Managing Chronic Pain:

First Do No Harm!

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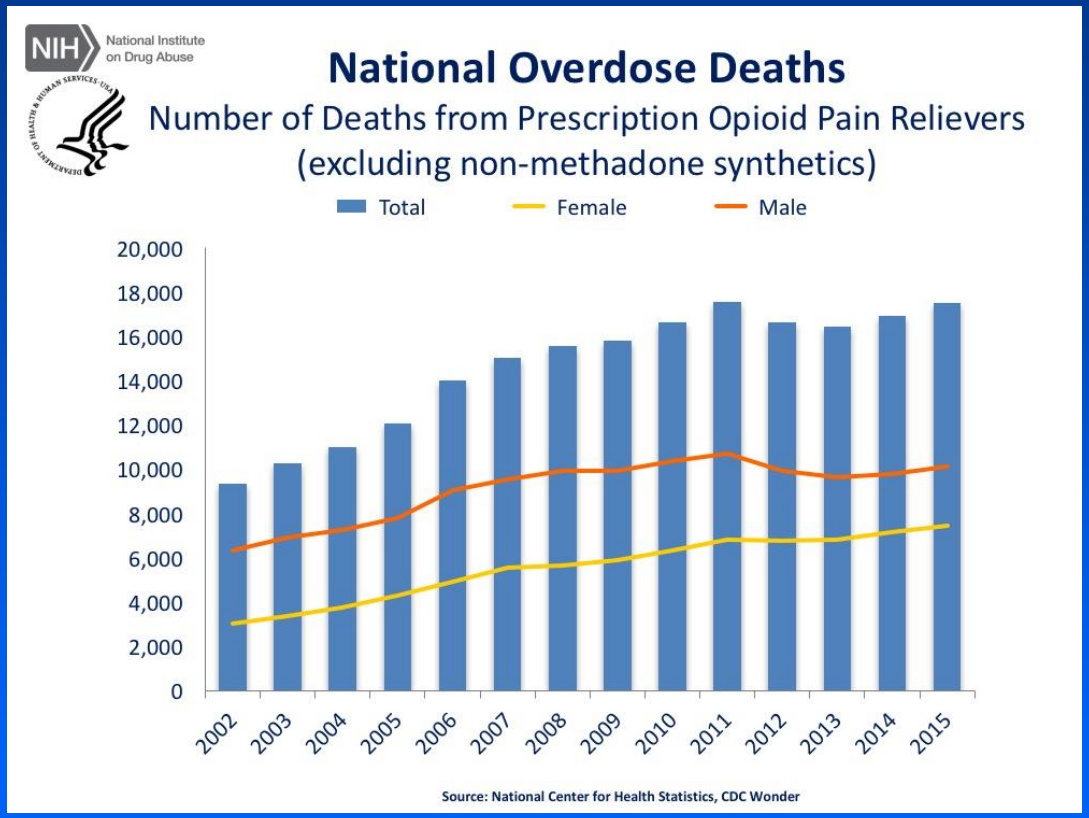
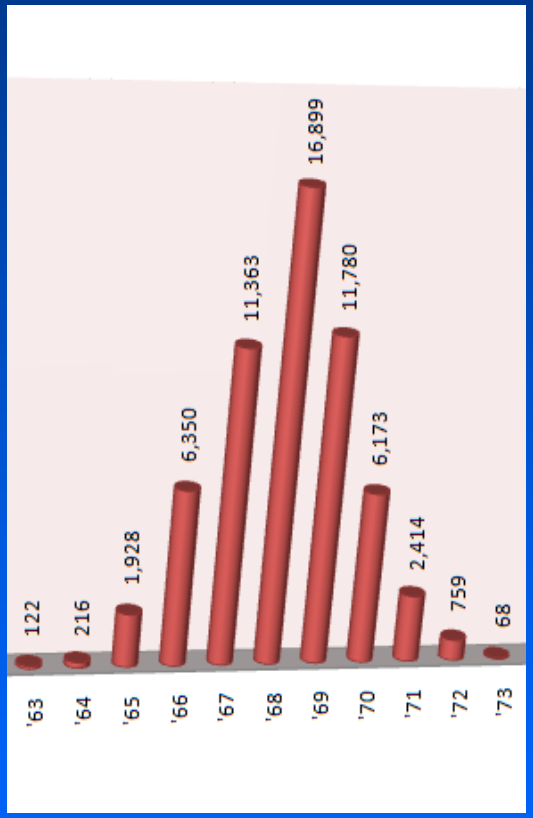
The Problem

