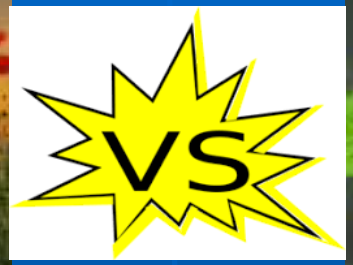
# Opioids V Medical Cannabis for Chronic Pain




Paul J. Christo, MD, MBA

# Title & Affiliation

Associate Professor
Director, Multidisciplinary Pain Fellowship (2003-2011)
Director, Blaustein Pain Treatment Center (2003-2008)
Division of Pain Medicine
Department of Anesthesiology and Critical Care Medicine
**Johns Hopkins Medicine**

# Disclosures

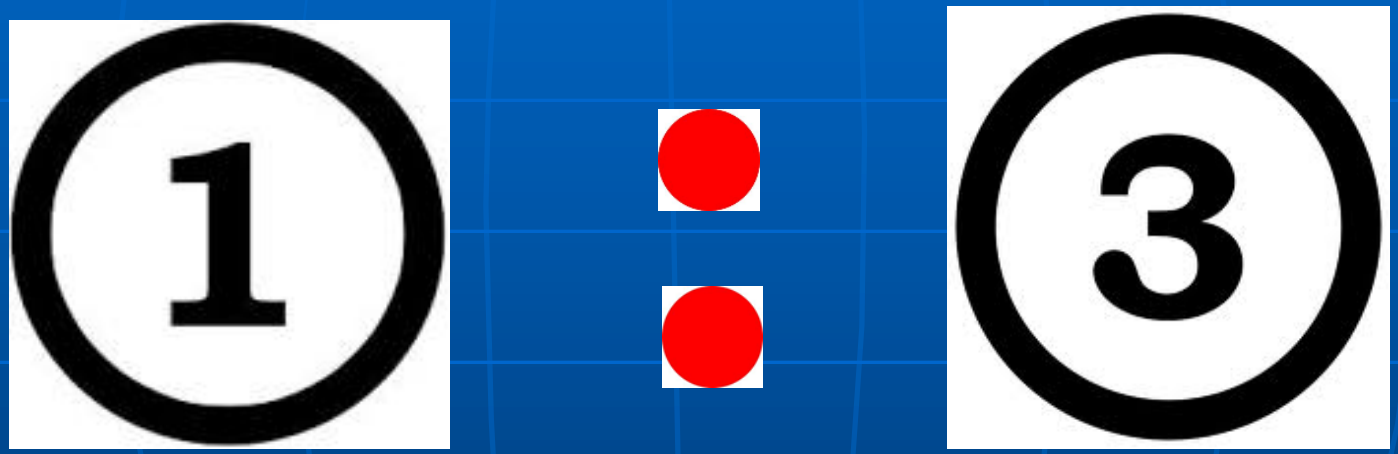
- Consultant/Advisory Board: GlaxoSmithKline Consumer Healthcare, Eli Lilly
- Media Work: Algiatry, LLC
- This presentation may contain references to off-label or investigational use of drugs or products

# Learning Objectives

- Describe the consequences of the opioid crackdown
- Identify some conditions to which opioids may respond
- Describe the trends in opioid prescribing

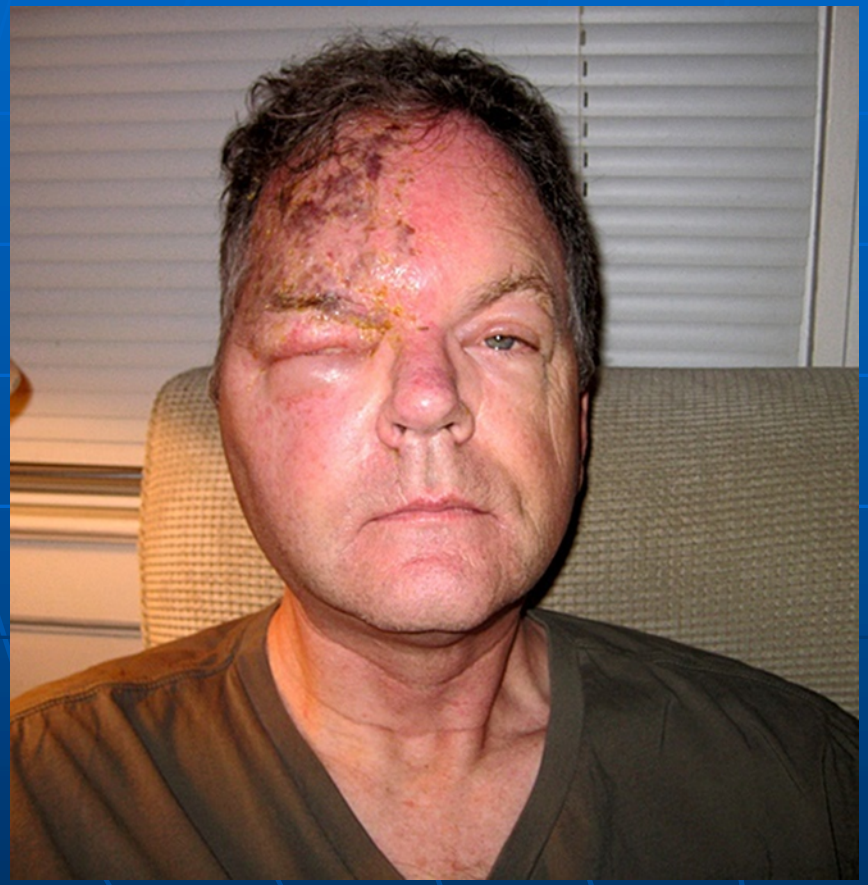
# How many?

