Opioids in the Elderly

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Disclosure

- I have no financial relationships or conflicts of interest to disclose.

The Cost of Pain

- 100M people have persistent pain in US
- Total cost of $560-635 Billion/year
- Opioid-related ADEs resulted in an increased length of stay (by 3.3 days), greater risk of re-admission, increased cost of $4,700 compared to cases without the opioid-related ADE's
- Estimated that 29% of preventable ADEs are caused by analgesics, with morphine being the most common

The National Sciences Academies of Sciences, Engineering, Medicine (NASEM) 2017
Bates DW, et al. JAMA. 1997;277:307–11; Oderda G, et al. J Pain Palliat Care Pharmacother 2013;27:62-70; Kane-Gill SL, et al. J Pain Palliat Care Pharmacother 2014;28(3):282-93

Pain in the Elderly

- Opioid prescribing highest in elderly (26.8%)
- 27% of elderly have chronic pain (65-84 yrs)
- 33.6% of eldest have chronic pain (>85 yrs)
- Often unable to perform ADLs , maintain independent living , less mobility, poor cognitive function and a higher level of disability

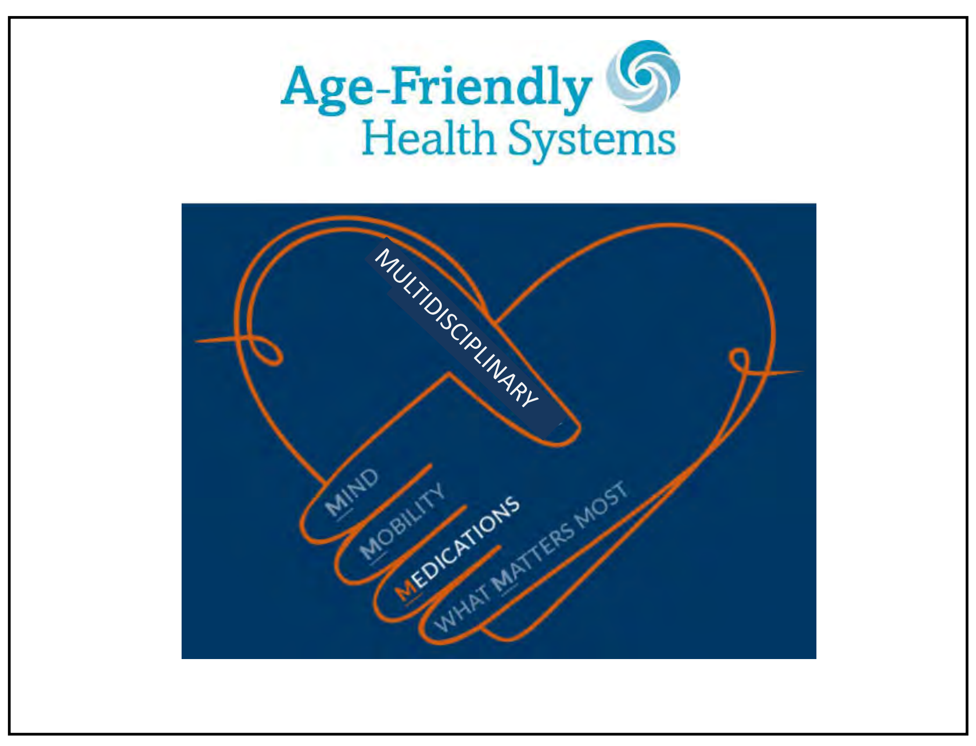
Gazelka H, et al. Concise review for clinicians| Volume 95, ISSUE 4, P793-800, April 01, 2020

