

Opioid Use in Older Adults: The Double-Edged Sword

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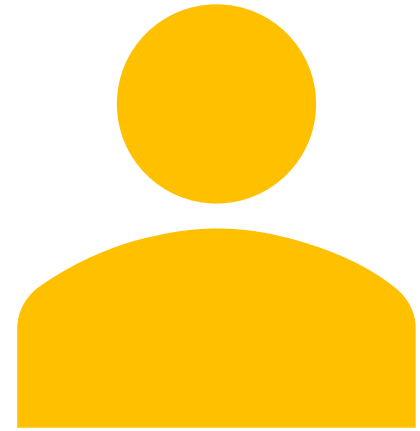
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Getting to know the audience

In which area do you primarily practice?

- Hospital
- Long-term care
- Outpatient specialty
- Outpatient internal/family medicine
- Other



1

Describe **physiological changes** in older adults as they impact choices in opioid therapy

2

Select appropriate **opioid therapy** for older adults

3

Describe **opioid misuse and management of opioid use disorder** in older adults

Objectives

DISCLAIMER:

When possible, chronic non-cancer related pain in older adults should be managed by non-pharmacologic methods in combination with non-opioid analgesics.

Challenges of Chronic Pain Management in Older Adults

- **Acetaminophen**
 - Efficacy
 - Toxicity
- **NSAIDs**
 - Toxicities: GI, renal, CV
- **Topicals**
 - Less effective
- **Adjuvant therapies**
 - TCAs: Toxicities
 - SNRIs
 - Antiepileptics
 - Muscle relaxants: Falls

*Older adults are
often excluded
from clinical trials*

What do we do if
moderate-severe
pain persists?



Opioids in Medicare Part D

Exhibit 1: Opioid Utilization in Part D, 2017

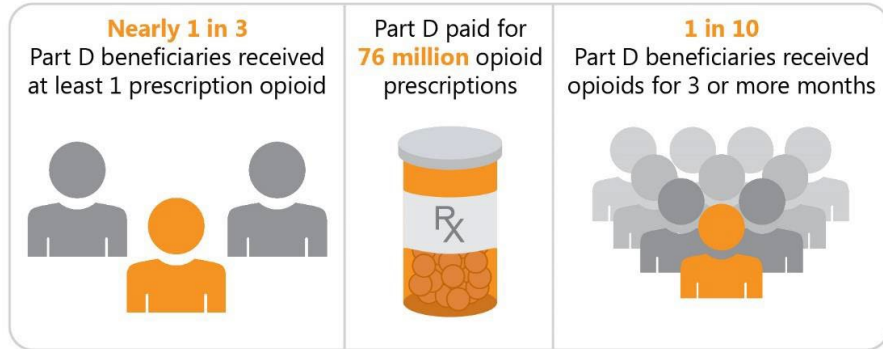
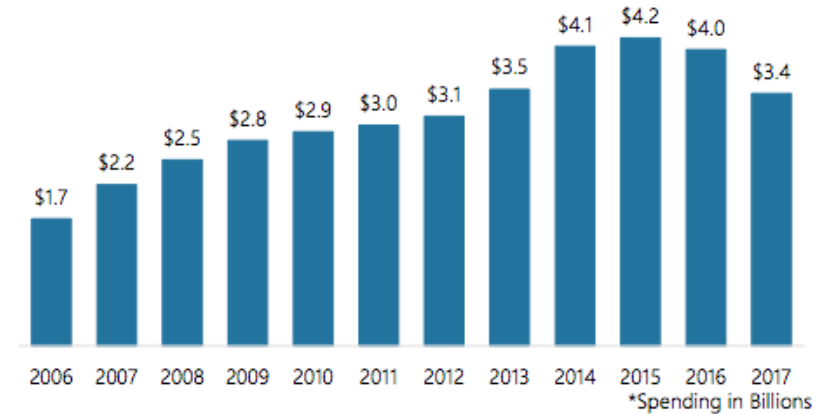


Exhibit 2: Overall spending for opioids in Part D decreased in 2017, but remained more than \$3 billion.



Source: OIG analysis of Medicare Part D data, 2018.

Decreased spending driven by lower prices not lower prescribing rates

A woman with short blonde hair is performing a sit-up exercise in a bright room with large windows. She is wearing a light-colored tank top and dark leggings. Her arms are extended forward, and her legs are bent at the knees. A large, semi-transparent white circle is overlaid on the left side of the image, containing the text.

Physiological Changes of Older Adults

- **Gastrointestinal**
- **Hepatic Metabolism**
- **Renal Excretion**
- **Distribution**
- **Pharmacodynamic**

Physiological Changes: Gastrointestinal

Change with normal aging	Clinical consequence of change
Delayed gastric emptying; reduced peristalsis	Alteration of drug absorption has little clinical effect
Reduced blood flow to GI tract	Increased risk of GI-related side effects, especially opioid-related gut mobility disturbance

Physiological Changes: Hepatic Metabolism

Change with normal aging	Clinical consequence of change
Decreased hepatic blood flow	Reduced first-pass metabolism
Reduced liver mass and functioning liver cells	<ul style="list-style-type: none">• Oxidative reactions (Phase I) may be reduced resulting in prolonged half-life<ul style="list-style-type: none">• CYP450 and MAO are Phase I enzymes• Conjugation (Phase II) is usually preserved• Difficult to predict precise effect in individual

