POM Clinical Pearls:

Fundamentals of Clinical Reasoning

I. Definitions and Key Concepts

Clinical Reasoning

Clinical reasoning is the cognitive process by which a clinician makes decisions regarding possible diagnoses and treatment strategies for an individual patient. It involves the application of biostatistics to the details of the patient's presentation (e.g. present and past medical history, exam findings, test results), along with the incorporation of the clinician's knowledge of pathophysiology.

In common usage, the term "clinical reasoning" often refers primarily to diagnostic reasoning (i.e. generating a differential diagnosis from known information), although in a broader sense it also refers to the selection and interpretation of diagnostic tests, as well as the reasoning behind treatment decisions.

Clinical reasoning is inherently probabilistic, and thus contains a significant amount of uncertainty. It is also a continuous, iterative process in which conclusions and probabilities are updated with each new piece of information available.

Differential Diagnosis

The differential diagnosis is a list of diagnoses (diseases or syndromes) which can explain a specific patient's presentation. It is usually placed in the estimated order of descending probability (i.e. the most likely diagnosis is listed first).

Diagnostic Framework

The diagnostic framework is a list of diagnoses which can explain the presence of a specific symptom, physical exam finding, or diagnostic test abnormality. Diagnostic frameworks are most commonly organized by organ system, but can also be organized by anatomic region, physiological mechanism, or category of microorganism (for suspected infections).

Examples of Diagnostic Frameworks:

Brief organ-system based framework

Dyspnea			
Cardiac	Pulmonary	Heme	Other
Heart failure Valvular heart disease CAD (i.e. angina-equivalent) Arrhythmias	Pneumonia Asthma COPD ILD Pleural effusion Pneumothorax	Anemia	Anxiety Metabolic acidosis

Thorough organ-system based framework

Chest Pain			
Cardiac	Pulmonary	GI	Other

• Coronary arteries
  ○ CAD / ACS
  ○ Vasospasm
• Myocardium
  ○ Myocarditis
  ○ Hypertrophic cardiomyopathy
  ○ Heart failure w demand ischemia
• Valves
  ○ Aortic stenosis
• Conduction System
  ○ Tachyarrhythmias
• Pericardium
  ○ Pericarditis
	• Pulmonary arteries
	  ○ Pulmonary embolism
	  ○ Pulmonary hypertension
	• Airways
	  ○ COPD / Asthma exacerbation
	• Pleura
	  ○ Plueritis
		• Esophagus
		  ○ Esophagitis
		  ○ GERD
		• Stomach
		  ○ Gastritis
		  ○ Peptic ulcer disease
		• Hepatobiliary
		  ○ Hepatitis
		  ○ Cholecystitis
		  ○ Cholangitis
		• Pancreas
		  ○ Pancreatitis
			• Rib fracture
			• Costocondritis
			• Herpes zoster
			• Psychogenic

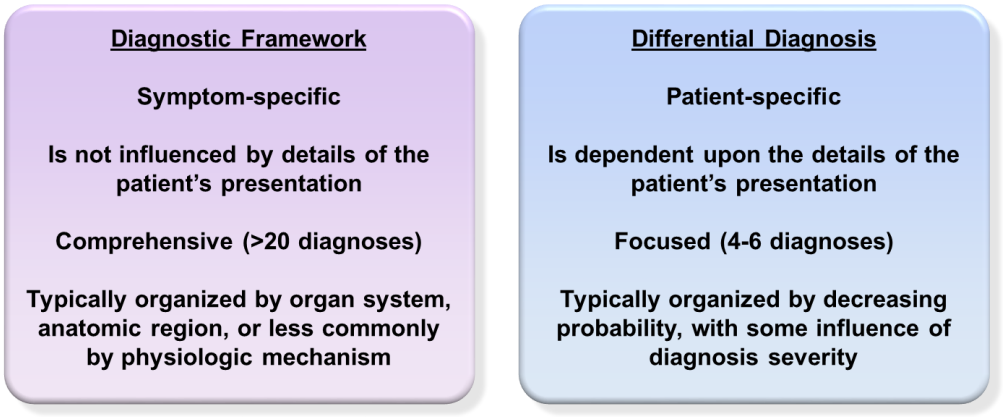
Physiology-based framework

Bilateral leg edema			
Increased venous hydrostatic pressure	Decreased oncotic pressure	Impaired lymphatic drainage	Miscellaneous
Heart failure Liver failure Kidney failure Venous insufficiency Medication side effect (e.g. NSAIDs, steroids)	Low dietary protein Liver failure Nephrotic syndrome	Primary lymphedema Lymphatic filariasis Post-surgical Post-radiation	Hypothyroidism

