Chronic Pain: Guiding Principles and Treatment in the Setting of Advancing Age and Frailty

Nicole Gise, MD

Assistant Professor

Geriatrics and Palliative Care

Director of Outpatient Palliative Care Program

Highland Hospital

University of Rochester Medical Center

MEDICINE *of* THE HIGHEST ORDER

UR MEDICINE | HIGHLAND HOSPITAL

Financial Relationships of Planners, Presenters and Others

The following planners, presenters and others have either indicated financial relationships with ineligible companies or that no financial relationships exist.
An *ineligible company* is any entity whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.
ACCME Standards for Integrity and Independence in Accredited Continuing Education

The following planners/presenters/others have disclosed financial relationships:	
Role: Name	**Financial Relationships** If financial relationships exist, include the name of the ineligible company and the nature of the relationship(s).
☐ *All of the relevant financial relationship(s) listed have been mitigated.*	

The following planners/presenters/others do not have any relevant financial relationships with ineligible companies:	
Role in CME Activity	**Names**
Presenters	Nicole Gise, MD

Commercial support for this activity *(Include the name of the ineligible company and nature of the support OR check the box "None")*
X None

Objectives

1. Explore the subjective nature of pain
2. Develop framework for identifying if an opioid is indicated
3. Discuss problematic use and aging
4. Touch on risk mitigation when using opioids
5. Discuss opioid selection
6. Do some math!

Abbreviations

APAP- acetaminophen

PCA- patient controlled analgesia

OUD- opioid use disorder

SUD- substance use disorder

OAT- opioid assisted therapy (ie methadone/buprenorphine maintenance)

OME- oral morphine equivalents

Cases

82 year old man with severe acute on chronic back pain

- Baseline severe spinal stenosis not a good surgical candidate
- On APAP, gabapentin 1200mg TID at home
- On oxycodone ER 80mg BID, oxycodone 10mg IR q 3 prn at home
  - Average 4 prn doses per day
  - Pain control at baseline is poor
- Admitted with spinal abscess after injection attempt
- Now on hydromorphone PCA with high use – used 30mg IV hydromorphone in the past 24 hours
  - Poor pain control
  - Unable to work with PT
  - No better despite significant increase in hydromorphone dosing
  - Becoming sedate, delirious

Cases

86 year old woman with severe OA and new diagnosis of uterine cancer

- Functionally struggling, now homebound due to pain
- APAP, topical OTC, topical diclofenac not helping
- Was hospitalized for perforated peptic ulcer due to NSAIDs
- Was on gabapentin and pregabalin in the past- poor relief and had hallucinations
- On high dose sertraline, trazodone for depression
- On oxycodone in the past- falls and confusion
- Lives alone, high fall risk, developing mild cognitive impairment

Why is this this so important?

Chronic Pain

Chronic pain is very common and increases with age

- ~40% of adults >65 report chronic joint pain
- ~15-30% older adults are taking prescription analgesic(s)
- ~70% report regularly using OTC analgesics

High impact on individual and society

- >600 billion estimated "cost" in US annually
  - Disability
  - Heath care costs/resource utilization
- Lower quality of life
- Accelerated functional/cognitive decline
- Risk for premature death

Domenichiello AF, Ramsden CE. The silent epidemic of chronic pain in older adults. Prog Neuropsychopharmacol Biol Psychiatry. 2019 Jul 13;93:284-290. doi: 10.1016/j.pnpbp.2019.04.006. Epub 2019 Apr 17. PMID: 31004724; PMCID: PMC6538291.

Objectives

1. **Explore the subjective nature of pain**
2. Develop framework on identifying if an opioid is indicated
3. Discuss problematic use and aging
4. Touch on risk mitigation
5. Discuss opioid selection
6. Do some math!

Pain

Pain experience is a complex interplay between our peripheral and central nervous system

Protective mechanism to prevent injury and tissue damage

There may or may not be an actual noxious stimuli

- This system can get highjacked- ex viral myalgias/arthralgias

True noxious stimuli may or may not cause pain

- Congenital pain insensitivity
- Anesthesia

- **All pain is "in your head"**
- **All pain is subjective and huge differences in pain experience exist**
- **Do not judge validity of pain!**

Objectives

1. Explore the subjective nature of pain
2. **Develop framework on identifying if an opioid is indicated**
3. Discuss problematic use and aging
4. Touch on risk mitigation
5. Discuss opioid selection
6. Do some math!

