

EBM Diagnosis

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Intro to diagnostic test characteristics

(naming what you didn't know you already know!)

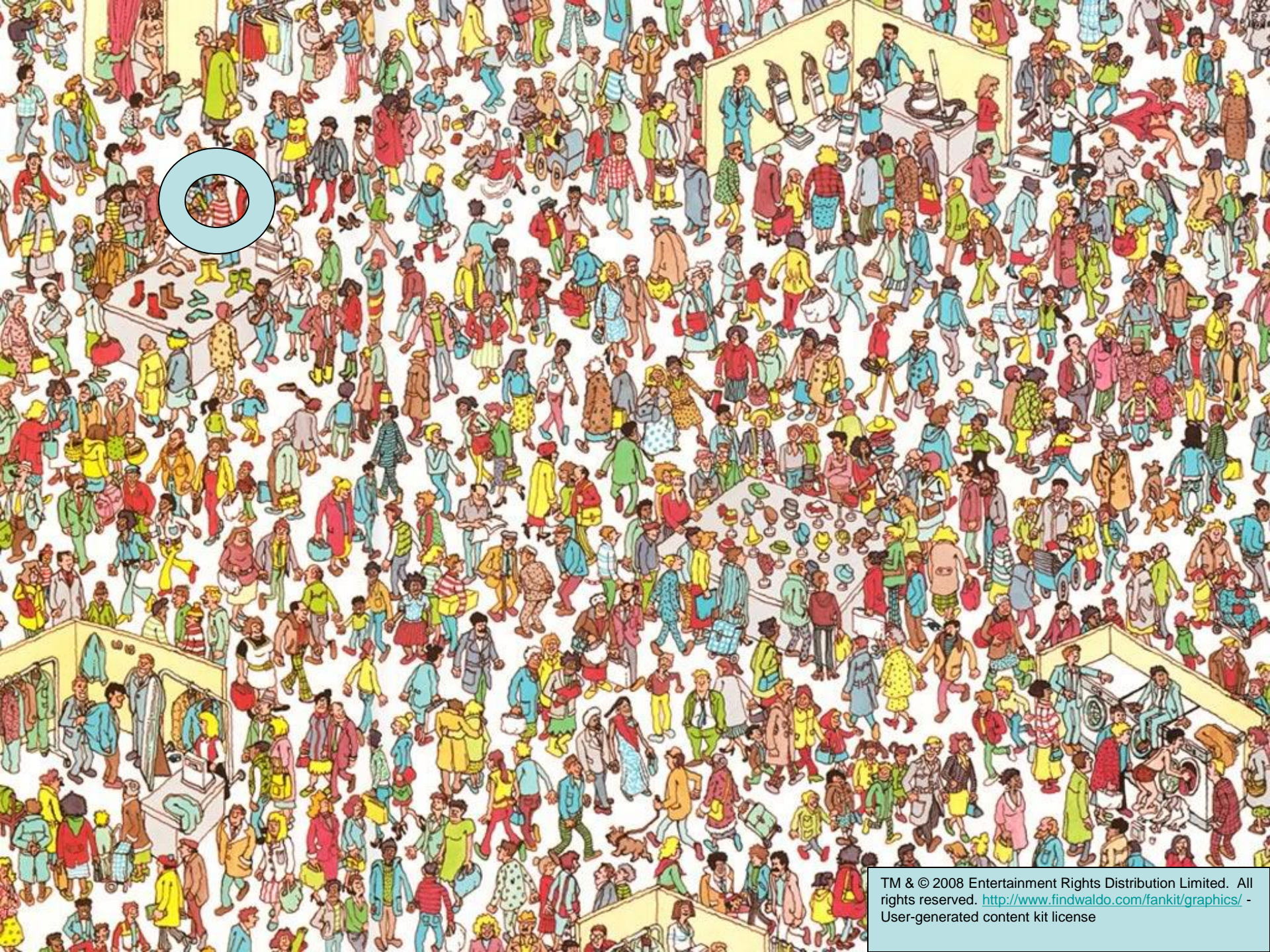
Validity criteria for a paper on a diagnostic test

(do I really want to read this? will I really use this?)

