A comparison of statistical methods for improving rare event classification in medicine

Thesis Defense

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Outline

Problem

Objectives

Methods

Case Studies

Simulation Study

Discussion

Conclusion

Imbalanced Learning Problem

- Predictive models learn poorly when datasets are imbalanced
- Over learning the majority and under learning the minority
- Results in low sensitivity and high specificity
- Need to improve predictive performance
- Many examples in medicine, diseases or adverse reactions taking place in small percent of the population

Aims

- Improve predictive performance for imbalanced dataset
- Utilizing measures of sensitivity, specificity, accuracy, and ROC analysis to evaluate performance
- Use and compare two methods to handle imbalance
  - Informed probability cutpoints for predicted probabilities
  - Sampling techniques to balance datasets
- Evaluate methods to recommend approaches in medicine

Methods

- Split data into training and test sets
- Create balanced datasets through sampling on test set
- Run predictive model on sampled data
- Get predicted probabilities on the hold-out test data
- Optimize probability cutoff for outcome

Model

Cross-validated lasso regression - Least Absolute Shrinkage and Selection Operator

- Lasso:
  - Shrinks estimates by penalizing size of coefficients
  - Performs variable selection by shrinking some to 0

$$\hat{\beta}_{lasso} = argmin \sum_{j=1}^{N} (y_i - \beta_0 - \sum_{j=1}^{p} x_{ij}\beta_j)^2$$

subject to $\sum_{j=1}^{p} |\beta_j| \leq t$ where t is the tuning parameter.

Cross Validation

- Cross validation:
  - Find the best "tuning measure" for model selection which determines amount of shrinkage of estimates
  - Split data into k parts and then train on each of those except one you validate against
  - Then pick the tuning measure that minimizes error

Advantages and Disadvantages

- Advantages:
  - Lower variance of the predicted values
  - More accurate predictions
  - Reduces the number of predictors
- Disadvantages:
  - Biased coefficients, inference not same as logistic regression
  - No standard errors or p-values out of the model

ROC & Cutoff Probabilities

ROC (with pROC package):

- Receiver Operating Characteristics
- ROC curve plots sensitivity vs specificity
- Each point on curve corresponds to a decision cutoff
- Youden's Index calculated the furthest upper left corner or "max" on curve
- Area under the curve (AUC) should be maximized

