Symptom Management in Palliative Care: Opioids 101

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Disclosures

- None

Objectives

- At the conclusion of this session, participants should be able to:
- Identify opioids commonly used in palliative care and hospice care
- Demonstrate ability to calculate equianalgesic doses between different opioids
- Recognize indications for use of methadone as a pain medication

Poll Everywhere Instructions

Text 22333 with the message:

valerievetter

Case 1 – CP

- 45 y/o with metastatic colorectal cancer admitted with a malignant bowel obstruction. Your team has dropped an NGT, requested a surgical consult, and have made CP NPO. At baseline, they take morphine ER 30 mg PO TID and morphine IR 15 mg PO every 4 hours prn (typically takes 2 per day).

- What should you order?

What should be ordered to account for CP's baseline pain?

Morphine 4 mg IV every 4 hours prn

0%

Morphine 5 mg IV every 3 hours

0%

Morphine 10 mg IV every 4 hours

0%

I have no idea!

0%

Case 2 - EE

68 y/o patient with end-stage COPD admitted from home hospice due to increased symptom management needs. EE was using concentrated morphine suspension (20 mg/mL) for dyspnea. He was ordered for 20 mg PO every 4 hours and every hour prn. Per EE's caregiver, he was using at least 12 prn doses per day, and still had significant dyspnea.

At time of admission, you decide to put EE on a morphine PCA (patient- controlled analgesia).

This patient should be started on a continuous or basal rate on the PCA.

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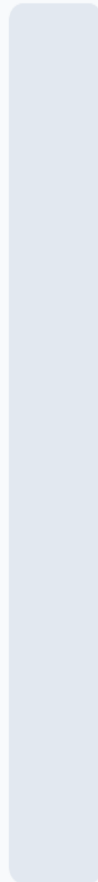

(A)
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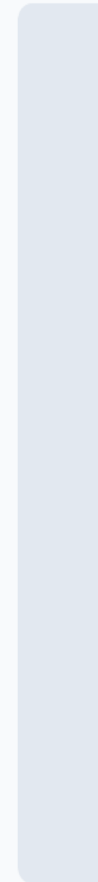

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Case 3 – HZ

83 y/o with HTN, CHF, CKD4 admitted from outside hospital for new pelvic mass. You have notified the gyn oncology team who will take HZ for an ultrasound and potentially exam under anesthesia tomorrow.

Overnight, covering provider is paged for pain and orders hydromorphone 1 mg IV x 1.

Later, you get paged....

Common Medications

- Morphine
- Oxycodone
- Hydromorphone
- Fentanyl
- Methadone

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Equianalgesic Dosing

American Academy of Hospice and Palliative Medicine (AAHPM), Equinalgesic Guide for Adults and Children with Communication Tool (Chicago: AAHPM, 2014).

Medication	PO	IM/IV
Morphine	30 mg	10 mg
Oxycodone	20 mg	N/A
Hydromorphone	7.5 mg	1.5 mg

Conversions Between PO and IV Route

Morphine

15 mg PO morphine = 5 mg IV

10 mg IV morphine = 30 mg PO

Hydromorphone

10 mg PO hydromorphone = 2 mg IV

1 mg IV hydromorphone = 5 mg PO

Hydromorphone 1 mg IV = Morphine 20 mg PO

Acute Pain: General Rules of Thumb

PO Route

- If able to tolerate PO medications, **this should be first choice**
- If no contraindications (allergy, renal dysfunction), then morphine is a good first choice
- Opioid naïve patients: Reasonable to start between 5 – 7.5 mg PO (moderate pain) or 10 – 15 mg PO (severe pain)

- *Note: 5 mg, 10 mg dosing – use liquid suspension*
- *Note: 7.5 mg, 15 mg dosing – can use tablet (or suspension if easier for pt)*

Acute Pain: PO Route Continued

What if patient cannot tolerate morphine?

