

Evidence for the Efficacy of Pain Medications

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Disclosure Statement

I, KariLynn Dowling,

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Objectives

At the conclusion of this session, attendees should be able to:

1. Summarize the current evidence for opioids in chronic and acute pain
2. Explain factors contributing to the imbalance between opioid prescribing rates and evidence for use
3. Identify appropriate scenarios for prescribing non-narcotic analgesics in place of opioids

Note

The information in this presentation does not extend to cancer pain treatment and end-of-life care.



Opioids in Chronic Pain

CDC Guideline

- ▣ Prescribing Opioids for Chronic Pain, March 2016
- ▣ “**No study** of opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for chronic pain **evaluated long-term (≥1 year) outcomes related to pain, function, or quality of life.**”¹
- ▣ Quality of Evidence: Insufficient

How did CDC find no evidence?

- ▣ AHRQ Report, “The Effectiveness and Risks of Long-Term Opioid Treatment of Chronic Pain” September 29, 2014
- ▣ Chronic Opioid Key Question Domains²
 - ▣ **KQ1: Effectiveness and comparative effectiveness**
 - ▣ KQ2: Harms and adverse events
 - ▣ KQ3: Dosing strategies
 - ▣ KQ4: Risk assessment and mitigation

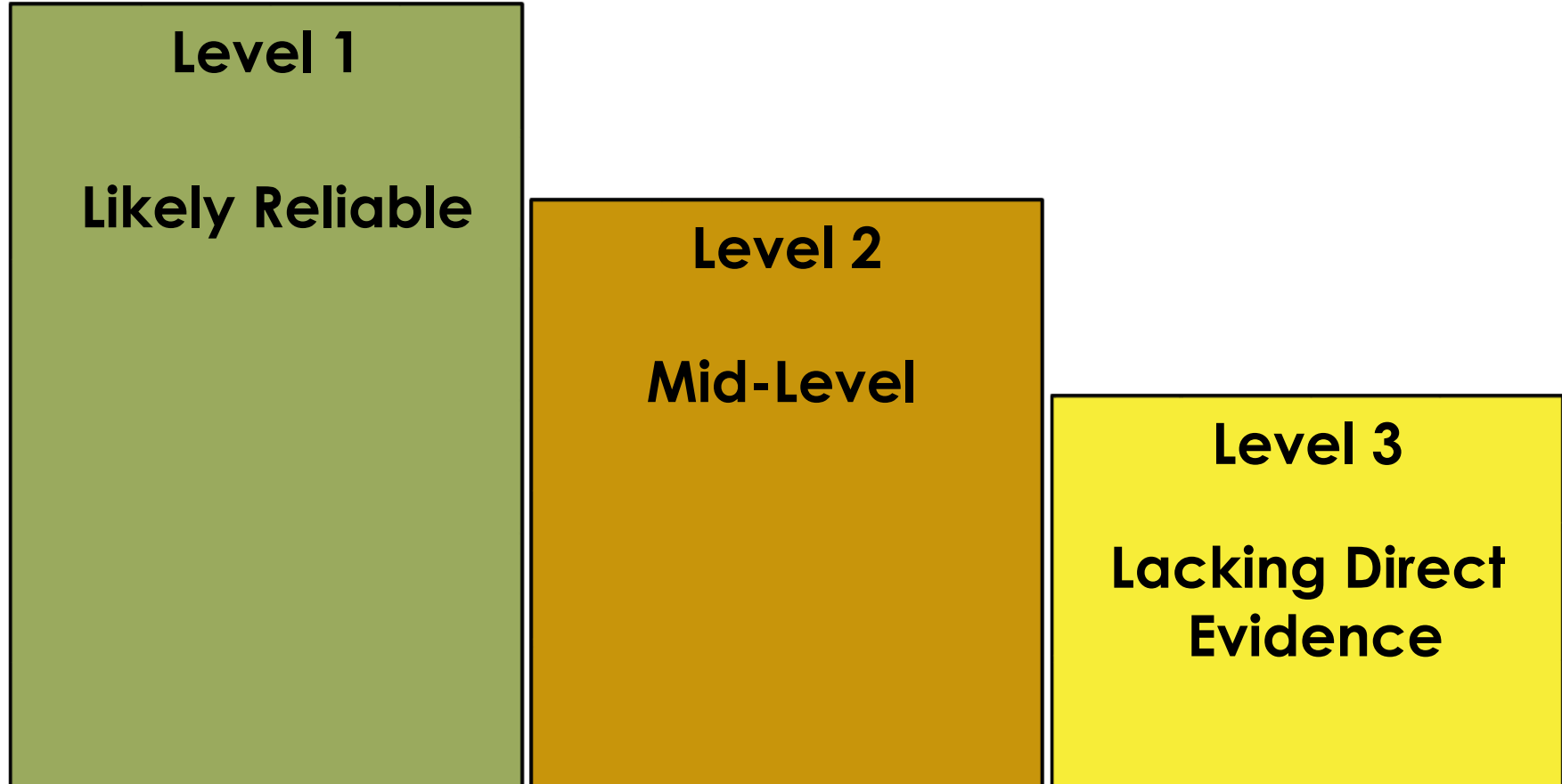
AHRQ Report²

- ▣ Literature review: 627 full articles
- ▣ 588 excluded
 - ▣ Major exclusions: age <18 years, opioid duration <3 months, acute pain, pregnant/breastfeeding, addiction treatment, end of life care, parenteral agent
- ▣ 39 included studies: **none** reported on pain, function, or QoL outcomes at ≥1 year

The Rest of the Story

- ▣ Were exclusion criteria too strict?
 - ▣ In CDC follow-up, most of the highest-quality trials identified were ≤ 6 weeks in duration¹
