



Opioid Management & Titration for Oncology Patients

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Disclosures and Disclaimers

- I have no financial disclosures
- Disclaimers
 - I am just trying to get you in the ballpark



Learning Objectives

1. Describe the pharmacologic properties of commonly used opioids, including onset, duration, and routes of administration.
2. Differentiate between short-acting and long-acting opioid formulations and identify appropriate clinical indications for each.
3. Explain the principles of opioid conversion and equianalgesic dosing across various routes and agents.
4. Identify risk factors and warning signs for opioid-related adverse effects (e.g., sedation, respiratory depression, constipation).

Case DB

35 y/o female with newly diagnosed AML that is admitted to hospital for initial induction chemotherapy with 7+3. She started treatment two days ago and is experiencing pain all over however is predominantly in hips. She is unable to lay comfortably in bed and pain is limiting sleep. States her world is collapsing her around her as her two young children are present at bedside.

- What are next steps?
- How do we address her pain?

There are many types of different pain problems in cancer care....

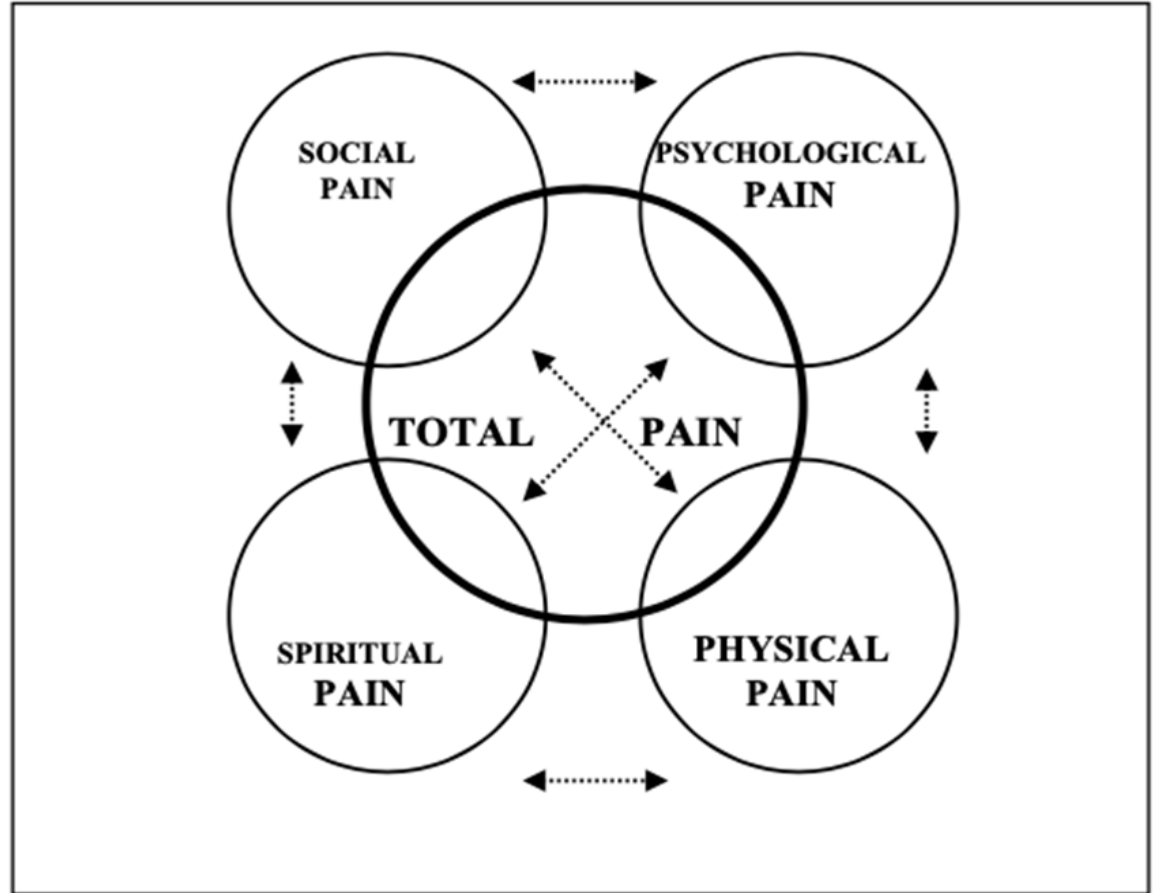


Yet, we don't always have the right tool for the job



Total Pain

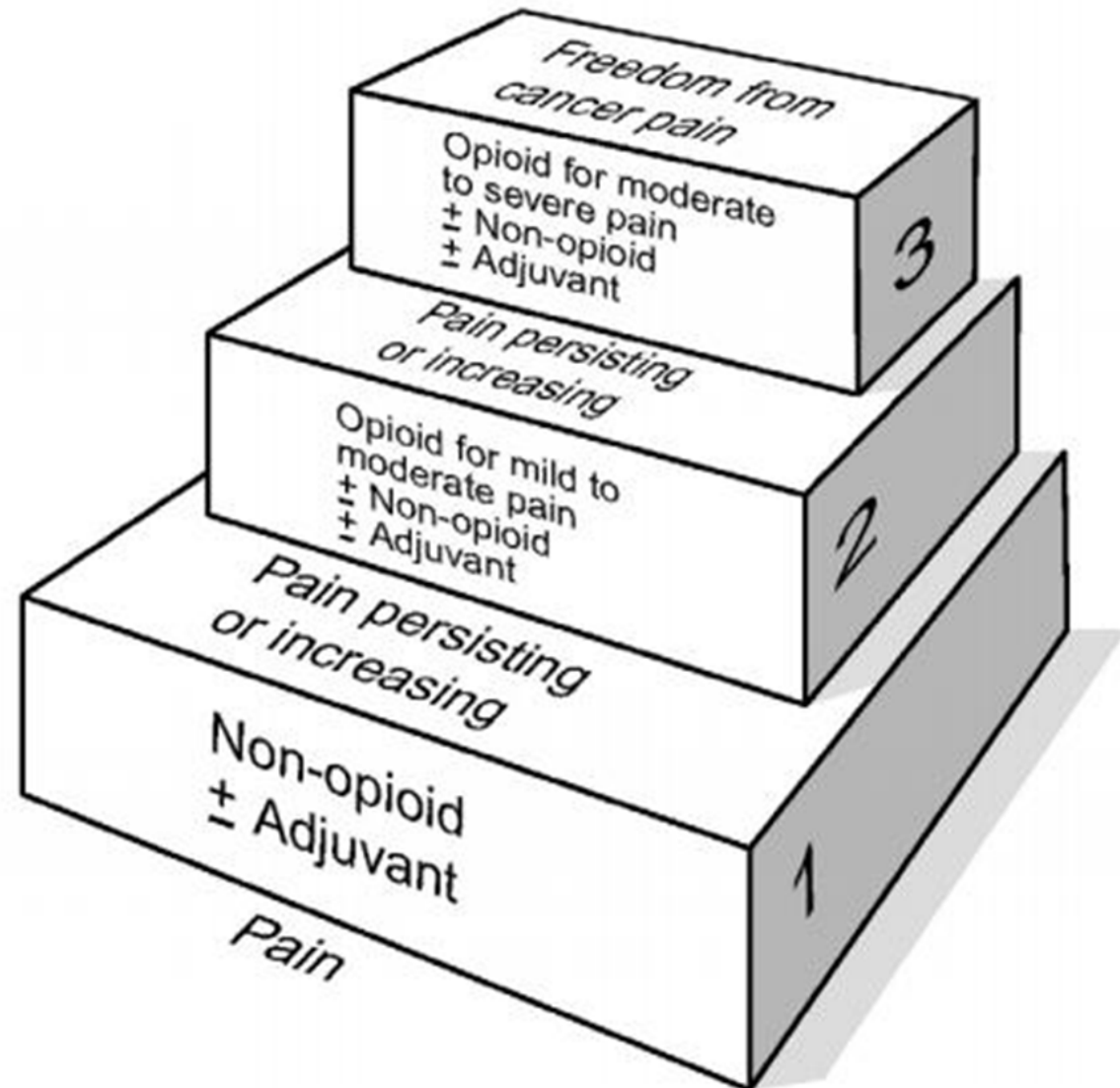
- Dame Cicely Saunders
 - Founder of the modern hospice movement
 - Pioneer who helped establish palliative care
- Utilize multi-disciplinary approach to address different aspects of pain



