Opioid Conversion in Older Adults with Pain

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1

Introduction

- **Pain prevalence with older adults**
- **Opioid use with older adults**
- **Opioid conversions**
- **Opioid history**
- **Opioid pharmacokinetics**
- **Opioid allergies**
- **Reviewing the literature**

2

Pain prevalence among older adults

- Pain prevalence among older adults estimates are 25% to 50% of community-dwelling elderly experience chronic pain.
- In long-term care settings, up to 85% of residents may have at least one pain-associated problem.
- Pain affects approximately 100 million American adults each year, resulting in a national cost of $635 billion annually.
- There is broad recognition that painful conditions warrant treatment, yet specific treatment protocols remain inconsistent across the medical community

3

Opioid use among older adults with chronic pain

- Management of chronic pain first with nonpharmacologic therapy and nonopioid pharmacologic therapy before initiating opioids.
- Nonopioid pharmacologic therapy may include antidepressants, antiarrhythmics, anticonvulsants, tranquilizers, and regional anesthesia.
- It is recommended that opioids be prescribed at the lowest effective dose, which is approximately **25% to 50%** of the adult recommended starting dose, and then slowly titrated to minimize adverse effects for patients **older than age 70 years.**
- The dosage should be reassessed 1 to 4 weeks after initiation or dose escalation. Immediate-release formulations of opioids should be initiated before extended-release or long-acting opioids are attempted.

4

Start low, Go Slow

- Lower doses (25%-50% of typical doses for younger adults) and gradually titrating based on efficacy and tolerability since older adults experience altered pharmacokinetics.
- The **American College of Surgeons Best Practices Guidelines for Acute Pain Management in Trauma Patients (2020)** recommends a decrease in the initial dose of an opioid **by 25% in 60-year-old** patients, and by **50% for 80-year-old** patients.

TABLE 1. Recommended Equivalent Starting Doses of Opioids for Elderly Patients

Opioid	Dose (mg)	Frequency
Tramadol	50	Every 4-6 h
Morphine	7.5	Every 4-6 h
Codeine	50	Every 4-6 h
Hydrocodone	5	Every 4-6 h
Hydromorphone	1-2	Every 4-6 h
Oxycodone	5	Every 4-6 h
Fentanyl transdermal	Not recommended for opioid-naive patients	
Methadone	Not recommended for opioid-naive patients	
Buprenorphine	5-μg/h patch changed every 7 d	
• Long-acting opioid formulations should be avoided in opioid-naive patients		
• Codeine is not recommended due to poor metabolism to morphine in a high percentage of the population		

5

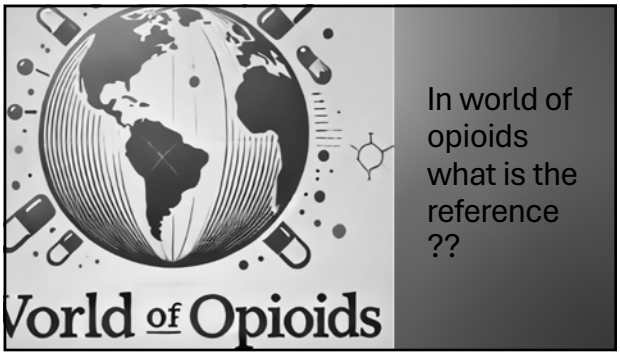
Co-prescribing of opioids with CNS-active medications

- Co-prescribing of opioids with CNS-active medications is increasing among older adults in the US. Co- prescribing of opioids and opioid potentiators, such as benzodiazepines, Z-drugs and gabapentinoids, among US adults ≥65 years increased from 29.6 per 1,000 people in 2007-2008 to 35.8 per 1,000 people in 2017-2018.
- Veterans Health Administration population found that 77% of veterans who received chronic opioid therapy also received psychotropics.
- Concurrent use with **≥2 CNS-active medications** increased the likelihood of **falls/fractures by 18% and ER visits by 21%**

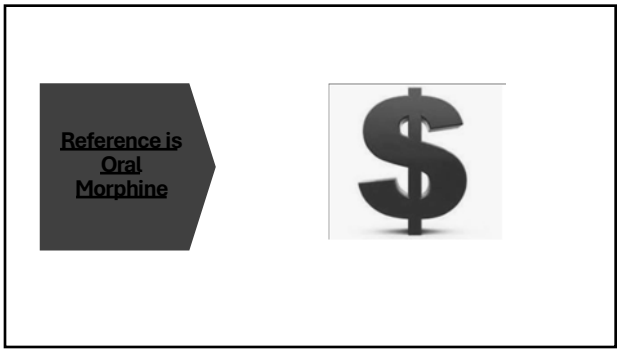
6


Any one Travel abroad ?
What's your currency reference to assess how expensive cheap or affordable anything is ?

