

# The Hidden Opioid Abuse Problem: Is it Geriatric Opioid Abuse or is Grandma Really a Junkie

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# Disclosure

- All planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.

# Learning Objectives

- Analyze patient-specific information to identify geriatric opioid abuse (GOA) in the setting of chronic opioid therapy, including risk factors for GOA and misdiagnosis.
- Analyze patient-specific information to identify comorbid conditions that may influence the clinical presentation of GOA, including the impact of advanced age on opioid pharmacokinetics and pharmacodynamics in the elderly.
- Given patient-specific information, design a care plan that addresses the management of Concurrent Chronic Noncancer Pain and opioid abuse in an elderly patient.

# Why It is So Difficult to Help Grandma?

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# Objectives

- At the end of this presentation, utilizing a case of an older patient on chronic opioid therapy (COT) for chronic noncancer pain (CNCP) with the comorbidity of geriatric opioid abuse (GOA) the participant will be able to:
  - Discuss the common presenting signs & symptoms of GOA
  - Understand why GOA may be difficult to diagnose
  - Assess the impact of common comorbidities present in older patients with GOA



## Case Study: RW is a 69-year-old female who presents, with her daughter, to your ambulatory care clinic for routine evaluation and refill of her medications

- CC
  - Increased pain, insomnia, memory impairment
- PMH
  - Chronic pain: osteoarthritis in bilateral hips & knees; degenerative disc disease (L4-L5)
  - Depression
  - Anxiety
  - Post-Traumatic Stress Disorder; assault (1987)
  - Type 2 Diabetes Mellitus
  - Osteoporosis
- FH
  - Parents
    - Both deceased; father from myocardial infarction; mother from cerebrovascular accident, parents divorced when patient was 11 years of age
    - husband alcoholic, abusive
  - 2 daughters, 1 son
    - both daughters w/history of tx for substance use disorders

## Case Study : Continued

- Medications (all taken orally)
  - Buspirone 10 mg three times daily
  - Cyclobenzaprine 10 mg three times daily
  - Duloxetine 20 mg twice daily
  - Metformin 500 mg twice daily
  - Morphine 15 mg every 6 hours
  - Mirtazapine 15-30 mg at bedtime
  - Pregabalin 100 mg three times daily
  - CaCO<sub>3</sub> 500 mg three times daily
- VS:
  - BP: 155/80 mm Hg, Ht: 5'2", Wt: 105 lb
  - HR: 100 bpm RR: 20 bpm
- Labs/Tests
  - SCr: 1.4 g/dL
  - LFTs: WNL
  - QTc: 480 ms
  - UDM: + morphine, hydromorphone
- Other Monitoring
  - Rx Monitoring Program: appropriate for 28 day fill cycle
  - Chart Rx refill list shows early fills for cyclobenzaprine, morphine, pregabalin

## Case Study: Continued

- PE
  - Well groomed, eye contact diverted at times
  - Affect is flat, somewhat engaged in conversation, cognition & memory seem slow and she has impaired word search, patient is hypervigilant
  - States her pain is ↑↑, but cannot discern a specific pain driver
  - She is focused on her cyclobenzaprine, morphine, & pregabalin

## Question 1:

**In the patient's medication list, which medications are at risk for abuse?**

- A** Buspirone, Cyclobenzaprine
- B** Cyclobenzaprine, Duloxetine
- C** Duloxetine, Morphine
- D** Morphine, Pregabalin

## Question 2: GOA is often underdiagnosed because

- A** Elderly patients do not abuse drugs
- B** Opioid abuse is a chronic disease of younger patients
- C** Health care providers rarely look for GOA
- D** Elderly patients do not present to clinic impaired from GOA

## Question 3: Which of the following system issues is the greatest barrier to the diagnosis of GOA?

- A** Definition of older adult varies
- B** Conflicting results from large studies
- C** Inadequate health care provider education on GOA
- D** Ease of admission to GOA rehab programs without notifying family

# GOA: The Hidden Opioid Abuse Epidemic

- GOA is a hidden & difficult diagnosis because of:
  - System Issues:
  - Scope of the problem:
    - As “baby boomers” started turning 65 yo in 2011, 10,000 people turned 65 yo daily, and this rate will continue for the next 20 years
    - All “boomers” will be  $\geq 50$  yo in 2020,  $\geq 65$  yo in 2030, and at that time nearly 20% of U.S. residents are expected to be 65 and older
    - $\geq 65$  yo group is projected to  $\uparrow$  to 88.5 million in 2050, more than doubling the number in 2008 (38.7 million)

Kalapatapu RK, et al. *Am J Addict* . 2010; 19:515-22.