Hybrid framework

Fever of Unknown Origin				
Infection			Malignancy	Autoimmune / Rheumatologic
Bacteria	Viruses	Parasites		
Tuberculosis Osteomyelitis Culture-negative endocarditis Lyme disease Q fever	CMV EBV Dengue Chikungunya	Malaria Babesiosis Amoebic liver abscess	Lymphoma Leukemia Renal cell carcinoma Hepatocellular carcinoma	Vasculitis Still's disease Reactive arthritis SLE

Confusingly, it's common on the wards and in clinics for clinicians to refer to a diagnostic framework as a "differential diagnosis". (i.e. "So medical student, can you tell me the differential diagnosis for vomiting?") However, even when the same term is used to describe differentials and frameworks, they are distinct concepts:



Key Features

Key features are individual elements of a presentation which are likely to help differentiate one diagnosis from another. They may be "pertinent positives" (i.e. symptoms or aspects of a symptom which are present) or "pertinent negatives" (i.e. symptoms or aspects of a symptom which are absent).

Semantic Qualifiers

Semantic qualifiers are qualitative abstractions of the symptoms of case, which can help the clinical reasoning process by ensuring the case is appropriately framed, by assisting in the recall of the most relevant illness scripts, and by facilitating efficient communication between clinicians.

Category of Qualifier	Examples
Onset	Abrupt vs. Gradual Acute vs. Chronic
Course	Continuous vs. Episodic Progressive vs. Stable
Site	Unilateral vs. Bilateral Proximal vs. Distal Diffuse vs. Focal
Trigger	Post-prandial vs. Exertional vs. Positional (i.e. worse when supine)
Quality	Painful vs. Painless Productive/Wet vs. Non-productive/Dry (for cough) Watery vs. Bloody (for diarrhea) Bilious vs. Non-bilious (for vomiting) Pleuritic vs. Non-pleuritic (for chest pain)

Examples:

"I've had this cough for 6 months, and it keeps getting worse. I've been bringing up lots of green phlegm"

Translates as: *Chronic, progressive, productive cough*

"My left leg swelled up yesterday, and it really hurts"

Translates as: *Acute, painful, unilateral leg swelling*

Illness Scripts

An illness script is a mental summary of the most relevant details of a specific disease, often organized in such a way as to facilitate a comparison to other diseases which can have a similar presentation. Expert clinicians and novice clinicians differ in the total number of illness scripts which they have committed to memory, and the choice of information each script contains (with experts focusing on the features which are the most discriminating from other similar diseases).

There is no universal organization to the information contained in an illness script, but common categories of information include pathophysiology, epidemiology/risk factors, clinical characteristics (e.g. symptoms, time course, associated exam findings and test abnormalities), means of definitive diagnosis, treatment, and prognosis.

Example of comparative illness scripts:

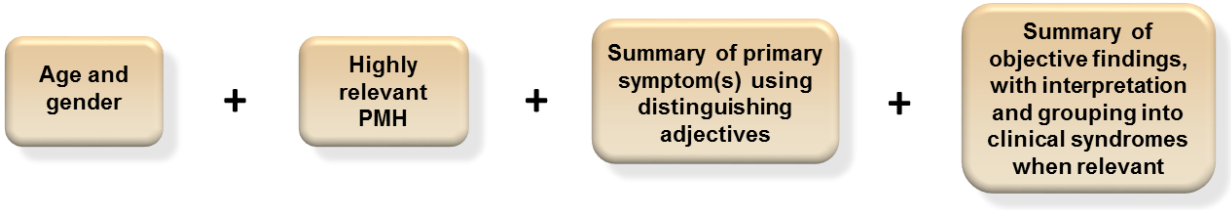
	Headache		
	Tension headache	Migraine headache	Cluster headache
Pathophysiology (Incompletely understood in all)	Myofascial pathway	Trigeminovascular pathway	Hypothalamic activation with secondary activation of the trigeminal-autonomic reflex
Epidemiology and risk factors	Age of onset: 20-50 ♀ predominance Most common	Age of onset: 10-40 ♀ predominance Strong genetic link Emotional stress is common trigger	Age of onset: 15-40 ♂ predominance Relatively rare
Clinical Presentation	Usually bilateral Duration: Mins-days Severity: Mild-mod Quality: "Tightness" Other: Usually not associated with other symptoms, or any physical signs	Starts as unilateral, but may become bilateral Duration: Hrs-days Severity: Mild-severe Quality: "Throbbing" Other: Preceded by prodrome (e.g. mood changes, food cravings, yawning). 25% will also have aura (scotoma, focal neuro findings). During headache, patients have nausea, photophobia, phonophobia, & allodynia. Patients prefer to sit in a dark, quiet room. Numerous distinct subtypes	Unilateral, near the eye Duration: < 3hrs Severity: Mod-severe Quality: "Piercing" Other: Ipsilateral autonomic symptoms (e.g. miosis, lacrimation, rhinorrhea). During headache, patients are restless, preferring to pace or rock. Headaches occur in clusters of 6-12 weeks, separated by asymptomatic remissions of 12+ months.
Diagnosis	Clinical	Clinical	Clinical
Treatment	Abortive: NSAIDs, acetaminophen Preventative: Usually none	Abortive: NSAIDs, triptans, dopamine antagonists, ergots Preventative: β blockers, anti-depressants, anticonvulsants	Abortive: 100% oxygen, triptans Preventative: Verapamil

Summary Statement

A *summary statement* is a 1-2 sentence summary of the most highly relevant key features of the presentation, as well as the most important pertinent positives and negatives from the physical exam and diagnostic tests. The use of semantic qualifiers for symptoms, as well as the grouping of related objective findings into a shared clinical syndrome (when possible), both work very well within summary statements.

Unfortunately, there is a lack of standardization in the terminology, structure, and content of the summary statement. For example, the term *problem representation* is commonly encountered in medical education literature. Also, some clinicians prefer this summary to be more comprehensive (5+ sentences), in which case it is more often referred to as an *impression* or an *assessment*, and may include mention of the leading diagnosis. Less commonly, clinicians prefer it to be as concise as a single phrase (e.g. "chronic episodic palpitations", "acute painful vaginal bleeding").

One suggested summary statement structure:



Examples:

> *"Mr. Chin is a 60 year old man with a history of poorly controlled diabetes, who is presenting with acute, positional, non-pleuritic dyspnea, with an exam and chest X-ray findings of volume overload, and with unremarkable labs and ECG."*

> *"Ms. Scott is a 46 year old woman with a history of HIV, who is presenting with chronic, stable, painless, watery diarrhea, and intermittent fevers. On exam, she was febrile but hemodynamically stable, with diffuse lymphadenopathy, and was noted to have thickening of the wall of her descending colon on CT abdomen."*

> *"Ms. Kumar is an 85 year old woman with a history of hypertension and hyperlipidemia, who is presenting with acute, unilateral, arm weakness, found to have flaccid paralysis of the right arm with hyporeflexia, normal labs, and an unremarkable head CT."*

> *"Emma is an 8 year old girl with a normal developmental history, who is presenting with acute, constant abdominal pain and non-bloody vomiting, found to be febrile and tachycardic, with right lower quadrant tenderness, and a white blood cell count of 20."*

> *"Mr. Williams is a 34 year old man with active methamphetamine abuse, presenting with acute onset of bizarre behavior, found on exam to be febrile, disoriented, and responding to internal stimuli. Routine labs and head CT are unremarkable, urine tox is positive for amphetamines and cocaine, and a lumbar puncture was only notable for mild pleocytosis."*

Rule-In vs. Rule Out

A diagnosis is considered to be "ruled in" when the probability of that disease is high enough that the balance of anticipated benefit and anticipated harm argues against further testing for it. When a diagnosis has been ruled in, it does *not* mean that the diagnosis is 100% certain, or that it can't be reconsidered at a later time when more information is available. A diagnosis should not be considered ruled-in unless all competing diagnostic possibilities have been ruled out.