Types of Pain

Acute pain goes away with resolution of stimulus which triggered pain

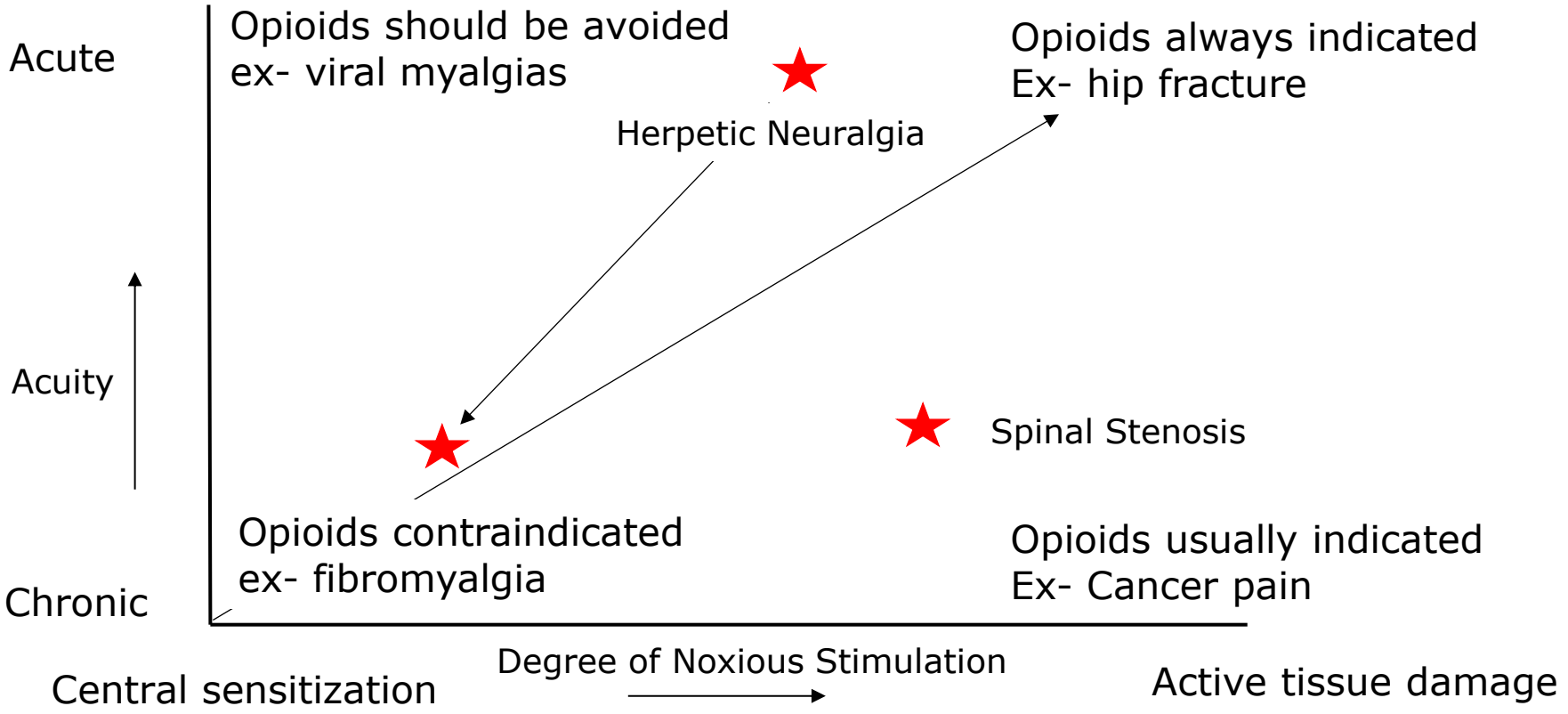
- Tissue recovery
- Resolution of viral infection

Chronic pain persists

- Stimulus resolution is not possible
  - Progressive malignant pain
  - Advanced degenerative disease with no operable interventions
- Stimulus resolved but with long term alteration in pain signaling
  - Neuropathy post chemotherapy or post-herpetic neuralgia
  - Phantom limb pain
- Central sensitization (i.e. no noxious stimulus existed)
  - Allodynia associated with fibromyalgia, depression
  - Opioid-induced hyperalgesia

➢ **Most appropriate treatment modalities will vary based on this spectrum**

Framework for Contemplating Opioids for Pain



WHO Step Ladder

Step 1- Mild Pain

- APAP
- ~~NSAIDS~~
- +/- Adjuvants

Adjuvants

- ~~Corticosteroids~~
- ~~Antidepressants~~
- ~~Gabapentinoids~~
- ~~Muscle relaxers~~
- Topicals

shutterstock.com · 2217909173

➢**High burden of nociceptive pain, CKD, medical comorbidities, side effect profile, and lower benefit for risk make NSAIDS and adjuvants low yield or contraindicated in many older/frail adults**

WHO Step Ladder

Step 1 - Mild Pain= APAP, perhaps topicals

- + consideration of low dose gabapentinoid or SNRI if significant neuropathic/sensitization component (ex- chronic post-herpetic neuralgia)

Step 2 (moderate or worsening/persistent pain despite step 1)

- Weak opioids
  - ~~Codeine based products~~
  - ~~Tramadol~~

➢**Weak opioids have more medication interactions, worse side effect profile vs benefit, proliferation of combination products, dose ceiling, higher abuse (hydrocodone)**

➢**For many older/frail adults skipping step 2 may be appropriate**

WHO Step Ladder

Step 3 - (severe or worsening/persistent pain despite steps 1+2)

- Strong opioids
  - Short acting- morphine, oxycodone, hydromorphone
  - Long acting- fentanyl, buprenorphine, methadone, SR forms
- ?Cannabis, Ketamine

➢**For many older/frail adults with if APAP and OTC topicals are not helping a very low dose strong opioid is probably best step for many patients**

Applicable to all steps!

