PO	TAB	Low	Paralysis agitans	70.8	56.2	99.9	21832.2
11.	Vancomycin	PO	MG	Low	Intestinal infection due to Clostridium difficile	61.9	63.8	99.7	21520.1
13.	Desmopressin	PO	MG	Low	Diabetes insipidus	75.5	48.1	100.0 ‡	19962.4
14.	Benzylpenicillin	IV	UNITS	Low	Carrier or suspected carrier of group B streptococcus	71.2	52.3	99.3	19827.0

E946.8: 'Other agents primarily affecting skin and mucous membrane causing adverse effects in therapeutic use'

PPV: positive predictive value

‡ actual value is slightly below 100%

Table 5. Comparison of drugs and routes with and without dose information predicting diagnoses; top ten (single listing of diagnoses) out of 351,266 compared prediction pairs, ordered by χ^2 gain descending.

	Drug	Route	PPV [%]	Sensitivity [%]	Specificity [%]	Unit	Dose	PPV [%]	Sensitivity [%]	Specificity [%]	Associated diagnosis	χ^2 statistic gain by including dose
1.	Diphenhydramine	PO	37.4	92.6	76.7	MG	High	89.2	92.2	98.3	Outcome of delivery, single liveborn	30120.2
2.	Multivitamins, other combinations	PO	1.0	82.1	65.4	TAB	High	63.6	62.8	99.9	Cystic fibrosis with pulmonary manifestations	21686.6
3.	Coagulation factor IX	IV	13.2	71.4	99.9	UNITS	High	50.0	71.4	100.0 ‡	Congenital factor IX disorder	14500.5
5.	Diphenhydramine	PO	14.4	91.8	70.9	MG	High	34.3	91.2	90.6	648.91	10455.2
6.	Calcium folinate	PO	5.3	47.2	99.4	MG	High	43.6	47.2	100.0 ‡	Malignant neoplasm of long bones of lower limb	9969.4
7.	Ethambutol	PO	10.2	83.3	99.9	MG	High	31.3	83.3	100.0 ‡	Pulmonary alveolar proteinosis	9663.8
8.	Multivitamins, other combinations	PO	0.6	70.2	65.4	TAB	High	35.0	47.8	99.7	Bronchiectasis with acute exacerbation	9042.6
9.	Pseudoephedrine	PO	30.9	61.3	99.6	MG	High	57.2	60.7	99.9	Benign neoplasm of pituitary gland and craniopharyngeal duct	8721.8
11.	Foscarnet	IV	17.2	100.0	100.0 ‡	MG	Low	31.3	100.0	100.0 ‡	Human herpesvirus 6 encephalitis	7718.8
12.	Diphenhydramine	PO	10.3	92.3	69.9	MG	High	24.7	92.2	89.4	664.11	7547.5

648.91: 'Other current conditions classifiable elsewhere of mother, delivered, with or without mention of antepartum condition'

664.11: 'Second-degree perineal laceration, delivered, with or without mention of antepartum condition'