Showing EBM is seriously useful

(and it is seriously fun to understand what you are doing, and why)





Pattern recognition vs probabilistic diagnostic reasoning

Pattern recognition	Probabilistic diagnostic reasoning
See it and recognize disorder	Clinical assessment generates pretest probability
Compare posttest probability with thresholds	New information generates posttest probability
(usually pattern recognition implies probability near 100% and so above threshold)	(May be iterative)
	Compare posttest probability with thresholds

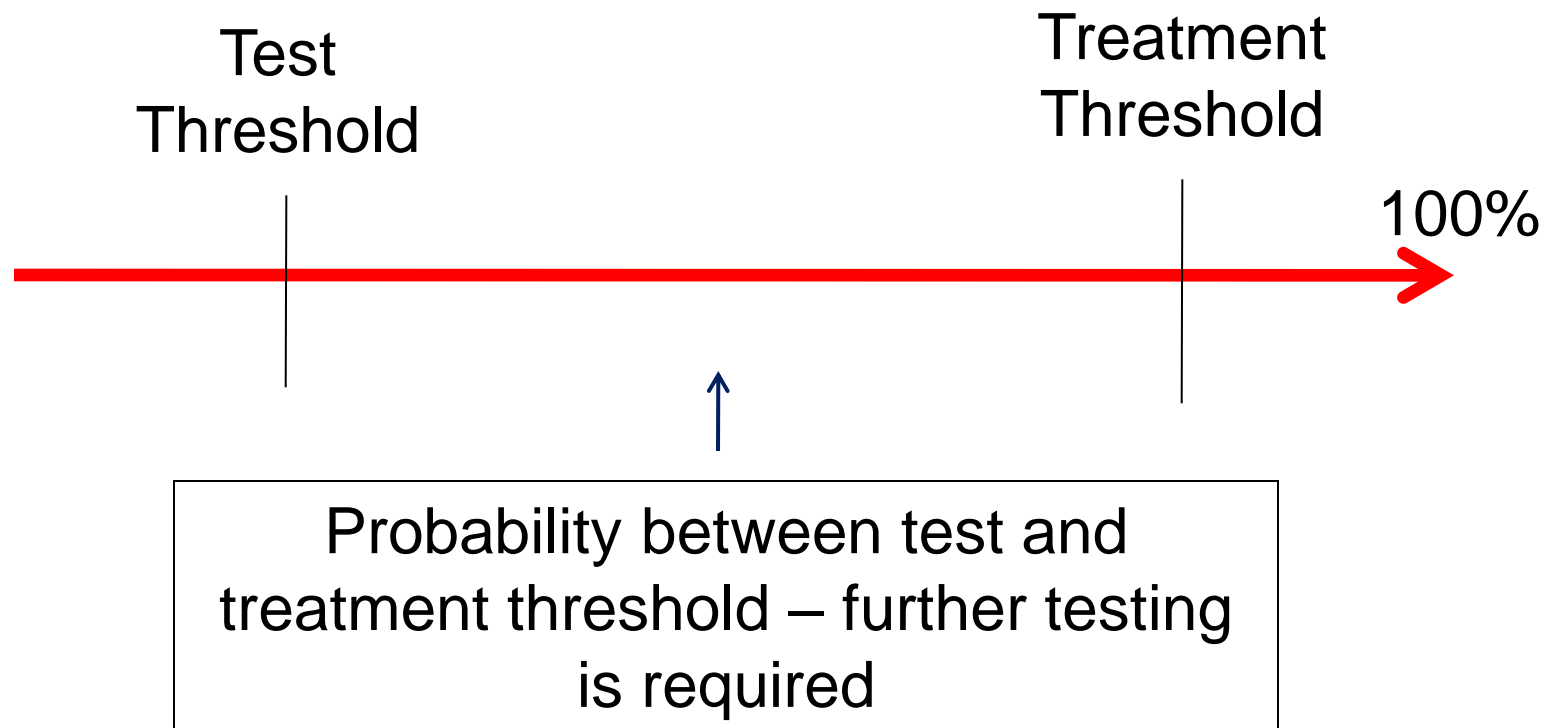
- clinicians select a small list of diagnostic possibilities, the differential diagnosis
- Clinicians then estimate the pretest probabilities using clinical experience (which can be prone to bias and random error), using studies of the same presenting complaint with thorough work-up to yield estimates of frequency of the diagnoses, or using validated clinical decision rules

- Green card = less likely ACS
- Yellow card = more likely ACS
- Blue card = neutral



