# Pain Treatment in the Opioid Epidemic: Opioids, Non-Opioids, and Alternative Therapies

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# Disclosure

- Salix Pharmaceuticals - Consultant

# Objectives

- List misconceptions associated with chronic pain
- Describe the goals of chronic pain therapy
- List opioid/non-opioid medications that can be used to treat pain and special considerations for each

Symptoms

Demands

Under treatment

Safety

Adverse Events

Overprescribing

Negative Feedback

Regulatory Action

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# What is the goal of pain management?

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INCREASE A PATIENT'S QUALITY OF LIFE

# CHRONIC PAIN DOES NOT = OPIOIDS!

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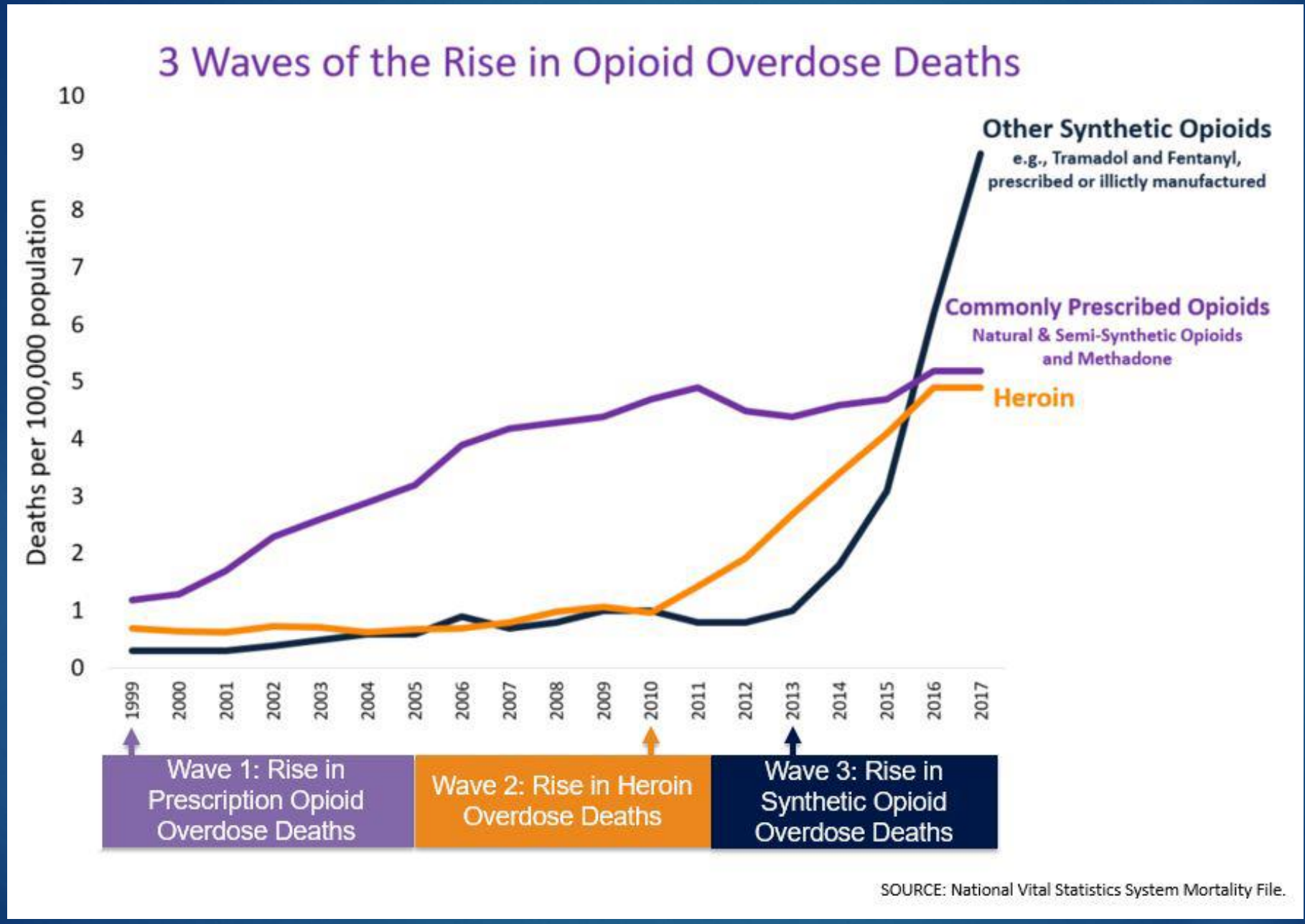


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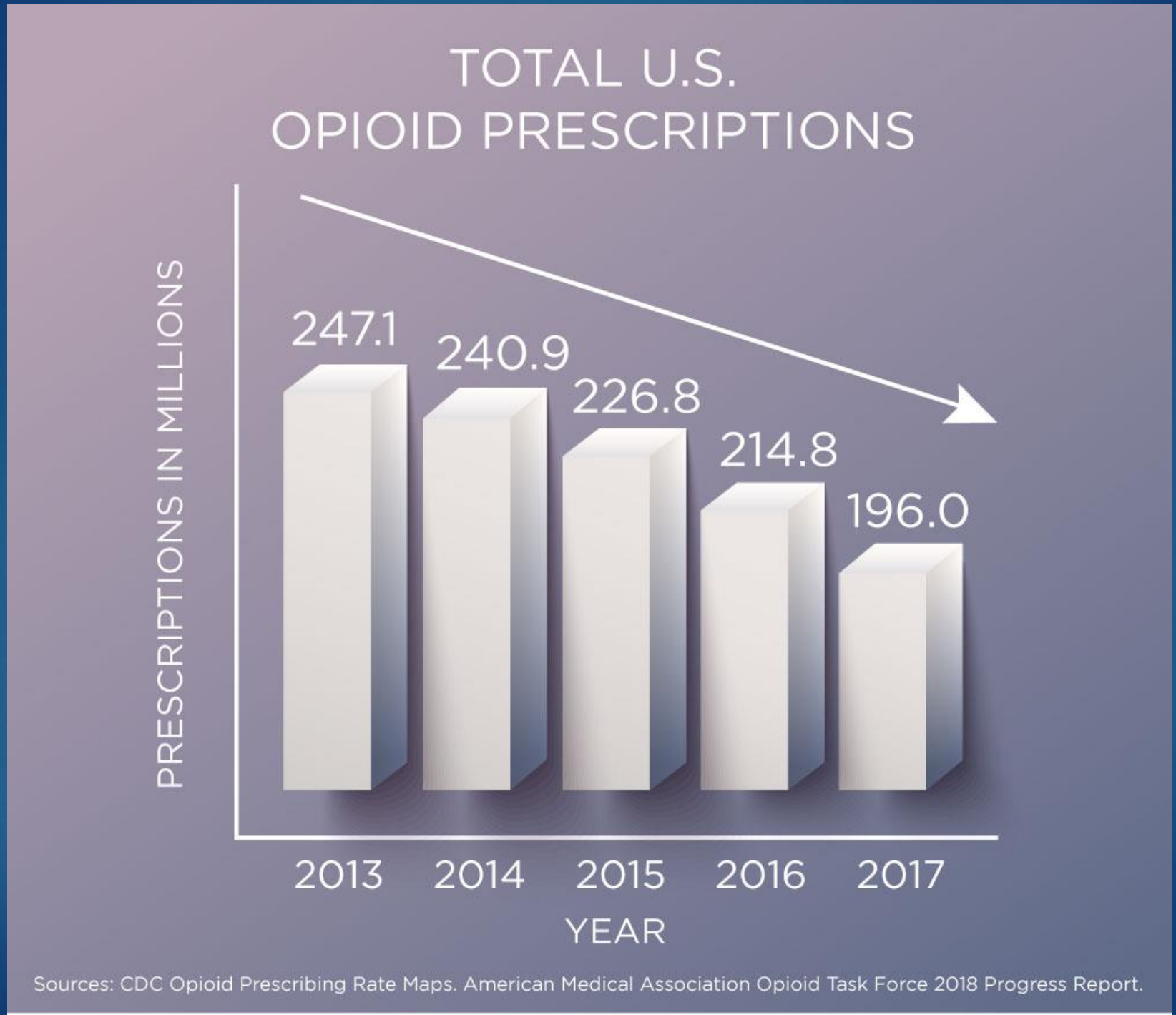