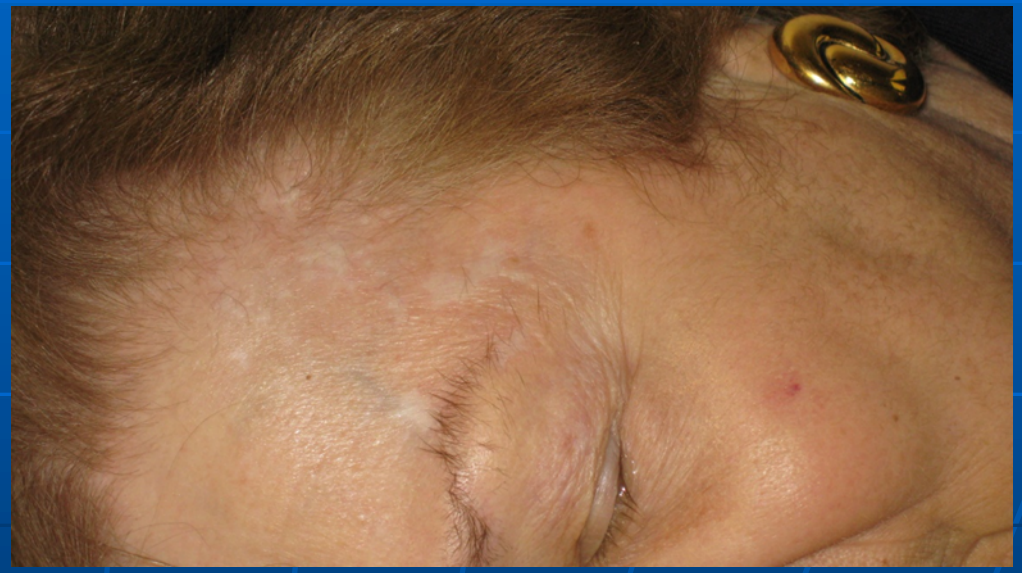
# Did you know?



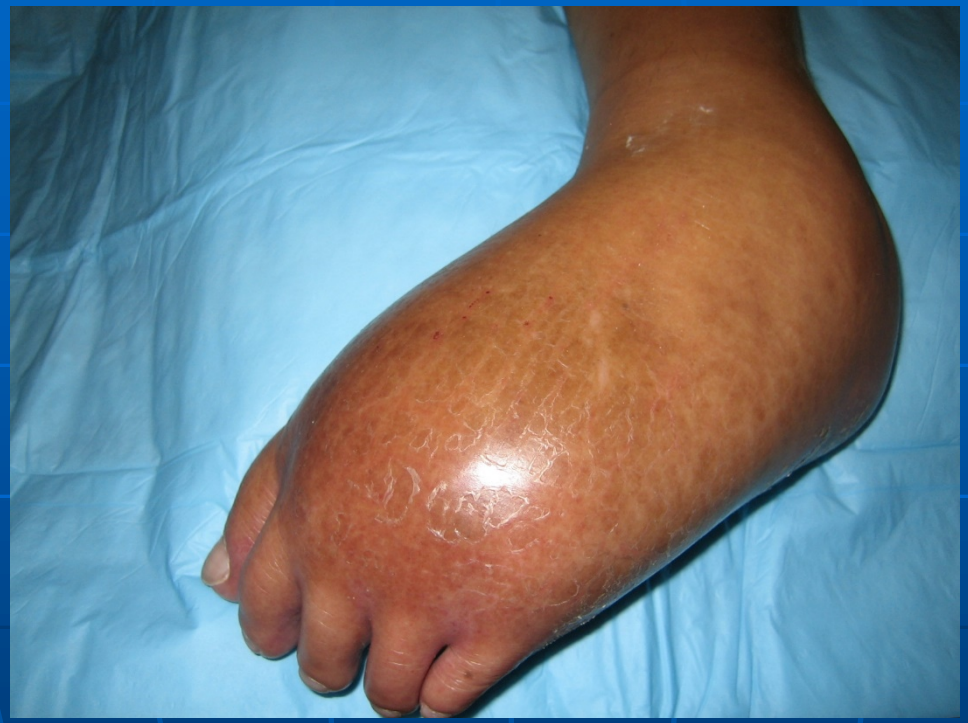

Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. *Relieving pain in America: a blueprint for transforming prevention, care, education, and research.* Washington (DC): National Academies Press (US); 2011