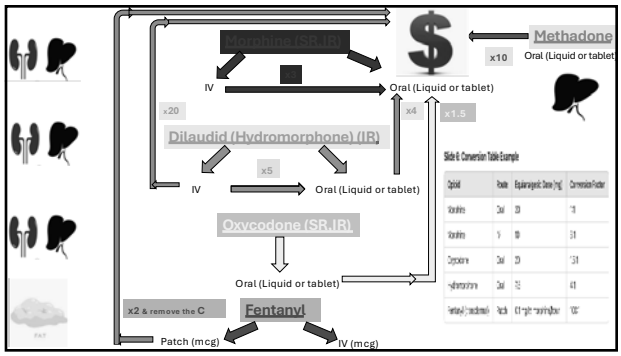
7


In world of opioids what is the reference ??
Vorld of Opioids

8


Reference is Oral Morphine

9



10

Slide 6: Conversion Table Example

Opioid	Route	Equianalgesic Dose (mg)	Conversion Factor
Morphine	Oral	30	1:1
Morphine	IV	10	3:1
Oxycodone	Oral	20	1.5:1
Hydromorphone	Oral	7.5	4:1
Fentanyl (transdermal)	Patch	0.1 mg IV morphine/hour	100:1

11

Morphine

- **IV Morphine is 3 times stronger than oral morphine**
- **Example 2 mg IV morphine is equivalent to 6 mg oral morphine**
- **My** Mnemonics is ..... ☺ M for mother which represents trinity in Christianity, so that is how I always remember it is a 3:1 ratio.
- **There are 2 forms of morphine SR (Sustained release) and IR (immediate release).**

12

History of Morphine

1. Discovery and Early Use

- **Origins**: Morphine is derived from the opium poppy (**Papaver somniferum**), a plant that has been used for medicinal purposes for thousands of years. The use of opium, the raw extract from poppy plants, dates back to **ancient civilizations**.

- **Isolation of Morphine**:

- First **isolated** in **1804** by a German pharmacist, **Friedrich Sertürner**. He named the compound after **Morpheus**, the Greek god of dreams, due to its ability to induce sleep and relieve pain.

- **Widespread Medical Use**:

- By **1817**, Sertürner had published his findings, and morphine began to be used widely for pain relief, particularly in Europe.

13

History of Morphine

2. Morphine in the 19th Century

- **Commercial Production**:

- In **1827**, the German pharmaceutical company **Merck** began the commercial production of morphine. It became a cornerstone of pain management and was used extensively for treating soldiers' injuries during conflicts like the **American Civil War** (1861–1865)

- **Introduction of the Hypodermic Needle**:

- Hypodermic **needle** in the **1850s** revolutionized the use of morphine. Doctors could now inject morphine directly into the bloodstream, providing faster and more effective pain relief.

- **"Soldier's Disease"**: By the end of the American Civil War, many soldiers who had been treated with morphine for their injuries became addicted.

14

Dilaudid (Hydromorphone)

- **IV Diladud is 5 times stronger than oral Dilaudid**
- **Example 1 mg IV Dilaudid is equivalent to 5 mg oral morphine**
- **My** Mnemonics is ..... ☺the other name of Dilaudid is hydromorphone and H for high five, so that is how I always remember it is a 5:1 ratio.
- **There is no extended or sustained release Dilaudid so it is a short acting IR (immediate release) medication for breakthrough pain.**

15

History of Dilaudid

1. Origins and Early Development (1920s)

- **Discovery**: Hydromorphone first synthesized in **1924** by Knoll, a German pharmaceutical company. It was derived from **morphine**.
- **Commercial Introduction**: In **1926**, the drug was introduced under the brand name **Dilaudid**, which is derived from "di-hydromorphinone." Its name reflects its chemical relationship to morphine, and it quickly became a popular pain-relief medication in Europe and the U.S.