- Chronic non-terminal pain affects up to 80 million people in US, and is the #1 cause of long term disability
- 300% increase in opioid prescribing since 1995
- Despite increased opioid use, no change in patient-reported pain, and sharp rises in disability rates due to chronic pain
- 180,000+ deaths from prescription opioids 2000-2015

US Annual Opioid Deaths



US Vietnam War Deaths

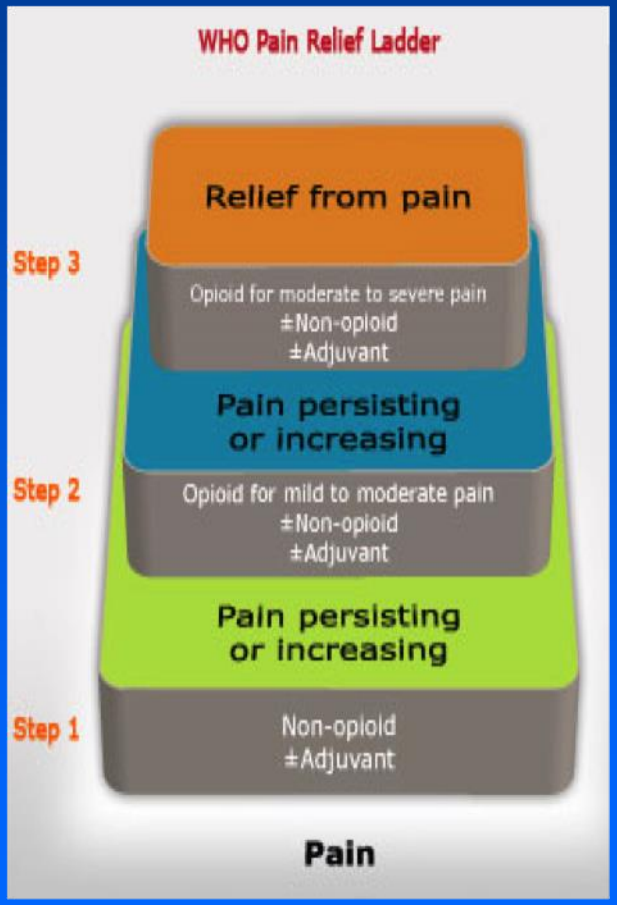


Our opioid prescribing patterns are leading to an explosion in opioid-related disability, addiction, and death.

How are we doing so much harm trying to do good?

Most of what we were taught about pain is wrong!

- You are a doc. You must "help"
- The WHO Pain Ladder is our guide
- Follow pain scores
- Treat chronic pain like acute pain
- All paths lead to opioids
- Minimal risk when used to treat chronic pain
- There is no ceiling for opioid treatment




"Ask your doctor if taking a pill to solve all your problems is right for you."

Do you need a pill for every ill?

- Nonpharmacologic therapy usually works!
  - Rest, Ice, Compression, Elevation (RICE)
  - Physical Therapy
  - Manipulation in selected cases
  - Massage therapy in selected cases
  - Injection therapy in selected cases
- Most acute pain improves within 1-2 weeks, regardless of treatment!

Start with the Basics

- Acetaminophen safest option overall.
- NSAID's vs. APAP?; NEJM study found equivalent. Anti-inflammatory effects of NSAID's oversold; primarily analgesics.
- NSAID's + APAP do have additive benefits
- Opioids aren't that good for acute pain
  - No better than NSAID's for most dental pain [Clin Pharmacol Ther 1999 Dec 66(6): 625-35; Clin Ther 2004 May 26(5): 769-78]
  - No better than NSAID'S for acute back pain (JAMA 2015 314(15): 1572-1580)

Opioids for Acute Pain

- Most chronic use starts with acute pain
  - Iatrogenic addiction is a huge problem!
  - Patients given opioids post-surgery 2-5 times more likely to end up using opioids long-term.
  - 44% of patients in a methadone maintenance program reported that their addiction began with opioids prescribed for pain.
- If you do use opioids for acute pain, prescribe no more than a 3 day supply (5-15 tabs) and re-evaluate carefully before extending therapy.