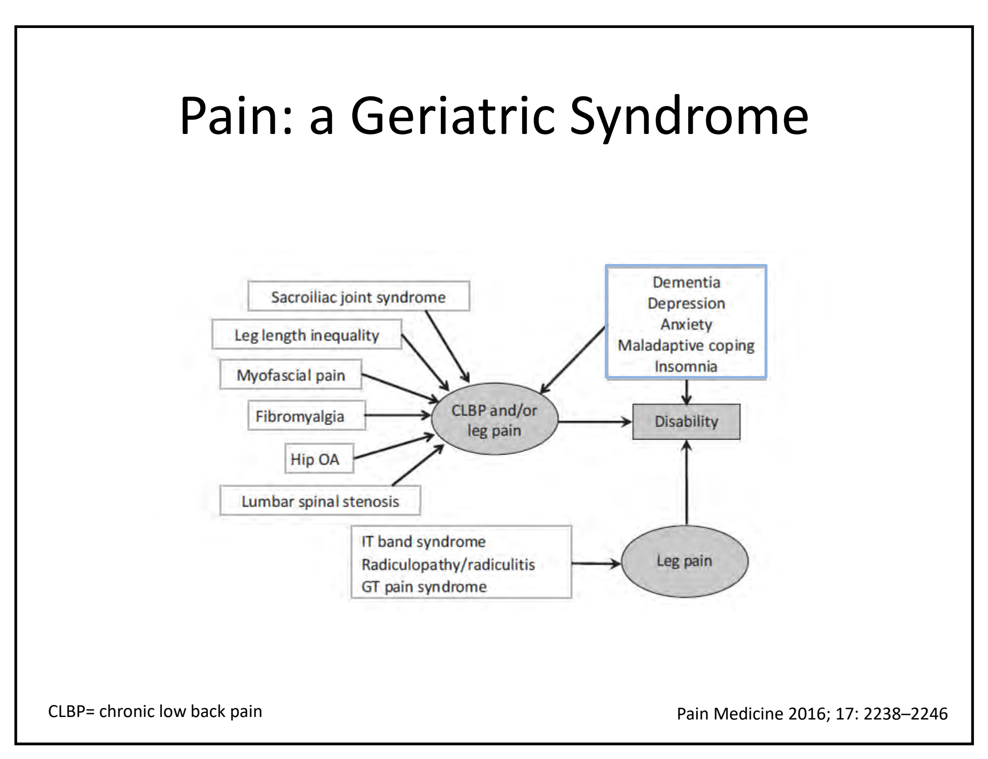
Agenda

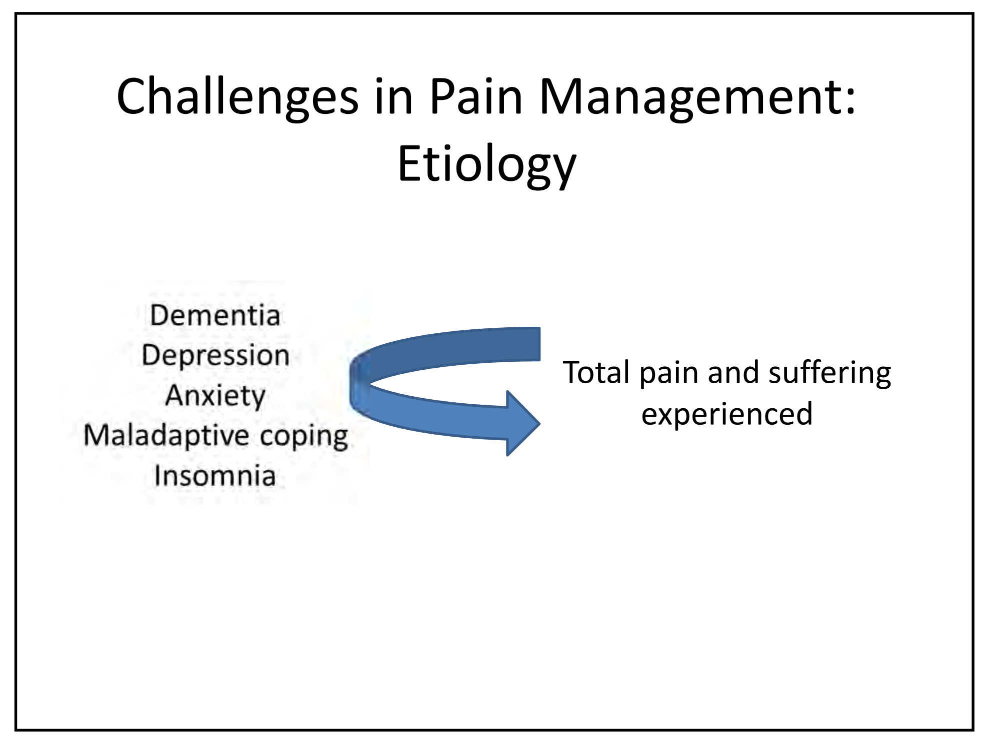
- Review pain management in general
  - Understand opioids' place in therapy for older adults
- Provide screening and monitoring guidelines to ensure safe management of opioids
- Highlight issues unique to opioid management in the older adult
- Apply recommendations to specific patient cases

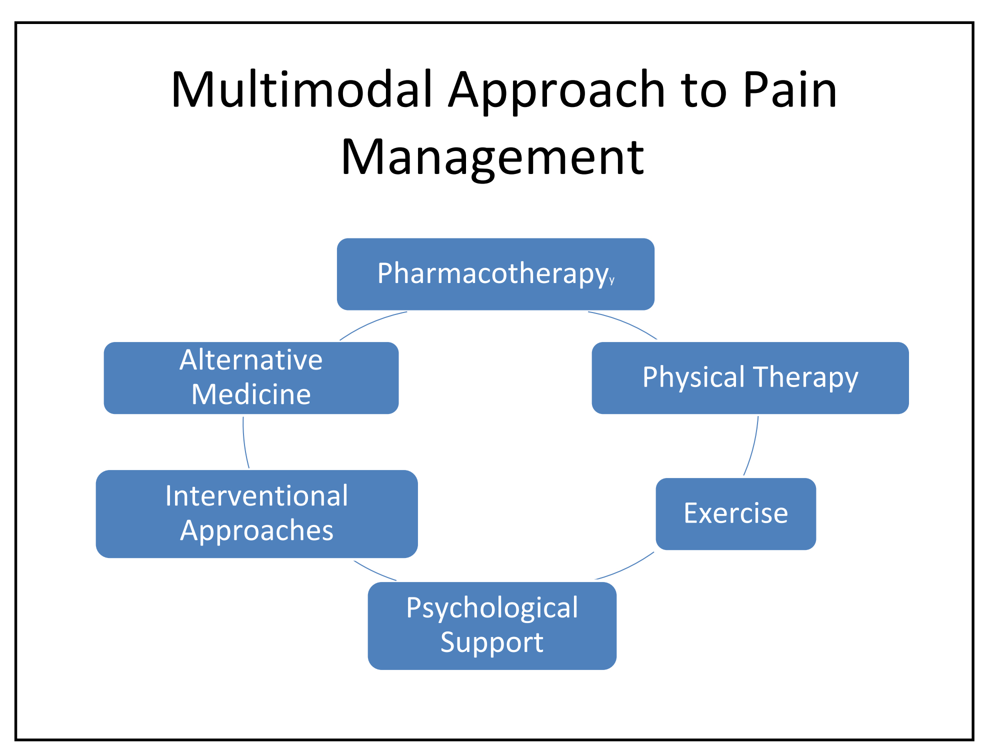
In which of the following cases would you feel comfortable prescribing opioids?

A. A 78 yo in hospice care for terminal lung cancer
B. A 68 yo with a history of depression, anxiety, and chronic pain , and a UTOX positive for cocaine, opioids, and benzodiazepines (prescribed)
C. A 66 yo who as hepatocellular carcinoma, recently enrolled in palliative care, with a comorbid severe alcohol use disorder
D. A 90 yo with chronic back, a neurocognitive disorder, and a history of falls
E. A 80 yo with severe lumbar stenosis with a family caregiver with an opioid use disorder


Age-Friendly
Health Systems
MULTIDISCIPLINARY
MIND
MOBILITY
MEDICATIONS
WHAT MATTERS MOST


Pain: a Geriatric Syndrome
Sacroiliac joint syndrome
Leg length inequality
Myofascial pain
Fibromyalgia
Hip OA
Lumbar spinal stenosis
CLBP and/or leg pain
Dementia
Depression
Anxiety
Maladaptive coping
Insomnia
Disability
IT band syndrome
Radiculopathy/radiculitis
GT pain syndrome
Leg pain
CLBP= chronic low back pain
Pain Medicine 2016; 17: 2238–2246


Challenges in Pain Management: Etiology
Dementia
Depression
Anxiety
Maladaptive coping
Insomnia
Total pain and suffering experienced


Multimodal Approach to Pain Management
Pharmacotherapy
Physical Therapy
Exercise
Psychological Support
Interventional Approaches
Alternative Medicine

Chronic Low Back Pain (LBP)

- American College of Physicians (2017) supports nonpharmacological interventions as first line for LBP
- Chronic LBP as a mixed pain syndrome
- The reported prevalence of LBP with a neuropathic component has been shown to range from 20% to up to 55%
- Combinations with NSAID or opioids demonstrate significant improvements

Shanthanna H, et al. PLoS Med. 2017; 14(8): e1002369; Morlion B. Curr Med Res Opinion. 2011;27 (1): 11-33.

