Statistics, Probability and Diagnostic Medicine

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Sponsored by the Clinical and Translational Science Institute (CTSI)
and the Department of Population Health / Division of Biostatistics

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Outline

- Define measures of diagnostic accuracy
- Statistics for qualitative tests
  - *Sensitivity, specificity*
  - *Positive* and *negative predictive values*
  - *Prevalence, likelihood ratio*
- Receiver-Operating Characteristic (ROC) plots
- Illustrative examples

Observed Data

- Suppose the observed data are organized as shown:

		Disease / Condition		**Row total**
		Present	Absent	
Test Results	Positive			T+
	Negative			T-
Column Total		D+	D-	N

Observed Data

- Suppose the observed data are organized as shown:

		Disease / Condition		Row total
		Present	Absent	
Test Results	Positive	True Positive (TP)	False Positive (FP)	T+
	Negative	False Negative (FN)	True Negative (TN)	T-
Column Total		D+	D-	N

Accuracy Measurements

- The ability to identify the presence or absence of the disease/condition
  - *Sensitivity* and *specificity*

- The ability to predict the presence or absence of the disease/condition
  - *Positive predictive value (PPV)* and *negative predictive value (NPV)*

Discriminating Accuracy

- *Sensitivity*: probability of a person with the disease having a positive test result

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

- *Specificity*: probability of a person without the disease having a negative test result

$$Specificity = \frac{TN}{D-}$$

Predictive Accuracy

- *Positive predictive value (PPV)*: probability of a person with a positive test result having the disease

$$PPV = \frac{TP}{T+}$$

- *Negative predictive value (NPV)*: probability of a person with a negative test result being disease-free

$$NPV = \frac{TN}{T-}$$

Liver Scan Example

How good is the liver scan at diagnosis of abnormal pathology? (Altman and Bland, 1994)

		Pathology		Row total
		Abnormal (+)	Normal (-)	
Test Results	Abnormal (+)	231	32	
	Normal (-)	27	54	
Column Total				

Liver Scan Example

How good is the liver scan at diagnosis of abnormal pathology? (Altman and Bland, 1994)

		Pathology		Row total
		Abnormal (+)	Normal (-)	
Test Results	Abnormal (+)	231	32	263
	Normal (-)	27	54	81
Column Total		258	86	344

Liver Scan Example

		Pathology		Row total
		Abnormal (+)	Normal (-)	
Test Results	Abnormal (+)	**231**	32	263
	Normal (-)	27	54	81
Column Total		**258**	86	344

$$Sensitivity = \frac{TP}{D+} = \frac{231}{258} = 0.90$$

Interpretation: In this study, 90% of patients with abnormal pathology has abnormal scan, i.e., the scan correctly identifies abnormal pathology 90% of the time.

Liver Scan Example

		Pathology		Row total
		Abnormal (+)	Normal (-)	
Test Results	Abnormal (+)	231	32	263
	Normal (-)	27	**54**	81
Column Total		258	**86**	344

$$Specificity = \frac{TN}{D-} = \frac{54}{86} = 0.63$$

Interpretation: In this study, 63% of patients with normal pathology has normal scan, i.e., the scan correctly identifies normal pathology 63% of the time.

Liver Scan Example

		Pathology		Row total
		Abnormal (+)	Normal (-)	
Test Results	Abnormal (+)	**231**	32	**263**
	Normal (-)	27	54	81
Column Total		258	86	344

$$PPV = \frac{TP}{T+} = \frac{231}{263} = 0.88$$

Interpretation: In this study, 88% of patients with abnormal scan has abnormal pathology, i.e., the scan correctly predicts abnormal pathology 88% of the time.

Liver Scan Example

		Pathology		Row total
		Abnormal (+)	Normal (-)	
Test Results	Abnormal (+)	231	32	263
	Normal (-)	27	**54**	**81**
Column Total		258	86	344

$$NPV = \frac{TN}{T-} = \frac{54}{81} = 0.67$$

Interpretation: In this study, 67% of patients with normal scan has normal pathology, i.e., the scan correctly predicts normal pathology 67% of the time.

