Diagnostic Reasoning

Cause, models and inference

Sean Collins
Physical Therapy, Plymouth State University

About this presentation

This presentation was developed for a continuing education course for the New Hampshire Association of Rehabilitation Administrators by the Plymouth State University Doctor of Physical Therapy Program

The slides were prepared as a project in Scrivener using Rmarkdown with the Slidify package io2012 framework; and compiled for HTML in RStudio.

All files are available in a GitHub repository:

https://github.com/scollinspt/differential_diagnosis (https://github.com/scollinspt/differential_diagnosis)

io2012 slide navigation:

- Press o to open the overview mode, you can use arrow keys to flip through slides
- Press g to open a box where you can type a slide number you want to Go To
- Press t to toggle a navigation list

Course Description

Advanced differential diagnosis for the practicing rehabilitation clinician

- Includes advanced knowledge for life long learning to improve differential diagnosis skills
  - Underlying causal connections
  - Reasoning patterns
- Focuses on screening for referral
  - Standard to complex clinical cases across practice settings
- Goal is to develop advanced diagnostic reasoning when faced with a myriad of presenting signs and symptoms, and the ability to develop novel differential diagnosis approaches for your practice setting

Course Objectives (5)

- Explain the use of causation, reasoning patterns and inference in differential diagnosis.
- Develop a causal network and consider the features of its structure in reasoning and making diagnostic inferences.
- Interpret a set of signs and symptoms in light of possible causes.
- Identify red flags that warrant a deeper consideration of alternative explanations for signs and symptoms.
- Generate a differential diagnosis and subsequent plan of action for complex patient cases across practice settings.

Part of a larger project

Includes:

- Consideration of the connection between research and practice
- Critique of a strictly empirical framework for decision making
- Development of the curriculum at Plymouth State DPT program
- Investigation of approaches of clinical reasoning
    - Cause, Models & Inference: Building a Knowledge Based Practice

Hope to encourage development of:

- Teaching and developing inferential reasoning based on causal models
- Development of specific Bayesian networks with practical relevance
- Continued discussion.....

Two experiences (1)

Bad answer to a question (1992)

- Told not worry about the answer, I would learn it with experience

Two experiences (2)

2005 PTJ Letter to the Editor (https://knowledgebasedpractice.wordpress.com/2015/01/30/complex-systems-letter-to-the-editor-2005/)

Bridge gap between research and practice with complex systems approach

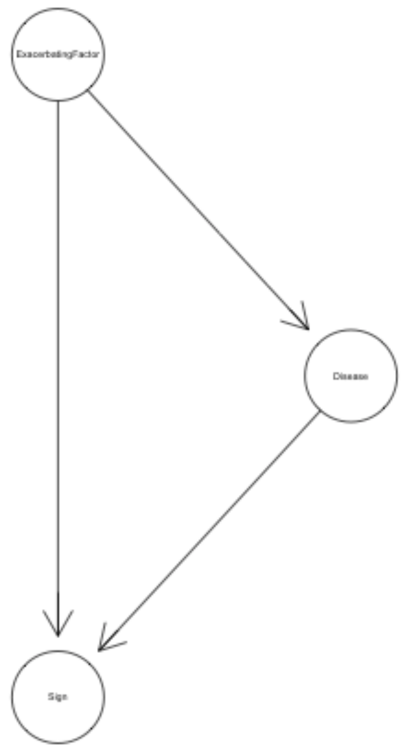
A complex system consists of interconnected parts. The simple study of the parts in isolation – reductionism – is the modus operandi of the scientific method, attempting to isolate sources of variation. Clinicians, however, are faced with all sources of variation at the same time and must deal constantly with the full burden of the complex system. They and their patient management become immersed, interconnected, and part of the complex system. This is a potential source of divergence between clinicians and scientists.