Kuerbis A, et al. *Clin Geriatr Med*. 2014; 30(3):629-54.

Center for Substance Abuse Treatment. Substance Abuse Among Older Adults. 1998. <https://www.ncbi.nlm.nih.gov/books/NBK64419>.

# GOA: The Hidden Opioid Abuse Epidemic

- GOA is a hidden & difficult diagnosis because of:
  - System issues
    - Definition of “older adult” can be 50 yo, or 60 yo, instead of 65 yo due to:
      - decrease in cognitive function
      - biological factors
      - psychological factors
      - changes in social factors
  - Small study sample sizes & heterogeneous populations

Taylor MH, et al. *Prim Care Companion CNS Disord*. 2012; 14: PCC.11r01320.

Kalapatapu RK, et al. *Am J Addict*. 2010; 19:515-22.

Kuerbis A, et al. *Clin Geriatr Med*. 2014 August; 30(3):629-54.

# GOA: The Hidden Opioid Abuse Epidemic

- Demographics of GOA may be changing
  - Administrative data from New York State licensed drug treatment programs to examine overall age trends and characteristics of older adults in opioid treatment programs in New York City from 1996 to 2012
  - Adults aged 50 and higher becoming the majority treatment population; the majority age group in opioid treatment were those 50–59 yr, with large increases in those over the age of 60
  - Small but consistent change in the type of primary opioid used, with increased reporting of non-heroin and prescription opioid use since 1996

# GOA: The Hidden Opioid Abuse Epidemic

- GOA is a hidden & difficult diagnosis because of:
  - System issues
    - Diagnostic criteria bias:
      - Due to lack of child care responsibilities &/or retirement from work, older patients with GOA may not meet the criteria of “failure to fulfill major role obligations at work or home” per DSM-IV-TR
      - Many elders w/ GOA enter treatment via social work avenues instead of employment or legal avenues
      - Changes in pharmacokinetics(PK)/pharmacodynamics (PD) and physiology may appear to ↓ opioid tolerance in elderly persons, which will negate the DSM criteria for ↑ opioid tolerance

# GOA: The Hidden Opioid Abuse Epidemic

- GOA is a hidden & difficult diagnosis because of:
  - System issues
    - Ageism & stereotyping
      - “grandma’s one last indulgence”
      - “what difference does it make? She won’t be around much longer”
    - Inadequate health provider education
      - In a crowded curriculum geriatrics accounts for a fraction of that curriculum; opioid abuse far less
    - Short appointment time

Bardach SH, et al. *The Gerontologist*. 2012;52:607-18.

Kalapatapu RK, et al. *Am J Addict*. 2010;19: 515-22.

Kuerbis A, et al. *Clin Geriatr Med*. 2014 August;30(3): 629-54.

Patterson TL, et al. *Psychiatric Services*. 1999;50:1184-8.

# GOA: The Hidden Opioid Abuse Epidemic

- GOA is a hidden & difficult diagnosis because of:
  - Patient issues
    - Denial, stigma, lack of awareness
      - ↑ isolation; ↓ social support
      - Chronic pain viewed as a natural part of aging
    - Effect of aging on physiologic systems
      - Dopaminergic & serotonergic receptor loss in prefrontal cortex and striatum; NMDA (N-methyl-D-aspartate) receptor loss in cortex, striatum, and hippocampus
    - Effect of comorbidities
      - GOA may present as dementia, insomnia/sleep apnea, depression, anxiety

Guerriero F.; 30(3):629-54. *World J Clin Cases*. 2017; 5:73-81.

