Measuring the Model Prediction Performance for Rare Events

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Outline

- Motivation
  - Predicting/Detecting the Rare Events (low prevalence/incidence)
- Metrics for evaluating model performance
  - Area under the ROC curve (AUC)
  - Average Positive Predictive Value (AP)
- Examples
- Summary and future work

Motivating Data

Digital Mammography Imaging Screening Trial (Pisano et al. 2005 *New England Journal of Medicine*)

Malignancy score		**7**	**6**	**5**	**4**	**3**	**2**	**1**	**Total**
Digital M	Category Total	11	29	69	1061	2224	6588	32588	**42570**
	Cancers	10	18	25	85	49	25	122	**334**
Film M	Category Total	17	29	70	942	2291	6910	32486	**42745**
	Cancers	13	24	25	74	35	33	131	**335**

42,760 screening participants underwent two screening technology, 335 were diagnosed with breast cancer at 15 months follow-up.

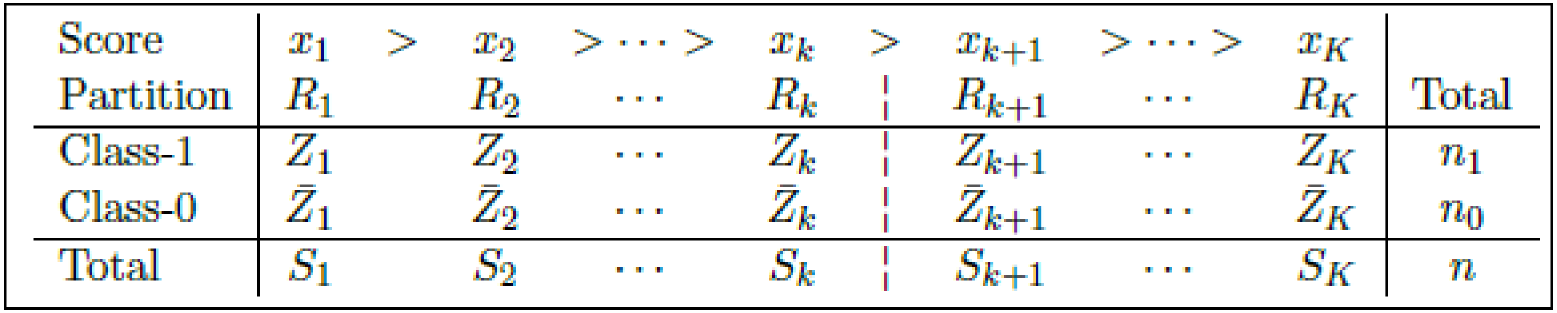
Predicting the Rare Events

- Cancer screening: detect from the asymptomatic population the diseased subjects, who make up a very small proportion (typically < 1%).
- Risk models
- Drug discovery: identify potential chemical compounds that are biologically active for some target (typically < 5%).
- Information retrieval
- Prediction of Rare events in your subject area?

Evaluating Model Performance for Predicting Rare Events

- Threshold Dependent Measure
  - Misclassification rate
  - Sensitivity and Specificity
  - Positive and Negative Predictive Value
- Threshold Independent Measure (Pre-clinical or pre-application stage)
  - Area Under the ROC* Curve (AUC)
  - Average Positive Predictive Value (AP)

*Receiver Operating Characteristic



Score	x_1	$>$	x_2	$> \cdots >$	x_k	$>$	x_{k+1}	$> \cdots >$	x_K	
Partition	R_1		R_2	$\cdots$	R_k		R_{k+1}	$\cdots$	R_K	Total
Class-1	Z_1		Z_2	$\cdots$	Z_k		Z_{k+1}	$\cdots$	Z_K	n_1
Class-0	$\bar{Z}_1$		$\bar{Z}_2$	$\cdots$	$\bar{Z}_k$		$\bar{Z}_{k+1}$	$\cdots$	$\bar{Z}_K$	n_0
Total	S_1		S_2	$\cdots$	S_k		S_{k+1}	$\cdots$	S_K	n

$$\widehat{AP} = \underset{w_1}{\left[\frac{Z_1}{S_1}\right]}\left[\frac{Z_1}{n_1}\right] + \underbrace{\left[\frac{Z_1+Z_2}{S_1+S_2}\right]}_{w_2}\left[\frac{Z_2}{n_1}\right] + \cdots + \underbrace{\left[\frac{Z_1+Z_2+\cdots+Z_K}{S_1+S_2+\cdots+S_K}\right]}_{w_K}\left[\frac{Z_K}{n_1}\right]$$

$$= \sum_{k=1} w_k \left[\frac{Z_k}{n_1}\right].$$

$$\widehat{AUC} = \frac{n}{n_0}\left\{\underbrace{\left[\frac{S_1+S_2+\ldots+S_K}{n}\right]}_{w'_1}\left[\frac{Z_1}{n_1}\right] + \underbrace{\left[\frac{S_2+\ldots+S_K}{n}\right]}_{w'_2}\left[\frac{Z_2}{n_1}\right] + \ldots + \underbrace{\left[\frac{S_K}{n}\right]}_{w'_K}\left[\frac{Z_K}{n_1}\right] - \frac{1}{2}\left(\frac{n_1}{n_0}\right)\right\} - \frac{1}{2}\left(\frac{n_1}{n_0}\right)$$

$$= \frac{n}{n_0}\sum_{k=1} w'_k \left[\frac{Z_k}{n_1}\right] - \frac{1}{2}\left(\frac{n_1}{n_0}\right)$$

Example 1: Two technology for Breast cancer screening

Malignancy score		7	6	5	4	3	2	1	Total
Digital M	Category Total	11	29	69	1061	2224	6588	32588	42570
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42,760 screening participants underwent two screening technology, 335 were diagnosed with breast cancer at 15 months follow-up.