# Acute ⟹ Chronic Pain

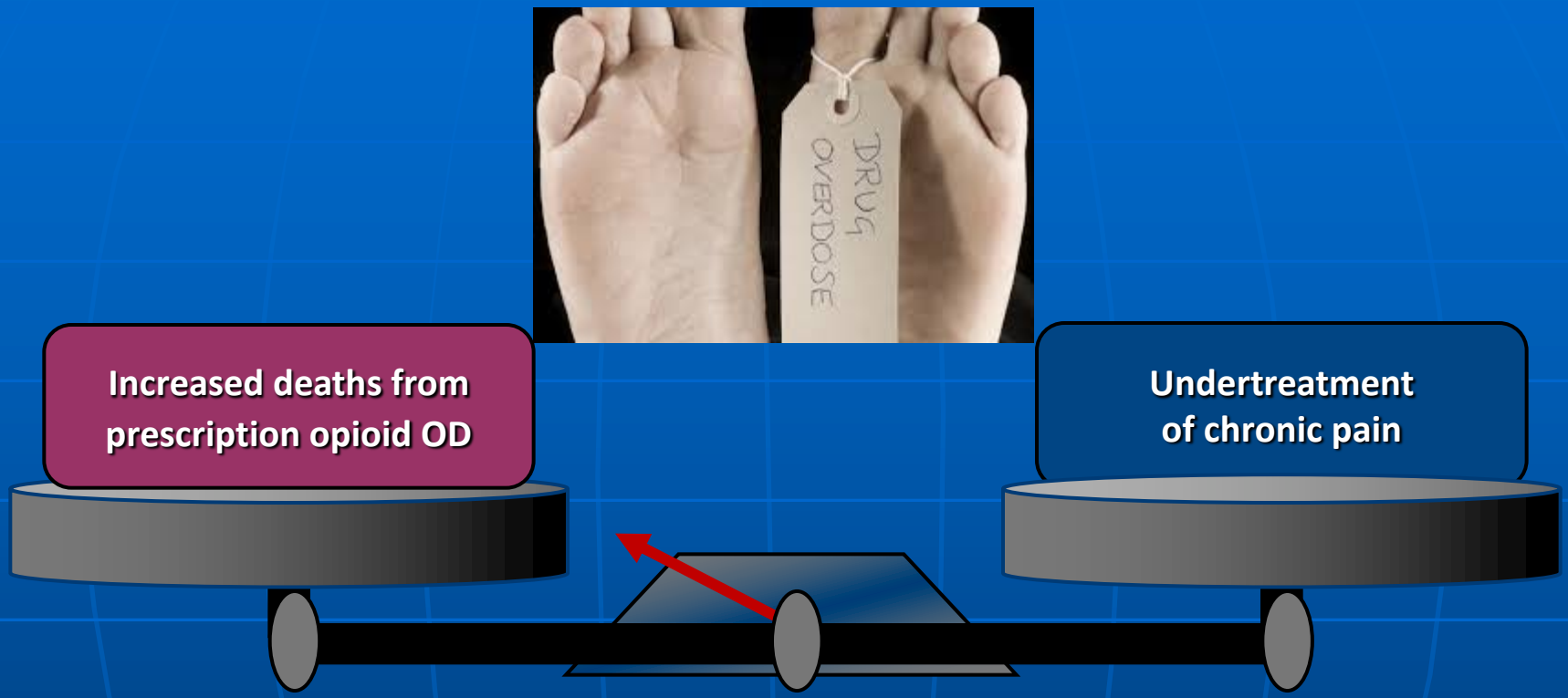




# Chronic Pain



# Deaths




- Quadrupling of deaths in last 15 years
- Failed efforts to consider addictiveness, low therapeutic ratio, lack of effectiveness

Frieden TR, Houry D. Reducing the risks of relief-The CDC Opioid-Prescribing Guideline. *N Engl J Med* 2016

# Pain ➡ Suicide

2X

Christo PJ. Opioids May be Appropriate for Chronic Pain. *J Law Med Ethics.* 2020 Jun;48(2):241-248

# New Evidence on Opioid Epidemic

- At least 60% of the overdose epidemic caused by illicit drugs, not prescription opioids
- The increase in opioid-related deaths primarily due to illicit fentanyl use
  - Illicitly manufactured fentanyl cannot be distinguished from prescription fentanyl in death certificate data
- Prescription Opioid Crisis = Polypharmacy Crisis?
  - More than 50% of deaths with opioid positive toxicology included alcohol
  - Average # of drugs identified in toxicologies = 6
- There has been a 20% decrease in opioid prescriptions between 2013-2017

U.S. Department of Health, (2018); American Medical Association (2018); Rudd RA, Aleshire N, et al. Increases in drug and opioid overdose deaths – U.S., 2000-2014. *MMWR Morb Mortal Wkl* Rept. 2016;64:1378-1382; Hannah HA, Arambula K, Ereman R, et al. Using local toxicology data for drug overdose mortality surveillance. *J Public Health Infom*. 2017;9(1):e143

# Changing Landscape of Opioid Epidemic

| Original Rx Deaths | Revised Rx Deaths | Date |
|---|---|---|
| 32,445 | **17,087** | 2016 |
| 33,000 | **15,000** | 2015 |