Kalapatapu RK, et al. *Am J Addict* . 2010; 19:515-22.

Kuerbis A, et al. *Clin Geriatr Med*. 2014 August.

# GOA: The Hidden Opioid Abuse Epidemic

- Epidemiology
  - Prevalence of opioid use
    - ~ 6–9% of community-dwelling older adults use COT for CNCP
    - 70% of nursing home residents with CNCP were prescribed COT
    - in a community-based study of older adults with CNCP and a mean age of 82 years, 25% of participants reported using COT

# GOA: The Hidden Opioid Abuse Epidemic

- Epidemiology

- Variance in reported prevalence of GOA

- 4/12,000 patients prescribed morphine for self administration became addicted

- 1.4% of adults  $\geq 50$  yo used prescription opioids nonmedically in the last year

- SUD tx in 1992 for prescription opioids was 0.7% for both age groups of 50–54 yo &  $\geq 55$  yo ; SUD tx in 2005  $\uparrow$  to 3.2% for ages 50–54 yo & 2.8% for  $\geq 55$  yo

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# GOA: The Hidden Opioid Abuse Epidemic

- Epidemiology
  - Prescription drug abuse is present in 12 to 15% of elderly individuals who seek medical attention
  - The number of Americans over age 50 abusing prescription drugs is projected to rise to 2.7 million in 2020 — a 190% increase from the 2001 figure of 910,000.

RW presents to your clinic for a refill of her medication. RW's daughter is with her. Her daughter states she thinks her mother may be running out of her pain medication early. Her daughter further elaborates that her mother's alertness & irritability wax and wane during the day.

- How would you screen for GOA?

## Question 4: Which of the following screening tools for opioid abuse have been validated in an older population?

- A** CAGE , ORT, AUDIT
- B** MAST, ASSIST, DARE
- C** No screening tests have been validated in a geriatric population
- D** All of the above screening tests have been validated in a geriatric population

## Question 5: Which screening tools have been recommended for screening for GOA?

- A** CAGE, MAST-G, AUDIT
- B** ORT, CAGE, MAST
- C** DIRE, ORT, CAGE
- D** DARE, DIRE, ORT

## Question 6: The use of medical cannabis may decrease GOA.

- A** True, medical cannabis has been shown to have an opioid-sparing effect in patients with CNCP prescribed COT
- B** True, medical cannabis has been shown to be a gateway drug & will decrease opioid prescribing
- C** True, medical cannabis has been shown to be a gateway drug & will decrease opioid prescribing
- D** False, medical cannabis has been shown to be a gateway drug & will increase opioid prescribing.

# GOA: Risk Factors

- Depression
- Less physically disabled
- Use of multiple medications
- PTSD
- History of illicit drug use

# Assessment of a Hidden Epidemic

- Presenting signs & symptoms
  - Have GOA on your radar screen
  - Changes in cognition, mood, memory, hygiene, nutrition, and sleep
  - ↑ in depression &/or anxiety
  - Call from concerned family member &/or friend
  - Changes in oxygen saturation at clinic visit

# Assessment of a Hidden Epidemic (cont'd)

- Screening Tests
  - There are no validated screening questionnaires for opioid abuse in the elderly
  - Use of a combination of: CAGE or CAGE-AID, Michigan Alcoholism Screening Test-Geriatrics (MAST-G), & Alcohol Use Disorders Identification Test (AUDIT) has been recommended

Center for Substance Abuse Treatment. Substance Abuse Among Older Adults. 1998. <https://www.ncbi.nlm.nih.gov/books/NBK64419>.

Kalapatapu RK, et al. *Am J Addict*. 2010; 19:515-22.

Satre DD, et al. *Am J Geriatr Psychiatry*. 2011; 19:695-703.