A diagnosis is considered to be "ruled out" when its probability is low enough that the balance of anticipated benefit and anticipated harm argues against further testing for it. When a diagnosis has been ruled out, it does *not* mean the diagnosis is impossible, or that it can't be reconsidered at a later time when more information is available.

Provisional Diagnosis (a.k.a. "the leading diagnosis", "the working diagnosis")

The provisional diagnosis is the diagnosis that is at the top of a differential diagnosis, but which has not yet been ruled in.

Empiric Treatment

A therapeutic intervention can be referred to as empiric treatment if it is provided to a patient with the intent to treat a possible diagnosis that has not yet been ruled in. Occasionally, empiric treatment can be used as a diagnostic test: if a patient's condition improves, it suggests they are more likely to have the diagnosis under consideration, whereas if they do not, it suggests they are less likely. It's important to realize that even when the leading diagnosis is the correct one, patients still might not initially improve to empiric treatment. Patients also frequently improve on their own, even if treatment for the wrong diagnosis is provided.

Clinical Prediction Rule

A clinical prediction rule is a decision support tool which takes the most statistically helpful pieces of information related to a specific clinical scenario, and reduces them to a simple scoring system or algorithm to assist the clinical reasoning process. They are used to help guide and inform clinical reasoning, not to supplant it. Clinical prediction rules should also be used only on the patients and in the specific situations in which they were validated.

Examples of Common Clinical Prediction Rules:

Category	Rule	Purpose
Diagnostic	Wells score	Diagnosis of DVT and PE
	HEART score	Diagnosis of ACS
	Lights' criteria	Differentiation of pleural effusions
	CAGE questions	Diagnosis of alcohol abuse/dependence

Therapeutic	CHA2DS2-Vasc score	Decision to use anticoagulation in a-fib
	CURB65 score	Decision to admit patients with pneumonia
	Centor criteria	Decision to use antibiotics in sore throat
Prognostic	TIMI score	Estimates short-term risk of death or ischemic events in patients with UA/NSTEMI
	APACHE-II score	Estimates short-term death in critical illness
	Ranson criteria	Estimates short-term death in pancreatitis
	MELD score	Estimates long-term death in cirrhosis
	Glascow coma scale	Estimates short and long-term prognosis in a variety of acute neurological injuries
	APGAR score	Estimates short-term prognosis in infants upon birth

Problem Lists

A problem list is a prioritized list that includes aspects of a person's current pathophysiological state, medical history, family history, and social history which either need to be addressed at the moment, or which might impact the patient's health at some point in the future. A problem list can include any of the following:

- Current or recent symptoms (e.g. shortness of breath, constipation, anxiety)
- Physical exam findings (e.g. heart murmur, abdominal mass)
- Test abnormalities (e.g. hyponatremia, anemia, lung nodule on chest X-ray)
- Chronic medical and psychiatric problems (e.g. hypertension, diabetes, depression)
- Old, seemingly resolved medical problems which could recur or lead to new problems (e.g. history of splenectomy, history of a cancer thought to have been cured)
- Life-threatening allergies (e.g. anaphylaxis to a common antibiotic)
- High-risk medications (e.g. anticoagulants, immunosuppression – including chronic prednisone) – the overwhelming majority of medications do *not* belong on the problem list
- Active or previous substance abuse
- Significant family history of life-threatening, hereditary disease (e.g. mother with BRCA1 mutation) – the overwhelming majority of the family history does *not* belong on the problem list
- Highly significant social factors (e.g. poverty, lack of insurance, home violence, homelessness, etc…)

Items in the problem list are ordered by acuity/priority (i.e. what item needs to be addressed the most urgently and/or is most likely to kill the patient), with the patient's chief complaint being accounted for near the top. Items should be lumped together if there is strong suspicion that they share a common primary etiology and/or pathophysiology, and share the same general treatment.

For example:

- Fever, tachycardia, and leukocytosis could be lumped together as sepsis.
- Insomnia, poor appetite, and suicidality could be lumped together as depression.
- Chest pain, elevated troponin, and ST elevations on ECG could be lumped together as a STEMI.