Non-medication interventions

- PT, activity program, yoga
- Minimally invasive procedures (knee injections for OA)
- "Alternative" therapies- acupuncture, TENs
- Behavioral interventions/pain coping resources
- Definitive treatment in those eligible
  - Joint replacement

➢**Always consider most appropriate non-medication intervention(s) as a replacement for or conjunction with medications**

Objectives

1. Explore the subjective nature of pain
2. Develop framework on identifying if an opioid is indicated
3. **Discuss problematic use and aging**
4. Touch on risk mitigation
5. Discuss opioid selection
6. Do some math!

Is developing a new addiction is rare in older adults?

Impulsive behavior and problematic drug/alcohol use trends down with age

Impact increases with age

- More likely to result in hospitalization, death

Increasingly common in older adults

- First time initiation of OAT doubled
- Prevalence of OUD in older adults tripled (2013→2018)
- 2-3x increase in ED visits related to problematic opioid use

Most addiction related to ETOH or prescription meds

Risks for developing new SUD ≥ 50

- Prior history of SUD, social isolation, depression
- Females at higher risk

Koechl B, Unger A, Fischer G. Age-related aspects of addiction. Gerontology. 2012;58(6):540-4. doi: 10.1159/000339095. Epub 2012 Jun 21. PMID: 22722821; PMCID: PMC3540205
.
Argyriou E, Um M, Carron C, Cyders MA. Age and impulsive behavior in drug addiction: A review of past research and future directions. Pharmacol Biochem Behav. 2018 Jan;164:106-117. doi: 10.1016/j.pbb.2017.07.013. Epub 2017 Aug 1. PMID: 28778737; PMCID: PMC5797988.

Dufort A, Samaan Z. Problematic Opioid Use Among Older Adults: Epidemiology, Adverse Outcomes and Treatment Considerations. Drugs Aging. 2021 Dec;38(12):1043-1053. doi: 10.1007/s40266-021-00893-z. Epub 2021 Sep 7. PMID: 34490542; PMCID: PMC8421190.

Published in final edited form as:
Nurs Outlook. 2018 ; 66(2): 112–120. doi:10.1016/j.outlook.2017.10.007.

Factors Associated with Prescription Opioid Misuse in Adults Aged 50 or Older

Yu-Ping Chang, PhD, RN, FGSA
School of Nursing, University at Buffalo, The State University of New York

Overt OUD is the tip of the iceberg

- Study of patients on opioid for chronic pain 35% reported misuse (taking more than prescribed in the past 30 days)
  - Higher pain severity, pain interference with function…pseudoaddiction?
  - Depression (GDS)
  - Younger age, specifically "boomer" generation (~1946-1964)
  - Higher education
  - Prior problematic alcohol/drug use

➢**Risk is lower with age but not zero, assessing risk and monitoring for misuse is still indicated**

Objectives

1. Explore the subjective nature of pain
2. Discuss problematic use and aging
3. Develop framework on identifying if an opioid is indicated
4. **Touch on risk mitigation**
5. Discuss opioid selection
6. Do some math!

Monitoring Therapy

Primary target should be based in function and quality of life

Do not escalate past modest dosing for chronic non-malignant pain

If not helping improve function or quality of life taper off

Monitor for side effects and mitigate when possible

- Stimulant laxative for constipation
- Dose reduction for sedation
- Opioid holiday or rotation for hyperalgesia/tolerance

Mitigate risk of overdose

- Naloxone- grandkids!!!
- Lockbox
- When possible avoid other sedating medications (ex- benzos)

Opioid Side Effects

Cognitive impairment/delirium/sedation

- More common with aging

Nausea, Constipation

- Declining gut motility with age can compound

Decreased coordination/falls

- High risk of fall related injury, hip fractures

Respiratory depression

- OSA, COPD, CHF can compound this

Tolerance/Hyperalgesia

➢**Older adults are higher risk of side effects due to opioids**
➢**Poorly controlled pain also associated with significant adverse effects**

Screening for Problem Use

Older adults are less likely to be screened for problematic use

Common symptoms can misattributed

- Cognitive changes, falls, driving accidents could be misattributed to aging when misuse is present
- Cognitive decline can create illusion of problematic use

Caregivers/facility staff are sometimes the problem

No clear validated tool, especially in older adults

Urine drug screening

- No clear consensus, differing expert opinion
- Hard to interpret (example: synthetic opioids generally do not screen positive on basic opioid testing)

But What if the Patient is not the Problem?