16

Oxycodone

- **Oral Oxycodone is 1.5 times stronger than oral morphine**
- **Example 10 mg Oxycodone is equivalent to 15 mg of oral morphine**
- **No** Mnemonics ⊗
- **There are 2 forms of oxycodone SR (Sustained release) and IR (immediate release).**

17

History of Oxycodone

1. Early Development (Early 1900s)

Origins: Oxycodone was first developed in **1916** in Germany. Chemists Martin Freund and Edmund Speyer at the University of Frankfurt.

Purpose: Goal was to create a less addictive and more effective alternative to **morphine** and **heroin**.

2. Adoption in the U.S. (1930s-1950s)

Introduction in the U.S.: Oxycodone entered U.S. market in **1930s**, initially in combination with other drugs such as **aspirin** or **acetaminophen**. One common brand at the time was **Percodan** (oxycodone combined with aspirin).

18

History of Oxodone

3. OxyContin and the Opioid Epidemic (1990s-Present)

OxyContin:

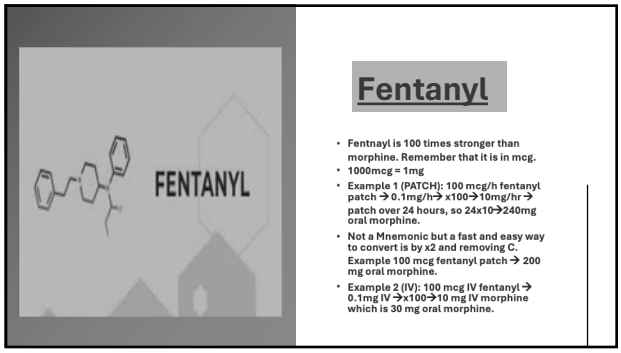
- In **1996**, Purdue Pharma introduced **OxyContin**, a time-released formulation of oxycodone. OxyContin was promoted as being less addictive because of its slow-release mechanism.

Rise in Prescriptions:

- Throughout late 1990s and early 2000s, prescriptions for OxyContin soared. The medical community shifted toward more liberal opioid prescribing for chronic pain, and OxyContin was seen as a safer option.

19

20



Fentanyl

- Fentnayl is 100 times stronger than morphine. Remember that it is in mcg.
- 1000mcg = 1mg
- Example 1 (PATCH): 100 mcg/h fentanyl patch → 0.1mg/h→ x100→10mg/hr → patch over 24 hours, so 24x10→240mg oral morphine.
- Not a Mnemonic but a fast and easy way to convert is by x2 and removing C. Example 100 mcg fentanyl patch → 200 mg oral morphine.
- Example 2 (IV): 100 mcg IV fentanyl → 0.1mg IV →x100→10 mg IV morphine which is 30 mg oral morphine.

21

History of Fentnayl

1. Development and Early Use (1960s)

- **Discovery**: Fentanyl was first synthesized in **1960** by **Dr. Paul Janssen**, the founder of Janssen Pharmaceutica, a Belgian pharmaceutical company.
- **Medical Use**: By modifying the molecular structure of certain synthetic opioids, Janssen created fentanyl, a drug **100 times more potent than morphine**. Fentanyl was initially used for pain management, particularly in surgical settings, where its rapid onset and powerful effects were ideal for anesthesia.

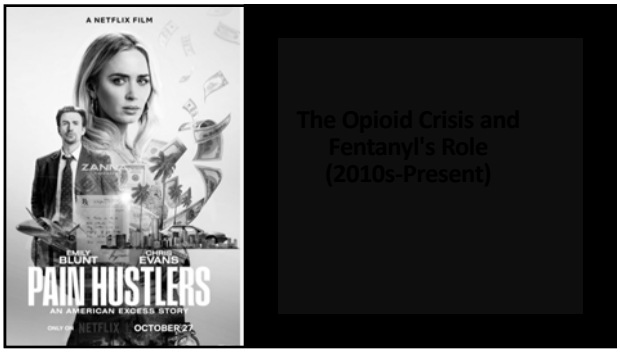
22

History of Fentnayl

2. Commercialization and Medical Applications (1970s-1990s)

- **Anesthetic Use**: Fentanyl became widely adopted as a surgical anesthetic under the brand name **Sublimaze**.
- **Introduction of Duragesic Patch**: In **1990**, Janssen introduced the **Duragesic patch**, a transdermal system that slowly releases fentanyl over time for patients suffering from chronic pain.
- **Lozenges and Lollipops**: Fentanyl lollipop approved for severe, breakthrough cancer pain in the 1990s. These innovations expanded fentanyl's use beyond surgery, making it an important tool in palliative care.

