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HANDOUTS

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PROACTIVE MEDICINE IN A REACTIVE WORLD

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Managing Chronic Pain in the Substance Use Disorder Patient: Theory & Practice

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Learning Objectives

- Differentiate addiction from chronic pain and physical dependence
- Identify appropriate medical and psychosocial treatment options for comorbid addiction along with pain
- Describe strategies for counseling patients regarding addiction and linkage to specialist treatment

About Me

- Triple-boarded in anesthesiology, pain medicine, and addiction medicine

- I run a super-specialty multidisciplinary pain clinic for veterans on high-dose opioids or with comorbid SUD issues

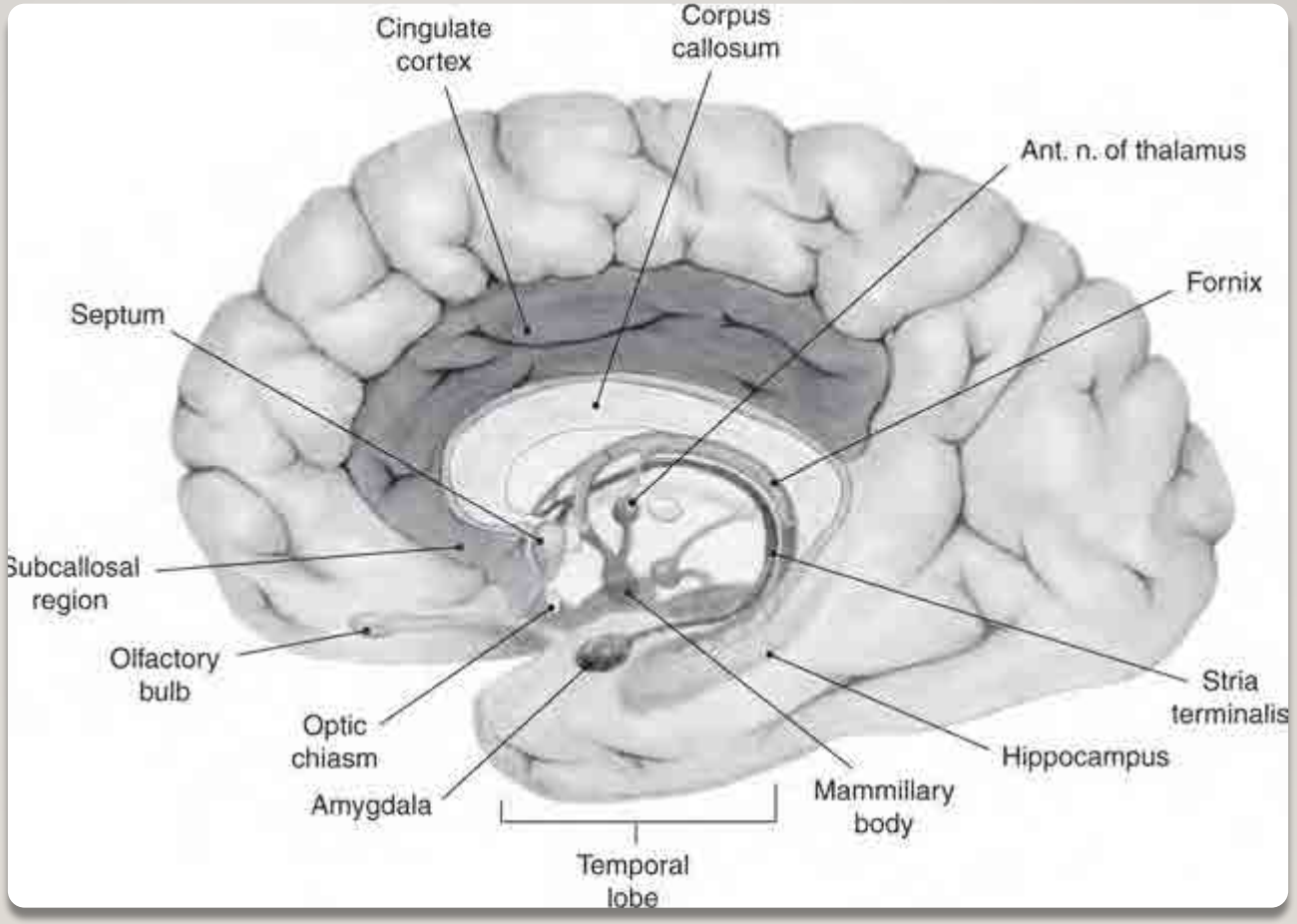
- This lecture is a combination of evidence-based practice, common sense, and good old-fashioned hard knocks of clinical practice

So how exactly does addiction happen?

Authors

Neurobiology I: Limbic System

- Emotion
- Behavior
- Memory
- Long-term motivation



From Herron A et al (2015) *The ASAM Essentials of Addiction Medicine: Second Edition.* New York, New York: LWW.

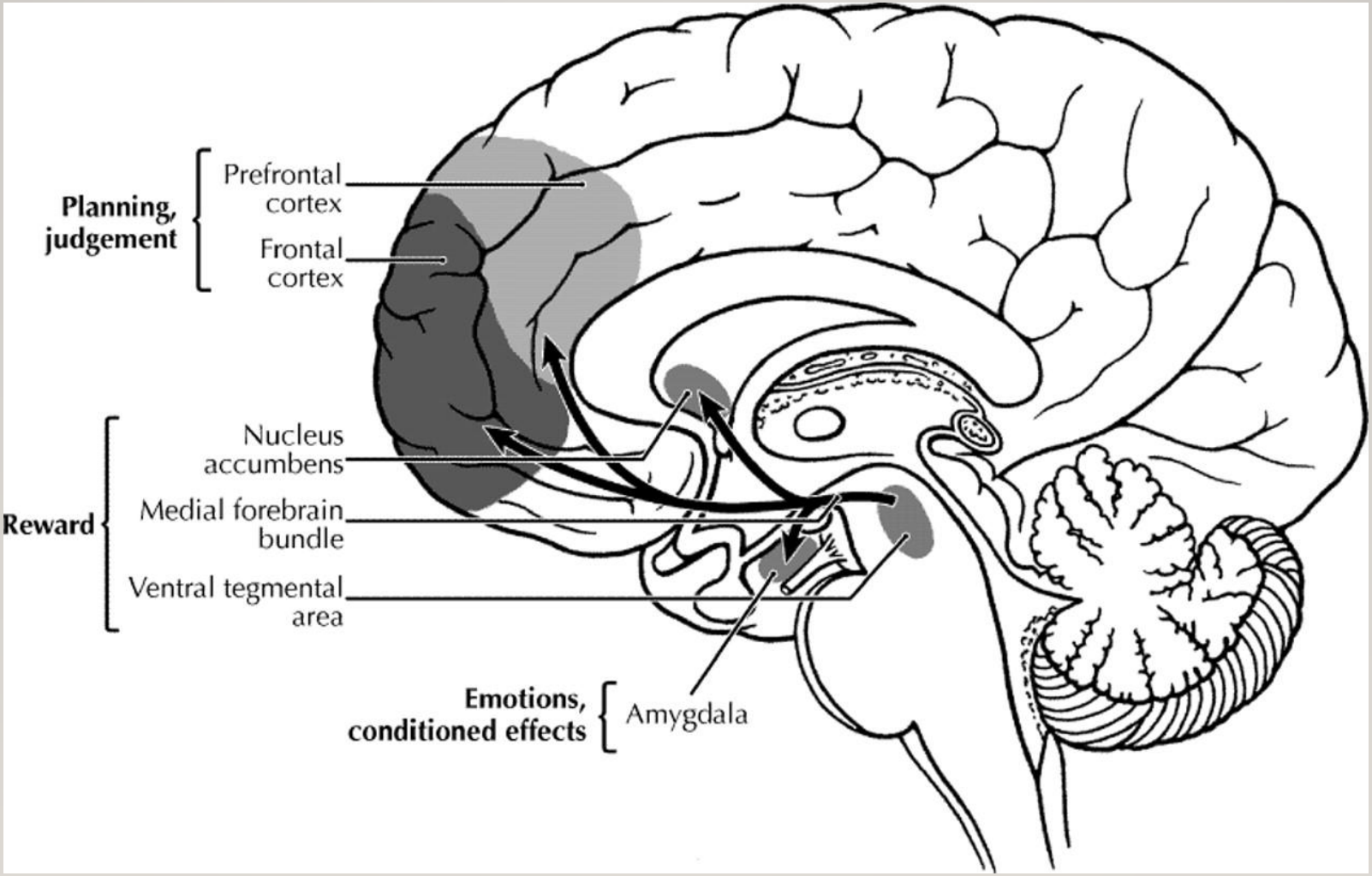
NB II: Mesolimbic i.e. "Reward" Pathway

- Ventral tegmental area (VTA) **__**dopaminergic__, GABAergic, glutamatergic

- VTA connects to:
  - **__Nucleus accumbens__** (reinforcement and reward for motor learning)
  - **__Prefrontal cortex__** (higher-order processing e.g. planning/executive functioning)

- Release of dopamine into NAcc regulates motivation and desire for stimuli and causes reinforcement and reward for motor learning

- Release of dopamine into PFC affects executive functioning (substances)


Planning, judgement
Prefrontal cortex
Frontal cortex
Reward
Nucleus accumbens
Medial forebrain bundle
Ventral tegmental area
Emotions, conditioned effects
Amygdala

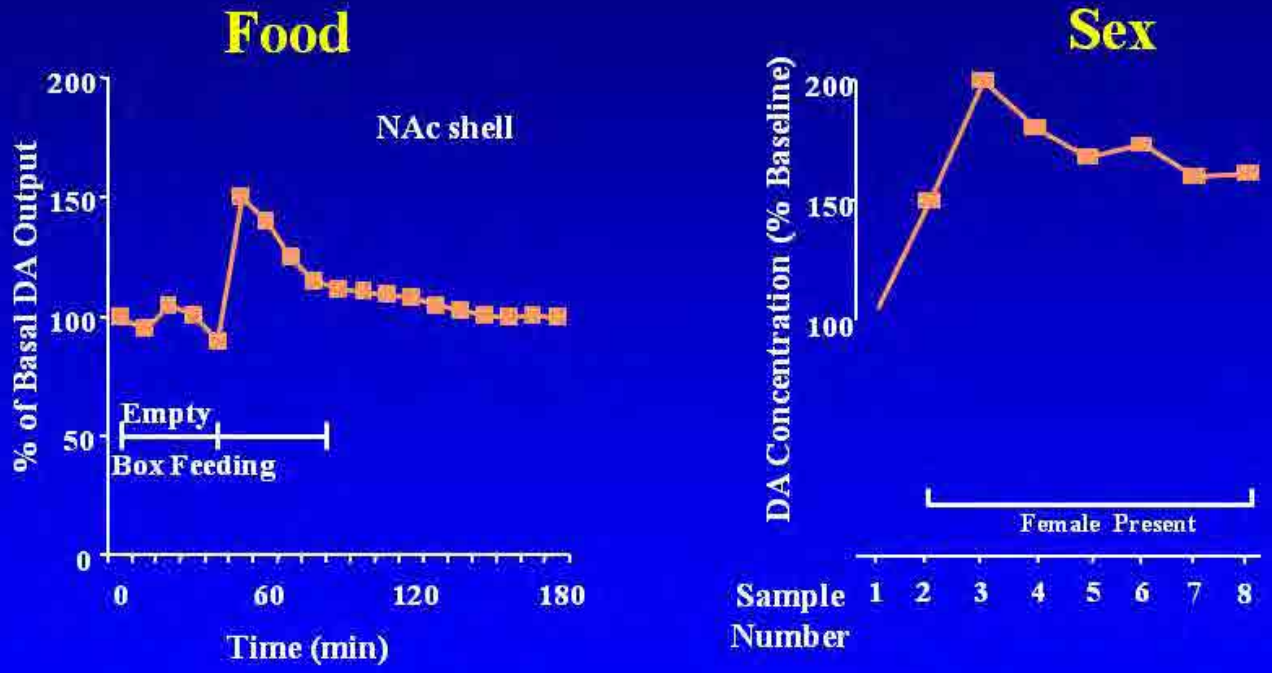
Dopamine: the "pleasure" neurotransmitter

- Released when we eat, drink, sleep, have sex, etc. (life-sustaining activities)

- **Drugs of abuse cause release of dopamine in much higher concentrations**, so regular life-sustaining activities don't provide as much euphoria

- This results in corruption of the reward pathway

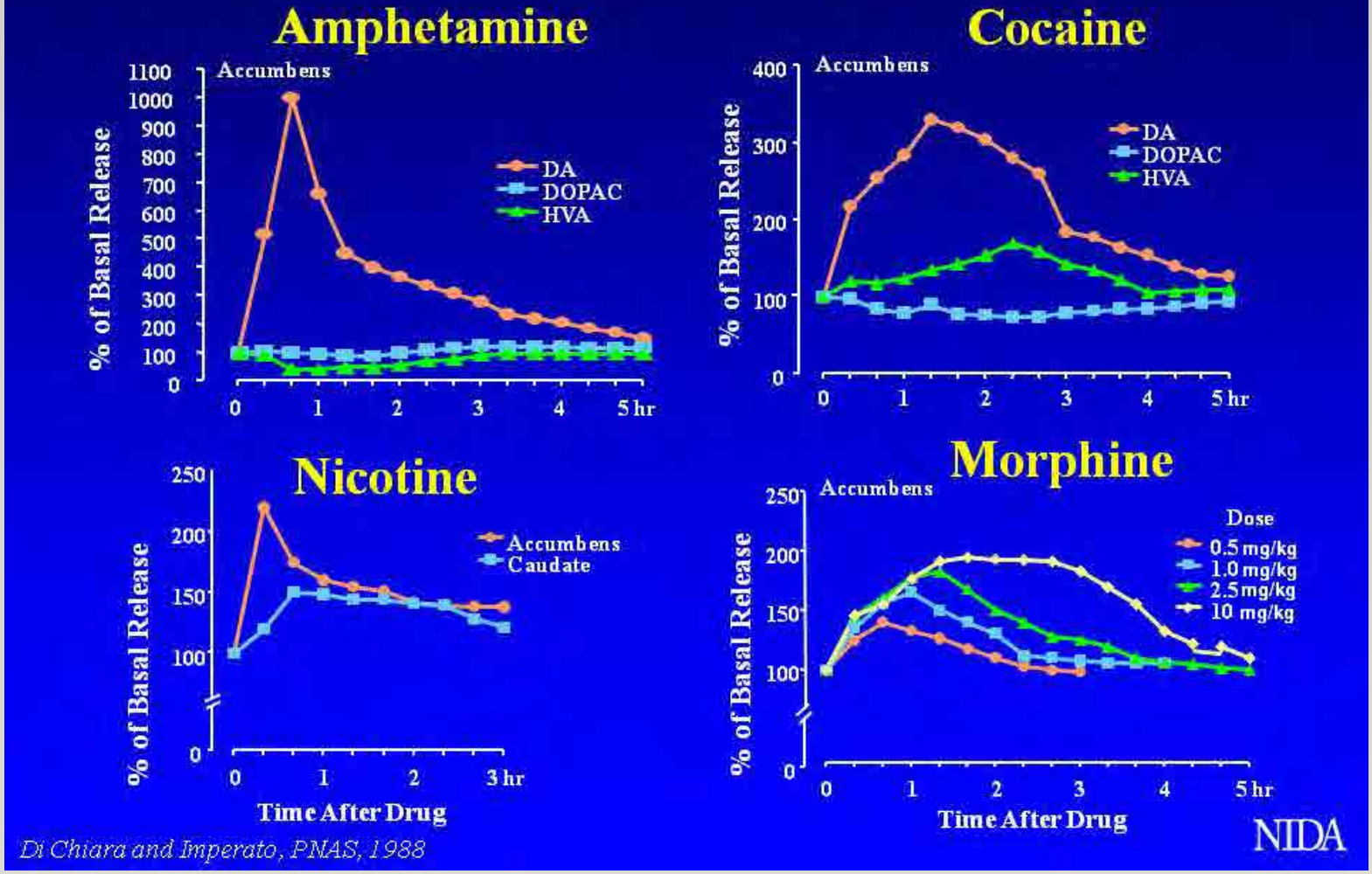
Natural Rewards Elevate Dopamine Levels



Di Chiara et al., Neuroscience, 1999., Fiorino and Phillips, J. Neuroscience, 1997.

NIDA

Effects of Drugs on Dopamine Release



Di Chiara and Imperato, PNAS, 1988

So what causes addiction in some but not others?

Genetic Factors

Responsible for **40-60%** of vulnerability to addiction

Environmental Associations

Low socioeconomic status

Poor parental support

Within-group peer deviance

Physical/psychological abuse

Unmarried status

Low level of education

Unemployed

Caucasian

Drug exposure

Mental Illness

30% of people with psychiatric diagnoses abuse drugs

- 25% EtOH
- 40% nicotine
- 15% other drugs

DSM-V: Substance Use Disorder (2013)

- 11 total criteria summarized by four categories:
  - **Impaired Control**: a craving or strong urge to use the substance; desire or failed attempts to cut down or control substance use
  - **Social problems**: substance use causes failure to complete major tasks at work, school, or home; social, work, or leisure activities are given up or cut back because of substance use
  - **Risky use**: use in risky settings; continued use despite known problems
  - **Pharmacologic effects**: tolerance and withdrawal symptoms
- Categorized as mild (2-3 criteria), moderate (4-5), or severe (>=6 criteria)
- Alcohol, cocaine, opioid, methamphetamine, benzodiazepine, etc. (includes gambling)

Loss of Control		
1	Substance taken in larger amounts or for a longer time than intended	"I didn't mean to start using so much."
2	Persistent desire or unsuccessful effort to cut down or control use of a substance	**"I've tried to stop a few times before, but I start using this drug again every time."**
3	Great deal of time spent obtaining, using, or recovering from substance use	"Everything I do revolves around using this drug." (In severe cases, most/all of a person's daily activities may revolve around substance use.)
4	Craving (a strong desire or urge) to use opioids	**"I wanted to use so badly, I couldn't think of anything thing else."**
Social Problems		
5	Continued opioid use that causes failures to fulfill major obligations at work, school, or home	**"I keep having trouble at work/ have lost the trust of friends and family because of using this drug."**
6	Continued opioid use despite causing recurrent social or personal problems	**"I can't stop using, even though it's causing problems with my friends/family/boss/landlord."**
7	Important social, occupational, or recreational activities are reduced because of opioid use	"I've stopped seeing my friends and family, and have given up my favorite hobby because of drugs."
Risky Use		
8	Recurrent opioid use in dangerous situations	"I keep doing things that I know are risky and dangerous to buy or use this drug."
9	Continued opioid use despite related physical or psychological problems	**"I know that using this drug causes me to feel badly/ messes with my mind, but I still use anyway."**
Pharmacological Problems		
10	**Tolerance** (the need to take higher doses of a drug to feel the same effects, or a reduced effect from the same amount)	"I have to take more and more of the drug to feel the same high."
11	**Withdrawal** (the experience of pain or other uncomfortable symptoms in the absence of a drug)	"When I stop using the drug for a while, I'm in a lot of pain."
Source: American Psychiatric Association. (2013). Substance Use Disorders. In *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.		

Behaviors more suggestive of POUD

Deterioration in function (work, social)

Illegal activities (selling medication, forging prescriptions, buying from non-medical sources)

Altering the route of administration (snorting, injecting)

Multiple episodes of ‘lost’ or ‘stolen’ prescriptions

Resistance to change therapy despite negative outcomes

Refusal to comply with toxicology testing

Concurrent, active abuse of alcohol, illegal drugs

Use of multiple physicians or pharmacies to obtain the prescription

Behaviors less suggestive of POUD

Medication hoarding

Requesting specific pain medications

Openly acquiring similar medications from other providers

Occasional unsanctioned dose escalation

Nonadherence to other recommendations for pain therapy

Miller et al. Prescription opioid use disorder: a complex clinical challenge. *Current Psychiatry*, 2012 August;11(8):14-22.

So how do you treat addiction?

Non-pharmacologic therapies for SUDs

From Herron A et al (2015) *The ASAM Essentials of Addiction Medicine: Second Edition*. New York, New York: LWW.

Pharmacologic treatment of SUDs

- **Alcohol**
  - •Disulfiram
  - •Acamprosate
  - •Naltrexone/nalmefene
  - •Topiramate/gabapentin may help
- **Opioids**
  - •Buprenorphine
  - •Methadone
  - •Naltrexone
- Benzodiazepines
  - •Carbamazepine for w/d
  - •Flumazenil for intoxication
- Stimulants
  - •No FDA-approved agents
  - •TCAs may help
- **Tobacco**
  - •NRT
  - •Varenicline
  - •Bupropion
  - •Nortriptyline
- Cannabinoids
  - •No FDA-approved agents
  - •Rimonabant (CB1 antagonist)

Complex persistent opioid dependence (CPOD)

- Somewhere between physiologic opioid dependence and OUD, coined by Manhapra and Ballantyne (no DSM or ICD code)

- CPOD is characterized by:
  - Poor pain control
  - Aberrant behaviors
  - Declining function
  - Medical/psychiatric instability
  - Difficulty tolerating opioid tapers (severe loss of function)

- "Although OUD commonly develops through the hedonic use of opioids, illicitly and/or via prescriptive pain treatment, **CPOD distinctly starts and persists within a therapeutic context of pain treatment** where LTOT is initiated and continued as a therapeutic strategy through shared decisions by the patient/provider dyad."

- Some patients benefit with buprenorphine

Manhapra et al. J Gen Intern Med 35(Suppl 3): S964-S71.

LETTER TO THE EDITOR

BUPRENORPHINE: NOT A SILVER BULLET, AND STILL CONTROVERSIAL

Utilizing buprenorphine in treating OUD has saved lives. While buprenorphine may have an improved side effect profile compared to other opioids, and while the liability related to prescribing it for pain may be somewhat lower versus other opioids, it is our firm belief that buprenorphine should not replace all full opioid agonist medications or be a first-line treatment strategy. As with any other clinical situation, the risks and benefits of all therapies should be considered. Multimodal pain care must be individualized and a plan discussed collaboratively with the patient and interdisciplinary team.

We applaud the pain community for its increasing awareness of substance use disorders within our patient population and commitment to address the issue more effectively. We must also exercise caution and remember that buprenorphine, while an excellent treatment modality for appropriate patients and clinical scenarios, is ultimately just a medication—not a panacea.

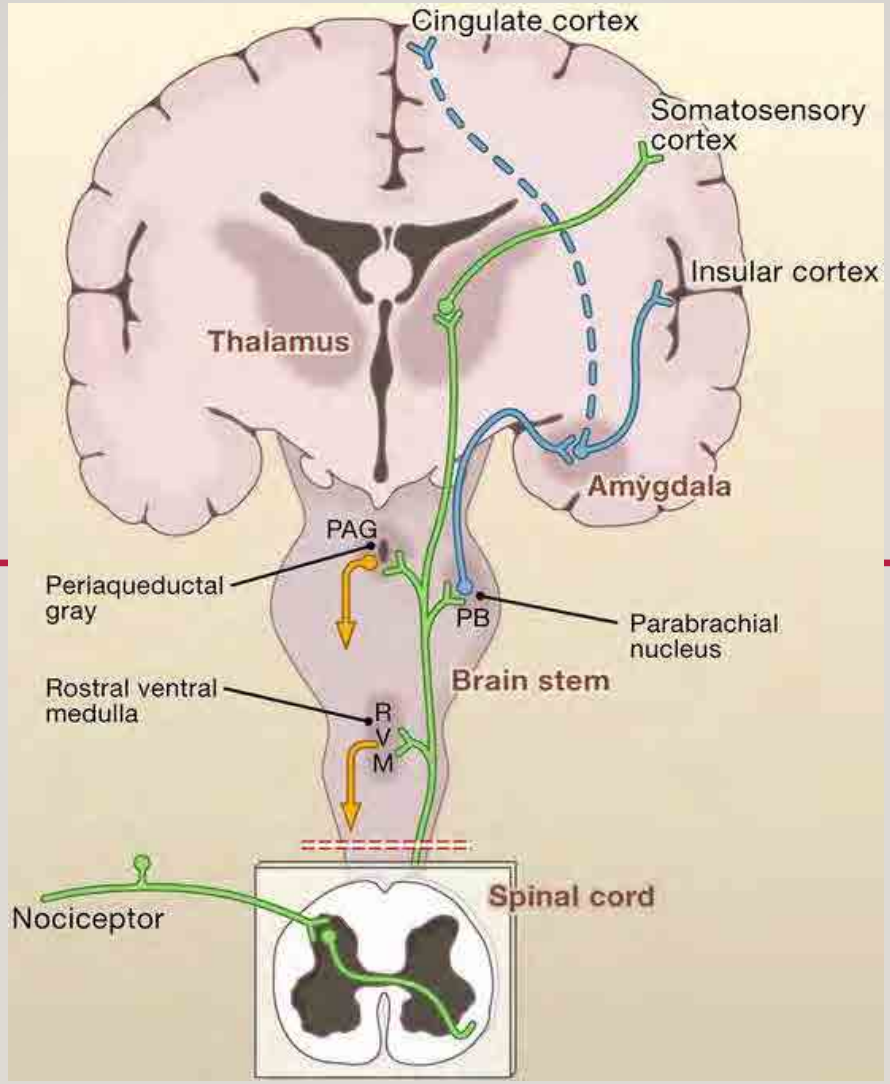
Potru et al. Journal of Opioid Management (2021)

Opioid Risk Tool (ORT)

Mark each box that applies	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Rx drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Rx drugs	5	5
Age between 16—45 years	1	1
History of preadolescent sexual abuse	3	0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	2	2
Depression	1	1
Scoring totals		

Webster LR, Webster R. Predicting aberrant behaviors in Opioid-treated patients: preliminary validation of the Opioid risk too. Pain Med. 2005; 6 (6) : 432

Pain Pathway (simplified)



Chen, Jun et al. (2013). Pain. 10.1007/978-1-4614-1997-6_32.

Mental Health, Pain, and Addiction

- My clinical experience is that, often, the highest opioid doses end up going to those with history of physical or emotional trauma (stated or unstated) □ **ORT!!!**

- > 50% of the opioids in the U.S. go to those with mental health disorders (16%)

- Treating physical pain, emotional suffering, or both?

- Manifestation of trauma as centralized pain syndromes (fibromyalgia, IBS, migraine, etc)

- Possible mechanisms:
  - Amygdala?
  - Glial cell activation?

Davis MA, Lin LA, Liu H, Sites BD. Prescription Opioid Use among Adults with Mental Health Disorders in the United States. J Am Board Fam Med. 2017 Jul-Aug;30(4):407-417. doi: 10.3122/jabfm.2017.04.170112. PMID: 28720623.

So how do I approach the patient with SUD and chronic pain clinically?

Big Question: do you want this patient in your clinic or not?

Everything starts from that!

American Society of Addiction Medicine: Definition of Addiction (2011)

- "Addiction is a **primary, ***chronic disease*** of brain reward, motivation, memory and related circuitry**. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

- Addiction is **characterized by** inability to consistently abstain, **impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission**. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death."

From Herron A et al (2015) *The ASAM Essentials of Addiction Medicine: Second Edition.* New York, New York: LWW.

Clinical Evaluation

- If long-term sobriety:
  - Will admit to issues in the past: "I don't want medications"
  - Will repeatedly ask if certain treatments are habit-forming
  - Will ask if treatments are likely to affect their mood
- If undiagnosed:
  - None of the above
  - Will perseverate on getting psychoactive medications
- If short-term sobriety, who knows
- Just remember that there are permanent brain changes that take **years** to change in some instances

Clinical Evaluation (cont)

- Disguise your addiction evaluation as a pain evaluation
  - Start by asking how long ago they started using pain medications
  - Ask in detail how they use their medications
  - Do they run out early often? Do they have withdrawal?
  - Some OUD patients will complain of compulsions to be "out of pain"
  - "Pseudoaddiction" – oy, don't get me started on Purdue Pharma

- Generate genuine empathy by imagining a close family member sitting in the exam room with you, dealing with both pain and addiction

- Frame everything in the context of safety, e.g. "I don't want anything bad to happen to you"

- Chronic pain patients with substance use disorders will have pain flares/exacerbations
  - Treat them appropriately
  - **Uncontrolled pain is a factor for relapse!!**
  - **SUD patients resemble opioid-TOLERANT they need MORE, not less**

Clinical Evaluation (continued) – Red Flags

- With an unexpected test result, it's time to (gently) ask more questions
- If you're unsatisfied with the answer or if it's inconsistent with objective findings (PDMP, UDS, random pill count, etc), it's time to ask more questions
- When someone says "the medication relaxes me" or "I take it and then I can finally go to sleep", it's time to ask more questions
- You may discover SUD, CPOD, or some underlying mental health issue
  - If so, it's time to refer to a specialist or start buprenorphine if OUD/CPOD

Treatment Considerations

- Think about a buprenorphine patch to bridge these patients if you don't want to give C-II medications
    - Virtually impossible to overdose, except with significant amounts of CNS depressants etc also
    - Maybe somewhat protective, although receptor occupancy likely too low
- Assume fentanyl products are in **all** pills from non-medical sources
    - This is a big problem with stimulants (pts opioid-naïve)

Buprenorphine Receptor Availability

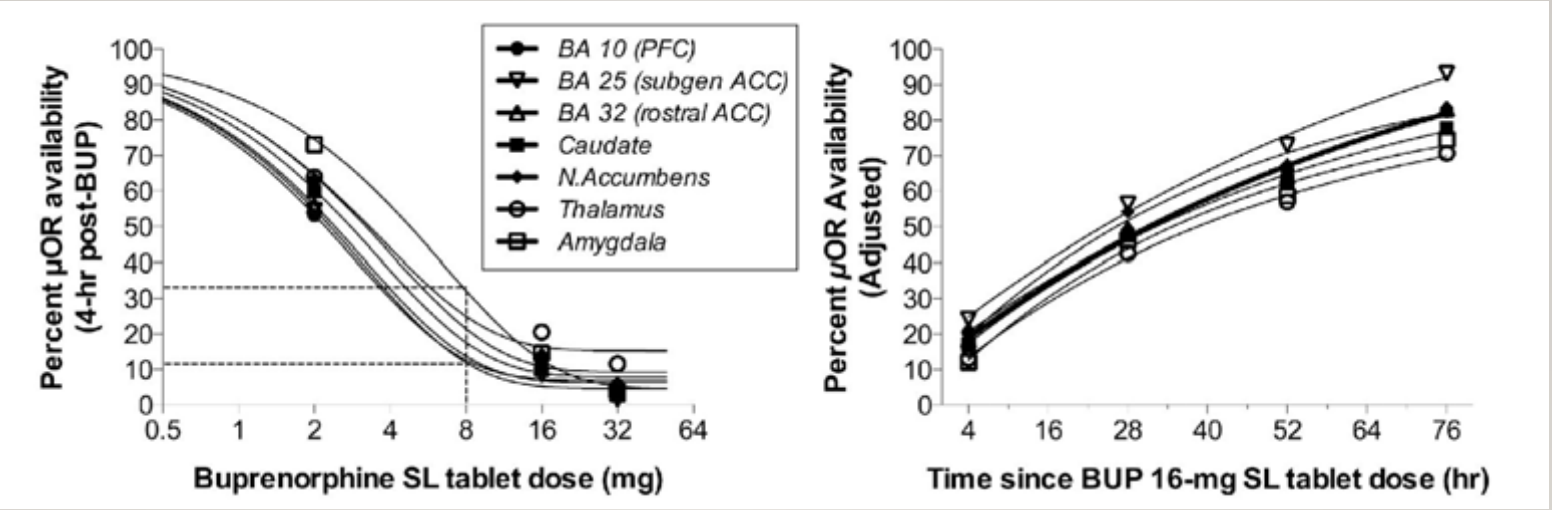


Table 1
Estimated percentages of mu-opioid receptor availability at different times following daily sublingual tablet buprenorphine (BUP) maintenance doses in heroin dependent volunteers.

Study details	1 mg (%)	2 mg (%)	4 mg (%)	8 mg (%)	12 mg (%)	16 mg (%)	24 mg (%)	32 mg (%)
Comer et al. (2005)*: $n = 7$ heroin vs. $n = 8$ controls; maintenance for 14 days at each dose, with tests at 15 h post-BUP/NAL		21–31		11–22				6–12
Greenwald et al. (2003)*: $n = 5$; maintenance for 12 days at each dose, with tests at 4 h post-BUP	71–85	53–72	36–55	20–35	13–24	9–20	4–15	2–12
Greenwald et al. (2007)*: $n = 10$; maintenance for 14 days minimum, with tests at: 4 h post-BUP 28 h post-BUP 52 h post-BUP 76 h post-BUP						27–31 54–61 65–75 77–94		

Greenwald MK, Comer SD, Fiellin DA. Buprenorphine maintenance and mu-opioid receptor availability in the treatment of opioid use disorder: implications for clinical use and policy. *Drug Alcohol Depend.* 2014;144:1–11. doi:10.1016/j.drugalcdep.2014.07.035

So let's say the patient might have some sort of SUD…how do I have the conversation?

Authors

How to talk to the SUD patient

- Avoid stigma/judgment and frame everything in the context of safety
- If you want to keep them: "I really want to help treat your pain, but I also need some help ensuring that what I'm going to do is safe for you."
- OR, if you'd prefer not to keep them, "Honestly, it's a little dangerous for me to care for you with the tools I have at my disposal. It's time for us to find you some real help."
- "When we've resolved/improved the other things going on in your life, we'll have you come back." **DO NOT DISCHARGE, ALWAYS HAVE THEM "FOLLOW-UP PRN"**
- Also, remember that **not prescribing opioids is not the same as discharge**!!

Let's talk a little bit more about buprenorphine…

Authors

Buprenorphine Formulations

Formulation	Indication	Strengths	Frequency	Nalox
Sublingual tablet (generic)	Opioid dependence	2 mg; 8 mg	Once daily	N
Sublingual tablet, film (generic, Suboxone)	Opioid dependence	2 mg/0.5 mg; 4 mg/1 mg; 8 mg/2 mg; 12 mg/3 mg	Once daily	Y
Sublingual tablet (Zubsolv)	Opioid dependence	0.7 mg/0.18 mg; 1.4 mg/0.36mg 2.9 mg/0.71 mg; 5.7 mg/1.4 mg; 8.6 mg/2.1 mg; 11.4 mg/2.9 mg	Once daily	Y
Buccal film (Bunavail)	Opioid dependence	2.1 mg/0.3 mg; 4.2 mg/0.7 mg; 6.3 mg/1 mg	Once daily	Y
Buccal film (Belbuca)	Chronic pain	75 mcg; 150 mcg; 300 mcg; 450 mcg; 600 mcg; 750 mcg; 900 mcg	Every 12 hours	N
Intravenous (Buprenex)	Acute pain	0.3 mg/mL	Every 6 hours as needed	N
Subcutaneous extended release injection (Sublocade)	Moderate-to-severe opioid use disorder	100 mg/0.5 mL; 300 mg/1.5 mL	Monthly	N
Transdermal patch (Butrans)	Chronic pain	5 mcg/hr; 7.5 mcg/hr; 10 mcg/hr; 15 mcg/hr; 20 mcg/hr	Every 7 days	N

Warner NS, Warner MA, Cunningham JL, et al. A Practical Approach for the Management of the Mixed Opioid Agonist-Antagonist Buprenorphine During Acute Pain and Surgery. *Mayo Clin Proc.* 2020;95(6):1253-1267.

Conversion to Buprenorphine (Webster)

For patients taking doses below the following amounts (~≤90 MME):

- Fentanyl transdermal: ≤25 μg/h
- Oxycodone: ≤60 mg/d
- Hydrocodone or morphine: ≤90 mg/d
- Hydromorphone: ≤16 mg/d
- Oxymorphone: <45 mg/d
- Tapentadol: Any dose

1. Discontinue after the last nighttime dose.
2. Consider initiating an adrenergic α_2 agonist (e.g., clonidine, lofexidine) or an immediate-release opioid (e.g., current opioid) to reduce the risk of withdrawal.
3. Initiate buprenorphine the following morning per the prescribing information, as either 10-μg/h transdermal buprenorphine or 150-μg buccal buprenorphine twice daily. Titrate buprenorphine as needed for pain per recommendations in the prescribing information.

In patients transitioning to buprenorphine from higher doses of opioids (~>90 MME):

- Fentanyl transdermal: >25 μg/h
- Oxycodone: >60 mg/d
- Hydrocodone or morphine: >90 mg/d
- Hydromorphone: >16 mg/d
- Oxymorphone: >45 mg/d

1. Discontinue after the last nighttime dose.
2. Consider initiating an adrenergic α_2 agonist (e.g., clonidine, lofexidine) or an immediate-release opioid (e.g., current opioid) to reduce the risk of withdrawal.
3. Initiate buprenorphine the following morning as either 20-μg/h transdermal buprenorphine once daily or 300-μg buccal buprenorphine twice daily and follow the recommendations in the prescribing information for upward titration as needed. Note that 20 μg/h is the highest dose of transdermal buprenorphine currently available in the United States. If these doses are ineffective, consider higher doses of the buccal formulation on the basis of risk/benefit analysis.

Short-acting opioids have been suggested to prevent withdrawal during the switch to buprenorphine [77].

Pain Medicine, 21(4), 2020, 714–723
doi: 10.1093/pm/pnz356

Is buprenorphine effective for chronic pain?

Webster et al – buprenorphine provides good analgesia

In some clinical settings, buprenorphine had similar or greater analgesic efficacy and antihyperalgesic effects as full μ-opioid receptor agonists [14,29–32]. Intravenous (IV) buprenorphine was as efficacious as or more efficacious than IV morphine in producing analgesia across various surgical models [14]. The effect size, or correlation between two variables, for change in pain intensity observed in clinical trials of transdermal and buccal buprenorphine vs placebo overlapped with those of several Schedule II opioids across trials of chronic noncancer pain, suggesting similar efficacy [29]. In addition, sublingual buprenorphine was as effective as IV morphine in managing acute renal colic pain [30]. Therefore, the characterization of buprenorphine as a partial μ-opioid receptor agonist does not clinically equate to partial analgesic efficacy.

In response to μ-opioid receptor binding, buprenorphine has been shown to have low intrinsic signaling activity that is sufficient to reach the analgesic threshold, while exhibiting a relative ceiling effect for respiratory depression (Figure 3B) [40–42]. At therapeutic doses, the

Pain Medicine, 21(4), 2020, 714–723
doi: 10.1093/pm/pnz356

Efficacy and tolerability of buccal buprenorphine in opioid-naive patients with moderate to severe chronic low back pain

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Abstract

Objectives: Buprenorphine HCl buccal film has been developed for treating chronic pain utilizing BioErodible MucoAdhesive (BEMA®) delivery technology. Buccal buprenorphine (BBUP; Belbuca™, Endo Pharmaceuticals) was evaluated for the management of moderate to severe chronic low back pain (CLBP) requiring around-the-clock analgesia in a multicenter, double-blind, placebo-controlled, enriched-enrollment, randomized-withdrawal study in opioid-naive patients.

Methods: Patients (n = 749) were titrated to a dose of BBUP (range, 150–450 µg every 12 h) that was generally well tolerated and provided adequate analgesia for ≥14 days, and then randomized to BBUP (n = 229) or placebo (n = 232), respectively. The primary efficacy variable was the change from baseline to week 12 of double-blind treatment in the mean of daily average pain intensity scores (numeric rating scale from 0 [no pain] to 10 [worst pain imaginable]).

Results: Patients were experiencing moderate to severe pain at study entry: mean (SD) = 7.15 (1.05). Following titration, pain was reduced to the mild range; 2.81 (1.07). After randomization, mean (SD) pain scores increased from baseline to week 12 more with placebo (1.59 [2.04]) versus BBUP: (0.94 [1.85]) with a significant between-group difference (−0.67 [95% CI: −1.07 to −0.26]; p = 0.0012). A significantly larger percentage of patients receiving BBUP versus placebo had ≥30% pain reduction (63% vs 47%; p = 0.0012). During double-blind treatment, the most frequent adverse events (AEs) with BBUP were nausea (10%), constipation (4%) and vomiting (4%). The most common AEs with placebo were nausea (7%), upper respiratory tract infection (4%), headache (3%) and diarrhea (3%).

Conclusions: These findings demonstrate the efficacy and tolerability of BBUP among opioid-naive patients requiring around-the-clock opioid treatment for CLBP.

Keywords

Chronic low back pain, Buccal buprenorphine, Opioid-naive patients

History

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Accepted 2 December 2015
Published online 23 December 2015

Rauck RL, Potts J, Xiang Q, Tzanis E, Finn A. Efficacy and tolerability of buccal buprenorphine in opioid-naive patients with moderate to severe chronic low back pain. Postgrad Med. 2016 Jan;128(1):1-11. doi: 10.1080/00325481.2016.1128307. Epub 2015 Dec 22. PMID: 26634956.

Efficacy and tolerability of buccal buprenorphine in opioid-experienced patients with moderate to severe chronic low back pain: results of a phase 3, enriched enrollment, randomized withdrawal study

Joseph Gimbel[a,*], Egilius L.H. Spierings[b], Nathaniel Katz[c,d], Qinfang Xiang[e], Evan Tzanis[f], Andrew Finn[g]

Abstract

A buccal film of buprenorphine (BBUP) was evaluated for safety and efficacy in a multicenter, double-blind, placebo-controlled, enriched-enrollment, randomized-withdrawal study in opioid-experienced patients (30 to ≤160 mg/d morphine sulfate equivalent) with moderate to severe chronic low back pain taking around-the-clock opioid analgesics. Patients' opioid doses were tapered to ≤30 mg morphine sulfate equivalent before open-label titration with BBUP (range, 150-900 μg every 12 hours). Patients who responded (received adequate analgesia that was generally well tolerated for 14 days) were randomized to receive buprenorphine (n = 254) or placebo (n = 257) buccal film. The primary efficacy variable was the change from baseline to week 12 of double-blind treatment in mean average daily pain-intensity scores using a rating scale of 0 (no pain) to 10 (worst pain imaginable). In the intent-to-treat population, mean pain scores were 6.7 after opioid taper and declined to 2.8 after the BBUP titration period. After randomization, mean pain scores were lower in the BBUP group than in the placebo group; the difference between groups in the mean change from baseline to week 12 was −0.98 (95% CI, −1.32 to −0.64; $P < 0.001$). A significantly larger percentage of patients receiving BBUP than placebo had pain reductions ≥30% and ≥50% ($P < 0.001$ for both). In the double-blind portion of the study, the only adverse event reported more frequently with BBUP than placebo and in ≥5% of patients was vomiting (5.5% vs 2.3%). These findings demonstrate the efficacy and tolerability of BBUP in opioid-experienced patients taking around-the-clock opioid treatment for chronic low back pain.

Gimbel J, Spierings ELH, Katz N, Xiang Q, Tzanis E, Finn A. Efficacy and tolerability of buccal buprenorphine in opioid-experienced patients with moderate to severe chronic low back pain: results of a phase 3, enriched enrollment, randomized withdrawal study. Pain. 2016 Nov;157(11):2517-2526. doi: 10.1097/j.pain.0000000000000670.

Treatment of Chronic Pain With Various Buprenorphine Formulations: A Systematic Review of Clinical Studies

Rohit Aiyer, MD,* Amitabh Gulati, MD,† Semih Gungor, MD,‡ Anuj Bhatia, MD,§ and Neel Mehta, MD‖

Table 1. Characteristics of Included Studies That Evaluated Buprenorphine/Naloxone Formulations for Chronic Pain

Reference	Year	Patient Population	Study Duration	N	Route and Dose	Comparator	Scale	Mean/Median Pain Score	Outcome and Results
Neumann et al[9]	2013	Chronic nonmalignant pain related to the spine or a large joint	6 mo	54	Average daily sublingual dose of buprenorphine/naloxone was 14.93 mg/3.73 mg	Oral methadone (20–60 mg, divided 3–4 times daily)	NRS	5.5 ± 1.9 after 6 mo compared to initial visit (6.3 ± 1.2)	There was significant difference in pain relief for both buprenorphine and methadone treatment groups ($P = .043$)

Table 3. Characteristics of Included Studies That Evaluated Buccal Buprenorphine Formulations for Chronic Pain

Reference	Year	Subjects	Study Duration	N	Route and Dose	Comparator	Scale	Mean/Median Pain Score	Outcome and Results
Gimbel et al[36]	2016	Moderate to severe chronic low back pain (nonneuropathic, neuropathic, or symptomatic for >6 mo)	12 wk	491	Buccal strengths of 150, 300, 450, 600, 750, and 900 μg every 24 h	Placebo buccal film	NRS	Placebo group 1.02 ± 1.87) and buprenorphine group 0.88 ± 1.79	There was statistical significant difference favoring buccal buprenorphine ($P < .001$) for pain relief.
Rauck et al[37]	2016	Moderate to severe chronic low back pain (nonneuropathic, neuropathic, or after low back pain surgery)	12 wk	749	Buprenorphine titration began at 75 μg once daily, progressed to 75 μg twice daily, and then to 150, 300, or 450 μg twice daily.	Placebo	NRS	Increase at week 12 from baseline in NRS scores was significantly greater in patients treated with placebo (1.59 ± 2.04) compared with those continuing with buprenorphine (0.94 ± 1.85); the mean treatment difference was −0.67 (95% CI, −1.07 to −0.26)	There was statistical significant difference between the groups ($P = .0012$) in favor of buccal buprenorphine for analgesia.
Webster et al[38]	2016	Chronic pain	7–16 d	39	Buccal 300-μg and 450-μg doses every 12h selected because they represent relative equivalence to 50% of the patients' morphine sulfate equivalent	Morphine sulfate, oxycodone, or placebo	NRS	There was no change from baseline in mean NRS scores through 9h, followed by slight increases from 9 to 12h that declined with the second dose.	There were no significant differences in pain ratings between treatments

Treatment of Chronic Pain With Various Buprenorphine Formulations: A Systematic Review of Clinical Studies

Rohit Aiyer, MD,* Amitabh Gulati, MD,† Semih Gungor, MD,‡ Anuj Bhatia, MD,§ and Neel Mehta, MD‖

Table 2. Characteristics of Included Studies That Evaluated SL and Intravenous Buprenorphine Formulations for Chronic Pain

Reference	Year	Patient Population	Study Duration	N	Route and Dose	Comparator	Scale	Mean/Median Pain Score	Outcome and Results
Ling et al[10]	2012	Patients had lingering noncancer pain	12 d	12	Intravenous 0.3 mg every 24 h	Buprenorphine (0.3 mg)/ naloxone (0.02 mg)	NRS and BPI	6.17 ± 1.57 (baseline for buprenorphine predose) 6.27 ± 1.71 (baseline for buprenorphine + ultra low-dose naloxone) 2.28 ± 1.78 (postdose for buprenorphine group) 2.62 ± 1.82 (postdose for buprenorphine + ultra low-dose naloxone group)	No significant difference between medications in pre- to postdose pain ratings
Jain et al[11]	2011	Forty-five treatment-seeking heroin-dependent males	6 d	45	SL 2 mg	Oral memantine 20 mg/d	VAS	VAS pain scores in the memantine group and the buprenorphine group were (+)10.00 (30–50) and (+)10.00 (−50 to [+]50), respectively	No significant difference between subjects in VAS ($P > .05$)
James et al[12]	2010	Osteoarthritis pain in the hip(s) and/or knee(s)	28 d	110	SL buprenorphine 200 and 400 μg tablets every 24 h	TDS buprenorphine (5, 10, and 20 μg/h)	BS-11	Mean treatment differences (95% confidence intervals) were 0.00 (−0.68 to 0.69), −0.11 (−0.85 to 0.63), and −0.13 (−0.95 to 0.68) for the morning, midday, and evening scores, respectively	There was no significant evidence for a difference in the BS-11 pain scores recorded on day 3 and day 7 for either of the treatment groups. Equivalence was shown for the 2 treatments with respect to BS-11 pain scores
Goebel et al[13]	2008	Chronic pain located in the region of lower face to upper thorax, area covered by dermatomes of the maxillary branch of trigeminal nerve (excluding eyes) to T3	6 d	18	Injection of 27 μg of buprenorphine in 5-mL 0.9% saline to the stellate ganglion (GLOA), and 5-mL normal saline into the buttock (intramuscular)	Reverse saline to the stellate plus intramuscular buprenorphine (SSB)	VAS	All patients had a median preinjection pain intensity of 6.7, before GLOA, and 6.2, before SSB. Five patients had ≤50% pain over 6 d (2 patients after GLOA, 2 patients after SSB, and 1 patient after both injections).	Pain reported over a 6-d period (the median of all pain daily entries within the first 6 d after injection) showed no differences between the groups (GLOA: 104%, SSB: 103%)
Spacek et al[14]	2002	Refractory trigeminal neuralgia	10 d	19	Stellate ganglion injection (GLOA) consisted of verum 0.045 mg buprenorphine in 1.5-mL 0.9% NaCl	Placebo-GLOA of 1.5 mL 0.9% NaCl	VAS	VAS after GLOA first week Verum-GLOA group: 2.4 ± 2.3 0.9% NaCl group: 2.7 ± 2.0	There was a significant difference in pain relief in both verum GLOA and placebo-GLOA interventions after the first week ($P < .001$)
Ehrna et al[15]	1996	Cancer pain	Up to 6 mo	131	Buprenorphine SL 0.2 mg every 6 h to every 8 h	Tramadol 100 mg every 8 h to every 12 h	VAS	Posttreatment scores: tramadol, 6.09 ± 2.78; buprenorphine, 4.74 ± 2.60	Analgesia significantly better in the tramadol group ($P < .05$)

Treatment of Chronic Pain With Various Buprenorphine Formulations: A Systematic Review of Clinical Studies

Rohit Aiyer, MD,* Amitabh Gulati, MD,† Semih Gungor, MD,‡ Anuj Bhatia, MD,§ and Neel Mehta, MD‖

Of the 25 studies reviewed, a total of 14 studies demonstrated clinically significant benefit with buprenorphine in the management of chronic pain:

- **1 study out of 6 sublingual and intravenous buprenorphine,**
- **the only sublingual buprenorphine/naloxone study,**
- **2 out of 3 studies of buccal buprenorphine, and**
- **10 out of 15 studies for transdermal buprenorphine showed significant reduction in pain against a comparator.**

No serious adverse effects were reported in any of the studies. We conclude that a transdermal buprenorphine formulation is an effective analgesic in patients with chronic pain, while buccal buprenorphine is also a promising formulation based on the limited number of studies.

Analgesic Effect of Buprenorphine for Chronic Noncancer Pain: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Stanley Sau Ching Wong, MD,*† Tak Hon Chan, NA,* Fengfeng Wang, PhD,*† Timmy Chi Wing Chan, MBBS,* Hung Chak Ho, PhD,*† and Chi Wai Cheung, MD*†

There is a relative paucity of literature on buprenorphine, especially for chronic noncancer pain. As far

CONCLUSIONS: Buprenorphine was associated with a statistically significant and small reduction in pain intensity compared to placebo. Both the transdermal and buccal routes provided pain relief. There was more evidence supporting its use for chronic low back pain. (Anesth Analg 2023;XXX:00–00)

DISCUSSION

In this meta-analysis of randomized controlled trials, buprenorphine was associated with a small reduction in pain intensity compared to placebo for chronic noncancer pain. Meta-analysis of 4 clinical trials versus active treatment showed no difference in analgesia. Both the transdermal and buccal route of administration provided statistically significant pain reduction, with no difference in analgesic effect between the 2 routes when analyzed using meta-regression. Chronic low back pain was the most commonly studied chronic pain condition. Buprenorphine produced a statistically significant and small reduction in pain intensity for chronic low back pain. It was also associated with large and small effect size reduction in pain intensity for studies with <12 weeks and those with >12 weeks of follow-up, respectively. Use of buprenorphine was associated with a higher incidence of adverse events, which were mostly mild to moderate. The incidence of serious adverse effects was rare, and not more frequent than placebo. Furthermore, buprenorphine was also associated with better sleep quality and higher patient rating for clinical treatment effectiveness. This was the first meta-analysis to quantitatively demonstrate the analgesic efficacy of buprenorphine versus placebo or

Conversion of Chronic Pain Patients from Full-Opioid Agonists to Sublingual Buprenorphine

Jonathan Daitch, MD, Michael Frey, MD, David Silver, PharmD, Carol Mitnick, ARNP, Danielle Daitch, BA, and Joseph Pergolizzi Jr., MD

Results: After initiation of buprenorphine SL therapy for more than 2 months, the mean pain scores on a scale from 0-10 decreased by 2.3 points ($P < 0.001$). Patient Quality of Life (QoL scale) was not significantly affected by buprenorphine SL therapy ($P = 0.14$). The success rate was highest for patients using morphine, oxycodone, and fentanyl before buprenorphine SL induction. These patient groups had a 3.7 point decrease in pain for those taking morphine, a 2.5 point decrease in pain for those taking oxycodone, and a 2.2 point decrease for those taking fentanyl. The smallest pain reduction was seen in the patient group using oxymorphone before conversion with a 1.1 point decrease in pain. Patients taking between 100-199 mg morphine equivalent per day experienced the greatest reduction (2.7 points) in pain scores. Patients taking between 200 and 299 mg morphine equivalent before buprenorphine SL induction exhibited a decrease of over 2 points on average. Patients taking > 400mg morphine equivalent reported the smallest reduction in pain scores, on average a 1.1 point decrease.

Pain Physician 2012; 15:ES59-ES66 • ISSN 2150-1149

Take Home Points

Addiction is a terrible neurobiological disease and not a "moral failing" – be compassionate

Always frame every discussion in the context of safety

Remember that uncontrolled pain is a risk for relapse

Think about prescribing buprenorphine for pain or OUD yourself. Very safe and often very effective for analgesia

Should we be using bup over full opioid agonists? Jury's still out.

If you are interested in difficult conversations…

Sudheer Potru, DO, FASA, FASAM

Anesthesiologist | Pain Physician | Addictionologist | Expert Witness | Researcher | Educator | Advocate

Screening & Treatment of Alcohol Use Disorders in Non-Specialty Healthcare Settings

Yilang Tang, MD, PhD

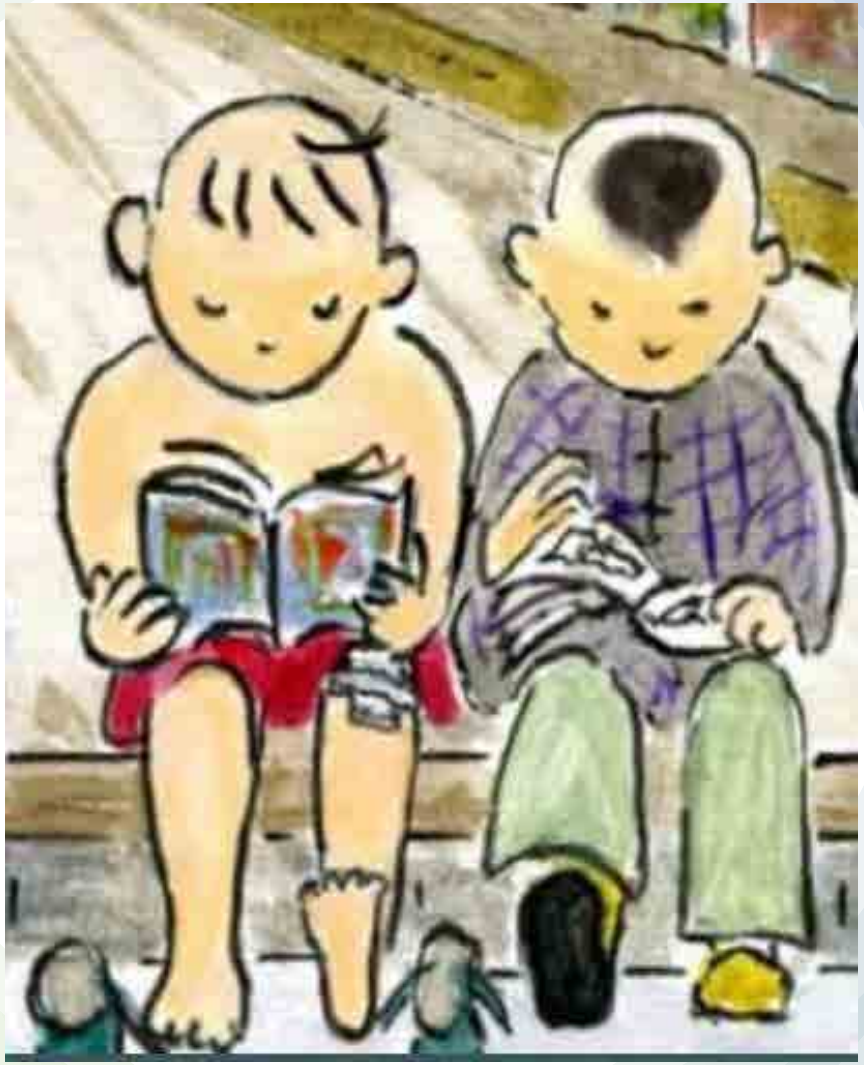
Department of Psychiatry and Behavioral Sciences

Emory University

Oct 24, 2024

SMA Annual Scientific Assembly

About Me



- I am a psychiatrist, ABPN board certified in both general and addiction psychiatry
- Completed medical training and first psychiatry residency training in Beijing, China
- Has practiced in both China and the United States
- Has conducted clinical and translational research
- Teach medical students, residents and fellows

Disclosure

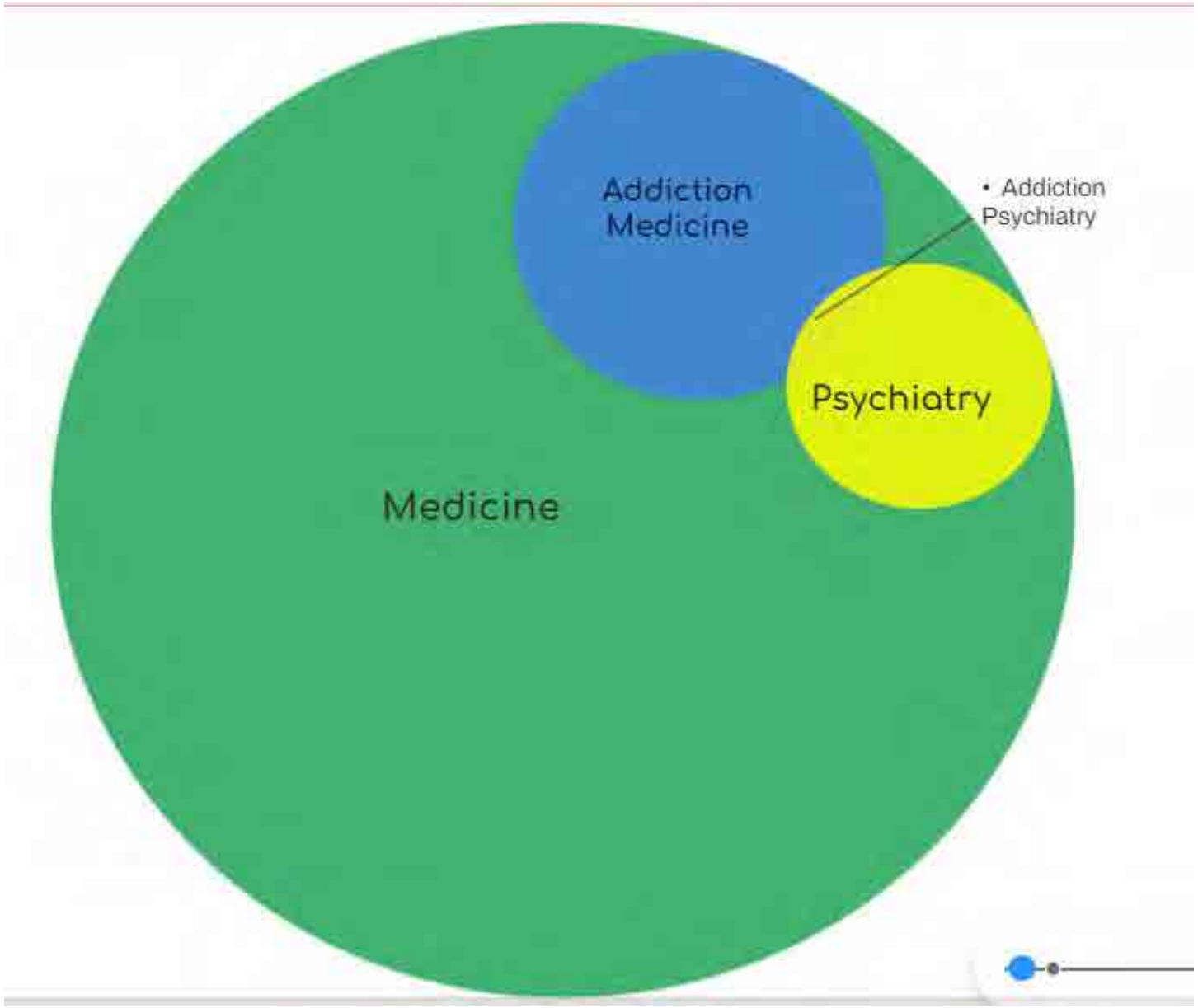
Dr. Tang has received grant support from the Veterans Administration for clinical trials

No Off-label use of medications is Discussed

A Few Important Definitions (NIAAA)

- **Binge Drinking:** a pattern of drinking alcohol that brings BAC to 0.08% or higher
- **Heavy Alcohol Use:** ≥ 5 drinks on any day or 15 or more per week for men, ≥ 4 drinks on any day or 8 for women
- **Alcohol Misuse:** Includes binge drinking and heavy alcohol use. Drinking in a manner, situation, amount, or frequency that could cause harm to the person who drinks or to those around them.
- **Alcohol-Related Disorders:** includes AUD, alcohol-induced disorders. Not a specific diagnosis but rather an umbrella term.
- **Alcohol-Induced Disorder**: Specific conditions that are caused by alcohol use.
- **Alcohol use disorder (AUD)** is a medical condition characterized by an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences. It encompasses the conditions that some people refer to as alcohol abuse, alcohol dependence, alcohol addiction, and the colloquial term, alcoholism. AUD can be mild, moderate, or severe.

What Am I talking about when I talk about non-Specialty Settings



Recent Findings on Alcohol and Health

- No Safe Alcohol Level: A significant meta-analysis has concluded that there is no safe level of alcohol use. The study analyzed data on 28 million people worldwide, found that alcohol is associated with 2.8 million deaths each year and is the seventh leading risk factor for premature death [1].
- Alcohol and Cardiovascular Disease: Some debate about the association between moderate alcohol consumption and a reduced risk of cardiovascular disease. However, the potential benefits are contested by evidence that suggests any amount of alcohol increases the risk of many other conditions [3].
- Changing Guidelines: The 2025 Dietary Guidelines for Americans, for example, may change the current advice on drinking due to the emerging evidence against alcohol's health benefits.

1. GBD 2016 Alcohol Collaborators, Lancet 2018
2. Harriet Rumgay et al. Lancet Oncology, 2021
3. Zhao et al. 2023, JAM Network Open,

Moderate Drinking and Health Benefits?

- No longevity benefit: Recent high-quality studies show that moderate drinking (1-14 drinks per week) does not increase lifespan compared to not drinking at all.
- Increased health risks: Even moderate alcohol consumption may raise overall risks of death and chronic diseases like cancer and heart disease compared to abstaining.
- Cancer risk: Low levels of alcohol use (less than 1 drink per day) can increase the risk of certain cancers.
- Flawed past studies: Earlier research suggesting health benefits from moderate drinking often had methodological issues, including:
  - Not accounting for other lifestyle factors like diet and exercise
  - Misclassifying former drinkers as abstainers
  - Focusing on older participants, potentially masking lifetime drinking effects
- No safe level: The WHO states there is no safe amount of alcohol consumption that does not affect health.
- Shifting public health message: Experts are increasingly encouraging alcohol-free lifestyles and urging a change in public health messaging to align with these findings.

CDC, About Moderate Alcohol Use | Alcohol Use | CDC

Outline

- 1. Describe AUD in various medical settings
- 2. Identify and Apply Evidence-Based Screening Tools
- 3. Develop Patient-Centered Intervention Plans
- 4. Enhance Communication Skills for Discussing Alcohol Use

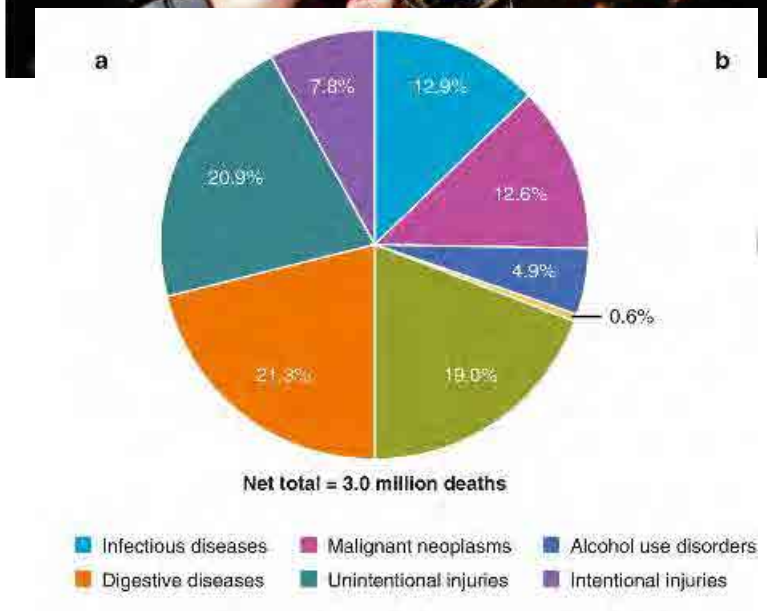
- **Why do we care?**
- **How do we do it?**
- **How do we really do it, step by step?**
- **Can we make a difference?**
- **How do we get paid?**

HEALTH

By the numbers: America's alcohol-related health problems are rising fast

By Isabella Cueto and J. Emory Parker June 27, 2024

Reprints



Deaths by alcohol

Number of deaths per year where underlying cause of death was alcohol-related

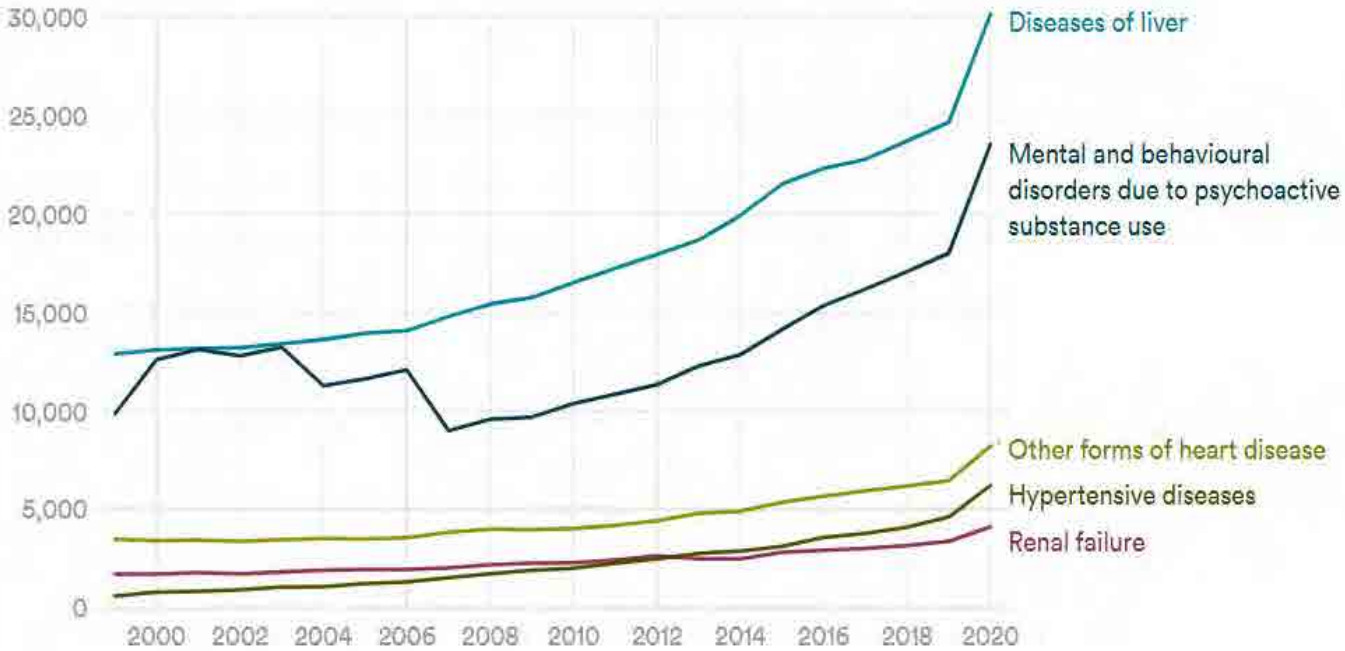


Chart: J. Emory Parker/STAT • Source: CDC WONDER

% of alcohol-attributable deaths (4.9%)

https://www.statnews.com/2024/06/27/alcohol-related-health-problems-rise/

1 in 5 deaths of US adults 20 to 49 is from excessive drinking, study shows

By Madeline Holcombe, CNN

Published 3:56 PM EDT, Tue November 1, 2022

- The estimates in this cross-sectional study of 694 660 mean deaths per year between 2015 and 2019 suggest that excessive alcohol consumption accounted for 12.9% of total deaths among adults aged 20 to 64 years and 20.3% of deaths among adults aged 20 to 49 years.
- An estimated 1 in 8 deaths among adults aged 20 to 64 years were attributable to excessive alcohol use
- 1 in 5 deaths among adults aged 20 to 49 years were attributable to excessive alcohol use.

Esser et al. 2022, JAMA Open Network

JAMA Psychiatry | Original Investigation

Prevalence of 12-Month Alcohol Use, High-Risk Drinking, and *DSM-IV* Alcohol Use Disorder in the United States, 2001-2002 to 2012-2013

Results From the National Epidemiologic Survey on Alcohol and Related Conditions

Bridget F. Grant, PhD; S. Patricia Chou, PhD; Tulshi D. Saha, PhD; Roger P. Pickering, MS; Bradley T. Kerridge, PhD; W. June Ruan, MS; Boji Huang, MD, PhD; Jeesun Jung, PhD; Haitao Zhang, PhD; Amy Fan, PhD; Deborah S. Hasin, PhD

- N= 43 093 participants in the National Epidemiologic Survey on Alcohol and Related Conditions and 36 309 participants in the National Epidemiologic Survey on Alcohol and Related Conditions III.
- Between 2001-2002 and 2012-2013, 12-month high-risk drinking, and *DSM-IV* AUD increased by **29.9%, and 49.4%,** respectively
- *DSM-IV* AUD increased from 8.5%(95%CI, 8.0%-8.9%) to 12.7%(95%CI, 12.1%-13.3%).

Grant et al. 2017

Excessive alcohol use is common and costly

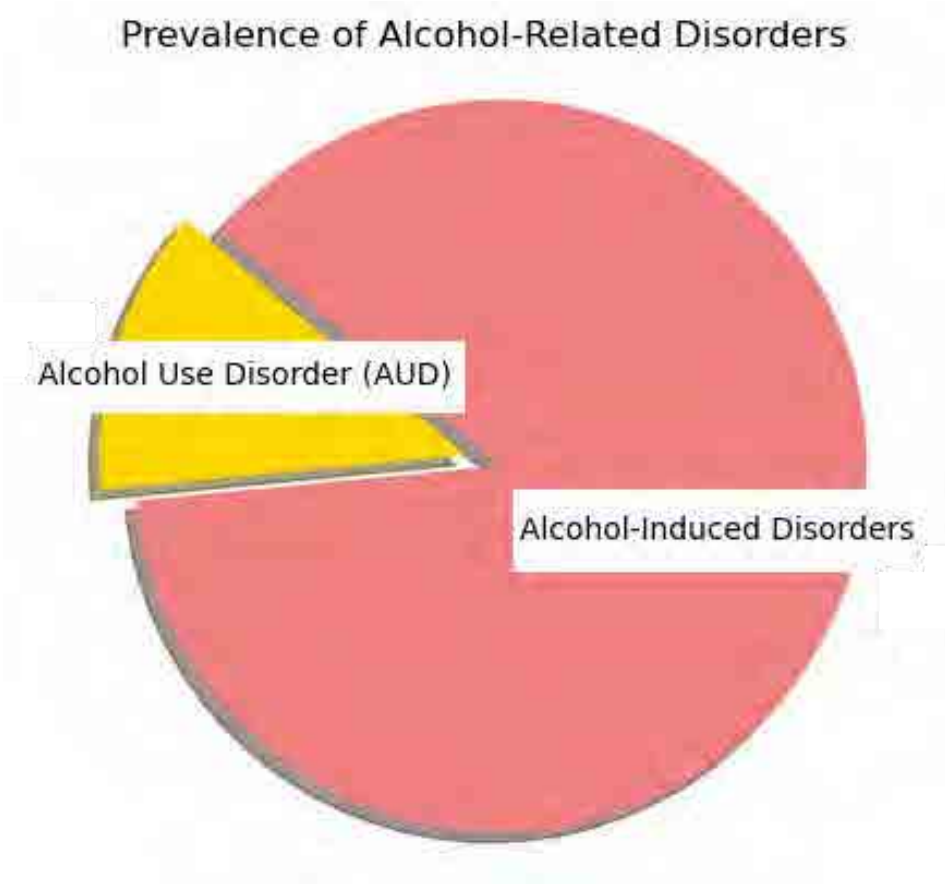
- Binge drinking. More than 37 million American adults binge drink
- Heavy drinking. about 7% of the adult population reported heavy drinking (2018)
- Drinking during pregnancy: nearly 1/7 (14%) pregnant people reported drinking alcohol in the past 30 days
- Costly and fatal. During 2015–2019, excessive alcohol use was responsible for more than 140,000 deaths and 3.6 million years of potential life lost each year, on average.

https://www.cdc.gov/alcohol-pregnancy/hcp/alcoholsbi/index.html

AUD and ARD in Medical Settings

Alcohol-related Disorders in Medical Settings

- Emergency Department:
  - 10-18% of ED patients screen positive for alcohol use disorders
  - Up to 50% of trauma patients have alcohol-related injuries
- Inpatient Settings:
  - 20-30% of hospitalized patients have AUD
  - Higher rates in certain specialties (e.g., gastroenterology, psychiatry)
- Primary Care Clinics
  - 10-15% of patients meet criteria for AUD
  - Often underdiagnosed due to time constraints and lack of screening



Common Presentation in Different Settings

- Emergency Department:
  - Acute intoxication and withdrawal
  - Alcohol-related injuries (falls, motor vehicle accidents)
  - Gastrointestinal complaints (pancreatitis, gastritis)
- Inpatient Settings:
  - Alcohol withdrawal syndrome
  - Liver disease (cirrhosis, alcoholic hepatitis)
  - Neurological complications (Wernicke-Korsakoff syndrome)
- Primary Care:
  - Chronic health issues (hypertension, diabetes)
  - Mental health concerns (depression, anxiety)
  - Social and occupational problems

Identify and Use Evidence-Based Tools

Recommendation Summary

Population	Recommendation	Grade
Adults 18 years or older, including pregnant women	The USPSTF recommends screening for unhealthy alcohol use in primary care settings in adults 18 years or older, including pregnant women, and providing persons engaged in risky or hazardous drinking with brief behavioral counseling interventions to reduce unhealthy alcohol use.	B
Adolescents aged 12 to 17 years	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening and brief behavioral counseling interventions for alcohol use in primary care settings in adolescents aged 12 to 17 years. See the Clinical Considerations section for suggestions for practice regarding the I statement.	I

Why Screening is Important?

- Alcohol-related disorders are common in medical settings
  - Alcohol use contributes to common health problems:
  - Alcohol use can promote disease progress while compromising self-care and treatment outcomes.
- Alcohol screening and brief intervention are effective and cost effective, especially in primary care settings.
- Early detection can avert greater harm and long-term complications
  - NO need to wait until “hitting the rock bottom” to intervene
- Screening and early intervention alcohol may help an entire family
  - Identifying individuals with alcohol problems may make a difference in the whole family’s health

https://www.niaaa.nih.gov/health-professionals-communities/core-resource-on-alcohol/screen-and-assess-use-quick-effective-methods

Evidence-based Screening Tools

Evidence-Based Screening for Alcohol Use Disorder

- **1. Alcohol Use Disorders Identification Test (AUDIT):**
  - Validated across genders and various racial/ethnic groups, suitable for primary care settings.
  - Purpose: Assesses alcohol consumption, drinking behaviors, and alcohol-related problems
  - 10 items. Scoring: >=8 positive screen
- **2. Single Alcohol Screening Question (SASQ):** Quick screening for unhealthy alcohol use
  - Question: "How many times in the past year have you had five (men)/four (women) or more drinks in a day?"
  - Positive screen if answering 1 or more times:
- **3. AUDIT-C:**
  - Components: First 3-item version of AUDIT
  - Scoring: 4+ (men), 3+ (women): Positive screen
- C.A.G.E: Not recommended

Huffsteler et al. 2020 https://bmcprimcare.biomedcentral.com/articles/10.1186/s12875-020-01147-4

The Alcohol Use Disorders Identification Test: Interview Version

Read questions as written. Record answers carefully. Begin the AUDIT by saying "Now I am going to ask you some questions about your use of alcoholic beverages during this past year." Explain what is meant by "alcoholic beverages" by using local examples of beer, wine, vodka, etc. Code answers in terms of "standard drinks". Place the correct answer number in the box at the right.

1. How often do you have a drink containing alcohol?
   (0) Never [Skip to Qs 9-10]
   (1) Monthly or less
   (2) 2 to 4 times a month
   (3) 2 to 3 times a week
   (4) 4 or more times a week

2. How many drinks containing alcohol do you have on a typical day when you are drinking?
   (0) 1 or 2
   (1) 3 or 4
   (2) 5 or 6
   (3) 7, 8, or 9
   (4) 10 or more

3. How often do you have six or more drinks on one occasion?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily
   Skip to Questions 9 and 10 if Total Score for Questions 2 and 3 = 0

4. How often during the last year have you found that you were not able to stop drinking once you had started?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

5. How often during the last year have you failed to do what was normally expected from you because of drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

7. How often during the last year have you had a feeling of guilt or remorse after drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

9. Have you or someone else been injured as a result of your drinking?
   (0) No
   (2) Yes, but not in the last year
   (4) Yes, during the last year

10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?
    (0) No
    (2) Yes, but not in the last year
    (4) Yes, during the last year

Record total of specific items here

If total is greater than recommended cut-off, consult User's Manual.

Patient Name _____ Date of Visit _____

1. Within the past year, how often did you have a drink of alcohol?

- ☐ a. Never
- ☐ b. Monthly (e.g. Special occasions/Rare)
- ☐ c. 2-4 times a month (e.g. 1x on weekend - "Fridays only" or "every other Thursday")
- ☐ d. 2-3 times a week (e.g. weekends – Friday-Saturday or Saturday-Sunday)
- ☐ e. 4 or more times a week (e.g. daily or most days/week)

2. Within the past year, how many standard drinks containing alcohol did you have on a typical day?

- ☐ a. 1 or 2
- ☐ b. 3 or 4
- ☐ c. 5 or 6
- ☐ d. 7 to 9
- ☐ e. 10 or more

3. Within the past year, how often did you have six or more drinks on one occasion?

- ☐ a. Never
- ☐ b. Less than monthly
- ☐ c. Monthly
- ☐ d. Weekly
- ☐ e. Daily or almost daily

SASQ

Alcohol: One drink =

12 oz. beer

5 oz. wine

1.5 oz. liquor (one shot)

		None	1 or more
MEN:	How many times in the past year have you had 5 or more drinks in a day?	○	○
WOMEN:	How many times in the past year have you had 4 or more drinks in a day?	○	○

USPSTF Guidelines (2018)

1

Screening for AUD should start with the AUDIT-C or Single Alcohol Screening Question (SASQ).

2

If the patient screens positive on one of these initial tests, proceed with a more specific tool such as the Alcohol Use Disorders Identification Test (AUDIT).

One drink a day….

What Is a Standard Drink?

12 fl oz of regular beer	=	8–9 fl oz of malt liquor (shown in a 12 oz glass)	=	5 fl oz of table wine	=	1.5 fl oz shot of distilled spirits (gin, rum, tequila, vodka, whiskey, etc.)
						
about 5% alcohol		about 7% alcohol		about 12% alcohol		about 40% alcohol

14grams of pure alcohol, the unit of a stand drink varies from one country to another (20 in Austria, 8 in UK)

Why is CAGE Not Recommended?

- **Limited scope and sensitivity:** primarily to detect alcohol dependence, it does not effectively screen for mild cases
- **Outdated diagnostic criteria**: It doesn't align well with current DSM-5 or ICD-11 criteria for alcohol use disorders.
- **Lack of information on drinking patterns:** CAGE does not provide information about quantity, frequency, or patterns of drinking
- **Potential for stigma:** the questions about feeling guilty or being annoyed by criticism, may be perceived as judgmental and could potentially increase stigma around discussing alcohol use.

What's "low-risk" drinking?

Avoiding the pitfalls in Screening

1. Do not start with “Do you drink…”
2. Use moralistic or judgmental language (abuse, alcoholism.)
3. Do not project your personal judgment or stereotypes
4. Assume patients won't be open to discussing alcohol use
5. Neglect to tie screening to clinical issues and intervention

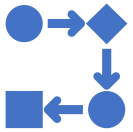
NIAAA Recommended 4 Steps

Step 1: Screening

Step 2: Advise or Assess

If NO to heavy drinking: Advise for Stay within US Dietary Guideline or Abstain

If YES to heavy drinking: Go to step 3



Step 3: Brief Intervention for heavy drinking and AUD

Follow up

Revisit drinking goals.

Acknowledge change is difficult.

Affirm progress.

Explore challenges and strategies to surmount them.

https://www.niaaa.nih.gov/health-professionals-communities/core-resource-on-alcohol/how-apply-core-resource-alcohol-clinical-practice#how_to_content

Brief Intervention for Heavy Drinking
Advise and Assist

- Ask permission: Start by setting the agenda to discuss alcohol use.
- Give feedback and advice: Discuss the patient’s current drinking, related risks, and goals.
- Link your concern about alcohol use with the patient’s relevant physical and mental health conditions and emphasize the benefits of cutting back.
- Advise cutting down by staying within the U.S. Dietary Guidelines or abstaining as warranted.
- Negotiate individualized drinking goals to include "no heavy drinking days" as needed.
- Check in: Ask what the patient thinks of this information.
- Build motivation: Briefly explore reasons for making a change, listening for the patient's own reasons.
- Offer support: Express empathy and encourage autonomy.
- Identify next steps: Work together to develop a plan for change.

≥ 5 drinks on any day or 15 or more per week for men, ≥ 4 drinks on any day or 8 for women

Brief Intervention for Alcohol Use Disorder
Advise and Assist

- Ask permission: Start by setting the agenda to discuss alcohol use.
- Give feedback and advice: Discuss the patient's current drinking, related risks, and goals.
- Inform them that you believe they have AUD, that they can get better, and that you're willing to help.
- Link your concern about alcohol use with the patient's other relevant physical and mental health conditions and emphasize the benefits of quitting.
- **Advise quitting by cutting down gradually. If the patient is hesitant to abstain, then negotiate individualized drinking goals.**
- Discuss treatment options. Consider prescribing an **FDA-approved medication** for AUD, providing a referral to specialty behavioral healthcare, and suggesting they try different mutual support groups.
- Check in: Ask what the patient thinks of this information.
- Build motivation: Briefly explore reasons for making a change, listening for the patient's own reasons. Use their responses to the AUD symptom checklist (see Step 2) as an opener, if applicable.
- Offer support: Express empathy and encourage autonomy.
- Identify next steps: Work together to develop a plan for change.

Table 1. Medications Used to Treat Alcohol Use Disorders

Medication	Year of First FDA Approval[a]	Mechanism of Action	Is a Generic Version Available?
Acamprosate calcium (oral) (Campral)	2004	Possible glutamate antagonist and gamma-aminobutyric acid (GABA) agonist (not fully known)—reduces symptoms of withdrawal and craving	Yes
Disulfiram (oral) (Antabuse)	1951	Alcohol antagonist—disulfiram plus alcohol will produce flushing, throbbing in head and neck, headache, nausea, vomiting, and other highly unpleasant symptoms	Yes
Naltrexone (oral)	1994 (for alcohol use disorders)	Opioid antagonist—blocks opioid receptors that are involved in alcohol and opioid cravings	Yes
Naltrexone (extended-release injectable) (Vivitrol)	2006	Opioid antagonist—blocks opioid receptors that are involved in alcohol and opioid cravings	No

Abbreviations: FDA, Food and Drug Administration.

[a] For more information on FDA approval of drugs, see U.S. Food and Drug Administration. Drugs@FDA: FDA Approved Drug Products. Retrieved from http://www.accessdata.fda.gov/scripts/cder/daf/

Naltrexone and acamprosate are listed as Essential Medicines by the WHO

For Screen Positive Patients

- More detailed assessment is indicated
- Meet alcohol use disorder? (DSM-5 criteria)
- Any physical signs of alcohol use disorder?
- Any alcohol-related disorders (medical issues?)
- Any laboratory abnormalities (elevated LFTs? GGT?)
- Problems with relationships, family or work performance
- Family history of alcohol use disorder

Substance Use Disorder
DSM-5 Criteria

A. A problematic pattern of substance use leading to clinically significant **impairment or distress**, as manifested by at least two of the following, occurring within a 12 month period:

- 1. The substance is often taken in larger amounts or over a longer period than was intended.
- 2. There is a persistent desire or unsuccessful efforts to cut down or control the substance use.
- 3. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from it's effects.

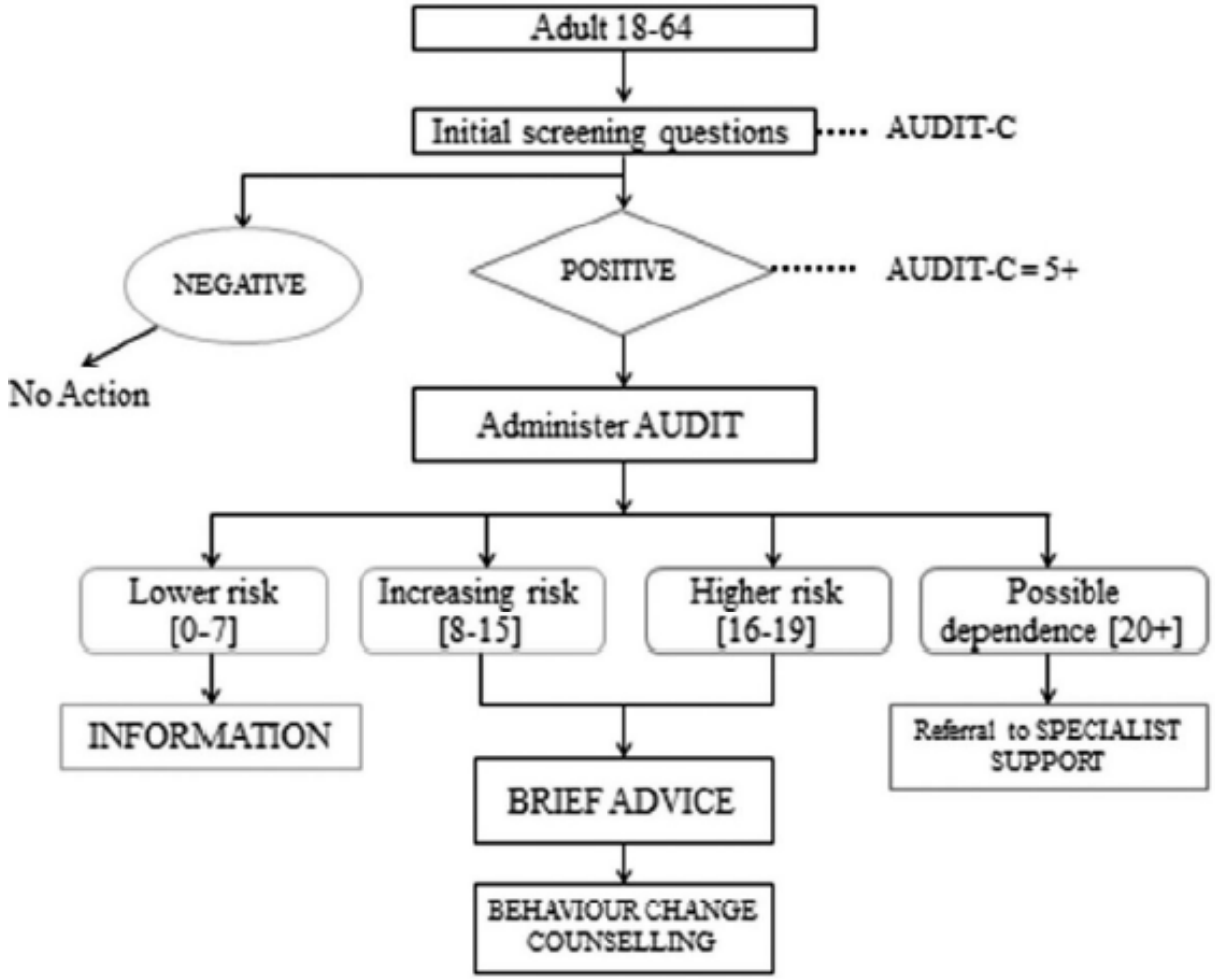
Substance Use Disorder
DSM-5 Criteria (2)

- 4. Craving, or a strong desire or urge to use the substance.
- 5. Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home.
- 6. Continued Substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance.
- 7. Important social, occupational, or recreational activities are given up or reduced because of substance use.

Substance Use Disorder
DSM-5 Criteria (3)

- 8. Recurrent substance use in situations in which it is physically hazardous.
- 9. Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
- 10. Tolerance
- 11. Withdrawal

Screening and Brief Intervention in United Kingdom



Does Screening and Intervention Work? What Does the Evidence Say?

Evidence of its Effectiveness

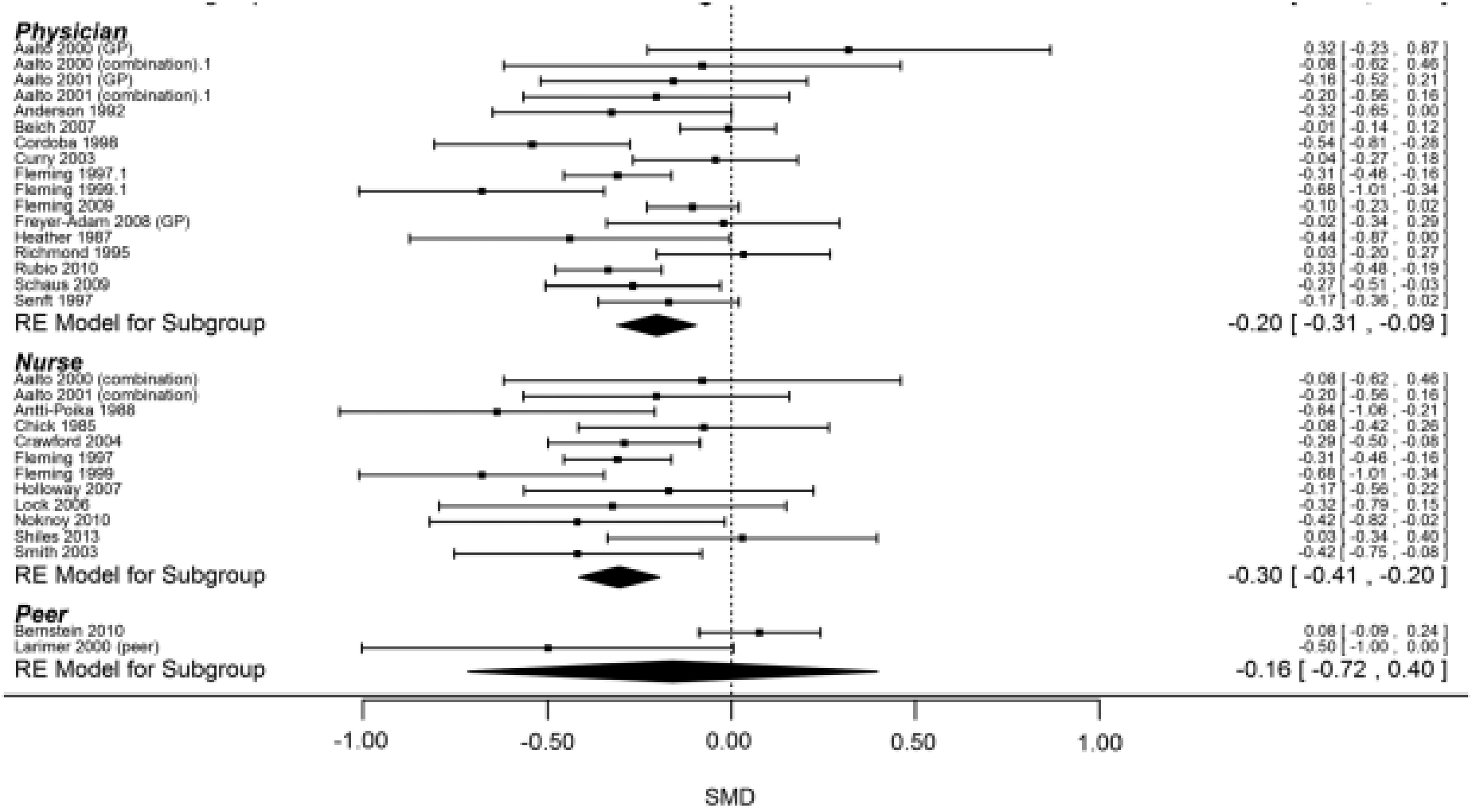
- Reduces Drinking Levels: brief interventions can effectively reduce alcohol use in patients who screen positive for heavy drinking.
- Cost-Effective: Implementing screening and brief intervention is cost-effective in primary care settings.
- Highly Ranked Preventive Practice: Based on cost-effectiveness and preventable disease burden, alcohol screening and brief intervention ranks higher than:
  - Hypertension screening
  - Cholesterol screening
  - Cancer screening
- Significant Public Health Impact: Has potential to reduce alcohol-related harm at both individual and population levels.

https://www.niaaa.nih.gov/health-professionals-communities/core-resource-on-alcohol/screen-and-assess-use-quick-effective-methods

Brief Interventions and Counseling

- Primary Care Settings: Proven to reduce alcohol consumption and related harms (NIAAA).
- Meta-Analysis Findings: Brief interventions reduce the quantity of alcohol consumed by 0.15 standard deviations (SDs) (Platt et al 2016).
- Nurse-Delivered Interventions: Particularly effective, with a reduction in quantity consumed by 0.23 SDs (Platt et al. 2016).

https://www.niaaa.nih.gov/health-professionals-communities/core-resource-on-alcohol/conduct-brief-intervention-build-motivation-and-plan-change.



- Brief Interventions play a small but significant role in reducing alcohol consumption. Interventions delivered by nurses were better than physicians or peers

Advice for At-Risk Drinking

- State your conclusion and recommendations clearly
  - “You are drinking more than is medically safe”
  - Relate to patient’s concerns and medical findings
  - Link alcohol use to his current medical conditions/medications
  - “I strongly recommend that you cut down (or quit) and I am willing to help.”

Asking about drinking is medical setting can be powerful

Creating ambivalence about change is one step closer to actual change….

A True Story (Professor K)

A prominent researcher on alcohol use disorder comes to his doctor for an annual physical. He is given a few forms to complete, including questions about tobacco and alcohol use. His doctor also asks him about his tobacco and alcohol use specifically.

"Of course I lied about my drinking."

"On the way home, I keep thinking, 'Why did I lie, do I drink too much?"
"In the following few months, I became more aware how much I drank, and I actually drank much less, "

When do I need to refer to specialty?

- Fail to respond to brief interventions
- Severe cases
- With comorbid psychiatric issues
- With other SUDs
- Medically fragile or complicated

Case discussion

Mr. J, a 45-year-old accountant, comes to your primary care clinic for a routine check-up. He appears well-groomed but seems slightly anxious.

Case Discussion

- **Step 1: Routine Screening**
  - The AUDIT-C was used and he scores 6, indicating a high risk of alcohol-related problems.
- **Step 2: Identifying Warning Signs**
  - Mild tremors in his hands, slightly elevated BP, c/o frequent heartburn and trouble sleeping, borderline elevation of AST and GGT
  - These signs and the AUDIT score raise your suspicion of potential AUD.

- **Step 3: Further Assessment**
  - Start a non-judgmental conversation about his alcohol use: He admits to drinking "a few beers" every night to relax
  - Weekends involve heavier drinking with friends (5-6 drinks)
  - He's had a few arguments with his wife about his drinking
  - He's missed a few Monday morning meetings due to hangovers

Case discussion

- **Step 4: Early Intervention**
  - MI techniques: Express empathy: "It sounds like alcohol is causing some issues in your life."
  - Develop discrepancy: "You mentioned wanting to advance in your career, but alcohol seems to be interfering with your work performance.“ “You care about your wife, but you have argued more recently.”
  - Roll with resistance: When he says, "But everyone drinks like this," you respond, "Many people do drink, but it affects everyone differently."
  - Support self-efficacy: "You've made positive changes in other areas of your life. You have the ability to make changes here too.“

- **Step 5: Collaborative Goal Setting**
  - Collaboratively set initial goals: Keeping a drinking diary for four weeks
  - Reducing drinking to no more than 2 drinks per day, no more 14 drinks/week
  - Having at least 2 alcohol-free days per week
- **Step 6: Follow-up and Monitoring**
  - You schedule a follow-up appt in a few weeks to review his progress and drinking diary.
- **Step 7: Ongoing Management**
  - At the follow-up: he partially met his goals (no more 14 drinks/week) but struggles with alcohol-free days
  - You discuss strategies for managing triggers and cravings. You recommend he join a local support group (AA)

Case discussion

- **Step 8: Consideration of Pharmacotherapy**
  - You prescribe naltrexone to help reduce cravings
  - You explain potential side effects and the importance of adherence
- **Step 9: Referral to Specialized Treatment**
  - He continues to struggle despite these interventions, and he reports feeling more and more depressed.
  - He has taken the med inconsistently. His wife has separated from him with a possible divorce.
  - You suggest a referral: You recommend an outpatient alcohol treatment program
- **Step 10: Ongoing Primary Care Support**
  - You assure him that you'll continue to be involved in his care: Regular check-ups to monitor his overall health
  - Coordination with the specialist alcohol treatment team
  - Continued support and encouragement in his recovery journey

Billing for service

CPT code	Description	2022 wRVU
99408	Alcohol and/or substance (other than tobacco) abuse structured screening (AUDIT, DAST), and a brief intervention, 15-30 mins	0.65
99409	…greater than 30 mins	1.30

Take Home Messages

You can make a difference

- Alcohol-related disorders are common in medical settings.
- Implement routine screening using validated tools (e.g., AUDIT-C or SASQ)
- Brief Intervention: Utilize motivational interviewing techniques for patients with risky drinking patterns
- Consider FDA-approved medications (naltrexone, acamprosate) as part of treatment plan for moderate to severe AUD
- Referral to Specialty Care: Facilitate timely referral to addiction specialists or treatment programs for patients requiring intensive or specialized care.
- Continuity of Care: Ensure a smooth transition between inpatient and outpatient settings, including referrals to specialized addiction treatment and support groups.

Key Resources

- NIDA Rethinking Drinking
- Screening and Brief Intervention and Referral to Treatment (SAMHSA)
- CDC Alcohol Use and Your Health

Questions and comments?

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Transforming the Brain: from Addiction to Recovery

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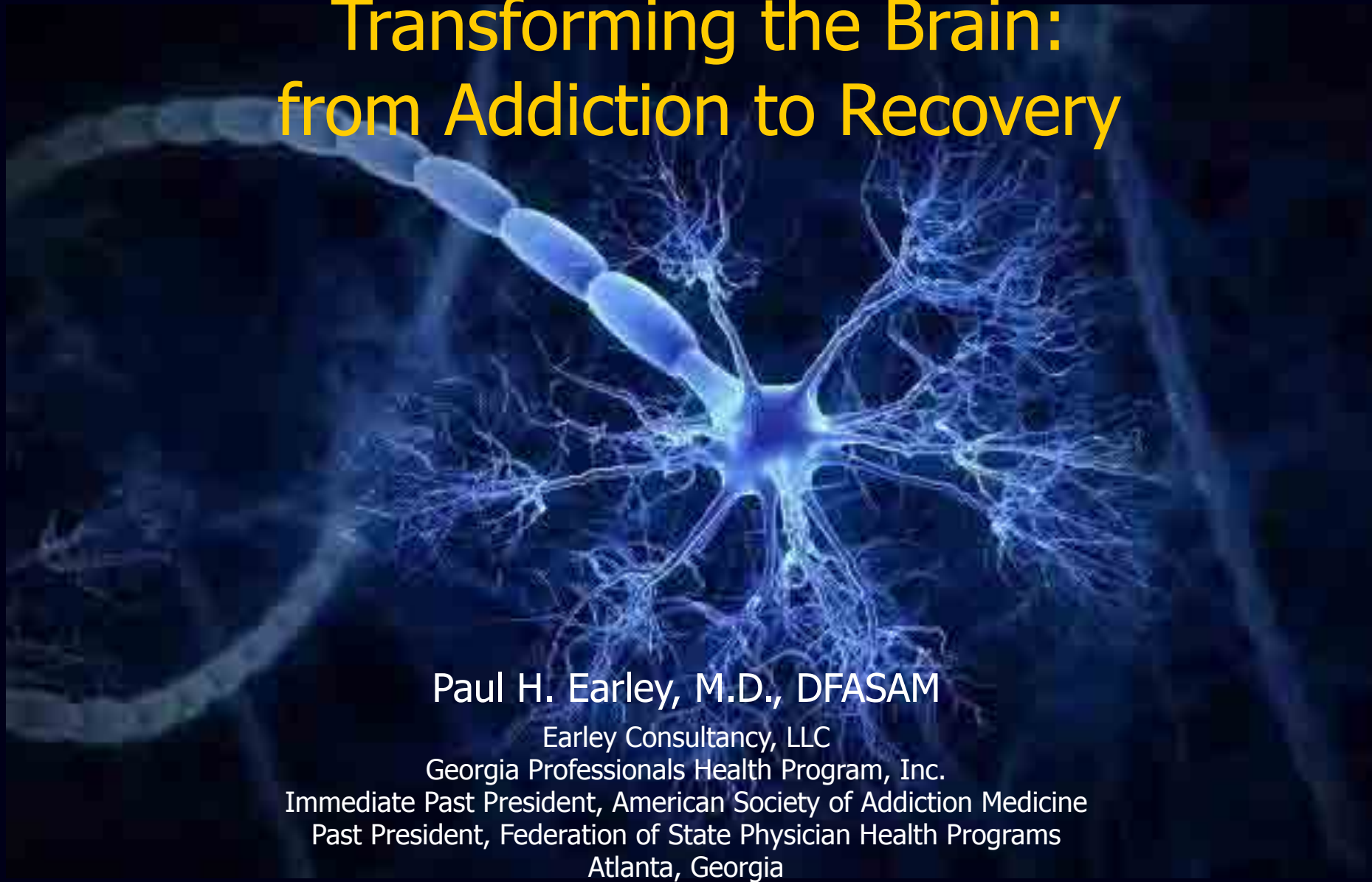
Transforming the Brain: from Addiction to Recovery



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SOUTHERN MEDICAL ASSOCIATION

Disclosure of Financial Relationships

Paul H, Earley, M.D., DFASAM

- Salary, Medical Director of the Georgia Professionals Health Program, Inc.
- Principal, Earley Consultancy, LLC providing consultation to the addiction treatment industry
- Stock in DynamiCare Health Inc. a software company that builds recovery support tools
- President of the American Society of Addiction Medicine, a volunteer position, from 2019-2021

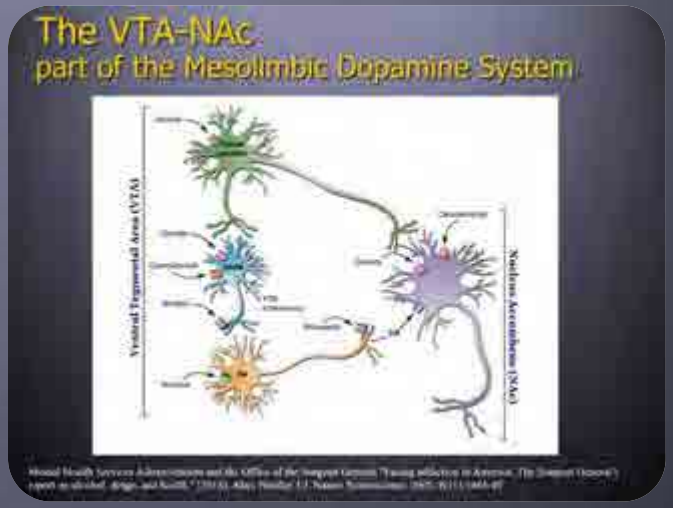
Premise of this Lecture

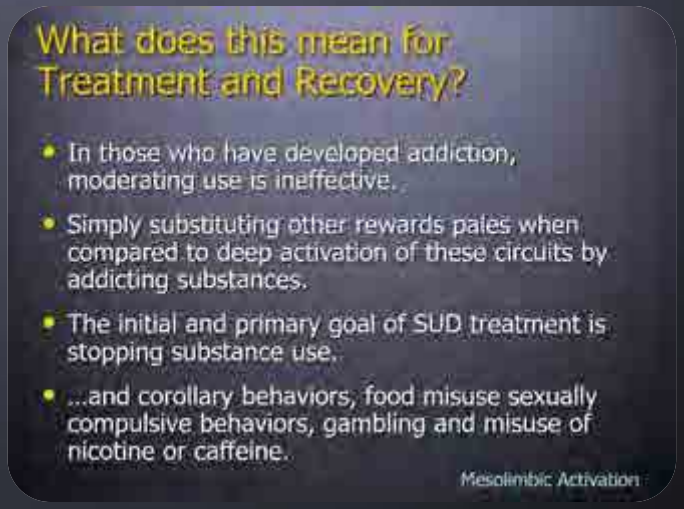
- Addiction reprograms the brain, but our understanding of how this occurs is limited.
- However, if we collect our current understanding as to how addiction modifies brain/behavioral circuits, we can use this information to aim our treatment to maximize recovery. Treatment will literally reprogram addiction's disrupted and distorted brain activities.
- Because addictions effects on the brain are so pervasive, treatment must rewire many behaviors and beliefs.
- This lecture uses this thought experiment as a way of refining addiction care by describing the reprograming necessary for recovery.

Format of this Lecture

- First, I will describe one of many ways in which drugs of misuse change brain circuity.

- Then, I will propose how treatment should be re-engineered to address this maladaptive re-programing.

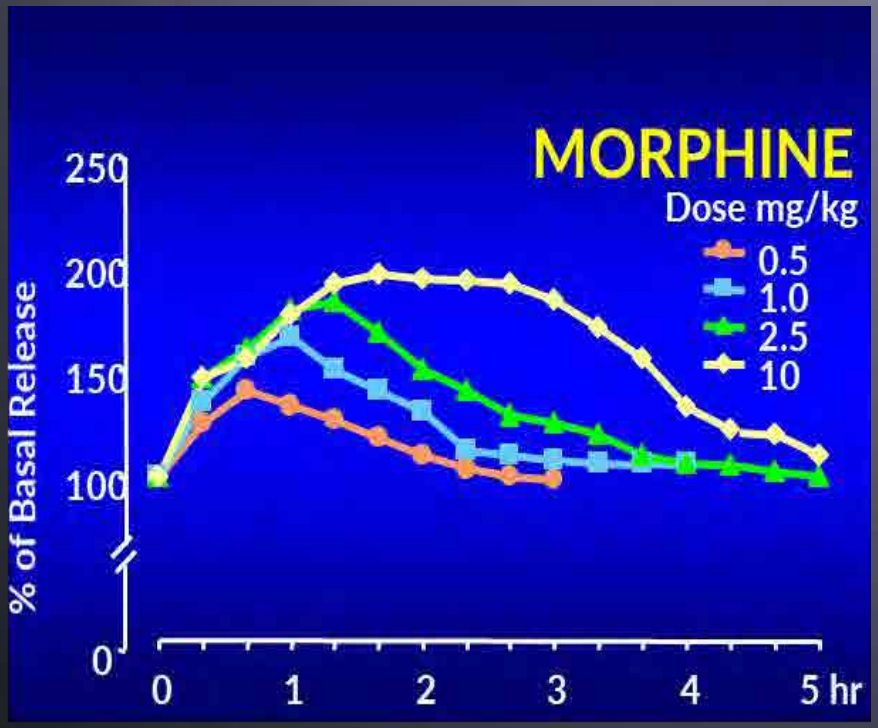


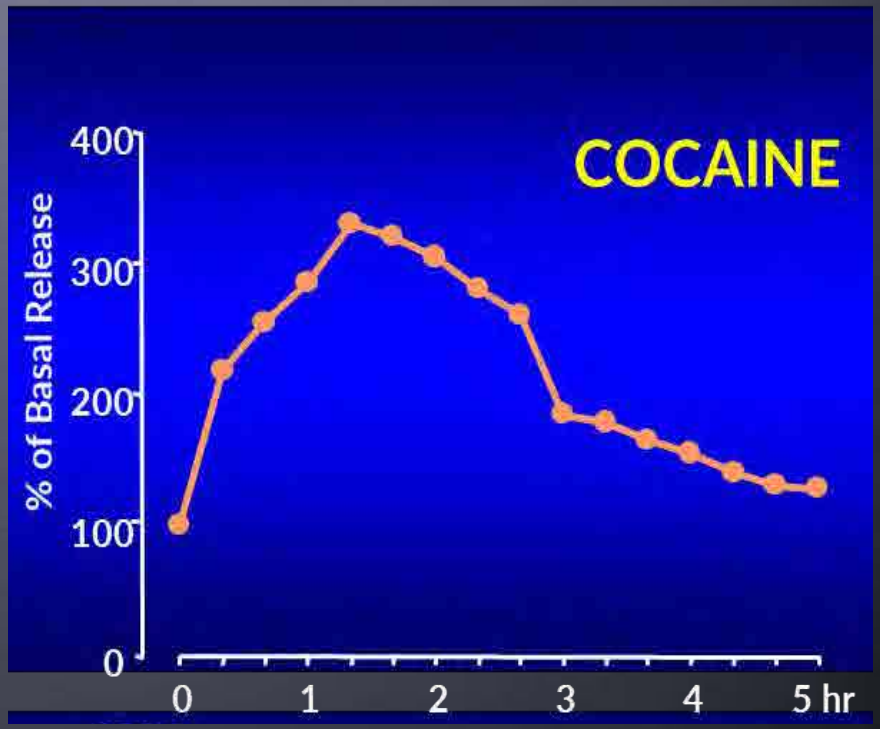


The Mesolimbic Reward Circuit

Why do Humans develop Addiction Diseases?

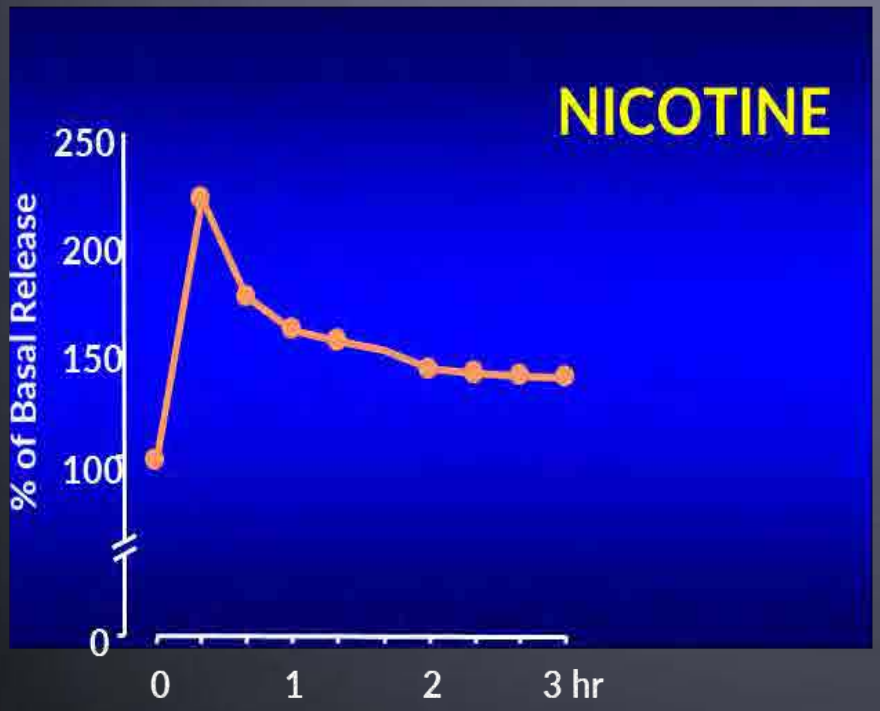
The Effect of Certain Drugs on Dopamine Levels

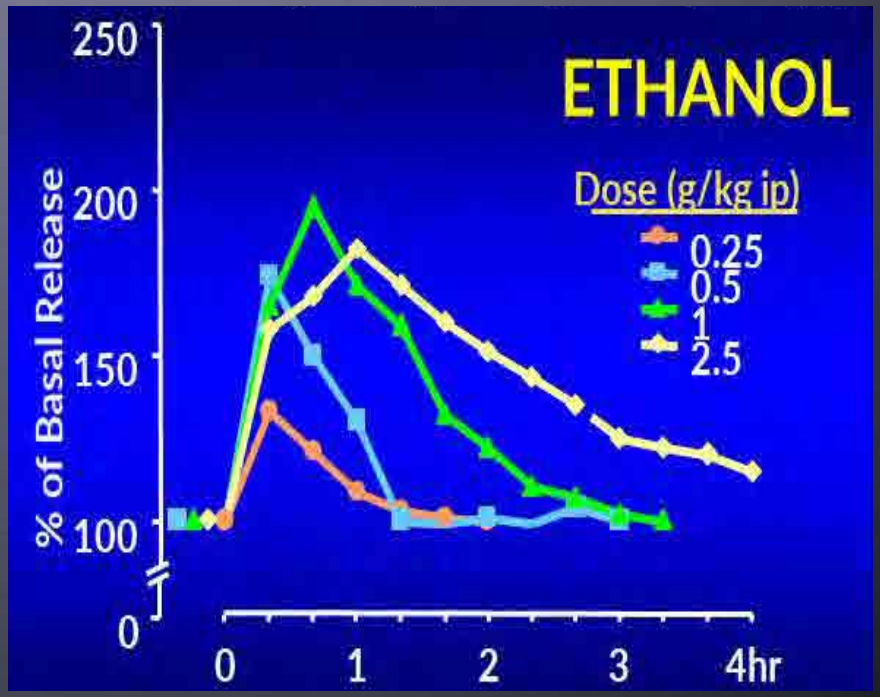




Adapted from: Di Chiara and Imperato, Proceedings of the National Academy of Sciences USA, 1988.