Caregivers (family/friends, and staff) sometimes are the issue

Traditional approach may still detect aberrant behaviors

Still consider UDS in those who can not develop problem use themselves

- Lack of expected drug strong evidence for diversion

Watch for waxing/waning response to same regimen

Increased toxicity in a more controlled environment

- Respiratory depression in the hospital when given home regimen

Try to use less divertible/commonly abused opioids, especially if concern

Change to forms that can be visualized- example: bup patch

Our Clinic Approach- Baseline Risk (ORT-R)

- 0-2 : Low Risk
- ≥ 3 : High Risk

Mark Each Box That Applies	Yes	No
Family history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Personal history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Age between 16-45 years	1	0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	1	0
Depression	1	0
Scoring total		

Our Clinic Approach

Prognosis

< 12 months

> 12 months

Risk Assessment

Low

- Discuss Narcan
- Discuss lock-box
- Routine office care

High

- Opioid patient instructions (AVS)
- Shorten prescribing intervals (2 weeks)
- Frequent visits (monthly)
- UDS if suspicion or random selected

Risk Assessment

Low

- Opioid patient instructions (AVS)
- Yearly UDS strongly encouraged
- Brief opioid screen yearly
- 3-month follow-ups expected

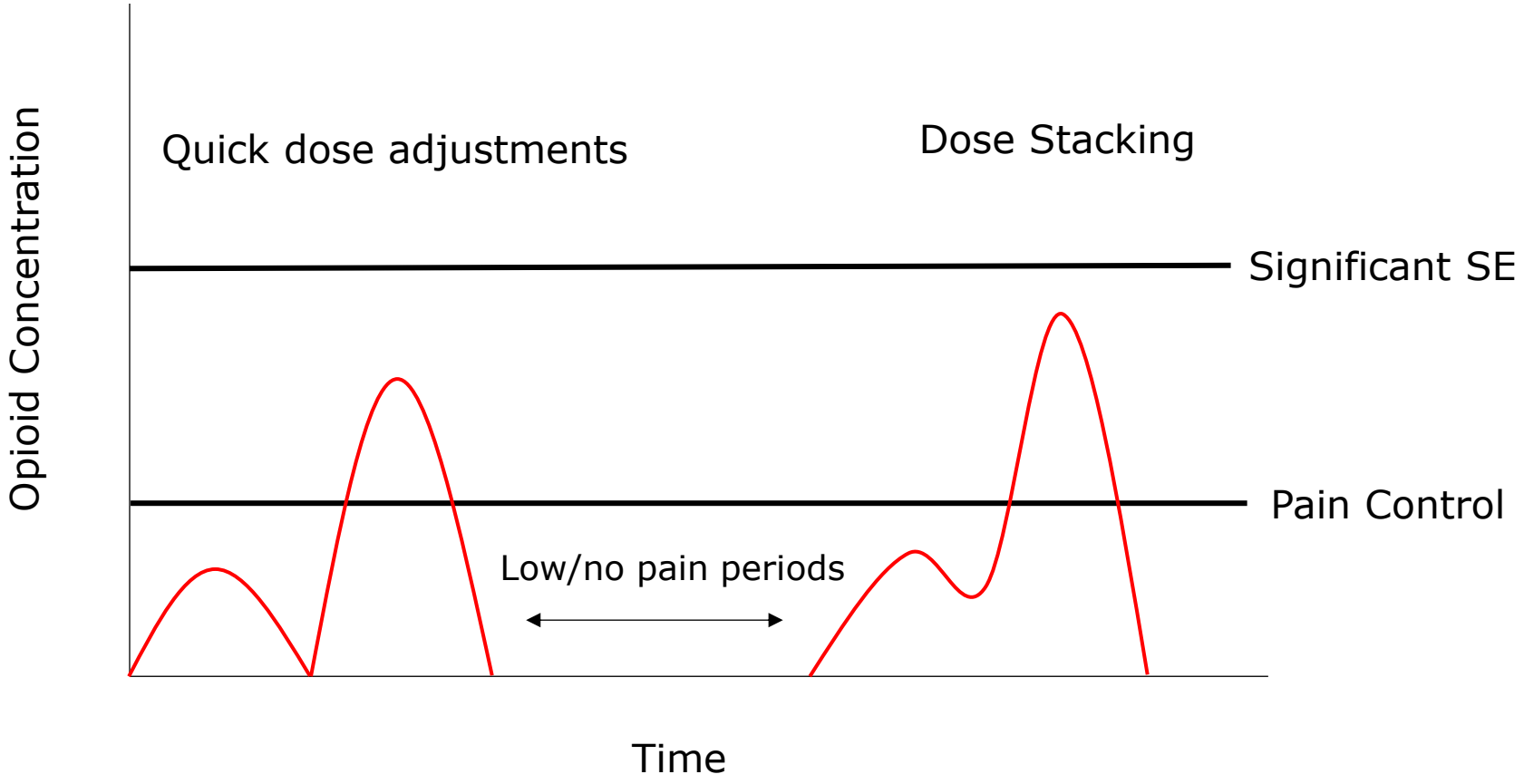
High

- Opioid patient instructions (AVS)
- Frequent visits (1-2 months)
- UDS q 6 months
- Brief opioid screen q 6 months
- Consider formal screening for OUD (SOAPP-R)
- Offer referral to SUD clinic

