Opioids and Cancer
Use, Misuse, Benefits, and Risks

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Frederick Moeller, MD: research grant, Vivozon; advisory/review panel Astra Zeneca, Boehringer Ingelheim.

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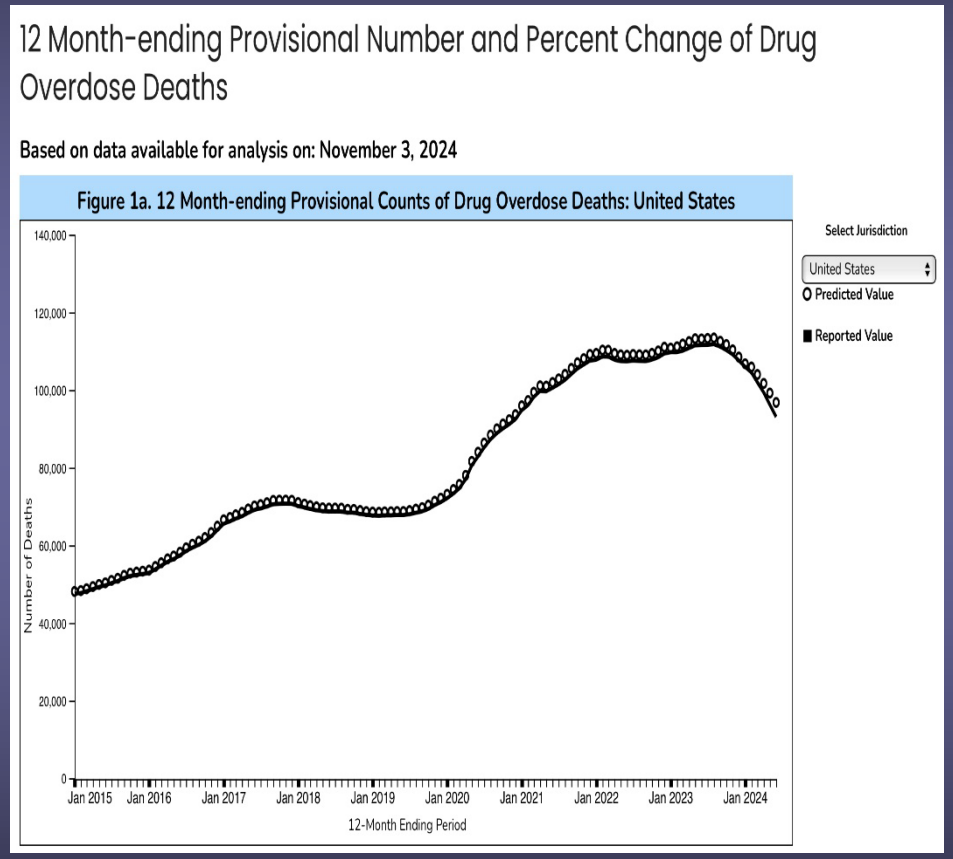
Objectives

- Describe the drug overdose epidemic in the US and Virginia and how prescription opioids played a part in this epidemic
- Discuss the CDC guidelines for use of opioids in the treatment of pain and how those guidelines may or may not be relevant for cancer pain

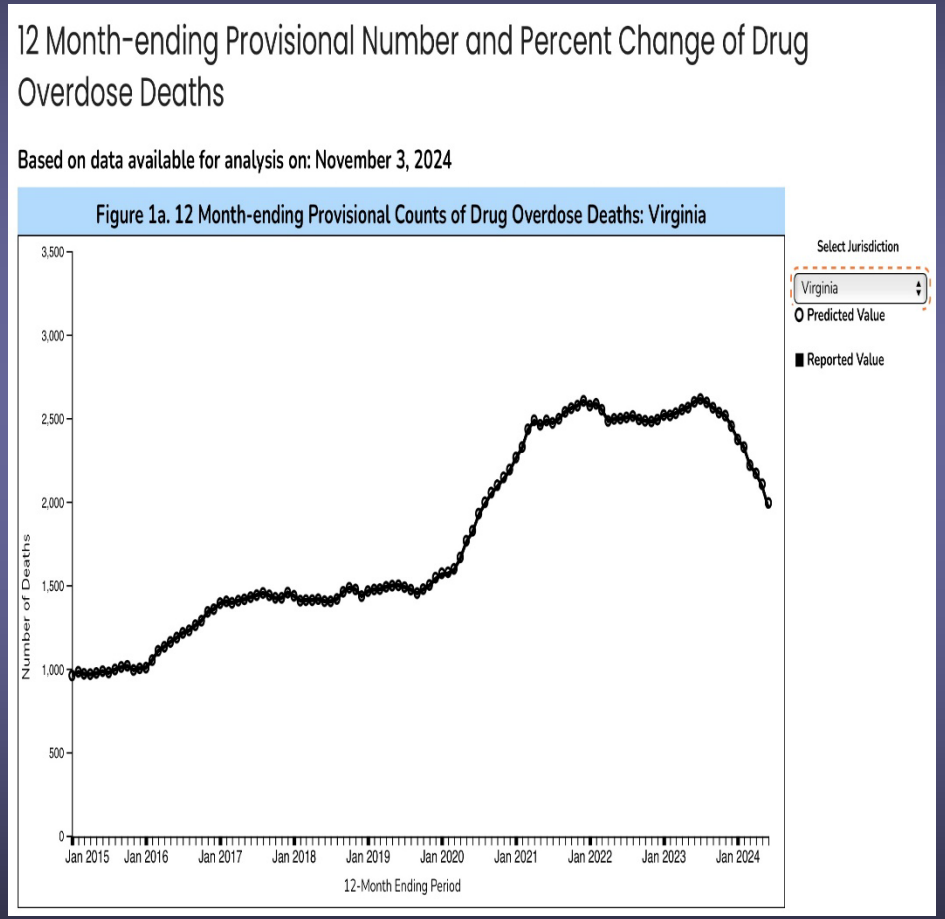
Why are We Concerned About Opioids?