# Assessment of a Hidden Epidemic (cont'd)

- Opioid Assessment Tools
  - Risk Assessment
    - Not validated in elderly
    - ORT, DIRE, SOAPP-R
  - Ongoing Assessment
    - Not validated in elderly
    - COMM, ABC, 5-Point Opiate Abuse Checklist

# Assessment of a Hidden Epidemic (cont'd)

- Other tools
  - Use of Rx monitoring program which may be regulated by individual state medical & pharmacy boards; or law enforcement
  - Use of urine drug testing as mandated by individual state medical & pharmacy boards

## Key Takeaways

1. The number of elderly patients will increase in the coming years. It should be expected that the number of geriatric patients with GOA should also increase. So, yes, Grandma could really be a junkie.
2. There are no validated tools to screen for GOA. SAMSHA recommends using: CAGE or CAGE-AID, MAST-G, and AUDIT has been recommended.

## Key Takeaways (cont'd)

3. GOA is underdiagnosed because of the
  - absence of validated diagnostic instruments in the geriatric population
  - multitude of medical co-morbidities
  - nonspecific clinical presentation in the elderly
  - lack of geriatric provider training or awareness of substance abuse disorders
  - absence of published literature on non-alcohol substance use disorders in this population
  - Health care provider bias &/or ageism
  
4. Due to the multitude of barriers to the diagnosis of GOA, GOA should always be on a provider's radar screen

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- C** Duloxetine, Morphine
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# Grandma's Brain on Opioids

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**Boston, Massachusetts**



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- Given patient-specific information, design a care plan that addresses the management of concurrent CNCP and opioid abuse in an elderly patient.

**Question 7: Which of the following PK parameters are most likely affected in a 78-year-old patient with CNCP on COT who is s/p gastric bypass surgery?**

- A** Absorption and distribution
- B** Distribution and metabolism
- C** Metabolism and excretion
- D** Absorption and excretion

**Question 8: Which of the following medications is NOT commonly used in combination with opioids as a cocktail of abuse?**

- A** Diphenhydramine
- B** Acetaminophen
- C** Gabapentin
- D** Clonidine

**Question 9: You are consulted about starting an opioid in a 77-year-old patient with CNCP and remote history of opioid use disorder (OUD). The prescriber only feels comfortable with codeine or hydrocodone and wants you to choose. What do you do?**

- A** Recommend acetaminophen/codeine; all grandmas love this drug!
- B** Recommend extended-release hydrocodone
- C** Educate the prescriber on other options
- D** Walk away

**Question 10: An 82-year-old patient with chronic low back pain (CLBP) and chronic renal impairment is unable to perform many activities of daily living (ADL). Recent use of nonopioid and nonpharmacologic modalities were ineffective for pain control. Which of the following opioids would you recommend?**

- A** Oral hydromorphone
- B** Oral morphine
- C** Transdermal fentanyl
- D** Transdermal buprenorphine

**Question 11: You are consulted about starting an opioid in a frail older adult with severe CNCP who resides in a nursing home. The formulary consists only of oxymorphone, levorphanol, tramadol, and tapentadol. What do you do?**

- A** No brainer – definitely select tramadol!
- B** Levorphanol – its long-acting so why not?!
- C** Possibly consider oxymorphone or tapentadol but ask more questions first
- D** Help change the formulary

## Question 12: Which of the following is an advantage of using buprenorphine in older adults with CNCP?

- A** Available as transdermal patch for ease of administration
- B** Lack of ceiling effect regarding analgesia
- C** Milligram-for-milligram conversion to and from other opioid medication
- D** Short half-life and rapid onset of action

# Pharmacokinetic Considerations – Opioid Use in Older Adults

Parameter	Change with Normal Aging	Common Disease Effects
<b>Absorption</b>	Slowing of GI transit time Worsening of bowel dysmotility	Disorders that alter gastric pH may reduce drug absorption; surgically-altered anatomy may impact absorption
<b>Distribution</b>	Increased fat-to-lean body weight ratio = increased Vd for fat-soluble drugs, decreased Vd for water-soluble drugs; Decreased serum albumin = increased free fraction of drugs	Aging and obesity may result in longer drug half-life Increased toxicity with high plasma protein-binding drugs
<b>Metabolism</b>	Oxidation is variable and may decrease; Conjugation is usually preserved; First-pass effect usually unchanged; Genetic enzyme polymorphisms; ↓ in hepatic blood flow & volume	Hepatic issues may disrupt oxidation (conjugation preserved)
<b>Excretion</b>	GFR decreases with age resulting in decreased excretion; ↓renal clearance will prolong effects of active metabolites	Renal disease can predispose to drug toxicity

AGS Panel on  
Pharmacological  
Management of Persistent  
Pain in Older Persons. *J Am  
Geriatr Soc.* 2009; 57:1331-  
46.