Acute And Chronic Pain Are Different

Acute Pain – a defense

- Is a symptom
- Has identifiable source and physical findings
- Has a protective function in response to disease or injury
- Associated with autonomic response (HR, BP changes, distress)
- Resolves with treatment or recovery of underlying process

Chronic Pain - learned

- Is a diagnosis
- Often without clear source or physical findings
- Is often maladaptive and becomes the disease itself
- Usually no observable physiologic changes
- After 3 months, is associated with physical, affective, behavioral and interpersonal consequences

Opioids for Chronic Pain

- Only 35-40% of patients benefit meaningfully
  - Little evidence for effectiveness for chronic noncancer pain [AHRQ 2014; Ann Int Med 2015 162(4)]
  - Limited efficacy in cancer pain (Pain Phys 2012; 15:ES39-58).
  - Tapering or discontinuing opioids may improve pain, function, and quality of life (Ann Int Med July 18, 2017)
- May aggravate chronic pain (opioid-induced hyperalgesia)
- Potent respiratory depressants
- Risks of endocrinopathy, enteropathy, fractures, immunologic
- Approximately 20-50% of patients treated with opioids for chronic pain eventually develop addiction
- **3.5 - 7+ relative risk for mortality**

OK, I get it. Opioids are bad.
So what should I do for pain?

Steps For Treating Chronic Pain

- Identify and treat local pain generators
- Promote healthy behaviors, increased physical activity
- Start with local, then adjuvant therapies
- Restore sleep
- Treat comorbid psychiatric illness
- THEN… Consider opioid initiation or continuation

Introduction to Adjuvant Therapies

- Tricyclics
- SSRI/SNRI medications
- Gabapentin and pregabalin
- Other anticonvulsants?

Tricyclic Antidepressants

- Mechanism in pain: Multiple receptor activities; serotonin and norepinephrine reuptake inhibition likely most important; alters pain signal transmission in spinal cord.
- Improves sleep quality; may be important.
- Also useful for vascular headaches, smoking cessation, depression, panic disorder, and anxiety.

Gabapentin and Pregabalin

- Gabapentin (Neurontin®, Horizant®)
- Pregabalin (Lyrica®)

- Mechanism in pain unclear. Bind to $\alpha_2\delta$ subunit of calcium channels, reducing glutamate release in excited afferent pain neurons. Decreases pain signal transmission.
- In neuropathic pain, may be more effective for "electric shock" type pain sensations.

SNRI's

- Improve pain through lowering central pain sensitivity
- Same mechanism as TCA's???
- Are pain benefits a class effect?
- Best data on pain is for duloxetine; less on venlafaxine, and very little on milnacipran.
- Conflicting data on duloxetine vs. venlafaxine

Match Drug to Type to Pain Type?

- Acetaminophen, NSAID's, and opiates can be effective for any kind of pain. However, they are typically less effective for neuropathic pain than for other types of pain.
- TCA's, SNRI's, and gabapentin/pregabalin are may be effective for any kind of pain. However, they are typically the most effective drugs for neuropathic pain.

Opioids for Chronic Pain

- Be clear that use is a TRIAL
- Start with short-acting opioids
- Start low and go slow; know your MED's
- Ongoing assessment of benefits and harms
- If tolerating and benefitting, then consider conversion to a long-acting opioid
- Avoid methadone unless you are very familiar with its pharmacokinetics and dynamics

Calculating morphine milligram equivalents (MME)

OPIOID (doses in mg/day except where noted)	**CONVERSION FACTOR**
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.

CDC Guideline on Prescribing Opioids For Chronic Pain

- Calculate opioid doses as morphine equivalents per day (MED)
- Reassess at >50 MED
- Doses >90 MED rarely (if ever) indicated:
  - >90 mg/day of morphine or hydrocodone
  - >60 mg/day of oxycodone
  - >50 mcg/hr of fentanyl
  - >20 mg/day of methadone

Opioid Dose Matters!