Physiological Changes: Renal Excretion

Change with normal aging	Clinical consequence of change
Reduced renal blood flow	Reduced excretion of drugs and metabolites eliminated by kidney leads to accumulation and prolonged effects.
Reduced glomerular filtration rate	
Reduced tubular secretion	

Physiological Changes: Distribution

Change with normal aging	Clinical consequence of change
Decreased body water	Reduced distribution of water soluble drugs <ul style="list-style-type: none">• Morphine
Increased body fat; lipid soluble drugs accumulate in reservoirs	Lipid soluble drugs have longer effective half-life <ul style="list-style-type: none">• Fentanyl
Lower concentration of plasma proteins; increased free fraction of highly protein-bound drugs	Increased potential for drug-drug interactions with other highly protein bound drugs

Physiological Changes: Pharmacodynamic

Change with normal aging	Clinical consequence of change
Decreased receptor density	Increased sensitivity to therapeutic and side effects
Increased receptor affinity	

Dosing & Initiation



Obtain history of use of opioids for dental or surgical procedures and beneficial or adverse responses to guide initial choice.

Start at 25-50% of typical adult dose

“Start low and go slow”

Extended interval for short-acting agents when initiating therapy

- Every 6 hours instead of 4 hours at initiation

Side Effects in Older Adults



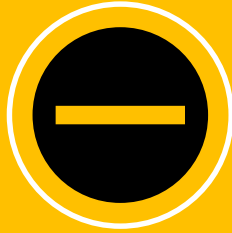
CNS effects
INCREASE incidence
of falls and fractures.

- Resolves after 2-3 days



Cognitive function

- Unaffected once dose is stable
- Impaired up to 7 days after dose increase



Constipation

- Be proactive!
Recommend a bowel regimen



Hormonal
suppression

- Decreased testosterone



Urinary retention

- Enlarged prostate

Getting to know the audience



What is your “go to” opioid for an older patient with chronic pain?

- Hydromorphone
- Morphine
- Oxycodone
- Fentanyl
- Whatever their insurance will pay for

Choosing an Appropriate Opioid

PREFERRED AGENTS

- **Oxycodone**
 - Flexibility in dosing
- **Hydromorphone**
 - Inactive metabolites
 - Preferred in renal disease
- **Fentanyl**
 - Better tolerated than oxycodone
 - Preferred in renal and/or hepatic disease
 - Not for opioid naïve

CAUTIOUS CHOICES

- **Morphine**
 - Active/toxic metabolites renally eliminated
- **Methadone**
 - CYP450 substrate (**3A4**, 2D6, 1A2)
 - P-glycoprotein substrate
 - Half-life (15-60 hours) exceeds duration of analgesia (8-12 hours)
 - Prolongs Qtc interval
 - Sequesters in fat tissue

**LESS
FREQUENTLY
USED OPIOIDS**



Levorphanol

Mechanism of action

- NMDA receptor antagonist
- Mu and kappa opioid receptor agonist
- Inhibits reuptake of serotonin and norepinephrine

Pharmacokinetics

- Half-life of drug is longer than duration of analgesia.
 - Typically dosed every 6-8 hours
- Do not adjust dose more frequently than every 4 days

Efficacy

- Neuropathic pain
- General pain syndrome



Compared to methadone:

- No cardiac toxicity
- No CYP450 metabolism
- Not a p-gp substrate

Buprenorphine Transdermal

Mechanism of action

- Partial mu receptor agonist
- Delta and kappa receptor antagonist
- High affinity and robust binding make it nearly impossible to displace, even with naloxone

Pharmacokinetics

- Highly lipophilic
- Long half-life (up to 32 hours)
- Transdermal formulation changed every 7 days

Efficacy

- Osteoarthritis
- Low back pain



Tapentadol

Mechanism of action

- Mu opioid receptor agonist
- Norepinephrine reuptake inhibitor

Pharmacokinetics

- No major drug-drug interactions
- No active metabolites
- Metabolism: glucuronidation, CYP2C9/19 substrate

Efficacy

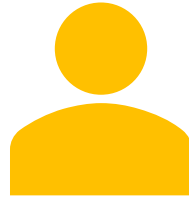
- Neuropathic pain
- Osteoarthritis
- Low back pain



Compared to tramadol:

- Not a prodrug
- No Qtc prolongation
- No serotonin reuptake inhibition

Getting to
know the
audience



**Which of the following have
you seen prescribed for older
patients with pain?**

- a. Buprenorphine
transdermal
- b. Levorphanol
- c. Tapentadol
- d. 2 of the above
- e. All of the above

Safe Opioid Use

Discuss with patient safe and secure storage of opioids to reduce risk of diversion

Consider periodic urine drug screening to monitor adherence to therapy

Frequent contact via phone or email to assess for and manage adverse effects

CMS
Policies
Effective
January 1,
2019


- 7-day supply limit for opioid naïve patients
- Opioid care coordination alert when cumulative MMED reaches or exceeds 90MMED
 - Pharmacy calls prescriber to confirm medical need
- Patient-specific point of sale claim edit
- Pharmacy limitation (“lock-in”)
- Prescriber limitation (“lock-in”)