Naples JG, et al. *Clin Geriatr  
Med.* 2016; 32(4):725-35.

# Pharmacodynamic Considerations – Opioid Use in Older Adults

- ↑ pain tolerance
- ↓ acetylcholine, dopamine, and serotonin receptors
- ↓ enzymatic degradation of monoamine oxidase
- ↓ responsiveness of beta-adrenergic receptors
- ↓ cortisol suppression

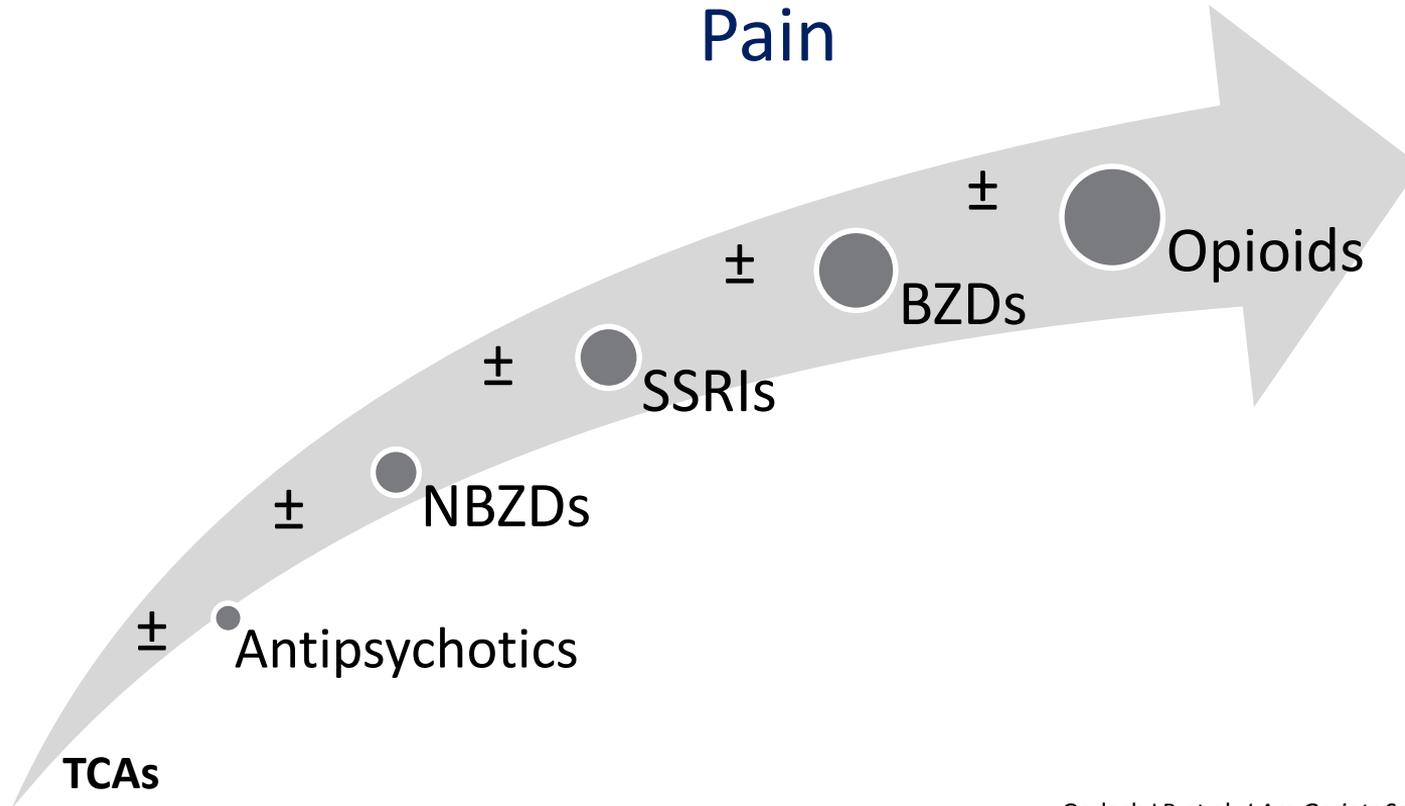
# Pharmacodynamic Considerations – Opioid Use in Older Adults (cont'd)