WHO Pain Ladder

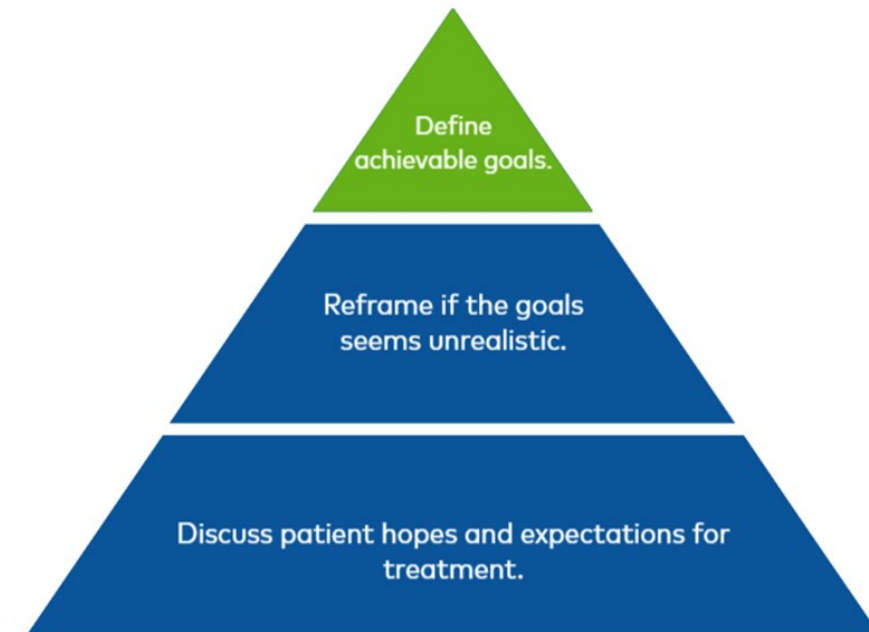
Level 3	Escalate to single-entity opioid agonists, most commonly morphine, oxycodone, hydromorphone, fentanyl, methadone
Level 2	Escalate to stronger agents including less potent opioid (ex: tramadol, hydrocodone) or combination agents (ex: APAP + hydrocodone)
Level 1	Start with agents such as acetaminophen, ibuprofen and naproxen

*Use of adjuvants can be considered at any pain level



Initiating Opioids

1. Are opioids appropriate for the patient's specific pain?
 - Define goals of care
 - Primarily focus on goals of opioid therapy
 - Discuss informed consent
 - Assess caregiver capacity, concerns, and support needs
 - Screen for risk factors for opioid misuse
 - Identify a primary prescriber
2. What opioid (drug/dose/route/frequency)?
 - Start low and go slow



Pharmacologic Properties

Case: JC

Current complaint "Pain medications just are not working like they used to!"

65 y/o male with metastatic NSCLC with diffuse osseous lesions with new disease progression seen on CT C/A/P that is being seen in clinic to discuss treatment plans however pain is poorly controlled. Previous analgesic regimen of acetaminophen 1000 TID and oxycodone 5 q6hr PRN (taken 1-3 times daily previously; currently taking oxycodone every 6 hours).

-What are your initial thoughts?

Pharmacokinetic Properties of Different Opioids

Opioid	Route	Onset of Analgesia	Peak Analgesic Effect	Duration of Effect	Steady state	Half-life
Morphine (IR) Oxycodone (IR) Hydromorphone (IR)	PO	30-40 mins	60-90 minutes	4 hours		2-4 hrs
Morphine (ER) Oxycodone (ER)	PO	1.5-3 hrs	3-4 hrs	8-12hours	24 hrs	4-6 hrs
Morphine Hydromorphone	IV	30-40 minutes	60-90 m	4 hours		2-4 hrs
Fentanyl	Transdermal	~6 hrs	20-72 hrs	72-96 hrs	3-6 days	17 hrs
Methadone	PO	30-60 min	3-5 days	4-8 hours	5-7 days	15-60 hrs