Oxycodone

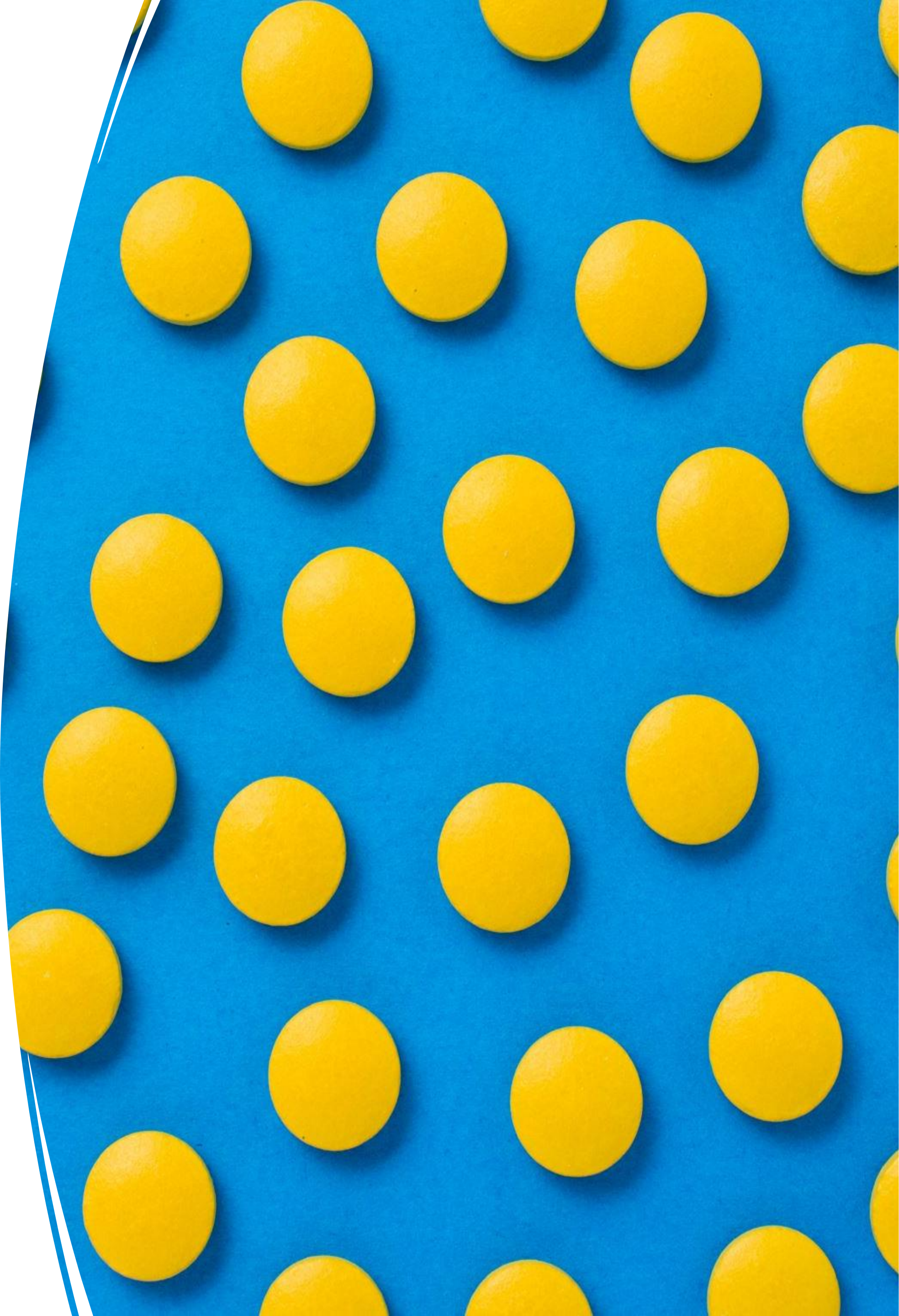
Opioid naïve patients:

