Finding Good Diagnosis Studies

- MESH Term ‘Sensitivity and Specificity’
- Sensitivity – prob that someone with disease will test positive (Pr [+|D])
  - “true positive”
- Specificity – prob that someone without the disease will test negative (Pr [-|d])
  - “true negative”

What are sensitivity and specificity actually measuring?

- Attributes of the ***test***
- 100% sensitive test
  - 100% of people with the disease will test positive
  - How clinically relevant is this information?
  - Is this the same as saying 100% of people with a positive test will have the disease?
- When we test a patient we do not know if she has the disease.

Positive and Negative Predictive Values

- More clinically relavent
- Positive Predictive Value – prob that someone with a positive test has the disease (Pr [D|+])
- Negative Predictive Value – prob that someone with a negative test does not have the disease (Pr [d|-])

Gold Standards

- Standards against which the tests we use in general practice are measured
- Usually expensive and invasive
- E.g. V-Q scan for PE measured against pulmonary angiography

How are blood donations screened for HIV? (may be a bit outdated)

- ELISA screening test
- + ELISA → repeat ELISA and confirmatory n blotrn Blot
- Repeat ELISA + and Western Blot - → blood discarded
- Repeat ELISA + and Western Blot + → donor informed he is HIV positive

ELISA Test for HIV

WESTERN BLOT

ELISA	Pos	Neg	
Pos	498	4	502
Neg	10	488	488
	508	492	1000

- **Sensitivity = true positive**= people with D who test positive / all people with D = 498/508=98.03% for the ELISA
- **Specifity = true neg** = people without D who test negative / all people without D = 488/492=99.19% for the ELISA
- **false pos** = people without D who test positive / all people without D = 4/492=0.81% (complement of specificity: 100 – 99.19 = 0.81)
- **false neg** = people with D who test neg / all people with D = 10/508 = 1.97% (complement of sensitivity)

What about PPV and NPV?

- PPV = people with + test and D / all people with + test = 498/502=99.2%
- NPV = people with - test and no D / all people with – test = 488/498 = 97.99%
- Can see the ELISA test is an extraordinarily good test.
- Why use Western Blot at all?

What's unusual about this population?

WESTERN BLOT

ELISA	Pos	Ne	
Pos	498	4	502
Neg	10	488	488
	508	492	1000

Let's look at a population with a more realistic prevalence.

ELISA	Pos	Neg	
Pos	1960	7984	9944
Neg	40	990016	990056
	2000	998000	1000000

Sensitivity = 1960 / 2000 = 0.98
Specificity = 990016 / 990000 = 0.992

PPV = 1960/9944 = 19.7%
NPV = 990,016/990,056 = 99.99%

What happened?

- The clinical *relevance* of a screening test is directly tied to the *prevalence* of the disease.
- Statistically based on Baye's Theorem and idea of prior probabilities
  - $$\Pr[D|+] = \frac{\Pr[+|D] \times \Pr[D]}{\Pr[+|D] \times \Pr[D] + \Pr[+|d] \times \Pr[d]}$$

Likelihood Ratios

- Determine a **pre**-test probability
  - Essentially the prevalence of a disease in your population
- Determine the likelihood ratio of the test
  - Odds of those with positive test result who have the disease to those with positive test results who do not (true + : false +)
- Use LR to calculate **post**-test probability

What constitutes a good screening test based on likelihood ratios?

- That which causes the biggest change from pre to post-test probabilities
- E.g.
  - pre-test know that 5% chance of person having a disease
  - Positive test raises that probability to 95%

The HCV Example

- Recall the 2 persons requesting HCV screening
  - Married, monogamous male received 2 units whole blood in 1969 for ruptured spleen
  - Single, female college student volunteers in day care impoverished area

Determine pre-test probabilities

- Lit search reveals following prevalences:
  - 1.6% (no known risk)
  - 10% (blood transfusion)
  - 65-95% (IVDA)