Opioids: The Double-Edged Sword



Effective for
Pain
Management



Risk of Abuse,
Misuse and
Dependence

2008 Article

The Consultant Pharmacist by C. Martin, PharmD



Pointed out:

- **More prescriptions, more abuse**
 - In 2008 at 13% of the population, they were receiving 33% of all medications
 - Medicare Part D expansion will result in increased prescribing
- Baby-boomers are aging who have a greater lifetime rate of using drugs than previous generations might result in **increased numbers of older drug users in 15 to 20 years**
 - Predicted use of psychotherapeutics without medical directions in adults > 50 years old will increase to 2.7 million by 2020
- Discussed doctor and pharmacy “shopping”, borrowing medications from friends and family; obtaining medications via the internet; “hoarding” old or unused medications just in case...
- Additional concerns **including overlooking substance abuse as the cause**
 - changes in behavior like memory impairment may be attributed to dementia; balance or incoordination attributed to Parkinson’s disease

Opioid Risk Tool

		Female	Male
Family Hx of Substance Abuse	Alcohol	1	3
	Illegal drugs	2	3
	Prescription drugs	4	4
Personal Hx of Substance Abuse	Alcohol	3	3
	Illegal drugs	4	4
	Prescription drugs	5	5
Age	16-45 years	1	1
Hx of preadolescent sexual abuse		3	0
Psychiatric disease	ADHD, OCD, bipolar, schizophrenia	2	2
	Depression	1	1
Total Score			

Adapted from: <https://www.drugabuse.gov/sites/default/files/files/OpioidRiskTool.pdf>

That cited Webster LR, et al. Pain Med 2005;6:432.

Opioid Risk Tool

Tool developed in 2005

		Female	Male
Family Hx of Substance Abuse	Alcohol	1	3
	Illegal drugs	2	3
	Prescription drugs	4	4
Personal Hx of Substance Abuse	Alcohol	3	3
	Illegal drugs	4	4
	Prescription drugs	4	4
Age	16-45 years		
Hx of preadolescent sexual abuse			
Psychiatric disease	ADHD, OCD, bipolar, schizophrenia		
	Depression	1	1
Total Score			

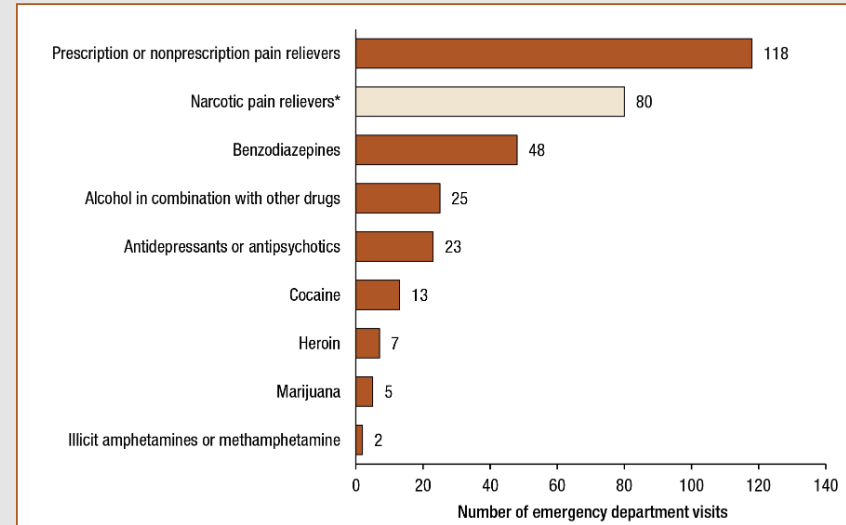
Scoring – Risk of future opioid abuse:
 ≤3: low risk
 4-7: moderate risk
 ≥ 8: high risk

2011 Drug Abuse Warning Network (DAWN) Report

In adults aged ≥ 65 years old:

- 750,529 drug-related emergency dept (ED) visits
- 2,056 drug-related ED visits on an average day
 - 290 of which were related to illegal drugs, alcohol with drugs, or nonmedical use of pharmaceuticals
- Of the 118 pain relievers; 80 were related to narcotic pain relievers

Figure 4. Number of emergency department visits for drug misuse on an average day for patients aged 65 or older, by selected types of drugs: 2011 DAWN



* Narcotic pain relievers are a subset of prescription or nonprescription pain relievers.

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, Drug Abuse Warning Network (DAWN), 2011.

First Time Admissions in Adults ≥ 55 years old

A.S. Huhn et al.