Major premises

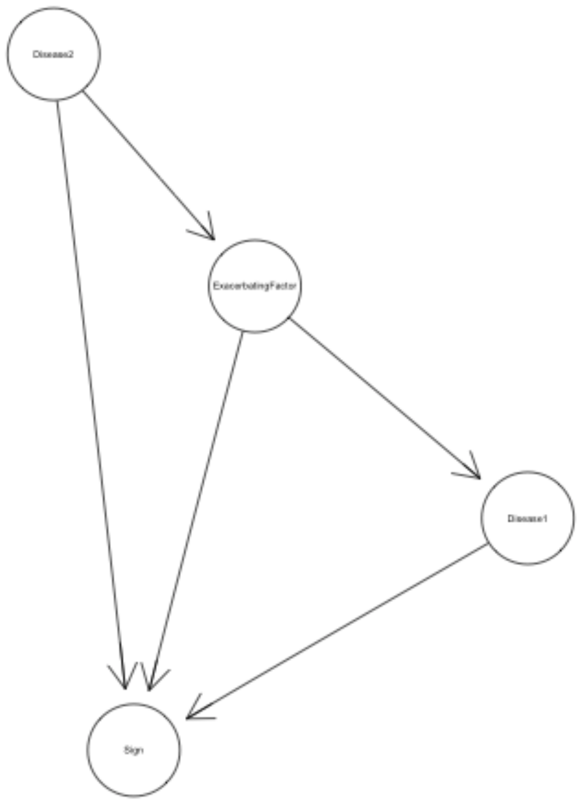
- Differential diagnosis requires abductive inference (infer cause from observed effects) and conditional probability
- Abductive inference requires knowing cause - effect relationships
- Knowing cause - effect relationships requires inductive inference
- What we know from induction is an estimate and is based on probability
- Causal conditional probability allows us to infer effects from cause
- Bayes theorem allows us to invert conditional probability to infer cause from effect
- This is still too simple to be useful in clinical practice since the true set of cause and effect relationships are part of a large causal network
- We can learn, communicate and utilize the structure of these networks
- Just like in our use of other foundational knowledge domains, rehabilitation professions must continue to look to the work being done in statistics, probability, computer science and philosophy to infuse knowledge, methods and innovation in our professions