- The US drug overdose death epidemic led to an estimated 93,000 overdose deaths in the 12-month period ending in June 2024 (CDC).
- There was an encouraging decline in overdose deaths in the first half of 2024

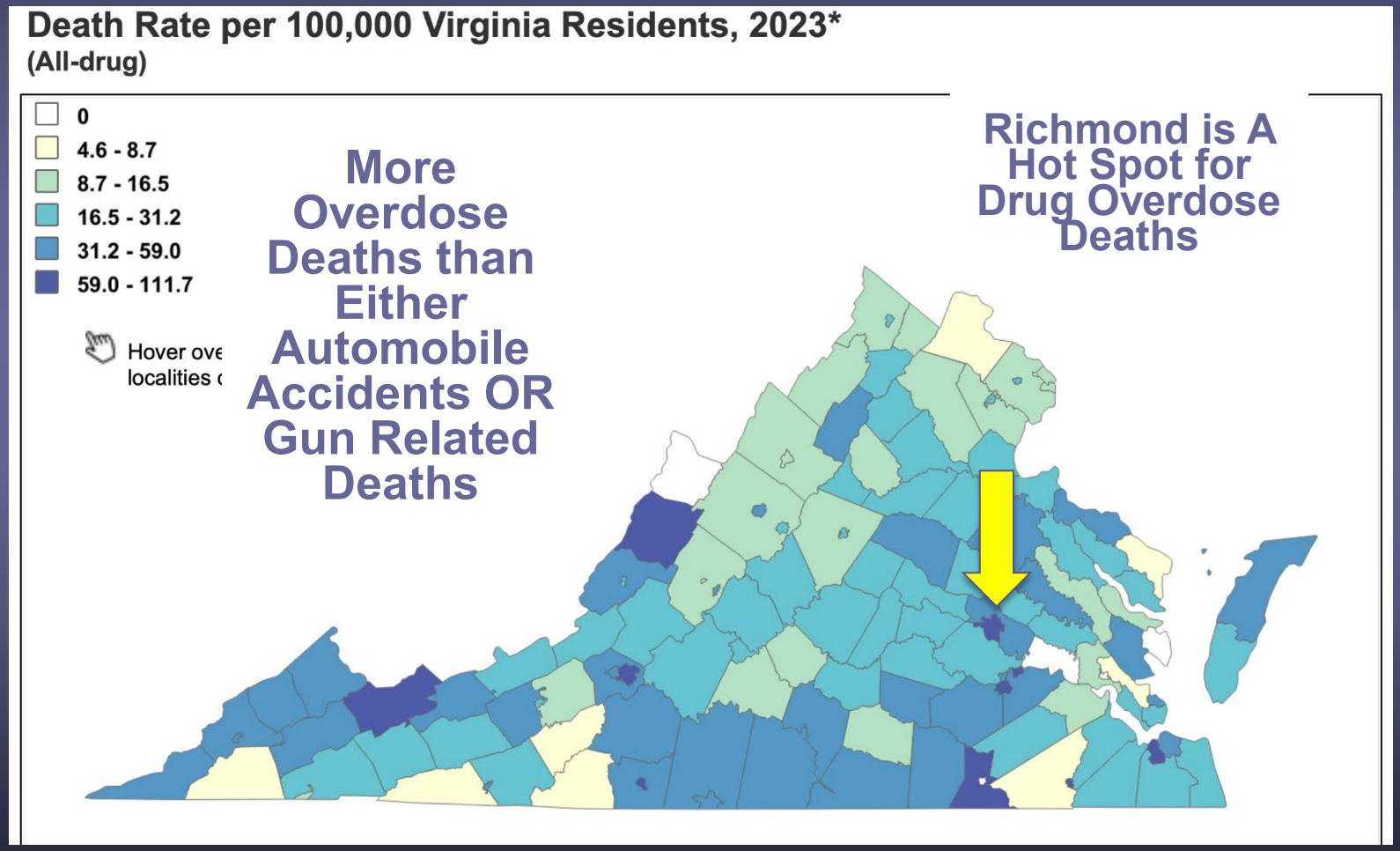


Where We Are in Virginia

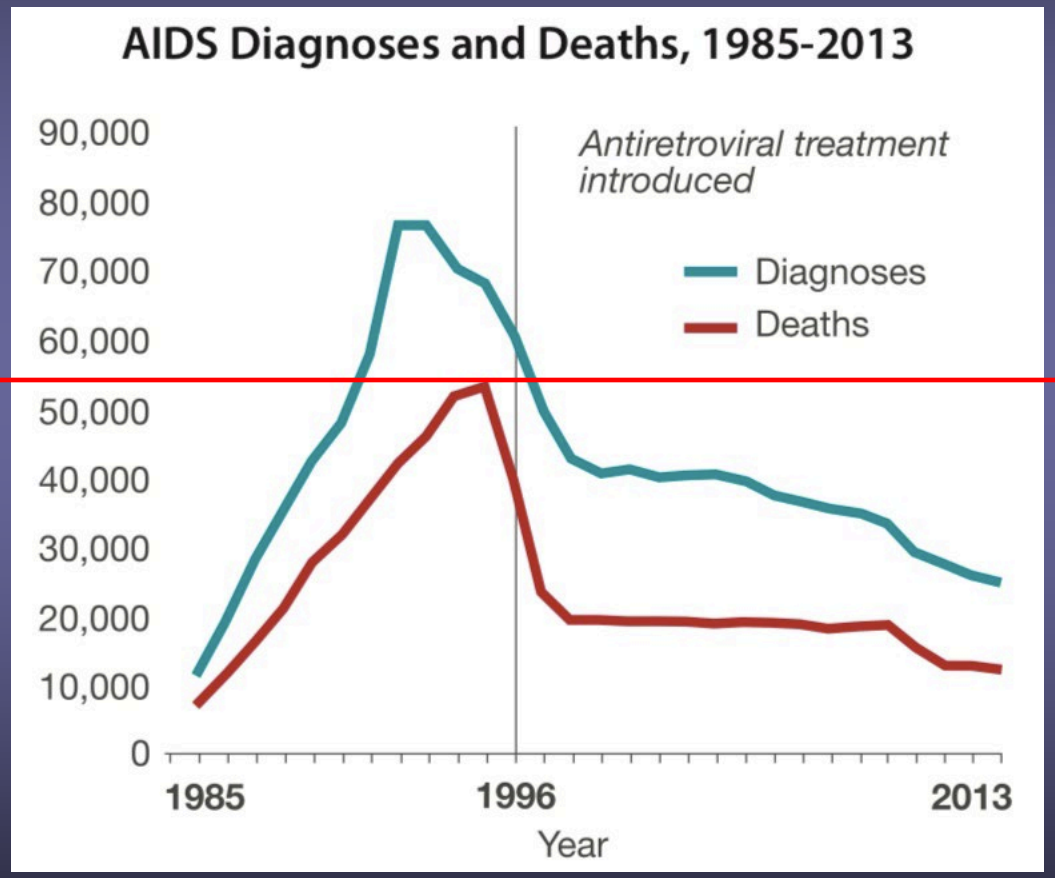
- Virginia saw an estimated 1,962 overdose deaths in the 12-month period ending in June 2024 (CDC).
- The encouraging decline nationally also took place in Virginia