Role of Multimodal Analgesia

- Using combinations of analgesics in lower doses offers broad coverage for the complex mechanisms of pain pathophysiology
- Using more options at lower doses or safer combinations reduces medication-related adverse effects
- Opioid-sparing – using other modalities, both pharm and nonpharmacological reduces or eliminates opioid requirements

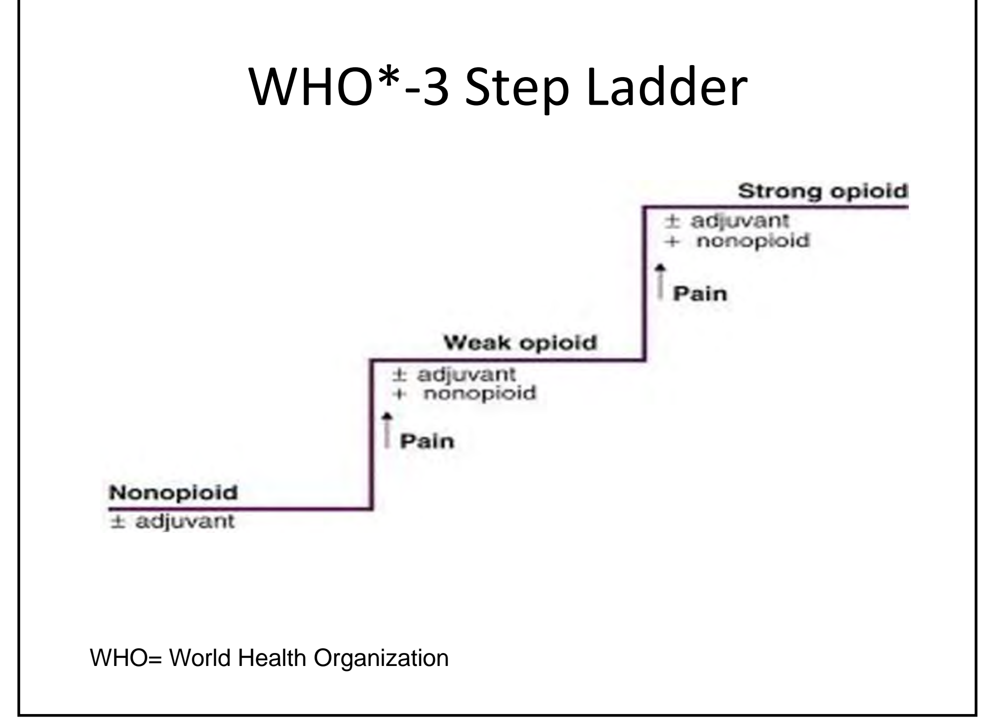
Multimodal Analgesia

- Total joint arthroplasty (1,540,462 surgeries, knee and hip)
- Compared opioid only vs. opioid +1 additional mode, opioid + 2 additional modes, opioid + > 2 additional modes
- Less frequent use of patient-controlled analgesia (PCA) with increasing modes (27.1% vs 19.1%, 12.6%, 6.1%)
- The "opioid only" group had the longest length and cost of hospitalization. This also decreased gradually with an increasing number of modes of analgesic options used
- NSAIDs were the most effective modalities
- Adding analgesic modes (vs. opioid only) resulted in:
  - 19% fewer respiratory complications (OR 0.81)*
  - 26% fewer GI complications (OR 0.74)*
  - Up to 18.5% less opioid use
  - 12.1% decrease in length of stay*

*$p<0.05$

Memtsoudis SG, et al. Anesthesiology 2018;128:891-902

WHO*-3 Step Ladder



WHO= World Health Organization

Acetaminophen – not so Lame

- Inhibits central prostaglandin synthesis without affecting peripheral prostaglandin synthesis
- Additive analgesia with opioids
- Oral = IV in efficacy
- Single doses provided 4 hours of at least 50% relief in 37% of patients with post-operative pain
- Reduced opioid consumption by 30% in first 4 hours
- No reduction in opioid-related adverse effects
- > 1 dose of 1000mg (IV or PO) showed anywhere from 6-10% reduction in opioid use

Hickman SR, et al Am J Health Syst Pharm 2018 Mar 15;75(6):367-75 McNicol ED, et al. Br. J Anaesth. 2011; 106(6):764-75. Stundner O, et al. Reg Anesth Pain Med 2019;44:565-72.

The United States Opioid Epidemic

The opioid crisis can be traced back to the 1990s:

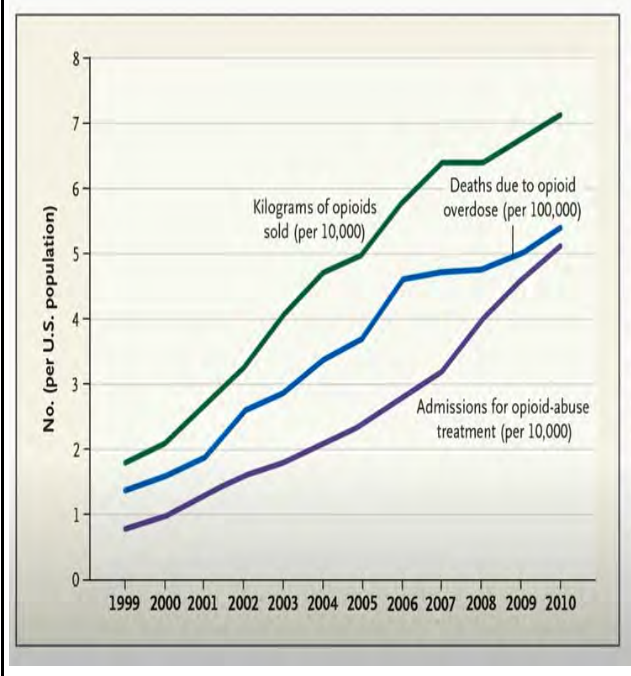
- Drug manufacturers heavily marketed opioids for chronic pain
- Reassured the public that opioids were not addictive

2016-2018 Statistics

- ~130 people die daily from an opioid overdose
- 11.4 million people misused Rx opioids
- ~ 2.1 million Americans were diagnosed with opioid use disorder (OUD)

- In 2017, the HHS declared a national emergency in regards to the opioid crisis

United States Department of Health and Human Services. (https://www.hhs.gov/opioids/).