Simple Network

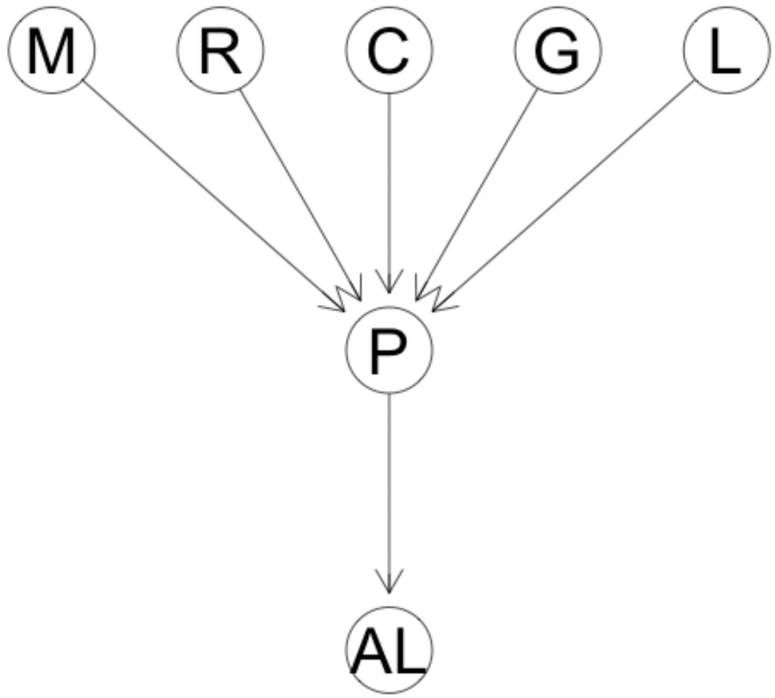
Simple Network



Simple Network



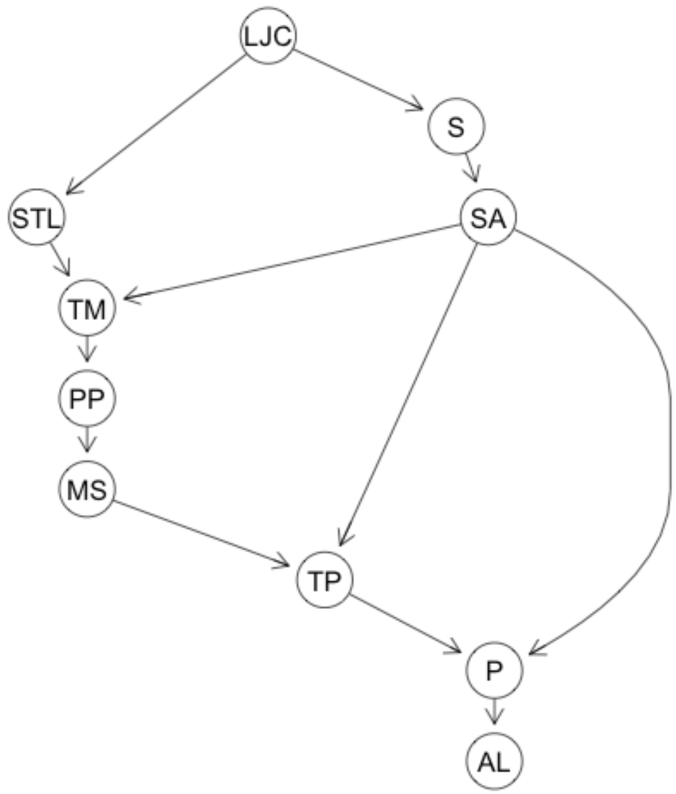
Differential diagnosis



	VARIABLE
L	Liver
G	Gall Bladder
C	Cardiac
R	Rib
M	Muscle
P	Thoracic Pain
AL	Activity Limitation

What are some of the challenges of differential diagnosis?

Another form of differential diagnosis



	VARIABLE
STL	Sitting Too Long
LJC	Low Job Control
SA	Sympathetic Activation
S	Stress
TM	Tight Muscles
PP	Poor Posture
MS	Muscle Strain
TP	Trigger Point
AL	Activity Limitation
P	Pain

Brief Outline of Day (tentative)

TIME	TOPIC	OBJECTIVE
8:30 - 10	Preliminaries	Causation, reasoning patterns and inference
10 - 10:15	Break	Sanity - your chance to break away (perhaps unnoticed)
10:15 - 12	Knowledge for network	Causal network, structure and reasoning
12ish - 1	Lunch	Hungry, possibly Hangry at this point.....
1 - 2:30	Case Set 1	Interpret a set of signs and symptoms; Generate a differential diagnosis
2:30 - 3	Break	By this point probably not this long - sort of a buffer in the schedule
3 - 4:30	Case Set 2	Red flags that warrant a deeper consideration; Generate a differential diagnosis

Preliminaries (8:30 - 10)

Causation, reasoning patterns and inference

Explain the use of causation, reasoning patterns and inference in differential diagnosis.

Establishing a foundation for knowledge

Epistemology

As a critical realist I do not fully subscribe to pure or hyper empirical approaches to knowledge; nor do I believe that rationalism or idealism individually provide the necessary framework for knowledge in practice

But all we need to start is a foundation - "common sense" realism:

- Law of causation
- Law of non contradiction (X cannot be & not be in the same way at the same time)
- Analogical use of language
- Basic reliability in sensory perception

Foundation for todays discussion (1 of 3)