- 2.5 – 5 mg PO (moderate pain)
- 5 - 7.5 mg PO (severe pain)

Hydromorphone

Opioid naïve patients:

- 1-2 mg PO (moderate pain)
- 2-4 mg PO (severe pain)



Acute Pain
IV Route

For patients that cannot take PO or severe pain that requires immediate relief

Morphine

Opioid naïve patients: Reasonable to start between 1- 2 mg IV (moderate pain) or 2-4 mg IV (severe pain)

Hydromorphone

Opioid naïve patients: Reasonable to start between 0.25 - 0.5 mg PO (moderate pain) or 0.5mg - 1 mg IV (severe pain)

Acute On Chronic Pain

Continue home pain medications!

Anticipate 30-50% increase in opioid needs (and maybe more!)

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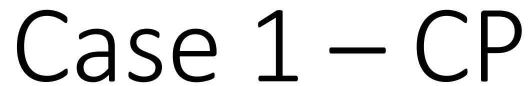
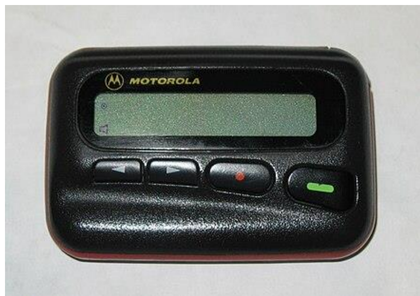


45 y/o with metastatic colorectal cancer admitted with a malignant bowel obstruction. Your team has dropped an NGT, requested a surgical consult, and have made GP NPO. At baseline, they take morphine ER 30 mg PO TID and morphine IR 15 mg PO every 4 hours prn (typically takes 2 per day).

Post-operatively, they are ordered for morphine 4 mg IV every 4 hours prn.



It’s 3 am…Beep!

CP is complaining of severe, uncontrolled pain.

The RN is asking you to come address.

Where did we go wrong? What should we have done?

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How do we address CP's pain?

Need to consider their baseline analgesic use:

Morphine ER 30 mg PO TID → 90 mg/day
Morphine IR 15 mg PO x 2 → 30 mg/day

What is the IV equivalent of this?

120 mg/3 = 40 mg IV

CP continued – dealing with baseline meds

At baseline, they use 40 mg IV morphine equivalent

Incorporate this as either scheduled medication or a continuous rate on PCA

Ideas:

- Morphine PCA 1.5 mg/hour (40 mg/24 hour = 1.67 mg/hour)
- Morphine 5 mg IV every 3 hours around the clock (40 mg/8)
- Morphine 6 mg IV every 4 hours (40 mg/6 → 6.7 mg)

Acute Pain Needs

CP may require additional pain medication secondary to pain from small bowel obstruction

They typically take morphine 15 mg PO every 4 hours prn pain.

15 mg PO/3 = 5 mg IV

Case 2 - EE

68 y/o patient with end-stage COPD admitted from home hospice due to increased symptom management needs. EE was using concentrated morphine suspension (20 mg/mL) for dyspnea. He was ordered for 20 mg PO every 4 hours and every hour prn. Per EE's caregiver, he was using at least 10 prn doses per day, and still had significant dyspnea.

At time of admission, you decide to put EE on a morphine PCA (patient-controlled analgesia).