Disease Prevalence

- *Prevalence*: the probability of a person in a population having the disease. In a randomized study (not case-control),

$$Prevalence = \frac{D+}{N}$$

- Liver scan example

$$Prevalence = \frac{258}{344} = 0.75$$

- *Prevalence* affects *PPV* and *NPV*

Prevalence

		Disease / Condition		Row total
		Present	Absent	
Test Results	Positive	TP	FP	T+
	Negative	FN	TN	T-
Column Total		D+	D-	N

- *Sensitivity* is calculated using only the group with disease
- *Specificity* is calculated using only the group without disease

Prevalence

		Disease / Condition		Row total
		Present	Absent	
Test Results	Positive	TP	FP	T+
	Negative	FN	TN	T-
Column Total		D+	D-	N

- *PPV* and *NPV* are calculated across the groups with and without disease
- Specific to the performance of a test on the study population

Prevalence

Population A		**Pathology** (+)	**Pathology** (-)	**Row total**
Test Results	(+)	231	32	263
	(-)	27	54	81
Column Total		258	86	344

Population B		**Pathology** (+)	**Pathology** (-)	**Row total**
Test Results	(+)	231	1184	1415
	(-)	27	1998	2025
Column Total		258	3182	3440

Population	A	B
Sensitivity	90%	90%
Specificity	63%	63%
Prevalence	75%	7.5%
PPV	88%	16%
NPV	67%	99%

- Given the same test, the rarer the disease the lower *PPV* and the higher *NPV*.
- High *sensitivity* required for a high *PPV* in rare diseases

Likelihood Ratio

- *LR*: the ratio of the probability of having a test result given the disease to the probability of having the same result without the disease
- *Positive LR*: reference = 1, high positive *LR* means test is useful in detecting condition

$$LR = \frac{TP/D+}{FP/D-} = \frac{sensitivity}{1 - specificity}$$

Likelihood Ratio

- Used to adjust for post-test probability
  Post-test odds = (pre-test odds)*LR
- Liver scan example

$$LR = \frac{sensitivity}{1\text{-}\,specificity} = \frac{0.90}{1-0.63} = \frac{0.90}{0.37} = 2.4$$

$$\text{pre-test odds} = \frac{0.75}{0.25} = 3$$

$$\text{post-test odds} = (2.4)3 = 7.2$$

$$\text{post-test prob} = \frac{7.2}{1+7.2} = .88$$

Receiver-Operating Characteristic (ROC)

- Used for tests with quantitative results
- Compare diagnostic tests
- Choose the optimal cut point to distinguish “abnormal” from “normal”
- For each cut point, calculate the *sensitivity* and *specificity*

ROC Plots

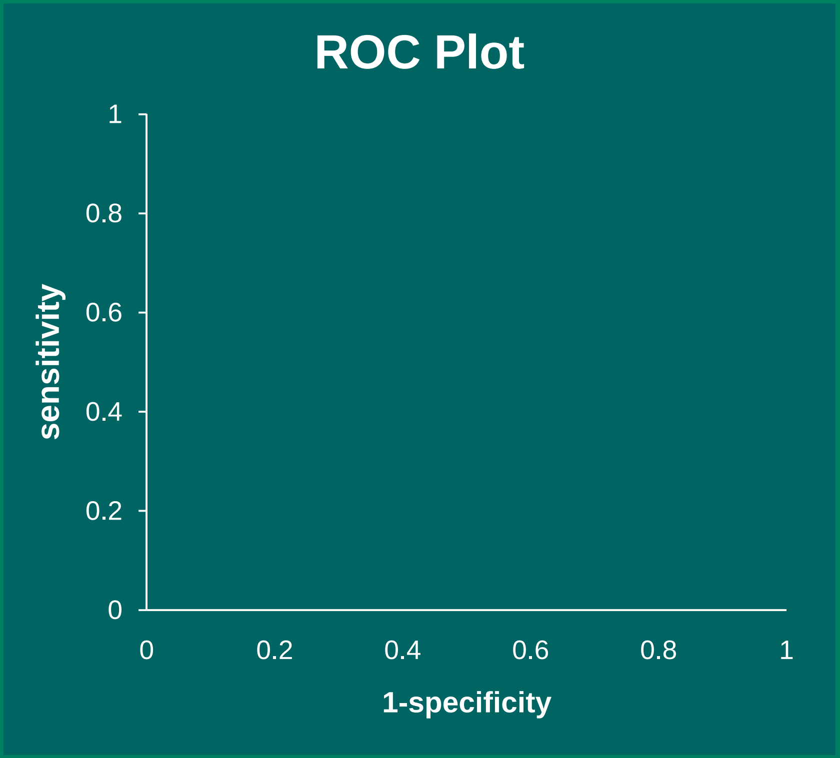
- CT scan example from Hanley and McNeil, 1982