ROC Curve

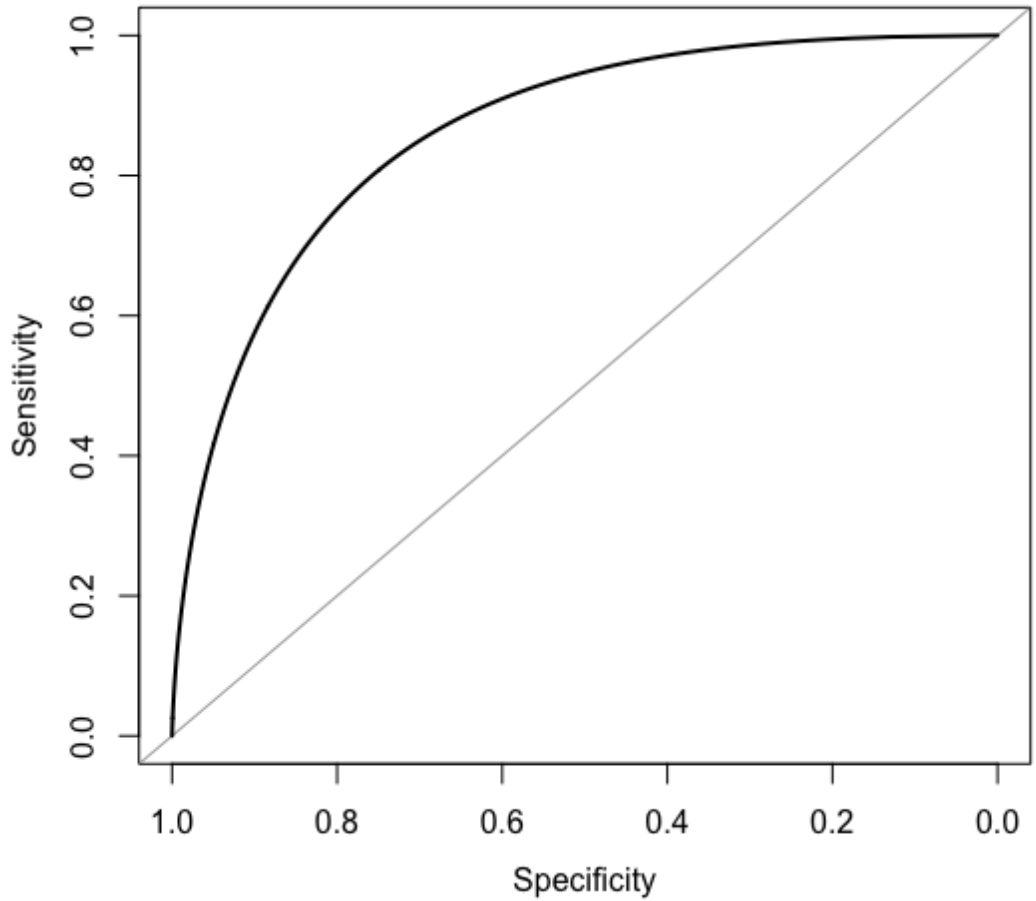

Figure 2: ROC Curve

Confusion Matrix

Correctly identify those w/ outcome:

$$Sensitivity = \frac{TP}{TP + FN}$$

Correctly identify those w/o outcome:

$$Specificity = \frac{TN}{TN + FP}$$

Correctly identify either group:

$$Accuracy = \frac{TP + TN}{TP + FP + TN + FN}$$

		Predicted class	
		P	N
Actual Class	P	True Positives (TP)	False Negatives (FN)
	N	False Positives (FP)	True Negatives (TN)

First Approach

No Sampling, Optimize Cut-off:

- Use original unsampled data and get predictions from the lasso model
  - Predictions return probability between 0 and 1 for each observation
- Use 0.5 standard probability cutoff to compare
- Find "best" probability cutoff
  - Youden's Index

Second Approach

Sampling:

- Create sampled data sets that are balanced
  - Down sample
  - Up sample
  - SMOTE
- Predict and use Youden's Index as cutoff