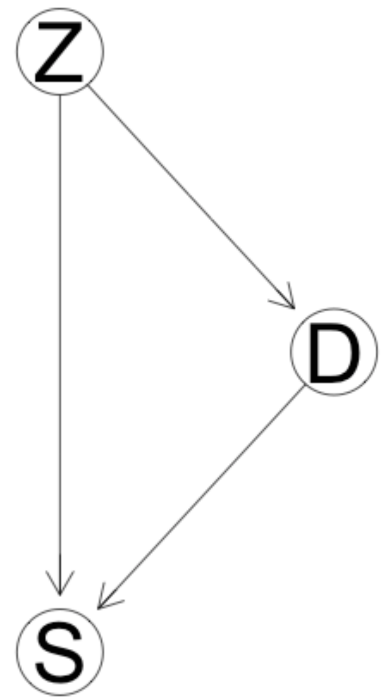
- Most of what we discuss we will make "discrete" (not as in be quiet about this, but as in a category, not continuous)
- Consistent with making continuous phenomena discrete (i.e. blood pressure becomes normal or hypertensive; blood values become anemia) we will assume normal is normal (not pathological), and that abnormal is abnormal (possibly pathological or at least a positive sign (+S))
- We will use
  - +D to indicate "Disease is present" as a fact
  - -D to indicate "Disease is not present" as a fact
  - +S to indicate that a "symptom or sign is present" as a fact
  - -S to indicate that a "symptom or sign is not present" as a fact
  - All test results and 'observable' clinical manifestations will be considered a sign
    - By observable we include all sensory modalities not just vision

Foundations (2 of 3)

- We must recognize that empirical variations in the association between S and D are due to:
  - Non deterministic associations (including non deterministic causal connections)
  - Measurement error of both S and D (validity and reliability)
  - Un measured variables ($Z \in (z_1, z_2, \ldots, z_n)$) that influence S and D in a potentially confounding manner
  - And that these reasons are not mutually exclusive

Confounding

Z is a confounder in this causal network



Foundations (3 of 3)

We will make use of 2x2 tables a lot

Relevant to disease and symptoms / signs:

	+D	-D
+S	True Positive (TP)	False Positive (FP)
-S	False Negative (FN)	True Negative (TN)

For use in probability equations:

	+D	-D
+S	a	b
-S	c	d

Conditional probability

$$P(D|S)$$

$$P(S|D)$$

$$P(D|S) = \frac{P(S|D) \cdot P(D)}{P(S)}$$

Causation underlying conditional probability

But, conditional probability helps establish causation

Causation based on probability

- Definite cause ($+D \rightarrow +S$)
  - $P(+S|+D) = 1$
- Probable cause ($+D \rightarrow +S$)
  - $P(+S|+D) > P(+S|-D)$
- Exacerbating factor ($+D \rightarrow +S$)
  - $P(+S|+D \wedge E) > P(+S|+D)$

Correlation and Causation

You have heard, and it is true:

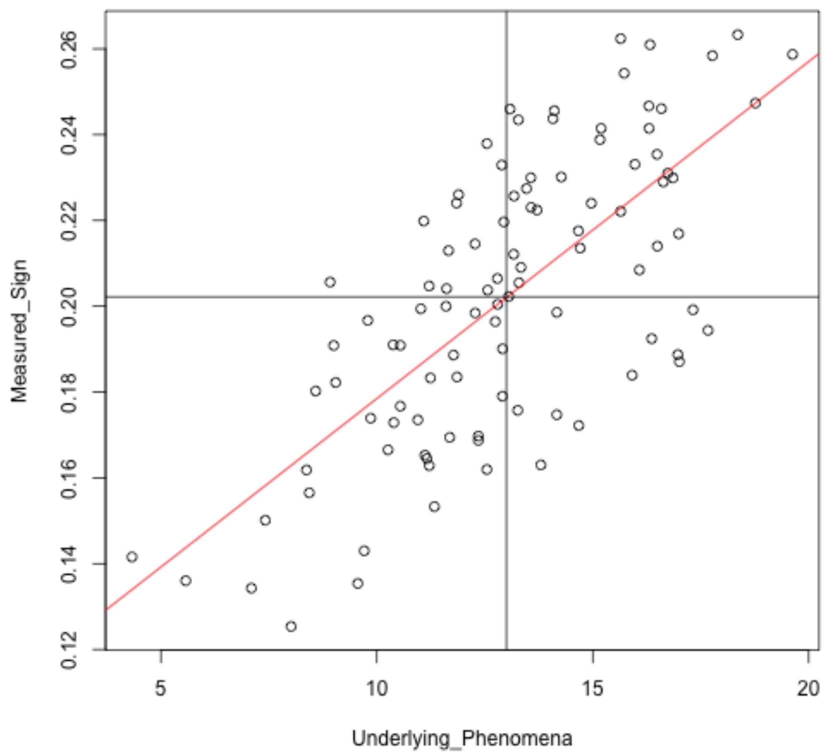
- Correlation does not imply causation

But it is also true that:

- Causation does imply correlation

Relationship between correlation and 2x2 table

Two continuous variable phenomena



Correlation (R) = 0.71

Conversion to 2x2 table

	+D	-D
+S	38	11
-S	12	39

Settling some terms:

What is Differential Diagnosis?

Do you have any examples to share?

At your table - briefly define and discuss:

1. Probability
2. Conditional Probability
3. Inference
4. Causation
5. Rule in / Rule out
6. Diagnosis / Disease / Conditions / Injury
7. Sensitivity / Specificity
8. Likelihood ratios

Reminder

Causation underlying conditional probability

- Definite cause ($+D \rightarrow +S$)
  - $P(+S| + D) = 1$
- Probable cause ($+D \rightarrow +S$)
  - $P(+S| + D) > P(+S| - D)$
- Exacerbating factor ($+D \rightarrow +S$)
  - $P(+S| + D \wedge E) > P(+S| + D)$

Conditional probability underlying pathology

- Etiology (a cause of disease)
  - $+E \to +D$
  - $P(+D| + E) > P(+D| - E)$ (assuming a probable cause)
- Risk factor (can be an etiology, can cause an etiology, or both (confounding))
  - $+R \to +D \vee +E$
  - $P(+D \vee +E| + R) > P(+D \vee +E| - R)$ (assuming a probable cause)
- Clinical manifestations
  - Symptoms (what people feel)
  - Signs -Observable (all sensory modalities) manifestations 1. Anatomical changes 2. Physiological changes 3. Behavioral changes (assumed but not able to identify either 1 or 2) 4. Tests and measures are typically of signs

Causation, reasoning patterns and inference

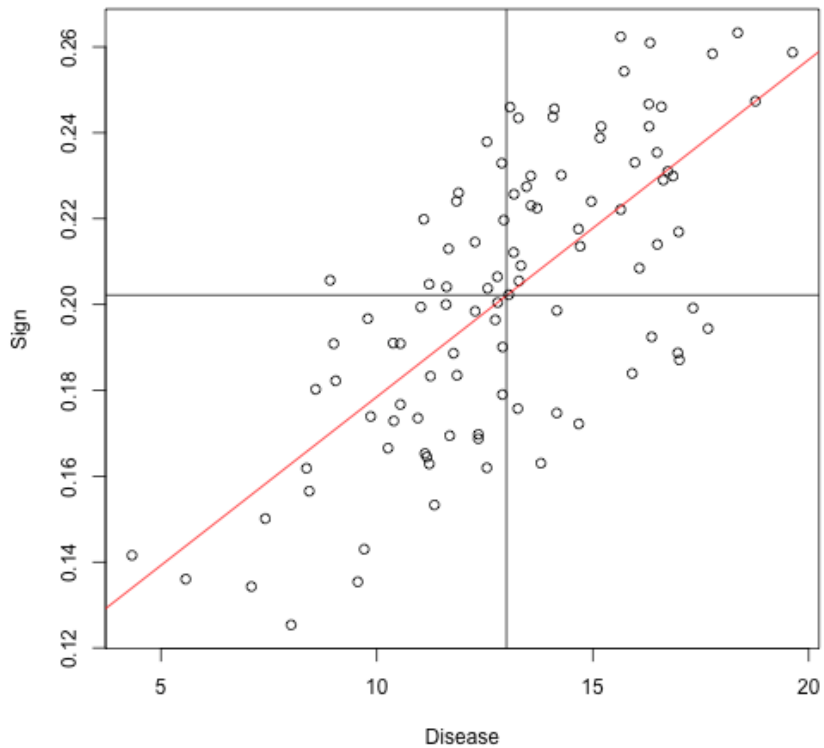
- Causation flows from cause TO effect:
  - $+D \rightarrow +S$
- Diagnostic inferences are cause FROM effect (abduction):
  - $+D \leftarrow +S$
- So while we start with gathering conditional probability on:
  - $P(+S| + D)$
- We really need the conditional probability of:
  - $P(+D| + S)$
- And this is only part of the picture, we also need:
  - $P(-D| - S)$
- And there are bound to be errors:
  - $P(-D| + S)$, $P(+D| - S)$