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**Perspective is key….**

**To Truly Measure Risk and Danger**

# Here Is What We Know…

- All drug deaths (including ANY drug/medication a patient takes) account for 60,000 to 70,000 annual deaths.
- All opioid deaths (including heroin/fentanyl and prescription opioids) account for 30,000 to 40,000

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# Now In Comparison

- Hospital-acquired infections deaths: 99,000 annually
- Tobacco, Alcohol, Guns and Traffic Accidents: >700,000 annually

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# An Even Closer Look…

- Fentanyl is responsible for 79% of all opioid overdose deaths
  - So your first reaction might be "no one should ever prescribe fentanyl"

- YET, only 5% of all fentanyl overdose deaths are due to pharmaceutical grade fentanyl

Schatman, Ziegler (2017) Pain Management, Presctiption Opioid Mortality and the CDC.

# It's Not An Opioid Epidemic… But A Polypharmacy Epidemic

72% of deaths involving oxycodone…..

also included alcohol, and/or benzodiazepines, cocaine, kratom, methamphetamine, and other opioids (which may not have been prescribed concurrently).

Schatman, Zieglar (2017) Pain Management, Presctiption Opioid Mortality and the CDC.

# A Few Definitions

To Understand the Risks and Who is Really in Danger?

# Chronic Non-Malignant Pain

*Pain has no predictable ending*

- Example chronic low back pain, failed surgical , rheumatoid arthritis, osteoarthritis, fibromyalgia
- Often can't be cured
- Frequently undertreated… But there is HUGE RISK of Overtreatment

# Issues With Most Chronic Pain Patients

- Tolerance:  a person's diminished response to a drug that is the result of repeated use

- Physical Dependence: caused by changes in the body as a result of constant exposure to a drug
  - Prednisone…..
  - Abrupt withdrawal of drug causes withdrawal symptoms

# Addiction

- a psychological condition that describes a compulsion to take a drug or engage in other harmful behaviors.
- The inability to limit or cease substance use.
- The irresistible urge to continue seeking and taking the drug despite serious negative consequences.
  - Will do "whatever it takes" to get the drug
  - CRAVING…….

# Our Goal When Treating With Medications

# Aim for Monotherapy

## But Know Combination Therapy May Be Required

TITRATE ONLY ONE DRUG AT A TIME

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# Pharmacotherapy Guidelines

Medication must result in:

- Significant pain relief and increase in functionality
- Tolerable side effects

- With the end result = greater function

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# Pharmacotherapy Guidelines

Both health care provider & patient must realize significant individual variability

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# Pharmacotherapy Guidelines

- Educate the patient

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# Non-Opiate Pharmacotherapy

- NSAIDs/Cox-2
- Acetaminophen
- Antidepressants
- Anticonvulsants
- Oral local anesthetics
- Alpha adrenergic agents
- Neuroleptics
- NMDA receptor antagonists
- Muscle relaxants
- Topical analgesics
- Emerging Agents

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# The 4 Pillars of Oral Pain Therapy

1) Anti-inflammatories

2) Anticonvulsants

3) Mood Modulators
   - SNRIs
   - SSRIs

4) Opiates

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# Non-Steroidal Anti-inflammatories (NSAIDS)

- Most commonly used analgesic for mild to moderate pain
- Have GI, Cardiovascular and Renal risks
- Annually, 100,000 patients are hospitalized for NSAID-related GI complications alone, direct costs ranging from $1800 to $8500 per patient per hospitalization, 16,500 persons die annually (Fine, 2013 AJMC)

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# Non-Steroidal Anti-inflammatories (NSAIDS) Cont'd

- FDA Latest Recommendations: Lowest Dose for the Shortest Period of Time

- Newest forms are targeted topical applied to the painful area – patch, gels and liquids - ex. Diclofenac gel (Voltaren gel), Diclofenac patch (Flector patch)

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# Acetaminophen

- Need to consider total acetaminophen daily intake now being targeted at 4000mg/day

- FDA is considering limiting doses of acetaminophen to 325mg in tablets

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# Acetaminophen Cont'd

- Caution with ETOH
- Overdoses can be unintentional but have costs, 56,000 ER visits, 26,000 hospitalizations, 458 deaths (D'arcy, 2011)
- Newest form is Acetaminophen IV (Orfirmev) – dosed pre-op, peri-op and post-op at 1000mg doses

# Antidepressants*

| Tricyclic | SSRI | SNRI |
|---|---|---|
| Amitriptyline (Elavil®) | Fluoxetine (Prozac®) | Duloxetine# (Cymbalta) |
| Desipramine (Norpramin®) | Paroxetine (Paxil®) | Venlafaxine (Effexor®) |
| Doxepin (Sinequan®) | Sertraline (Zoloft®) | Milnacipran# (Savella) |
| Imipramine (Tofranil®) | Fluvoxamine (Luvox®) | Desvenlafaxine (Pristiq) |
| Nortriptyline (Pamelor®) | Citalopram (Celexa) | |

* = Partial list # = FDA approved for at least one pain disorder

SSRI = selective serotonin reuptake inhibitor SNRI = serotonin norepinephrine reuptake inhibitor

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# Antidepressants and Pain

- Improve pain symptoms regardless of the presence or absence of co-morbid major depression.

- Chronic pain and major depression
  - Shared neurobiology
  - Appear to have a shared neuro-anatomy (in the brain and spinal column)
  - Neuro-chemistry (norepinephrine and serotonin), with similar hypothalamic-pituitary-adrenal (HPA) axis, autonomic nervous system (ANS), and inflammatory cytokine disturbances

Jain & Jain (2017) Antidepressants in the Treatment of Chronic Pain, Practical Pain Management.

# Side Effects of Antidepressants

- Weight Gain
- Sexual Dysfunction
- Sedation/Fatigue
- Nausea
- Anxiety

# Antidepressant Clinical Pearls

- Selection of antidepressant
  - Based on insurance and indication
- Consider Drug/Drug Interactions
  - CYP450… 2D6 – SSRIs, less citalopram
  - Serotonin Syndrome potential…. Tramadol
- Slow titration

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# Anticonvulsants

- Carbamazepine*
- Divalproex sodium*
- Gabapentin*
- Pregabalin*
- Clonazepam
- Phenytoin
- Lamotrigine
- Topiramate*
- Zonisamide
- Oxcarbazepine
- Levatriacetam
- Lacosamide

***Has FDA indication for pain/headache**

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# Clinical Syndromes and Anticonvulsant Use

- Postherpetic neuralgia
  - gabapentin
  - Pregabalin
- Diabetic neuropathy
  - carbamazepine
  - phenytoin
  - gabapentin
  - Lamotrigine
  - pregabalin
- HIV-associated neuropathy
  - Lamotrigine
- Trigeminal neuralgia
  - carbamazepine
  - lamotrigine
  - Oxcarbazepine
- Fibromyalgia
- pregabalin
- Central poststroke pain
  - lamotrigine

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# Anticonvulsant Pearls

- Start Low and Go Slow
  - Gabapentin 100mg or 300mg QHS to start
  - Goal dose 1800mg/day, up to 2400mg/day

  - Pregabalin 25mg, 50mg, 75mg QHS to start
  - Goal dose: 300mg-450mg/day

- Consider Long-acting Anticonvulsant
  - Lessened side effects
  - More likely to reach therapeutic dose

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# N-Methyl D-aspartate Receptor Antagonist

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# Drugs with Potential NMDA-R Antagonist Properties

- Dextromethorphan
- **Ketamine**
- **d-Methadone**
- Amantadine
- Memantine
- Amitriptyline

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# Methadone Benefits

- High bioavailability
- Lack of known metabolic products
  - Decrease in neurotoxicity
- Multiple receptor affinities
  - Mu opioid
  - Inhibitor of Serotonin Reuptake
  - NMDA-R

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# Methadone Cautions….