- ▣ What about trials with greater methodological limitations?³
 - ▣ Lack of blinding/unclear allocation concealment
 - ▣ Small sample sizes
 - ▣ High exclusion and dropout rates

Review: Levels of Evidence⁴



Review: NNT

- Number Needed to Treat
- How many patients must receive the intervention for one to have the desired outcome?
- Same concept for number needed to:
 - Harm (NNH)
 - Kill (NNK)

Opioids in Knee or Hip Osteoarthritis³

- 2014 Cochrane analysis of nontramadol opioids
- Median 4 weeks treatment (range 3 days-3 months)
- NNT
 - Decreased pain: 10
 - Improved function: 11
- NNH: 14

Opioids in Low Back Pain⁵

- ▣ Short-term Use (≥ 1 month)
- ▣ 4 to 15 weeks follow-up
- ▣ “Strong” opioids (morphine, hydromorphone, oxymorphone, tapentadol, oxycodone)
 - ▣ NNT 5-13 for at least 30% relief
 - ▣ NNT 5-18 for at least 50% relief

Opioids in Neuropathic Pain⁶

- ▣ “Intermediate-term” treatment (≤ 12 weeks)
 - ▣ NNT 4 for at least 33% relief
 - ▣ NNT 5.9 for at least 50% relief
- ▣ No significant changes to emotional or physical function

What about specific opioids?

- ▣ Overall weak evidence
- ▣ Sustained-release morphine and transdermal fentanyl have the “best” of the weak evidence
 - ▣ TD Fentanyl: three prospective studies with use ≥ 10 months⁷, 1 refractory pain trial with 50% dropout⁸
 - ▣ SR Morphine: 5 studies with varied methods⁷

Specific Opioids, continued

- ❑ Oxycodone: effective in 1 uncontrolled study with high dropout rate⁷
- ❑ Methadone: insufficient evidence to support use in chronic noncancer pain⁹
- ❑ Hydrocodone: **no studies** evaluating efficacy are available⁷

Tramadol Cochrane Reviews

- ▣ 2006: Provides a small degree of pain relief for hip or knee OA (mean duration 35 days)¹⁰
- ▣ 2009: For neuropathic pain, NNT 3.8 (50% pain relief) and NNH 8.3¹¹

