Thesis Proposal

Predictive Modeling with Imbalanced Data?

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Introduction

- Don't go into background problem too much? (for stats paper)
- Do I open on the imbalanced learning problem?
- How much to describe the dataset?
- start with opioid problem
- how much increase in opioid use
- how need to identify patients at increased risk is immediate
- this presents a statistical problem in classifying patients when identifying a rare outcome
- cite some other issues in health with rare outcomes and what people have done
- give fair bit of background (stats in medical, etc) find where people try to predict rare outcomes
- hopefully no ones done exactly what we've done
- no one's explored the tradeoffs of cut-points and sampling, what we've sought to do in order to achieve best prediction
- last paragraph, we sought to identity patients at risk for COT at a safety hospital at Denver, predictive performance, few sentences on what we're doing and what methods and dataset

Predictive modeling with imbalanced data has been found to have report low sensitivity (reference?). To combat this issue of overlooking many true postitives,

Methods

Data

To illustrate this issue, we are using electronic health record data from Denver Health from the years 2008 to 2014 of patients for patients with chronic opioid therapy (COT). This

is an urban, safety-net hospital. Five percent of the 27,705 patients were reported with the outcome, which was defined as receipt of $\geq$ 90-day supply of opioids with $<$ 30-day gap in supply over a 180-day period or receipt of $\geq$ 10 opioid prescriptions over one year. The data also contained demographic information on the patient including age, race, gender, history of chronic pain, and length of hospital stay.

Statistical Methods

The analysis was done in RStudio version 1.1.383.

We used a roughly 2/3rd temporal split of the data to create training and testing datasets, where years 2008-2011 were used to train (65%), and 2012-2014 were used to test (35%).

The model used for this analysis was cross validated lasso regression. This was chosen as it has been found to perform better predictor selection than stepwise selection (reference on this?), and as we were not interested in having interpretable coefficients.

The predictors were first narrowed from ? to 35 (?) based on clinical relevance.

We first evaluated the prediction performance of the dataset without sampling to see the effects of the imbalanced data on the accuracy, sensitivity, and specificity. This was to serve as a baseline to compare with the techniques available to mitigate the issue of poor sensitivity. The predicted probability cut-point used here was rounding at the standard 0.5 that would be appropriate in balanced datasets.

The first approach used to improve performance was to choose a more informed probability cut-point for the data. This was done using the Youden Index, which finds the maximum of the receiver operating characteristic (ROC) curve (reference here!) with the pROC package.

The second approach was through sampling the dataset. Three types of sampling methods were compared–down sampling, up sampling, and Synthetic Minority Over-sampling Technique (SMOTE). Down sampling takes a random sample from the majority class, in this case those who are not classified as having chronic opioid therapy, in order to match the size of the minority class (reference?). Up sampling does the reverse to take random samples of the minority class in order to match the majority (reference?). SMOTE combines sampling both from the majority and minority, but instead of taking identical copies of the minority it creates synthetic observations (reference). For each of the three sampling techniques, the probability cut-point was optimized using the Youden Index as before.

Results

As expected, without using an optimized cut-point or sampling technique, the sensitivity of the model was extremely poor at 8%, with high specificity and accuracy (99% and 96%). Simply choosing a more informed probability cut-point to 0.043 instead of 0.5 improved the

sensitivity to 85% and brought the specificity down to 73%. This cut-point is intuitive as the outcome is present at 5% in the dataset, which would be consistent with a 0.5 cutoff in a evenly split dataset. The up and down sampled datasets both showed the same improved sensitivity with probability cut-points at about 0.4, also with close specificities of 74 and 73%. SMOTE on the other hand, resulted in 74% sensitivity and 84% specificity. However, there were improvements in accuracy for SMOTE at 86% as compared to the other three approaches, which had accuracies at 86-87%.

There was no change to the negative predicted value across the approaches, and a decrease in positive predicted value. In terms of the ROC analysis, the area under of the curve for each approach was about the same at 86-87%. See Table 2 for full results for the cut-point, sensitivity, specificity, accuracy, negative predicted value, positive predicted value, and area under the curve.