- QTC Prolongation
  - EKG prior to starting and then every 6mos to 1yr
- Half-Life – 72hr
- Individual Variability
- Will the patient take as prescribed?
- Can I trust them?

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# Methadone

- Cheap medication
- Beneficial in neuropathic pain, opioid tolerance, hyperalgesia

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# Methadone Dosing

- Starting dose
  - If rotating from another opioid then reduce dose by 75% (equianalgesic dose)… but be careful!
  - 2.5mg-5mg po QHS… to start
  - Increase every 4-7 days
  - USE WITH CAUTION!!!

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# Ketamine

- Dissociative anesthetic agent, NMDA Receptor Antagonist
- IV or IM – usually reserved for inpatient, mouthwash for mucositis
- Used in chronic pain with an acute pain crisis or cancer related pain
- Lots of off-label uses

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# Ketamine

- IV Pushes
  - 5-10 mg pushes Q4hr
  - Onset 1-5 mins
- IV Infusions
  - 0.1-0.2 mg/kg/hr, titrate 0.05 mg/kg every 24 hrs

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# Ketamine Adverse Effects

- **Hypertension**, tachycardia

- Hallucinations, vivid dreams, delirium

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# Muscle Relaxants

- Cyclobenzaprine (Flexeril®)
- Carisoprodol (Soma®)
- Methocarbamol (Robaxin®)
- Metaxalone (Skelaxin®)
- Orphenadrine citrate (Norflex®)

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# Cyclobenzaprine (Flexeril)

- Structurally similar to tricyclics
- Centrally acting
- Nocturnal muscle spasm effects

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# Cyclobenzaprine

- SIDE EFFECTS:
  - Drowsiness
  - Cardiac dysrhythmias
  - Anticholinergic
    - Dry mouth
    - Blurred vision
    - Urine retention
    - Constipation
    - Increased intraocular pressure

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# Carisoprodol (Soma)

- Precursor of meprobamate
- Centrally active
- Reduction of muscle spasm

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# Carisprodol

- Side effects:
  - Sedation, drowsiness, dependence
  - Withdrawal symptoms
    - Agitation
    - Anorexia
    - N/V
    - Hallucination
    - Seizures
- No longer recommended due abuse and addiction
- SOMA rhymes with COMA for a reason!

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# Methocarbamol (Robaxin)

- Investigative usage: MS
- Daily dosage: 1000 mg qid
- Side effect: drowsiness
- Mechanism of action:
  - Centrally active
  - Inhibits polysynaptic reflexes
- Clinical effects:
  - Reduction of muscle spasms

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# Metaxalone (Skelaxin)

- Daily dosage: 400-800 mg tid
- Clinical effects:
  - Reduction in muscle spasm
- Side effects:
  - Nausea
  - Drowsiness
  - Dizziness

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# Topical Analgesics:  Key Facts

- Topical agents are active within the skin, soft tissues and peripheral nerves.
- In contrast to transdermal, oral or parenteral medications, use of a topical agent does not result in clinically significant serum drug levels.
- Other benefits include lack of systemic side effects and drug-drug interactions.
- The mechanism of action of a topical analgesic is unique to the specific agent considered.

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# Topical Treatments for Chronic Pain

- Diclofenac (patch/gel/lotion)
- Aspirin
- Capsaicin
- Local anesthetics
  - lidocaine patch 5%/eutectic mixture of local anesthetics
- Tricyclic antidepressants
- Investigational agents

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# Emerging Analgesics

- Botulinum Toxin (Type A, Type B)
- Cannabinoids
- CGRP Inhibitors (Calcitonin Gene-Related Peptide)
- Low dose naltrexone

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# Onabotulinumtoxin A (Botox Injections)

- Indication: Migraine Headaches
  - >/15 more headache days/month

- Injected bilaterally in 7 muscle groups in forehead and occipitally

- A response **rate** of 65% is expected after 3 courses of treatment with onabotulinumtoxin A (**Botox**) in patients with chronic **migraine**.

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# Cannabinoids

- Two active combonents
  - THC – activates cannabinoid receptors in brain
    - Produces "high
  - CBD – activates other cannabinoid receptors
    - Does not produce "high"
  - Potential uses
    - Analgesia, Anxiolytics, Muscle relaxants, Insomnia

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# FDA Approved

- Dronabinol
  - Marinol and nabilone (Cesamet)- synthetic THC
- Epidiolex (Indication: Seizure Disorder)
  - Purified CBD

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# Other Forms of CBD

- Online and Local Dispensaries
- Forms: oral or topical oils, SL sprays, edibles, inhalants, cream
- Problems: Inconsistent CBD amounts, THC and other contaminants

# Drugs that Increase CBD Levels

- Clarithromycin, erythromycin
- Omeprazole
- Diltiazem, verapamil, amiodarone,
- Warfarin, clopidogrel
- Amitriptyline, morphine
- Citalopram, bupropion, alprazolam

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# CGRP (Calcitonin Gene-Related Peptide)

- Indications: Migraine Headaches
- Bio-Identical Hormone (monoclonal antibody)
- Injected monthly or quarterly and oral formulation
- Side Effects:
  - injection site reactions
  - constipation

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# Low Dose Naltrexone

- Investigational Uses: Fibromyalgia, MS, CRPS
- A glial/immune cell modulator, which decreases pain by helping reduce inflammation.
- Dosing: 0.5 mg to 4.5 mg/day
- Side Effects
- Small Study population

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Toljan K, Vrooman B. Low-Dose Naltrexone (LDN)-Review of Therapeutic Utilization. *Med Sci (Basel)*. 2018;6(4):82. Published 2018 Sep 21. doi:10.3390/medsci6040082

# Opioids

## BUT FIRST….THE CDC GUIDELINES

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# Recommendation #1

1

- Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.
- Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient.
- If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

# Recommendation #2

2

- Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks.

- Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

# Recommendation #3


- Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

# Recommendation #4

4

- When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

# Choose predictable pharmacokinetics and pharmacodynamics to minimize overdose risk

- In general, avoid the use of immediate-release opioids combined with ER/LA opioids.
- Methadone should not be the first choice for an ER/LA opioid.
  - Only providers familiar with methadone's unique risk and who are prepared to educate and closely monitor their patients should consider prescribing it for pain.
- Only consider prescribing transdermal fentanyl if familiar with the dosing and absorption properties and prepared to educate patients about its use.

# Recommendation #5

5

- When opioids are started, clinicians should prescribe the lowest effective dosage.

- Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

# Start low and go slow

- Start with lowest effective dosage and increase by the smallest practical amount.

- If total opioid dosage ≥50 MME/day
  - reassess pain, function, and treatment
  - increase frequency of follow-up; and
  - consider offering naloxone.

# Start low and go slow (cont'd)

- Avoid increasing opioid dosages to ≥90 MME/day.

- If escalating dosage requirements
  - discuss other pain therapies with the patient
  - consider working with the patient to taper opioids down or off
  - consider consulting a pain specialist.

# Recommendation #7

7

- Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation.
- Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently.
- If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

# Recommendation #8

8

- Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms.

- Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.

# Recommendation #9

9

- Clinicians should review the patient's history of controlled substance prescriptions using state PDMP data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him/her at high risk for overdose.

- Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.

## Recommendation #10

10

When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

## Recommendation #11

11

Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

# Avoid concurrent opioids and benzodiazepines whenever possible

- Taper benzodiazepines gradually.
- Offer evidence-based psychotherapies for anxiety.
  - cognitive behavioral therapy
  - specific anti-depressants approved for anxiety
  - other non-benzodiazepine medications approved for anxiety
- Coordinate care with mental health professionals.