Conditional Probability 2x2

	+D	-D
+S	$P(+S] + D)$	$P(+S] - D)$
-S	$P(-S] + D)$	$P(-S] - D)$

Causal Relationship to Conditional Probability

Disease → Measured Sign



Correlation (R) = 0.71

$D \rightarrow S$

	+D	-D
+S	38(a)	11(b)
-S	12(c)	39(d)

- Sensitivity: $P(+S| + D) = \dfrac{a}{a+c}$
- Specificity: $P(-S| - D) = \dfrac{d}{b+d}$
- 1 - Sensitivity: $P(-S| + D) = \dfrac{c}{a+c}$
- 1 - Specificity: $P(+S| - D) = \dfrac{b}{b+d}$
- $P(D) = \dfrac{a+c}{a+b+c+d}$
- $P(S) = \dfrac{a+b}{a+b+c+d}$

$D \rightarrow S$

Data fills table and is used to generate summary statistics

	+D	-D
+S	38(a)	11(b)
-S	12(c)	39(d)

And summary statistics can be used to generate "simulated" data

	+D	-D
+S	76	22
-S	24	78

- Sensitivity (Rate of True Positives): $P(+S| + D) = \dfrac{a}{a + c}$ = 0.76
- Specificity (Rate of True Negatives): $P(-S| - D) = \dfrac{d}{b + d}$ = 0.78
- 1 - Sensitivity (Rate of False Negatives): $P(-S| + D) = \dfrac{c}{a + c}$ = 0.24
- 1 - Specificity (Rate of False Positives): $P(+S| - D) = \dfrac{b}{b + d}$ = 0.22
- $P(D) = \dfrac{a + c}{a + c + b + d}$ = 0.5
- $P(S) = \dfrac{a + b}{a + b + c + d}$ = 0.49

$KneeFracture \rightarrow OttawaKneeRule$

From: http://getthediagnosis.org/finding/Ottawa_Knee_Rule.htm (http://getthediagnosis.org/finding/Ottawa_Knee_Rule.htm)

Sensitivity 100%; Specificity 49%

	+D	-D
+S	100	51
-S	0	49

- Sensitivity (Rate of True Positives): $P(+S|+D) = \dfrac{a}{a+c}$ = 1
- Specificity (Rate of True Negatives): $P(-S|-D) = \dfrac{d}{b+d}$ = 0.49
- 1 - Sensitivity (Rate of False Negatives): $P(-S|+D) = \dfrac{c}{a+c}$ = 0
- 1 - Specificity (Rate of False Positives): $P(+S|-D) = \dfrac{b}{b+d}$ = 0.51
- $P(D) =$ 0.5
- $P(S) =$ 0.755

$HF \to S3$

From: http://getthediagnosis.org/diagnosis/Congestive_Heart_Failure.htm#1311 (http://getthediagnosis.org/diagnosis/Congestive_Heart_Failure.htm#1311)