CDC Division of Unintentional Injury Prevention (2018)

- CDC classification included many deaths from illicit opioids ⟹ heroin and fentanyl
- Prescription Opioid–Related Deaths actually stable since 2012

CDC Morbidity & Mortality Weekly Report (2017)

- Illicitly manufactured fentanyl a major driver of opioid overdose deaths in multiple states
- Added funding to improve toxicologic testing for wider range of fentanyl analogs (e.g.,carfentanil, acetylfentanyl)

O'Donnell JK, Halpin J, Mattson C, et al. Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 – 10 States, July-Dec. 2016). *MMWR*, (66); 2017; Seth P, Rudd RA, Noonan RK, Haegerich TM. Qantifying the epidemic of prescription opioid overdose deaths. *Am J Public Health*. 2018;108 (4):500-502; Automation of Reports and Consolidated Orders System (ARCOS) of the DEA 1999. Transactional Data Warehouse 2015

# Opioid Crackdown

## Vicki

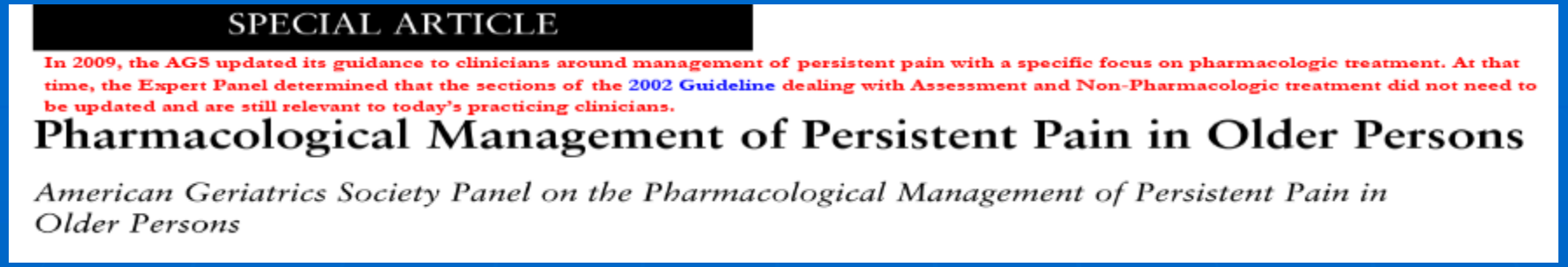
- "After 20 years of being on opioids during which I worked full time, raised three successful children, and took care of my house, I'm now on my last month of pain medications. I'm not sure what I'm going to do now that I can't do much of anything. I have no hope for the future, and don't care if I live or die anymore. This is no kind of existence."

Pain News Network, 2018

# Toll on Pain Care

- Drug Enforcement Policies
  - Involuntary Tapers
  - Patient Abandonment
  - Practitioner Flight
    - Fear of state or federal government sanctions
- CDC Guideline
  - Arbitrary adoption by regulators and health care organizations
    - Opioid reduction without expanding other resources for pain care
      - Leading more people to illicit opioid markets with greater harm ?

Addiction psychiatrist questions involuntary tapering of opioid (https://youtube/pRmPizyuZFM), last accessed Feb. 2019; Ziegler SJ. Patient Abandonment in name of Opioid Safety. *Pain Med.* 2013, 14 (3):323-324; Why I am Closing My Pain Practice? https://www.painnewsnetwork.org/stories/2018/1/17/whi-i-am-closing-my-pain-practice; Bonnie RJ, Schumacher MA, Clark JD, et al. Pain Management and Opioid Regulation: Continuing Public Health Challenges. *Am J Public Health* 2019;109(1):31-34



SPECIAL ARTICLE

In 2009, the AGS updated its guidance to clinicians around management of persistent pain with a specific focus on pharmacologic treatment. At that time, the Expert Panel determined that the sections of the 2002 Guideline dealing with Assessment and Non-Pharmacologic treatment did not need to be updated and are still relevant to today's practicing clinicians.

Pharmacological Management of Persistent Pain in Older Persons

*American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons*

AUGUST 2009–VOL. 57, NO. 8 JAGS

**Nonselective NSAIDs and COX-2 selective inhibitors may be considered rarely, and with extreme caution, in highly selected individuals** (high quality of evidence, strong rec)

- **All patients taking nonselective NSAIDs and COX-2 selective inhibitors should be routinely assessed for gastrointestinal and renal toxicity, hypertension, heart failure, and other drug–drug and drug–disease interactions (weak quality of evidence, strong recommendation).**

**All patients with moderate to severe pain, pain-related functional impairment, or diminished quality of life due to pain should be considered for opioid therapy** (low quality of evidence, strong recommendation)

- **Patients taking opioid analgesics should be reassessed for ongoing attainment of therapeutic goals, adverse effects, and safe and responsible medication use (moderate quality of evidence, strong recommendation)**

# Guidance on the Management of Pain in Older People

## British Geriatric Society

"Opioids may be considered for patients with moderate to severe pain, particularly if the pain is causing functional impairment or is reducing their quality of life."