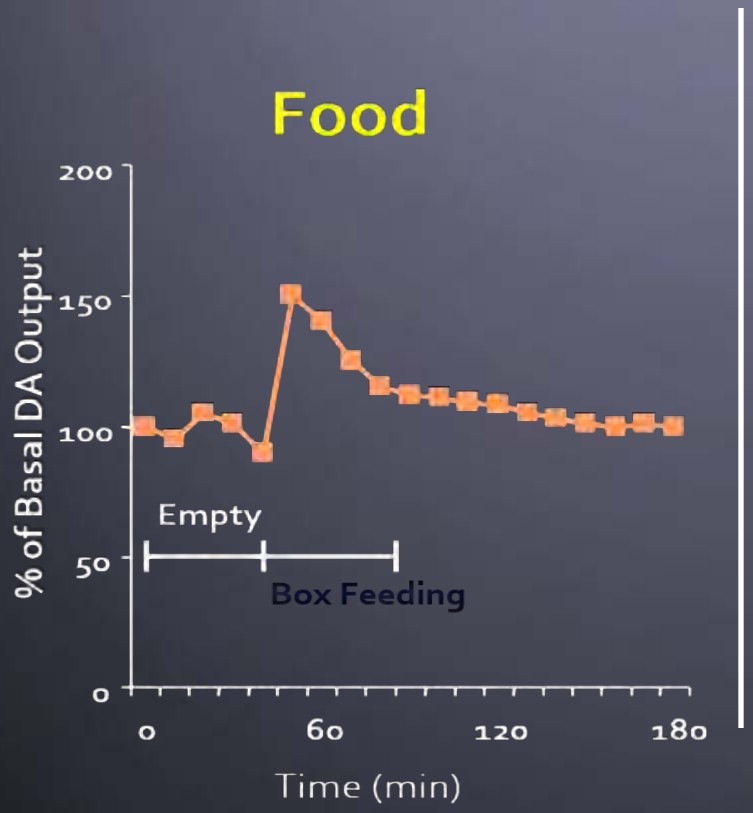
Effects of Drugs on Dopamine Levels

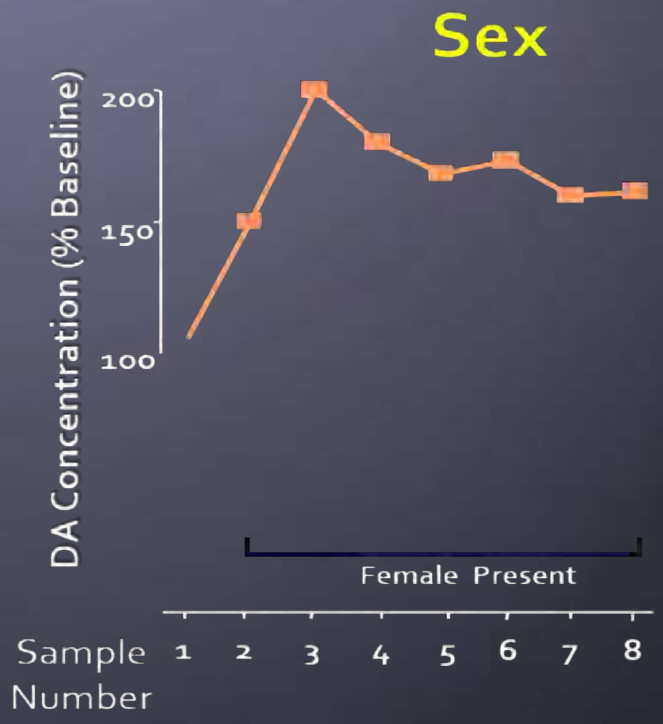




Adapted from: Di Chiara and Imperato, Proceedings of the National Academy of Sciences USA, 1988.

Natural Rewards produce the Same Dopamine Activation





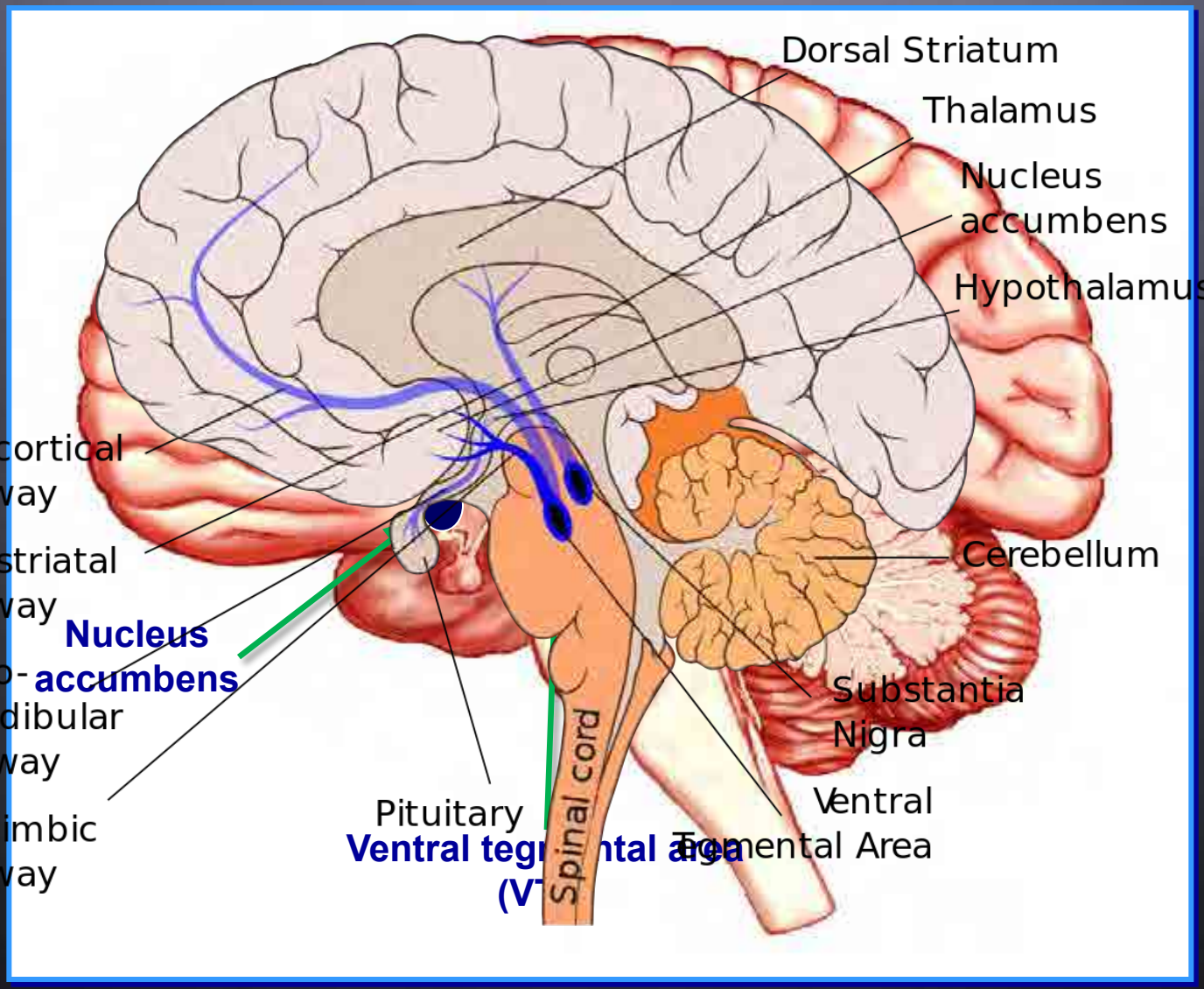
Adapted from: Di Chiara et al, Neuroscience, 1999.
Adapted from: Fiorino and Phillips, J Neuroscience, 1997.

Dopamine / Reward Model

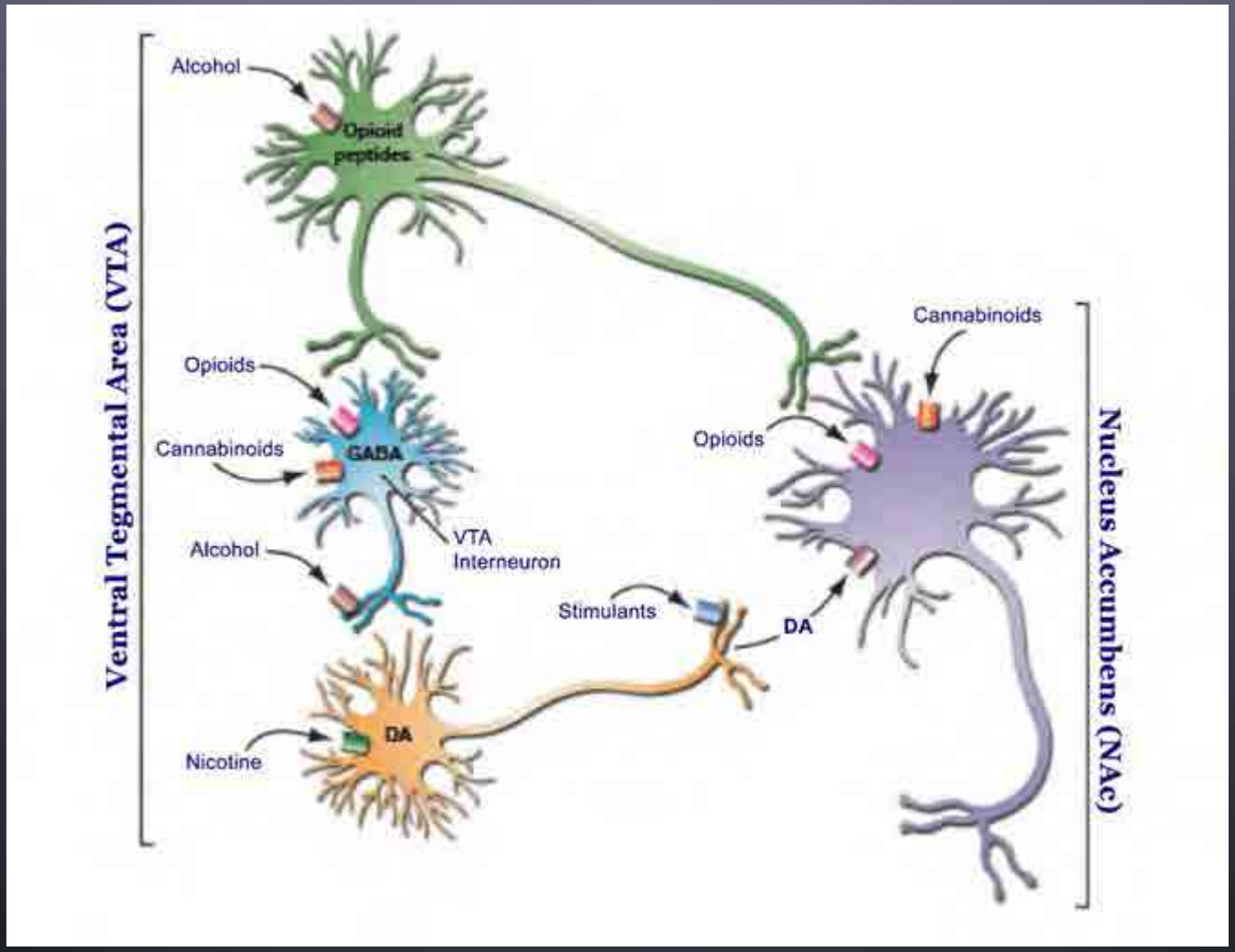
- Dopamine neurons in the Ventral Tegmental Area (VTA) project to shell of the Nucleus Accumbens (NAc).
- This primitive brain structure drives life-sustaining activities,[1] foraging for food and water, escaping from harm, reinforcing sexual activity and child-rearing and establishing the criticality and drive for these activities.
- All drugs of misuse seem to activate this circuit, albeit through a variety of neurotransmitter substrates.
- The use of certain drugs in certain people motivates their continued use, their learning to be more efficient at such behaviors, their up-ranking their use to high importance and their de-ranking other behaviors and motivators as less important.

[1] Alcaro A, Huber R, Panksepp J. Behavioral functions of the mesolimbic dopaminergic system: an affective neuroethological perspective. Brain Res Rev. 2007 Dec;56(2):283-32

Dopamine Reward Circuit



The VTA-NAc
part of the Mesolimbic Dopamine System



Mental Health Services Administration and the Office of the Surgeon General "Facing addiction in America: The Surgeon General's report on alcohol, drugs, and health." (2016). Also: Nestler, EJ. Nature Neuroscience 2005; 8(11):1445-49

What does this mean for Treatment and Recovery?

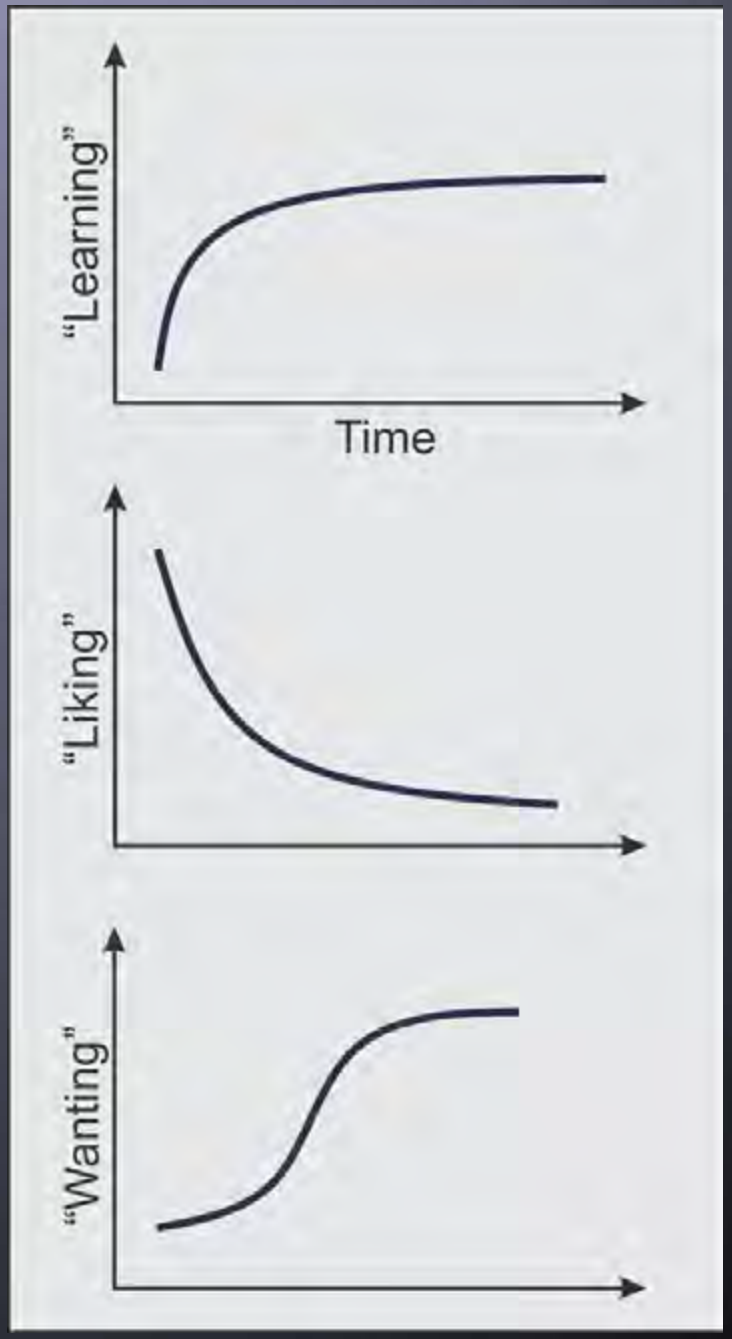
- In those who have developed addiction, moderating use is ineffective.
- Simply substituting other rewards pales when compared to deep activation of these circuits by addicting substances.
- The initial and primary goal of SUD treatment is stopping substance misuse.
- …and corollary behaviors, food misuse sexually compulsive behaviors, gambling and misuse of nicotine or caffeine.

Mesolimbic Activation

However, this activation of the mesolimbic dopamine center is more complex than an on/off switch…

Incentive Salience

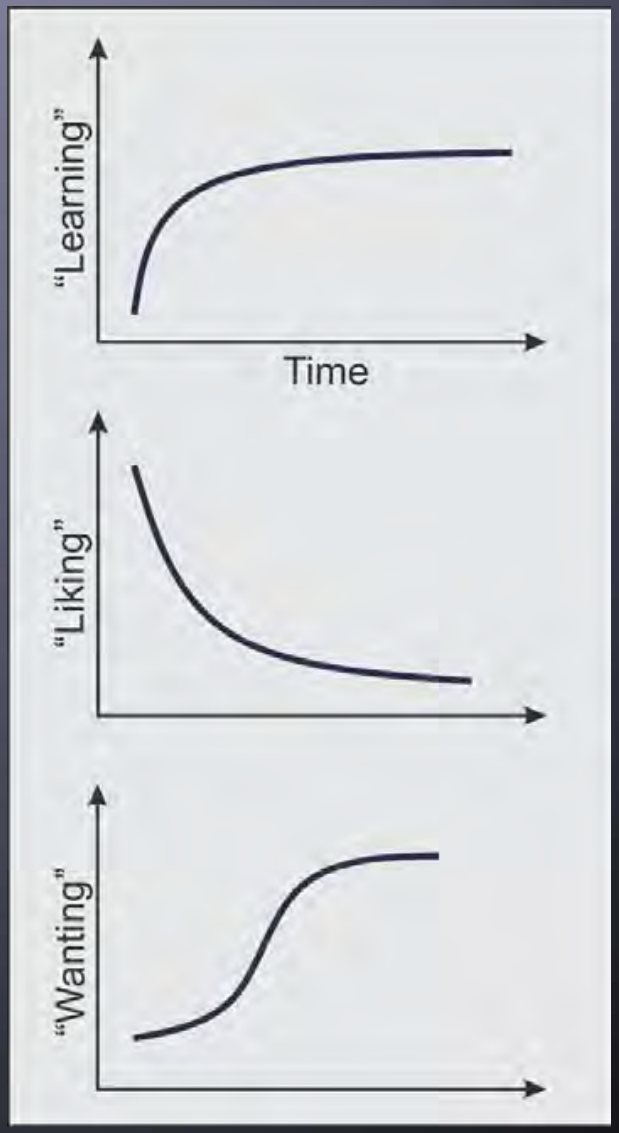
- Berridge, after destroying the VTA in rats, noted they continue to enjoy food but do not work for it.
- This seminal study and subsequent research led to the conclusion that the VTA□NAc produces wanting rather than reward.



Berridge, K. C. and T. E. Robinson (2003). "Parsing reward." Trends in Neurosciences 26(9): 507-513.

Incentive Salience

- It is not pleasure that drives addiction but "Incentive Salience"
- "This explains why life's intense pleasures are less frequent and sustained than intense desires." [1]



[1] Berridge, K. C. and T. E. Robinson (2003). "Parsing reward." Trends in Neurosciences 26(9): 507-513.

What does this mean for Treatment and Recovery?

- Using the thought experiment: "Don't you see how you will feel better if you stop using?" may seem helpful in the abstract but does not compute on an emotional level for most individuals early in recovery.
- Some patients benefit from learning how to parse "wanting" from "liking." Doing so provides insight.
- Most individuals are relieved to learn that their brain has become highly skilled at substance procurement and use and much of this response is automatic.
- Normalizing drug (alcohol) hunger reduces negative self concept.

Incentive Salience

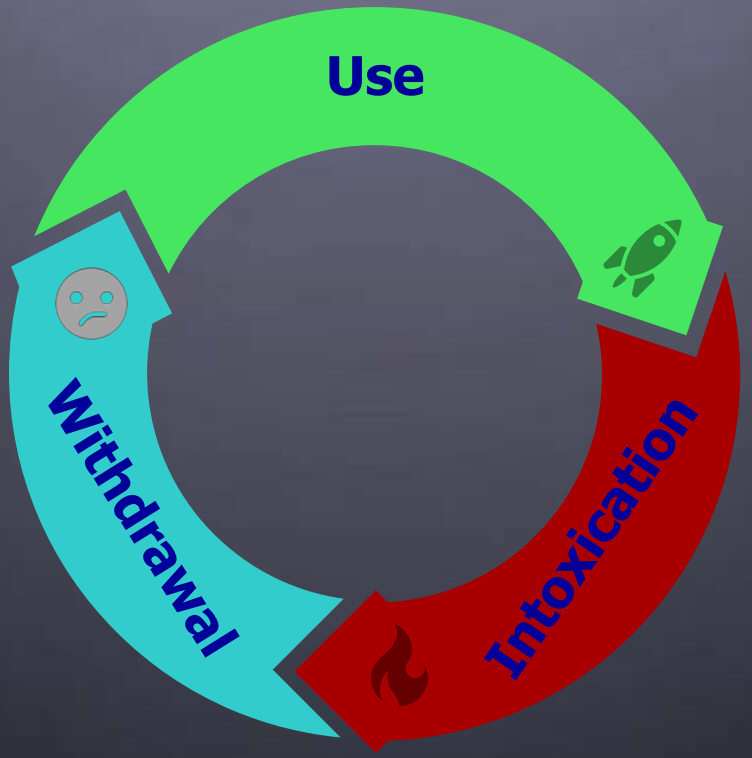
Two Cycles drive Continued Use

Cycle One - Defined by drug physiology

Use

Substance use in those with addiction becomes more about relief than pleasure.

Quick Cycle



Withdrawal

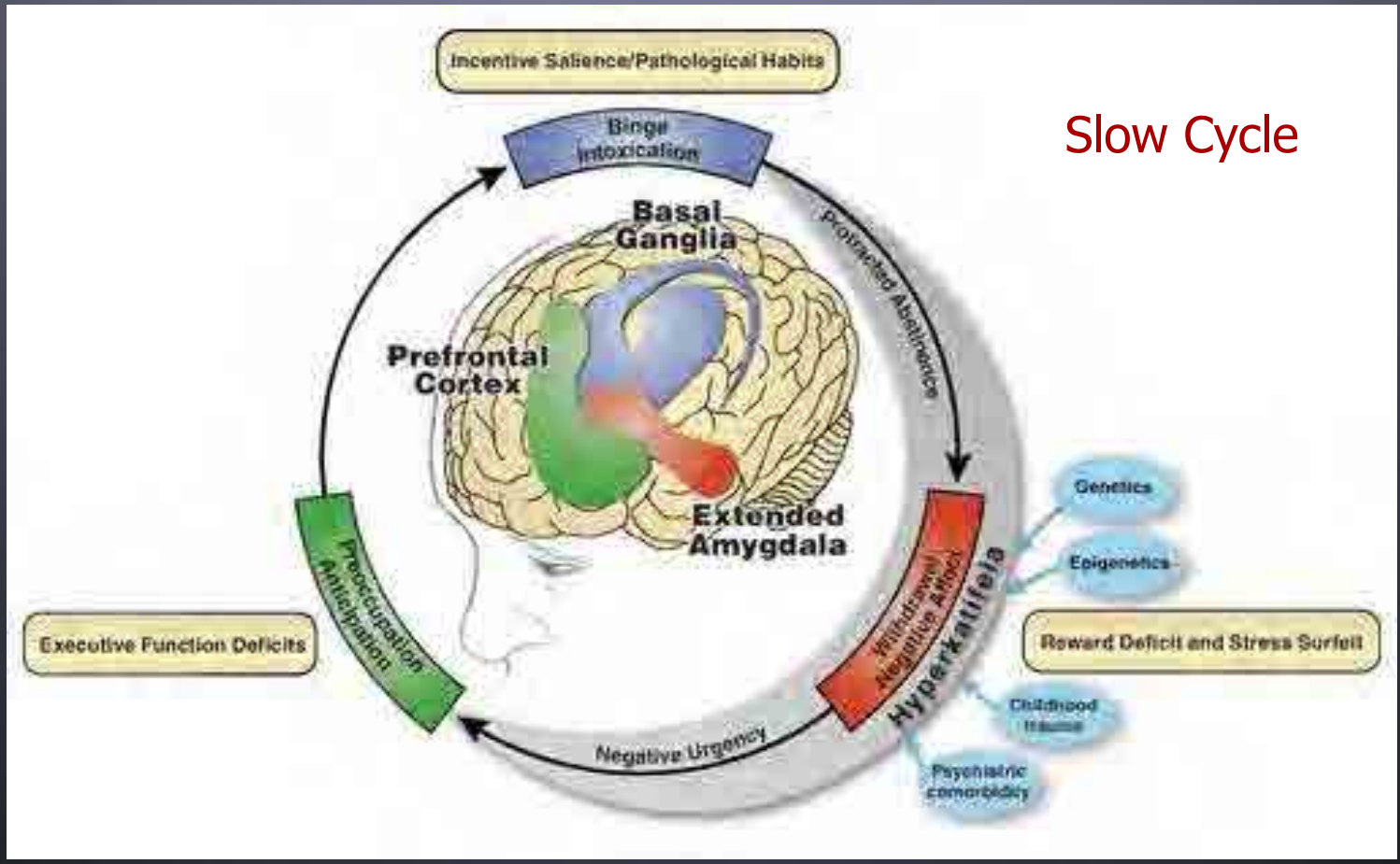
Depending on the substance, withdrawal can begin hours later or rapidly after cessation of use.

Intoxication

Intoxication returns the individual back to their new normal.

Two Cycles drive Continued Use

Cycle Two - Defined by brain physiology



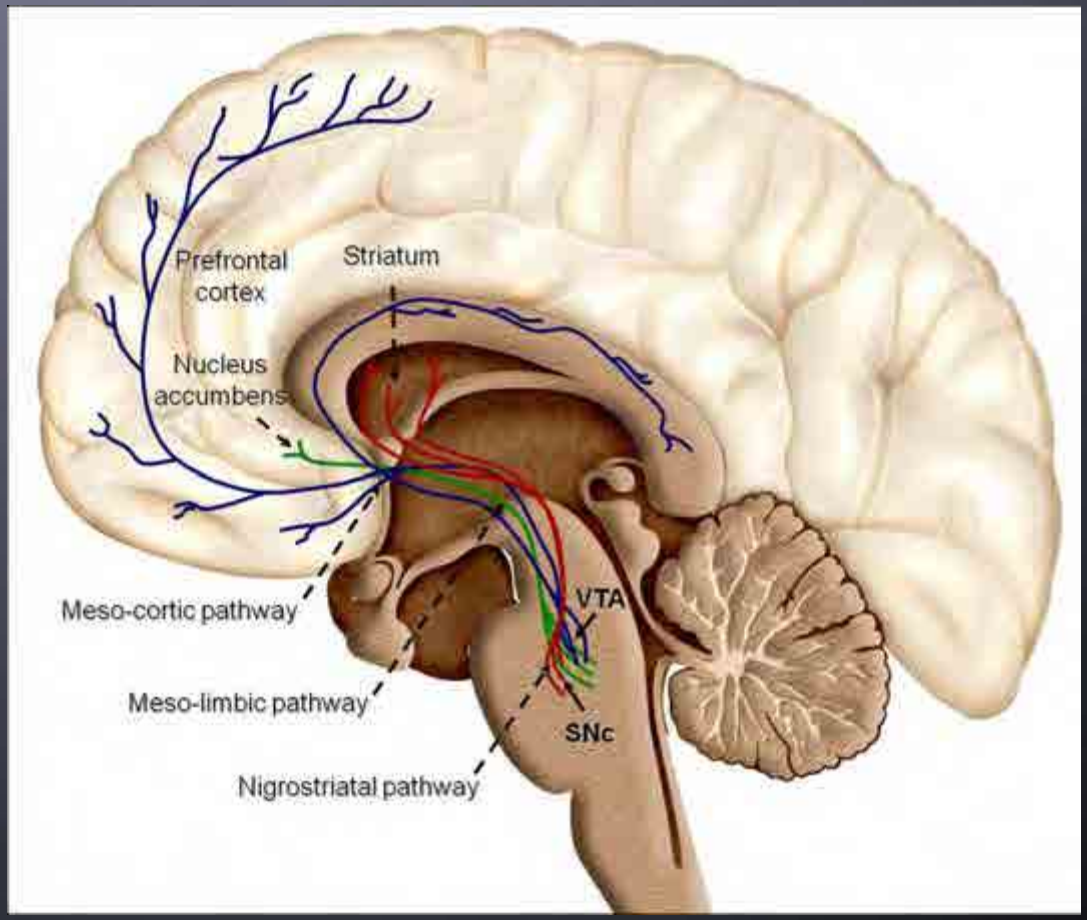
Koob, G. F., Powell, P., & White, A. (2020). Addiction as a coping response: Hyperkatifeia, deaths of despair, and COVID-19. American Journal of Psychiatry, 177(11), 1031–1037

What does this mean for Treatment and Recovery?

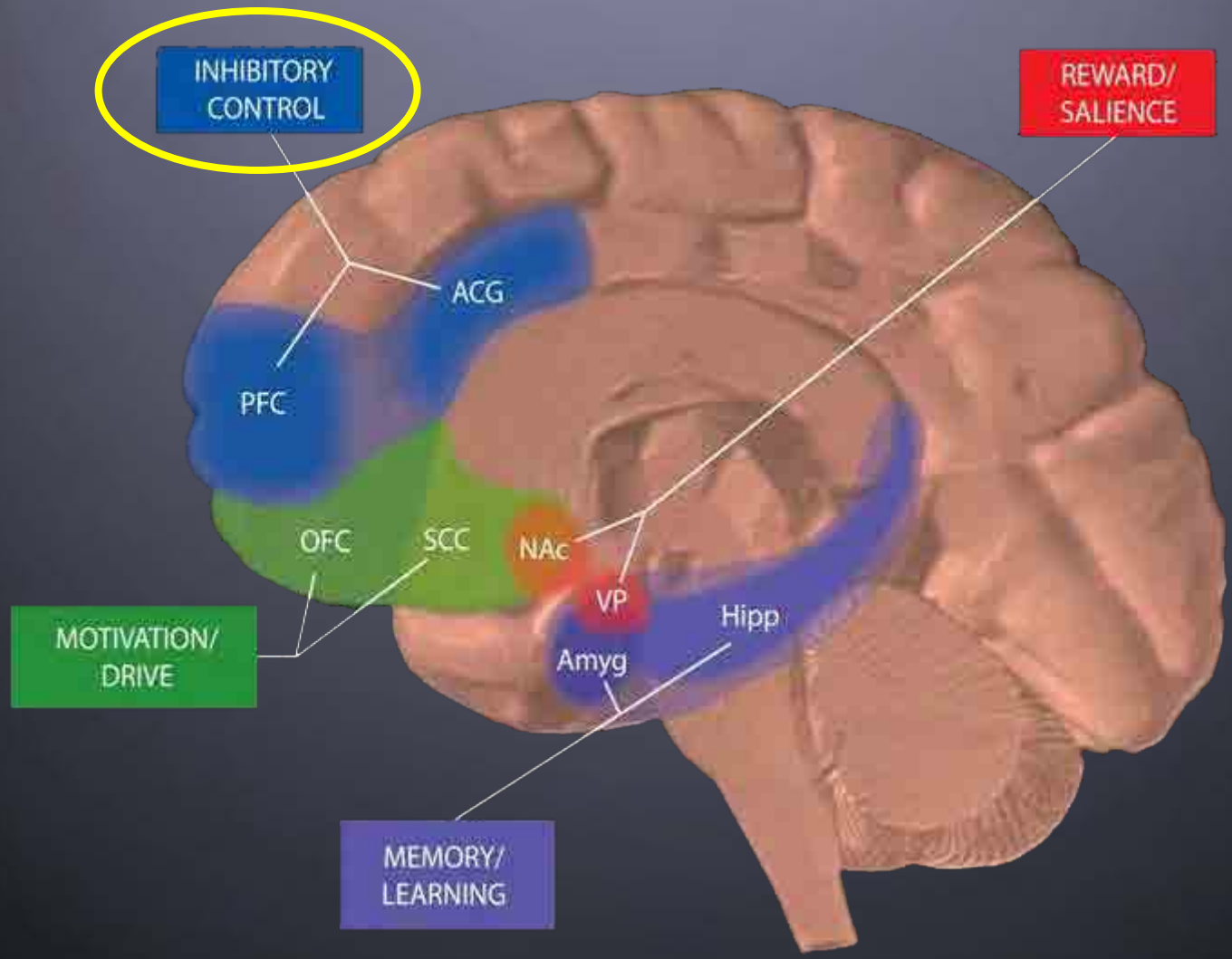
- Patients should be taught about these cycles, normalizing them part of early recovery.
- Patients should learn how to recognize the stages when they occur and have a plan for when they do occur to prevent relapse.

Downstream effects of the Mesolimbic Dopamine System

Dopaminergic cells have far-flung effects throughout the brain.

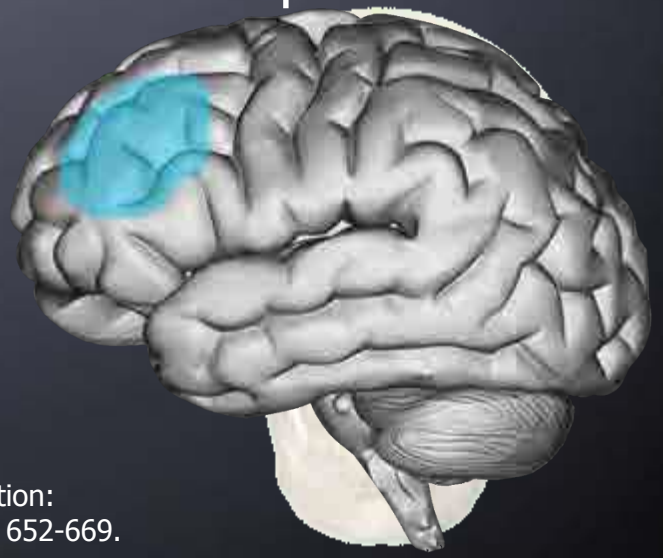


Brain Centers & Addiction



Addiction derails Inhibitory Controls

- The dorsolateral (DLPC) and orbitofrontal (OFC) prefrontal cortices are involved in inhibitory decisions, immediate versus delayed responses and weighing the importance of various goal-related behaviors.
- Addiction produces decreased sensitivity to non-drug reinforcers and decreased ability to inhibit maladaptive or disadvantageous behaviors.
- Inhibitory control problems may be picked up on neuropsychological



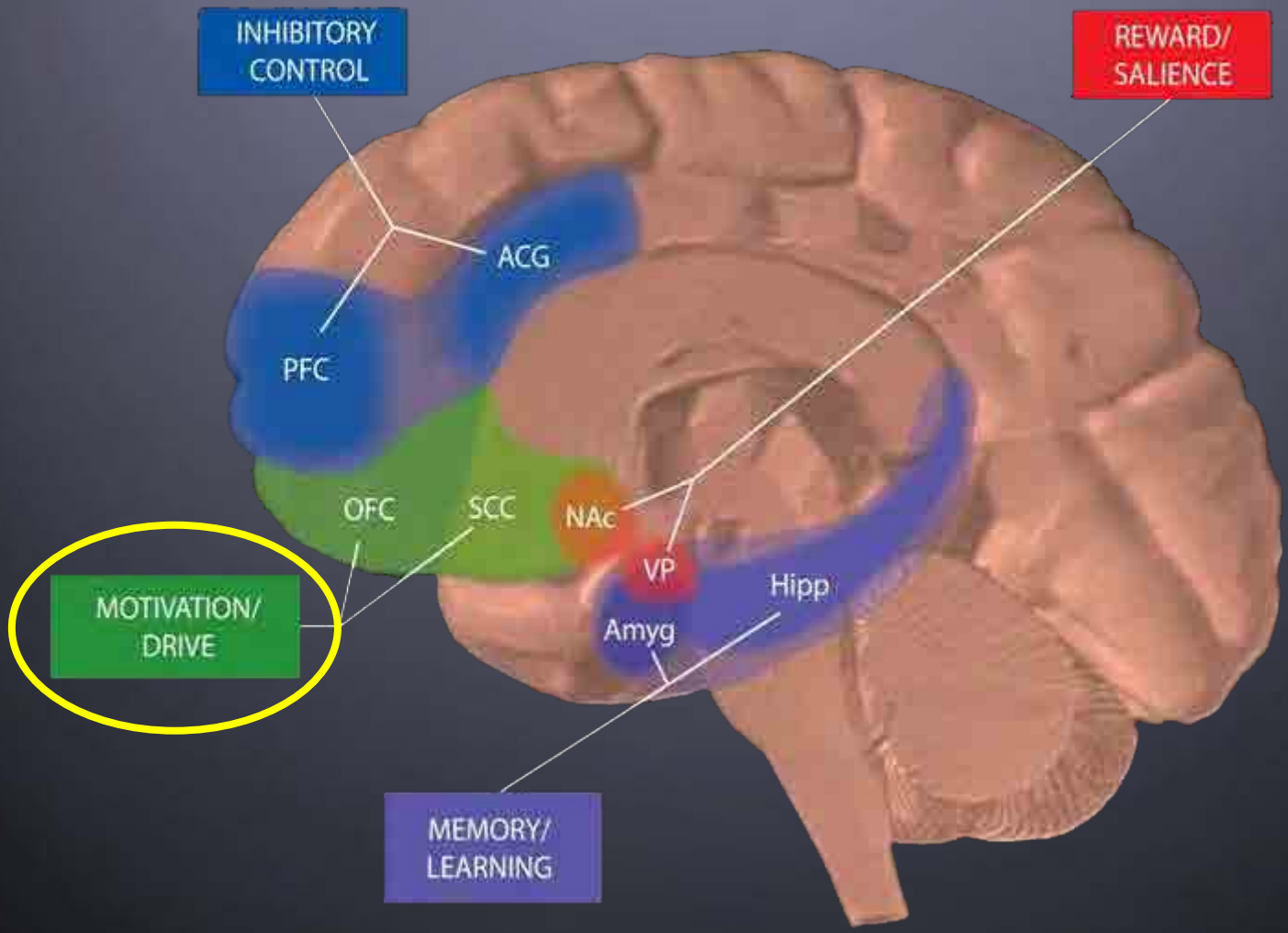
Goldstein, R. Z. and N. D. Volkow (2011). "Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications." Nature Reviews: Neuroscience 12(11): 652-669.

What does this mean for Treatment and Recovery?

- In most cases, external constraints must be used to interrupt destructive use.
- We cannot expect individuals in early recovery to execute conscious, effective decisions not to use.
- Environmental cues, emotional states and stress induced craving must be minimized.
- Exposure to even indirect substance triggers must be delayed until inhibitory controls come back online.

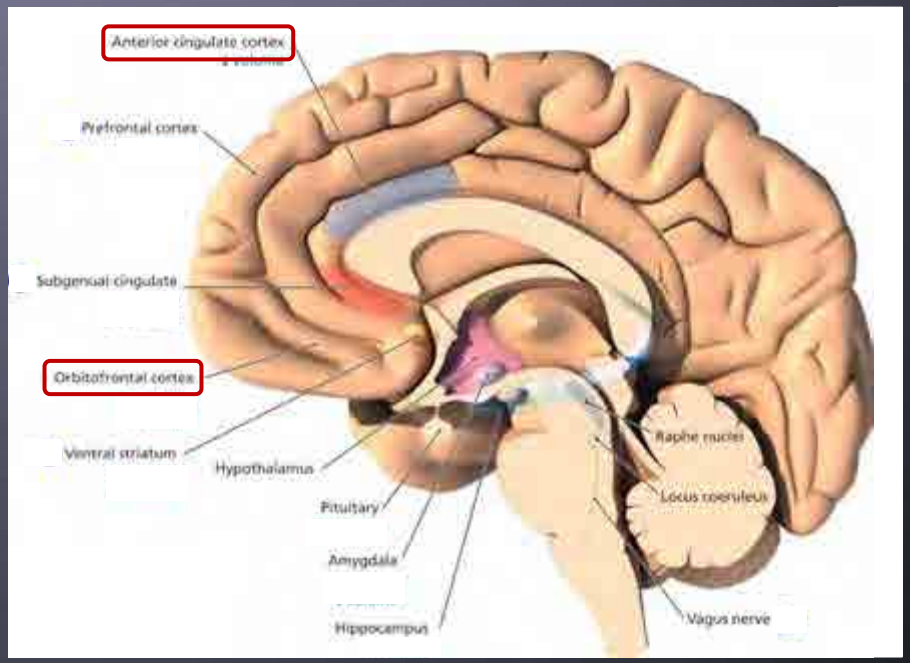
Loss of Inhibitory Controls

Brain Centers & Addiction



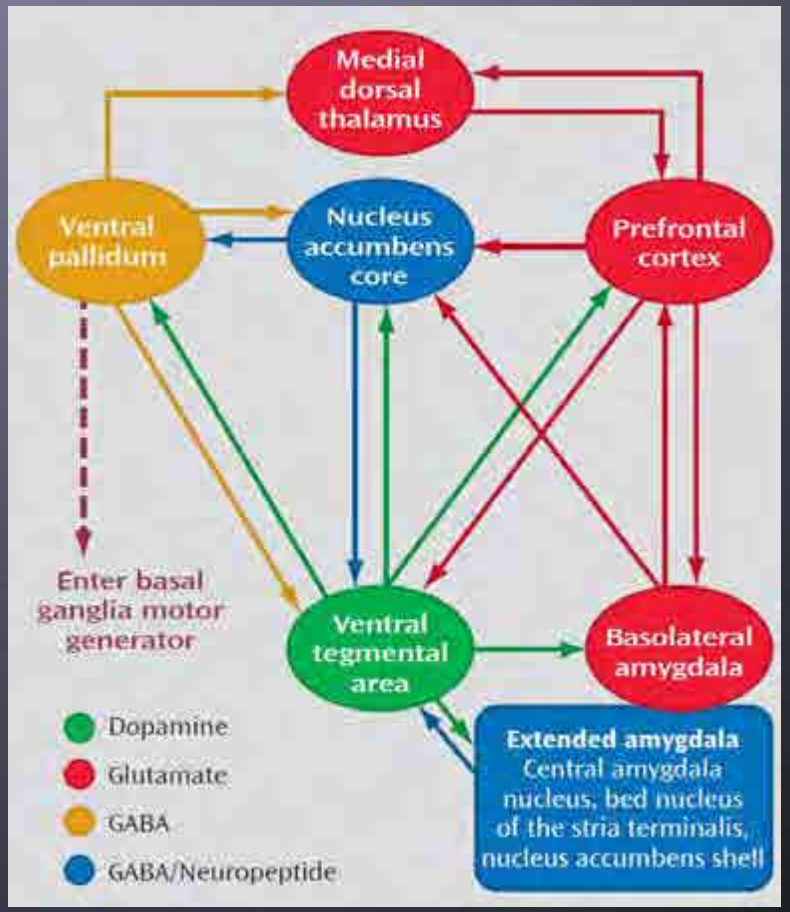
Addiction hijacks Attention and Motivation

- Under non-addicted conditions:
  - The Prefrontal Cortex (PFC) is creates a representation of goals, assigns a value to them and selects actions to attain goals.
  - The Anterior Cingulate Cortex focuses attention and monitors performance.



Addiction hijacks Attention and Motivation

- When addicted, addiction-related stimuli initiate a supraphysiological glutamatergic response sent to the nucleus accumbens which stimulates drug seeking.
  - Pathways from the OFC activate well learned drug foraging behaviors.
  - Activity in the ACC focus sustained attention on drug procurement behaviors.
- At the same time, changes in this circuit reduce the capacity of the prefrontal cortex to initiate responses to healthy goals.

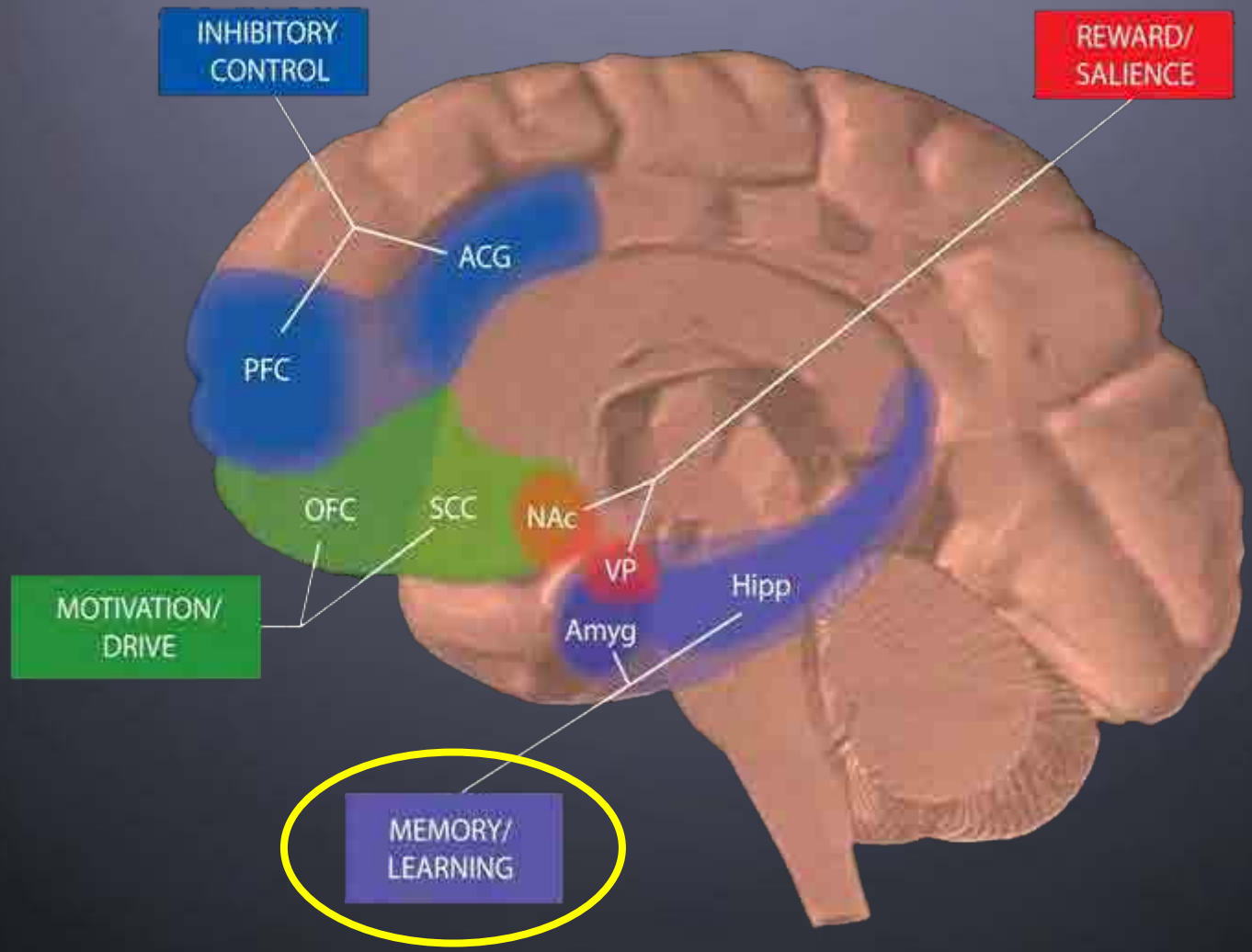


Kalivas, Peter W., Volkow, Nora. "The neural basis of addiction: a pathology of motivation and choice." American Journal of Psychiatry (2014).

What does this mean for Treatment and Recovery?

- Attentional problems are expected. Do not reflexively prescribe medications.
- One way of reclaiming attention is to track what is distracting (i.e., cravings). This means even the smallest craving should be acknowledged in early recovery.
- We should never judge an individual by stating "He is not motivated to get better."
- Contingency Management techniques can rewire the brain, rebuilding the motivation for healthier goals.

Brain Centers & Addiction



Addiction & Memory

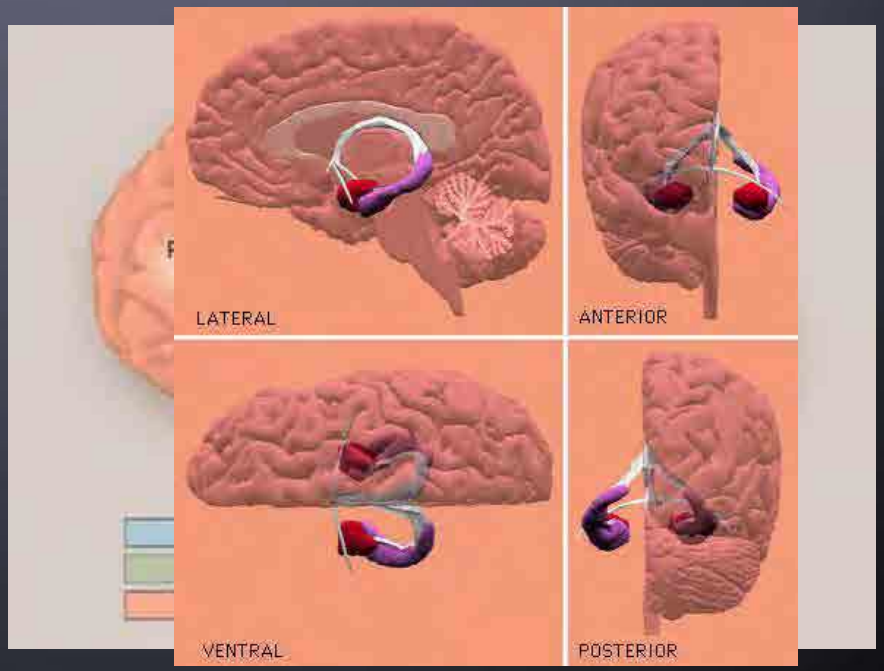
- Addiction shares striking similarities with neural plasticity associated with natural reward-based learning and memory.*
- Addiction affects memory in many ways:
  - Addiction sensitizes the brain to drug cues (many of which are unconscious).
  - Addiction entrains drug or alcohol foraging through Procedural Memory.
  - Addiction Flashbacks: PTSD-like recall of substance related events.

* Kelley, A. (2004). "Memory and Addiction: Shared Neural Circuitry and Molecular Mechanisms." Neuron 44(1): 161-179.

Procedural Memory

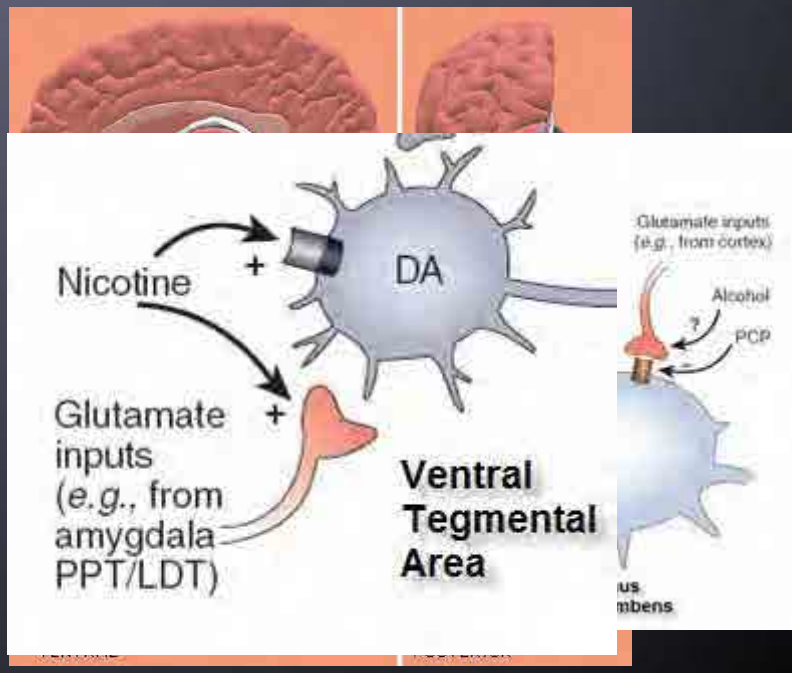
Brain structures in Procedural Learning

- Striatum and basal ganglia: two parallel information processing pathways diverge from the striatum, both acting in opposition to each other in the control of movement. The striatum is comprised predominately of GABA neurons. The system is activated by dopamine.
- Supplementary Motor Area: participate in the development of skills requiring internal elaboration of motor behavior.
- Cerebellum: Records the movement component of memory. Fine tunes procedural skills, increasing their efficacy. The automation of unconscious behavior occurs here.
- Amygdala: attaches emotional qualities and intensity to a memory.



Cue-based Craving

- The brain embeds the experience of substance use, adding environmental stimuli to produce an "addiction memory*."
- Building credence to the aphorism to "change playmates, playgrounds, and playthings."
- A strong cue remains embedded in the amygdala awaiting reactivation.
- The Amygdala signals the VTA through glutaminergic circuits that establish the hunger and urgency associated with a cue-based craving.
- Memory stored in the hippocampus and eventually becomes episodic memory located in the temporal lobe.



* Boening, J. (2001). "Neurobiology of an addiction memory." Journal of Neural Transmission 108(6): 755-765.

Addiction and Procedural Learning

- The basal ganglia are involved with behavioral learning. It is as automatic as stopping at a water fountain when thirsty.
- Attentional circuits (Anterior Cingulate) and dopamine-mediated incentive salience (VTA and NAc) direct the basal ganglia to record behaviors that result in drug procurement.
- Repeated use over time perfects and automates alcohol and drug procurement (basal ganglia and cerebellum).
- When stimulated by related cues (amygdala), automatic and partially automatic relapse behaviors ensue.
- Like all procedural learning, the knowledge is automated, rigid, life-long and partially unconscious.

What does this mean for Treatment and Recovery?

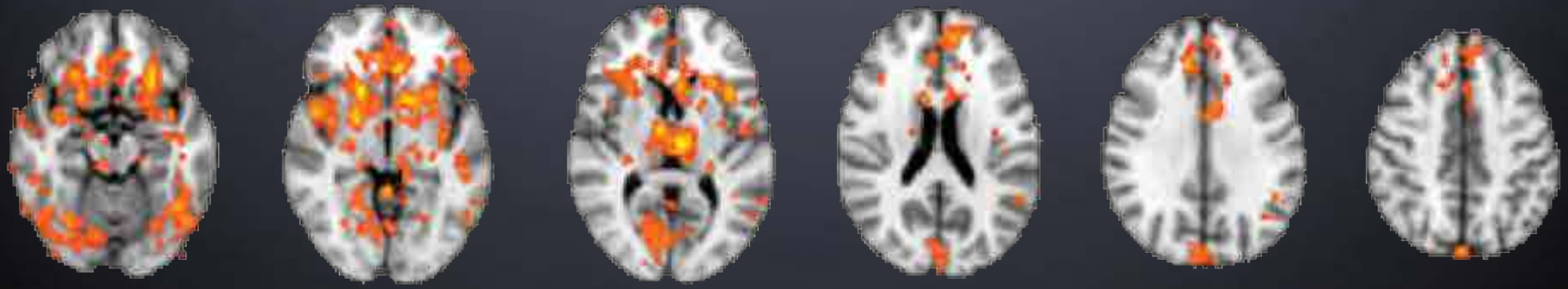
- Relapse is entrained at the procedural level, is automated, rigid, life-long and at least partially unconscious.
- Listening to lectures about what to do in recovery, by themselves, is ineffective. Recovery skills must be practiced.

What happens with PTSD?

- The acute trauma is either too overwhelming or is repeated, preventing the individual from reprocessing the trauma
- The trauma "tape" becomes stuck in visual memory
- The victim numbs to avoid emotionally experiencing the trauma
- Dreams and further meaning-extraction does not occur, rending the organism susceptible to recurrence
- The victim may engage in "trauma re-enactment" to reactivate the release of endorphins and dopamine

Addiction Flashbacks

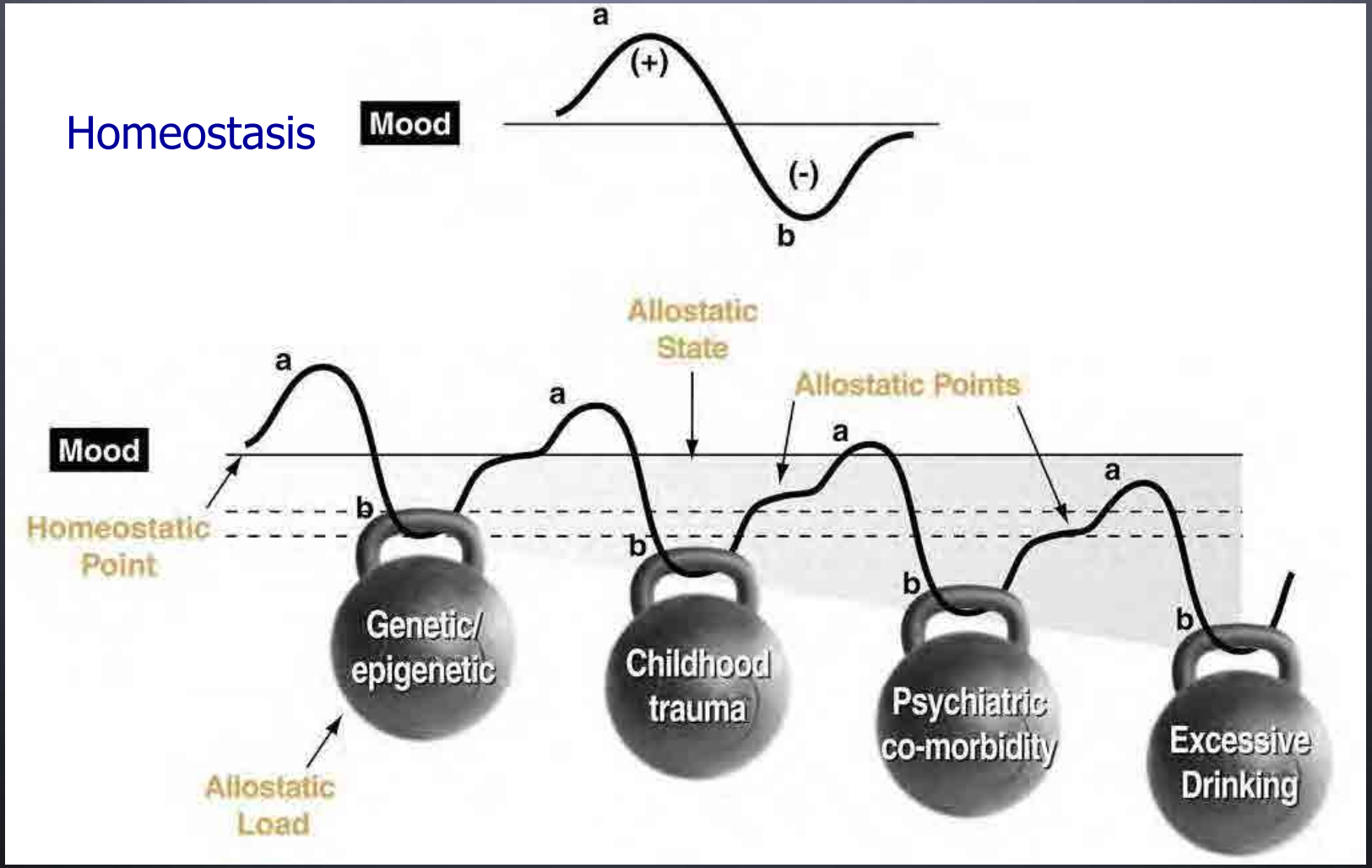
- Intrusions have sensory properties (mental images, i.e., not just verbal thoughts).
- Come to mind unbidden (i.e., not those deliberately recalled).
- Most likely shares the same circuitry with PTSD



What does this mean for Treatment and Recovery?

- Cognitive learning might be easier to attain, but is nearly useless in treating addiction. Procedural learning is vastly superior.
- Addiction psychotherapy should unearth "substance-related video clips," teaching the individual how to manage them when they occur.
- At the very least, treatment should build a list of substance cues that define a plan to extinguish each of them in the first years of recovery.
- Individuals who are susceptible to PTSD are more susceptible to addiction. Techniques such as EMDR, brain spotting and exposure therapy are critical for a substantive recovery.
- Therapists and members of twelve-step groups should validate that some memories are fixed, they never go away.

Stress, Trauma, and Mood Disorders



Koob, G. F. and J. Schulkin (2019). "Addiction and stress: An allostatic view." Neuroscience & Biobehavioral Reviews 106: 245-262.

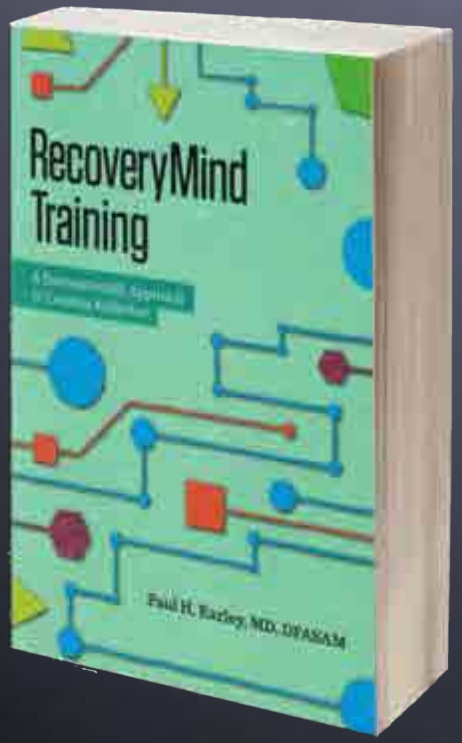
What does this mean for Treatment and Recovery?

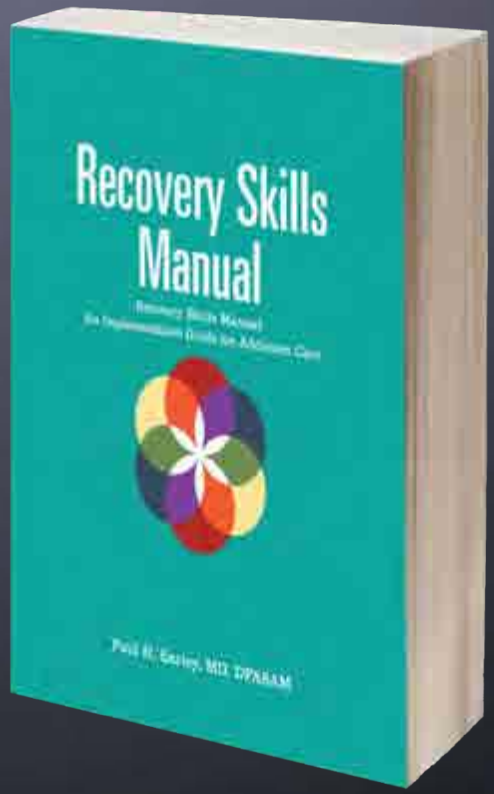
- Individuals prone to Addiction may have genetic "allostatic loading" to respond poorly to stress and trauma. Therapeutic tools aimed at stress tolerance and developing a balance outlook on life are relapse prevention tools.
- Childhood trauma is especially progenerative for addiction. Best case damage repair through therapy is imperative in such cases.
- When an independent depressive illness is diagnosed, treat aggressively. When in doubt, treat using medications and therapy.

Stress, Trauma, and Mood Disorders

For More Information

- Web-based information: ww.paulearley.net
- E-mail: paulearley@earleyconsultancy.com





THE OPIOID CRISIS HITS HOME: SOLUTIONS FOR OUR PRACTICE

ONE PILL CAN KILL:

SONG FOR CHARLIE PRESENTS: "FENTAPILLS - YOU NEED TO KNOW" (YOUTUBE.COM)

HTTPS://WWW.DEA.GOV/ONEPILL/TEENS

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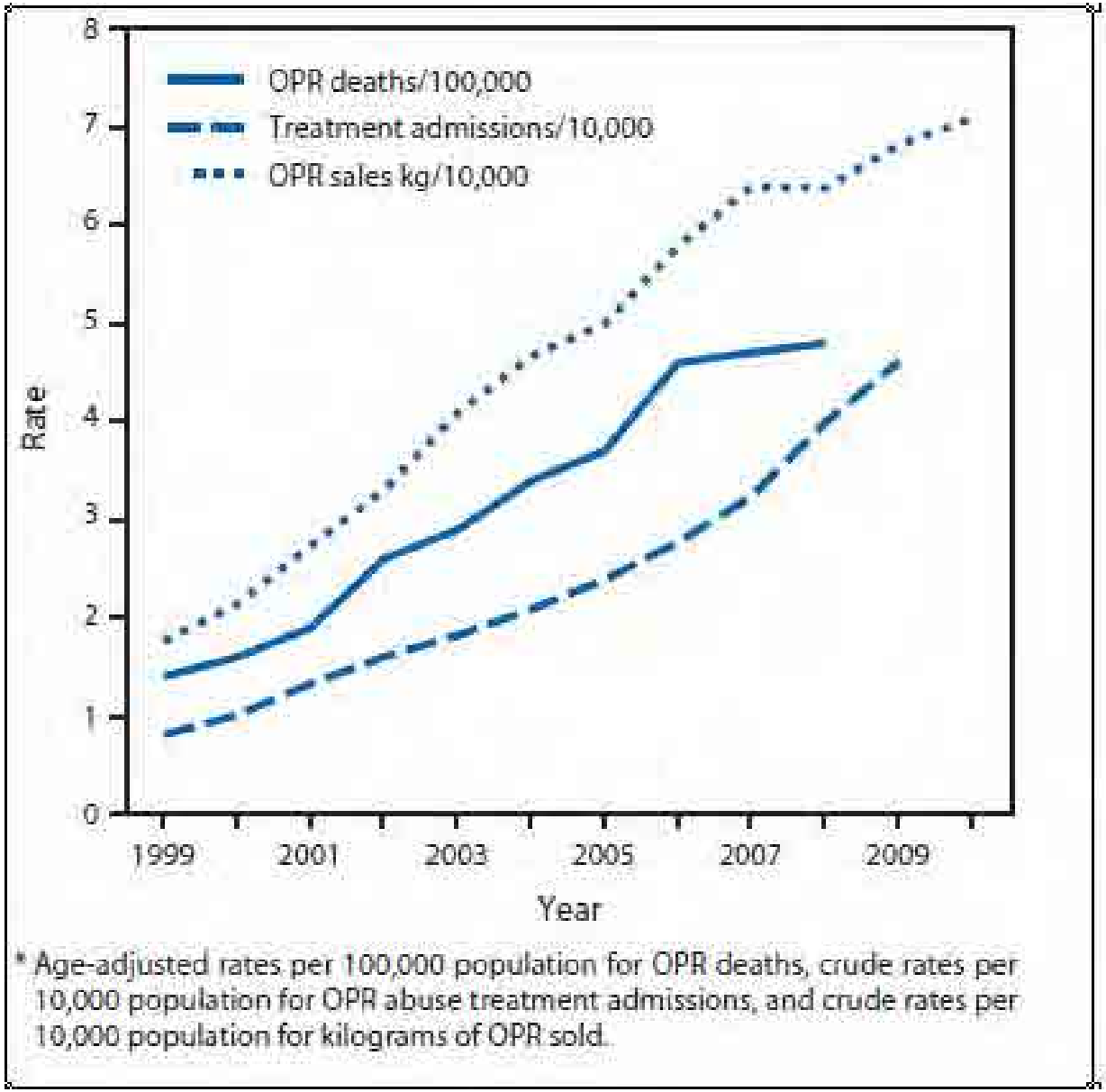
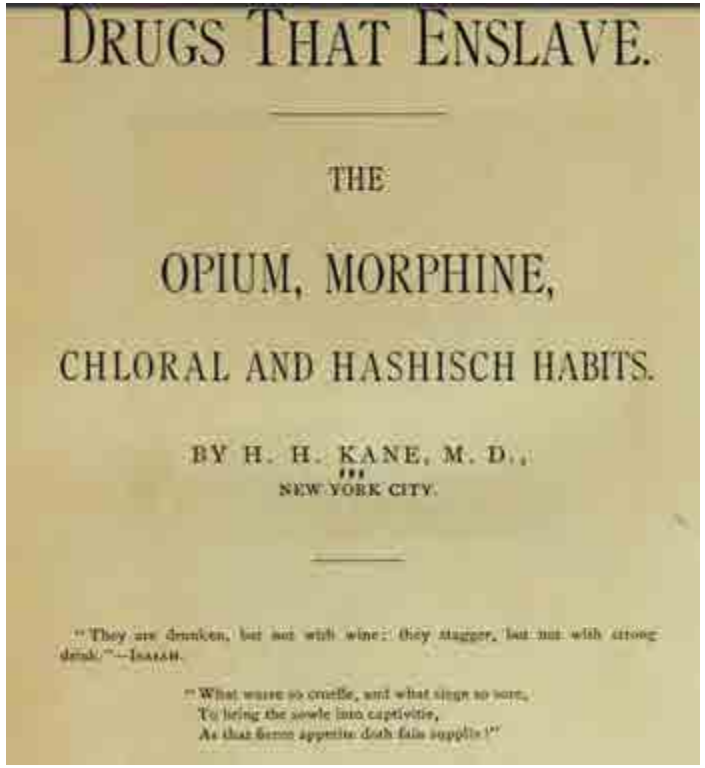
RATES OF OPIOID PAIN RELIEVER (OPR) SALES, DEATHS AND TREATMENT ADMISSIONS INCREASED IN PARALLEL: 1999 - 2008



2011-CDC-MMWR Vol. 60 No. 43 p.1487-1492

FIRST OPIOID EPIDEMIC IN THE UNITED STATES: 1855 - 1914



DRUGS THAT ENSLAVE.

THE

OPIUM, MORPHINE,

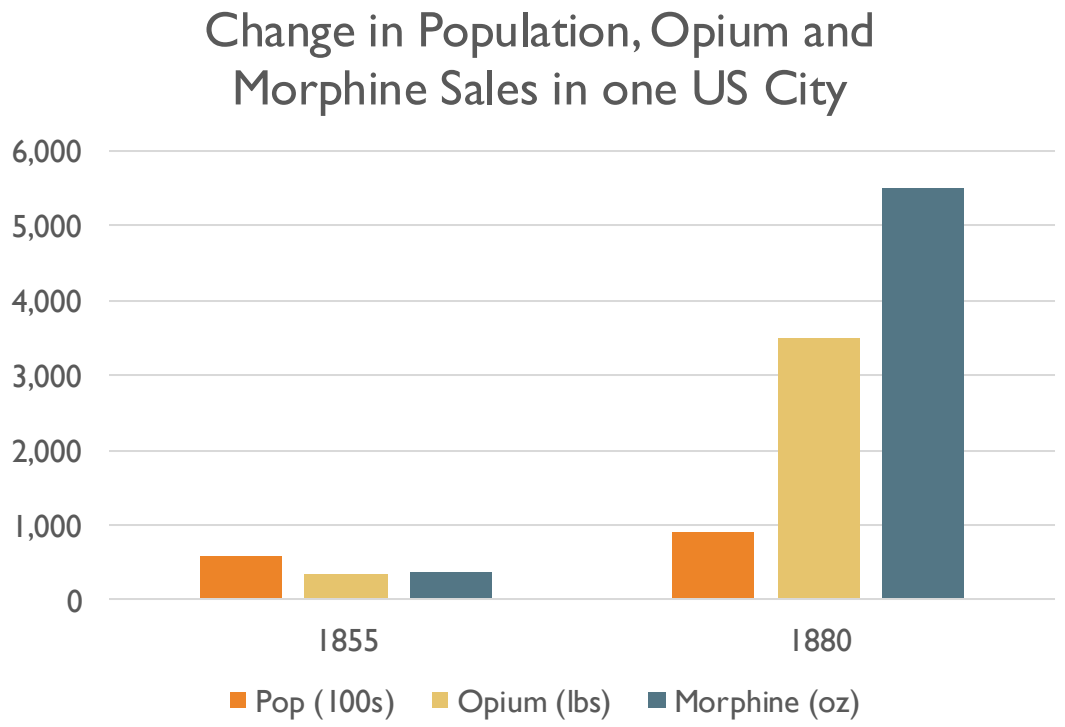
CHLORAL AND HASHISCH HABITS.

BY H. H. KANE, M. D.,

NEW YORK CITY.

"They are drunken, but not with wine; they stagger, but not with strong drink."—Isaiah.

"What worse or cruelle, and what siege so sore,
To bring the soule into captivitie,
As that fierce appetite doth false supplie?"



IATROGENIC ORIGINS OF THE OPIUM AND MORPHIA "HABIT"

- "Finding ***pain***, nervousness, and hysteria constantly claiming his attention, and that nothing relieves them so well as opium (or its alkaloid morphia which is six times the parent strength),
- The physician resorts to their use more and more freely, expecting that as soon as the more distressing symptoms pass away to pursue another more permanent treatment."
- "The patient, however, having once experienced relief, insists upon the further use of the drug, sometimes feigns illness to procure it…drifts rapidly into the ***habit***…"
- "Today thousands of educated and respectable people in all countries and all classes are habitues;
  - Slaves to a habit that is more demanding that the hardest task master, that they loathe…yet binds them in chains they are wholly unable to break…Suicide is on the increase.

1881-Kane-Drugs That Enslave-The Opium, Morphine, Chloral and Hashisch Habits-New York

SOLUTIONS: RESTRICT MEDICAL USE
TREAT DRUG-INDUCED NARCOTIC DEPENDENCE

- 1898- Bayer introduces Heroin
  - Diacetylmorphine- non-addicting alternative to morphine and cough suppressant
- 1899- Bayer introduces Aspirin
  - Acetylsalicylic acid- non-addicting pain reliever
- 1910- Bayer stops marketing Heroin
- 1914- Harrison Narcotic Tax Act
- 1935- US Narcotic Farm – Lexington, KY
  - State of the art treatment- detox & rehabilitation- 22% to 40% success
  - Laboratory to study narcotic dependence
  - Described opioid tolerance, withdrawal and its treatment by methadone.
- 1960- Iatrogenic opioid dependence was rare, but illicit heroin addiction and related deaths rising.
- 1962- Dole, Nyswander, Kreek- Methadone maintenance treatment for opioid dependence

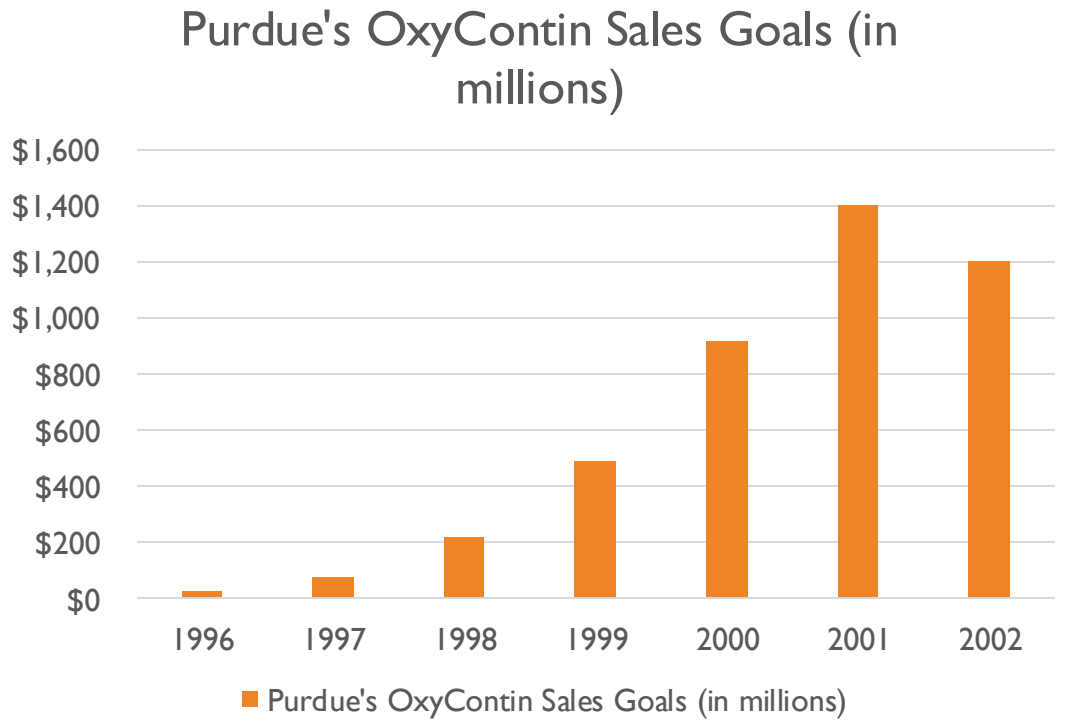
PALLIATIVE CARE MOVEMENT TO LONG-TERM OPIOIDS FOR PAIN

- Perceived undertreatment of chronic pain
  - Laws or regulations passed in >20 states to allow use of opioids for chronic pain
- Expert opinion that risk of abuse or addiction is low in medical settings
  - 1980- Porter & Jick- NEJM Letter to the Editor= Case series
    - Addiction diagnosed in <1% of hospitalized patients treated with opioids; most prescribed <20 mg MEDD
  - 1986- Portenoy RK- Low risk of abuse in palliative care settings
  - 1989- Weissman & Haddox- Pseudoaddiction (i.e. fake addiction)- Case report
    - 17-year-old with acute leukemia & chest wall pain treated with iv morphine and iv meperidine
      - Patient increasing complaints, agitation, pain becomes more diffuse
      - Increasing opioids improves his comfort and opioid doses decrease as pulmonary infiltrates resolve.
- 1996- Purdue Pharma introduces OxyContin- FDA-approved for cancer-related pain
  - Immediate marketing plan to expand to low back pain market
  - 6 – 7 million cancer patients vs. 35 million back pain patients

https://kffhealthnews.org/news/purdue-and-the-oxycontin-files/

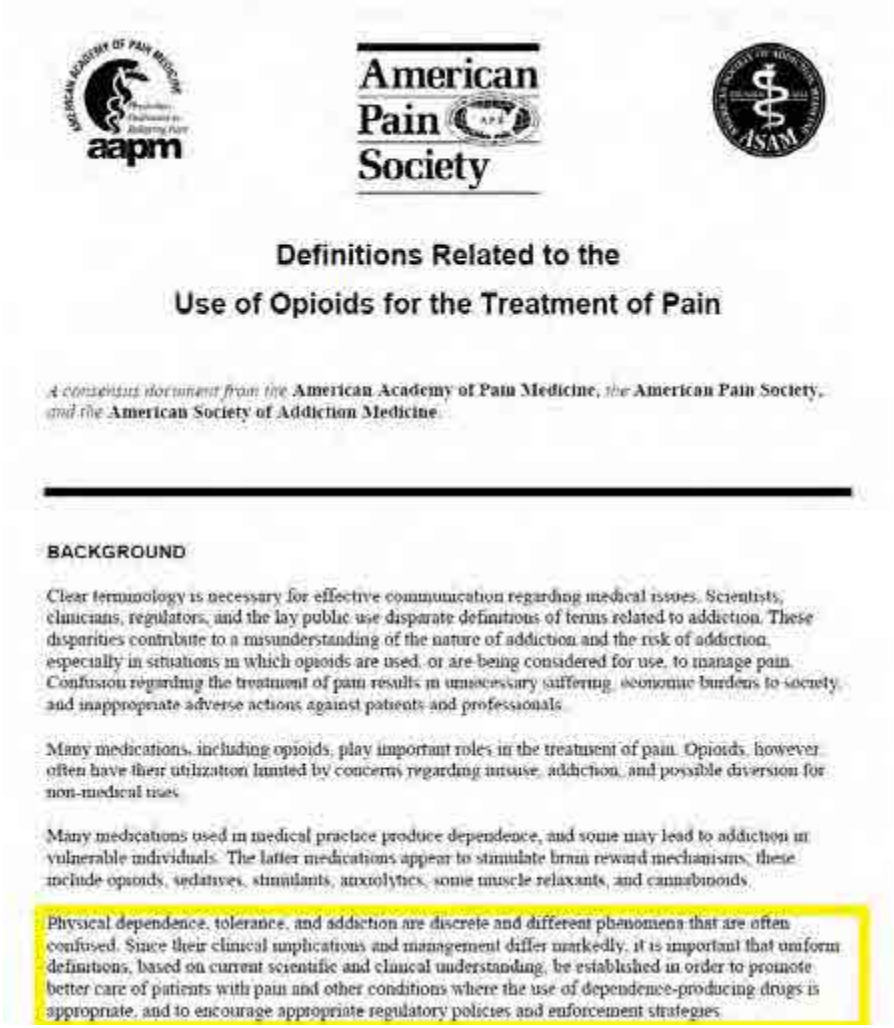
PURDUE PHARMA'S OXYCONTIN MARKETING PLANS

- FDA-approved OxyContin for cancer pain in 1996
- Increase sales by targeting non-cancer pain
- Key Messages: OxyContin is safe and effective for non-malignant pain
  - For patients:
  - 1997- "Partners Against Pain®"
  - For providers:
  - 1997- $250K educational grant to develop consensus guidelines for opioids for non-malignant pain
  - 1999- $90K for Addiction, Physical Dependence ,& Tolerance Terminology Visual



https://kffhealthnews.org/news/purdue-and-the-oxycontin-files/
Accessed July 8, 2024

2001 AMERICAN PAIN SOCIETY, AAPM, AND ASAM: CONSENSUS STATEMENT



American Pain Society

aapm

ASAM

Definitions Related to the Use of Opioids for the Treatment of Pain

A consensus document from the **American Academy of Pain Medicine**, *the* **American Pain Society**, *and the* **American Society of Addiction Medicine**

BACKGROUND

Clear terminology is necessary for effective communication regarding medical issues. Scientists, clinicians, regulators, and the lay public use disparate definitions of terms related to addiction. These disparities contribute to a misunderstanding of the nature of addiction and the risk of addiction, especially in situations in which opioids are used, or are being considered for use, to manage pain. Confusion regarding the treatment of pain results in unnecessary suffering, economic burdens to society, and inappropriate adverse actions against patients and professionals.

Many medications, including opioids, play important roles in the treatment of pain. Opioids, however, often have their utilization limited by concerns regarding misuse, addiction, and possible diversion for non-medical uses.

Many medications used in medical practice produce dependence, and some may lead to addiction in vulnerable individuals. The latter medications appear to stimulate brain reward mechanisms; these include opioids, sedatives, stimulants, anxiolytics, some muscle relaxants, and cannabinoids.

Physical dependence, tolerance, and addiction are discrete and different phenomena that are often confused. Since their clinical implications and management differ markedly, it is important that uniform definitions, based on current scientific and clinical understanding, be established in order to promote better care of patients with pain and other conditions where the use of dependence-producing drugs is appropriate, and to encourage appropriate regulatory policies and enforcement strategies.

- "Physical dependence (withdrawal)
- Tolerance and
- Addiction are discrete and different phenomena that are often confused."
- "Most specialists in pain medicine and addiction medicine agree that patients treated with prolonged opioid therapy usually do develop physical dependence and sometimes develop tolerance, ***but do not usually develop addictive disorders***." (*emphasis added*)
- No references, no data, no peer review

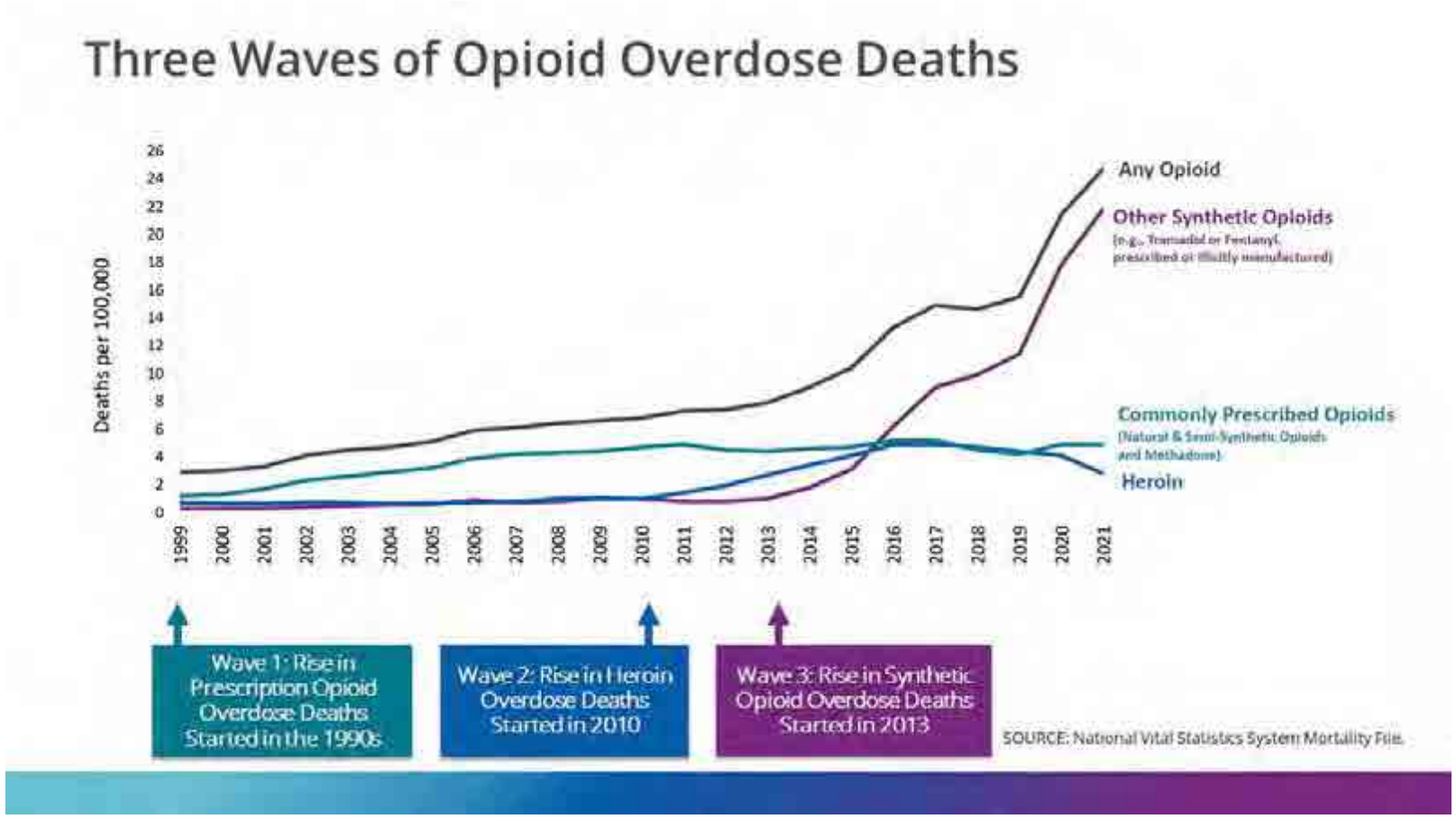
POPULATION EXPOSURE TO LONG-TERM OPIOIDS UNLEASHES WAVES OF OVERDOSE DEATHS

Wave 1: Increased opioid prescribing for non-malignant pain.

Some patients develop high tolerance and drug hunger that exceeds the supply from their pain treatment provider. Some turn to "doctor shopping" or "pill mills"

Wave 2: Illicit Heroin. Illicit drug dealers step up to meet growing demand.

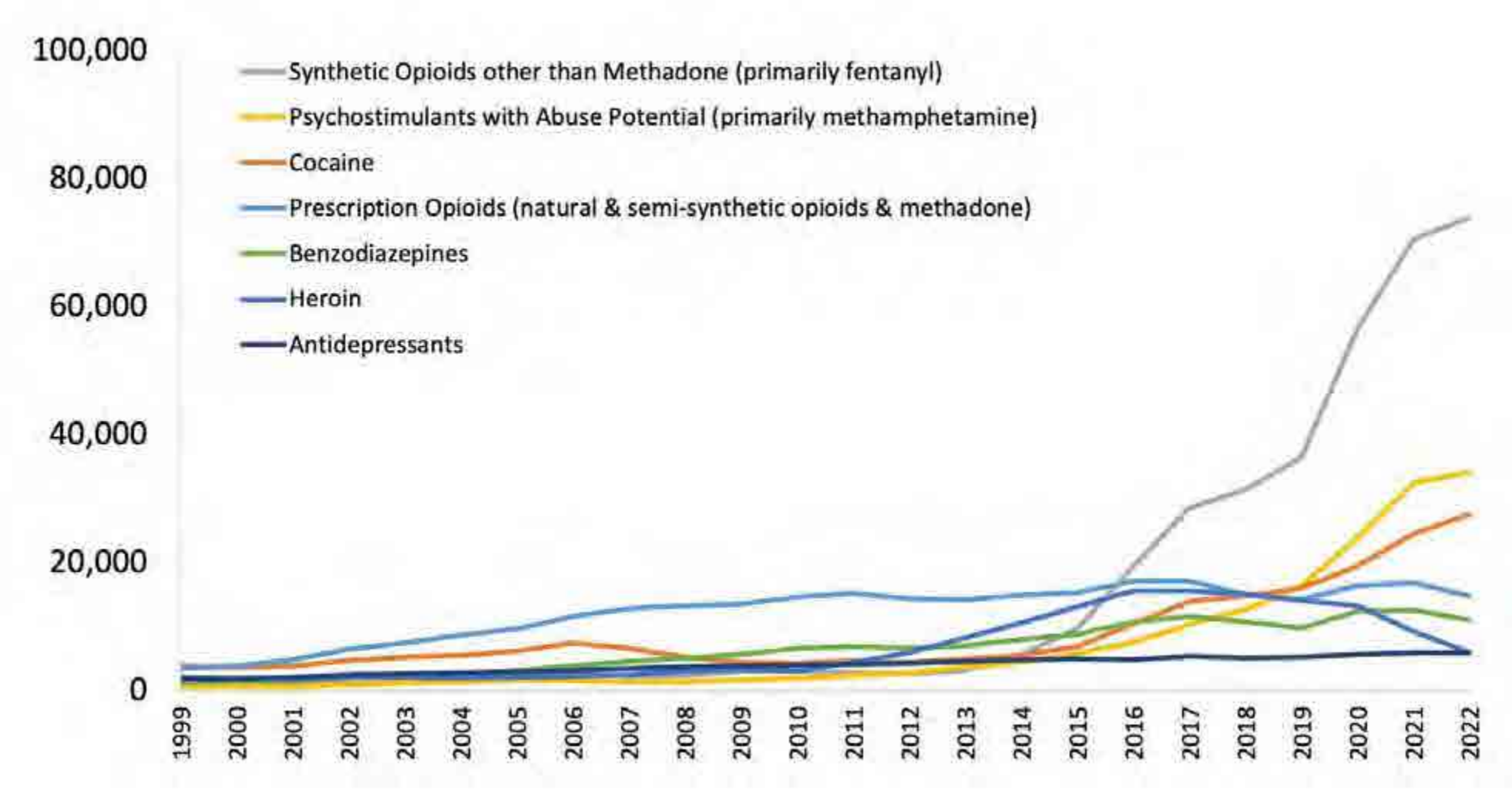
Wave 3: Synthetic opioids, Drug dealers introduce fentanyl into any white powder and into counterfeit pills to increase sales



https://www.cdc.gov/overdose-prevention/about/understanding-the-opioid-overdose-epidemic.html

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

U.S. DRUG OVERDOSE DEATHS- 1999 - 2022



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PRIMARY PREVENTION: NON-OPIOID THERAPIES RECOMMENDED

- "All patients with pain should receive treatment that provides the greatest benefits relative to risks."
- "Non-opioid therapies are at least as effective as opioids for many common types of acute pain."
  - Maximize nonpharmacologic and nonopioid therapies
- "Non-opioid therapies are preferred for subacute and chronic pain."
  - Maximize nonpharmacologic therapies (e.g. exercise)
  - Maximize nonopioid medications (e.g. NSAIDs)

CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022

Deborah Dowell, MD[1]; Kathleen R. Ragan, MSPH[1]; Christopher M. Jones, PharmD, DrPH[2]; Grant T. Baldwin, PhD[1]; Roger Chou, MD[3]

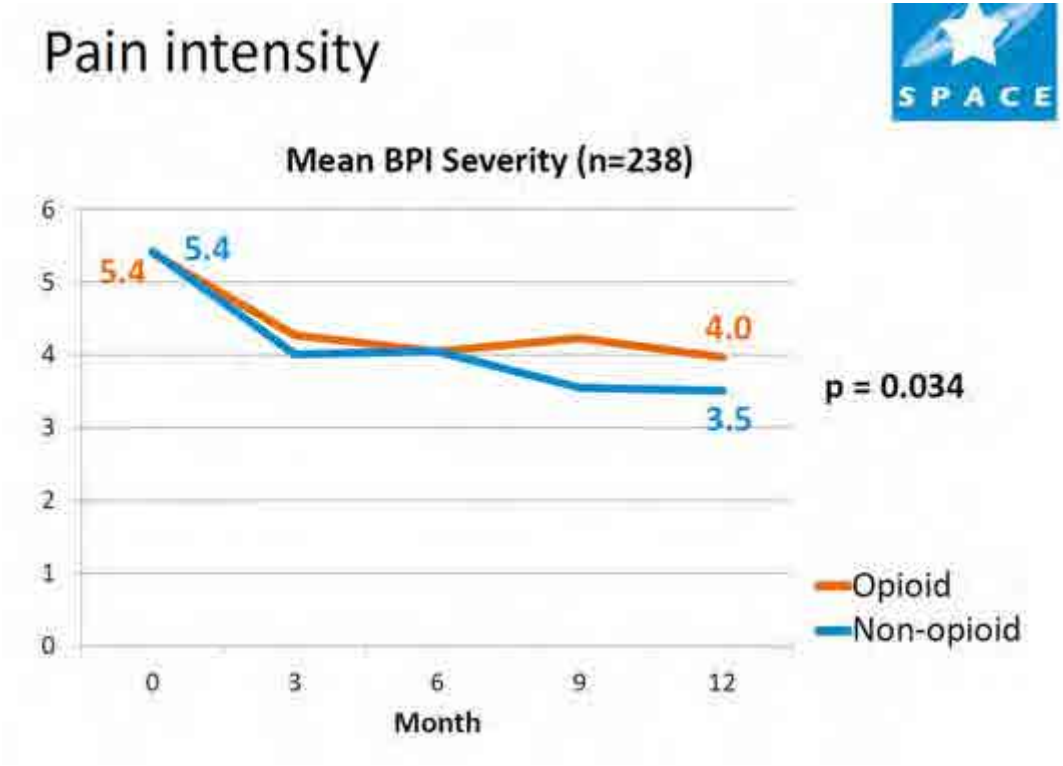
1Division of Overdose Prevention, National Center for Injury Prevention and Control, CDC;

2Office of the Director, National Center for Injury Prevention and Control, CDC;

3Pacific Northwest Evidence-based Practice Center and Oregon Health & Science University, Portland, Oregon

SPACE TRIAL

- One year VHA trial in Primary Care for Low Back Pain and Osteoarthritis
- N = 240
- Open-label for patients and clinicians
- Individualized collaborative care management
- Assessments masked
- Average opioid dose 26 mg vs. 1 mg MEDD
- No difference in function
- Pain and adverse events worse in opioid group
- No overdose deaths or emergent OUD



Krebs E. JAMA 2018

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EDUCATE PATIENTS ABOUT THE MEDICATION: WHAT ARE OPIOIDS?

- Chemicals that activate opioid receptors in our brains
- Exogenous opioids mimic natural neurotransmitters- e.g. endorphins and enkephalins (active for msec)
- 3-types of Opioids (active for min.- hours)
  - Opiates- chemicals occurring in the opium poppy - e.g. opium, morphine, codeine
  - Semi-synthetics – e.g. oxycodone (Oxycontin®), buprenorphine, hydrocodone, diacetylmorphine
  - Synthetics – e.g. fentanyl, carfentanyl, methadone
- All opioids are potentially addicting
- All opioids can cause death by stopping breathing

OPIOID EFFECTS:

Acute Intoxication

- Pain and cough relief
- Euphoria and anxiety/depression relief
- Pupillary constriction – "Pinpoint pupils"
- Sleepiness > drowsiness > coma (unresponsive)
- Muscle relaxation, slurred speech
- Slowed breathing > gurgling, chest rattling > apnea
- Slowed digestion, decreased bowel sounds
- Lower body temperature, lower heart rate

Chronic Use

- Tolerance and hyperalgesia (increased pain sensitivity)
- Withdrawal:
  - Dilated pupils
  - Fever, sweating, runny nose, watery eyes
  - Nausea, vomiting, diarrhea
  - Muscle aches, bone aches, muscle spasms (i.e. "kicking the habit")
  - Yawning, chills, piloerection (i.e. "cold turkey")
  - Insomnia, dysphoria, irritability

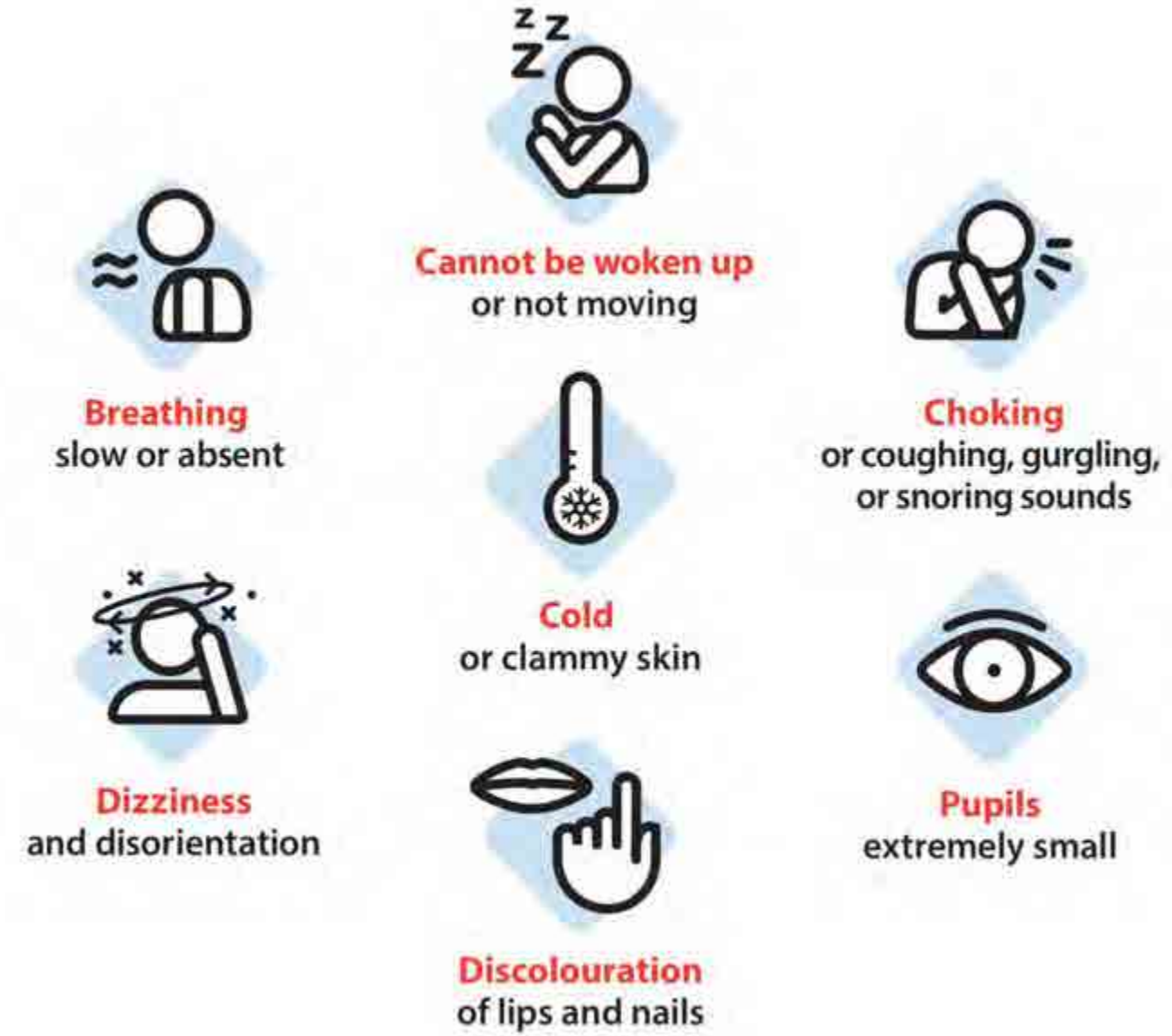
EDUCATE PATIENTS ABOUT THE RISKS OF COUNTERFEIT PILLS: WHY ARE FENTANYL AND ANALOGUES MORE DANGEROUS?

https://www.clearvuehealth.com/im/opioidlethaldoses/

- Potency
- Illicit manufacturing processes:
- https://www.youtube.com/watch?v=16m_5zSE1h8

TEACH PATIENTS HOW TO RECOGNIZE AND RESPOND TO OPIOID OVERDOSE

- Administer naloxone (spray into one nostril)
- Turn the person on their side
- Call 911 immediately-
  - Describe symptoms- unresponsive, not breathing, etc.
- Rescue breathing – one breath every 5 seconds, if needed.
- If needed, readminister naloxone (spray into the other nostril)



Walgreens: https://www.youtube.com/watch?v=SqgWKvsFYuA
canaPHEM: https://www.youtube.com/watch?v=WnjgrRNMfKM
Spectrum Health: https://www.youtube.com/watch?v=LmxZkNW7VKM

WHAT ABOUT INFORMED CONSENT FOR OPIOIDS?

- My recommendation is to inform all patients with chronic pain for whom you are prescribing opioids about the risks of developing opioid dependence/OUD.
- For those with chronic pain who are considering opioids review all 6 of the ICD-10 features (or all 11 DSM-5 criteria) and explain that up to 41% of patients on LTOT develop these symptoms. (Boscarino JA: 2015 Subst Abuse Rehab)
- Opioids are not the first-line treatment for chronic pain. Overtime, daily opioid use can make pain worse and require increasing doses.
- Increasing tolerance is a warning sign that it may be difficult to discontinue the medication when adverse events like constipation, falls, oversedation outweigh modest benefits.
- Encourage your patient to express any concerns and questions. Reassure them that you want to work with them to prevent and treat any emerging opioid dependence symptoms that develop. The earlier you become aware, the more effective prevention and treatment will be.
  - "I'm not worried about you abusing the drug; I'm worried about the drug abusing you."

GEORGIA'S 9-1-1 MEDICAL AMNESTY LAW

- The law expands access to naloxone by authorizing trained first responders, including law enforcement officers, firefighters, and EMS personnel to administer the medication.
- Additionally, the law establishes limited civil and criminal immunity for medical professionals who prescribe naloxone, **and laypeople who administer it to a person suspected of suffering from an opioid overdose**.
- More information at: https://www.gnrhealth.com/the-georgia-9-1-1-medical-amnesty-law/

AGENDA

- The Opioid Epidemic:
  - One Pill Can Kill- How Did We Get Here?
  - Opioid pain relievers + Marketing
- **What can we do about it?**
- Primary prevention: Opioid-sparing pain care
- Secondary prevention: Mitigate risks in patients on long-term opioids
  - Educate patients about overdose and recommend/co-prescribe naloxone
  - Mitigate risks of opioid therapy for chronic pain
    - Lowest effective dose
    - Close monitoring (PDMP, urine drug tests)
    - Shared decision-making for increasing and tapering opioids and benzodiazepines
- **Tertiary prevention:**
  - Use shared decision-making to treat opioid dependence with indicated medication

OPIOID DEPENDENCE (ICD-10)

Opioid Dependence (3 or more features)	Example Behaviors
A strong desire to take the drug	Distracting intrusive thoughts about the next dose of opioids
Difficulties in controlling opioid use	Taking a larger dose than prescribed; unable to stop when indicated Repeatedly driving under influence
Persisting in opioid use despite harmful consequences	Request for more opioids after adverse events (e.g. overdose) Continued use despite poor performance or family/friend concerns
Higher priority given to opioid use than to other activities and obligations	Spending a lot of time frequenting EDs & clinics to obtain opioids Progressive neglect of tasks and role obligations Stopping previously enjoyed activities (e.g. sports, friends, etc.)
A physiologic withdrawal state	Sweating, nausea, vomiting, diarrhea, muscle/bone aches, runny nose
Tolerance	Requires larger doses for effect (e.g. pain relief)

https://www.pbm.va.gov/PBM/AcademicDetailingService/Documents/508/IB10-933_OUD-ProviderAD-EducationalGuide_508Ready.pdf

WHAT IF THE PERSON IS OPIOID DEPENDENT (HAS DSM-5 OUD)? OFFER MEDICATION

- Medication is the gold-standard for treating opioid use disorder/opioid dependence.
  - Medication reduces the risk of relapse by about 50% compared to placebo; improves retention 75% vs. 0% (Kakko, 2003)
  - Medication reduces the risk of opioid overdose death by about half (OR MMT = 0.41, Bup = 0.62) (Larochelle, 2018)
    - Reduces opioid craving
    - Prevents relapse
    - Reduces risk of overdose death, if relapse occurs
- Counseling and/or mutual help groups (AA/NA/Smart Recovery) can help.
  - I recommend both medication and counseling for most people with OUD
- **Detoxification without initiating maintenance medication can increase the risk of opioid overdose by reducing tolerance without protecting against relapse**.

1. Kakko J, et al. 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomised, placebo-controlled trial. Lancet. 2003 Feb 22;361(9358):662-8
2. Larochelle MR, et al. Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality: A Cohort Study. Ann Intern Med. 2018 Aug 7;169(3):137-145.

THREE FDA-APPROVED MEDICATIONS FOR OPIOID DEPENDENCE

Three FDA-approved medications	Best for whom?	Where available? (See Findtreatment.gov)
Naltrexone (opioid blocker- long-acting injectable recommended over once daily oral tablet)	Those without opioid tolerance and those who prefer non-opioid options	Most accredited SUD treatment programs and physicians' offices
Buprenorphine (partial opioid agonist available as once daily sublingual film/tablet or long-acting injectable)	Those with moderate to high opioid tolerance and withdrawal	Many SUD treatment programs and physicians' offices
Methadone (full opioid agonist available as once daily oral liquid)	Those with high opioid tolerance who would benefit from daily clinic contact until stabilized	Only licensed and accredited Opioid Treatment Programs (OTPs a.k.a. Methadone Clinics)

REFERENCES

- Boscarino JA, Hoffman SN, Han JJ. Opioid-use disorder among patients on long-term opioid therapy: impact of final DSM-5 diagnostic criteria on prevalence and correlates. Subst Abuse Rehabil. 2015 Aug 19;6:83-91
- Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022. MMWR Recomm Rep. 2022 Nov 4;71(3):1-95.
- Drexler K, Edens EL, Trafton JA, Compton WM. In the balance: No new diagnosis needed in addition to opioid use disorder to study harms associated with long-term opioid therapy. Addiction. 2024 Jan;119(1):6-8
- Kakko J, Svanborg KD, Kreek MJ, Heilig M. 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden. Lancet. 2003 Feb 22;361(9358):662-8.
- Larochelle MR, Bernson D, Land T, *et al.* Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality: A Cohort Study. Ann Intern Med. 2018 Aug 7;169(3):137-145.
- Porter J, Jick H. Addiction rare in patients treated with narcotics. N Engl J Med. 1980 Jan 10;302(2):123.
- Portenoy RK. Opioid therapy for chronic nonmalignant pain: clinician's perspective. J Law Med Ethics. 1996 Winter;24(4):296-309
- Weissman DE, Haddox DJ. Opioid pseudoaddiction--an iatrogenic syndrome. Pain. 1989 Mar;36(3):363-366.

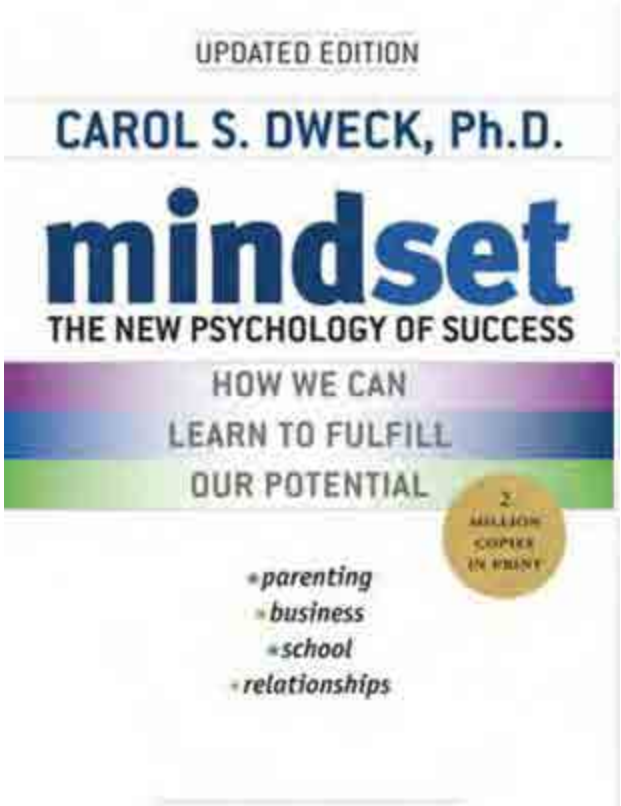
QUESTIONS?

Finding Joy in Medicine
A story of Adversity, Creativity and Community

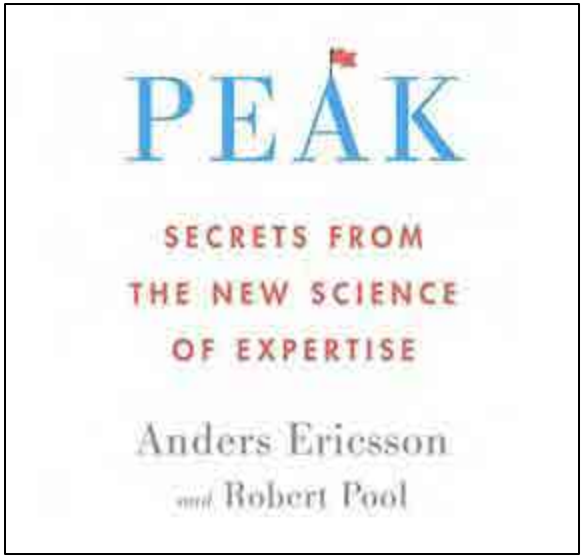
Reza Manesh, MD & Rabih Geha, MD

Purpose

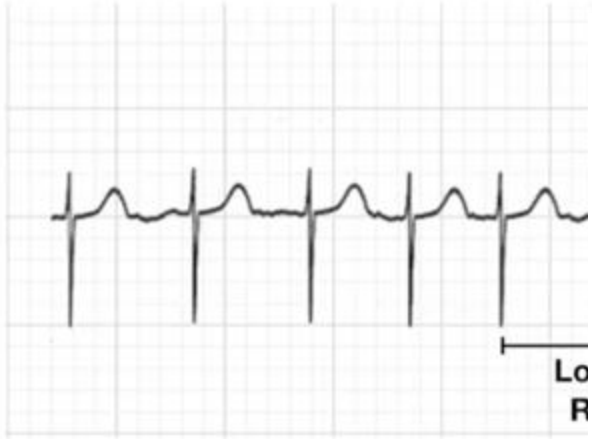
Mistakes

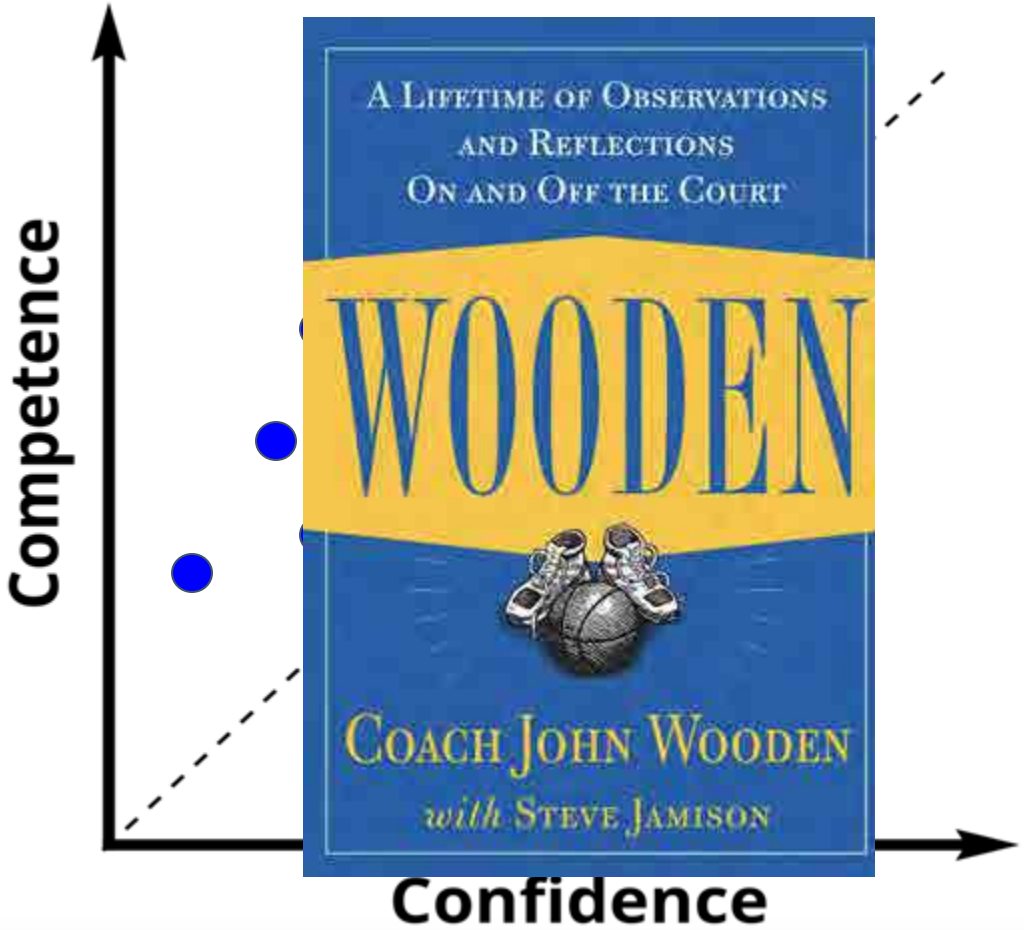

UPDATED EDITION
CAROL S. DWECK, Ph.D.
mindset
THE NEW PSYCHOLOGY OF SUCCESS
HOW WE CAN
LEARN TO FULFILL
OUR POTENTIAL
2 MILLION COPIES IN PRINT
•parenting
•business
•school
•relationships

Passion

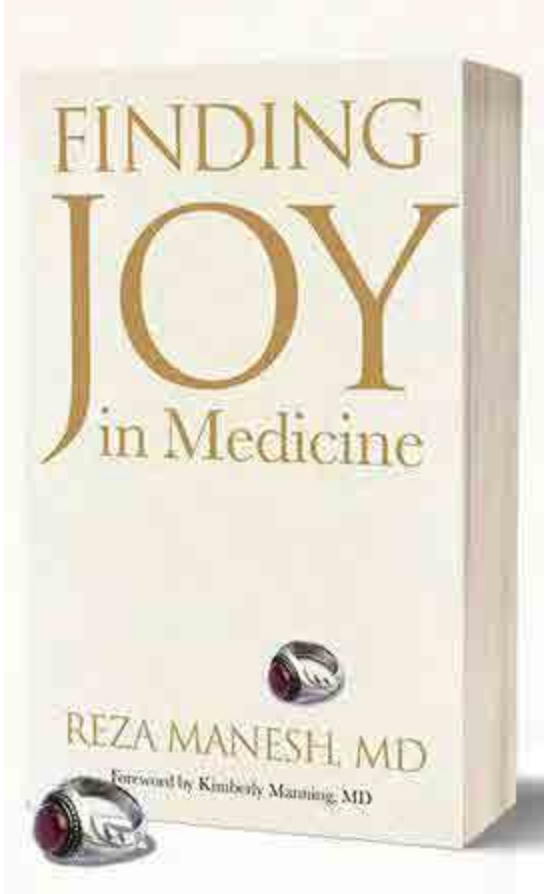

PEAK
SECRETS FROM
THE NEW SCIENCE
OF EXPERTISE
Anders Ericsson
and Robert Pool

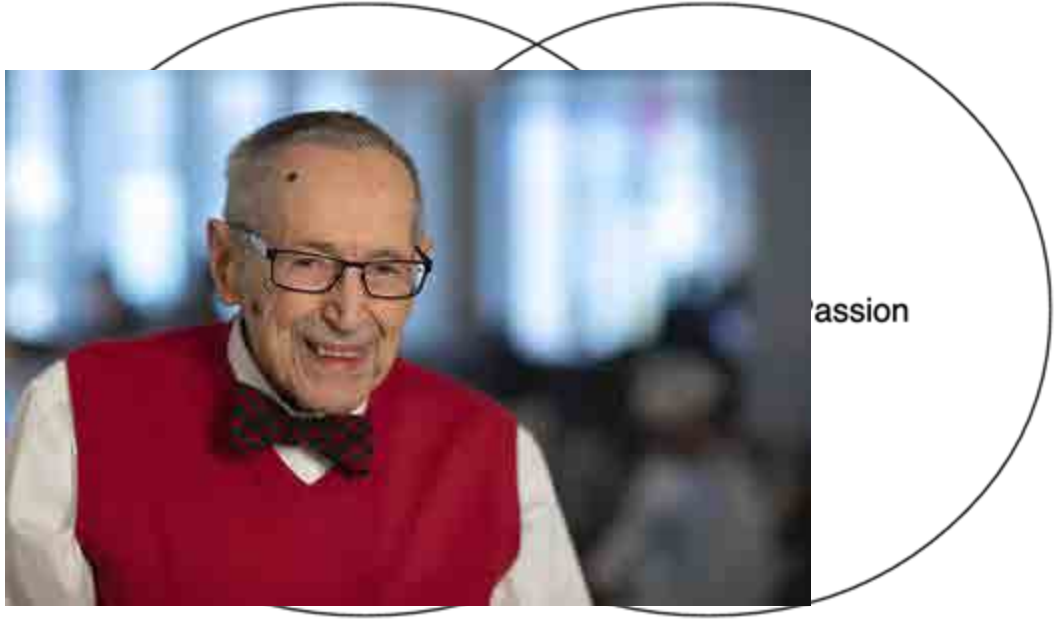
Imposter Syndrome





Our Formula


FINDING
JOY
in Medicine
REZA MANESH, MD
Foreword by Kimberly Manning, MD


assion

DDx in Neurology = Localization x Time Course

Localization

"Where"

CNS

- Brain
- Brainstem
- Cerebellum
- Spinal Cord

PNS

- Root(s)
- DRG
- Plexus
- Nerve(s)
- NMJ
- Muscles

Time Course

"When"

Hyperacute
Sec-Min

- Vascular
  - Stroke
  - Hemorrhage
  - SAH
- Seizure
- Migraine
- Trauma

Acute
Hours-Days

- Infections
  - Bacteria
  - Viral
- Inflammatory
  - GBS
  - MS Flare

Subacute
Wks-Months

- Infections
  - TB
  - Fungal
- Inflammatory
  - CIDP
  - Antibody-Mediated
- Neoplasm

Chronic
Months-Years

- Degenerative

Toxic/Metabolic

Dx


THE CURB SIDERS
INTERNAL MEDICINE

Dx ABOUT US PODCAST MORNING REPORT RESOURCES RESIDENCY MATCH SPACED LEARNING LANGUAGES

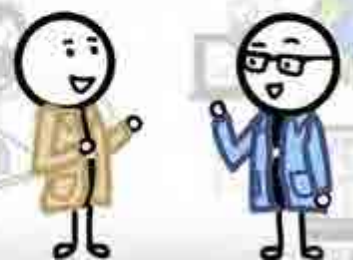
The Clinical Problem Solvers

Democratizing clinical reasoning education

Podcast

Morning Report

Frameworks - Scripts



+ RLR CPSolvers

Get Involved!