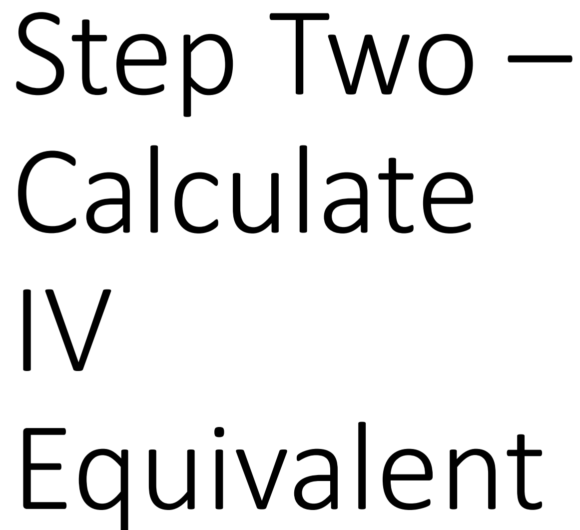
Step One – Calculate 24 Hour Needs

20 mg PO every 4 hours and every hour prn. Per EE's caregiver, he was **using at least 10 prn doses per day**, and still had significant dyspnea.

20 mg x 6 = 120 mg

20 mg x 12 = 240 mg

360 mg/24 hours



Step Two – Calculate IV Equivalent

At baseline, EE is using 360 mg of PO morphine/day

Medication	PO	IM/IV
Morphine	30 mg	10 mg

360 mg/3 = 120 mg IV morphine/day

Step Three – Basal Rate

EE requires 120 mg IV morphine/day

120 mg/24 hours = 5 mg/hour

Step Four – Demand Doses

Dealer's Choice

5 mg every 6-10 minutes
6 mg every 6-10 minutes
7 mg every 6-10 minutes

Case 3 – HZ

83 y/o with HTN, CHF, CKD4 admitted from outside hospital for new pelvic mass. You have notified the gyn oncology team who will take Mrs. Z for an ultrasound and potentially exam under anesthesia tomorrow.

Overnight, covering provider is paged for pain and orders hydromorphone 1mg IV x 1.

How do we avoid...

HZ is relatively opioid naïve

Hydromorphone 1 mg IV =Morphine 20 mg PO

Given age and co-morbidities, probably should have started with:

- Hydromorphone 0.25 mg IV x 1 (can repeat if pain still uncontrolled)
- Hydromorphone 1 mg PO x 1 (can repeat if pain still uncontrolled)

Avoid morphine given her CKD

Opioid Rotation and Cross-Tolerance

Consider for patients:

- On opioids for long period of time with worsening pain control
- Who have contraindication to current opioid
  - Renal failure
  - Cachexia (fentanyl patch)
- Have a new symptom (dyspnea) that would benefit from opioid
  - Typically morphine IR or hydromorphone most helpful for dyspnea

Cross-tolerance

- Rule of thumb is to decrease by about 25-50% when rotating opioids
- Special considerations: fentanyl, methadone

McPherson ML. Why equianalgesic tables are only part of the answer to equianalgesia. *Ann Palliat Med*. 2020;9(2):537-541. doi:10.21037/apm.2020.03.05

Coming Attractions

Methadone
Fentanyl
Ketamine
Buprenorphine

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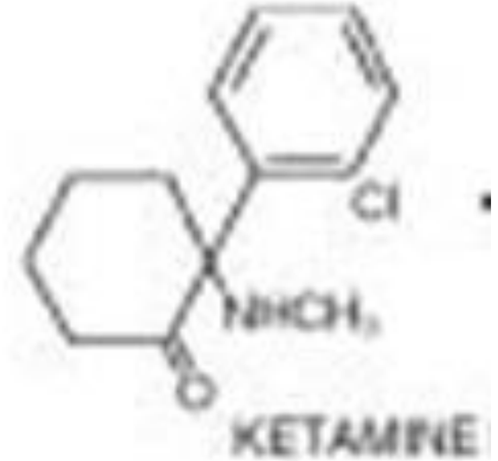

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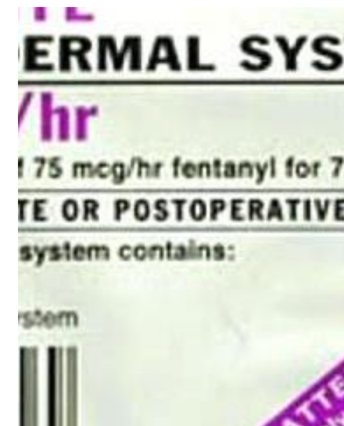