		Disease Status		Row total
		Abnormal	Normal	
CT Ratings	Definitely abnormal (5)	33	2	35
	Probably abnormal (4)	11	11	22
	Unsure (3)	2	6	8
	Probability normal (2)	2	6	8
	Definitely normal (1)	3	33	36
Column total		51	58	109

sensitivity	*specificity*	**1-***specificity*
0.65	0.97	0.03
0.86	0.78	0.22
0.90	0.67	0.33
0.94	0.57	0.43

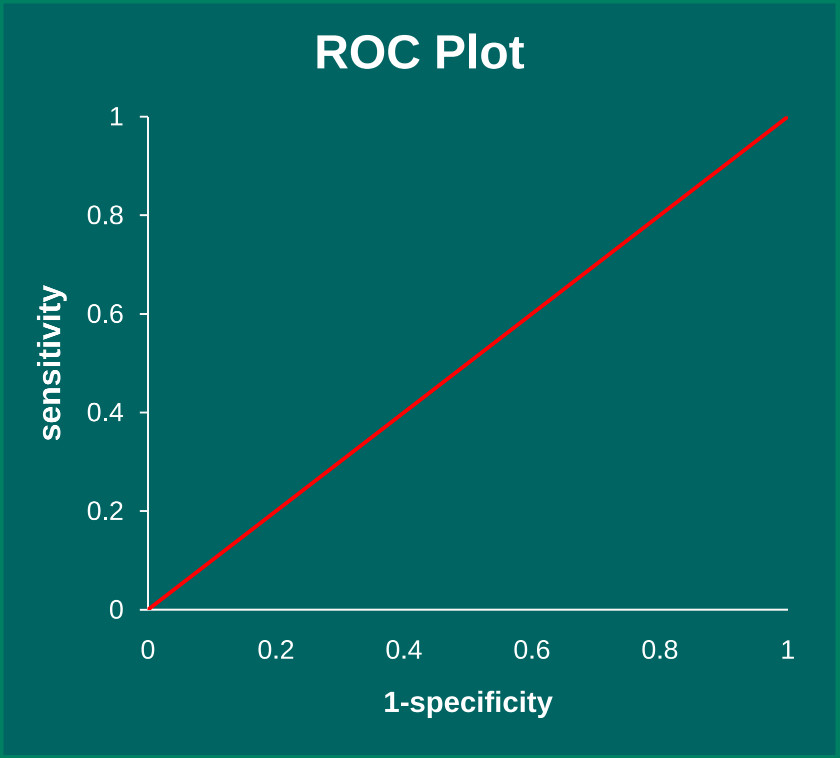
Receiver-Operating Characteristic (ROC)

- Plot *sensitivity* vs. (1-*specificity*)



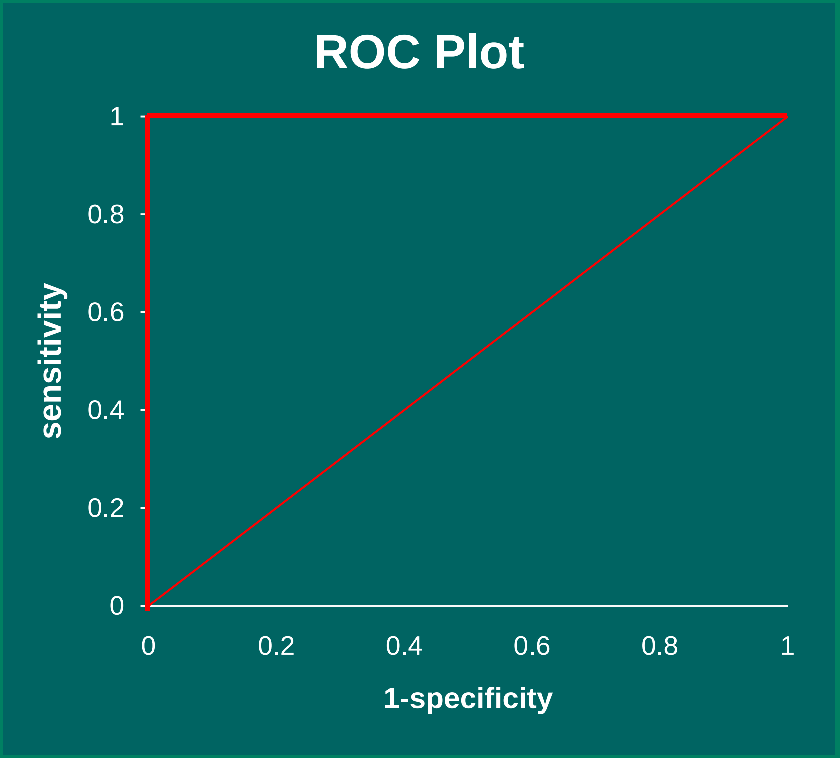
Receiver-Operating Characteristic (ROC)