Drug and Alcohol Dependence 193 (2018) 142–147

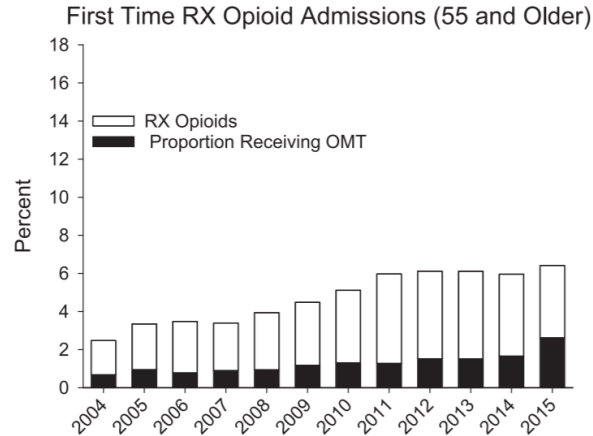
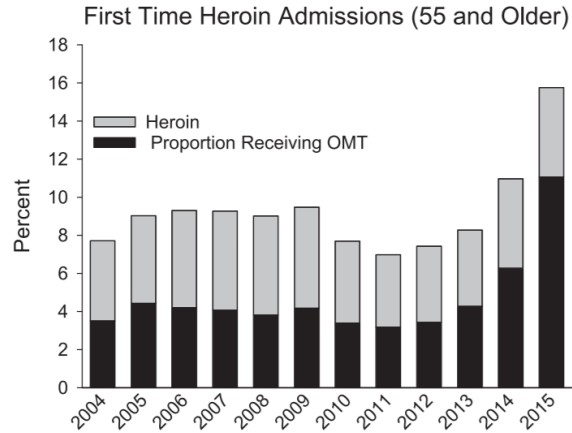
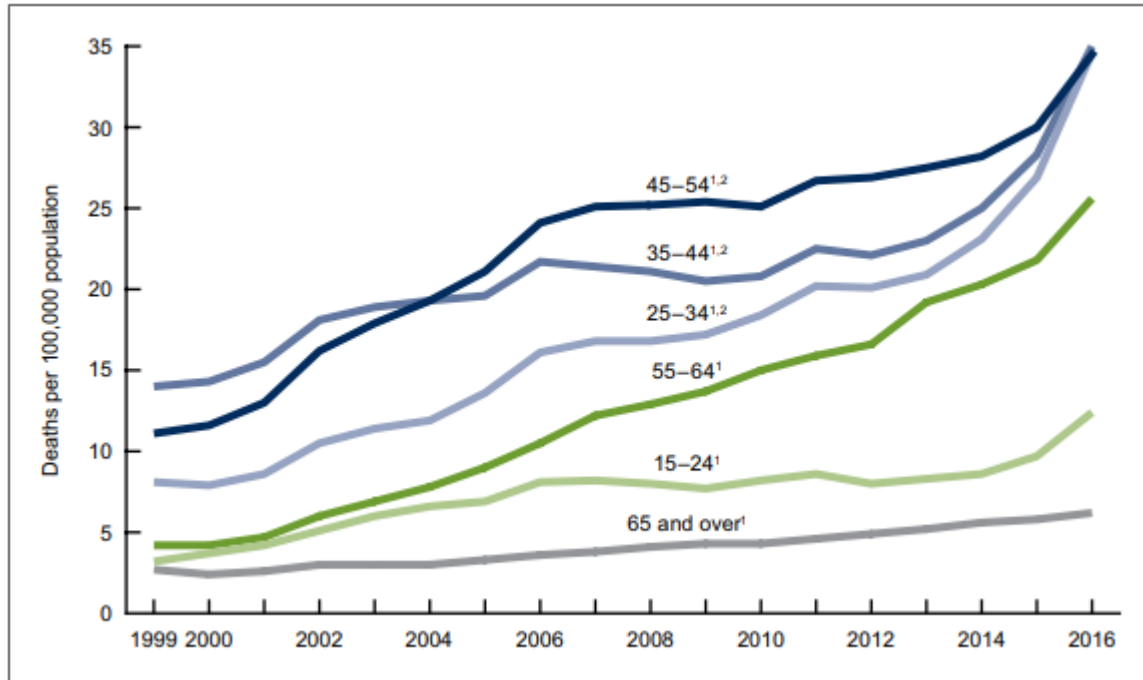


Fig. 2. Left: percent of older adults (55 and older) presenting to treatment for the first time with opioid use disorder using heroin as their primary drug of choice. Right: percent of older adults presenting to treatment for the first time with opioid use disorder using prescription opioids as their primary drug of choice. Both graphs show the relative proportion (in black) of older adults where opioid maintenance therapy (OMT) was planned as part of treatment for opioid use disorder (OUD). RX = prescription.

Drug Overdose Death Rates, by Age Group: United States 1999-2016



When to Recommend Naloxone?

Naloxone an opioid antagonist is available for reversal of opioid overdose

In Virginia, as of 2017 – Prescribers of opioids for chronic pain – if morphine milligram equivalents (MME) > 120 mg or are prescribed an opioid in combination with a benzodiazepine – must prescribe naloxone.

In general, anyone in an opioid treatment program (OTP) or office-based opioid treatment (OBOT) program

History of past overdose

How would you describe his use of oxycodone/acetaminophen?

Poll: Case Study Mr. J

Mr. J a 72-year-old male with a history benign prostatic hypertrophy, hypertension, and osteoporosis. He was recently discharged after undergoing hip replacement surgery.

At discharge he was prescribed oxycodone/acetaminophen 1-2 tablets every 6 hours as needed for pain #56 (a 7-day supply). He calls the orthopedic clinic after 5 days asking for a “refill”. Upon questioning he reported that the medication was wearing off after 3-4 hours, so he started taking it 5 to 6 times per day (which he looked up on the internet that it can be prescribed every 4 hours).

- Legitimate medical use
- Abuse
- Misuse
- Diversion
- Dependence

How would you describe her use of oxycodone/acetaminophen?