- Risk increases sharply as doses rise

Relative risk of opioid overdose death	
Maximum prescribed daily opioid dose, mg/d	
1-<20	1 [Reference]
20-<50	1.88 (1.33-2.67)
50-<100	4.63 (3.18-6.74)
≥100	7.18 (4.85-10.65)

JAMA. 2011;305(13):1315-1321

Pain-Enjoyment-Activity Scale

1. What number best describes your pain on average in the past week:

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

3. What number best describes how, during the past week, pain has interfered with your general activity?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

3+ point change generally considered clinically significant

Ready to Stamp Out Pain?

Case 1

45 y/o man new to you, his former doc, Dr. Feelgood, recently “left practice” and he will soon need refills. History of fairly good health, but chronic headaches, neck pain and spasms 5 years after a MVA. No hx surgery or PT.

Pain managed well on meds. He works part-time, smokes cigarettes.

Asking for Soma 350 mg – 1 TID, OxyContin 80 mg BID and Vicodin 5/500 – 2 QID.

Exam – NAD, friendly, non-specific exam.

What would you do for him at this first visit?

A) Prescribe the medications so that he doesn't go through withdrawal.
B) Prescribe the OxyContin, but not Soma.
C) I would tell him "I don't kiss on the first date."
D) I would rotate his opioids to methadone.

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Before that first kiss:

1) Check MAPS.
2) Check urine toxicology.
3) Check records.
4) Establish use agreement and expectations.

Concept of Universal Pain Precautions:

- Prescription monitoring programs
- Urine toxicology
- Complete assessment and records
- Controlled substance use agreements

Michigan Automated Prescription System

Selected Prescription Detail Report

Patient Name : Doe John DOB : 01/01/2001

Patient Name	Birth Date	Medication		Rx Number	Practitioner Name	Dispenser Name
Address	Issue Date	Form / Qty	Rx Type	Transmission Form	Practitioner DEA#	Dispenser DEA#
	Fill Date	Strength	Auth Refills	Payment Type	Practitioner Address	Dispenser Address
DOE, JOHN	01/01/2001	DIAZEPAM		935281	UNIVERSITY OF MICHIGAN MEDICAL CENT	BILLNAT CORP, DBA
12345 ANYSTREET	10/26/2013	TAB 60.00	Original	Written Prescription	AU7007467	BB5563538
ANYTOWN	10/26/2013	10 MG	0	Commercial PBM Ins	UH-B2D301	SAV-ON FAMILY PHARMACY
					ANN ARBOR, MI, 481095008	ROMULUS, MI, 481740000
DOE, JOHN	01/01/2001	LORAZEPAM		917149	UNIVERSITY OF MICHIGAN MEDICAL CENT	BILLNAT CORP, DBA
12345 ANYSTREET	06/04/2013	TAB 90.00	Original	Written Prescription	AU7007467	BB5563538
ANYTOWN	06/04/2013	1 MG	0	Commercial PBM Ins	UH-B2D301	SAV-ON FAMILY PHARMACY
					ANN ARBOR, MI, 481095008	ROMULUS, MI, 481740000
DOE, JOHN	01/01/2001	ZOLPIDEM TARTRATE		207359	UNIVERSITY OF MICHIGAN MEDICAL CENT	BILLNAT CORPORATION
12345 ANYSTREET	10/08/2012	TAB 7.00	Original	Written Prescription	AU7007467	BB9218670
ANYTOWN	10/08/2012	10 MG	0	Commercial PBM Ins	UH-B2D301	DBA SAV-ON HUNTER PHARMACY
					ANN ARBOR, MI, 481095008	HARPER WOODS, MI, 482250000
DOE, JOHN	01/01/2001	APAP/HYDROCODONE BITARTRATE		207362	UNIVERSITY OF MICHIGAN MEDICAL CENT	BILLNAT CORPORATION
12345 ANYSTREET	10/08/2012	TAB 20.00	Original	Written Prescription	AU7007467	BB9218670
ANYTOWN	10/08/2012	500 MG-5 MG	0	Commercial PBM Ins	UH-B2D301	DBA SAV-ON HUNTER PHARMACY
					ANN ARBOR, MI, 481095008	HARPER WOODS, MI, 482250000

Urine Toxicology

- Two basic varieties
  - EIA: Sensitive and cheap, but subject to false positives, and misses some drugs
  - Gas Chromatography/Mass Spectroscopy: More precise and highly accurate, but labor intensive and expensive
  - If in doubt about a result, have a quick chat with your friendly toxicology lab director!

Controlled Substance Use Agreement

Appendix C.