- Reference line - useless test

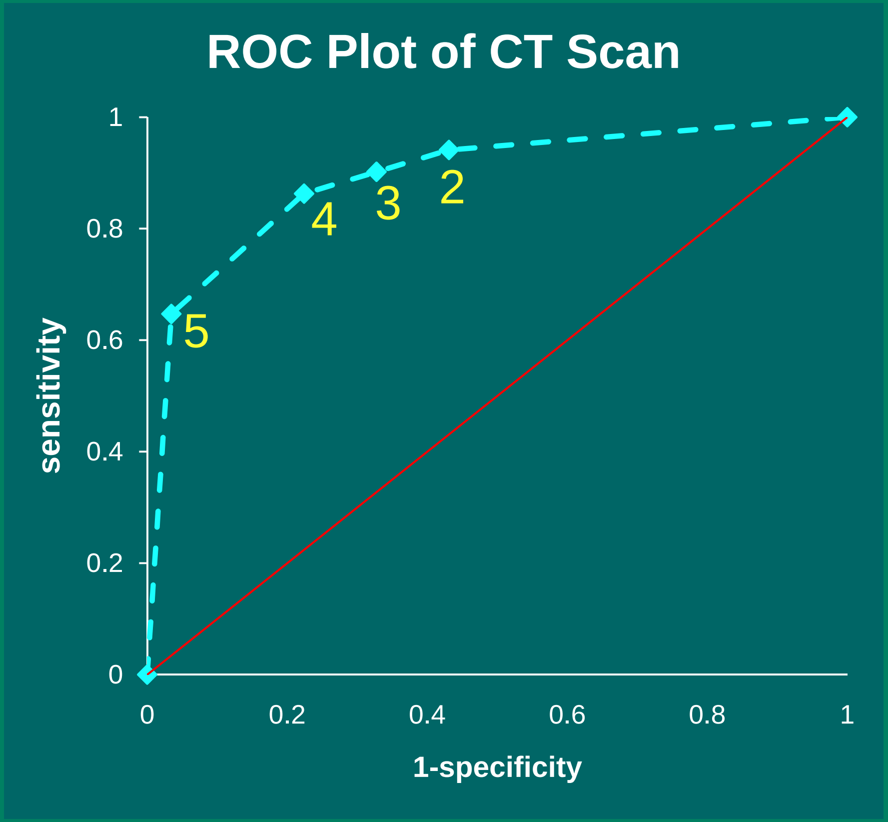


ROC Plots

- Test with perfect discrimination



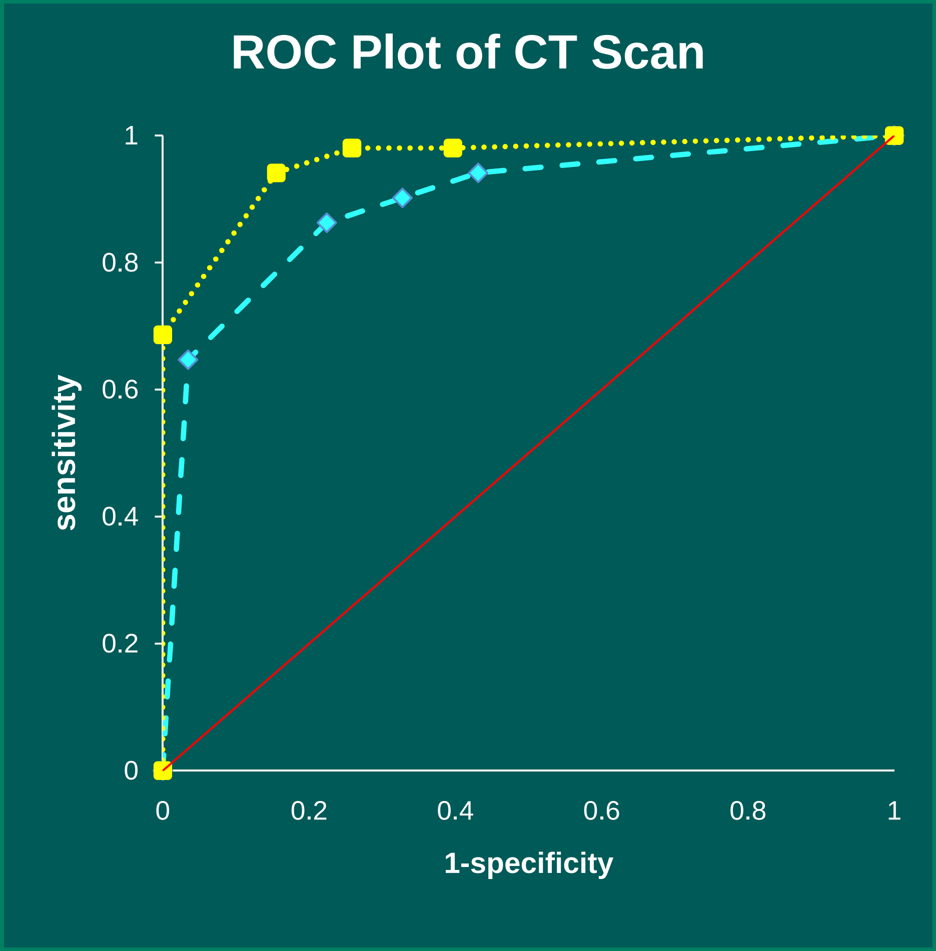
ROC Plots



	sensitivity	**1-***specificity*
5	0.65	0.03