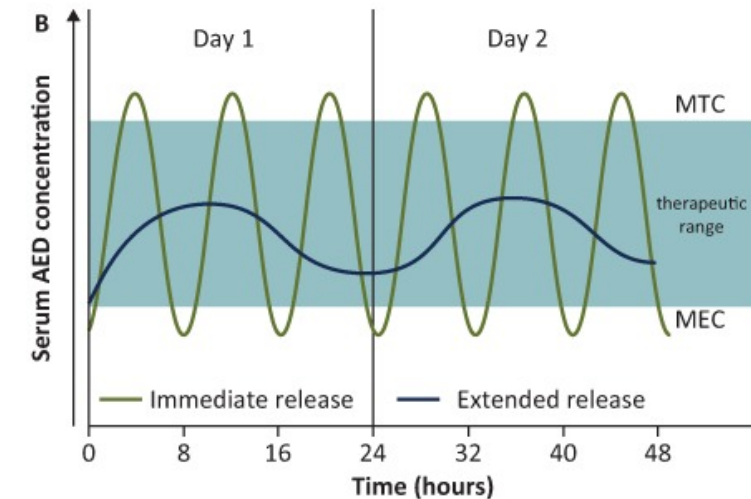
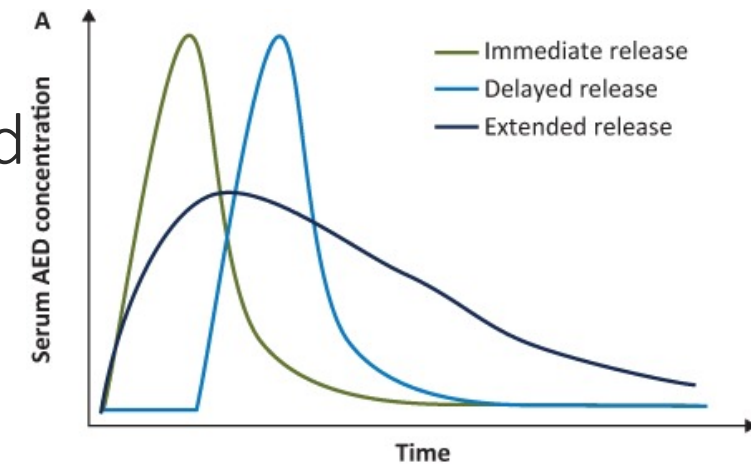
Cancer-Related Pain Patient Experience

Immediate Release Only

- Roller coaster/peaks and valleys
- Sedation Peaks
- End-of-dose failure
- Frequent dosing

Extend Release with as needed

- Stable control/rolling hills
- Smoother analgesia
- Better overnight control
- Better adherence



Wheless JW, Phelps SJ. A Clinician's Guide to Oral Extended-Release Drug Delivery Systems in Epilepsy. J Pediatr Pharmacol Ther. 2018 Jul-Aug;23(4):277-292. doi: 10.5863/1551-6776-23.4.277. PMID: 30181718; PMCID: PMC6117810.

AED, antiepileptic drug; MEC, minimal effective concentration; MTC, minimal toxic concentration.

Opioid Formulations

Commonly Available Oral Opioid Formulations

Opioid	Immediate Release		Extended Release	
Morphine	Tablets (mg)	15, 30	Tablet (MSContin; mg)	15, 30, 60, 100, 200
	Solution	10 mg/5 mL, 20 mg/ 5 mL 20 mg/mL	Capsules (Kadian; mg)	10, 20, 30, 40, 50, 60, 80, 100, 200
Oxycodone	Tablets	5 , 10 , 15 , 20 , 30	Tablet (Oxycontin; mg)	10 ,15, 20, 30, 40, 60, 80
	Solution	5 mg/5 mL, 20 mg/mL	Capsules (Xtampza ER; mg)	9, 13.5, 18, 27, 36
Hydromorphone	Tablets	2 , 4 , 8		
	Solution	1 mg/5 mL, 1 mg/mL		
Fentanyl			Patch (mcg/hr)	12, 25, 50, 75, 100

Wisconsin Medicaid, BadgerCare Plus Standard, and SeniorCare Preferred List

Analgesics, Opioids Short-Acting		
codeine/apap		P
hydromorphone		P
hydrocodone/apap 325mg		P
hydrocodone/ibuprofen		P
morphine		P
oxycodone solution, tablets		P
oxycodone/apap 325mg		P
tramadol 50mg tab		P
tramadol/apap 325mg		P
butorphanol spray		NP
codeine		NP
dihydrocodeine/apap/caffeine	SCN	NP
fentanyl transmucosal lozenges		NP
levorphanol		NP
hydrocodone/apap solution, tabs*		NP
hydromorphone liquid, suppository		NP
meperidine		NP
oxycodone capsules, concentrate		NP
oxymorphone		NP
pentazocine/naloxone		NP
tapentadol (Gen-Nucynta)		NP
tramadol HCL solution		NP
tramadol 25mg, 75mg tablet	SCN	NP
tramadol 100mg tablet		NP
Dilaudid Liquid		NP
Roxybond Tablet	SCN	NP
Xyvona tablet	SCN	NP