# Recommendation #12


Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

# If you suspect opioid use disorder (OUD)

- Discuss with your patient and provide an opportunity to disclose concerns.
- Assess for OUD using DSM-5 criteria. If present, offer or arrange MAT.
  - Buprenorphine through an office-based buprenorphine treatment provider or an opioid treatment program specialist
  - Methadone maintenance therapy from an opioid treatment program specialist
  - Oral or long-acting injectable formulations of naltrexone (for highly motivated non-pregnant adults)
- Consider obtaining a waiver to prescribe buprenorphine for OUD (see http://www.samhsa.gov/medication-assisted-treatment/buprenorphine-waiver-management)

# OPIOID SIDE EFFECTS AND ADVERSE EVENTS

| SIDE EFFECTS | ADVERSE EVENTS |
|---|---|
| Respiratory depression | Falls or fractures |
| Opioid-induced constipation (OIC) | Addiction |
| Myoclonus (twitching or jerking) | Overdose |
| Sedation, cognitive impairment | Hospitalization |
| Sweating, miosis, urinary retention | Disability or permanent damage |
| Allergic reactions | Death |
| Hypogonadism | |
| Tolerance, physical dependence, hyperalgesia | |

# OPIOID-INDUCED RESPIRATORY DEPRESSION

## MORE LIKELY TO OCCUR:

- In elderly, cachectic, or debilitated patients
- If given concomitantly with other drugs that depress respiration
- In patients who are opioid-naïve or have just had a dose increase
- Opioids are **contraindicated** in patients with respiratory depression or conditions that increase risk

## HOW TO REDUCE RISK:

- Ensure proper dosing and titration
- **Do not overestimate** dose when converting dosage from another opioid product
  - Can result in fatal overdose with first dose
- Instruct patients to swallow tablets/capsules whole
  - Dose from cut, crushed, dissolved, or chewed tablets/capsules may be fatal, particularly in opioid-naïve individuals

# DRUG INTERACTIONS COMMON TO OPIOIDS

**Other CNS Depressants**

- Concurrent use can increase risk of respiratory depression, hypotension, profound sedation, or coma
- Reduce initial dose of one or both agents

**Partial Agonists* or Mixed Agonist/Antagonists †**

- Avoid concurrent use with full opioid agonist
- May reduce analgesic effect and/or precipitate withdrawal

**Skeletal Muscle Relaxants**

- Concurrent use may enhance neuromuscular blocking action and increase respiratory depression

**Anticholinergic Medication**

- Concurrent use increases risk of urinary retention and severe constipation
- May lead to paralytic ileus

*Buprenorphine †pentazocine, nalbuphine, butorphanol

# SPECIAL POPULATIONS

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# OLDER ADULTS

## RISK FOR RESPIRATORY DEPRESSION

- Age-related changes in distribution, metabolism, excretion; absorption less affected

## ACTIONS

- Monitor
  - Initiation and titration
  - Concomitant medications (polypharmacy)
  - Falls risk, cognitive change, psychosocial status
- Reduce starting dose to 1/3 to 1/2 the usual dosage in debilitated, non-opioid-tolerant patients
- Start low, go slow, but GO
- Routinely initiate a bowel regimen
- Patient and caregiver reliability/risk of diversion

SOURCE: American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. J Am Geriatr Soc. 2009;57:1331-46. Chou R, et al. J Pain. 2009;10:113-30.

# WOMEN OF CHILDBEARING POTENTIAL

Neonatal opioid withdrawal syndrome is a potential risk of opioid therapy

## GIVEN THIS POTENTIAL RISK, CLINICIANS SHOULD:

- Discuss family planning, contraceptives, breast feeding plans with patients
- Counsel women of childbearing potential about risks and benefits of opioid therapy during pregnancy and after delivery
- Encourage minimal/no opioid use during pregnancy, unless potential benefits outweigh risks to fetus
- Refer to a high-risk OB/Gyn who will ensure appropriate treatment for the baby

- Perform universal screening to avoid neonatal abstinence syndrome

- For women using opioids on a daily basis, consider methadone or buprenorphine

SOURCES: Chou R, et al. J Pain. 2009;10:113-30; ACOG Committee on Obstetric Practice, August 2017

# Short-acting Opioids

- Tylenol with codeine - falling out of favor related to FDA warnings for rapid metabolizers and slow metabolizers
- Doses are limited by the amount of acetaminophen – 4000mg/day max
- Side effect potential – high for nausea and vomiting

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# Codeine

- Available in 15,  30,  60 mg
- “mild opioid”  130 mg = morphine 30 mg
- May be combined with Tylenol, Butalbital
- Max dose 60 mg q4hr (higher dose not more analgesia, more side effects
- Half-life 2.9 hr

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# Codeine

- Metabolites: codeine-6-glucuronidate
  morphine (10%)
- Renal excretion
- Caution ultra-rapid metabolizers CYP2D6 convert to morphine more rapidly with increased effects
- Caution alcohol, benzodiazepines

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# Moderate Short-acting opioids

- Hydrocodone with acetaminophen
- Oxycodone with/without acetaminophen
- Tramadol
- Tapentadol - dual mode of action as an agonist of the mu-opioid receptor and as a norepinephrine reuptake inhibitor

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# Hydrocodone

- IR - 2.5/325, 5/325, 7.5/325, 10/325, Long-acting formulation
- Lowest effective dose to start
- Hepatic monitoring (acetaminophen)
  - Educate about other acetaminophen containing products

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# Hydrocodone

- Monitor other CNS depressant products
  - BENZODIAZEPINES
- Adverse effects: Respiratory depression, sedation, constipation
- 1:1 morphine equivalency

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# Oxycodone with/without Acetaminophen

- IR - 2.5/325, 5/325, 7.5/325, 10/325
- IR 5mg,10mg,15mg……20mg, 30mg (WHAT???)
- Lowest effective dose to start

- Hepatic Failure – use oxycodone lowest dose
- Oxycodone with Acetaminophen
  - Educate about other acetaminophen containing products

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# Oxycodone with/without Acetaminophen

- Monitor other CNS depressant products
  - BENZODIAZEPINES

- Adverse effects: Respiratory depression, sedation, constipation
- 1:1.5 Morphine Equivalency

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# Tramadol

- Non-opioid– affinity for mu-receptor 10x less than codeine, inhibits serotonin/norepinephrine
- Dosing: 50mg IR, 100mg, 200mg, 300mg ER
  - Start low, go slow (max of IR 100mg QID PRN)
- Adverse Effect: dizziness, nausea, constipation
- **Warning: Serotonin Syndrome/Seizure Risk: use in caution with MAOIs, TCAs, Triptans, SSRI, SNRI, Opioids**
- 1:0.1mg Morphine Equivalency

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# Tapentadol

- IR – 50mg, 75mg, 100mg, Long-acting formulation
- Lowest effective dose to start, max 700mg/day
- Hepatic insuff - use with caution, Renal: CrCL<30: avoid use
- Monitor other CNS depressant products
  - BENZODIAZEPINES
- Adverse effects: Respiratory depression, sedation, constipation
- 1: 0.4mg morphine equivalency

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# Strong Short-Acting Opioids

- Morphine
- Hydromorphone
- Fentanyl *not for acute pain or opioid naïve patient

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# Morphine

- IR - 2.5/325, 5/325, 7.5/325, 10/325, Long-acting formulation
- Lowest effective dose to start
- Reduce dosing in hepatic and renal insufficiency d/t metabolic accumulation
- Monitor other CNS depressant products
  - BENZODIAZEPINES
- Adverse effects: Respiratory depression, sedation, constipation

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# Hydromorphone

- Used most often inpatient IV, poor choice for oral d/t short half-life
- Dosing: 2mg, 4mg, 8mg, also available LA (better option for outpatient – but not opioid naïve)
- Caution renal/hepatic impairment
  - Better option in renal failure, but use with caution

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# Hydromorphone

- Monitor other CNS depressant products
  - BENZODIAZEPINES
- Adverse effects: Respiratory depression, sedation, constipation
- 1:7mg Morphine equivalency

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# When Should A Patient Titrate to A Long-Acting/Extended Release Opioid?