Level 1

Level 2



Opioids in Acute Pain

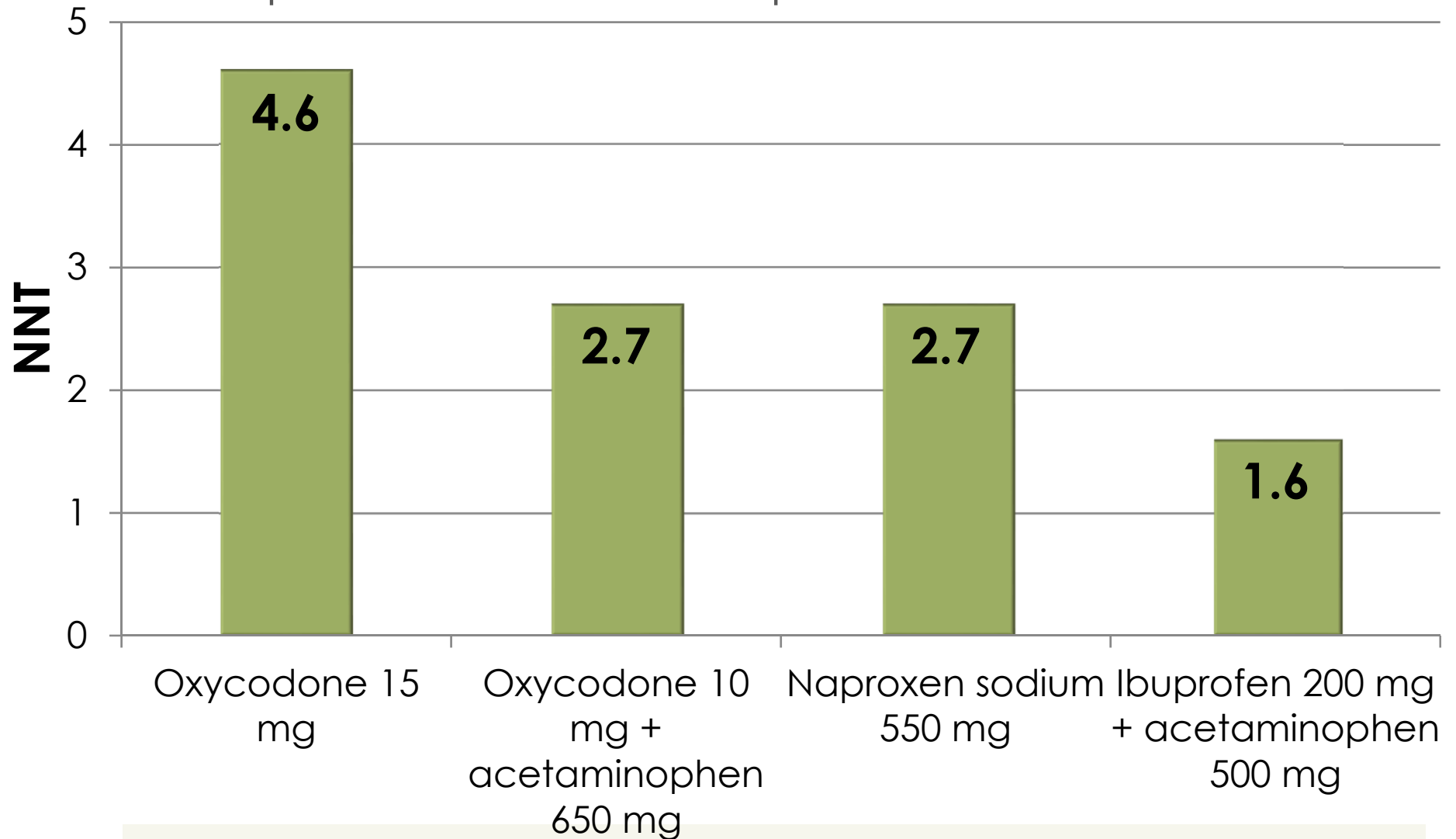
Analgesic Strength

For acute pain, opioids >> other analgesics, right?

Not necessarily!