Overdose Death Rates Are Not Equal Across Regions and Patient Demographics

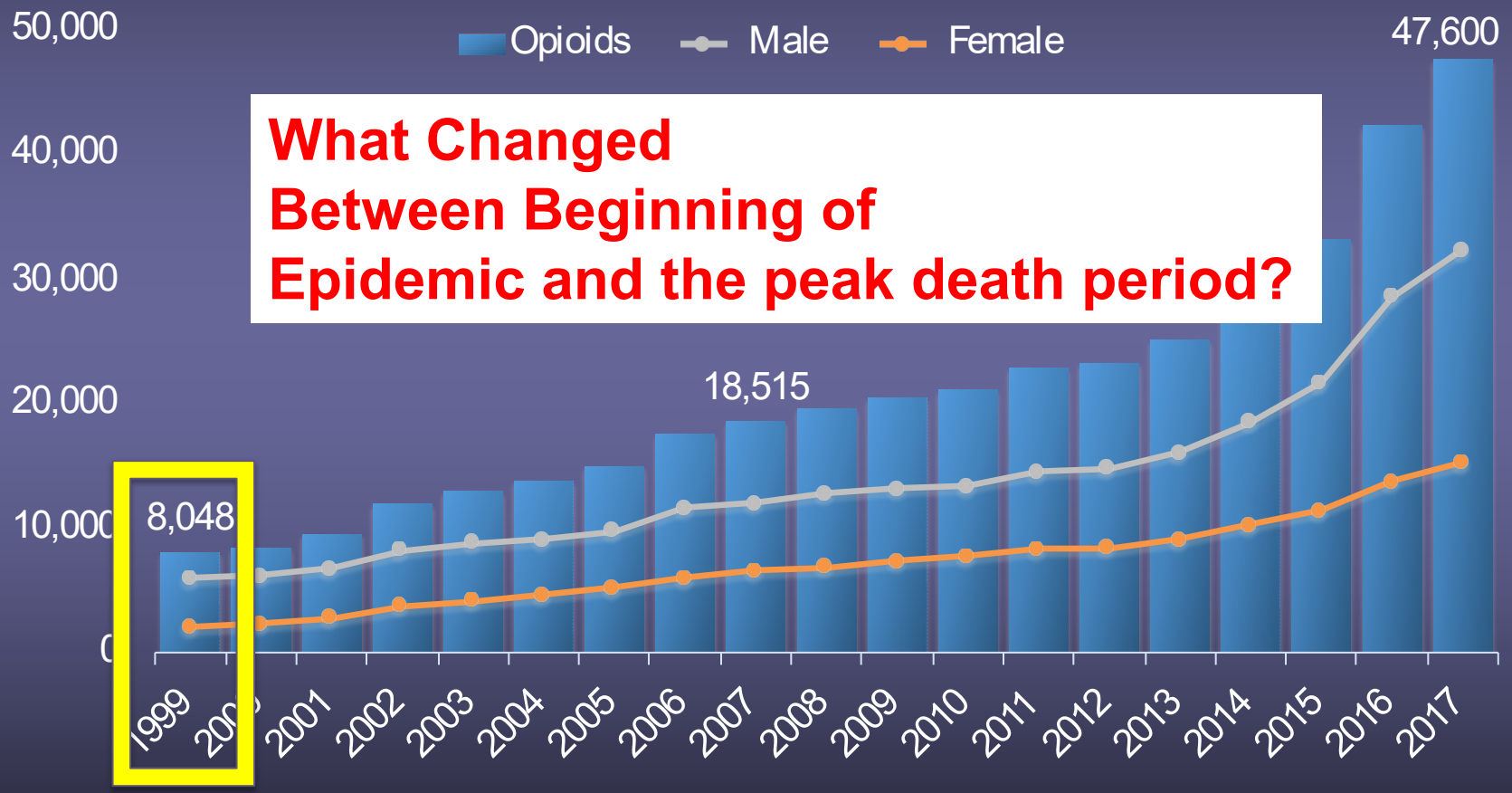


Putting the Overdose Death Rates in Perspective



