Pain in 2017: Standing up to the Challenge

Mass PI Spring Meeting

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Audience Poll # 1

The presenter of this lecture is a/ an:

A. Paid consultant for drug/ device companies

B. Investor in drug/ device companies

C. Paid speaker bureau member for drug/ device companies

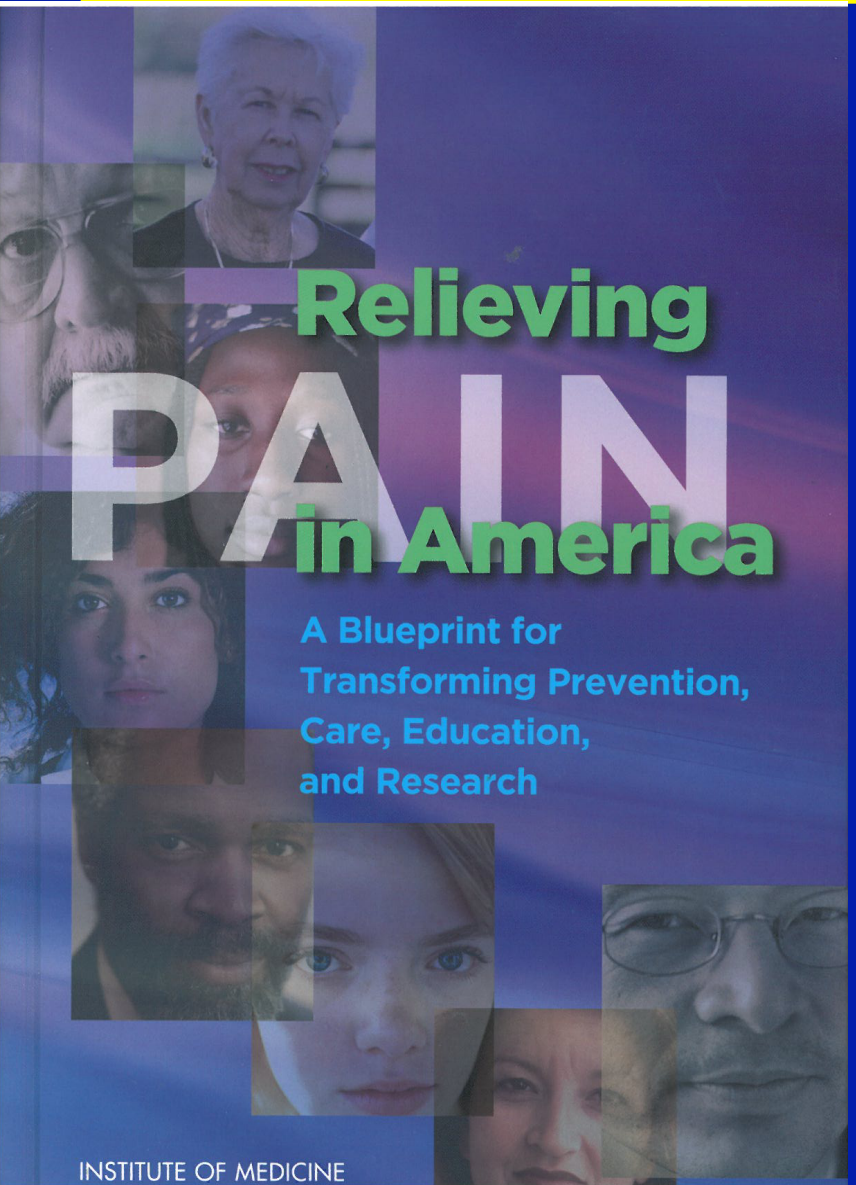
D. Grantee from drug/ device companies

E. None of the above – no relevant commercial financial relationships

Disclosures

- No relevant commercial interests
- BC/BS (past Opioid Policy Advisor)
- Mass DPH: PDMP Council, DFC
- Governor's medical education task force (through Tufts)
- AAPM participant, AMA Task Force, IPRCC appointee

Pain: a Public Health Issue



IOM, WHO have declared pain a public health issue:

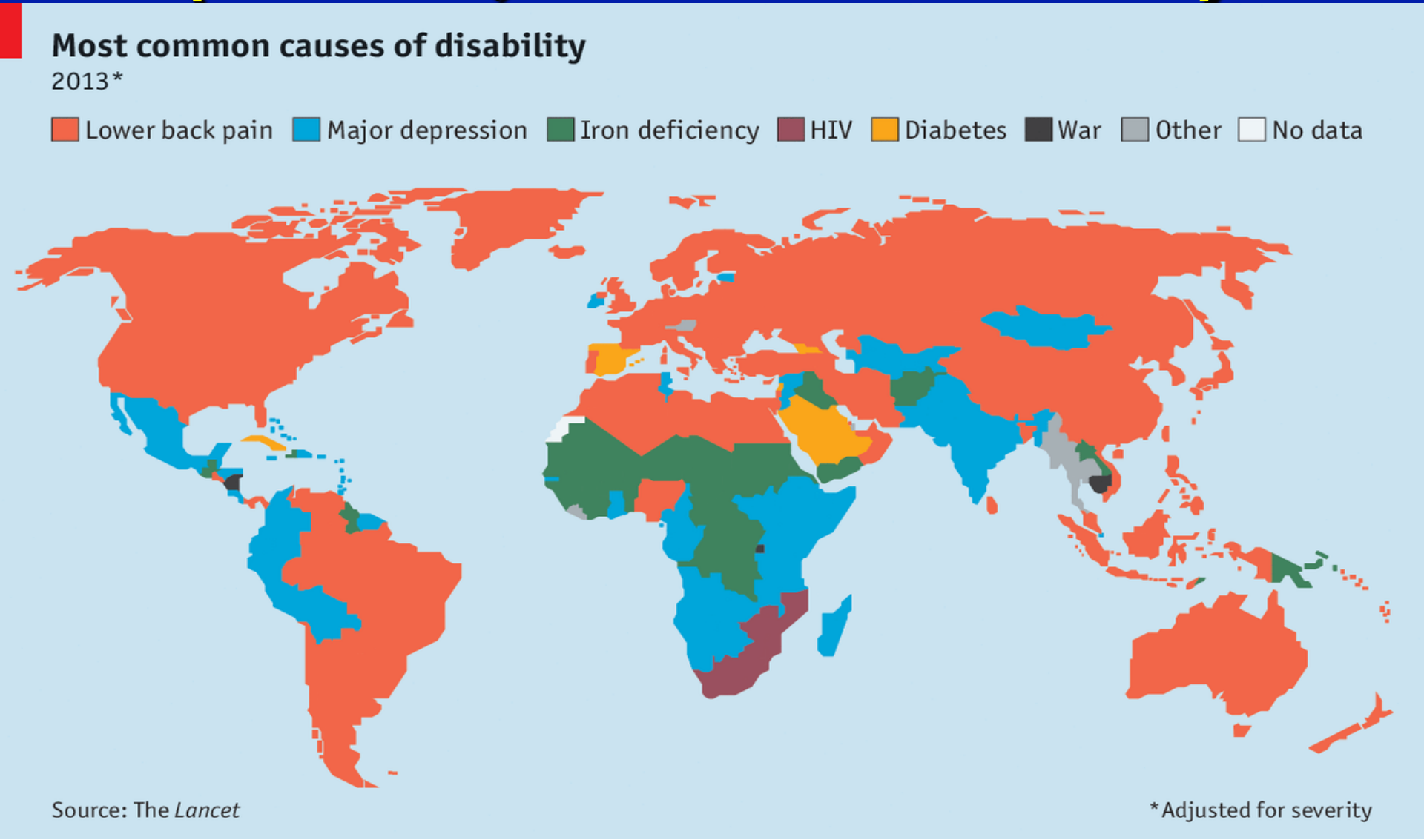
- High prevalence, burden
- Amenable to prevention (e.g., acute-to-chronic)
- Population-based, clear relation to SES
- Human rights dimension including inequities
- Moral imperative to transform our thinking