CPSolvers Academy

This website is best viewed on a computer.

Clinical Unknown with The Clinical Problem Solvers

2024 Southern Medical Association Annual Scientific Assembly

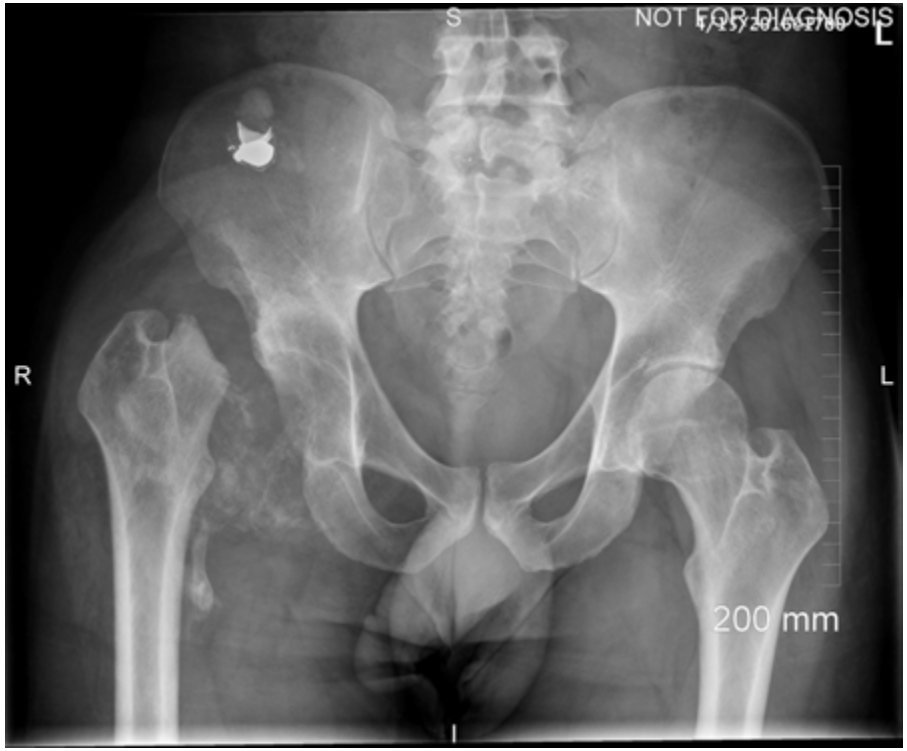
Aliquot 1

- ***HPI***: 35 yo AAM presenting to ER with 5 month history of inability to use the right lower extremity (RLE).
- ***PMH***: C3-C4 myelopathy, gun shot wound (GSW) to hip & stomach, L5-S1 herniated nucleus pulposus, hypertension
- ***PSHx***: anterior cervical diskectomy and fusion of C3-C4, exploratory laporotomy for GSW, right L5-S1 metrix lumbar diskectomy
- ***SHx***: ½ PPD smoker, alcohol & marijuana dependence, works as one of the Memphis "flippers"

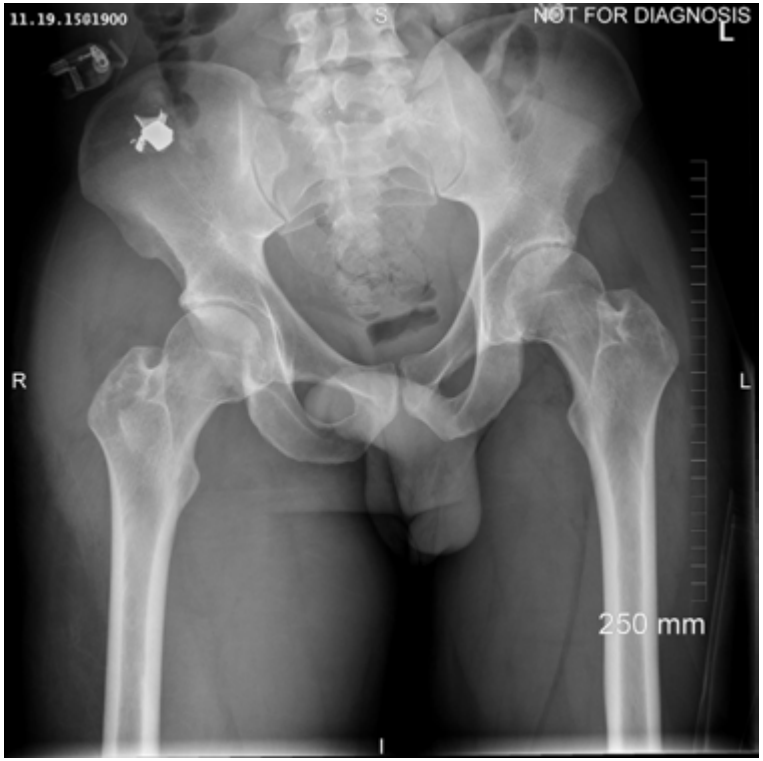
ROS: + for right leg paresthesias, numbness; - for fevers, chills, sweats, weight loss, recent trauma

Aliquot 2

- NEURO:
- EXTREMITIES: Examination of right lower extremity shows intact skin without pain or discomfort with range of motion of the hip, knee, ankles, or toes. Sensation decreased from L3 to S1. 3 out of 5 strength in his hip flexors, 1 out of 5 in his quadriceps, and 0 out of 5 in his hamstrings, tibialis anterior (TA), and gastroc soleus (GSC), and extensor hallucis longus (EHL) muscle groups in the right lower extremity. He has brisk capillary refill x 5. Examination of the left lower extremity shows intact skin without ecchymoses or effusion. No tenderness to palpation about bony prominences and neurovascularly intact.



Aliquot 3



- Patient was admitted to orthopedic surgery service for further evaluation of suspected septic arthritis
- Interventional radiology was consulted, and they performed a fluoroscopic-guided right hip aspiration
- Results listed below:
  - Color: orange
  - Consistency: cloudy
  - WBC- 412
  - RBC- 33,060
  - No crystals identified
  - Negative bacterial, fungal, TB, and spirochetal cultures
  - Pathology: hypocellular with no malignant cells
- Testing for reversible causes including HIV, acute hepatitis panel, and syphilis serologies were all negative

Final Diagnosis?

Charcot Arthropathy of the Hip Introduction

- Charcot arthropathy of the hip is an uncommon but debilitating disorder resulting from repetitive joint stress in the setting of neurovascular compromise[1].

- The most common cause is tabes dorsalis from tertiary syphilis although HIV, HCV, IBD, and syringomyelia have been implicated in previous cases[2,3,4,5]

Charcot Arthropathy Discussion

- Charcot arthropathy was first described in 1831 by Mitchell (5). It can occur in 5-10% of patients with tabes dorsalis from tertiary syphilis. Time from diagnosis of syphilis to development of Charcot arthropathy ranges from three to fifteen years (5). Areas most affected by this disorder include the knees, ankles, hips, joints, and lumbar spine. Charcot arthropathy of the hip is usually secondary to syphilis but HIV, HCV, syringomyelia, and IBD should be excluded as they have been implicated in previous reports (2,3, 4, 5).

- This case is unique as no previous cases to our knowledge report “flipping” or similar activities as a cause of Charcot arthropathy of the hip. While tertiary syphilis is the most common etiology, any activity causing constant mechanical stress to the joint can lead to neuropathic arthropathy. Optimal treatment is controversial but involves treating underlying cause and possible arthrodesis[6]. A complete history and physical examination can help distinguish Charcot arthropathy from similar diseases such as septic arthritis and occult malignancy.

References

- 1. Cavalli G. and Praderio L. Charcot's Arthropathy of the Hip. J Rheumatol 2013;40;1770.
- 2. Johnson J.T.H. Neuropathic Injuries of the Hip. Journal of Clinical Orthopedics and Related Research 1973;90;29-32
- 3. Veins NA, Watters TS, and Vinson EN et al. Neuropathic Arthropathy of the Hip as a Sequela of Undiagnosed Tertiary Syphilis. Clinical Orthopedics and Related Research 2010;468;3126-3131
- 4. Drago L, Vechhi ED, Pasqualini M et al. Rapid, progressive neuropathic arthropathy of the hip in a patient co-infected with human immunodeficiency virus, hepatitis C virus and tertiary syphilis: case report.
- 5. Memarpour R, Tashtoush B, Isaac L et al. Syringomyelia with Chiari I Malformation Presenting as Hip Charcot Arthropathy: A Case Report and Literature Review. Case Reports in Neurological Medicine 2015;2015;1-6
- 6. Rapala K. and Obrebski M. Charcot's Arthropathy of the Hip Joints: A Late Manifestation of Tabes Dorsalis Treated by Total Joint Arthroplasty 2 Cases. Journal of Arthroplasty 2007;22;771-774

"The Janus Paradox. The Two Faces of ACE2 in Cardiovascular Disease“

2024 Dr. Robert D. & Mrs. Alma W. Moreton Original Research Award

Friday, October 25, 2024

Carlos M Ferrario, MD, FAHA, FASH, FAPS, FISH, FACC

Professor Emeritus, Department of Surgery

Atrium Health -Wake Forest Baptist

Wake Forest School of Medicine

Winston Salem, NC 27157

Chief Operating Officer, Inter American Society of Hypertension (IASH)

Immediate Past President -Inter American Society of Hypertension (IASH)

Founder -Consortium for Southeastern Hypertension Control (COSEHC™)

DISCLOSURE

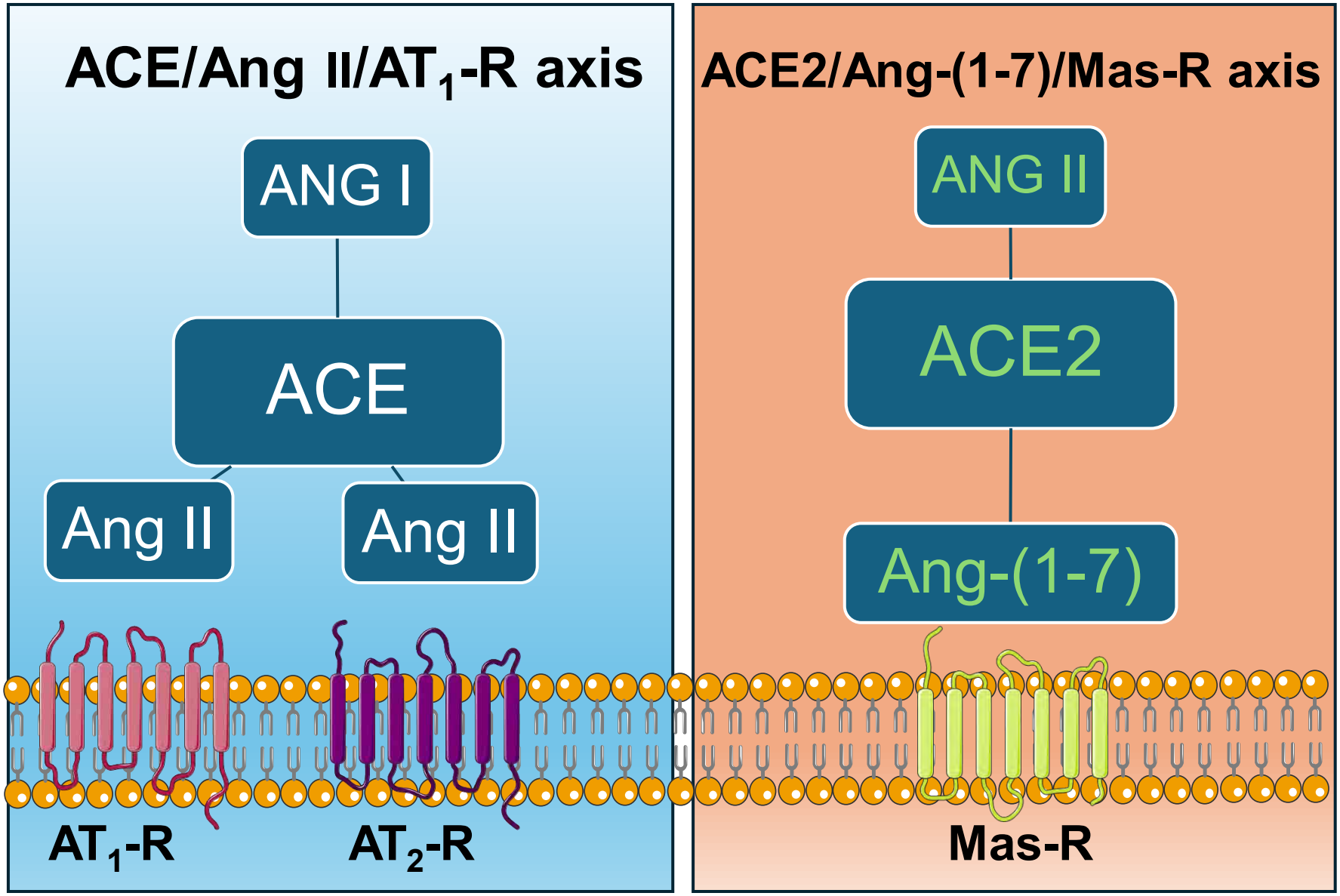
CMF IS THE RECIPIENT OF NATIONAL INSTITUTES OF HEALTH GRANTS HL-051952 AND R21 AG070371-01.

JANUS - GOD OF ENDINGS AND BEGINNINGS

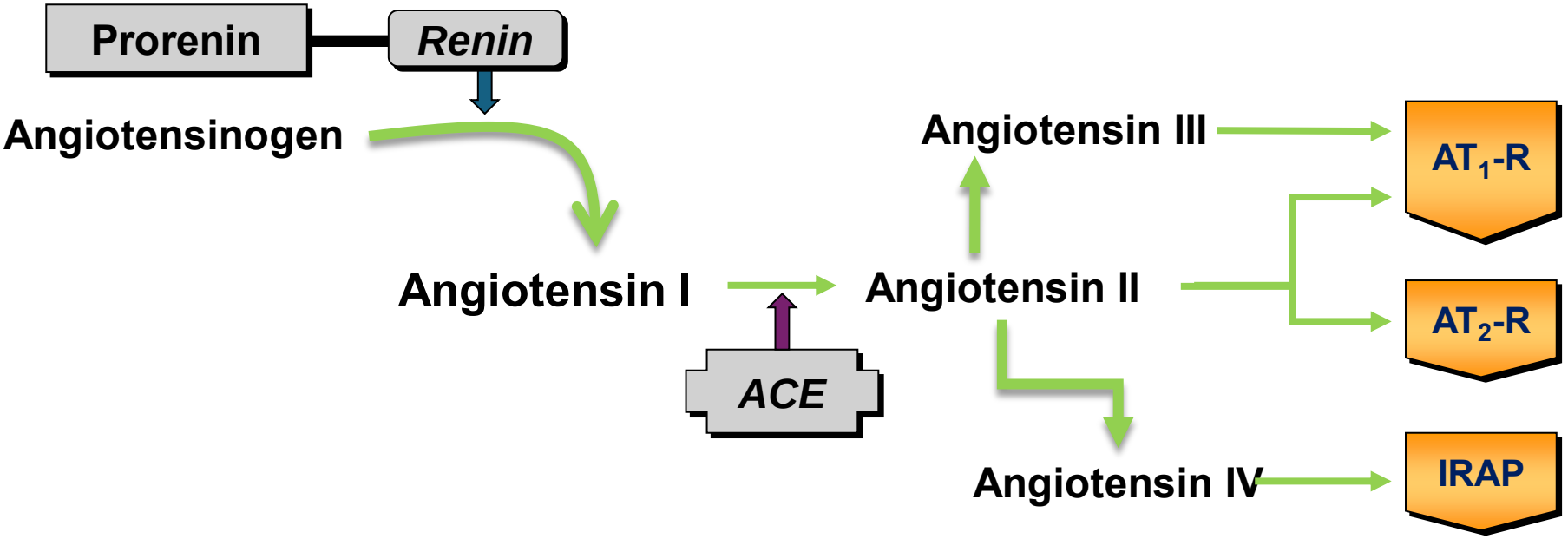
"May he grant the graces to open the doors to new beginnings and help those courageous enough to find those gateways and step through them."

JANUS - GOD OF ENDINGS AND BEGINNINGS

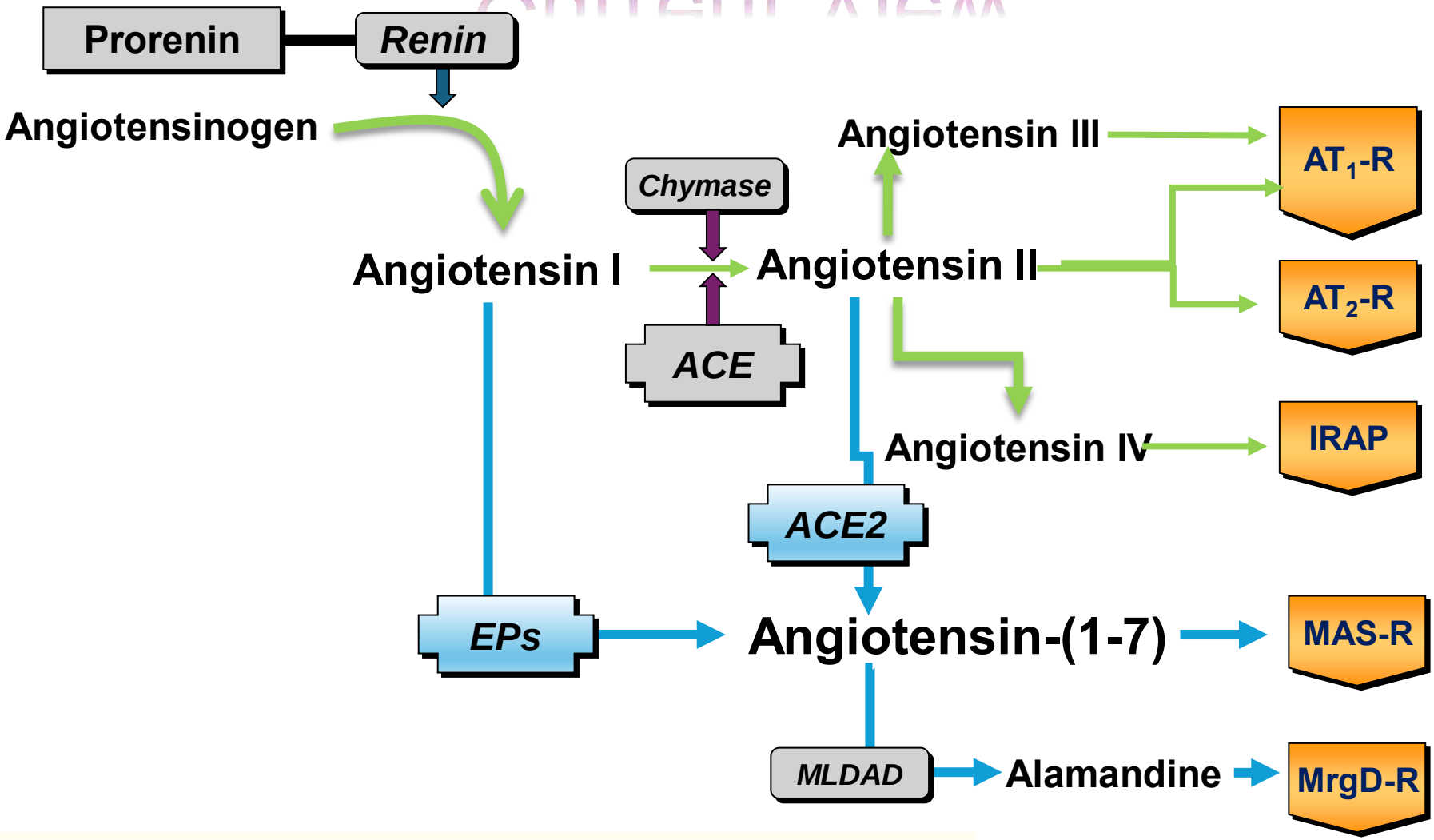
JANUS - GOD OF ENDINGS AND BEGINNINGS



The Renin Angiotensin System. Original View



The Renin Angiotensin System. Current View



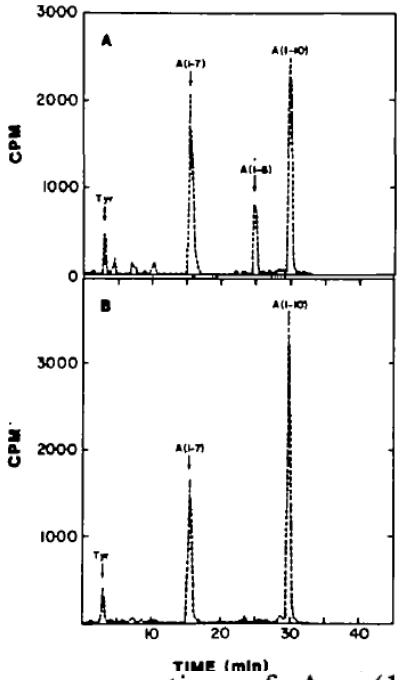
Eps, neprilysin, thimet oligopeptidase (TOP), and prolyl oligopeptidase (POP).
MLDAD, mononuclear leukocyte-derived aspartate decarboxylase.


R Santos


M Schiavone


KB Brosnihan

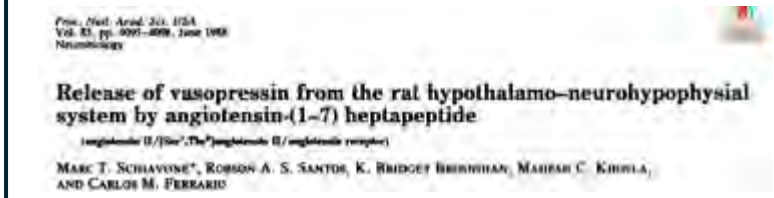

CM Ferrario



Chromatographic depiction of radiolabeled ^{125}I-Ang I metabolism in canine brain stem homogenates in the absence (A) and the presence (B) of the ACE inhibitor enalapril.

generation of Ang-(1–7). Since in our experiments Ang-(1–7) was the major product of labeled Ang I metabolism in brain punch hydrolysates, the data raise questions about its possible biological functions. Although Ang-(1–7) has weak agonistic pressor and drinking effects,[18] the spectrum of biological actions of angiotensins is certainly not limited to either body fluid or cardiovascular regulation. Further studies are necessary to investigate the possible biological actions of this peptide.

Santos RA, et al. Converting enzyme activity and angiotensin metabolism in the dog brainstem. Hypertension. 1988;11(2 Pt 2):I153-7.

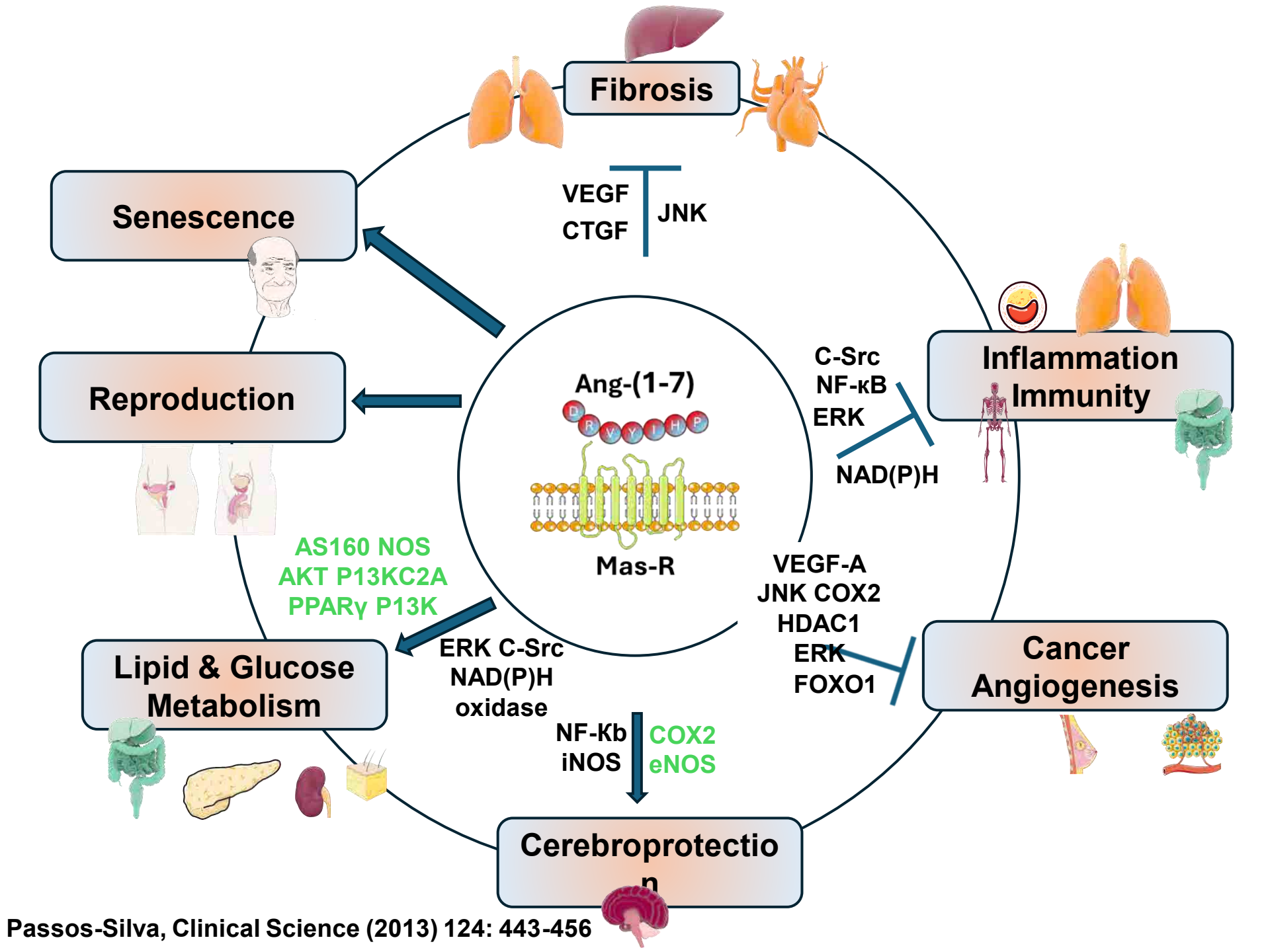


Release of vasopressin from the rat hypothalamo–neurohypophysial system by angiotensin-(1–7) heptapeptide

MARC T. SCHIAVONE*, ROBSON A. S. SANTOS, K. BRIDGET BRENNIHAN, MAHESH C. KHOSLA, AND CARLOS M. FERRARIO

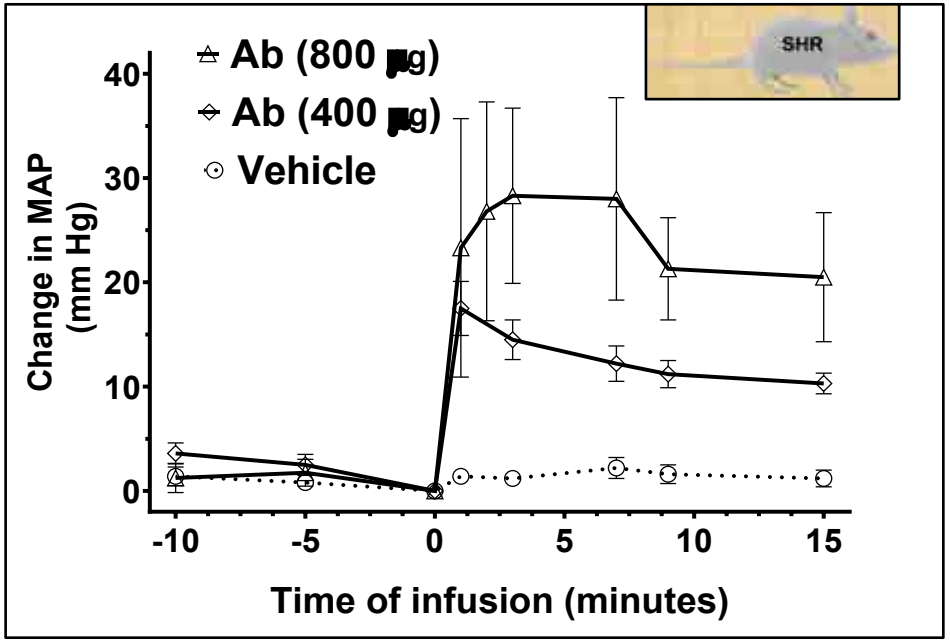
terminus of the Ang II molecule. However, our observation that the AVP-releasing activity of Ang-(1–7) is similar to that of Ang II, together with the metabolic studies showing generation of Ang-(1–7) in brain and peripheral tissues, suggest that Ang-(1–7) is an endogenously generated centrally active angiotensin peptide.

Schiavone MT et al. Release of vasopressin from the rat hypothalamo-neurohypophysial system by angiotensin-(1-7) heptapeptide. Proc Natl Acad Sci U S A. 1988;85(11):4095-8.



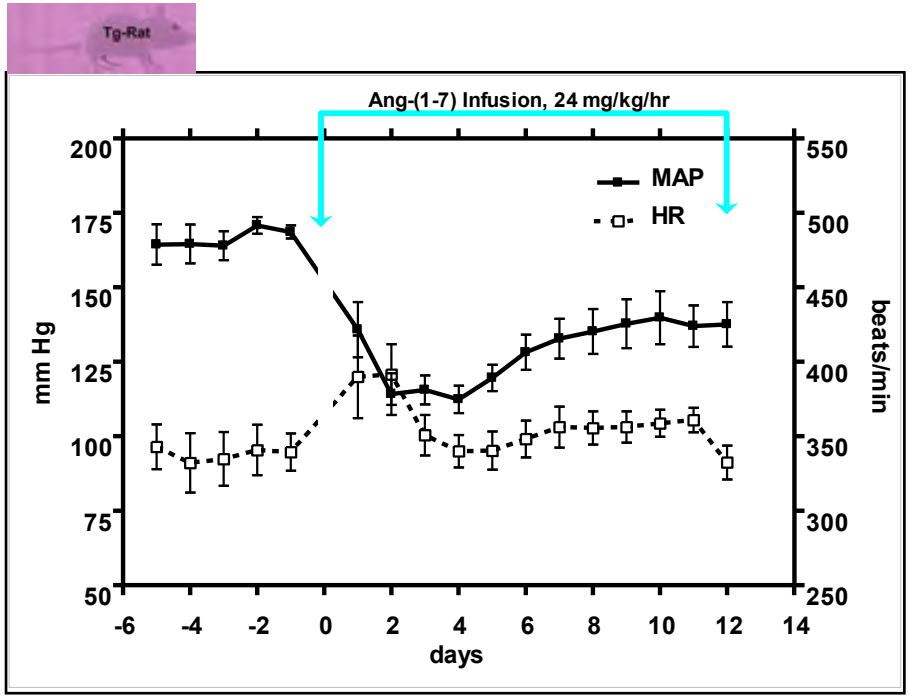
Passos-Silva, Clinical Science (2013) 124: 443-456

Ang-(1-7) Antihypertensive Actions



Ang-(1-7) immunoneutralization with a monoclonal antibody causes a substantial worsening of hypertension in SHR.

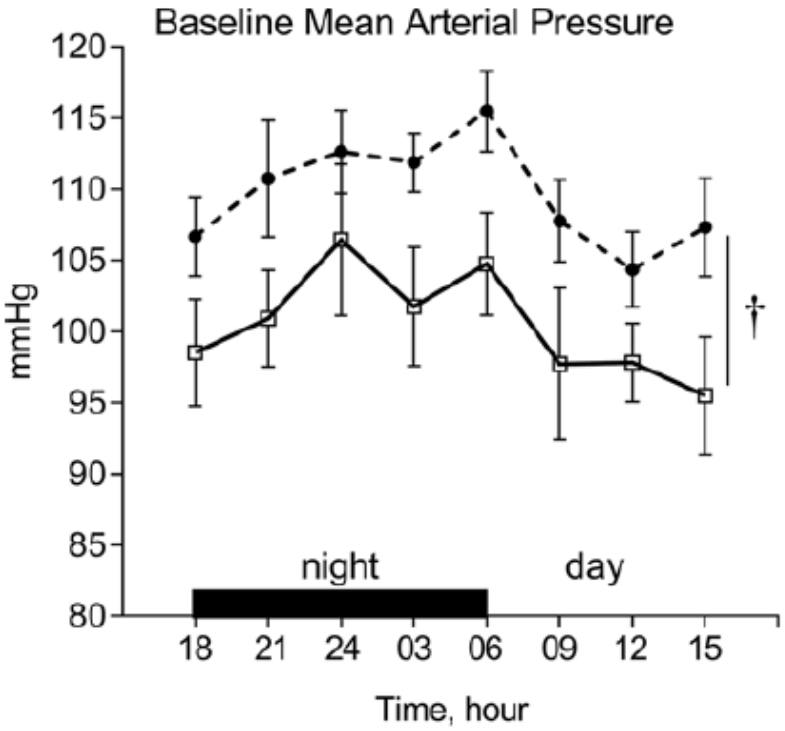
Iyer et al. Hypertension 2000; 36 (3), 417-422

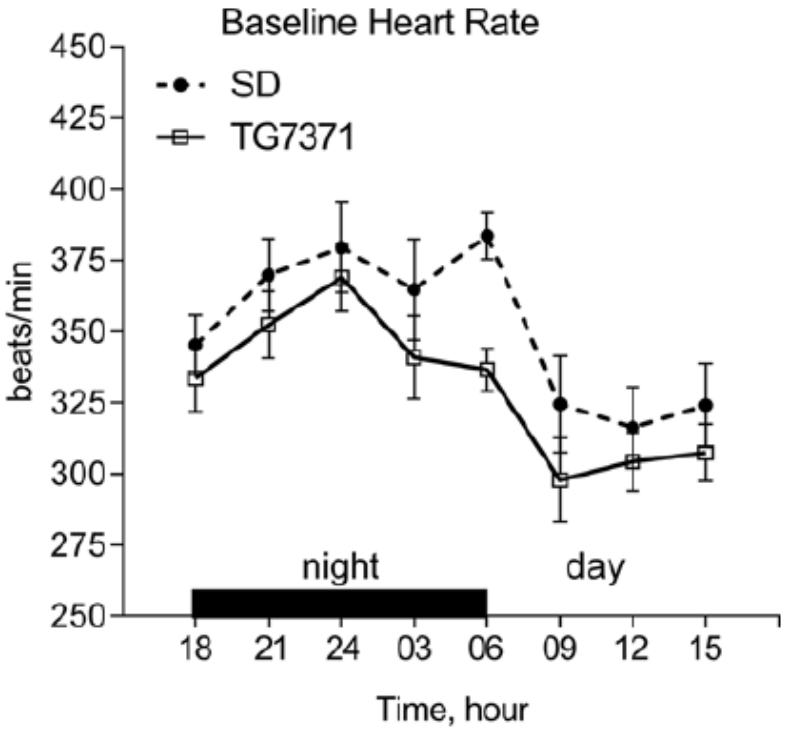


Chronic Ang-(1-7) infusion lowers the elevated blood pressure of transgenic hypertensive rats expressing the renin gene (TGR(mRen2)27).

Moriguchi et al. Hypertension 1995; 25 (6), 1260-1265

Expression of an Ang-(1-7)-producing fusion protein induces a hypotensive phenotype due to organ vasodilation and consequent fall in peripheral resistance

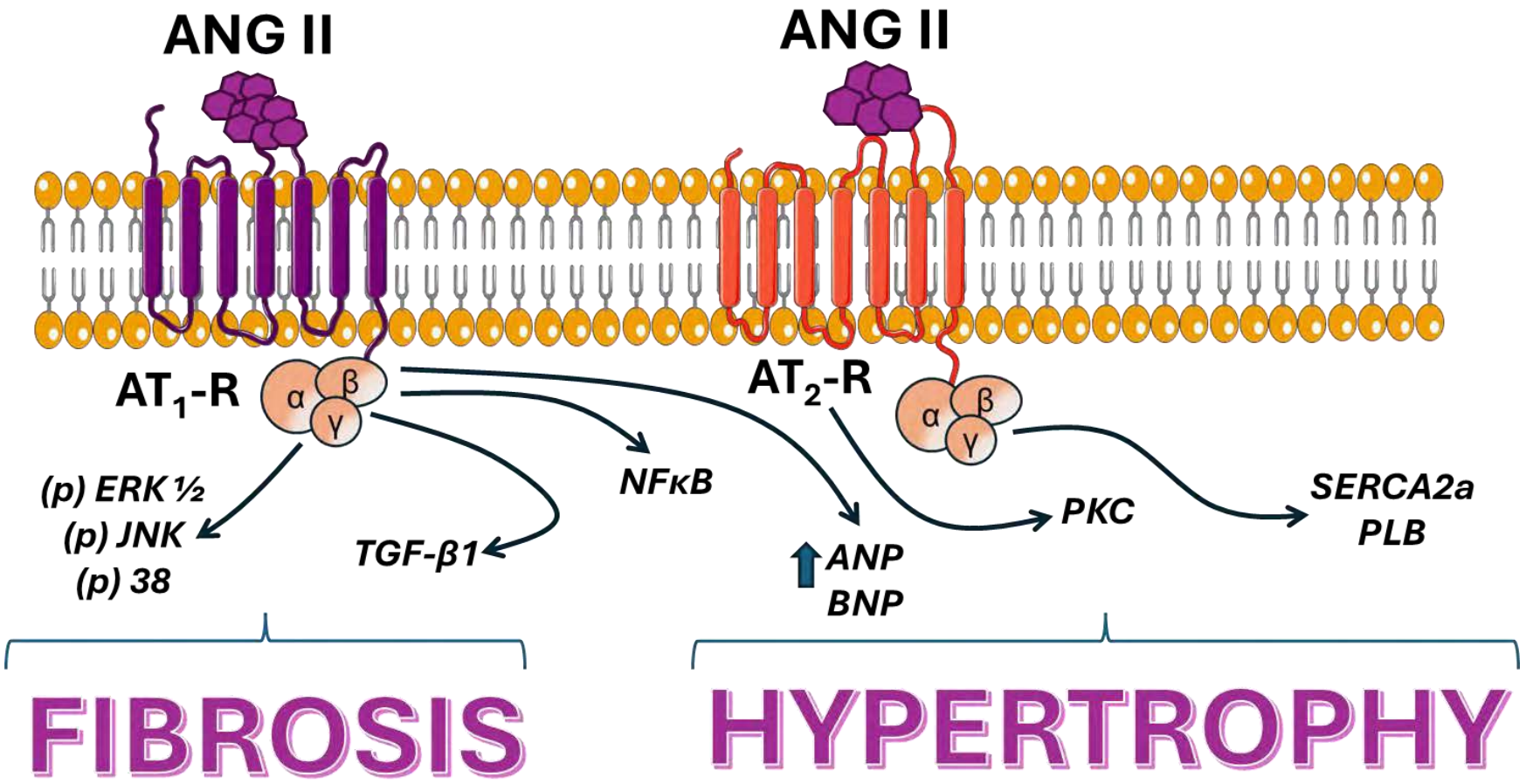




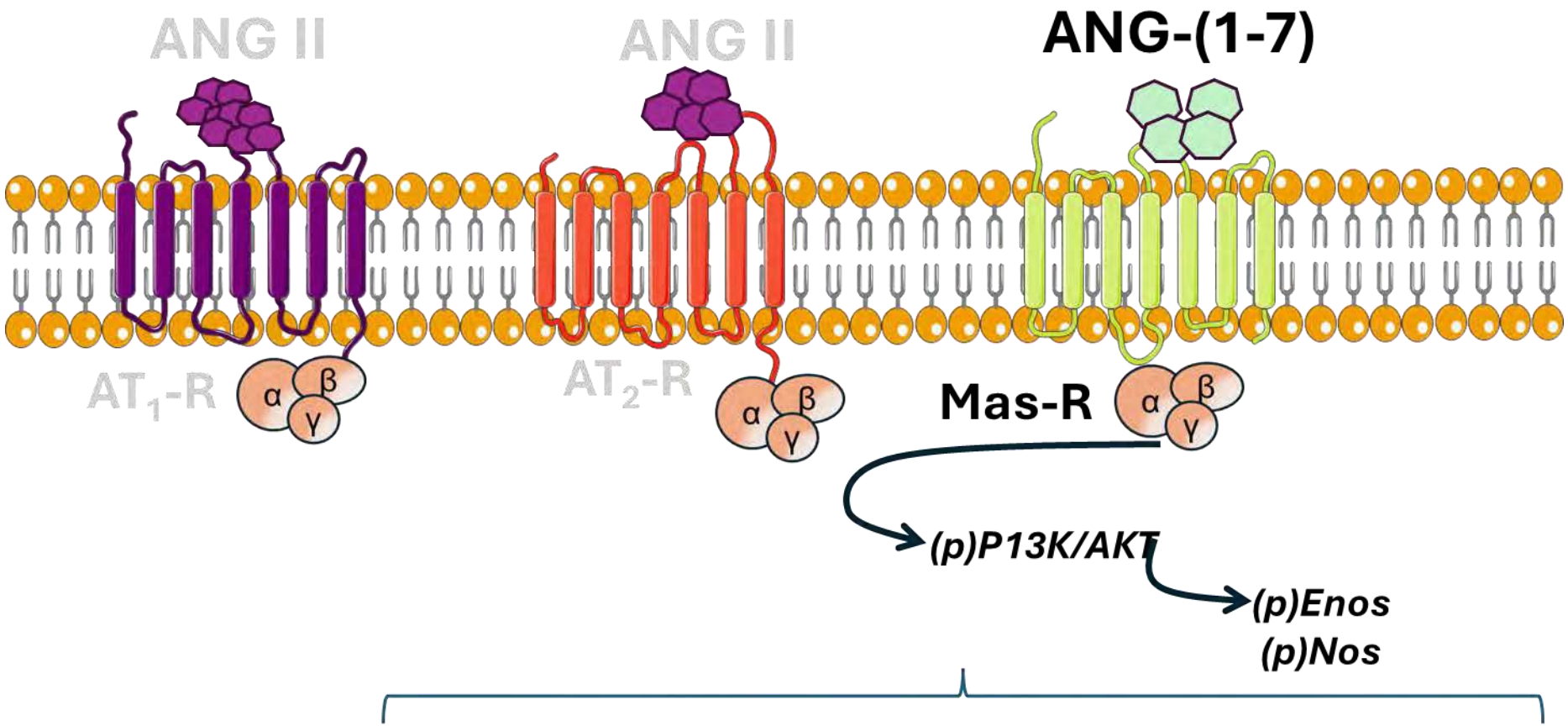
- **In homozygous transgenic rats (TG7371), the expression of a fusion protein containing the Ang-(1-7) sequence causes sustained normalization of the elevated blood pressure and augmented blood flow in the kidney, mesentery, muscle, heart, and skin compared to control SD rats.**

Alves et al. Clinical Science 2021; 135 2197–2216

The classic view of angiotensin II receptors is that there are two types of receptors: the angiotensin II type 1 receptor (AT1-R) and the angiotensin II type 2 receptor (AT2-R)



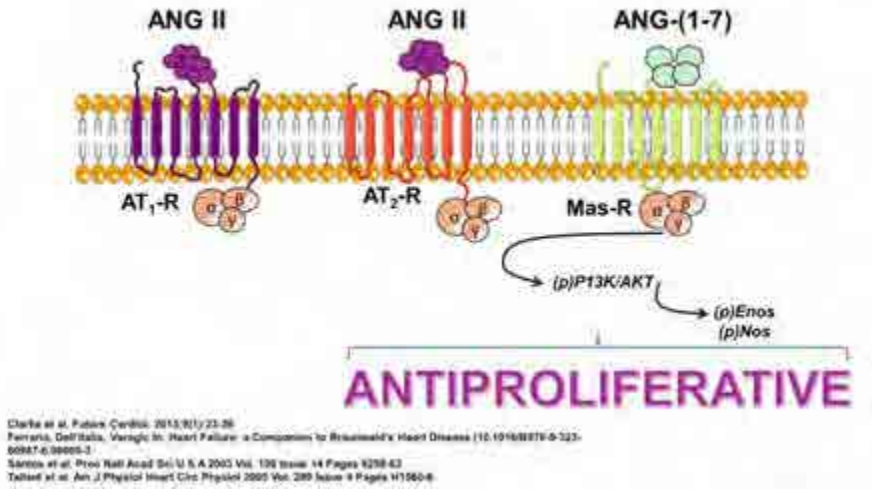
Ferrario et al. Hypertension 1997 Vol. 30 Issue 3 Pt 2 Pages 535-41



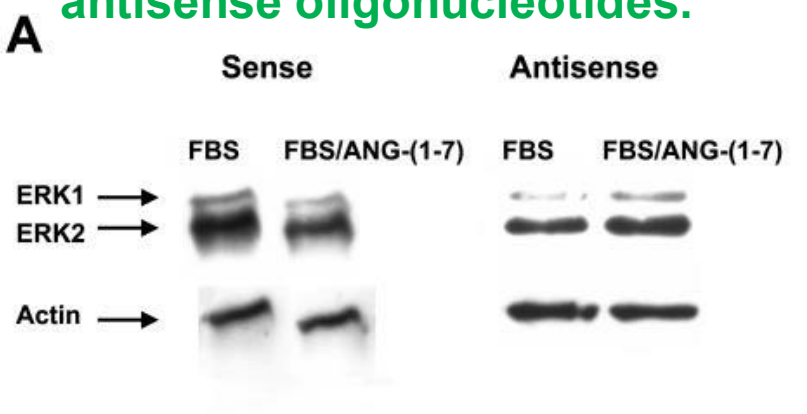
ANTIPROLIFERATIVE

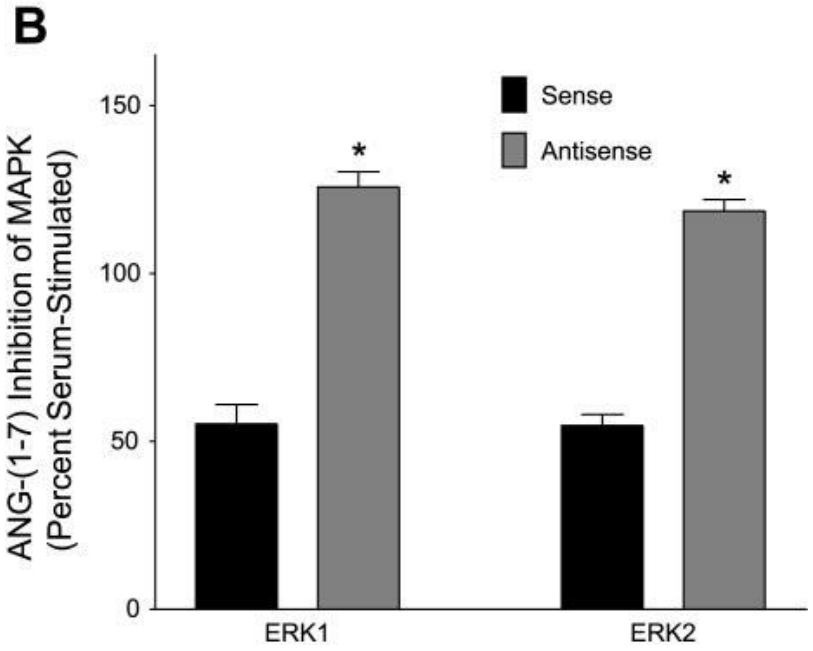
VASODILATOR

Clarke et al. Future Cardiol. 2013;9(1):23-38.
Ferrario, Dell'Italia, Varagic In: Heart Failure: a Companion to Braunwald's Heart Disease (10.1016/B978-0-323-60987-6.00005-3
Santos et al. Proc Natl Acad Sci U S A 2003 Vol. 100 Issue 14 Pages 8258-63
Tallant et al. Am J Physiol Heart Circ Physiol 2005 Vol. 289 Issue 4 Pages H1560-6



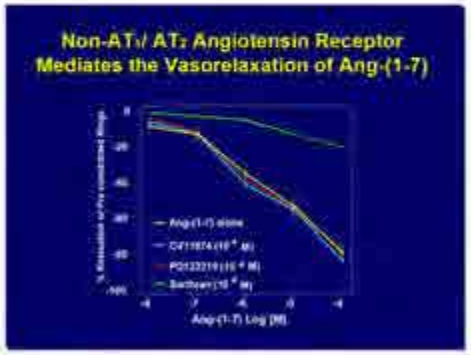
Inhibition of ANG-(1–7)-mediated MAPK activity by Mas receptor antisense oligonucleotides.



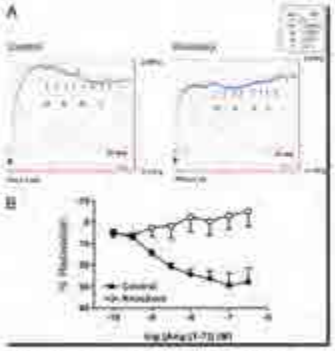


Tallant, Ferrario, Gallagher. Am J Physiol Heart Circ Physiol 2005 Vol. 289 Issue 4 Pages H1560-6

The *mas* Receptor Mediates the Vasorelaxation of Ang-(1-7)



Li et al. Hypertension 29, 394-400, 1997

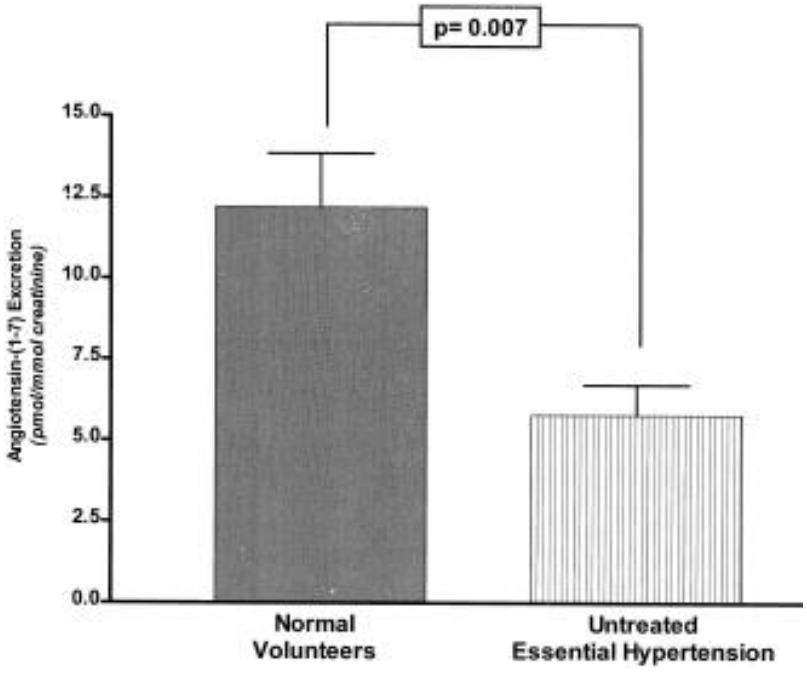


Inhibition of vascular Ang-(1-7)-mediated endothelial relaxation in mas knockout mice. Santos et al. Proc Nat Acad Of Med, 2003

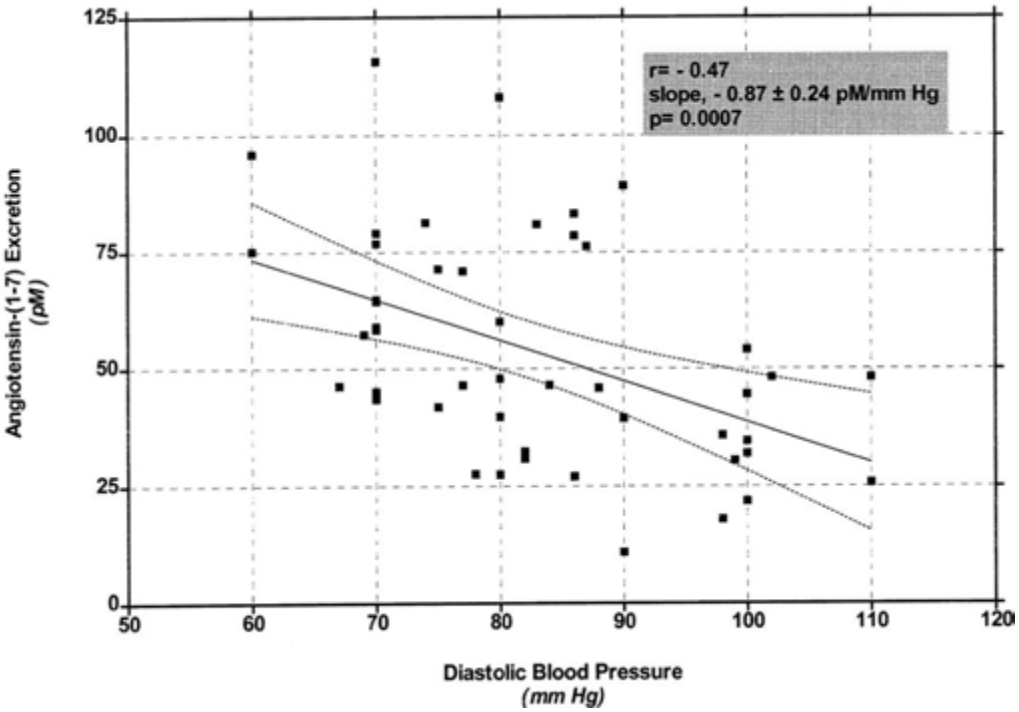
Does clinical evidence support a role for Ang-(1-7) in the modulation of cardiovascular diseases (CVDs)?

- **Hypertension:**
  - Hypertensive patients treated with Ang (1-7) showed significant blood pressure reductions, likely due to vasodilatory and natriuretic effects.
- **Heart Failure:**
  - Clinical investigations in heart failure patients have demonstrated that Ang-(1-7) levels are inversely related to disease severity. Therapeutic administration of Ang-(1-7) has been associated with improved cardiac output and reduced ventricular remodeling.
- **Atherosclerosis:**
  - Clinical data on Ang-(1-7) in atherosclerosis are limited, but preclinical studies support its anti-inflammatory and anti-atherosclerotic roles. Ang-(1-7) inhibits monocyte adhesion and vascular smooth muscle proliferation, key events in atherogenesis.

Does a Deficit in Ang-(1-7) Contribute to Human Essential Hypertension?

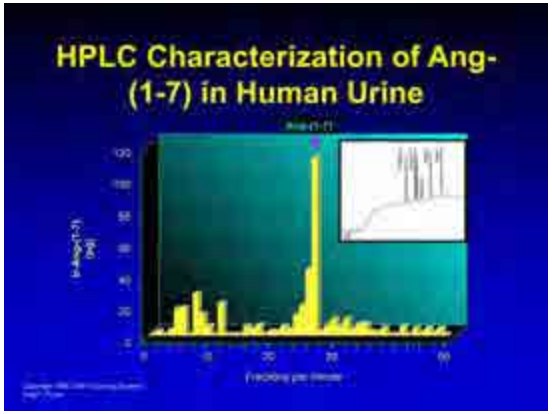


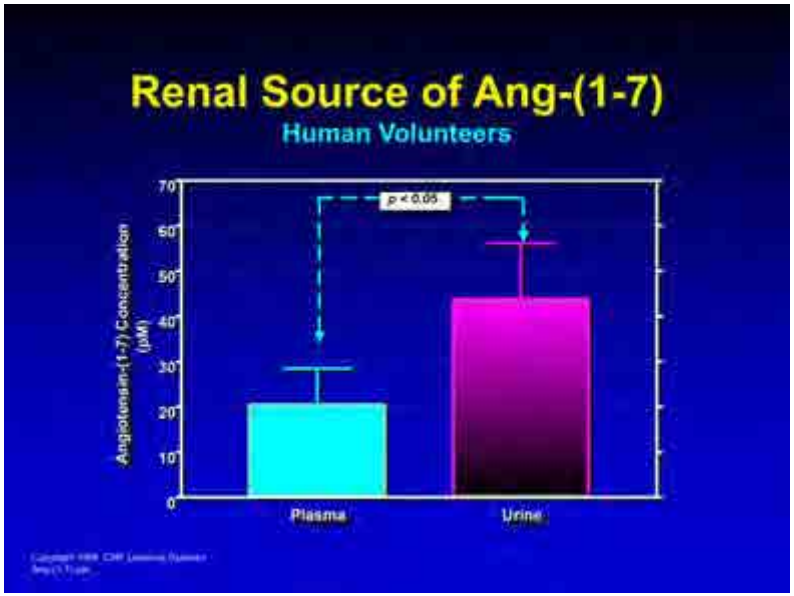
Ferrario et al. Am J Hypertens. 1998;11(2):137-46.



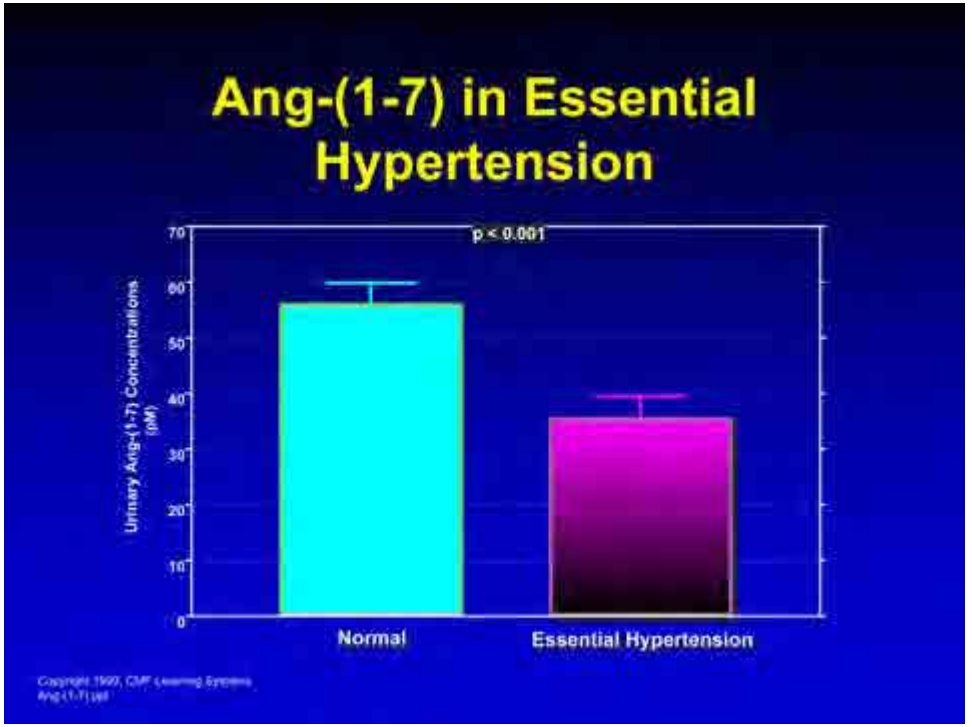
Luque et al. J Hypertens 1996 .14 (6): 799-805

Does a Deficit in Ang-(1-7) Contribute to Human Essential Hypertension?



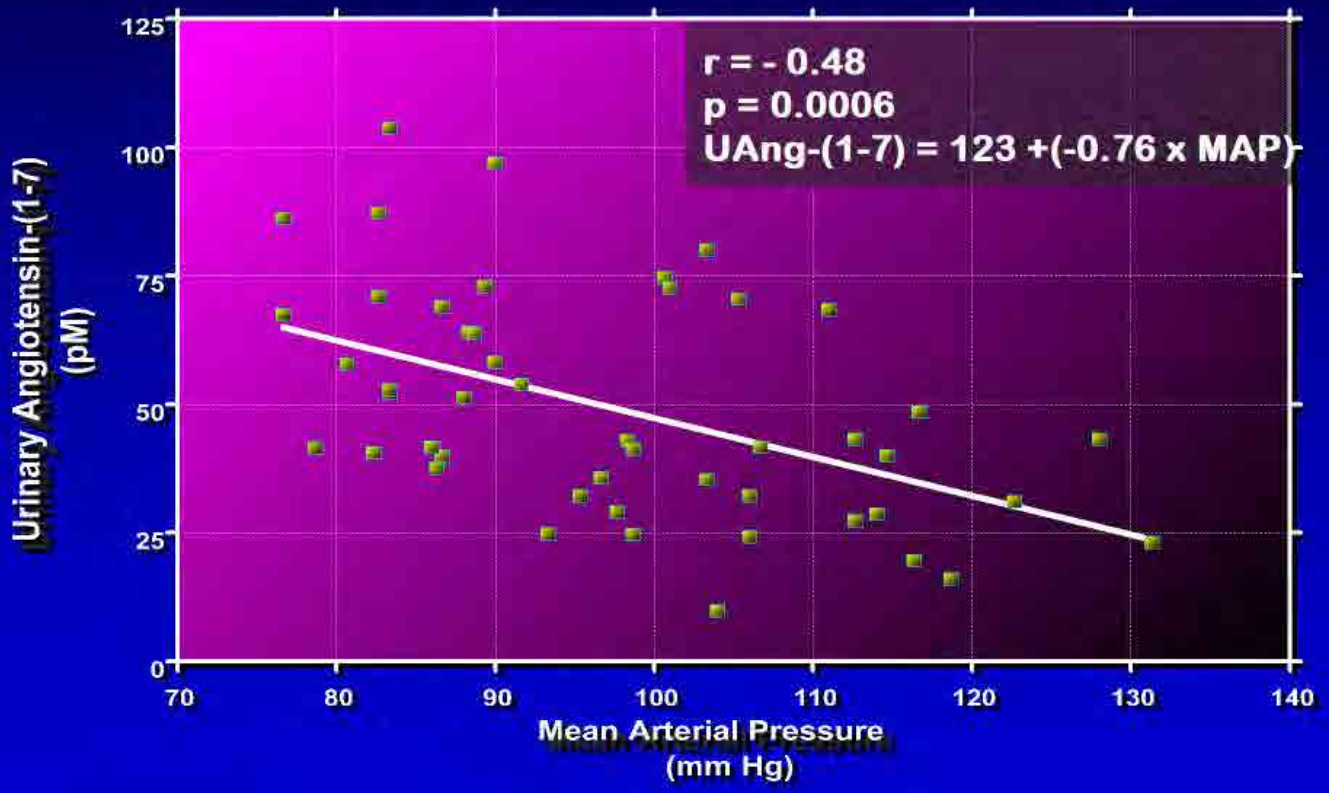


Ferrario et al. Am J Hypertens. 1998;11(2):137-46.



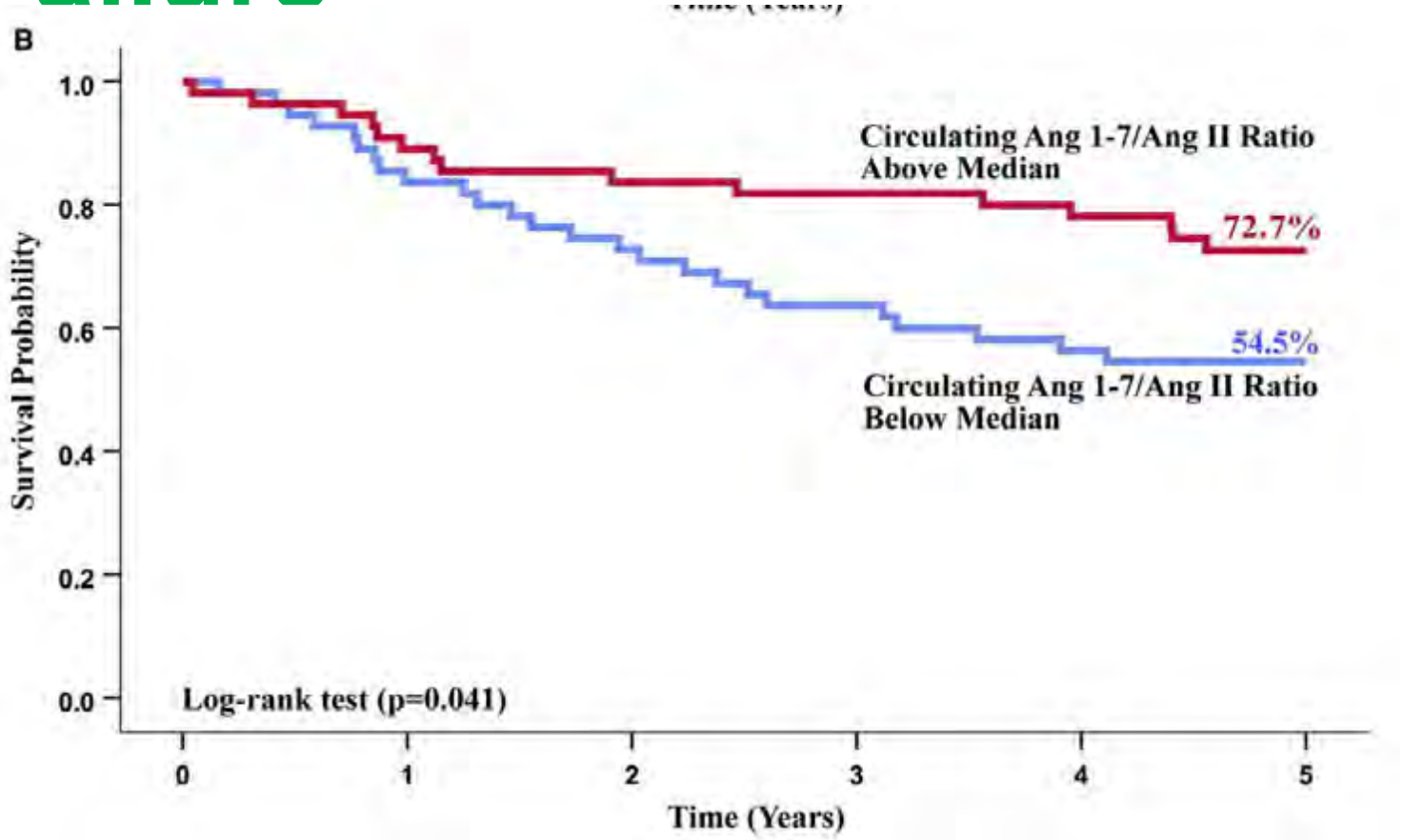
Luque et al. J Hypertens 1996 .14 (6): 799-805

Urinary Ang-(1-7) and High Blood Pressure



Luque et al. J Hypertens 1996 .14 (6): 799-805

Ang-(1-7) in Human Heart Failure



Ang II mediates HF progression, while Ang 1–7 offers protection in HF. Plasma Ang 1–7/Ang II ratio is an important prognostic tool in risk stratification across the broad spectrum of HF.

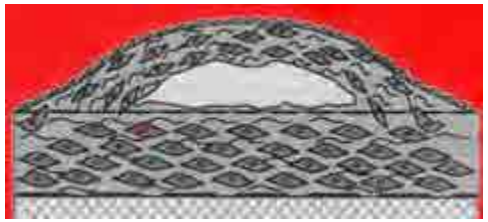
Wang et al. Circulation: Heart Failure 2020 Vol. 13 (7) e006939.

NOVEL CONCEPTS

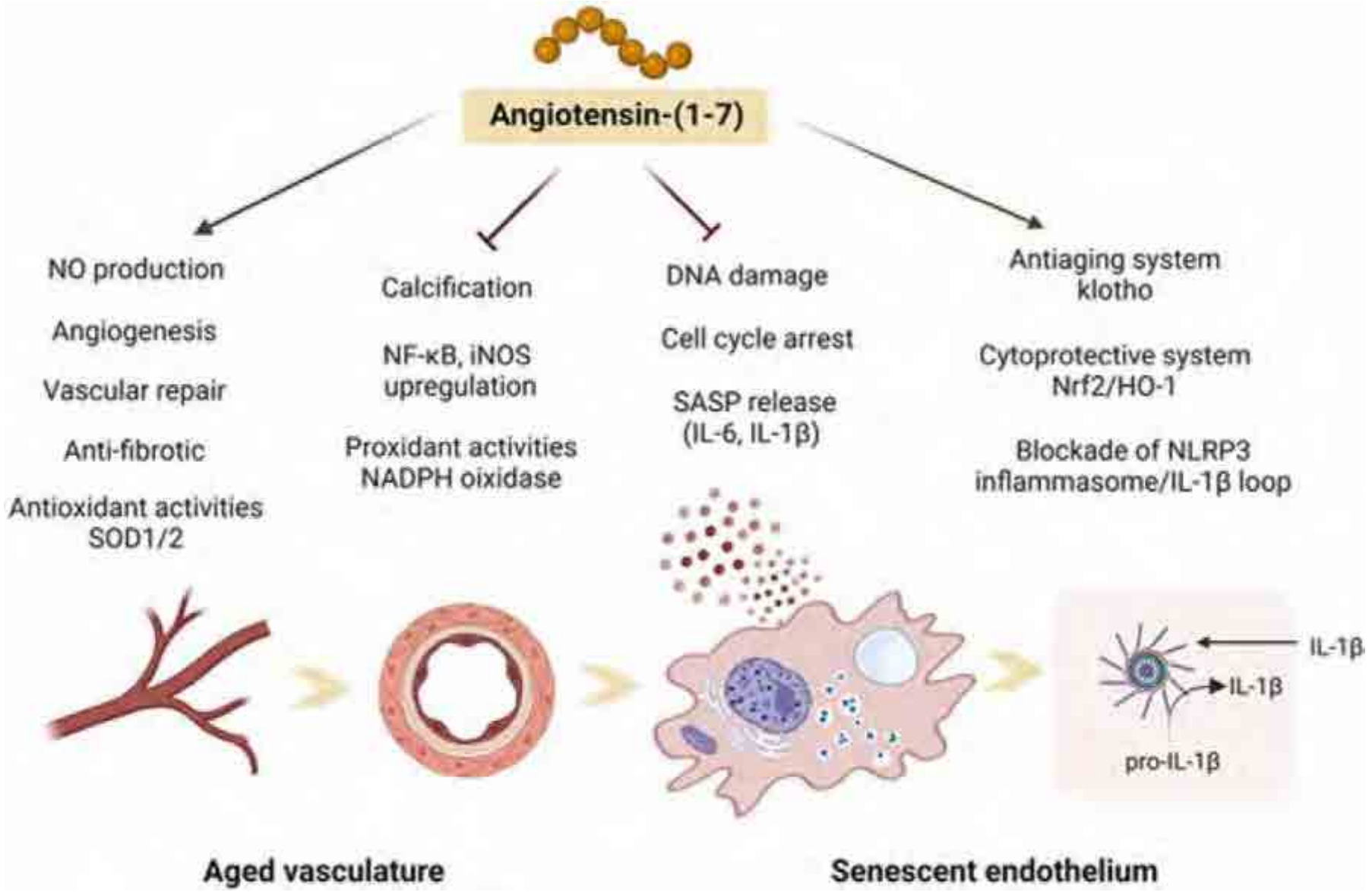
LDL and Ang II

Endothelial Dysfunction Inflammation Plaque Formation

Ang-(1-7)

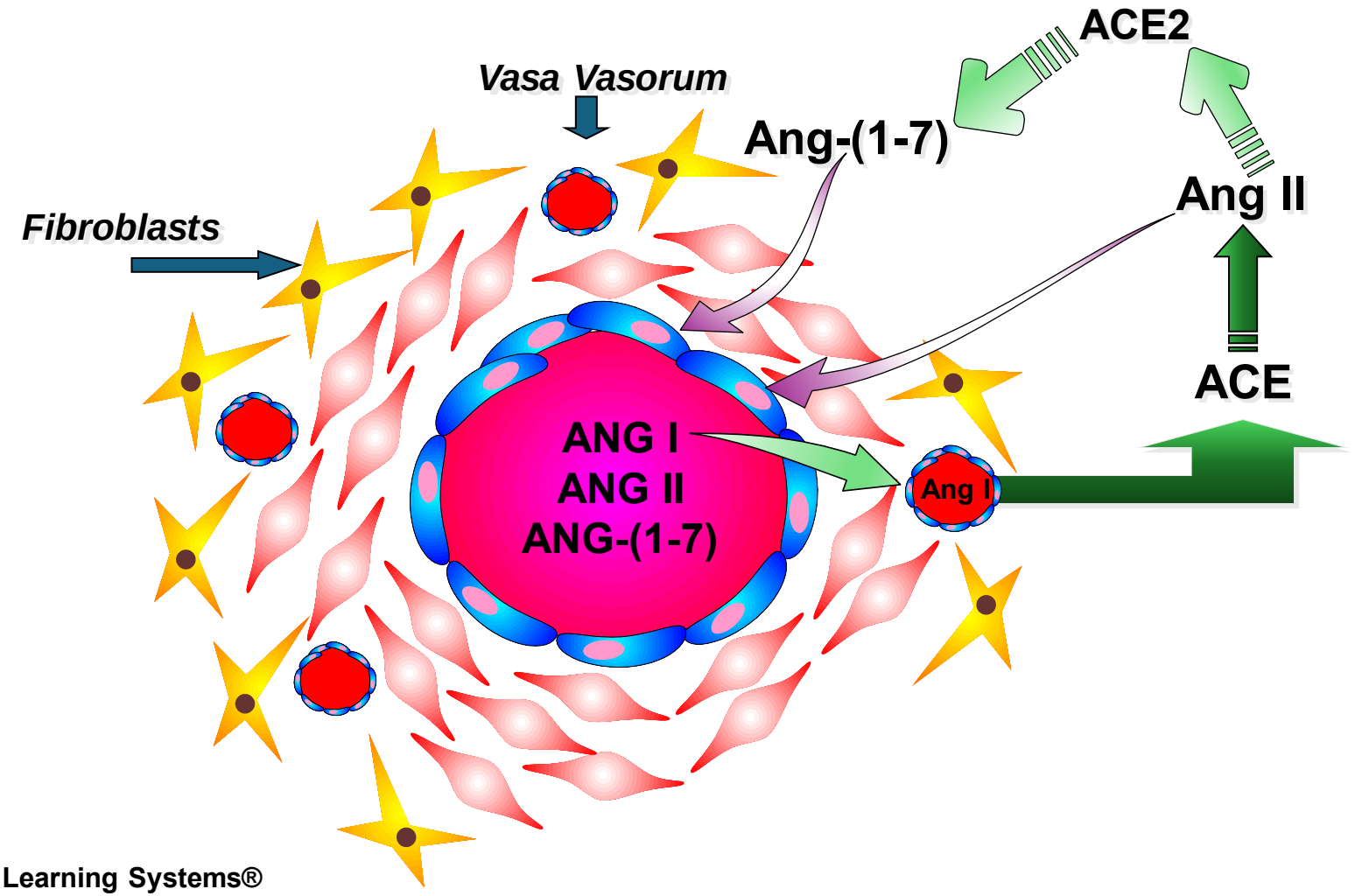


Plaque Regression & Plaque Stabilization



Valencia et al. Peptides 2022. 152. 170775

Ang II – Local Biosynthesis

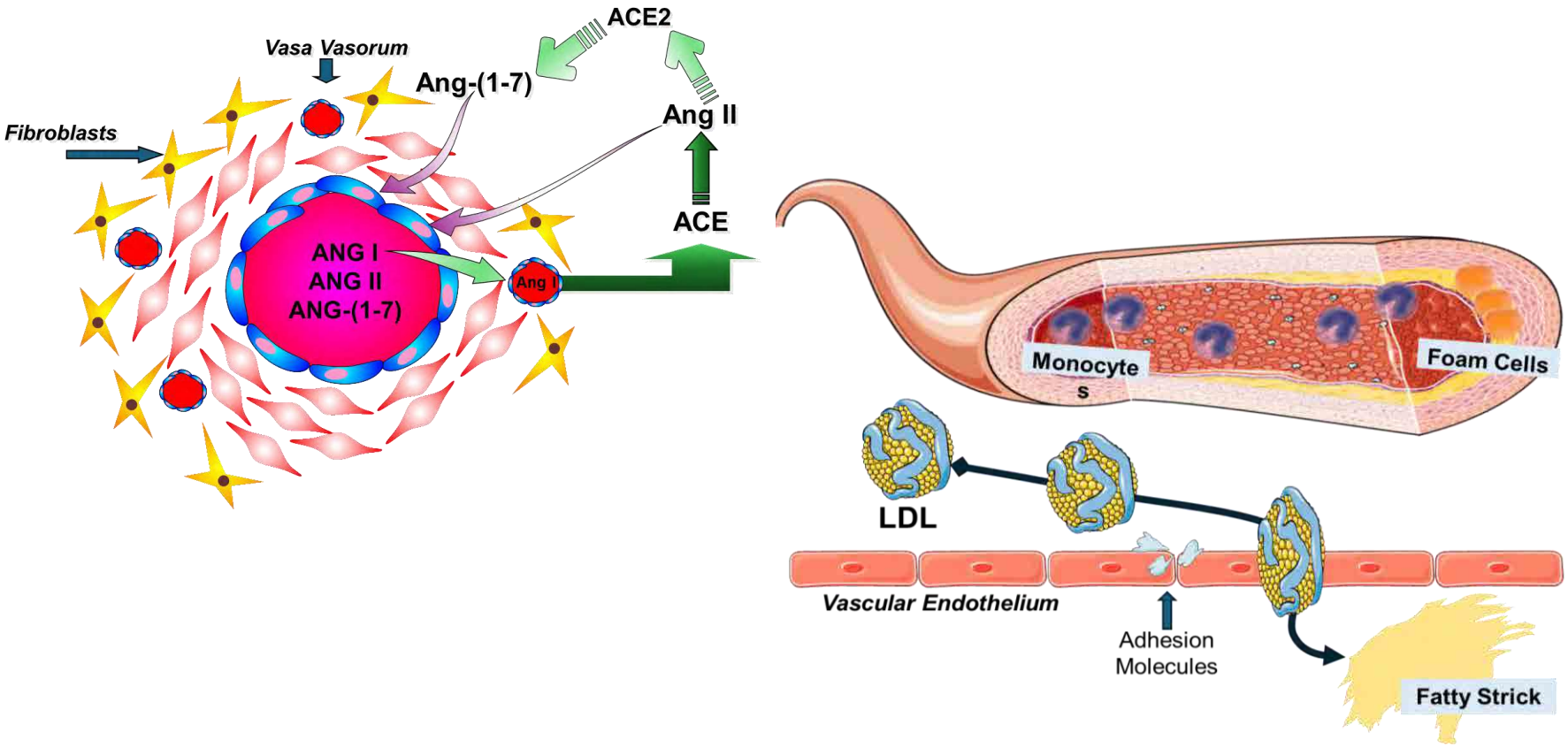


CMF Learning Systems®

Strawn WB, Ferrario CM. Mechanisms linking angiotensin II and atherogenesis. Curr Opin Lipidol. 2002;13(5):505-12

Strawn WB, Chappell MC, Dean RH, Kivlighn S, Ferrario CM. Inhibition of early atherogenesis by losartan in monkeys with diet-induced hypercholesterolemia. Circulation. 2000;101(13):1586-93.

The Angiotensin System in the Development of Atherosclerosis



CMF Learning Systems®

Strawn WB, Ferrario CM. Mechanisms linking angiotensin II and atherogenesis. Curr Opin Lipidol. 2002;13(5):505-12

Strawn WB, Chappell MC, Dean RH, Kivlighn S, Ferrario CM. Inhibition of early atherogenesis by losartan in monkeys with diet-induced hypercholesterolemia. Circulation. 2000;101(13):1586-93.

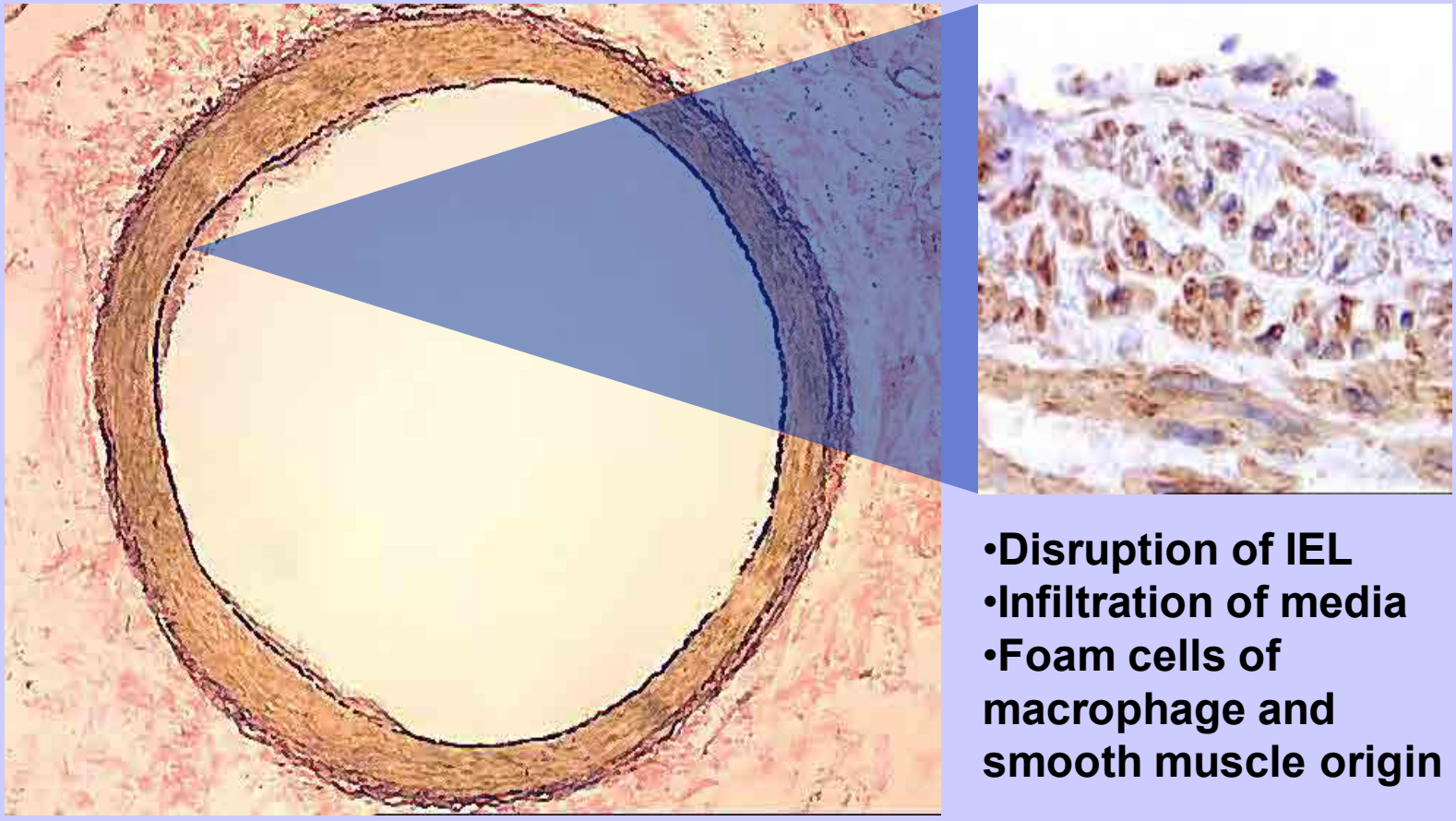
Experimental Atherosclerosis

Cynomolgus Monkeys (Macaca fascicularies)

- **Spontaneous Atherosclerosis, (Prathap et al. DOI:10.1002/path.1711100205)**
- **Diet-induced atherosclerosis bears high similarity with human lesions.**
- **Coronary artery lesions similar to those present in humans (Stary & Manilow. DOI: 10.1016/0021-9150(82)90019-3).**
- **Lesion progression from initial foam cell accumulation (Small et al., 1984. DOI: 10.1172/JCI111366).**
- **Carotid atherosclerosis correlates with plasma lipid concentrations (Kaplan et al., 1984. DOI: 10.1016/s0022-5347(17)50506-6).**
- **Plasma LDL uptake increased in aortas with diet-induced fatty streaks (Ghosh et al. 1987. DOI: 10.1093/cvr/21.1.14)**

Strawn WB and Ferrario CM. Circulation. 2000;101(13):1586-93.

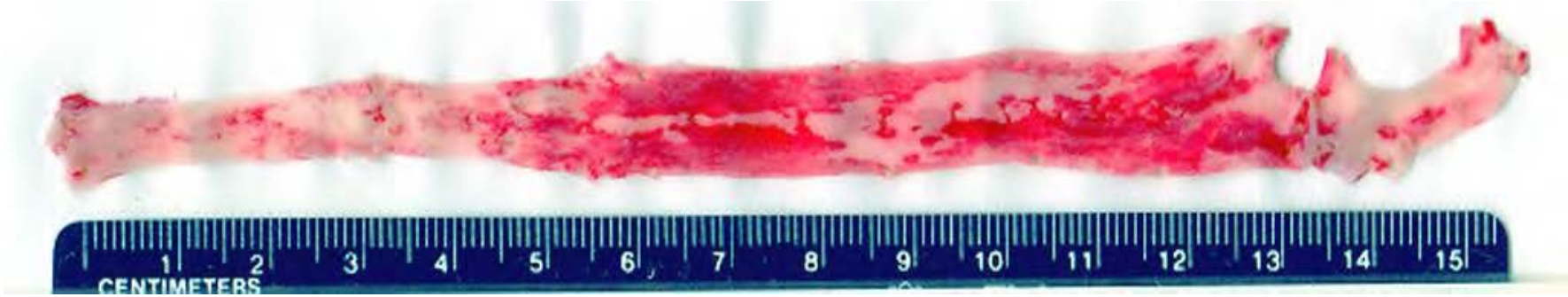
Coronary Artery Fatty Streak in Vehicle-Treated Monkey



- Disruption of IEL
- Infiltration of media
- Foam cells of macrophage and smooth muscle origin

Strawn and Ferrario. Circulation. 2000;101(13):1586-1593.

Oral Treatment with Losartan Blocks the Development of Experimental Atherosclerosis in Monkeys

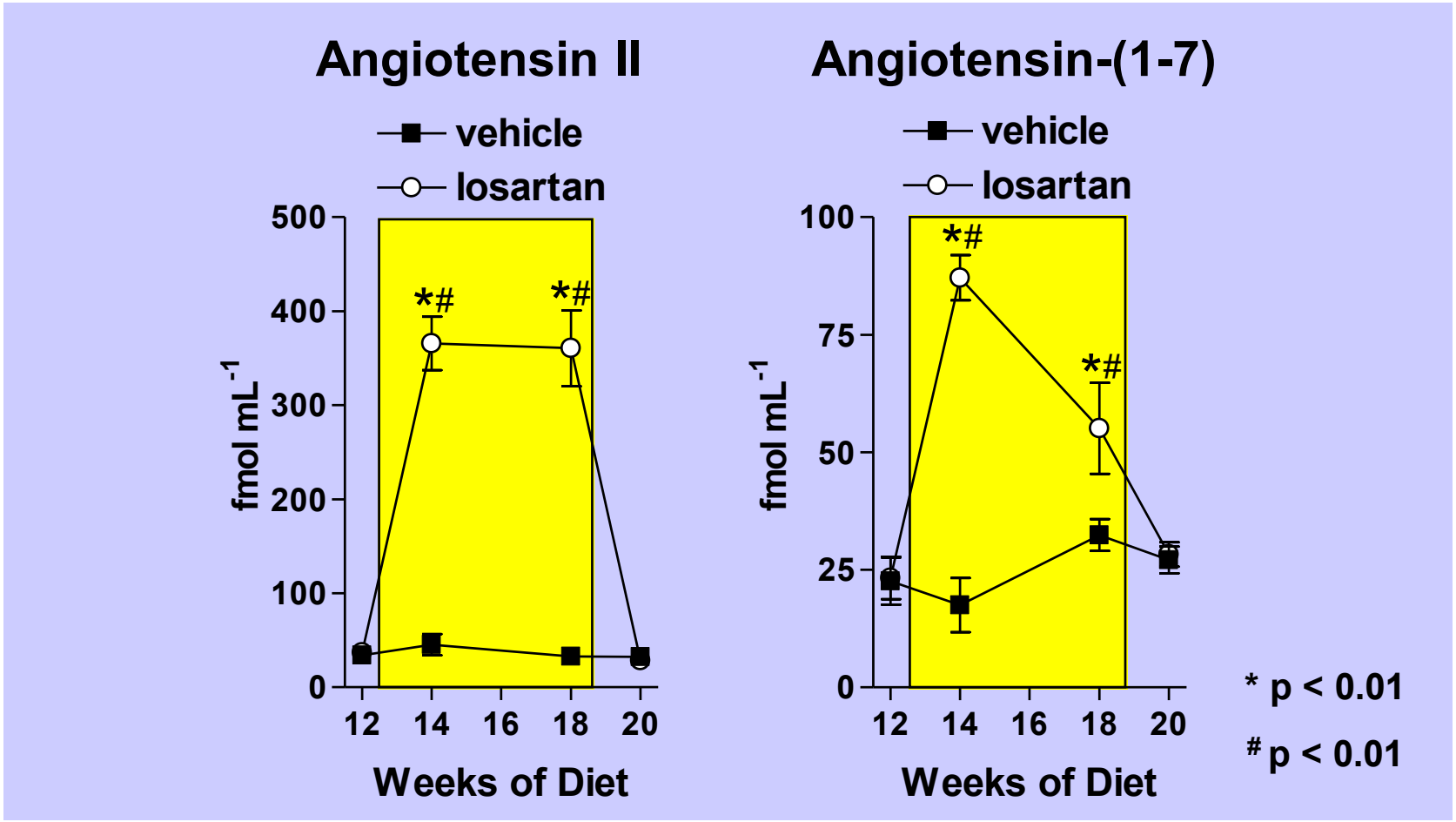


Control feeding of a 4-week High-Cholesterol Diet

Feeding of a 4-week High-Cholesterol Diet in Monkeys medicated with Losartan

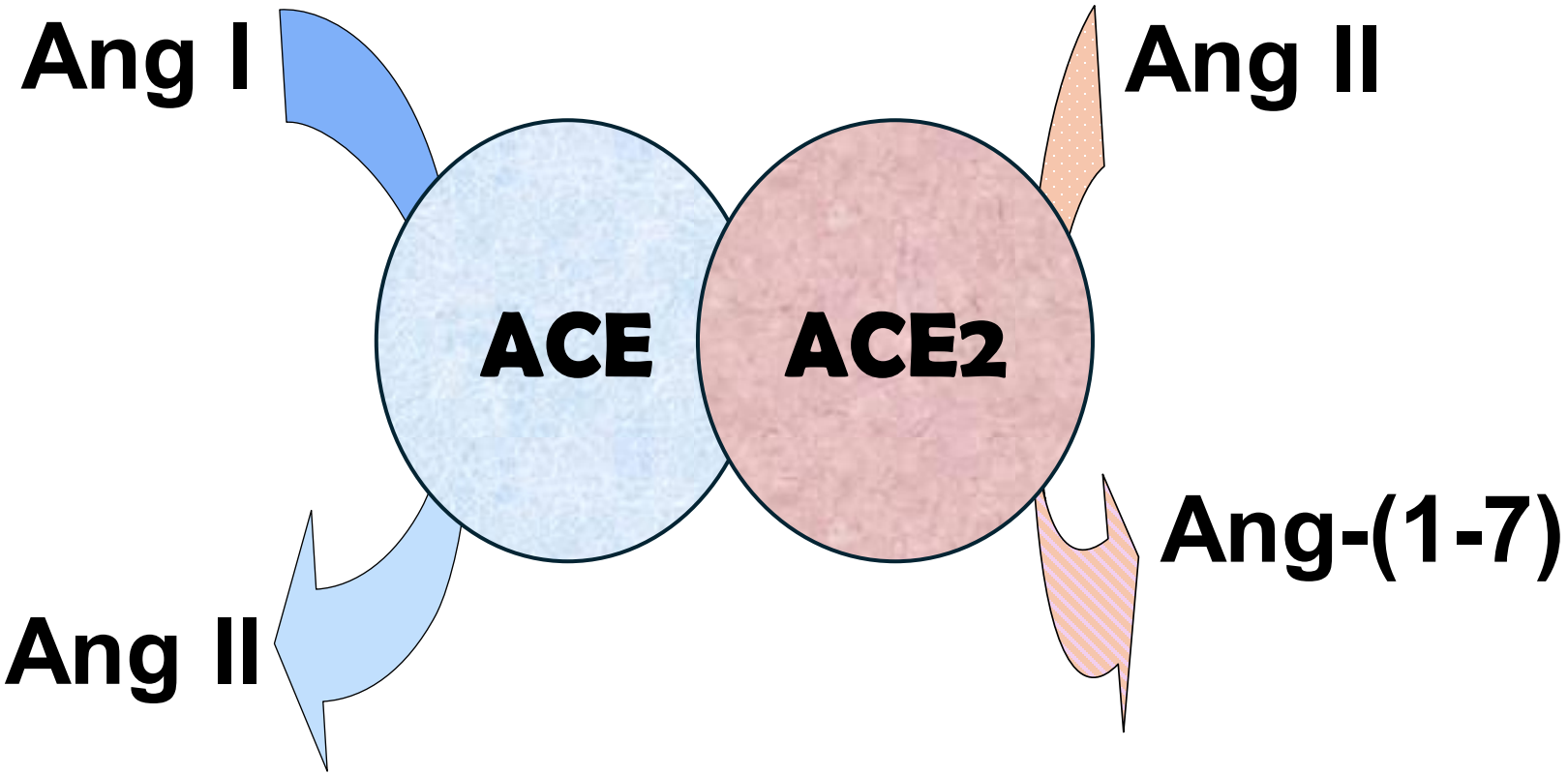
Strawn WB and Ferrario CM. Circulation. 2000;101(13):1586-93.

Plasma Angiotensin Peptide Concentrations



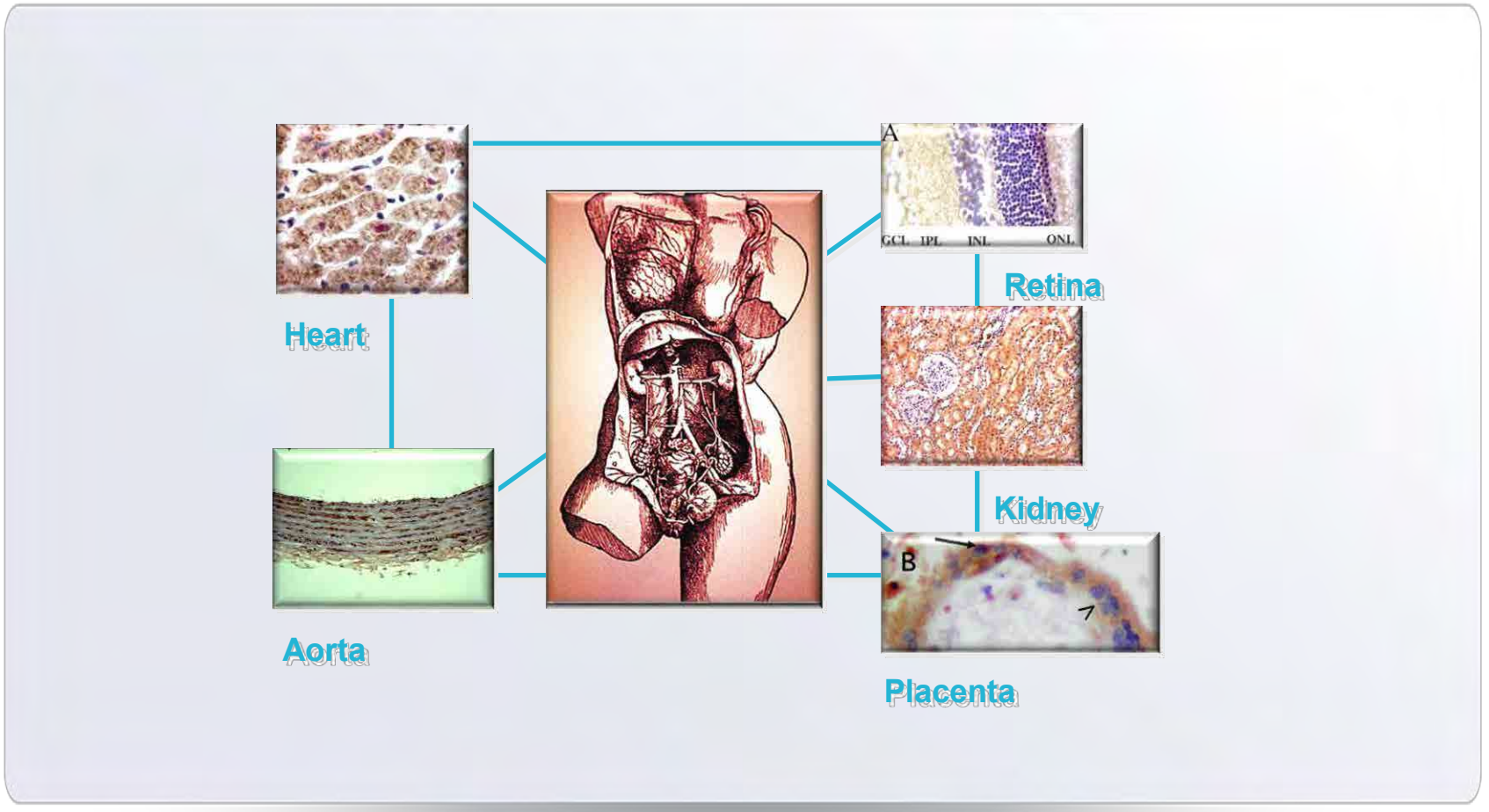
Strawn WB and Ferrario CM. Circulation. 2000;101(13):1586-93.

JANUS - GOD OF ENDINGS AND BEGINNINGS

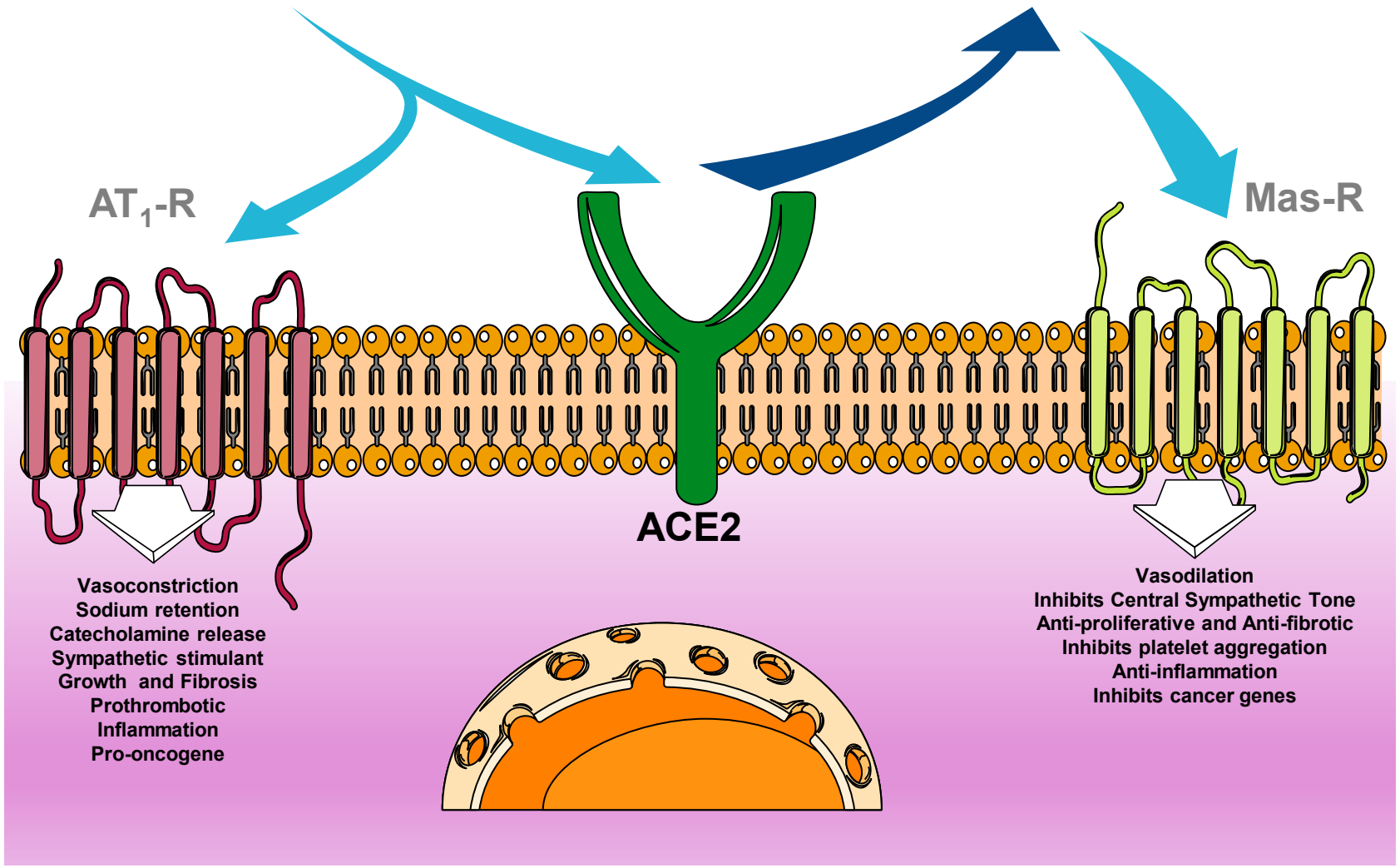


Ferrario and Jessup. Current Hypertension Reviews 2007. Vol. 3 Issue 2 Pages 97-104

Angiotensin Converting Enzyme 2



Ferrario, CM. Curr Opin Nephrol Hypertens. 2011 Jan;20(1):1-6.


ANGIOTENSIN II
ANGIOTENSIN-(1-7)
AT1-R
Mas-R
ACE2
Vasoconstriction
Sodium retention
Catecholamine release
Sympathetic stimulant
Growth and Fibrosis
Prothrombotic
Inflammation
Pro-oncogene
Vasodilation
Inhibits Central Sympathetic Tone
Anti-proliferative and Anti-fibrotic
Inhibits platelet aggregation
Anti-inflammation
Inhibits cancer genes

LANDMARK STUDY

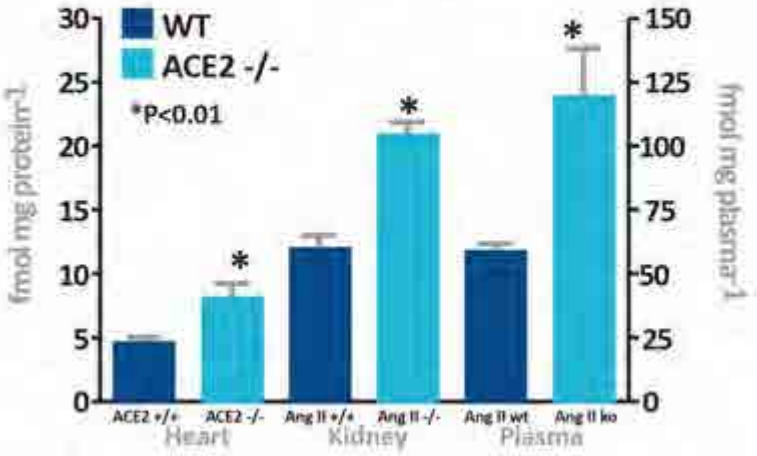
articles

Angiotensin-converting enzyme 2 is an essential regulator of heart function

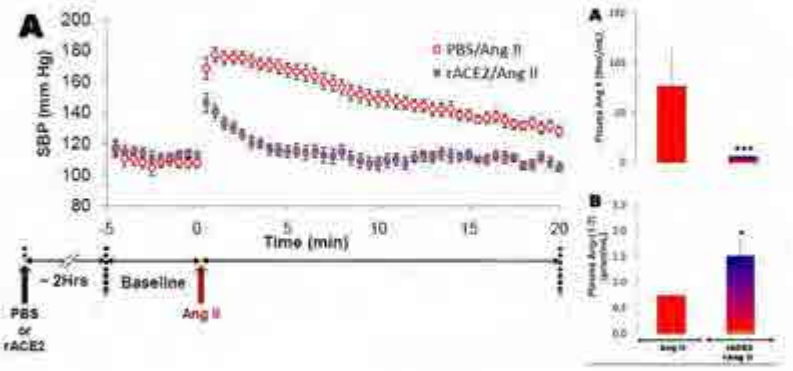
Michael A. Crackower*†‡, Renu Sarao*§‖, Gavin Y. Oudit‡‖¶#, Chana Yagil☆, Ivona Kozieradzki*§, Sam E. Scanga*†, Antonio J. Oliveira-dos-Santos*, Joan da Costa*, Liyong Zhang*†‡§, York Pei#, James Scholey#, Carlos M. Ferrario††, Armen S. Manoukian*†, Mark C. Chappell††, Peter H. Backx‡¶#, Yoram Yagil☆ & Josef M. Penninger*†‡§

Crackower et al. NATURE | VOL 417 | 20 JUNE 2002

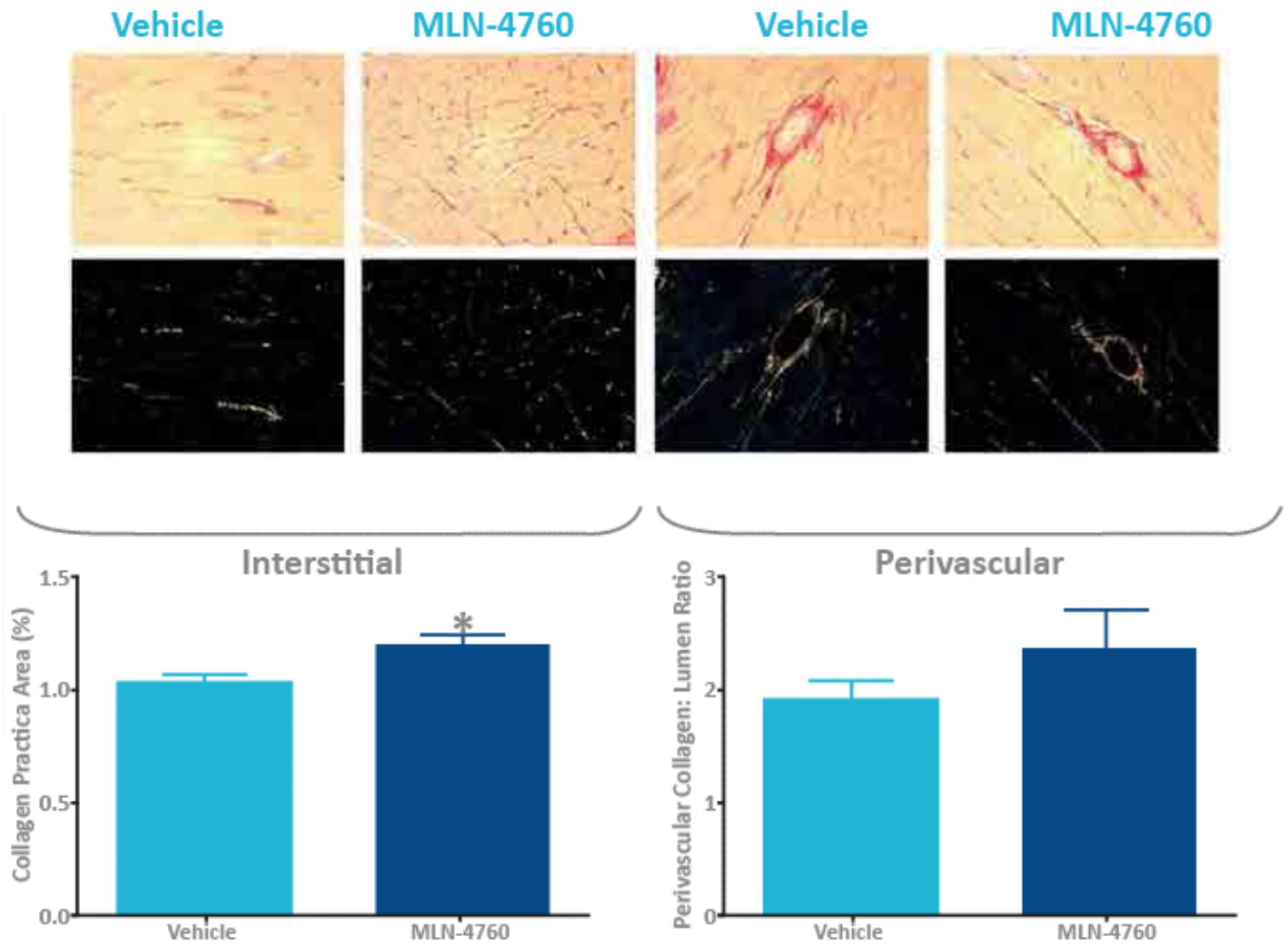
Angiotensin II is Increased in ACE2$^{-/-}$ Mice



Antihypertensive Effect of Human Recombinant ACE2 in Mice

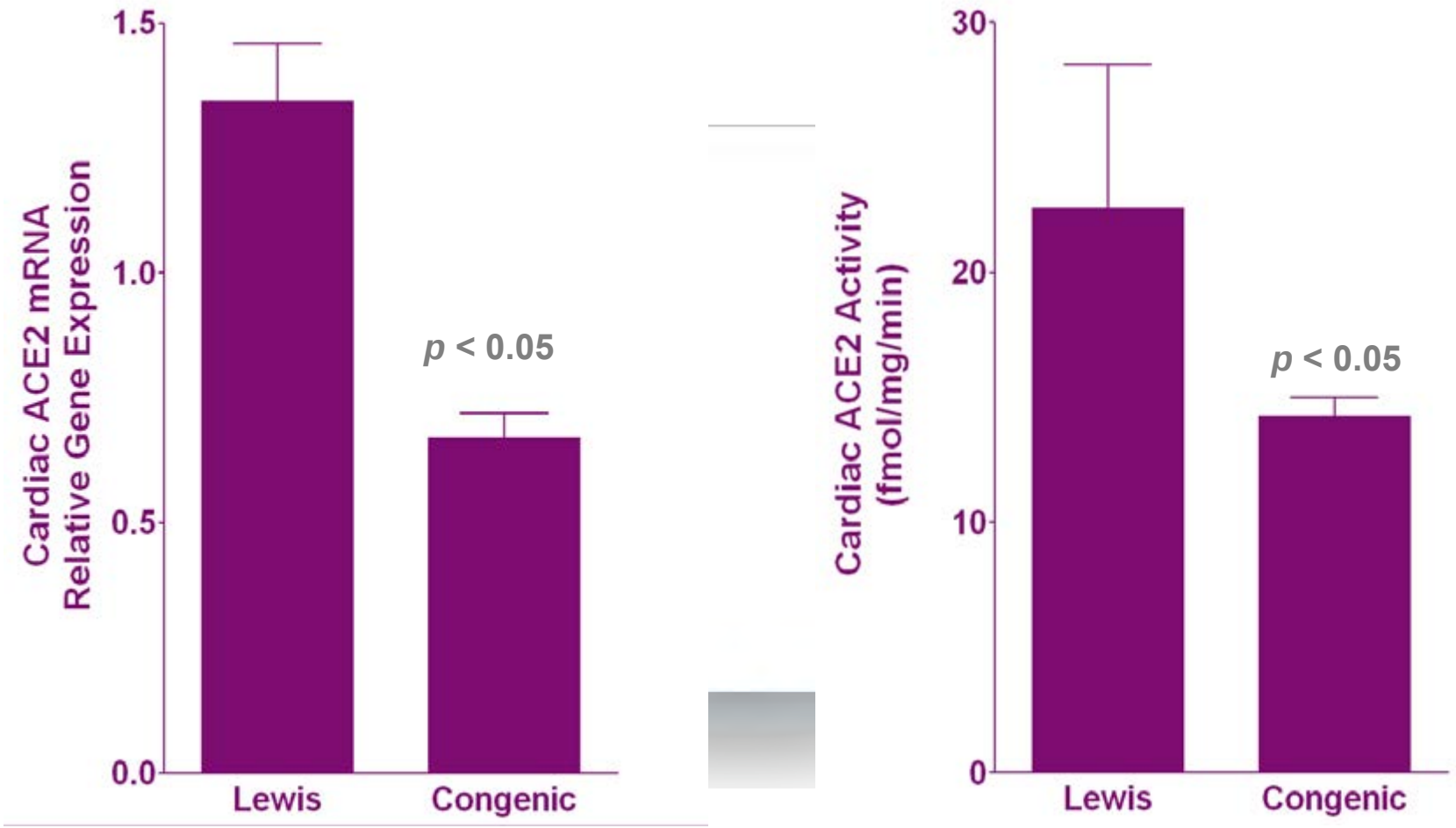


ACE2 Inhibition Exacerbates Cardiac Hypertrophy

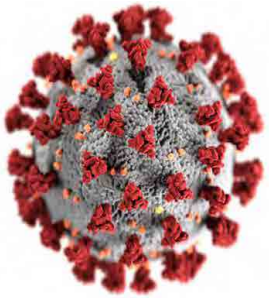


Trask AJ, et al. Am J Hypertens. 2010 Jun;23(6):687-93.