Opioid Sales, Admissions for Opioid-Abuse Treatment, and Deaths Due to Opioid Overdose in the United States, 1999–2010.

Data are from the National Vital Statistics System of the Centers for Disease Control and Prevention, the Treatment Episode Data Set of the Substance Abuse and Mental Health Services Administration, and the Automation of Reports and Consolidated Orders System of the Drug Enforcement Administration.

DEA Increases Restrictions to Opioid Prescribing

- **2014**: Hydrocodone-containing products reclassified from Schedule III to Schedule II
- **2014**: Tramadol placed in Schedule IV
- **2018**: Emergency rules propagated to place fentanyl analogues in Schedule I
- **2018**: Proposal to set annual opioid production limits for oxycodone, hydrocodone, oxymorphone, hydromorphone, morphine and fentanyl

21 C.F.R. § 1308 (2018). United States Drug Enforcement Administration. (https://www.dea.gov

CDC Prescribing Opioids for Pain Guidelines

- The CDC introduced national chronic pain guidelines in 2016, which set national standards for opioid prescribing.
- Explicitly states that opioids are NOT first-line therapy for chronic pain
- Recommends limiting acute pain opioid Rx to 3-7 day supplies
- Recommends safe quantities and durations of long-term opioid therapy

Bottom line: National efforts to curb opioid prescribing have made opioids more difficult to obtain for recreational use.

Centers for Disease Control and Prevention. (https://www.cdc.gov/drugoverdose/pdf/Guidelines_Factsheet-a.pdf).

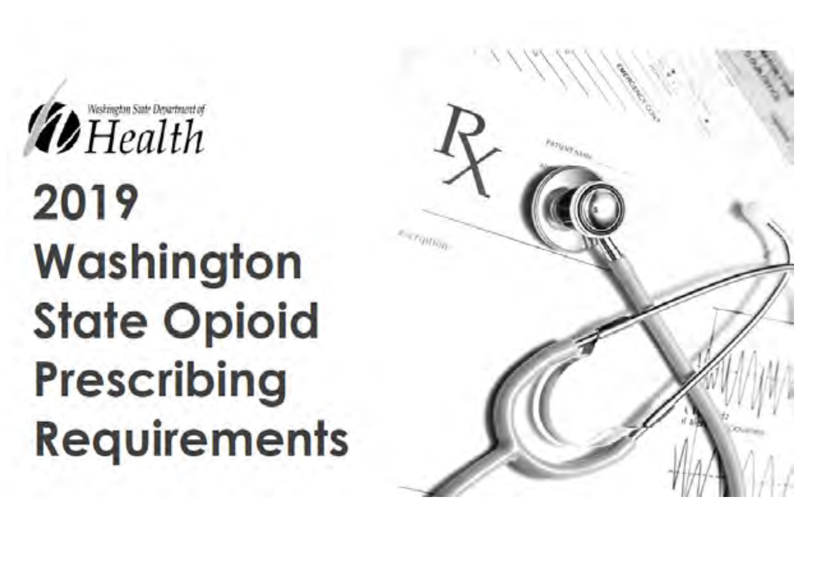
Have we actually decreased opioid prescriptions?

- ~40% of patients who do not take opioids within 24 hours of discharge still go home with an opioid prescription
- Who is doing the prescribing?
- Systems-level challenges

Chen EY, et al. JAMA Surg. 2018 Feb; 153(2): e174859. ; 59(10); 1-3.

Provider's barriers to mitigating risk

- Productivity demands
- Limited access to resources
- Inconsistencies among providers (opioids a polarizing topic)
- OUD underreported and undertreated



2019 Opioid Prescribing Rules: www.doh.wa.gov/opioidprescribing

Opioid Rules for Ambulatory Care

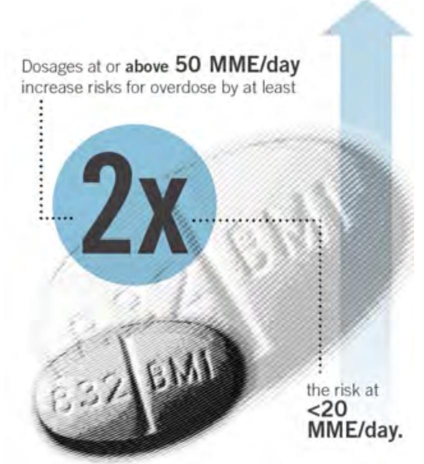
- Apply to ALL pain
  - Except active cancer/palliative care; excludes inpatient and procedural
- Prescription Monitoring Program (PMP)
  - All prescribers must register and PMP must be checked for every Rx
- Risk screening
  - For severe pain, respiratory depression/overdose, opioid use disorder
  - Follow-up visits and naloxone Rx based on risk
- Patient notification
  - Education about risks, safe use, storage and disposal
- Alternatives to opioids
  - Multimodal approach = Better pain management

Mitigating Risk: Limiting opioid quantities

Acute Pain (0-6 weeks)	**Subacute Pain (6-12 weeks)**	**Chronic Pain (>12 weeks)**
Maximal duration of prescription (without documented rationale): 7 days 14 days post-op pain	Maximal duration of prescription (without documented rationale): 14 days	Mandatory pain consult if over 120 MEDs Complete written agreement for treatment