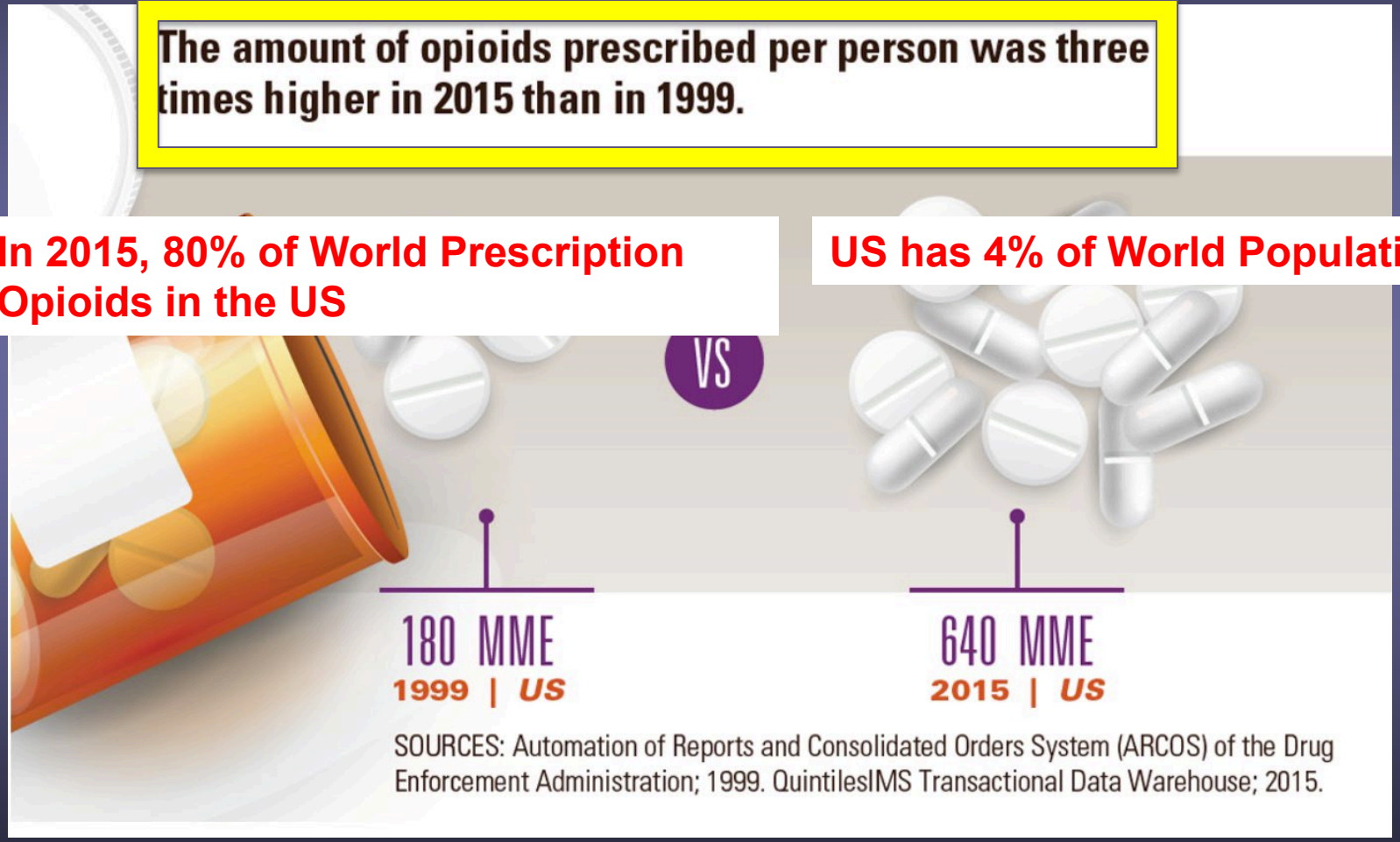
- More People in US are dying from Drug Overdose than Died of AIDS at the Peak of the HIV Epidemic