4	0.86	0.22
3	0.90	0.33
2	0.94	0.43

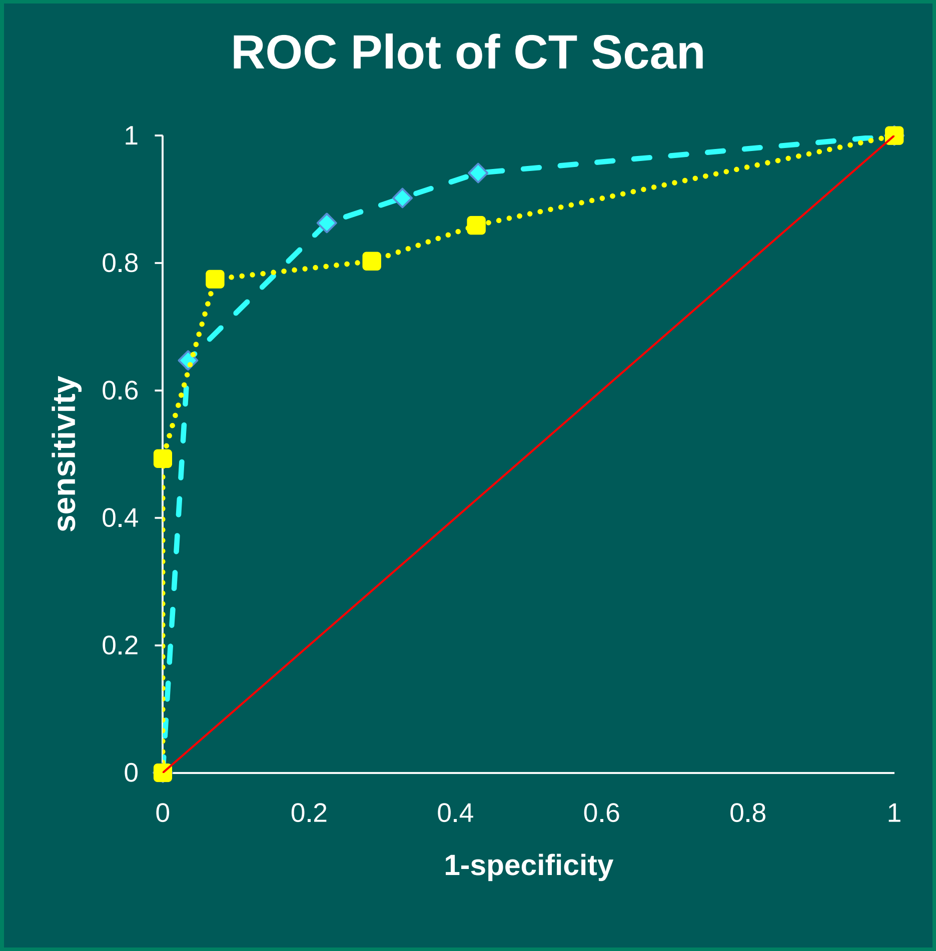
ROC Plots

- Comparing tests:
  - Curve above and to the left indicates better performance
  - Test 1 has higher accuracy than Test 2