- When healing will take place over an extended period of time, greater than 1 month
- When patient is experiencing pain around the clock
- When pain is rated as moderate to severe in intensity
- Rule of thumb: NO MORE THAN 4 SHORT ACTING OPIOID DOSES IN A 24 HOUR PERIOD…. If needed then convert to an ER/LA Opioid

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# Long-acting/Extended Release Opioids

- Slower onset of action 30-90 min., duration of action can extend up to 72 hours
- Each pill contains more medication than the short-acting equivalents
- For pain that lasts throughout the day
- Should be scheduled
- Alcohol can degrade ER mechanism and allow medication to be absorbed rapidly Davies & D'Arcy, 2013

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# Fentanyl Transdermal

- IR – 12 mcg, 25 mcg, 37.5mcg, 50mcg, 62.5mcg, 75mcg, 87.5mcg, 100mcg – per hour
- Lowest effective dose to start
- Reduce dosing in mild to mod hepatic/renal impairment
- Monitor other CNS depressant products
  - BENZODIAZEPINES

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# Fentanyl

- Only use in Opioid Tolerant
  - 60mg of morphine or equivalency for 1 week
- Adverse effects: Respiratory depression, sedation, constipation
- Fentanyl lozenges, suckers…. No longer recommended
- Difficulty weaning patients off fentanyl!
- 25mcg fentanyl patch equivalent to 60mg of morphine

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# Buprenorphine

- May only prescribe preparations with indication for pain
  - Buprenorphine transdermal (Butrans)/sublingual (Belbuca)
- The only C III opioid available
- Dosing: Transdermal – 5mcg/7.5mcg(branded)10mcg/15mcg/20mcg
- Sublingual – 75mcg, 150mcg, 300mcg, 450mcg, 600mcg, 750mcg, 900mcg

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# Buprenorphine

- Lowest effective dose to start
- Avoid use in end stage hepatic or renal disease
- Monitor other CNS depressant products
  - BENZODIAZEPINES
- Adverse effects: Respiratory depression, sedation, constipation, QTC prolongation potential

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# Alternative Therapies

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# Interventional Options

- Joint Injections
  - Hip, knees, shoulders, elbows, ankles, wrists
  - Short term pain relief…. But can provide significant pain relief

- Epidural Spinal Injections
  - Cervical and lumbar – most common
  - MRI - "disc herniation, displacement"

- Facet Blocks/Radiofrequency Ablation
  - Cervical and lumbar – most common
  - MRI Findings: "Facet arthropathy, arthritis"
  - RFA – 6-12 mos of pain improvement

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# Interventional Options

- Implantable Spinal Cord Stimulator
  - Spinal cord stimulation to decrease pain sensations
  - Issues with paresthesias associated with placement
  - Requires trial, prior to placement

- Implantable Pain Pump
  - Opioids directly into spinal cord region
  - Must have close follow up, someone to "fill" pump

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# Pain and Physical Exercise Problems and Opportunities


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Goldenberg DL. *J Clin Psychiatry* 2008;69:S30-S34.

# COGNITIVE BEHAVIORAL THERAPY AND MINDFULNESS MEDITATION AS TREATMENT OPTIONS FOR CHRONIC PAIN

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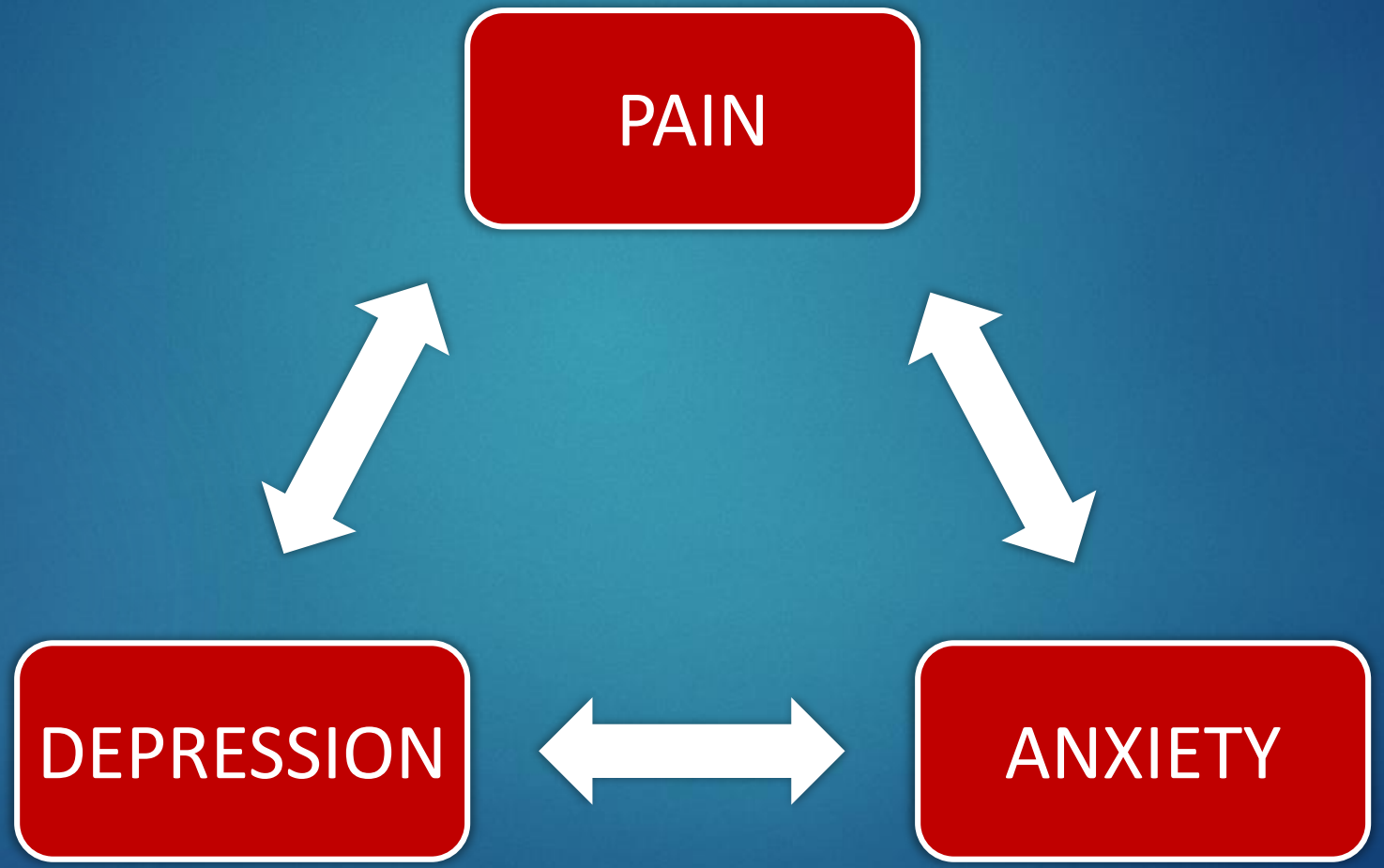
# Toxic Triple Threat

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# Cognitive Behavioral Therapy