- Age-related increase in sensitivity to opioids
  - Risk of respiratory depression is significantly higher in patients in the seventh–ninth decades of life compared with younger patients
    - PK-PD models indicate that EC50 (the effect-site concentration producing half-maximal effect) decreases linearly with age (e.g., EC50 of an 80-year-old is ~half that of a 40-year-old)
      - No PK-PD data for most commonly used opioids (e.g., morphine)
  - How might this impact decisions for dosing?
    - IR vs. SR morphine dosing simulations to predict analgesic response and risk of respiratory depression

# Comorbidities of Concern

- Arthritis
- Osteoporosis
- Diabetes mellitus
- HTN, HF, PAD, CAD
- Obstructive airway disease
- Depression
- Anxiety
- Malignancy
- Sensory impairments
- Dementia
- Organ dysfunction
- Stroke
- Musculoskeletal disorders
- Sleep disorders

# CNS Polypharmacy in Older Adults with Chronic Pain



# Cocktails of Concern

- Opioids
- Gabapentinoids
- Clonidine
- Antihistamines
- Antiemetics (e.g., prochlorperazine)

# Opioid Comparisons: Use This, Not That?

	CODEINE	HYDROCODONE
PK/PD	CYP2D6 → morphine (5-10%) CYP3A4 → norcodeine (10%) UGT 2B7, UGT 2B4 → C6G	CYP2D6 → hydromorphone CYP3A4 → norhydrocodone
SAFETY CONCERNS	Lack of efficacy → ↑ misuse? CYP2D6*2x2 genotype → ultra-rapid metabolizers	Risk of accumulation in renal impairment

# Opioid Comparisons: Use This, Not That?

## (cont'd)

	MORPHINE	HYDROMORPHONE
<b>PK/PD</b>	Phase II (UGT 2B7, UGT 1A3) → M6G (active), M3G (inactive)	Phase II (UGT WB7, UGT 1A3) → H3G (inactive)
<b>SAFETY CONCERNS</b>	Immunosuppression Accumulation of metabolites in renal impairment ↑ risk of neurotoxicity with M3G	Accumulation of H3G in renal impairment → ↑ risk of neurotoxicity

UGT=UDP-glucuronosyltransferase

M6G=morphine-6-glucuronide

M3G=morphine-3-glucuronide

H3G=hydromorphone-3-glucuronide

# Opioid Comparisons: Use This, Not That? (cont'd)

	OXYCODONE	OXYMORPHONE
<b>PK/PD</b>	CYP3A4 → noroxycodone CYP2D6 → oxymorphone	Phase II → 6-OH-oxymorphone, O3G
<b>SAFETY CONCERNS</b>	Accumulation of active metabolites in renal impairment	↑ bioavailability in hepatic impairment Changes in absorption with fed vs. fasting states

O3G=oxymorphone-3-glucuronide

# Opioid Comparisons: Use This, Not That? (cont'd)

	TRAMADOL	TAPENTADOL
<b>PK/PD</b>	CYP2D6 → O-desmethyl tramadol CYP3A4, CYP2B6 (minor) Phase II → inactive metabolites	Phase II → inactive metabolites
<b>SAFETY CONCERNS</b>	<ul style="list-style-type: none"> <li>↑ risk of serotonin syndrome</li> <li>↑ risk of BP, HR changes</li> <li>↑ risk of bleeding</li> </ul>	<ul style="list-style-type: none"> <li>↑ risk of BP, HR changes</li> </ul>