Hypertension Reduces ACE2 Gene Expression and Activity

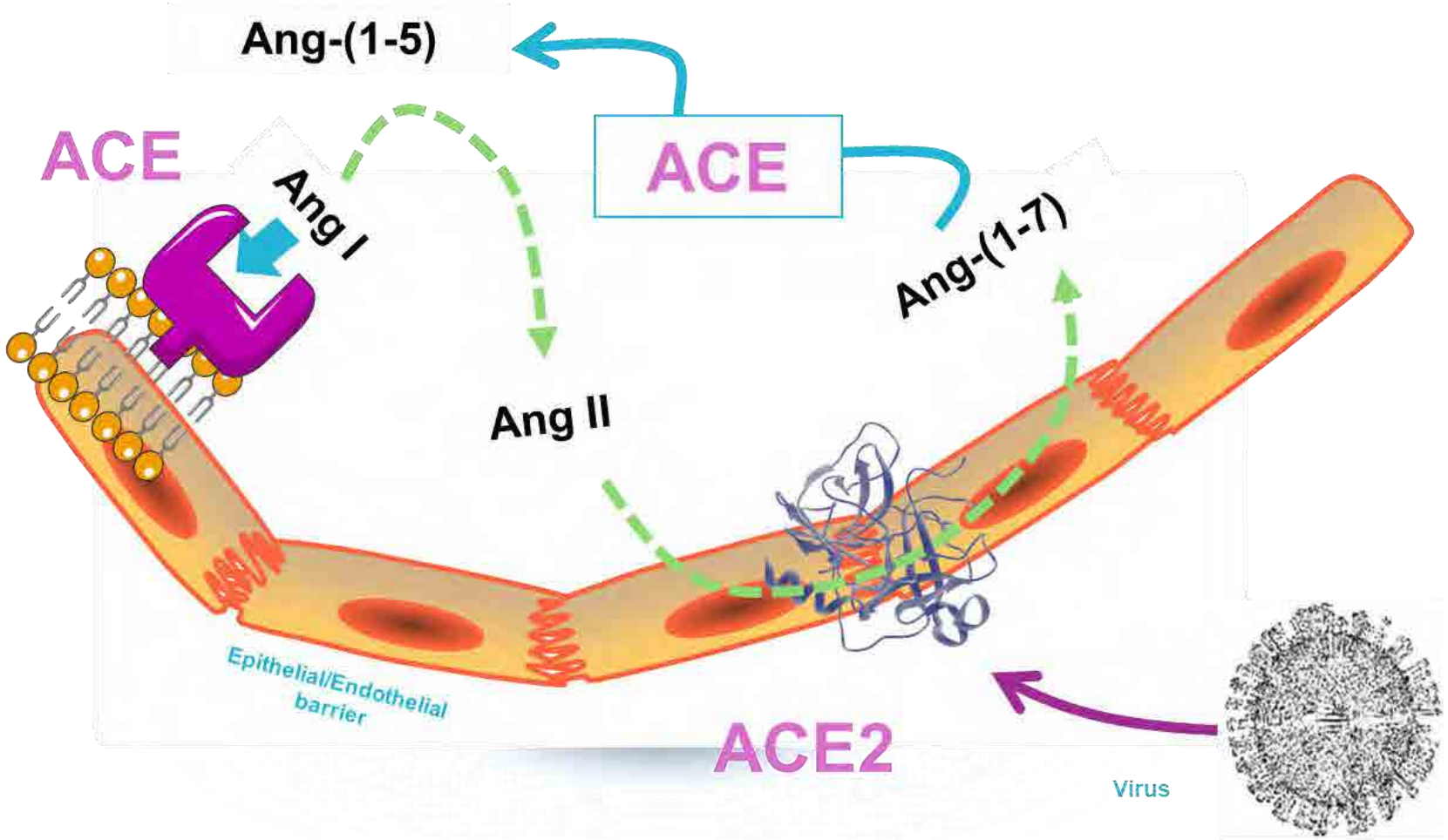


Jessup JA, et al. Am J Physiol Heart Circ Physiol. 2006 Nov;291(5):H2166-72.

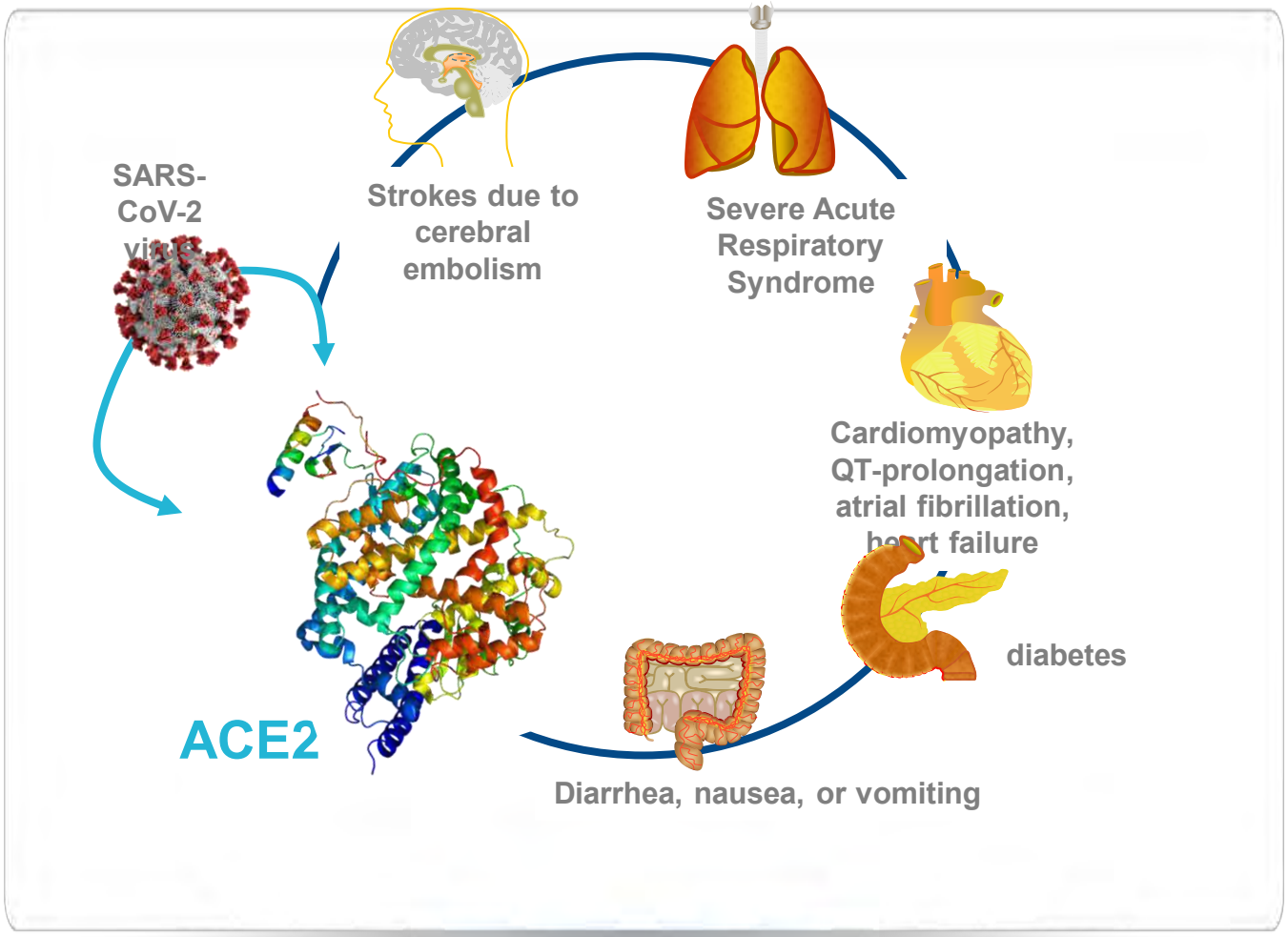


SARS-CoV-2 virus

The Awakening

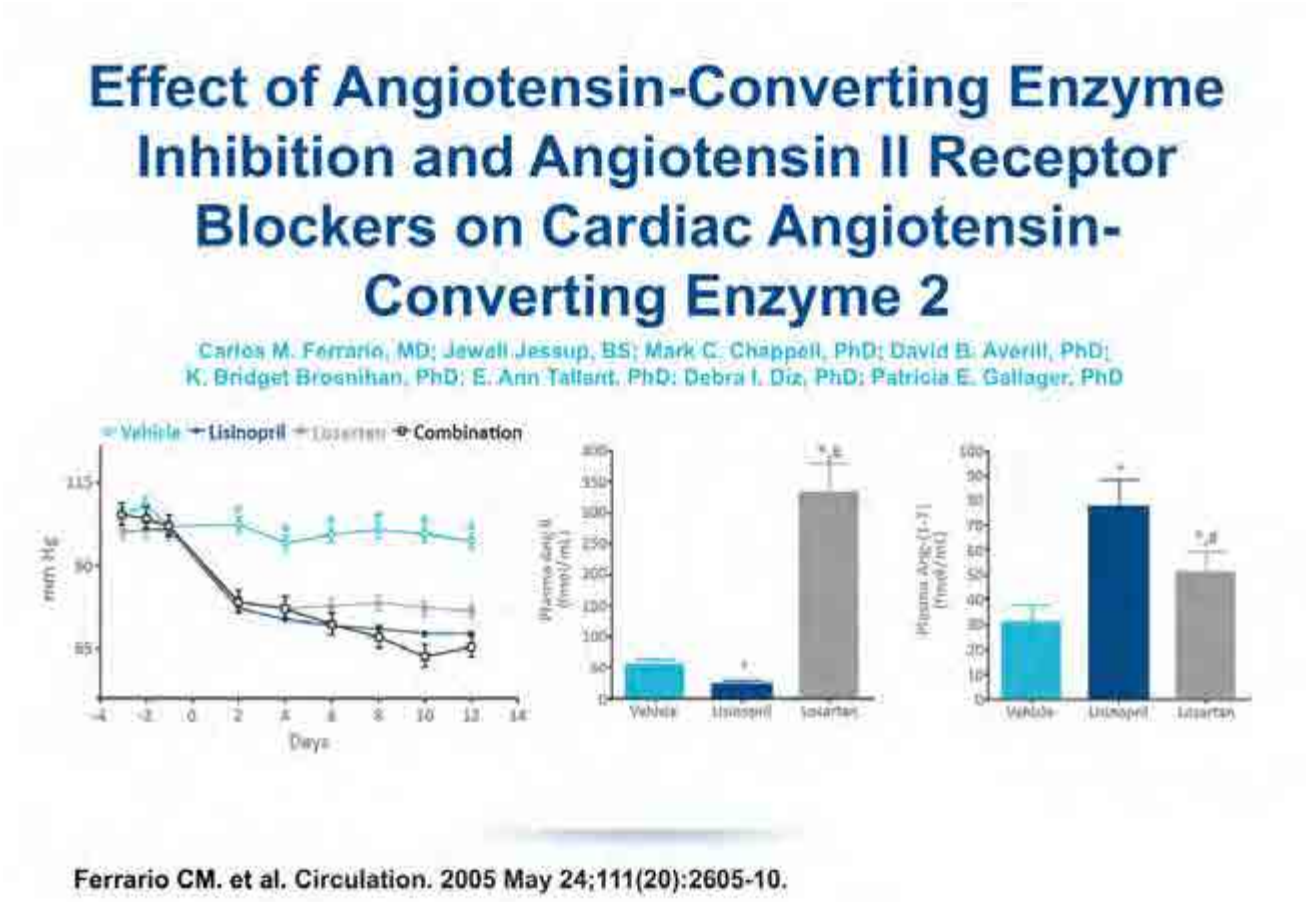


The SARS-CoV-2- and ACE2

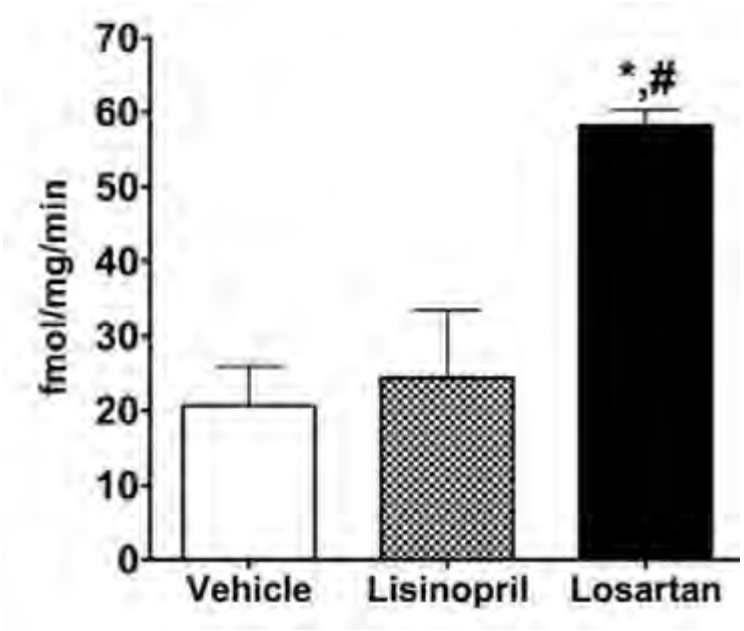


ACE2: The Awakening

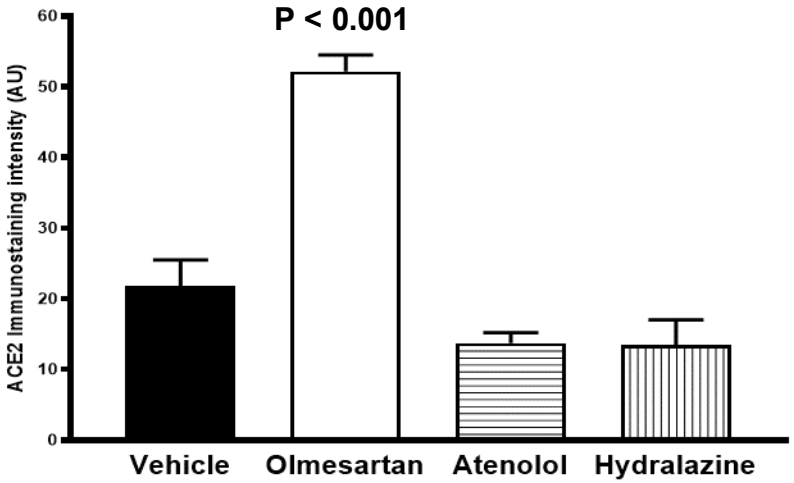
Health care professionals, physicians, researchers, and even patients are actively debating the benefits of continuing treatment with ACE inhibitors and ARBs in patients infected with the COVID-19 virus given the identification of ACE2 as the functional receptor for the family of coronaviruses.

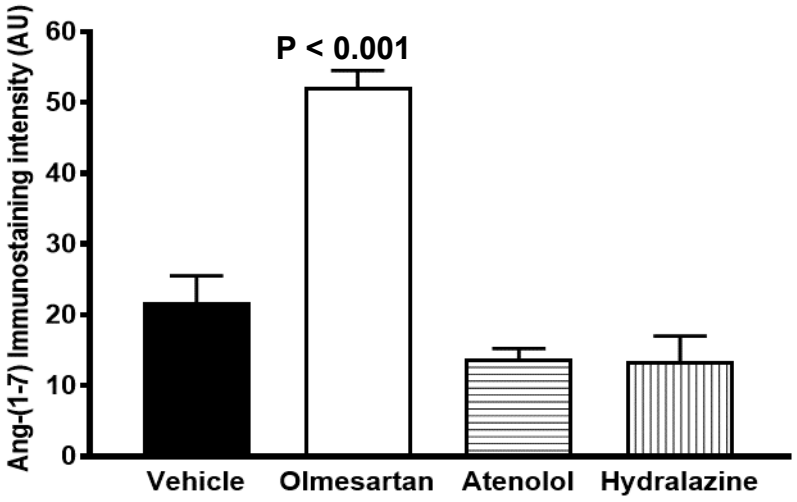


Do ACE inhibitors or ARBs worsen COVID-19 clinical evolution?



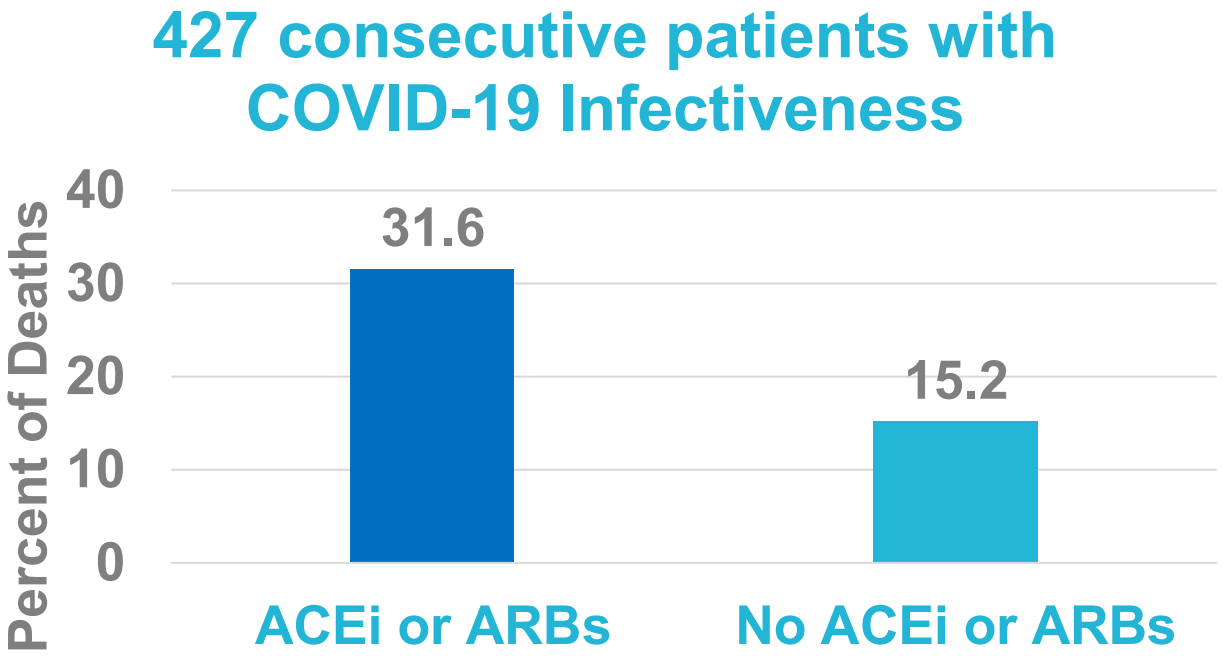
Ferrario et al. Circulation. 2005;111:2605-2610





Igase et al. Am J Physiol Heart Circ Physiol. 2005, 289(3), H1013-1019.

RAS Inhibition and SARS-CoV-2 Mortality



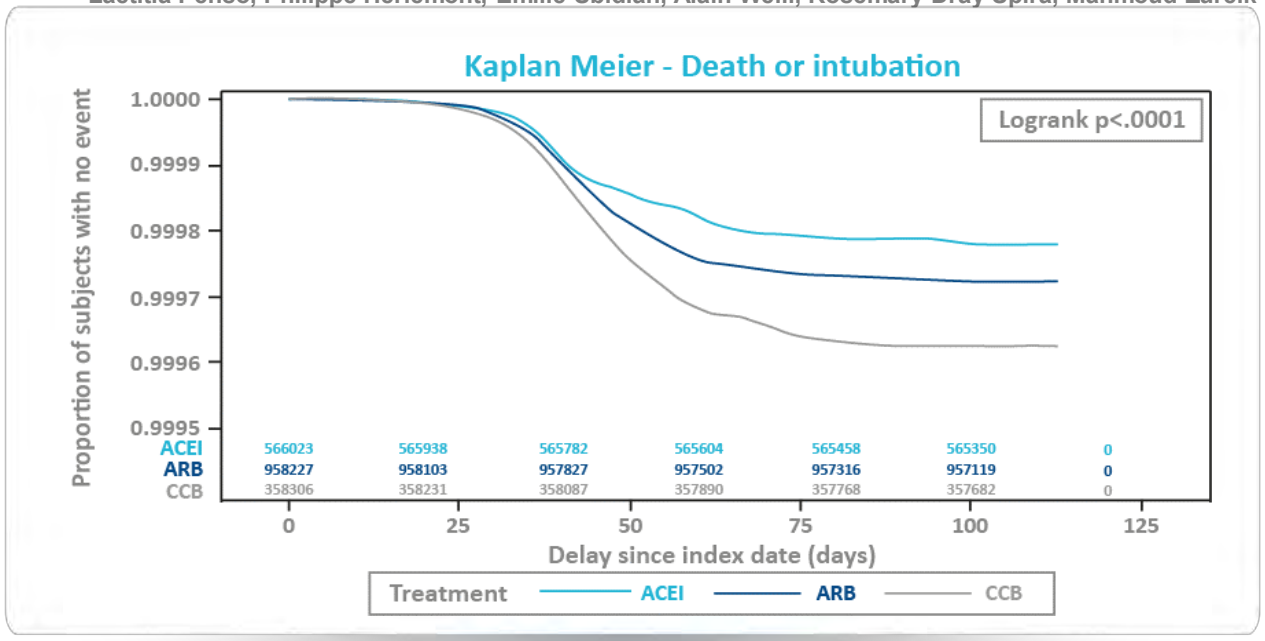
Conclusion: The apparently increased mortality of patients with COVID-19 receiving long term treatment with ACE inhibitors or ARBs is not due to the drugs themselves, but to the conditions associated with their use.

Cugno M, et al. Adv Ther. 2021 May;38(5):2709-16.

COVID-19
Antihypertensive Drugs and Covid-19 Risk

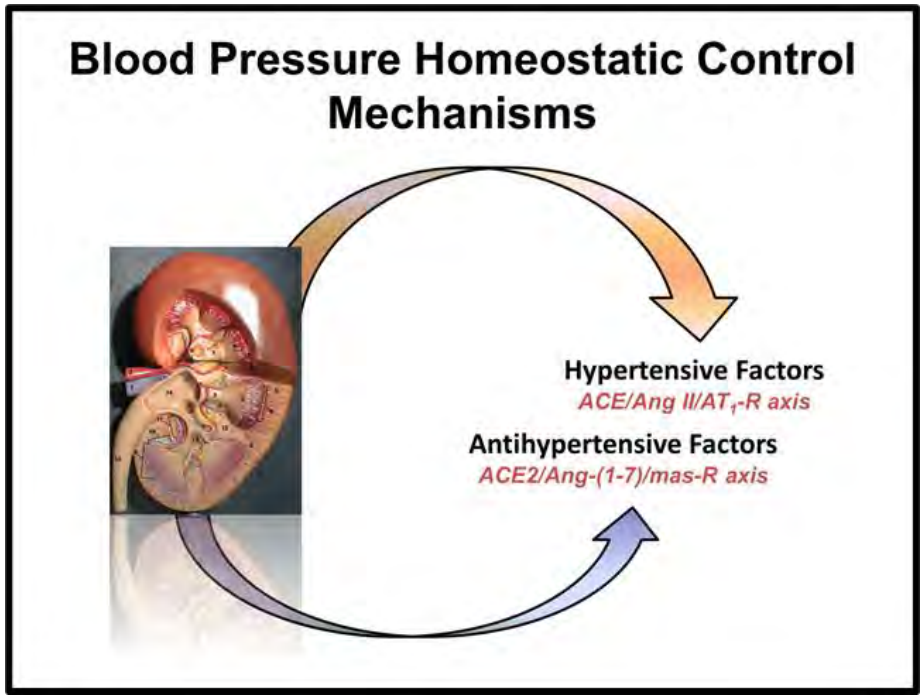
A Cohort Study of 2 Million Hypertensive Patients

Laura Semenzato,* Jerémie Botton,* Jerôme Drouin, Bérangère Baricault, Clémentine Vabre, François Cuenot, Laetitia Penso, Philippe Herlemont, Emilie Sbidian, Alain Weill, Rosemary Dray-Spira, Mahmoud Zureik



Lower COVID-19 risk in hypertensive patients treated over a long period with ACE inhibitors or ARBs compared with CCBs.

Semenzato L, et al. Hypertension. 2021 Mar 3;77(3):833-42.



- **The binding of the SARS-Cov-2 spike protein to ACE-2 has the potential to disturb this balance, by downregulating the protective effects of the ACE2/Ang-(1-7)/Mas pathway while simultaneously releasing the brake on the ACE/Ang II/AT_1-R pro-inflammatory and pro-thrombotic arm of the RAS system.**

- Soluble ACE2 proteins have been studied to intercept SARS-CoV-2-CoV-2 from binding to membrane-bound ACE2 and prevent cell entry of SARS-CoV-2 altogether (Batlle D, et al. Cell. 2022;185(11):1837-9).
- Continuos intravenous Ang-(1-7) (Martins et al. DOI: 10.1186/s13613-024-01369-0) or administration of a MAS receptor activator (Lobo et al. DOI: 10.1016/j.eclinm.2023.102383) have not yielded conclusive results in COVID-19 patients.

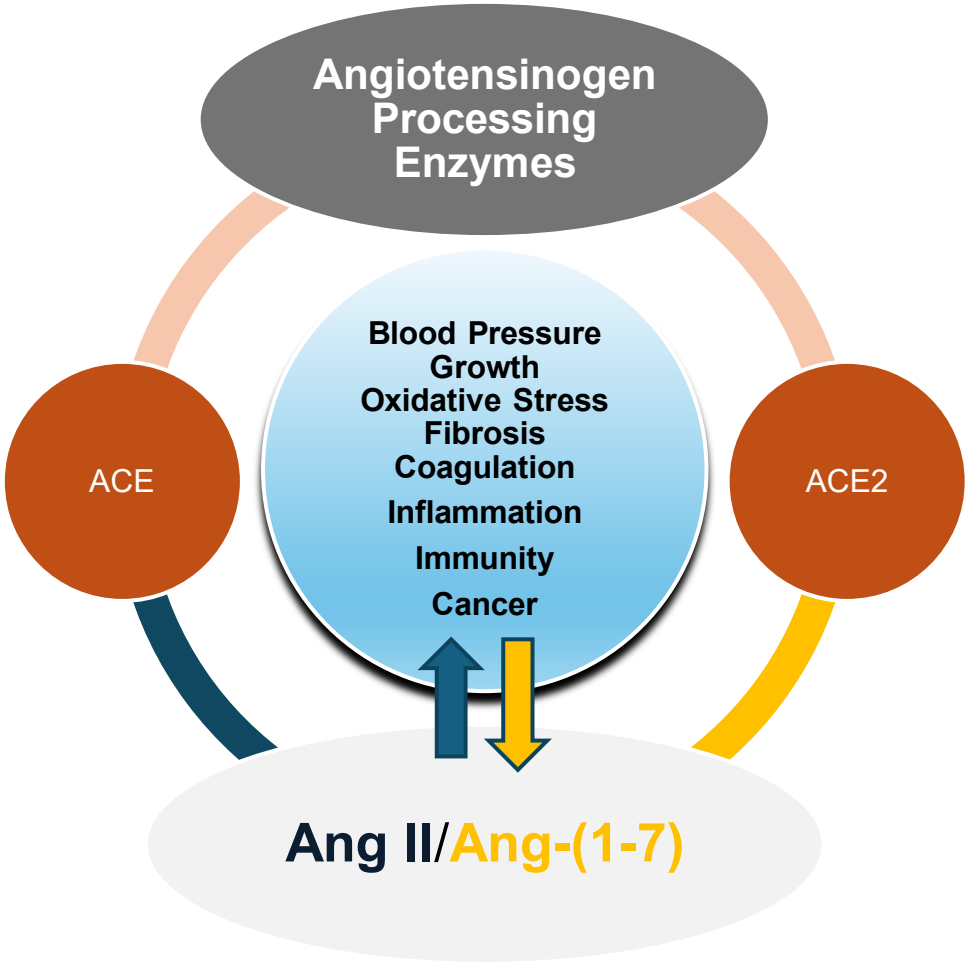
SUMMARY

The ACE2/Ang-(1-7)/mas-receptor axis constitutes a fundamental regulatory, internal cellular control component of the RAS;

The imbalance of the two arms of the RAS may explain the cardiovascular adaption associated with dysregulation of the blood pressure control mechanisms;

The expression of the ACE2/Ang-(1-7)/mas-receptor axis in cardiac, vascular, and renal tissues underscores the significant differences in the biochemical constitution of the RAS in blood versus tissues, adding to the complexity of the system.

Cardiovascular Adaptation Depends on Balance of Ang II/Ang-(1-7) Activity



Thank you for your Attention

Ferrario CM, et al. Kidney Int Suppl (2011). 2022;12(1):36-47.


ACE
ACE2

A Physician's Role in Addressing Health Disparities - A Review of Strategies

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Personal/ Professional Financial Relationships: Jada Bussey-Jones

External Industry Relationships *	Company Name	Role
Equity, stock, or options in biomedical industry companies or publishers	None	
Board of Directors or officer	None	
Royalties from Emory or from external entity	None	
Industry funds to Emory for my research	None	
Other	None	

All images of people in this PPT (other than my family) were downloaded from Google Images and are openly available on the WWW.

Objectives

By the end of this sessions, participants should be able to:

- Define health inequities and key drivers
- Describe the role of medical decision making & impact on adverse health outcomes
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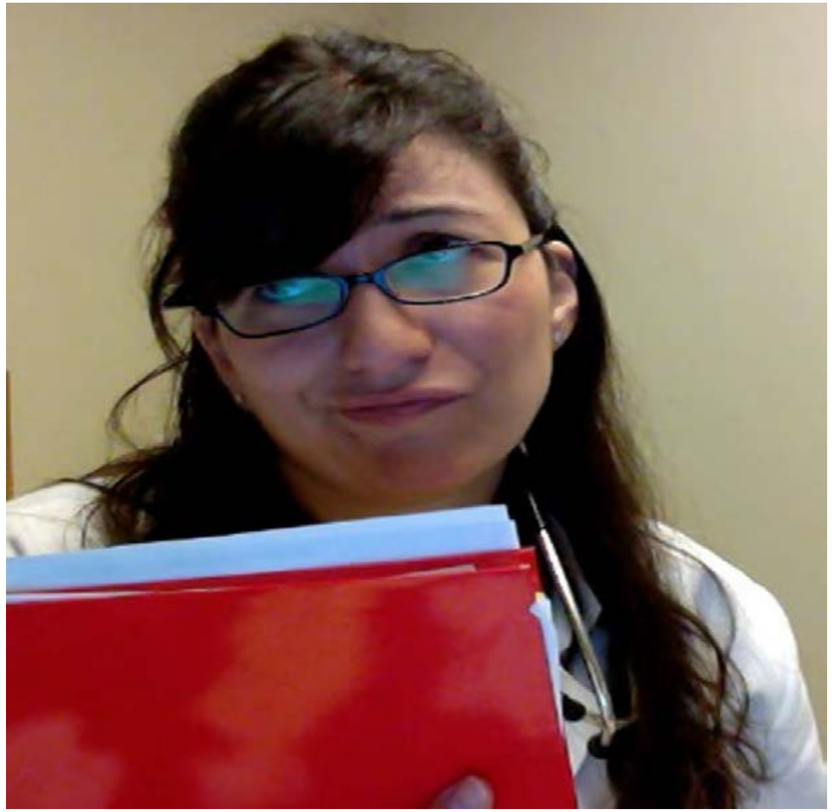
Case

68-year-old man with HTN, HL, CHF who has been readmitted for the 3rd time this month with CHF exacerbation. As the intern presents the case, her frustration is evident.

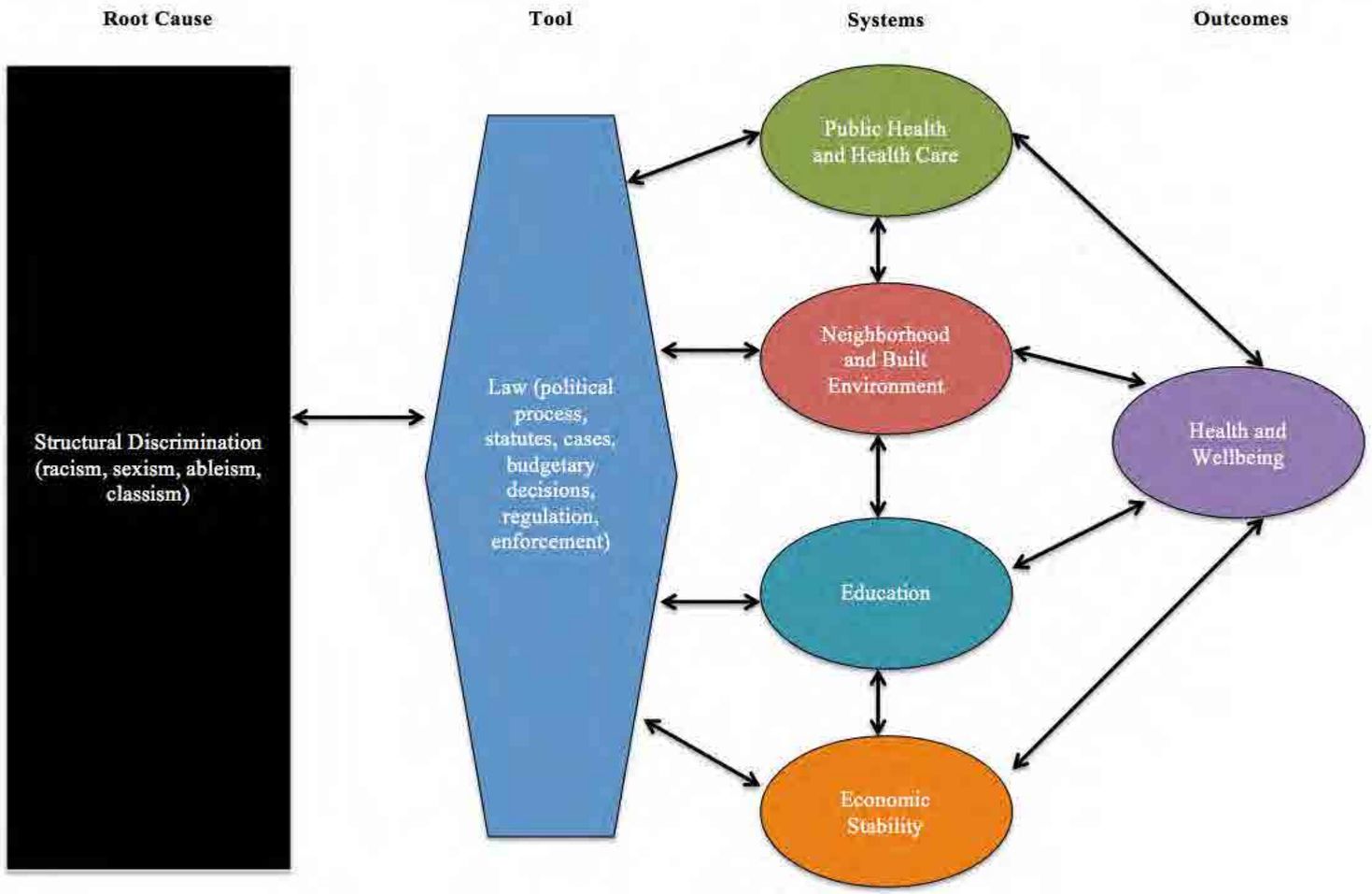


What are the potential issues?

Clinical care only 10-20%

- Ischemia?
- Atrial Fib
- Thyroid dysfunction?

This is how we are trained to think!



Revised SDOH Framework created by Ruqaiijah Yearby (2020)

Dobson, R., Rice, D.R., D'hooghe, M. et al. Social determinants of health in multiple sclerosis. Nat Rev Neurol 18, 723–734 (2022)

Yearby R. Structural Racism and Health Disparities: Reconfiguring the Social Determinants of Health Framework to Include the Root Cause, 48 J. of L. Med. & Ethics 518-526 (September 2020)

Case

- A 36 yr old BF w/ hx of unprovoked DVT and PE presents in labor.
- After undergoing C-section 2/2 to prolonged delivery. Doing well.
- On POD 1 she has pleuritic chest pain and SOB.
- Because of her history, the pt. requests a stat CT Chest and treatment with heparin.

- What do you do next?

That is not what happened…

The nursing staff and physicians believed that her pain medications were causing delirium and decided to observe the patient.

The patient continues to have symptoms and to vocally express desire for CT chest.

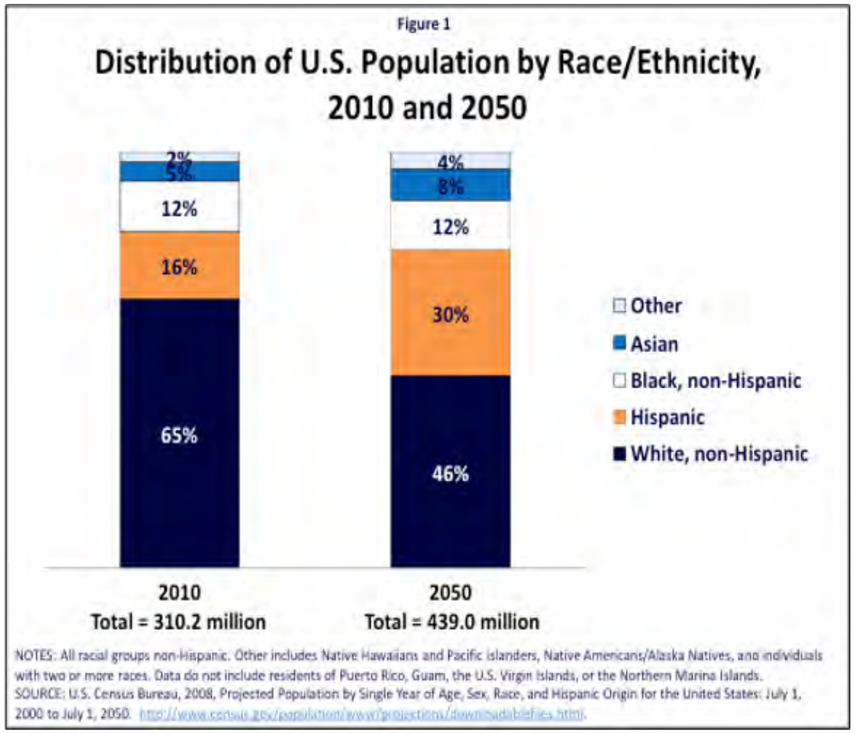
After pleading with staff, CT is ultimately performed revealing multiple submassive thrombi.

Sound familiar…

If it can happen to Serena…

Why is this important

- Increasing diversity in US
- Current climate…impact:
  - Our profession
  - Our patients
  - Our communities



- Goal is to think about our role…

Implicit Bias

Implicit Bias:

Attitudes or stereotypes that affect our understanding, actions, and decisions in an unconscious manner

- are pervasive
- do not necessarily align with our declared beliefs
- Generally, but not always, favor our own ingroup
- are malleable

Ohio State University Kirwin Institute for the Study of Race and Ethnicity.
http://kirwaninstitute.osu.edu/research/understanding-implicit-bias/ Accessed 10/4/17

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My Biases

We are not born to exhibit racial prejudice – we learn it…early in life

- Newborn infants demonstrated no spontaneous preference for faces from either their own-or other-ethnic groups.
- 3-month-old infants demonstrated a significant preference for faces from their own ethnic group.

*David J. Kelly, University of Sheffield, United Kingdom

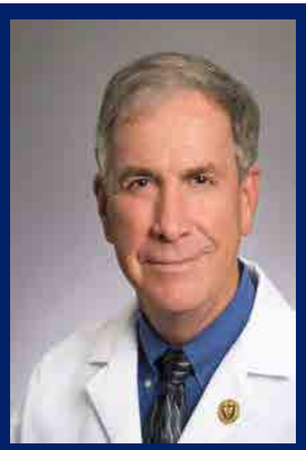
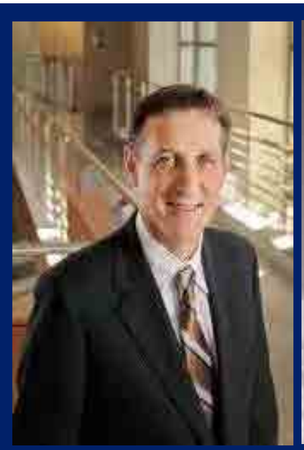
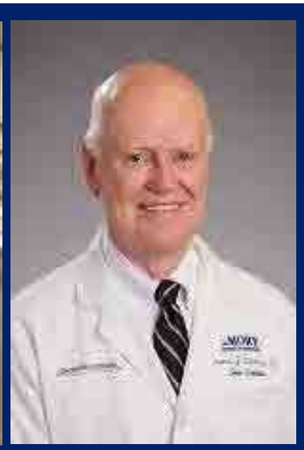
picture a doctor

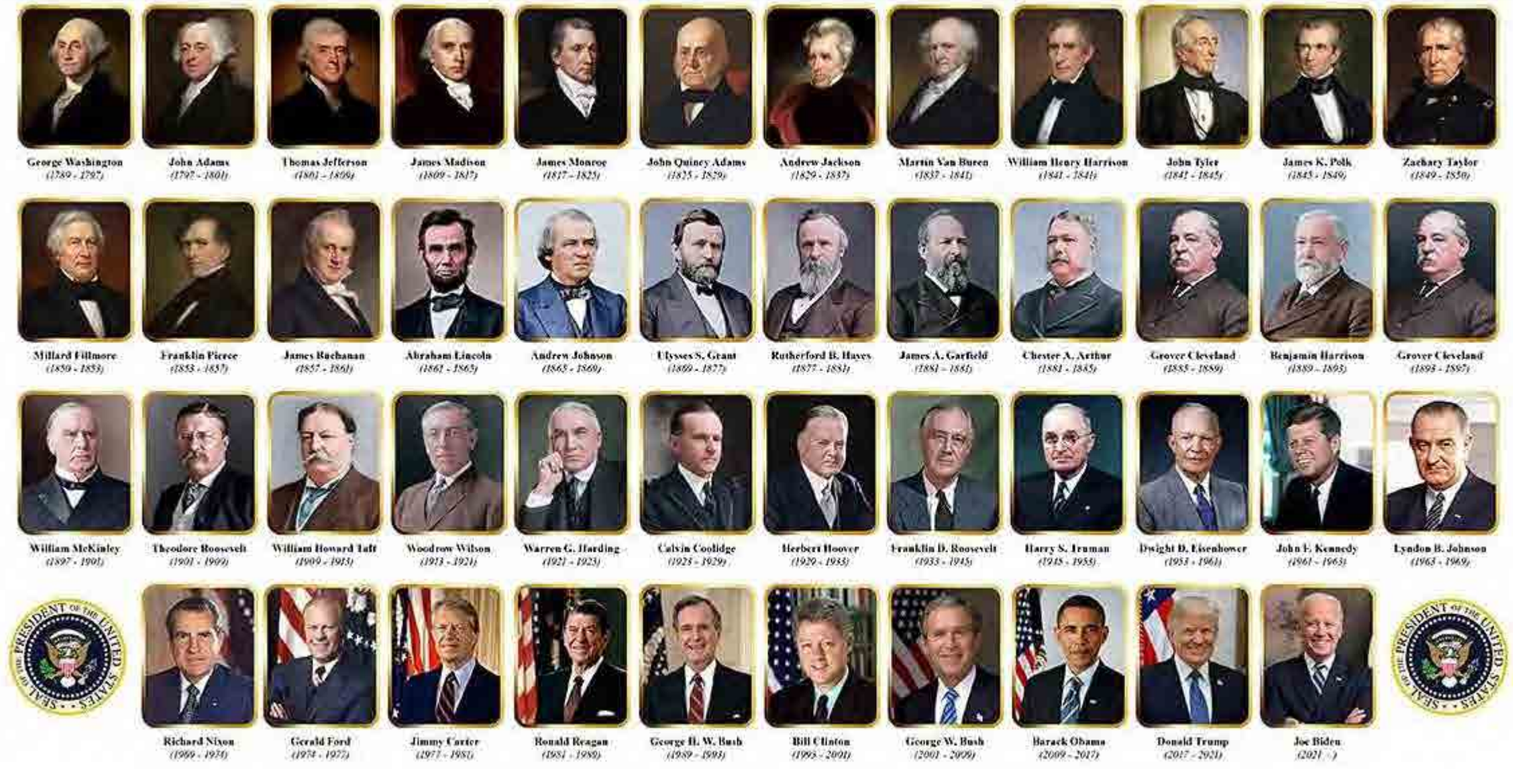
picture a boss Google search 2020

RYSE

Jan 6
Jan 12
Jan 13





Clear if unspoken message about who leads

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Impact of implicit bias on clinical & workplace decisions

- Recruitment
- Hiring decisions
- Salary & resource allocation
- Performance reviews
- Retention/Promotion
- Teamwork
- Clinical Environment

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IOM: RACE & MEDICAL CARE

Across Healthcare

- Minorities receive fewer procedures and poorer quality medical care than whites.

Difference Persist After Controlling For

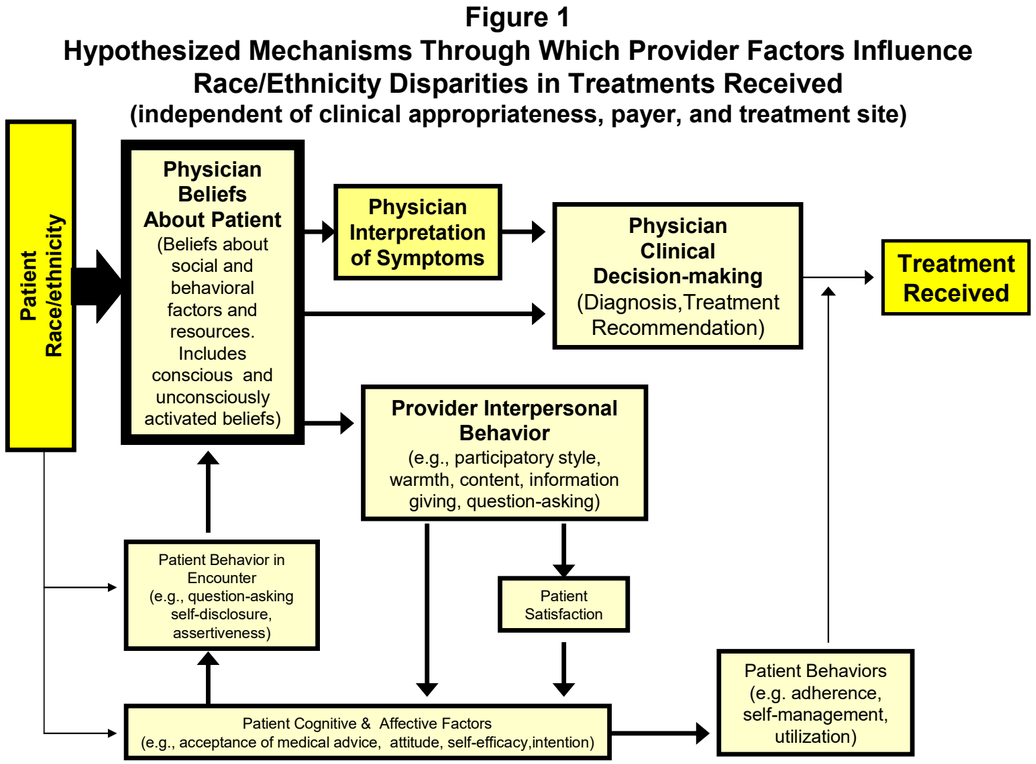
- Insurance
- SES
- Stage and severity of disease, co-morbidity
- Medical facility

Persist in Medicare & the VA Health System

- Differences in economic status and insurance coverage are expected to be minimized

Institute of Medicine, 2002
Shulman KA. N Engl J Med 1999; 340: 618–626

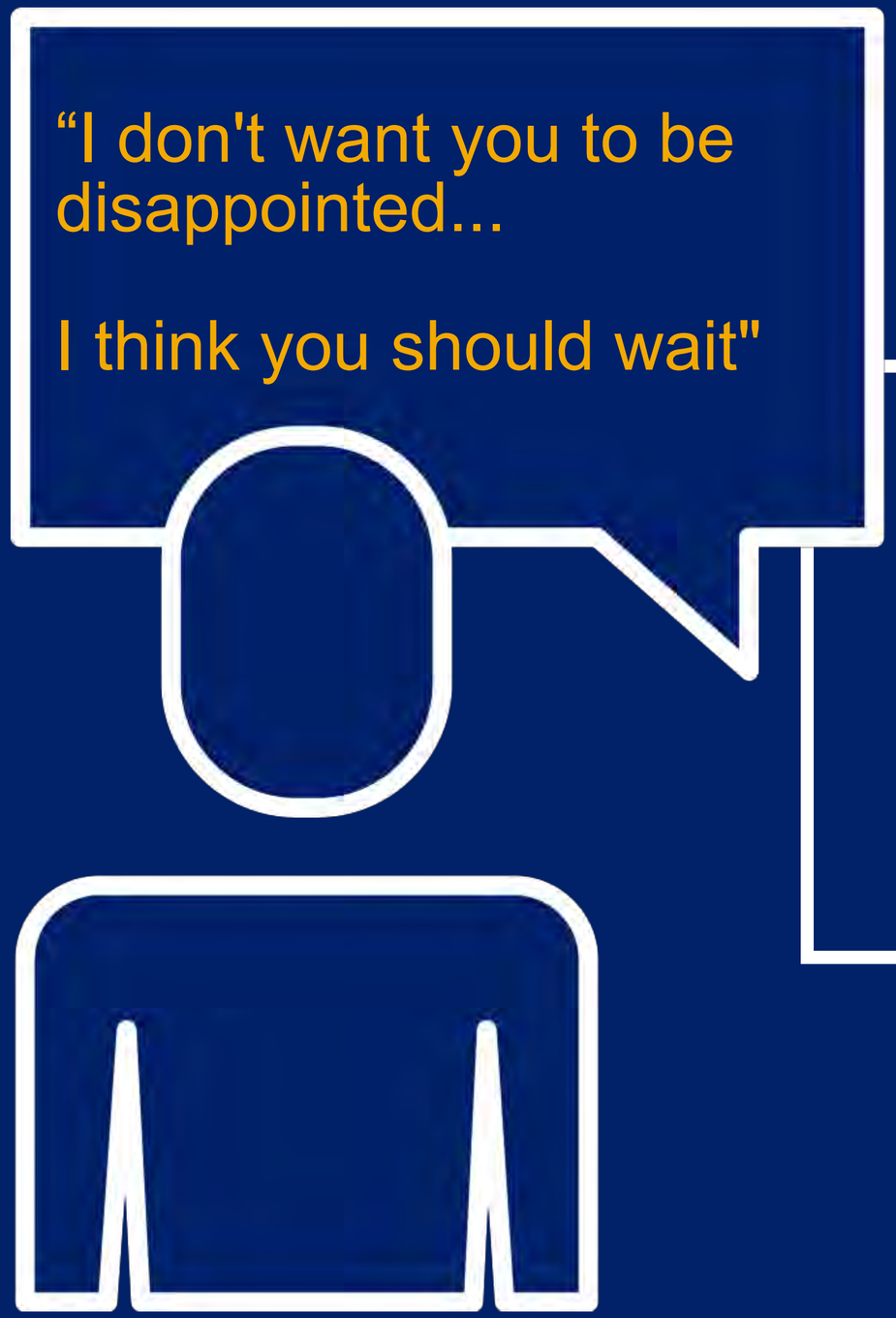
Michelle Van Ryn: Evidenced-Based Framework



- Symptom interpretation/ diagnosis
- Interpersonal behaviors
  (engagement, courtesy, warmth, info)
- Clinical decisions

van Ryn M, Fu SS. Paved with good intentions: do public health and human service providers contribute to racial/ethnic disparities in health?. *Am J Public Health*. 2003;93(2):248–255.

Workplace



Case

- Black American Woman Associate Professor in rank 6 years
- Requests consideration for promotion

Context: Me

- Him: 2 white men recently unsuccessful
- Me: Service on DOM P&T Committee

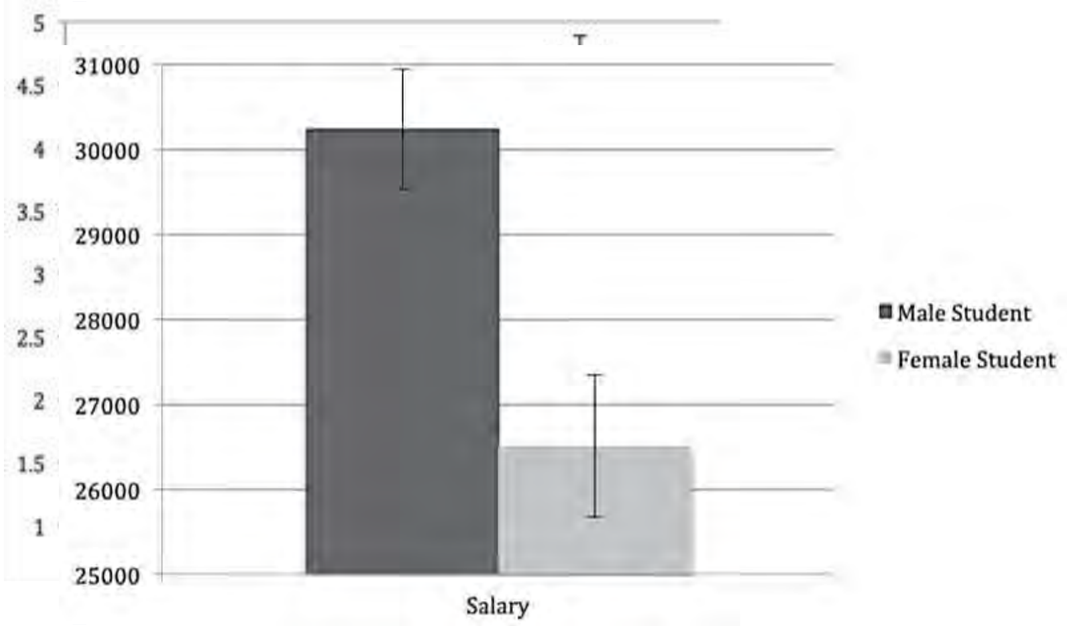
Evidence: URiM & Women Faculty

- **Barriers for Success**
  - Less Mentorship
  - Bias experiences
  - Disproportionate share of non-career advancing activities
- **Consequently:**
  - Less likely to achieve senior promotion
  - Remain in rank longer
  - Lower levels of job satisfaction
  - More likely to leave academia

Nickens 2000, Palepu 1998, Diggs 2009, Liu 2010, Thomas 2000, Helm 2000, Diggs 2009

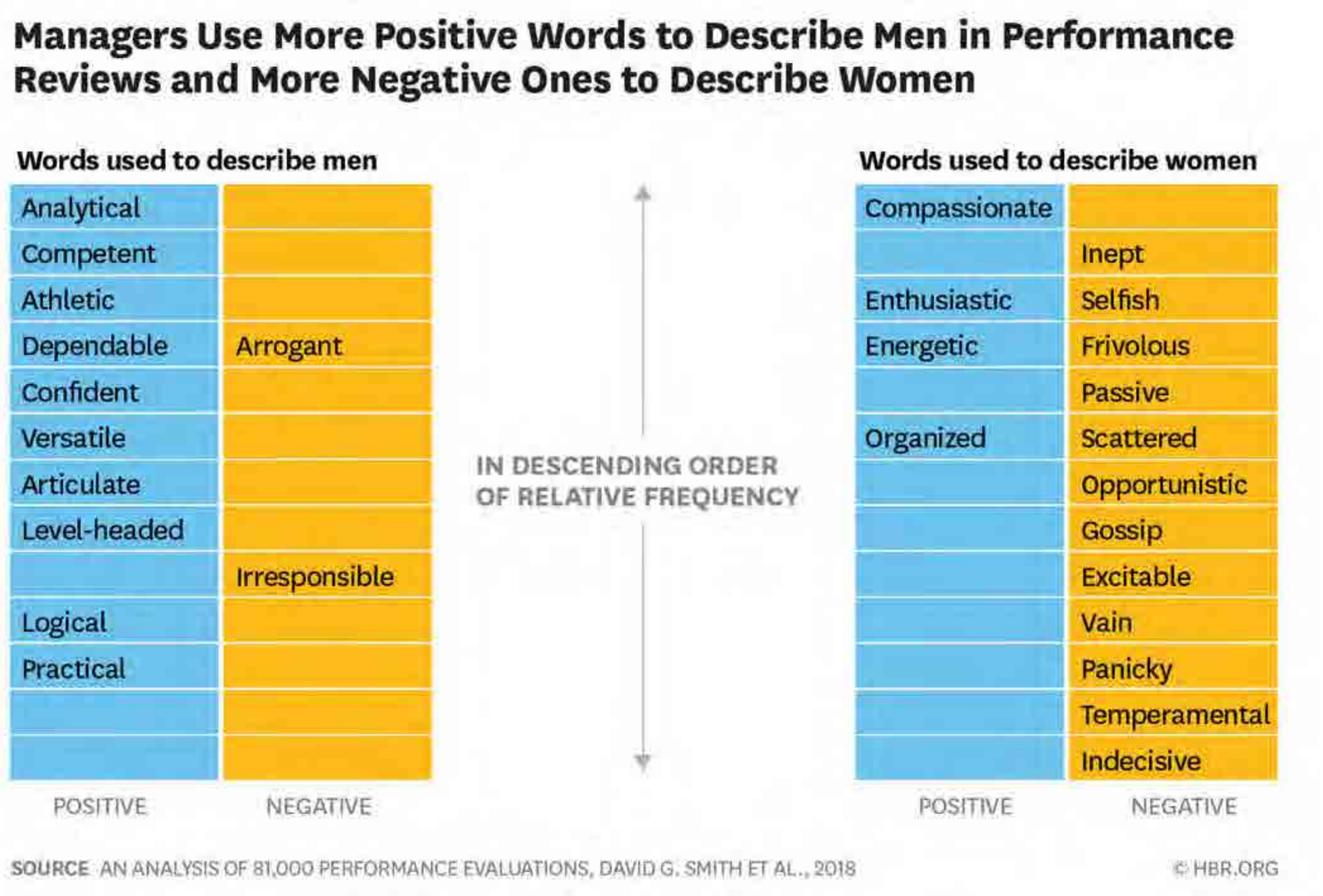
Implicit Bias & Workplace Decisions: Compensation, Resource Allocation

- Science faculty (n=127) at research-intensive universities rated applications for students applying for lab manager positions
- Applications randomly assigned male or female names
- Faculty asked to judge student competency, hireability, interest in mentoring, and assign salary



Emory Bias Training: Moss-Racusin CA et al. PNAS 2012;109:16474-16479

Unconscious Bias and Workplace Decisions: Performance Evaluations



"What are you girls gossiping about?"

"Where are you really from?"

“You speak really good English”

“She’s so bossy”

”That presentation was ***SUPRISINGLY*** good”

“Your name is hard to pronounce. I’ll just call you Jane”

"That's so gay."

Microaggressions

- Brief and common usually verbal indignities
- Often unintentional,
- Communicate hostile or negative racial insults and
- Potentially harmful or unpleasant for the target person or group.

Run #LikeAGirl:

Microaggression & Internalized bias

Microaggression and internalized bias….

Always #LikeAGirl Campaign Ad:
"Super Bowl XLIX" - YouTube

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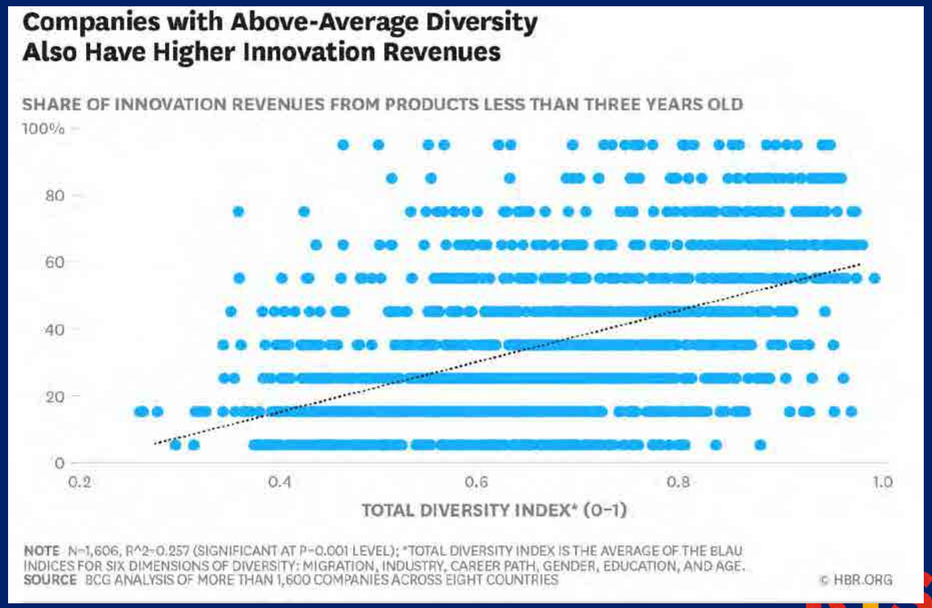
Why diversity is important?
NOT just for marginalized groups…

Business Case for Diversity



Rohner, U. and B. Dougan (2012). Gender diversity and corporate performance. Technical report, Credit Suisse Research Institute, Zurich.

Clinical care: Diversity can be mitigating factor

- Women less likely to die after MI when treated by female MDs
- women were 32% less likely to die (and 16% less likely to have complications) w/ female surgeon
- Female MDs are more likely to follow guidelines (CHF, DM, preventive care)
- Women ask patients about social circumstances & spend more time w/ pts

Tsugawa Y, et al. Comparison of hospital mortality and readmission rates for Medicare patients treated by male vs. female physicians. *JAMA Intern Med.* 2017;177(2):206–213.
Kim C, et al. Is physician gender associated with the quality of diabetes care? *Diabetes Care*. 2005;28(7):1594–1598.
Lurie N, et al. Preventive care for women. Does the sex of the physician matter? *N Engl J Med*. 1993;329(7):478–482.
Frank E, Harvey LK. Prevention advice rates of women and men physicians. *Arch Fam Med.* 1996;5(4):215-219.
Baumhäkel. Influence of gender of physicians and patients on guideline-recommended treatment of chronic heart failure in a cross-sectional study. Eur J Heart Fail. 2009 Mar;11(3):299-303.
Roter D,. Sex differences in patients' and physicians' communication during primary care medical visits. Med Care. 1991 Nov;29(11):1083-93.
Greenwood BN, Carnahan S, Huang L. Proc Natl Acad Sci U S A 2018;115:8569-8574.

Clinical care: Diversity can be mitigating factor

- Black pts get more preventive services w/ black MDs;
- URM MDs more likely to serve minority, poor, and Medicaid populations.
- Gender, race, and language concordance associated w/ improved outcomes – satisfaction, adherence, trust, infant mortality, MI outcomes, etc.

Alsan M, Garrick O, Graziani GC. National Bureau of Economic Research, 2018
Cantor JC, Miles EL, Baker LC, Barker DC. Inquiry 1996;33:167-180.
Cooper-Patrick, L. JAMA. 1999; 282: 583–589

Hot off the press: Increased Black PCPs in county associated with improved life expectancy for Blacks

JAMA Network™

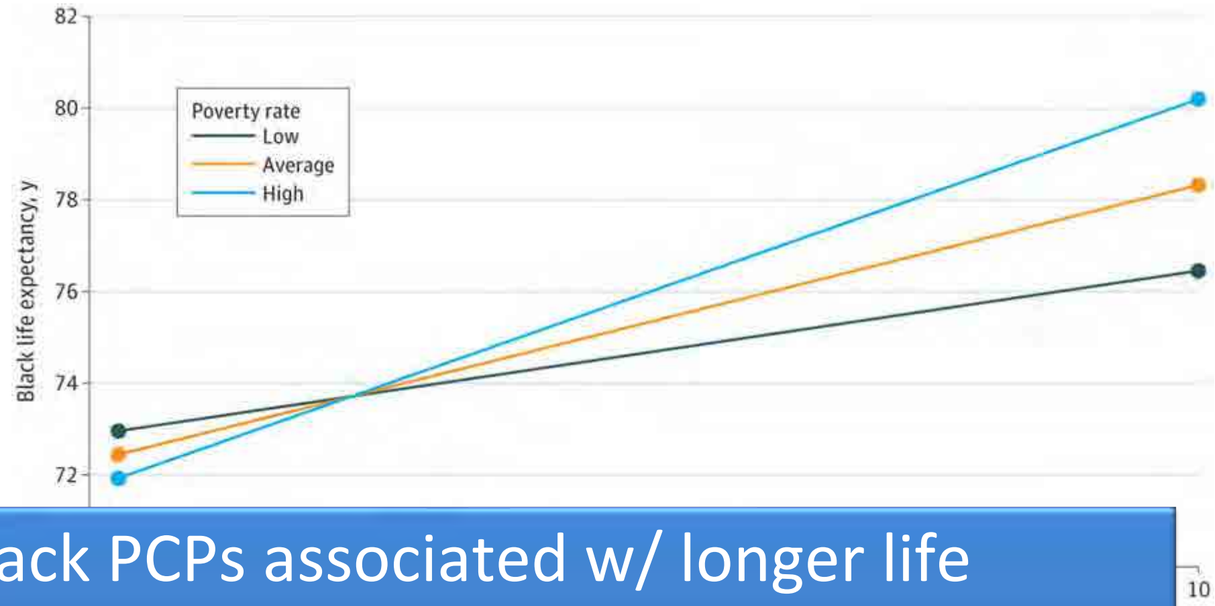
HEALTH

In counties with more Black doctors, Black people live longer, 'astonishing' study finds

By Usha Lee McFarling April 14, 2023 Reprints

ADOBE

Black people in counties with more Black primary care physicians live longer, according to a new national analysis that provides the strongest evidence yet that increasing the diversity of the medical workforce may be key to ending deeply



- Black PCPs associated w/ longer life
- Less mortality inequities
- Higher poverty associated w/ max impact
- Did not have see the Black PCP

Snyder JE, Upton RD, Hassett TC, Lee H, Nouri Z, Dill M. Black Representation in the Primary Care Physician Workforce and Its Association With Population Life Expectancy and Mortality Rates in the US. JAMA Netw Open. 2023;6(4):e236687. doi:10.1001/jamanetworkopen.2023.6687

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Department of Medicine

In clinical care…

Reduce Bias in Clinical & Work Environments

COUNTER STEREOTYPE IMAGING

See the individual as the opposite of the stereotype??

COMMON IDENTITY FORMATION

A find common interests

INDIVIDUATION

Learning more about personal background

PERSPECTIVE TAKING

"Putting yourself in the other person's shoes"

Navigating bias.

- Counter narrative imaging
- Individuation & Common Identity formation
- Perspective taking
- Checklists
- Bias pause
- Avoid bias landmines:
  - Tired/ sleep deprived
  - Rushed
  - Hungry
  - Ambiguity

Supporting each other to address biases…

Strategy: Structural Change / Support

Example: Faculty Review Committee

- Developed database of development, awards, grants, etc.
- Group of recently promoted faculty
- Quarterly meeting ~6 faculty per session
- Review EVERY faculty at least T-2 years prior to next rank

Outcomes

- More senior faculty post intervention (OR: 3.94, 95% CI: 1.65-9.42)
- More non-URiM senior women (OR: 11.6, 95% CI: 2.52-53.7),
- Trend toward increased URiM women faculty

	2013			2020		
	Grady GIM	SOM	AAMC	Grady GIM	SOM	AAMC
Total						
Faculty	46	2,210	159,943	50	2,883	184,682
URiM	10 (22%)	246 (11%)	13,825 (9%)	12 (24%)	393 (14%)	17,484 (9%)
Women	24 (52%)	839 (38%)	61,121 (38%)	31 (62%)	1,283 (45%)	79,174 (43%)
Assistant						
All	31 (67%)	1,208 (55%)	71,903 (45%)	23 (46%)	1,642 (57%)	86,485 (47%)
URiM	6 (60%)	162 (66%)	7,732 (56%)	6 (50%)	289 (74%)	9,777 (56%)
Women	17 (71%)	534 (64%)	31,457 (51%)	12 (39%)	612 (48%)	41,243 (52%)
Associate						
All	10 (22%)	353 (16%)	32,231 (20%)	17 (34%)	551 (19%)	37,781(20%)
URiM	4 (40%)	37 (15%)	2,489 (18%)	3 (25%)	48 (12%)	3,271 (19%)
Women	7 (29%)	102 (12%)	11,027 (18%)	13 (42%)	172 (13%)	15,006 (19%)
Professor						
All	5 (11%)	370 (17%)	35,789 (22%)	10 (20%)	461 (16%)	39,001 (21%)
URiM	0 (0%)	14 (6%)	1,880 (14%)	3 (25%)	30 (8%)	2522 (14%)
Women	1 (0%)	65 (8%)	7,669 (13%)	6 (19%)	93 (7%)	10,421 (13%)

Jones D, Fluker SN, Walker TA, Manning KD, Bussey-Jones JC. An innovative approach to career development and promotion of diverse faculty. J Hosp Med. 2023 Mar;18(3):234-238.

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Outcomes

- *Majority* Grady GIM faculty at senior rank (58% associate or full professor)
- 100% success of subm… …kets through 201…
- …men w/ senior promotion
- 42% URiM w/ senior promotion

Context: ~1% of all professors are black women…

- Open call for all leadership roles
- Interview/ selection cmtes
- Remove my bias for those “tapped”
- Address perception of exclusion, “I could have done that job”, “I didn’t even know that job was open”.

Strategy: Transparency

Opportunity

(salary, opportunity, office, others...)

Participation & Promotion Yr 1

- 14 participants – all junior
- 11 of 14 promotion eligible (time in rank)
- Mean time in rank 9 yrs (range 5 -18 yrs)
- 9 (81%) of 11 promoted within 2 yrs

SOM wide URIM FACULTY DEVELOPMENT PROGRAM

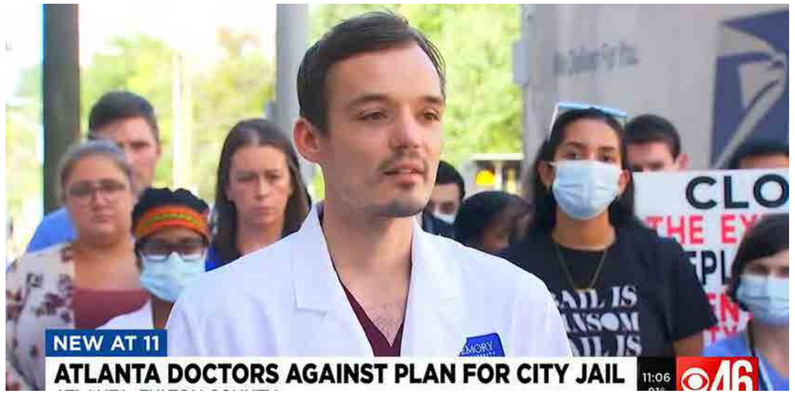
- Suggests faculty were ready/ near ready at the time of participation

- *Intervention may address barriers:*
  - *Explicitly names promotion as achievable, valuable goal for URiM*
  - *Increases confidence: addressing fear of rejection, past advice, lack of information.*
  - *Encourages active rather than passive response (ask your leader!)*

Advocacy Course

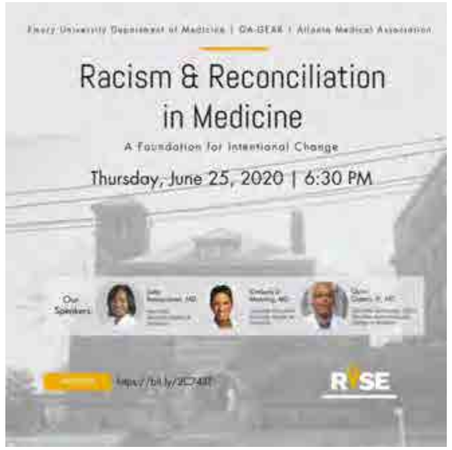
Objectives:

- To train health professionals, learners, and community members advocacy skills related to vulnerable populations.
- To foster longitudinal working relationships with Institutional Government Relations Offices in support of an aligned advocacy mission for vulnerable populations.
- To promote experiential advocacy with legislators and policy makers around health equity
- To engage in community-based advocacy and community-partnerships, learning to work within communities and to be a voice for their expressed concerns.

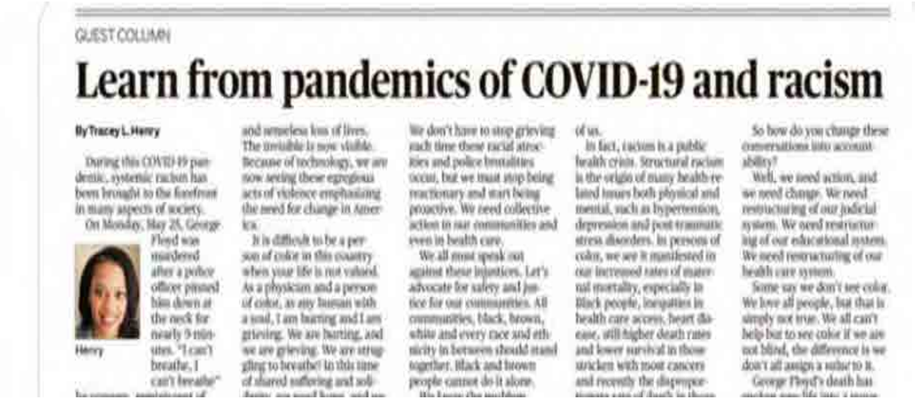


When clinical care is not enough…

Town Halls



OpEds



GUEST COLUMN

Learn from pandemics of COVID-19 and racism

By Tracey L. Henry

During this COVID-19 pandemic, systemic racism has been brought to the forefront in many aspects of society.

On Monday, May 25, George Floyd was murdered after a police officer pinned him down at the neck for nearly 9 minutes. "I can't breathe, I can't breathe"

Henry

and senseless loss of lives. The invisible is now visible. Because of technology, we are now seeing these egregious acts of violence emphasizing the need for change in America.

It is difficult to be a person of color in this country when your life is not valued. As a physician and a person of color, as any human with a soul, I am hurting and I am grieving. We are hurting, and we are grieving. We are struggling to breathe! In this time of shared suffering and soli-

We don't have to stop grieving each time these racial atrocities and police brutalities occur, but we must stop being reactionary and start being proactive. We need collective action in our communities and even in health care.

We all must speak out against these injustices. Let's advocate for safety and justice for our communities. All communities, black, brown, white and every race and ethnicity in between should stand together. Black and brown people cannot do it alone.

of us.

In fact, racism is a public health crisis. Structural racism is the origin of many health related issues both physical and mental, such as hypertension, depression and post-traumatic stress disorders. In persons of color, we see it manifested in our increased rates of maternal mortality, especially in Black people, inequities in health care access, heart disease, still higher death rates and lower survival in those stricken with most cancers and recently the dispropor-

So how do you change these conversations into account-ability?

Well, we need action, and we need change. We need restructuring of our judicial system. We need restructuring of our educational system. We need restructuring of our health care system.

Some say we don't see color. We love all people, but that is simply not true. We all can't help but to see color if we are not blind, the difference is we don't all assign a value to it.

George Floyd's death has

Podcasts

Demonstrations

Legislative Advocacy

What else? Structural change…

IRB System Change

eGFR System Change

Promotion Packet

In Summary

- Medical and nonmedical determinants of equity/ disparities
- “Isms”/ Bias pervasive
  - Impact society, clinical care & our profession
- Diversity itself can improve this
- Proactive an intentional work in clinical and professional domains needed
  - Awareness, reflection on biases
  - Structural changes, intervention

Expanding what doctor, professor, leader looks like… For learners, patients, colleagues, & community

Questions?

Real Time Bias Management: Breakout #1

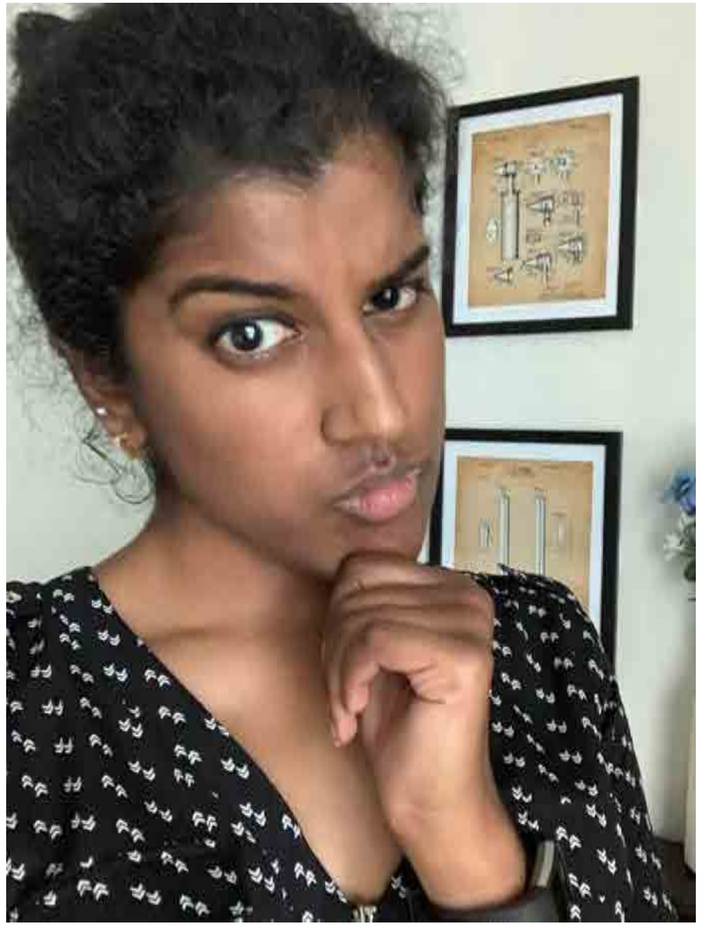
Case 1: 6 minutes

- 30 year old female BMI 78
- Admitted with exacerbation of chronic pain due to worsening hidradenitis
- Nurse asks you to see the patient to evaluate pain at 11:55 am for chest pain
- ***What are some potential bias landmines?***
- ***What might mitigate your bias response?***

Reflection…

- An instance you wished you had intervened during an encounter?
- A time you did intervene?

UPSTANDING

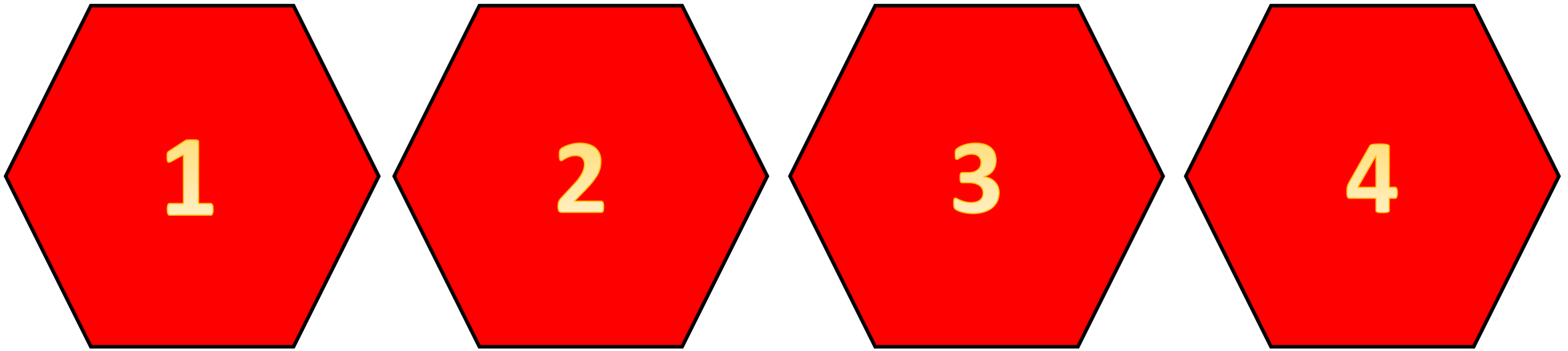


1 **RECOGNIZE**

2 **EVALUATE**

3 **ASSUME RESPONSIBILITY**

THE BYSTANDER EFFECT:
What STOPS us in our tracks?



DIFFUSION OF RESPONSIBILITY

AMBIGUITY

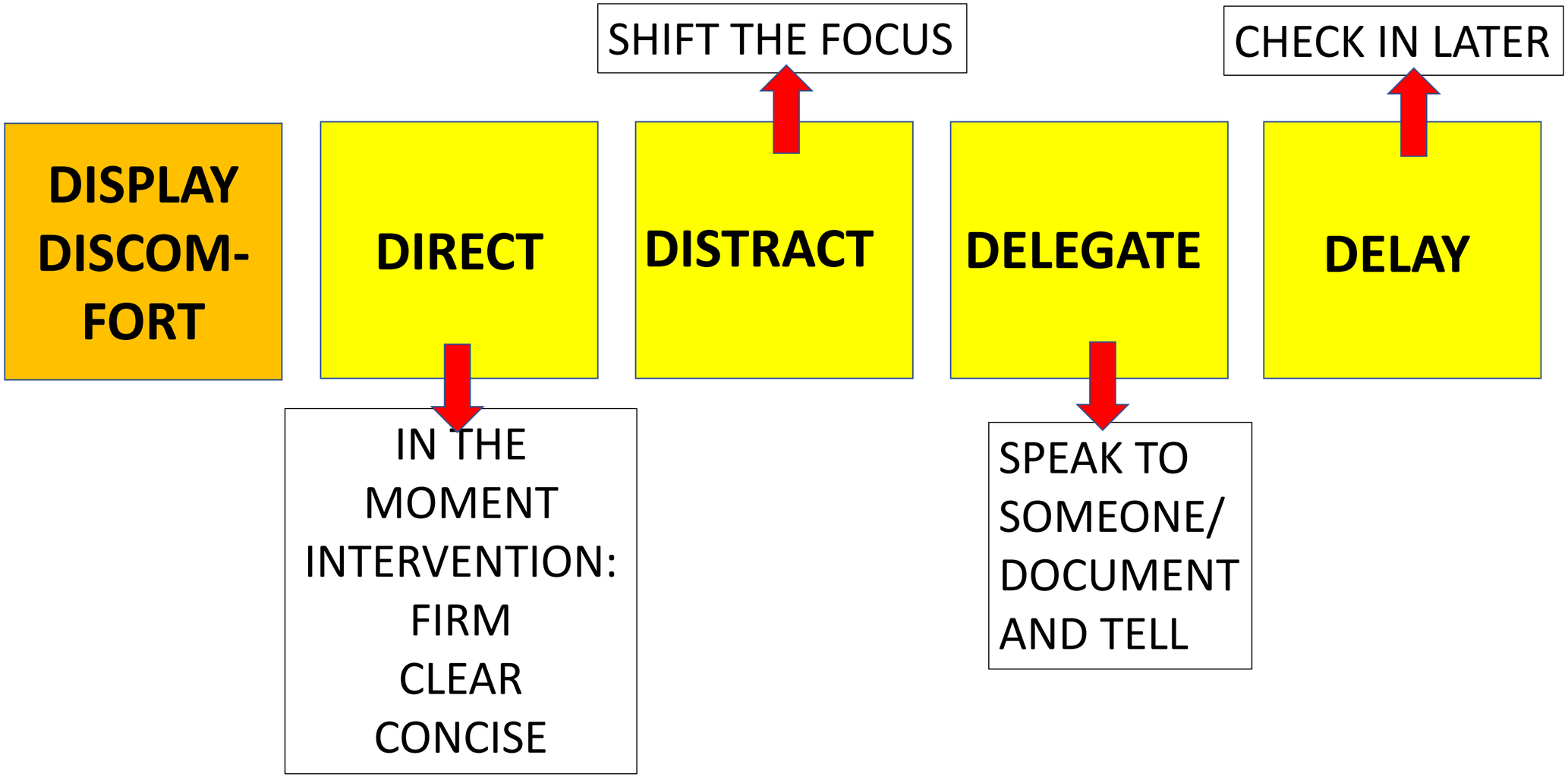
PERCEIVED COST

APPREHENSION

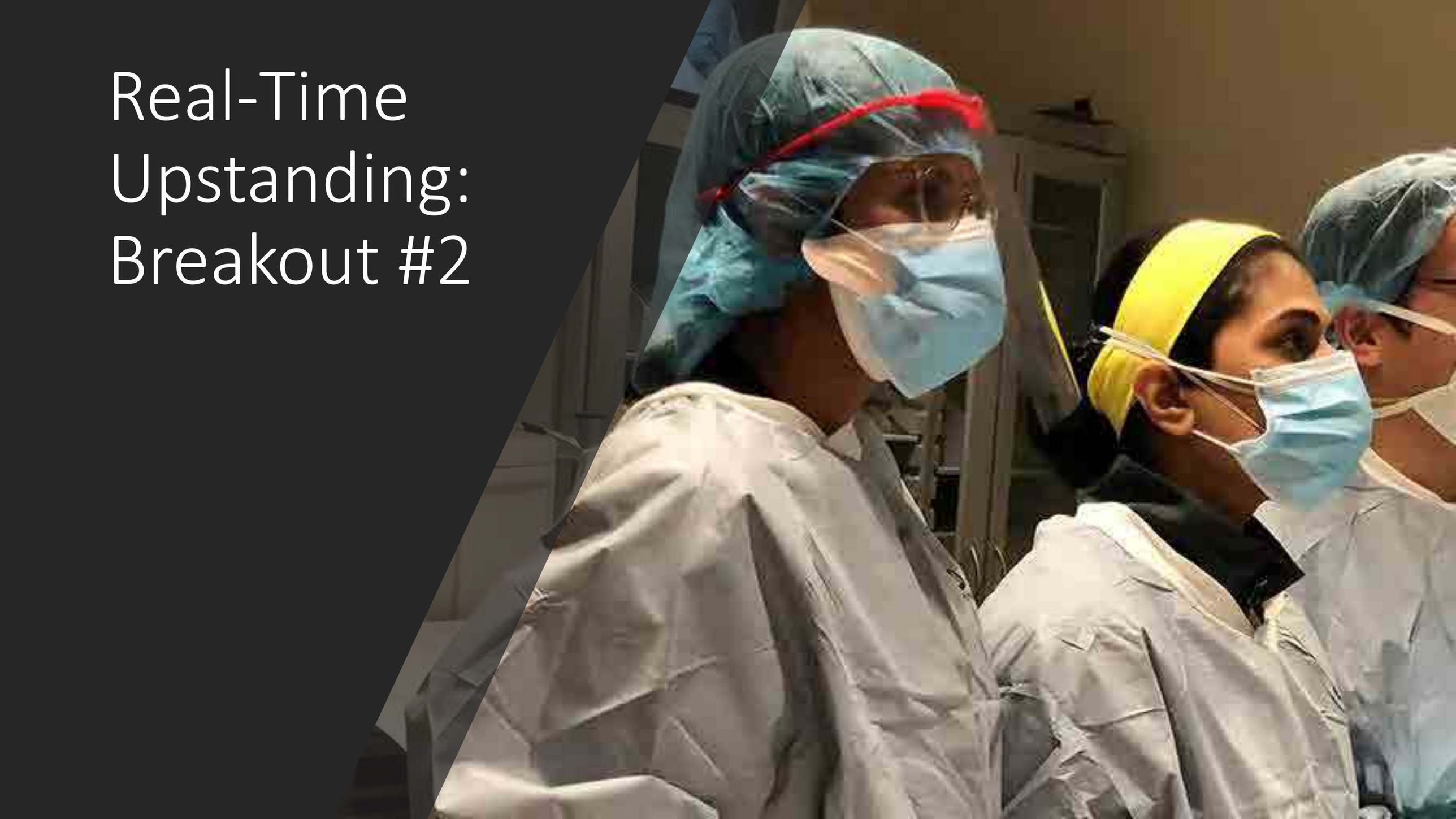
J Pers Soc Psychol 1968;10:215-221

The 5Ds of UPSTANDING

THE 5 D APPROACH TO UPSTANDING



Real-Time Upstanding: Breakout #2



OW*TFD: example

- **O**bserve: Concrete, factual observations, not evaluative, “I noticed you said…”
- **W**hat did you mean? Or “Can you say more about that?”
- **T**hink/**F**eel: Emotions, “I am concerned that other students might misunderstand…”
- **D**esire: Specific request or inquiry about desired outcome,
  - “It would be helpful not to generalize about…” or
  - “Would it be possible to debrief a bit more with you when we have time?”

RYSE

EMORY UNIVERSITY SCHOOL OF MEDICINE

Department of Medicine

ENVIRONMENTAL IMPACT ON PATIENT HEALTH

Presented by

Earl Stewart, Jr., MD, FACP

2023 Climate and Health Fellow, MSCCH

Internal Medicine Physician, WellStar Cobb Hospital

Objectives

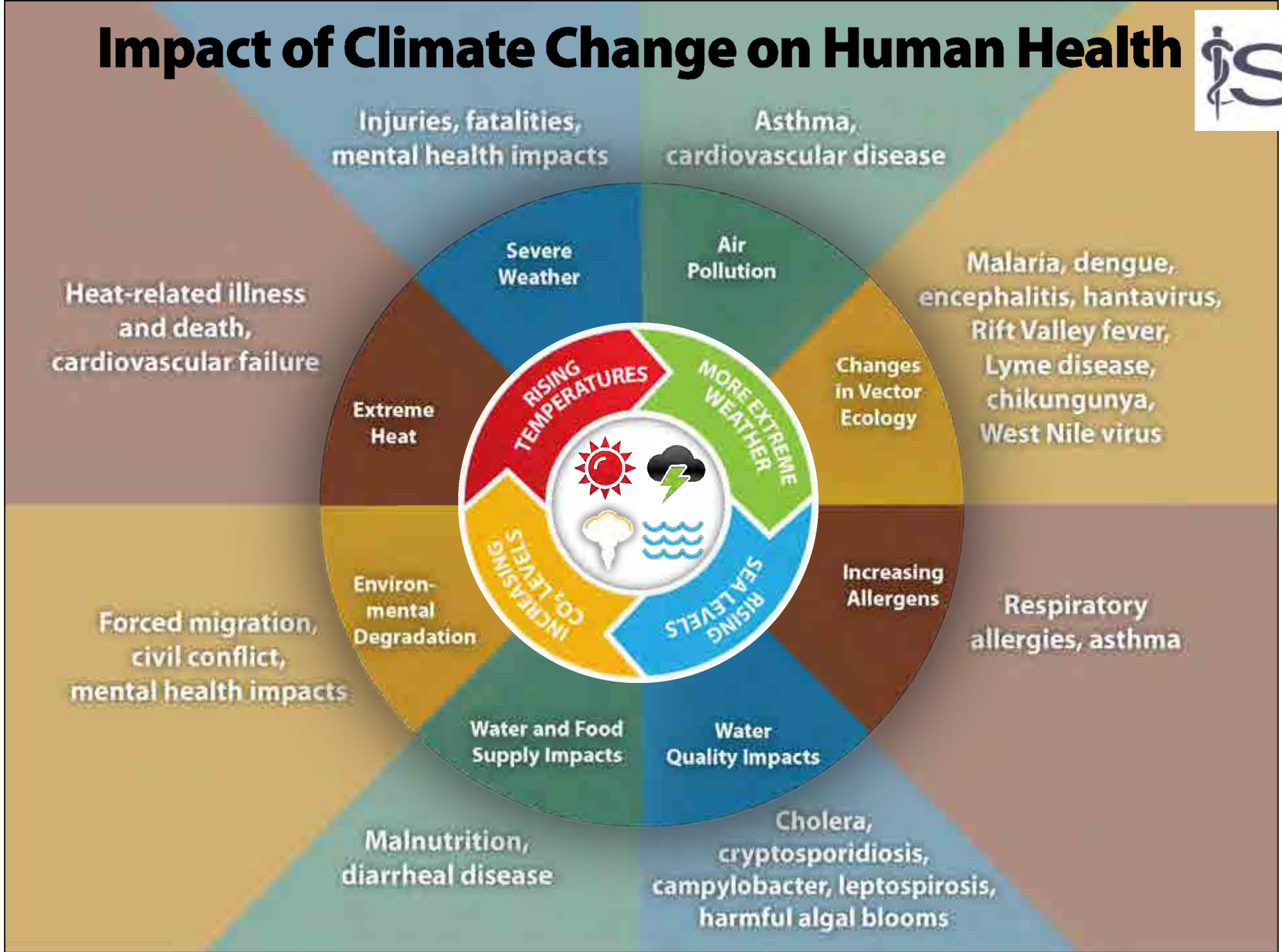
Define the environment and an introduction to environmental justice principles

Provide an evidence-based approach on environmental influences on health

Discuss how the environment holistically impacts patient health outcomes

The speaker has disclosed no financial relationships with ineligible organizations.

Impact of Climate Change on Human Health



What is the *environment*?

environment noun

en·vi·ron·ment in-ˈvī-rə(n)-mənt -ˈvī(-ə)r(n)-

Synonyms of *environment* >

1 : the circumstances, objects, or conditions by which one is surrounded

2 a : the complex of physical, chemical, and biotic factors (such as climate, soil, and living things) that act upon an organism or an ecological community and ultimately determine its form and survival

b : the aggregate of social and cultural conditions that influence the life of an individual or community

What is *environmental justice*?

Environmental justice means the just treatment and meaningful involvement of all people, regardless of income, race, color, national origin, Tribal affiliation, or disability, in agency decision-making and other Federal activities that affect human health and the environment so that people:

(i) are fully protected from disproportionate and adverse human health and environmental effects (including risks) and hazards, including those related to climate change, the cumulative impacts of environmental and other burdens, and the legacy of racism or other structural or systemic barriers; and

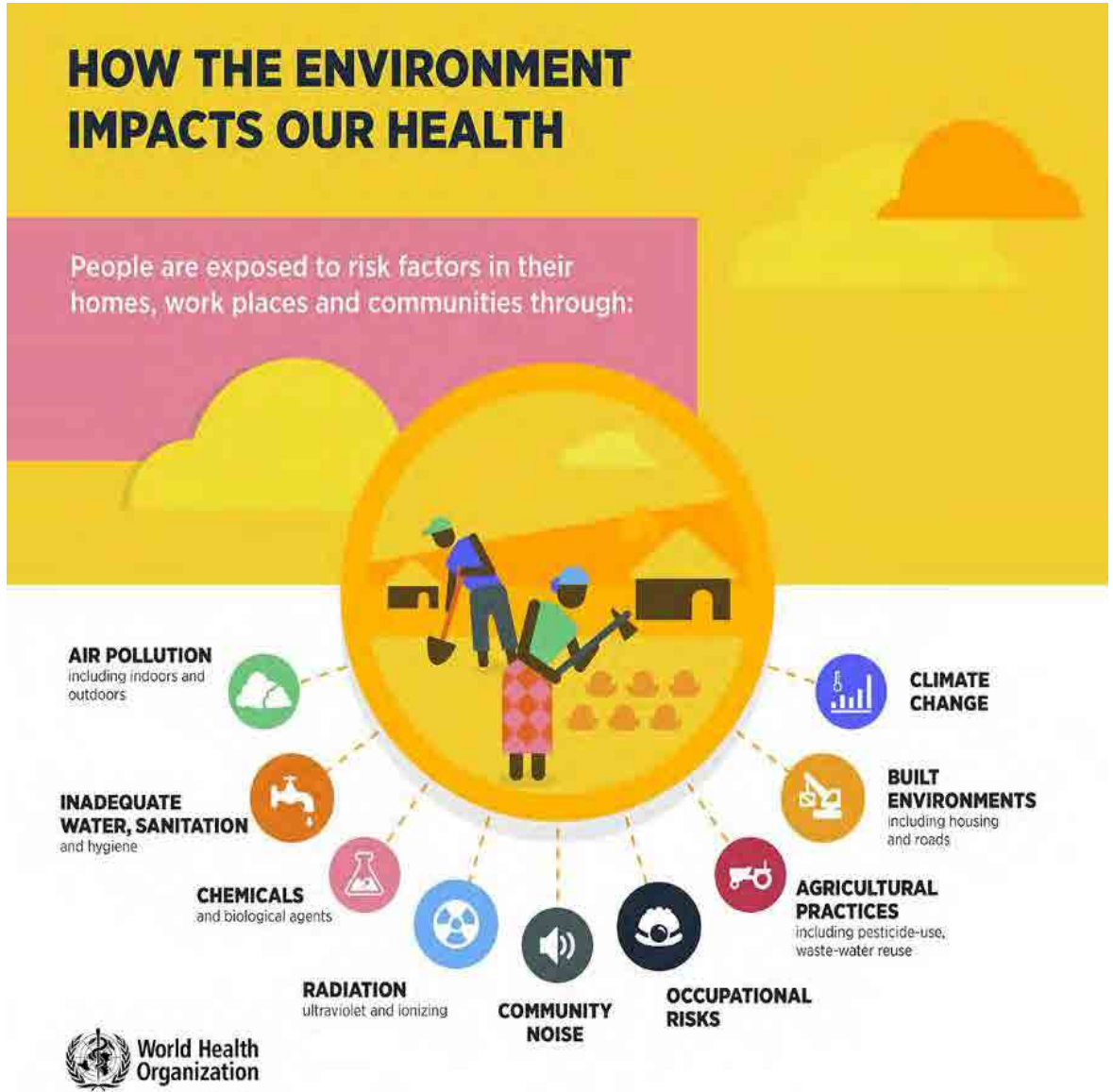
(ii) have equitable access to a healthy, sustainable, and resilient environment in which to live, play, work, learn, grow, worship, and engage in cultural and subsistence practices.

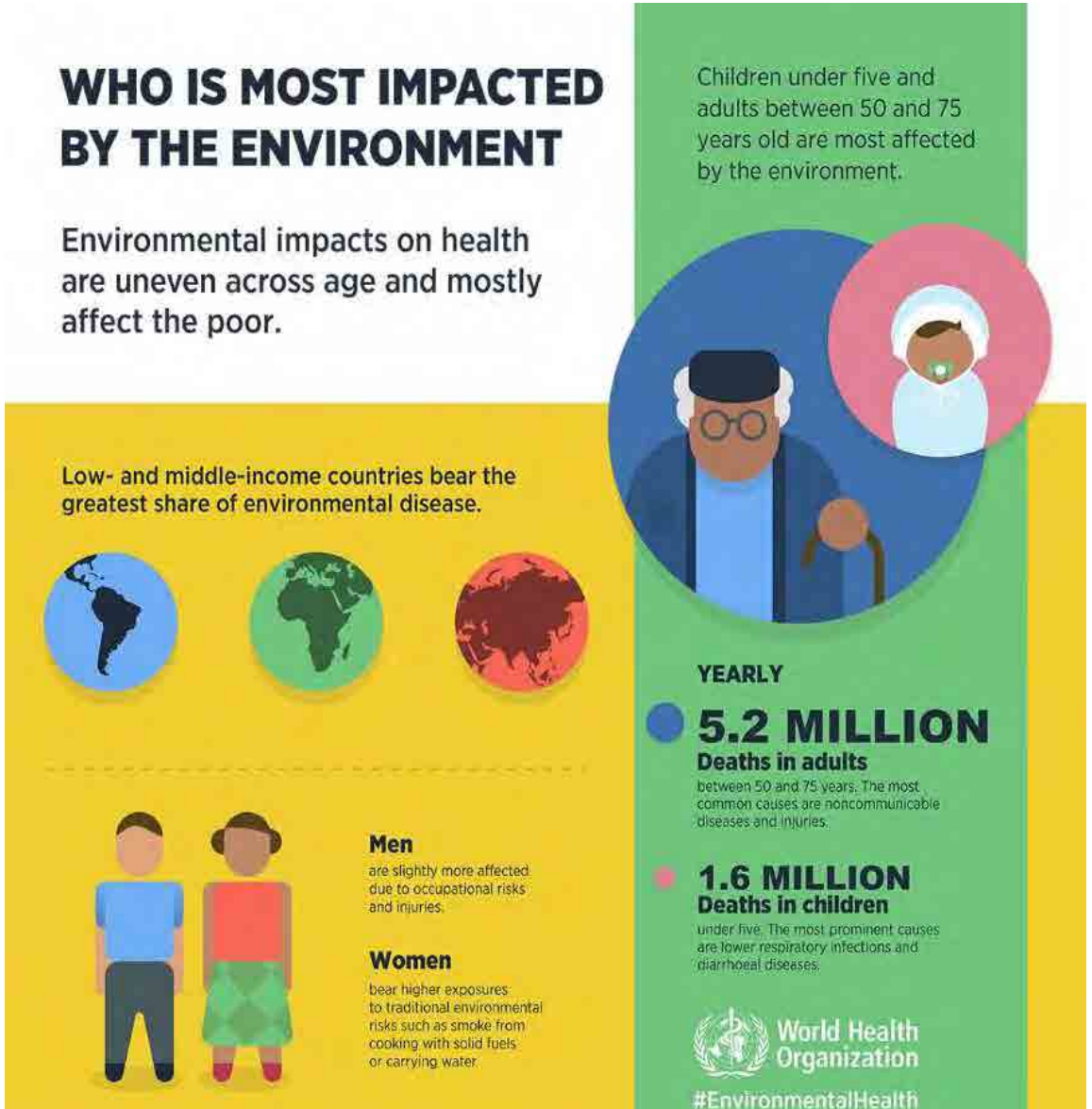
The following pages detail how the Department of Energy (DOE) implements environmental justice within the Department.

https://www.energy.gov/lm/what-environmental-justice
https://www.epa.gov/environmentaljustice/learn-about-environmental-justice

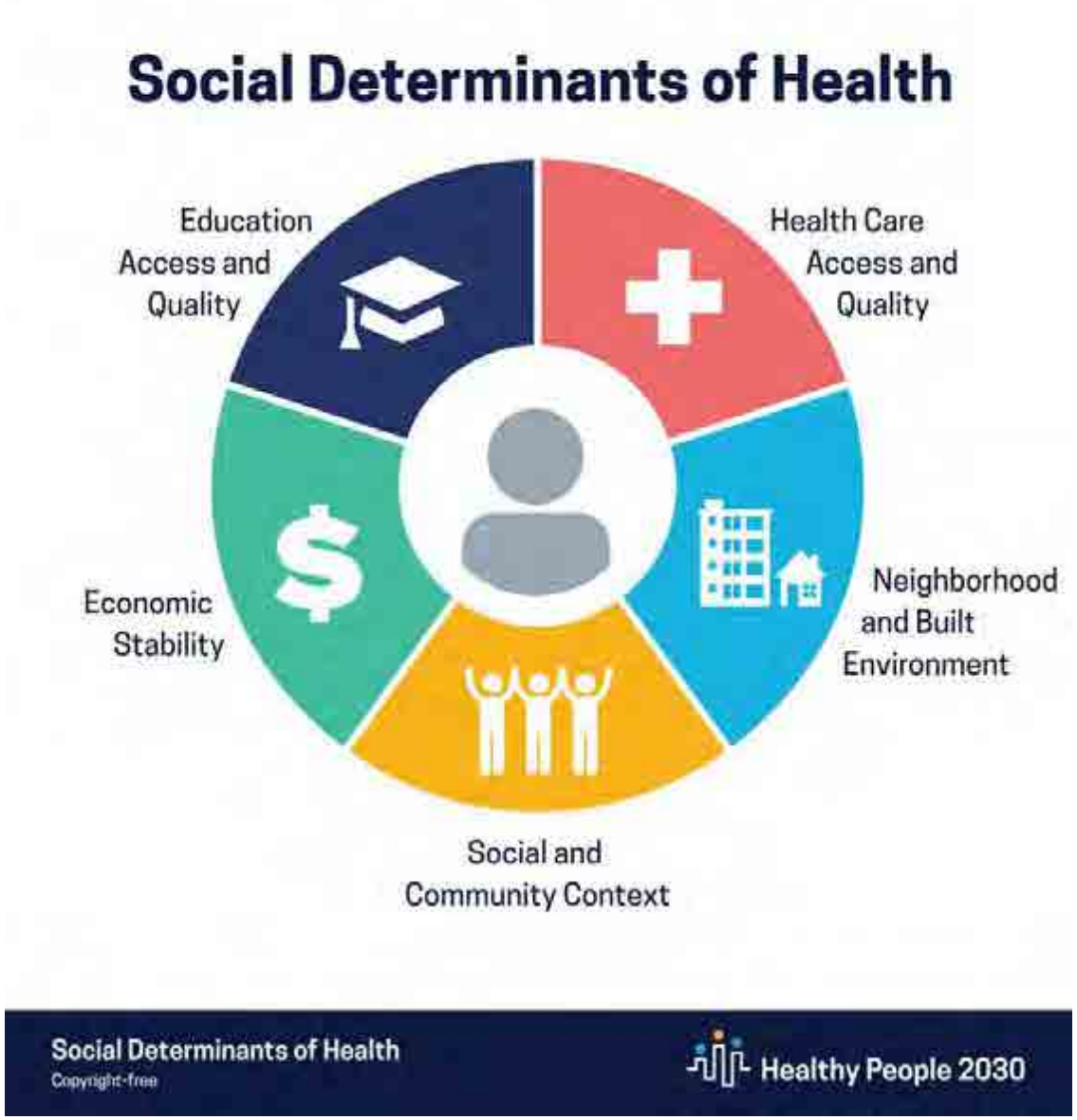
- https://centerforearthethics.org/blog/the-right-to-a-healthy-environment/

Environmental Impacts on Health





How do we fix this?



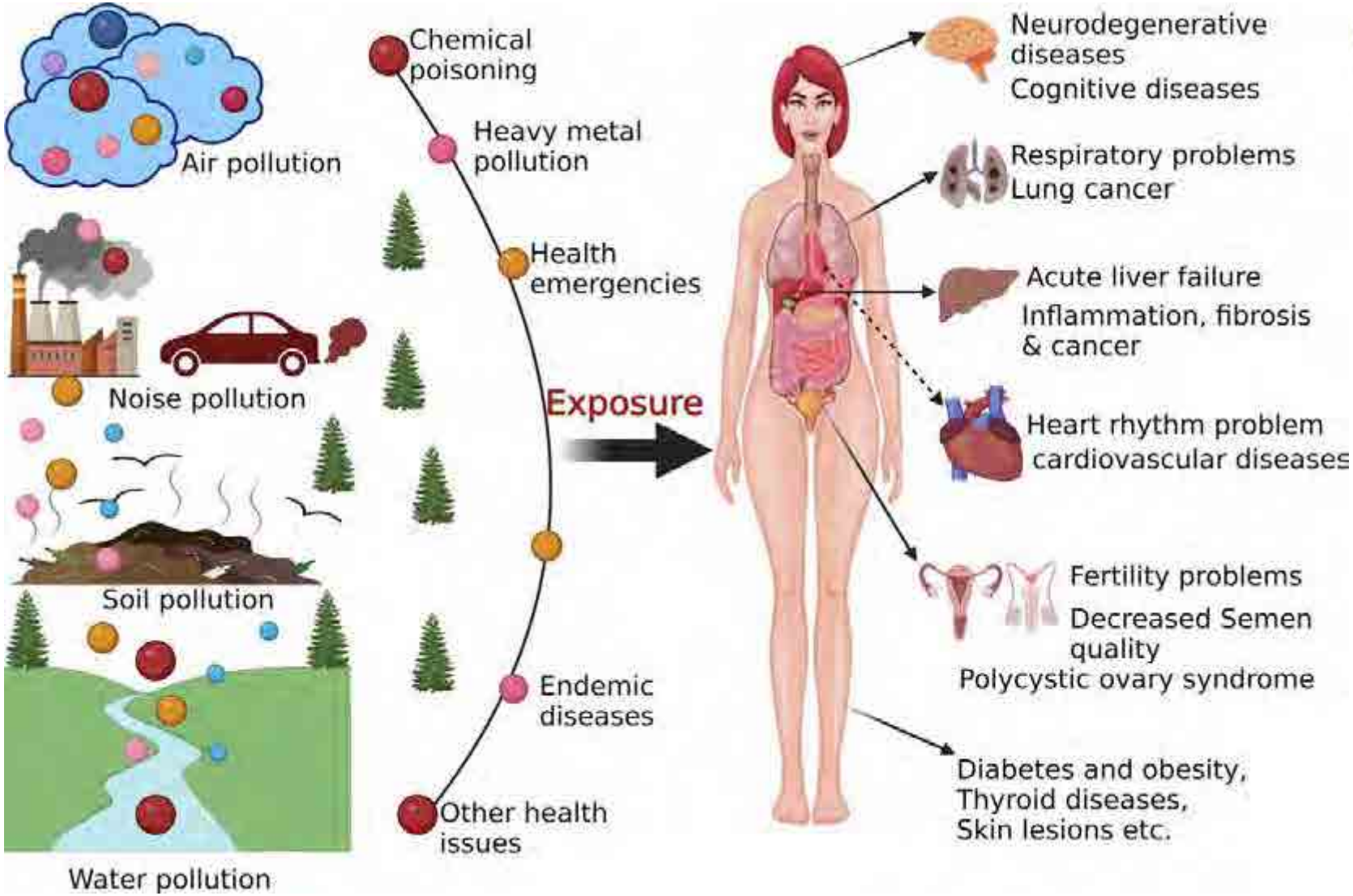
Healthy People 2030, U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. Retrieved [date graphic was accessed], from https://health.gov/healthypeople/objectives-and-data/social-determinants-health

ENVIRONMENTAL INFLUENCES ON . . . PHYSICAL HEALTH

ENVIRONMENTAL INFLUENCES ON . . . PHYSICAL HEALTH

WHO

Clean air, stable climate, adequate water, sanitation and hygiene, safe use of chemicals, protection from radiation, healthy and safe workplaces, sound agricultural practices, health-supportive cities and built environments, and a preserved nature are all prerequisites for good health.



Sharma, Amit Kumar, et al. “Mapping the impact of environmental pollutants on human health and environment: A systematic review and meta-analysis.” *Journal of Geochemical Exploration*, vol. 255, Dec. 2023, p. 107325, https://doi.org/10.1016/j.gexplo.2023.107325.

Heavy Metals

Pollutant	Source	Impacts on Human Health
Lead	Paints, Lead-acid batteries	Encephalopathy, Peripheral Neuropathy, Anemia. Damage to the Liver, kidney, and brain, neurobehavioral changes, and abnormalities in fertility and pregnancy
Mercury	Thermal power plants, hospital waste	Hypertension, Myocardial infarction, Proteinuria, cardiovascular diseases.
Arsenic	Wood preservatives, pesticide	Respiratory Cancer, Dermatomes, Genetic toxicity

Shetty, Shilpa S., et al. “Environmental pollutants and their effects on human health.” *Heliyon*, vol. 9, no. 9, Sept. 2023, https://doi.org/10.1016/j.heliyon.2023.e19496.

Particulate Matter

Pollutant	Source	Impacts on Human Health
$PM_{2.5}$, PM_{10}	Vehicular emission, Agricultural waste, Fuel, and wood burning	Chronic Pulmonary disease, bronchitis, asthma, respiratory and cardiovascular illness and mortality stroke, change in blood pressure.

Shetty, Shilpa S., et al. “Environmental pollutants and their effects on human health.” *Heliyon*, vol. 9, no. 9, Sept. 2023, https://doi.org/10.1016/j.heliyon.2023.e19496.

Pesticides

Pollutant	Source	Impacts on Human Health
Organochlorine compound	Dichloro-diphenyl-trichloroethane, DT, Dichlorodiphenyldichloroethane, Dicofol, Eldrin, Dieldrin	Damage human liver, kidney, neural and immune systems, and induces birth defects cancer, causes neurotoxicity, reproductive toxicity Inflammation of the upper respiratory tract and bronchitis, blood effects such as aplastic anemia
Carbamates	Sprays	Impair child development and IQ Decrease lung function Central nervous system tumor
Pyrethrin &Pyrethroids	Sprays, dust, and pet shampoos	Paranesthesia, respiratory tract, eyes, and skin irritations cardiovascular disease

Shetty, Shilpa S., et al. “Environmental pollutants and their effects on human health.” *Heliyon*, vol. 9, no. 9, Sept. 2023, https://doi.org/10.1016/j.heliyon.2023.e19496.

Plastics

Pollutant	Source	Impacts on Human Health
High-density polyethylene	Plastic containers, pipes	Mild dermatitis, Respiratory damage, Hormone disruption
Low-density polyethylene	Shrink wraps, squeeze bottles	Mild dermatitis, Burning sensation in eyes, Asthma
Polyvinyl chloride	Cosmetic containers wrap	Respiratory damage, immune system damage

Shetty, Shilpa S., et al. “Environmental pollutants and their effects on human health.” *Heliyon*, vol. 9, no. 9, Sept. 2023, https://doi.org/10.1016/j.heliyon.2023.e19496.

Plastics Additives

Pollutant	Source	Impacts on Human Health
Bisphenol A	Food storage containers,	Ovarian disorder
Phthalates	Personal care products, Vinyl flooring, Polyvinyl chloride plastics	Endocrine disruptor Interference with testosterone, sperm motility, testicular cancer
Dioxins	Tobacco smoke, Combustion of wood, coal, oil, Pesticides	Carcinogen interferes with testosterone
Polycyclic aromatic hydrocarbons (PAHs)	Tobacco smoke, burning coal, oil, gas, wood, garbage	Developmental and reproductive toxicity
Polychlorinated biphenyls (PCBs)	Contaminated fish, meat, and dairy products	Interferes with thyroid hormone

Shetty, Shilpa S., et al. “Environmental pollutants and their effects on human health.” *Heliyon*, vol. 9, no. 9, Sept. 2023, https://doi.org/10.1016/j.heliyon.2023.e19496.

ENVIRONMENTAL INFLUENCES ON . . . FINANCIAL HEALTH

Financial Health

- Air pollution leads to an increase in respiratory and cardiovascular diseases, which increases health care costs for individuals and governments.

- Reduced tourism and investments – it's natural that people are likely to avoid visiting polluted cities or countries; there might be lower potential for investments which can result in decreased business opportunities and a loss of income for the local population.

- Increased energy costs – **one of the connections between economy and air pollution are higher costs of energy**. The buildup of pollution can cause equipment to fail and need repair or replacement, leading to an increase in energy costs for businesses and individuals.