Poll: Case Study Ms. Z

Ms. Z is a 68-year-old female with a history of osteoarthritis, breast cancer, and diabetes recently started complaining of right knee pain. She reports acetaminophen and ibuprofen “just were not cutting it.”

A neighbor offered her some oxycodone/acetaminophen that they had left over from a recent surgery. She has been using the oxycodone/acetaminophen 2 to 3 times daily with significant pain relief. She denies any history of substance use disorder.

- Legitimate medical use
- Abuse
- Misuse
- Diversion
- Dependence

Definitions

Abuse

One of the following over the last 12 months (*DSM-IV term*)

- Recurrent use resulting in failure to fulfill obligations (home, work); in physically hazardous situations; linked to legal problems; continued use despite social or interpersonal problems
- Purposely take medications for uses other than prescribed, doses greater than prescribed

Misuse

An Rx medication is taken incorrectly – too often, wrong dose, too long, or incorrect indication

Diversion

Transfer of a legally rx'd controlled medication to another individual

Dependence

(*DSM-IV term*)

Traditionally linked to physical dependence resulting in withdrawal when the medication is discontinued

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Legitimate medical use

Abuse – Ms. Z

Misuse

Diversion – neighbor

Dependence

Access and Diversion

Many older adults are prescribed opioids by doctors

Senior-living communities

- Sharing their prescriptions

Family members

Purchase on the internet

Those in the hospital or long-term care facility

- Diversion by staff

DSM-IV to DSM-5 Changes in Terminology

DSM-IV

- **Abuse** – 4 of the current combined “use” disorder criteria
- **Dependence** – 7 of the current combined “use” disorder criteria including tolerance and withdrawal

DSM-5 refers to all as a substance “use” disorder



✓ Use Disorder



Screening for an Opioid Use Disorder

Patient Scenario...

Screening for an Opioid Use Disorder

Mrs. P is a 67-year-old female with a past medical history of ankylosing spondylitis, COPD, and chronic pain.

Medications include: Methadone 10 mg – 2 tablets 3 times daily; oxycodone 10 mg every 3 hours PRN

In the past 4 months has requested fills early, so provider has switched to 7 and 14-day supplies UDS: + methadone, + morphine, + oxycodone

Interview between provider and patient to screen for an opioid use disorder; as you listen PLEASE NOTE how many questions the patient answers positively

Is taken in larger amounts or over a longer period than intended

There is a continued desire or unsuccessful efforts to “cut down” or control use

A large amount of time is spent attempting to obtain, use, or recover from the effects of opioids or heroin

Craving to use opioids or heroin

Recurrent use results in a failure to fulfill obligations at work, school, or home

Despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of substance; they continue to use

Important social, occupational, or recreational activities are given up or reduced because of the use of opioids or heroin

Substance use in situations in which it is physically hazardous.

Use of the substance is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.

Tolerance, as defined by either of the following:

- A need for markedly increased amounts of opioids or heroin to achieve intoxication or desired effect.
- Markedly diminished effect with continued use of the same amount.

Withdrawal, as manifested by either of the following:

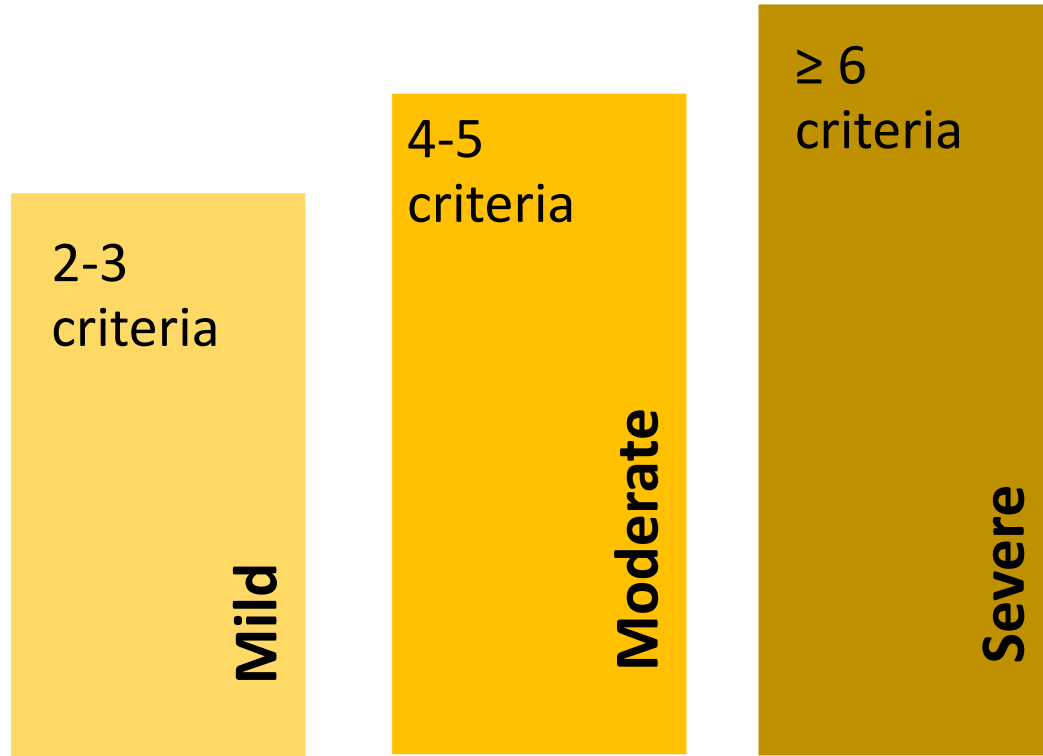
- Opioid withdrawal
- Taking an opioid (or a closely related one) to relieve or avoid withdrawal symptoms.