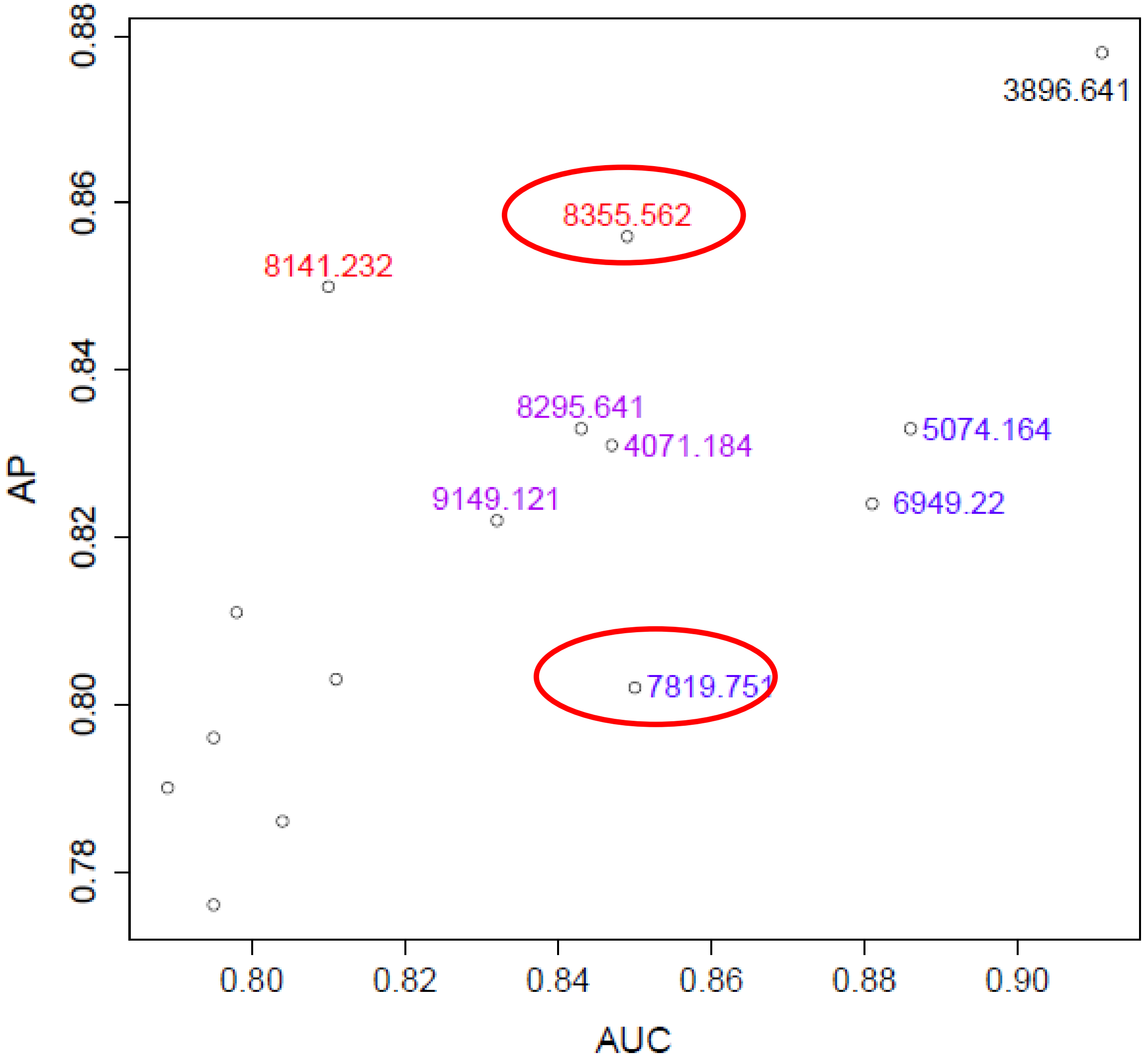
Given that 335 breast cancer diagnosed in 42,760 screening participants at 15 months follow-up, the prevalence π is 0.783%.