Patient-Provider Agreement for Ongoing Use of Controlled Medication

BIRTHDATE

NAME

The use of the following medicine(s)_____
(list medicine names)

Is only one part of my treatment for_____.

Primary Prescribing Doctor: _____

What should I know about this medication?

This controlled medication may help me.

Opioid pain medications often have side effects, which may include but are not limited to:

- Itching
- Rash
- Severe constipation
- Trouble urinating or passing stool
- Depression getting worse
- Problems thinking clearly

Anxiety & Sleep medicine(s) can cause:

- Dizziness
- Memory problems

Combining drugs can cause:

- Overdose
- Trouble breathing
- Death

Stimulant medicines (such as for ADHD) can cause:

- High blood pressure
- Fast or irregular heart beats

I could become addicted to this medicine.

If I must stop this medicine for any reason, I need to stop it slowly. Stopping it slowly will help me avoid feeling sick from withdrawal symptoms. If I decide to stop my medication, I will contact my doctor.

If I or anyone in my family has ever had drug or alcohol problems, I have a higher chance of getting addicted to this medicine.

If I take this medicine and drink alcohol or use illegal drugs I:

- May not be able to think clearly
- Could risk hurting myself (such as a car crash)
- Could become ill or even die

My doctor can only prescribe this medicine if I do not use illegal drugs.

If I do not use this medication exactly as prescribed, I risk hurting myself and others.

I will not increase my medicine dose without being told to do so by my doctor.

This medicine will not be refilled early.

I am in charge of my medicine.

- I know my medicine will not be replaced if it is stolen or lost.
- I will not share or give this medicine to other people.

Case 2

- 44 y/o M with a history of low back pain radiating to left leg, present since motorbike injury at age 24.
- On opiates for approximately 20 years; now taking methadone 60 mg QID.
- PMH significant for depression, anxiety, and substance abuse; denies current drug use.
- Unemployed, lives with parents. No hobbies, volunteering, or social activities.

Case 2 Continued

- States at visit, “I feel like my body is falling apart. I hurt all over.” Pain is 6/10 at best, 10/10 at worse, 8/10 most of the time.
- Exam: Appears tearful and depressed. Moves slowly. Diffusely tender to palpation over lower back and left leg.
- MAPS shows no other prescribers
- Urine tox shows prescribed medications

What is the strongest indication to change his regimen?

A) Total daily methadone dose of 240 mg/day

B) 8/10 pain most of the time

C) Prior history of drug abuse

D) Signs of depression

E) Low level of function

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E) Low level of function

Benefits must outweigh risks!

- Patient is on a massive dose of methadone; maximum recommended dose is 20 mg/d!
- Diffuse pain suggests opiate-induced hyperalgesia
- Despite extraordinary opiate doses, patient is almost completely nonfunctional.

Why To Taper or Remove

- Lack of benefit
- Excessive dosing
- Medication overdose
- Opioid induced hyperalgesia/toxicity
- Non-compliance with evaluation, meds, etc.
- Suspicion for misuse of medication

Approaching Tapering

- Have an honest talk with the patient about risk and benefits from treatment
- Be clear that intent is not punitive
- Set targets for increasing activities and socialization.
- Mental health interventions
- Plan a gradual taper, with frequent follow-up

How to Taper

Calculate starting daily MED

Usual Taper:

1. Reduce by 10% of starting dose every week until at 20% of original dose
2. May then need to slow taper; e.g. 5%/week.

Rapid Taper: Reduce by 25-50% of starting dose every week until off

May use clonidine 0.1 mg QID PRN for withdrawal symptoms (agitation, piloerection, sweats).

May use OTC loperamide PRN for diarrhea

May use antiemetics PRN for nausea

Case 3

Your next case is a 44 year old woman with chronic pelvic pain, interstitial cystitis, cyclic vomiting syndrome, irritable bowel syndrome, and depression. She cries at every visit, and reports poor sleep at night. Trials of nortriptyline, Lyrica, and Vicodin have done little to improve her pain.

Case 3

What should your next step be?