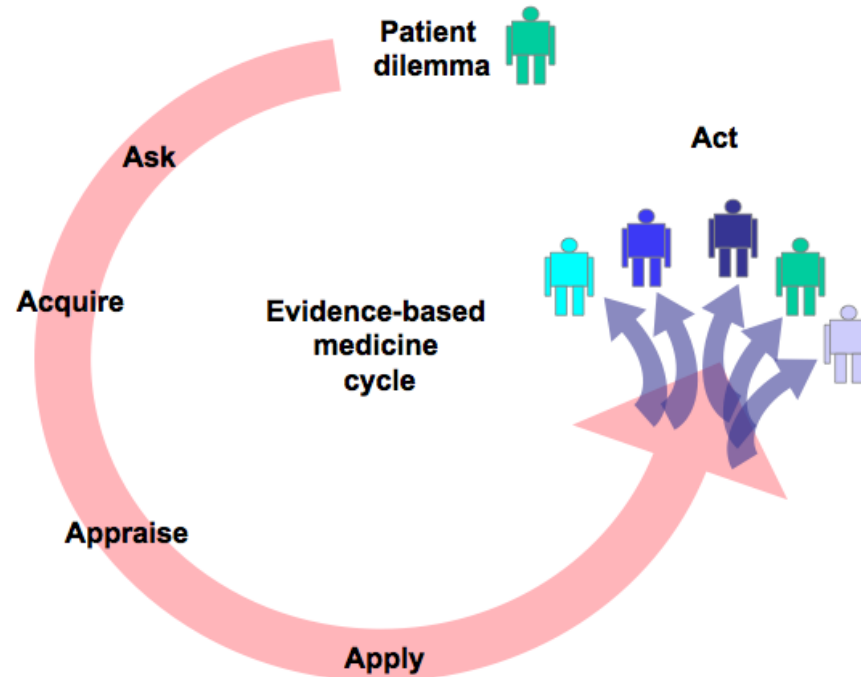
- 47 year old, businessman, presents to the ER
- athlete
- with a 1 hour history of squeezing retro-sternal chest pain radiating to both arms
- diaphoretic
- nauseated
- BP 110/70 mmHg, HR 74/min
- S1, S2, no murmur,
- ECG 1 mm ST-segment depression leads V1-V4

Test and Treatment in the Diagnostic Process



Let's Think About A Diagnostic Test Study:

In patients with concern for ACS how reliable is a new high sensitivity troponin compared to a standard troponin assay for early diagnosis of MI?



Diagnosis

Sensitive cardiac troponin assays were more accurate than a standard troponin assay for early diagnosis of AMI

Reichlin T, Hochholzer W, Bassetti S, et al. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. N Engl J Med. 2009;361:858-67.

Clinical impact ratings:  ★★★★★☆☆  ★★★★★☆☆

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Are the results valid?

What are the results?

How can I apply the results to the patient care?

Critical appraisal

Are the results valid?

- Did participating patients present a diagnostic dilemma?
- Did investigators compare the test to an appropriate, independent reference standard?
Gold Standard
- Were those interpreting the test and reference standard blind to the other results?
- Did investigators perform the same reference standard to all patients regardless of the results of the test under investigation?

Critical appraisal

What are the results?

- What likelihood ratios were associated with the range of possible test results?

(Ah ha, math😊, we'll come back to this)

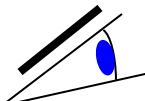
Critical appraisal

How can I apply the results to the patient care?

- Will the reproducibility of the test results and the interpretation be satisfactory in my clinical setting?
- Are the study results applicable to the patients in my practice?
- Will the test results change my management strategy?
- Will the patients be better off as a result of the test?

Exam Tip.... Setting Up Your 2 x 2 Table

- Single biggest error is setting this up incorrectly....