A potential exception to this is when separate problems have distinct approaches to acute management, even if they share common mechanism. For example, an elevated creatinine and low urine output could be bundled together as renal failure, while hyperkalemia remained a distinct item on the problem list as hyperkalemia is a more critical problem than renal failure in general, and has a specific set of treatments that are not relevant for the other aspects of renal failure.

If there is uncertainty as to whether two items are part of the same process, it's preferable to list them separately.

The purposes of problem lists include:

- Help clinicians make connections between individual features of a presentation to aid in generating a differential diagnosis.
- Ensure that all active abnormalities have been accounted for and are being addressed.
- Prevent new treatments for acute problems from interacting with chronic problems (e.g. starting a new antibiotic in a patient on warfarin).
- Aid in a diagnostic time-out (discussed below under "debiasing strategy").
- Help facilitate communication between health care professionals by organizing a clinician's thoughts and management plan, and to maximize the chance that problems don't "slip through the cracks" after handoffs in care.
- Aid in billing insurance companies appropriately.

Problem lists are not static, and should be continuously updated to reflect new emerging problems, complete resolution of problems which can be removed from the list, and new information that allows the clinician to more accurately lump or split two or more problems.

The clinician's choices during the construction of a problem list (e.g. how to lump vs. split, choice of problems to include, order of problems) depends upon the patient's overall acuity of illness, and the clinician's primary focus. The problem list from a specialist called to consult on a medically complex patient may look different that the problem list from that patient's primary medical team. An inpatient problem list often looks quite different from an outpatient one.

Examples of Problem Lists:

A 50 year old woman in the ED with dyspnea, in whom the diagnostic data is currently incomplete.	The same patient on hospital day #2, after a diagnosis has been made	The same patient seen in primary care clinic 1 month later, after full recovery from her acute illness.
• Hypoxemia • Chest pain • Elevated d-dimer • Hyperglycemia • Long-standing hypertension • Osteoporosis • Remote history of IV drug use • Marginal housing	• Acute pulmonary embolism • Diabetes, new diagnosis • Long-standing hypertension • Osteoporosis • Remote history of IV drug use • Marginal housing	• Diabetes • Hypertension • Warfarin use • History of PE • Osteoporosis • Remote history of IV drug use • Marginal housing • Colon cancer screening due 2019

II. Steps to Generating a Differential Diagnosis

There are multiple good approaches to generating a differential diagnosis, one of which is a comparison of illness scripts for the chief complaint. When done unconsciously, this becomes a form of pattern recognition, which can be relatively quick and is generally accurate when done by experienced clinicians. However, pattern recognition can fall short when the patient presents with an unusual chief complaint, has a particularly atypical presentation of a common chief complaint, or the clinician is inexperienced (i.e. their illness scripts are too few in number, or too incomplete).

An alternative, more systematic but time-consuming approach is as follows:

1. Acquire data – A differential diagnosis is only as accurate and complete as the information that goes into it.

2. Identify key features – Not every piece of data from a patient's presentation is helpful at distinguishing possible diagnoses from one another. There's a reasonable argument that any question during the patient interview, physical exam maneuver, or test ordered should only be undertaken if it will result in some useful information. However, for several reasons, there is a significant amount of extraneous information acquired during the initial patient evaluation, and it's critical for clinicians to sift through it and identify what's actually important.

3. Craft a summary statement – This step forces the clinician to identify the most highly relevant key features, and to identify the primary problem(s), which usually (though not always) includes the patient's chief complaint.

4. Choose a diagnostic framework – The choice of framework is based upon the primary problem as described in the summary statement.