Discussion

- there do appear to be variables with strong associations, but the question of model choice depends on what method– get different vars from lasso if you're doing cutpoint or sampling

sampling gives a case control in your data and I think should give fewer variables– checked, does not. there are more vars for the sampling cases (by 2 or 3)*

trade offs to discuss with physician, at what point do the sens, spec need to be

Across the different samples, we saw similar improvements for sensitivity.

Conclusion

References

ROC, Youden, SMOTE, LASSO, cross-validation Chronic Opioid Therapy, up-sampling, down-sampling

A Statistical Model for Prediction of Future Chronic Opioid Use among Hospitalized Patients

Appendix

Include full table 1? Yes include the full table before but pull out some of the ones from the smaller table to quote

Among these set of variables, which ones are most important in classifying. supervised learning problem (because observed outcome)

Table 1:

Variable	**Yes COT** 1,457 (5%)	**No COT** 26,248 (95%)	**p-value**
Age 15-35	10%	22%	<.001
Age 45-55	35%	24%	<.001
Age 55-65	28%	21%	<.001
Discount payment or Medicaid	76%	61%	<.001
History of chronic pain	76%	53%	<.001
Discharge diagnosis chronic pain	50%	29%	<.001
Surgical patient	48%	39%	<.001
Past year:			
Benzodiazepine	16%	5%	<.001
Non-opioid analgesics	25%	9%	<.001
Number of opioid prescriptions:			
0	38%	80%	
1	17%	11%	
2	14%	4%	
3	9%	2%	
4-9	23%	3%	<.001
Receipt of opioid at discharge	56%	28%	<.001
MME per hospital day > 10	80%	52%	<.001

Table 2: Results

Data	**Threshold**	**Specificity**	**Sensitivity**	**NPV**	**PPV**	**Accuracy**	**AUC**	**Covariates**
Unsampled 0.5	0.5	99	8	96	35	96	86	31
Unsampled	0.043	73	85	99	12	73	86	31
Down sampled 0.5	0.5	81	75	99	15	81	86	34
Down sampled	0.401	73	85	99	12	74	86	34
Up sampled 0.5	0.5	82	75	99	15	82	87	34
Up sampled	0.399	74	85	99	12	74	87	34
SMOTE 0.5	0.5	86	71	99	17	85	86	33
SMOTE	0.472	84	74	99	17	84	86	33