	<u>Disease Present</u>	<u>Disease Absent</u>
<u>Test Positive</u>	TRUE POSITIVE	FALSE POSITIVE
<u>Test Negative</u>	FALSE NEGATIVE	TRUE NEGATIVE

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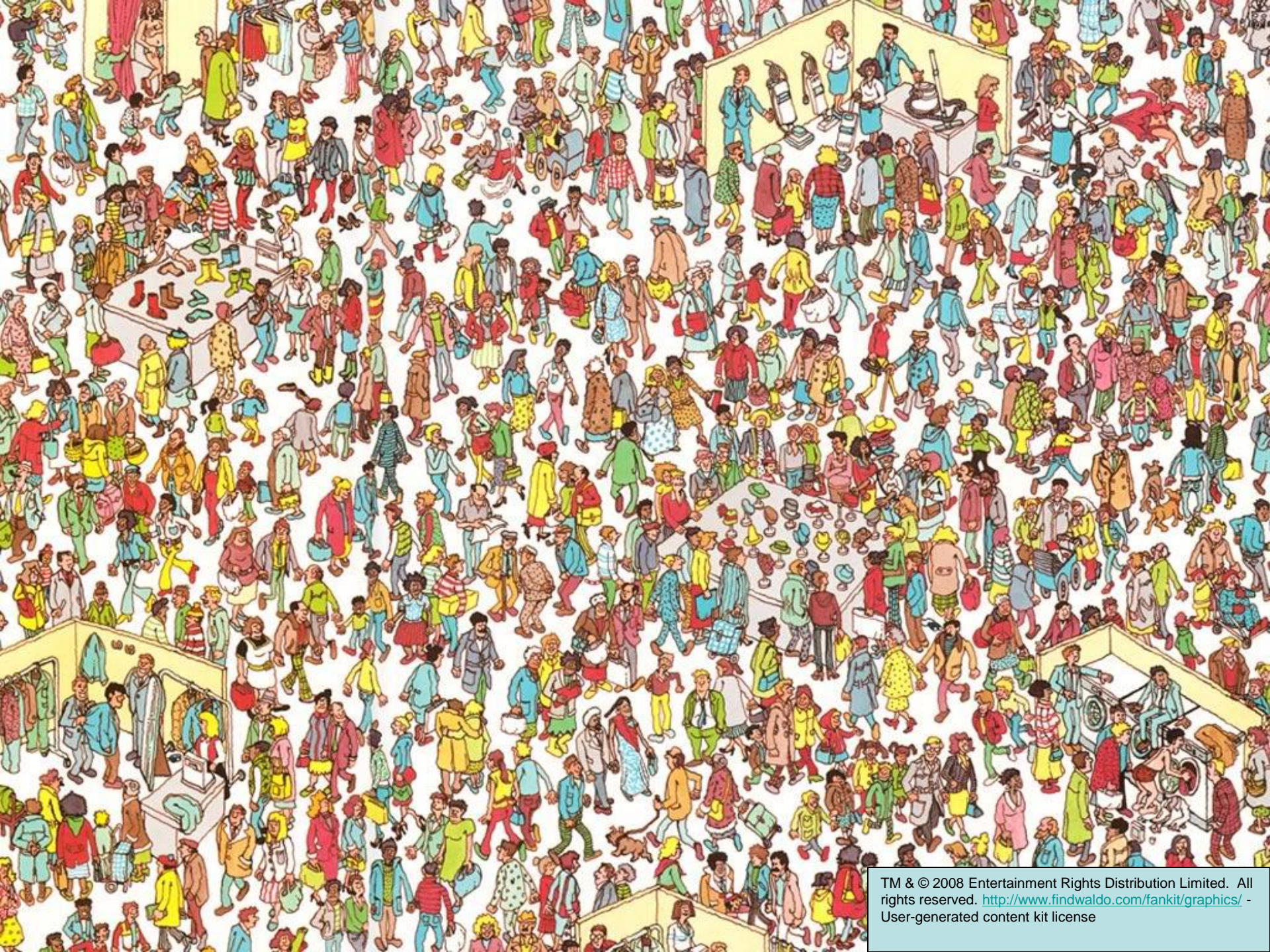
Sensitivity= Likelihood of a positive test when disease is present



Specificity Likelihood of a negative test when disease is absent

Where you are --- What you see --- What you think











	<u>Disease Present</u>	<u>Disease Absent</u>
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Thinking about LRs

	<u>Waldo Present</u>	<u>Waldo Absent</u>
<u>Test Positive</u>		
<u>Test Negative</u>		

Diagnostic test: Looking for someone with red & white striped cap & shirt, blue bottoms

Likelihood Ratios

	<u>Disease Present</u>	<u>Disease Absent</u>
<u>Test Positive</u>	TRUE POSITIVE	FALSE POSITIVE
<u>Test Negative</u>	FALSE NEGATIVE	TRUE NEGATIVE