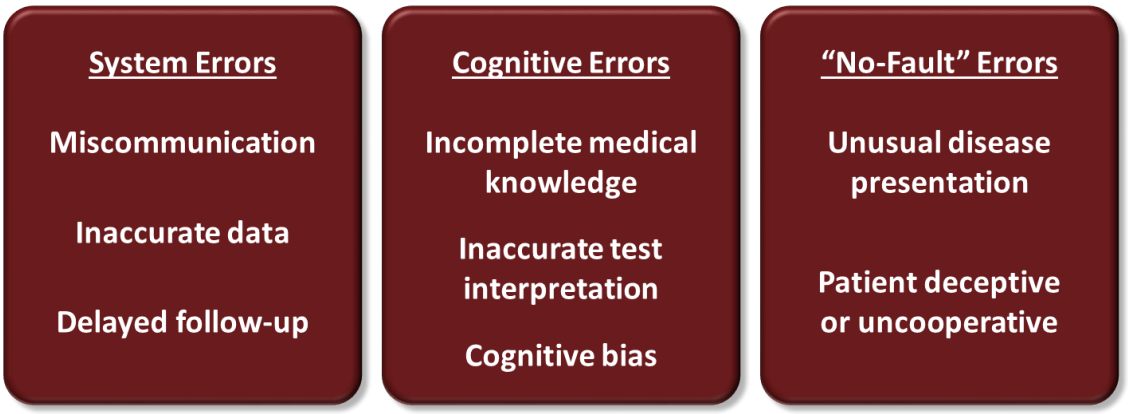
5. Apply the key features to the framework – The probability of specific diagnoses listed in the framework either rise or fall based upon the individual key features.

6. Create the differential diagnosis – This is primarily done by picking the most probable diagnoses after the key features have been applied to the framework. There is also some consideration of the danger of a missed diagnosis when crafting the differential, such that a less likely but highly dangerous diagnosis might be included on the list while a more likely but benign diagnosis is left off. A typical differential for common presenting symptoms is around 4-6 diagnoses long. The less data there is, the greater the uncertainty, and the longer the differential will be. In other words, as more data on the patient accumulates, the differential will shorten until eventually it contains just one diagnosis, which is then "ruled in".

As a word of caution, a clinical syndrome is usually not the final diagnosis. For example, it's fine to include "sepsis" on the differential diagnosis for a patient presenting with fever, but once sepsis has been ruled in, the clinician must then create a differential diagnosis for the patient's sepsis. Likewise, "heart failure" is perfectly fine to be on a differential diagnosis for a patient presenting with dyspnea, however, once heart failure has been ruled in, the underlying etiology of the heart failure must be sought (e.g. ischemia, hypertension, alcohol abuse, amyloidosis, etc…).

III. Common Pitfalls

Sources of Diagnostic Error



(Cognitive errors are the most common)

Cognitive Bias

Cognitive bias is any tendency for doctors to favor one particular viewpoint over another in a way that's not fully supported by logic or data. There are many forms of cognitive bias, some of which impact diagnostic reasoning, and some of which impact decisions about therapy.

Examples of Diagnostic Biases:

Anchoring bias	The clinician inadequately adjusts the initial diagnostic hypothesis when new information becomes available. The clinician holds on to the initial working diagnosis despite conflicting information due to "anchoring" on a specific feature of the presentation learned early on. Similar to confirmation bias.
Attribution bias	The clinician places greater than appropriate weight on diagnoses which can be "blamed" on a patient's behavior, substance abuse, or lack of compliance. Most commonly associated with psychiatric and minority patients.
Availability bias	The clinician places greater weight on diagnoses that come readily to mind due to recent patients with the same diagnoses, or to having recently read about a specific condition.
Base rate neglect bias	The clinician ignores the prevalence of disease, and focuses just on how typical or atypical a patient's symptoms/signs are for that disease.
Confirmation bias	The clinician places greater weight on data that confirms a specific diagnostic hypothesis, and less weight on data that refutes it. Similar to anchoring bias.
Exhaustion bias	The clinician fails to consider diagnoses when new information becomes available, if previous attempts to diagnose the patient exhausted a thorough battery of tests.
Gender bias	The clinician places greater than appropriate weight on a patient's gender when determining the probability of a disease. Can occur when gender does not affect the probability of a disease, or when it does affect the probability but the effect is smaller than estimated.
Momentum bias	The clinician prematurely accepts a diagnosis as accurate that had been already attached to the patient, without being adequate skeptical of it, or without reaching his/her own conclusions.
Multiple alternatives bias	The clinician may feel overwhelmed by a lengthy differential diagnosis, and may prematurely narrow the differential to a smaller subset with which he/she is more familiar.
Order bias	The clinician tends to preferentially remember and process the initial (primacy effect) and end (recency effect) of any presentation of data.