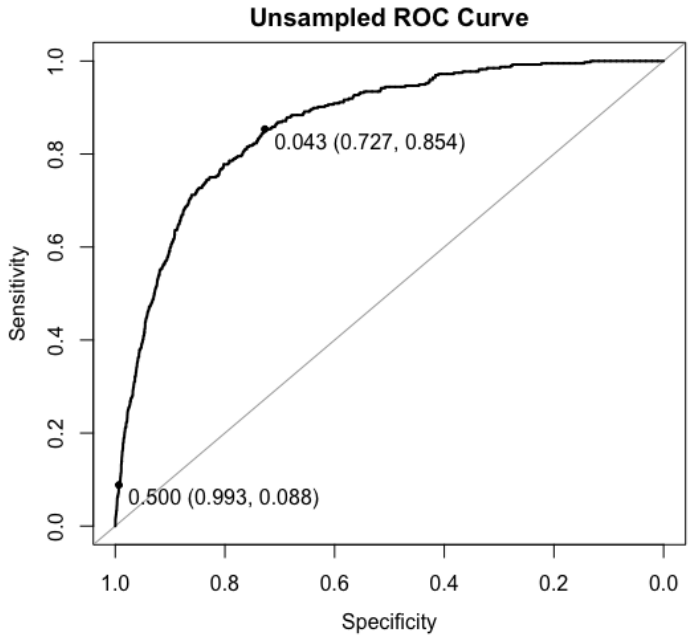

Figure 1: ROC for Original Data: Younden and 0.5 cutoffs

		Chronic Opioid Use		P-Value
	Total (N=27,705)	Yes (N=1,457)	No (N=26,248)	
Gender, n (%)				
Female	12,933 (46.7)	652 (44.7)	12,281 (46.8)	0.13
Race, n (%)				
Hispanic	10,798 (39.0)	580 (39.8)	10,218 (38.9)	0.01
Non-Hispanic White	10,645 (38.4)	555 (38.1)	10,090 (38.4)	
African American	4,842 (17.5)	273 (18.7)	4,569 (17.4)	
Other or Unknown	1,420 (5.1)	49 (3.4)	1,371 (5.2)	
Age at Index Admission (Years), n (%)				
15-<35	6,017 (21.7)	150 (10.3)	5,867 (22.4)	<0.0001
35-<45	4,734 (17.1)	267 (18.3)	4,467 (17.0)	
45-<55	6,919 (25.0)	506 (34.7)	6,413 (24.4)	

		Chronic Opioid Use		P-Value
55-<65	5,880 (21.2)	400 (27.5)	5,480 (20.9)	
65-<75	2,745 (9.9)	110 (7.5)	2,635 (10)	
75-ł85	1,410 (5.1)	24 (1.6)	1,386 (5.3)	
Mean (SD)	48.1 (16.0)	50.2 (11.6)	48.0 (16.2)	
Median (25th, 75th)	49 (37, 59)	51 (43, 58)	49 (36, 59)	
Insurance Status, n (%)				
Discount Payment Plan*	8,499 (30.7)	576 (39.5)	7,923 (30.2)	<0.0001
Medicaid	8,575 (31.0)	531 (36.4)	8,044 (30.6)	
Medicare	6,260 (22.6)	259 (17.8)	6,001 (22.9)	
Commercial	2,402 (8.7)	50 (3.4)	2,352 (9.0)	
Other/Unknown/Self-Pay	1,969 (7.1)	41 (2.8)	1,928 (7.3)	
Three Year History of, n (%)				
Tobacco Use Disorder	9,682 (34.9)	716 (49.1)	8,966 (34.2)	<0.0001
Alcohol Use Disorder	7,167 (25.9)	408 (28.0)	6,759 (25.8)	0.06
Stimulant Use Disorder	1,719 (6.2)	118 (8.1)	1,601 (6.1)	0.003
Opioid Use Disorder	672 (2.4)	44 (3.0)	628 (2.4)	0.13
Chronic Pain	14,914 (53.8)	1,105 (75.8)	13,809 (52.6)	<0.0001
Acute Pain	10,073 (36.4)	611 (41.9)	9,462 (36.0)	<0.0001
Top 3 Mental Health Disorders, n (%)				
Depression	6,318 (22.8)	491 (33.7)	5,827 (22.2)	<0.0001
Anxiety Disorder	3,677 (13.3)	265 (18.2)	3,412 (13.0)	<0.0001

		Chronic Opioid Use		P-Value
Bipolar Disorder	2,362 (8.5)	135 (9.3)	2,227 (8.5)	0.3
Any Mental Health Disorder n (%)	9,805 (35.4)	634 (43.5)	9,171 (34.9)	<0.0001
Top 3 Chronic Medical Conditions, n (%)				
Hypertension	11,799 (42.6)	773 (53.1)	11,026 (42.0)	<0.0001
Respiratory Disease	7,060 (25.5)	444 (30.5)	6,616 (25.2)	<0.0001
Diabetes Mellitus	5,701 (20.6)	376 (25.8)	5,325 (20.3)	<0.0001
Any Chronic Medical Condition, n (%)	17,535 (63.3)	1,102 (75.6)	16,433 (62.6)	<0.0001
Charlson Comorbidity Index from 3 Year Diagnosis History				
Mean (SD)	1.9 (2.2)	2.4 (2.5)	1.9 (2.2)	<0.0001
Median (25th, 75th)	1 (0, 3)	2.0 (1, 3)	1.0 (0, 3)	
Discharge Diagnoses, n (%)				
Chronic Pain_	8,346 (30.1)	729 (50.0)	7,617 (29.0)	<0.0001
Acute Painŕ	4,586 (16.6)	255 (17.5)	4,331 (16.5)	0.32
Neoplasm¤	1,447 (5.2)	170 (11.7)	1,277 (4.9)	<0.0001
Top 3 Surgical Procedures During Initial Hospitalization, n (%)				
Digestive System	3,437 (12.4)	225 (15.4)	3,212 (12.2)	<0.001
Musculoskeletal System	3,037 (11.0)	258 (17.7)	2,779 (10.6)	<0.0001
Cardiovascular System	2,312 (8.3)	157 (10.8)	2,155 (8.2)	<0.001
Patients Who Had Surgical Procedure During Index Hospitalization, n (%)	10,956 (39.5)	700 (48.0)	10,256 (39.1)	<0.0001
Number of Healthcare Encounters in the One Year Preceding the Index Admission, n (%)				