What is the Role of Prescription Opioids in the Overdose Epidemic?



Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released

How did We Get Here?



What is the reason for the widespread prescription of opioids by US physicians leading to the epidemic?

FOCUS ON PAIN

Hospitals, Pharma, Doctors

Track Performance
Improving Pain Management for Hospitalized Patients

Choose Metrics and Develop a Data Collection Plan

Metrics for a pain management quality improvement project are based on the project's scope and aims. Although interest is high on outcomes, a tunnel-vision approach that focuses only on the end result will miss what can happen in the intermediary steps if the end outcomes are not achieved. Thus, metrics should include structure, process and outcomes related to the specific aims of quality improvement goals. Data collection should include at least three key steps in the process-improvement measurement including 1) identifying problems or opportunities for improvement, 2) obtaining baseline measurements, and 3) results after the new improved process has been implemented. Measurements should also be repeated periodically to monitor the new process. Measures should be few, easy to collect and cover short periods to be most useful.

Evidence-based quality measures can be devised to suit the aims of specific projects. Example indicators include:

- Pain is treated with regularly administered analgesics
- A multimodal approach is used
- Pain is prevented and controlled to a degree that facilitates function and quality of life
- Patients are adequately informed and knowledgeable about pain management.[29]

Society of Hospital Medicine

New England Journal of Medicine January 10th, 1980

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

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1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