Fentanyl

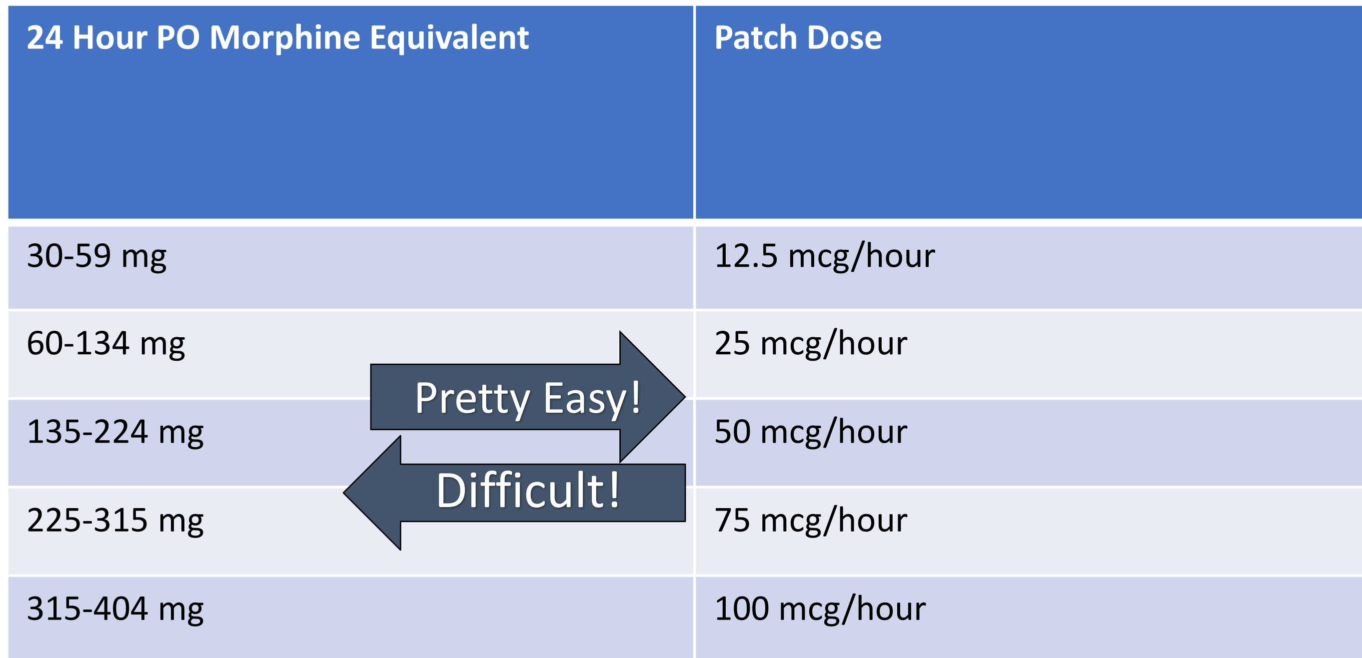
PROS:

- OK in renal insufficiency
- Transdermal Patches bypass Oral, GI route

CONS:

- Not dialyzable. Do not use in dialysis
- Not as straightforward as other conversions
- Not to be used in opioid-naïve patients

Fentanyl (Transdermal Patch)



24 Hour PO Morphine Equivalent	Patch Dose
30-59 mg	12.5 mcg/hour
60-134 mg	25 mcg/hour
135-224 mg	50 mcg/hour
225-315 mg	75 mcg/hour
315-404 mg	100 mcg/hour

American Academy of Hospice and Palliative Medicine (AAHPM), Equinalgesic Guide for Adults and Children with Communication Tool (Chicago: AAHPM, 2014).