Analgesics, Opioids Long-Acting		
fentanyl transdermal 12mcg, 25mcg, 50mcg, 75mcg, 100mcg		P
morphine ER tablets		P
tramadol ER tab (Gen-Ultram ER)		P
Butrans transdermal		P
Hysingla ER		P
buprenorphine transdermal		NP
fentanyl transdermal 37.5mcg, 62.5mcg, 87.5mcg		NP
hydrocodone ER tablet (Gen-Hysingla ER)		NP
hydrocodone ER capsule (Gen-Zohydro ER)		NP
hydromorphone ER		NP
methadone tablet, solution		NP
morphine ER capsules		NP
oxycodone ER		NP
oxymorphone ER		NP
tapentadol ER (Gen-Nucynta ER)		NP
tramadol ER capsule (Gen-Conzip)	SCN	NP
tramadol ER tab (Gen-Ryzolt)		NP
Belbuca Film		NP
Conzip	SCN	NP
Oxycontin		NP

Opioid Escalations/Conversions

General Opioid Tenets

- Safe and Effective
 - Safety main priority
- Start low and Go Slow

	Less Effective	More Effective
More Safe	Acceptable quadrant	Preferred Quadrant
Less Safe	Least acceptable quadrant	Not Acceptable Quadrant

Case JC (revisited)

65 y/o male with metastatic NSCLC with diffuse osseous lesions with new disease progression seen on CT C/A/P that is being seen in clinic to discuss treatment plans however pain is poorly controlled.

On follow-up later that week:

Providers appropriately increase oxycodone to 10 mg every 4 hours as needed with improvement in pain but notes if he waits until 5 hours pain is uncontrolled and pain is awakening from sleep.

-Thoughts/Next Steps?

Opioid Escalation

1. Is an opioid dose escalation appropriate?
2. How quickly can we increase the dose?
3. How much do I increase the dose?