Regarding the opioid/heroin

DSM-5 Criteria



Severity of Opioid Use Disorder



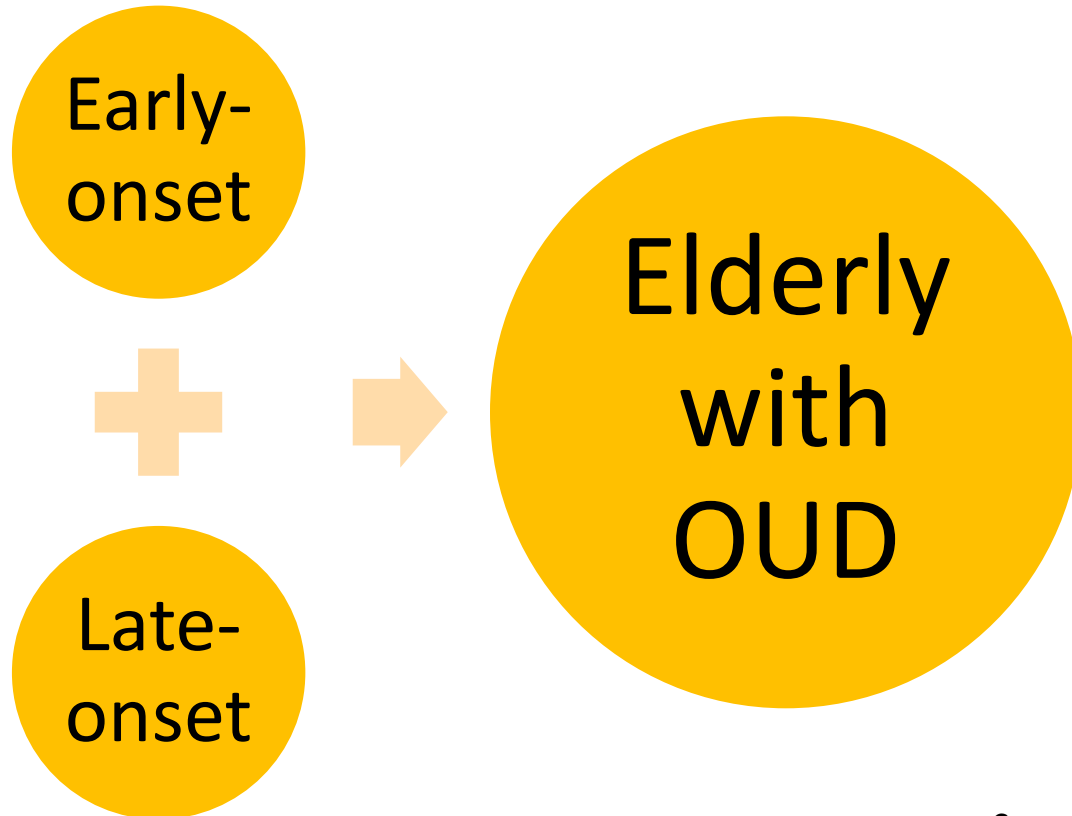
POLL

Based on how the patient answered the screening questions, how would you classify the severity of their Opioid Use Disorder?

- Mild
- Moderate
- Severe



Who Makes up the Older OUD Population?



Heroin

Rx opioid

Older adults more likely to use ETOH; less likely to use other illicit substances for both heroin and Rx opioids

For both – more likely to live in urban areas

Older adults (>55 yo) were more likely to be male, AA or Hispanic than < 55yo

IN & IV

Older adults (>55 yo) were more likely to be male, AA, less likely to be Hispanic than < 55yo

Oral > IN vs. < 55 yo

TEDS-A: Treatment Episode Data Set – Admissions
Huhn AS, et al. Drug Alcohol Depend 2018;193:142-7.

TEDS-A database

IN = intranasal
IV = intravenous

Case Scenario

Mr MA is a 62-year-old male with a history of benign prostatic hypertrophy, hypertension, and chronic pain. He has a history of cocaine use disorder back in his 20s-30s. He has been in “recovery” from cocaine use for over 25 years.

- In 2002 he had a work-related injury and experienced lower back pain
- For 15 years he was prescribed oxycodone/acetaminophen. He reports he only ever took the oxycodone/acetaminophen exactly as prescribed.
- In Nov 2017 his prescriber informed him he would no longer be prescribing him oxycodone/acetaminophen. No attempts to taper were made.
- Mr. MA found himself purchasing prescription opioids from neighbors and off the street. He switched to heroin (intranasal) in March 2018 because it helped with pain and was much cheaper.

Case Scenario Continued...