## IS IT EFFECTIVE IN CHRONIC PAIN?

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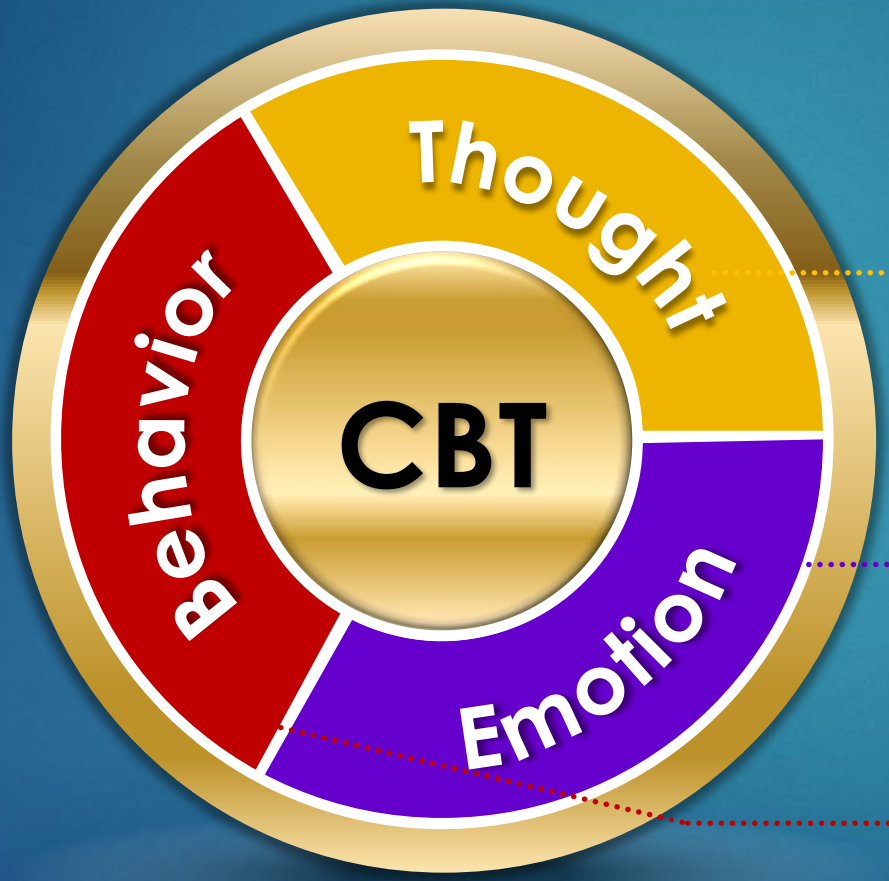
# Model of CBT




What we ***think*** affects how we act and feel

What we ***feel*** affects what we think and do

What we ***do*** affects how we think and feel

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# The Neurobiology of CBT

## DOES CBT CHANGE THE BRAIN?

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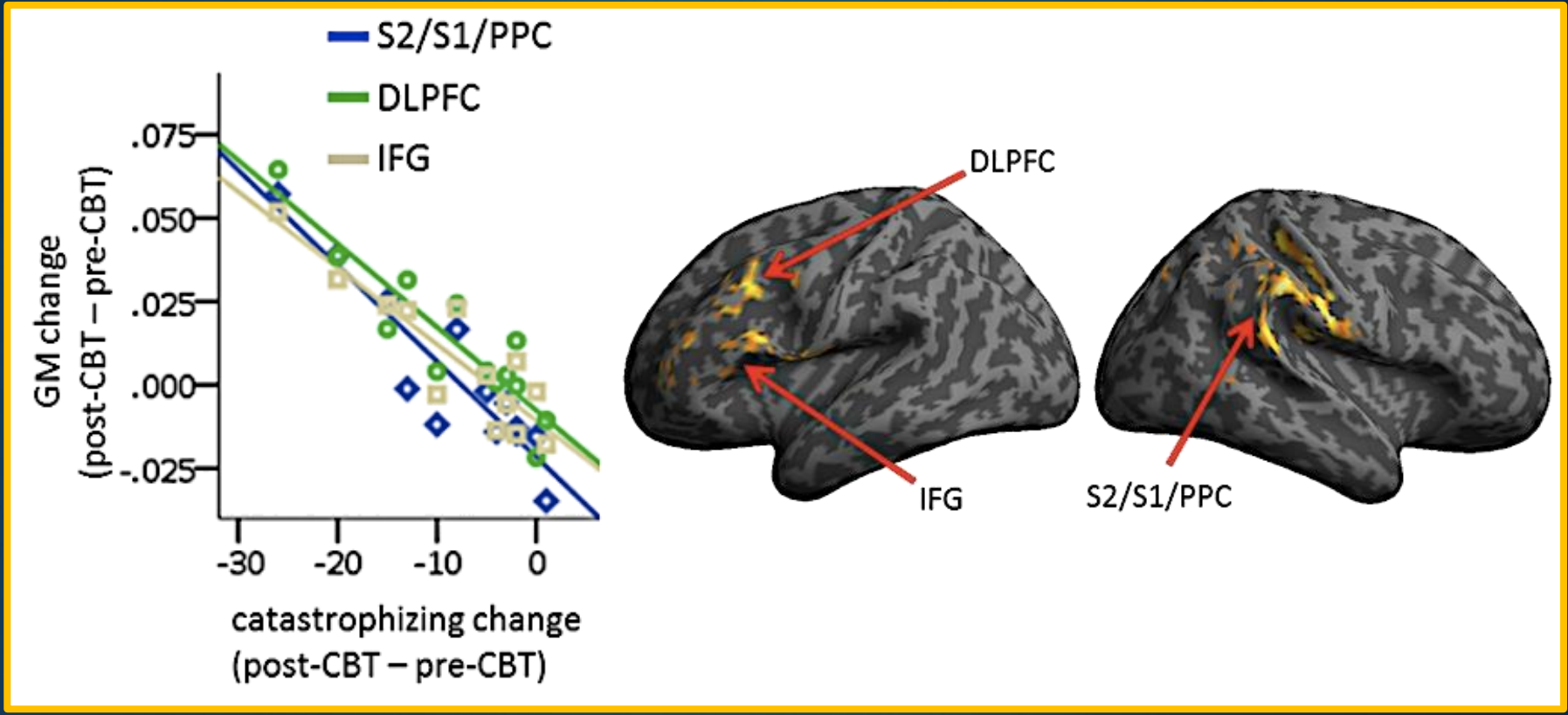
# CBT Reduces Catastrophizing and This Has Brain Correlates

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# Findings from the Seminowicz Study

***An 11-week CBT intervention for coping with chronic pain resulted in increased GM volume in prefrontal and somatosensory brain regions, as well as increased dorsolateral prefrontal volume associated with reduced pain catastrophizing.***

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# CBT As A Clinical Intervention

## HOW DOES IT WORK?

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# When Is The Last Time You Saw This Patient ?


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# Catastrophizing: A Cognitive Distortion

**Catastrophizing:**
**Irrational thought(s) that events will turn out far worse than reasonable.[1]**

**Magnification**

**Rumination**

**Helplessness**

**PAIN**

**One of the most consistent findings has been that catastrophizing is associated with heightened pain experience.[2]**

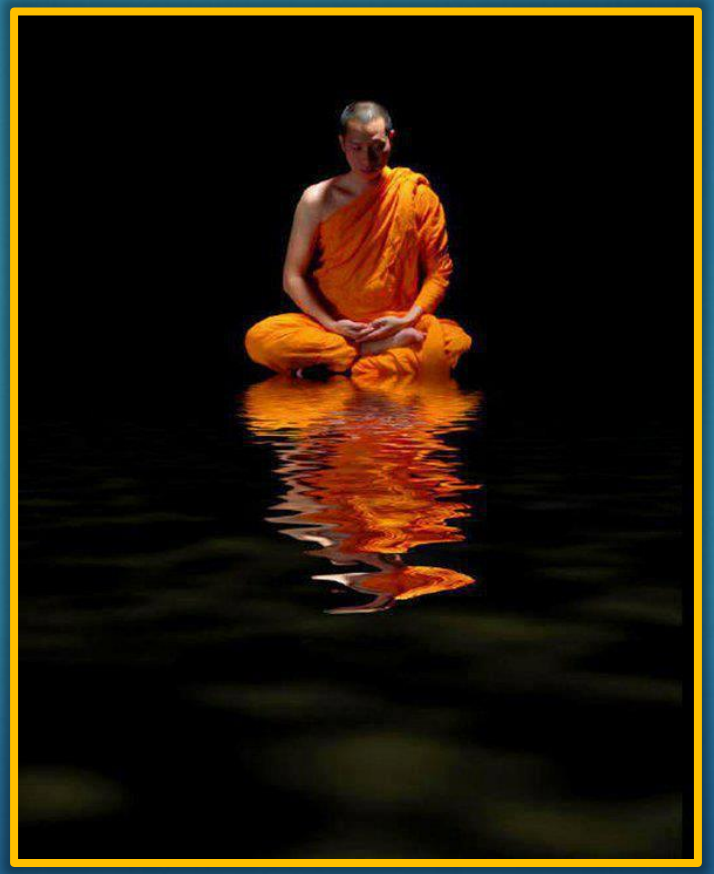

1. http://psychcentral.com/lib/what-is-catastrophizing/0001276.
2. Sullivan MJ, et al. *Clin J Pain.* 2001;17(1):52-64.