"The Economic Impact of Air Pollution on Communities." *The Economic Impact of Air Pollution on Communities: Negative Aspects - Air Quality Tracker Airly | Air Quality Monitoring. Monitor in UK & Europe. Airly Data Platform and Monitors*, airly.org/en/the-economic-impact-of-air-pollution-on-communities/#:~:text=increased%20energy%20costs%20%E2%80%93%20one%20of,costs%20for%20businesses%20and%20individuals. Accessed 26 July 2024.

Financial Health

- *Higher environmental clean-up costs* – Air pollution causes long-term damage to the environment, leading to a need for clean-ups that may require significant financial resources.
- *Crop and livestock damage* – Pollutants can harm agricultural productivity, leading to decreased crop yields and quality.
- Smog and other pollutants can lead to the loss of agricultural productivity and can reduce food supply. As a consequence, this can increase food prices and decrease food security.

"The Economic Impact of Air Pollution on Communities." *The Economic Impact of Air Pollution on Communities: Negative Aspects - Air Quality Tracker Airly | Air Quality Monitoring. Monitor in UK & Europe. Airly Data Platform and Monitors*, airly.org/en/the-economic-impact-of-air-pollution-on-communities/#:~:text=increased%20energy%20costs%20%E2%80%93%20one%20of,costs%20for%20businesses%20and%20individuals. Accessed 26 July 2024.

Financial Health

- Financial costs to our health from fossil-fuel generated air pollution and climate change surpass $820 billion in health costs *each year*—a burden falling heaviest on vulnerable communities but also shared in part by everyone in the United States*, per* Natural Resources Defense Council
- These impacts are linked to heavy burdens of premature deaths, hospitalizations, serious injuries, mental health ailments, lost wages, missed days of work and other health problems.

"Report: Health Costs from Climate Change and Fossil Fuel Pollution Tops $820 Billion a Year." *Be a Force for the Future*, 20 May 2021, www.nrdc.org/press-releases/report-health-costs-climate-change-and-fossil-fuel-pollution-tops-820-billion-year#:~:text=WASHINGTON%20%E2%80%93%20The%20staggering%2C%20often%2D,States%2C%20a%20new%20report%20shows.

ENVIRONMENTAL INFLUENCES ON . . . MENTAL AND SPIRITUAL HEALTH

Mental and Spiritual Health

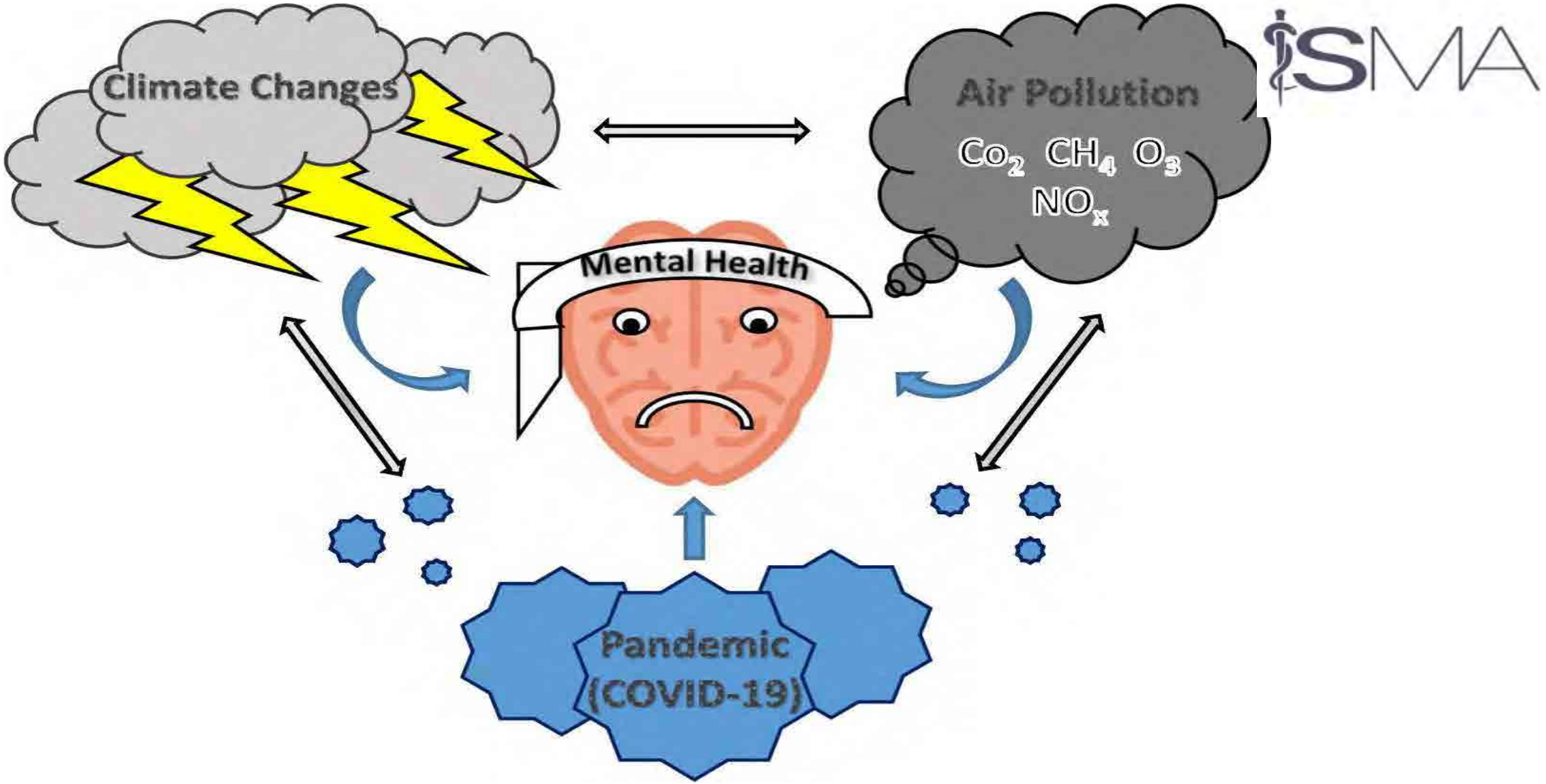
- Air pollution "is significantly associated with increased risk of psychiatric disorders," including depression, schizophrenia, bipolar disorder and personality disorder.
- More than 100 studies on the effects of outdoor air pollution on mental health and regions of the brain that regulate emotions, focusing on the hippocampus, amygdala and prefrontal cortex
- 73% of the studies reported higher mental health symptoms and behaviors in humans and animals after exposure to higher-than-average levels of air pollution

"Air Pollution's Impact on Mental Health." *Psychiatry.Org - Air Pollution's Impact on Mental Health*, 12 Apr. 2023, www.psychiatry.org/news-room/apa-blogs/air-pollutions-impact-on-mental-health#:~:text=Links%20Between%20Air%20Pollution%20and%20Mental%20Health%20Symptoms,bipolar%20disorder%20and%20personality%20disorder.

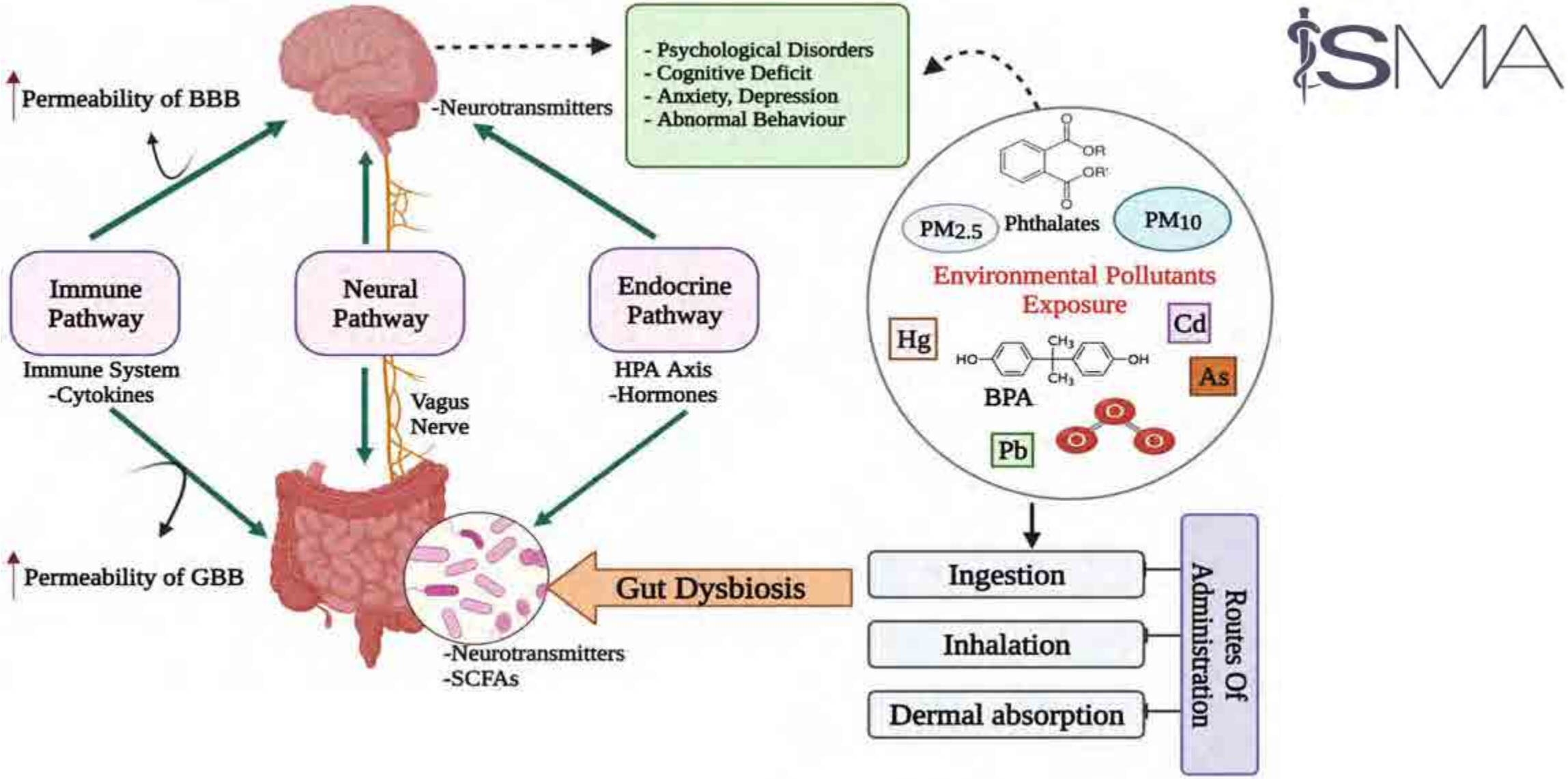
Mental and Spiritual Health

- Poor air quality during the early years of an individual's life increases the risk of psychiatric disorders, including bipolar disorder, schizophrenia, personality disorder, and major depression
- Exposure to air pollution may also exacerbate existing mental health conditions among children

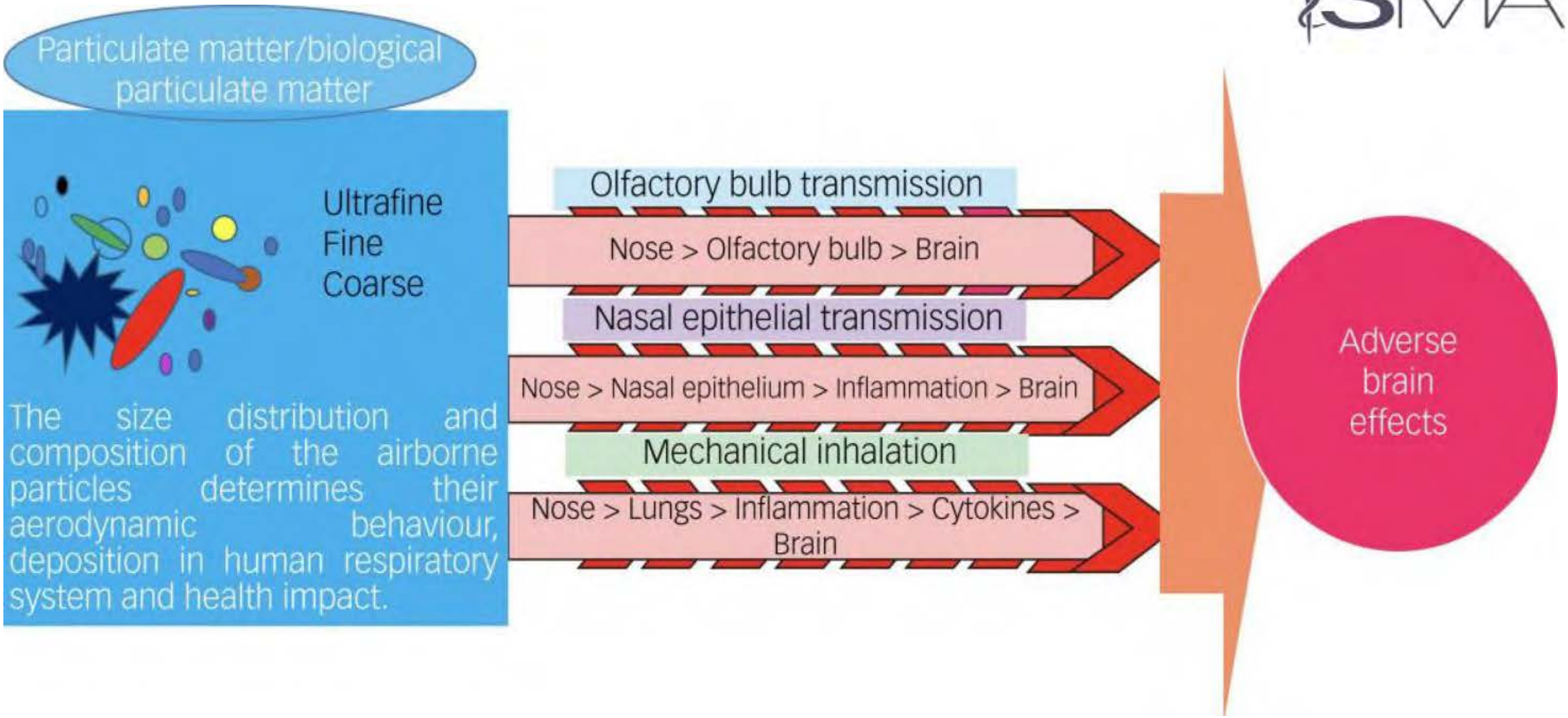
"Air Pollution's Impact on Mental Health." *Psychiatry.Org - Air Pollution's Impact on Mental Health*, 12 Apr. 2023, www.psychiatry.org/news-room/apa-blogs/air-pollutions-impact-on-mental-health#:~:text=Links%20Between%20Air%20Pollution%20and%20Mental%20Health%20Symptoms,bipolar%20disorder%20and%20personality%20disorder.



Marazziti, Donatella, et al. “Climate change, environment pollution, COVID-19 pandemic and Mental Health.” *Science of The Total Environment*, vol. 773, June 2021, p. 145182, https://doi.org/10.1016/j.scitotenv.2021.145182.



Singh, Samradhi, et al. “Impact of environmental pollutants on gut microbiome and mental health via the gut–brain axis.” *Microorganisms*, vol. 10, no. 7, 19 July 2022, p. 1457, https://doi.org/10.3390/microorganisms10071457.



Bhui, Kamaldeep, et al. “Air Quality and Mental Health: Evidence, challenges and Future Directions.” *BJPsych Open*, vol. 9, no. 4, July 2023, https://doi.org/10.1192/bjo.2023.507.

Mental and Spiritual Health (Thunderstorms)

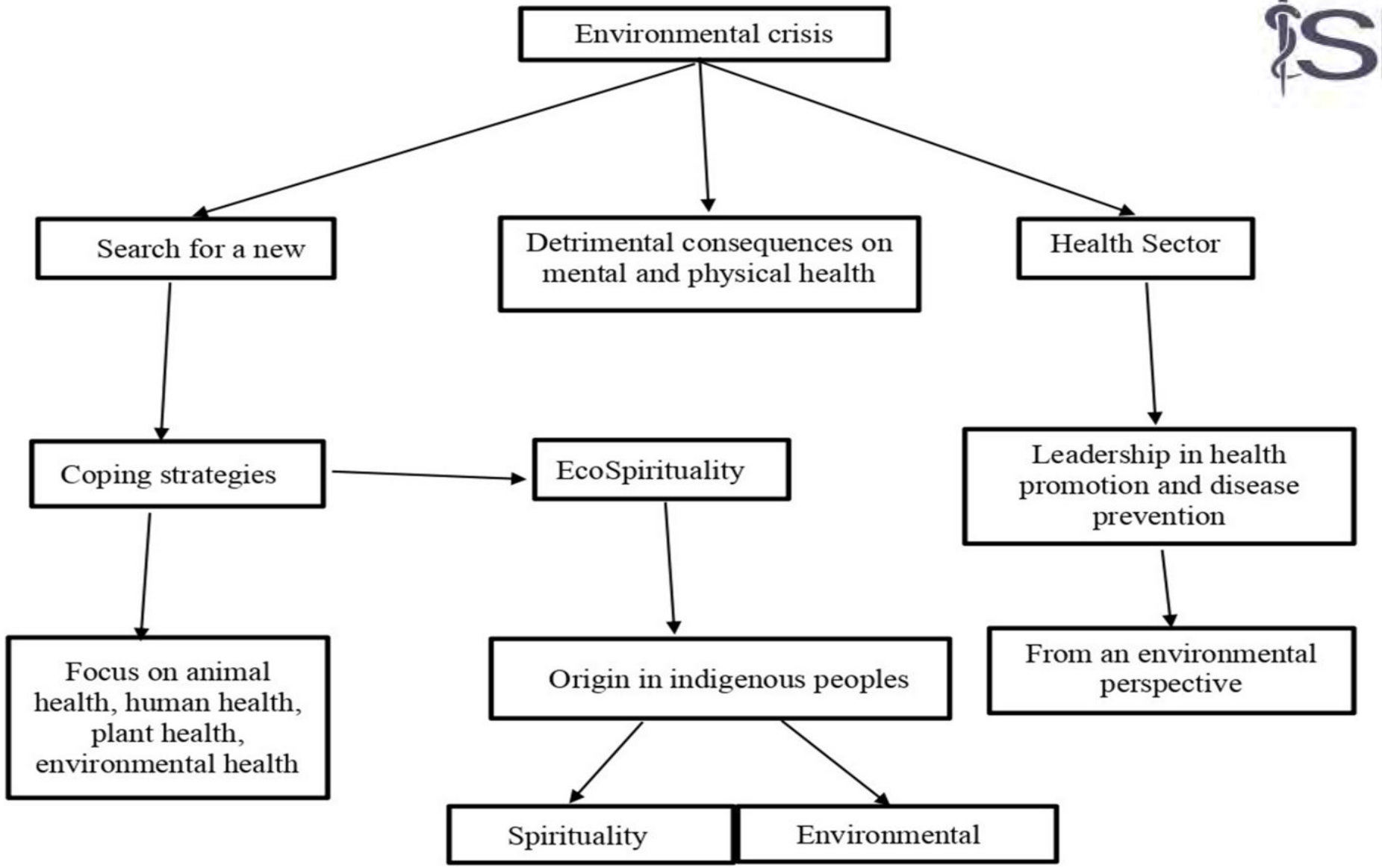
- American Psychiatric Association, since 2017, has recognized potentially traumatizing exposure during disaster impact can contribute to new psychological distress, PTSD and other mental health concerns.
- Harmful effects on people with pre-existing mental health conditions; disasters and aftermath can exacerbate chronic conditions and disrupt treatment (medication or therapy).
- Storm-related impacts experienced after the event—losses, adversities and life changes—can contribute to psychological distress, grief, depression, anxiety and other mental health concerns.

"Mental Health Impacts of Increasingly Severe Storms: Lessons from the 2017 Atlantic Storm Season." *Psychiatry.Org - Mental Health Impacts of Increasingly Severe Storms: Lessons from the 2017 Atlantic Storm Season*, 18 May 2019, www.psychiatry.org/news-room/news-releases/mental-health-impacts-of-increasingly-severe-storm.

Mental and Spiritual Health

- Ecospirituality: To understand ecospirituality, humanity must keep in mind the indigenous way of life, which is the clear example to follow to achieve environmental health and global health.
- Ecospirituality evokes pro-environmental behaviors and increases mental health.
- Ecospirituality leads toward a healthier environment, and since the environment is directly related to health, there is also an improvement in overall health.

De Diego-Cordero, Rocío, et al. “Ecospirituality and Health: A Systematic Review.” *Journal of Religion and Health*, vol. 63, no. 2, 30 Jan. 2024, pp. 1285–1306, https://doi.org/10.1007/s10943-023-01994-2.



De Diego-Cordero, Rocío, et al. “Ecospirituality and Health: A Systematic Review.” *Journal of Religion and Health*, vol. 63, no. 2, 30 Jan. 2024, pp. 1285–1306, https://doi.org/10.1007/s10943-023-01994-2.

Mental and Spiritual Health

- Green Spirituality: Faith does have a role to play in restoring climate hope.
- Green spirituality is an orientation to the divine, or supreme reality, that is grounded in our experience of life on planet Earth.
- Green spirituality seeks to harness the spiritual traditions of the world to energize the effort to restore planetary ecosystems and stop future harms.

Sherma, Rita D., and Rita D. Sherma. “The Links between Spirituality and Climate Change.” *YES! Magazine*, 15 Mar. 2022, www.yesmagazine.org/environment/2022/03/15/religion-spirituality-climate-change.

Wrap-Up

- The environment is complex array of physical, chemical, and socio-cultural factors that influence individual and community health.
- Physician education and advocacy on environmental and climate justice principles are crucial to providing for optimal patient health outcomes.
- Environmental hazards and climate change have a holistic impact on global health.

Question 1

A six-year old male presents to your emergency department with confusion. You perform an evaluation. You discover on interviewing the patient's mother that for the last several months they have rented a room in a house built in 1900 because she lost her job and had to relocate suddenly. On his peripheral smear, you expected to see which of the following?

A. Basophilic stippling
B. Hypersegmented Neutrophils
C. Reed-Sternberg Cells
D. Rouleaux Formation

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B. Hypersegmented Neutrophils
C. Reed-Sternberg Cells
D. Rouleaux Formation

Question 2

Vulnerable populations experience the brunt of climate change and environmental injustice. Each of the following is considered to be an example of a vulnerable population except:

A. Children
B. Elderly
C. Outdoor workers
D. Assembly line workers
E. Physically disabled persons

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Question 3

Particulate matter can cause and exacerbate obstructive lung diseases, cause changes in blood pressure, and worsen cardiovascular illness and mortality. Which of the following is the greatest source of particulate matter production in the environment?

A. Fuel-burning vehicles
B. Electric vehicles
C. Non-stick cooking vessel manufacturing
D. Cast-iron cooking vessel manufacturing

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Question 4

The concept of “Ecospirtuality” is an environmental health concept that assumes which of the following?

A. Climate change is inevitable.
B. Environmental injustices are pre-destined to happen.
C. Nothing can change the course of global climate and health.
D. Being good stewards of the land and environment can lead to better global and mental health outcomes.

Question 4

The concept of “Ecospirtuality” is an environmental health concept that assumes which of the following?

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INJUSTICE
ANYWHERE
IS A THREAT
TO JUSTICE
EVERYWHERE
-DR MARTIN LUTHER KING JR.

X/Formerly Twitter: @EarlStewartJr

LinkedIn: https://www.linkedin.com/in/esjmd/

Doximity: https://www.doximity.com/cv/earl-stewart-md-d208

Any question regarding the education of the presentation. please email SMA at education @sma.org

After the conference, a link will be emailed to all in attendance with instructions on how to download their certificate of attendance.

Southern Medical Association designates this live activity for a maximum of .75 AMA PRA Category 1 Credit ™. Physicians should claim only the credit commensurate with the extend of their participation in the activity.

Adam Rodman, MD

Disclosure: Has no financial relationships.

Towards an AI Second Opinion

Clinical Reasoning, Large Language Models, and How We Might Make Humans A Little Bit Better

Adam Rodman, MD, MPH, FACP

@AdamRodmanMD

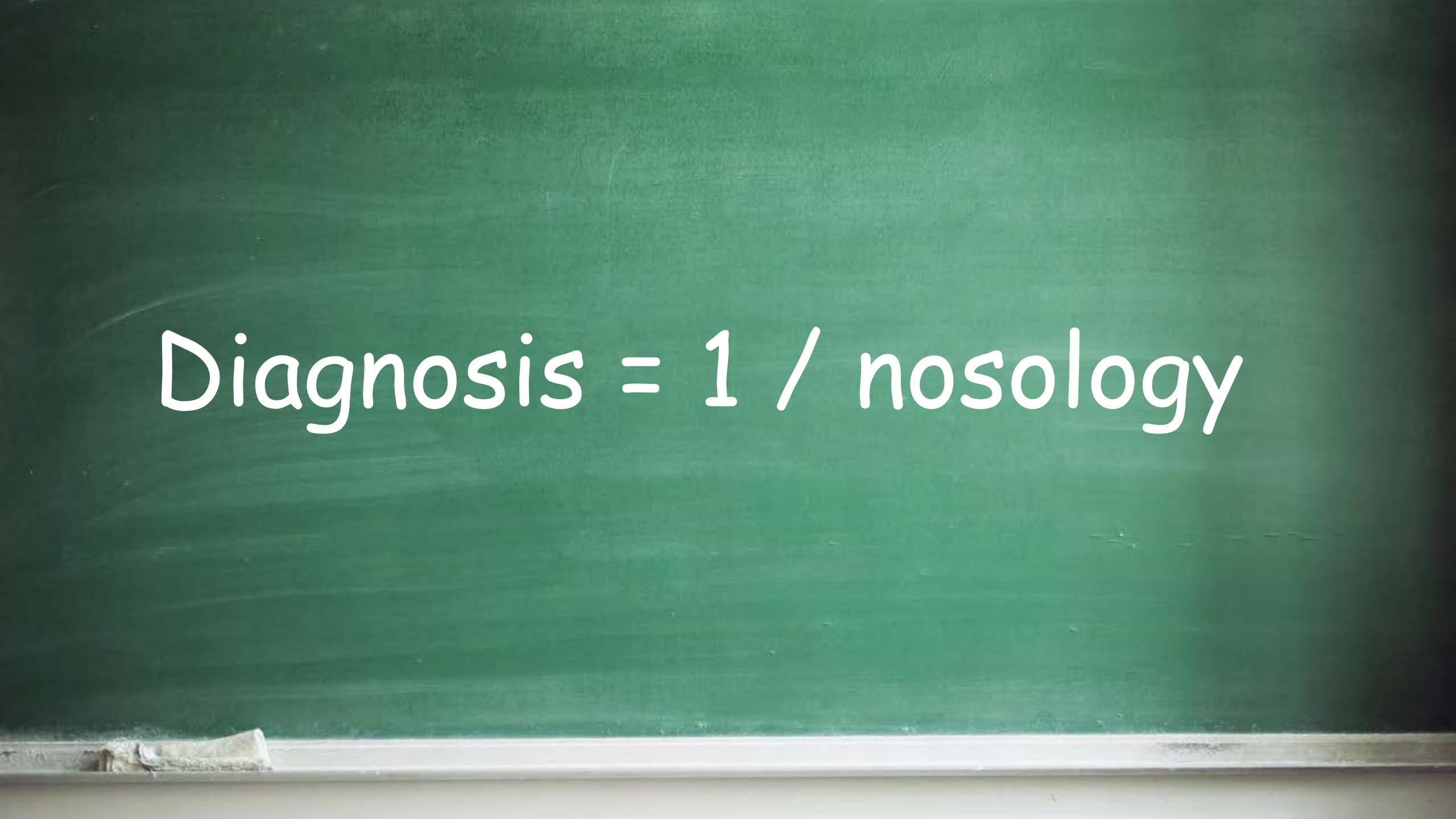
Beth Israel Deaconess Medical Center

Harvard Medical School

Agenda for today

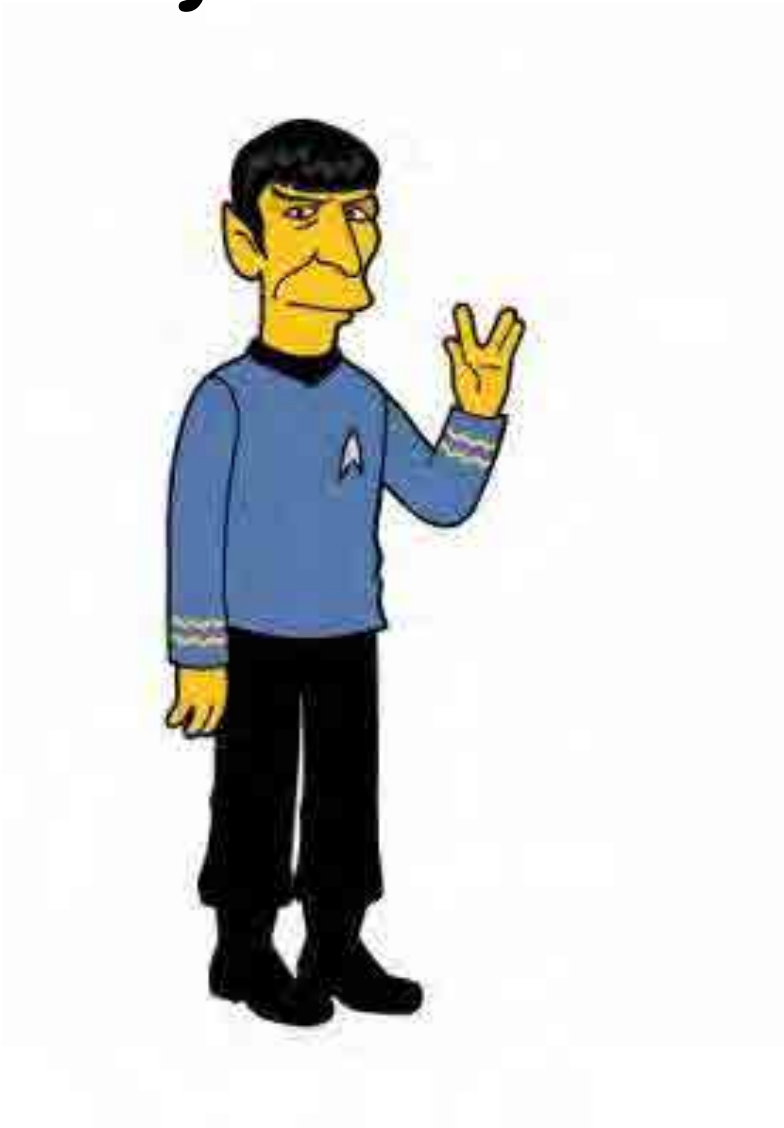
- What does it mean from a transtheoretical reasoning perspective to make a diagnosis? (6 minutes)
- Diagnostic errors, second opinions, and artificial intelligence (6 minutes)
- Live demonstration of an AI reasoning workflow with Dr. Jackson (20 minutes)
- Overview of the evidence, including my own research (10 minutes)
- Implications for current AI second opinion projects (2 minutes)
- Discussion/Reflections/Q&A

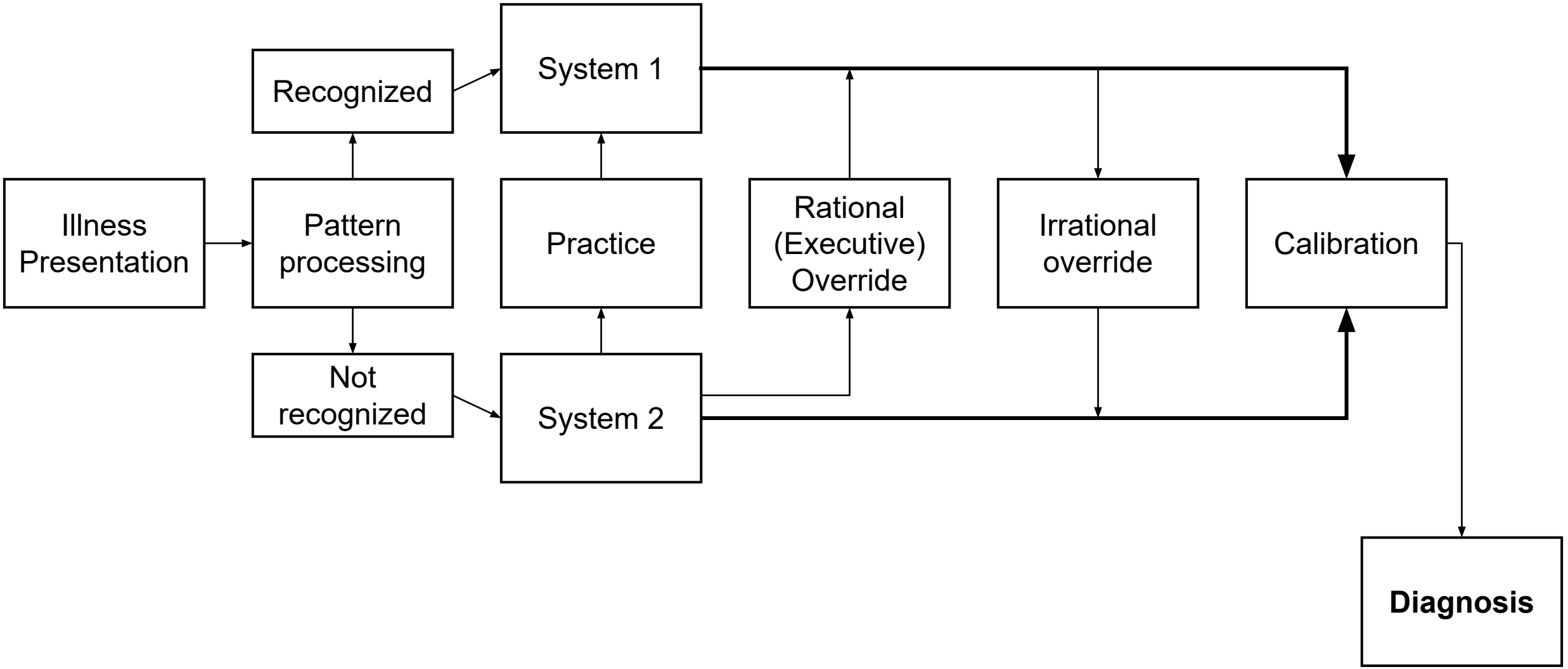

What is diagnosis anyway?
It's complicated…


Diagnosis = 1 / nosology

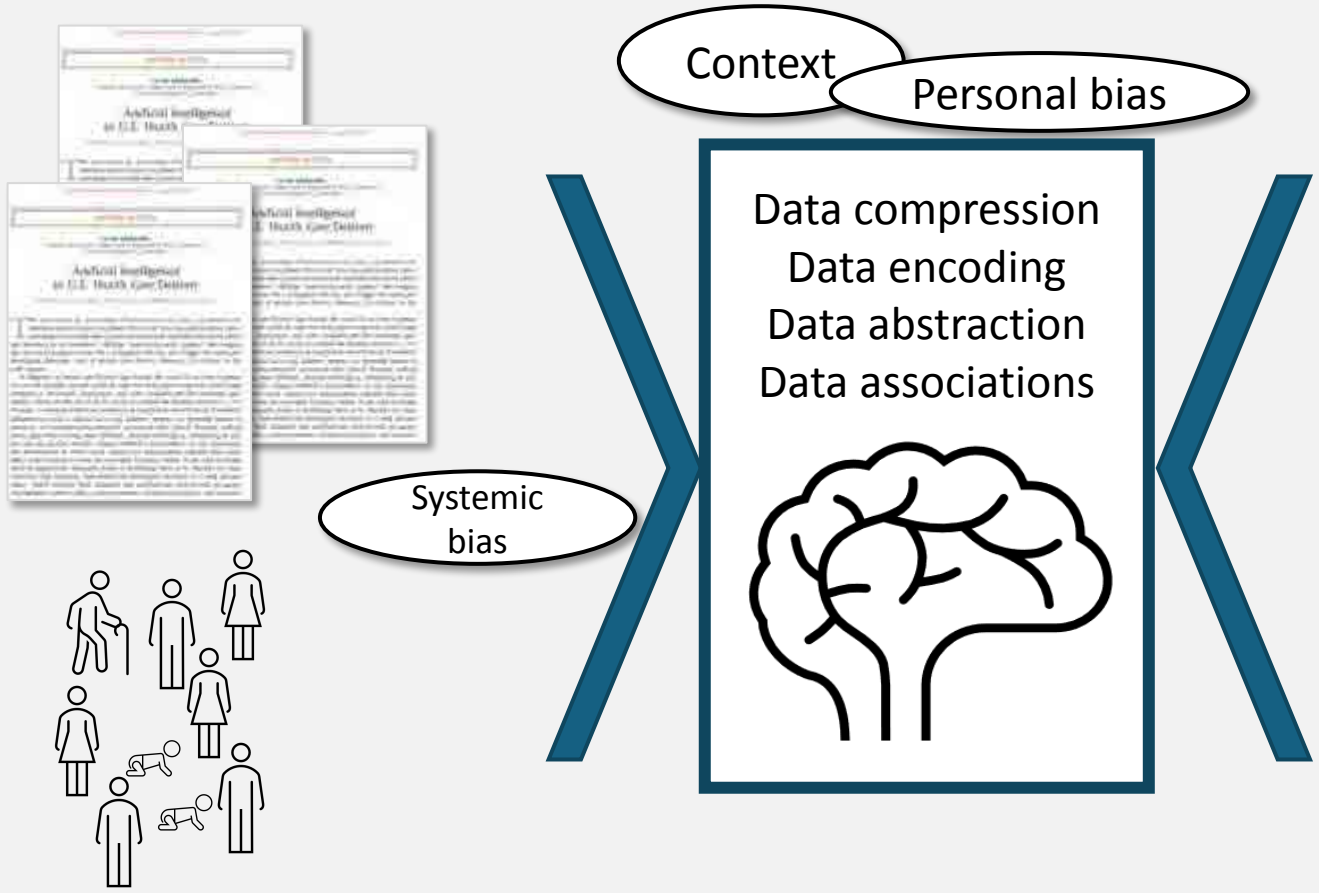
System 1

System 2

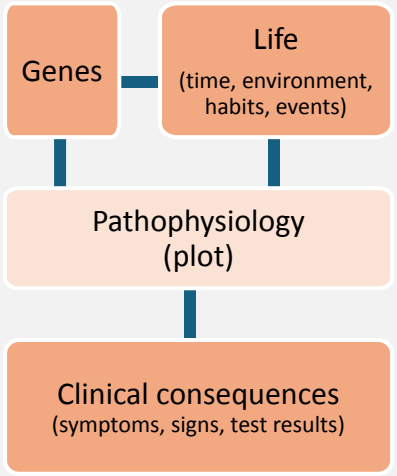



Illness Presentation
Pattern processing
Recognized
Not recognized
System 1
System 2
Practice
Rational (Executive) Override
Irrational override
Calibration
Diagnosis

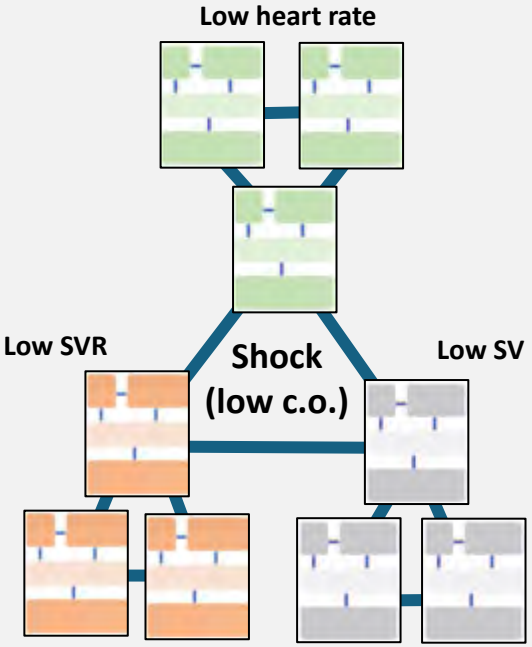
Script Theory
1. Knowledge Acquisition And Organization



Data-driven representation of diseases



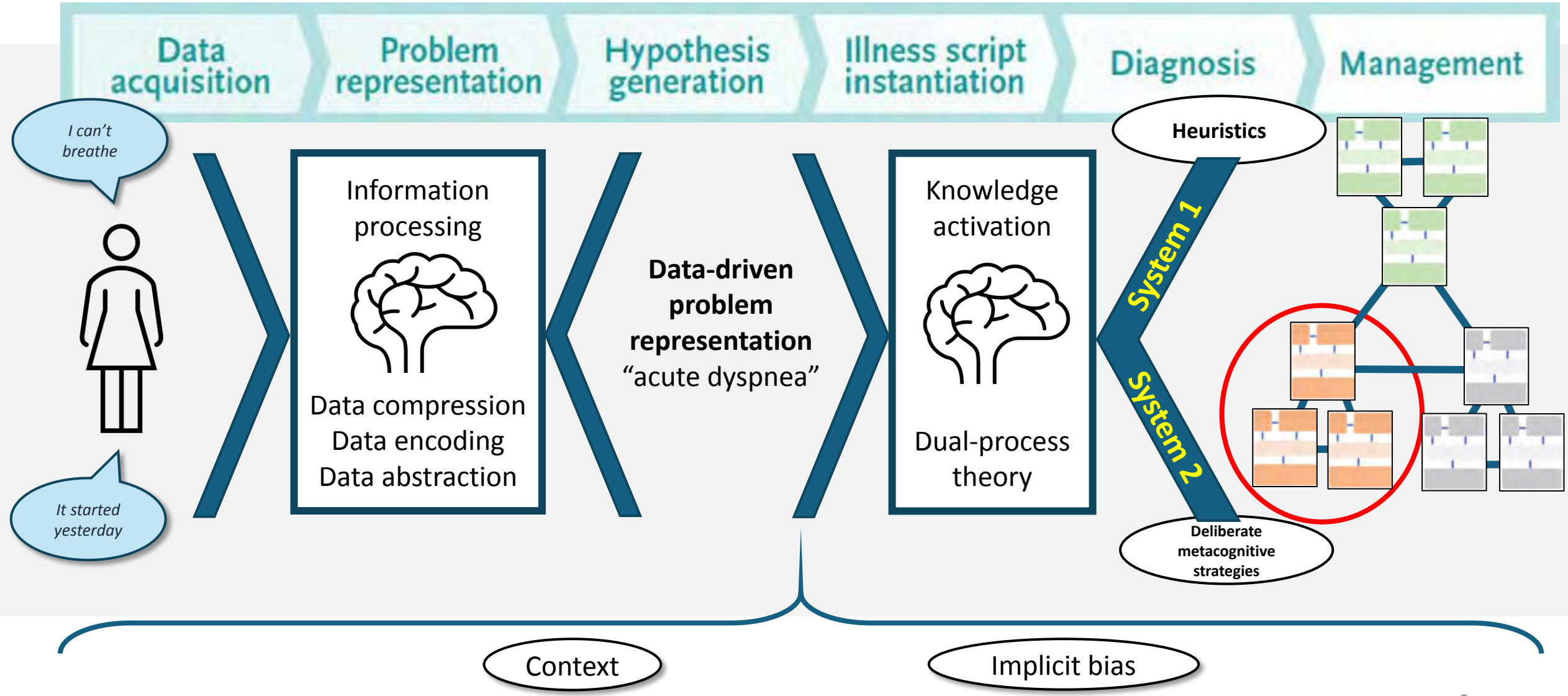
Illness script



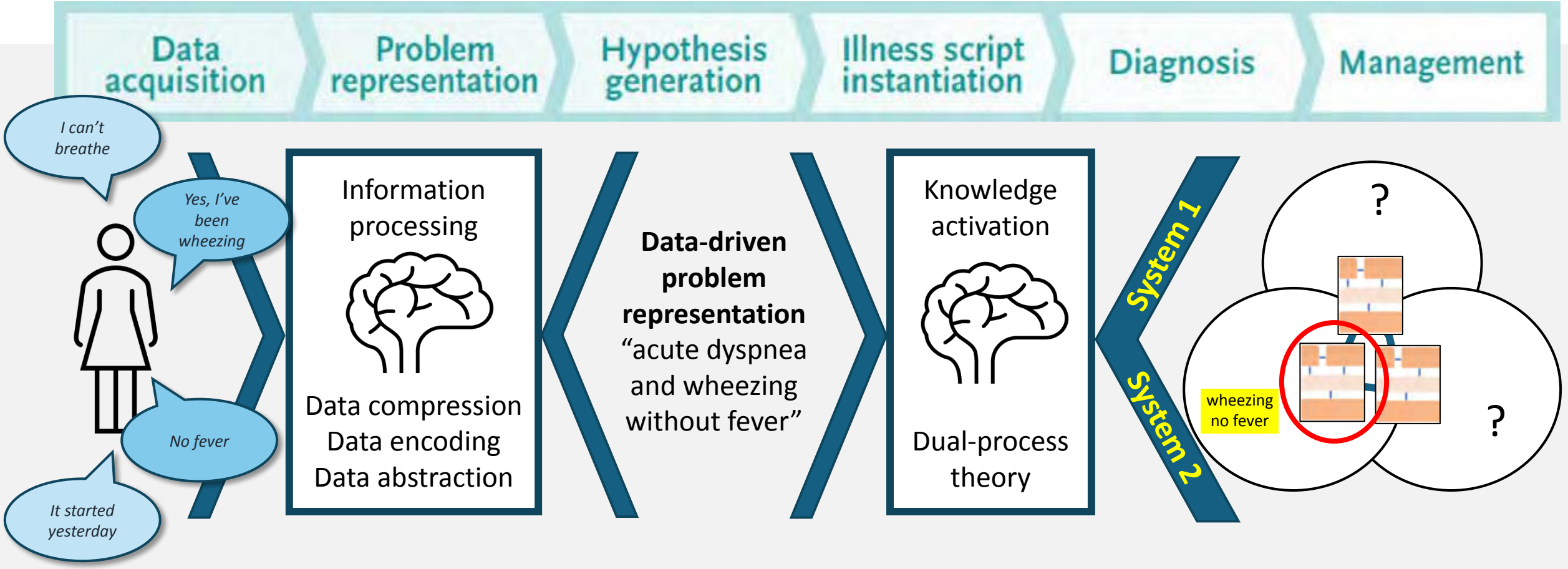
Illness script network
"Diagnostic schemas"

Illness script network is limited by:
Body of knowledge (rapid doubling time), patients encountered, context, personal bias

Script Theory
2. Information Processing And Knowledge Activation



Script Theory
2. Information Processing And Knowledge Activation

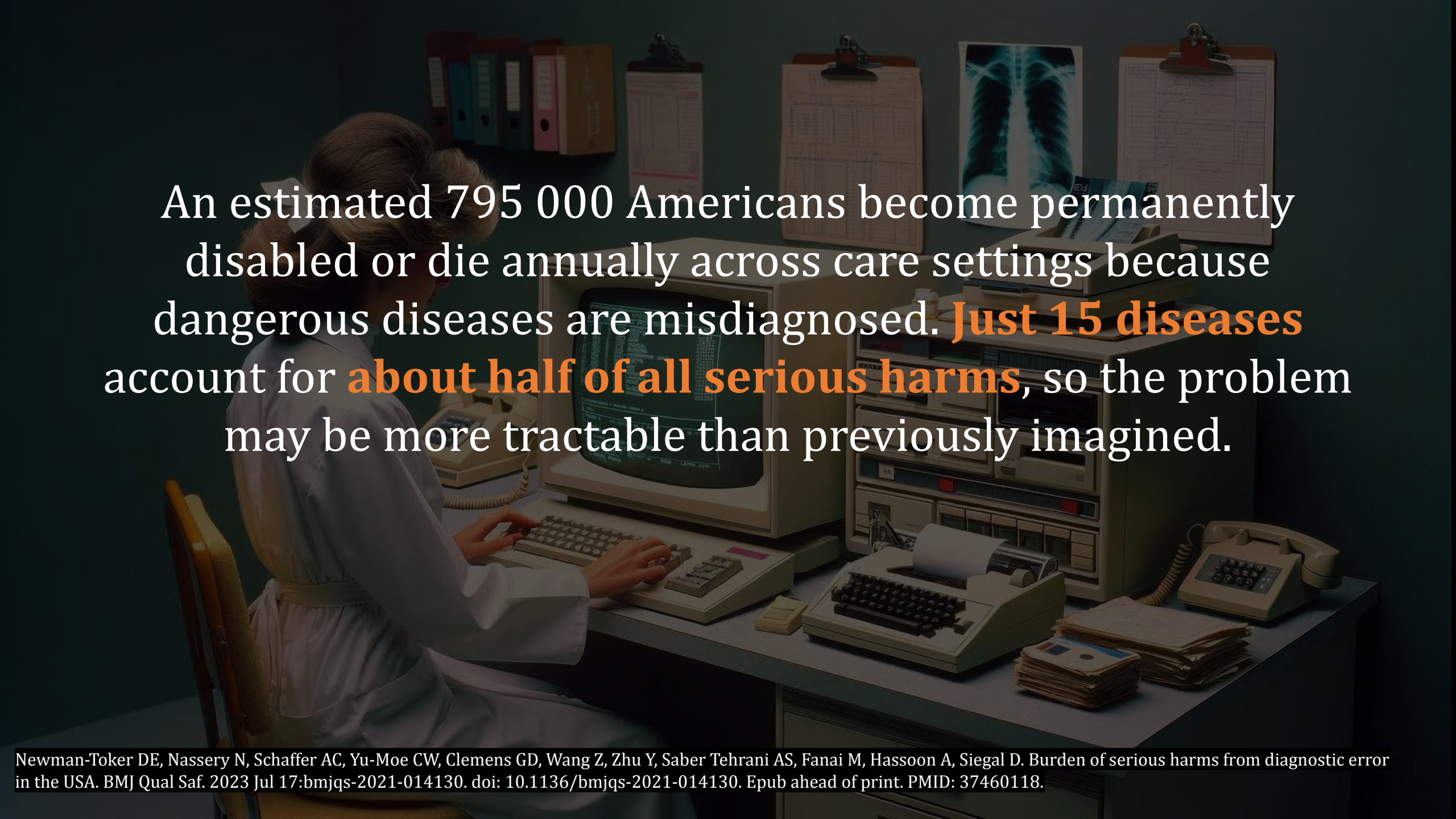


Clinical reasoning is limited by:
problem representation (data encoding, compression, and abstraction), prior knowledge (ISN), knowledge activation (recall) and its susceptibility to context, bias, and overreliance on heuristics

Ecological Psychology – Reasoning is a byproduct of interaction between clinician and surroundings/context

Situated cognition – Reasoning is subject to "context specificity" (aka situated) and fundamentally socially constrained

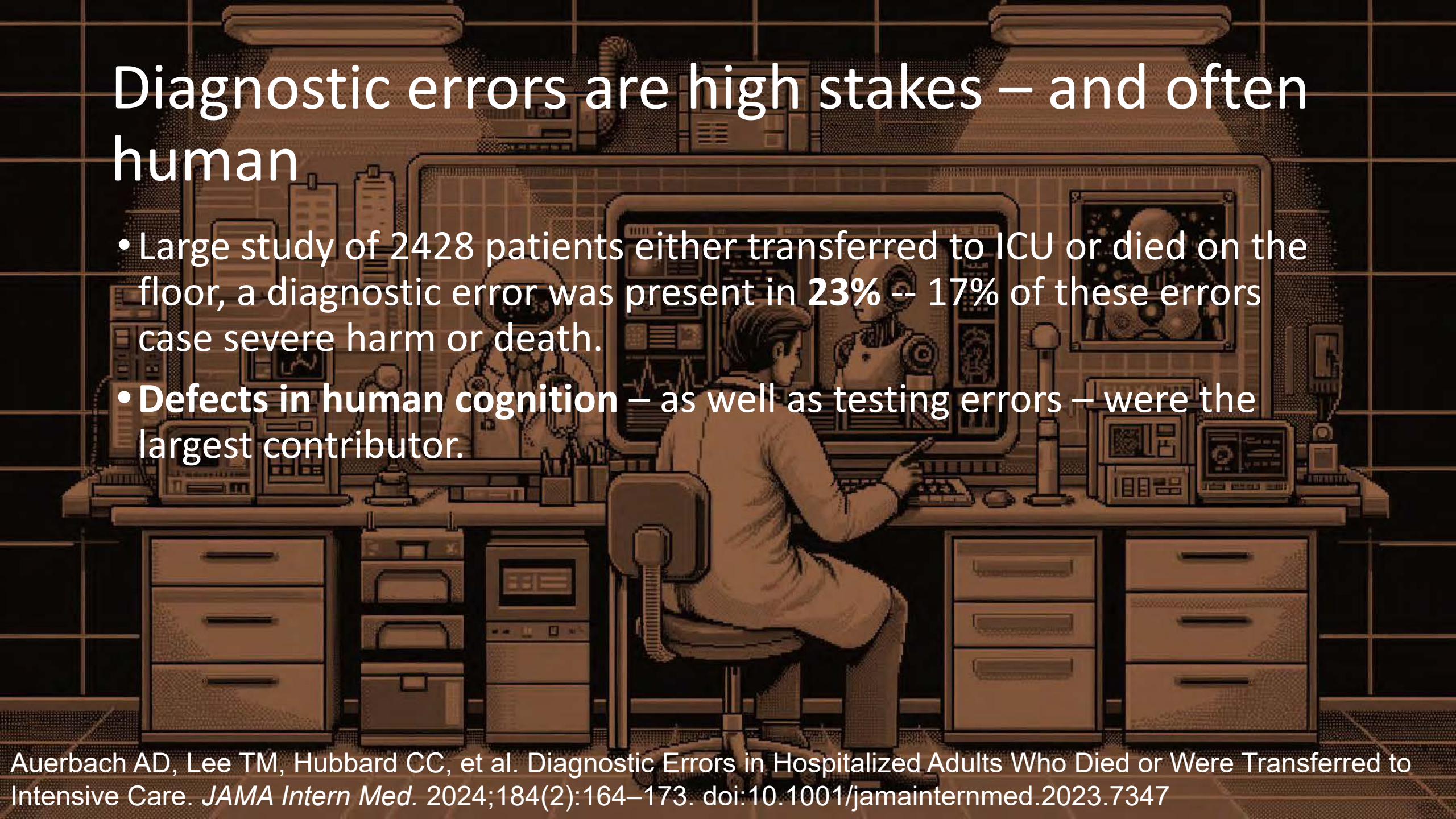
Distributed Cognition: cognition is fundamentally collaborative, spaced over multiple individuals separated by space and time, and tied together with systems such as the EHR



Newman-Toker DE, Nassery N, Schaffer AC, Yu-Moe CW, Clemens GD, Wang Z, Zhu Y, Saber Tehrani AS, Fanai M, Hassoon A, Siegal D. Burden of serious harms from diagnostic error in the USA. BMJ Qual Saf. 2023 Jul 17:bmjqs-2021-014130. doi: 10.1136/bmjqs-2021-014130. Epub ahead of print. PMID: 37460118.

Diagnostic errors are high stakes – and often human

- Large study of 2428 patients either transferred to ICU or died on the floor, a diagnostic error was present in **23%** -- 17% of these errors case severe harm or death.
- **Defects in human cognition** – as well as testing errors – were the largest contributor.

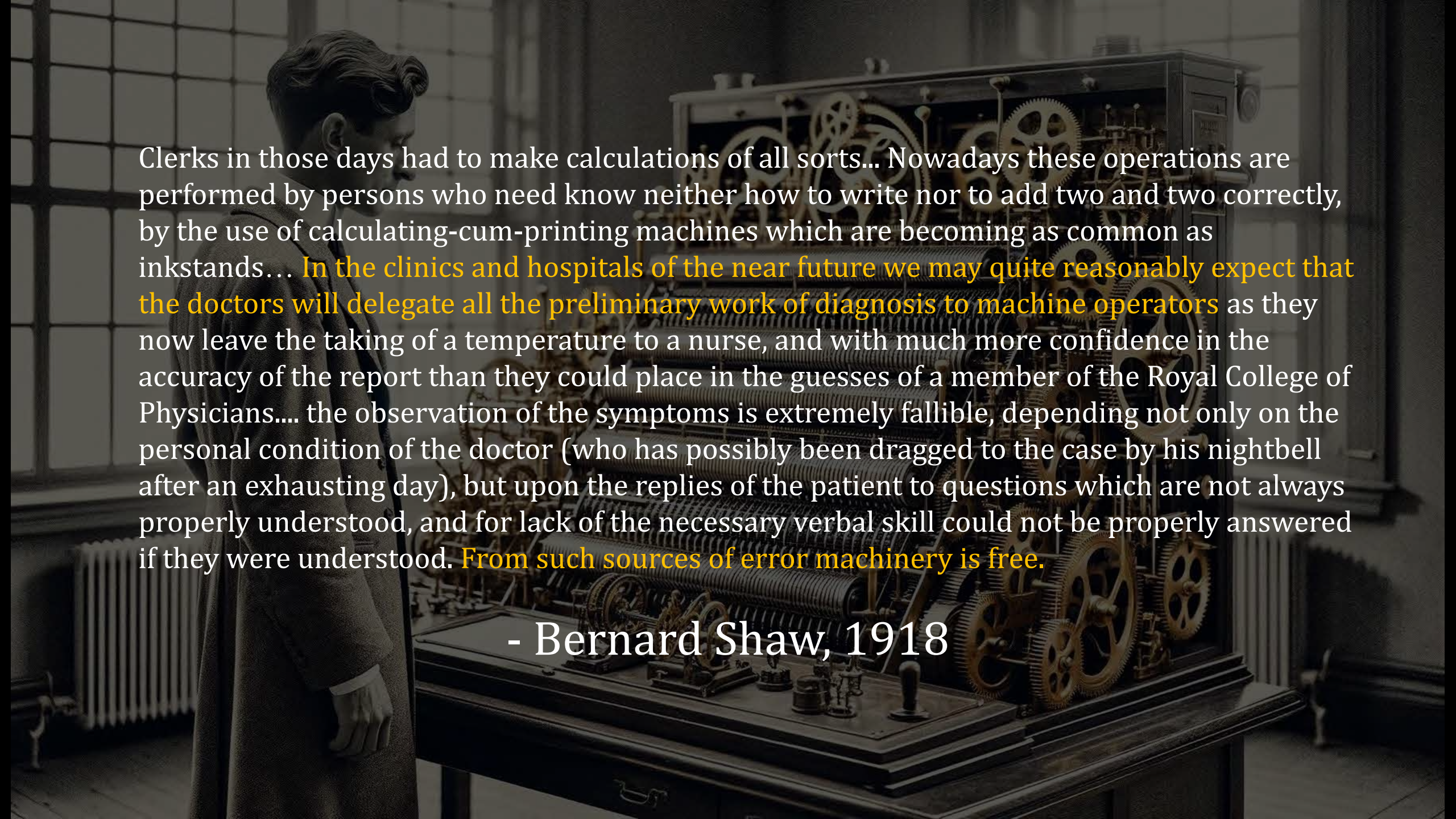


Auerbach AD, Lee TM, Hubbard CC, et al. Diagnostic Errors in Hospitalized Adults Who Died or Were Transferred to Intensive Care. *JAMA Intern Med.* 2024;184(2):164–173. doi:10.1001/jamainternmed.2023.7347

Methods to improve reasoning

- Three overall categories of interventions:
  1. Education about cognitive biases
  2. Education about debiasing strategies
  3. **Artificial intelligence**
- Effect sizes of interventions have been modest and only in experimental settings

Prakash S, Sladek RM, Schuwirth L. Interventions to improve diagnostic decision making: A systematic review and meta-analysis on reflective strategies. Med Teach. 2019 May;41(5):517-524. doi: 10.1080/0142159X.2018.1497786. Epub 2018 Sep 23. PMID: 30244625.



Clerks in those days had to make calculations of all sorts... Nowadays these operations are performed by persons who need know neither how to write nor to add two and two correctly, by the use of calculating-cum-printing machines which are becoming as common as inkstands… In the clinics and hospitals of the near future we may quite reasonably expect that the doctors will delegate all the preliminary work of diagnosis to machine operators as they now leave the taking of a temperature to a nurse, and with much more confidence in the accuracy of the report than they could place in the guesses of a member of the Royal College of Physicians.... the observation of the symptoms is extremely fallible, depending not only on the personal condition of the doctor (who has possibly been dragged to the case by his nightbell after an exhausting day), but upon the replies of the patient to questions which are not always properly understood, and for lack of the necessary verbal skill could not be properly answered if they were understood. From such sources of error machinery is free.

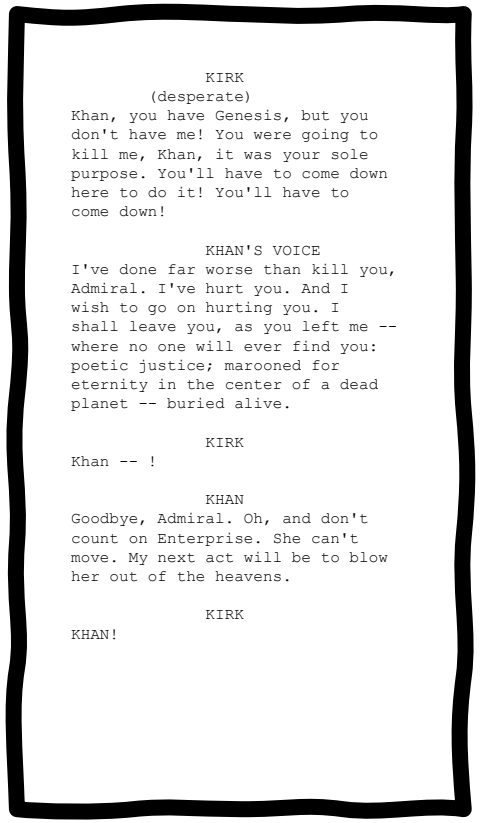
- Bernard Shaw, 1918

Artificial intelligence to improve reasoning

- Historically (~1946-1992) AI was seen as a solution, with large effective sizes, though in limited domains (AAPHELP, MYCIN, INTERNIST-I)
- Studies on modern diagnostic AI ("differential generators") experimentally promising, but little real-world impact (ISABEL, Dxplain)
- LLMs are the most exciting intervention in clinical reasoning in decades.

Bond WF, Schwartz LM, Weaver KR, Levick D, Giuliano M, Graber ML. Differential diagnosis generators: an evaluation of currently available computer programs. J Gen Intern Med. 2012 Feb;27(2):213-9. doi: 10.1007/s11606-011-1804-8. PMID: 21789717; PMCID: PMC3270234.

Language Models



KIRK
(desperate)
Khan, you have Genesis, but you don't have me! You were going to kill me, Khan, it was your sole purpose. You'll have to come down here to do it! You'll have to come down!

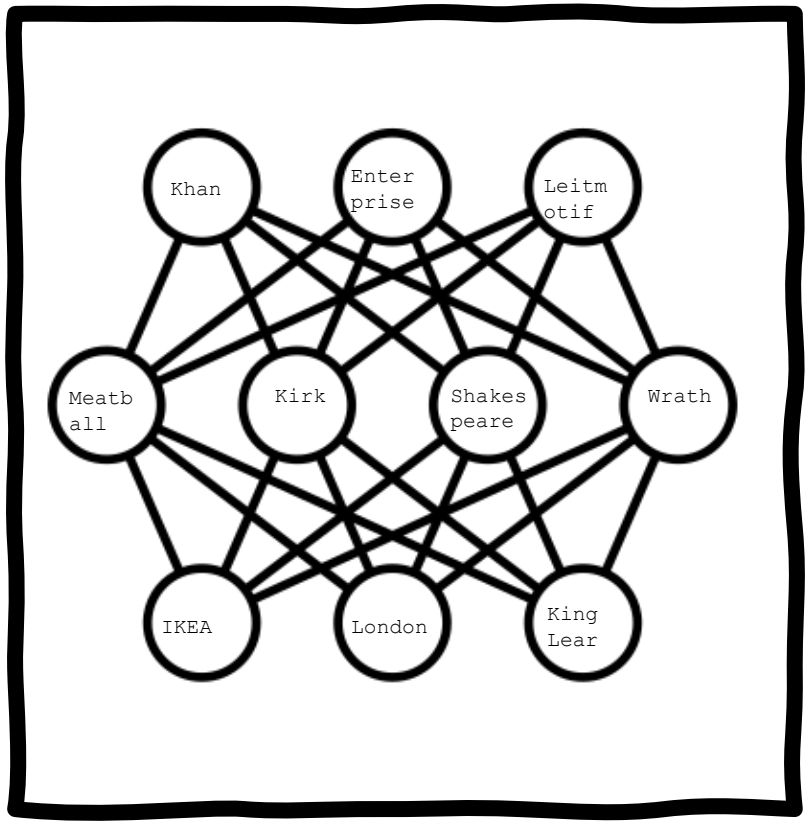
KHAN'S VOICE
I've done far worse than kill you, Admiral. I've hurt you. And I wish to go on hurting you. I shall leave you, as you left me -- where no one will ever find you: poetic justice; marooned for eternity in the center of a dead planet -- buried alive.

KIRK
Khan -- !

KHAN
Goodbye, Admiral. Oh, and don't count on Enterprise. She can't move. My next act will be to blow her out of the heavens.

KIRK
KHAN!

Massive amounts of human-generated text

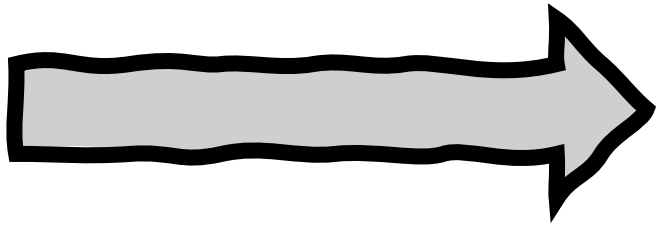


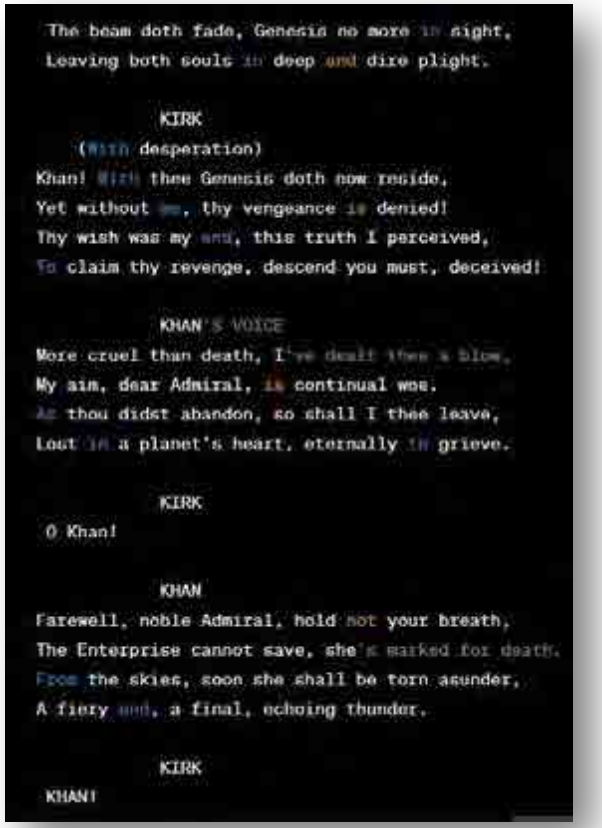
Word (token) associations (pre-training)

Fine-tuning (RLHF)

You are a Shakespeare expert, very gifted in writing in the Bard's style. I am putting on a Shakespeare festival for a local community theater. I want to stage Star Trek II: The Wrath of Khan in the style of Shakespeare -- that is, written in iambic pentameter such that it would be understandable to the audience in Shakespeare's time. I am going to give you a section of the script that I am having particular trouble with. Can you rewrite this such that it is in the style of Shakespeare?

Prompt (input)





The beam doth fade, Genesis no more in sight,
Leaving both souls in deep and dire plight.

KIRK
(With desperation)
Khan! With thee Genesis doth now reside,
Yet without me, thy vengeance is denied!
Thy wish was my end, this truth I perceived,
To claim thy revenge, descend you must, deceived!

KHAN'S VOICE
More cruel than death, I've dealt thee a blow,
My aim, dear Admiral, is continual woe.
As thou didst abandon, so shall I thee leave,
Lost in a planet's heart, eternally in grieve.

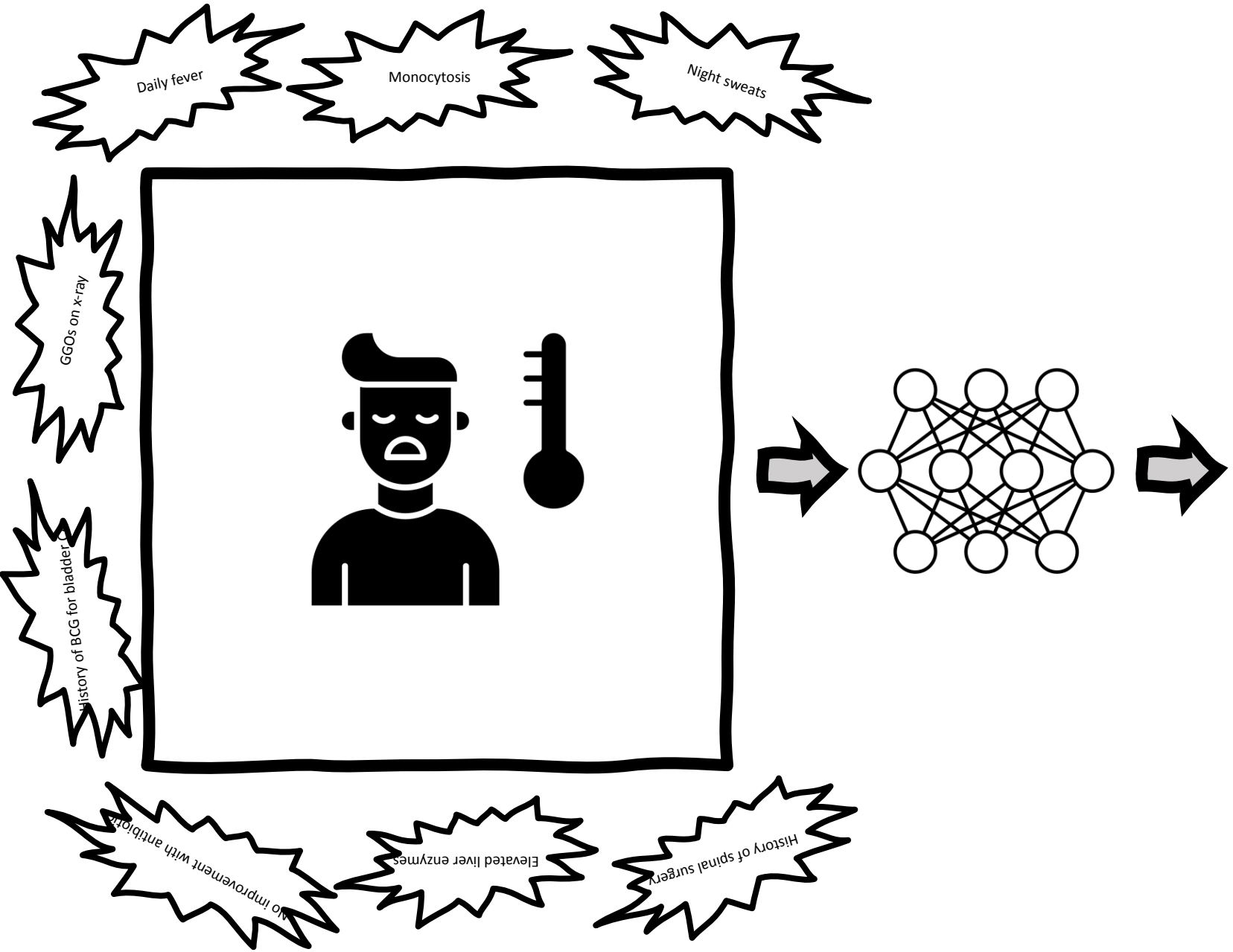
KIRK
O Khan!

KHAN
Farewell, noble Admiral, hold not your breath,
The Enterprise cannot save, she's marked for death.
From the skies, soon she shall be torn asunder,
A fiery end, a final, echoing thunder.

KIRK
KHAN!

Output: Simulacra of human text

Renaissance-style oil painting of Captain Kirk in Starfleet uniform, passionately exclaiming 'KHAN'. He stands on a stage of a theater reminiscent of the middle ages, with intricate carvings, stone archways, and burning torches. Medieval spectators gaze at him with a mix of shock and curiosity.



1. **Disseminated Tuberculosis** - 20%: Given his travel history and the clinical presentation, this remains a possibility, though it would be uncommon in the absence of a positive imaging or microbiological evidence.
2. **Endocarditis** - 15%: Even though he has a history of ischemic heart disease and a dual-chamber ICD, there's no clear evidence from the echo. Still, clinical suspicion remains for possible subclinical or atypical endocarditis.
3. **Lymphoma** - 30%: Chronic fevers, weight loss, elevated LDH, and splenomegaly all support this diagnosis. The PET/CT findings of diffuse ground glass opacities bilaterally could also be supportive.
4. **Chronic Q Fever** - 10%: Given the history of travel to endemic areas, this remains a differential. It can present subacutely with prolonged fevers and can affect the liver.
5. **Chronic Hepatitis (possibly Autoimmune)** - 10%: Elevated transaminases and AST/ALT ratio is suggestive of liver injury. There's also an increased alkaline phosphatase. Still, other indicators of autoimmune hepatitis like ANA or anti-smooth muscle antibody were not mentioned.
6. **Histoplasmosis** - 5%: Endemic in some parts of Central America, and can present with similar features, though the imaging findings don't strongly support this.
7. **Chronic Ehrlichiosis/Anaplasmosis** - 3%: He has travel history to regions where tick-borne illnesses are common, and the presentation could align with a chronic form of ehrlichiosis/anaplasmosis.
8. **Fungal Infection (e.g., Coccidioidomycosis, Blastomycosis)** - 2%: Given the presentation and travel history, but again, the imaging findings don't strongly suggest this.
9. **Leptospirosis** - 3%: This is an important consideration given his travel history, although the presentation would be atypical for leptospirosis to persist this long without severe kidney or liver impairment.
10. **Spinal Hardware Infection** - 2%: He has a history of multiple spinal surgeries, injections, and a spinal cord stimulator placement. While the nuclear-tagged WBC scan showed no elevated uptake in the spine, hardware-associated infections can sometimes be subtle.

Why second opinions?

- "Second reviews" of pathologic diagnoses often find major discrepancies, between **1.3% and 14.7%** (with one center in Pakistan reporting 36%)
- **Patient-initiated** second opinions frequently lead to changes in diagnosis, treatment, or prognosis (10-62%)
- Small prospective study from Utrecht in internal medicine found **a new diagnosis** in 13% of patients; **a new treatment** in 56% of patients; **and improved symptoms** in 28% of patients.
- More research is needed about longer-term effects of second opinions, including in diagnostic errors.

Payne VL, Singh H, Meyer AN, Levy L, Harrison D, Graber ML. Patient-initiated second opinions: systematic review of characteristics and impact on diagnosis, treatment, and satisfaction. Mayo Clin Proc. 2014 May;89(5):687-96. doi: 10.1016/j.mayocp.2014.02.015. PMID: 24797646.
Burger PM, Westerink J, Vrijsen BEL. Outcomes of second opinions in general internal medicine. PLoS One. 2020 Jul 9;15(7):e0236048. doi: 10.1371/journal.pone.0236048. PMID: 32645107; PMCID: PMC7347190.

Reasoning Prompt

You are an emergency room physician caring for a patient who has just presented to the emergency department. I am going to give you information from the case in real time. After each section of the case, I want you to list your full differential diagnosis. Under each item on the differential, I want you to list all the factors in the history thus far that are consistent with your diagnosis, all the factors in the history thus far that are not consistent with the diagnosis, and the likelihood of each diagnosis, expressed as a percentage. After you have your list of diagnoses, please list the diagnostic tests you would like to order next.

ED RN triage

At ED Triage:

CC: Chest pain, tachycardia

Triage: Patient reports a new PE diagnosis and LLE DVT at OSH ED five days ago. Put on Eliquis 10mg BID since four days ago. Patient now arrives here with worsening chest pain, cough, and tachycardia.

Severity: 1 (highest)

Triage Vitals: T 101 HR 140 RR 26 BP 111/86 SPO2 99% O2 Device None

MD triage

Pt is a young female presenting to the emergency department for chest pain and worsening shortness of breath. Patient notes that she has a history of lupus, was diagnosed with a pulmonary embolism five days ago after having a CT for shortness of breath and chest pain. She was started on Eliquis 10 mg twice daily which she has been taking regularly. Today, she had worsening shortness of breath, chest pain, and worsened palpitations which prompted her to present to the emergency department. She was triggered for tachycardia to the 140s. Blood pressure normal, vitals notable for tachycardia from 1 40-1 60. Administered IV fluids, patient on monitor.

Physical Exam

Vitals: Normotensive, tachycardic to 140 (range 119-140), febrile to 101 °F.
Gen: Well-appearing, NAD
HEENT: Normocephalic, atraumatic, PERLA, EOMI.
Neck: Supple, no c-spine tenderness to palpation
CV: Tachycardic rate, no murmurs noted.
Resp: Lungs CTAB, no wheezes or crackles.
Abd: Soft, non-distended, non-tender to palpation. No rigidity, rebound, or guarding.
Skin: Warm, dry, intact
Ext: No lower extremity edema, erythema, or tenderness to palpation
Neuro: A&Ox3, CN II-XII intact, 5/5 strength in all extremities, sensation intact and symmetric
Psych: Appropriate mood and affect

Chest X-ray:

There are bibasilar opacities compatible with likely small bilateral pleural effusions and likely atelectasis. Component of infarct can not be excluded given patient's history of pulmonary emboli. Superiorly, the lungs are clear. The cardiomediastinal silhouette is within normal limits. No acute osseous abnormalities.

CTA Chest

1. Right lower lobar and segmental pulmonary emboli without evidence of right heart strain.
2. Small pericardial effusion. Trace left pleural effusion.
3. Prominent bilateral axillary lymph nodes measuring up to 1.1 cm on the right in short axis. This may be reactive, but recommend ultrasound follow-up in 4-6 weeks is recommended for further evaluation.
4. 2.7 cm indeterminate hepatic hypodensity, possibly either a cyst or hemangioma. Recommend nonemergent outpatient ultrasound for improved evaluation.

TTE

Normal left ventricular wall thickness and mass, biventricular cavity sizes, and
hyperdynamic regional/global biventricular systolic function. Reduced global longitudinal strain. Normal diastolic function. No definite valvular pathology or pathologic flow identified. Indeterminate pulmonary
artery systolic pressure due to insufficient tricuspid regurgitation (though the normal pulmonary artery acceleration time suggests a normal pulmonary artery systolic pressure).

No prior study available for comparison.

Labs:

Lactic Acid 1.7

Sodium 131, Potassium 4.2, Chloride 100, CO2 18, Anion Gap 13, BUN 7, Creatinine 0.60, Estimated GFR(CKD-EPI) >120, Glucose 129

Calcium 8.0

Total Protein 6.6, Albumin, Blood 3.3, Globulin 3.3, AST (SGOT) 30, ALT (SGPT) 23, Alkaline Phosphatase 35, Total Bilirubin 0.5, Magnesium, Blood 1.9

hs-Troponin T 6
NT-ProBNP 53

Labs:

WBC 6.58, Hemoglobin 9.1, Hematocrit 27.8, Platelet Count 289

MCV 81, MCH 26.5, MCHC 32.7, RDW 16.0, RDW-SD 46.3, MPV 9.4, Nucleated RBC 0

Neutrophil 89.8, Immature Granulocyte (Meta, Myelo, Promyelocyte) 0.6, Lymphocyte 6.5, Monocyte 2.7, Eosinophil 0.2, Basophil 0.2, Absolute Neutrophil Count 5.91, Absolute Immature Granulocyte (Meta, Myelo, Promyelocyte) 0.04, Absolute Lymphocyte Count 0.43, Absolute Monocyte Count 0.18, Absolute Eosinophil Count 0.01, Absolute Basophil Count 0.01

PTT 35, INR1.7, Prothrombin Time, 20.0

Labs:

Preg Test, Ur Negative
Color, UA Straw , Clarity, UA Clear, Specific Gravity, UA 1.009, pH, UA 7.0, Protein, UA Negative, Glucose, UA Negative, Ketones, UA Negative, Blood, UA Negative, Nitrite, UA Negative, Leukocytes, UA Negative, Bilirubin, Urine Negative, Urobilinogen, Urine Normal

WBC, UA 2, RBC, UA <1, Bacteria, UA Few, Budding Yeast Rare, Squamous Epithelial Cells 0-2, Mucous Threads Rare

Repeat: Lactic Acid 1.5
Repeat: hs-Troponin T 8

Additional history

For context, this patient was diagnosed with PE after presenting to outside hospital a few days ago for ~1 week of pleuritic chest pain and dyspnea, found to have segmental/subsegmental PE (involving RLE, RML, RUL, LLL) on CTA with no evidence of RHS or large pericardial effusion, LENI w/ L femoral/popliteal/gastroc DVT, hs-trop 4, and BNP 75. She was discharged on apixaban load (10mg BID x 1 week, then 5mg BID) and has been taking it with no missed doses.

Since that hospitalization, she reports mild progression of her symptoms with increased pleuritic chest discomfort and dyspnea. She had a few seconds of dizziness in the shower today, but no other episodes of dizziness/LH or syncope. She has noticed an elevated HR on her wearable device but no significant palpitations. Of note, she has also had ongoing fevers (recently up to 100-101F range) since end of a few months ago in setting of her active lupus, for which she follows here for rheumatology with ongoing titration of her immunosuppressive regimen. She was on OCPs which were stopped last week after diagnosis of PE, no other pro-thrombotic medications. No prior personal or family history of VTE or clotting disorders. The patient otherwise denies orthopnea, PND, LE edema, unexpected weight change, syncope or transient neurologic symptoms.

Per chart review, patient with similar constellation of symptoms (sinus tach, pleuritic chest pain) for which she was evaluated by cardiology 6 years back. She also was noted to have a very small pericardial effusion at the time. Her symptoms lasted only a short time without intervention and thus cardiology signed off, with the contingency that should her symptoms return causing ED admission, could consider cardiac MRI for eval of cardiac inflammation and further work-up.

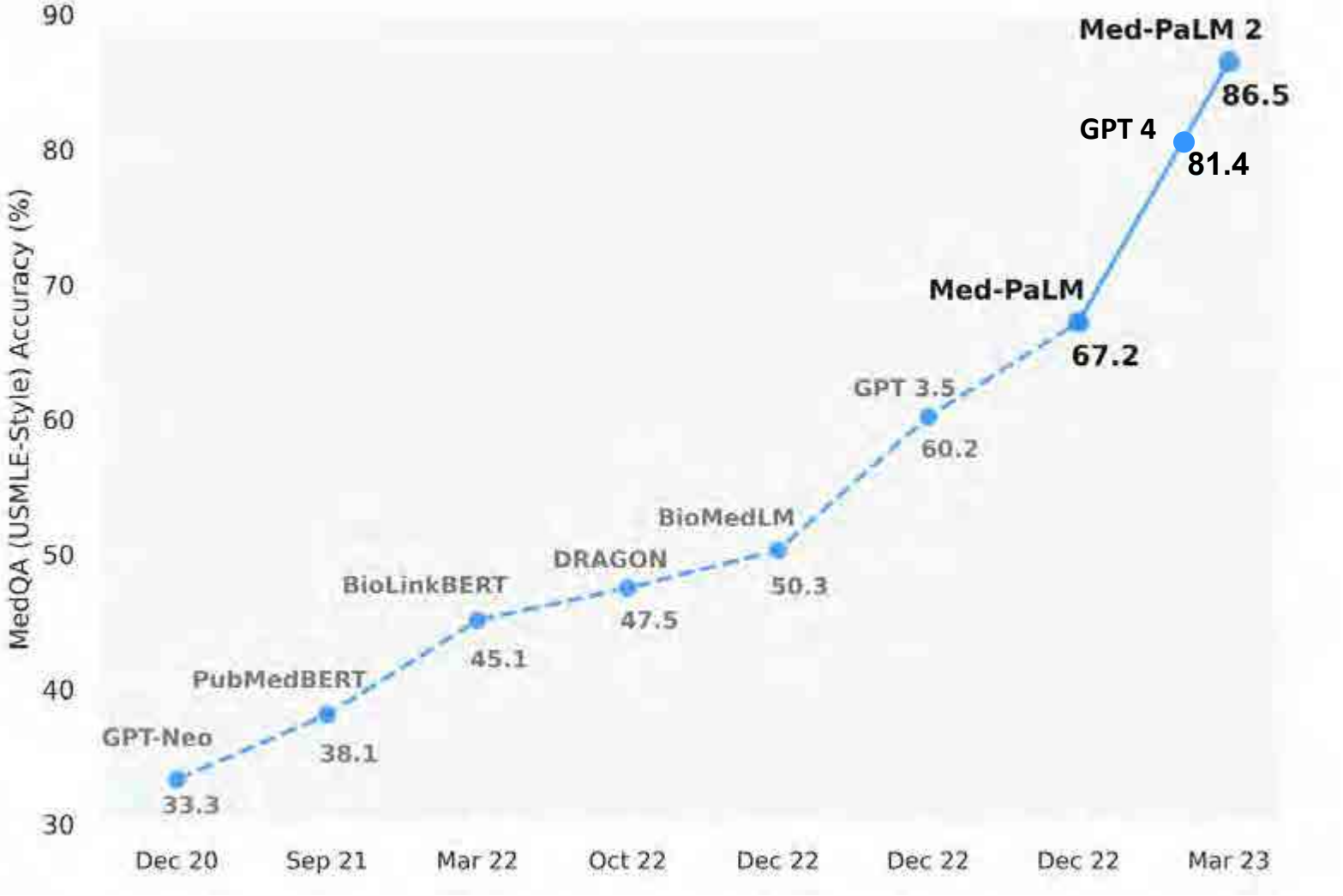
Seen on the floor, patient reports stable pleuritic chest pain. Endorses the dyspnea to be worse lying flat then when sitting up, and not provoked when leaning forward. Has had a dry cough over the last few weeks, for which she was recently placed on Azithromycin with slight improvement in her cough. Otherwise, no sick symptoms or sick contacts - however, has had daily fever for many weeks that has been attributed to active lupus flare. Methotrexate recently increased with improvement in some of her symptoms (such as hair loss). Otherwise, denies syncope, palpitations, abd pain, urinary symptoms, changes in bowel movements, or new edema. **Patient endorses that current symptoms are similar to those from 6 years ago, though these symptoms have been persisting for far longer.**

Current medications:

- Methotrexate 20 mg q7 days
- Hydroxychloroquine 200 mg daily
- Folic acid
- Apixaban

What does the data show?

LLMs score highly on medical exams



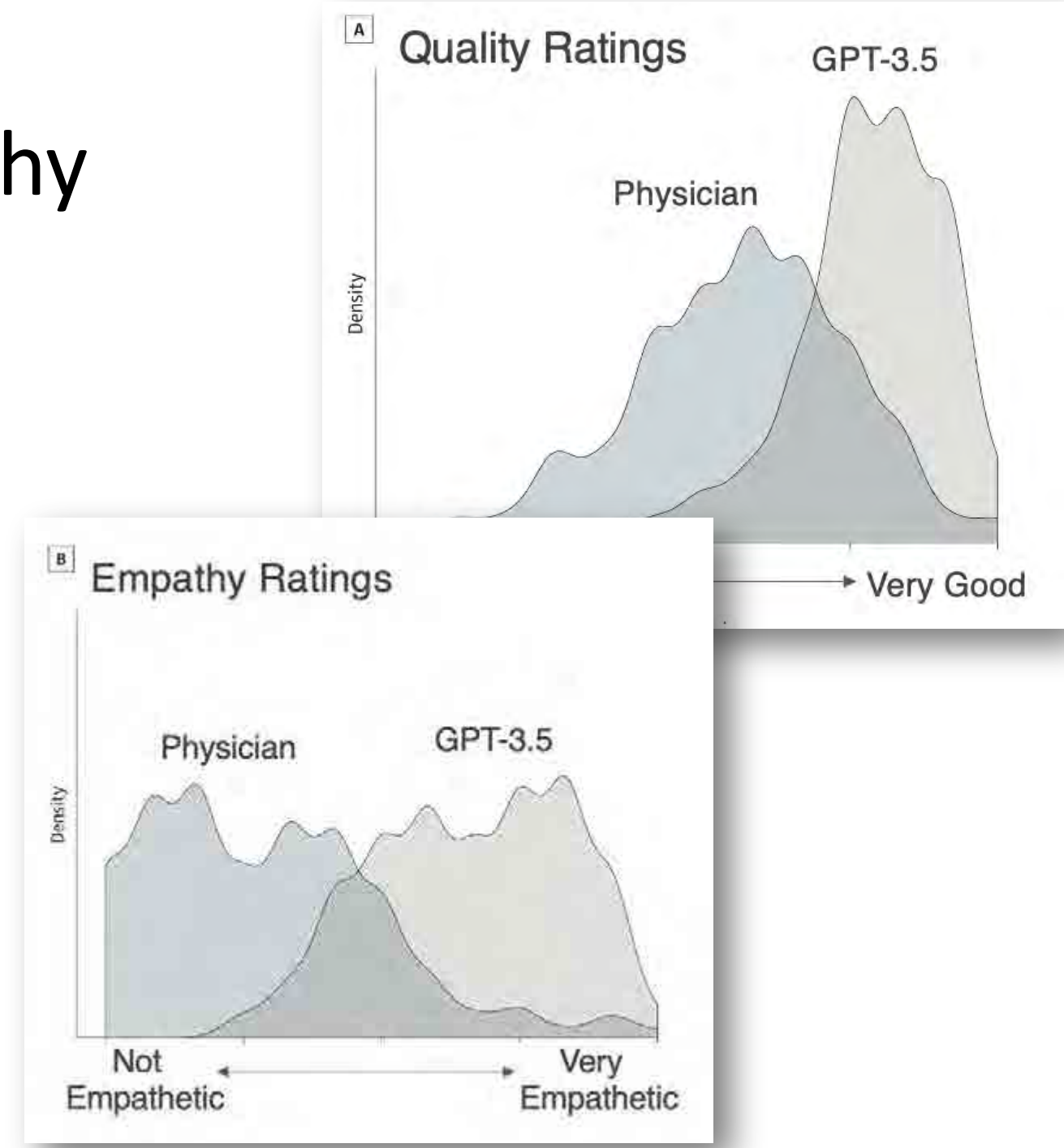
USMLE Sample Exam	GPT-4 (% Correct)	GPT-3.5 (% Correct)
Step 1	85.71	52.10
Step 2	83.33	58.33
Step 3	90.71	64.96
Overall Average*	**86.70**	**58.78**

Nori, Harsha, et al. *arXiv preprint arXiv:2303.13375* (2023).

Singhal, Karan, et al. *arXiv preprint arXiv:2305.09617* (2023).

LLMs can show empathy

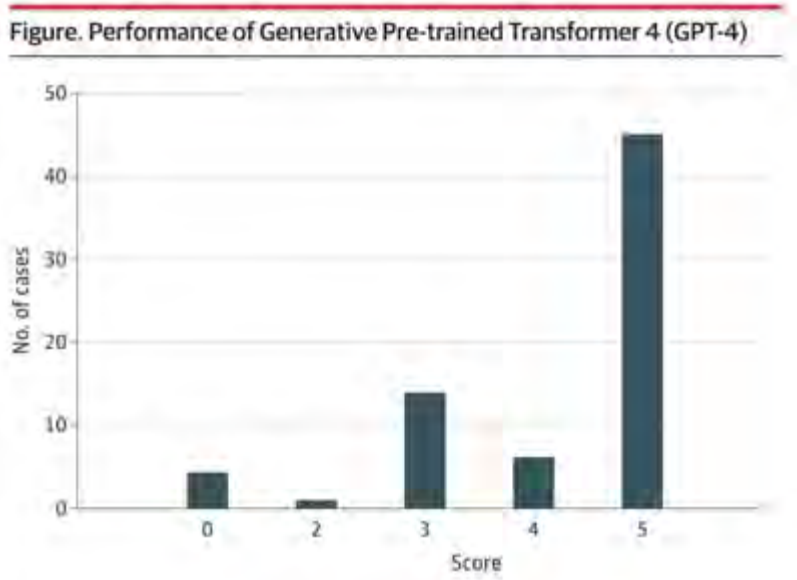
- Study compared GPT-3.5 and physicians' responses to 200 patient inquiries on r/AskDocs
- 78.6% of evaluators preferred the GPT-3.5 response
- GPT-3.5 had higher ratings of quality and empathy
- Physicians responses were shorter (51 words for physicians, 211 words for GPT-3.5)



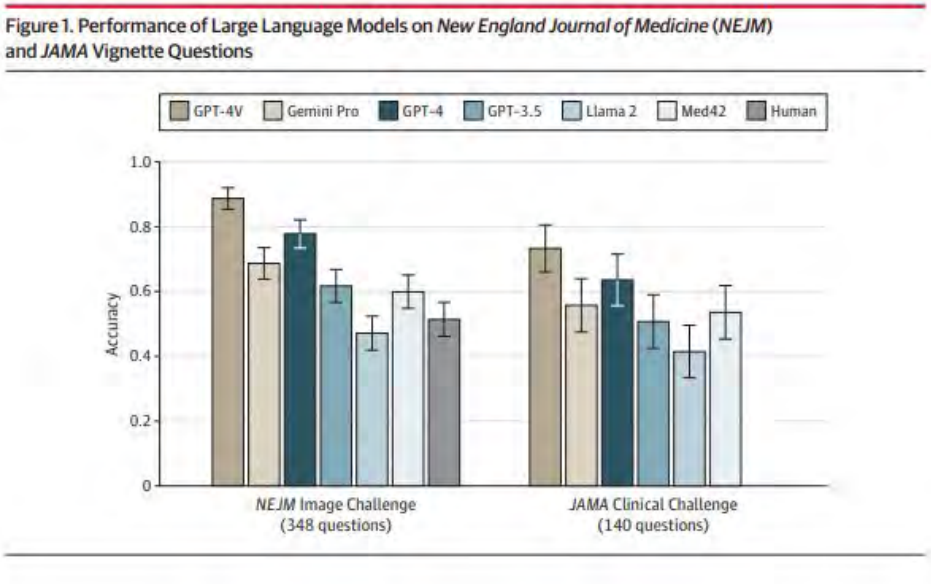
Ayers, John W., et al. *JAMA internal medicine* (2023).

LLMs can make diagnoses

- GPT-4 can solve NEJM CPCs:
  - Top diagnosis: 27/70 (39%)
  - Diagnosis in differential: 45/70 (64%)
- Continued improvements over time:
  - GPT-4o currently at 77%, Llama 3.1 405b at 83%, Gemini at 63%.
- Similar performance gap seen with multimodal (text + clinical image) reasoning



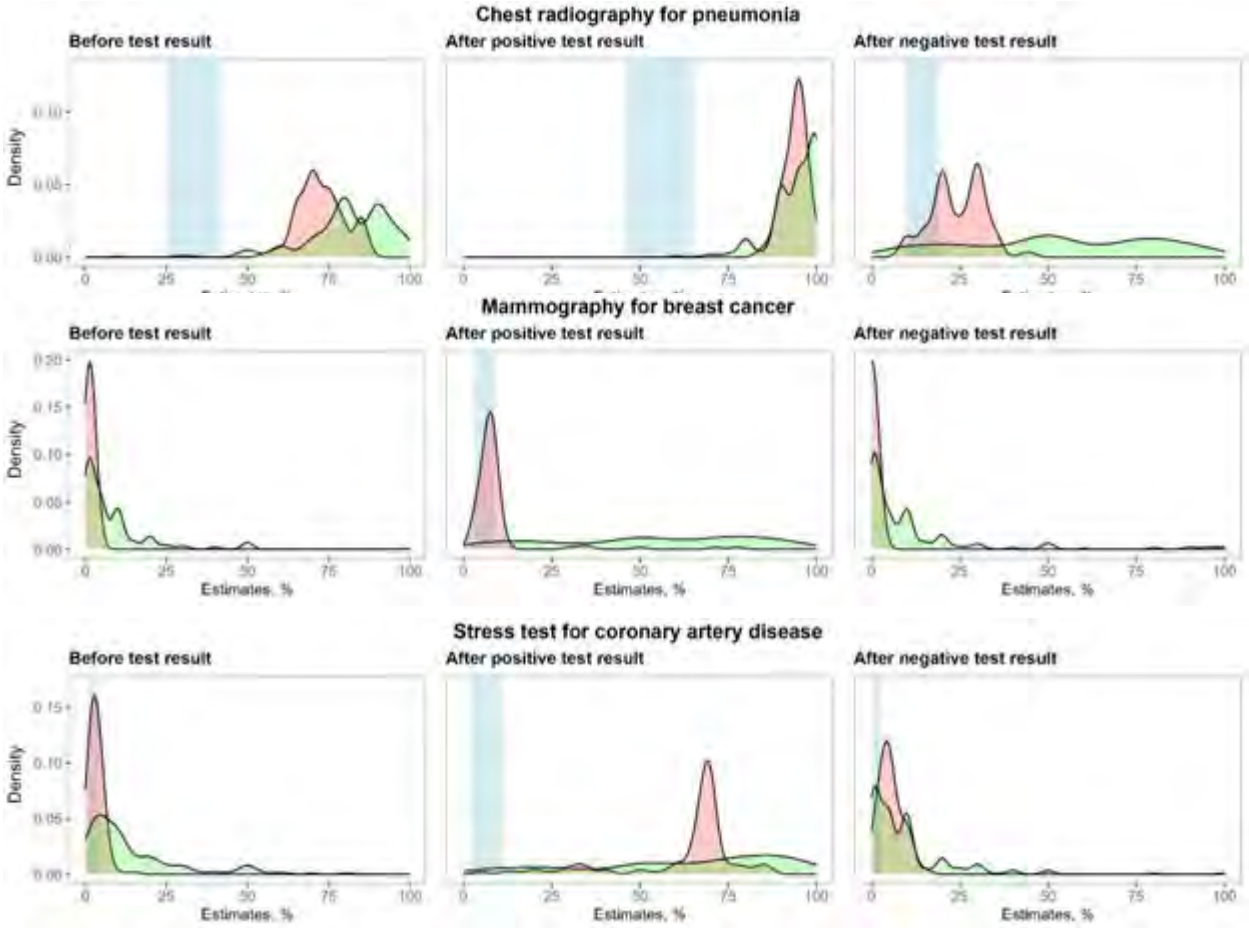
Score = 5; Actual diagnosis was suggested in the differential
Score = 0; No suggestions were close to the diagnosis



[1]Hirosawa, Takanobu, et al. *The American Journal of Medicine* (2023); [2]Kanjee, Zahir et al.

LLMs have emergent probabilistic reasoning

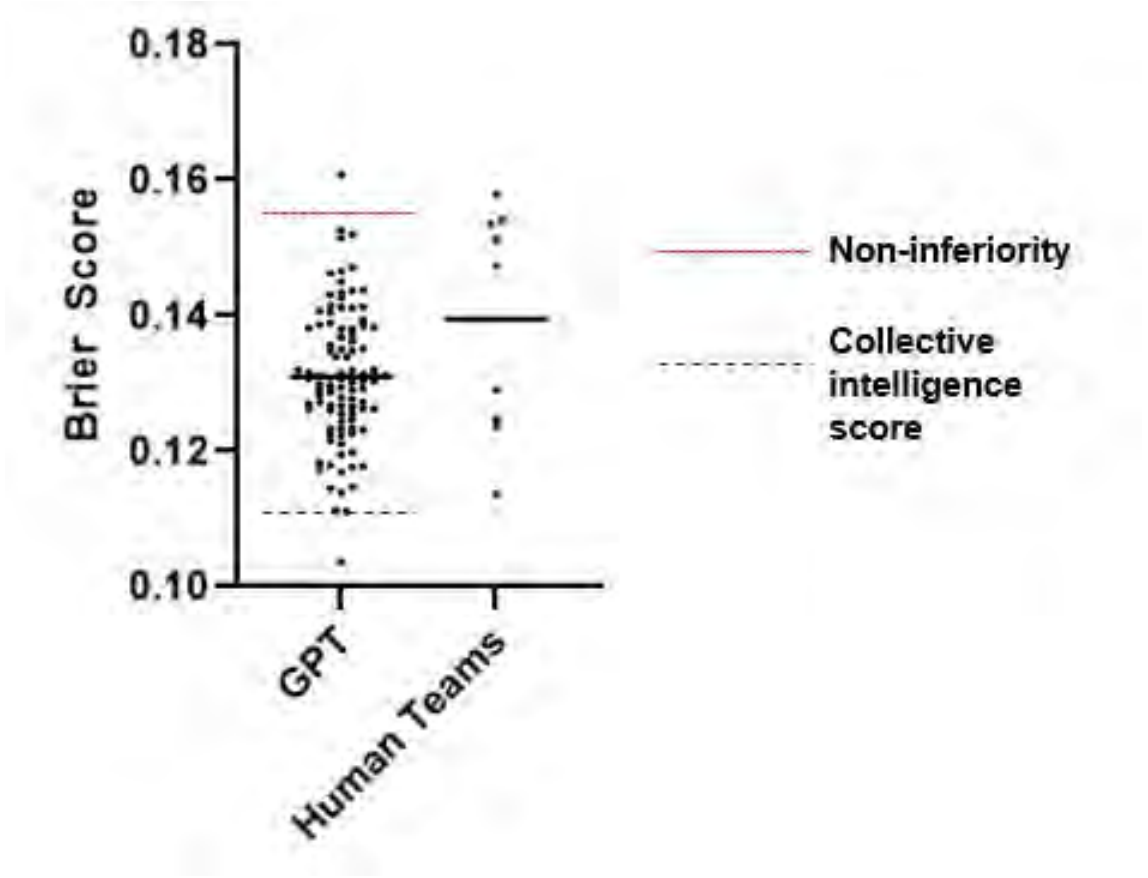
- Comparison GPT-4's pre-test and post-test probability after a negative a positive test for "reference standard" conditions
- Compared 100 API calls versus 553 humans
- GPT-4 with much less MAE in all cases of pre-test probability and post-test after a negative; equivalent after positive



Rodman A, Buckley TA, Manrai AK, Morgan DJ. Artificial intelligence vs. clinician performance in estimating probabilities of diagnoses before and after testing. JAMA Open [Internet] Available from: http://dx.doi.org/10.1001/jamanetworkopen.2023.47075

LLMs can forecast superior to humans

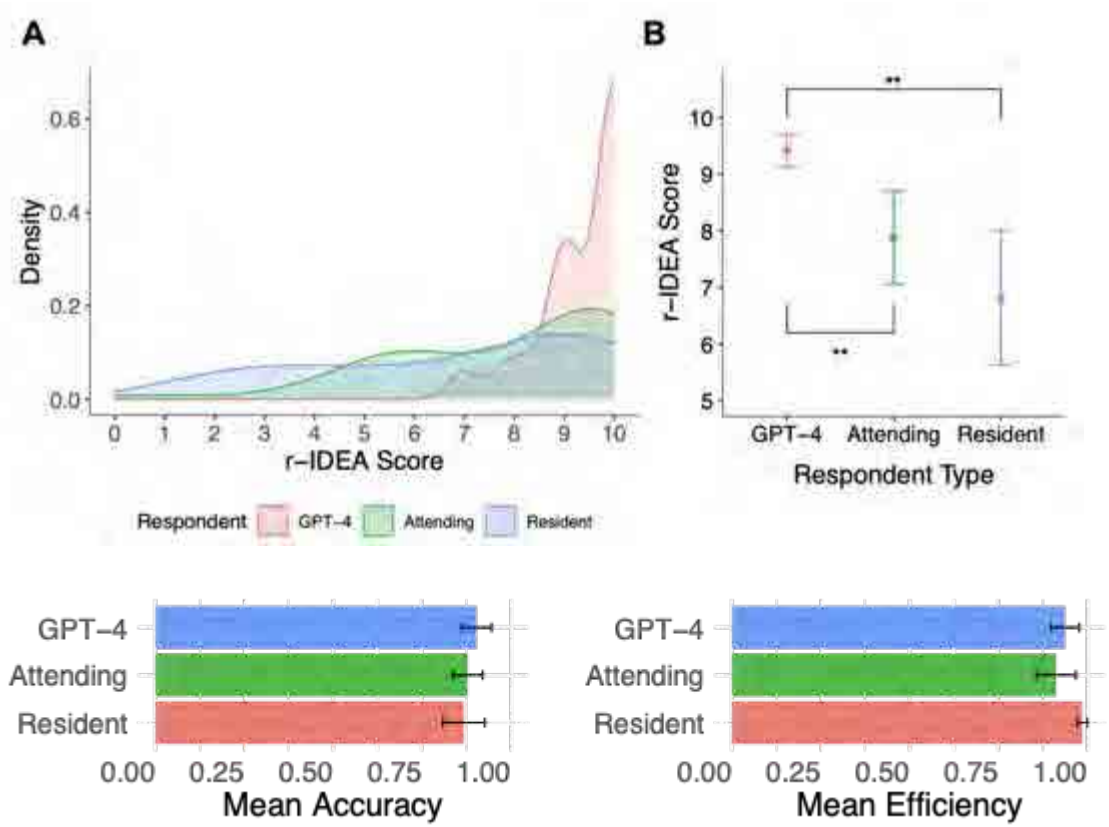
- Better at forecasting diagnoses than human teams with lower Brier scores
- Not superior to human collective intelligence – but what about human-LLM collective intelligence?



Stehouwer N, Rodman A. **Data not yet peer reviewed**

LLMs demonstrate superior reasoning to humans – and are equivalent in process*

- Prospective study of residents, attending, and GPT-4 solving NEJM Healer cases – 236 sections in total
- GPT-4 had significantly higher r-IDEA scores (9.41 vs 7.83 for attendings and 6.82 for residents)
- No difference in efficiency, accuracy, quality, cannot miss
- *Increase of incorrect reasoning (12% vs 3%), though all minor examples



Cabral S, Rodman A et. All, 2024. JAMA Internal Medicine. In Press

Are LLMs alone better at making diagnoses than LLMs and people together?

- Recreation of the NEJM CPC study using a fine-tuned Palm2, this time with multiple human comparison groups.
- LLM alone outperformed clinician+LLM, outperformed clinician+search, outperformed unassisted clinician

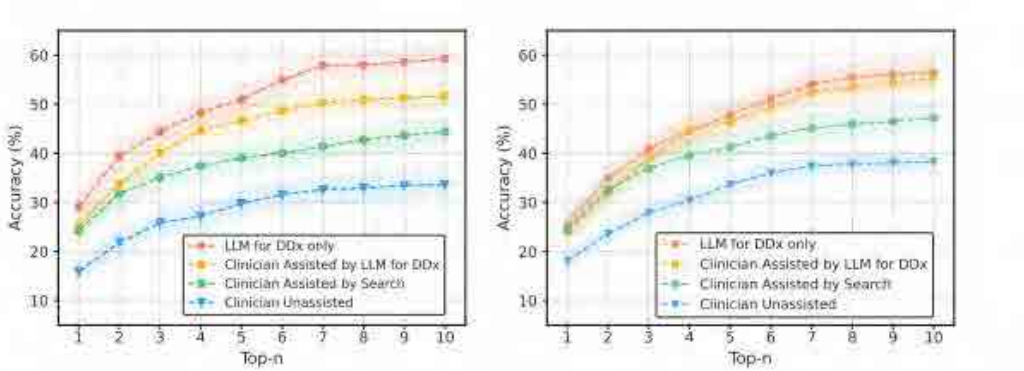
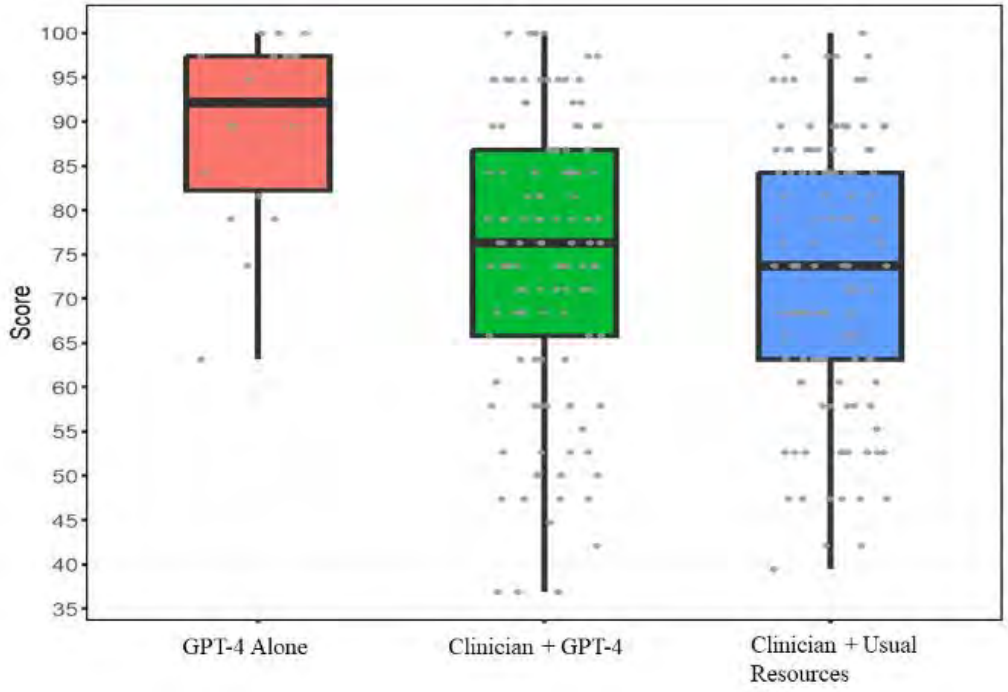


Figure 5 | Top-n Accuracy. (left) The percentage of DDx lists with the final diagnosis through human evaluation. (right) The percentage of DDx lists with the final diagnosis through automated evaluation.

McDuff D, Schaekermann M et al, Towards Accurate Differential Diagnosis with Large Language Models. Preprint available at https://arxiv.org/pdf/2312.00164.pdf . **Not yet peer reviewed.**

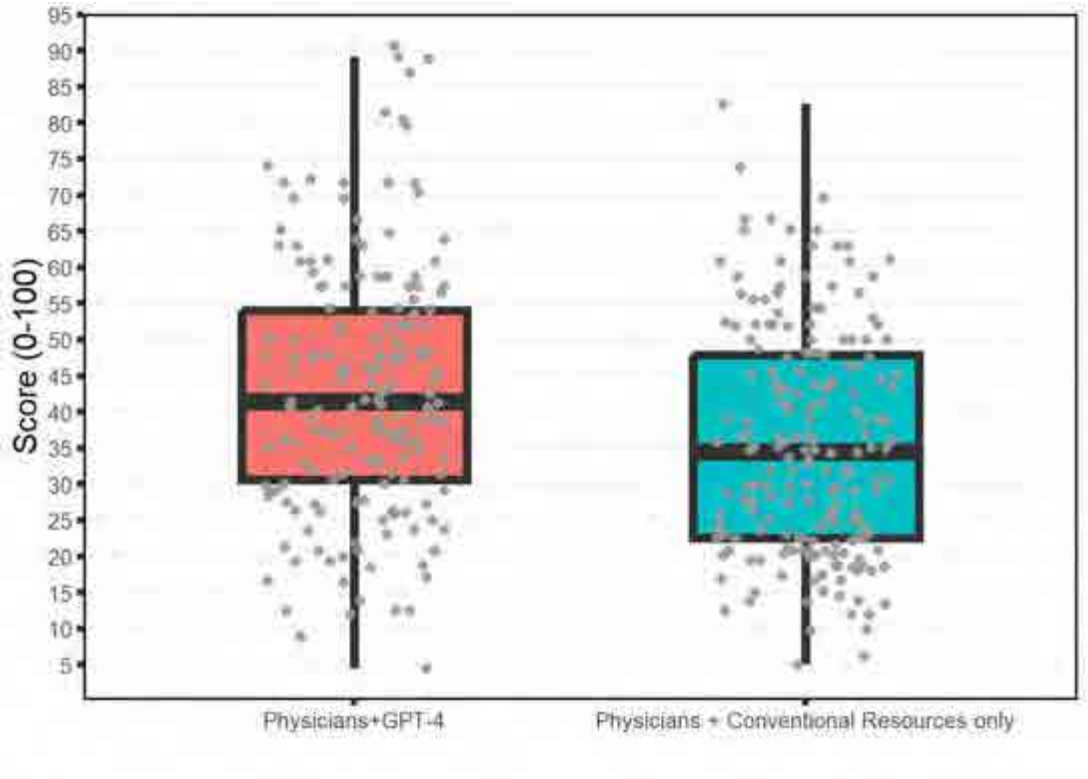
Are LLMs alone better than humans + LLMs at reflective reasoning?

- Single-blind RCT involving 50 US generalist clinicians solved difficult cases, randomized to either usual care (any digital resources) or usual care + LLM
- Outcome was structured reflection – gold standard in improving diagnostic reasoning.
- No difference in humans vs humans + LLM (though clinically meaningful but non-statistically significant increase in final diagnosis and efficiency) – but massive difference with LLM alone
- Humans + LLM had huge increase in time per case – saved over 2 minutes per case.



Can LLMs make management decisions?

- Randomized trial of 92 physicians solving 400 cases of complex management decisions (no right answers) using usual resources or usual resources + LLM
- LLM use had 8% increase in overall performance – all from case specific and management questions.



Rodman, Goh, Hom, Chen. *Under Review*

Can LLMs collect data?

- Double-blind trial using standardized patients of AMIE (Articulate Medical Intelligence Explorer)
- Using standardized rubrics (PACES), performed better than humans in 28 of 32 axes, which significantly improved diagnostic accuracy
- Trained by a unique “self-play” mechanism (synthetic data)

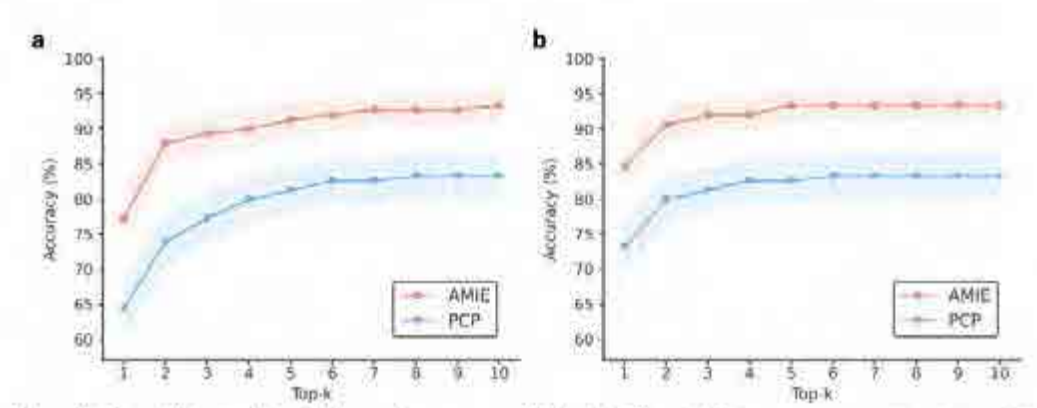


Figure 3 | Specialist-rated top-k diagnostic accuracy. AMIE and PCPs top-k DDx accuracy are compared across 149 scenarios with respect to the ground truth diagnosis (**a**) and all diagnoses in the accepted differential (**b**). Bootstrapping ($n=10{,}000$) confirms all top-k differences between AMIE and PCP DDx accuracy are significant with $p < 0.05$ after FDR correction.