23



The Opioid Crisis and Fentanyl's Role (2010s-Present)

24

Methadone

- Methadone conversion to morphine is challenging due to methadone's non-linear pharmacokinetics and the fact that its potency increases with higher doses.

Variable Potency:

- Methadone is estimated to be **approximately 3 to 10 times more potent** than oral morphine when given orally, depending on the dose.

Daily oral morphine equivalent	*Conversion ratio of oral morphine: oral methadone*
<100 mg	3:1
100–300 mg	5:1
301–600 mg	10:1
601–800 mg	12:1
801–1000 mg	15:1
Over 1000 mg	20:1[a]

25

History of Methadone

1. Origins and Development

- **World War II**:
  - Methadone was first synthesized in **Germany** in the late 1930s. During **World War II**, due to shortages of morphine and other opioids, German scientists, led by chemists **Max Bockmühl** and **Gustav Ehrhart** at the pharmaceutical company **IG Farben**, developed a synthetic opioid to serve as an alternative painkiller.
- **Introduction to the United States**:
  - After the war, the formula for methadone was brought to the United States as part of post-war reparations.
  - In 1947, the drug was introduced in the U.S. under the name **Dolophine** (a name that some believe was derived from the Latin word "dolor," meaning pain).

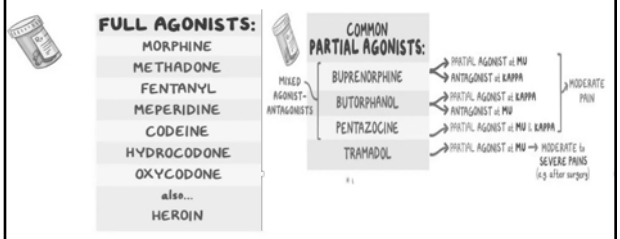
26

History of Methadone

- **Opioid Addiction Crisis**:
  - By the 1960s, the U.S. was facing a growing heroin addiction crisis. During this time, methadone was explored as a potential treatment for heroin dependency.
- **Pioneering Research**: **Drs. Vincent Dole** and **Marie Nyswander** at **Rockefeller University** in New York were among the first to advocate for methadone as a treatment for heroin addiction. This discovery led to the establishment of methadone **maintenance therapy** (MMT) in the mid-1960s.
- **Widespread Adoption**: Methadone maintenance programs (MMT) began to proliferate in the late 1960s and early 1970s.

27

Full Agonist versus Partial Agonist



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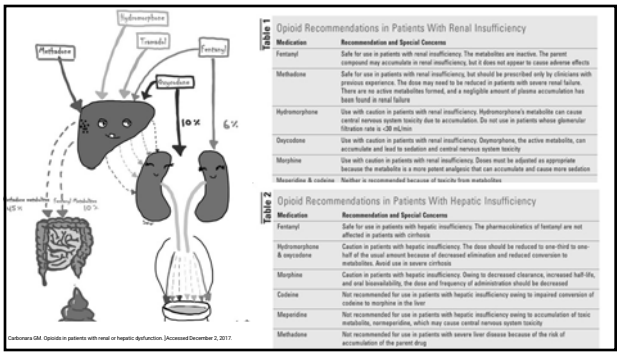

Carbonaro GM. Opioids in patients with renal or hepatic dysfunction. [Accessed December 2, 2017.