Audience Poll # 2

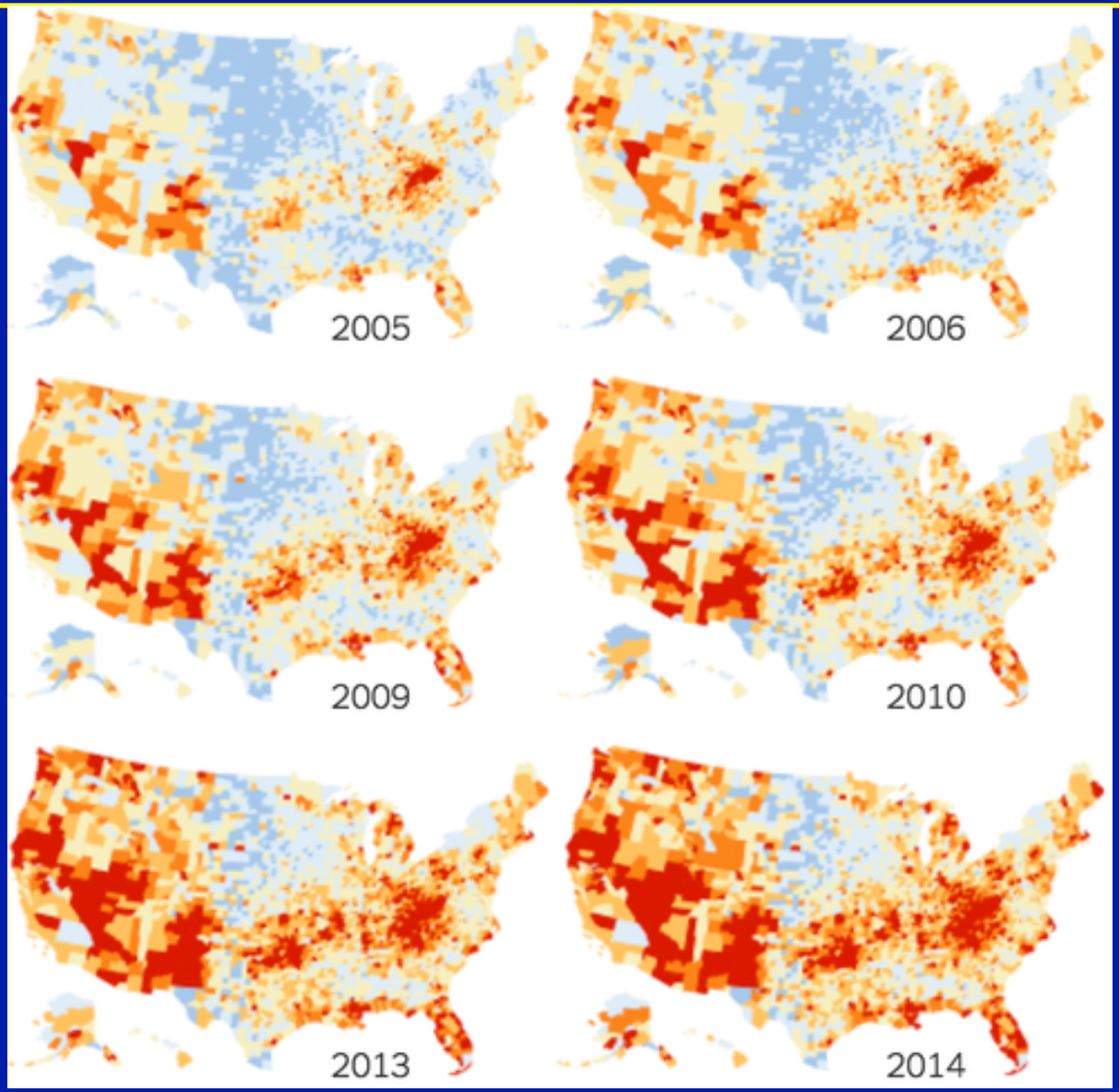
The leading cause of disability worldwide in adults living in developed nations is

A. Cancer
B. Mental illness
C. Firearm and other violence
D. Heart disease
E. Low back pain

Worldwide Disability (Lancet, Economist 2015)



US Opioid Death Rates



Audience Poll # 3

Factors associated with an increased risk of opioid abuse include:

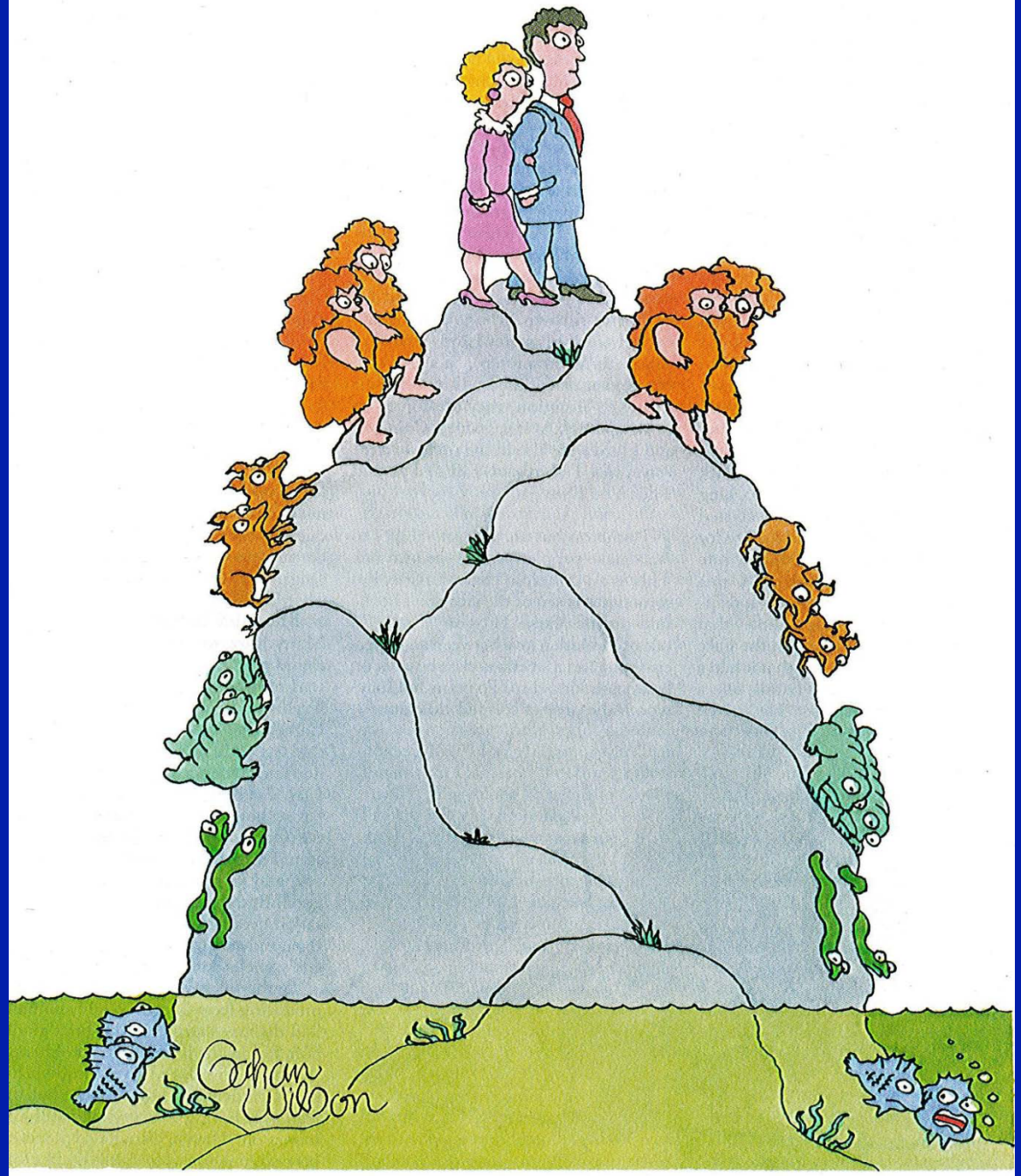
A. Younger age (18-25)
B. Male gender
C. Psychiatric disorder (including exposure to violence, e.g., sexual assualt)
D. Individual or family substance abuse Hx
E. All of the above

John Bonica (1917-1994)

- Many patients with chronic pain have conflicts that center around obtaining medications, failure in obtaining relief, and obtaining certification of the sick role.
- The physician who is unaware of the psychosocial dimensions of chronic pain will fail to identify the vulnerable patients… become frustrated and wonder whether the patient is a drug addict or the psychological symptoms are the cause rather than the effect of the pain.

Evolving Viewpoint (1)

- Portenoy and Foley (Pain 1986; N=38):
  - A single committed physician who will evaluate ongoing medical and psychological problems should be available.
  - The physician must be able to make the clinical judgment that higher doses will not be salutary or the treatment should be stopped altogether.
  - Most patients in the [literature] have required modest doses; the need for high doses must be scrutinized to ensure drug is appropriately used and that pain is the symptom being treated.
  - Present survey provides suggestive evidence for safety and efficacy in selected patients BUT paucity of data dictates caution and use in [otherwise] refractory patients.



"Well, that was a total waste of time!"

Evolving Viewpoint (2)

- Portenoy (JPSM, 1996):
  - Available data do not support doctrinaire pronouncements about the role of opioid therapy in CNCP.
  - Controlled clinical trials of long-term opioid therapy are needed, but the lack of such trials should not exclude empirical treatment where medical judgment supports it and therapy is monitored and documented.
  - Documentation of pain, side effects, functional status, and drug-related behaviors must be ongoing and explicit.

Volkow, McLellan JAMA 2011

- Opioid analgesics are among the most effective medications (including noncancer pain) but they are also associated with serious and increasing public health problems.
- Increased abuse in part a consequence of more aggressive pain Rx (incl noncancer).
- Better education of physicians, nurses, dentists, and pharmacists is needed to reduce public health risks while improving the quality of care of patients with pain.

CDC Grand Rounds 2012

- 700 MED in 2007 per person (up from 96 in 1997) equates to 5 mg hydrocodone Q4H RTC for 3 weeks for entire US population.
- Persons who abuse opioids have learned to exploit this new practitioner sensitivity to patient pain.
- Among patients prescribed opioids
  - 80% take <100 MED from 1 practitioner ➔ 20% PPK ODs
  - 10% take ≥100 MED from 1 practitioner ➔ 40% "
  - 10% take ≥100 MED from multiple practitioners ➔ 40% " plus divert PPKs to others.
    - Prevention of OD deaths should focus on this last group.

Physicians for Responsible Opioid Prescribing (7/25/12)

- "An increasing body of medical literature suggests that long-term use of opioids may be neither safe nor effective for many patients [with CNCP], especially when prescribed in high doses"
- Petitioned FDA to revise opioid label for CNCP:
  - Drop "moderate" from "moderate-to-severe"
  - Cap daily dose at 100 mg MED
  - Cap duration at 90 days
- Senate Finance Committee (Baucus, Grassley)
- Petition rebuffed by APS, AAPM, PAINS etc

Gertrude Stein (1874-1946)

Everybody gets so much information all day long that they lose their common sense.

FDA Response to PROP (9/10/13)

- "The petition is granted in part and denied in part"
- ER/LA opioids ~ disproportionate safety concerns
  - Use only when alternative treatments inadequate
- All NDAs for ER/LA opioids must include post-marketing studies to assess risks of opioid use
  - misuse, abuse, hyperalgesia, overdose, death
- Assess each patient's risk pre-Rx, monitor all patients for development of these behaviors
- New black box: emphasize risks (incl NOWS)
- Don't base Rx solely on pain intensity

Opioid Guidelines: Shared Elements (CDC 2013)

- P Ex, pain Hx, past medical Hx, family/social Hx
- Urine drug testing, when appropriate
- Consider all treatment options, weighing benefits and risks of opioid therapy, and using opioids when alternative treatments are ineffective
- Start patients on lowest effective dose
- Pain treatment agreements
- Document/ monitor ongoing pain, Rx progress, PDMP
- Use greater vigilance at high doses
- Using safe and effective methods for discontinuing opioids (e.g., tapering, specialist referrals)

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CDC Guideline Process

- Secret panel (initially)
  - No patients/ advocates
- 1 pain specialist
- Distorted evidence review
- Little/ no opportunity to comment upon draft

Evidence Review

- Released 15 March 2016
- Based upon AHRQ 2014
- Unlike earlier reviews, now raised threshold for study inclusion to be > 1 year
- ➔ Zero studies included on efficacy, effectiveness of opioids for CNCP!

Whom to Believe (1)?

- 2009 APS/AAPM Guideline on Opioids for CNCP:
  - OSHU methodologists, GRADE evidence
  - Literature search through November 2007
  - 8,034 abstracts screened
  - 14 systematic reviews and 57 primary studies
- Conclusion: “Clinicians should consider a trial of COT for CNCP when potential benefits are likely to outweigh risks, and there is no alternative therapy that is likely to pose as favorable a balance of benefits to harms.”
- 2010 Cochrane Review: similar conclusion

Whom to Believe (2)?