LR(+) = *Likelihood of a positive test in the presence of disease as compared to the likelihood of a positive test in the absence of disease*

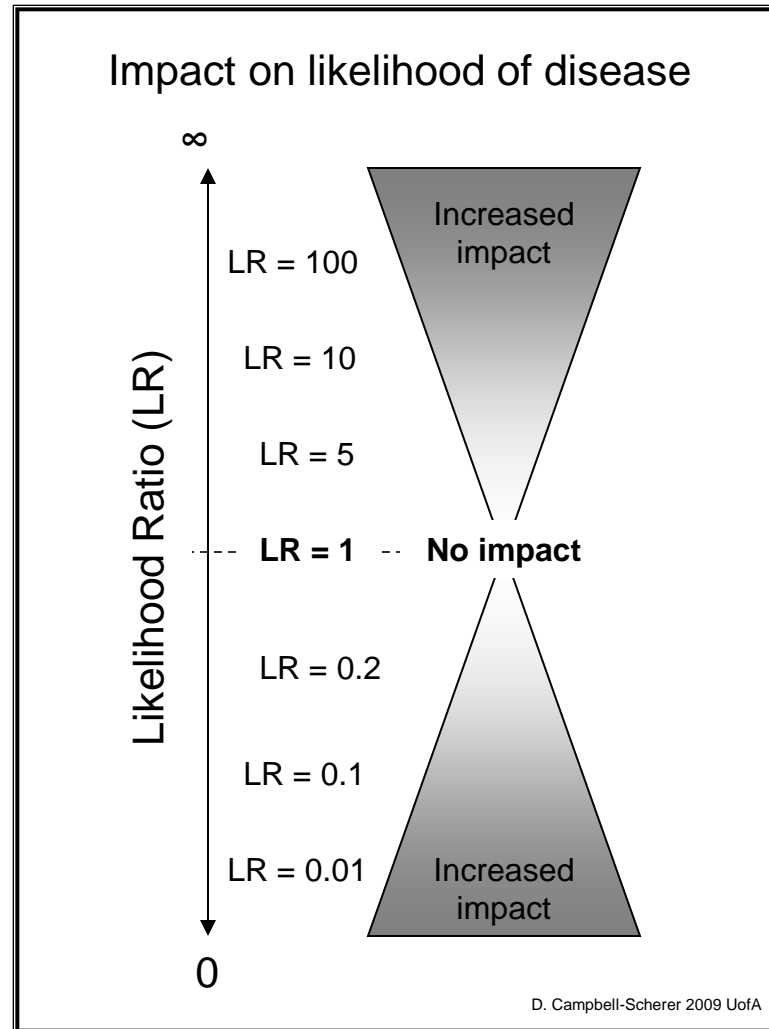
$$= (TP/(TP+FN)) / (FP/(FP+TN))$$

$$= \text{sensitivity} / (1-\text{specificity})$$

LR(-) = *Likelihood of a negative test in the presence of disease as compared to the likelihood of a negative test in the absence of disease*

$$= (FN/(TP+FN)) / (TN/(FP+TN))$$

$$= (1-\text{sensitivity}) / \text{specificity}$$





Back to our case

4 sensitive cardiac troponin assays vs a standard troponin assay for early diagnosis of acute myocardial infarction in the emergency department*

Test	Sensitivity (95% CI)	Specificity (CI)	+LR	-LR	Area under the ROC curve (CI)
Abbott-Architect Troponin I†	86% (79 to 92)	92% (90 to 94)	11	0.15	0.96 (0.94 to 0.98)
Roche High-Sensitive Troponin T†	95% (90 to 98)	80% (77 to 83)	4.8	0.06	0.96 (0.94 to 0.98)
Roche Troponin I†	84% (76 to 90)	94% (91 to 95)	14	0.17	0.94 (0.92 to 0.97)
Siemens Troponin I Ultra†	89% (82 to 94)	92% (89 to 94)	11	0.12	0.96 (0.94 to 0.98)
Roche Troponin T (standard assay)‡	72% (64 to 80)	97% (96 to 98)	24	0.29	0.90 (0.86 to 0.94)