Down Sampling

- Under-sample majority to equal minority

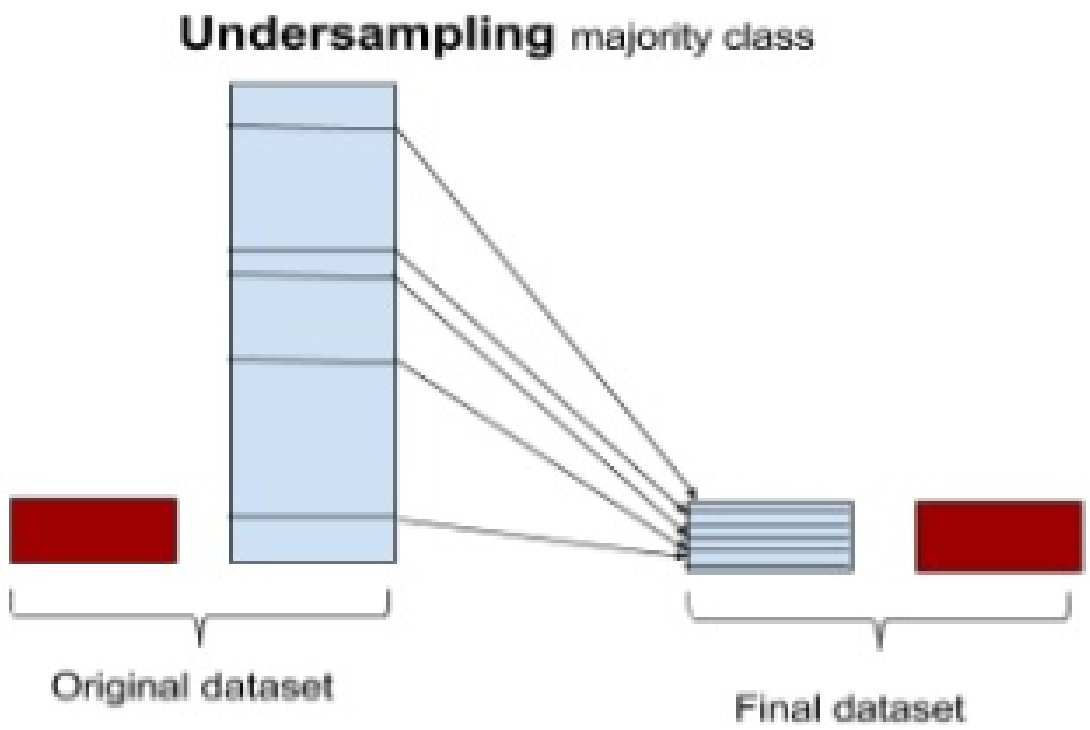

Figure 3: Down sample

Up Sampling

- Over-sample minority to equal majority

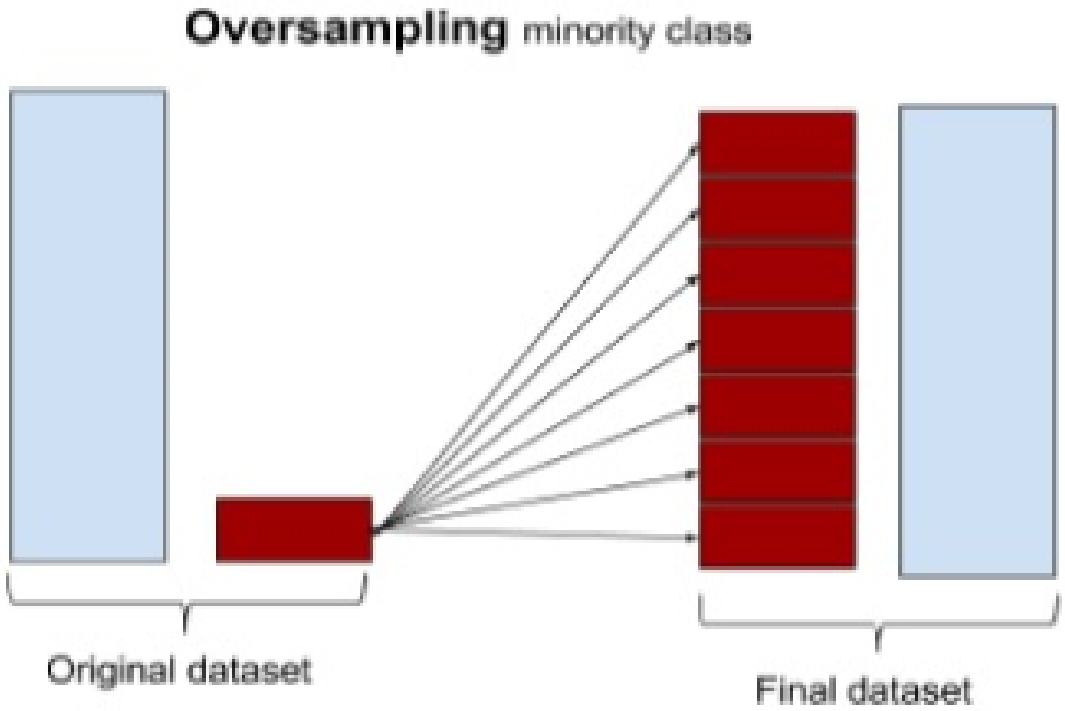

Figure 4: Up sample

SMOTE

- Synthetic Minority Over-sampling Technique

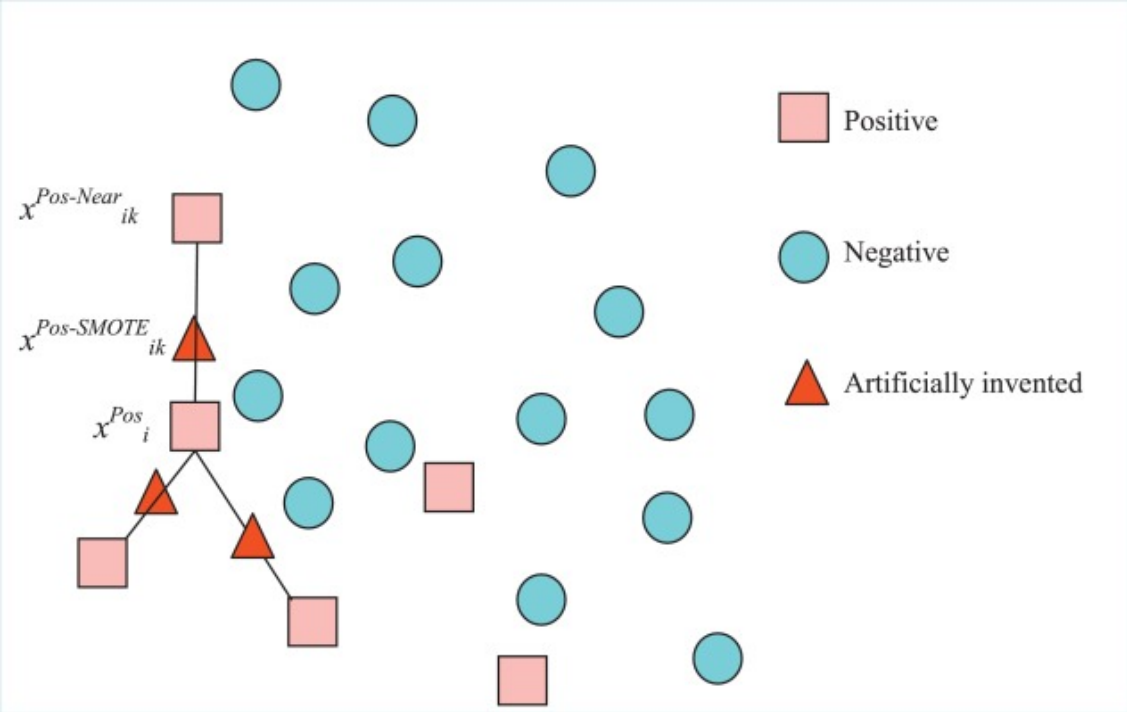

Figure 5: SMOTE

Models

- Model 1: No Sampling
  - 0.5 cutoff
  - Youden's Index
- Model 2: Down Sampling
  - Youden's Index
- Model 3: Up Sampling
  - Youden's Index
- Model 4: SMOTE
  - Youden's Index

Case Studies

We used these methods on two case studies to see how results may differ between two real world examples with rare outcomes.

- Case Study 1: Predicting chronic opioid therapy in hospitalized patients (5%)
- Case Study 2: Predicting surgical site infections in hospitalized patients (3.4%)

Case Study 1

- Data from Denver Health electronic health records (EHR)
- Definition of Chronic Opioid Therapy (COT) one year following the index hospital discharge:

  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.

- 27,705 patients where 5% developed COT within a year
- 35 explanatory variables
  - Ex: age, race, history of chronic pain, discharge diagnosis