A) Prescribe fluoxetine
B) Prescribe duloxetine
C) Prescribe methadone
D) Prescribe her zolpidem
E) Ask her about her dreams

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Chronic Pain Patients Are Different

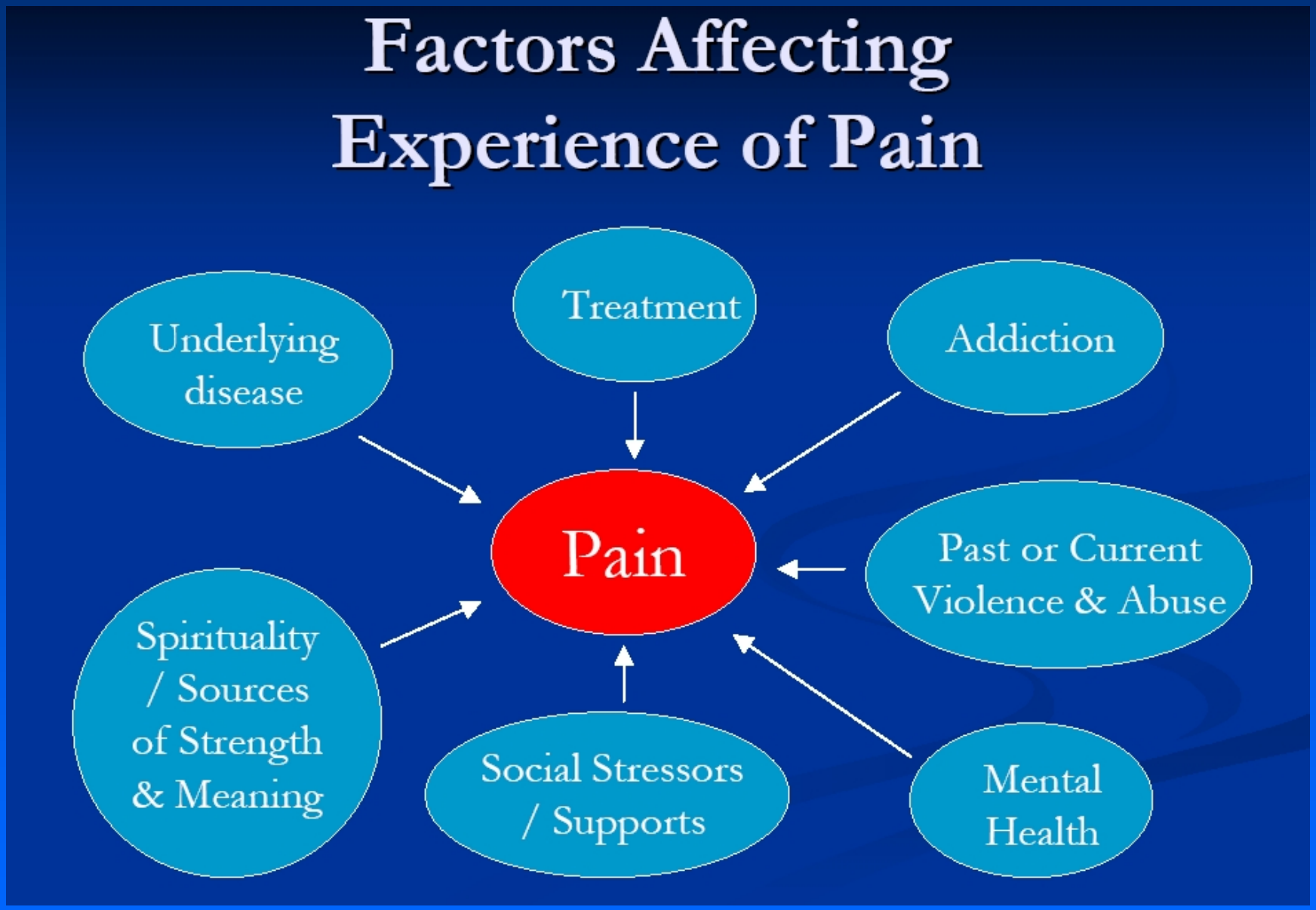
High prevalence of complex psychosocial issues

- Mood and anxiety disorders
- PTSD
- Personality Disorders
- History of suicide attempts
- History of emotional/physical sexual abuse
- Past or present substance abuse (not just opioids)
- Impaired coping skills
- Low employment and income levels

Pain 156 (2): 231-242 (2015)

Understanding the Pain-Depression-Addiction Nexus is critical to successfully treating these patients!