# What Do You Think of When I Say Meditation?

**Dates Back 5000+ Years**

**Buddha: Meditation Icon (500 BC)**

**Buddhist & Hindu-Based Most Popular**

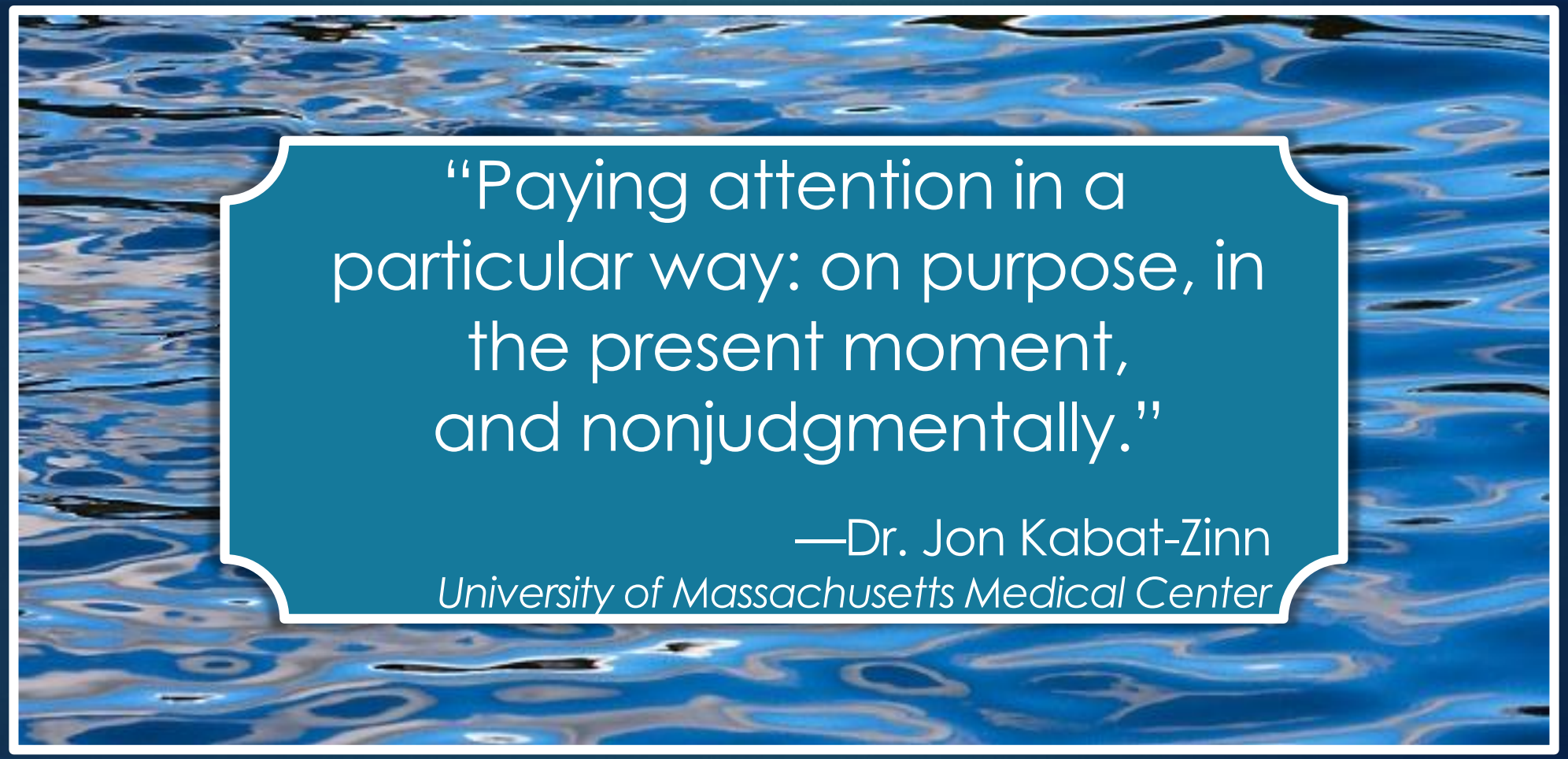


**Spread to West Thousands of Years Later**

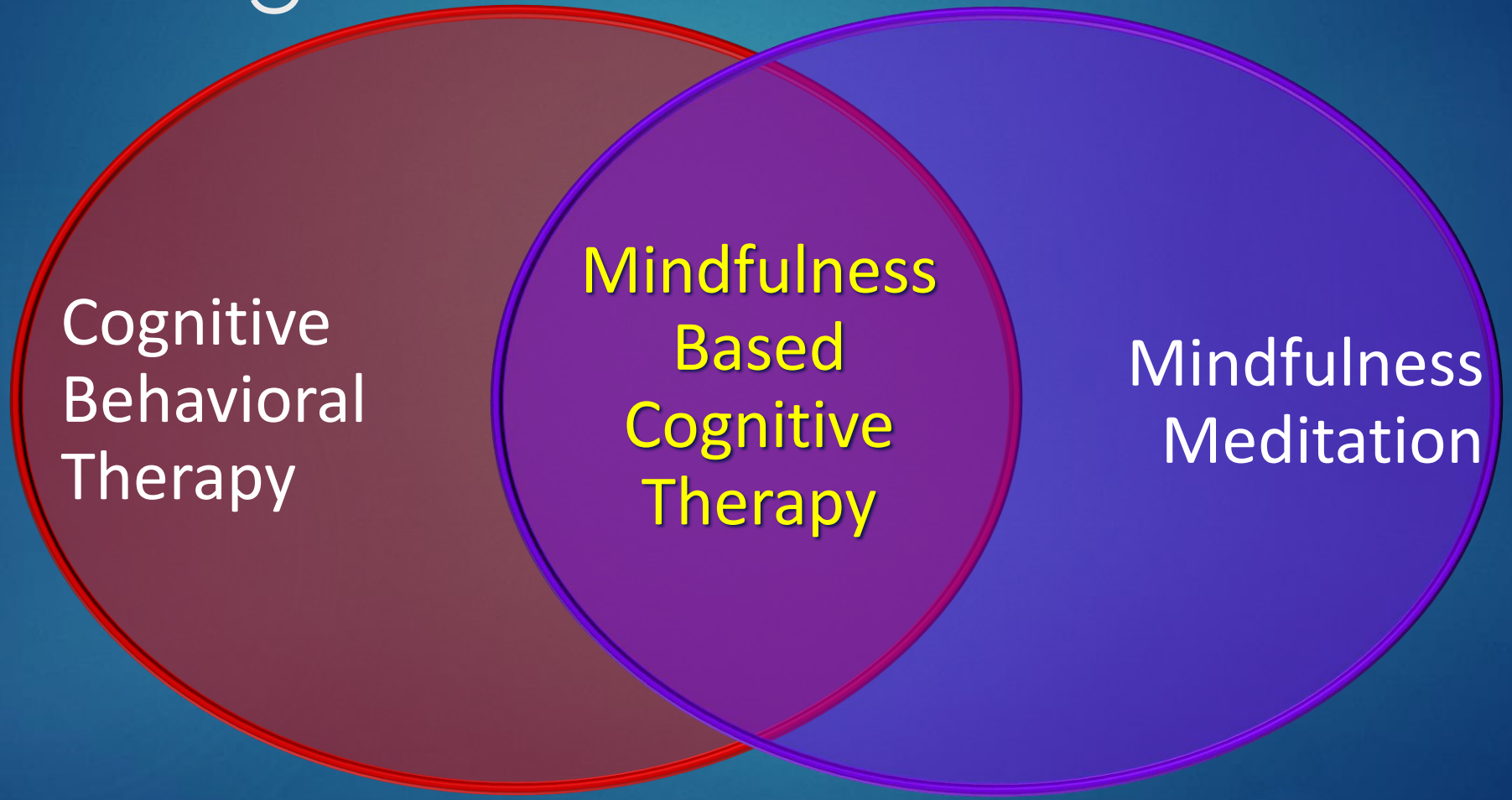
**Popular in the West Mid-20th Century**