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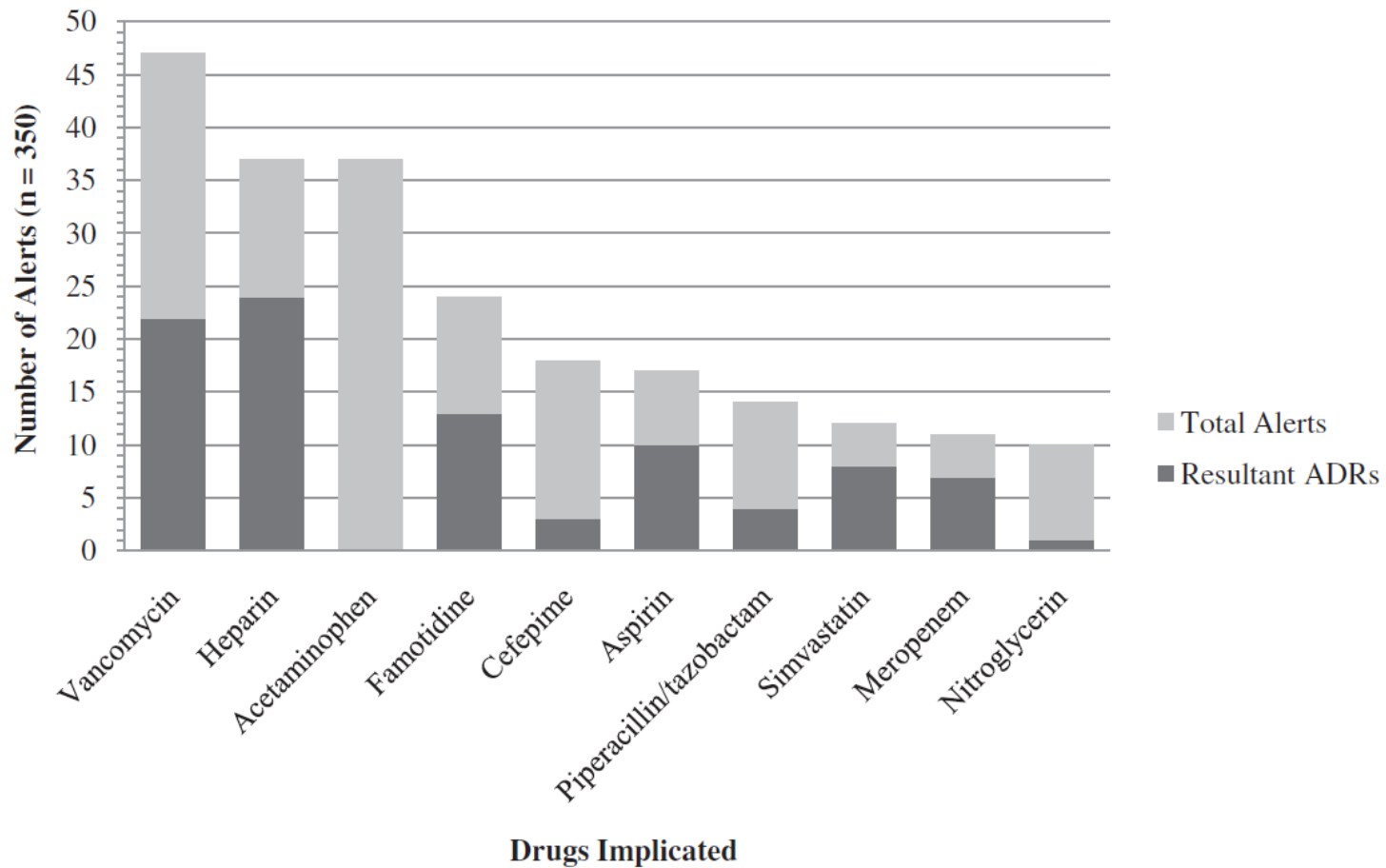
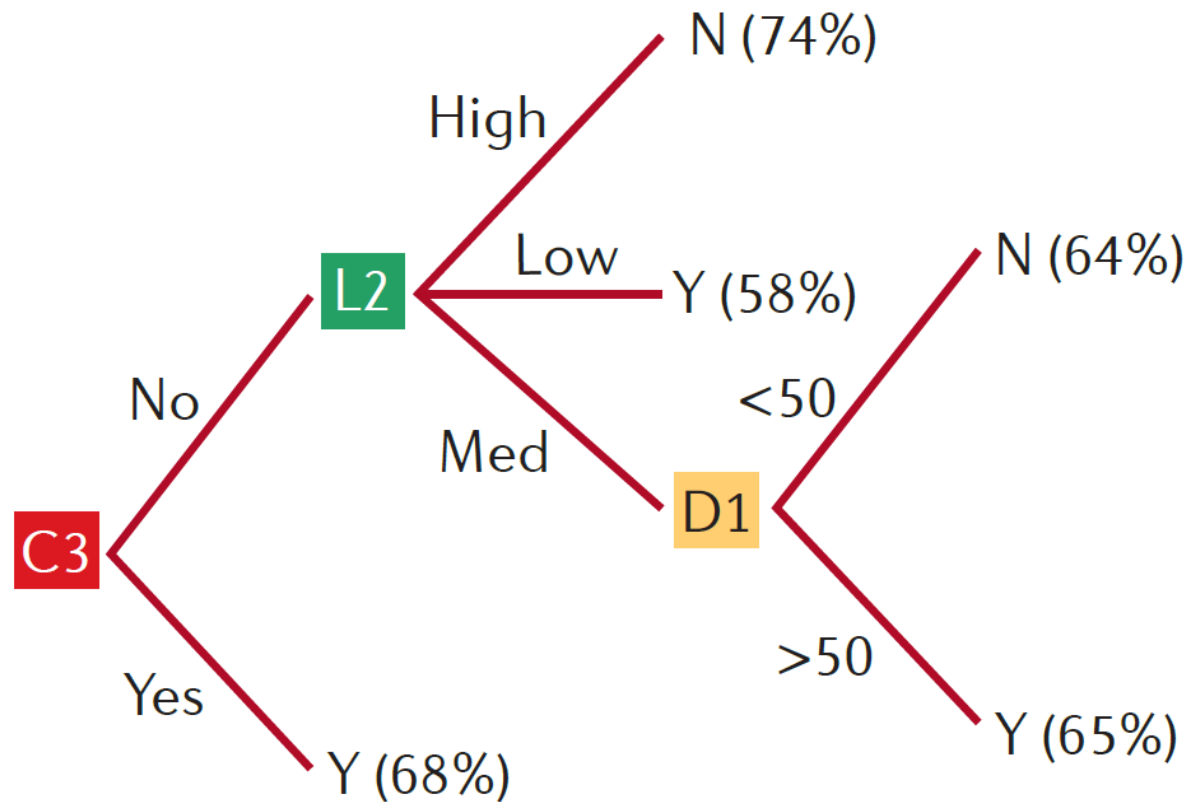