Citations of 1980 letter

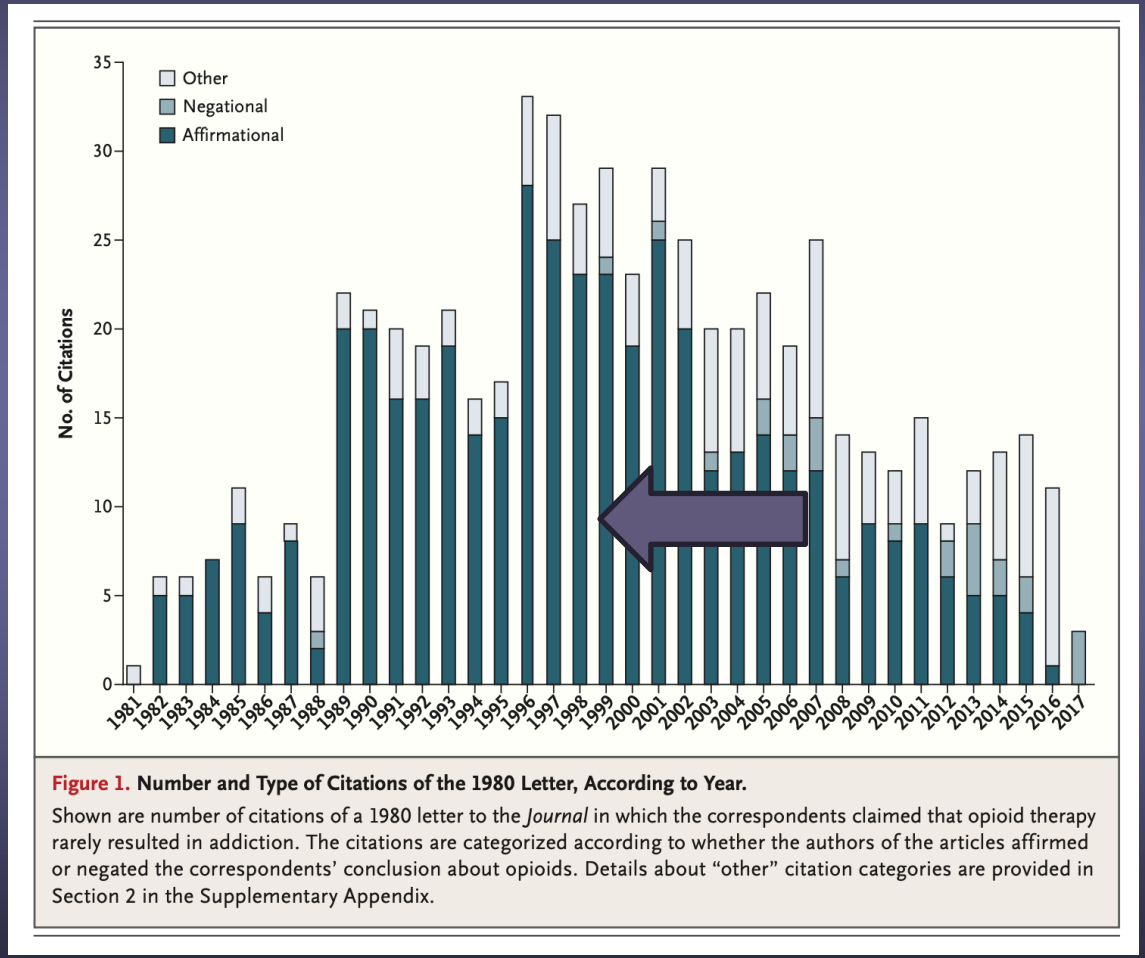

Figure 1. Number and Type of Citations of the 1980 Letter, According to Year.

Shown are number of citations of a 1980 letter to the *Journal* in which the correspondents claimed that opioid therapy rarely resulted in addiction. The citations are categorized according to whether the authors of the articles affirmed or negated the correspondents' conclusion about opioids. Details about "other" citation categories are provided in Section 2 in the Supplementary Appendix.

- Leung et al., reviewed citations of the 1980 letter showing multiple citations affirming that ***opioid use for "real" pain is at low risk of addiction***

Response to Increased Opioid Prescribing

CDC Clinical Practice Guideline for Prescribing Opioids for Pain – United States, 2022

Recommendations and Reports / November 4, 2022 / 71(3);1–95

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View suggested citation

Summary

This guideline provides recommendations for clinicians providing pain care, including those prescribing opioids, for outpatients aged ≥18 years. It updates the CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016 (MMWR Recomm Rep 2016;65[No. RR-1]:1–49) *and includes recommendations for managing acute (duration of <1 month), subacute (duration of 1–3 months), and chronic (duration of >3 months) pain. The recommendations do not apply to pain related to sickle cell disease or cancer or to patients receiving palliative or end-of-life care. The guideline addresses the following four areas: 1) determining whether or not to initiate opioids for pain, 2) selecting opioids and determining opioid dosages, 3) deciding duration of initial opioid prescription and conducting follow-up,*

Article Metrics

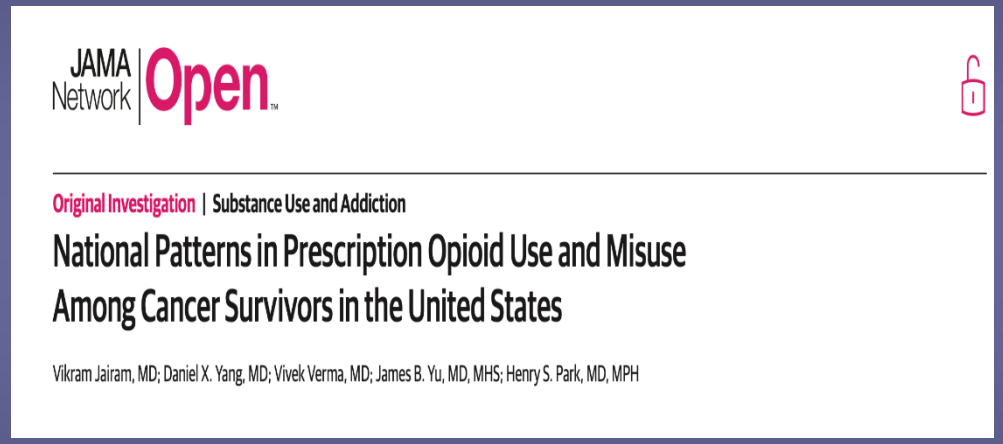
Altmetric:

2827

News (325)
Blogs (16)
Policy documents (9)
X (334)
Facebook (9)
Wikipedia (8)
Reddit (2)
Video (2)
Clinical guidelines (3)
Bluesky (2)

- CDC guidelines for Prescribing Opioids Developed in Response to Epidemic
- Explicitly exclude cancer pain or palliative or end-of-life care
- Is there a risk in the cancer patient population?

Are Cancer Patients at Risk of Opioid Use?