Acute Postoperative Pain¹²

For 1 person to reach 50% pain relief, treat:



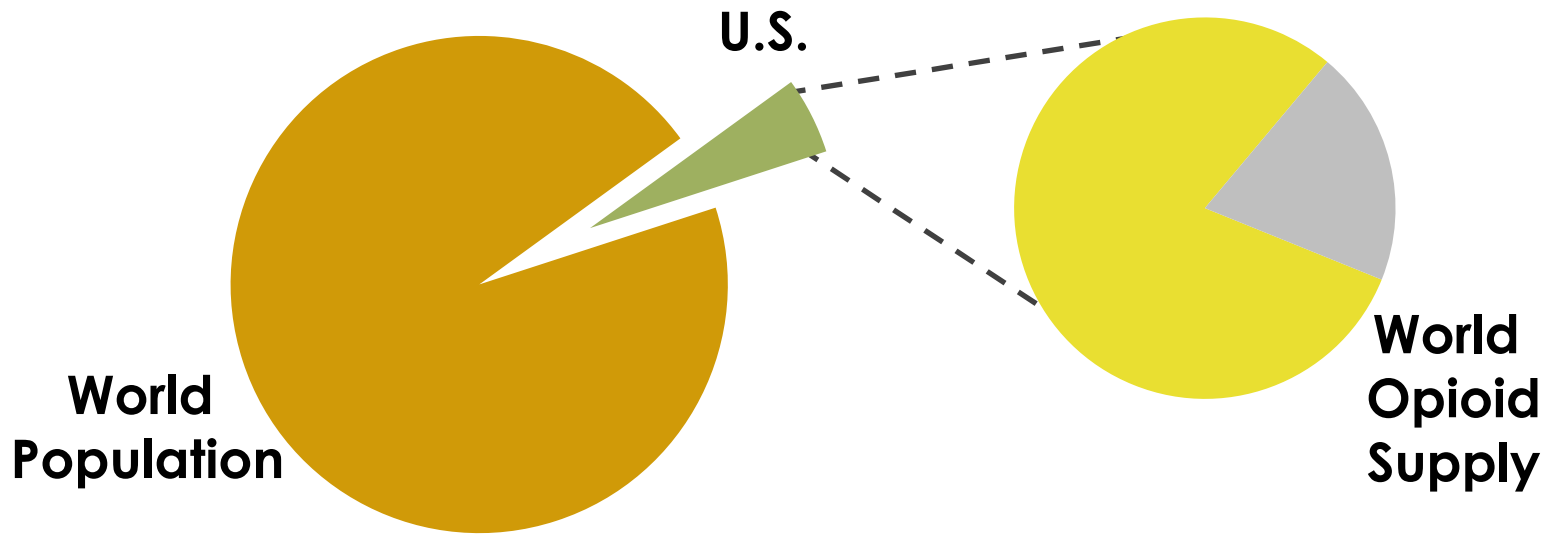
Acute Pain NNT, Continued¹³

Medication	# Patients Studied	NNT
Celecoxib 400 mg	298	2.1
Ibuprofen 400 mg	5456	2.5
Naproxen 400 mg	197	2.7
Ibuprofen 200 mg	3248	2.7
Oxycodone 10 mg + acetaminophen 1000 mg	83	2.7
Morphine 10 mg IM	948	2.9
Tramadol 50 mg	770	8.3

Other Acute Pain Studies

- Wisdom tooth extraction
 - Ibuprofen 200 mg/APAP 325 mg combo provided better relief than opioids¹⁴
- Lumbar disc herniation
 - Opioids associated with higher rate of cross-over to surgery¹⁵
- Renal colic
 - 10 of 13 studies in a review reported lower pain scores for patients receiving NSAIDs¹⁶

The US makes up **5%** of the world's population, and consumes **80%** of the world's opioids.¹⁷



How did we arrive here?