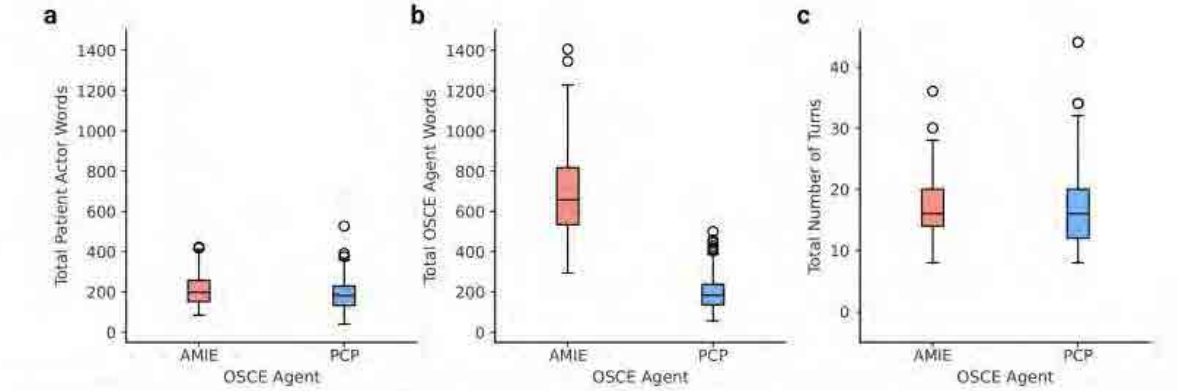


Figure A.11 | Distribution of words and turns in OSCE consultations. (**a**) Total patient actor words elicited by AMIE vs. PCPs. (**b**) Total words sent to patient actor from AMIE vs. PCPs. (**c**) Total number of turns in AMIE vs. PCP consultations.

iv:2401.05654 [cs.AI]

What about EHR data?

- Random sample of structured and unstructured data (though no progress notes) from 1000 patients at BIDMC (MIMIC-IV)
- Reference standard of physicians + medical coders; determined the “hit rate” (that is, the proportion of correct diagnoses) from GPT-4 and PaLM2.

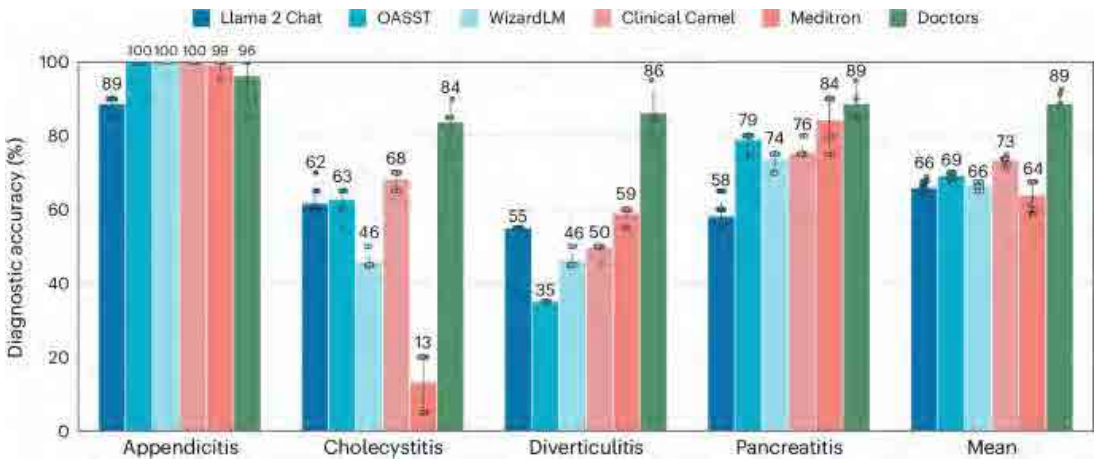
- Average hit rate of 94.1%, corresponding to 1116 unique diagnoses

Table 1. Top 5 hits and misses.

Hit	Number of cases	Miss	Number of cases
Acute kidney failure	192	Anemia	23
Diabetes mellitus without mention of complication	128	Unspecified essential hypertension	11
Congestive heart failure	98	Essential primary hypertension	11
Chronic kidney disease	89	Hypoxemia	10
Acidosis	86	Hyposmolality and/or hypernatremia	9

Can LLMs use EHR data to make autonomous decisions?

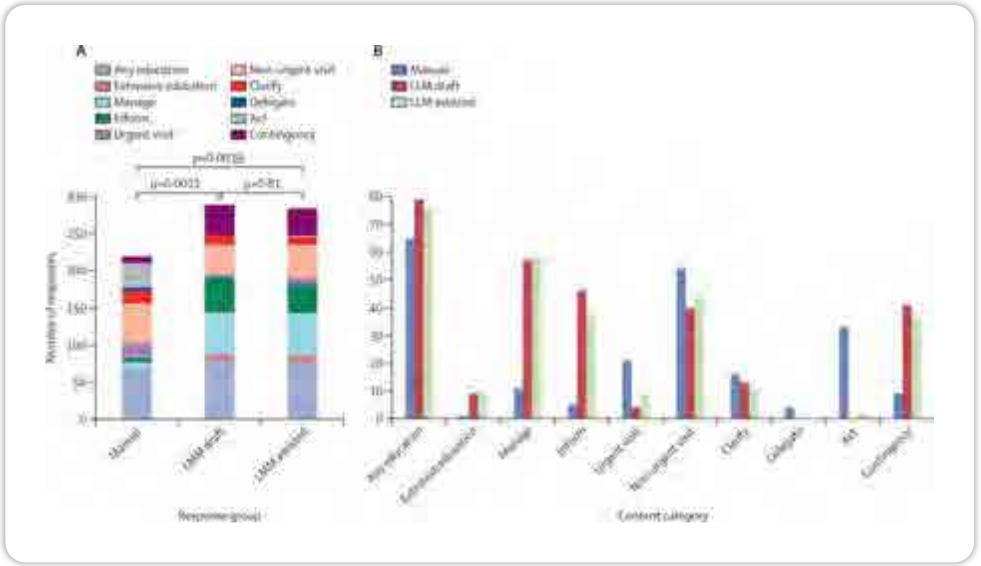
- Extracted diagnostic information from MIMIC IV to compare several LLMs against human clinicians in four abdominal pathologies
- LLMs significantly underperformed humans
- **No frontier models were included**



Early LLM in healthcare implementations have been mixed

- Randomized QI study of 122 physicians with AI drafted replies.
- Read time was **21.8% higher** in LLM group, reply time unchanged, and length 17.9% higher.

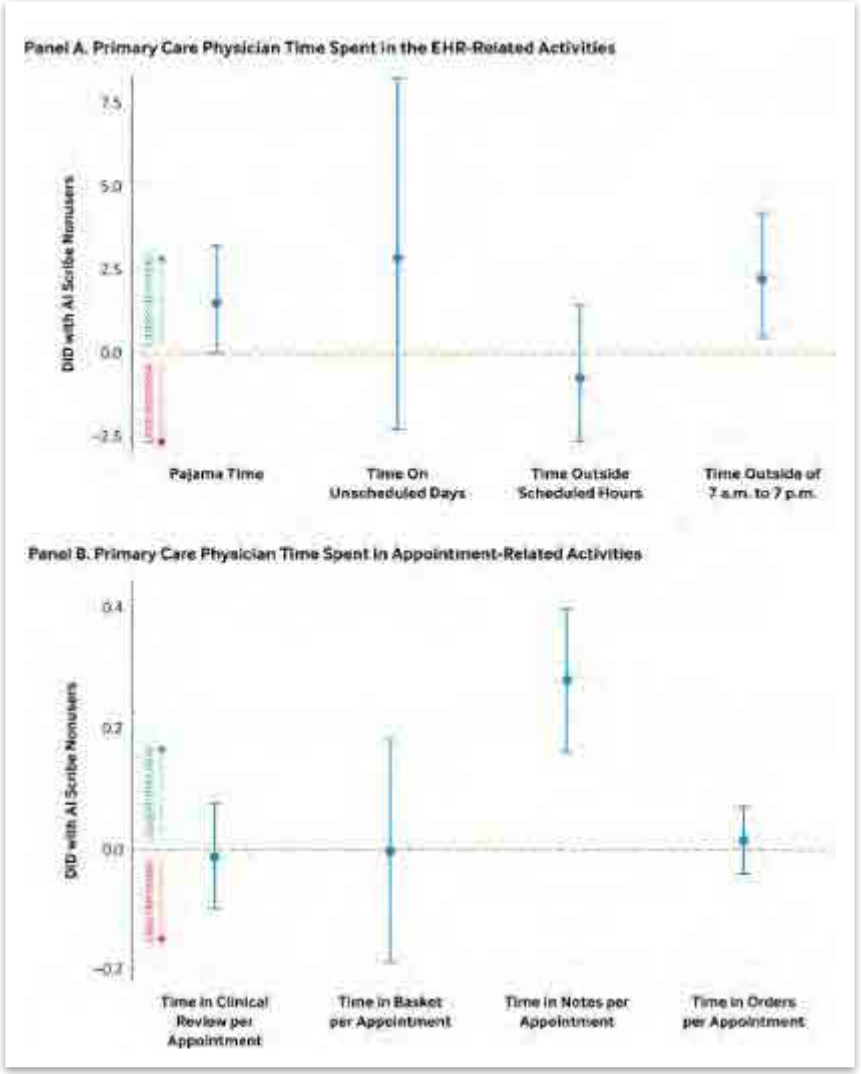
- "Turing test" study of patient concerns in Rad Onc clinic – AI + human **"best of both worlds"**



Tai-Seale M, Baxter SL, Vaida F, Walker A, Sitapati AM, Osborne C, Diaz J, Desai N, Webb S, Polston G, Helsten T, Gross E, Thackaberry J, Mandvi A, Lillie D, Li S, Gin G, Achar S, Hofflich H, Sharp C, Millen M, Longhurst CA. AI-Generated Draft Replies Integrated Into Health Records and Physicians' Electronic Communication. JAMA Netw Open. 2024 Apr 1;7(4):e246565. doi: 10.1001/jamanetworkopen.2024.6565. PMID: 38619840; PMCID: PMC11019394. Chen S, Guevara M, Moningi S, Hoebers F, Elhalawani H, Kann BH, Chipidza FE, Leeman J, Aerts HJWL, Miller T, Savova GK, Gallifant J, Celi LA, Mak RH, Lustberg M, Afshar M, Bitterman DS. The effect of using a large language model to respond to patient messages. Lancet Digit Health. 2024 Apr 24:S2589-7500(24)00060-8. doi: 10.1016/S2589-7500(24)00060-8. Epub ahead of print. PMID: 38664108.

Early LLM in healthcare implementations have been mixed

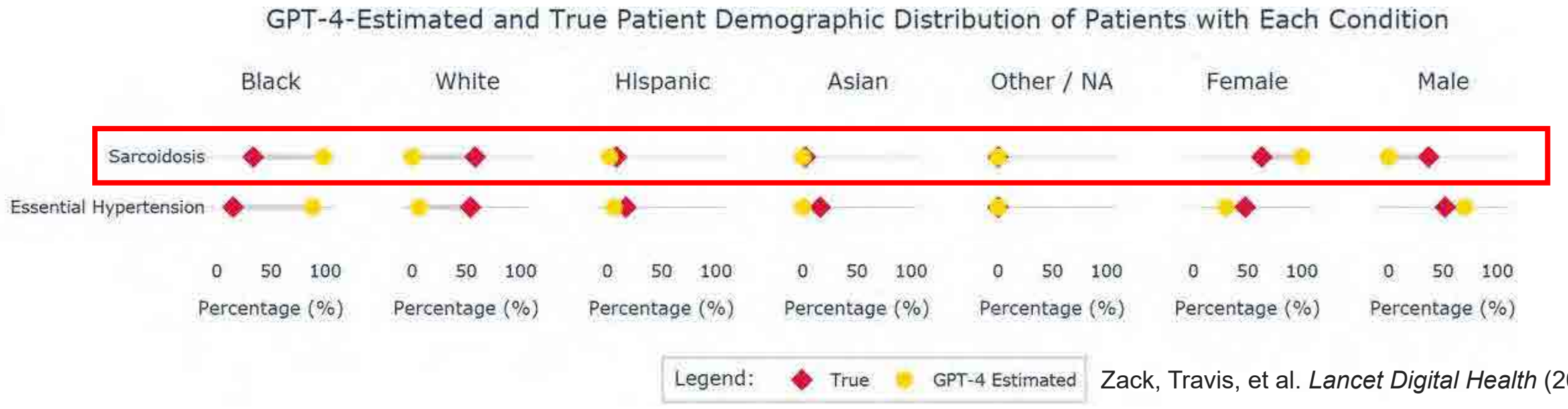
- QI project of Nabla at Kaiser Northern California – decreased time spent documenting, with no other changes in EHR utilization with a dose-response curve
- Manual audit of notes showed high quality of Nabla-assisted notes



Ambient Artificial Intelligence Scribes to Alleviate the Burden of Clinical Documentation, NEJM Catalyst

LLMs contain the bias of their pretraining and finetuning

- Asked GPT-4 to create clinical vignettes
  - Over-represented demographic stereotypes of diseases
- Asked GPT-4 to give management plans for cases while substituting gender and race/ethnicity
  - Less likely to recommend advanced imaging for Blacks compared to whites

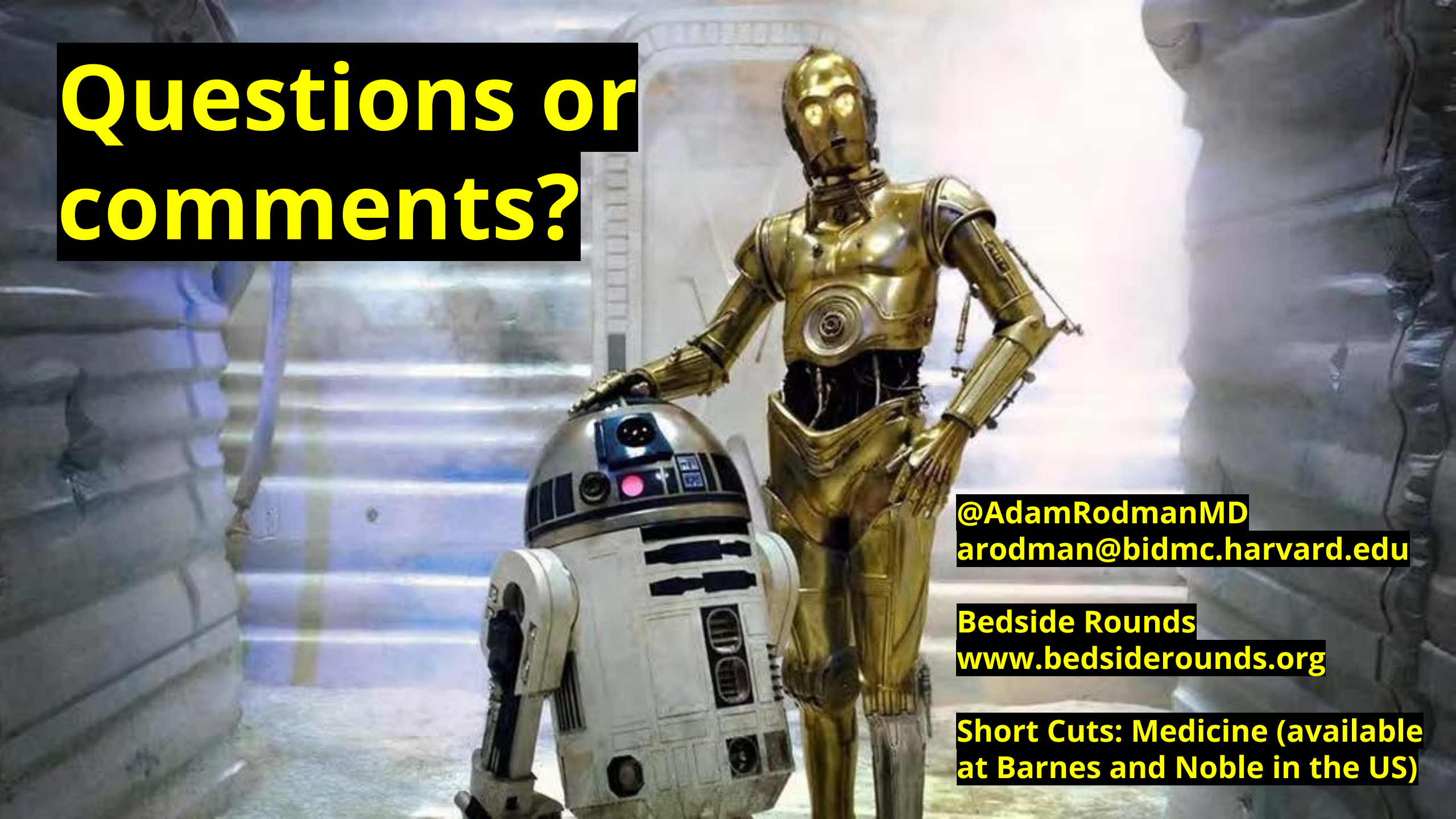


Zack, Travis, et al. *Lancet Digital Health* (2023).

What are the challenges to an AI second opinion service?

- Human-computer interaction is tricky:
  - **Which clinicians** should be targeted and **when**?
  - **Which cases** benefit the most from a second opinion?
  - **How** does an AI second opinion affect quality and resource utilization?
- Automation bias affects all CDS systems
- How does this affect diagnostic deskilling in the future?
  - LLMs will **never** be able to replace human diagnosticians (though other AI technologies might)

Questions or comments?



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Bedside Rounds
www.bedsiderounds.org

Short Cuts: Medicine (available at Barnes and Noble in the US)

Professional Boundaries

Just say No

PROFESSIONAL BOUNDARIES in Medicine

Presented by

Rodney Overstreet, BSN, CRNA, MNA

CRNA, UAB Medical West

Upon completion of this activity, learners should be to:

1. List strategies to minimize risk of sexual misconduct
2. Discuss sexual boundaries, impact of trauma and implicit bias
3. Describe components of HB 458 and reporting requirements for sexual assault

Disclosure

Speaker has nothing to disclose.

Rodney W. Overstreet CRNA

Act 1

Poor Boundaries

Are you in a FOG?

3 ways people manipulate us and push our boundaries:

- Fear
- Obligation
- Guilt

Self-sacrificing behaviors have become habits:

- Medical training
- COVID
- Increasing responsibilities

What are boundaries?

Types of Boundaries

- Emotional
- Physical
- Sexual
- Workplace
- Material
- TIME!

How to Set Boundaries

Be Clear!

Use simple, firm language

- I want
- I need
- I expect
- I would like
- Do not apologize
- Do not let it slide
- Do not over-explain

Barriers to Healthy Boundaries

Individuals with low EQ, people from different cultural backgrounds, and those already operating with poor boundaries.

Feeling overwhelmed, poor interoception and/or mindfulness and not knowing where to start…

Ignoring our own needs and dealing with habitual boundary steppers!

Boundaries in the Workplace

- Physical Boundaries- Our comfortable halo
- Emotional Boundaries- How we are spoken to and treated
- Workplace Boundaries- Set the tone and role model the behavior that you expect
- Time Boundaries- Clearly communicate expectations for appointments, meetings, work hours, and off time
- Material Boundaries- Decide if you are comfortable lending space or equipment

Boundary Infringement

- Physical- Inform others that you don’t hug or shake hands, etc.
- Emotional- Call out or address the behavior when you are calm
- Workplace- Bring attention to infringements. Don’t let it slide
- Time- Remind colleagues and staff about your limits and rules
- Material- Don’t feel guilty or apologize for your boundaries

Role Play

We will now take a moment to examine real-world examples of boundary infringements we have encountered. We will identify the types of boundaries that were breached and role-play these scenarios using enhanced communication tools. The objective is to address these situations more effectively and promote healthier interactions.

Side Effects of Poor or No Boundaries

- Increased stress
- Physical and/or emotional exhaustion
- Psychosomatic issues
- Low self-esteem
- Difficulty communicating
- Feelings of powerlessness
- Passive aggressive behavior
- Difficulty making decisions
- Strained relationships
- Increased sick days
- Attrition

Burnout and Boundaries

Ultimately, these boundary infringements add up, accumulate, and become too much for the provider to bear. These long-term professional burdens result in burnout and fleeing the organization or profession as a means of self-protection. The only safe route the individual may see is physical separation from the institution or practice of caregiving.

“You can’t pour from an empty cup.”

Whether you’re just getting started or checking the fence line:

-Reflect honestly on the challenges and barriers to developing/strengthening boundaries (I hate conflict, I want to be a team player)

-Shift your focus to the reasons why setting the boundary is important (I have to take care of myself first)

-Identify the values you would honor by implementing the boundary (I can be a better parent, partner, or practitioner)

-Prioritize self-care to replenish your physical, emotional, and mental resources, reinforcing your ability to maintain boundaries effectively.

Act 2

Healthy Boundaries

Q & A

Thank You!

References

- Set Boundaries, Find Peace: A Guide to Reclaiming Yourself by Nedra Glover Tawwab
- Campbell L. Why Personal Boundaries are Important and How to Set Them. Psych Central. Published May 17, 2016.
- Lampe, L., Hitching, R., Hammond, T. E., Park, J., & Rich, D. (2023). Being a 'good' doctor: Understanding and managing professional boundaries is challenging and can lead to stress and burnout. *Australasian psychiatry : bulletin of Royal Australian and New Zealand College of Psychiatrists*, *31*(6), 764–767. https://doi.org/10.1177/10398562231191662

Break the Silence: Empowering Intimate Partner Violence Screening

Alexa Jenkins, M.S., RMHCI

Disclosures

The presenter has no financial disclosures.

Objectives

- Identify key features from medical history and exam that suggest IPV
- Screen for IPV using validated tools
- Address shame, stigma, and bias
- Create integrative referral network

Intimate Partner Violence

- Assaultive or coercive behavior that may include physical injury, psychological abuse, sexual assault, progressive isolation, stalking, deprivation, intimidation, financial abuse, and reproductive coercion

- This behavior is perpetrated by current or former romantic partners

Incidence of Intimate Partner Violence

41% OF WOMEN AND 26% OF MEN EXPERIENCE PHYSICAL VIOLENCE, SEXUAL VIOLENCE OR STALKING

---

61 MILLION WOMEN & 53 MILLION MEN HAVE EXPERIENCED PSYCHOLOGICAL AGGRESSION

ON AVERAGE THERE ARE 20,000 DAILY CALLS TO DOMESTIC VIOLENCE HOTLINES

Why Screen in Medical Settings?

- Long term health consequences: Chronic migraines, STIs, GI disorders, depression, anxiety, suicidal ideation, PTSD, metabolic and cardiovascular disorders due to prolonged stress and trauma
- Victims of IPV have up to 50% greater number of primary care visits than non-victims
- Annual healthcare utilization costs are 42% higher for IPV victims
- IPV victims are at much higher risk for substance use disorders and suicide attempts
- Healthcare visits may be the only time the patient sees anyone outside of their household

At Risk Populations

- Pregnant Women
- Adolescents
- LGBTQ+
- Firearms in the home increases homicide risk by 500%
- Couples with income, educational, or job status disparties
- Childhood history of experiencing or witnessing domestic violence
- Women with disabilities have 40% higher rate of intimate partner violence

Mandated Reporting

ABUSE OF CHILDREN, ELDERS, AND PEOPLE WITH DISABILITIES GENERALLY FALL UNDER MANDATED REPORTER LAWS

KNOW YOUR LOCAL LAWS. SOME STATES REQUIRE MANDATED REPORTING OF DOMESTIC VIOLENCE BUT MANY STATES DO NOT.

Men are not viewed as intimate partner violence victims, even though they are.

Boyfriend seen dodging SUV before woman fatally runs him over, Michigan officials say

BY **MITCHELL WILLETTS**
MAY 15, 2024 11:42 AM

A Michigan woman is accused of fatally running over her boyfriend, officials say. *Getty Images/iStockphoto*

Only have a minute? Listen instead

-01:54

Powered by **Trinity Audio**

A Michigan woman is accused of murder after investigators say she fatally ran over her boyfriend with an SUV.

LOCAL

Woman dead after being run over by vehicle in suspected domestic dispute in Jackson

Pam Dankins
Mississippi Clarion Ledger

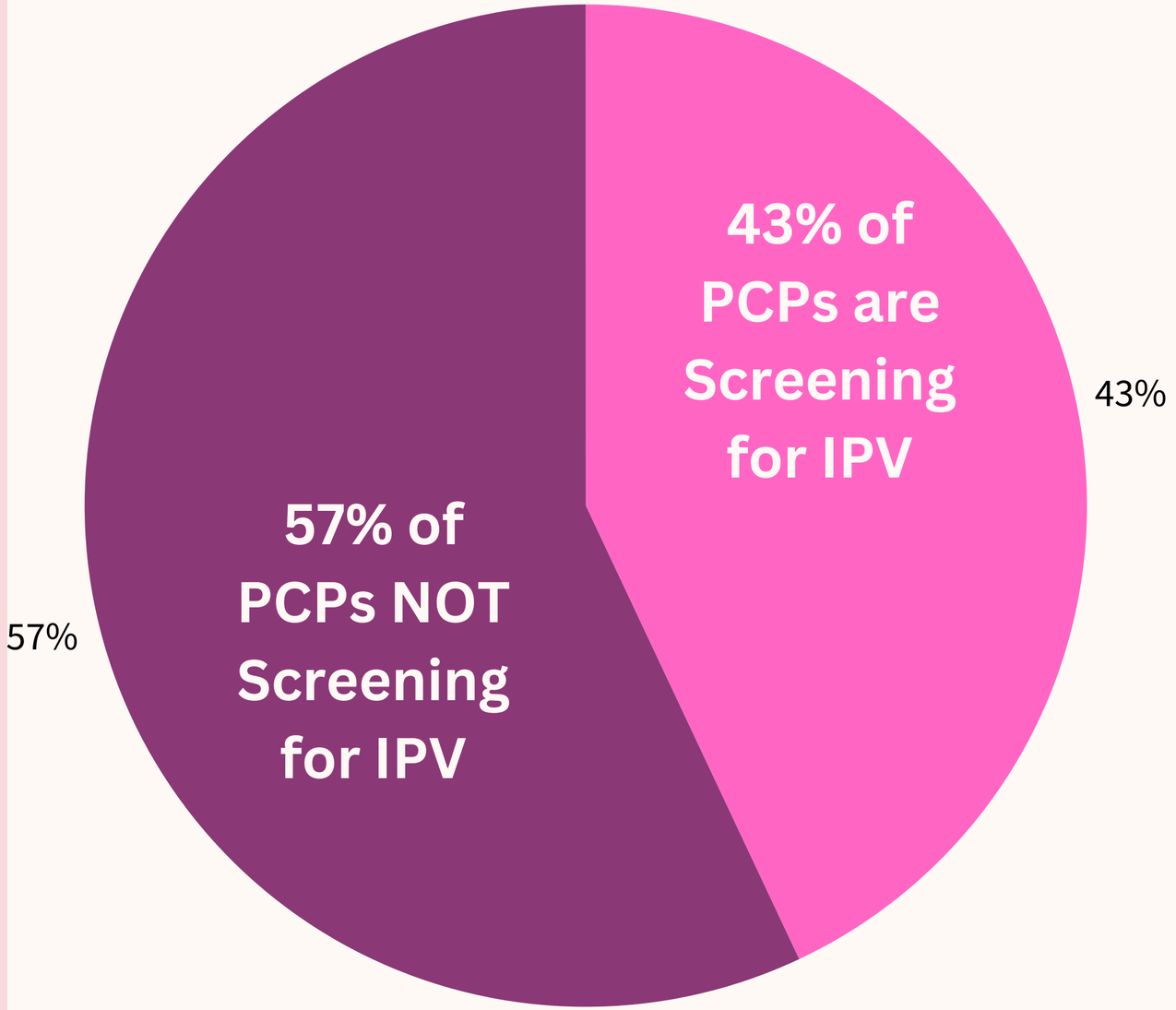
Published 10:03 a.m. CT April 23, 2024 | **Updated 3:53 p.m. CT April 23, 2024**

Show video info

A woman died at a hospital Monday after being run over several times by a vehicle in a suspect domestic dispute, according to Jackson Police Detective Tommie Brown.

OIG 2024 Report

OF 1,186 RESPONDENTS, ONLY 43% OF PRIMARY CARE CLINICIANS SCREENED FOR IPV AND REFERRED PATIENTS TO BH SERVICES ACCORDING TO USPSTF GUIDELINES



What are the barriers in your own health system to screening for intimate partner violence?

OIG Reported Physician Barriers to Screening

- TIME LIMITATIONS
- NO BEHAVIORAL HEALTH RESOURCES
- PATIENT SAFETY IF IPV LISTED IN EHR
- MANDATORY REPORTING LAWS
- INADEQUATE TRAINING

You cannot save the patient, but you can help them.

On average, it can take 7 or more attempts for an intimate partner violence victim to leave

ONE MORE DAY
ONE MORE DAY
ONE MORE DAY
ONE MORE DAY
ONE MORE DAY

Screening Recommendations

- USPSTF Grade B recommendation
- All women of reproductive age should be screened
- USPSTF found no evidence for screening on a particular interval

BIAS:

- No recommendation for men or older women
- No recommendations for sexual and gender minorities

Presenter Recommendations

- Annual screening of all patients 12+
- All screening tools should be administered in private
- If both men and women are routinely screened it helps identify IPV cases and normalizes screening process

IPV Assessment in Adults

"HITS" A domestic violence screening tool for use in the community

HITS Tool for Intimate Partner Violence Screening: Please read each of the following activities and fill in circle that best indicates the frequency with which you partner acts in the way depicted.

How often does your partner?	Never	Rarely	Sometimes	Fairly often	Frequently
1. Physically hurt you	O	O	O	O	O
2. Insult or talk down to you	O	O	O	O	O
3. Threaten you with harm	O	O	O	O	O
4. Scream or curse at you	O	O	O	O	O
	1	2	3	4	5

Each item is scored from 1-5. Thus, scores for this inventory range from 4-20. A score of greater than 10 is considered positive.

IPV Assessment in Adults

3b. HARK questions*

H **HUMILIATION**

Within the last year, have you been humiliated or emotionally abused in other ways by your partner or your ex-partner?

A **AFRAID**

Within the last year, have you been afraid of your partner or ex-partner?

R **RAPE**

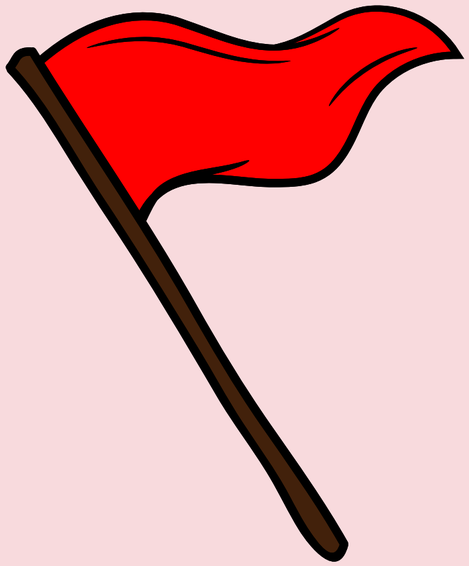
Within the last year have you been raped or forced to have any kind of sexual activity by your partner or ex-partner?

K **KICK**

Within the last year, have you been kicked, hit, slapped or otherwise physically hurt by your partner or ex-partner?

**screening questions developed in general practice Hardip Sohal (2011).*

History and Physical Exam Red Flags



CHRONIC UNEXPLAINED PELVIC PAIN

FREQUENT SEXUALLY TRANSMITTED INFECTIONS

MULTIPLE UNWANTED PREGNANCIES

UNEXPLAINED BRUISING OR FREQUENT BROKEN/FRACTURED BONES

DEPRESSION, ANXIETY, SUICIDAL IDEATION, SUBSTANCE USE

What do you think stops patients from reporting intimate partner violence?

Barriers to help seeking behavior

- LOW SELF ESTEEM
- EMBARASSMENT & SHAME
- LACK OF FINANCIAL RESOURCES
- FEAR OF FURTHER VIOLENCE
- FEAR OF NOT BEING BELIEVED
- CHILDREN

Trauma Informed Care

Create a Referral Network

- National Domestic Violence Hotline
- Love Is Respect
- MaleSurvivor
- RAINN
- YWCA
- Local domestic violence shelters
- Coordinate with local social work & mental health organizations and ask them to share resource list
- Peer support groups

Case 1

27-year old female patient presents to clinic for third STI check in the past 6 months. She scored positive on the HARK, admitting to her boyfriend humiliating her. She denies any physical abuse but you've noticed bruising around her neck and wrists.

1. How would you treat the patient while respecting that she is not ready to discuss physical abuse?
2. What resources would you offer the patient?

Case 2

66-year-old male presents to the hospital for a hand fracture. Patient states he got into a fight with his male partner and fractured his finger. Patient says that he and his partner physically fight all the time but they always make up.

1. Do you have any mandated reporter responsibilities?
2. What resources would you offer the patient?

Key Takeaways

- Know the laws in your state
- Leaving the relationship takes time - screen, screen, and screen again
- Make sure you have resources ready
- Trauma informed care helps build clinician-patient trust

References, Resources, Slides

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Breaking Bread and Barriers: Cultivating Solutions for Mississippi Food Deserts

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LYSSA WEATHERLY, MD

The authors stated above have no financial disclosures to report.

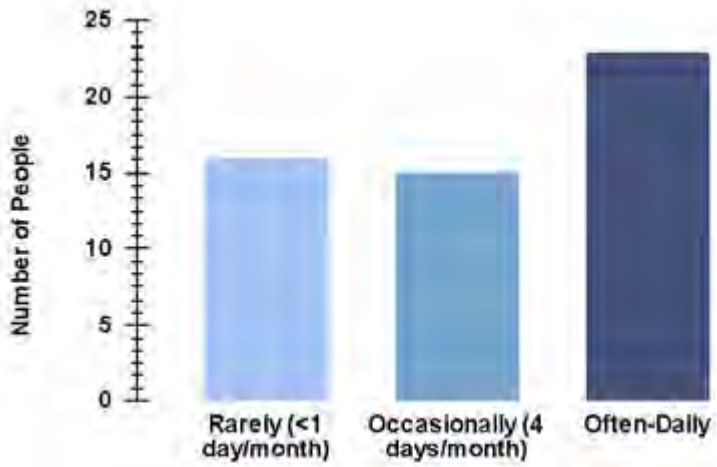
Food Insecurity & Food Deserts

- Having uncertain availability, or ability, to acquire nutritionally adequate foods.
- Areas with limited access to fresh, affordable, and healthy food:
  - 33% of residents living > 1 mile from a grocery store in an urban area.
  - 33% of residents living > 10 miles from a grocery store in a rural area.
  - 20% or more of an area's residents live at or below the poverty line.
- 6% of the United States population lives in a food desert.
  - What about Mississippi?

"Dollar Store Diner" Recipe Book				
	Snack	Break-fast	Lunch	Dinner
Average cost per serving	$1.20	$1.58	$1.05	$2.05
Caloric Value (kcal)	150	265	295	430
Average time of preparation (minutes)	13	15	35	24
Electronic copies distributed	442			
Physical copies distributed	135			

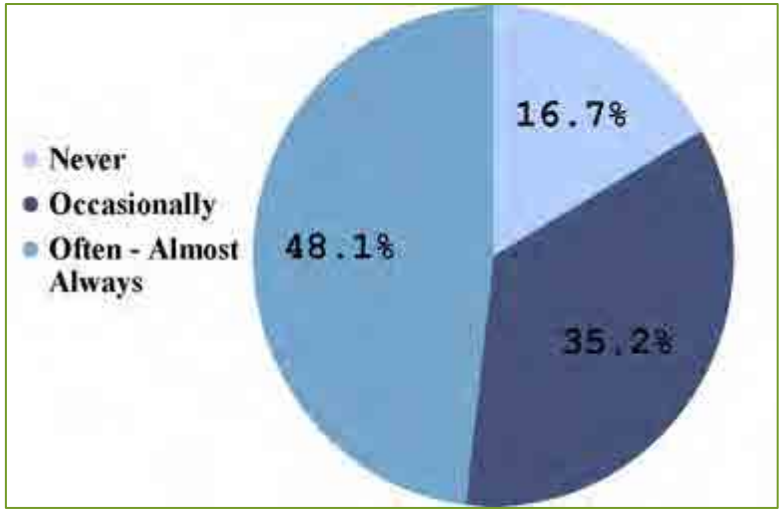
U.S. Household Food Security Survey Module: Six-Item Short Form, Economic Research Service, USDA

Many respondents reported food insecurity, with 73.5% of the sample sometimes or often running out of food, as well as 53.2% of the sample limiting food consumption due to financial restraints.



Frequency of fast-food consumption

Likelihood of using recipe book to make meals at home



Intervention Tool

CONCLUSIONS

Residents of a food desert are often restricted to consuming foods with a long shelf-life and lack accessibility to fresh fruits and vegetables.

Healthcare providers should consider the barriers to diet modifications, especially the cost of groceries, when making recommendations to patients.

Providing low-income individuals with food demonstrations and affordable recipes using ingredients sold at local dollar stores can mitigate obstacles imposed by practicing a healthy diet.

Working with patients directly to overcome a tangible barrier to healthy living can increase trust and partnership in the patient-physician relationship, leading to more effective overall patient care.

REFERENCES

1. Stuff JE, Casey PH, Szeto KL, et al. Household food insecurity is associated with adult health status. J Nutr. 2004;134(9):2330-2335. doi:10.1093/jn/134.9.2330

2. Vilar-Compte M, Burrola-Méndez S, Lozano-Marrufo A, et al. Urban poverty and nutrition challenges associated with accessibility to a healthy diet: a global systematic literature review. Int J Equity Health. 2021;20(1):40. doi:10.1186/s12939-020-01330-0

3. Poverty, food insecurity, and nutritional outcomes in children and adults. Journal of Health Economics. 2004;23(4):839-862. doi:10.1016/j.jhealeco.2003.12.008

4. State-Level Estimates of Low Income and Low Access Populations. Tableau Software. Accessed March 6, 2023. https://public.tableau.com/shared/Q9PN83QZ3?:display_count=yes&:origin=viz_share_link&:embed=y&:showVizHome=n&:tabs=n&:toolbar=n&:apiID=host0#navType=0&navSrc=Parse

5. Stats of the States - Heart Disease Mortality. Published February 25, 2022. Accessed March 6, 2023. https://www.cdc.gov/nchs/pressroom/sosmap/heart_disease_mortality/heart_disease.htm

Inadequate Care: The Impact of living in an Underserved Community on Chronic Disease Management

Ahmad Elhaija[2,3], Shubhreet Bhullar[1,3]

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3. International Healthcare Organization, Los Angeles, CA, USA

Background/Knowledge Gap

- International Healthcare Organization (IHO) is a 501c(3) non-profit organization based in Los Angeles, California, formerly known as the International Collegiate Health Initiative (ICHI). Our team is comprised of doctors, nurses, medical students, non-profit advisors, and healthcare administrators. We provide high-quality medical care through our healthcare safety net systems.

- Significant Challenges in Healthcare Access, such as Acculturation and Language Barriers, for Latino populations in urban locales like Maywood and Bell in Southeast Los Angeles
  - Acculturation Issues: Cultural differences, Social Isolation, Economic Pressure, Immigration Status
  - Language Barriers: Complex medical jargon, Lack of interpreter services, Mistranslation
- Challenges in accessing healthcare in these locales reflect broader trends in the Hispanic population's health in the U.S.[1]

[1]CITY AND COMMUNITY HEALTH PROFILES LOS ANGELES COUNTY MAYWOOD. (2018). Retrieved from http://publichealth.lacounty.gov/ohae/docs/cchp/2018/Maywood.pdf

Methods/Design

- Cross-sectional survey of 120 participants
- General health, Demographic information, and Family history
- Healthcare access, Diet, Lifestyle, and Insurance coverage
- Impact of Lack of Healthcare Services and Desired Improvements

Results/Findings

Table 1. *Sample Characteristics of Survey Respondents*

Survey Questions / Gender	Male	Female
	56	64
	Yes (%)	No (%)
Have health insurance	88	12
Have access to healthcare services in their area	78	22
Have chronic or hereditary conditions/diseases	59	41
Consider themselves healthy	62	38
Partake in drug or alcohol use	42	58
Exercise or engage in physical activity more than once a week	74	26
Eat fruits and vegetables daily	40	60
Get 7-9 hours of sleep every night	42	58
Visit a healthcare professional once every year	71.6	
Visit a healthcare professional 2 or more times every year	6	
Visit a healthcare professional once every 2-3 years	22.4	

- 88% insured; 78% had healthcare services
- 71.6% had annual physician consultations
- 59% with chronic/hereditary conditions
- 42% use drugs/alcohol
- 74% physically active weekly
- 42% get adequate sleep
- 40% consume daily fruits/vegetables
- Education: 50 secondary education, 46 Bachelor's degrees, 2 professional diplomas, 2 Master's degrees

Conclusions/Implications

- Acculturation, Language proficiency, and Immigration status influence healthcare access
- Intricate Factors of Healthcare Inequality: personal beliefs, past experiences, and systemic barriers
- Recommendations: Enhancing community outreach programs, Offering flexible consultation schedules, Providing targeted health education sessions
- This study elucidates the significance of Acculturation and Education Healthcare
- Foundation for policy change and interventions to promote Inclusively Accessible Healthcare

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Dupilumab Use in Treatment of Refractory Bullous Pemphigoid

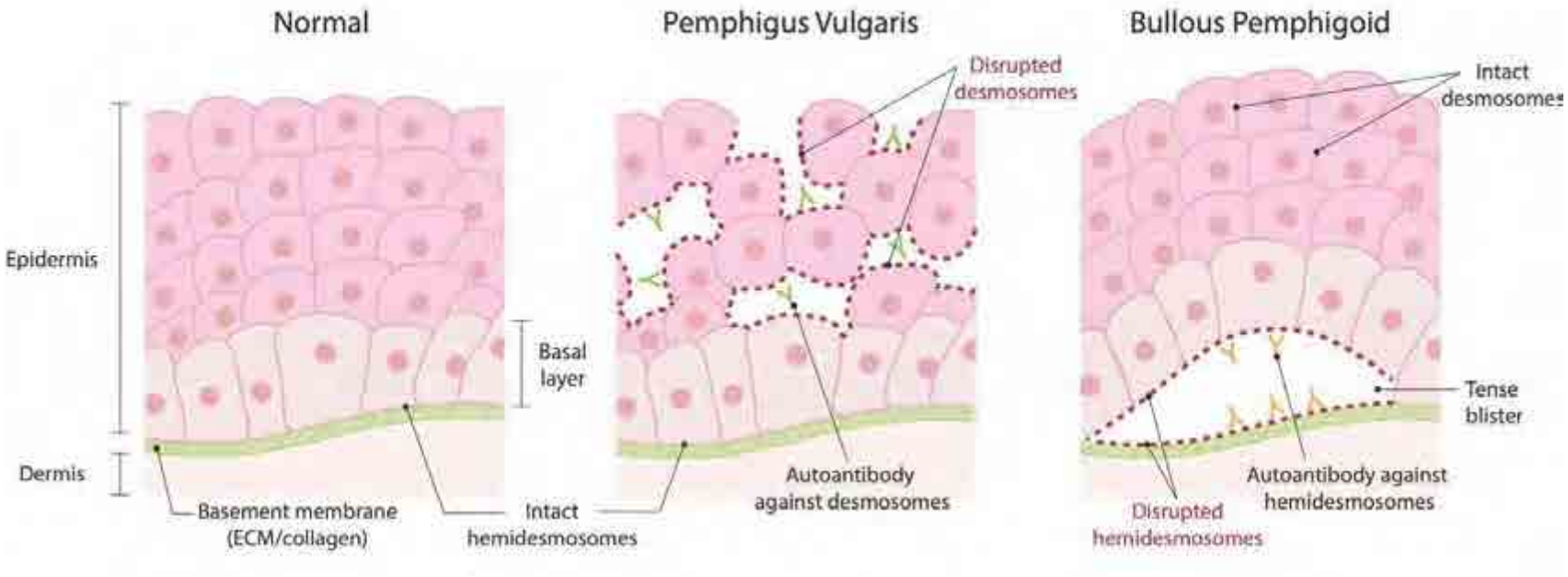
Jordan Beam, MS3 – Heersink School of Medicine

Jo Herzog, MD

My fellow presenters and I have no financial disclosures.

Bullous Disorders

- What is a bullous disorder?
- Types
  - Autoimmune
  - Mechanical
  - Metabolic
  - Allergic
- Offending agents
- Traditional tx



Edens, M. H., Khaled, Y., & Napeñas, J. J. (2016). Intraoral pain disorders. *Oral and Maxillofacial Surgery Clinics of North America*, *28*(3), 275–288. https://doi.org/10.1016/j.coms.2016.03.008
Oiseth, S., Jones, L., & Maza Guia, E. (2024, May 17). *Bullous pemphigoid and Pemphigus vulgaris*. Lecturio. https://www.lecturio.com/concepts/bullous-pemphigoid-and-pemphigus-vulgaris/
Drug-Induced Bullous Pemphigoid: Rapid Resolution with Corticosteroid Therapy. (2024). *Journal of Medicinal and Chemical Sciences*, *7*(2). https://doi.org/10.26655/jmchemsci.2024.2.3

Case Presentation

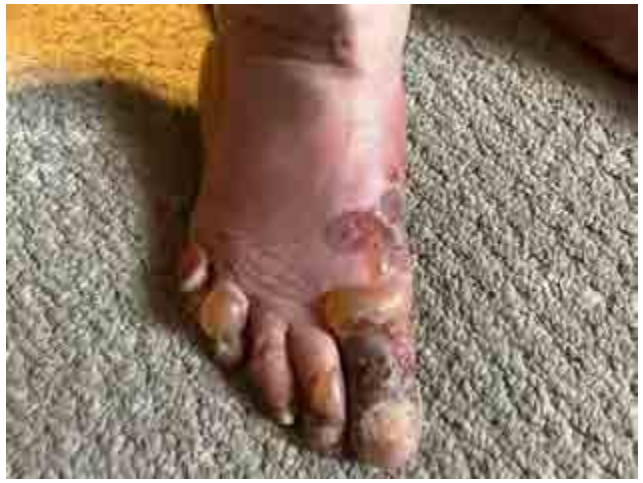
HPI: 83 y/o female with a 6 month hx of bullous pemphigoid that failed traditional treatment (steroids, dapsone)

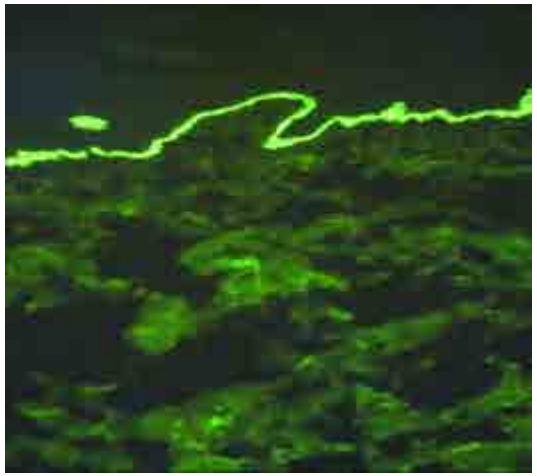
PMH: CHF, HTN, DM, HLD, Hyperthyroidism

Medications: Furosemide, pravastatin, losartan, hydralazine, levothyroxine, metformin

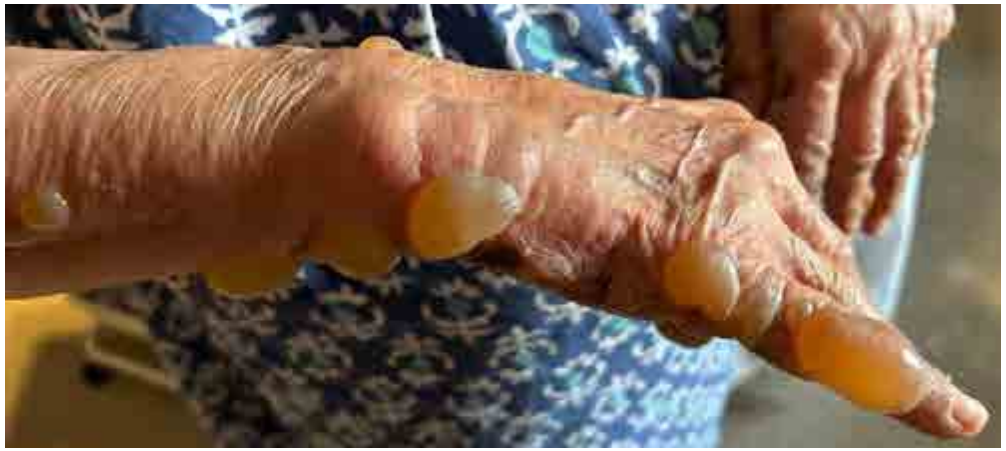
PE: tense bullae with eye involvement

Tests: thin, wavy linear deposition of IgG, IgG4, and C3 along basement membrane zone (direct) and IgG (indirect)



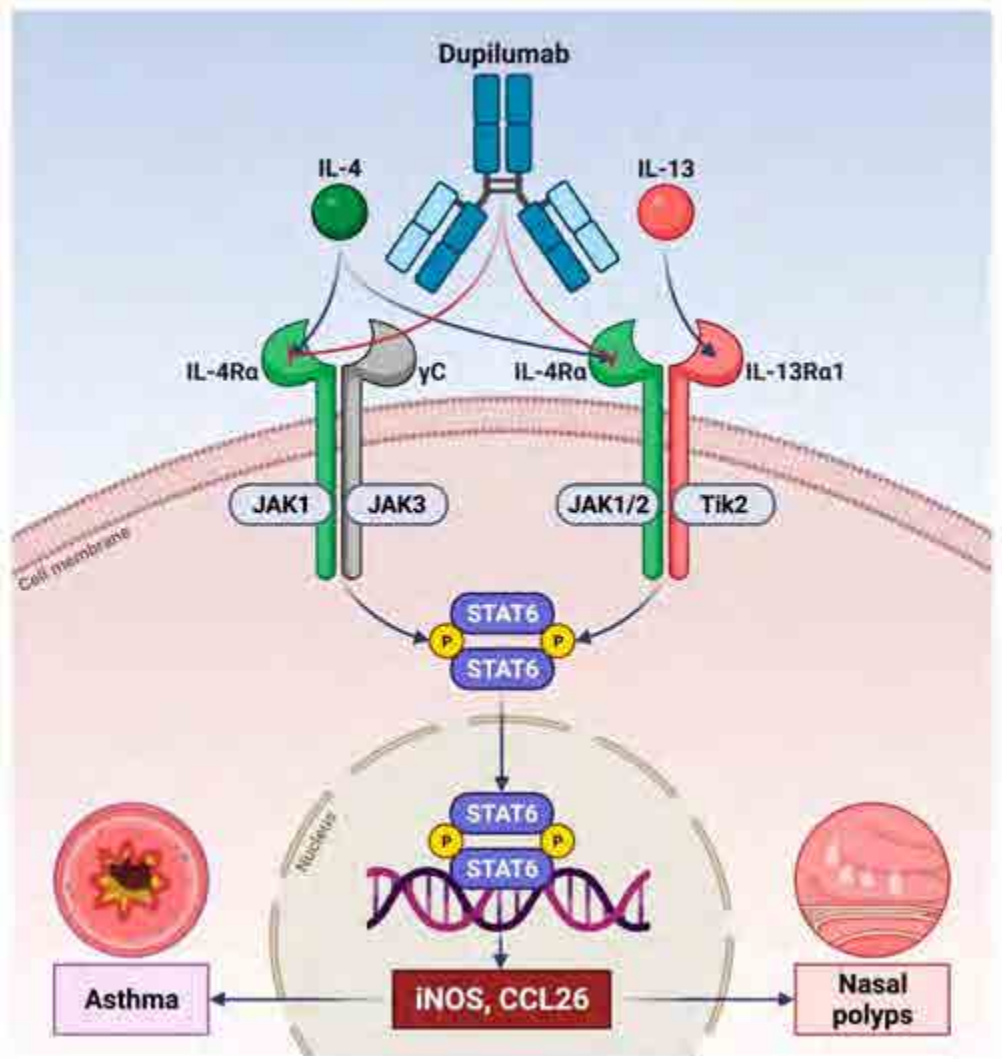


https://www.researchgate.net/publication/334253361_Reverse_Koebner_Phenomenon_in_Bullous_Pemphigoid_-_A_Case_Report



Treatment

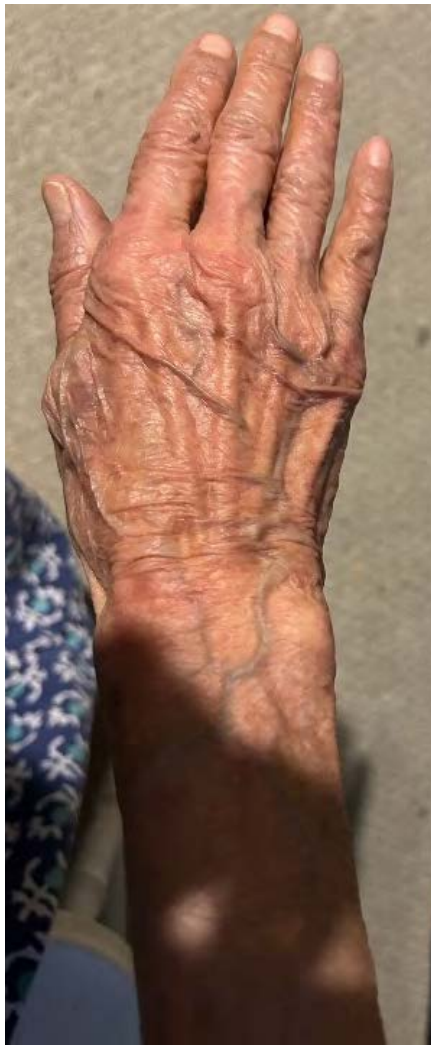
- Patient's furosemide was d/c
- Anemia began to improve, started back on steroids + niacinamide + doxycycline + dapsone
- BP and anemia stable, no significant improvement
- Dupilumab was considered



Russo R, Cozzani E, Gasparini G, Parodi A. Targeting interleukin 4 receptor α: A new approach to the treatment of cutaneous autoimmune bullous diseases? Dermatol Ther. 2020 Jan;33(1):e13190. doi: 10.1111/dth.13190. Epub 2020 Jan 2. PMID: 31863534; PMCID: PMC7154653.

Follow Up and Lit Review

- Condition gradually improved, dapsone and steroids slowly tapered
- Receives dupilumab injections every 2 weeks
- Remains well on dupilumab monotherapy



- Multiple case reports of furosemide associated bullous pemphigoid
- Possibility of dupilumab in bullous disorders in literature

Baz, K., Ikizoglu, G., Kaya, T., & Koca, A. (2002). Furosemide-induced bullous pemphigoid. *JEADV. Journal of the European Academy of Dermatology and Venereology/Journal of the European Academy of Dermatology and Venereology*, *16*(1), 81–82. https://doi.org/10.1046/j.1468-3083.2002.383_1.x

Takeichi, S., Kubo, Y., Arase, S., Hashimoto, T., & Ansai, S. (2009). Brunsting-Perry type localized bullous pemphigoid, possibly induced by furosemide administration and sun exposure. *European Journal of Dermatology*, *19*(5), 500–503. https://doi.org/10.1684/ejd.2009.0715

HCA Florida Blake Hospital

I-PASS Module Digital Integration to Admission Tracker–An ACGME Survey directed QI initiative

Behman J., OyesanmiO., Lin Y.

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UPDATES 06/27/24 TO 06/28/24

TEAM	INTERN / SENIOR	DATE	PT NAME (3,3)	ROOM #	ILLNESS SEVERITY	ACTION ITEMS W/ F/U PLAN	SITUATION / CONTINGENCY	NIGHT TEAM - UPDATE?
Blue	Mikul	6/28	LYN,DAN	412A	Stable	hx of melana, Severe coronary calfication req CABG; EGD showed no active bleed; on Heparin drip with Serial H/H;	if active GIB occurs or obvious drop in H/H, transfuse w/ goal Hgb <8 (CAD), hold Heparin gtt and reconsult GI (rascon) for me pls	
Purple	Luc/Gabby	06/28	YVO,FOR	432A	Stable	Hx COPD 3L, HFrEF (EF 40%), afib (was on eliquis, now held), chronic pain, CKD, seizure disorder. Had hemorrhagic shock because of large abdominal hematoma from ground level fall, transfused a lot of blood products and given alot of fluids, it resolved. Had iatrogenic fluid overload and developed heart failure. Baseline 2-3L, was requiring 6L of oxygen and BiPAP at bedtime. She was back on her 3L breathing improved, but however she has been weak not really clearing her secretions and developed atelectasis whole right side of her lung. She was placed on BiPAP today 6/26	We are monitoring if the atelectasis gets better on BiPAP. We are considering ICU however she seems to be doing well on BiPAP. It is improving. She is on BiPAP q3h for 1 hour and BiPAP at night. Diuresing her with lasix 40mg BID IV as her CXR looks slightly more congested than yesterday	
Purple	Luc/Gabby	6/28	KUU,ERI	CVI4	Stable	Has multivessal CAD w/>90% stenosis in all 3 of the	If chest pain get a CXR. Call CTS they are managing perioperatively. For arrhythmias get stat labs and correct abnormalities as needed. He has sundowning but generally does not get agitated, just reorient. Avoid antipshycotics unless indicated	
		6/27	LYN,DAN	412a	Watcher	Patient with NSTEMI and melena w/ acute anemia. s/p 2u pRBCs. Took ASA before arrival. Plan for EGD tomorrow and eventual ischemic workup. Trop uptrending 92->5000	HH 2200. trend trop. If starts hemorrhaging, contact GI for possible emergent EGD.	
		6/27	BEL,ROG	415b	Stable	Baker acted. Pt with new mediastinal mass, dyspnea.	SI, states that he wants to leave AMA. May become agitated	
Red	Jen/Priyanka	6/27	WEL,WAY	430A	Stable	nursing reports multiple bouts of diarrhea, pt just finished 2 weeks of po vanc 3 days ago for it	Start po vanc if diarrhea worsens	no report of worsening diarrhea
	Riddhy	6/28	FAW,DOU	408A	Watcher	frank blood in urine. stat H&H	if <7, order transfusion	repeat was 7.3

I-PASS
BETTER HANDOFFS. SAFER CARE.

I	Illness Severity	• Stable, "watcher," unstable
P	Patient Summary	• Summary statement • Events leading up to admission • Hospital course • Ongoing assessment • Plan
A	Action List	• To do list • Time line and ownership
S	Situation Awareness and Contingency Planning	• Know what's going on • Plan for what might happen
S	Synthesis by Receiver	• Receiver summarizes what was heard • Asks questions • Restates key action/to do items

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Results

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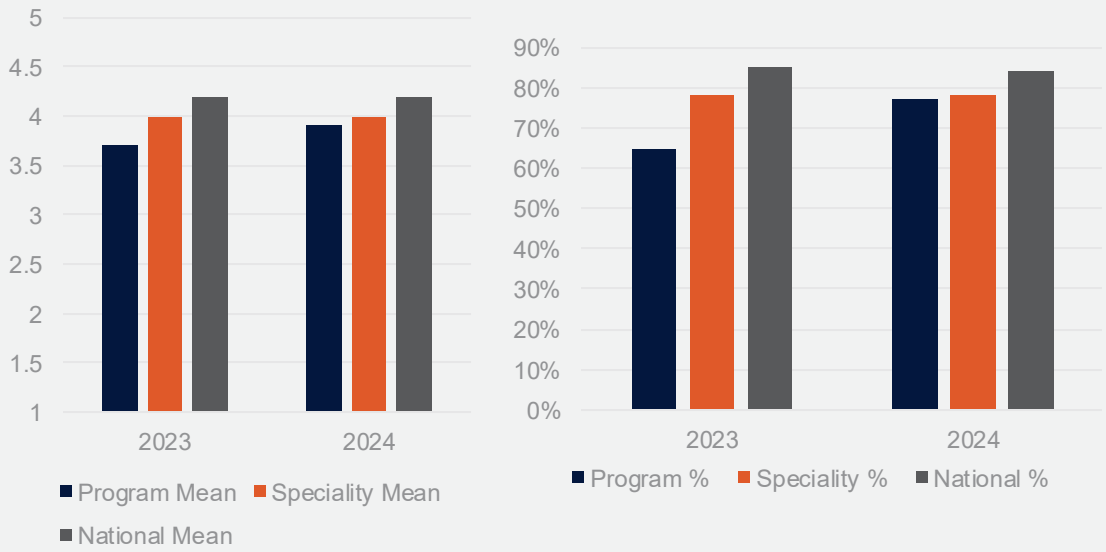
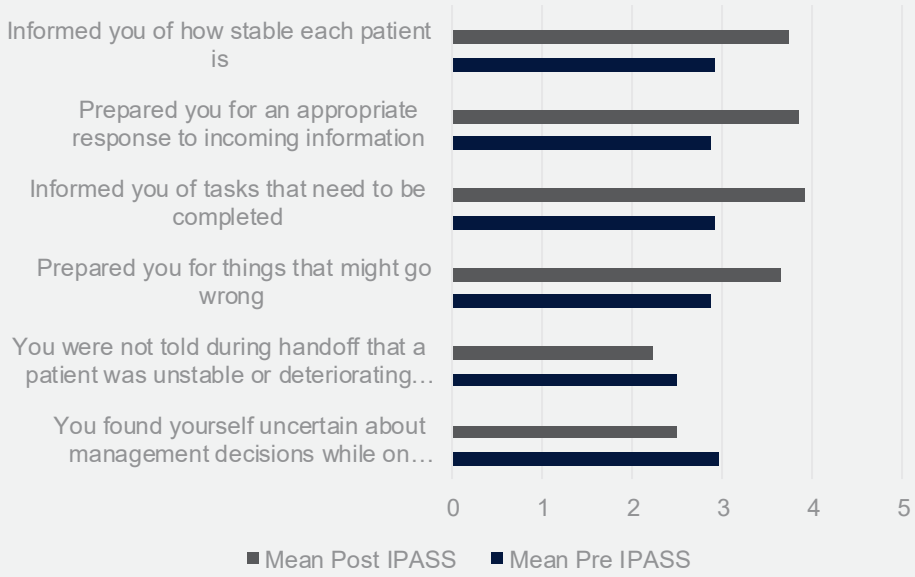
ACGME Survey - Transition of Care % Compliance



Resident Survey On Pre/Post IPASS Implementation. N=26



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Discussion & Future

- ACGME Survey Directed QI Initiative
- Innovative and versatile integration of validated TOC module
- Now included personalized bootcamp for all incoming interns+

* Continued improvement and growth through annual ACGME survey

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HCA Florida Blake Hospital

References

1. https://www.mededportal.org/doi/10.15766/mep_2374-8265.9311
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9923540/
3. The Joint Commission Center for Transforming Healthcare. Improving transitions of care: Hand-off communications. Oakbrook Terrace, Illinois: The Joint Commission, 2014.
4. https://www.hopkinsmedicine.org/news/articles/reducing-medical-errors-in-patient-handoffs
5. https://www.psqh.com/analysis/patient-handoffs-gap-mistakes-made/
6. https://www.acgme.org/globalassets/pfassets/programresources/residentsurvey_cprcrosswalk.pdf

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Hansen's Disease (Leprosy) in the United States of America: A Systematic Review

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LSU Health NEW ORLEANS

No disclosures

Hansen's Disease (Leprosy) in the United States of America: A Systematic Review

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No disclosures

Hansen's Disease (Leprosy) in the United States of America: A Systematic Review

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No disclosures

Background (1/2)

- Leprosy, also known as Hansen's disease (HD), is a chronic infectious disease acquired from *Mycobacterium (M.) leprae* and rarely from *M. lepromatosis*

- Transmitted via respiratory droplets after prolonged contact w/ infected person as well as via zoonotic transfer from infected nine-banded armadillos and other small mammals
  - Incubation period usually 5-10 years but can be longer
- Primarily affects the skin, extremities, peripheral nerves, mucous membranes & occasionally internal organs including kidneys and testes

- Despite becoming less globally prevalent over time, HD remains major cause of debilitating disabilities with psychosocial impact

Background (2/2)

- Ridley-Jopling classification, established in 1966, categorizes HD into 5 types based on clinical & histological data: tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), and lepromatous leprosy (LL)

- In 1982, WHO introduced simplified classification scheme: multibacillary (MB) & paucibacillary (PB)[4]
  - PB includes ≤5 skin lesions; equivalent to TT and BT
  - MB involves >5 lesions, spanning BB, BL, and LL, w/ higher AFB counts in skin smears

- Classification schemes help guide treatment and patient monitoring

- Multi-drug treatment (MDT) consists of dapsone, rifampicin, & clofazimine
  - Duration of 6 months for PB and 12 months for MB

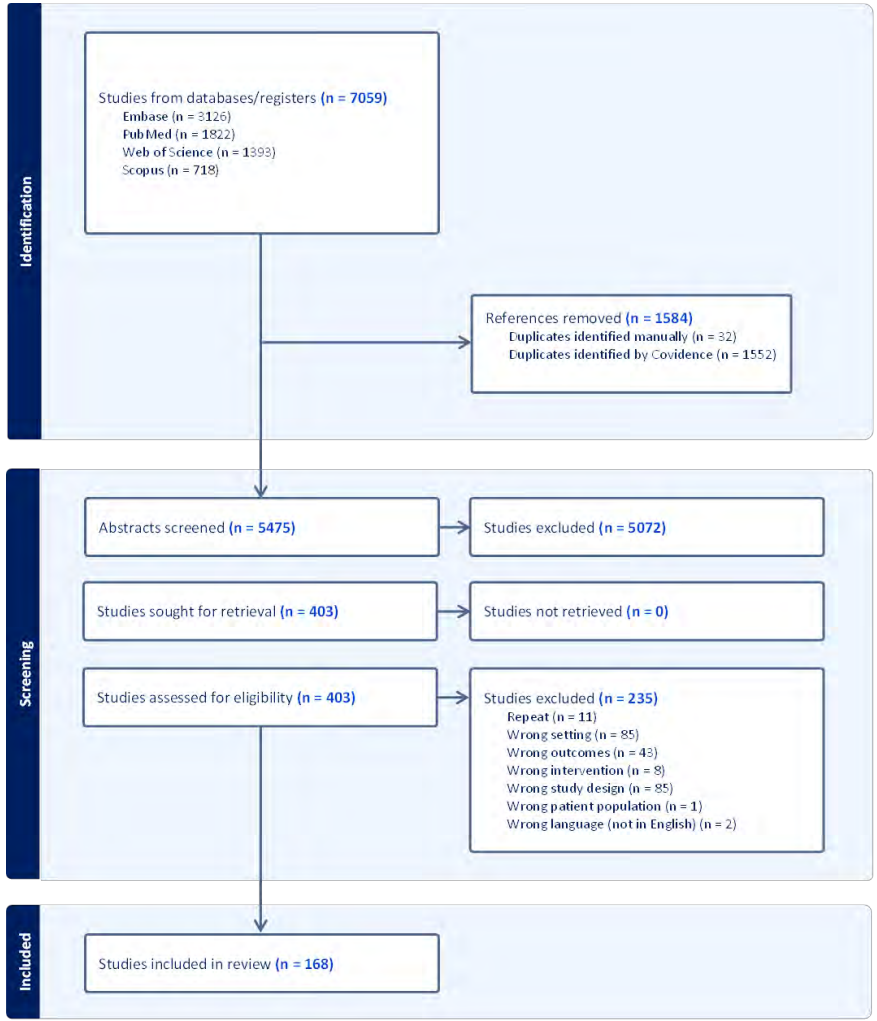
Methods

- 4 databases (Medline via PubMed, ISI Web of Science, Embase, Scopus) were searched for relevant studies
  - All full-length studies in English until June 2, 2023

- 7,059 studies were identified
- 5,475 unique abstracts were screened by 2 independent reviewers

- 403 publications, from 1896 to 2023, met inclusion criteria

- 168 publications were included after excluding for reasons related to wrong study setting, wrong outcomes, and wrong study design



Results

- Publications covered time span from Jan 1798 to June 2023
  - 111 (>80%) publications from after 1980

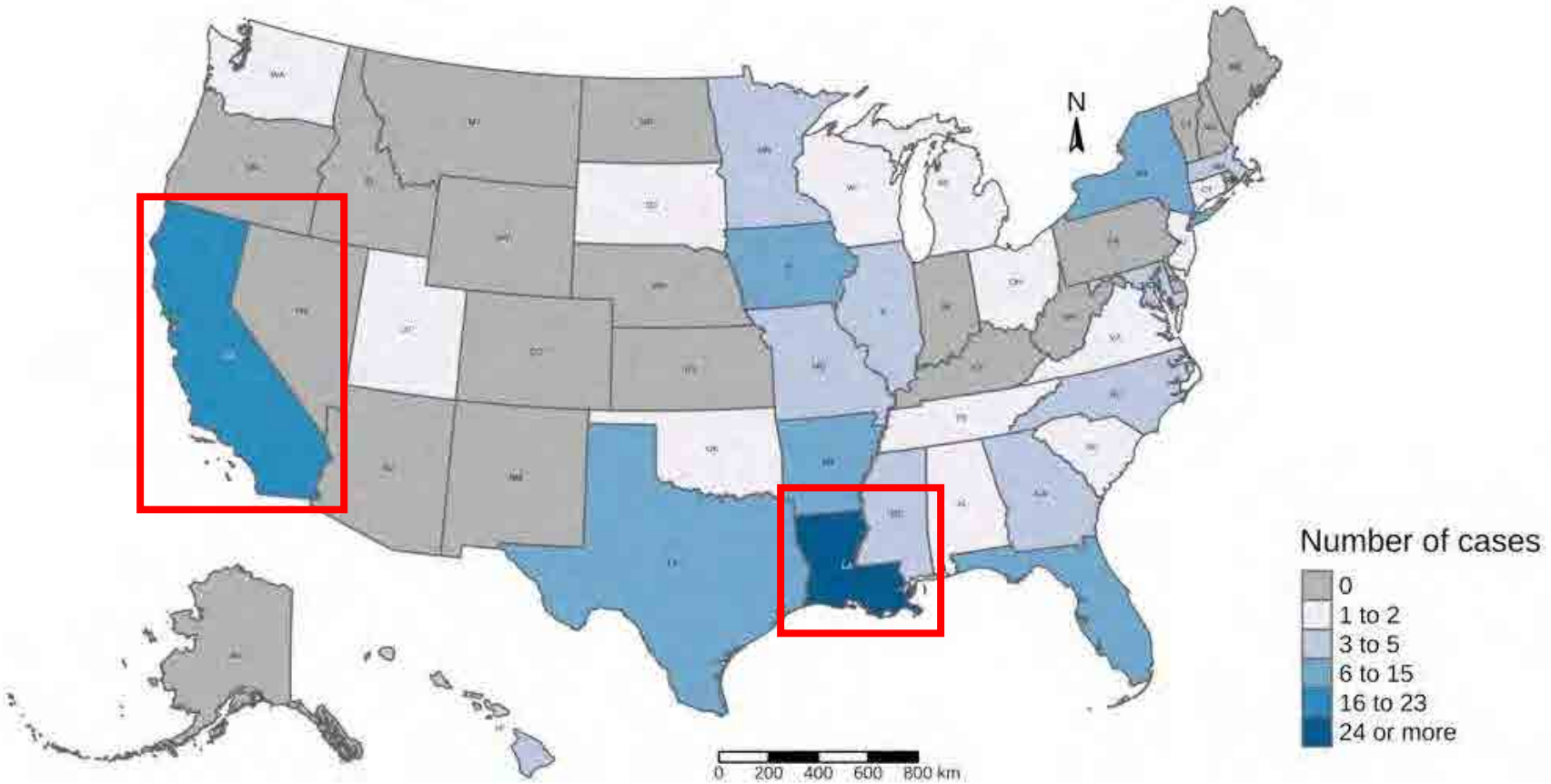
- Sample sizes in individual studies ranged from 1 to 46

- 328 unique cases were identified

- Median age (range) = 43 yrs (3.5 – 87 yrs)
- Majority (80%) cases were male

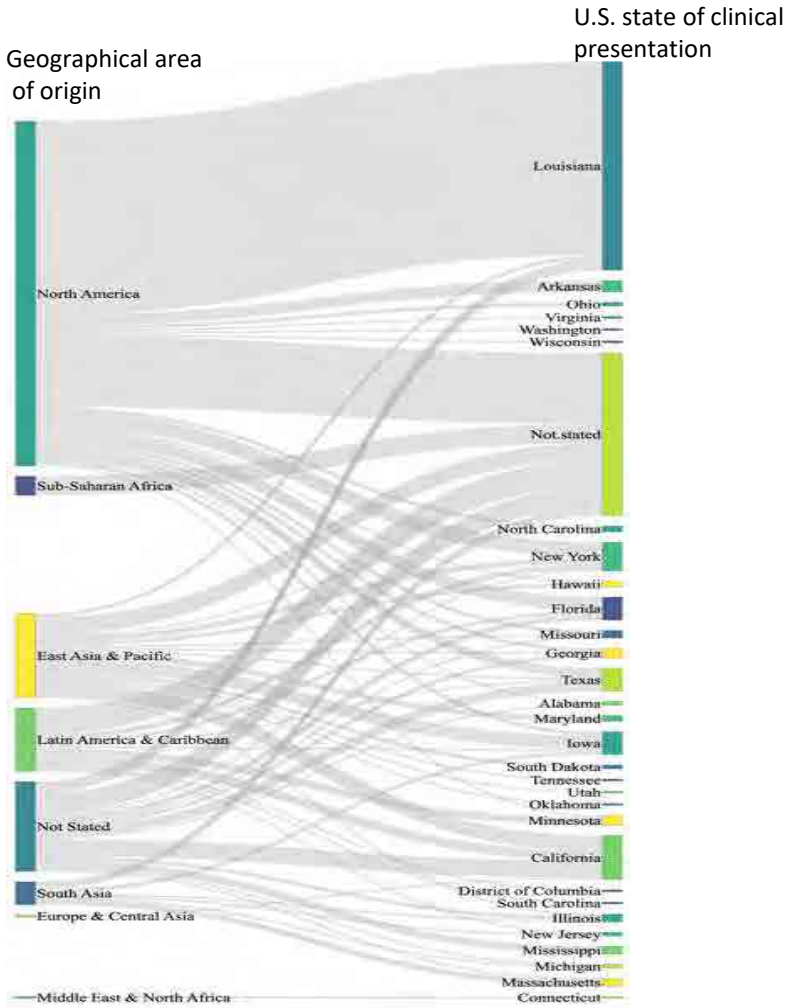
- 169/328 (51.5%) were White, 44/328 (13.4%) were Asian, 34/328 (10.4%) were Black
- 4% were Native Hawaiian or other Pacific Islander

Geographic distribution of cases based on state of clinical presentation



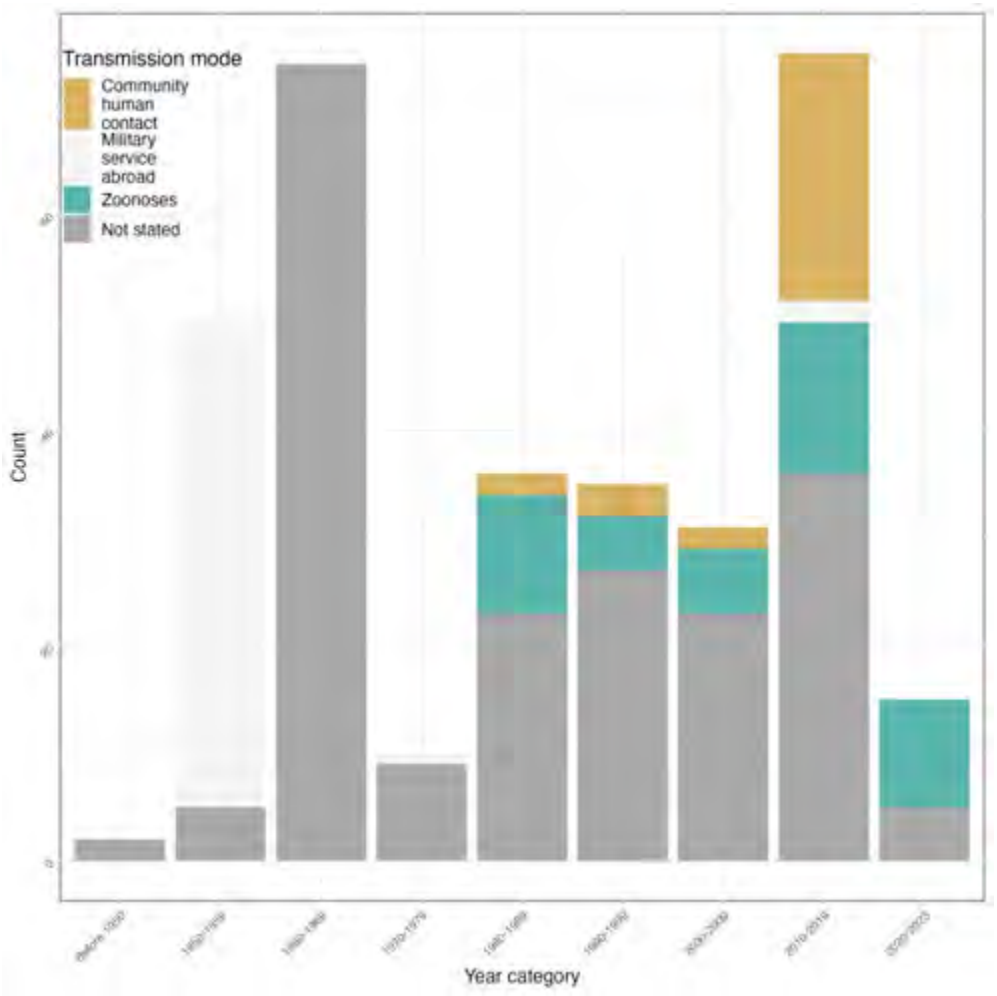
Case dispersal patterns across the U.S.

- Most cases were born in North America, specifically in the U.S.
- Most cases of HD that came from outside of N. America came from East Asia and the Pacific and dispersed widely across the continental U.S.
- Most cases in the U.S. have been based in Louisiana, with other focal concentrations in California, New York, Florida, Iowa, and Arkansas



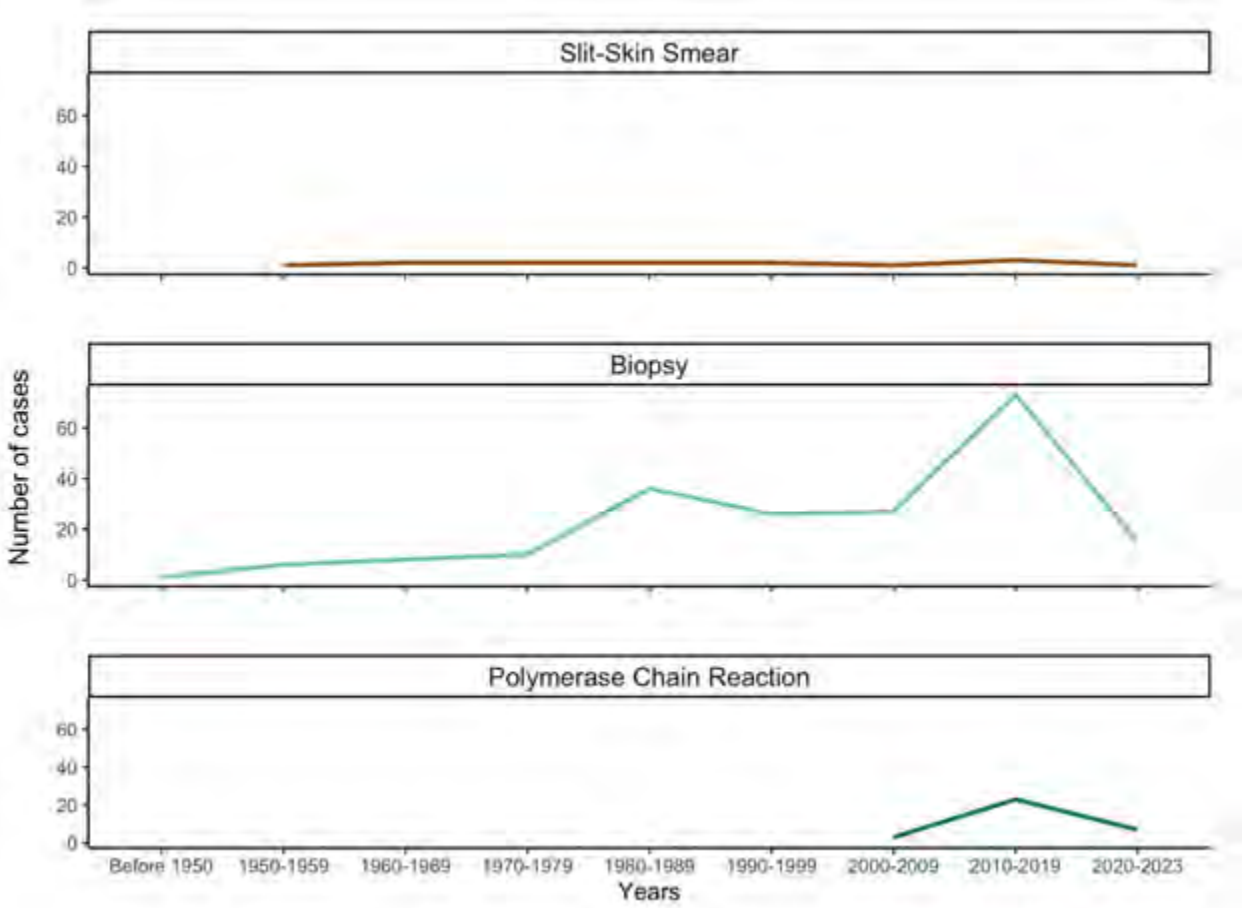
- Most publications did not report the likely or confirmed transmission mode
- In studies reporting this information, most cases were transmitted via prolonged community contact with infected persons
- Majority of cases published in 1950s were contracted while on military service abroad
- Growing number of zoonotic cases from armadillos

Transmission mode over time



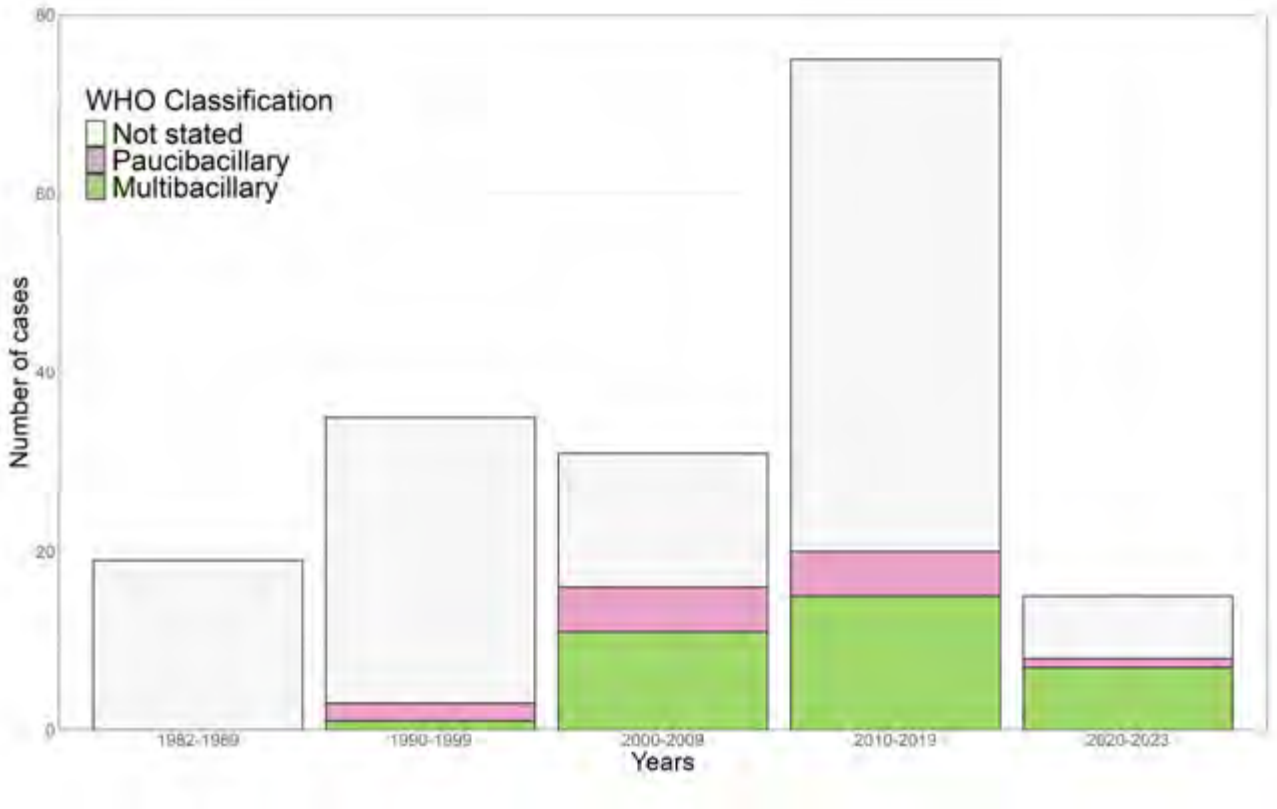
Diagnostic modalities reported over time

- Most cases reported were confirmed based on pathology
- PCR started being used for diagnostics in 1990
- Diagnostic modality was not discussed in large proportion of published cases



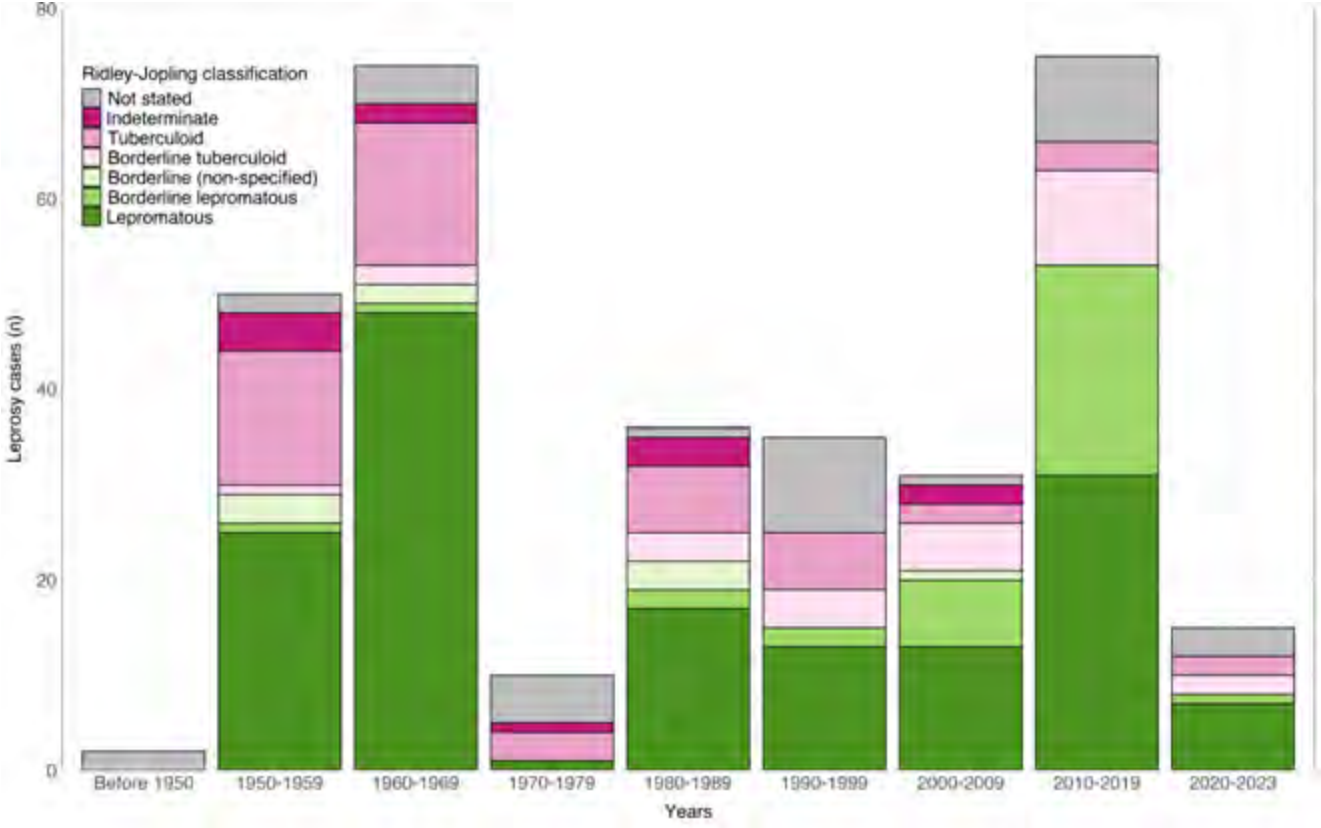
WHO classifications of cases over time

- Majority of reported WHO classifications were multibacillary
- Much information was missing across publications



Ridley-Jopling classifications of cases over time

- Majority of reported Ridley-Jopling classifications were Lepromatous (LL)
  - LL is multibacillary with polymorphic lesions
- More widely reported than WHO classification



Discussion

- One-third of all cases presented to the National Hansen's Disease Program (NHDP) in Louisiana

- State of residence and state of diagnosis trends aligned. Majority of cases were from the U.S. and resided in states providing NHDP resources.

- Prior to 1960, most cases were associated with military service abroad (86.5%)
- Since 1980, growing proportion of cases (22.8%) associated with likely zoonotic transmission

- Skin biopsy remained the dominant diagnostic modality (61.6%) through 2023, with PCR utilized more since 2000

Discussion

- Based on Ridley-Jopling classification, most cases included in this review (47.3%) were lepromatous

- Based on WHO classification, where applicable and reliable data were available, 21.8% were MB and 8.3% were PB

- Multi-drug regimens with rifampicin, dapsone, and clofazimine have dominated treatment protocols since 1980, but other antibiotics have been increasingly used over the past decade
  - Clarithromycin
  - Minocycline
  - Fluoroquinolones

Conclusion

- Studies reporting on HD in the U.S. are limited
- Our analysis showcases potentially emerging trends such as increased zoonotic transmission in the southern U.S.
- Limitations included lack of complete information across many metrics
- Case counts do not represent full scope of cases that have been reported to surveillance centers over time
- Further research is needed to clarify burden of HD and changing geographic and demographic distributions
- Standardized reporting methods for diagnostics and treatment are needed in study of HD in the U.S.

References

- Maymone MBC, Laughter M, Venkatesh S, et al. Leprosy: Clinical aspects and diagnostic techniques. Journal of the American Academy of Dermatology. 2020;83(1):1-14. doi:10.1016/j.jaad.2019.12.080
- Sato H, Frantz JE. Termination of the leprosy isolation policy in the US and Japan : Science, policy changes, and the garbage can model. BMC Int Health Hum Rights. 2005;5(1):3. doi:10.1186/1472-698X-5-3
- WHO GLP. Leprosy Factsheet. World Health Organization; 2023. https://www.who.int/news-room/fact-sheets/detail/leprosy
- Ploemacher T, Faber WR, Menke H, Rutten V, Pieters T. Reservoirs and transmission routes of leprosy; A systematic review. PLoS Negl Trop Dis. 2020;14(4):e0008276. doi:10.1371/journal.pntd.0008276
- Gilmore A, Roller J, Dyer JA. Leprosy (Hansen's disease): An Update and Review. Mo Med. 2023;120(1):39-44.
- Jariyakulwong N, Julanon N, Saengboonmee C. Lepromatous leprosy with a suspected 30-year incubation period: A case report of a practically eradicated area. J Taibah Univ Med Sci. 2022;17(4):602-605. doi:10.1016/j.jtumed.2021.12.005
- Makhakhe L. Leprosy review. South African Family Practice. 2021;63(1). doi:10.4102/safp.v63i1.5311
- Gama RS, Leite LA, Colombo LT, Fraga LADO. Prospects for new leprosy diagnostic tools, a narrative review considering ELISA and PCR assays. Rev Soc Bras Med Trop. 2020;53:e20200197. doi:10.1590/0037-8682-0197-2020
- Song S, Lim J, Park S, et al. Diagnosis of New Leprosy Patients through Various Histological Findings according to Biopsy Sites. Ann Dermatol. 2022;34(6):487. doi:10.5021/ad.20.224
- Chen KH, Lin CY, Su SB, Chen KT. Leprosy: A Review of Epidemiology, Clinical Diagnosis, and Management. J Trop Med. 2022;2022:8652062. doi:10.1155/2022/8652062
- Alrehaili J. Leprosy Classification, Clinical Features, Epidemiology, and Host Immunological Responses: Failure of Eradication in 2023. Cureus. 2023;15(9):e44767. doi:10.7759/cureus.44767
- Pardillo FEF, Fajardo TT, Abalos RM, Scollard D, Gelber RH. Methods for the Classification of Leprosy for Treatment Purposes. Clinical Infectious Diseases. 2007;44(8):1096-1099. doi:10.1086/512809
- Parkash O. Classification of leprosy into multibacillary and paucibacillary groups: an analysis. FEMS Immunol Med Microbiol. 2009;55(1):1-5. doi:10.1111/j.1574-695X.2008.00491.x

TULANE UNIVERSITY SCHOOL of MEDICINE

Student Clinic Council
Tulane University School of Medicine

fitclinic
FIT (Formerly Incarcerated Transitions) Clinic

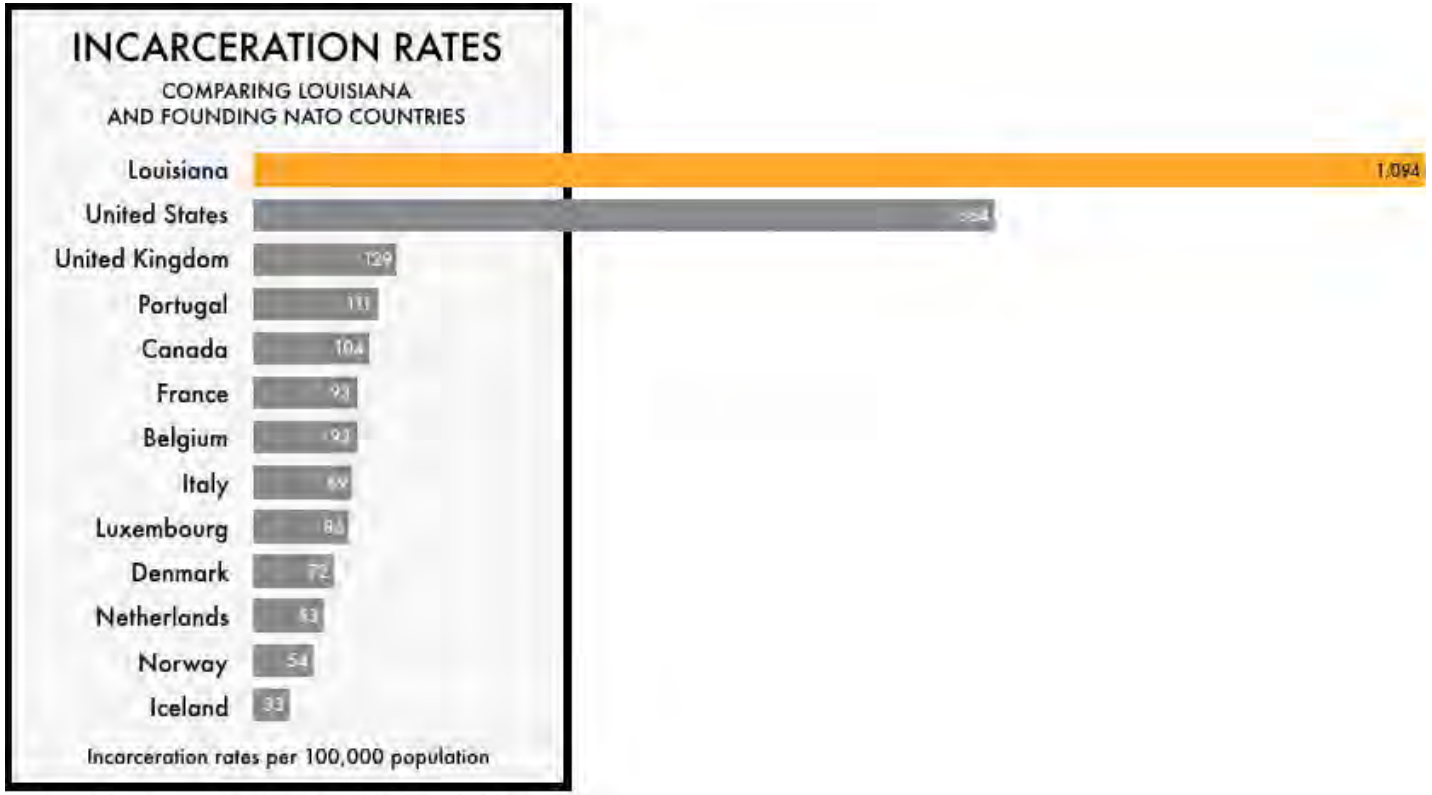
Understanding Substance Use and Misuse Related to Incarceration History in a New Orleans Student Clinic Population

Vidhatri Raturi M.S.[1,2], Haley Watts B.S.E.[1], Thomas Stall M.S.W.[1], Danielle Metz A.A.[1,2], Haki Sekou [2,3], Anjali Niyogi M.D.[1,2], M.P.H., Helen Pope M.D.[1]

[1]Tulane University School of Medicine [2]Formerly Incarcerated Transitions Clinic [3]Voice of the Experienced

Incarceration History and Health

- Justice impacted individuals face a higher burden of chronic, mental, physical, and communicable conditions than their non-justice impacted counterparts
- For every year of incarceration, life expectancy is shortened by 2 years
- 12x increased risk of overall mortality and 129x increased risk of overdose mortality within 2 weeks of release
- Incarceration exacerbates the Social Determinants of Health



Source: https://www.prisonpolicy.org/global/2021.html

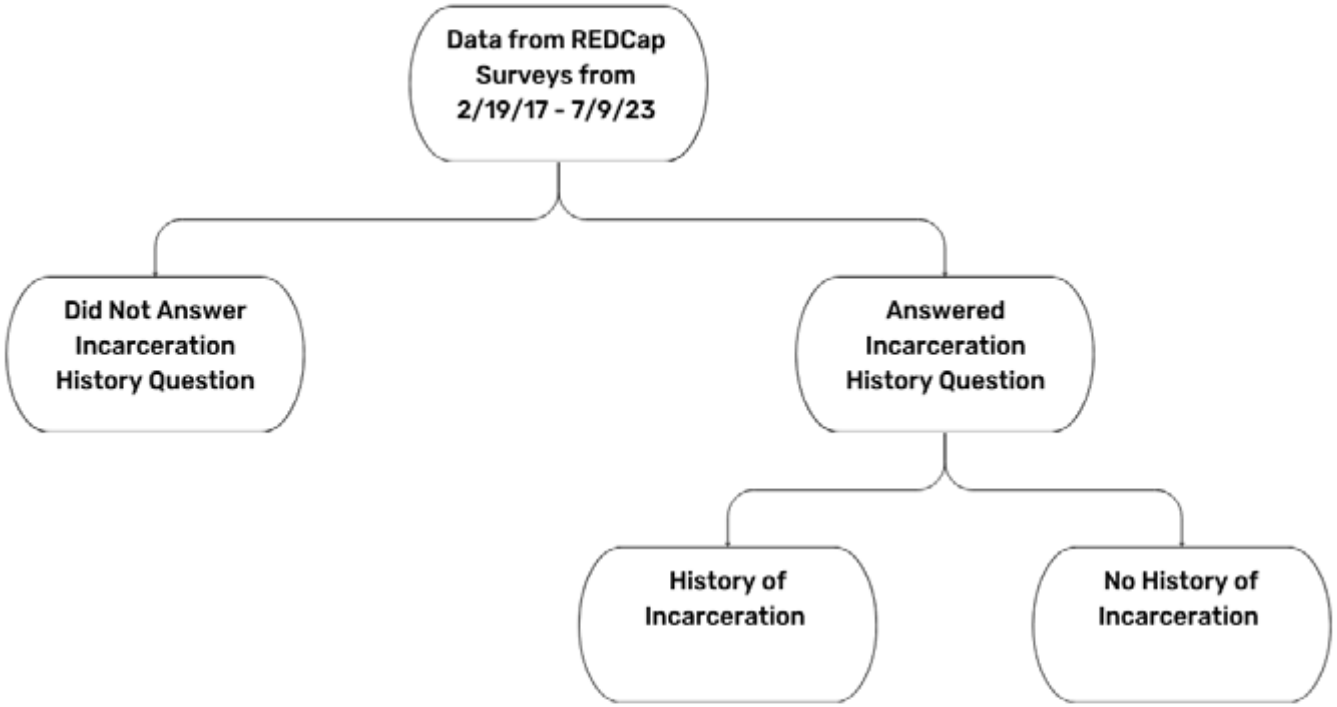
Substance Use and Misuse in Incarcerated Populations

- 65% of individuals incarcerated in prisons are affected by an active Substance Use Disorder
- 85% of incarcerated people in prisons either meet the criteria for Substance Use Disorder, were under the influence of alcohol or drugs at the time of the incident they were convicted for, or were convicted for a drug related incident
- Prevalence of cigarette smoking is 2x greater in incarcerated populations compared to their non-incarcerated counterparts

Study Objectives

- Understand how many formerly incarcerated individuals Tulane Student Run Clinics serve
- Evaluate the prevalence of substance use and misuse among formerly incarcerated and their non-formerly incarcerated counterparts
- Provide information necessary for student clinics to best serve their formerly incarcerated patients

Methods



Questions Regarding:

- Smoking
  - History
  - Cessation
  - Within the past 30 days
- Alcohol
  - Use
  - Misuse Within the Past 30 Days
- Illicit Drug
  - Within the Past 30 Days

Analysis :

- Chi Square Test

Results

- 47.6% (969) of patients answered the incarceration history question (n = 2,035)
- Of those who answered the question, 71% (692) of patients indicated a history of incarceration
- Both groups were predominantly male, and Black, with the average age being in the early 40s

		Incarceration History		No Incarceration History		P-value
History of Smoking		N = 491		N = 154		0.029
	Yes	411	84%	117	76%	
	No	80	16%	37	27%	
Smoking Cessation		N = 362		N = 101		0.047
	Wants to Stop Smoking	114	31%	21	21%	
	Considering Cessation	67	19%	28	28%	
	Not Interested in Cessation	181	50%	52	51%	
Alcohol Use		N = 282		N = 154		0.00001
	Yes	149	53%	44	29%	
	No	133	47%	110	71%	
Smoking in the Past 30 Days		N = 591		N = 277		0.00015
	Yes	315	53%	104	38%	
	No	276	47%	173	62%	
Illicit Drug Use in the Past 30 Days		N = 691		N = 276		0.047
	Yes	118	17%	33	12%	
	No	573	83%	243	88%	
Alcohol Misuse in the Past 30 Days		N = 138		N = 62		0.0397
	Yes	52	38%	33	53%	
	No	86	62%	29	47%	

Discussion

- High rate of incarceration in Orleans Parish
- Higher rates of substance use disorders in formerly incarcerated persons
- Higher rates of mortality post release from substance-related conditions

Conclusion

- A large number of patients receiving care in Tulane's student clinics are justice impacted.
- Community and providers at student-run clinics should be familiar with these statistics and incorporate targeted screening to better meet patient needs

References

Kang-Brown, J, Montagnet C, Heiss J. *People in Jail and Prison in 2020*.; 2021. https://www.vera.org/downloads/publications/people-in-jail-and-prison-in-2020.pdf

Nelson S, Horton P. *Where People in Prison Come From: The Geography of Mass Incarceration in Louisiana*. Prison Policy Initiative; 2023.

National Center on Addiction and Substance Abuse, Columbia University. BehindBars II: Substance Abuse and America's Prison Population. https://files.eric.ed.gov/fulltext/ED509000.pdf. Published February 2010

Binswanger, I. A., Krueger, P. M., & Steiner, J. F. (2009). Prevalence of chronic medical conditions among jail and prison inmates in the United States compared with the general population. Journal of Epidemiology and Community Health, 63(11), 912–919.

Valera P, Reid A, Acuna N, Mackey D. The smoking behaviors of incarcerated smokers. Health Psychology Open. 2019;6(1). doi:10.1177/2055102918819930

J. Travis, B. Western, S. Redburn (Eds.), The growth of incarceration in the United States: Exploring causes and consequences, National Academies Press, Washington, DC (2014)

Tsai, J., & Gu, X. (2019). Utilization of addiction treatment among U.S. adults with history of incarceration and substance use disorders. *Addiction science & clinical practice*, *14*(1), 9. https://doi.org/10.1186/s13722-019-0138-4

Rezaei S, Akbari Sari A, Arab M, Majdzadeh R, Mohammad Poorasl A. Economic burden of smoking: a systematic review of direct and indirect costs. Med J Islam Repub Iran. 2016 Jul 13;30:397. PMID: 27579287; PMCID: PMC5004566.

Ahalt C, Buisker T, Myers J, Williams B. Smoking and Smoking Cessation Among Criminal Justice–Involved Older Adults. Tobacco Use Insights. 2019;12. doi:10.1177/1179173X19833357

Rowell-Cunsolo, T. L., & Bellerose, M. (2021). Utilization of substance use treatment among criminal justice-involved individuals in the United States. *Journal of substance abuse treatment*, *125*, 108423. https://doi.org/10.1016/j.jsat.2021.108423

Saloner, B., Bandara, S. N., McGinty, E. E., & Barry, C. L. (2016). Justice-Involved Adults With Substance Use Disorders: Coverage Increased But Rates Of Treatment Did Not In 2014. *Health affairs (Project Hope)*, *35*(6), 1058–1066. https://doi.org/10.1377/hlthaff.2016.0005

Dumont DM, Brockmann B, Dickman S, Alexander N, Rich JD. Public health and the epidemic of incarceration. Annu Rev Public Health. 2012 Apr;33:325-39. doi: 10.1146/annurev-publhealth-031811-124614. Epub 2012 Jan 3. PMID: 22224880; PMCID: PMC3329888.

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ORTHOPAEDIC SURGERY

UAB MEDICINE

Postoperative complications following internal fixation of periprosthetic tibia fractures with plating, nailing, or revision TKA

Garrett Hawkins, BS, MS3 – UAB Heersink School of Medicine

Matthew T Yeager, BA; Austin Atkins, MD; Clay A Spitler, MD; Joey P Johnson, MD

Background

- Periprosthetic tibia fractures (PPTFs) – fracture in the presence of a non-native joint.
- Complex injuries that are likely to increase as total knee arthroplasty (TKA) becomes more common.
- A study at Mayo Clinic found subsequent PPTFs in 0.40% of cases following TKA.
- Scarcity in literature describing these fractures.

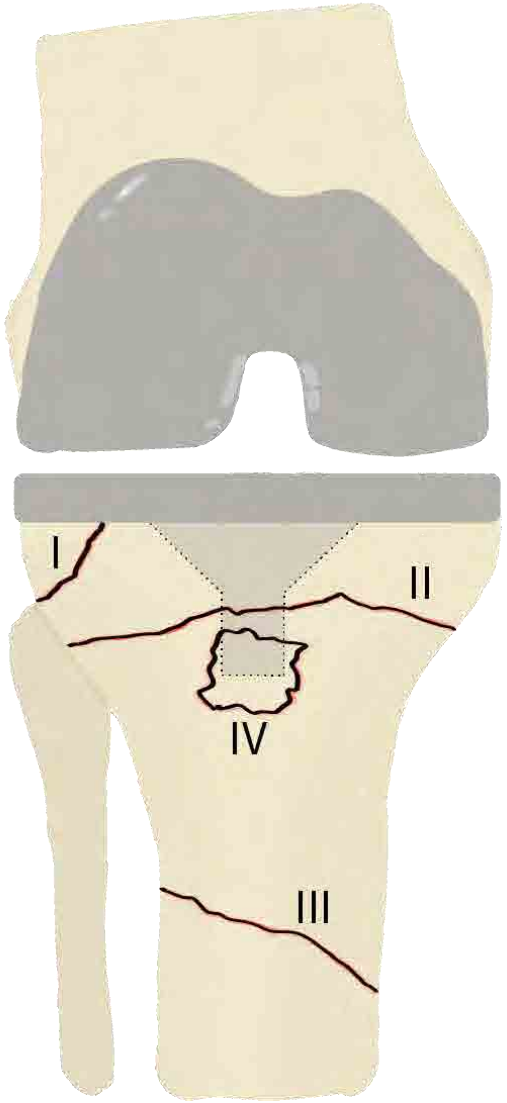


Figure 1. Felix Classification

Williams SN, Wolford ML, Bercovitz A. Hospitalization for Total Knee Replacement Among Inpatients Aged 45 and Over: United States, 2000-2010. *NCHS Data Brief*. 2015;(210):1-8.

Felix NA, Stuart MJ, Hanssen AD. Periprosthetic fractures of the tibia associated with total knee arthroplasty. Clin Orthop Relat Res. 1997;(345):113-124.