# Opioid Comparisons: Use This, Not That? (cont'd)

	METHADONE	LEVORPHANOL
PK/PD	CYP3A4, CYP2B6, CYP2C19, CYP2C9, CYP2D6 → inactive metabolites	Phase II → inactive metabolites
SAFETY CONCERNS	<ul style="list-style-type: none"> <li>↑ risk of QTc prolongation</li> <li>↑ risk of serotonin syndrome</li> <li>↑ risk of BP, HR changes</li> <li>↑ risk of bleeding</li> </ul>	<ul style="list-style-type: none"> <li>↑ risk of serotonin syndrome</li> <li>↑ risk of BP, HR changes</li> <li>↑ risk of bleeding</li> </ul>

# Should We Fuss with Fentanyl?

- Advantages
  - Inactive metabolites
  - Can be used in renal impairment
  - May not significantly impact cognitive or psychomotor function
- Disadvantages
  - Variable absorption with transdermal patch
  - Increased Vd due to lipophilicity of medication
  - Immunosuppression has been demonstrated in humans

# What About Buprenorphine?

- Advantages

- Partial agonist w/ ceiling effect for analgesia & adverse events
- Better safety profile
  - Buprenorphine causes less cognitive impairment than do certain other opioids
- More optimal choice for patients that have demonstrated aberrant behavior/addiction
- Do not need DEA “X” number for CNCP treatment

- Disadvantages

- By some protocols, if on opioid medication, need to decrease until  $\leq 30$  morphine milligram equivalents (MME) daily
- May not be adequate for severe pain
- Insurance obstacles
- No clearly defined MME dose

PK Parameter	Buprenorphine (SL & Topical)
Protein Binding	96%
Bioavailability	SL: 29%; Topical:~ 15%
Half-life Elimination	SL:~37 hr; Topical: ~26 hrs
Onset of Action	10-30 min
Duration of Action	6 hr
Time to Peak Effect	N/A
Hepatic dysfunction:	Mild-moderate dysfunction: adjust dose and monitor
Renal dysfunction	No dose adjustment
Geriatric	Monitor

# Best Practices

- Therapy considerations
  - Age-related physiological changes
  - Polypharmacy
  - Comorbidities
  - Realistic goals of therapy
  - Risk factors for opioid-related adverse effects
  - Role of nonopioid and nonpharmacologic interventions

## Best Practices (cont'd)

- Choose an opioid based on drug- and patient-specific factors
- Start low and go slow
- Use longer dosing intervals
- Monitor therapy regularly
  - 8 “A’s”: analgesia, adverse effects, ADLs, aberrant behaviors, adjuvants, affect, access to treatment, adherence

# Management of Opioid-Related Adverse Effects in Older Adults

Adverse Effect	Frequency	Management
Constipation	+++	Routine assessment; preventive measures
Nausea	+++	Low dose, slow titration
Sedation, confusion, delirium	+	Low dose, slow titration
Falls, fractures	±	Monitor fall risk
Respiratory depression	±	Low dose, slow titration
Immunosuppression	Rare	Monitor for signs/symptoms of infection
Addiction	Rare	Monitor; consider PMH

## Key Takeaways

1. Normal aging processes, comorbidities, and polypharmacy can impact the safety of opioids for CNCP in older adults
2. Buprenorphine may be an ideal and safer opioid analgesic for a patient with opioid use disorder and/or CNCP
3. Approach to therapy should be individualized with close monitoring of achievement of realistic goals while balancing adverse effects

**Question 7: Which of the following PK parameters are most likely affected in a 78-year-old patient with CNCP on COT who is s/p gastric bypass surgery?**

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- Analyze patient-specific information to identify geriatric opioid abuse (GOA) in the setting of chronic opioid therapy, including risk factors for GOA and misdiagnosis.
- Analyze patient-specific information to identify comorbid conditions that may influence the clinical presentation of GOA, including the impact of advanced age on opioid pharmacokinetics and pharmacodynamics in the elderly.
- Given patient-specific information, design a care plan that addresses the management of concurrent CNCP and opioid abuse in an elderly patient.

# Questions?