- 2014 AHRQ Evidence Report (+ 2015 Ann Int Med) on Opioids for CNCP:
  - OSHU methodologists, GRADE evidence
  - Literature search 2008 - October 2013
  - 3793 articles screened, 3161 excluded
  - Of 632 remaining, excluded 595 most often for “inadequate duration” (= ≤ 1 yr)
  - Zero studies remained to address effectiveness !

Whom to Believe (3)?

- "We focused on outcomes reported after at least 1 year of opioid therapy, with the exception of outcomes related to overdose and injuries (fractures, falls, motor vehicle accidents), studies on treatment of acute exacerbations of chronic pain, studies on dose initiation and titration, and studies on discontinuation of opioid therapy, for which we included studies of any duration."
- Conclusion: "No study of opioid therapy versus placebo or no opioid therapy evaluated long-term (>1 year) outcomes related to pain, function, or quality of life."

Evidence Review

- Based upon AHRQ 2014
- Unlike earlier reviews, now raised threshold for study inclusion to be > 1 year
- ➔ Zero studies included on efficacy, effectiveness of opioids for CNCP!

Recommendation #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.

"Any improvement since I brought the balloon?"

Recommendation #2

- Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and 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 provider responsibilities for managing therapy.

Recommendation #4

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

Recommendation #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) per day, and should avoid increasing dosage to ≥90 MME per day or carefully justify a decision to titrate dosage to ≥90 MME per day.

Audience Poll # 4

CDC guideline recommendations adjust dosage thresholds to reflect individual variability to opioid effects based upon:

A. Age

B. Gender

C. Weight (or BMI, BSA)

D. Physical status (frail, organ dysfunction…)

E. None – there are no such adjustments

Individual Responses Vary

- Genetic: preclinical, clinical ➔ PK, PD
- Age, gender, body weight/ BMI
- Physical status (including organ dysfunction)
- Psychosocial (= meaning of the illness and its pain): litigation/ compensation, job/ family satisfaction, spousal solicitousness, premorbid depression, abuse
- Clinician-patient interaction (?enabling, medicalizing a somatoform disorder)

Recommendation #6

- Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids.
- Three days or less will often be sufficient; more than 7 days will rarely be needed.

Recommendation #7

- Clinicians should evaluate benefits and harms with patients within 1–4 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

- 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

- Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or 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

- 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

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

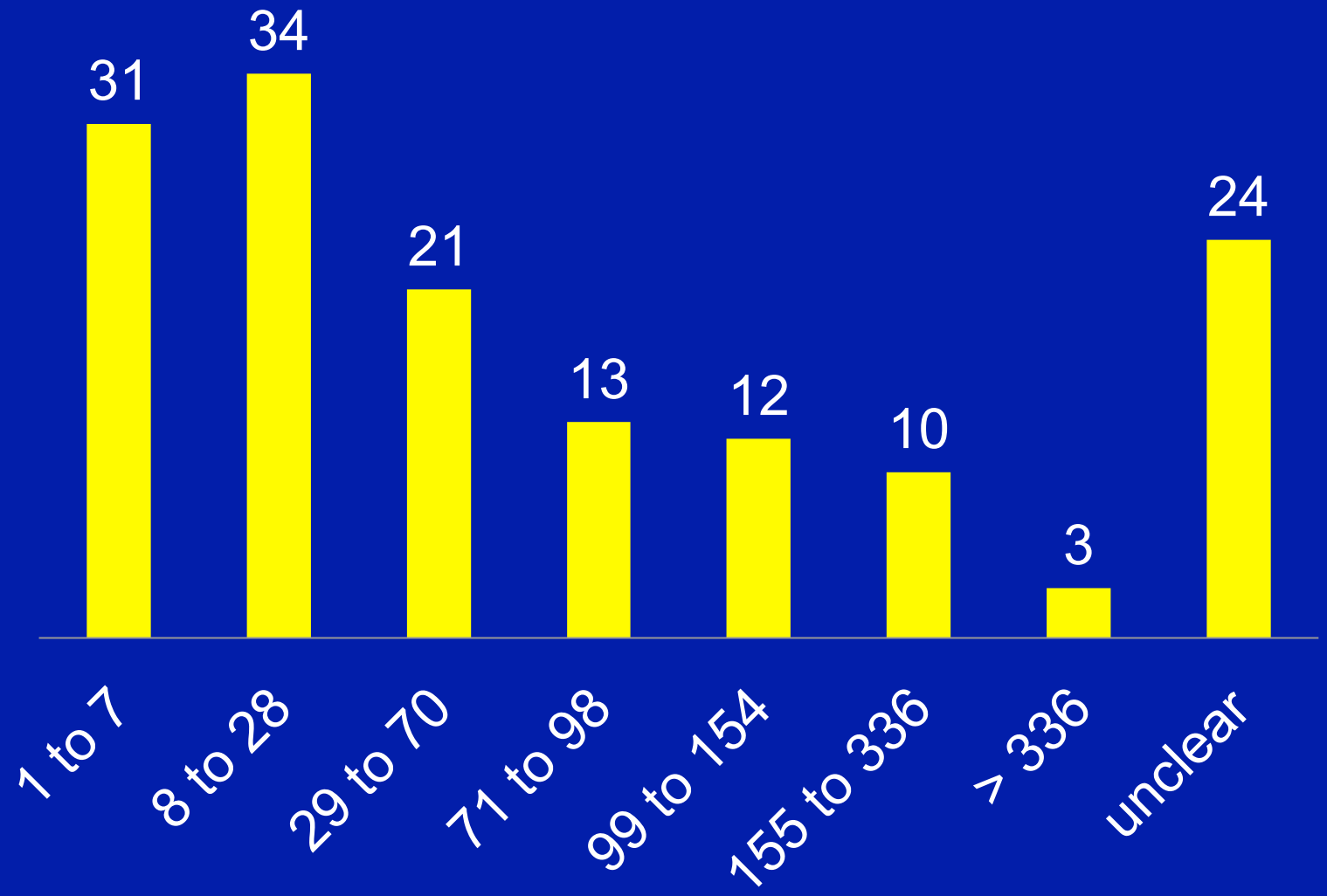
Recommendation #12

- 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.