Case Study 1: Results

Table 1: Results for Chronic Opioid Therapy

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

ROC Plot

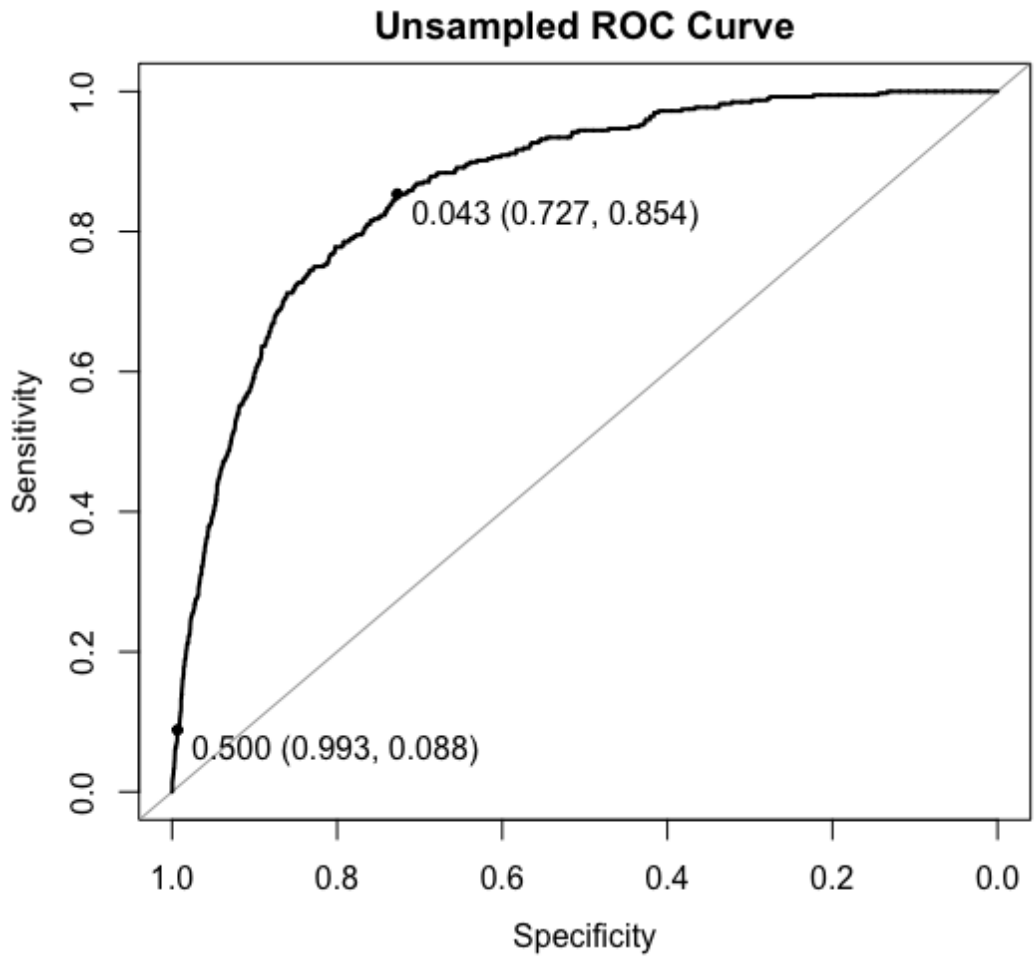

Figure 6: ROC for Original Data: Youden's Index and 0.5 cutoffs

Case Study 2

- Need to identity post-operative complications without the use of manual chart reviews by nurses
- Surgical site infections (SSI) are the most common complication
- $>$50% of SSIs occur after patient discharge
- Data from 6,840 patients at the University of Colorado Hospital from 2013-2016
- 136 independent variables were all binary indicators
  - Ex: Antibiotic prescriptions, procedure codes, ICD-9 codes

Case Study 2: Results

Table 2: Results for Surgical Site Infections

Model	Threshold	Sensitivity	Specificity	NPV	PPV	Accuracy	AUC	Covariates
Unsampled 0.5	0.50	0	0	0	0	0	0	0
Unsampled	0.04	80	90	99	24	90	89	35
Down sampled	0.48	82	87	99	20	87	89	20
Up sampled	0.45	79	91	99	24	90	89	123
SMOTE	0.15	89	79	99	14	80	88	88

Simulation Study

- We conducted a simulation study to look at how to methods performed at a greater range of prevalences
- We chose 3%, 5%, 10%, 20%, 40%, and 50% outcomes
- Goals:
  - Evaluate performance differences
  - Determine at what point it's no longer necessary to worry about imbalance

Simulation Methods

- Selected 10 of the strongest predictors to run a logistic regression
- Set the results as the values for the coefficients for the linear predictor
- Simulated the new outcome with a logistic distribution

$$F(x) = \frac{e^z}{1 + e^z}$$

- Controlled prevalence by adjusting the intercept
- Implemented sampling and lasso regression with additional 15 predictors (30 total) to get results

Simulation Results Part 1

Table 3: Results for 3, 5 and 10%

	Threshold	Sensitivity	Specificity	Accuracy	AUC	Coefficients
3%						
Unsampled 0.5	0.50	2	100	97	79	6
Unsampled	0.03	70	75	74	79	6
Down Sampled	0.49	70	74	74	78	9
Up Sampled	0.48	70	74	74	78	27
SMOTE	0.41	70	74	74	78	15
5%						
Unsampled 0.5	0.50	4	100	95	78	7
Unsampled	0.05	69	74	74	78	7
Down Sampled	0.49	69	74	74	78	9
Up Sampled	0.49	69	74	74	78	23
SMOTE	0.41	69	74	74	78	16
10%						
Unsampled 0.5	0.50	8	100	91	77	8
Unsampled	0.10	68	74	73	77	8
Down Sampled	0.49	68	74	73	77	9
Up Sampled	0.49	68	74	73	77	18
SMOTE	0.42	68	73	73	77	19