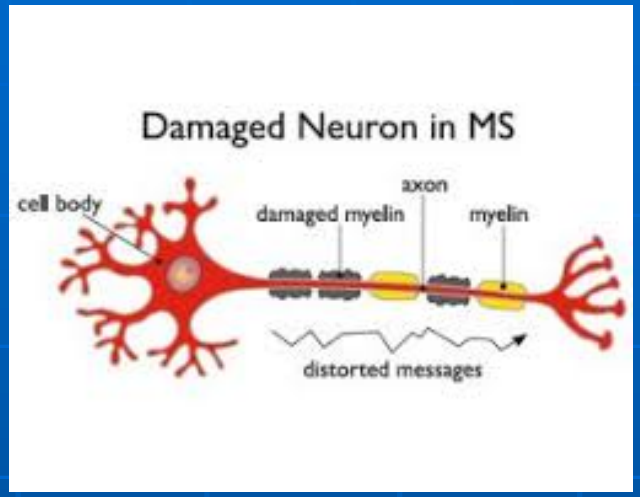
Abdulla A, Adams N, Bone M, et al; British Geriatric Society. *Age Ageing*. 2013 Mar;42 Suppl 1:i1-57

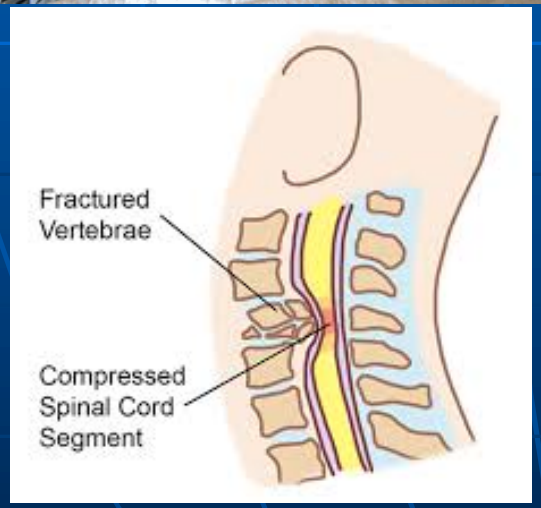
# Safer Pharmacologic Option

- Consider adverse effects of NSAIDs
  - Nephrotoxicity, bleeding, cardiotoxicity
- Consider life-threatening drug resistance from combining antiretrovirals (ART) with certain anticonvulsants or antidepressants
  - Reduced blood levels of the ART

Wegrzyn EL, Chaghtai AM, Argoff CE, et al. The CDC Opioid Guideline: Proponent Interpretation Has Led to Misinformation. *Clinical Pharmacology & Therapeutics* 2018; 103 (6): 950-953

# Painful Debilitating Diseases




# Opioids and Addiction

**Assumption: Opioids leading chronic pain patients to addiction and overdose deaths**

**Evidence: "Addiction occurs in a small percentage of people exposed to opioids – even with pre-existing vulnerabilities" – *Nora Volkow*, Director of NIDA**

**Fishbain et al – 3.27% risk of addiction in review of 67 studies**

**Cochrane Review - 0.5% incidence of de novo addiction & prevalence 4.5%**

**Reality: Opioids for chronic pain not associated with a major risk of addiction (OUD)**

Volkow ND, McLelllan TM. Opioid abuse in chronic pain – Misconceptions and mitigation strategies, *N Engl J Med.* 2016;374 (13):253-1263; Fishbain DA, Cole B, Lewis J, et al. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic opioid therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. *Pain Med.* 2008;9:444-459; Minozzi S, Amato L, Davoli M. Development of dependence following treatment with opioid analgesics for pain relief: A systematic review. *Addiction* 2013;108(4):688-98

# Opioid Evidence Base
## CDC Guideline

CDC Guideline viewed only RCTs ≥52 weeks as adequate

Problem: no other analgesics held to that standard

In fact: several 52 week open label studies of ER/LA opioids show benefit and safety

Wegrzyn EL, Chaghtai AM, Argoff CE, et al. The CDC Opioid Guideline: Proponent Interpretation Has Led to Misinformation. *Clinical Pharmacology & Therapeutics* 2018; 103 (6): 950-953

# Opioid Evidence Base
## Cochrane

Cochrane review shows over 20% of pts with chronic pain have long term relief from different painful conditions

# Opioid Evidence-Base

REVIEW

## Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects

CMAJ 2006;174(11)

Andrea D. Furlan, Juan A. Sandoval, Angela Mailis-Gagnon, Eldon Tunks

Chronic non-cancer-related pain (CNCP) includes

# Opioid Evidence Base

"Chronic non-cancer pain is a major health problem, for which opioids provide one Rx option. However, evidence is needed about side effects, efficacy, and risk of misuse or addiction."