Pain as the 5th Vital Sign

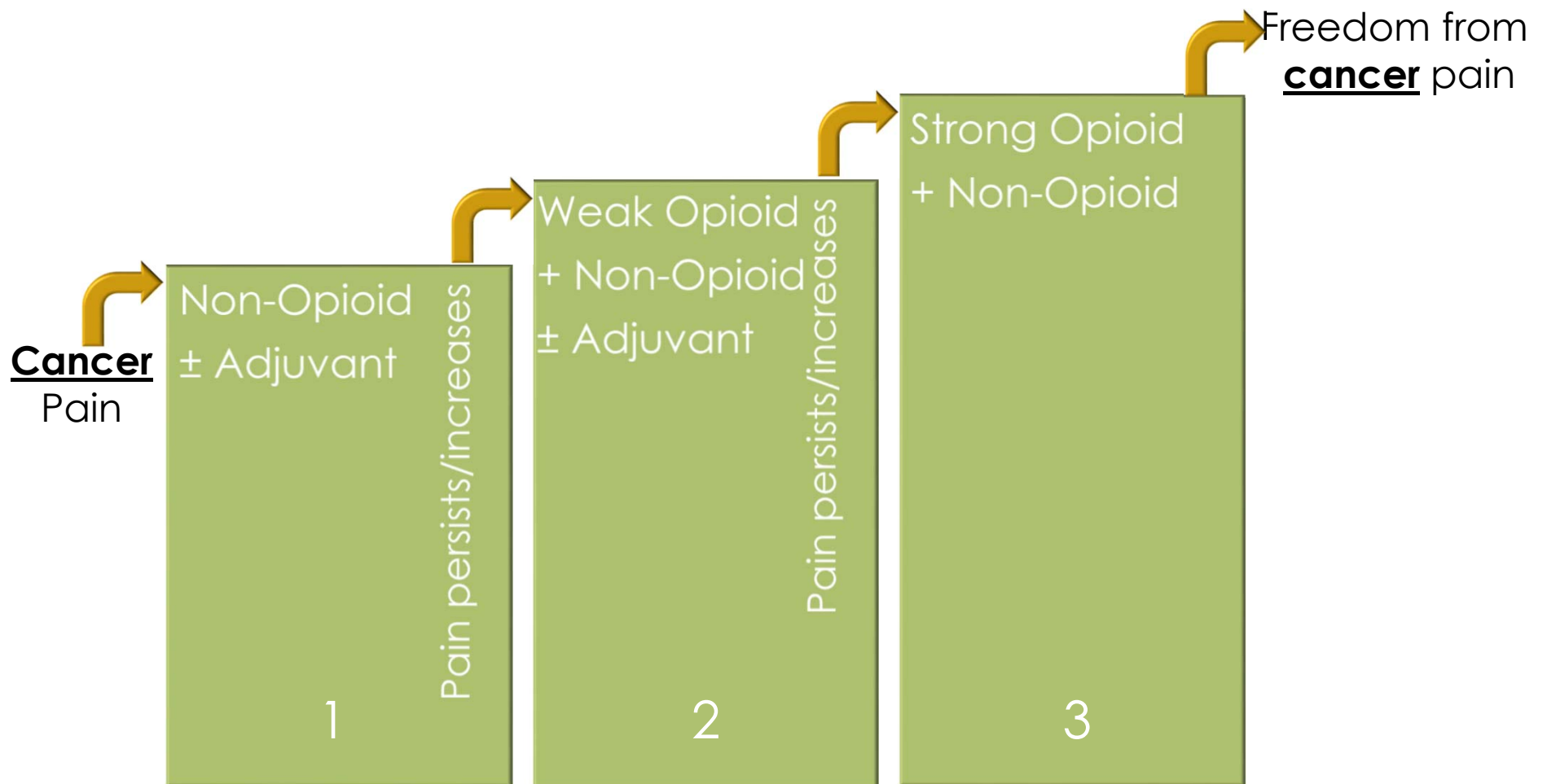
- ❑ “Bloodletting of the 21st century”
- ❑ Quality measures suggesting any level of pain is unacceptable
- ❑ Widely-adopted practice intended to improve care, caused unanticipated harm instead



“Opioids are much stronger than other analgesics”¹²

- ❑ No ceiling effect when given IV
 - ❑ Psychotherapeutic effects for emotional distress
 - ❑ Skillful advertising
 - ❑ Ubiquitous WHO pain ladder
-

WHO Pain Ladder¹⁸



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Moving Forward: Prescribing Choices

Selecting Analgesics

- After thorough work-up and clear diagnosis, look at the evidence for THAT indication
 - Low back pain ≠ knee pain ≠ pelvic pain, etc.
- Opioids may not be inferior to other analgesics, but in most cases they also do not outperform other analgesics
- What we know: the population that will benefit from opioids is much smaller than the population that currently receives them

Considerations: Dose

- ▣ What is the ultimate goal for the patient: reduced pain, or improved function?
- ▣ Current evidence suggests higher doses do not benefit, and may decrease, functionality
- ▣ What is the threshold?
 - ▣ APS/AAPM says no evidence for 200 or more morphine milligram equivalents (MME)¹⁹
 - ▣ CDC says reassess at 50 MME, avoid 90 MME¹