Simulations Results Part 2

Table 4: Results for 20, 40, and 50%

	Threshold	Sensitivity	Specificity	Accuracy	AUC	Coefficients
20%						
Unsampled 0.5	0.50	21	97	82	76	8
Unsampled	0.20	66	73	72	76	8
Down Sampled	0.49	66	73	72	76	9
Up Sampled	0.49	66	73	72	76	13
SMOTE	0.42	66	72	71	75	23
40%						
Unsampled 0.5	0.50	49	84	70	74	9
Unsampled	0.39	66	71	69	74	9
Down Sampled	0.49	66	71	69	74	9
Up Sampled	0.49	65	71	69	74	10
SMOTE	0.41	64	71	68	73	28
50%						
Unsampled 0.5	0.50	63	72	68	73	9
Unsampled	0.49	63	72	68	73	9

Sensitivity and Specificty by Prevalence

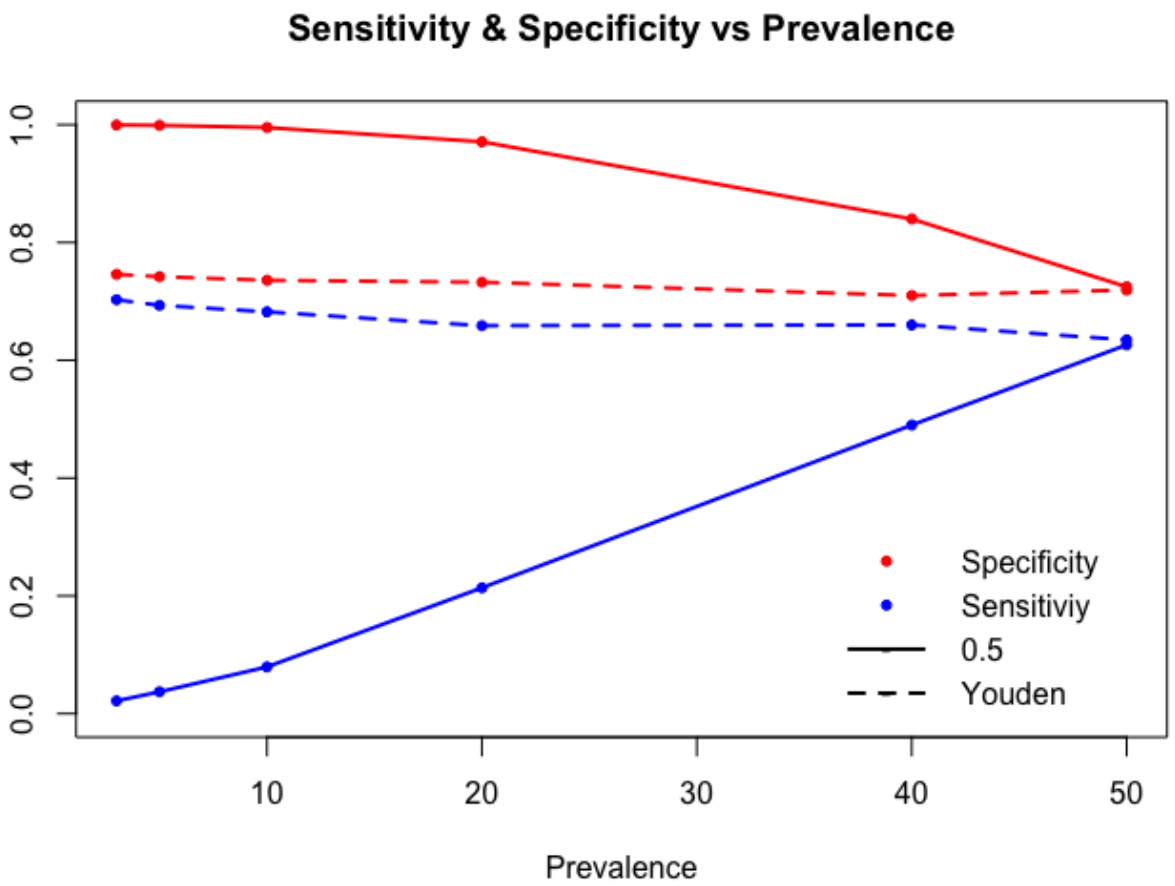

Figure 7: Comparing Youden's Index vs 0.5 cutoff results across prevalence

Youden's Index by Prevalence

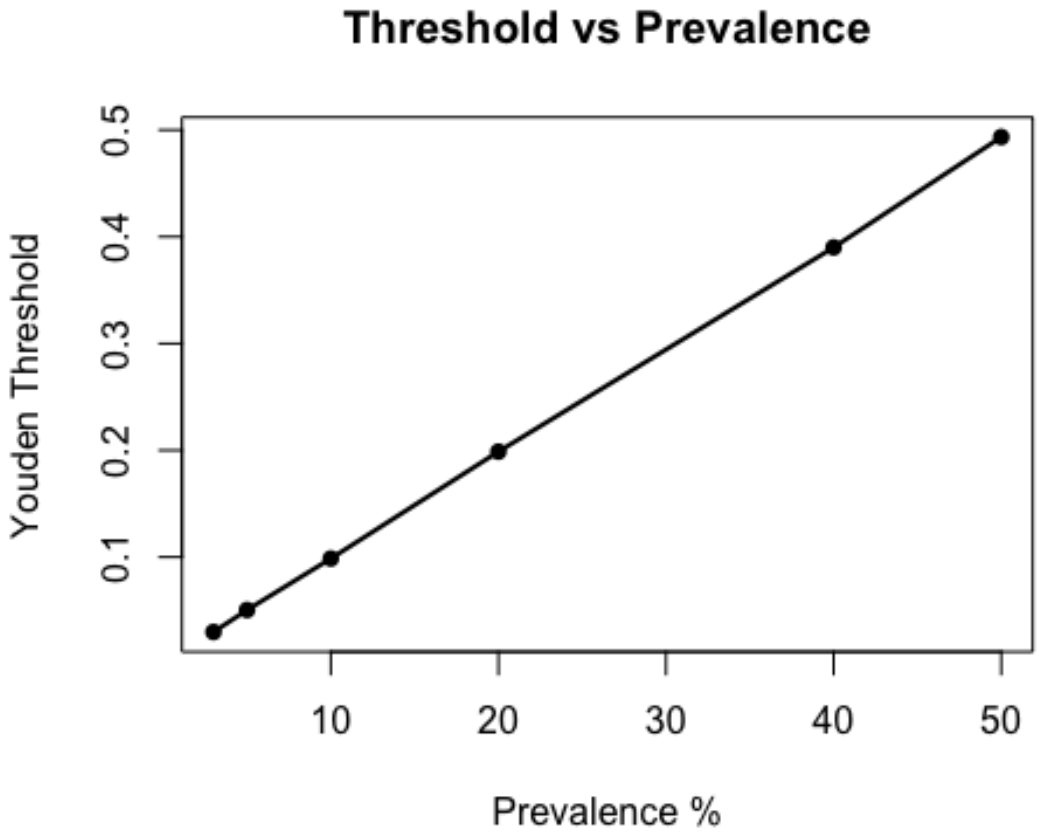

Figure 8: Youden's Index matches prevalence

Discussion

- Not much difference between Youden's + sampling vs. Youden's alone
- Over sampling and SMOTE had highest number of coefficients
- Threshold equals prevalence
- Sensitivity low even in less extreme imbalanced data for 0.5 cutoff
- Costs are unknown

Conclusion

I don't really see any value in sampling, but I'm not sure I should say that, or if I should still give some credit to sampling? (in one or two instances it had lower coefficients or slightly higher accuracy/AUC but it seems insignificant and variable to me)

- When costs are known, these approaches may be used with more intentional decision making
- Further Investigation:
- Choosing cutoff with training set rather than test set

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Funding??

Thank you for attending.

Case Study 1

- Design: Denver Health retrospective analysis electronic health record (EHR) data from 2008 to 2014.
- Patients: Hospitalized patients at an urban, safety-net hospital.
- Definition of Chronic Opioid Therapy (COT) one year following the index hospital discharge:

  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.

Case Study 1: Patient Population

- 27,705 patients
- Majority had incomes <185% of the Federal Poverty Level
- 70% were ethnic minorities
- 5% with COT
- Excluded Patients:
  - <15 or >85 years old
  - Those in prison, jail, or police custody
  - Those who died within one year following their index hospitalization
  - Patients with <2 healthcare visits to Denver Health three years preceding their index hospitalization
  - Undocumented persons receiving emergent hemodialysis
  - Obstetric patients

Case Study 2

Add more details on this case study here