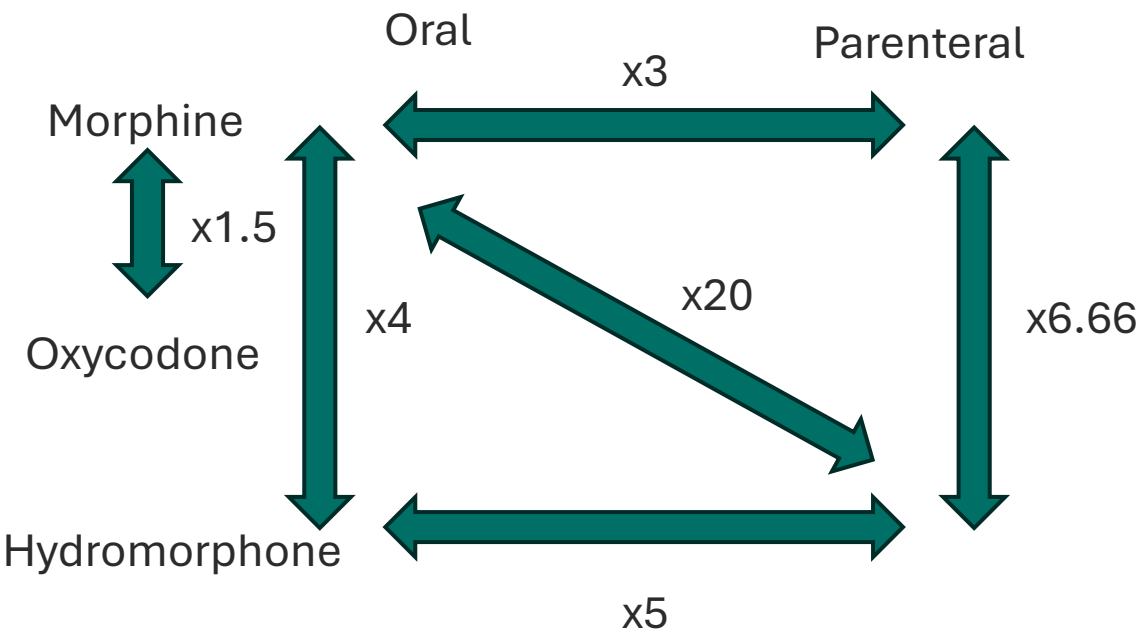


Opioid Escalation Process

1. Calculate total daily opioid

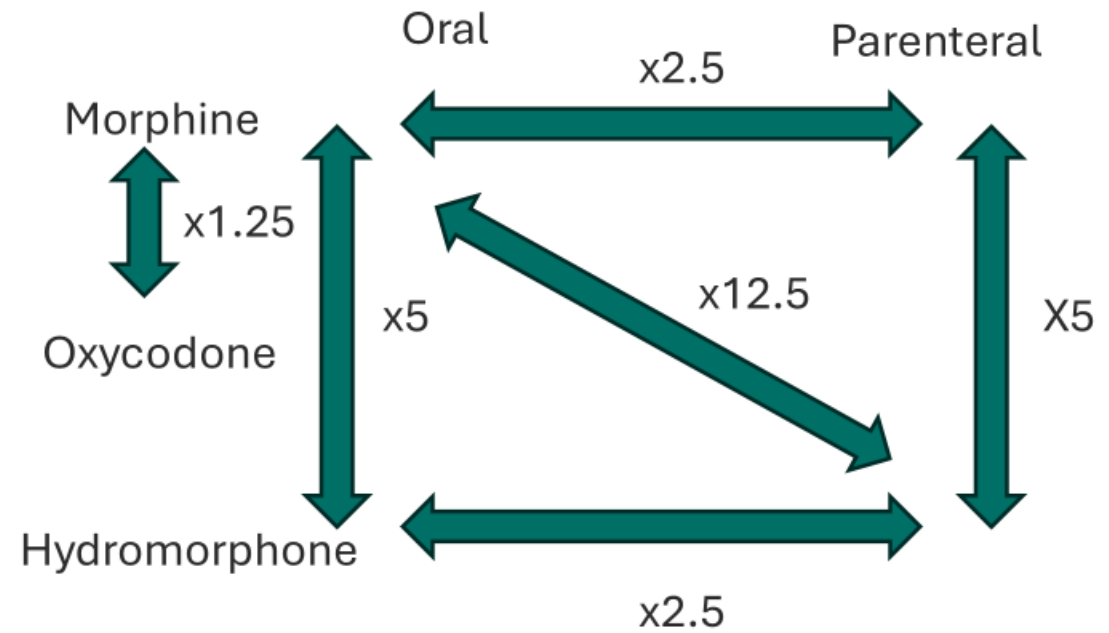
Opioid Equianalgesic Table (2010-original)

Opioid	IV	PO
Morphine	10	30
Oxycodone		20
Hydromorphone	1.5	7.5



Opioid Equianalgesic Table (2018 update)

Opioid	IV	PO
Morphine	10	25
Oxycodone		20
Hydromorphone	2	5



Opioid Escalation Process

1. Calculate total daily opioid

○ 60 mg oxycodone $\frac{25 \text{ mg morphine}}{20 \text{ mg oxycodone}}$ = 75mg morphine

Opioid Escalation Process

1. Calculate total daily opioid
 - 60 mg oxycodone IR= 75 OME
2. Determine if regimen is failing
 - Using >4 breakthrough doses daily
3. Add/Increase Basal Opioid
 - My goal=Aim for 2-3 PRN uses daily
 - Typically aim for basal opioid to equal 2/3 daily OME
 - Opioid escalation for uncontrolled pain
 - Mild/moderate: 25-50% dose increase
 - Severe/uncontrolled: 50-100% dose increase
 - Frail/elderly: 10-25% dose increase

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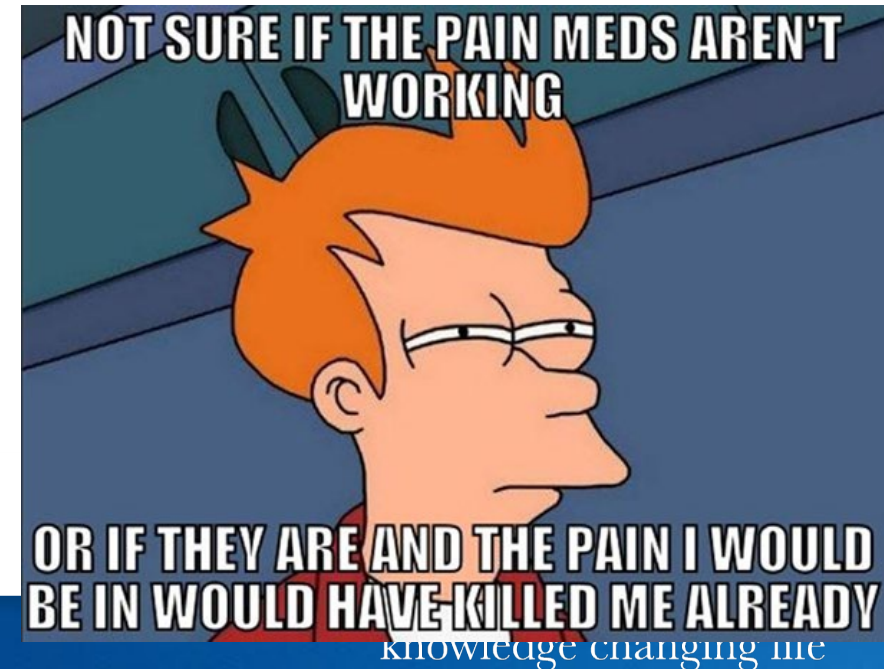
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65 y/o male with metastatic NSCLC with diffuse osseous lesions with new disease progression seen on CT C/A/P that is being seen in clinic to discuss treatment plans however pain is poorly controlled.