Table 1 Opioid Recommendations in Patients With Renal Insufficiency

Medication	Recommendation and Special Concerns
Fentanyl	Safe for use in patients with renal insufficiency. The metabolites are inactive. The parent compound may accumulate in renal insufficiency, but it does not appear to cause adverse effects
Methadone	Safe for use in patients with renal insufficiency, but should be prescribed only by clinicians with previous experience. The dose may need to be reduced in patients with severe renal failure. There are no active metabolites formed, and a negligible amount of plasma accumulation has been found in renal failure
Hydromorphone	Use with caution in patients with renal insufficiency. Hydromorphone's metabolite can cause central nervous system toxicity due to accumulation. Do not use in patients whose glomerular filtration rate is <30 mL/min
Oxycodone	Use with caution in patients with renal insufficiency. Oxymorphone, the active metabolite, can accumulate and lead to sedation and central nervous system toxicity
Morphine	Use with caution in patients with renal insufficiency. Doses must be adjusted as appropriate because the metabolite is a more potent analgesic that can accumulate and cause more sedation
Meperidine & codeine	Neither is recommended because of toxicity from metabolites

Table 2 Opioid Recommendations in Patients With Hepatic Insufficiency

Medication	Recommendation and Special Concerns
Fentanyl	Safe for use in patients with hepatic insufficiency. The pharmacokinetics of fentanyl are not affected in patients with cirrhosis
Hydromorphone & oxycodone	Caution in patients with hepatic insufficiency. The dose should be reduced to one-third to one-half of the usual amount because of decreased elimination and reduced conversion to metabolites. Avoid use in severe cirrhosis
Morphine	Caution in patients with hepatic insufficiency. Owing to decreased clearance, increased half-life, and oral bioavailability, the dose and frequency of administration should be decreased
Codeine	Not recommended for use in patients with hepatic insufficiency owing to impaired conversion of codeine to morphine in the liver
Meperidine	Not recommended for use in patients with hepatic insufficiency owing to accumulation of toxic metabolite, normeperidine, which may cause central nervous system toxicity
Methadone	Not recommended for use in patients with severe liver disease because of the risk of accumulation of the parent drug

29

Q.1

Max is a 72-year-old man with hyperparathyroidism, renal failure, and severe osteoporosis. He has been receiving long-term opioid therapy with oxycodone at 10 mg taken orally every 8 hours around the clock for hip pain following fracture and surgery. His creatinine level increased from 1.2 mg/dl to 2.4 mg/dl in 1 week. His daughter reports that he has been very drowsy and irritable recently. His pain control has also been poor. What is the best possible opioid to switch to?

A. Morphine
B. Hydromorphone
C. Codeine
D. Methadone

30

ALLERGIES

- **Morphine**, codeine, hydrocodone, **Hydromorphone, Oxycodone**, and belong to a class of opioids called **Phenanthrenes.**
- **Fentanyl** belong to a class of opioids called **Phenylpiperidines .**
- **Methadone** belong to a class of opioids called **Phenylheptylamines**.

31

Q.2

- Mr. K is a 68-year-old man with lung cancer and metastasis to the spine. He is currently receiving chemotherapy. He had an allergic reaction to morphine in the past that included rash, hives, itching, and some swelling of his tongue. He has back pain that is not resolved by taking ibuprofen. His oncologist has recommended that acetaminophen not be used on a regular basis. What would you recommend for managing his severe pain from bone metastasis?

A. Morphine

B. Codeine

C. Oxycodone

D. Fentanyl

32

LETS REVIEW THE LITERATURE

SHOULD WE TREAT PAIN IN THE ELDERLY PALLIATIVE CARE CANCER PATIENTS DIFFERENTLY?

Methods

- **Study Design**: Prospective observational study conducted in a hospice in Rijeka, Croatia.
- **Population**: The study included 137 patients, aged over 18 years, with a life expectancy of less than three months. Patients were divided by age, using 65 years as the cutoff for "elderly."
- **Exclusion Criteria**: Delirium, inability to consent, or cognitive impairments that precluded accurate pain assessment.
- **Evaluation Tools**: Assessment utilized the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative (EORTC QLQ-C15-PAL) and the Edmonton Symptom Assessment System (ESAS).
- **Analgesic Use**: Doses of opioids were converted to mgoday of oral morphine equivalent (OME) for standardized comparison.

Results

- **Demographics**: The mean age of participants was 71.8 years, with the most common cancer types being lung, gastrointestinal, and hepatobiliary cancers.
- **Pain Scores**: Younger patients exhibited significantly higher pain scores than older patients (5.34 vs. 3.91, p=0.01).
- **Analgesic Use**:
  - Older patients used opioids less frequently (68.8% vs. 85.7% in younger patients) and at lower doses (mean of 90.42 mg OME vs. 135.19 mg OME on admission).
  - By the last week of care, older patients had a mean daily dose of 109.98 mg OME compared to 165.61 mg for younger patients (p=0.03).
  - Notably, older patients used non-steroidal anti-inflammatory drugs (NSAIDs) less frequently, while the use of paracetamol was more common.
- **Survival Rates**: No significant differences in survival between the age groups were found (37.36 days for younger patients vs. 37.98 days for older patients).