MED – Morphine Equivalent Dose
MME – Morphine Milligram Equivalents

Mitigating Risk: Calculating MME



Improve Safety

- Higher doses associated with higher risk of side effects, overdose and death
- Potentially similar pain relief and function with lower MME
- Helps stratify patient risk

https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf

Calculating MME

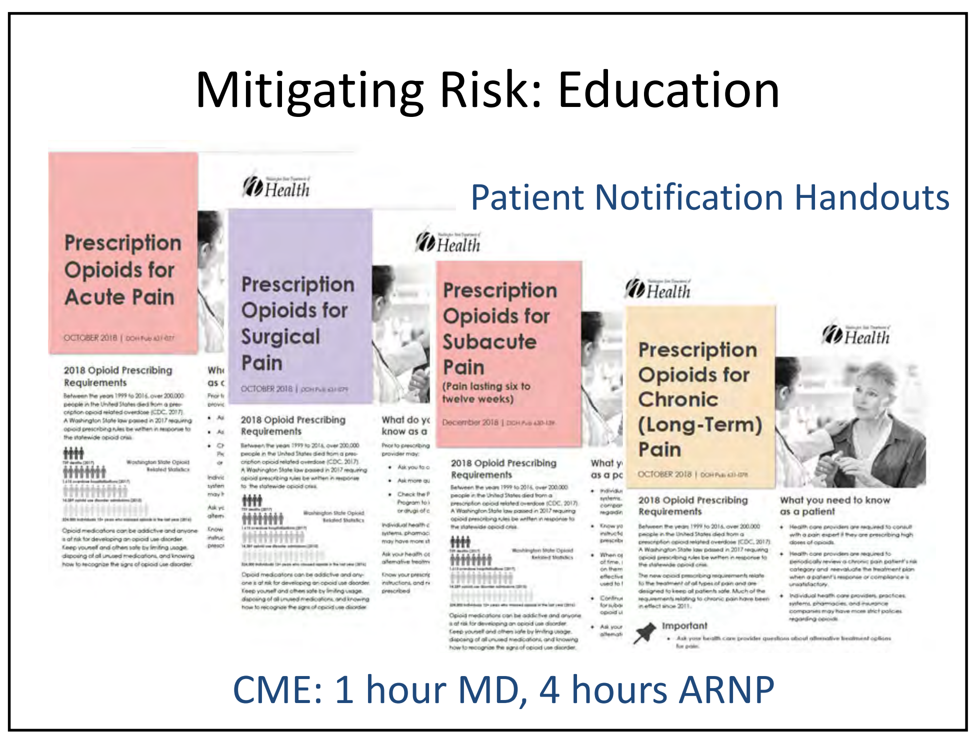
OPIOID (doses in mg/day except where noted)	CONVERSION FACTOR
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

- Pain consult when MME >120
- Provide naloxone when

  MME >90 for MD

  MME > 50 for ARNPs

https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf



Mitigating Risk: Screening Patients

- Avoid prescribing to patients with moderate or severe sleep apnea
- Ensure treatment for depression is optimized
  - Opioids may transiently improve mood but not sustained
  - Help to avoid potential Opioid Use Disorder (OUD)
- Avoid concurrent CNS medications
- Use additional caution with renal or hepatic insufficiency, or with patients ≥ 65y

Stratify Risk and Reevaluate

- Reevaluate within 1-4 weeks of starting long-term therapy
- Chronic pain: review quarterly (high-risk patients), semiannually (moderate-risk), annually (low-risk)
- UTOX – frequency based on risk
- Work with patients to taper opioids down or off when
  - Opioid dosage ≥ 50 MME/day without evidence of benefit
  - Concurrent benzodiazepines that can't be tapered off
  - Patients experiencing overdose, other serious adverse/warning signs

UTOX

86 yo community dwelling patient returning to clinic today. She is on chronic oxycodone 10mg TID for lumbar stenosis.

UTOX today comes back negative.

Why? What are your next steps?

Pt states she ran out of oxycodone 4 days ago.
Re-evaluate narcotic need and possibly deprescribe.

Caregiver/family member is not giving oxycodone to the pt.
Evaluate living situation. May need to possibly switch to a non-opioid agent.

She is selling it to supplement her income.

TABLE 2. **Length of Time Drugs of Abuse Can Be Detected in Urine**

Drug	Time
Alcohol	7-12 h
Amphetamine	48 h
Methamphetamine	48 h
Barbiturate	
Short-acting (eg, pentobarbital)	24 h
Long-acting (eg, phenobarbital)	3 wk
Benzodiazepine	
Short-acting (eg, lorazepam)	3 d
Long-acting (eg, diazepam)	30 d
Cocaine metabolites	2-4 d
Marijuana	
Single use	3 d
Moderate use (4 times/wk)	5-7 d
Daily use	10-15 d
Long-term heavy smoker	>30 d
Opioids	
Codeine	48 h
Heroin (morphine)	48 h
Hydromorphone	2-4 d
Methadone	3 d
Morphine	48-72 h
Oxycodone	2-4 d
Propoxyphene	6-48 h
Phencyclidine	8 d

Mayo Clin Proc. • January 2008;83(1):66-76

Mitigating Risk: Reminders

Opioid Safe Storage & Disposal

Only take opioids if you have strong pain that does not lessen by other methods.

Do not share your medications with others. Do not sell your medication.

Keep your medication in a safe place away from children and pets.

Discard expired or unused medication by taking it to a safe disposal location which can be found at www.takebackyourmeds.org

Naloxone is a prescription medicine that temporarily reverses an opioid overdose. In the state of Washington you can get naloxone without a prescription from any pharmacy. Cost may vary.

Allergies to Narcotics

79 yo male pt involved in a MVA and sustained a broken arm and ribs. He is allergic to morphine (severe hives).

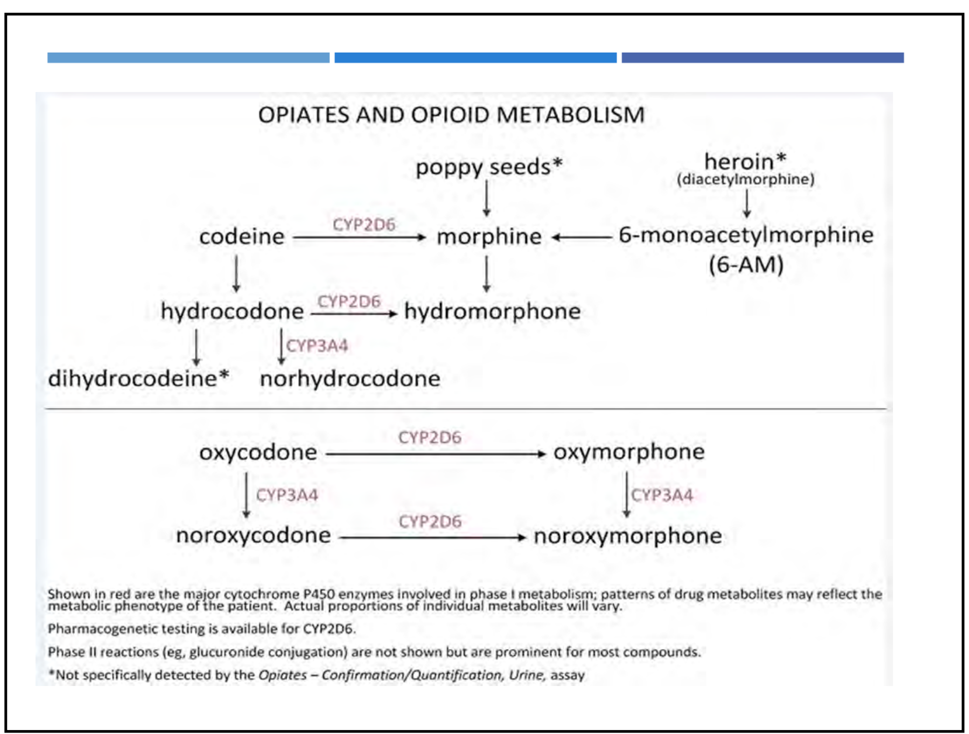
What narcotic would you recommend?