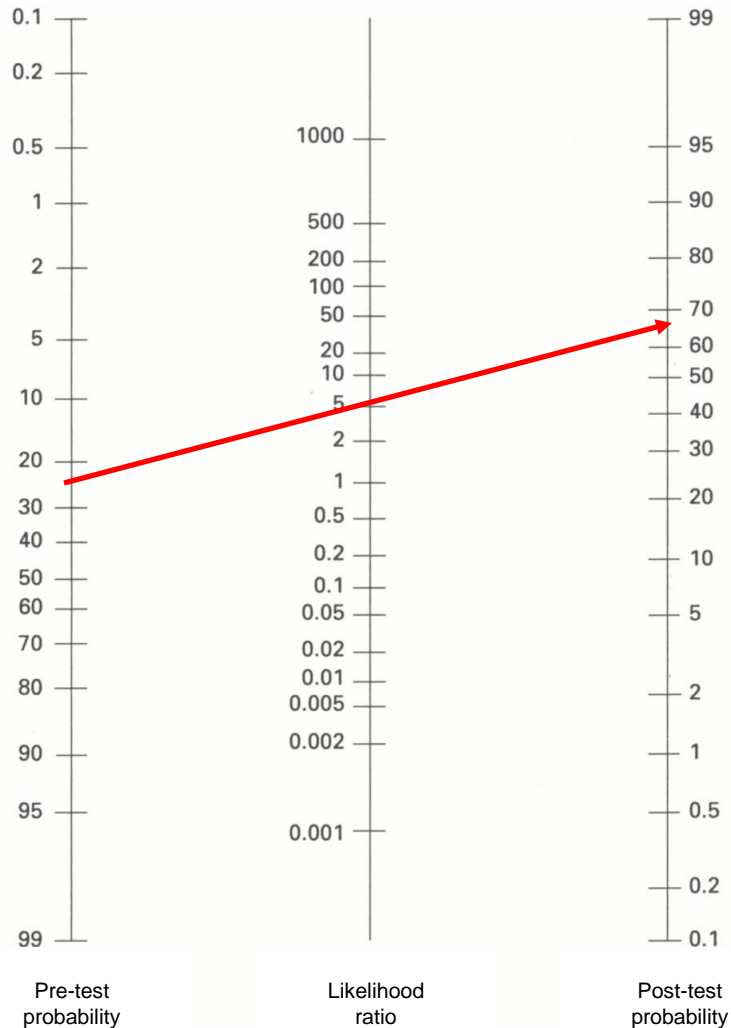
*ROC = receiver-operating characteristic; diagnostic terms and CI defined in Glossary. LRs calculated from sensitivity and specificity in article. The gold standard was final clinical diagnosis at 60 days.

†At 99th percentile.

‡At 10% coefficient of variation.

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Graphic example for Fagan Nomogram for Bayes theorem



Reference

*Bayes nomogram (adapted from Fagan).
Fagan TJ. Nomogram for Bayes theorem [Letter]. N Engl J Med 1975;293:275.
Jaeschke R. Guyatt GH. Sackett DL. Users' guides to the medical literature. III. B. The Evidence-Based Medicine Working Group. JAMA 1994; 271:703-7.
Glasziou, P. Evid Based Med 2001;6:164-166*

Some Fun Examples of LR from our cases.....