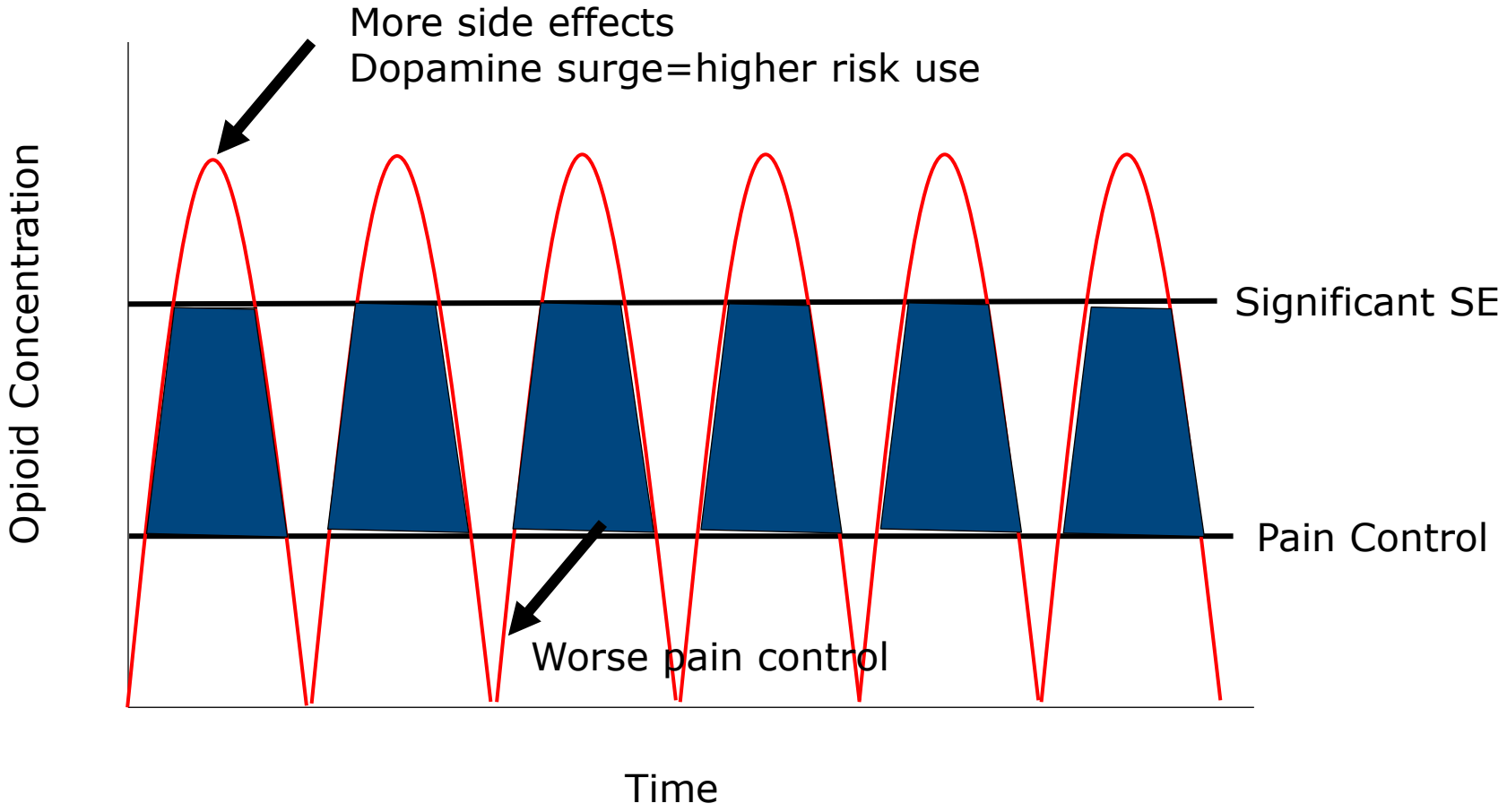
Objectives

1. Explore the subjective nature of pain
2. Discuss problematic use and aging
3. Develop framework on identifying if an opioid is indicated
4. Touch on risk mitigation
5. **Discuss opioid selection**
6. Do some math!