Methadone

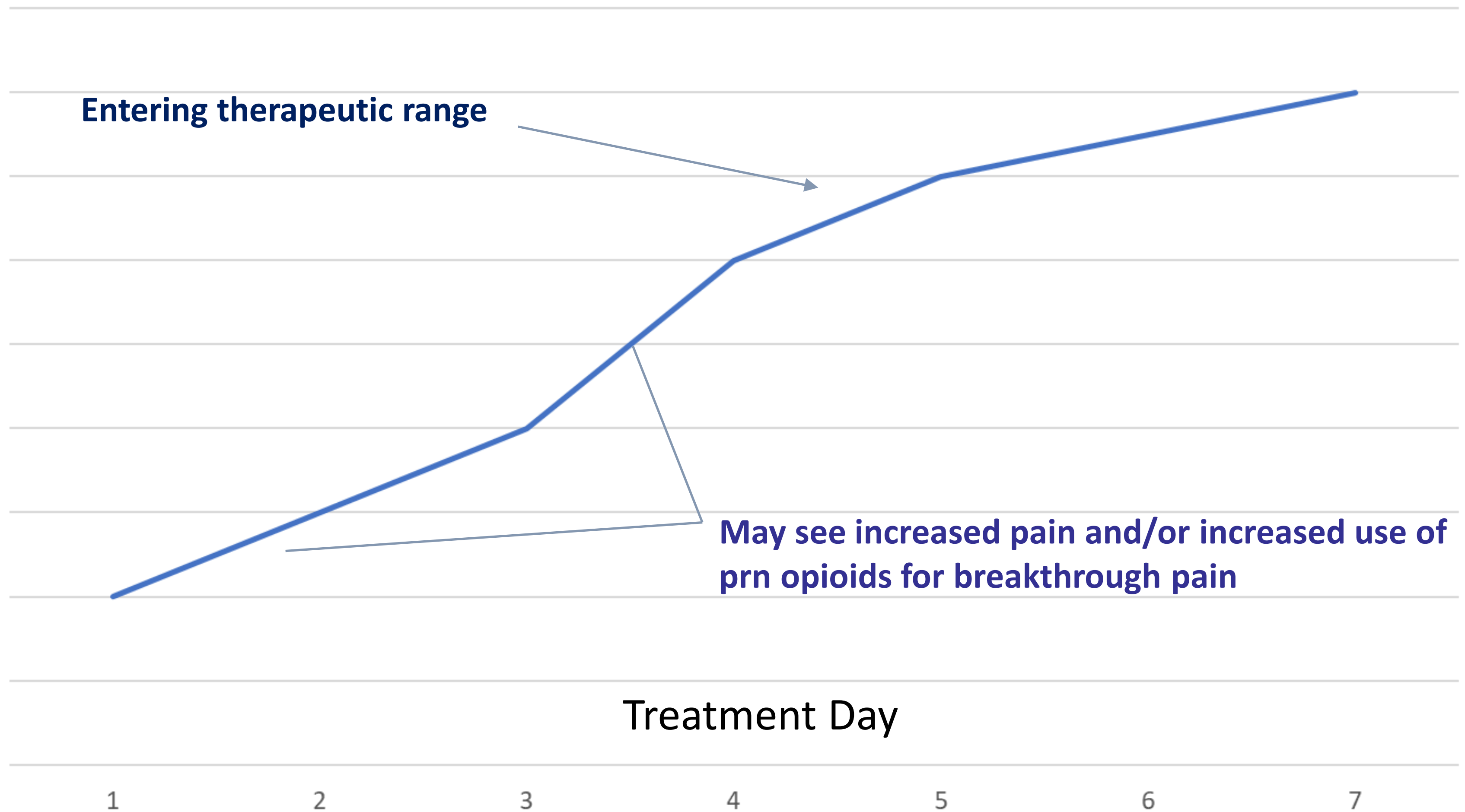
PROS:

- Excellent pain medication
- Unique receptor activity
- Inexpensive
- Has both oral and IV formulation