Factors Affecting Experience of Pain



Psychiatry for the Primary Doc

- Take a "real" psychosocial history
- Uncover anxiety back to childhood, current stresses, pending litigation…
- Recognize the Pain – Mood disorder nexus
- Substance abuse vs. chemical coping
- Therapy is hard
- Finding a qualified therapist (and payment) is harder
- Detoxification is essential !

Case 4

45 year old woman seen by you tomorrow. You have been treating her for two years with MS-ER 30 mg TID, HC/APAP 10/325 x 8/d, sometimes takes 12 and Xanax 2 mg TID for chronic, generalized abdominal pain and anxiety. She is divorced, unemployed, is worried about her bills and cannot sleep at night. Pain 8/10. She has never had misuse or unexpected drug test results, but occasionally runs out of her meds, has called early for more, cries every time seen.

What is most wrong with this picture?

A) Taking MS-ER 90 mg/day
B) Taking HC/APAP 10/325 8 tabs/day
C) Taking Xanax 2 mg TID
D) High levels of distress

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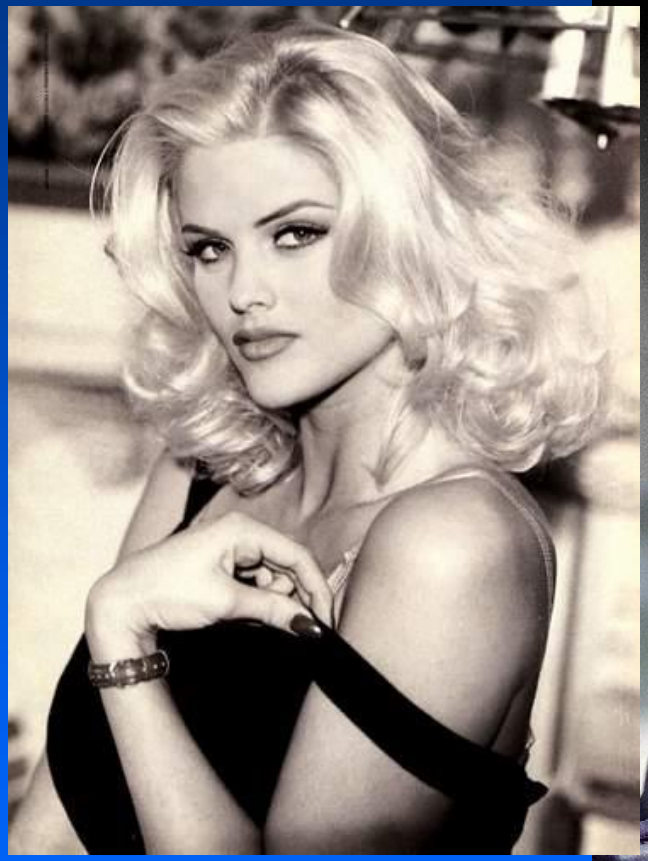
Benzodiazepines