ROC Plots

- Comparing tests:
  - Cross-over
  - Compare the areas under the curves (AUC)

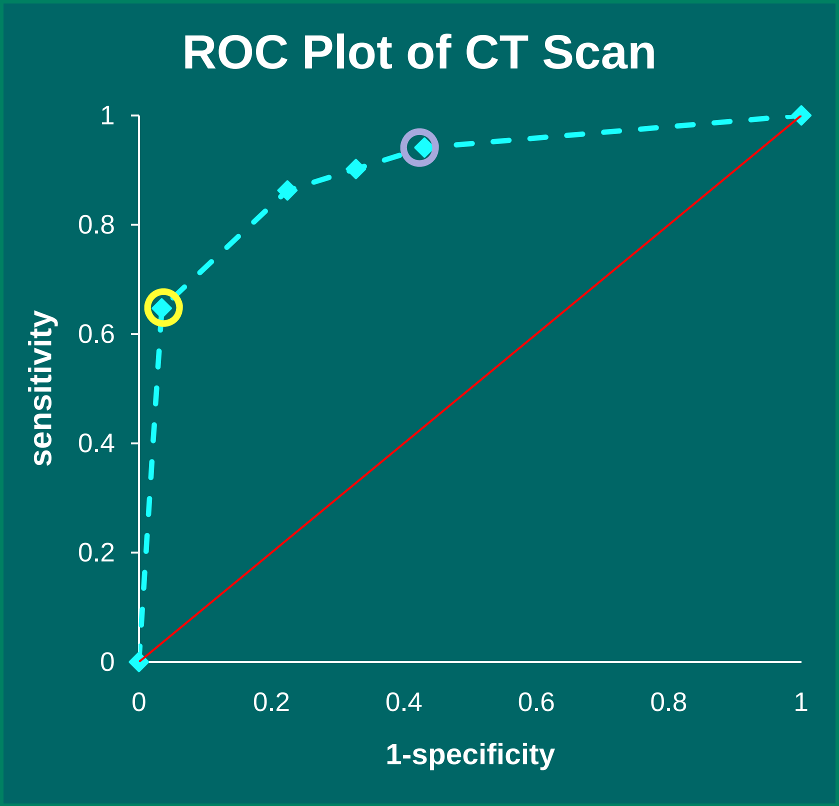


ROC Plots

- Area under the ROC curve gives the global assessment of performance of the test.
- It is the probability of a random person with the disease has a higher (more positive) value than a random person without the disease.
- For an uninformative test, the area under the ROC curve = 50%.

ROC Plots

- Having determined a good test, pick the best cut point
- Consider:
  - Cost of false diagnose
  - Prevalence of disease



Summary

- *Sensitivity* and *specificity* are properties of diagnostic tests
- *PPV* and *NPV* are predictive measures and affected by *prevalence*
- *LR* used to adjust post-test probability
- Use ROC curves and AUCs to compare performance of multiple tests
- Optimal cut point based on ROC curve depends on costs of false diagnoses and disease prevalence

Resources

- The Clinical and Translation Science Institute (CTSI) supports education, collaboration, and research in clinical and translational science: www.ctsi.mcw.edu
- The Biostatistics Consulting Service provides comprehensive statistical support

  http://www.mcw.edu/biostatsconsult.htm

Free drop-in consulting

- MCW/Froedtert/CHW:
  - Monday, Wednesday, Friday 1 – 3 PM @ Froedtert Pavilion, Room #L777A (TRU Offices)
  - Tuesday, Thursday 1 – 3 PM @ Health Research Center, H2400
- VA: 1^{st} and 3^{rd} Monday, 8:30-11:30 am
  - VA Medical Center, Building 111-B-5423
- Marquette: 2^{nd} and 4^{th} Monday, 8:30-11:30 am
  - Olin Engineering Building, Room 338D

ROC Plots

- The best cut point can be chosen by minimizing the expected costs.
- It is affected by:
  - Cost of false diagnoses
  - Prevalence of disease