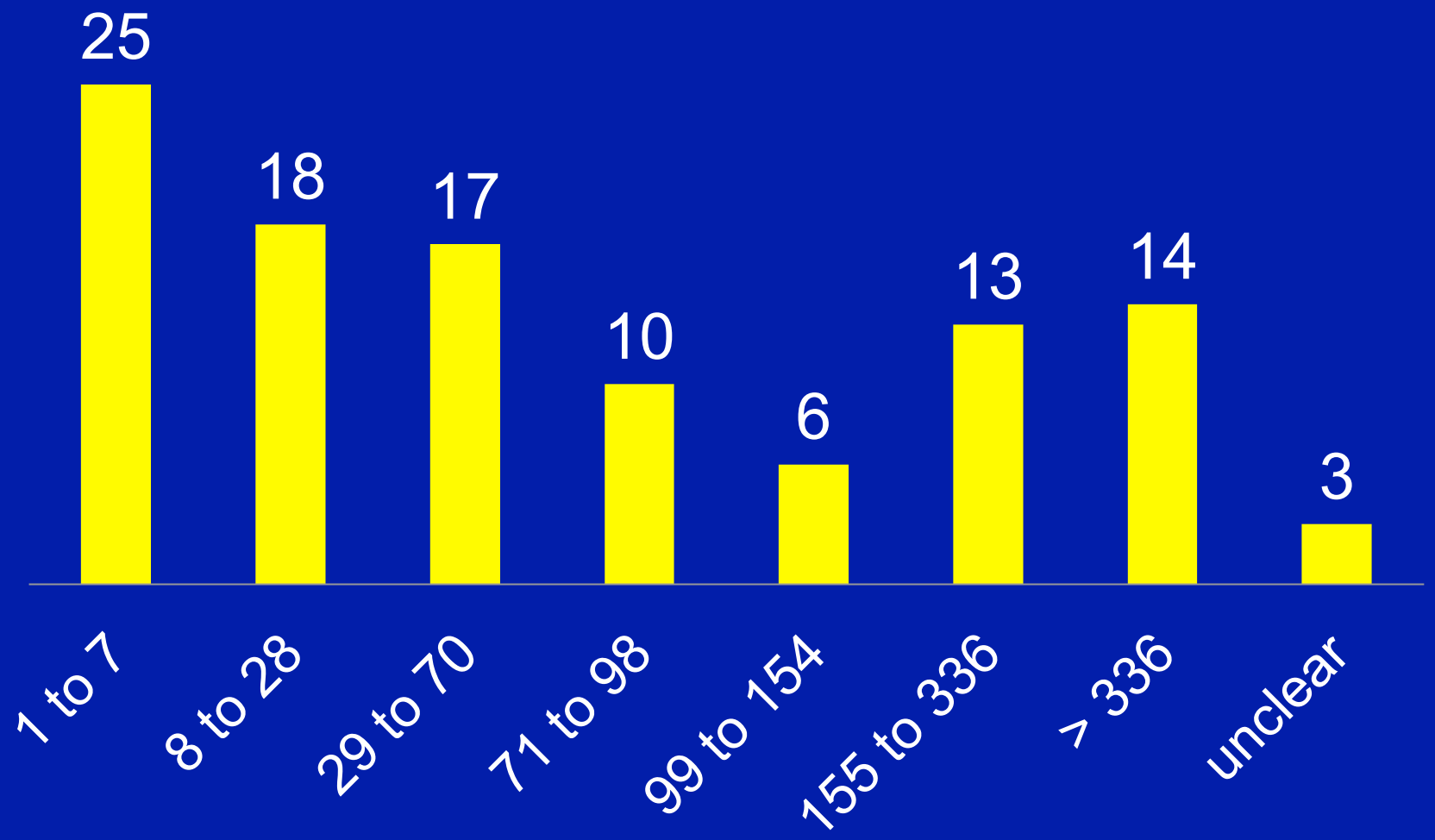
Maimonides (1135-1204)

If anyone declares to you that he has actual proof, from his own experience, of something that he requires for the confirmation of his theory - even though he be considered a man of great authority, truthfulness, earnest words and morality - yet, just because he is anxious for you to believe his theory, you should hesitate.

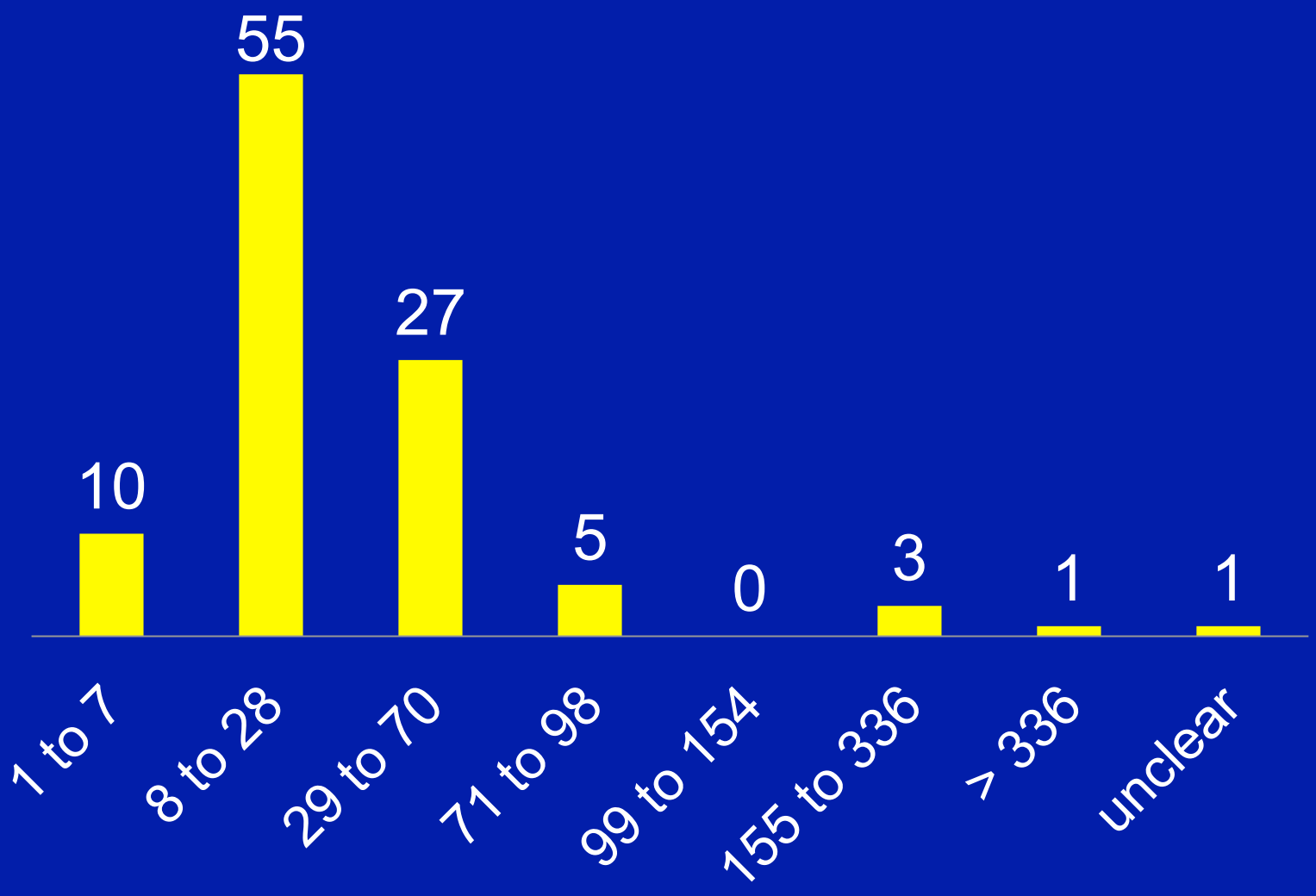
Opioids: AHRQ (2014)



Opioids: Cochrane (2010)