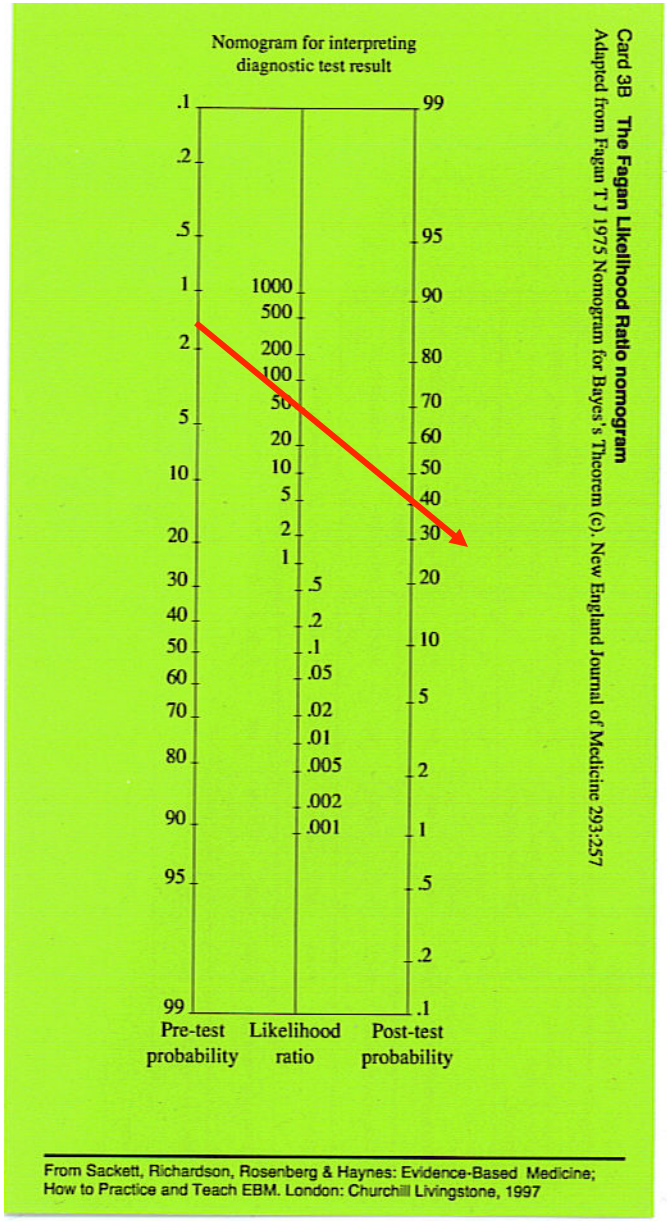
Determine LR+ for a test

- LR+ = sensitivity / 1-specificity
  - E.g. serum ferritan sens/spec = 0.90/0.85 (gold standard of bone marrow biopsy)
  - LR+ = 0.90 / 1-0.85 = 6
  - People with low ser ferritan 6 times more likely to have iron-deficiency anemia; esta good test
- LR+ for HCV = 48

Determine Post-Test Probabilities

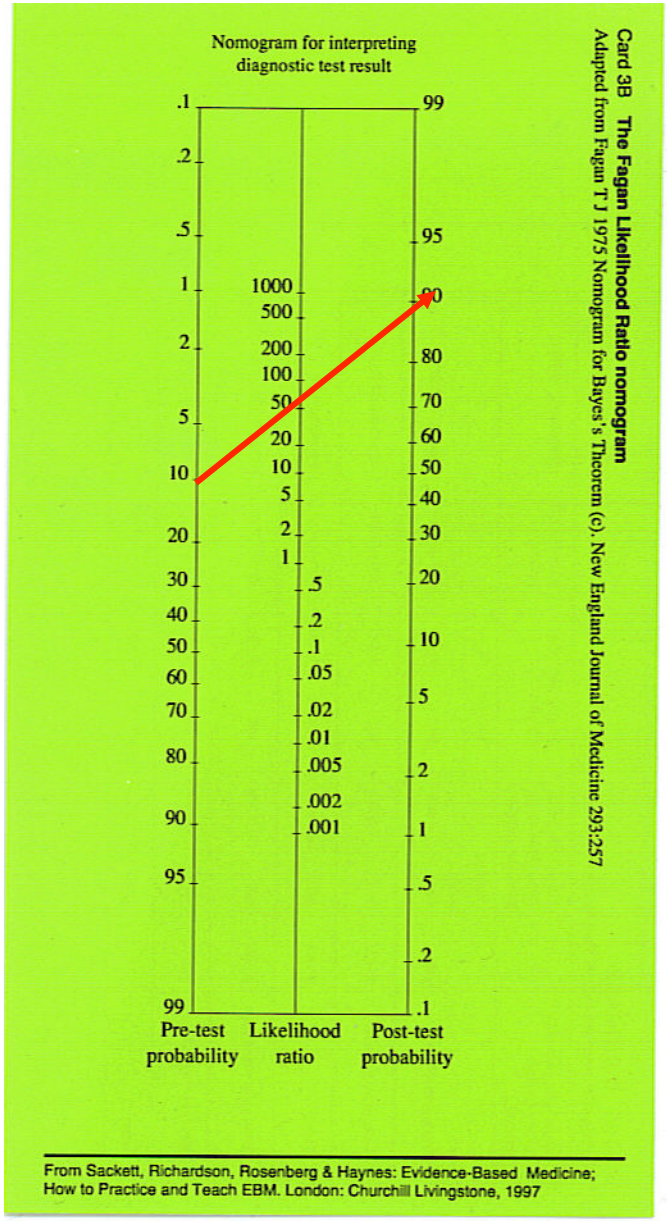
- Multiply pre-test odds by LR
  - say pre-test odds D = 50:50=1
  - Post-test odds = 1x6 = 6
  - Post-test prob = 6/6+1 = 86%
- Easier approach is to use normograms developed for this purpose