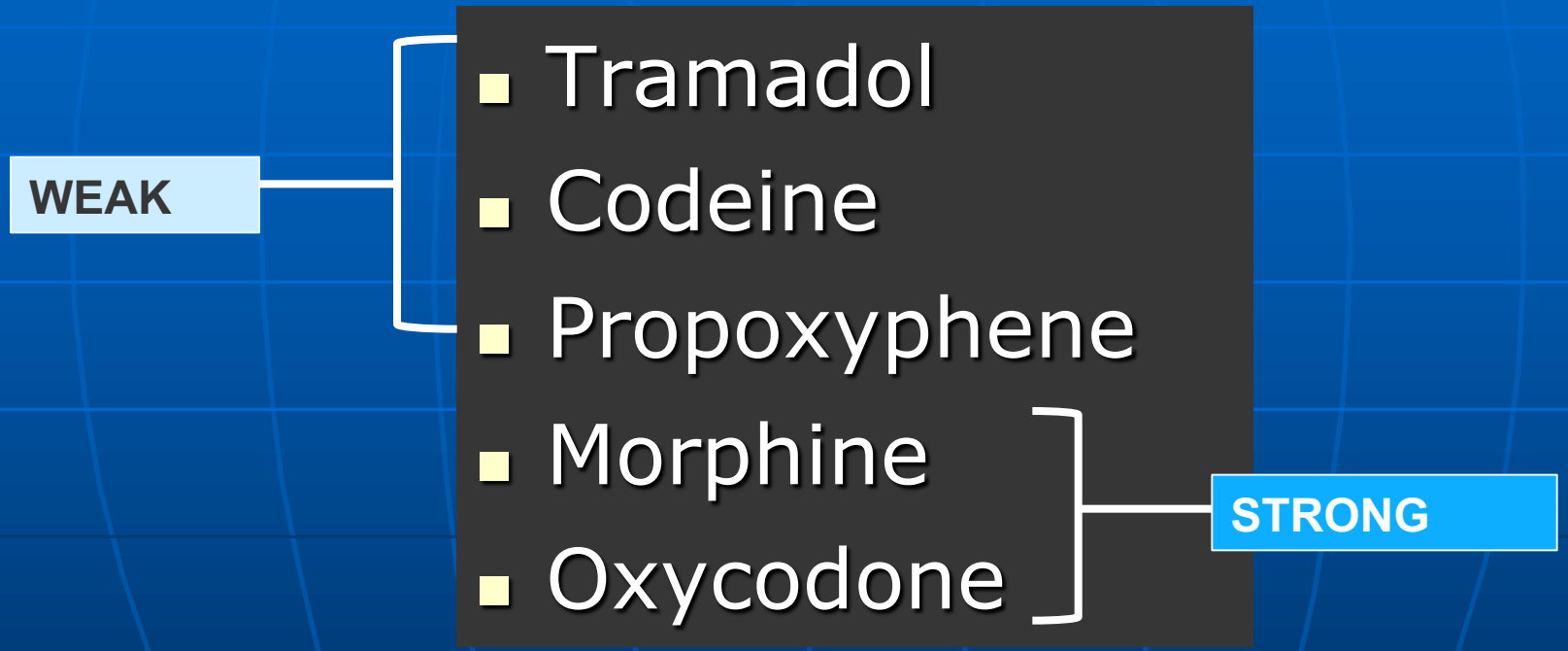
Furlan A et al *CMAJ* 2006;174(11):1589-1594

# Opioid Evidence Base
## Meta-analysis 41 Trials (n =6,019)

- Nociceptive (OA, RA, LBP): 80%
- Neuropathic (PHN, DPN, phantom): 12%
- Fibromyalgia:7%
- Mixed = 1%
- Study quality high: 87%

Furlan A et al *CMAJ* 2006;174(11):1589-1594

# Opioid Evidence Base
## Meds Studied




Furlan A et al *CMAJ* 2006;174(11):1589-1594

# Opioid Evidence Base
## Efficacy Outcomes: Pain & Function

"Opioids were more effective than placebo for both pain and functional outcomes in patients with nociceptive or neuropathic pain or fibromyalgia."

Furlan A et al *CMAJ* 2006;174(11):1589-1594

# Opioid Evidence Base
## Safety Outcomes: AE's

"Dropout rates averaged 33% in the opioid groups and 38% in the placebo groups."

Furlan A et al *CMAJ* 2006;174(11):1589-1594

# Cannabis-Based Medicines
## Analgesia in Chronic Pain

| Evidence | Finding |
| --- | --- |
| Aviram et al (syst review & meta analysis) | No effect in most studies or uncertain significance of pain reduction |
| Stockings et al (syst review & meta analysis) | NNT 24 & pain intensity change of 3 mm on 100 mm VAS |
| Hauser et al (overview SR) | Inconsistent effects for *neuropathic* pain, small effects, ? clinical utility |
| Cochrane Report | Very low quality evidence for herbal cannabis in chronic *neuropathic* pain |
| Hauser et al (syst review & meta analysis) | Overall no supportive evidence for *cancer* pain |

Aviram J et al. *Pain Physician* 2017;20:E755-E796; Stockings et al. *Pain* 2018;159:1932-1954; Hauser W et al. *Eur J Pain* 2018;22:455-470; Hauser et al. *Schmerz* 2019

# Cannabis Evidence-Base

**Medical Cannabis for the Treatment of Chronic Pain: A Review of Clinical Effectiveness and Guidelines**

Four overviews (systematic review of systematic reviews), one systematic review of guidelines, and six guidelines

Banerjee S, McCormack S. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019 Jul. CADTH Rapid Response Reports.