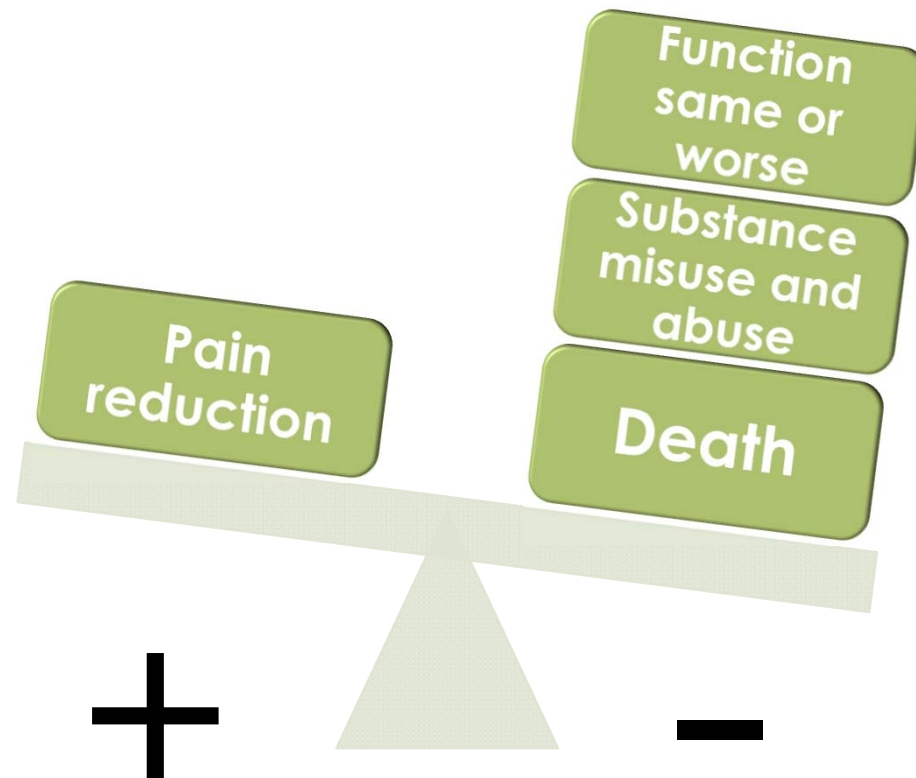
Considerations: Other Meds

- ❑ Avoid opioid-benzodiazepine combos
- ❑ Odds Ratio (OR) of controlled substance-related death²⁰
 - ❑ Opioid only: 3.4
 - ❑ Benzodiazepine only: 7.2
 - ❑ Combination of at least one opioid and one benzodiazepine: **14.9**
- ❑ Benzodiazepines present in 31%-61% of opioid overdose deaths¹

Considerations: Disease States

- ▣ All of the following require or strongly suggest selecting non-opioid therapies^{1,7,19}
 - ▣ Past/present substance use disorder
 - ▣ History of overdose attempt
 - ▣ Childhood trauma (ACEs)
 - ▣ Sleep apnea, respiratory disease
 - ▣ Uncontrolled mental health disorders
 - ▣ Decreased cognitive function

Long-Term Opioids



Conclusions

- ❑ Low-to-moderate quality body of evidence for efficacy of opioids in acute and chronic painful conditions
- ❑ Rates of meaningful outcomes after a year or more of use are unknown
- ❑ Superiority of opioids to other analgesics is generally not substantiated at this time
- ❑ Finding the small set of patients who will benefit from opioids requires careful evaluation

Case #1

A 64-year-old female complains of chronic low back pain. Which of the following would you NOT screen for to determine if opioids are a safe and effective treatment option for the patient?

- a) Respiratory disease
- b) Pain scale rating
- c) Childhood trauma
- d) Cognitive decline

Case #2

A 19-year-old male has just undergone wisdom tooth extraction. Assuming no therapeutic contraindications, which of the following is most likely to provide at least 50% pain relief?

- a) Oxycodone
- b) Oxycodone + acetaminophen
- c) Ibuprofen
- d) Ibuprofen + acetaminophen

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