- Retrospective data from 169,162 respondents
- 5139 (5.2%) were cancer survivors
- Cancer survivors divided into more recent (< 12 months 1,243) vs less recent (>12 months 3896)

Opioid Use and Misuse by Group

Table 1. Unadjusted and Adjusted Analysis of Prescription Opioid Use or Misuse by Reported Cancer History

	Prescription opioid use				Prescription opioid misuse			
Cancer history	Weighted % (95% CI)	*P* value[a]	OR (95% CI)	*P* value[b]	Weighted % (95% CI)	*P* value[a]	OR (95% CI)	*P* value[b]
No cancer history	30.5 (30.2-30.9)	NA	1 [Reference]	NA	4.3 (4.2-4.4)	NA	1 [Reference]	NA
More recent cancer history	54.3 (50.2-58.4)	<.001	1.86 (1.57-2.20)	<.001	3.5 (2.4-5.2)	.339	1.27 (0.82-1.96)	.36
Less recent cancer history	39.2 (37.3-41.2)	<.001	1.18 (1.08-1.28)	<.001	3.0 (2.4-3.6)	<.001	1.03 (0.83-1.28)	.76

Abbreviation: NA, not applicable; OR, odds ratio.

[a] *P* values calculated from χ^2 comparisons of rates of prescription opioid use and misuse by reported cancer history.

[b] Multivariable models adjusted for age, sex, race, survey year, education level, insurance status, income, urban/rural status, employment status, marital status, self-reported health status, depression history, alcohol use disorder, and nonopioid drug use disorder.

- Cancer survivors more likely to be prescribed opioids
- Cancer survivors ***no less likely to misuse opioids***
- *Factors associated with prescription opioid misuse included younger age, alcohol use disorder, and non-opioid drug use disorder*

Can CDC Guidelines be Helpful in Cancer Patients?

CDC Guidelines for Use of Opioids for Pain

Recommendation 1 Acute Pain

- ***Nonopioid therapies are at least as effective as opioids for many common types of acute pain.***
- Clinicians should *maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider opioid therapy for acute pain if benefits are anticipated to outweigh risks to the patient*.
- Before prescribing opioid therapy for acute pain, *clinicians should discuss with patients the realistic benefits and known risks of opioid therapy.*

https://www.cdc.gov/mmwr/volumes/71/rr/rr7103a1.htm

CDC Guidelines for Use of Opioids for Pain

Recommendation 2 Subacute (1-3 months) and Chronic (> 3 months) Pain

- ***Nonopioid therapies are preferred for subacute and chronic pain***.
- Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider initiating opioid therapy if expected benefits for pain and function are anticipated to outweigh risks to the patient.
- Before starting opioid therapy for subacute or chronic pain, clinicians should discuss with patients the realistic benefits and known risks of opioid therapy, should work with patients to establish treatment goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks

CDC Guidelines for Use of Opioids for Pain

Recommendation 3

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

Recommendation 4

- When opioids are initiated for opioid-naïve patients with acute, subacute, or chronic pain, clinicians should prescribe the **lowest effective dosage**.

Recommendation 5

- For patients already receiving opioid therapy, clinicians should carefully weigh benefits and risks and **exercise care when changing opioid dosage.**

CDC Guidelines for Use of Opioids for Pain

Recommendation 6

- When opioids are needed for acute pain, clinicians should prescribe **no greater quantity than needed for the expected duration of pain severe enough to require opioids**

Recommendation 7

- Clinicians should **evaluate benefits and risks with patients** within 1–4 weeks for subacute or chronic pain or of dosage escalation. Clinicians should regularly reevaluate benefits and risks of continued opioid therapy with patients

Recommendation 8

- Before starting and periodically during continuation of opioid therapy, clinicians should **evaluate risk for opioid-related harms and discuss risk with patients. Offering naloxone**

CDC Guidelines for Use of Opioids for Pain

Recommendation 9

- When prescribing initial opioid therapy for acute, subacute, or chronic pain, and periodically during opioid therapy for chronic pain, **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 combinations that put the patient at high risk for overdose**

Recommendation 10

- When prescribing opioids for subacute or chronic pain, clinicians should consider the **benefits and risks of toxicology testing** to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances

CDC Guidelines for Use of Opioids for Pain

Recommendation 11

- Clinicians should use **particular caution when prescribing opioid pain medication and benzodiazepines** concurrently and consider whether benefits outweigh risks of concurrent prescribing of opioids **and other central nervous system depressants**