# Cannabis Evidence-Base
## Key Findings

- *Some* suggestion of benefit with cannabis-based medicines for neuropathic pain
  - However, benefits need to be weighed against harms
- Findings are *inconsistent* for effect of cannabis-based medicines in patients with fibromyalgia, musculoskeletal pain, Crohn's disease, and MS

Banerjee S, McCormack S. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019 Jul. CADTH Rapid Response Reports.

# Cannabis Evidence-Base
## Cochrane Review

**Cannabis-based medicines for chronic *neuropathic* pain in adults**

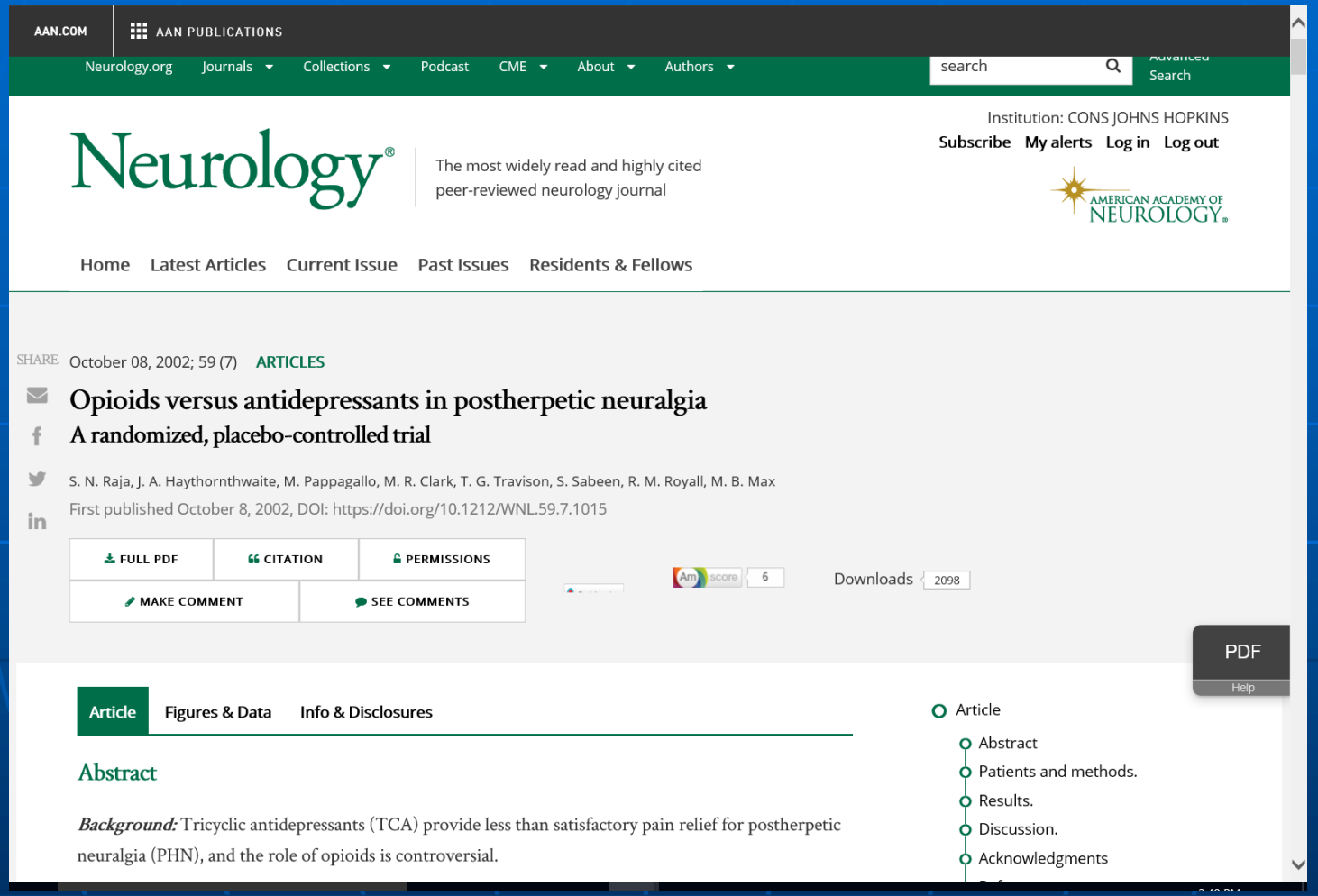
**AUTHORS' CONCLUSIONS**

- The potential benefits of cannabis-based medicine (herbal cannabis, plant-derived or synthetic THC, THC/CBD oromucosal spray) in chronic neuropathic pain *might be* outweighed by their potential harms

Cochrane Database Syst Rev. 2018 Mar 7;3:CD012182

# Opioid Evidence Base

## Opioids vs Antidepressants in Postherpetic Neuralgia




*Neurology.* 2002 Oct 8;59(7):1015-21.**Opioids versus antidepressants in postherpetic neuralgia: a randomized, placebo-controlled trial.** Raja SN[1], Haythornthwaite JA, Pappagallo M, Clark MR, Travison TG, Sabeen S, Royall RM, Max MB