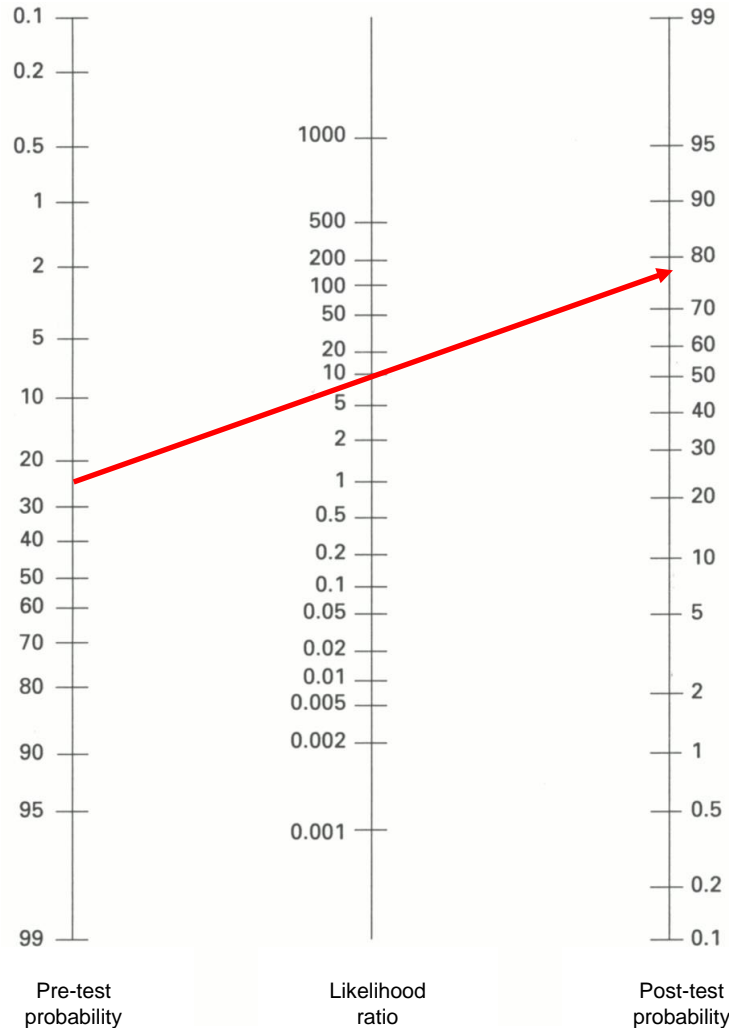
- Diaphoresis:
- LR= 2.0 (1.9-2.2)
- Chest pain radiation both arms:
- LR= 9.7 (4.6-20)
- Nausea or vomiting:
- LR = 1.9 (1.7-2.3)
- History of MI
- LR = 1.5-3
- Chest pain sharp or stabbing:
- LR= 0.3 (0.2-0.5)
- Pleuritic chest pain:
- LR = 0.2 (0.2-0.3)
- Chest pain with palpation:
- LR = 0.2-0.4

JAMA Rational Clinical Exam, Ch 35. Myocardial Infarction p.467, 2009

Bringing it back to the patient: 1 hour history of squeezing retro-sternal chest pain radiating to both arms