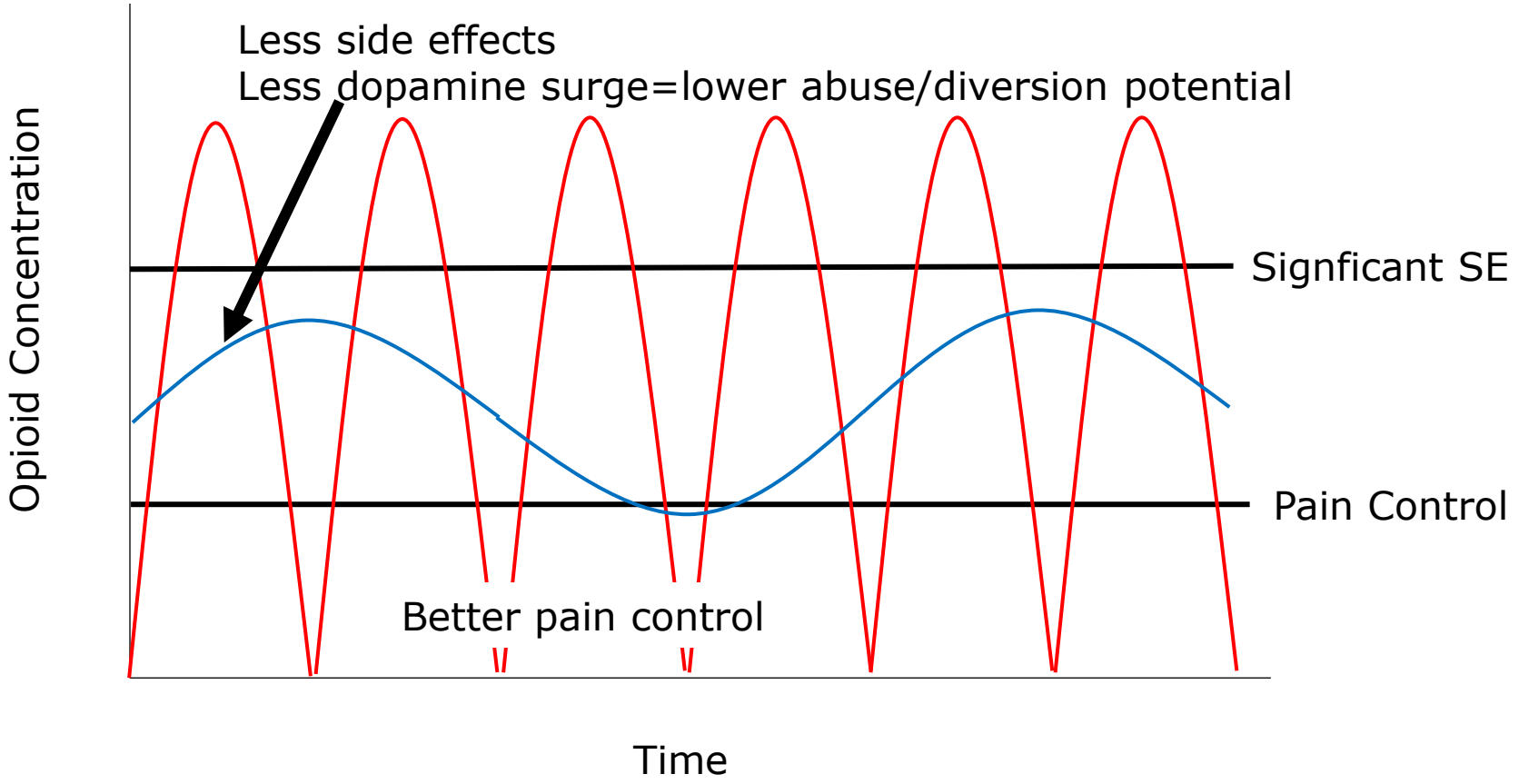
Short Acting Preparations-Acute Pain



Short Acting Preparations-Chronic pain



Short vs Long Acting Preparations- Chronic Pain



Short Acting Strong Opioids

Morphine

- Many forms- tabs, ER tabs, SL solution, liquid, IV
- Avoid with significant CKD
- Starting dose (opioid naive) 5-7.5mg po/2mg IV

Oxycodone

- Closely linked to opioid misuse on population scale
- More "likeable" compared to morphine
- More dopaminergic rush in animal models
- Only widely available in tab/ER forms
  - Prior authorizations abound
- Starting dose (opioid naïve) 2.5-5mg

Wightman R, Perrone J, Portelli I, Nelson L. Likeability and abuse liability of commonly prescribed opioids. J Med Toxicol. 2012 Dec;8(4):335-40. doi: 10.1007/s13181-012-0263-x. PMID: 22992943; PMCID: PMC3550270.

Short Acting Strong Opioids

Hydromorphone

- Misuse risk unclear, probably lower than oxycodone, higher than morphine
- OK with hepatic/renal failure (with dose reduction)
- Available po/liquid/IV formulations (ER exists but not widely available)
  - Shortages have been a problem
- Starting dose = 1-2mg po or 0.25mg IV (opioid naïve)

➢**Best for acute pain- chronic pain should trigger consideration of long acting**
➢**Morphine is best barring significant CKD- my cutoff is CCL~45**
➢**If morphine contraindicated I use hydromorphone**
➢**Oxycodone is still frequently being used as 1st line short acting… it should not be**

Long Acting Opioids

Morphine ER

- Minimum starting dose 15mg BID= 30mg OME… opioid tolerant only
- Can not be crushed/tablet altered (ex- dysphagia, PEGs)
- BID vs TID dosing
- Avoid with CKD