		Chronic Opioid Use		P-Value
0	23,280 (84.0)	1,196 (82.1)	22,084 (84.1)	0.03
1	3,413 (12.3)	197 (13.5)	3,216 (12.3)	
2+	1,012 (3.7)	64 (4.4)	948 (3.6)	
Mean (SD)	0.2 (0.6)	0.2 (0.7)	0.2 (0.6)	
Median (25th, 75th)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)	
Past Year Benzodiazepine Receipt, n (%)	1,606 (5.8)	227 (15.6)	1,379 (5.3)	<0.0001
Past Year Receipt of Non-Opioid Analgesics (NSAIDs, neuropathic agents, topical capsaicin & lidocaine), n (%)				
	4,875 (17.6)	620 (42.6)	4,255 (16.2)	<0.0001
Past Year Number of Opioid Prescriptions Filled, n (%)				
0	21,543 (77.8)	549 (37.7)	20,994 (80.0)	<0.0001
1	3,167 (11.7)	249 (17.1)	2,918 (11.1)	
2	1,331 (4.8)	197 (13.5)	1,134 (4.3)	
3	646 (2.3)	132 (9.1)	514 (2.0)	
9-Apr	1,018 (3.7)	330 (22.6)	688 (2.6)	
Receipt of Opioid at Discharge, n (%)	8,028 (29.0)	817 (56.1)	7,211 (27.5)	<0.0001
Milligrams of Morphine Per Hospital Day, n (%)				
0	9,655 (34.8)	189 (13.0)	9,466 (36.1)	<0.0001
0.01 < 10	3,320 (12.0)	108 (7.4)	3,212 (12.2)	
10 < 51	7,337 (26.5)	490 (33.6)	6,847 (26.1)	
51 < 100	4,413 (15.)	371 (25.5)	4,042 (15.4)	
100+	2,980 (10.8%)	299 (20.5)	2,681 (10.2)	

		Chronic Opioid Use		P-Value
Mean (SD)	37.7 (65.4)	64.4 (76.7)	36.2 (64.4)	
Median (25th, 75th)	12.5 (0, 54.7)	45.5 (14.3, 90.2)	10.8 (0, 52.2)	
Length of Hospital Stay (days)				
1	8,449 (30.0)	383 (26.3)	8,066 (30.7)	0.0003
2	5,655 (20.4)	282 (19.4)	5,373 (20.5)	
5-Mar	7,801 (28.2)	450 (30.9)	7,351 (28.0)	
6+	5,800 (20.9)	342 (23.5)	5,458 (20.8)	
Mean (SD)	4.7 (9.0)	4.9 (7.7)	4.6 (9.1)	
Median (25th, 75th)	2 (1, 5)	3 (1, 5)	2 (1, 5)	
Number of Subsequent Hospitalizations within 12 Months post Hospital Discharge				<0.001
Mean (SD)	NA	1.48 (2.20)	0.54 (1.21)	
Median (25th, 75th)	NA	1 (0,2)	0 (0,1)	