Pre-test probability ~2%



Post-test probability ~40%

Pre-test probability 10%



Post-test probability 90%

Some pre-test probabilities

Table 3b1.1 Some pretest probabilities

Patient problem	Clinical setting	Target disorder	Pretest probability
Melena in a 50-year-old man who drinks 25 units of alcohol a week but has no stigmata of liver disease	Emergency room in North America	Varices	5%
		Benign ulcer	55%
		Gastritis	40%
Symptomless 60–69-year-olds	Primary care	Undiagnosed colon cancer: all patients	0.5%
		positive family history	1.5%
Symptomless	Primary care	≥ 75% stenosis of one or more coronary arteries	
Woman 30–39 y/o			0.3%
60–69 y/o			8%
Man 30–39 y/o			2%
60–69 y/o			12%
Non-anginal chest pain			
Woman 30–39 y/o			1%
60–69 y/o			19%
Man 30–39 y/o			5%
60–69 y/o			28%
Atypical angina			
Woman 30–39 y/o			4%
60–69 y/o			54%
Man 30–39 y/o			22%
60–69 y/o			67%
Typical angina pectoris			
Woman 30–39 y/o			26%
60–69 y/o			91%
Man 30–39 y/o			70%
60–69 y/o			94%
Symptomless 50 y/o with a solitary pulmonary nodule	Primary care	Cancer for any nodules	50%
		For 3 cm nodules	65%

SnNout and SpPin

- Sensitivity and specificity still useful if they are very high
- If a test has a high Sensitivity a Negative result rules out the disease (SnNout)
- If a test has a high Specificity a Positve result rules in the disease (SpPin)

Some SpPins and SnNouts

Table 3b1.3 Some SpPins and SnNouts

Target disorder	SpPin (& specificity) [presence rules in the target disorder]	SnNout (& sensitivity) [absence rules out the target disorder]
Ascites (by imaging or tap)*	Fluid wave (92%)	History of ankle swelling (93%)
Pleural effusion†	Auscultatory percussion note loud and sharp (100%)	Auscultatory percussion note soft and/or dull (96%)
Increased intracranial pressure (by CAT scan or direct measurement)‡		Loss of spontaneous retinal vein pulsation (100%)
Cancer as a cause of lower back pain (by further investigation)§		Age >50 or cancer history or unexplained weight loss or failure of conservative therapy (100%)
Sinusitis (by further investigation)¶		Maxillary toothache or purulent nasal secretion or poor response to nasal decongestants or abnormal transillumination or history of coloured nasal discharge
Alcohol abuse or dependency**	Yes to ≥3 of the CAGE questions (99.8%)	
Splenomegaly (by imaging)††	Positive percussion (Nixon method) and palpation	
Non-urgent cause for dizziness‡‡	Positive head-hanging test and either vertigo or vomiting (94%)	