Morphine. Allergy was reported a long time ago

Oxycodone

Hydrocodone

Fentanyl Patch



Considerations in the Elderly

- More affordable then alternative options
- Invasive/surgery not advised
- Other medications not options- NSAIDs/CNS meds
- Low risk of end-organ damage (GI, renal, hepatic, CV)
- Decreases disability
- Increased quality of life (QOL)

- Increased risk of falls/fractures, delirium
- Exacerbates comorbidities (constipation, urinary retention, cognitive impairment)
- Polypharmacy
- Potential target of elder abuse
- Possible risk of substance use disorder (SUD)
- Decrease QOL

Opioid Selection, Dosage, Duration, Follow Up and Discontinuation

Prescribing Opioids

- Administer regularly; use or titrate to desired lowest effective dose
  * Avoid extended release formulations when starting treatment
- Document baseline status
- Assess in ~ 3 days for tolerability
- Assess over ~1-4 weeks for benefit in pain/function
  - If benefits and tolerated → Continue
  - If no benefits or not adequately tolerated → taper and discontinue

Establish and Measure Progress

- Establish realistic treatment goals for pain and function
- Assess and document progress using 3-item PEG Assessment Scale*
  - Pain average (0-10)
  - Interference with Enjoyment of Life (1-10)
  - Interference with General Activity (0-10)

Age-Related Changes affecting Pain Management

- Pharmacokinetic changes
  - Decreased renal function
  - Decreased liver mass and hepatic blood flow
  - Changes to distribution
- Pharmacodynamic changes
  - Increased sensitivity at μ-opioid receptors
  - Decrease in integrity of GI mucosa and its defense mechanism

Mr. B is a 73 yo patient with refractory multiple myeloma and chronic tumor related pain.

Prolonged hospital stay for back pain following a mechanical fall.

SCr elevated at 1.8 but almost back to baseline when discharged.

Discharged to SNF on morphine ER 60mg q 12h and morphine IR 15mg q4h prn.

What changes would you make to pain regimen?

Nothing, this might be this patient's baseline

Reduce dose and /or decrease frequency of morphine

Consider changing to an agent less likely to accumulate in renal dysfunction

Opioid Metabolism Summary

	Morphine	Hydromorphone	Oxycodone	Fentanyl	Methadone
Use in CRI	Caution	Caution-dose reduce	Caution-dose reduce	Yes	Yes
Analgesically active metabolites	Yes	No	Yes	No	No
Neuro-excitatory active metabolites	Yes	Yes	No	No	No

Prescribing Opioids: Opioid Conversion

Opioid	P0	IV
Morphine	30	10
Oxycodone	20	-
Hydromorphone	7.5	1.5
Hydrocodone	30	-
Tramadol	100	-

Fentanyl 25mcg/hr = Morphine 50mg/day

Dosing Pearl: when switching opioids, start new opioid at 50-75 % of equivalent dose d/t incomplete cross tolerance

www.aahpm.org

Tolerance

Which of the following will NOT develop tolerance to opioids?

- o Nausea and Vomiting
- o Constipation
- o Sedation
- o Confusion
- o Respiratory Depression

Tramadol: not a true opioid

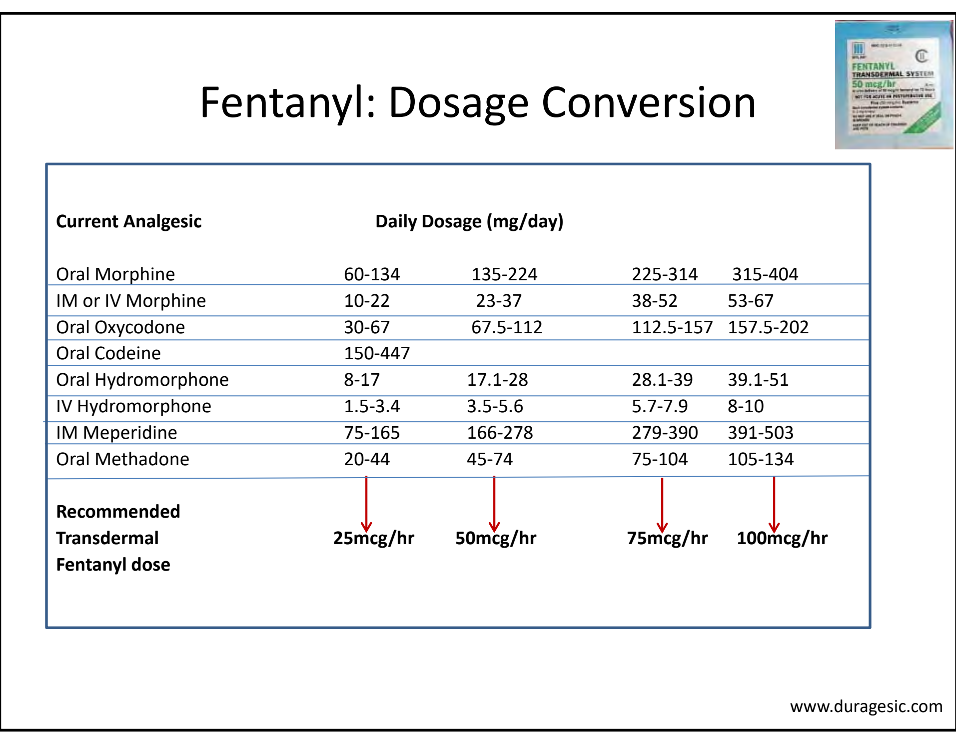
- Weak μ- receptor agonist and SNRI inhibitor
- Use for mild to moderate pain- 10% as potent as morphine
- Lowers seizure threshold (contraindicated)
- S/e include appetite loss, constipation, nausea, dizziness, drowsiness
- Active metabolite renally excreted
- Dosed: (25mg) 50mg QID. Max 300mg/d in elderly