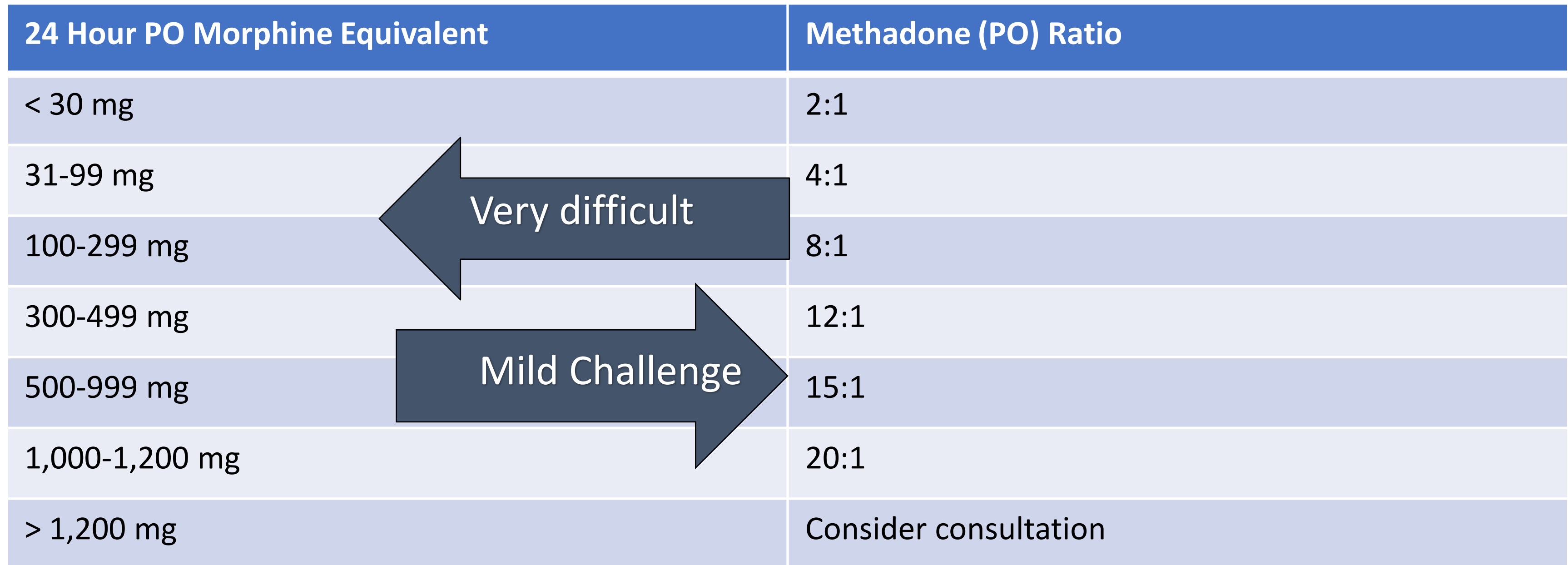
CONS:

- Dosing can be tricky
- QTc Prolongation
- Bad Rep: “Heroin Drug”
- Elimination half-life of methadone is longer than its analgesic effect
- Avoid rapid escalation

Methadone Pharmacology



Methadone



24 Hour PO Morphine Equivalent	Methadone (PO) Ratio
< 30 mg	2:1
31-99 mg	4:1
100-299 mg	8:1
300-499 mg	12:1
500-999 mg	15:1
1,000-1,200 mg	20:1
> 1,200 mg	Consider consultation

American Academy of Hospice and Palliative Medicine (AAHPM), Equianalgesic Guide for Adults and Children with Communication Tool (Chicago: AAHPM, 2014).