- Opioid choice
- Opioid dose (hypothetically choose oxycodone ER)
 - 75-90 daily OME
 - 20 mg oxycodone ER q12hr with 10 mg oxycodone IR q4hr PRN

5 Step Approach to Opioid Conversion

1. Globally assess the patient to determine source of pain exacerbation
2. Determine the total daily usage of current opioid
3. Decide which opioid analgesic we will be switching to
4. Individualize the dosage based on assessment from Step 1
5. Patient follow-up and continual reassessment



Assessment

P- Precipitating and palliating

Q- Quality

R- Region and radiation

S- Severity

T- Temporal

U- You aka How is the pain affecting you? Function, sleep, mood, etc.

Case JC: Revisited

65 y/o male with metastatic NSCLC with diffuse osseous lesions with disease progression that remains poorly controlled as outpatient with opioid escalation that he is admitted to hospital. Prior to admission opioid use is oxycodone IR 10 mg taken every 4 hours and oxycodone ER 20 mg twice daily in addition to adjuvants. Admission imaging demonstrated new compression fractures as well as labs notable for acute kidney injury (eGFR <30).

- What is next step for pain management in regards to opioids?
- What is appropriate PRN medication and dose?

Opioid conversion

$$\frac{\text{Oral morphine equivalents}}{\text{mg of current opioid}} = \frac{\text{Equivalent mg new opioid}}{\text{Equivalent mg current opioid}}$$

$$\frac{\text{Oral morphine equivalents}}{100\text{mg of oxycodone}} = \frac{25 \text{ mg oral morphine}}{20 \text{ mg oral oxycodone}}$$

$$X(20) = (25)(100)$$

$$X = \text{OME} = (25)(100)/20 = 2500/20$$

$$X = 125 \text{ OME (old calculation 150 OME)}$$

Opioid	IV	PO
Morphine	10	25
Oxycodone		20
Hydromorphone	2	5

Opioid conversion

X= 125 OME

- 10-20% dose of PRN hydromorphone
- $125 \text{ OME} / 10 = 12.5 \text{ OME}$

12.5 mg morphine  5 mg hydromorphone 2.5 mg hydromorphone
25 mg morphine

But... Pain exacerbation and no 2.5 mg tablet

Opioid	IV	PO
Morphine	10	25
Oxycodone		20
Hydromorphone	2	5

Case JC: Revisited

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- What is next step for pain management in regards to opioids?
- What is appropriate PRN medication and dose?

PCA: When to use

- Indications
 - Severe uncontrolled pain
 - Rapid opioid titration needed
 - Mucositis/esophagitis/inability to tolerate PO
 - Frequent IV PRN medications
 - Incident pain requiring relief

PCA: How to use

- Components
 - Type of opioid
 - Bolus dose/Bolus lockout/Basal rate
 - “The demand dose tells you what the patient needs. The basal rate reflects what they consistently require.”
- Opioid Naïve:
 - Bolus only
- Opioid Tolerant:
 - Convert extended-release opioid into IV formulation of chosen opioid and divide by 24
 - Select IV bolus dose with effective dose

Case JC

- 125 OME (50 OME in extended release and 12.5 OME PRN dose)
- What are the initial PCA dosing recommendations:

50 mg PO morphine  2 mg IV hydromorphone  4 mg IV hydromorphone
25 mg PO morphine

4 mg IV hydromorphone/24hr= .166 mg/hr

12.5 mg PO morphine  2 mg IV hydromorphone  1 mg IV hydromorphone
25 mg PO morphine

Initial settings:

- IV hydromorphone 0.4 mg/20 min lockout/0.2 mg/hr

PCA: Transitioning back off

Stepwise Approach

1. Calculate 24h opioid use
2. Convert to oral equivalent
3. Reduce 25–50% for cross-tolerance
4. Divide into long-acting regimen
5. Add PRN breakthrough

The Others....