Oxycodone ER

- Minimum starting dose 10mg BID= 30mg OME… opioid tolerant only
- Can not be crushed/tablet altered (ex- dysphagia, PEGs)
- BID vs TID dosing
- High abuse potential
- Usually requires PA

Long Acting Opioids

Fentanyl patch

- Minimum starting dose 12.5mcg= 45mg OME… opioid tolerant only
- Dangerous with applied heat/fever
- ? Poor absorption with cachexia
- Generally q 72 hour dosing

➢**Long acting best choice for chronic pain**
➢**All traditional long acting agents have significant downsides for many older adults**
➢**All require at least some degree of opioid tolerance**

Long acting alternatives…

Methadone

Long acting by property not formulation

- Available in liquid and can be crushed- dysphagia, PEGs
- For pain usually BID or TID dosing is still helpful
- Very cheap even without insurance

Doesn't just hit the mu-receptor

- For many is more helpful for neuropathic pain
- Can help consolidate adjuvants, can reduce hyperalgesia

Marked dosing range

- Helpful for very high OME (i.e. 100s-1000s)
- Can be used at low dose in opioid naive
  - Starting dose of 2.5-5mg/day≈ 7.5-15mg OME

Less abuse/diversion, probably lower risk of side effects

Methadone- Stipulations

If you are doing anything other than starting very low dose you need to be very comfortable with dosing

- Huge variability in ½ life and dose required- always dose reduce 30-50%!
- Delayed pain response and delayed overdose- 5-7 days to steady state
- Dosing scale is not linear, it's logarithmic
- Calculating back to other opioids is hard

Patient/caregiver should be reliable

- Self escalation or accidental dosing could have more severe consequences

More medication interactions to watch for (examples: cipro, fluconazole)

Needs intermittent EKG for QT monitoring

- CI with QTc >500, use with caution close to this- 470 is my approx. cutoff
- Dose dependent effect
- Bundle branch blocks overestimate QTc, correction exist but are burdensome

Buprenorphine

Available in long acting patch (Butrans)

- Avoids oral route
- Can be changed weekly- good for less reliable patients

Partial opioid agonist

- Lower abuse/diversion potential
- Lower risk of respiratory depression and systemic side effects

Low starting dose

- Can be used at low dose in opioid naive
  - Starting dose of 5mcg≈ 10-15 mg OME

Also available in SL forms for those with higher OME needs

Buprenorphine – Stipulations

If you are doing anything other than butrans patch you need to be very comfortable with dosing

- Partial agonist with high affinity= precipitated withdrawal in opioid tolerant
- Micro-induction required (high opioid dosing)
- OME does not translate very well into dosing
- Transitioning back to other opioids is hard
- High dose buprenorphine (SL forms) interferes with short acting prns

Prior Auth need is common

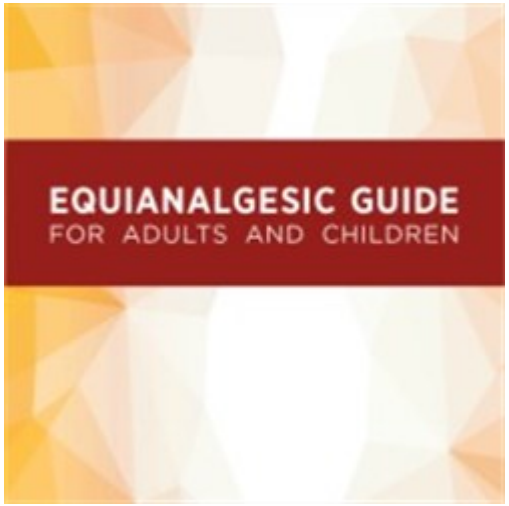
- And as opposed to methadone it is expensive

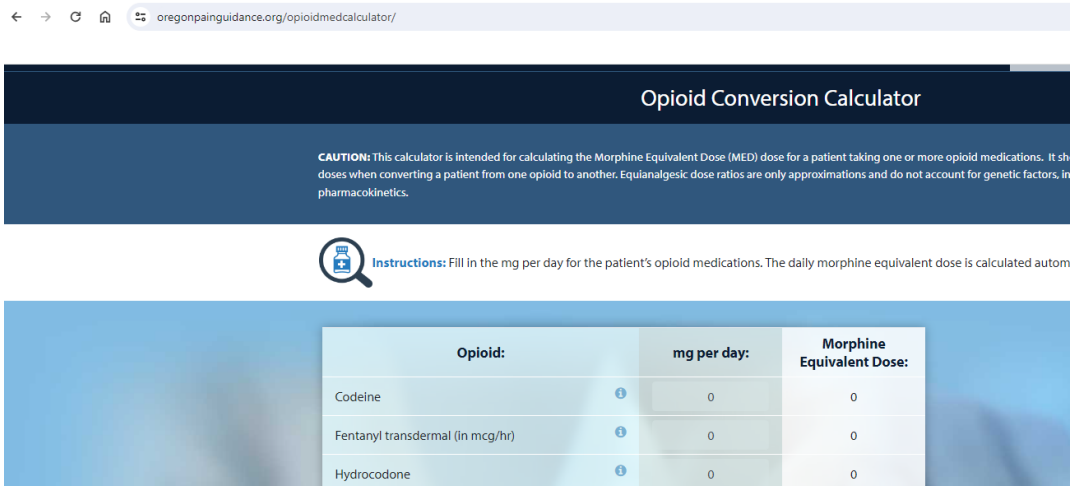
Dosing opioids

Start with lowest starting dose for opioid naïve

Use oral morphine equivalents (OME) as the universal base

When escalating or rotating always do the math!