NSAIDs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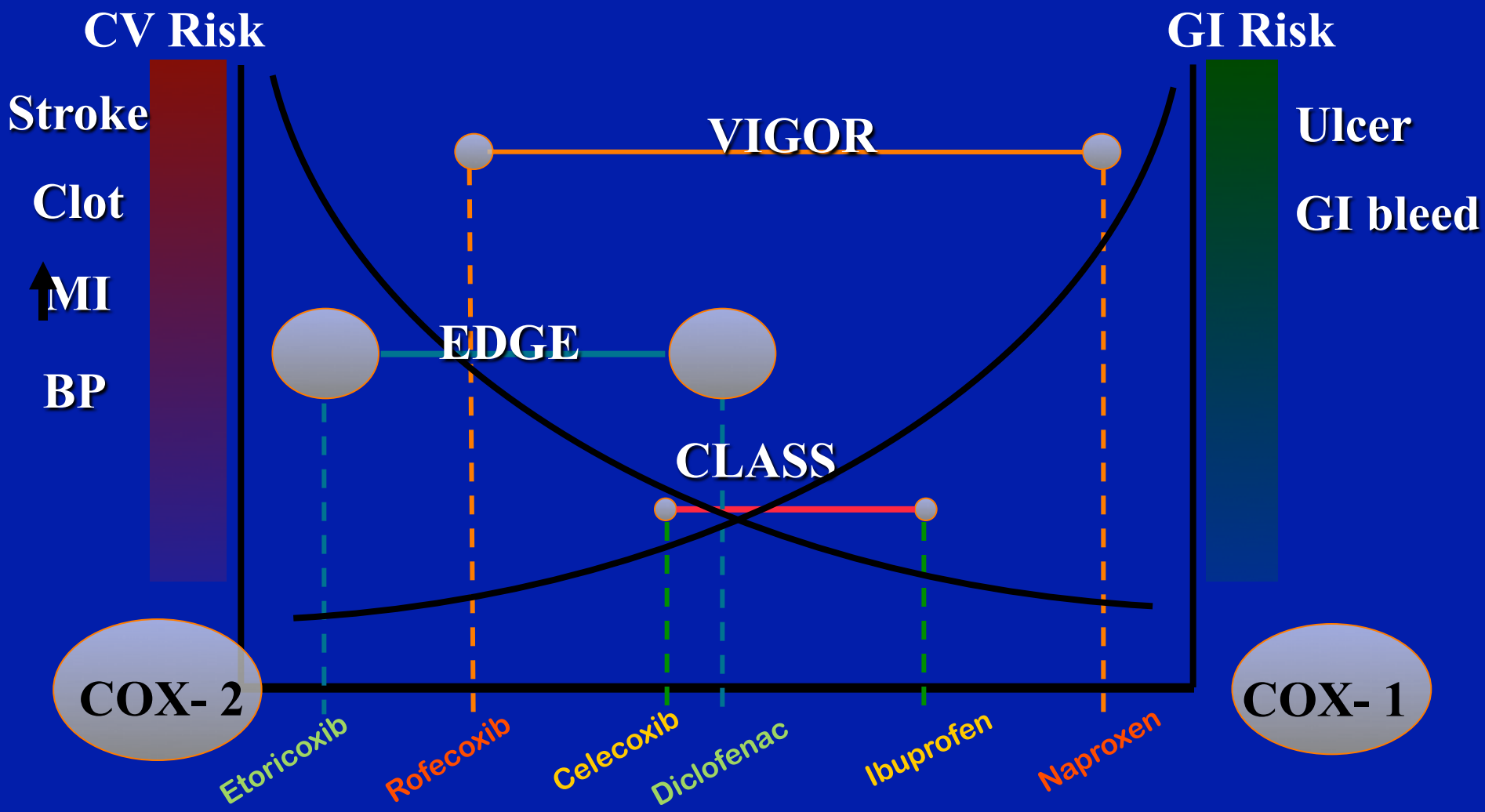