- Methadone

Equianalgesic Conversion TO Methadone		
Dose-dependent potency changes well-established in the literature.		
Oral Morphine Equivalent	Mg of oral Methadone = Mg of oral Morphine (ratio)	
under 60 mg/day	Do not start higher than 7.5 mg methadone per day	
61-200 mg/day*	1	10
over 200 mg/day	1	20
IV methadone is twice as potent as oral methadone		
Doses above 2000 mg oral morphine have not been studied for conversion to methadone – please use caution in these circumstances		
*May consider 1:20 conversion ratio in patients older than 65 or with other comorbidities		

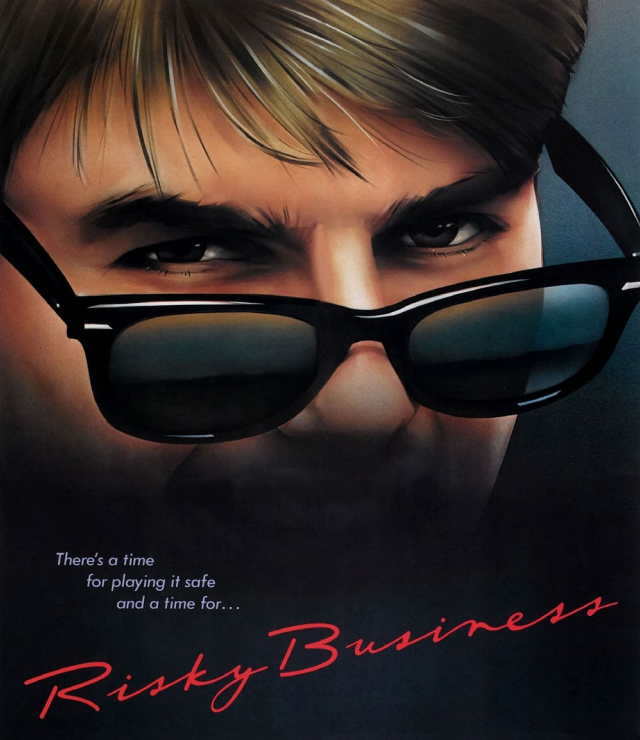
- Fentanyl
 - Patch (transdermal): 1 mcg/hr=2 mg morphine (OME)
 - Ex: Fentanyl patch 25 mcg/hr= 50 OME

The Others...

- Buprenorphine
 - Partial opioid agonist ≠ partial analgesic
 - Safest opioid with respiratory suppression threshold and decreased dependency
 - Select for high risk patients and is not high risk medication
 - Topic warrants another lecture that I am happy to give
 - Email for PowerPoint and questions
 - jbauman@mcw.edu

Buprenorphine	Oral Morphine Equivalent/24hrs (OME)								
	7	15	30	48	60	80	100	120	300
Transdermal (TD) patch	5mcg/hr q7days		10mcg/hr q7days	20mcg/hr q7days					
Buccal patch	75mcg daily	150mcg q12hrs	300mcg q12hrs	450mcg q12hrs	600mcg q12hrs	750mcg q12hrs		900mcg q12hrs	
Sublingual (SL) tabs						1mg BID (split 2mg tabs)		1mg TID	2mg TID

Case, A.A., Kullgren, J., Anwar, S. *et al.* Treating Chronic Pain with Buprenorphine—The Practical Guide. *Curr. Treat. Options in Oncol.* 22, 116 (2021). <https://doi.org/10.1007/s11864-021-00910-8>



"Risky Business" aka Side Effects

Constipation

- Every patient with opioid prescription NEEDS bowel regimen
 - Scheduled vs PRN
 - Anticipate everyone will develop constipation due to decreased peristalsis
 - Tolerance is not developed that typically occurs with other side effects
- "Your #2 is our #1"
- Medications
 - Stimulant (gold standard) +/- laxative
 - Ex: Senna (titrated up to 4 tablets)
 - No added benefit seen with docusate

Neurotoxicity

- Types
 - Myoclonus
 - Hallucinations
 - Hyperalgesia/allodynia
 - Delirium
 - Sedation
- Offending Agents
 - Morphine
 - Hydromorphone metabolites
 - Renal failure
- Treatment
 1. Rotate/decrease opioid
 2. Medication management
 - Gabapentin
 - Levitriacetam
 - Steroids

Nausea

- Etiology
 - Irritation of chemoreceptor trigger zone (similar to chemotherapy-induced nausea)
- Natural history of OIN
 - Tolerance develops in 3-7 days
 - Co-prescription of antiemetics for the first 1-2 weeks of opioid use in opioid-naïve patients.

Thank you and Questions