Figure Drugs most commonly associated with alerts and the number of resultant ADRs.

J Crit Care. 2012 Jun;27(3):242-9.



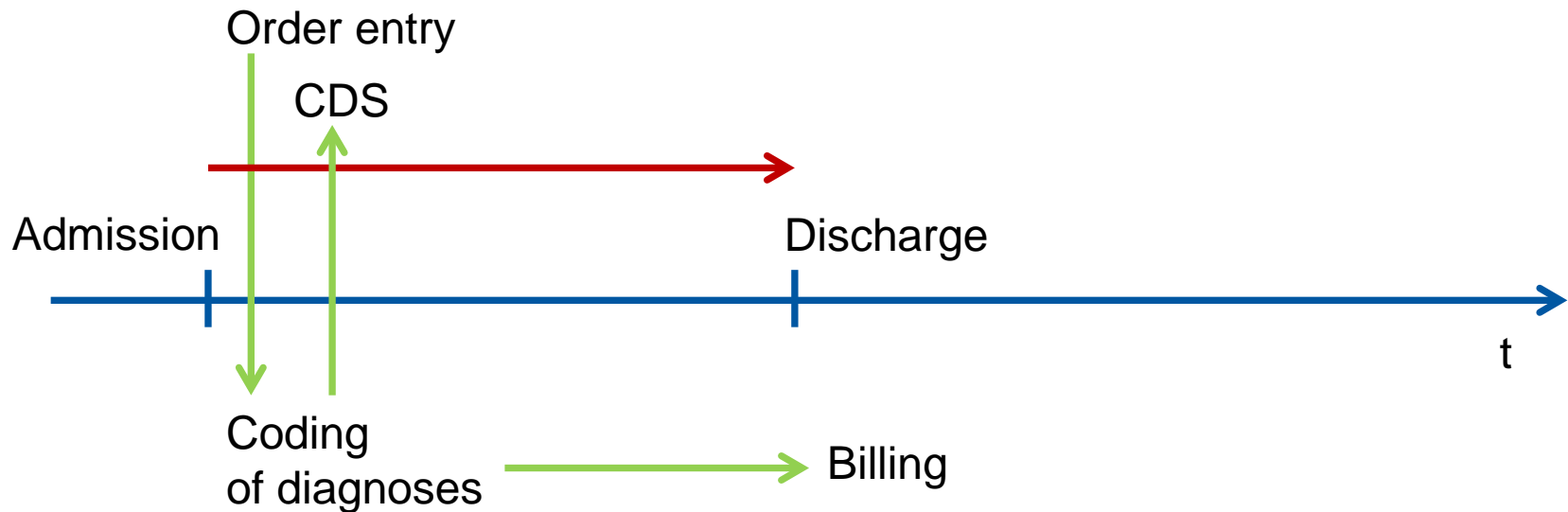
Machine learning



Nat Rev Genet. 2012 May 2;13(6):395-405.



Use of Structured Information on Medication Orders



Thank you!

Questions?



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