Fentanyl: Use in the Elderly

- Transdermal Fentanyl not indicated for patients with acute or post-surgical or intermittent pain
- Use in opioid tolerant patients only!
  - Morphine 60mg/day, oxycodone 30mg/day, hydromorphone 8mg/day for at least a week
- Absorbs into skeletal muscle and fat
  - Avoid in cachetic patient due to inadequate absorption

Fentanyl Dosing

- Takes 12-18 hours for pt to feel pain relief
  - Continue oral narcotics to cover this time frame
- Takes 20 hours for 50% of drug to leave the body
  - Start long acting opioids at least 12 hour after patch removed (at 50% of dose, 100% of dose after 24 hours)
  - continue short acting prn breakthrough opioids
- Allow 9 or more days prior to dose increase
- Heat increases absorption
- Don’t cut patch



Fentanyl: Dosage Conversion

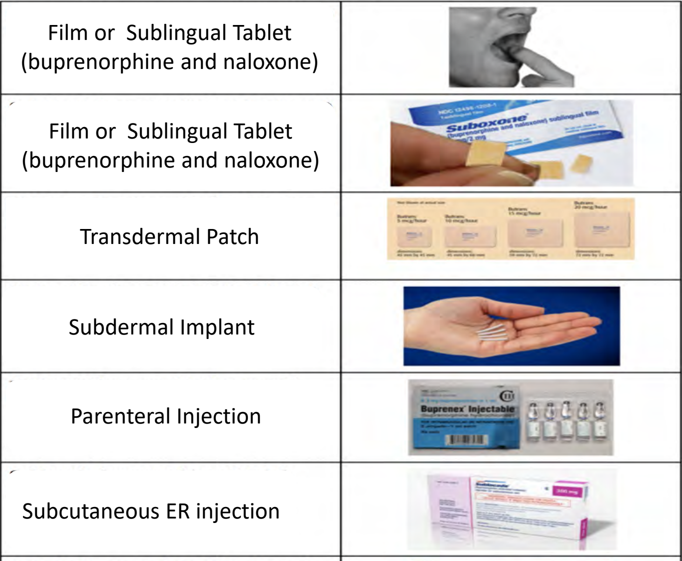
Current Analgesic	Daily Dosage (mg/day)			
Oral Morphine	60-134	135-224	225-314	315-404
IM or IV Morphine	10-22	23-37	38-52	53-67
Oral Oxycodone	30-67	67.5-112	112.5-157	157.5-202
Oral Codeine	150-447			
Oral Hydromorphone	8-17	17.1-28	28.1-39	39.1-51
IV Hydromorphone	1.5-3.4	3.5-5.6	5.7-7.9	8-10
IM Meperidine	75-165	166-278	279-390	391-503
Oral Methadone	20-44	45-74	75-104	105-134
Recommended Transdermal Fentanyl dose	**25mcg/hr**	**50mcg/hr**	**75mcg/hr**	**100mcg/hr**

www.duragesic.com

Buprenorphine

- For mild to moderate pain relief
- High affinity agonist for mu opioid receptor and antagonist at kappa-opioid receptor
- Long duration of action
- Less "potent" than full agonists due to ceiling effect
  - Lower risk of respiratory depression, no increased analgesia at higher doses, less constipation, less sedation
- Metabolites – Norbuprenorphine does not cross blood brain barrier

Buprenorphine : Multiple Formulations
C-III designation



Film or Sublingual Tablet (buprenorphine and naloxone)	
Film or Sublingual Tablet (buprenorphine and naloxone)	
Transdermal Patch	
Subdermal Implant	
Parenteral Injection	
Subcutaneous ER injection	

Buprenorphine: Use in the Elderly

- Less cognitive dysfunction than other opioids
  - Less impairment with driving when compared with equal doses of morphine
  - Less psychomotor adverse effects than fentanyl (comparable to placebo)
- Several studies have shown benefit in elderly- with improved pain, sleep and QOL
- Pharmacokinetics not altered with age, no dosage adjustments needed
- Only opioid not associated with fracture risk

1. Giacomuzzi S et al. Driving impairment on buprenorphine and slow release oral morphine in drug-dependent patients. Forensic Sci In. 2005
2. Davis, M. P. (2012). "Twelve reasons for considering buprenorphine as a frontline analgesic in the management of pain." J Support Oncol 10(6): 209-219
3. Pergolizzi J, et al. Opioids and the management of chronic severe pain in the elderly: consensus statement of an international Expert Panel with focus on the six clinically most often used World Health Organization Step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). Pain Pract. 2008