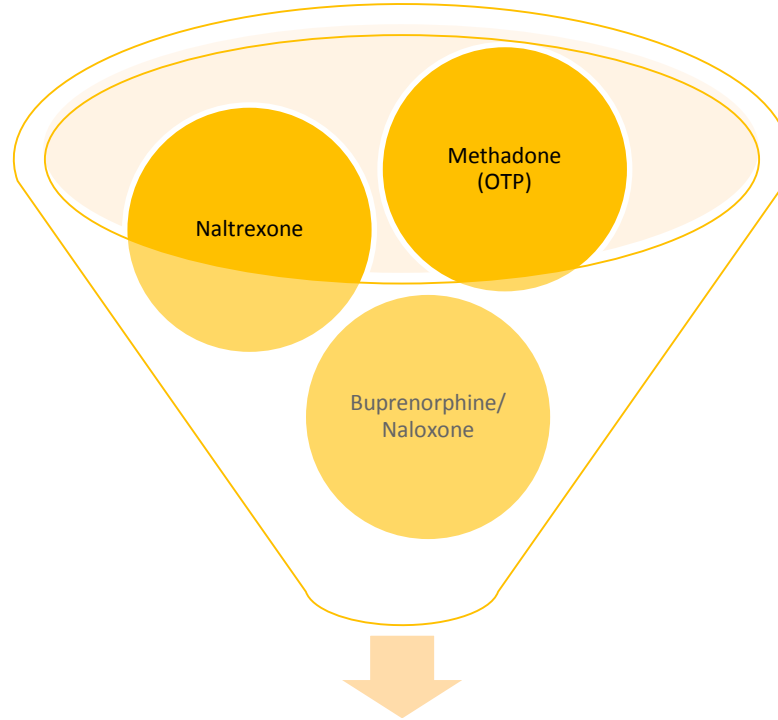
In May 2018 Mr. MA presents to the Substance Use Disorder Clinic because he is “Too old to mess with this stuff.” He reports he had no idea that he could become “addicted to his pain medications”

- Had he been screened with the opioid risk tool – He would have scored a 4 (moderate risk to develop future opioid abuse or an opioid use disorder)

What treatment options can we offer him?

Opioid Use Disorder Medication Assisted Therapy Treatment Options

Non-pharmacologic therapy:
Psychosocial Treatment

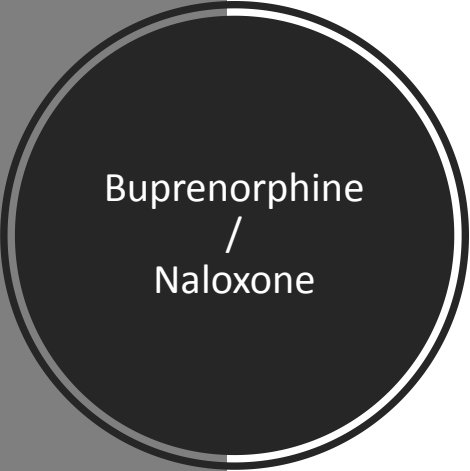


MAT = Medication
Assisted Therapy

Goal is abstinence from Opioid Use



MOA	Full opioid agonist
Access	Via Opioid Treatment Program (OTP) licensed facilities
Cost	Daily fee
Dosing	Day 1: 5-10 mg every 4 hours up to 40 mg OR 10-30 mg, followed by 10 mg 3-4 hours later Dose is titrated over 2 weeks
Usual range	60-120 mg per day
Monitoring	Urine drug screens, QTc prolongation, drug interactions



Buprenorphine
/
Naloxone

MOA	Partial opioid agonist/opioid antagonist (as an abuse deterrent)
Access	Outpatient by DATA waived providers only
Cost	Each prescription – 3/7/14/21/28 day supply
Dosing	Day 1: 2 to 8 mg of buprenorphine (max 8 mg) Day 2: day 1 dose + additional (max 16 mg)
Usual range	8-16 of buprenorphine daily [max usually 24 mg daily]
Monitoring	Urine Drug Screens, LFTs



Naltrexone

MOA	Opioid antagonist
Access	No restrictions on prescribing or dispensing
Cost	Each prescription/monthly
Dosing	Must be opioid free for 7-14 days prior to initiation Induction: 12.5-25 mg test dose; 25 mg 4 hours later Maintenance: 50 mg daily or can consider using 100 mg on Mondays and Wednesdays, and 150 mg on Fridays if the patient is abstinent from opioids and cooperative
Usual range	350 mg/week
Monitoring	Urine Drug Screens, LFTs

Geriatric Considerations with MAT Options

	Renal or Hepatic Dosage Adjustments	Drug Interactions	Other considerations
Naltrexone	No specific adjustments Metabolite is renally excreted; AUC is increased in 5-10 times in hepatic cirrhosis; not recommend in acute hepatitis or hepatic failure	Opioids	
Buprenorphine/ Naloxone	No specific recommendations	Opioids, CNS depressants, Benzodiazepines, QTc prolongation	
Methadone	If renal function CrCl < 10 mL/min administer 50-75% of dose No hepatic adjustments; start lower, titrate slower	QTc prolongation, CYP3A4 inducers/inhibitors, benzodiazepines	QTc prolongation Long half-life Central sleep apnea