# Opioid Evidence Base

## Opioids vs TCA in PHN

- Opioids and TCA (nortrip) decreased pain more than placebo ($p<0.001$) and no detrimental cognitive effects
- Trend toward greater pain reduction and lower NNT with opioids vs TCA
- Sustained release morphine compared to nortrip more effective in decreasing PHN pain when two drugs compared
- Comparison of TCA and opioid suggested opioids probably decrease PHN pain better than TCA

*Neurology*. 2002 Oct 8;59(7):1015-21.**Opioids versus antidepressants in postherpetic neuralgia: a randomized, placebo-controlled trial.** Raja SN[1], Haythornthwaite JA, Pappagallo M, Clark MR, Travison TG, Sabeen S, Royall RM, Max MB

# Cannabis Side Effects

## Short Term in Pain

- Rare serious adverse events
- No deaths every reported

## Long Term in Chronic Pain

- Very little information
- May be increased risk of chronic bronchitis, impaired memory, attention, decision-making, planning, psychological D/O
  - In recreational cannabis smokers
  - Most reversible with smoking cessation

## Problematic Use

- Risk about 10% and similar to lifetime recreational use

Sharon et al. *Curr Opin Anesthesiol* 2019, 32:623-628; Nugent SM et al. *Ann Intern Med* 2017;167:319-331; Feingold D et al. *Pain Med* 2017;18:294-306

# Cannabis as Substitute

VIEWPOINT

## Should Physicians Recommend Replacing Opioids With Cannabis?

**Keith Humphreys, PhD**
Veterans Affairs Health Services Research and Development Center; and Stanford University, Palo Alto, California.

**Richard Saitz, MD, MPH**
Department of Community Health Sciences, Boston University School of Public Health, Boston, Massachusetts; Clinical Addiction Research and Education Unit, Section of General Internal Medicine, and Grayken Center for Addiction, Boston Medical Center, Boston, Massachusetts; and Associate Editor, *JAMA*.

**Recent state regulations** (eg, in New York, Illinois) allow medical cannabis as a substitute for opioids for chronic pain and for addiction. Yet the evidence regarding safety, efficacy, and comparative effectiveness is at best equivocal for the former recommendation and strongly suggests the latter—substituting cannabis for opioid addiction treatments is potentially harmful. Neither recommendation meets the standards of rigor desirable for medical treatment decisions.

### Efficacy of Cannabis for Chronic Pain and for Opioid Use Disorder

Recent systematic reviews[1,2] identified low-strength evidence that plant-based cannabis preparations alleviate neuropathic pain and insufficient evidence for other types of pain. Studies tend to be of low methodological quality, involve small samples and short-follow-up periods, and do not address the most common causes of pain (eg, back pain). This description of evidence for efficacy of cannabis for chronic pain is similar to how efficacy studies of opioids for chronic pain have been described (except that the volume of evidence is greater for opioids with 96 trials

rescheduling, Good Samaritan laws, incarceration practices, and availability of evidence-based opioid use disorder treatment and naloxone. Furthermore, the aggregate population associations (eg, between medical cannabis and opioid overdose) may be opposite of those seen within individuals. In the only individual-level analysis, which included 57 146 people aged 12 and older, of a nationally representative sample, medical cannabis use was positively associated with greater use and misuse of prescription opioids.[4]

The largest prospective study of cannabis as a substitute for opioids was a 4-year cohort study of 1514 patients with chronic pain who had been prescribed opioids.[5] Cannabis use was associated with more subsequent pain, less self-efficacy for managing pain, and no reductions in prescribed opioid use. There was no substitution; rather, cannabis was simply added to the mix of addictive substances taken by patients with pain.

For opioid use disorder, there is concern that the New York State Health Commissioner has defined opioid addiction to include people being treated with US Food and Drug Administration–approved, efficacious,

# Abuse-Deterrent Opioids

## Effectiveness and Value

**Economic modeling – ADF opioids have potential to substantially reduce incidence of abuse in chronic pain patients**

**But – Significantly higher cost**

**Call for: further research generating real-word evidence for health and economic impact on opioid abuse epidemic**

Abuse-Deterrent Formulation of Opioids: Effectiveness and Value. *Institute for Clinical and Economic Review*, 2017.

# Ethical Pain Care

- Provide opioids for cancer pain and at the end of life
- Consider opioids for certain patients with chronic, non-cancer pain
  - Severe pain, unresponsive to other therapies, adversely affects quality of life or function
- Preserve access for patients whose function and quality of life are improved
- Don’t substitute cannabis with a low or inconsistent effect on chronic pain conditions

Christo PJ. Opioids May be Appropriate for Chronic Pain. *J Law Med Ethics.* 2020 Jun;48(2):241-248
Chou R, et al. *J Pain*. 2009;10:113-130; Dowell D, et al. *JAMA*. 2016;315:1624-1645; Schneider JP. A patient centered approach to the opioid overdose crisis. *J Mississippi State Medical Association* 2018;59(5):232-233

# Touches us