Objectives

- This study's objectives:
  - Describe PPTFs in the cohort with related demographic data
  - Describe how methods of internal fixation impact post-op complications

Methods

- Retrospective cohort study at a single level 1 trauma center (2013-2022)
- Demographic data, comorbidities, and fracture/injury/operative characteristics were collected from the EMR
- Differences in post-op complications were investigated in those treated with revision TKA (rTKA), nailing, or plating

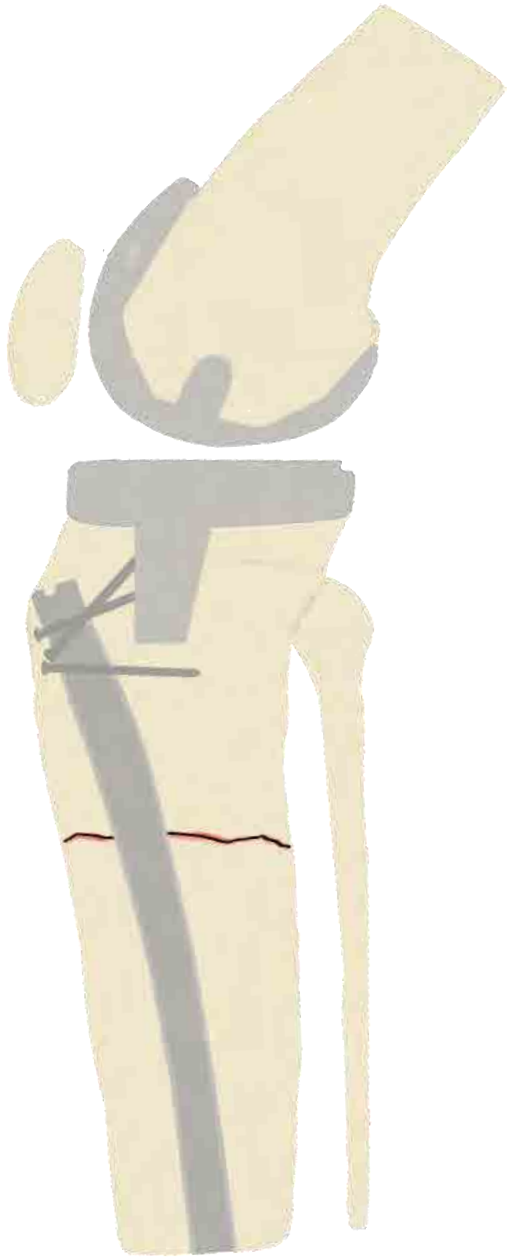
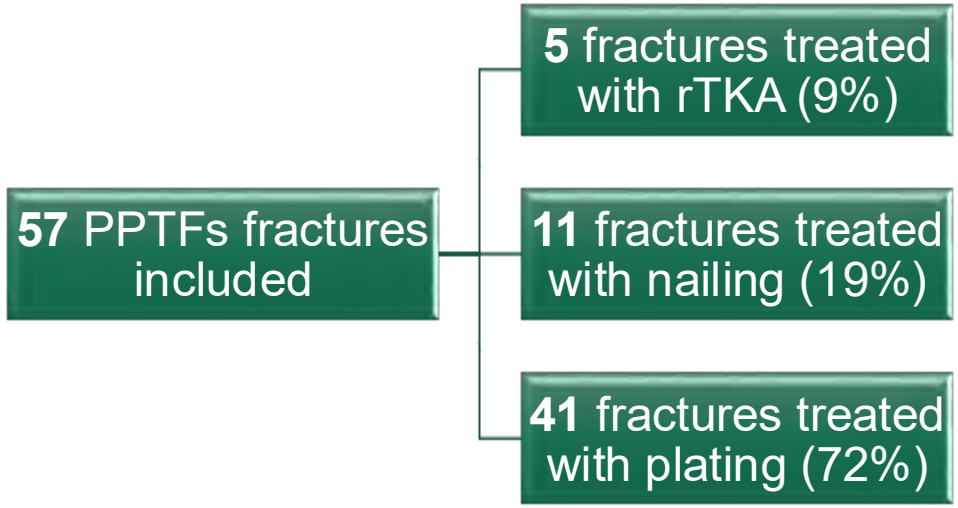


Figure 2. IMN

Results



Demographics

	rTKA	Nail	Plate	P-value
Age (years), mean [SD]	62 [10]	64 [15]	67 [12]	0.619
Gender, N [%]				0.134
Male	1 [20]	6 [55]	10 [24]	
Female	4 [80]	5 [45]	31 [76]	
Race, N [%]				0.951
White	4 [80]	8 [73]	31 [76]	
Black	1 [20]	3 [27]	10 [24]	
BMI, mean [SD]	40 [8]	34 [6]	35 [10]	0.541

Results (continued)

Postoperative Complications

	rTKA	Nail	Plate	P-value
MI	0 [0]	1 [9%]	0 [0]	0.119
DVT	0 [0]	1 [9%]	0 [0]	0.119
Sepsis	0 [0]	2 [18%]	3 [7%]	0.405
Reop for bone healing	0 [0]	0 [0]	6 [21%]	0.280
Reop for infection	0 [0]	0 [0]	9 [27%]	0.129
Implant removal	1 [20%]	0 [0]	7 [18%]	0.412
Amputation	1 [20%]	0 [0]	1 [3%]	0.141
Unplanned reoperations	3 [60%]	0 [0]	14 [34%]	**0.027**

We have nothing to disclose

THANK YOU

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SUBLINGUAL ASENAPINE FOR AGITATION IN MALABSORPTIVE STATES: THREE PATIENT CASES

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Disclosure: No conflict of interest

INTRODUCTION

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- Gastric malabsorptive conditions may prevent patients from deriving benefit from orally administered medications intended for enteric absorption
- While malabsorption is an increasingly common issue, current data on alternative oral options for agitation in these patients is very sparse
- Asenapine is a second-generation antipsychotic displaying efficacy from its' potent antagonism of many serontonergic (5-HT_{2A} Ki=0.06 nM) and dopaminergic receptors (D_2 Ki=1.3)
- Asenapine's sublingual (SL) form bypasses gut absorption, has a fast peak (30 min to 1.5 hrs), with noted efficacy for acute agitation within 15 min
- Clinicians should be aware of the inherent differences in orally disintegrating tablets (ODT) and SL, which are significant
- We report on three patients, one with short bowel syndrome, one with viral gastritis, and one with aortic dissection who were trialed on SL asenapine for agitation after failing alternative antipsychotics
- The aim is to showcase asenapine as a viable option for acute agitation, especially in these niche malabsorptive states where only minimal data exist

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CASES

Patient	Reason for gastric malabsorption	History of psychiatric illness	Oral medications trialed for agitation (prior to SL asenapine)	Effective dose of SL asenapine used	Time to noted benefit of SL asenapine
Mr. A	SBS secondary to NEC	Yes	Olanzapine ODT Risperidone ODT	5 mg twice daily	1 day
Ms. B	Viral gastritis / vomiting	Yes	Olanzapine tablet Chlorpromazine tablet	5 mg every morning plus 10 mg every evening	3 days
Mr. C	Aortic dissection with end-organ failure	No	Olanzapine tablet	5 mg twice daily	3-5 days

Table 1: Summary of Sublingual Asenapine Use for Depicted Patients

Abbreviations: SL=Sublingual; SBS=Short Bowel Syndrome; NEC=Necrotizing Enterocolitis; IM=Intramuscular; IV=Intravenous; ODT=Orally Disintegrating Tablet; mg=Milligrams

DISCUSSION & CONCLUSION

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- All 3 patients had significant response to SL asenapine, which was uniquely selected out of a concern for gut absorption or difficulty with route of delivery
- Response was rapid and was seen not only through a reduction of subjective agitation, but objectively seen through a reduction in as-needed medication use
- For patients A and B, it should be noted that the use of SL asenapine was limited by inconsistencies in actual sublingual administration
- It is quite possible that the necessity to switch from SL asenapine to an alternative agent was secondary to the patient swallowing the tablet, reducing the bioavailability to nil
- To date, there are no guidelines which assist clinicians in choosing the most appropriate medication for patients with agitation or delirium when gut absorption cannot be relied upon
- There is an urgent need for review of alternative agents for agitation management and overall psychiatric care in patients with acquired or congenital gut malformations
- Consult-liaison clinicians may consider sublingual asenapine a viable option for medically complex patients where rapid onset is needed, and intestinal absorption is known to be compromised or is questionable

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REFERENCES

- Boucher BA, Wood GC, Swanson JM. Pharmacokinetic changes in critical illness. *Crit Care Clin*. Apr 2006;22(2):255-71, vi. doi:10.1016/j.ccc.2006.02.011
- Forsberg J, Bedard E, Mahmoud SH. Bioavailability of Orally Administered Drugs in Critically Ill Patients. *J Pharm Pract*. May 6 2022:8971900221100205. doi:10.1177/08971900221100205
- Salazar JA, Carey AN, Duggan CP. Nutritional and medical approaches to intestinal failure. *Curr Opin Clin Nutr Metab Care*. May 1 2023;26(3):201-209. doi:10.1097/MCO.0000000000000918
- Mendelson J, Upton RA, Everhart ET, Jacob P, 3rd, Jones RT. Bioavailability of sublingual buprenorphine. *J Clin Pharmacol*. Jan 1997;37(1):31-7. doi:10.1177/009127009703700106
- Markowitz JS, DeVane CL, Malcolm RJ, et al. Pharmacokinetics of olanzapine after single-dose oral administration of standard tablet versus normal and sublingual administration of an orally disintegrating tablet in normal volunteers. *J Clin Pharmacol*. Feb 2006;46(2):164-71. doi:10.1177/0091270005283839
- FDA. Highlights of Prescribing Information: Saphris Package Insert. Food and Drug Administration. Accessed June 14th, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022117s020s021lbl.pdf
- Huhn M, Nikolakopoulou A, Schneider-Thoma J, et al. Comparative Efficacy and Tolerability of 32 Oral Antipsychotics for the Acute Treatment of Adults With Multi-Episode Schizophrenia: A Systematic Review and Network Meta-Analysis. *Focus (Am Psychiatr Publ)*. Oct 2020;18(4):443-455. doi:10.1176/appi.focus.18306

Reduced Utero-placental Perfusion and Acute Seizure Exposure induce modest learning impairment, Alzheimer's disease markers, and reduced cerebrovascular perfusion in Mice at 2 months Postpartum

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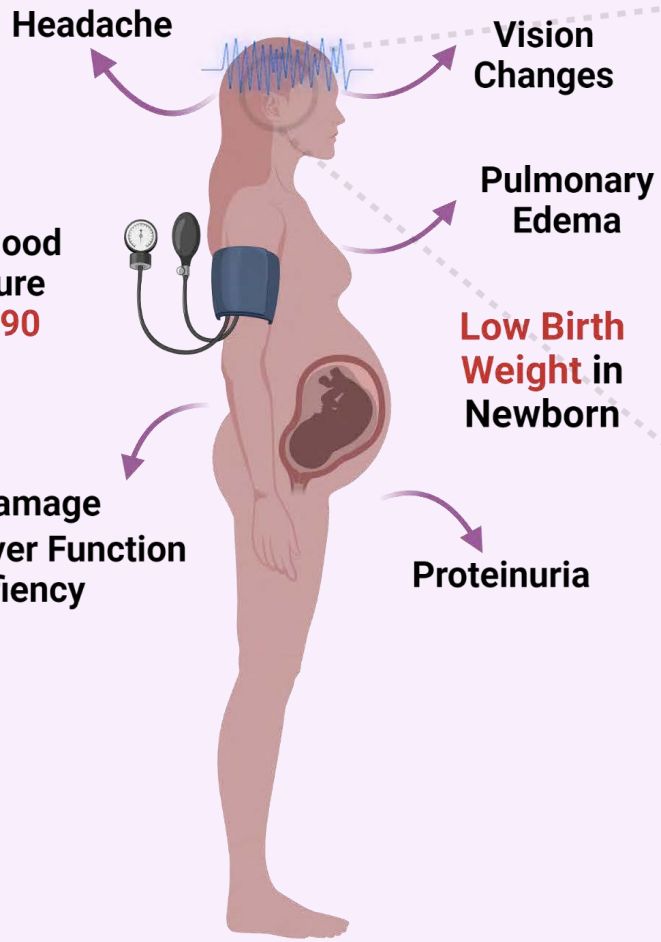
No Disclosures

PREECLAMPSIA & COGNITIVE IMPAIRMENT



POSTPARTUM COMPLICATIONS

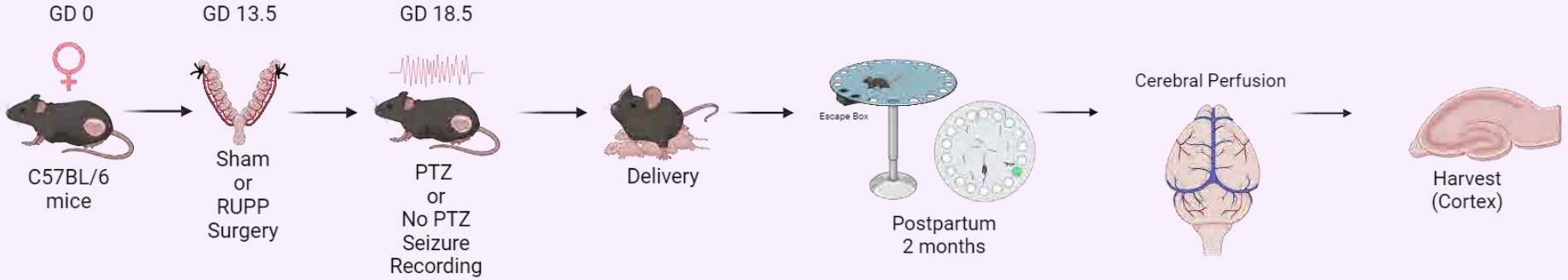
EARLY POSTPARUM

Neuronal Death & Impaired Neurogenesis
+ Vascular Injury
+ Neuroinflammation

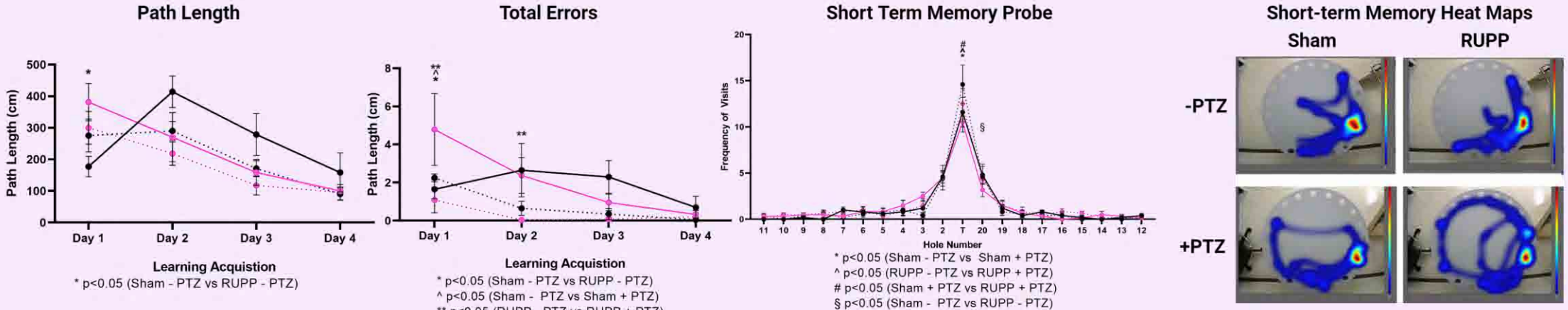
YEARS POSTPARTUM

White Matter Lesion & Cognitive Impairments
+ Vessel Rupture due to Increased Blood Pressure
+ Vascular Dementia, Stroke
+ Increased risk of Mortality from Alzheimer's Disease in Women with History of Preeclampsia

STUDY DESIGN



MICE EXPOSED TO RUPP SHOWED MODEST LEARNING IMPAIRMENTS & IMPAIRED SHORT TERM MEMORY AT 2MO POSTPARTUM



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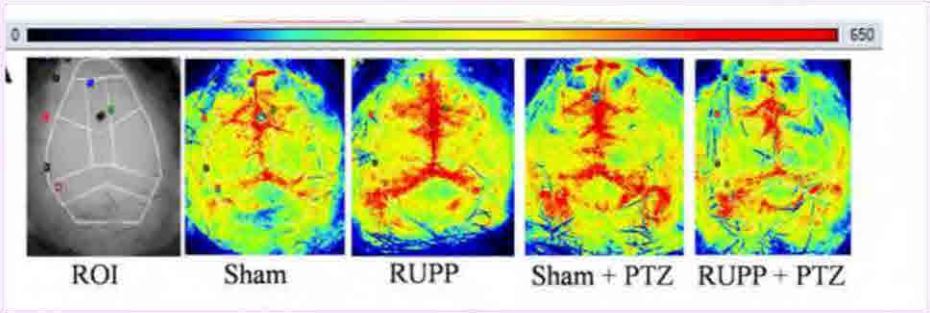
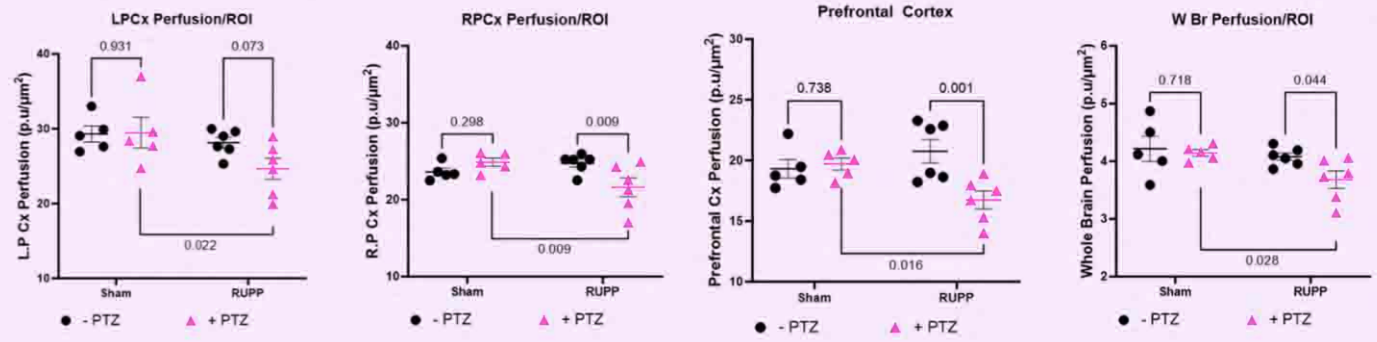
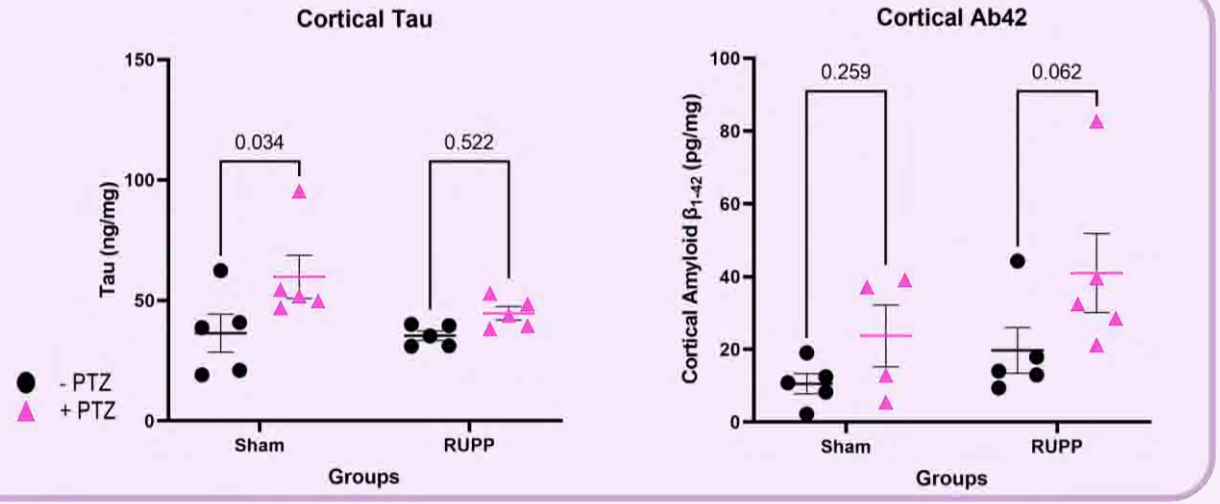
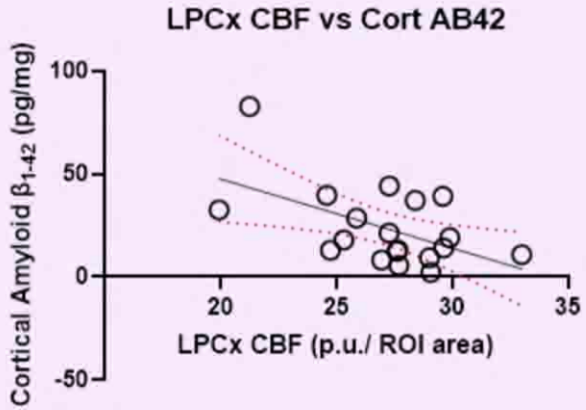
MICE EXPOSED TO RUPP + SEIZURES HAD REDUCED BASELINE CEREBRAL PERFUSION





MICE EXPOSED TO SEZIURES HAD SIGNIFICANT INCREASE IN TOTAL TAU AND Aβ42 IN CORTEX





WORKS CITED

1. Bangen KJ, Preis SR, Delano-Wood L, et al. Baseline white matter hyperintensities and hippocampal volume are associated with conversion from normal cognition to mild cognitive impairment in the Framingham Offspring Study. Alzheimer disease and associated disorders. 2018. Accessed July 26, 2023. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5821543/?report=reader.

2. Jones-Muhammad M, Warrington JP. Cerebral blood flow regulation in pregnancy, hypertension, and hypertensive disorders of pregnancy. MDPI. September 4, 2019. Accessed July 26, 2023. https://www.mdpi.com/2076-3425/9/9/224.

3. Theilen LH, Fraser A, Hollingshaus MS, et al. All-cause and cause-specific mortality after hypertensive disease of pregnancy. Obstetrics and gynecology. August 2016. Accessed July 26, 2023. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4961555/.

4. Protein misfolding, congophilia, oligomerization, and ... - science. Accessed July 27, 2023. https://www.science.org/doi/10.1126/scitranslmed.3008808.

5. Testo AA, McBride C, Bernstein IM, Dumas JA. Preeclampsia and its relationship to pathological brain aging. Frontiers. September 26, 2022. Accessed July 26, 2023. https://www.frontiersin.org/articles/10.3389/fphys.2022.979547/full.

6. Basit S, Wohlfahrt J, Boyd HA. Pre-eclampsia and risk of dementia later in life: Nationwide cohort study. The BMJ. October 17, 2018. Accessed July 26, 2023. https://www.bmj.com/content/363/bmj.k4109.long.

7. RC; S-PPFJ. Cerebral white matter lesions after pre-eclampsia. Pregnancy hypertension. Accessed July 26, 2023. https://pubmed.ncbi.nlm.nih.gov/28501273/.

8. Zambrano MD, Miller EC. Maternal stroke: An update - current atherosclerosis reports. SpringerLink. June 22, 2019. Accessed July 26, 2023. https://link.springer.com/article/10.1007/s11883-019-0798-2.

9. Richard M. Burwick MD, a, b, et al. Assessment of blood-brain barrier integrity and neuroinflammation in preeclampsia. American Journal of Obstetrics and Gynecology. June 20, 2019. Accessed July 26, 2023. https://www.sciencedirect.com/science/article/pii/S0002937819307884?casa_token=SbOg2Jn01vYAAAAA%3AFHebiydsauhAUi4mr5WzCejE9AoBQe0YJRbtMM-uCqtCliERpbfOf_cKJeFjNSfRX1i9DH3X4Q.

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Surgical Management Options for Infants with Pierre Robin Sequence: Establishing a Standard

Grant B. Torres, MS; Kimberley C. Brondeel, MD; Emily L. Geisler, MD; Petros Konofaos, MD, PhD

Background

- Pierre Robin Sequence (PRS)
  - Triad: micrognathia, glossoptosis, and airway obstruction
  - Often associated with cleft palate
- Isolated PRS, Syndromic PRS
- Epidemiology
  - 1:8,000 – 1:14,000
  - 1:5,000 - 1:6,000 in United States, United Kingdom/Ireland, Netherlands

Background

- Conservative Management

  prone positioning, nasopharyngeal airway, CPAP, nasogastric tube

- Surgical Management

  Airway

  Tracheostomy

  Tongue-lip adhesion (TLA)

  Mandibular Distraction Osteogenesis (MDO)

  Feeding

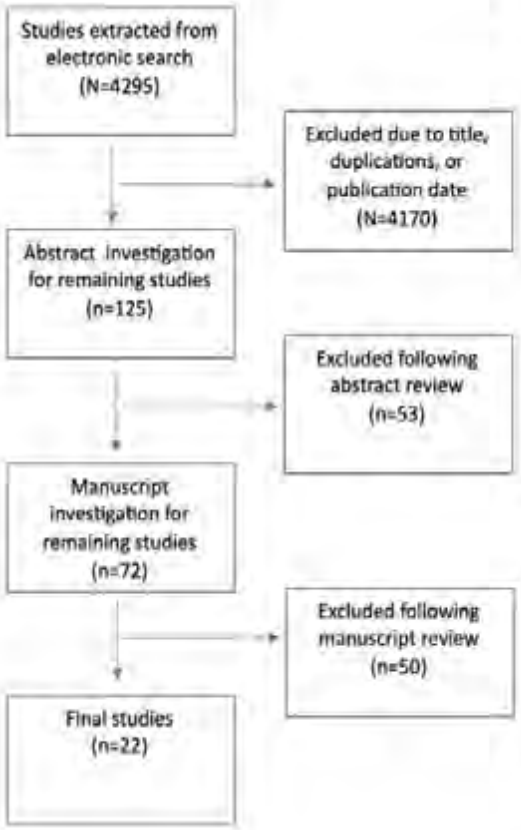
  Gastrostomy

Background

- New trends in diagnostics/therapeutic markers
  - Polysomnography data: Apnea/hypopnea index (AHI), O2 nadir
- Objective data to establish standards for treatment success
- Currently, there is no gold standard in management for PRS
- **This review: comprehensive evaluation of most recent data regarding airway and feeding outcomes for infants with PRS**

Methods

- Systematic Literature Review
- PubMed, Embase
- MDO, TLA outcomes in infants with PRS
- 22 studies: MDO, TLA, MDO-TLA comparisons



Inclusion Criteria

1) Articles written in English
2) Original articles including randomized control trials, retrospective cohorts, prospective cohorts, cross-sectional studies, and case series (excluding case reports)
3) Articles pertaining to MDO or TLA specifically in PRS subjects.

Exclusionary Criteria

1) Studies with fewer than 10 subjects
2) Studies without a reported follow-up duration of at least 1 year
3) Studies investigating non-primary MDO or TLA subjects
4) Studies with insufficient data on our outcomes of interest
5) Articles using repeat PRS subjects as articles already included in our review
6) Articles without full text via the University of Texas Medical Branch Moody Medical Library database or subscriptions

Outcomes of Interest

1) Airway outcomes
   - Primary: OSA resolution (PSG Data)
     1) AHI (decreased number of apnea episodes, mean AHI pre-op, mean AHI post-op)
     2) O2 nadir (mean oxygen saturation nadir pre-op, mean oxygen saturation nadir post-op)
   - Secondary: tracheostomy avoidance (tracheostomy prevention or decannulation), reoperations, complications
2) Feeding outcomes
   - Primary: achievement of full oral feeds
   - Secondary: growth/weight assessments, gastrostomy prevention

Results: Airway

	MDO	**TLA**
OSA Relief	95.8% (46/48)	48.8% (20/41)
AHI	All study groups (12) report significant differences between preoperative and postoperative AHI	No study groups (4) report significant differences between preoperative and postoperative AHI
O2 Nadir	All study groups (6) report significant differences between preoperative and postoperative O2 nadir	No study groups (1) report significant differences between preoperative and postoperative O2 nadir
Tracheostomy Avoidance	95.7% (446/466)	95.2% (121/127)

Results: Feeding

Achievement of full oral feeds

- MDO: multiple studies report 100% (44/44) within 1 month
- TLA: 42.5% (31/73) at 9 months, 61.6% (45/73) at 18 months
  - Latest/Largest cohort

Growth/Weight Assessments

- Improvement in both, no significant differences between MDO/TLA
  - Weight percentiles, weight-for-age Z-scores, etc

Gastrostomy Avoidance

- MDO = 80% (40/50), TLA = 44.7% (42/94)

Results: Other

- Reoperations
  - MDO = 1.5% (7/466), TLA = 11.0% (14/127)
- Mortality
  - MDO = 0.6% (3/466), TLA = 1.6% (2/127)
- Complications
  - MDO: minor infections, device realignment
  - TLA: minor infections
    - Relatively fewer minor complications seen with TLA

Discussion: Advantages/ Disadvantages

	Advantages	**Disadvantages**
MDO	advancement/prolongation of the mandible corrects micrognathia-induced glossoptosis	requires specialized surgical training/equipment, distraction process requires intensive care monitoring, subsequent operation for hardware removal
TLA	simplicity of the procedure, immediate relief of airway obstruction, and relatively fewer complications	does not correct micrognathia, relies on mandibular “catch-up” growth to fully achieve long-term airway stabilization

Discussion: Trends

- Trends in PRS management
- American Cleft Palate-Craniofacial Association (ACPA) & International Society of Craniofacial Surgeons
- Surveys
  - 2010: 48% MDO, 28% TLA
  - 2018: 74% MDO, 13% TLA
    - US surgeons: 82% MDO, 11% TLA
    - Int’l surgeons: 39% MDO, 19% TLA

Discussion: Airway

PSG Data

- MDO: significant improvement in all studies
- TLA: no significant improvement in studies
  - Comparison studies: MDO nearly doubles TLA success rate in OSA Relief

- Rate of reoperations was markedly lower in MDO than in TLA

- PSG data + fewer reoperations = MDO > TLA

Discussion: Feeding

- Both MDO and TLA improve feeding function
  - Similar growth and weight assessments
- Achievement of full oral feeds: MDO > TLA
- Gastrostomy Avoidance: MDO > TLA

Discussion: Miscellaneous

- MDO
  - Normalization of mandibular body, condylar positioning
  - Improved laryngoscopy grading
  - Effective for syndromic PRS patients

  - Predictors of Failure:
    - Neurological impairment, low birth weight, syndromic status
    - CNS abnormalities, laryngomalacia, preoperative intubation

Conclusion

- MDO exhibits consistently superior resolution of airway obstruction
  - PSG data
  - Lower rate of reoperations
  - Laryngoscopy data
- Reinforces previous notions
  - Time until and overall achievement of oral feeds
  - Gastrostomy avoidance

Pulmonary Function Tests as an Indicator of Postoperative Pulmonary Complications in Patients Undergoing Abdominal Wall Reconstruction

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Introduction

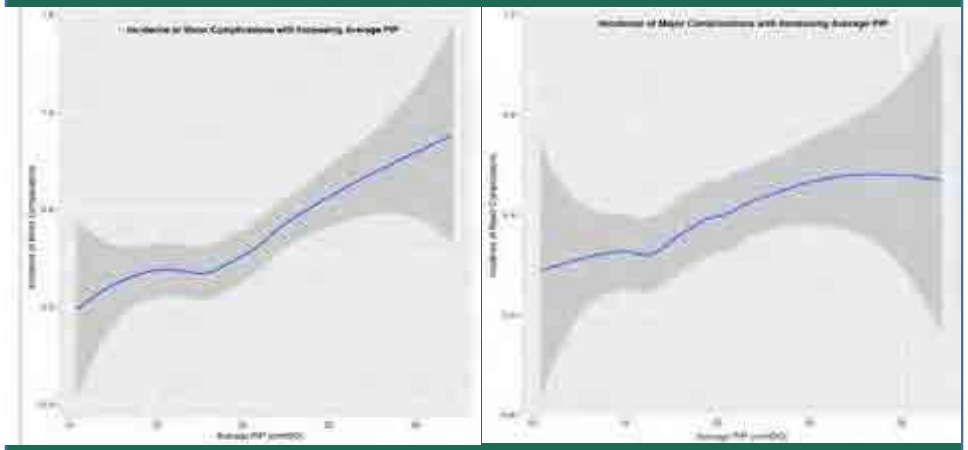
- Abdominal Wall Reconstruction is a common technique used in large and complex hernia repair. Postoperative respiratory complications are not uncommon following any surgery, but current studies do not have a consensus on how to predict their development.
- Prior studies have looked at various aspects of respiratory function following AWR. Risk factors including increased age, male sex, congestive heart failure (CHF), lung disease, obesity, and obstructive sleep apnea (OSA) have all been shown to cause an increase in respiratory failure.
- Of yet, no correlation has been found linking an increase in intraoperative Peak Inspiratory Pressure (PIP) and an increased rate of postoperative pulmonary complications.
- **The purpose of this study is to determine if there is a link between PIP and the development of respiratory complications.**

Methodology

- An IRB-approved retrospective review was completed on all patients who underwent AWR due to ventral hernia development at our tertiary care center from January of 2017 to September of 2022.
- Variables included were patient demographics, procedure information and intraoperative PFTs, and postoperative respiratory outcomes.

Results

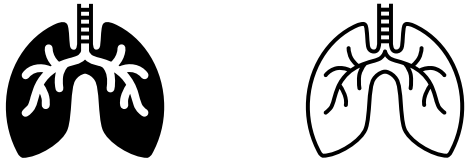
- Overall, the cohort had an average age of 55 years; Average BMI was 33.67.
- **There was no significant difference in age at procedure, BMI, smoking status, or history of diabetes mellitus between the two groups.**
- **30.5% developed a respiratory complication while 5.95% developed a major complication**
- **Post operative complications Mean PIP: 21.65cmH2O**
  - **No complications: 18.55cmH2O**
  - **P<0.001**



*A major complication was defined as any post-operative complication requiring mechanical ventilation or a BiPAP to correct (e.g. ARDS) while a minor complication was that which was corrected successfully without.

Conclusion

- Intraoperative elevations in PIP are associated with increased susceptibility to major and minor pulmonary complications following AWR independent of relevant patient risk factors.
- These findings hold potential significance in guiding postoperative care strategies for patients undergoing AWR.
- A larger, more extensive retrospective review will be performed to further analyze these results.



Disclosures

None

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THE UNIVERSITY OF ALABAMA AT BIRMINGHAM.

Initiation and Optimization of Goal Directed Medical Therapy for Heart Failure: A Quality Improvement Project in the Primary Care Setting

Kashaf Aqeel Zaidi, MD; Parikshit Chapagain, MD; Patrick Nguyen, MD; Shuva Shah, MD; George D. Everett, MD

Background

Heart failure impacts over 64 million people worldwide and the number continues to rise.

Clinical trials have established the effectiveness of pharmacological therapies and electrophysiological devices to reduce heart failure hospitalizations and to improve mortality, particularly in Heart Failure with Reduced Ejection Fraction (HFrEF).

Recent studies highlighted suboptimal utilization and dosing of goal directed medical therapy regimens.

Primary care physicians have been encouraged to initiate and titrate GDMT to achieve maximum benefit for the patients.

However, this has not been able to reach optimal implementation. Limiting factors include physician, patient, and drug factors

Objective

To assess the frequency of utilization of goal directed medical therapy (GDMT) for heart failure. To assess for optimal dosing, dose titration, and limitations to medication titration.

Methods

250 patients with Heart Failure were randomly selected from the primary clinic population.

The patients with heart failure with reduced ejection fraction were selected for chart review.

Charts were individually reviewed to assess the utilization of GDMT, including individual medication groups angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), angiotensin-neprilysin inhibitors (ARNi), mineralocorticoid receptor antagonists (MRA), and sodium-glucose transport (SGLT) II inhibitors.

Exclusion criteria included patients who had heart failure with preserved ejection fraction and those who had stopped following with the clinic.

A statistical analysis was performed to assess the percentage of patients on optimal doses of GDMT.

Among those who weren't, personal interviews were conducted with their PCPs to identify limitations to dose titration, if any.

Training was provided regarding optimal medications and appropriate dose titrations to the residents.

Results

Figure 1: Percentage of patients who are optimizable without contraindications.

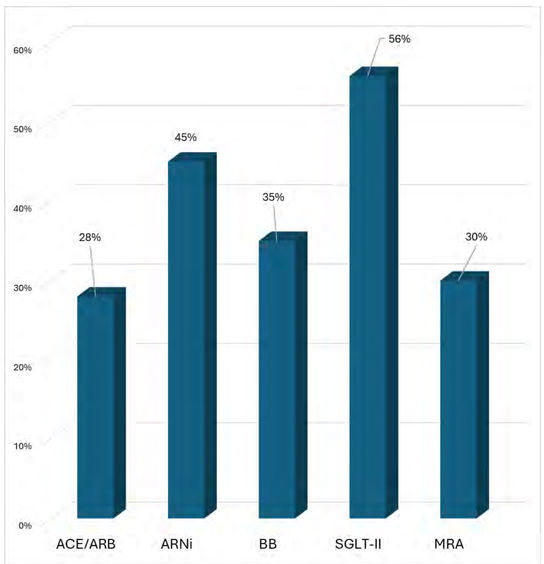
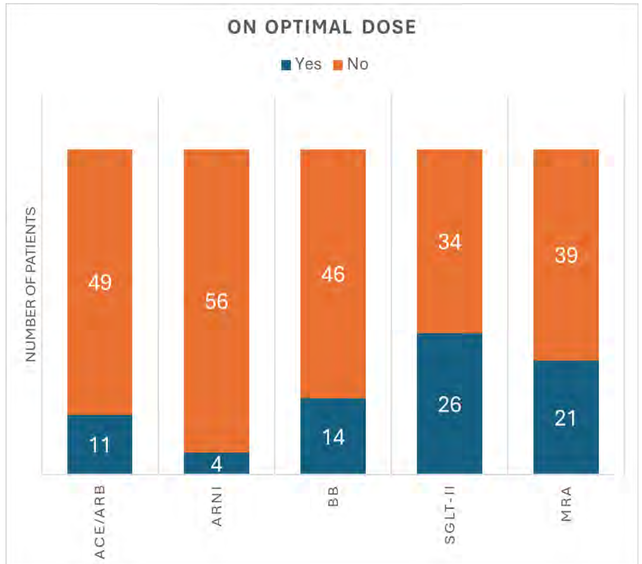


Figure 2: Percentage of patients on optimal doses of GDMT



Results

The mean age for the patients in this group was 65.7 +/- 13.8 years and 66% of them were males.

94% of the patients were on a beta blocker, while only 25% were on optimal dosage. 39% on Jardiance. 50% on mineralocorticoid receptor antagonist, 72% were on optimal dose, while 74.6% were on ACE/ARB/ARNi but only 21.5% were on the optimal dose.

Figure 1 shows the percentage of patients who were optimizable without contraindications.

Common drug factors limiting optimization were side effects including cough, bradycardia, hyperkalemia, urinary tract infections.

Common limiting factors for the patients were GFR < 30, cost, lack of insight.

Among physician factors were an inadequate knowledge regarding optimal doses and side effects, reliance on cardiology to optimize medications, and infrequent clinic visits.

Conclusions

There is sub-optimal initiation and optimization of GDMT at the primary care level. It is an ongoing study, and we will continue to re-evaluate periodically to ensure adequate implementation.

References

AHA/ACC/HFSA. (n.d.). 2022 AHA/ACC/HFSA guideline for heart failure. https://www.heart.org/-/media/Files/Professional/Quality-Improvement/Get-With-the-Guidelines/Get-With-The-Guidelines-HF/HF-Awareness-Week-2023/2023New-Heart-Failure-Guidelines-Impact-on-the-Patient-Journey-The-Healthcare-Professional-Perspecti.pdf

Jarjour, M., & Ducharme, A. (2023). Optimization of GDMT for patients with heart failure and reduced ejection fraction: Can physiological and biological barriers explain the gaps in adherence to heart failure guidelines? Drugs in Context, 12, 1–14. https://doi.org/10.7573/dic.2023-5-6

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Anti-neutrophil cytoplasmic antibody (ANCA) associated Pulmonary Vasculitis: Exploring the role of Extracorporeal Membrane Oxygenation

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INTRODUCTION

- Diffuse alveolar hemorrhage (DAH) can occasionally be the initial manifestation of Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis.
- Historically, vasculitis with DAH had a case fatality rate as high as 50%.
- Extracorporeal membrane oxygenation (ECMO) has emerged as the next critical intervention for managing respiratory failure when conventional ventilation methods are insufficient.
- This abstract highlights the crucial role of ECMO in managing severe respiratory failure in patients with ANCA-positive vasculitis.

CASE PRESENTATION

- A 68-year-old male, fairly active at baseline

Presenting symptoms:
- Dyspnea and persistent hemoptysis for 4 days

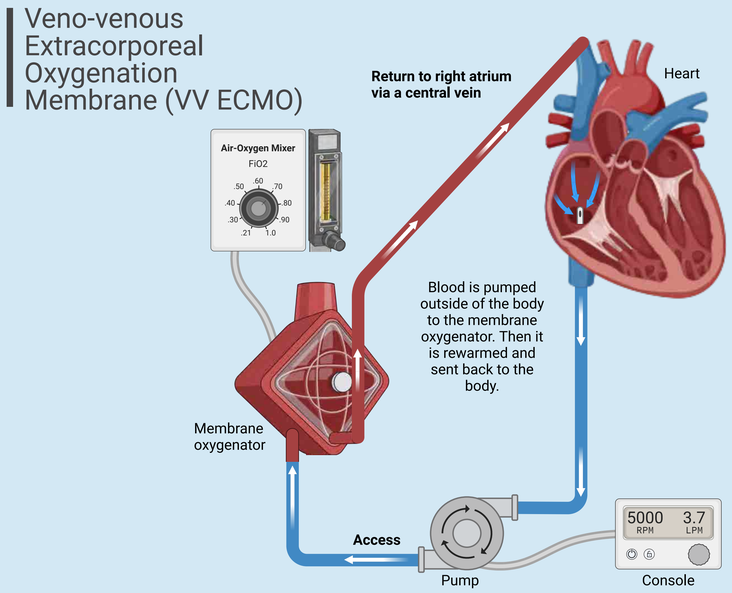
Physical Examination:
- Hypoxic, on a high-flow nasal cannula with 100% FiO2
- Using accessory muscles of respiration, Bilateral chest crackles
- No lower extremity edema, No joint swelling

Bedside echocardiogram:
- Hyper-dynamic LV and RV
- Collapsible inferior vena cava

Lab results:
- Hemoglobin: 8 mg/dL
- No leukocytosis
- Normal procalcitonin
- COVID-19 antigen test: negative

CT scan of the chest with contrast:
- Bilateral opacities
- No pulmonary embolism detected

ILLUSTRATION



WORKING DIAGNOSIS/MANAGEMENT

Initial intervention:
- Increasing oxygen requirements
- Required intubation within 24 hours of admission

Bronchoscopy findings:
- Consistent with Diffuse Alveolar Hemorrhage
- Progressively more hemorrhagic aliquots
- No airway bleeding noted

Post-intubation:
- Continued hypoxia
- Examination: bilateral diminished breath sounds
- Pronation attempted

Working Diagnosis: Inflammatory process
- Low likelihood of infectious process
- Started on pulse dose steroids
- Autoimmune antibody panel sent

Condition deterioration and transfer:
- Despite aggressive management and maximum mechanical ventilatory support, he continued to deteriorate.
- Transferred to an institute with ECMO availability due to hospital limitations.

OUTCOME/FOLLOW UP

- Positive anti-proteinase 3 (PR3) antibody level of >177 IU/L confirmed ANCA-associated vasculitis.
- Patient maintained on VV ECMO and successfully weaned off after five days. He maintained oxygenation.
- Unfortunately later he suffered cardiac arrest.

DISCUSSION

- **Role of ECMO:** ECMO provides valuable time for immune-modulating therapies to take effect in ANCA associated vasculitis complicated by DAH.
- **Timely Intervention:** Early referral to centers equipped with ECMO should be considered.
- **Types of ECMO:**
  - **Veno-Venous (VV) ECMO:** Provides support to the lungs, used for severe respiratory failure when the heart function is adequate.
  - **Veno-Arterial (VA) ECMO:** Provides support to both the heart and lungs by maintaining systemic circulation and oxygenation.

REFERENCES

1. O'Neil ER, Quinn RE, Olson TL, Rycus PT, Anders MM, Chartan CA, Vogel TP, Silva-Carmona M, Coleman RD. Extracorporeal Membrane Oxygenation Support for Antineutrophil Cytoplasmic Antibody-associated Vasculitides: An ELSO Registry Analysis. ASAIO J. 2022 Apr 1;68(4):553-560. doi: 10.1097/MAT.0000000000001539. PMID: 34324445.
2. Yusuff H, Malagon I, Robson K, Parmar J, Hamilton P, Falter F. Extracorporeal membrane oxygenation for Life-threatening ANCA-positive pulmonary capillaritis. A review of UK experience. Heart Lung Vessel. 2015;7(2):159-67. PMID: 26157742; PMCID: PMC4476770.
3. Mark E McClure, Rona M Smith, Pasupathy Sivasothy, Lisa C Willcocks, Extracorporeal membrane oxygenation for life-threatening ANCA-associated vasculitis with pulmonary haemorrhage, Rheumatology, Volume 60, Issue Supplement_3, June 2021, Pages iii54–iii56, https://doi.org/10.1093/rheumatology/keab043
4. Wang, L., Wang, J., Xu, Y., Jiao, J., Xie, L., & Mo, G. 2021 Aug 12. A novel therapeutic strategy using extracorporeal membrane oxygenation in patients with anti-neutrophil cytoplasmic antibodies-associated vasculitis: a case report and literature review. Annals of Translational Medicine. [Online] 9:15

Association of A1AT Heterozygotes with Pulmonary Fibrosis and Mortality

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THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER

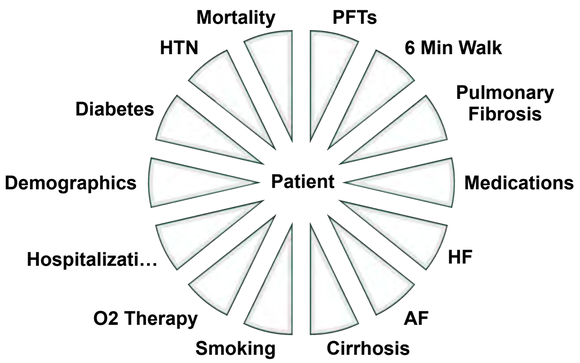
Background

- AAT deficiency is a rare disease associated with the development of early COPD and mortality
- The purpose of this study is to investigate the relationship of heterozygotes to the development of pulmonary fibrosis and all-cause mortality

Methods

- Cross-sectional study involving 1137 patients who underwent genetic testing between 2018-2023
- MM classified as “normal” (homozygotes)
- One abnormal allele was classified as abnormal (heterozygous)
- MS removed and combined with MM due to clinically less severe disease

DATA COLLECTION



Data

All-Cause Mortality				
Study	Age	Male Sex	Cirrhosis	COPD
MM + MS vs Heterozygotes	p = <.001 CI 1.03-1.07	p = .3	p = .010 CI 1.20 – 4.09	p = .3
MM (MS Removed) vs Heterozygotes	p = <.001 CI 1.03-1.07	p = .4	p = .018 CI 1.11 - 4.27	p = .2

Pulmonary Fibrosis				
Study	Age	Male Sex	Cirrhosis	COPD
MM + MS vs Heterozygotes	p = <.001 CI 1.01-1.05	p = .02 CI 1.07-2.2	p = .02	p = .001 CI .22-.60
MM (MS Removed) vs Heterozygotes	p = .004 CI 1.03-1.07	p = .031 CI 1.04-2.2	p = .078	p = .004 CI .27-.79

Results

- The mean age was 62.1 ± 1.1 years
- 62.5% of the population were males
- The mean pack-years smoked was 35.5

- For all-cause mortality, both the MM vs. heterozygotes & the combined MM + MS vs. heterozygotes were significant
  - Age
  - Cirrhosis
- For pulmonary fibrosis, there was significance for
  - Age
  - Male Sex
  - COPD

Conclusion

- As more entries have been recorded into our alpha-1 antitrypsin patient database, we have been experimenting with different methods to analyze our data
- Typically, MS genotypes are associated with a clinically less severe disease presentation
- Prior to this study, our research group was curious if including the MS patients in the heterozygous group was driving us towards the null hypothesis
- This study grouped the MS genotype with the MM genotype (combined model) and removed MS from both groups (removed model)
- There was no difference in which variables were statistically significant in relationship to all-cause mortality and pulmonary fibrosis

TIPS and Tricks: A Novel Technique For TIPS Graft Extraction in a Hypercoagulable Patient

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Introduction

The Transjugular Intrahepatic Portosystemic Shunt (TIPS) treats portal hypertension and end-stage liver disease by creating a shunt between the portal and hepatic veins via a catheter through the jugular vein[1]. While generally safe, TIPS rarely can cause coagulation, necessitating removal.

Learning Objectives

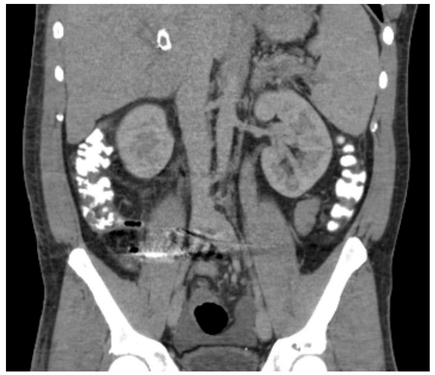
1. Identify patient-specific risk factors for re-occlusion of TIPS stent
2. Describe approaches to help manage cases of re-occlusion and stent removal
3. Understand the risks and benefits of different TIPS stent removal and retrieval techniques

Case Presentation

A 36-year-old male with an unspecified coagulopathy and previous successful TIPS placement presented with recurrent portal vein thrombosis involving the graft site following an initial positive response to the TIPS procedure. A CT scan (Figure 1) was performed and revealed a thrombus at the hepatic site of the TIPS stent and confirmed using CT angiography. The TIPS stent was determined to be the cause of the repeated PVT and deemed necessary for removal.

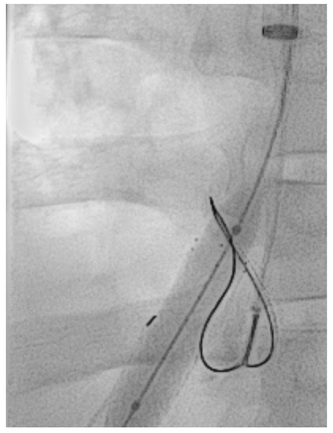
Under fluoroscopy, we inserted a balloon catheter into the TIPS stent and secured a loop snare around the inflated balloon. As the balloon deflated, we tightened the snare and advanced a vascular sheath over the structure and pulled on the system, causing the balloon-graft-snare complex to collapse into the sheath and ultimately allowing us to completely remove the stent. We proceeded to monitor our patient for further occlusions or clotting using contrasted imaging. No further occlusion occurred.

Figure 1



CT scan of occlusion at hepatic end extending into atrial-IVC junction.

Figure 2



A balloon with a loop snare was used to snare the free end of the graft, by advancing and inflating the balloon catheter within the stent and tightening the loop snare around the balloon, enabling removal of the collapsed complex.

Discussion

The Transjugular Intrahepatic Portosystemic Shunt (TIPS) is a well-established intervention; however, coagulopathies are among the significant complications[2] due to altered hemodynamics that result in thrombus formation within the shunt. Managing compilations starts with pre-procedural patient selection to mitigate the risk of thrombotic events with particular caution for patients with underlying coagulopathies such as disseminated intravascular coagulation (DIC)[3].

Although rare, when coagulative complications occur, management involves pharmacological and interventional approaches. Anticoagulation therapy is a common preventative approach but must be carefully monitored for bleeding[3]. When pharmacological management fails or in cases of stent migration to surrounding anatomy, mechanical stent removal becomes necessary[1] as in our patient.

However, there is limited literature on techniques for stent removal or replacement. Prior methods involve a variety of complex technical methods such as fluoroscopically using a snare to grasp and remove the stent[1], using specialized retrieval equipment to collapse and extract the stent[4], and repositioning of stent via using a balloon catheter to adjust positioning[5]. Repositioning is advantageous as it is less invasive so long as the stent remains intact and functional but is not an option in coagulative scenarios.

Conclusion

Prior literature describes methods to remove TIPS stents, such as mechanical snare retrieval and endovascular replacement, each with their own sets of complications and benefits. Interventionalists should prioritize preventing coagulation by thorough patient prescreening, utilizing preventative anticoagulation therapy, and emphasizing precision in stent placement to prevent occlusion. Our case underscores the importance of proactive monitoring to efficiently diagnose complications to determine course of action efficiently enhance patient outcomes in TIPS.

Question

What is a possible complication in using traditional TIPS stent removal techniques with endobronchial forceps?

A. Stent misalignment
B. Infection at the removal site
C. Development of a tear in the stent
D. Incomplete stent removal

References

1. Suhocki PV, Lungren MP, Kapoor B, Kim CY. Transjugular intrahepatic portosystemic shunt complications: prevention and management. Semin Intervent Radiol. 2015;32(2):123-132. doi:10.1055/s-0035-1549376.
2. Lee EW, Eghtesad B, Garcia-Tsao G, et al. AASLD Practice Guidance on the use of TIPS,variceal embolization, and retrograde transvenous obliteration in the management of variceal hemorrhage. Hepatology. 2024;79(1):224. Doi:10.1097/HEP.0000000000000530
3. Boike JR, Thornburg BG, Asrani SK, et al. North American Practice-Based Recommendations for Transjugular Intrahepatic Portosystemic Shunts in Portal Hypertension. Clin Gastroenterol Hepatol. 2022;20(8):1636-1662.e36. doi:10.1016/j.cgh.2021.07.018.
4. Cwikiel W, Bergenfeldt M, Keussen I. Endovascular Removal of the Viatorr Stent-Grafts. Report of Two Cases. Pol J Radiol. 2015;80:277-280. doi:10.12659/PJR.893642
5. Mirchia K, Thibodeau R, Goel A, et al. A successful endovascular repositioning of migrated transjugular intrahepatic portosystemic shunt (TIPS) stent. Radiol Case Rep. 2021;16(2):278-283. doi:10.1016/j.radcr.2020.11.010

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Vaping Induced Diffuse Alveolar Hemorrhage Complicated by Pericarditis in a 19-year-old: A Case Report

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Introduction

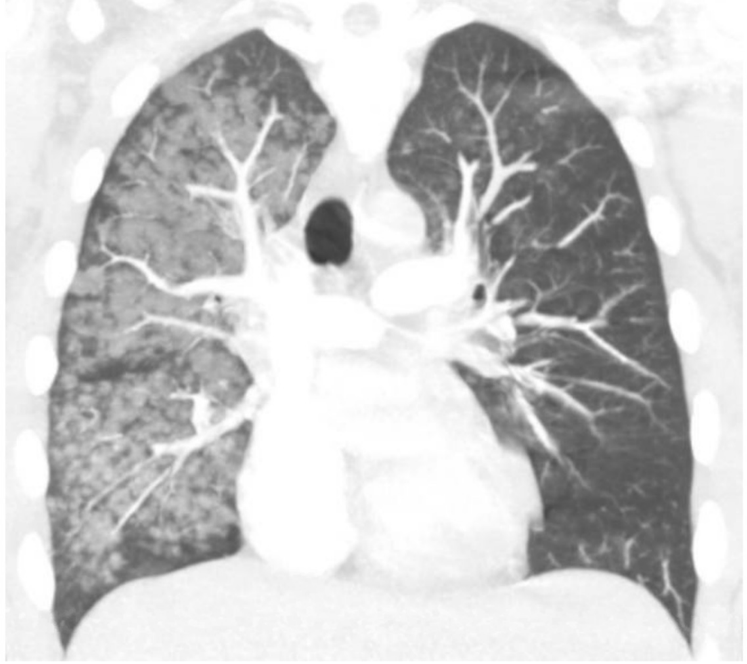
- Diffuse alveolar hemorrhage (DAH) has highly variable clinical presentation and is defined as bleeding into the alveolar spaces from the pulmonary microcirculation, often associated with vasculitis causing vascular injury.
- However, it can also originate from vascular inflammation due to inhalation or cytotoxic drug therapy
- Separately, pericarditis is a disease process defined by inflammation of the pericardial sac, the etiologies or which falls into infectious and noninfectious causes.
- Diagnosis requires at least two of the following findings: 1). Characteristic positional chest pain, 2). Pericardial friction rub, 3). Characteristic EKG changes, 4). New or worsening pericardial effusion
- Here, we present a case of a 19-year-old male with clinically diagnosed alveolar hemorrhage due to inhalational lung injury, complicated by pericarditis.

Case Description

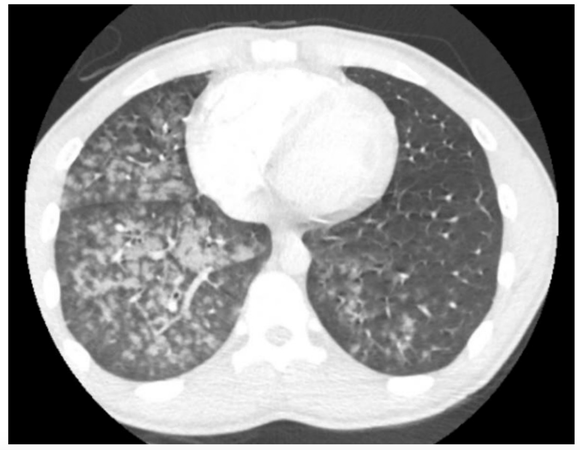
- Previously healthy 19 year old male presented with acute onset hemoptysis (approximately 250 mL) in the setting of chronic vaping/marijuana use since age 13, as well as new onset Percocet use (snorting). On arrival, he was anxious but otherwise well appearing and hemodynamically stable, in no respiratory distress, saturating well, with no further episodes of hemoptysis. CT chest was negative for PE and demonstrated a pattern consistent with diffuse alveolar hemorrhage. Labs for vasculitis/autoimmune causes of DAL were obtained including ANA, ANCA, anti-GBM, and QuantiFERON gold and were all unremarkable. Of note, he was found to have ST segment elevations with PR segment depression on EKG, and in the setting of positional chest discomfort and TTE demonstrating trace pericardial effusion, a diagnosis of pericarditis was made.

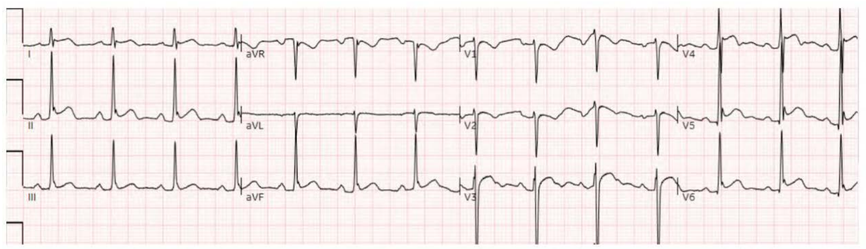
Discussion

A clinical diagnosis of DAH was made given the patient's history and imaging findings. Due to cessation of bleeding and lack of respiratory distress, pulmonology did not proceed with bronchoscopy. It is unclear if the patient's concomitant pericarditis was the consequence of his inhalational lung injury. Ultimately, he was treated with a regimen of colchicine 0.6 mg twice daily. Due to this patient's risk of bleeding, minimal symptoms of pericarditis, and high incidence of recurrence in patients treated with steroids for the first time, the decision was made not to initiate high-dose ibuprofen with taper. He was to follow up with cardiology, and obtain a repeat chest X-ray 3 months later.



CT PE: "Diffuse pulmonary nodules, right more than left. The pattern is compatible with diffuse alveolar hemorrhage, as can be seen in inhalational lung injury."





EKG on presentation: Diffuse ST segment change and PR depression, consistent with pericarditis.

Conclusion

The use of vaporized products has dramatically increased in recent years, and the medical complications still remain widely unknown. This report emphasizes the importance of pediatric and adult providers to be aware of the prevalence of vaping amongst their patients and to counsel patients on potentially life-threatening respiratory complications. Furthermore, as the rise of vaping continues, there must be an increased emphasis on research regarding pulmonary and cardiac toxicity of vaping.

References

1.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3651925/#:~:text=Abstract,diagnosis%20and%20rule%20out%20infection.
2.https://www.ncbi.nlm.nih.gov/books/NBK431080/
3.https://www.acc.org/Latest-in-Cardiology/ten-points-to-remember/2020/01/07/10/59/Management-of-Acute-and-Recurrent-Pericarditis

When a Common Virus Takes a Dangerous Turn: CMV and Splenic Infarctions

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Introduction

- Cytomegalovirus (CMV) is usually asymptomatic in immunocompetent patients.
- In immunocompromised, CMV can be complicated by thrombosis mainly reported as DVT or pulmonary embolism.
- This is a unique case of CMV - induced splenic infarctions in an immunocompetent patient .

Case Presentation

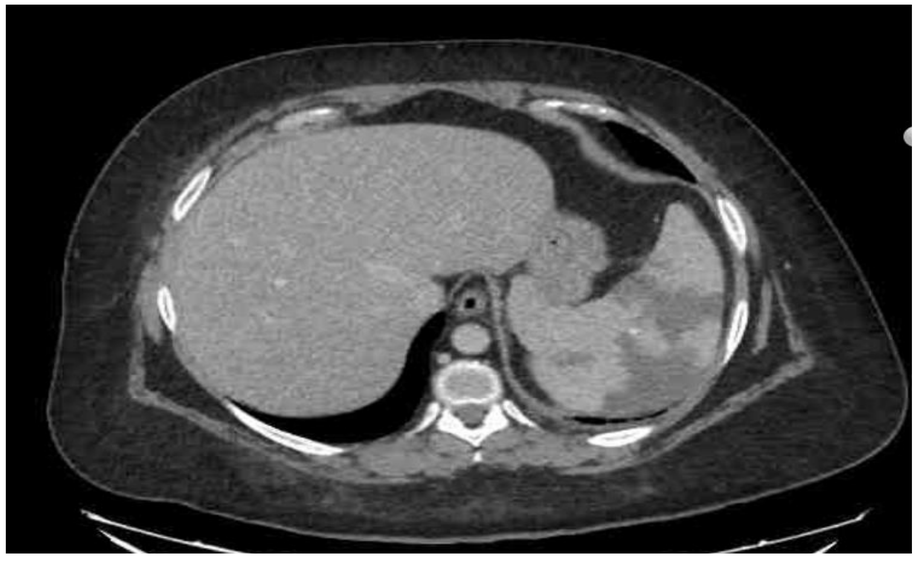
- A 42-year-old female with no significant past medical history presented to the hospital with complaints of worsening fever, cough, left sided abdominal pain, nausea and vomiting for 13 days.
- On presentation, vitals were pertinent for a heart rate of 124 and a fever of 100.7 °F.
- Physical examination was notable for left lower abdominal tenderness.
- Routine lab tests and a chest x- ray were normal.
- Viral screening showed CMV IgG elevated 3 times and IgM elevated 5 times above the normal limit.
- With supportive treatment, her fever and cough gradually improved; however, the abdominal pain persisted.
- Abdominal CT scan with contrast showed multiple regions of peripheral wedge shaped decreased attenuation, indicating splenic infarction.
- Therapeutic anticoagulation with heparin was initiated.
- Further workup revealed slightly raised levels of Anticardiolipin IgG and IgM antibodies, prolonged Lupus Anticoagulant and Lupus Anticoagulant PTT Mix.
- Protein C and S activity were within normal ranges, there was no evidence of the Factor V Leiden mutation.

Final Diagnosis /Follow up

- CMV induced splenic infarcts.
- She was discharged on oral apixaban and completed a total of 6 months of treatment.
- She followed up with the hematology clinic to confirm absence of coagulation disorders.
- A repeat ct scan was done 3 months later to insure resolution of infarcts.

Discussion

- Various mechanisms behind CMV- induced thrombosis have been suggested, such as vascular damage that triggers coagulation factors and enhances platelet and leukocyte adhesion.
- In our case, the most likely mechanism appears to be CMV- induced production of antiphospholipid antibodies.
- Despite elevated antibodies, the borderline level and lack of prior thrombosis or adverse pregnancy outcomes made antiphospholipid syndrome unlikely, confirmed by normal repeat antibody levels in follow-up visits.



Learning Points

- Recognize that CMV can lead to serious complications even in immunocompetent patients.
- Consider CMV among the differentials for a patient presenting with symptoms of viral infection and thrombosis, with no other obvious triggers.

A Multidisciplinary Treatment Approach for Thrombotic Cutaneous Gangrene Secondary to Vasculopathy in a Patient with Ulcerative Colitis

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Introduction

- Inflammatory bowel disease (IBD) patients are three times more hypercoagulable than the general population
- Thrombotic cutaneous gangrene is *diagnosed* in 6% of IBD patients with both well-controlled and uncontrolled disease, however, it is *found* in about 40% of postmortem examinations
- Etiology is multifactorial and may be due to:
  - Underlaying endothelial damage
  - Altered levels of coagulation enzymes
  - Increased anticoagulation antibodies
  - Therapy side effects
- Factors Va, VIIa, VIIIa, Xa, fibrinogen, von Willebrand factor, platelets and cryoglobulins are usually elevated
- Antithrombin III, protein C and S are decreased due to protein losing enteropathy
- Treatment includes anticoagulation and systemic IBD therapy, but is not standardized

Case Presentation

- 51-year-old African American female with poorly controlled ulcerative colitis on Ustekinumab
  - Presented with right flank bruising, nausea, dizziness and 15lb weight loss; CT showed pan colitis
  - No prior history of thrombosis or anticoagulation use
  - Discharged on antibiotics and topical ointment
- Re-presented with bruising, blistering and drainage of her left flank, toe bruising and left peri-areolar erythema
  - Given IV steroids, vitamin K and cryoprecipitate; hypercoagulable workup initiated
  - Skin lesions became gangrenous and tender; biopsy showed focal dermal hemorrhage, mixed diffuse inflammatory infiltrates
  - Colonoscopy confirmed severe acute pan-colitis
- Treatment: IV solumedrol then oral prednisone, one infusion of infliximab, heparin drip, argatroban transitioned to apixaban
- Left flank infarcted and she underwent excision and debridement down to muscle fascia; managed with negative pressure wound therapy dressing, transitioned inpatient to outpatient
- She has since returned with another flare, indicating biologics failure and is being assessed for a total colectomy

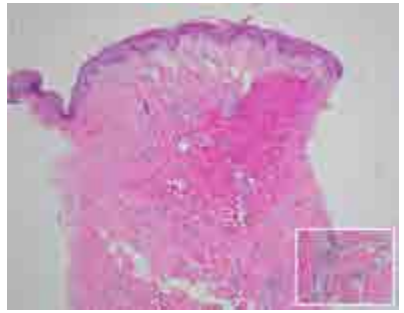

Figure 1. Biopsy showed focal dermal hemorrhage and mixed diffuse inflammatory infiltrates

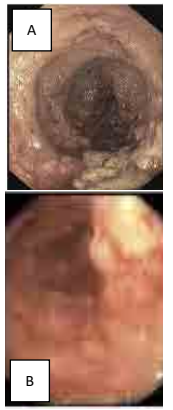

Figure 2. Unchanged sigmoid (A) before (B) after biologics

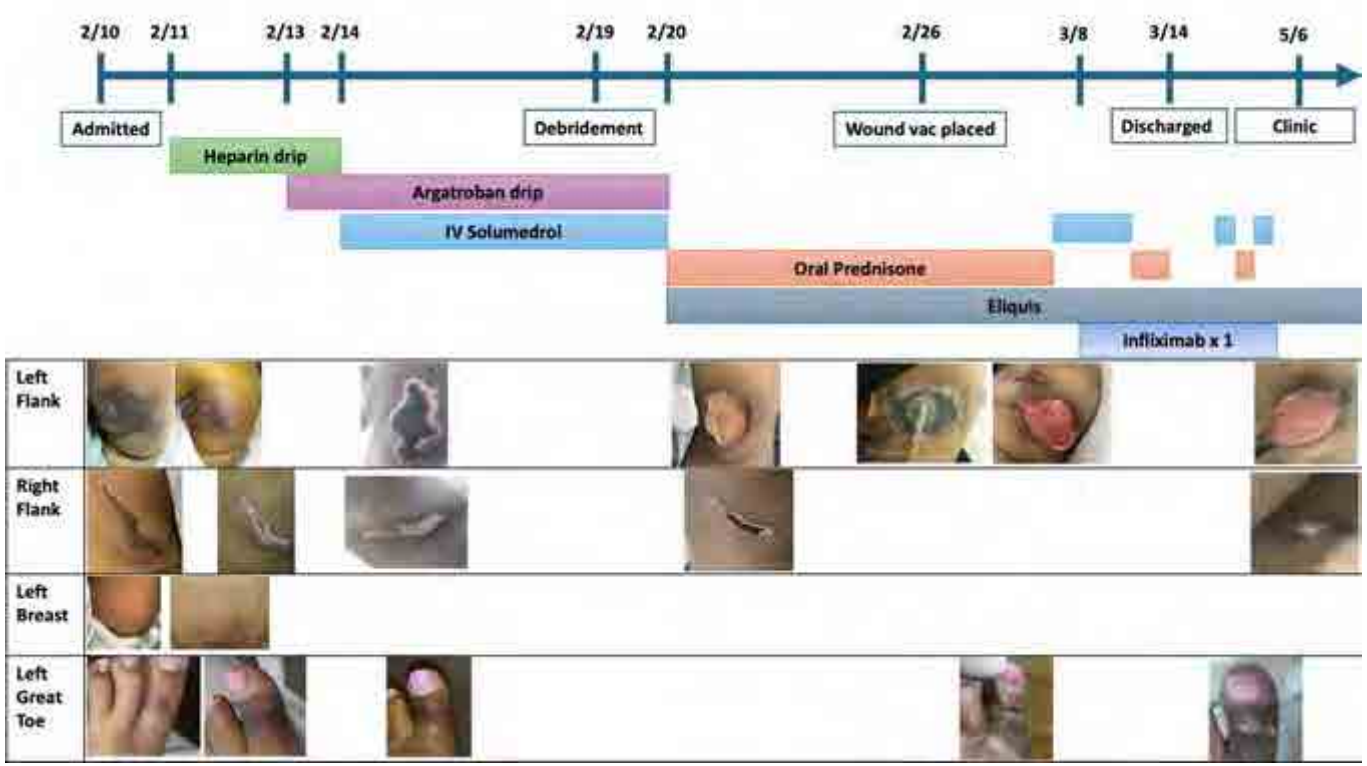

Figure 3. Timeline of treatment durations and affects on skin lesions

Patient	Anticoagulation	IBD treatment	Worsening	Resolution	Other
33yo WF	✓	✓		✓	
33yo WF	✓			✓	
29 MiM		✓		✓	
38 WM	✓	✓	✓		Amputation
57 WM	✓		✓	✓	Skin graft
36 F	✓	✓	✓		GI Bleed, Death

Figure 4. Similar case presentations in the literature and response to therapy
W= white, F = female, M = male, Mi = mixed race

Coagulation Factors		
	IBD patients	Our Patient
Fibrinogen	Increased	Decreased
Factor V	Increased	Decreased
Factor VIII	Increased	Slightly increased
Plasma coagulation inhibitors		
Antithrombin III	Decreased	Decreased

Figure 5. Changes in coagulation and fibrinolytic systems in patients with IBD as compared to our patient

Rationale/Lessons Learned

Our algorithm was driven by our patient's symptoms. A combination of wound breakdown and increasing pain, prompted us to debride her wound. Dressing change sensitivity and need to speed up granulation led us to place a wound vac.

Management/Outcome/Follow-up

These lesions are diverse in presentation and treatment response, occurring both in well and poorly controlled disease. Yet, vasculopathies are known to follow a set life cycle. Is there a fundamental difference in patients who develop these lesions? Does the histopathological life stage of a lesion affect treatment response? A better understanding of the pathophysiology can help devise a targeted prevention, treatment and follow-up strategy.

References

-Barahimi, M., Lee, S., Clark-Snustad, K. (2021). Pustular Rash in Crohn's Patient on Ustekinumab Raises Concern for Drug-Induced Paradoxical Psoriasis. *Case Reports in Gastroenterology. 15 (1),* 662-666.
-Barros, L. L., *et al.* (2023). Fatal Presentation of Thrombotic Cutaneous Gangrene Associated With Acute Severe Colitis. *The American Journal of Gastroenterology. 118(12S),* S28.
-Bernett, C. N., Krishnamurthy, K. (2023). Cutaneous Crohn Disease. StatPearls. http://www.ncbi.nlm.nih.gov/books/NBK470311/
-Cheeley, J., Morales-Pico, B., John, S. (2018). Cutaneous thrombotic vasculopathy related to poorly controlled ulcerative colitis. *Journal of American Academy of Dermatology Case reports. 4 (1),* 672-4.
-Chu, C.H., Davis, C. (2017). Urticarial Reaction to Ustekinumab during the treatment of plaque psoriasis in a hepatitis c-positive patient. *Drug Safety Case Reports. 4(1),*9.
-Galambus, J., *et al.* (2022). Thrombotic cutaneous gangrene associated with ulcerative colitis. *Journal of American Academy of Dermatology Case Reports. 28 (1),* 71-73.
-Komatsu, Y. C., *et al.* (2013). Skin gangrene as an extraintestinal manifestation of inflammatory bowel disease. *Anais Brasileiros de Dermatologia. 89(6),* 967-969.
-Kong, L., *et al.* (2023) Development of bullous pemphigoid during treatment of psoriasis with ustekinumab: a case report and literature review. *Frontiers in Medicine.*
-Owczarek, D., *et al.* (2014). Inflammatory bowel disease: Epidemiology, pathology and risk factors for hypercoagulability. *World Journal of Gastroenterology. 20(1),* 53-63.
-Santiago, M.B., Paz, A. (2019). Acute peripheral and/or Cutaneous ischemic syndrome. *Journal of Clinical Rheumatology. 27(2),* 73-79.
-Seyedian, S. S., Nokhostin, F., Malamir, M.D. (2021). A review of the diagnosis, prevention and treatment methods of inflammatory bowel disease. *Journal of Medicine and Life. 12(2),* 113-122
-Singh, S., Noshirwani, K. (1996). An unusual cutaneous manifestation of ulcerative colitis: thrombotic skin gangrene. *Postgraduate Medicine Journal. 72(852),* 623-4.
-Wilk, M., Zelger, B.G., Zelger, B. (2023). Vasculitides and occluding vasculopathies, challenges in recognizing histopathological patterns and their solutions. *Frontiers in Medicine. 9(1).*
-Yu, M.A., *et al.* (2016). Thrombotic Cutaneous Gangrene: A Rare Dermatologic and Hematologic Extraintestinal Manifestation of Ulcerative Colitis. *The American Journal of Gastroenterology. 113(1),* S1193-4.
-Zezos, P., *et al.* (2009). Elevated markers of thrombin generation and fibrinolysis in patients with active and quiescent ulcerative colitis. *Med Sci Monit. 15(11),* CR563-72.
-Zhang, J., *et al.* (2017). D-Dimer levels are correlated with disease activity in Crohn's patients. *Oncotarget. 8(38),* 63971-63977.

Disclosures: None

A Rare Cause of Miliary Pattern Lung Disease in a Patient with History of Tuberculosis

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Introduction

A chronic cough and a miliary pattern on chest imaging have a broad differential including bacterial infections, fungal infections, immune sources, and lastly malignant processes. We report a case of a 53-year-old female with a history of latent tuberculosis who had completed a 6-month treatment with isoniazid upon immigration from a tuberculosis endemic area, who presents with a 5-month history of cough, fatigue, weight loss and night sweats.

Case Summary

A 53-year-old female with history of latent tuberculosis treated with 6 months of Isoniazid presented to her PCP with a 5-month history of cough, weight loss and night sweats. She immigrated from the Philippines 35 years prior. She concurrently experienced a 10-pound weight. Physical exam and vitals were unremarkable. CXR showed diffuse pulmonary micronodules concerning for miliary tuberculosis (Figure 1, a). Patient was sent to the emergency department. Labs showed elevated alkaline phosphatase with bone and liver isoenzyme elevated. Labs were otherwise normal. Chest CT showed innumerable pulmonary nodules with a dominant nodule in the left upper lobe, a small left sided pleural effusion, pleural thickening, and multiple sclerotic osseus lesions (Figure 1, b). Infectious work up was negative. Endobronchial biopsy was then pursued showing poorly differentiated adenocarcinoma. The molecular analysis showed a EGFR mutation. Staging showed bone and brain metastases. She underwent radiation to pelvic and sacral metastases and initiated tyrosine kinase inhibitor therapy with Osimertinib. One year later she shows no evidence of metastatic disease on imaging

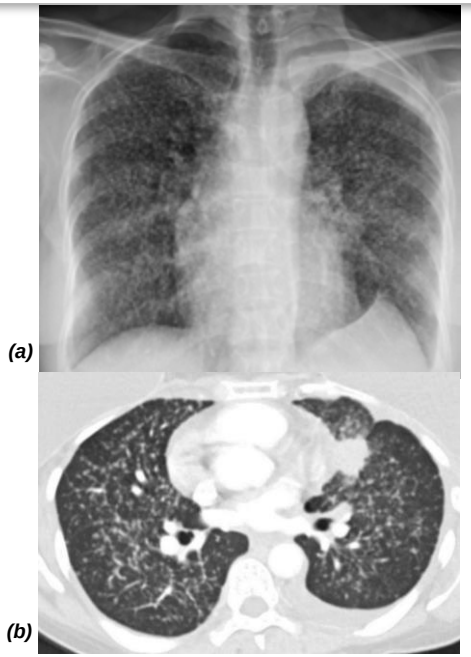

Figure 1. (a) Radiograph of the chest, AP view, showing diffuse pulmonary micronodules. (b) CT of the Chest, Axial View, showing diffuse pulmonary micronodules and left upper lobe dominant nodule.

Discussion

- Lung adenocarcinoma is the most common primary lung cancer, with a mean age of diagnosis at 71 and a male predominance.[1,2]
- It is commonly discovered incidentally on imaging in an asymptomatic individual but can present with a cough, unintentional weight loss, shortness of breath or hemoptysis.[2]
- Well-known risk factors include tobacco use and occupational exposures to silica, asbestos, radon, heavy metals, and diesel fumes[2].
- A past tuberculosis infection is a lesser-known independent risk factor for developing lung cancer in young patients, regardless of smoking history.[3]
- The differential of the miliary pattern on chest imaging include bacterial infections such as tuberculosis, mycoplasma and nocardia, fungal infections such as histoplasmosis and blastomycosis, immune sources including hypersensitivity pneumonitis and sarcoidosis, and lastly malignant processes (specifically EGFR positive NSCLC)[4,5,6].
- Due to the risk of early brain metastasis associated with EGFR positive lung adenocarcinoma[7], early diagnosis and treatment is vital.

Key Points

- There is a wide differential for chronic cough and miliary pattern on chest imaging and the etiologies have significant overlap in clinical presentation.
- A past infection with tuberculosis is a lesser-known risk factor for lung cancer in young patients, independent of smoking history.
- Miliary pattern lung cancer is concerning for EGFR positive adenocarcinoma, which has been associated with distant metastasis to the brain making timely diagnosis and treatment crucial.

References

(1) Myers DJ, Wallen JM. Lung Adenocarcinoma. In: StatPearls. Treasure Island (FL): StatPearls Publishing; June 12, 2023.
(2) May L, Shows K, Nana-Sinkam P, Li H, Landry JW. Sex Differences in Lung Cancer. Cancers (Basel). 2023;15(12):3111. Published 2023 Jun 8. doi:10.3390/cancers15123111
(3) Hwang SY, Kim JY, Lee HS, et al. Pulmonary Tuberculosis and Risk of Lung Cancer: A Systematic Review and Meta-Analysis. J Clin Med. 2022;11(3):765. Published 2022 Jan 30. doi:10.3390/jcm11030765
(4) Mitsudomi T, Yatabe Y. Epidermal growth factor receptor in relation to tumor development: EGFR gene and cancer. FEBS J. 2010;277(2):301-308. doi:10.1111/j.1742-4658.2009.07448.x
(5) Togashi Y, Masago K, Kubo T, et al. Association of diffuse, random pulmonary metastases, including miliary metastases, with epidermal growth factor receptor mutations in lung adenocarcinoma. Cancer. 2011;117(4):819-825. doi:10.1002/cncr.25618
(6) Sharma BB. Miliary nodules on chest radiographs: A diagnostic dilemma. Lung India. 2015;32(5):518-520.
(7) Tan L, Wu Y, Ma X, et al. A Comprehensive Meta-Analysis of Association between EGFR Mutation Status and Brain Metastases in NSCLC. Pathol Oncol Res. 2019;25(2):791-799. doi:10.1007/s12253-019-00598-0

Southern Medical Association Virtual Abstract Competition 2024

Northeast Georgia Medical Center
GRADUATE MEDICAL EDUCATION

Giant Cell Arteritis Presenting as Lingual Necrosis

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Background

- Giant Cell Arteritis (GCA) is an immune-mediated medium/large vessel vasculitis that can manifest as systemic, neurologic, or ophthalmologic complications.
- Presentation: scalp tenderness, headaches, jaw or tongue claudication, myalgias, transient ischemic attacks, and vision changes
- Incidence: ~10 /100,000 people
- Prevalence: Caucasian, Females >age of 50, Peak at 70 years
- Vascular aging plays a key role in the development of GCA, although several risk factors such as vascular disease, smoking, early menopause, low body mass index and expression of major histocompatibility complex molecules, particularly HLA-DRB1, have been linked with disorder
- According to the American College of Rheumatology (ACR), GCA is diagnosed after fulfilling 4 of the 5 criteria:
    - Age over 50 years
    - Reduced temporal pulse
    - New-onset headache
    - ESR greater than 50 mm/h
    - Abnormal temporal artery biopsy

Initial Presentation

- 83-year-old female with past medical history significant for mild Alzheimer's dementia, carotid artery disease, coronary artery disease, hypertension, and hyperlipidemia who presented to the emergency department with concerns of severe headache, nausea, vomiting, altered mental status, dysarthria, dysphagia, diplopia, and transient left arm weakness.
- Vitals - unremarkable
- Laboratory values – WBC 14.9 K/uL, Na 133 mEq/L, HST 213 ng/L
- Physical Examination - chronic anisocoria, agitation, moderate dysarthria and dysphagia, and normal strength of the upper and lower extremities
- Admitted for stroke-like symptoms; however, the stroke work-up was negative and she was deemed as having a transient ischemic attack.

Case Presentation

- On day 2, she developed white-gray discolorations of her tongue with small lesions and plaques on the right lateral tongue resembling thrush or leukoplakia.
- The lesions progressed to nodular ulcerations with restricted tongue movement and hyponasal quality to her voice over the next seven days.
- There were no ulcerations noted in the buccal cavity itself.
- CT maxillofacial showed no obvious soft tissue inflammation or airway narrowing.
- She was treated with oral nystatin solution and fluconazole for glossitis with oral thrush.
- The tongue discoloration transitioned to a diffuse blackish appearance with a large right sided tongue ulceration after 10 days noted in Figure 1a-b.

Figure 1a-b

Case Presentation

- Laboratory values – **ESR 105 mm, CRP 13.8 mg/dL**
- Figure 2a-c showed CT soft tissue neck – **2.5 by 3 cm heterogenous, necrotic or cystic enhancement of the anterior tongue extending down to the floor of the mouth concerning for a necrotic tumor versus vascular-induced necrosis.** There was **no focal artery occlusion**, however a slightly **asymmetrical vascularity** was noted with the lingual arteries concerning for vasculitis on the CTA head and neck.

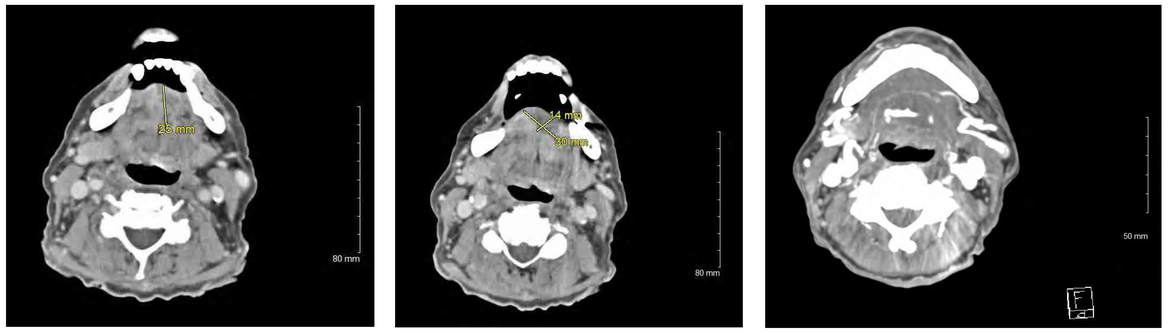


Figure 2a-c

- **ID** and **ENT** specialists were consulted due to concerns of tongue necrosis.
- Oral swab returned positive for **HSV-1** and she was started on IV **Acyclovir**.
- She completed a 5-day course of cefepime.
- A **lingual biopsy** was recommended, however the patient's family declined.
- **Rheumatology** was consulted to rule out giant cell arteritis and other vasculitis as the underlying etiology of the tongue necrosis.
- She was started on **high dose steroids** of IV solumedrol 60 mg per day for 7 days for clinical suspicion of vasculitis and empiric IV piperacillin-tazobactam for secondary oral infections.
- **CTA aorta thoracic** revealed mild atherosclerosis of the aorta without findings of aortitis.
- ID recommended continuation of acyclovir for 6 weeks as HSV is known to cause vasculopathy and likely contributed to the progression of tongue necrosis.
- A **temporal biopsy** was also recommended, however the patient's family declined.
- She tested negative for **anti-proteinase 3** and **myeloperoxidase antibodies** ruling out granulomatosis with polyangiitis.
- The hospitalization was complicated by worsening encephalopathy with significant lethargy. IV steroids were transitioned to oral steroids for possible steroid-induced psychosis, and acyclovir was also replaced by valacyclovir to reduce risk of neurotoxicity. The patient's mentation gradually improved, and the tongue necrosis stabilized without any further progression.
- After approximately 4 weeks, the family consented for debridement and biopsy the tongue. **The biopsy revealed ulcerated squamous mucosa with marked reactive changes and chronic inflammation without signs of malignancy** (Figure 3a-c).

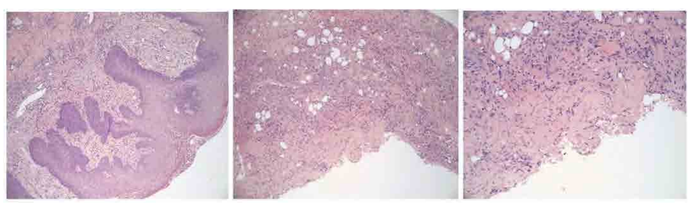


Figure 3a-c

- The biopsy results were consistent with autoimmune conditions such as vasculitis.
- Rheumatology prescribed a **steroid taper** upon discharge starting at prednisone 60 mg daily. The prednisone dose was decreased by 10 mg every 7 days. The option of trialing Tocilizumab was discussed with the family, however they requested to hold off on immunosuppressive therapy.
- Upon discharge, laboratory values noted improvement in inflammatory markers. Patient was scheduled to follow up with a Head/Neck Cancer and Reconstructive Surgeon after discharge for microvascular free flap to maintain tongue mobility and prevent tethering.
- Patient was discharged with Rheumatology follow-up for continued management of giant cell arteritis and steroid taper.

Discussion

- **Gold Standard - Histopathology** from the biopsy revealing transmural inflammation, multinucleate giant cells and in certain cases focal fibrinoid necrosis.
- **Lingual necrosis causes** – malignancy, medication side effects, radiation and chemotherapy exposure, embolism or hemorrhage and infectious (syphilis, herpes and tuberculosis)
- Systemic vasculitis such as Anti-Neutrophil Cytoplasmic Antibody (ANCA) positive vasculitis, most commonly granulomatosis with polyangiitis, can also present with tongue necrosis.
- Tongue necrosis and vision loss associated with GCA are irreversible complications that can lead to permanent vision loss or tongue amputation.
- **High dose glucocorticoids should be initiated as soon as GCA is suspected**, even prior to biopsy, if there is strong clinical suspicion.
- According to the European League Against Rheumatism (EULAR) guidelines, patients with active GCA should be given an initial **40-60 mg/day of prednisone-equivalent dosage immediately to induce remission of active disease**
- **In cranial ischemic symptoms, such as amaurosis fugax or vision loss, pulse steroids with IV methylprednisolone 0.25-1 g/day for three days is advised to decrease long term prognosis of permanent vision loss.**
    - Treatment should be followed with oral steroids at 40-60 mg of oral prednisone daily, which can be adjusted in regard to pre-existing health conditions and concerns for steroid side effects
- **Studies showed that administration of doses higher than 60 mg/day would exceed receptor saturation after several days resulting in genomic and nongenomic side effects**
- There is an increasing use of immunosuppressants as adjuvant therapy to minimize total exposure to glucocorticoids as long-term steroids use can lead to higher risks of infection, cardiovascular disease, osteoporosis, osteonecrosis, and diabetes amongst other known less- desired side effects
- **According to the Giant-Cell Arteritis Actemra (GiACTA) trial, patients treated with tocilizumab at 162 mg weekly or biweekly + a 26-week prednisone taper sustained GCA remission with greater disease control and fewer flares.**
- In Min Cho et al., the patient received a single dose of IV tocilizumab at 6 mg/Kg with clinical improvement within several days despite previous steroid therapy resistance.
- However, tocilizumab has not yet been proven to act as a first-line treatment.
- There was limited evidence, or no benefit found with use of Methotrexate, TNF-a inhibitors, such as infliximab and etanercept, or purine analog, azathioprine.
- Several cases documented autoamputation of the necrotic region and appropriate reepithelization after several weeks

References

- Brar AS, Nanda R, Narayanan R, Pathy SK. Giant Cell Arteritis With Bilateral Central Retinal Artery Occlusion and Tongue Necrosis. Cureus. 2024 May 2;16(5):e59554. doi: 10.7759/cureus.59554. PMID: 38826883; PMCID: PMC11144274.
- Bilton EJ, Mollan SP. Giant cell arteritis: reviewing the advancing diagnostics and management. Eye (Lond). 2023 Aug;37(12):2365-2373. doi: 10.1038/s41433-023-02433-y. Epub 2023 Feb 14. PMID: 36788362; PMCID: PMC9927056.
- Ciofalo A, Gualtieri G, Iannella G, Pasquariello B, Manno A, Angeletti D, Pace A, Greco A, Allegorie G, de Vincentiis M, Magliulo G. Giant Cell Arteritis (GCA): Pathogenesis, Clinical Aspects and Treatment Approaches. Curr Rheumatol Rev. 2019;15(4):259-268. doi: 10.2174/1573397115666190227184014. PMID: 30807250.
- Cho, Y.M., El-Koury, L., Paramo, J. et al. Tongue necrosis secondary to giant cell arteritis, successfully treated with tocilizumab: a case report. BMC Musculoskelet Disord 24, 382 (2023). https://doi.org/10.1186/s12891-023-06465-z
- Cho YM, El-Koury L, Paramo J, Horowitz DM, Li JY, Kello N. Tongue necrosis secondary to giant cell arteritis, successfully treated with tocilizumab: a case report. BMC Musculoskelet Disord. 2023 May 15;24(1):382. doi: 10.1186/s12891-023-06465-z. PMID: 37189114; PMCID: PMC10184088.
- Grayson PC, Ponte C, Suppiah R, Robson JC, Gribbons KB, Judge A, Craven A, Khalid S, Hutchings A, Sreeda D, Luqmani RA, Watts RA, Merkel PA; DCVAS Study Group. 2022 American College of Rheumatology/EULAR classification criteria for Takayasu arteritis. Ann Rheum Dis. 2022 Aug;81(8):1106-1114. doi: 10.1136/ard-2022-223482. Epub 2022 Aug 4. PMID: 35933154.
- Rose EC, Carroll LS, Evans S, Mayer A. Giant cell arteritis complicated by tongue necrosis and bilateral cerebellar ischaemic stroke. BMJ Case Rep. 2021 Dec 8;14(12):e244846. doi: 10.1136/bcr-2021-244846. PMID: 34880035; PMCID: PMC8655573.
- Hellmich B, Agueda A, Monti S, Buttgereit F, de Boysson H, Brouwer E, Cassie R, Cid MC, Dasgupta B, Dejaco C, Hatemi G, Hollinger N, Mahr A, Mollan SP, Mukhtyar C, Ponte C, Salvarani C, Sivalingam R, Tan K, Tomasson G, Turesson C, Schmitt W, Villiger PM, Watts R, Young C, Luqmani RA. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis. 2020 Jan;79(1):19-30. doi: 10.1136/annrheumdis-2019-215672. Epub 2019 Jul 3. PMID: 31270110.
- Mollan SP, Gr edh O, O'Sullivan E, Mackie SL. Practice points for ophthalmologists from the 2020 British Society for Rheumatology Giant Cell Arteritis guidelines. Eye (Lond). 2021 Mar;35(3):699-701. doi: 10.1038/s41433-020-1090-y. Epub 2020 Jul 16. PMID: 32678347; PMCID: PMC8027007.
- Villiger PM, Adler S, Kuchen S, Wermelinger F, Dan D, Fiege V, Bütikofer L, Seitz M, Reichenbach S. Tocilizumab for induction and maintenance of remission in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet. 2016 May 7;387(10031):1921-7. doi: 10.1016/S0140-6736(16)00560-2. Epub 2016 Mar 4. PMID: 26951241.
- Pinjus R, Hansen MS, Hamann S, Mollan SP. An update on the clinical approach to giant cell arteritis. Clin Med (Lond). 2022 Mar;22(2):107-111. doi: 10.7861/clinmed.2022-0041. PMID: 35304369; PMCID: PMC8966800.
- Buttgereit F, Dejaco C, Matteson EL, Dasgupta B. Polymyalgia Rheumatica and Giant Cell Arteritis: A Systematic Review. JAMA. 2016 Aug 23-30;316(8):836-44. doi: 10.1001/jama.2016.9029. PMID: 27552619.
- Buttgereit F, da Silva JA, Boers M, Burmester GR, Cutolo M, Jacobs J, Kirwan J, Kohler L, Van Riel P, Wiek C, Bijlsma JW. Standardised nomenclature for glucocorticoid dosages and glucocorticoid treatment regimens: current questions and tentative answers in rheumatology. Ann Rheum Dis. 2002 Aug;61(8):718-22. doi: 10.1136/ard.61.8.718. PMID: 12117676; PMCID: PMC1754186.
- Ponte C, Rodrigues AF, O'Neill L, Luqmani RA. Giant cell arteritis: Current treatment and management. World J Clin Cases. 2015 Jun 16;3(6):484-94. doi: 10.12998/wjcc.v3.i6.484. PMID: 26090367; PMCID: PMC4468993.
- Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, Brouwer E, Cid MC, Dasgupta B, Rech J, Salvarani C, Schett G, Schulz-Kuoja H, Sparks R, Unizony SH, Collinson N, Trial of Tocilizumab in Giant-Cell Arteritis N Engl J Med. 2017 Jul 27;377(4):317-328. doi: 10.1056/NEJMoa1613849. PMID: 28745999.
- Stone JH, Han J, Aringer M, Blockmans D, Brouwer E, Cid MC, Dasgupta B, Rech J, Salvarani C, Spiera R, Unizony SH, Bao M; GiACTA investigators. Long-term effect of tocilizumab in patients with giant cell arteritis: open-label extension phase of the Giant Cell Arteritis Actemra (GiACTA) trial. Lancet Rheumatol. 2021 May;3(5):e358-e336. doi: 10.1016/S2665-9913(21)00038-2. Epub 2021 Mar 19. PMID: 38279290.
- Spiera RF, Mitnick HJ, Kupersmith M, Richmond M, Spiera H, Peterson MG, Paget SA. A prospective, double-blind, randomized, placebo controlled trial of methotrexate in the treatment of giant cell arteritis (GCA). Clin Exp Rheumatol. 2001 Sep-Oct;19(5):495-502. PMID: 11579844.
- Hoffman GS, Cid MC, Rendt-Zagar KE, Merkel PA, Weyand CM, Stone JH, Salvarani C, Xu W, Visvanathan S, Rahman MU, Infliximab-GCA Study Group. Infliximab for maintenance of glucocorticosteroid-induced remission of giant cell arteritis: a randomized trial. Ann Intern Med. 2007 May 1;146(9):621-30. doi: 10.7326/0003-4819-146-9-200705010-00004. PMID: 17470830.
- Martínez-Taboada VM, Rodríguez-Valverde V, Carreño L, López-Longo J, Figueroa M, Belzunegui J, Moya EM, Bonilla G. A double-blind placebo controlled trial of etanercept in patients with giant cell arteritis and corticosteroid side effects. Ann Rheum Dis. 2008 May;67(5):625-30. doi: 10.1136/ard.2007.082115. Epub 2007 Dec 17. PMID: 18086726.
- Zaragoza JR, Ivanov R, Chaffart-Sí, Tongue necrosis as an initial manifestation of giant cell arteritis: case report and review of the literature. Case Rep Rheumatol. 2015;2015:901795. doi: 10.1155/2015/901795. Epub 2015 Jan 31. PMID: 25802790; PMCID: PMC4329787.
- Cantín De Sesone J, Gutiérrez Guédez LA, Rodríguez Cambrón AB, Burgos F. Tongue necrosis secondary to giant cell arteritis. BMJ Case Rep. 2023 May 16;16(5):e254888. doi: 10.1136/bcr-2023-254888. PMID: 37192780; PMCID: PMC10193075.

The Southern Medical Association and the Evolution of Medical Research

Thomas F. Heston MD FACNM

Clinical Associate Professor
Washington State University

Presented at the Southern Medical Association's 116th Annual Meeting 2024
Atlanta, GA

Disclosure

I do not have any relevant financial interests or conflicts of interest to disclose related to the content of this presentation.

Learning Objectives

1. Understand key milestones in medical research.
2. Explore current trends and technologies.
3. Discuss the future of medical research.

Major Advances in Medicine and Bioethics: 1910-2024

Time	Medical Advances	Applications	Methodology & Ethics
1910s	Infectious disease and sanitation	Public health campaigns	Observational studies and case-based learning; no ethical oversight of research
1920s	Surgical advancements	Sterilization, aseptic techniques	Early discussions on research standardization
1930s	Cardiology as a specialty	Introduction of the EKG	The AMA begins addressing ethics in research
1940s	Antibiotic research	PCN, sulfa in WWII	Nuremberg (1947): informed consent, voluntary
1950s	Vaccines	Salk polio vaccine	Thalidomide scandal (1957-1961)
1960s	Cardiovascular surgery	First successful CABG	RCTs & data standardization
1970s	Oncology, chemotherapy	Multi-agent therapies	Belmont Report (autonomy, beneficence, justice) in response to the Tuskegee Syphilis Study (1932-1972)
1980s	HIV/AIDS treatments	Antiretroviral therapies	FDA Phase I-IV clinical trials
1990s	Genomic research	Human Genome Project	Expansion of role of IRBs
2000s	Stem cell research	Tissue regeneration	Patient safety & adverse event reporting
2010s	Personalized medicine	CAR-T, immunotherapy	Integration of EHRs in clinical research
2020s	COVID-19, AI	mRNA vaccines	Development of pandemic-related ethics

Key Milestones in Medical Research 1910 - 1960

- **1910s. Early focus on infectious diseases and surgery**
  - SMA first annual meeting was in **1906**. Early meetings focused on sanitation, public health
  - SMJ inaugural issue was **July, 1908** (*Wood EG. Clinical Notes on Apoplexy 1908;1(1):1)*
  - Mortality rates in major surgeries were 25-30% prior to **aseptic technique**
- **1920s - 1930s. Bacteriology and antimicrobial era**
  - SMA meetings discussed **serum therapy**, reducing fatality diphtheria rates from 50% to 10%
  - **PCN** discovered in 1928 & **sulfonamide** in 1932 marking the start of the antibiotic era.
- **1940s. Advancements during World War II**
  - **Blood transfusion** techniques saved thousands of lives; PCN; beginning of EM specialty
- **1950s. Surge in surgical innovations**
  - **Heart-lung machine** enabled longer and more complex cardiac operations
  - **CABG**, artificial valves

PROGRAM

OF THE

SOUTHERN MEDICAL ASSOCIATION

FOURTH ANNUAL MEETING

NASHVILLE, TENN.

November 8, 9, 10, 1910.

Southern Medical Association

FIRST GENERAL MEETING

Auditorium of Y. W. C. A.

Seventh Avenue, North, Between Church and Union Sts.

TUESDAY, NOV. 8, 10.00 A. M.

Call to order by Chairman Committee on Arrangements.

Prayer by Dr. R. M. Inlow, Pastor First Baptist Church, Nashville, Tenn.

Address of Welcome, W. D. Haggard, Nashville.

Response to Address of Welcome, Seale Harris, Mobile, Ala.

Introduction of President W. W. Crawford, Hattiesburg, Miss.

Report of Committee on Arrangements, G. C. Savage, Chairman.

Report of Vice Presidents.

Report of Councilors.

Report of Secretary-Treasurer.

Election of Nominating Committee.

Business.

Address by J. B. Murphy, President-elect A.M.A., Chicago.

Adjournment for Dinner.

SOUTHERN MEDICAL JOURNAL

PUBLISHED MONTHLY

VOLUME I NASHVILLE, TENN., JULY, 1908 NUMBER I

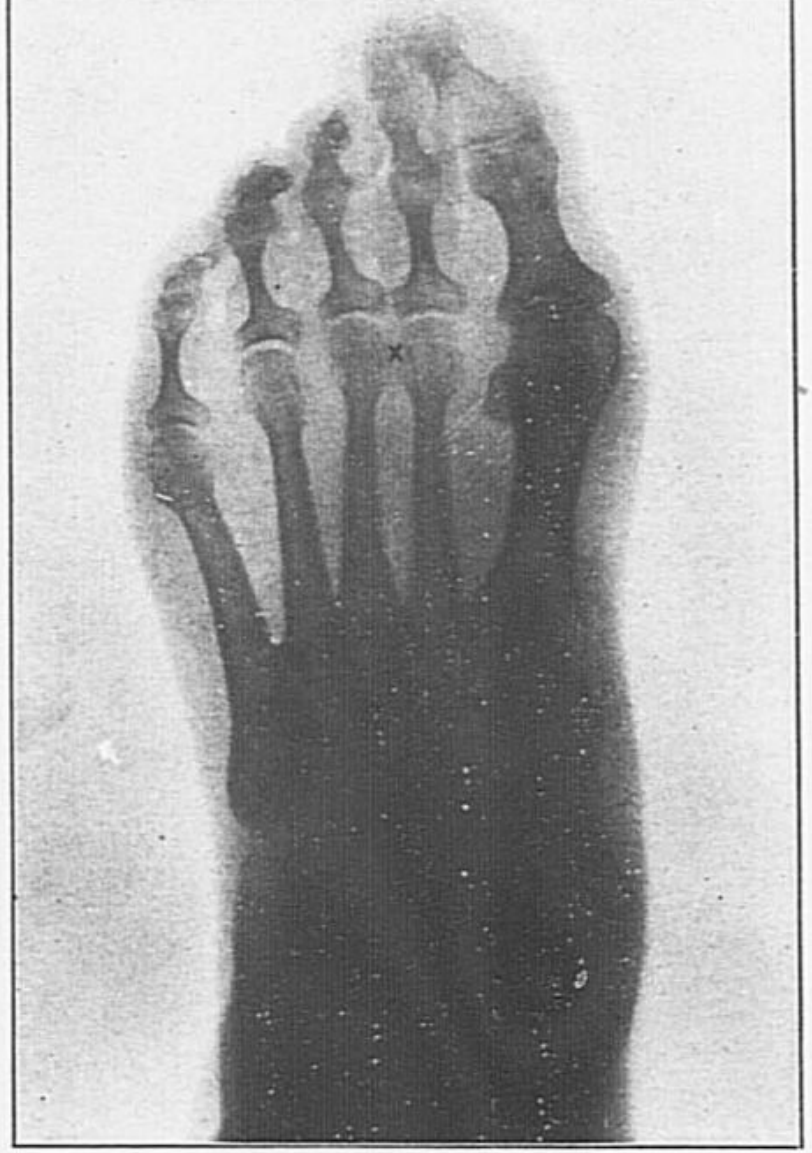
CLINICAL NOTES ON APOPLEXY.

E. G. WOOD, M.D., C.M., PROFESSOR OF MEDICINE, UNIVERSITY OF NASHVILLE.

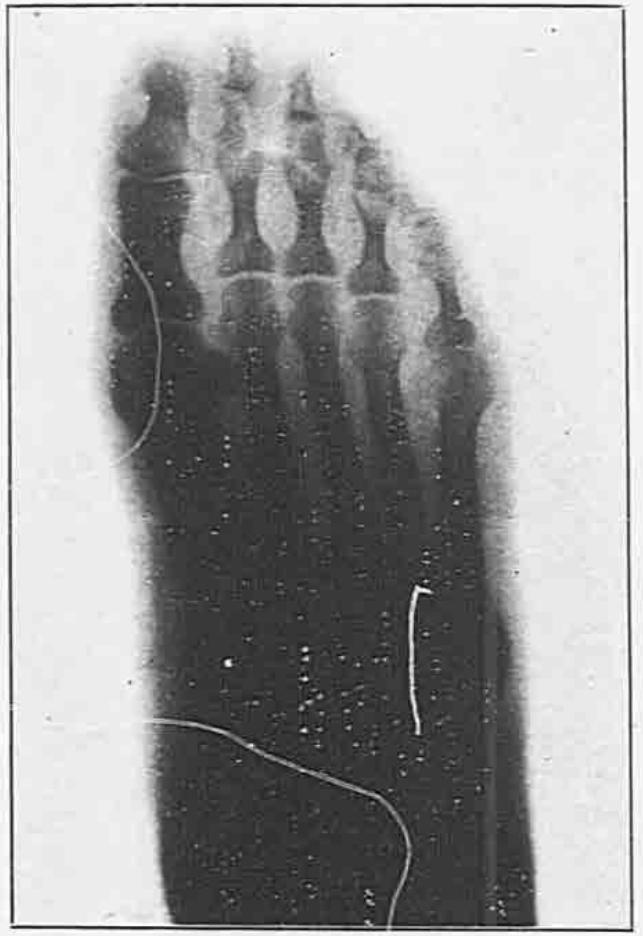
In the remarks I have to make the term *apoplexy* will be used in its broadest sense, and as a general term will embrace not only the acute cerebral attack or "stroke" due to hemorrhage, but also that resulting from the plugging of a vessel. The apoplectic seizures occasionally met with in intracranial tumor or abscess, in general paralysis of the insane and in a few other conditions, will not be considered.

A "stroke" or an attack of apoplexy is vascular in origin and is due either to rupture of a blood vessel in the brain, cerebral hemorrhage, or to plugging of a vessel, cerebral embolism or thrombosis. Cerebral hemorrhage is usually due to arteriosclerosis, either primary, or as an associated condition in chronic Bright's disease. In nearly all cases the rupture can be traced to three factors, viz: powerful left ventricle, high arterial pressure and weakened vessel wall. Cerebral hemorrhage is especially frequent between the ages of forty and sixty, that is, during the period when arterial degeneration is marked, while the power of the heart is still good. After sixty the heart becomes weaker, intra-arterial pressure is lower and rupture is progressively less frequent. As

bones. The use of the Rœntgen ray for a diagnosis of affections of this portion of the foot, is practically valueless, save to clear up any possible doubt that may exist as to the presence of exostosis, or of mal-positions of the



No. 4. Radiograph of foot giving symptoms of Morton's toe.



No. 5. Radiograph of foot with symptoms identical to No. 4.

Scott EL. Diagnosis of Painful Feet. SMJ 1908;1(1):6-12.

Key Dates in Medical Research 1910 - 1960

- **1928. Discovery of penicillin (Alexander Fleming)**
  - Large scale production by 1945 (ACH died of PNA @ Portland VA in 1939)
  - SMA 1950: The enhancement of serum penicillin levels in man by benemid
  - SMA 1960: presentation of trends addressing PCN resistance
- **1943. Streptomycin isolated (Selman Waksman)**
  - SMA 1950: presentations on use of streptomycin in TB
- **1950s. Development of polio vaccine (Jonas Salk)**
  - SMA 1960: 1959 outbreak in Arkansas; effectiveness of Salk vaccine 85%
- **1953. Discovery of DNA structure (Watson & Crick)**
- **1960. First oral contraceptive approved by the FDA**
  - SMA 1990: development of follicular cysts in triphasic vs monophasic OC

Key Milestones in Medical Research 1960 - 2024

- **1960s - 1970s. The rise of cardiovascular research**
  - Focused on chronic diseases, primarily heart disease and cancer; chemotherapy developed
  - RCTs became the gold standard in clinical research
  - IRBs began forming; Belmont Report; Tuskegee Syphilis Study, thalidomide scandal
- **1980s. Molecular biology and genetics**
  - HIV/AIDS crisis; antiretroviral therapies developed
  - **Good Clinical Practice** international guidelines developed for research
- **1990s - 2000s. The "War on Cancer" & Evidence Based Medicine**
  - EBM becoming more structured and formalized into clinical practice
  - Genome sequencing and targeted therapies improve cancer treatments
- **2010s - 2020s. Big data & personalized medicine**
  - Personalized medicine (genomics), immunotherapy (CAR-T), mRNA (COVID-19)
  - Ethical issues regarding emergency use authorizations for vaccines

Key Dates in Medical Research 1960 - 2024

- **1967. First heart transplant**
  - SMJ 1965: clinical experience with organ transplantation[1] - “current status in this area of medical experimentation”
- **1978. First “test tube baby” born (IVF)**
  - SMJ 1987: case report from Medical College of Georgia[2]
- **1996. Dolly the sheep cloned**
  - SMJ 2006: ethics article arguing against the illusory quest for immortality via cloning[3]
- **2003. Human Genome Project completed**
  - SMJ 1990: mapping and sequencing of the human genome[4]
- **2020. mRNA vaccines for COVID-19**
  - SMA 1990: development of follicular cysts in triphasic vs monophasic OC

1. Starlz TE et al. Clinical experience with organ transplantation. South Med J 1965;58(2):131-147. 2. Butler WJ et al. In vitro fertilization and birth after ultrasonically guided transurethral aspiration of oocytes. South Med J 1987;90(5):659-662. 3. Sulmasy DP. Promethean medicine: spirituality, stem cells, and cloning. South Med J 2006;99(12):1419-142. 4. Antonarakis SE. The mapping and sequencing of the human genome. South Med J 1990;83(8):876-878

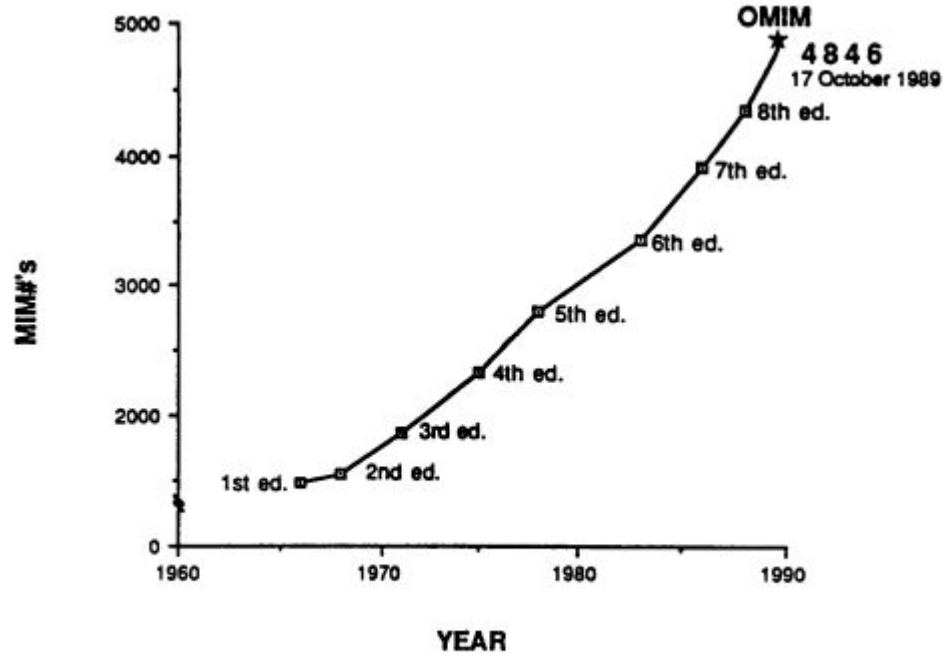


FIGURE 1. Number of gene entries cataloged in *Mendelian Inheritance in Man* (MIM) by McKusick.[1]

As of September 6, 2024 there are 27,502 gene entries in the MIM database (omim.org)

Antonarakis SE. The mapping and sequencing of the human genome. South Med J 1990;83(8):876-878

Key Trends in Biostatistics 1900-2024

- **1900s. Development of hypothesis testing**
  - Fisher's significance testing framework introduced p-values, ANOVA
  - Pearson's contributions to correlation, the chi-squared test, foundation of regression analysis
- **1940s-1950s. Formalization of clinical trials**
  - 1948 Bradford Hill trial of streptomycin treatment in TB was the first RCT
  - Randomization and blinding became fundamental techniques
- **1970s. Advances in multivariate analysis**
  - Cox proportional hazards, logistic regression, generalized linear models, survival analysis
- **1980s-2000s. Computational revolution**
  - Bootstrapping, Monte Carlo simulations, rise of Bayesian statistics
- **2010s-2020s. Evolving approaches to statistical rigor**
  - Reproducibility crisis prompts greater attention to robustness and fragility metrics
  - Increased use of meta-analyses and systematic reviews

The First Randomized Controlled Clinical Trial

Group	Improvement	No Improvement	Total
Bed Rest & Streptomycin	38	17	55
Bed Rest Alone	17	35	52
Total	55	52	107

p = 0.000166

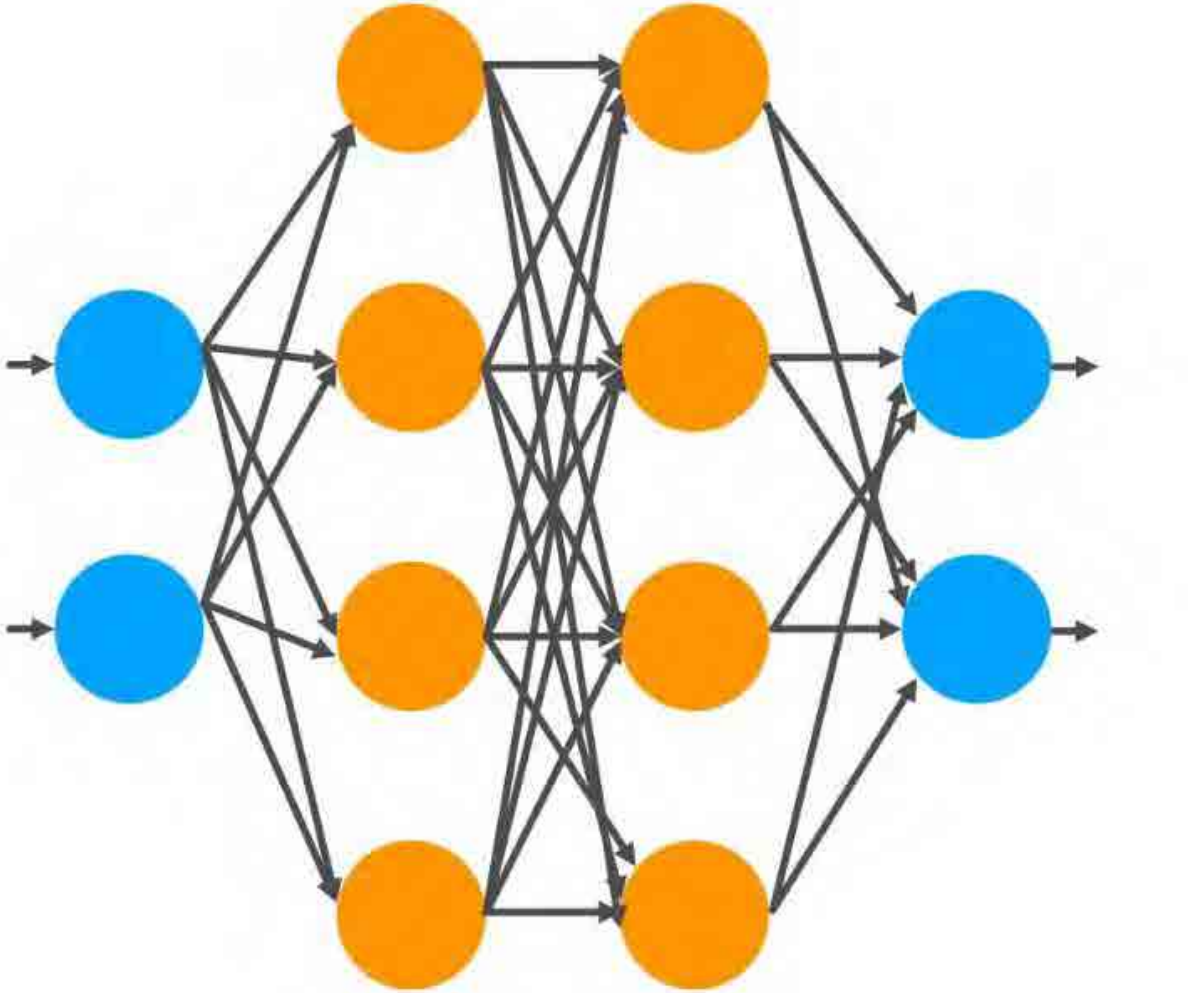
Treating physicians not blinded, but physicians interpreting CXRs were blinded

Streptomycin Treatment Of Pulmonary Tuberculosis: A Medical Research Council Investigation. British medical journal. 1948;2(4582):769-782.

Future Directions: AI

- **Diagnostics**
  - Early disease detection (imaging, pathology)
  - Predictive analytics
- **Drug Discovery**
  - AI's ability to identify potential drug candidates faster developed
  - Identification of personalized therapies
- **Clinical Trials**
  - Improved patient recruitment
  - Improved adaptive trials
- **Ethical Considerations**
  - Data privacy and security
  - Algorithmic bias
  - Need for regulatory frameworks

Algorithmic and Complexity Biases

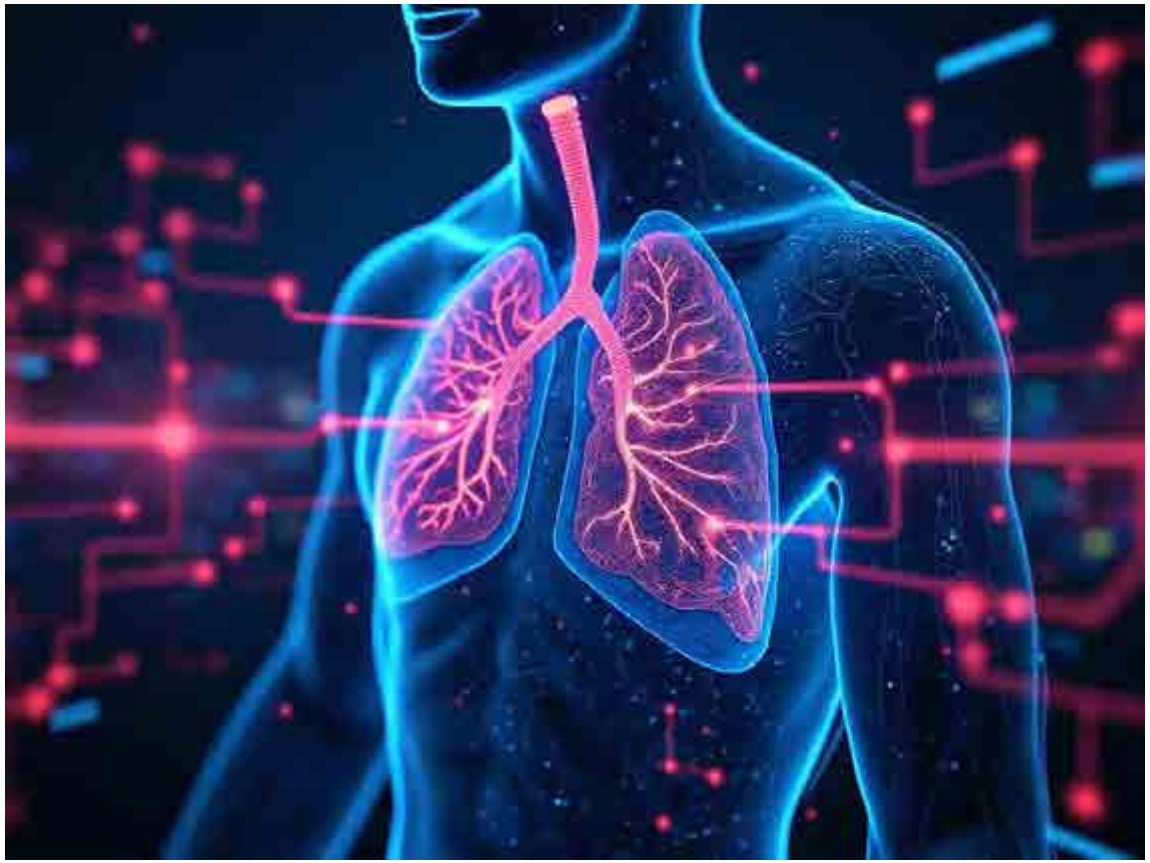


SMJ: AI in Education

Emerging Role of Artificial Intelligence in Academic Pulmonary Medicine

William J. Healy, MD[1]; Ali Musani, MD[2]; David J. Fallaw, MD[3]; and Shaheen U. Islam, MD, MPH[1]

SMJ 2024;117(7):369-370.