3 out of 5 older adults take painkillers Regularly

>30% of all Medicare Part D participants received a opioid Rx in 2016

1 in 5 older adults take a CNS medication

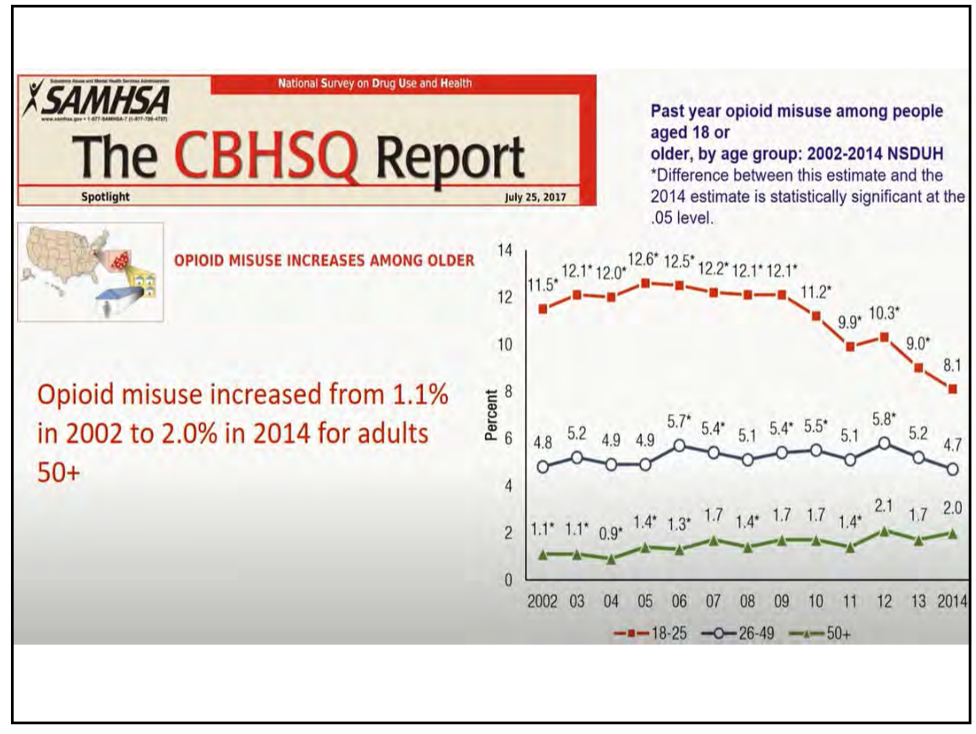
11% take a benzodiazepine

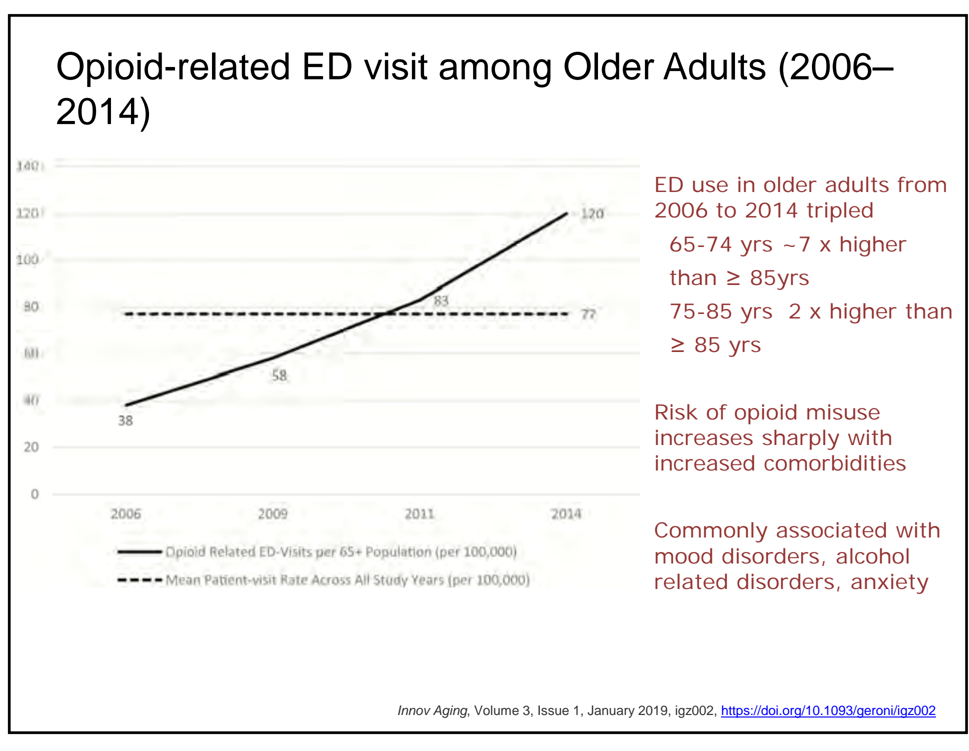
~ 50% of older adults consume alcohol

53% of older drinkers have harmful/hazardous drinking patterns when accounting for comorbidities

Increased substance/drug exposure increases risk for Substance Use Disorder (SUD)

Health in Aging.org July 2020. Carter MW et al. Innovations in Aging. 2019; 1: 1-13.





Red Flags Suggestive of Substance Use Disorder (SUD)

Patterns/behavior suggestive of possible SUD:

- Patient appears sedated, confused, or intoxicated
- Patient reports taking one large bolus daily instead of BID, TID etc. or needing higher doses
- Early request for refills
- Multiple scripts from different providers

Wolters Kluwer. (https://www.wolterskluwercidi.com/blog/watch-these-red-flags-when-prescribing-or-dispesing -controlled-substances/).

Alternative Drugs of Abuse

- There has been a rise in reports of misuse of the following non-scheduled prescription and OTC drugs in recent years. Opioid restrictions may have contributed to this rise.

Prescription	Over-the-Counter
• Gabapentin • Bupropion • Quetiapine • Albuterol • Olanzapine • Venlafaxine	• Loperamide • Dextromethorphan • Promethazine

- Non-scheduled drugs are typically not monitored by state prescription drug monitoring programs, nor are they routinely detected by urine drug screens.

ClinCalc. (http://clincalc.com/). Schifano F, et al. Brain Res. 2018;8:73

Opioid Use Disorder Treatment

- CDC recommends clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies)
  - Buprenorphine or Methadone maintenance through an office-based treatment provider or an opioid treatment program specialist
  - Oral or long-acting injectable formulations of naloxone (for highly motivated non-pregnant adults)

SBIRT

SBIRT stand for Screening, Brief Intervention, and Referral to Treatment.

Purpose: a practice model to identify early signs of drug and alcohol misuse and referral to brief therapy to prevent progression to dependence and abuse.

General Model:

SCREENING	BRIEF INTERVENTION	REFERRAL TO TREATMENT
Provider assesses patient for risky substance use behavior	Provider converses with patient, provides feedback and advice	Provider refers patient to brief therapy or additional treatment as necessary

McHugh RK, et al. Psychiatr Clin North Am. 2011;33:511-25

Opioid Summary

- Opioids are not 1st line therapy for pain
- Establish an explicit, multimodal plan for management
  - Encompassing realistic expectation about pain intensity and function and patient's responsibility for management
  - Reviewing benefits and harms of opioids
- Monitor progress
  - Include monitoring for potential harms
  - Attempt to deprescribe if appropriate

“ More than 90% of patients are willing to stop a medication if their doctor says it is possible”

Reeve E, Wolff JL, Skehan M, Bayliss EA, Hilmer SN, Boyd CM (2018) “Assessment of attitudes toward deprescribing in older Medicare beneficiaries in the United states.” JAMA Internal Medicine; Published online 15 Oct 2018