Cases

82 year old man with severe acute on chronic back pain

- **On oxycodone ER 80mg BID, oxycodone 10mg q 3 prn at home**
  - **Average 4 prn doses per day**

What is his home OME?

- 80mg x2 =160mg oxycodone
- 10mg x 4 = 40mg oxycodone
- 160mg+40mg= 200mg oxycodone
- 200mg oxycodone ($\frac{30mg\ oral\ morphine}{20mg\ oral\ oxycodone}$) = 300 OME baseline need

82 year old man with severe acute on chronic back pain

- 300 OME baseline
- Now on hydromorphone PCA with high use – used 30mg IV hydromorphone in the past 24 hours and is not doing well

What is his hospital OME?

- 30mg IV hydromorphone ($\frac{30mg\ oral\ morphine}{1.5mg\ IV\ hydromrophone}$)=600 OME

My Considerations

High OME requirements

Both acute and chronic components

Strong neuropathic component, on very high dose gabapentin

Doubling of opioid w/o any improvement and perhaps worsening worrisome for a component of opioid induced hyperalgesia

Developing neuropsychiatric side effects (confusion, sedation)

Methadone it is!

- QTc OK
- No major medication interactions

Dosing?

- 600 OME ($\frac{1\ oral\ methadone}{15\ oral\ morphine}$) = 40mg methadone= 20-30 mg depending on dose reduction
- Using well above home dosing, concern that methadone may be much more clinically helpful = larger dose reduction
- Start 10mg BID, revisit dosing after 5-7 days

It was a lifesaver! He is doing much better 4+ years later

Cases

86 year old woman with severe OA and new diagnosis of uterine cancer

- Functionally struggling, now homebound due to pain
- APAP, topical OTC, topical diclofenac not helping
- Was hospitalized for perforated peptic ulcer due to NSAIDs
- Was on gabapentin and pregabalin in the past- poor relief and had hallucinations
- On high dose sertraline, trazodone for depression
- On oxycodone in the past- falls and confusion
- Lives alone, high fall risk, developing mild cognitive impairment

My Considerations

Failing on step 1 (APAP/OTC topicals)

Has tried and failed many adjuvants

Other non-opioid options are contraindicated

- Ex- TCA, NSAIDs

Weak opioids still have risk and lower likelihood of significant benefit

- Tramadol/serotonin syndrome

Very chronic pain and high risk of side effects

- Favors long acting as opposed to short acting

Opioid naïve

Methadone or Buprenorphine is most appropriate option

No clear contraindications to methadone- start 2.5mg qhs x 1 week, then increase to BID.

- 2 week visit-pain a bit better subjectively but a bit less clear cognitively… no changes
- 1 month follow-up… 2 falls, having trouble splitting pills, some missed doses needing oversight from daughter

Methadone doing more harm than good….Stop!

After return to baseline started buprenorphine patch 5mcg

- Daughter can manage
- Subjective modest reduction in pain scores
- Significant improved function/QOL- able to get out to appointments, store
- Tolerating well

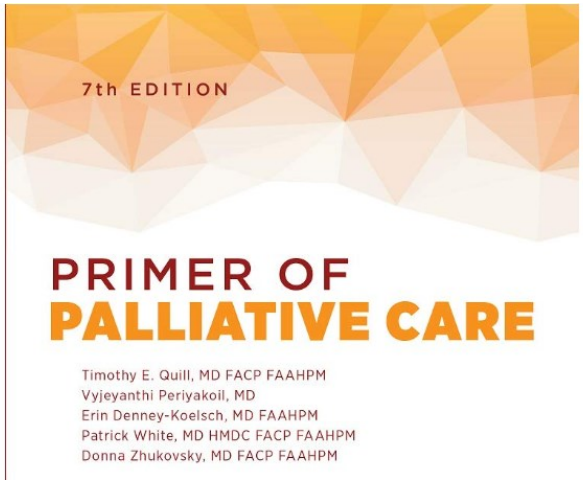
Continue buprenorphine with close oversight

QUESTIONS?

Feel free to contact me with questions/math confirmations:

nicole_gise@urmc.rochester.edu

Equianalgesic tables for purchase:



Primer of Palliative Care, 7th Edition | AAHPM Learn

UR MEDICINE | HIGHLAND HOSPITAL

MEDICINE *of* THE HIGHEST ORDER