MAT Comparison

Medication	% opioid free on active medication	% opioid free on placebo	Citations
Naltrexone ER	36	23	Krupitsky et al. 2011
Buprenorphine/ Naloxone	20-50	6	Fudala et al. 2008, Weiss et al. 2011
Buprenorphine/ Naloxone	60	20	Woody et al. 2008
Methadone	60	30	Mattick 3t al. 2009

Long-acting Options

Medication	Route of Administration	Frequency	Other Considerations
Buprenorphine	Subcutaneous	Every 4 weeks	
Buprenorphine	Implant	Every 6 months	Must be on ≤ 8 mg of buprenorphine daily
Naltrexone	Intramuscular	Every 4 weeks	

Back to Mr. MA

Mr. MA met the criteria for OUD - severe

Decision is made to start him on Buprenorphine/naloxone

To initiate, he must be in moderate opioid withdrawal; his Clinical Opioid Withdrawal Scale (COWS) today is 14

- Received 4 mg/1 mg of buprenorphine/naloxone with minor improvement
- Received a second dose 4 mg/1 mg of buprenorphine/naloxone
- Day 2 of induction dose was increased to 8 mg/2 mg buprenorphine/naloxone 2 films SL daily

Scoring:

- Mild: 5-12
- Moderate: 13-24
- Mod/Severe: 25-36
- Severe: >36

COWS screens for:

1. Pulse rate

2. Sweating

3. Restlessness

4. Pupil size

5. Bone/joint aches

6. Runny nose or tearing

7. GI upset

8. Tremor

9. Yawning



10. Anxiety/Irritability

11. Gooseflesh Skin

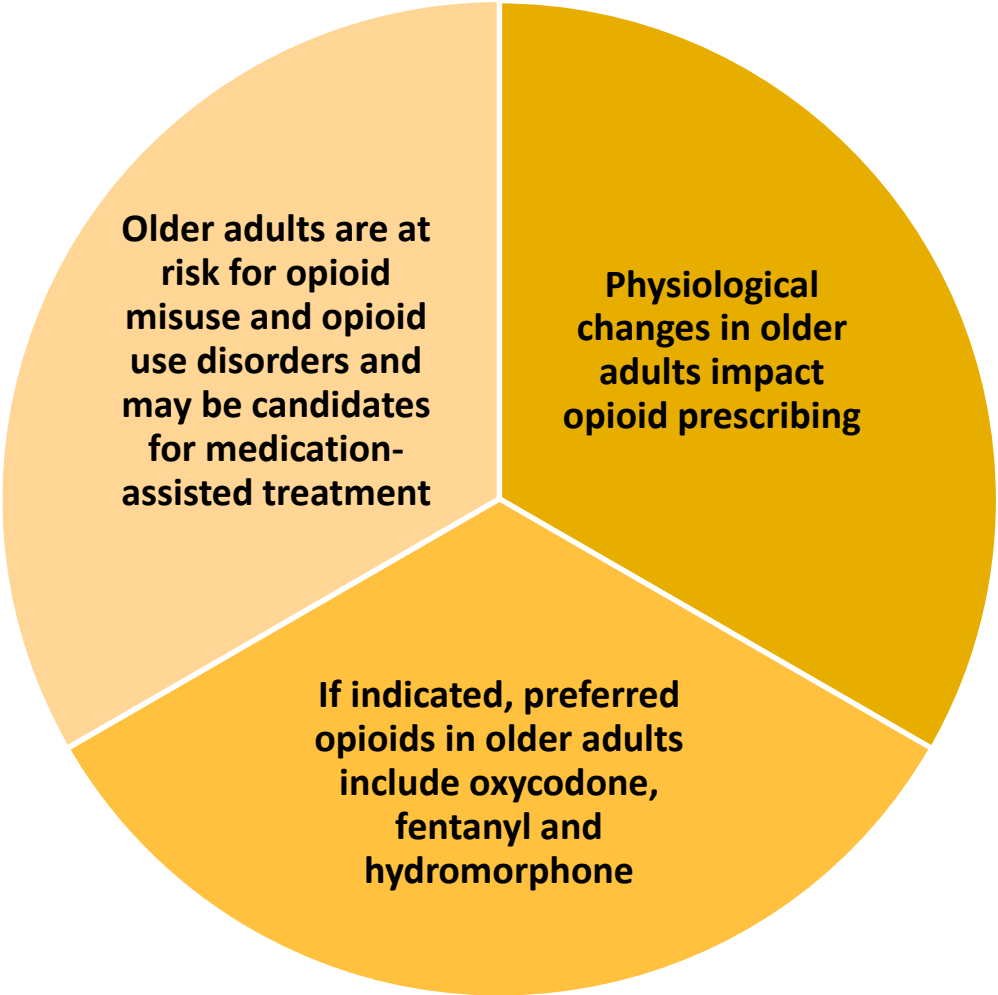
Back to Mr. MA

- Has been maintained on 16 mg of buprenorphine (as combo product) for over 5 months
- Attends narcotics anonymous weekly at his local church and one group per week at our clinic.
- Urine drug screens (UDS) consistently negative for any opioids or morphine metabolites
- Occasionally UDS positive for marijuana (states it helps with his pain)





Take Home Points



Older adults are at risk for opioid misuse and opioid use disorders and may be candidates for medication-assisted treatment

Physiological changes in older adults impact opioid prescribing

If indicated, preferred opioids in older adults include oxycodone, fentanyl and hydromorphone