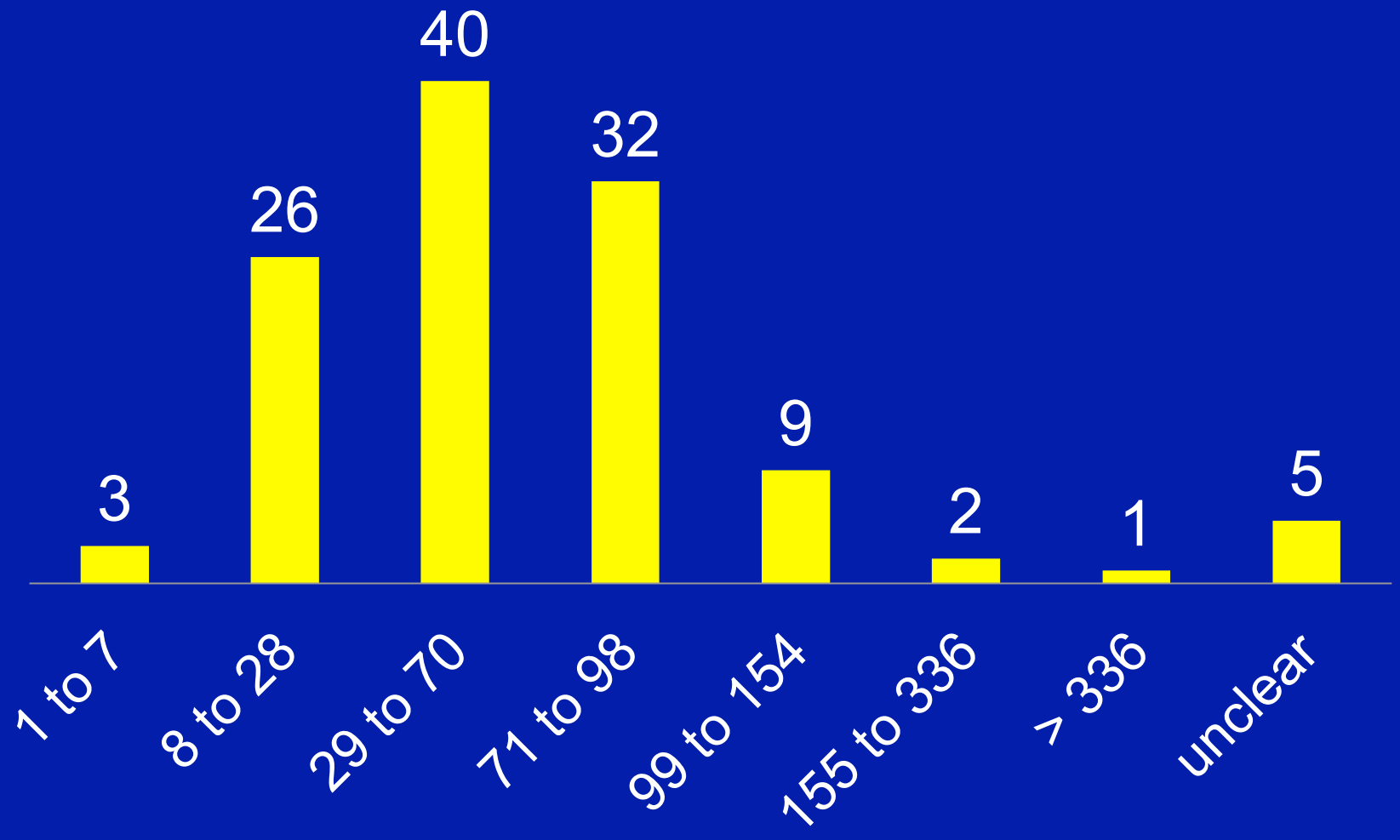
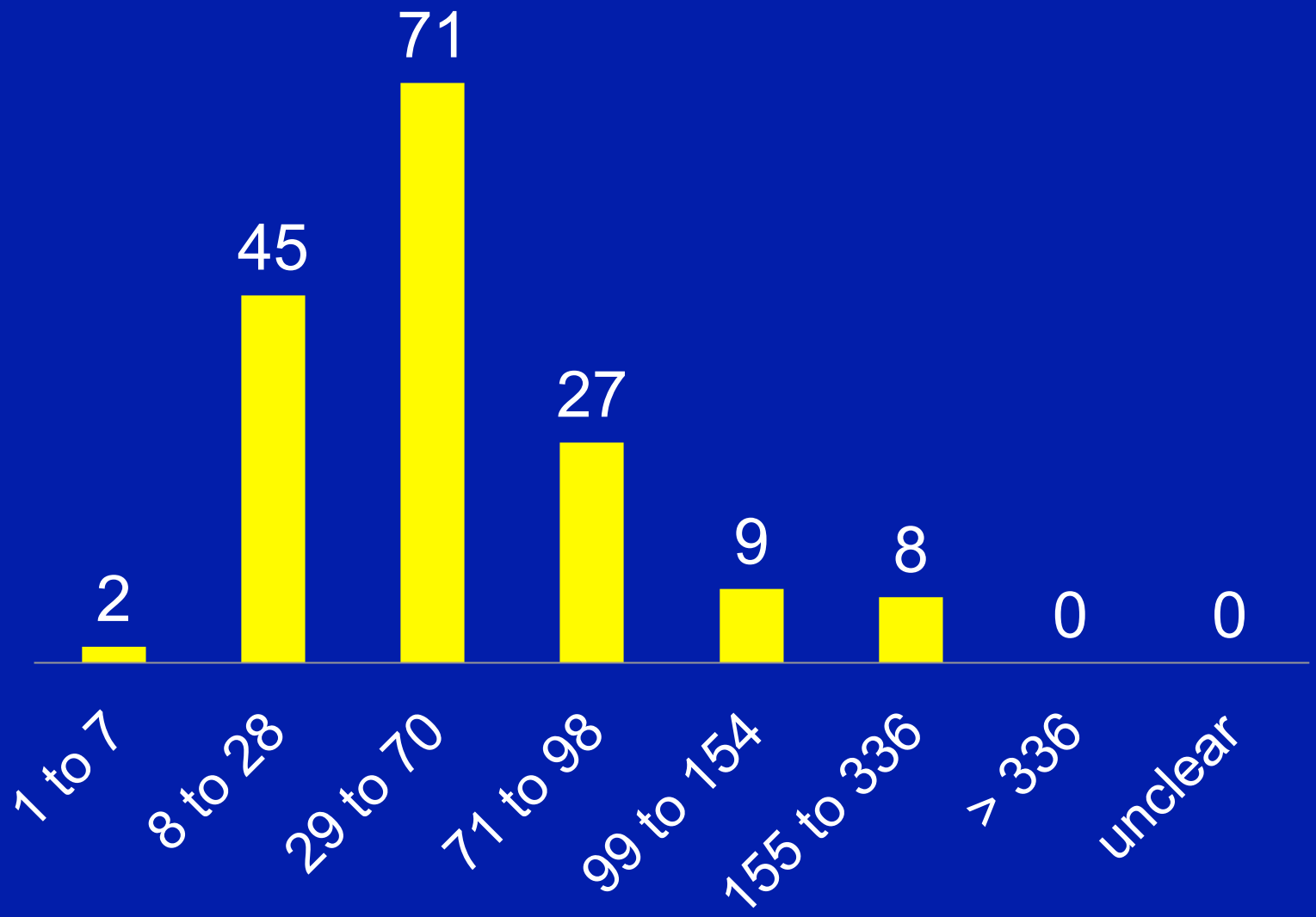
Continuum of Risk: COX-1 vs COX-2