Patient with signs/symptoms of Acute Coronary Ischemia





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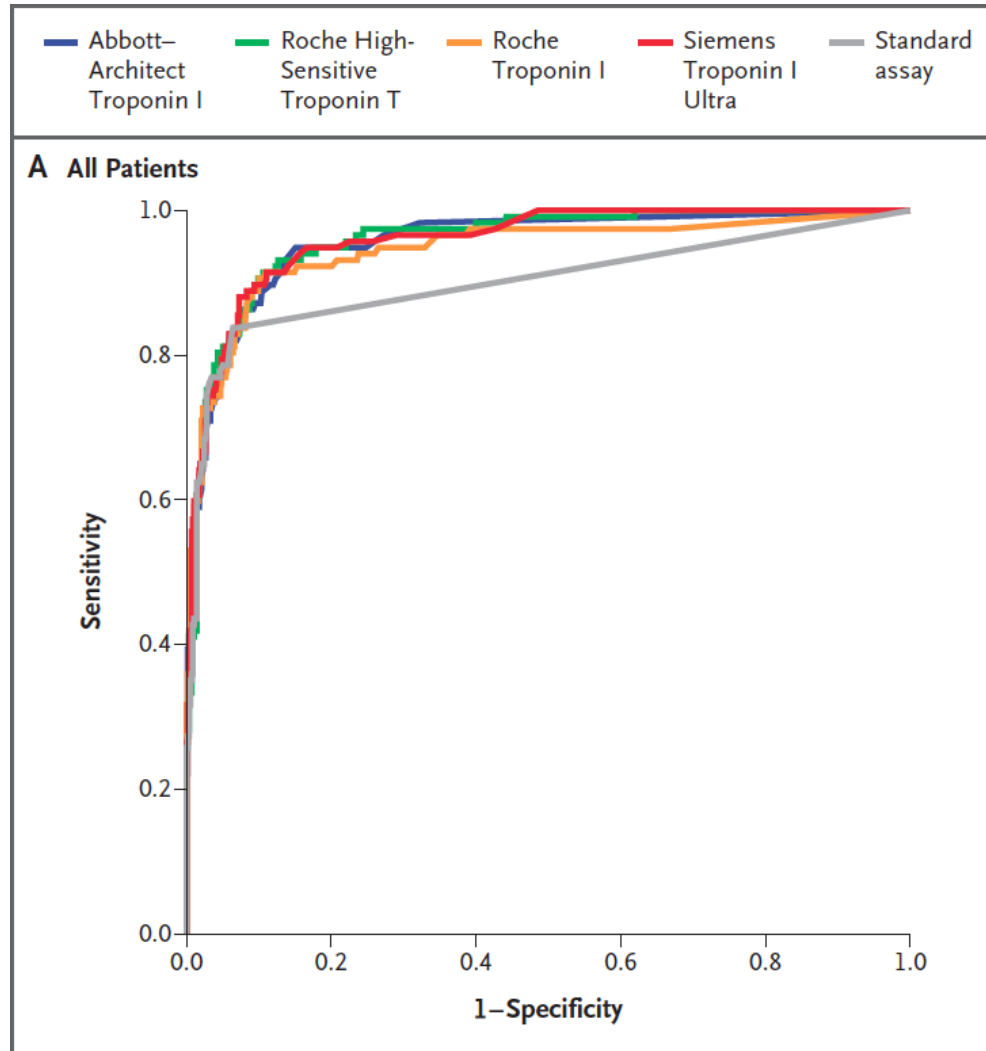
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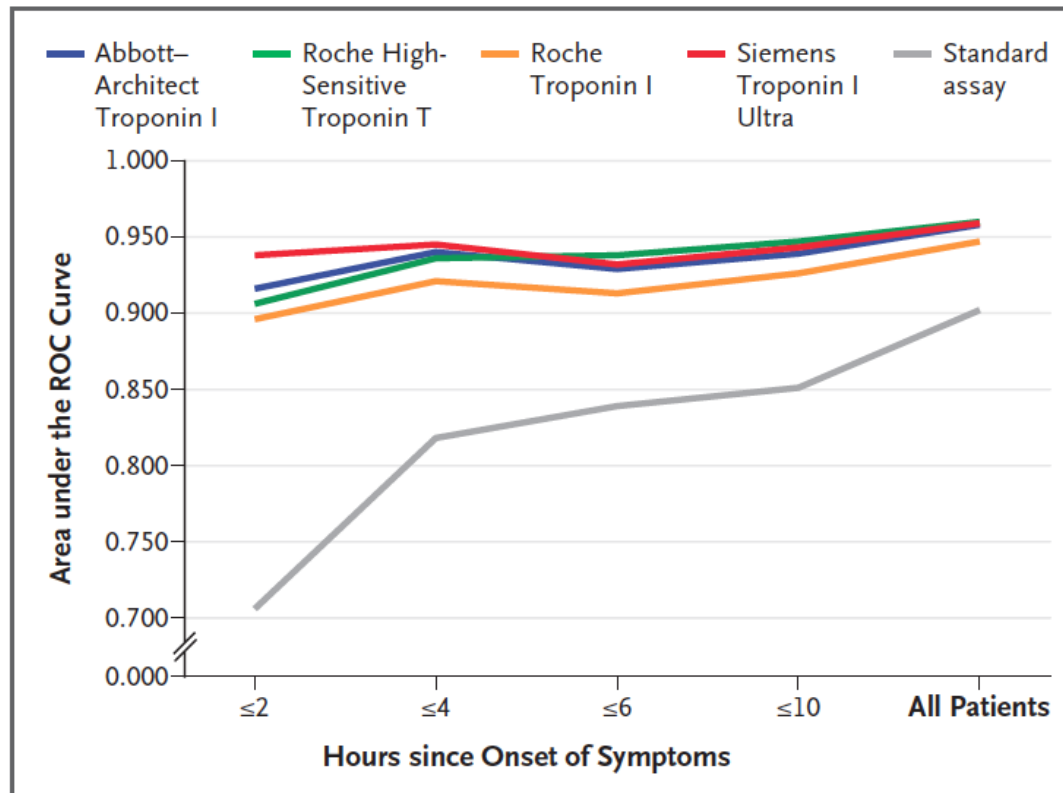


Figure 3. Diagnostic Accuracy of Cardiac Troponin Assays at Presentation According to Time since Onset of Chest Pain.

The area under the receiver-operating-characteristic curve (AUC) is shown, according to the time since the onset of chest pain, for the four sensitive cardiac troponin assays and the standard assay performed on blood samples obtained at presentation for the diagnosis of acute myocardial infarction.

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[ROC Curves Website](#)