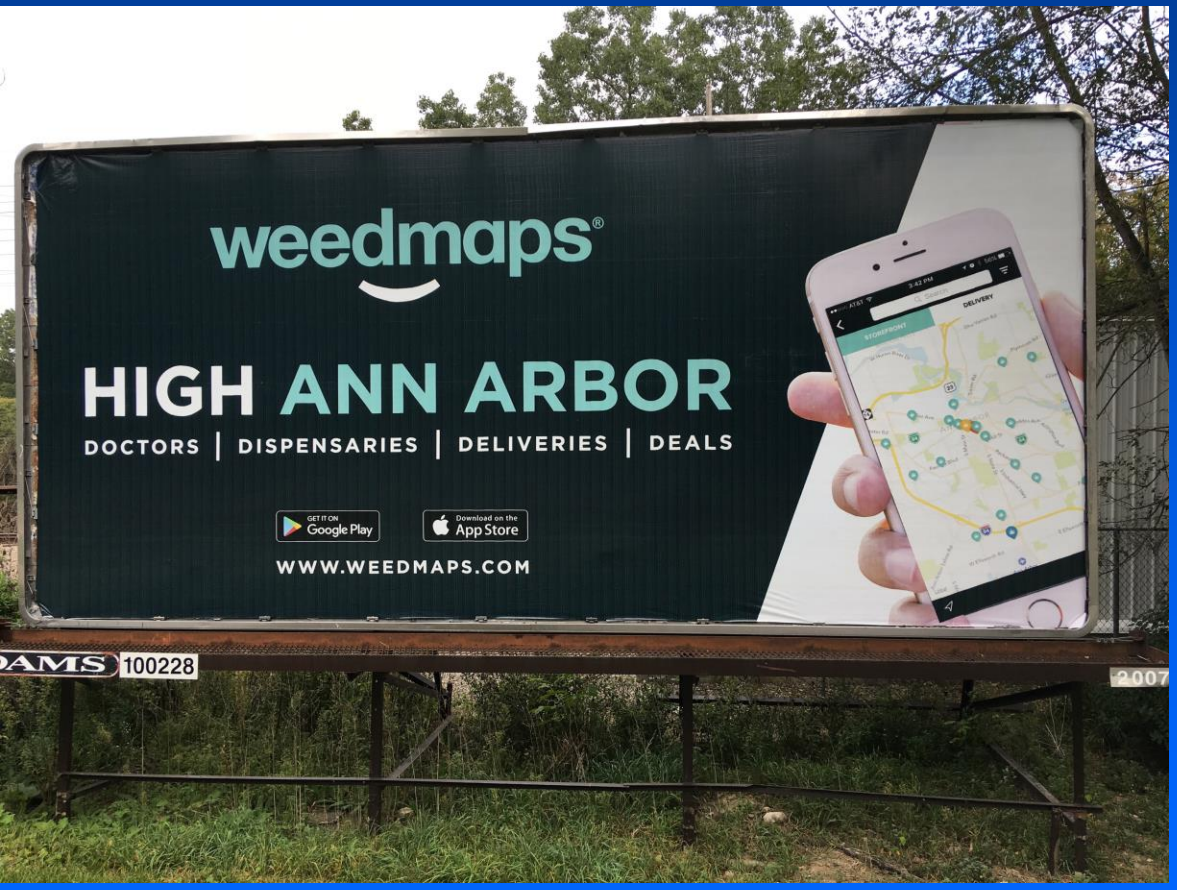
- Ineffective for insomnia >1-2 weeks of use
- Not first line for anxiety management
- Not recommended for use >2-4 weeks
- Worse than placebo for muscle spasms
- Substantial risk of addiction
- Impair cognitive function
- Increase risk of falls and delirium
- May increase risk of dementia

About 50% of opioid overdose deaths involve concurrent benzo use



Opioids + Benzos = Dead Patient

So, what about “medical” marijuana?



“Medical Marijuana” and Pain

- Evidence supporting efficacy for pain is poor
- Concerning data for impact on depression, anxiety, paranoia, and PTSD
- Sharply increased risk of psychotic disorders in young patients; risk for schizophrenia
- IQ decrease over time
- Marker of risk for addiction and drug diversion
- Medicolegal risk to prescriber ???

Stay Grounded In Your Role:

FIRST…
Do No Harm

THEN…
Cure Sometimes

Comfort Always

UMHHC MEDICATION PRESCRIPTIONS

University of Michigan Hospitals and Health Centers

1500 E. Medical Dr.
Ann Arbor, MI 48109
(734) 936-5582 (Taubman Clinic)
(734) 763-5459 (Back and Pain Center)

Rx For: , KIMBERLY
Date: 07/28/2012
Reg:
Address: RD
, MI,

DOB:
Ht:
Wt:

Allergies and Intolerances: nalbuphine naproxen penicillin

Rx: **One new aging dog – should be adopted from the shelter**
Sig:

Dispense#: Quantity: 1 (one) dog — Write Quantity:

Refill#: Quantity: — Write Quantity:

Provider: BERLAND, DANIEL WILLIAM, MD **Clinic:**

Signature: **DEA#:** **NPI#:** 1063417731 **Dr#:** 015629

Questions and Comments ??

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MICHIGAN MEDICINE
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Essential Reading

- CDC Opioid Guideline

  The new standard of care for opioid use

  https://www.cdc.gov/drugoverdose/prescribing/guideline.html

- The Heather Ashton Manual

  Invaluable resource for benzo management

  benzo.org.uk

- Unlearn Your Pain – Dr. Howard Schubiner

  Treating the trauma-anxiety-pain nexus

  unlearnyourpain.com