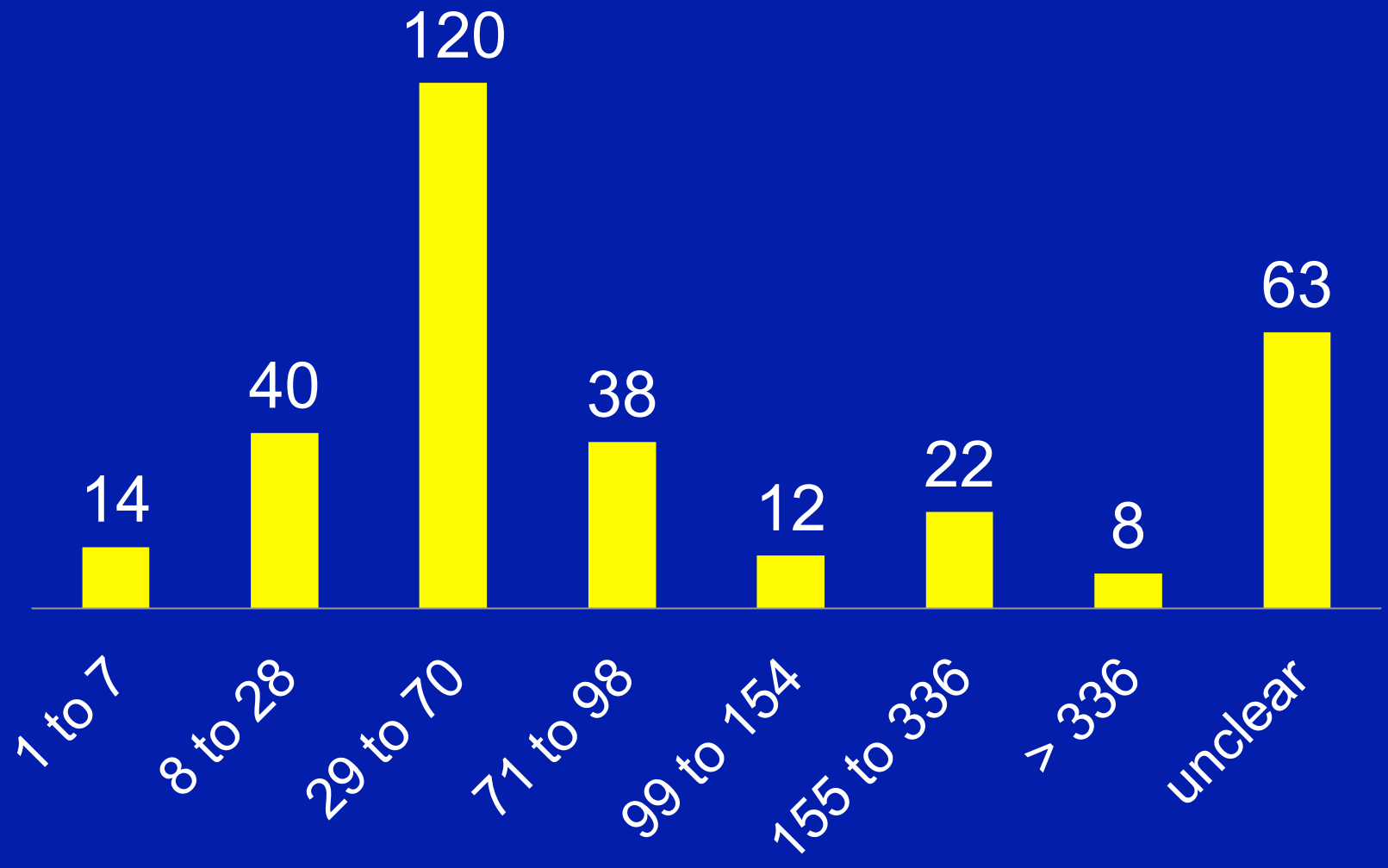
Anticonvulsants



Antidepressants



Behavioral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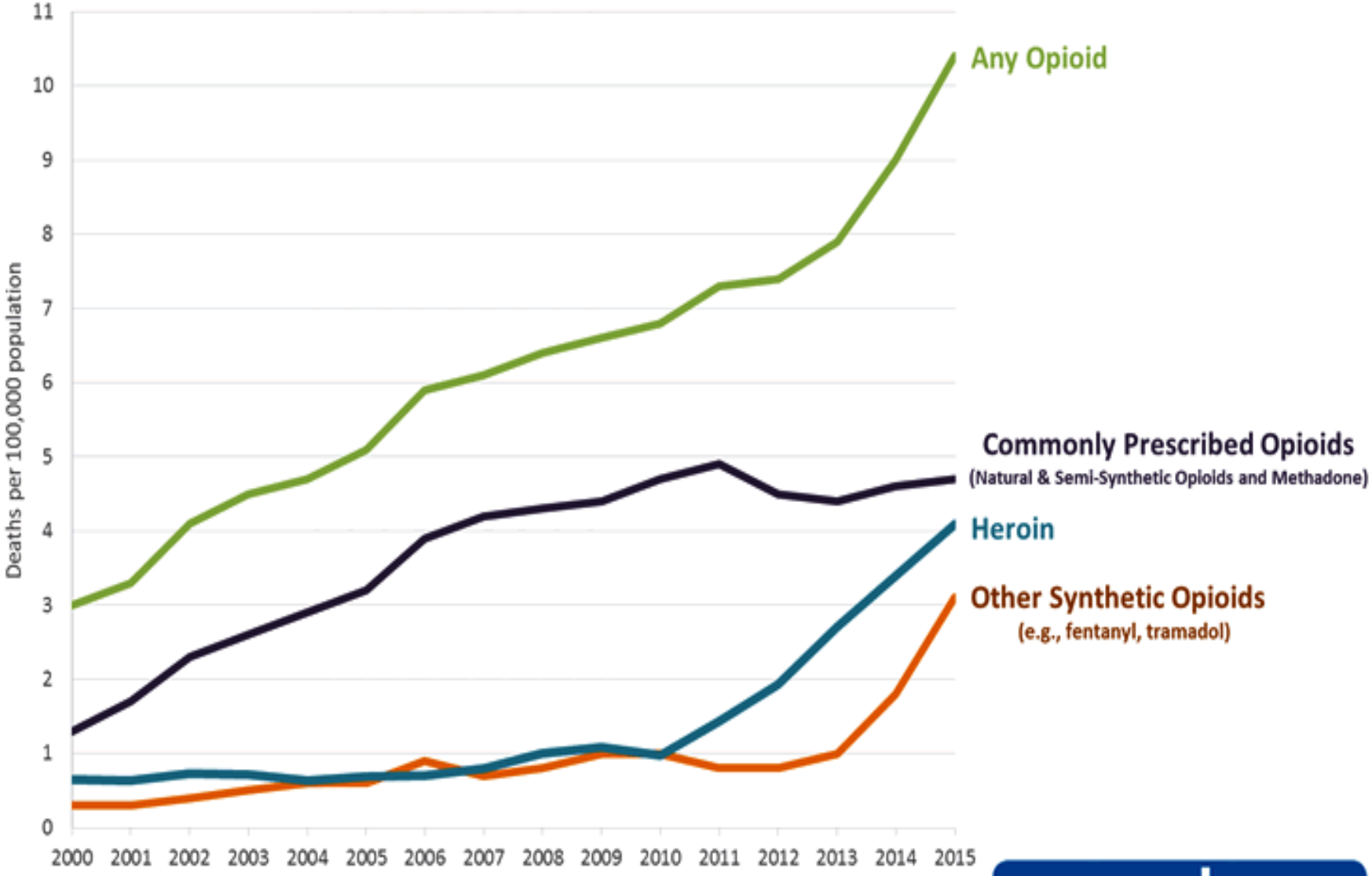
MA Chapt 52 – 2016 (1)

- "An Act Relative to Substance Use Treatment, Education and Prevention" (Effective 3-14-16)
- Highlights (MMS "Physician Fact Sheet")
  - CHECK Mass Prescription Awareness Tool (MassPAT) ***[NOTE: ORANGE = REQ'D BY LAW]***
  - DETERMINE GOALS of using opioid Rx
  - DO a risk assessment
  - PRESCRIBE for 7 day limit (5 days for ED) for initial Rx in adults, all Rx for minors with parental notification. Document exceptions in med record. "Lowest dose for least number of days."

MA Chapt 52 – 2016 (2)

- Highlights (MMS Fact Sheet [continued])
  - EXPLAIN expected benefits, side effects, risks
  - DISCUSS amount prescribed, dosing, option for partial fill or “voluntary non-opiate directive”
  - DOCUMENT goals, exceptions, reasons, patient education and Rx plan in medical record
  - Take special precautions when Rx long-term opioid therapy (see MMS Opioid Rx Guidelines)
  - DOCUMENT Rx agreement if ER/LA opioid or long-term opioid
  - CONSIDER specialist referral, co-Rx naloxone

Overdose Deaths Involving Opioids, United States, 2000-2015



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2016. https://wonder.cdc.gov/.

www.cdc.gov
Your Source for Credible Health Information

Opioid Crisis: Consequences

- Multidimensional response: legislative, regulatory (NASPER), educational, scientific (ADFs)
- Myriad efforts, not all coordinated
  - Not all evidence-based (e.g., dose thresholds, MEDD)
  - Climate of fear for prescribers, NNU for patients
- Rifts between government agencies (FDA, CDC)
- Reduction of opioid availability across the board
- Impetus to reformulate/ develop new drugs
- Increased interest and data to support behavioral & interventional techniques (HF SCS, cold RF…)
- Calls to end pain assessment, delink $ HCAHPS
- Polarized, volatile, ultimately unstable situation