Grok: *I generated an image with the prompt: 'Emerging Role of Artificial Intelligence in Academic Pulmonary Medicine'.*

Future Directions: Surgery

- **Telesurgery**
  - Integration with virtual reality for remote surgeries as well as for surgical planning
  - Potential for surgery in extreme environments (space, war zones)
- **3D Printed Organs and Tissues**
  - Patient-specific prosthetics and implants
  - 3D printing can now enable the fabrication of living tissues
  - Stacked scaffolds of living tissues => bioprinting of organs for transplantation
- **Robotic Surgery**
  - AI-enhanced surgical robots
  - Haptic feedback systems
  - Advances in minimally invasive surgery

Smart Glasses

Photo of smart view glasses and intraoral scanner (2020), by Quang Tri NGUYEN via Unsplash.

Real Time, Remote, and Recorded: Medical Student Experiences with Smart Glasses in Obstetrical Simulation

Aparna Sridhar, MD, MPH[1]; Julia Burrows, MD[2]; Catherine Nameth, PhD[3]; and Yue Ming Huang, EdD, MHS[4]

SMJ 2023;116(8):686-689.

Key Points

- Smart glasses move with users and capture their perspective while being compatible with live conferencing platforms. They are well suited for streaming procedures and simulation experiences.
- This article describes a pilot innovation study exploring the feasibility of this novel tool for teaching simulation of vaginal birth and understanding student experiences with the glass usage.
- The overall responses of the students were largely positive, with high satisfaction rates.
- The pilot study paves the way for future studies to understand the use of this technology with patients and learners in different specialties.

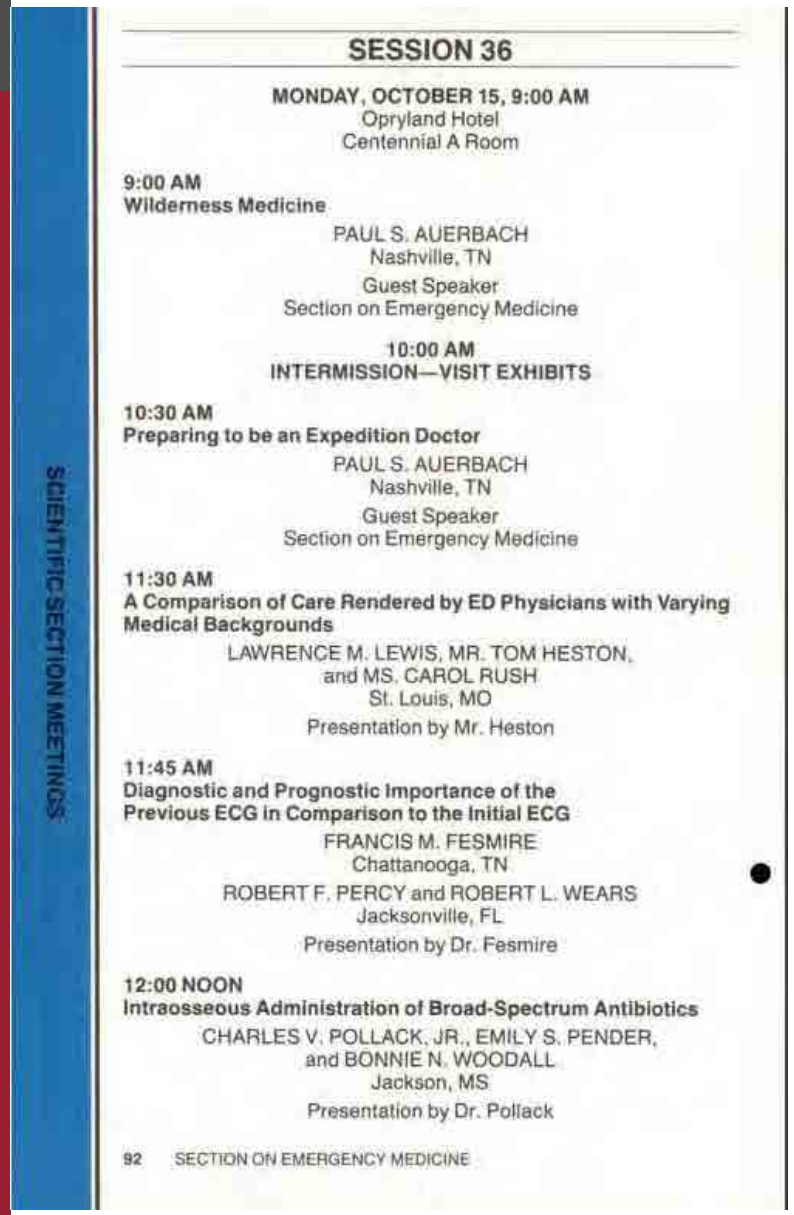
Future Challenges in Medical Research

- **Antimicrobial resistance**
  - Superbugs: MRSA, C.difficile, TB, carbapenem-resistent enterobacteriaceae
  - Development of new antibiotics has been slowed by bureaucracy, costs, need for innovation
  - Pharmaceutical industry has often prioritized more profitable drugs over antibiotics
  - Rapid evolution of bacterial resistance requires constant innovation
- **Improving global health**
  - Expanding access to surgery, medications, and expertise
  - The prevention and response to pandemics
- **Sustainable research**
  - NIH budget “buying power” decreased due to inflation and rising costs of research
  - Competition for funding is intense
  - Need for diversified funding sources
  - Value based care & preventive medicine

Micro-Trends: a Personal Journey

- **1990-1992. Student presenter**
  - 1990: Comparison of care by ED physicians with varied backgrounds
  - 1991: Gender differences in chest pain evaluation and management
  - 1992: Predictors of weight loss in hypertension prevention
- **2024. Reconnection with mentor**
  - 2024: ChatGPT's inconsistent risk-stratification of chest pain
  - Explored AI's limitations in clinical decision-making in the evaluation of chest pain
  - No gender or racial bias was found, indicating success of early research
- **2024. Mentorship and new research**
  - Abstract with mentee: Optimizing thyroid scintigraphy for hyperthyroidism
  - Focus on improving diagnostic accuracy with Technetium-99

From Student to Physician Researcher



SCIENTIFIC SECTION MEETINGS

SESSION 36

MONDAY, OCTOBER 15, 9:00 AM
Opryland Hotel
Centennial A Room

9:00 AM
Wilderness Medicine
PAUL S. AUERBACH
Nashville, TN
Guest Speaker
Section on Emergency Medicine

10:00 AM
INTERMISSION—VISIT EXHIBITS

10:30 AM
Preparing to be an Expedition Doctor
PAUL S. AUERBACH
Nashville, TN
Guest Speaker
Section on Emergency Medicine

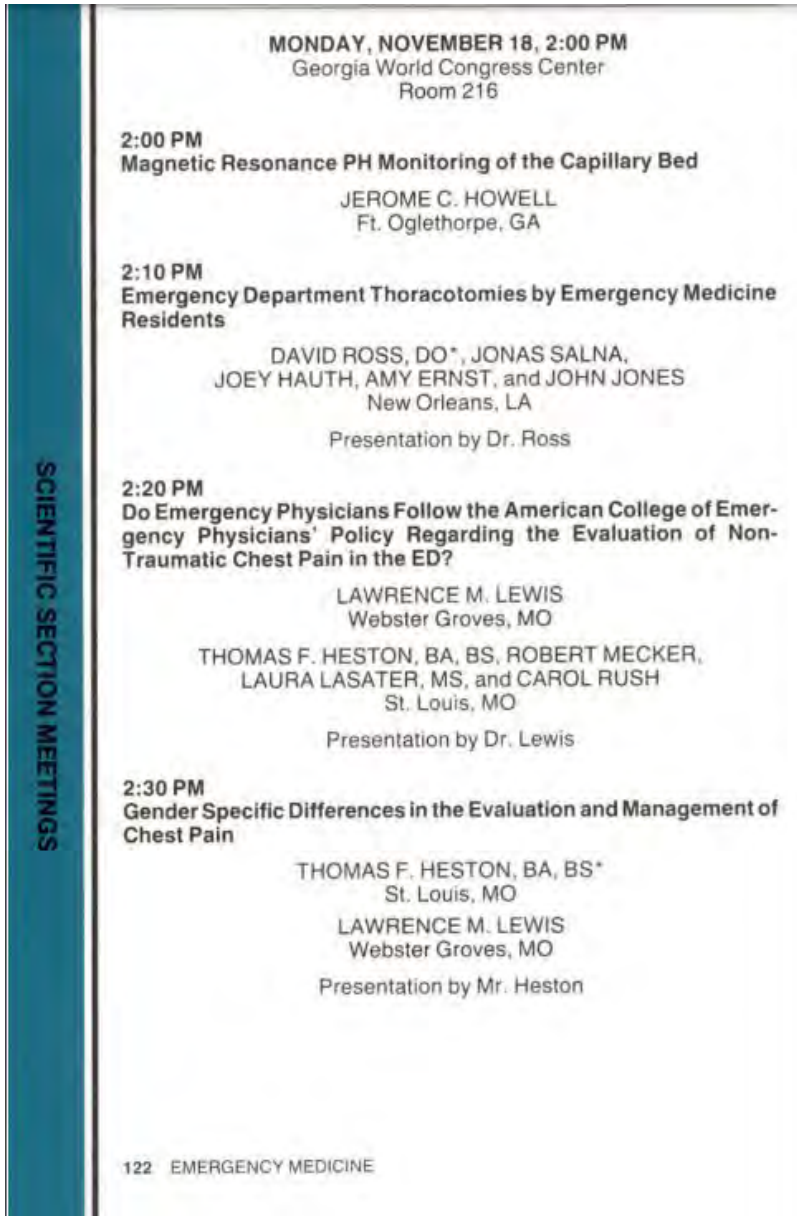
11:30 AM
A Comparison of Care Rendered by ED Physicians with Varying Medical Backgrounds
LAWRENCE M. LEWIS, MR. TOM HESTON, and MS. CAROL RUSH
St. Louis, MO
Presentation by Mr. Heston

11:45 AM
Diagnostic and Prognostic Importance of the Previous ECG in Comparison to the Initial ECG
FRANCIS M. FESMIRE
Chattanooga, TN
ROBERT F. PERCY and ROBERT L. WEARS
Jacksonville, FL
Presentation by Dr. Fesmire

12:00 NOON
Intraosseous Administration of Broad-Spectrum Antibiotics
CHARLES V. POLLACK, JR., EMILY S. PENDER, and BONNIE N. WOODALL
Jackson, MS
Presentation by Dr. Pollack

92 SECTION ON EMERGENCY MEDICINE

1990 My 1st medical meeting. “Tom Heston”



SCIENTIFIC SECTION MEETINGS

MONDAY, NOVEMBER 18, 2:00 PM
Georgia World Congress Center
Room 216

2:00 PM
Magnetic Resonance PH Monitoring of the Capillary Bed
JEROME C. HOWELL
Ft. Oglethorpe, GA

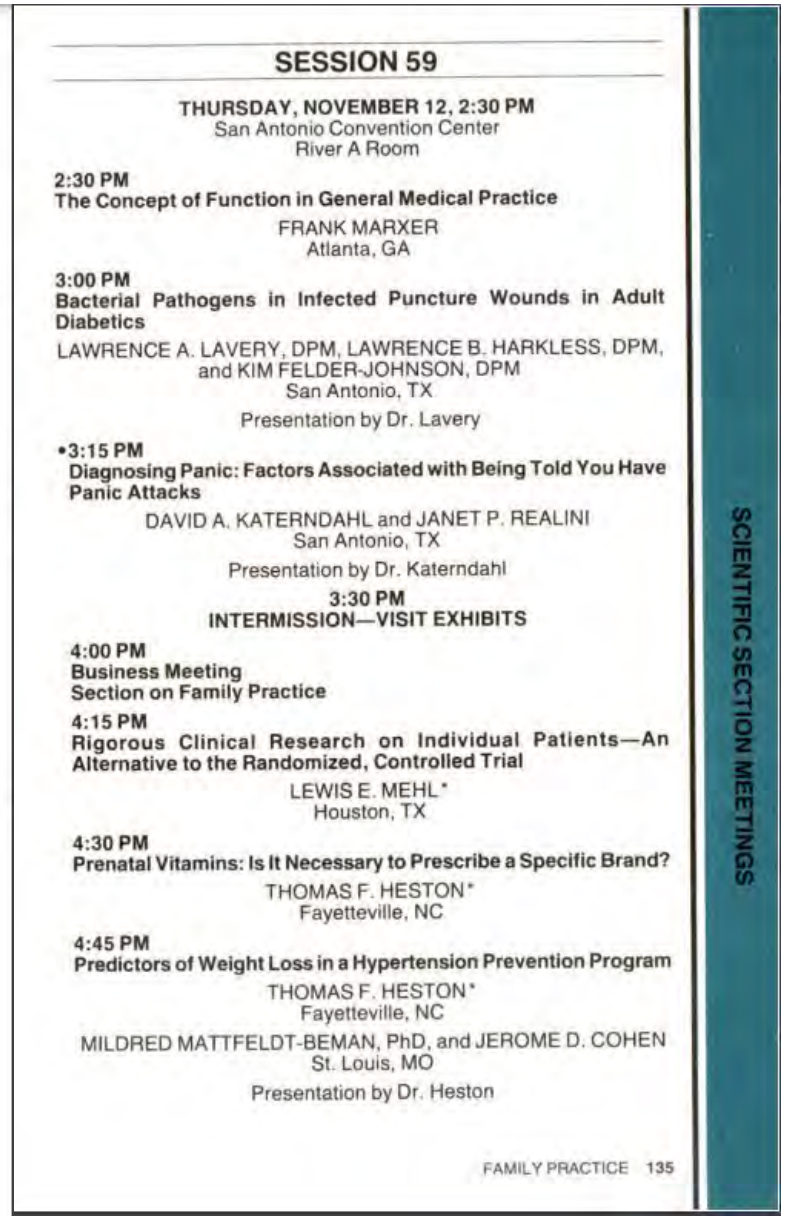
2:10 PM
Emergency Department Thoracotomies by Emergency Medicine Residents
DAVID ROSS, DO*, JONAS SALNA, JOEY HAUTH, AMY ERNST, and JOHN JONES
New Orleans, LA
Presentation by Dr. Ross

2:20 PM
Do Emergency Physicians Follow the American College of Emergency Physicians' Policy Regarding the Evaluation of Non-Traumatic Chest Pain in the ED?
LAWRENCE M. LEWIS
Webster Groves, MO
THOMAS F. HESTON, BA, BS, ROBERT MECKER, LAURA LASATER, MS, and CAROL RUSH
St. Louis, MO
Presentation by Dr. Lewis

2:30 PM
Gender Specific Differences in the Evaluation and Management of Chest Pain
THOMAS F. HESTON, BA, BS*
St. Louis, MO
LAWRENCE M. LEWIS
Webster Groves, MO
Presentation by Mr. Heston

122 EMERGENCY MEDICINE

1991. 2nd Meeting. “Thomas F Heston”



SCIENTIFIC SECTION MEETINGS

SESSION 59

THURSDAY, NOVEMBER 12, 2:30 PM
San Antonio Convention Center
River A Room

2:30 PM
The Concept of Function in General Medical Practice
FRANK MARXER
Atlanta, GA

3:00 PM
Bacterial Pathogens in Infected Puncture Wounds in Adult Diabetics
LAWRENCE A. LAVERY, DPM, LAWRENCE B. HARKLESS, DPM, and KIM FELDER-JOHNSON, DPM
San Antonio, TX
Presentation by Dr. Lavery

•3:15 PM
Diagnosing Panic: Factors Associated with Being Told You Have Panic Attacks
DAVID A. KATERNDAHL and JANET P. REALINI
San Antonio, TX
Presentation by Dr. Katerndahl

3:30 PM
INTERMISSION—VISIT EXHIBITS

4:00 PM
Business Meeting
Section on Family Practice

4:15 PM
Rigorous Clinical Research on Individual Patients—An Alternative to the Randomized, Controlled Trial
LEWIS E. MEHL*
Houston, TX

4:30 PM
Prenatal Vitamins: Is It Necessary to Prescribe a Specific Brand?
THOMAS F. HESTON*
Fayetteville, NC

4:45 PM
Predictors of Weight Loss in a Hypertension Prevention Program
THOMAS F. HESTON*
Fayetteville, NC
MILDRED MATTFELDT-BEMAN, PhD, and JEROME D. COHEN
St. Louis, MO
Presentation by Dr. Heston

FAMILY PRACTICE 135

1992. “Dr. Heston”

Optimizing Thyroid Scintigraphy for Hyperthyroidism Using Technetium-99 Pertechnetate

Xiangyu Gao[1], Thomas F. Heston[1,2]
1. Washington State University Elson S. Floyd College of Medicine, Spokane, WA, 99202.
2. University of Washington School of Medicine, Spokane, WA, 99202.

Washington State University

INTRODUCTION

Hyperthyroidism affects 0.2-1.3% of the global population, with Graves' disease being the most common cause (70%). Subacute thyroiditis is an important differential diagnosis. Serum thyroid hormones are useful but nonspecific in distinguishing between Graves' disease and thyroiditis. Nuclear imaging with Iodine-123 (I-123) is useful and identifies nodules, taking 2-24 hours for imaging; Technetium-99m Pertechnetate (Tc-99m) is faster and less expensive. I-123 has well-defined uptake patterns, while Tc-99m patterns are less standardized for differentiating the etiology.

METHODS

A retrospective review of conducted on 78 patients evaluated for hyperthyroidism at an outpatient imaging center. Final clinical diagnoses were: 7% normal, 24% thyroiditis, 45% Graves, 20% multinodular goiter, and 4% autonomous nodule. Those with Graves or thyroiditis and were evaluated. Tc-99m pertechnetate 5 mCi IV was administered. Imaging was performed at 5 and 25 minutes post-injection. Camera-based uptake ratios of the thyroid to neck, salivary gland, mediastinum, and lung were calculated. Correlation and ROC analyses were used to assess diagnostic performance; Fisher's z-transformation compared correlation coefficients for equivalence or superiority.

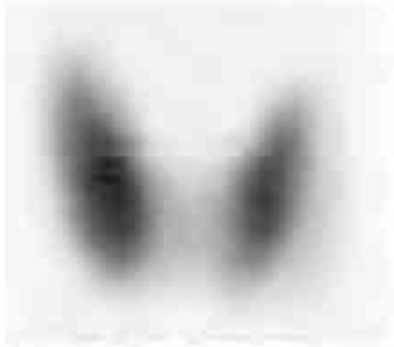


Figure 1. Tc-99m thyroid scintigraphy at 25 minutes post-injection.

Thyroid to region ratio	5 min	25 min
Mediastinum	0.679	0.563
Salivary Glands	0.663	0.581
Neck	0.643	0.581
Right Lung	0.635	0.529

Table 1. Correlation coefficients with diagnosis of subacute thyroiditis vs Graves Disease

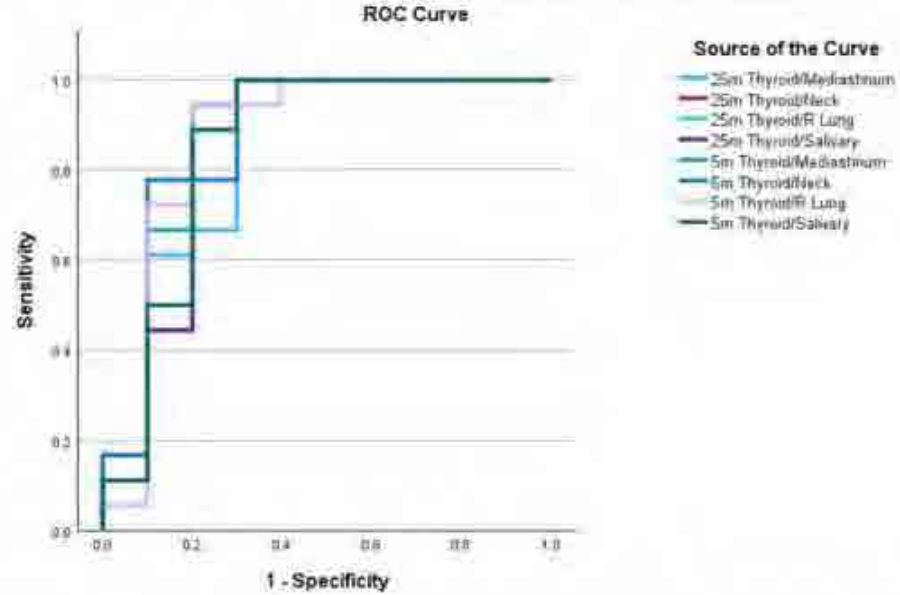


Figure 2. ROC analysis of thyroid to region uptake ratios in differentiating Graves vs subacute thyroiditis for patients presenting with hyperthyroidism.

RESULTS

- Strong correlation of all uptake ratios (**Table 1**) with clinical diagnosis ($p \leq 0.002$).
- Correlation coefficients ranged from 0.529 for the 25-minute thyroid-to-right lung uptake ratio, to 0.679 for the 5-minute thyroid-to-mediastinum ratio (**Table 1**).
- These correlations of the 5 min vs 25 min uptake ratios are equally strong based on Fisher's z-transformation ($p>0.05$).
- ROC analysis found that the uptake ratios with area under the curve being > 0.85 in all cases except 25 min Thyroid/Mediastinum (0.839) (**Figure 2**).

CONCLUSION

- In differentiating Graves from thyroiditis: the 5-minute Tc-99m ratios are non-inferior to 25-minute ratios and highly accurate diagnostically.
- In this setting, the use of Tc-99m instead of I-123 may be useful due to its lower cost, lower radiation exposure, and shorter scan time.

REFERENCES

Chaudhary V, Bano S. Imaging of the thyroid: Recent advances. Indian J Endocrinol Metab. 2012 May;16(3):371-8.

Wiersinga WM, Poppe KG, Effraimidis G. Hyperthyroidism: aetiology, pathogenesis, diagnosis, management, complications, and prognosis. The Lancet Diabetes & Endocrinology. 2023;11(4):282-298. doi:10.1016/S2213-8587(23)00005-8

Alshahrani A, Syed QM, Khan AH, et al. Assessment of normal reference values for thyroid uptake of technetium-99m pertechnetate in a Saudi population. Ann Saudi Med. 2021;41(2):88-99. doi:10.5144/0256-4947.2021.88

SMA: A Century of Medical Progress

- **Contributions to medical advances**
  - Early focus on **public health and sanitation** (1910s)
  - **Dissemination** of antibiotic research and surgical innovations (1940s - 1950s)
  - **Platform for emerging technologies** and bioethics discussions (1960s - present)
  - Transition from a regional to national organization reflects its unique value
- **Value of mentorship in advancing medical science**
  - Facilitates **knowledge transfer** across generations
  - Encourages **innovative thinking** and continuity in research
  - Enriches **professional development** and career satisfaction
- **Looking forward**
  - Continued commitment to **evidence-based, ethical research**
  - Embracing **new technologies** while preserving the human element in medicine
  - Fostering a **culture of mentorship** to shape the future of medicine

Thank you!

Thomas F Heston MD

tom.heston@wsu.edu

EvidenceNOW
BUILDING STATE CAPACITY
AN AHRQ INITIATIVE

TENNESSEE
HEART HEALTH
NETWORK

TSMA

The Power of Partnerships in Hypertension/Cardiovascular Care:

James E. Bailey, MD, MPH
Tennessee Population Health Consortium
University of Tennessee Health Science Center

Disclosures

Jim Bailey, MD

Grant/Research Support: **NIMHHD, AHRQ, CDC, UnitedHealthcare Services, TN Dept of Health, Shelby County Government**

Board Member: **Coalition for Better Health**

Other: **President, The Healthy City, Inc.**

*All clinical recommendations are **evidence-based and free of commercial bias***

Objectives

1. **Identify Key Collaborators in Hypertension and Cardiovascular (CV) Care**
    - Roles of various healthcare professionals, non-clinical lay health workers, and community-based organizations involved in managing CV conditions
2. **Understand the Benefits of Multidisciplinary Collaboration**
    - How partnerships between different healthcare providers (including primary care physicians, cardiologists, nurses, pharmacists, dieticians, community health workers, and health coaches) enhance patient outcomes in CV care
3. **Implement Strategies for Effective Partnership and Coordination**
    - Practical strategies for building and maintaining effective partnerships and coordinating care across different providers and organizations to optimize patient management and treatment outcomes


If you want to go fast
go alone.
If you want to go far
go together.
African proverb

Identifying Key Collaborators

Primary Care Physicians

Nurse Practitioners

Dieticians

Cardiologists

Nurses

Medical Assistants

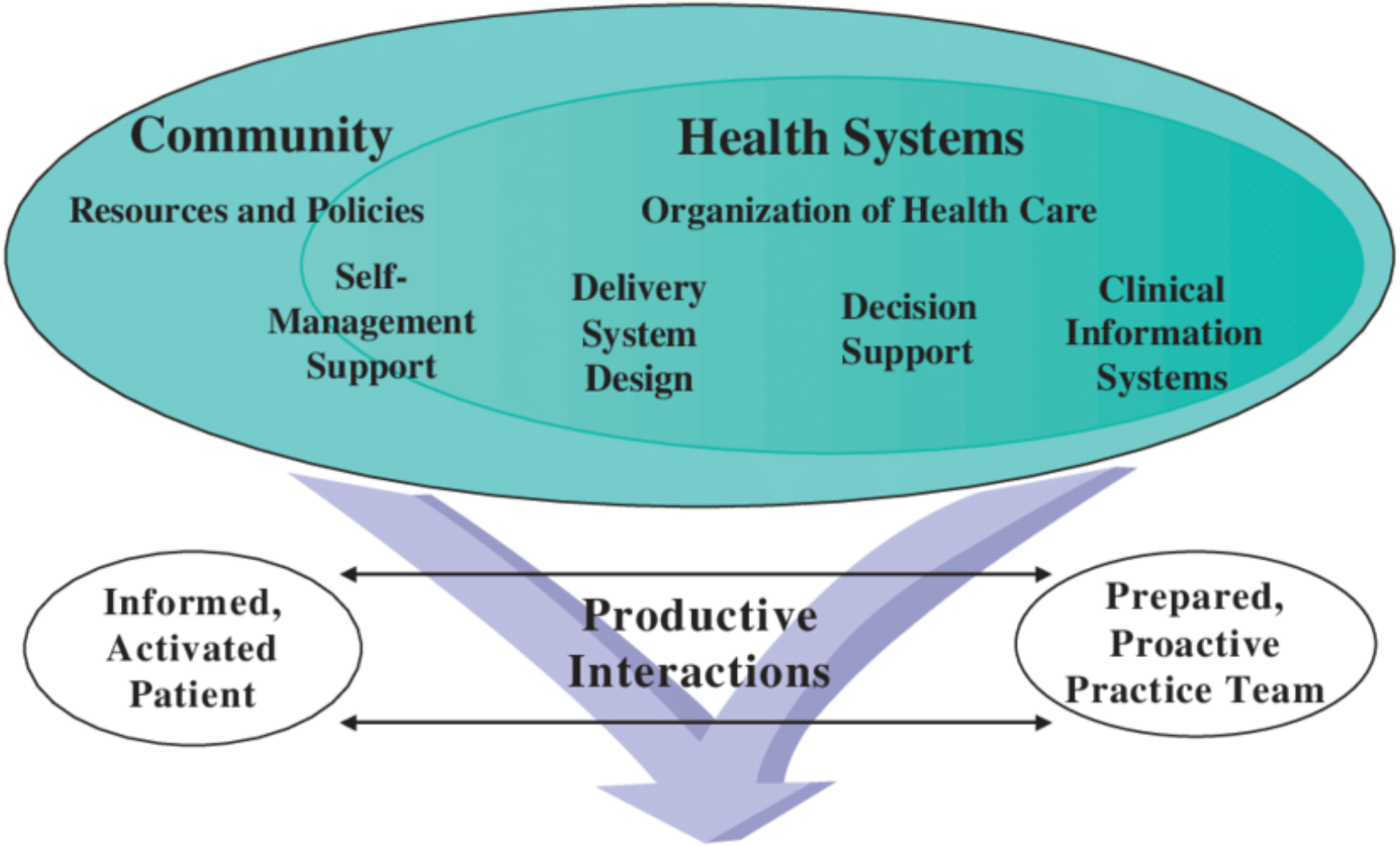
Community Health Workers

Pharmacists

Health Coaches

Identifying Key Collaborators

The Chronic Care Model



Developed by The MacColl Institute

Background: Place-based Neighborhood-level Access

- Numerous studies demonstrate clearly that neighborhood availability of primary care strongly predicts ”realized access (i.e. primary care utilization)[1]

[1] Harrington et. al. Realizing neighbourhood potential? The role of the availability of health care services on contact with a primary care physician, *Health & Place*. 16 (4), July 2012

Figure 2. Clinical Summary: Behavioral Weight Loss Interventions to Prevent Obesity-Related Morbidity and Mortality in Adults

Population	**Adults with a BMI ≥30[a]**
Recommendation	**Offer or refer to intensive, multicomponent behavioral interventions.** **Grade: B**

Risk Assessment	More than 35% of men and 40% of women in the United States have obesity. Obesity is associated with health problems such as increased risk for coronary heart disease, type 2 diabetes, various types of cancer, gallstones, and disability. Obesity is also associated with an increased risk for death, particularly among adults younger than 65 years.
Interventions	• Effective intensive behavioral interventions were designed to help participants achieve or maintain a ≥5% weight loss through a combination of dietary changes and increased physical activity • Most interventions lasted for 1 to 2 years, and the majority had ≥12 sessions in the first year • Most behavioral interventions focused on problem solving to identify barriers, self-monitoring of weight, peer support, and relapse prevention • Interventions also provided tools to support weight loss or weight loss maintenance (eg, pedometers, food scales, or exercise videos)
Relevant USPSTF Recommendations	The USPSTF has made recommendations on screening for abnormal blood glucose levels and type 2 diabetes, screening for high blood pressure, statin use in persons at risk for cardiovascular disease, counseling for tobacco smoking cessation, aspirin use in certain persons for prevention of cardiovascular disease, behavioral counseling interventions to promote a healthful diet and physical activity for cardiovascular disease prevention in adults with and without common risk factors, and screening for obesity in children and adolescents.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to https://www.uspreventiveservicestaskforce.org.

Social Determinants of Health

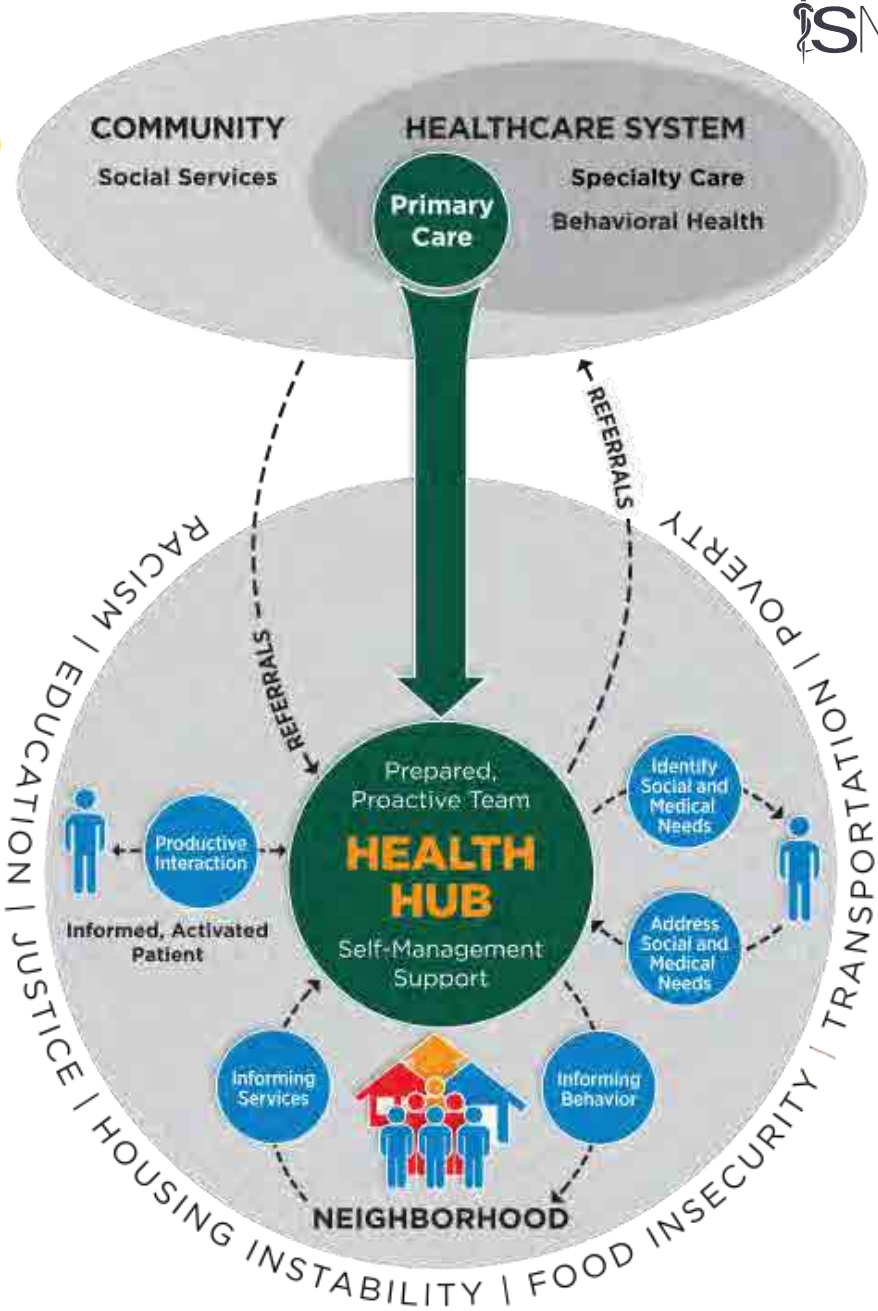
Poor People's Campaign
A NATIONAL CALL for MORAL REVIVAL

Better Jobs Better Education Better Homes

"Of all the forms of inequality, **injustice in health care is the most shocking and inhuman**." — Dr. Martin Luther King, Jr.

Neighborhood Health Hub Model

A new place-based model to extend primary care into neighborhoods of greatest need



Benefits of Multidisciplinary Team-based Care

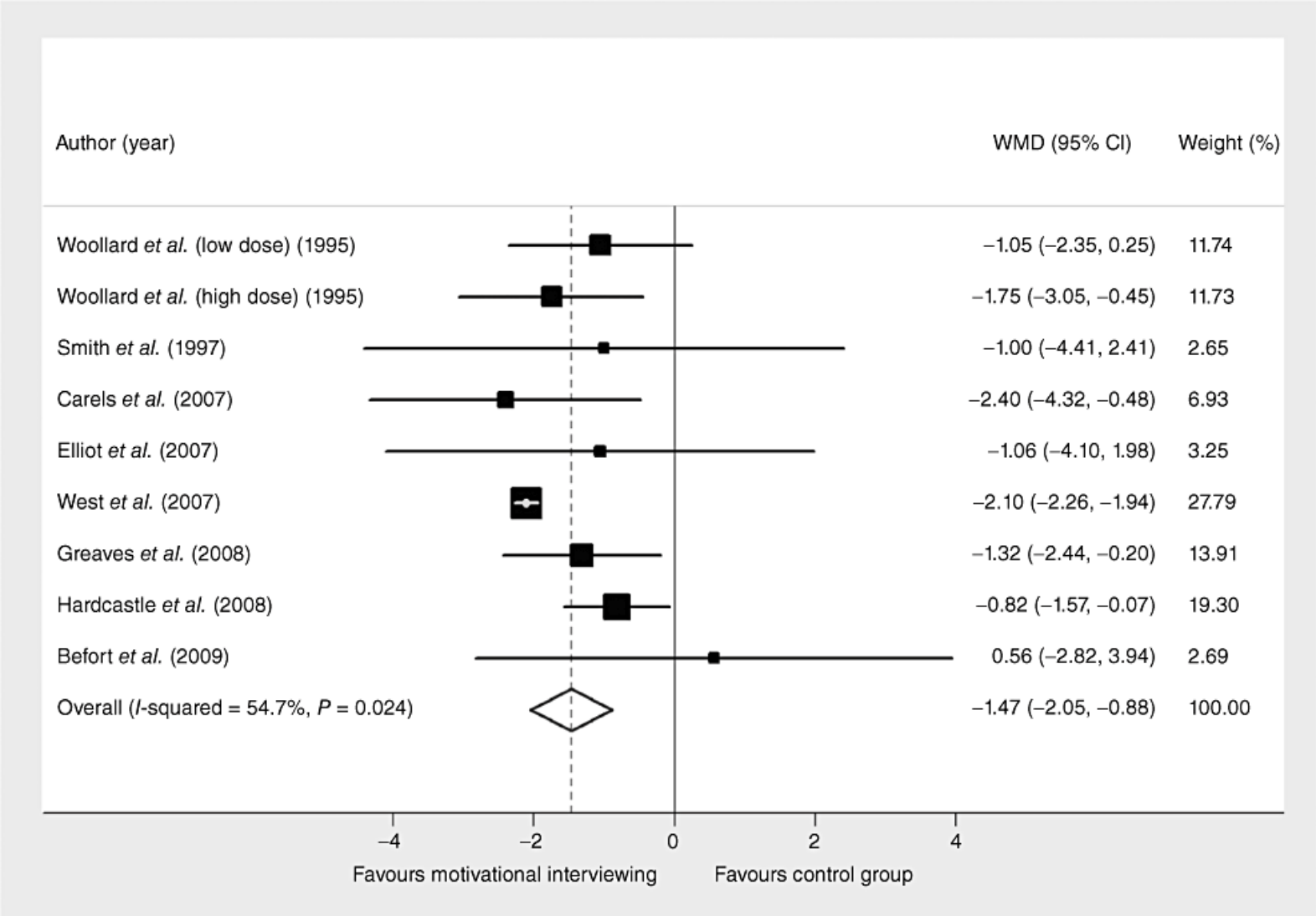
- **Extensive evidence demonstrates :**
  - Multidisciplinary team-based care enhances patient outcomes
  - Care coordination care and communication among different providers improve patient management, treatment adherence, and overall outcomes
  - Effectiveness of motivational interviewing and health coaching in improving patient engagement and outcomes

Best Counseling Approach = MI-Based Health Coaching

- **Effective weight loss trials used highly diverse interventionists[1]**
  - **Behavioral therapists**
  - **Psychologists**
  - **Registered dieticians**
  - **Exercise physiologists**
  - **Health coaches**
- **Motivational interviewing (MI) more effective than education for weight loss[2]**

[1] USPSTF, Behavioral Weight Loss Interventions to Prevent Obesity-Related Morbidity & Mortality in Adults, *JAMA*, 2018
[2] Armstrong et al. Metaanalysis of RCTs, *Obesity Reviews*, 12(9) 2011

MI more effective than Education for Weight Loss



Armstrong et al. Metaanalysis of RCTs, *Obesity Reviews*, 12(9) 2011

Welcome to the MODEL Study!

Comparative Effectiveness of Diabetes Self-Care Interventions in African-American Adults: A Three-Arm Randomized Controlled Trial

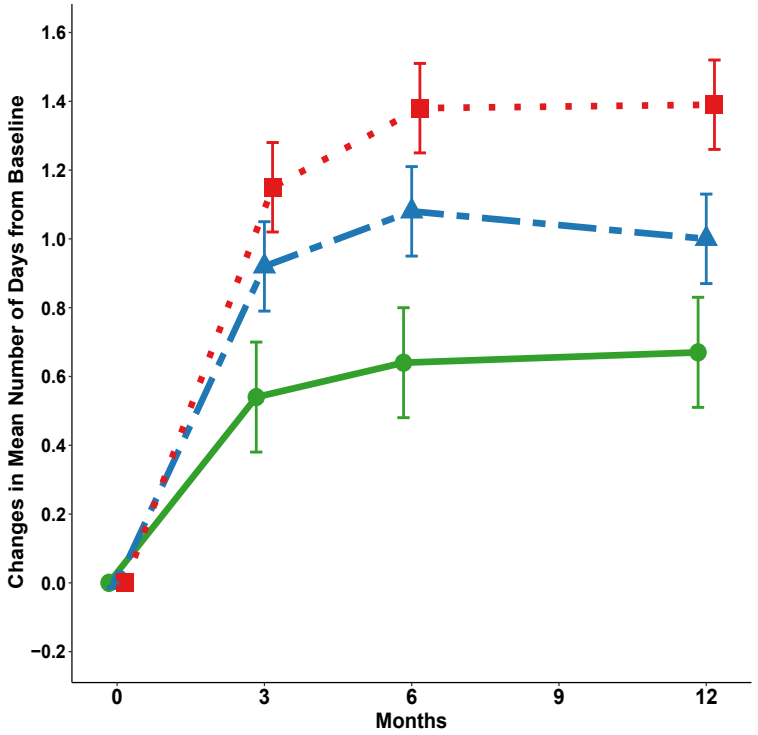
MODEL
MANAGEMENT OF DIABETES in EVERYDAY LIFE

***Study Design*: Pragmatic, patient-level randomized controlled trial**

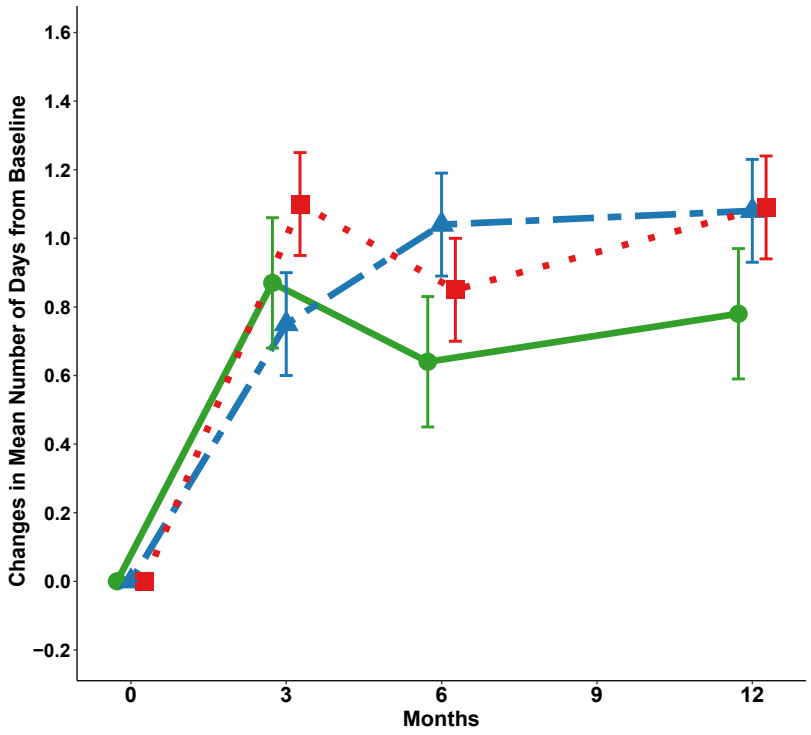
Adults ≥ 18 with Uncontrolled Diabetes and Multiple Chronic Conditions (N = 666)

- **Health Coaching (HC) + EM (N = 258)**
- **Text Messaging (TM) + EM (N = 253)**
- **Educational Materials (EM) Only (N = 155)**

A. Change in General Diet



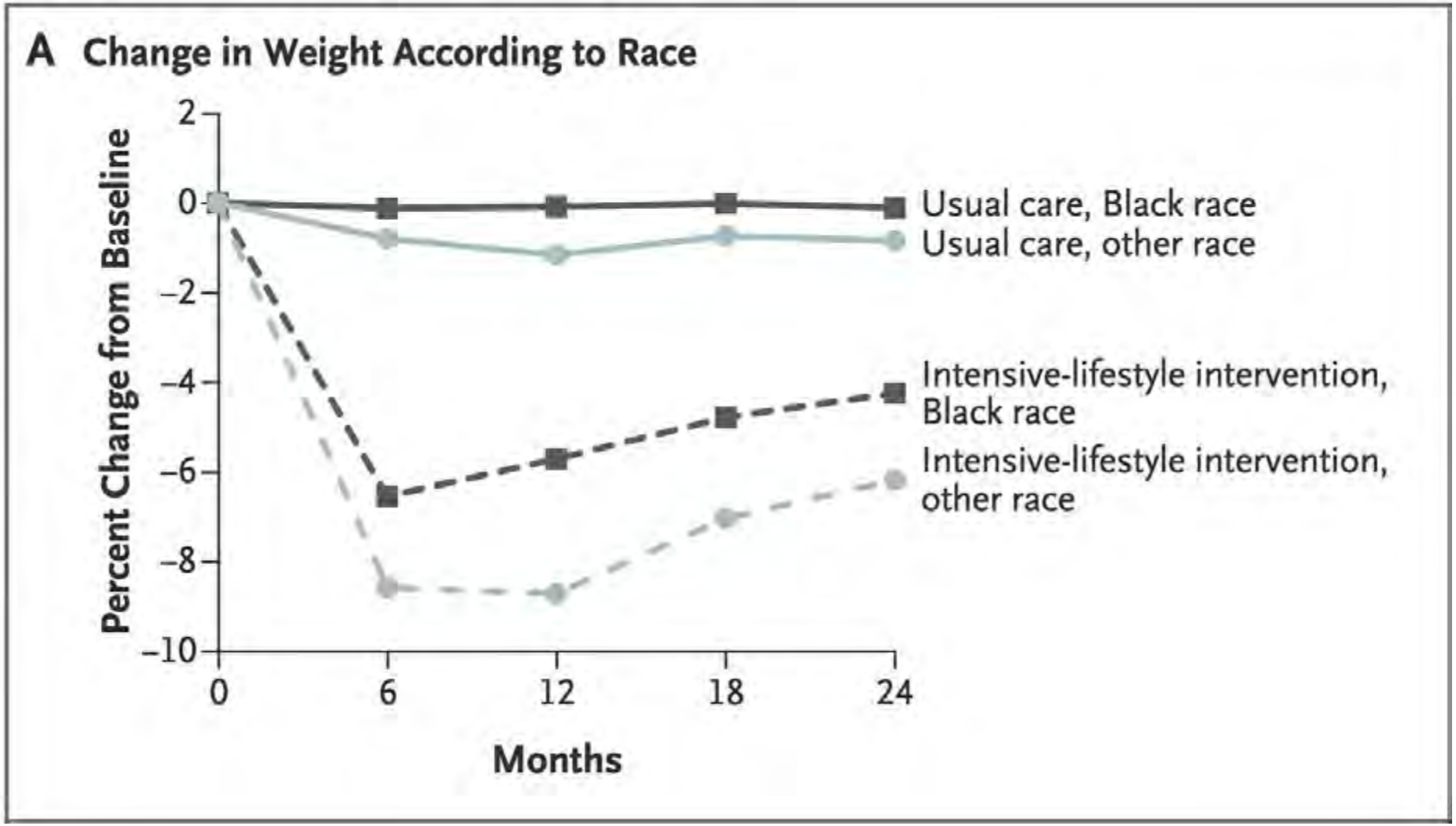
B. Change in Exercise



Conclusion

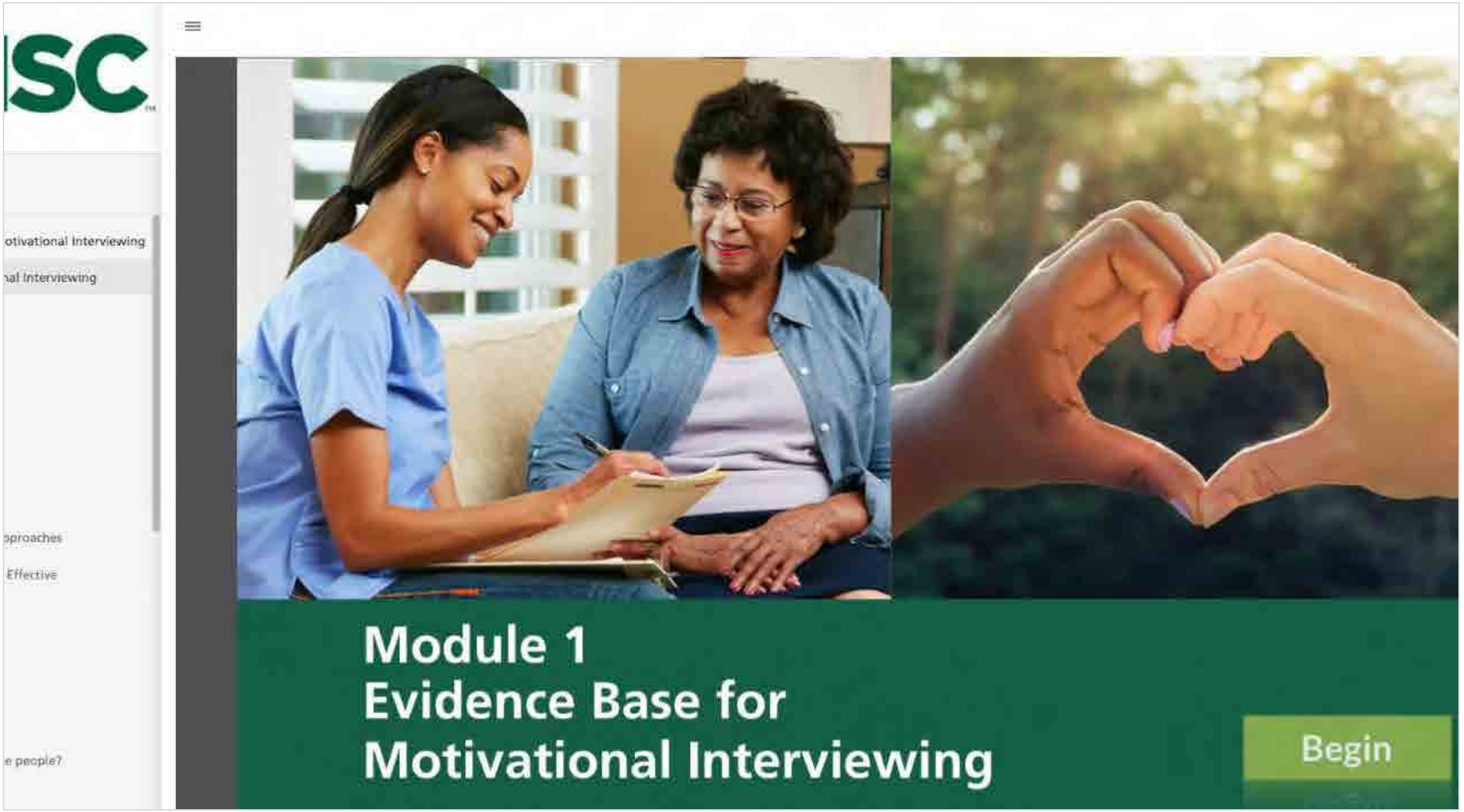
- Although TM+EM is more effective than EM alone in improving healthy eating, TM+EM, HC+EM, and EM alone are all effective for improving self-care behaviors and HbA_{1c}
- Low-cost EM, HC+EM, and TM+EM should be made more routinely available in primary care

Promoting Successful Weight Loss in Primary Care in Louisiana (PROPEL)



Katzmarzyk et al., Weight Loss in Underserved Patients — A Cluster-Randomized Trial, *NEJM*, 2020

Training Community Members as Engagement Experts

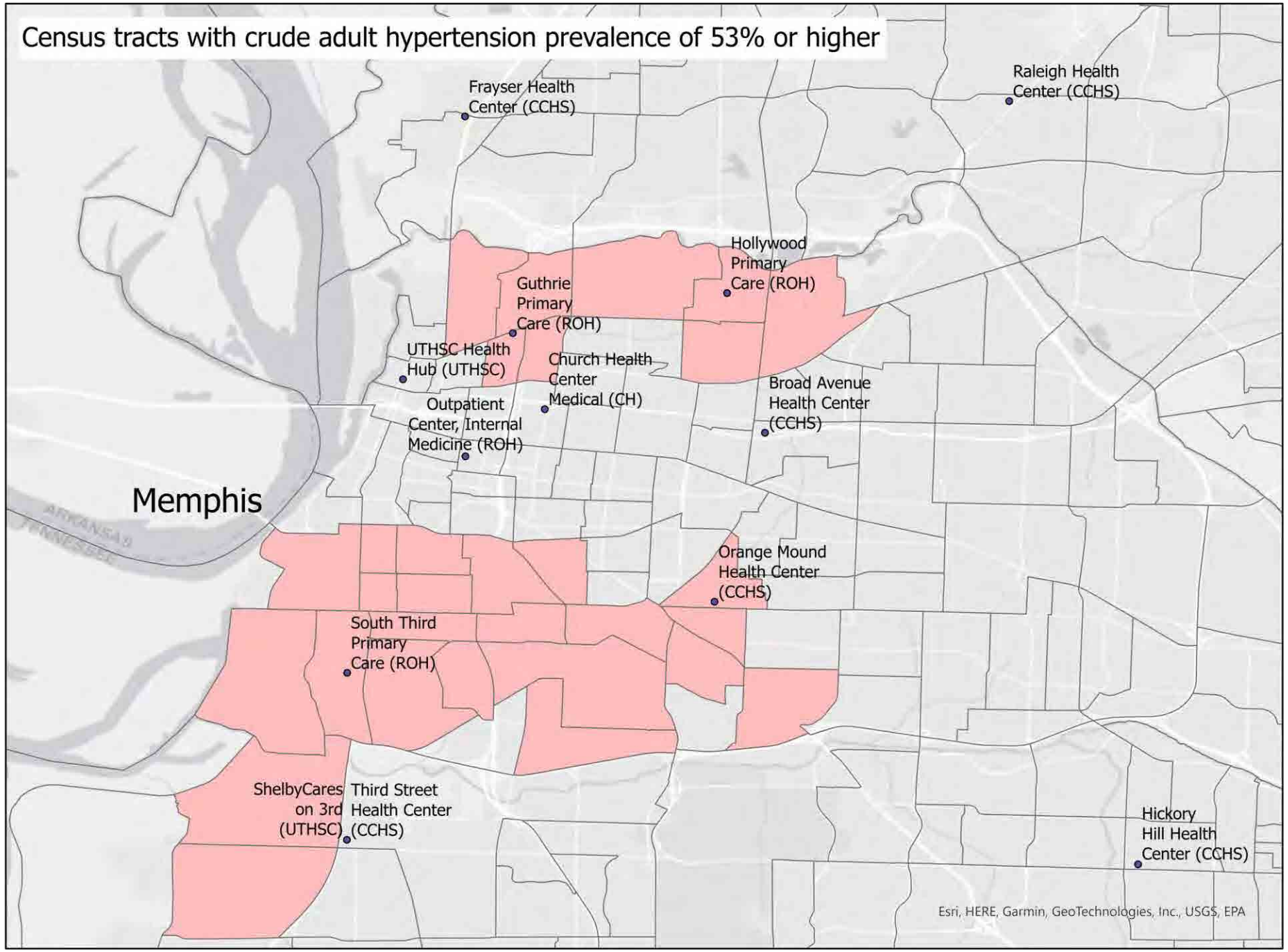


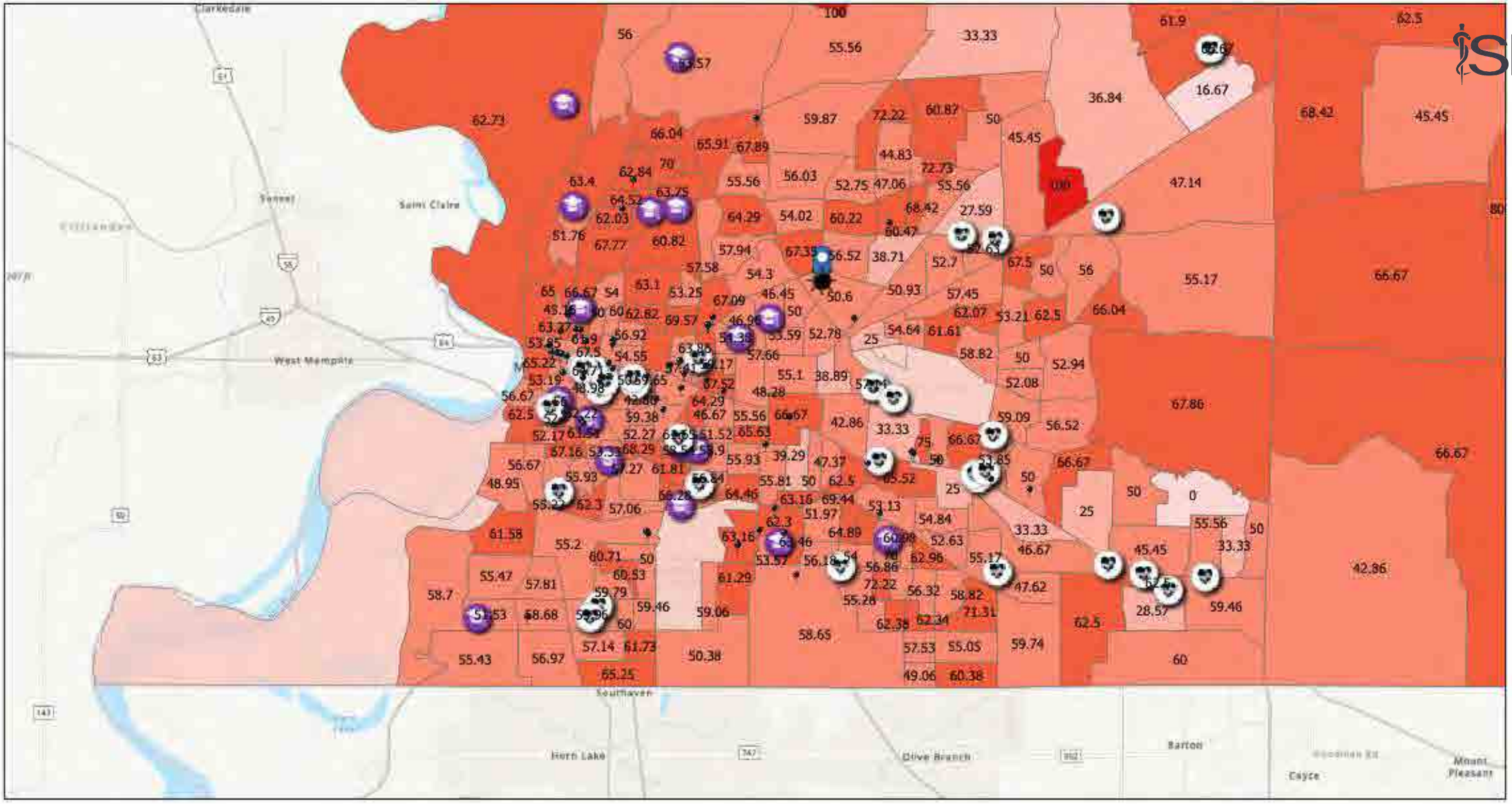
The Neighborhood Health Hub Model:

Extending Primary Care into Medically Underserved Neighborhoods to Improve Cardiovascular Outcomes

UTHSC HEALTH HUB

SHELBYCARES
A COMMUNITY PARTNERSHIP WITH MAYOR LEE HARRIS, SHELBY COUNTY GOVERNMENT, AND THE UT HEALTH SCIENCE CENTER COLLEGE OF MEDICINE


Census tracts with crude adult hypertension prevalence of 53% or higher
Frayser Health Center (CCHS)
Raleigh Health Center (CCHS)
Hollywood Primary Care (ROH)
Guthrie Primary Care (ROH)
UTHSC Health Hub (UTHSC)
Church Health Center Medical (CH)
Outpatient Center, Internal Medicine (ROH)
Broad Avenue Health Center (CCHS)
Memphis
Orange Mound Health Center (CCHS)
South Third Primary Care (ROH)
ShelbyCares on 3rd (UTHSC)
Third Street Health Center (CCHS)
Hickory Hill Health Center (CCHS)
Esri, HERE, Garmin, GeoTechnologies, Inc., USGS, EPA



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CBO

2023 Hypertension Indicated (meets or exceeds 130 over 80)

0.00 - 20.00

20.01 - 40.00

40.01 - 60.00

60.01 - 80.00

80.01 - 100.00

Base Layer with 22 and 23 and 24

0 2.5 5 10 mi

0 3.75 7.5 15 km

Arkansas GIS Office, Esri, TomTom, Garmin, SafeGraph, METI/NASA, USGS, EPA, NPS, USDA, USFWS

UTHSC in Uptown

UTHSC HEALTH HUB

ISMA

Health Hubs employ health coaches to provide life-saving primary and preventive services:

- **Screening** for obesity, hypertension, diabetes, and social needs
- **Coaching** (individual and group) using an evidenced-based communication approach to help patients set their own health goals & increase healthy eating, physical activity, lose weight, and control their chronic conditions
- **Connecting to care** to get people the primary, specialty, and mental health care and social services they need most

ShelbyCares on 3rd

Expanding Care in Westwood Neighborhood

SHELBYCARES

A COMMUNITY PARTNERSHIP WITH MAYOR LEE HARRIS,
SHELBY COUNTY GOVERNMENT, AND
THE UT HEALTH SCIENCE CENTER COLLEGE OF MEDICINE

Services Delivered

- 6555 visits to date including:
  - 1091 screening visits
  - 1044 initial health coaching visits
  - 2080 health coaching follow-up visits
  - 2,340 group session attendees

- 1269 total unique patients served.
  - 94% of patients served are Black/African American

- 989 total patients screened for obesity, hypertension, and/or diabetes.
  - 56% positive for obesity (BMI > 30)
  - 48% have uncontrolled hypertension (e.g., ≥ 140/90)
  - 34% have high blood sugar (e.g., > 125 mg/dl)

Outcomes

Regular Health Coaching Clients experienced:

- 4.1 pound avg. weight loss of among those with obesity
- 10% decrease in avg. systolic blood pressure (BP) from 152.9 to 138.1 mmHg
- 6% decrease in avg. diastolic BP from 90.9 to 85.7 mmHg
- 18% decrease in avg. random blood glucose from 211.0 to 173.5 mg/dl

HEAL Diabetes Participants experienced:

- Average weight loss of 5.6 pounds
- 12% decrease in avg. blood sugar (A1c) from 7.8 to 6.9%

Strategies for Effective Partnership

- Build trust by listening and supporting community leadership
- Find critical community members to help extend care into the community
- Hear patient expert/community member perspectives
- Facilitate community leadership
- Foster effective collaboration and establish shared goals

Listening to Build Trust

Soulsville Community Panel Themes

Key Challenges

1) **Accessing Quality Care**
   - Long wait times, short visits, pushing pills with little education and support
   - Need consistent, culturally relevant incentives and encouragement
2) **Economics and Environment**
   - Lack of amenities (e.g. grocery stores, pharmacies) and abandoned properties
   - Inadequate public infrastructure (e.g. garbage pickup, policing, transportation)
   - Human consequences (e.g. homelessness, early childhood trauma)

Community-Driven Solutions

1) **Bring Healthcare Closer into the Community**
   - Address social and mental health needs/connect people to needed services
   - Health workers that get to know families and follow-up long-term
2) **Build Social Network of Support**
   - Building connections & figuring out solutions together
   - Holding up history and soul of neighborhood -"What was, what is, and what can be"

Community-driven Solutions:

Tailoring Care Solutions to Meet Community Needs

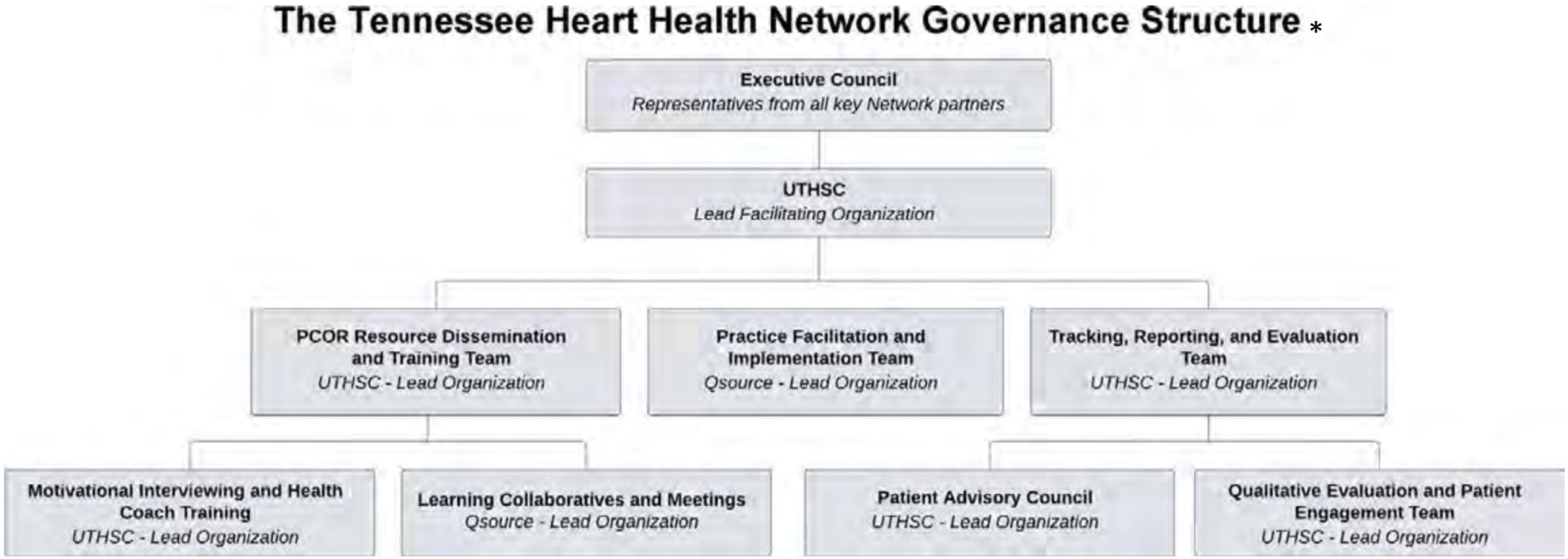
- The MODEL Study tailored its interventions based on extensive input through:
  - Patient Advisory Council
  - Community Advisory Council
  - Surveys and Focus Groups

Bailey et al., The management of diabetes in everyday life study. *Contemporary Clinical Trials*, 2020
Gatwood et al., Development of a tailored text message intervention. *TBM*, 2019


THE BEAUTIFUL THING ABOUT LEARNING IS THAT NOBODY CAN TAKE IT


soulsville

Representative Governance



* Grant CG, Mzayek F, Mamudu HM, Surbhi S, Kabir U, Bailey JE. Building Statewide QI Capacity, *Joint Commission Journal on Quality and Patient Safety,* 2024

Building Strong Relationships with Patients

- 20 Patient Advisory Council members representing diverse and medically underserved populations across TN met monthly to:
  - Give expert advice on ways to make cardiovascular care more patient-centered
  - Participate in educational sessions
  - Share their stories regarding care experience and their path to better heart health
- Patient stories disseminated to providers and policymakers (https://tnhearthealth.org/patient-video-stories/)

Building Strong Relationships with Payers, Providers, & Public Health

- Executive Council engaged:
  - Payers (Tennessee Medicaid, Medicaid MCOs, commercial plans)
  - Providers (health systems, community health centers, primary care)
  - Public health & more (TN Dept. of Public Health, TN Primary Care Assoc.)
- Population Health Subcommittee developed, adopted, and disseminated:
  - Health Coach Training and Certification Standards
  - Service Codes for Use by Health Coaches in Team-based Care
  - FAQs, all available at https://tnhearthealth.org/resources/reimbursement/

Takeaways

If you want to go fast, go alone. If you want to go far, go together.

- **Identify Key Collaborators**, meet them where they live and work to develop trusted partnerships
- **Multidisciplinary Team-based Care and Collaboration** is evidence based
  - Partnerships between different healthcare providers, our patient-neighbors, and community organizations enhance patient outcomes in cardiovascular care
- **Effective Partnerships** require building trust through listening and sharing power:
  - Engaging patient and provider experts
  - Representative governance

For more information contact Jim Bailey, MD at jeb@uthsc.edu or go to www.TNHeartHealth.org

Primary Palliative Care for Frail Older Adults

Mary Thomas, MD, MPH

Southern Medical Association

Annual Scientific Assembly

October 26, 2024

Disclosures

- No financial relationships

Objectives

- Define physical frailty
- Identify available physical frailty assessment tools
- Explore strategies for integrating primary palliative care and serious illness communication into clinical practice

Let's Meet our Patient

- Alex is an 80 year old man with history of Alzheimer's dementia w/o behavioral disturbance (diagnosed 6 years ago) who is partially dependent, HFpEF, CKD 3, macular degeneration, and recurrent falls who presents to primary care clinic for a routine check up.
- His son tells you that he has progressively needed more assistance with his IADLs and ADLs due to cognitive changes. He now needs assistance with bathing. He has also been losing weight.
- Alex says he feels well although is tired sometimes. He enjoys watching TV and describes his mood as happy at home. He has no concerns today.

Physical Exam

- General: well groomed, thin appearing man sitting in wheelchair, in no apparent distress
- HEENT: dentures present (which he adjusts several times during conversation), HOH, no hearing aids present
- MSK: sarcopenia, kyphosis
- Extremities: 1+ pitting edema lower extremities, chronic venous stasis dermatitis, toenail onychomycosis
- Neuro: plantar surface sensation intact, LE & UE strength 3/5, decreased grip strength bilaterally
- Timed up and go test: 45 secs
- Weight loss: 15 lbs over past year

What things come to mind in caring for Alex?

What makes you worried about frailty in Alex?

Frailty as a Clinical Syndrome

- Physical or phenotypic frailty – dysregulation of multiple physiologic processes/systems that leads to a decline in reserve and resistance to stressors and increased vulnerability to adverse outcomes
- Index frailty– accumulation of health conditions and impairments

Frailty ≠ Age ≠ Disability ≠ Comorbidity

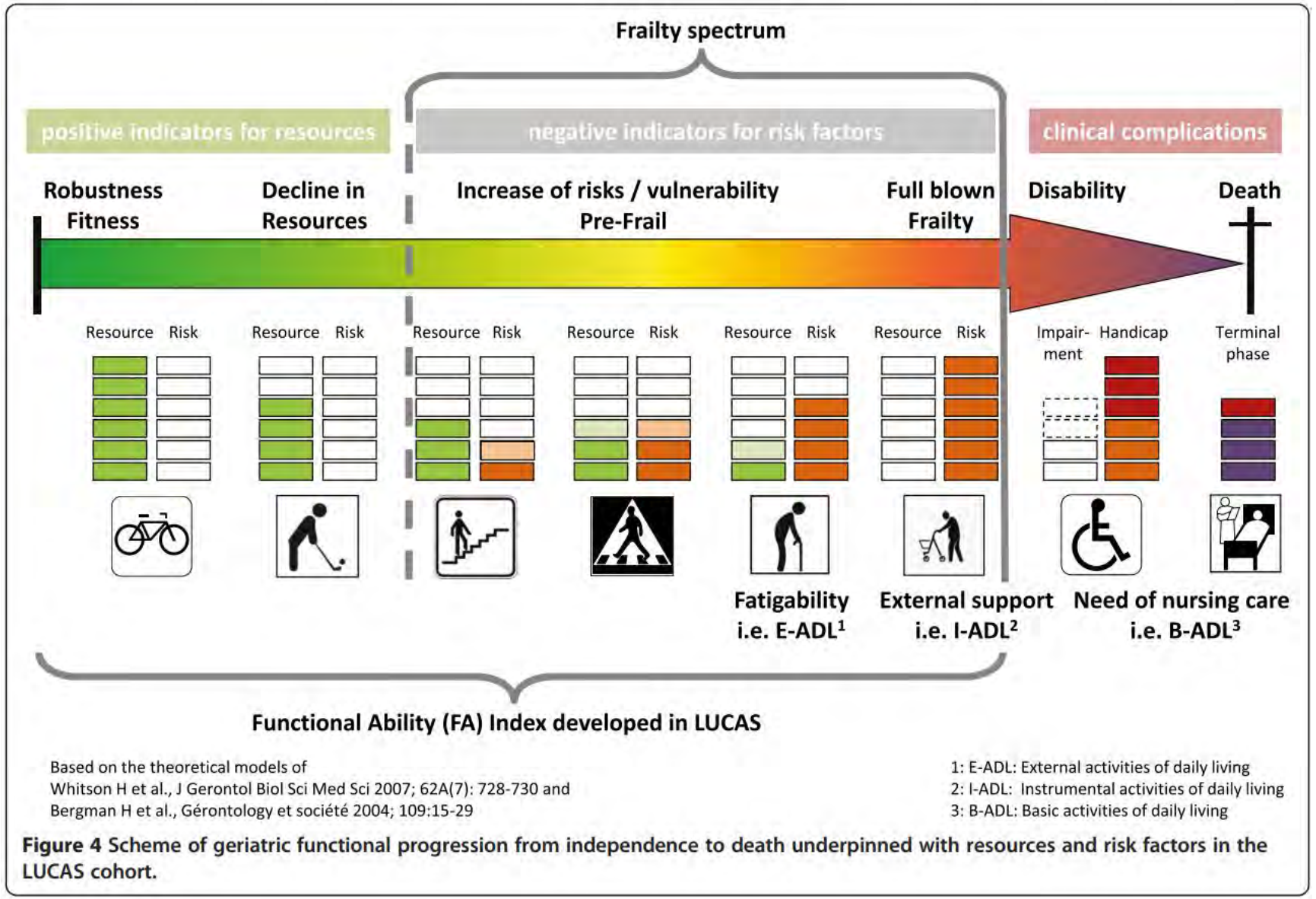
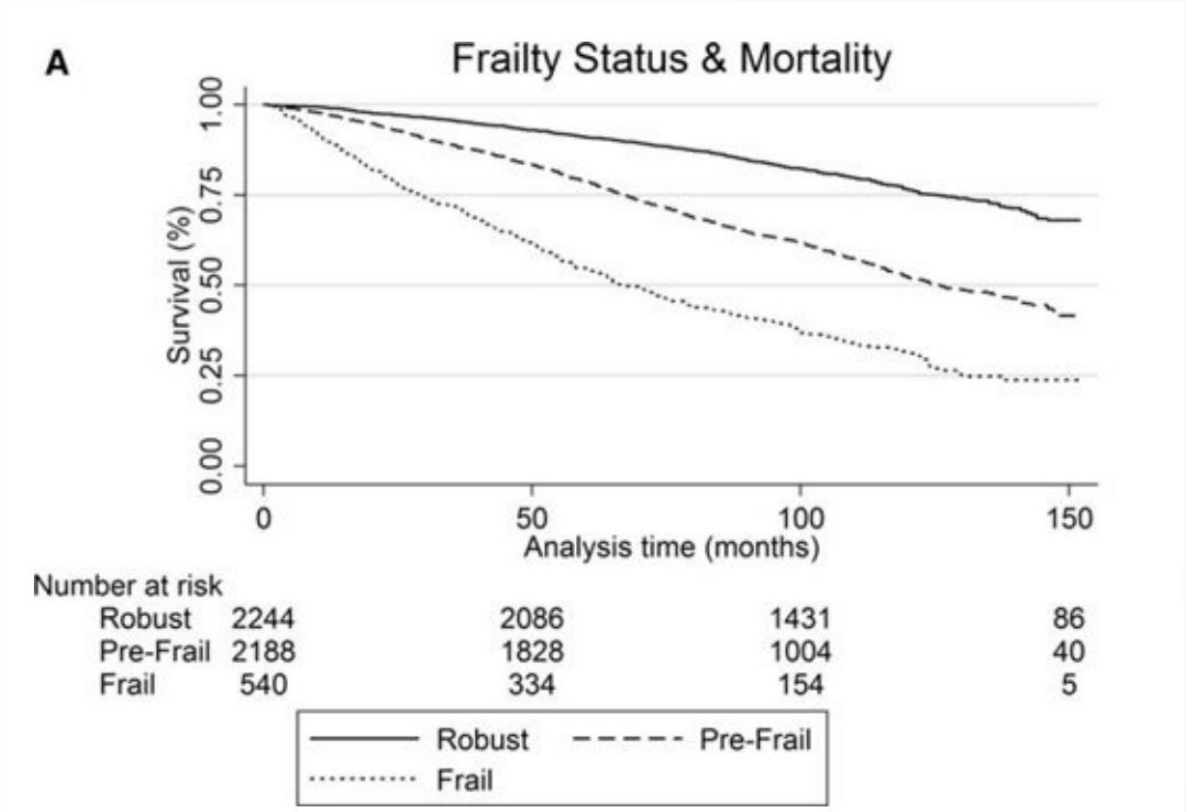


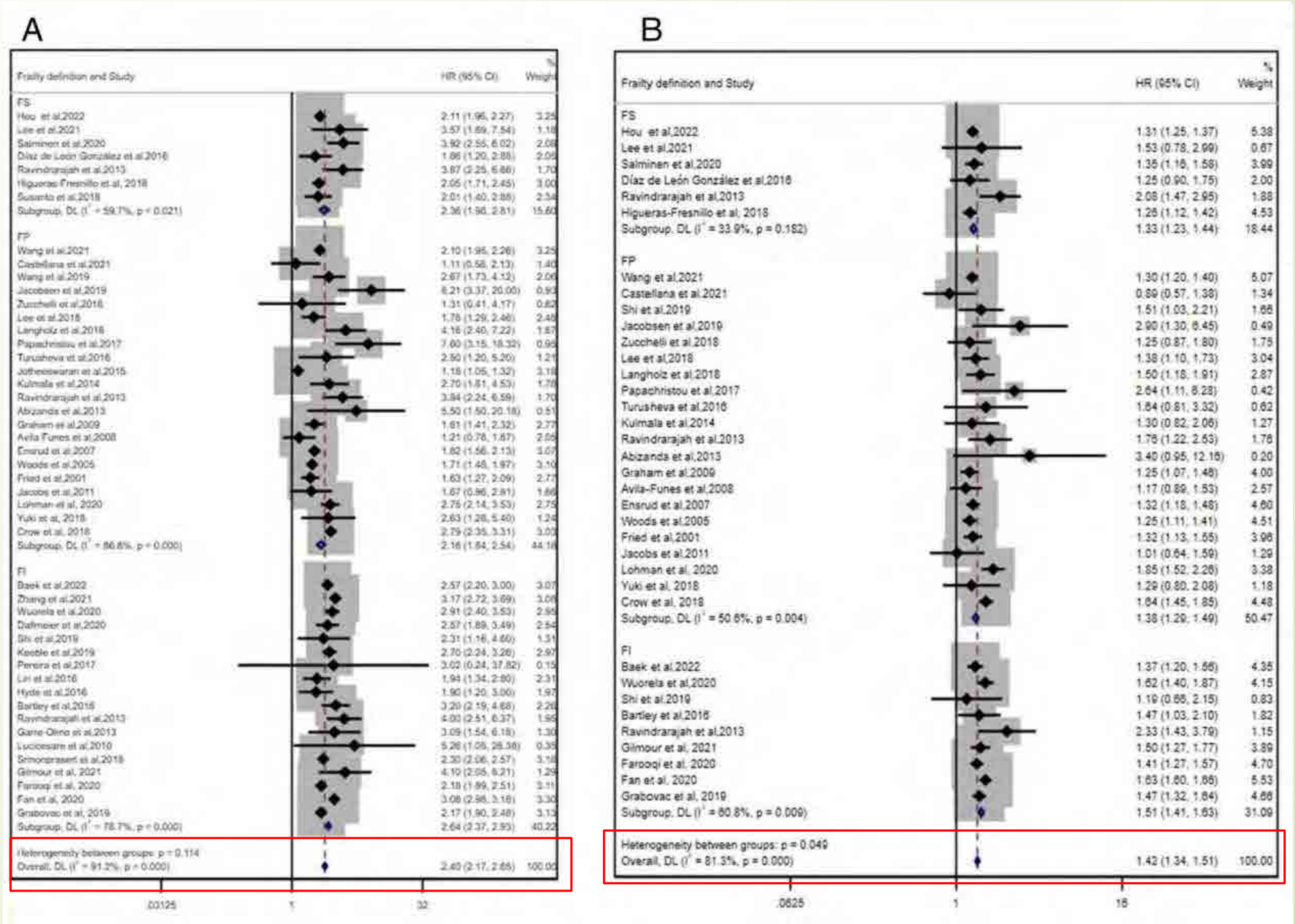
Figure 4 Scheme of geriatric functional progression from independence to death underpinned with resources and risk factors in the LUCAS cohort.

Dapp, et al., 2014

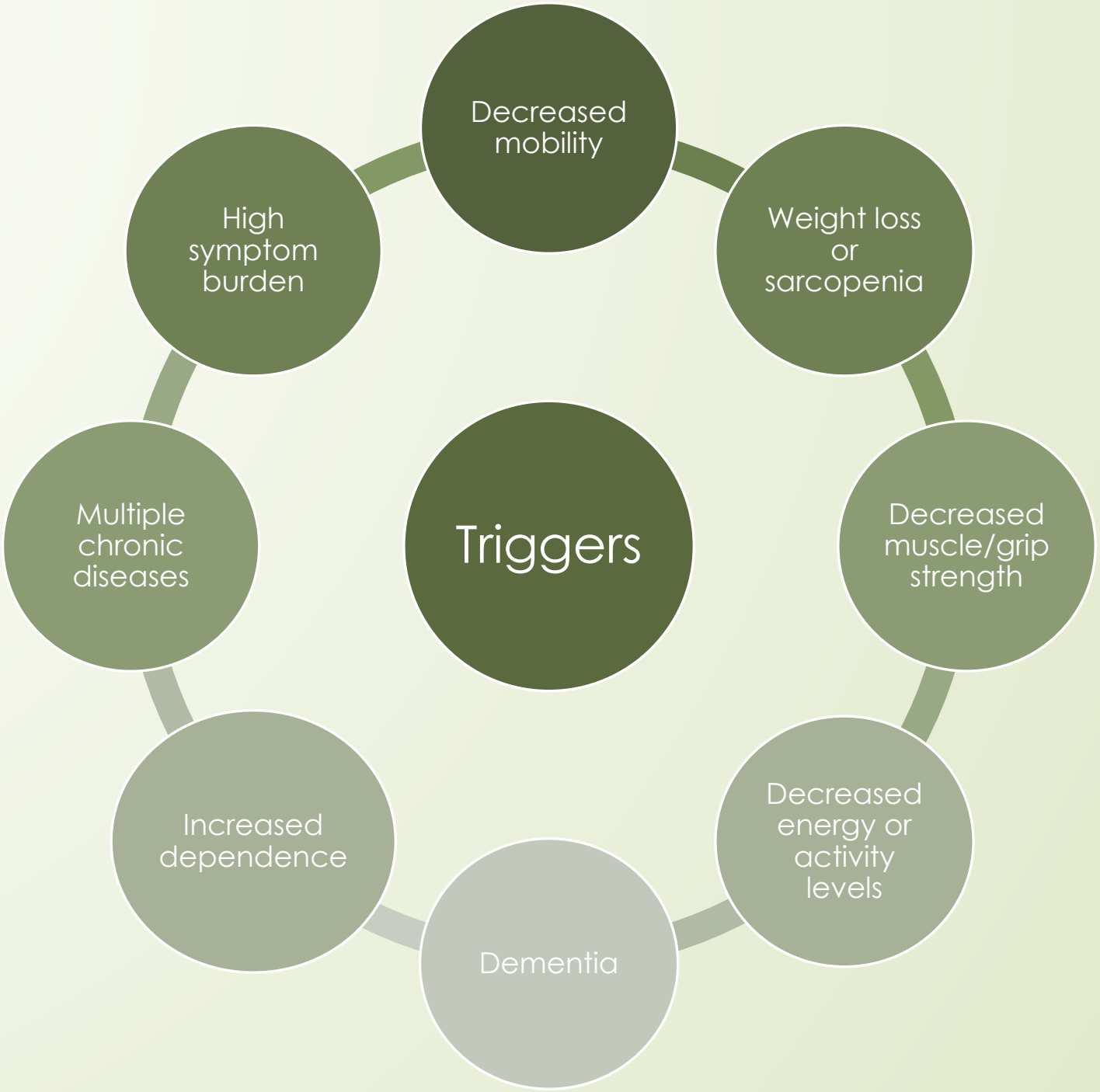


Mortality Risk Along the Frailty Spectrum

Crow, et al., 2018



Ekram, et al., 2021


Decreased mobility
Weight loss or sarcopenia
Decreased muscle/grip strength
Decreased energy or activity levels
Dementia
Increased dependence
Multiple chronic diseases
High symptom burden
Triggers

How would you assess Alex for frailty?

"Letting go" by David Millen

Given in loving memory of Dona Goodman

Criteria for Physical Frailty

Weight loss

- Unintentional weight loss of > 10 pounds in past year or at least 5% weight loss of previous year's body weight

Exhaustion

- Last week "I felt that everything I did was an effort" and "I could not get going"

Slowness

- Amount of time to walk 15 ft

Low activity level

- Kcal expenditure per week based on gender

Weakness

- Measured using grip strength

Instrument	Components	Pros	Cons
Gait speed	4 meter walk test	Strong predictor of future disability & all-cause mortality	No additional domains assessed, patient must be able to walk
Edmonton Frail Scale	Cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, functional performance	Multidimensional, includes cognition, multiple languages	Takes slightly longer than other assessments
FRAIL Scale	5 item questionnaire - Fatigue, resistance, ambulation, illness, loss of weight	Very quick (< 5 mins), can be completed prior to encounter, multiple languages	Self-report, no cognitive domain, diagnostic validity
Clinical Frailty Scale	Scale with pictures and text - physical fitness, symptom burden, functional independence	Scoring for people with dementia, helpful with prognostication, multiple languages	Relies heavily on clinical judgement, distinguishing disability from frailty

CLINICAL FRAILTY SCALE

1 VERY FIT — People who are robust, active, energetic and motivated. They tend to exercise regularly and are among the fittest for their age.

2 FIT — People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g., seasonally.

3 MANAGING WELL — People whose **medical problems are well controlled**, even if occasionally symptomatic, but often are **not regularly active** beyond routine walking.

4 LIVING WITH VERY MILD FRAILTY — Previously "vulnerable," this category marks early transition from complete independence. While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up" and/or being tired during the day.

5 LIVING WITH MILD FRAILTY — People who often have **more evident slowing**, and need help with **high order instrumental activities of daily living** (finances, transportation, heavy housework). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation, medications and begins to restrict light housework.

6 LIVING WITH MODERATE FRAILTY — People who need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 LIVING WITH SEVERE FRAILTY — **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~6 months).

8 LIVING WITH VERY SEVERE FRAILTY — Completely dependent for personal care and approaching end of life. Typically, they could not recover even from a minor illness.

9 TERMINALLY ILL — Approaching the end of life. This category applies to people with a **life expectancy <6 months**, who are **not otherwise living with severe frailty.** (Many terminally ill people can still exercise until very close to death.)

SCORING FRAILTY IN PEOPLE WITH DEMENTIA

The degree of frailty generally corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

In **very severe dementia** they are often bedfast. Many are virtually mute.

DALHOUSIE UNIVERSITY

Rockwood K et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–495.

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Clinical Frailty Scale

Acute Frailty Network

10K+
Downloads

E
Everyone

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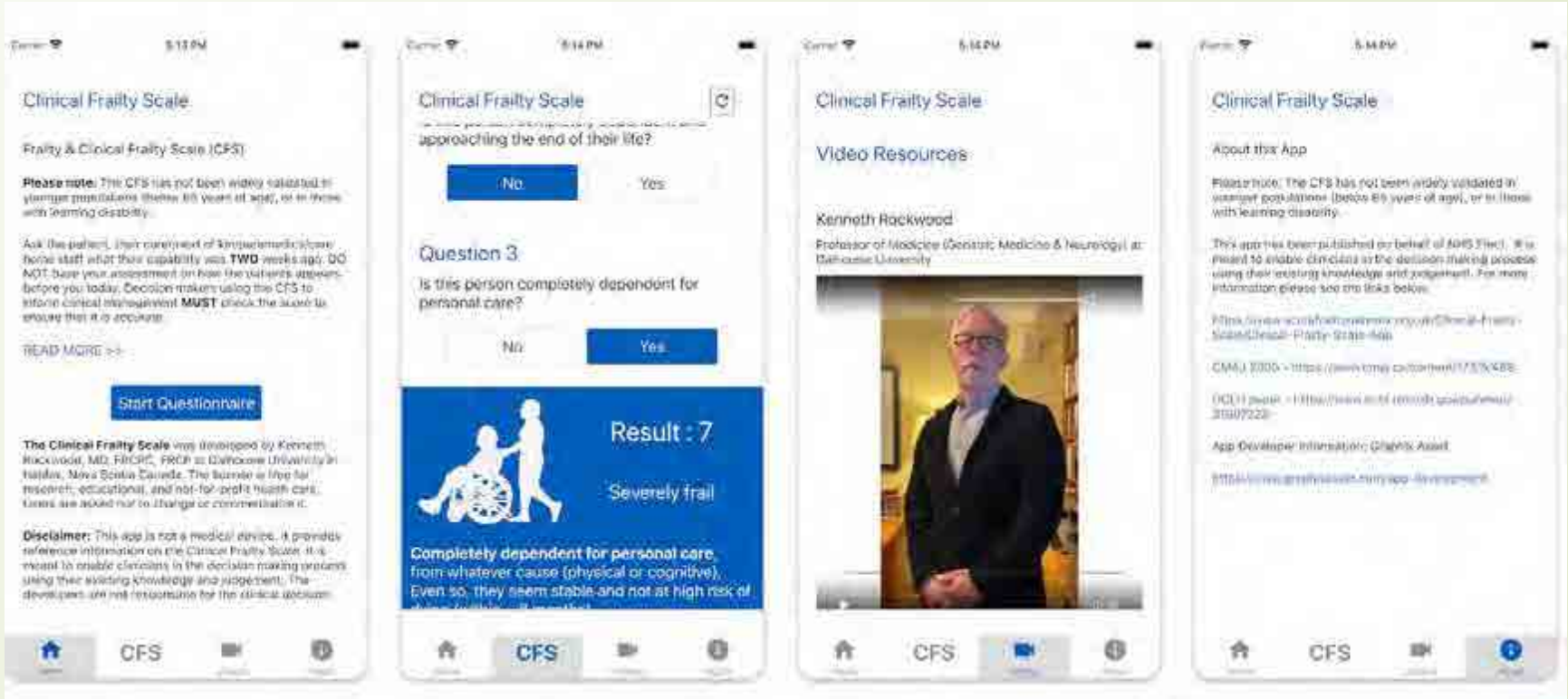
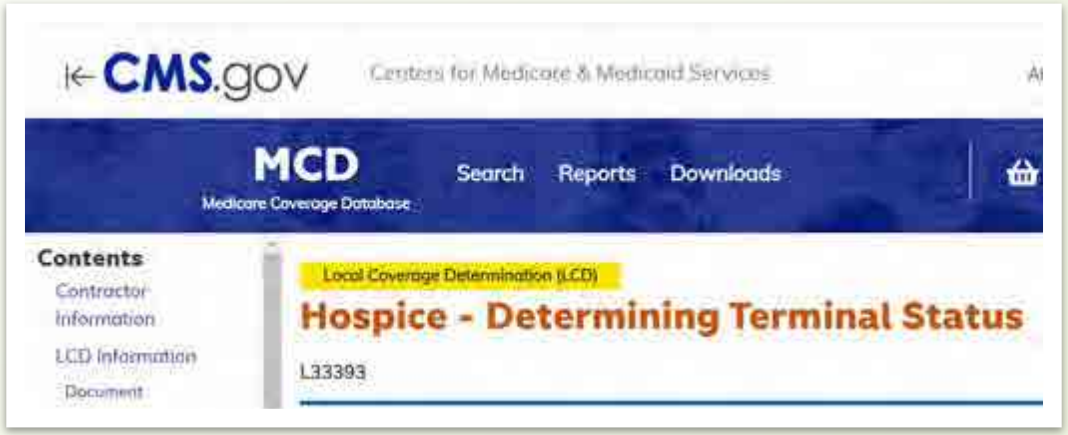
This app is available for all of your devices



Functional Assessment Staging Tool (FAST Scale)



Stage	Stage Name	Characteristic
1	Normal Aging	No deficits whatsoever
2	Possible Mild Cognitive Impairment	Subjective functional deficit
3	Mild Cognitive Impairment	Objective functional deficit interferes with a person's most complex tasks
4	Mild Dementia	IADLs become affected, such as bill paying, cooking, cleaning, traveling
5	Moderate Dementia	Needs help selecting proper attire
6a	Moderately Severe Dementia	Needs help putting on clothes
6b	Moderately Severe Dementia	Needs help bathing
6c	Moderately Severe Dementia	Needs help toileting
6d	Moderately Severe Dementia	Urinary incontinence
6e	Moderately Severe Dementia	Fecal incontinence
7a	Severe Dementia	Speaks 5-6 words during day
7b	Severe Dementia	Speaks only 1 word clearly
7c	Severe Dementia	Can no longer walk
7d	Severe Dementia	Can no longer sit up
7e	Severe Dementia	Can no longer smile
7f	Severe Dementia	Can no longer hold up head

Primary Palliative Care

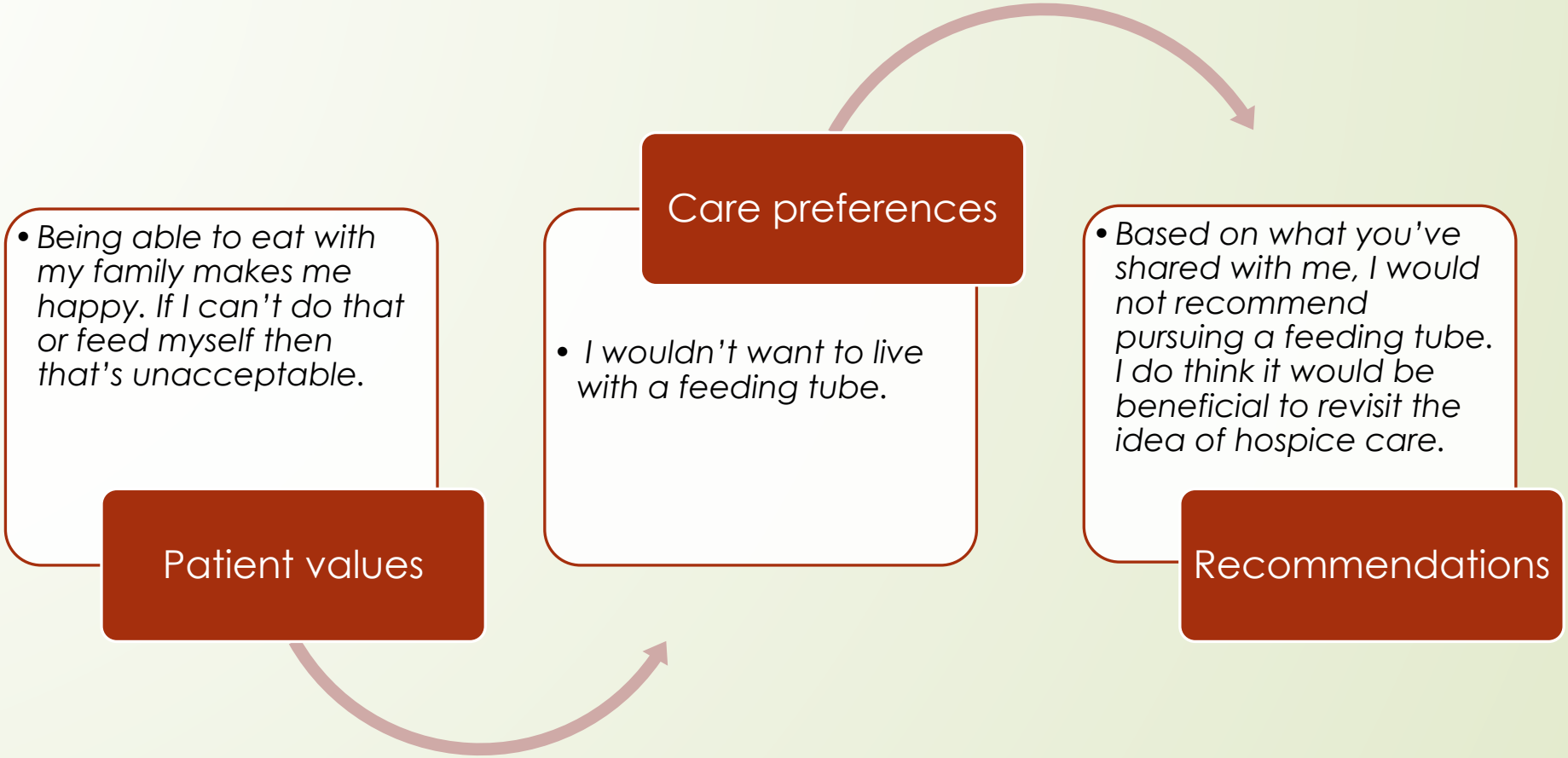
- Assess for frailty
- Determine factors that affect QOL
- Symptom management
- Communicate about prognosis
- GOC, ACP, and EOL planning
- Determine need for referral to specialty palliative care
  - Refractory symptoms
  - Pain management
  - Multiple complex conditions with unclear prognosis
  - Complex family dynamics or disagreements
  - Existential or spiritual distress
  - Requests for medical aid in dying

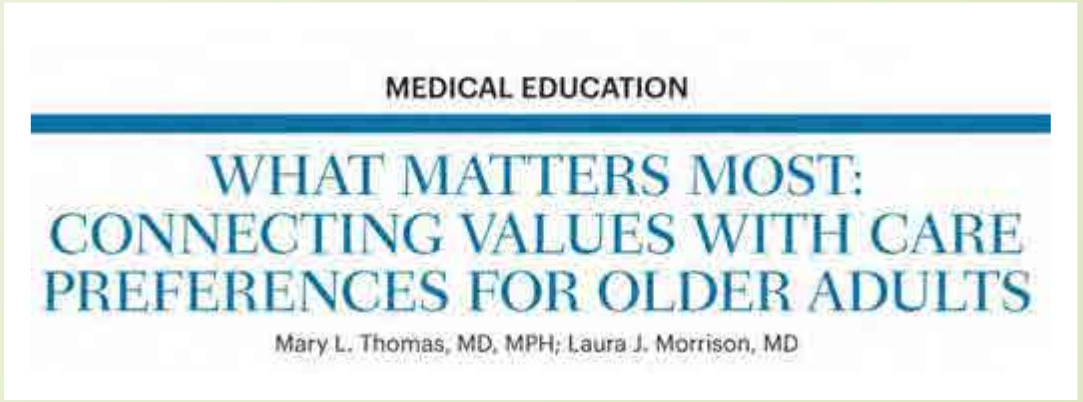
Alex's son shares his worry that fatigue, pain, and other symptoms have limited his quality of life. It is becoming challenging for Alex to leave the house.

How would you introduce GOC and ACP to your discussion with Alex and his son?

An Approach: REMAP

Step	What you say or do
1. Reframe why the status quo isn't working.	You may need to discuss serious news (eg a scan result) first. "Given this news, it seems like a good time to talk about what to do now." "We're in a different place."
2. Expect emotion & empathize.	"It's hard to deal with all this." "I can see you are really concerned about [x]." "Tell me more about that—what are you worried about?" "Is it ok for us to talk about what this means?"
3. Map the future.	"Given this situation, what's most important for you?" "When you think about the future, are there things you want to do?" "As you think towards the future, what concerns you?"
4. Align with the patient's values.	As I listen to you, it sounds the most important things are [x,y,z].
5. Plan medical treatments that match patient values.	Here's what I can do now that will help you do those important things. What do you think about it?


Patient values
• Being able to eat with my family makes me happy. If I can't do that or feed myself then that's unacceptable.
Care preferences
• I wouldn't want to live with a feeding tube.
Recommendations
• Based on what you've shared with me, I would not recommend pursuing a feeding tube. I do think it would be beneficial to revisit the idea of hospice care.


MEDICAL EDUCATION
WHAT MATTERS MOST: CONNECTING VALUES WITH CARE PREFERENCES FOR OLDER ADULTS
Mary L. Thomas, MD, MPH; Laura J. Morrison, MD

Communicating Uncertain Prognosis

Ask what they know

Clarify what is being asked & the information that is desired

- We want to be helpful in the way they want us to be helpful
- Not always asking about death
- Sometimes they are asking about something specific (functional, cognitive, life event)

Acknowledge the uncertainty, name the emotion

- *"Things are uncertain right now. I can only imagine how scary this must be."*

"I wish" statements

- *"I wish I knew the exact answer to your question. We can't know for sure."*

Ask permission to give anticipatory guidance

- *"Is it okay if I tell you what we do know about the progression of dementia?"*

Prognosis Communication Pearls

- Minutes to hours, hours to days, etc.
- “While it is possible, I would be surprised if…”
- Best, worst, and most likely case scenario

ACP Pearls

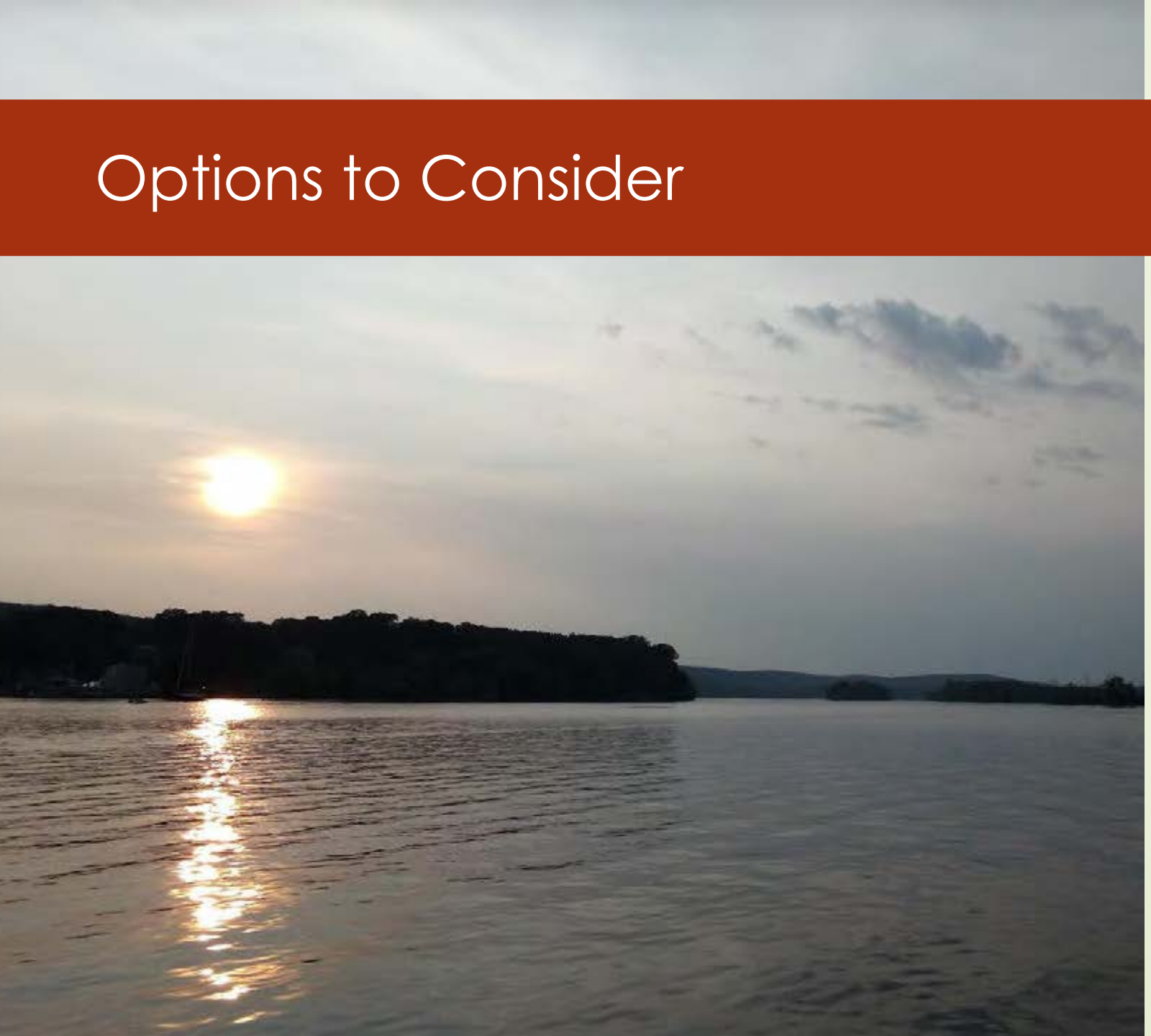
Healthcare proxy discussions

- Is the patient the decision maker for someone else?
- Does the proxy know they are the proxy?
- Can the proxy fulfill these duties?
- Sometimes patients associate ACP and GOC solely with burial plans or estate planning
  - *"What do they know about your wishes in medical situations? Tell me more about your conversations with them."*

Reframe

- *"Your son might need to make some tough decisions which can be scary. Sharing your wishes with him now can be a loving thing to do to try to help him through that."*

Options to Consider



- MOLST/POLST forms
- Geriatrics home care
- VNA services
- Area Agency on Aging
- Do not hospitalize order
- Palliative bridge program
- Hospice evaluation

SMA

PALLIATIVE CARE NETWORK OF WISCONSIN

ABOUT ADVOCACY FAST FACTS PUBLICATIONS RESOURCES CONTACT DONATE

Tools for Being a Better Educator

Search by Keyword | Filter by Category | SUBMIT

- Part 3: Communication Skills Resource Guide
- Part 2: Non-Pain Symptom Management Resource Guide
- Part 1: Pain Assessment and Management Resource Guide

Geriatric Fast Facts — by System | by Topic | by Science | by ACGME-C | by Age Friendly 4Ms

Determine blood pressure goals in older adults and possible medications

Laboratory Evaluation of Kidney Function - #8

Review key renal function lab values in a geriatric patient

Ocular Effects of Systemic Medications - #27

Identify and manage ophthalmic complications of systemic medications

Review of System

Cardiovascular
Endocrine
Gastrointestinal
Head, eye, ear, nose, throat
Hematologic/Lymphatic
Musculoskeletal
Neurologic
Psychiatric
Pulmonary & Respiratory Functions
Renal and Urinary
Sexuality
Skin

Geriatric Topic

Aging Principles
Cognitive, Affective & Behavioral Health
Complex or Chronic Illness in Older Adults
Falls, Balance, Gait Disorders
Injury and Trauma
Medication Management
Palliative and End of Life Care
Prevention, Safety and Transitions of Care

Science Principles

Behavioral & Social Sciences including Bioethics
Connective Tissue Changes
Immunosenescense
Impaired homeostasis
Population Health including Social Determinants
Post-mitotic tissue and age related degeneration

ACGME-C

Medical Knowledge
Patient Care
Communication Skills
Professionalism
Practice-based Learning and Improvement
Systems-based Practice

Age Friendly 4Ms

(What) Matters Most
Medications
Mentation
Mobility

Takeaways

- Physical frailty can be assessed for relatively quickly with the Edmonton Frail Scale, Clinical Frailty Scale, and the FRAIL scale.
- VitalTalk's REMAP communication strategy can be used to map values and care preferences and guide decision making.
- Palliative Care and Geriatrics Fast Facts are quick and readily accessible ways to look up clinically relevant evidence-based material.


Thank you!
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Sources

- Rockwood K, Theou O. Using the Clinical Frailty Scale in Allocating Scarce Health Care Resources. *Can Geriatr J*. 2020;23(3):210-215. Published 2020 Sep 1. doi:10.5770/cgj.23.463
- Chu W, Chang SF, Ho HY. Adverse Health Effects of Frailty: Systematic Review and Meta-Analysis of Middle-Aged and Older Adults With Implications for Evidence-Based Practice. *Worldviews Evid Based Nurs*. 2021;18(4):282-289. doi:10.1111/wvn.12508
- Clinical Frailty Scale Education Tool, Dr Elizabeth Moloney & Dr Lisa Kiely, 07 Apr 2020. Panopto. Published 2020. Accessed September 15, 2024. https://ucc.cloud.panopto.eu/Panopto/Pages/Viewer.aspx?id=ce9a4d94-fc1c-44ca-8a39-ab9600f624f3
- Crocker TF, Brown L, Clegg A, et al. Quality of life is substantially worse for community-dwelling older people living with frailty: systematic review and meta-analysis. *Qual Life Res*. 2019;28(8):2041-2056. doi:10.1007/s11136-019-02149-1
- Crow RS, Lohman MC, Titus AJ, et al. Mortality Risk Along the Frailty Spectrum: Data from the National Health and Nutrition Examination Survey 1999 to 2004. *J Am Geriatr Soc*. 2018;66(3):496-502. doi:10.1111/jgs.15220
- Dapp U, Minder CE, Anders J, Golgert S, von Renteln-Kruse W. Long-term prediction of changes in health status, frailty, nursing care and mortality in community-dwelling senior citizens—results from the Longitudinal Urban Cohort Ageing Study (LUCAS). *BMC Geriatr*. 2014;14:141. Published 2014 Dec 19. doi:10.1186/1471-2318-14-141
- Ekram ARMS, Woods RL, Britt C, Espinoza S, Ernst ME, Ryan J. The Association between Frailty and All-Cause Mortality in Community-Dwelling Older Individuals: An Umbrella Review [published correction appears in J Frailty Aging. 2022;11(2):247. doi: 10.14283/jfa.2021.24]. *J Frailty Aging*. 2021;10(4):320-326. doi:10.14283/jfa.2021.20
- Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56(3):M146-M156. doi:10.1093/gerona/56.3.m146
- Home. VitalTalk. https://www.vitaltalk.org/
- Hoogendijk E, Dent E. Recent Developments in Frailty Identification, Treatment, and Prevention in Older Adults: A Review. *Innov Aging*. 2023;7(Suppl 1):868. Published 2023 Dec 21. doi:10.1093/geroni/igad104.2796
- Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging*. 2012;16(7):601-608. doi:10.1007/s12603-012-0084-2
- Ng YX, Cheng LJ, Quek YY, Yu R, Wu XV. The measurement properties and feasibility of FRAIL scale in older adults: A systematic review and meta-analysis. *Ageing Res Rev*. 2024;95:102243. doi:10.1016/j.arr.2024.102243
- O'Caoimh R, Sezgin D, O'Donovan MR, et al. Prevalence of frailty in 62 countries across the world: a systematic review and meta-analysis of population-level studies. *Age Ageing*. 2021;50(1):96-104. doi:10.1093/ageing/afaa219
- Peng Y, Zhong GC, Zhou X, Guan L, Zhou L. Frailty and risks of all-cause and cause-specific death in community-dwelling adults: a systematic review and meta-analysis. *BMC Geriatr*. 2022;22(1):725. Published 2022 Sep 2. doi:10.1186/s12877-022-03404-w
- Waite SJ, Maitland S, Thomas A, Yarnall AJ. Sarcopenia and frailty in individuals with dementia: A systematic review. *Archives of Gerontology and Geriatrics*. 2021;92:104268. doi:https://doi.org/10.1016/j.archger.2020.104268

When Met with Hesitation or "No"

- Explore why
  - *"May I ask how come?"*
  - *"You seem hesitant."* (silence)
- Acknowledge that you respect their decision
- *"Is there someone else you'd like me to talk to about these things?"*
- *"I worry that by not talking about these things you could receive care that you don't want and not receive care that you do want."*
- *"Why don't we take a step back…"*
- Operate in the hypothetical
- Offer to set up a follow-up visit with patient and decision maker

PAUSE Talking Map

STEP	WHAT YOU SAY OR DO
PAUSE, make the time	***"There is something I'd like to put on our agenda today."*** Take a moment to introduce the topic.
ASK permission and explain why.	***"I would like your opinion on something. Occasionally one of my patients gets sick suddenly and I can't talk to them."*** *"Then I worry that I can't provide the best care for them."* *"For example, one of my patients told me that they would never want to be a vegetable. That's very important for me to know, even when that person is far from being that sick."* *"What do you think about that?"*
UNDERSTAND big picture values.	***"Have you ever heard about advance directives or living wills?"*** *"If the disease was getting worse and might take your life, what would be most important to you?"* *"Some people think that we should focus on comfort, others say adding days to your life is the most important. What do you think?"*
SUGGEST choosing a surrogate.	***"Have you ever thought about who would be the best person to make medical decisions if you were too sick to make them yourself?"***
EXPECT emotion respond empathically.	***"I can see this is making you feel concerned." [names the emotion]*** *"What I am hearing you say is you want to keep fighting."* [Reflects the patient's words back]

ADAPT Tool

Step	What you say
1. Ask what the patient knows, what they want to know	What have other doctors told you about what your prognosis, or the future? How much have you been thinking about the future?
2. Discover what info about the future would be useful for the pt	For some people prognosis is numbers or statistics about how long they will live. For other people, prognosis is about living to a particular date. What would be more helpful for you?
3. Anticipate ambivalence	Talking about the future can be a little scary. If you're not sure, maybe you could tell me how you see the pros and cons of discussing this. If clinically deteriorating: From what I know of you, talking about this information might affect decisions you are thinking about.

4. Provide information in the form the patient wants	To provide using statistics: The worst case scenario is [25th percentile], and the best case scenario is [75th percentile]. If I had 100 people with a similar situation, by [median survival], 50 would have died of cancer and 50 would still be alive with cancer. To provide without statistics: From my knowledge of your situation and how you cancer has been changing /responding, I think there is a good/50-50/slim chance that you will be able to be around [on that date/for that event].
5. Track emotion	I can see this is not what you were hoping for. I wish I had better news. I can only imagine how this information feels to you. I appreciate that you want to know what to expect.

Goals of Care Note Section

- Understanding
- Information preferences
- Prognosis
- Goals
- Fears/worries
- Function
- Trade-offs
- Family
- POA/proxy

To Facilitate Discussion

- Includes personal, spiritual, medical, and legal wishes
- Written with the American Bar Association's Commission on Law & Aging
  - Meets 46 states' legal requirements
  - Burial wishes are not legally binding
- Available in 40 languages
- Can be completed at home
  - Stimulates discussion with patient and their family
- Can be scanned into EMR