Conclusion

- The findings suggest that elderly cancer patients in palliative care utilize lower doses of opioids and different analgesics without resulting in higher pain levels or shortened survival.
- This indicates that a strategy of starting at lower doses and cautiously titrating opioids may be beneficial, reinforcing the principle of 'start low, go slow'

33

LETS REVIEW THE LITERATURE

JKMS

Effect of Opioids on All-cause Mortality and Sustained Opioid Use in Elderly Patients with Hip Fracture: a Korea Nationwide Cohort Study

Methods

- A retrospective observational cohort study was conducted involving patients from the Korean National Health Insurance Service-Senior cohort.
- The study included patients aged 65 years and older with acute hip fractures from 2002 to 2015.
- Patients were categorized into past opioid users, current users, and those who sustained use (opioids used 3-12 months after fracture).
- Generalized estimating equations and multivariable-adjusted Cox proportional hazards models were employed to analyze the outcomes, measuring adjusted rate ratios (aRR) and hazard ratios (HR) for mortality.

Results

- The cohort comprised 12,927 patients with a mean age of 77 years; 57.22% were past opioid users, while 88.75% reported current use post-fracture.
- No significant difference in mortality rates was observed between current and non-current users of opioids across all measured time frames (30 days to 1 year).
- Among survivors, past opioid use increased the likelihood of sustained opioid usage by 1.52 times (aRR: 1.52; 95% CI: 1.45–1.58; P < 0.001).
- The shift in opioid use saw a rapid initial increase following fracture, followed by a decline at three months post-injury.

Conclusion

- Both current and past opioid use did not correlate with increased all-cause mortality in the elderly population following hip fractures.
- The study indicates that prior opioid use substantially raises the risk of continued opioid consumption post-fracture.
- These findings emphasize the necessity of careful monitoring and management strategies for opioid use within this demographic.

34

LETS REVIEW THE LITERATURE

Research article

The association between initial opioid type and long-term opioid use after hip fracture surgery in elderly opioid-naive patients

Methods

- A nationwide population-based cohort study was conducted using data from Danish health registries from 2006 to 2015.
- The study included elderly patients aged ≥65 years who had undergone hip fracture surgery and redeemed at least one opioid prescription within three months post-surgery.
- Long-term opioid use was defined as the redemption of one or more opioid prescriptions each within three different three-month periods after surgery.
- The primary outcomes measured included the type of opioid initially redeemed, long-term opioid use rates, and adjustments through logistic regression analyses yielding adjusted odds ratios (aOR) compared with morphine as the reference.

Results

- The study cohort comprised 26,790 opioid-naïve patients, with 21% of subjects dying within nine months of surgery.
- Among 21,205 patients who survived, 15% transitioned to long-term opioid use.
- Significant findings indicated that certain opioid types are linked to an increased likelihood of long-term use when compared to morphine:
  - Oxycodone: 14% (aOR 1.76, 95% CI 1.52–2.03)
  - Fentanyl: 29% (aOR 4.37, 95% CI 3.12–6.12)
  - Codeine: 13% (aOR 1.55, 95% CI 1.14–2.09)
  - Tramadol: 13% (aOR 1.96, 95% CI 1.39–1.80)
  - Buprenorphine: 33% (aOR 5.27, 95% CI 4.14–6.94)
  - More than one opioid type: 27% (aOR 3.83, 95% CI 3.31–4.44)
- A noted decrease in the proportion of long-term opioid users was observed from 18% before 2010 to 13% thereafter.

Conclusion

- The study's findings indicate that certain opioids, especially buprenorphine and fentanyl, are associated with a greater risk of long-term use compared to morphine following hip fracture surgery.
- Healthcare providers should consider these associations when prescribing opioids to elderly postoperative patients, emphasizing careful selection based on potential long-term consequences.
- Additionally, the decreased initiation of long-term opioid use after 2010 suggests improvements in prescribing practices, indicating a trend towards more conscientious opioid management strategies.

35

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36