Outcome bias	The clinician favors diagnoses with better prognoses.
Posterior probability bias	The clinician's estimate of the likelihood of a disease is excessively influenced by previous similar presentations within the same patient.
Psych bias	The clinician attributes symptoms to a known primary psychiatric diagnosis before adequately considering non-psychiatric etiologies.
Representativeness bias	The clinician only considers a diagnosis if the presentation is a classic example of it. Can be a problem with overreliance on incomplete illness scripts.
Specialist deference bias	The clinician defers judgment regarding diagnosis to a person labeled as a "specialist", irrespective of their actual expertise or whether the specialist's opinion is consistent with the data.
Sunk cost bias	The clinician is resistant to consider alternatives when he/she has invested time and resources to look for a specific diagnosis.
Technology bias	The clinician always trusts diagnostic tests relying on technology over the history and exam, irrespective of whether or not the technology is actually superior.
Visceral bias	The clinician favors a diagnosis of either better or worse prognosis due to personal emotional involvement (positive or negative) with the patient, which may be caused by countertransference.
Zebra bias	The clinician places inappropriate weight on the consideration of rare diagnoses because they are fun to read about, represent unusual learning opportunities, or because such diagnoses have been overrepresented in educational conferences. It is a special case of base rate neglect.

Examples of Therapeutic Biases:

Aggregate bias	The clinician falsely believes that his/her patients are atypical or exceptional, and thus clinical practice guidelines based on aggregate data do not apply.
Cluster bias	The clinician errs on the side of providing identical treatment regimen to a cluster of patients who present at the same time with similar, but not identical presentations.
Commission bias	The clinician errs on the side of action rather than inaction, in the belief that active intervention is the best way to prevent harm to the patient. It is the opposite of omission bias, and more likely in overconfident physicians.
Deference bias	The clinician errs too greatly on the side of offering treatment that the patient requests, even if not medically appropriate.
Framing bias	The clinician's opinion about the best course of action is impacted by how the situation is framed.
Limited perspective bias	The clinician's opinion about the best course of action in a common scenario is impacted by the fact that he/she is only exposed to the adverse consequences of one therapeutic option; thus, over time, the clinician becomes increasingly adverse to that option in favor of those treatment options in which the adverse consequences are hidden from view.
Omission bias	The clinician errs on the side of inaction rather than action, in the belief that watchful waiting is the best way to prevent harm to the patient. It is the opposite of commission bias. It also includes the belief that adverse outcomes that are part of the nature course of the disease process are preferable to those that are a direct consequence of physician intervention, even when those outcomes are otherwise of identical severity.
Secondary gain bias	The clinician's opinion about appropriate treatment is subconsciously swayed by personal secondary gain. When done consciously, this does not represent true bias.
Triage bias	The clinician allows the environment to which the patient has been triaged dictate the types of treatment the patient receives, instead of revising the location of care.
Visceral bias	The clinician allows personal emotional involvement with a patient (positive or negative) to unduly influence the treatments offered. As with visceral bias in diagnosis, this is often caused by countertransference.

Base Rate Neglect Bias

This form of cognitive bias, also called base rate fallacy, deserves special attention due to how common and problematic it is. When a clinician's diagnostic reasoning is clouded by base rate neglect, they focus too much attention on the specifics of a patient's presentation, and not enough on the prevalence of the disease under consideration in the general population. A common axiom among clinicians designed to combat this bias is as follows:

> In general, an atypical presentation of a common disease is a more likely explanation for a patient's presentation than a typical presentation of a rare disease.

Debiasing Strategy

Debiasing strategies are conscious, deliberate techniques used to limit the impact of cognitive bias on diagnostic reasoning. They can include:

- A "Diagnostic Timeout" – Before ruling in a diagnosis, ask "what else could this be?", irrespective of how obvious the leading diagnosis appears. Also, closely examine any feature of the presentation that is not easily explainable by the leading diagnosis.
- Ask a colleague for a second opinion
- Metacognition – Reading and thinking about cognitive bias *may* decrease its effect.