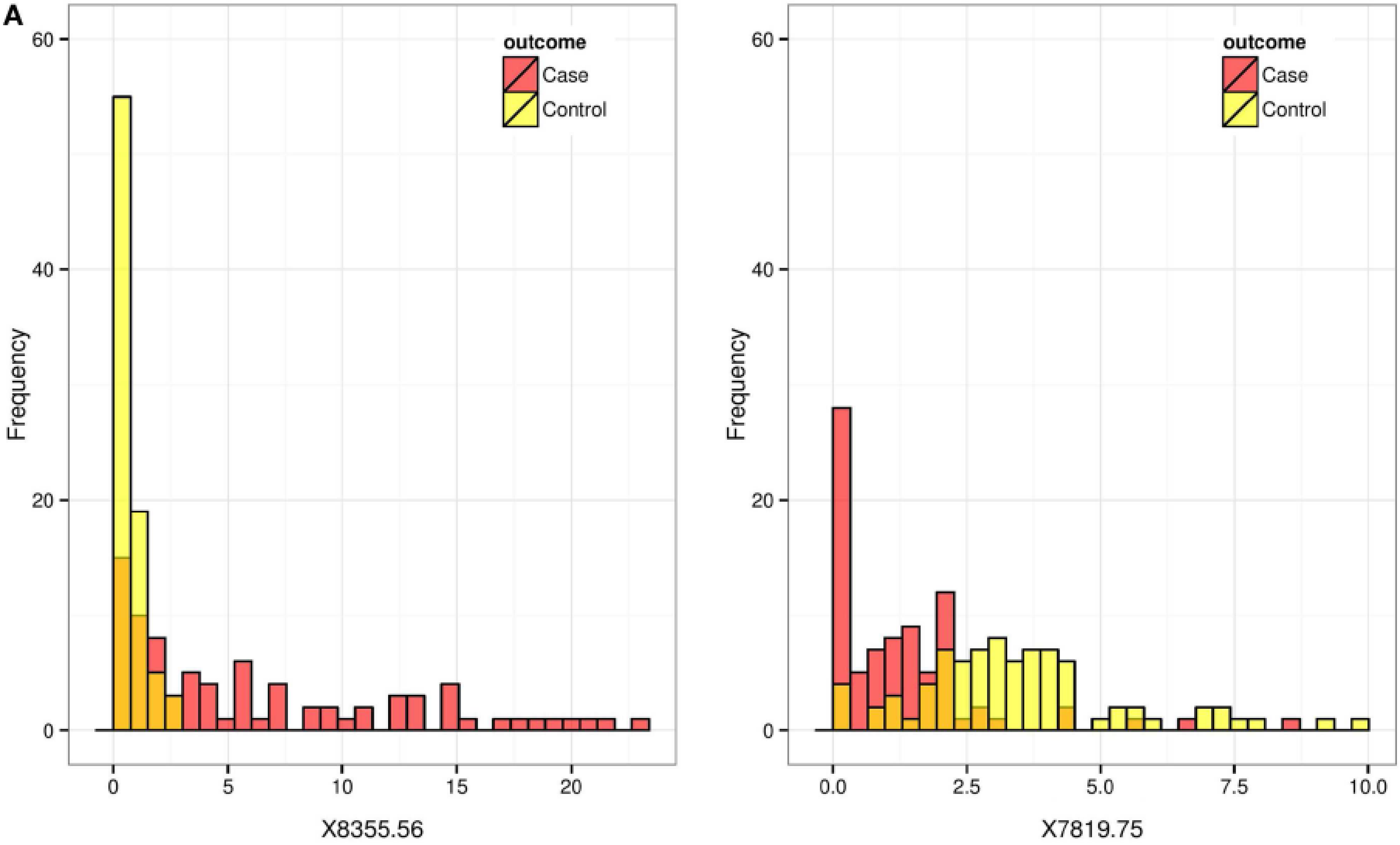
	Seven-point Malignancy Scale	
	$\widehat{AUC}$ (s.e.)	$\widehat{AP}$ (s.e.)
Film mammography	0.735 (0.012)	0.166 (0.022)
Digital mammography	0.753 (0.012)	0.144 (0.021)

Remark: Resampling method can be used for the inference of the difference in AP when we have paired data.

Example 2: Biomarkers for prostate cancer

779 potential biomarkers were assessed in 83 late-stage prostate cancer patients and 82 normal subjects. (Adam *et al*. 2002 Cancer Research)




A
outcome
Case
Control
60
40
20
0
Frequency
0
5
10
15
20
X8355.56
outcome
Case
Control
60
40
20
0
Frequency
0.0
2.5
5.0
7.5
10.0
X7819.75

A Thought Experiment

- The biomarker study is based on a case-control study (# disease ≈ # non-disease); its goal is to identify potential screening markers.
- How AP and the ranking of biomarkers is affected when the prevalence is much lower as in a screening setting?

Inflate the controls by replicating them

Biomarker	AUC	AP		
	n_0 X 1 $\pi = 0.5$	n_0 X 1 $\pi = 0.5$	n_0 X 10 $\pi = 0.1$	n_0 X 100 $\pi = 0.01$
8355.562	**0.849**	0.856	0.606	0.571
7819.751	**0.850**	0.802	0.370	0.062

Summary and future work

- AP is a single numerical measure, similar to AUC
  - Connection between AP and AUC
  - Empirical estimation of AP and its asymptotic variance
- Assessing risk prediction and survival models