Recommendation 12

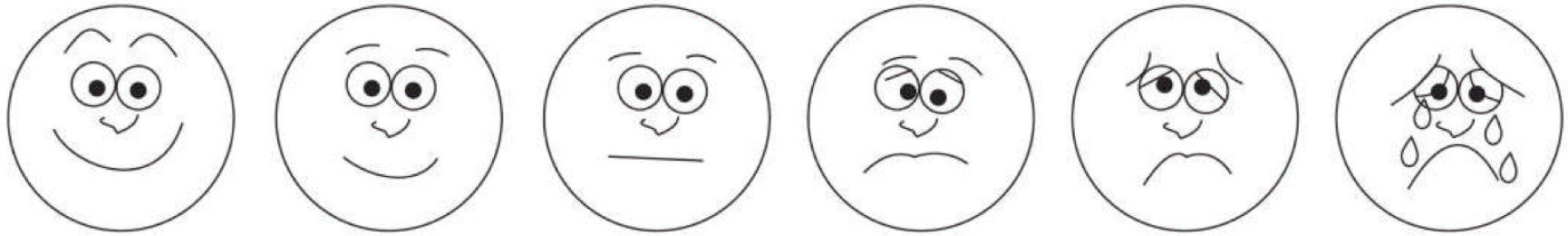
- Clinicians should **offer or arrange treatment with evidence-based medications to treat patients with opioid use disorder**. Detoxification on its own, without medications for opioid use disorder, is not recommended for opioid use disorder because of increased risks for resuming drug use, overdose, and overdose death

Pain (Cancer related or not)

- Subjective phenomenon
- No “absolute” amount of pain based on type of injury or disorder
- Although pain is subjective doesn’t make it “fake”
- Pain is associated with significant morbidity and mortality (suicide, overdose)
- *Function is a better measure of severity*, especially for patients with substance use

Previous Way of Measuring Pain

Faces Pain Scale



0	2	4	6	8	10
Very happy, no hurt	Hurts just a little bit	Hurts a little more	Hurts even more	Hurts a whole lot	Hurts as much as you can imagine (don't have to be crying to feel this much pain)

Sub-optimal as Goal is "no hurt" which is purely subjective

Functional Pain Measure

Functional Pain Scale

Optimal as Goal is Objective Measure of Function

Instructions:

Ask the patient if pain is present. If the patient has pain, ask him or her to rate the pain subjectively as either "tolerable" or "intolerable." Finally, find out if the pain interferes with function. If the patient rates the pain as "tolerable," establish whether the pain interferes with any activity. If the pain is "intolerable," determine whether the pain is so intense as to prevent passive activities. See the chart below for guidelines.

Rating	Description
0	No pain
1	Tolerable (and does not prevent any activities)
2	Tolerable (but does prevent some activities)
3	Intolerable (but can use telephone, watch TV, or read)
4	Intolerable (but cannot use telephone, watch TV, or read)
5	Intolerable (and unable to verbally communicate because of pain)

Scoring:

The patient's subjective rating of pain and the objective determination of the pain's interference with activities will produce a corresponding score on a scale of 0-5. A lower score equates to less severe pain and less interference with functional abilities, if any. Ideally, all patients should reach a 0 to 2 level, preferably 0 to 1. It should be made clear to the respondent that limitations in function only apply if limitations are due to the pain being evaluated.

Factors For Discussion

- Palliative, end of life care (what parameters are being used for this?
- Pain vs. Function (elimination of pain vs elimination of cognitive function)?
- Assessment and discussion with patients and family (who is more at risk, what does the family/patient want)?
- What constitutes opioid use disorder in the context of being prescribed opioids for cancer pain?

Cases on the Ends of the Spectrum

- 70-year-old female with metastatic melanoma, no history of substance misuse
- Several rounds of cancer treatment, most recent round led to significant side effects and treatment terminated
- Patient with severe pain, unable to sleep, not able to interact with family because of pain
- Not taking pain medication
- Contacted addiction medicine provider because worried that she might become addicted to tramadol

Cases on the Ends of the Spectrum

- 35-year-old male with metastatic melanoma. Pre-cancer history of opioid and alcohol use disorder.
- Responded well to cancer treatment, now in remission.
- Pain started during treatment, continues to be a problem after 6 months.
- Prescribed opioids, with escalating dose, now >100 MME.
- Urine drug screens show illicit opioids as well as prescribed opioids.
- When confronted says “you started me on these meds”

Case: Taper in Progress

- 60-year-old female with history of breast cancer; now no evidence of disease
- Seen in supportive care clinic for approx. 6-7 years
- Initially reported 10/10 pain and other symptoms on ESAS
- Abnormal UDS late last year (negative for fentanyl, positive for cocaine and buprenorphine); appropriate UDS earlier this year
- Following with physical therapy, psychiatry (prescribed clonazepam for anxiety)
- Nicotine patch for smoking cessation
- Amenable to tapering: reduce oxycodone, increase buprenorphine-naloxone
  - Discussed risks of combining benzodiazepines & opioids
  - Plan to taper opioids quickly to ensure safety, has medication to manage withdrawal symptoms as needed

Summary

- Use of opioids for pain has benefits and risks ***regardless of cancer diagnosis***
- Factors that make individuals more likely to develop an opioid use disorder upon exposure to opioids are also a risk for cancer patients
- ***Communication with patients and family*** about risks and benefits on the front end can mitigate problems on the back end