S3 heart sound in dyspneic patients presenting to the ED

Sensitivity 13%; Specificity 99%
Study: JAMA. 2005 Oct 19;294(15):1944-56 PMID: 16234501

	+D	-D
+S	13	1
-S	87	99

- Sensitivity (Rate of True Positives): $P(+S| + D) = \dfrac{a}{a+c}$ = 0.13
- Specificity (Rate of True Negatives): $P(-S| - D) = \dfrac{d}{b+d}$ = 0.99
- 1 - Sensitivity (Rate of False Negatives): $P(-S| + D) = \dfrac{c}{a+c}$ = 0.87
- 1 - Specificity (Rate of False Positives): $P(+S| - D) = \dfrac{b}{b+d}$ = 0.01
- $P(D) = 0.5$
- $P(S) = 0.07$

$LungCA \rightarrow Clubbing$

From: http://getthediagnosis.org/diagnosis/Lung_Cancer.htm (http://getthediagnosis.org/diagnosis/Lung_Cancer.htm)

Digital clubbing in patients with lung cancer

Sensitivity 37%; Specificity 91%
Study: JAMA. 2001;286:341-347. http://jama.ama-assn.org/cgi/content/full/286/3/341 (http://jama.ama-assn.org/cgi/content/full/286/3/341)

	+D	-D
+S	37	9
-S	63	91

- Sensitivity (Rate of True Positives): $P(+S| + D) = \dfrac{a}{a+c}$ = 0.37
- Specificity (Rate of True Negatives): $P(-S| - D) = \dfrac{d}{b+d}$ = 0.91
- 1 - Sensitivity (Rate of False Negatives): $P(-S| + D) = \dfrac{c}{a+c}$ = 0.63
- 1 - Specificity (Rate of False Positives): $P(+S| - D) = \dfrac{b}{b+d}$ = 0.09
- $P(D) =$ 0.5
- $P(S) =$ 0.23

Side note: Likelihood Ratios

$LungCA \rightarrow Clubbing$

	+D	-D
+S	37	9
-S	63	91

Positive Likelihood Ratio

$$+LR = \frac{Sensitivity}{1 - Specificity}$$

$$+LR = \frac{P(+S| + D)}{1 - P(-S| - D)}$$

$$+LR = \frac{a(b + d)}{b(a + c)}$$ = 4.1111111

- Sensitivity (Rate of True Positives): $P(+S| + D) = \frac{a}{a + c}$ = 0.37
- Specificity (Rate of True Negatives): $P(-S| - D) = \frac{d}{b + d}$ = 0.91
- 1 - Sensitivity (Rate of False Negatives): $P(-S| + D) = \frac{c}{a + c}$ = 0.63
- 1 - Specificity (Rate of False Positives): $P(+S| - D) = \frac{b}{b + d}$ = 0.09

Side note: Likelihood Ratios

$LungCA \rightarrow Clubbing$

	+D	-D
+S	37	9
-S	63	91

Negative Likelihood Ratio

$$-LR = \frac{1 - Sensitivity}{Specificity}$$

$$-LR = \frac{1 - P(+S| + D)}{P(-S| - D)}$$

$$-LR = \frac{c(b + d)}{d(a + c)}$$ = 0.6923077

- Sensitivity (Rate of True Positives): $P(+S| + D) = \frac{a}{a + c}$ = 0.37
- Specificity (Rate of True Negatives): $P(-S| - D) = \frac{d}{b + d}$ = 0.91
- 1 - Sensitivity (Rate of False Negatives): $P(-S| + D) = \frac{c}{a + c}$ = 0.63
- 1 - Specificity (Rate of False Positives): $P(+S| - D) = \frac{b}{b + d}$ = 0.09

Bayes formula

Probability of cause from effect

Computes the probability of disease given the sign/symptom ($P(D|S)$)

$$P(+D|+S) = \frac{P(+S|+D) \cdot P(D)}{P(S)}$$

$P(+D|+S)$= 0.8043478

Based on some assumptions:

- Sensitivity (Rate of True Positives): $P(+S|+D) = \frac{a}{a+c}$ = 0.37
- $P(D) = \frac{a+c}{a+c+b+d}$ = 0.5
- $P(S) = \frac{a+b}{a+b+c+d}$ = 0.23

It's all about the priors!