**60s & 70s Researching the Benefits**

# Mindfulness: What Is It?



# Meditation + CBT = MBCT
# "*A Marriage Made in Heaven*"

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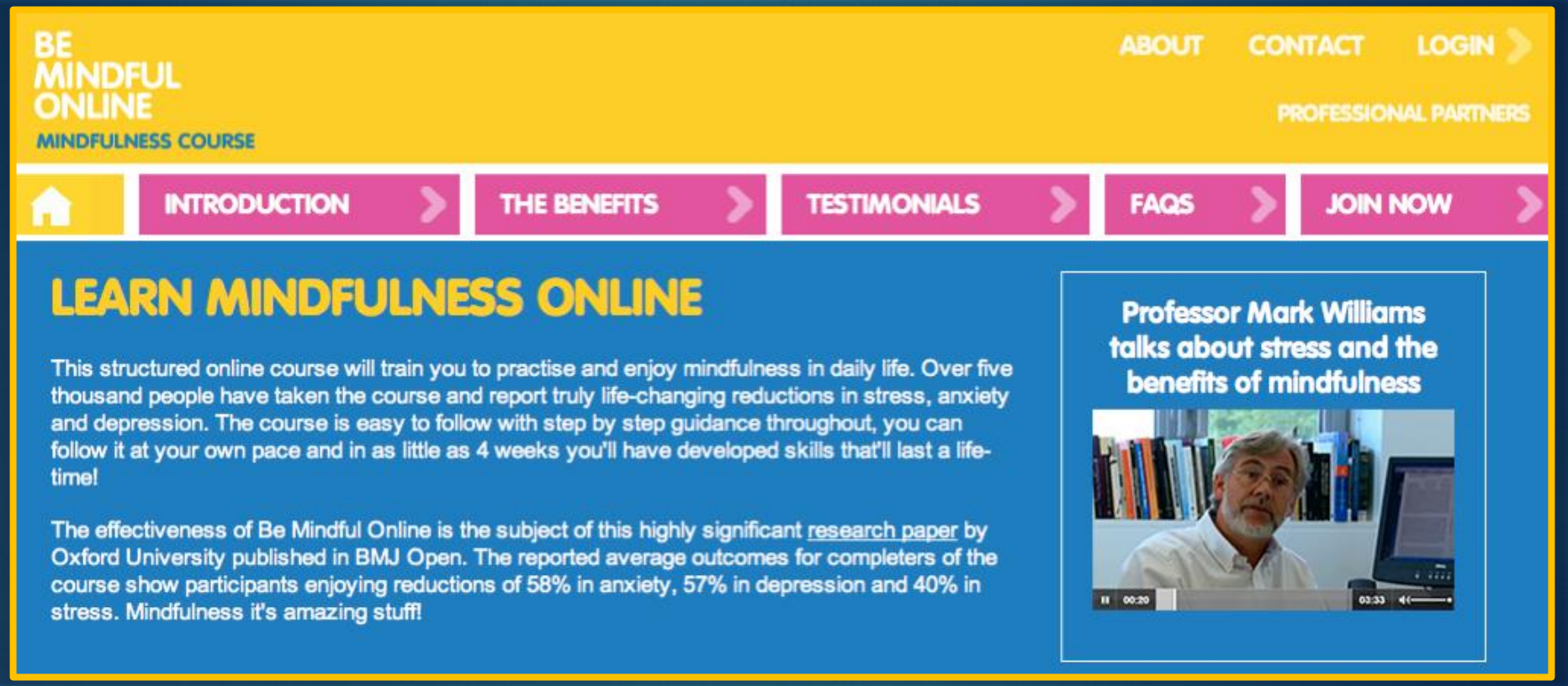
# Online Mindfulness Program: Is It Effective?




www.bemindfulonline.com.

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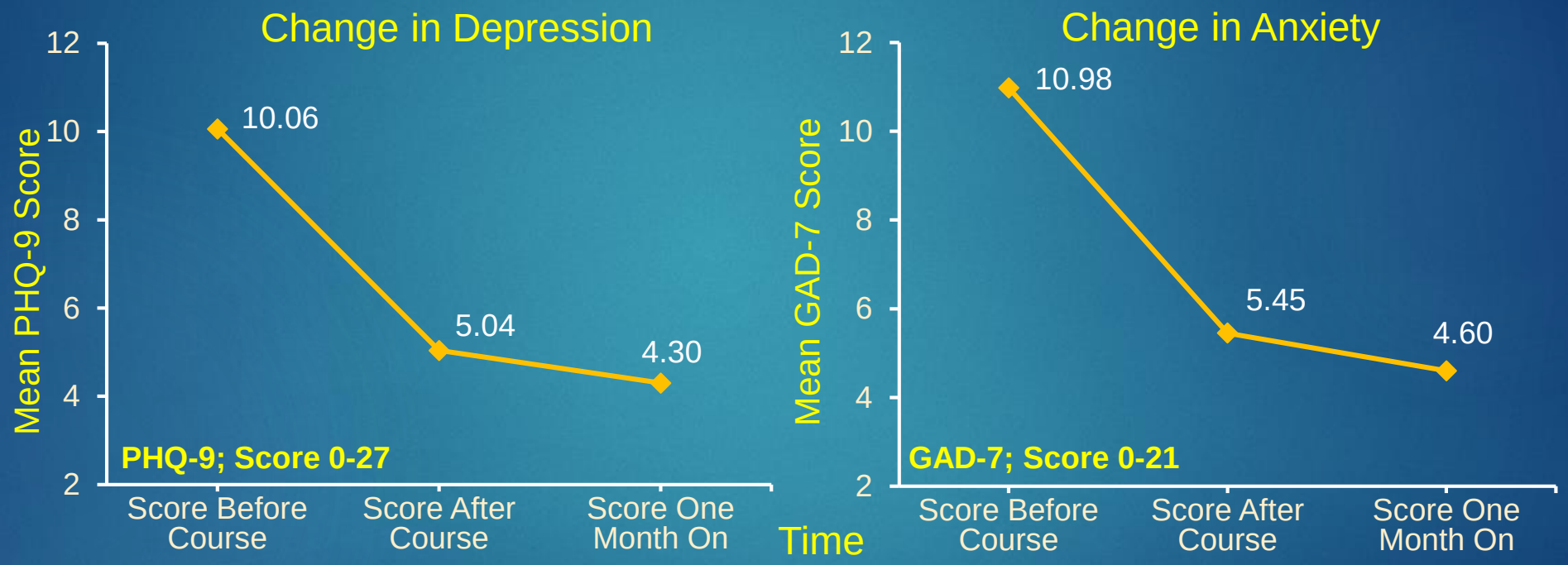
# Online Mindfulness Training: Looks Promising!

Change from pre- to post-course and follow-up (1 month after course completion)




A follow-up investigation of an online mindfulness course (N = 273). Self-referrals; 10 sessions, guided meditation videos, and automated emails, with elements of MBSR and MBCT, completed at a pace to suit the individual (minimum length 4 weeks).

item scale.

Krusche A, et al. *BMJ Open*. 2013;3(11):e003498.

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I Am Happy To Take Questions?

Thank You!

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