But this based on one sample; and this sample may have an elevated $P(D)$ and $P(S)$

The $P(D)$ and $P(S)$ are the "priors" - or "baseline" probabilities of the disease and the sign

$$P(+D| + S) = \frac{P(+S| + D) \cdot P(D)}{P(S)}$$

For example, for Small Pox, with S = spots:

- $P(+S|+D)= 0.76
- $P(D)= 0.0011
- $P(S)= 0.08

$P(+D| + S)$= 0.01045

It's all about the priors!

But for chicken pox, with S = spots:

- $P(+S | +D)$= 0.9
- $P(D)$= 0.075
- $P(S)$= 0.08

$P(+D | +S)$= 0.84375

What are the challenges related to Differential Diagnosis?

- Difference between knowledge (justified true belief) when there is a probabilistic justification and when there is a direct observation (the example of knowing someone in China is making a doll right now, or knowing that someone is taking a breath right now even though you do not see it happening)

- Relate to inductive inference and the process of developing general theories about how the world works, of what is true about the world

Inversion of causation -

24% of people having a stroke have difficulty with speech; is not the same and does not mean mean that 24% of people that are having difficulty with speech are having a stroke

Chapters from a book on differential diagnosis

- Screening for Hematologic Disease
- Screening for Cardiovascular Disease
- Screening for Pulmonary Disease
- Screening for Gastrointestinal Disease
- Screening for Hepatic and Biliary Disease
- Screening for Urogenital Disease
- Screening for Endocrine and Metabolic Disease
- Screening for Immunologic Disease
- Screening for Cancer
- Screening the Head, Neck, and Back
- Screening the Sacrum, Sacroiliac, and Pelvis
- Screening the Lower Quadrant: Buttock, Hip, Groin, Thigh, and Leg
- Screening the Chest, Breasts, and Ribs
- Screening the Shoulder and Upper Extremity

Relate the pathology terms to causation

Abductive inference & Bayesian probability

expectations about the world - our "baseline" or "apriori" probability

top diseases in terms of prevalence and then the distribution of these conditions among groups of people - looks a lot like "stereotyping"

Break (10 - 10:15)

Sanity - your chance to break away (perhaps unnoticed)

Knowledge for network (10:15 - 12)

Causal network, structure and reasoning

Develop a causal network and consider the features of its structure in reasoning and making diagnostic inferences.

fill in knowlege we gain during a clinical encounter and how that changes our "Bayesian" interpretation of the probability of ruling out and ruling in

Sources of Data in New Hampshire

New Hampshire Department of Health and Human Services (http://www.dhhs.nh.gov/data/)

http://www.dhhs.nh.gov/data/ (http://www.dhhs.nh.gov/data/)

Build some graphical models of common sets of symptoms (start with symptoms, progress to signs)

Case Set 1 (1 - 2:30)

Interpret a set of signs and symptoms; Generate a differential diagnosis

Interpret a set of signs and symptoms in light of possible causes.

Generate a differential diagnosis and subsequent plan of action for complex patient cases across practice settings.

Interpret a set of signs and symptoms in light of prior and posterior probabilities regarding possible causes.

Generate a differential diagnosis and subsequent plan of action for complex patient cases across practice settings.

Break (2:30 - 3)

By this point probably not this long - sort of a buffer in the schedule

Case Set 2 (3 - 4:30)

Red flags that warrant a deeper consideration; Generate a differential diagnosis

Identify red flags that warrant a deeper consideration of alternative explanations for signs and symptoms.

Generate a differential diagnosis and subsequent plan of action for complex patient cases across practice settings.

Identify red flags that warrant a deeper consideration of alternative explanations for signs and symptoms.