Methadone Pearls

- PO to IV Conversion
  - 2 → 1 Conversion (Oral to IV)
  - Important to continue methadone if patient is NPO
- To Hold, or Not to Hold (that is the question)
  - Answer is “probably do not hold”
- What if patient has acute pain at time of methadone administration?
  - Ok to give short acting medication with methadone

Case Scenario

Ms. P has metastatic breast cancer with bony metastases and neuropathic pain. You decide to start her on methadone 5 mg PO BID and morphine IR 7.5 mg PO every 4 hours prn.

On day 3, the nurse pages you to tell you that Ms. P continues with horrible pain and wants something done about it. Per MAR review, you see that she has used 2-3 doses of prn morphine over past 24 hours.

What would you do?

A Increase methadone by 10% — 0%

B Increase methadone by 50% — 0%

C Stop methadone - it's not working — 0%

D Increase dose and/or frequency of prn morphine and encourage its use — 0%

None of the above — 0%

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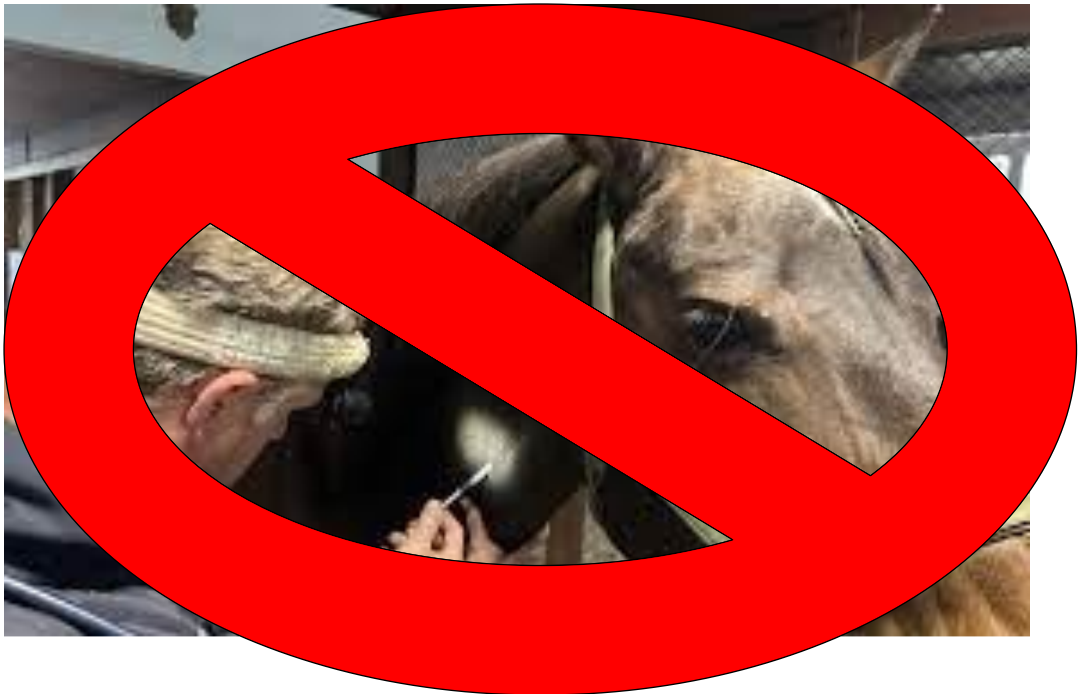
Ketamine

May see this more, as it is becoming a standard of care for intractable, acute on chronic pain



Ketamine – How Does it Work?

Niesters M, Martini C, Dahan A. Ketamine for chronic pain: risks and benefits. *Br J Clin Pharmacol*. 2014;77(2):357-367. doi:10.1111/bcp.12094

Produces strong analgesia in neuropathic pain states

- Inhibition of NMDA reception (NMDAR)
- NMDAR are activated and up-regulated in chronic pain states
- Ketamine can halt nociceptive input brain[42]

May also affect other receptor systems, such as opioidergic, muscarinic, and monomingeric receptors

Jury is still out on how to best use ketamine in patients with chronic pain

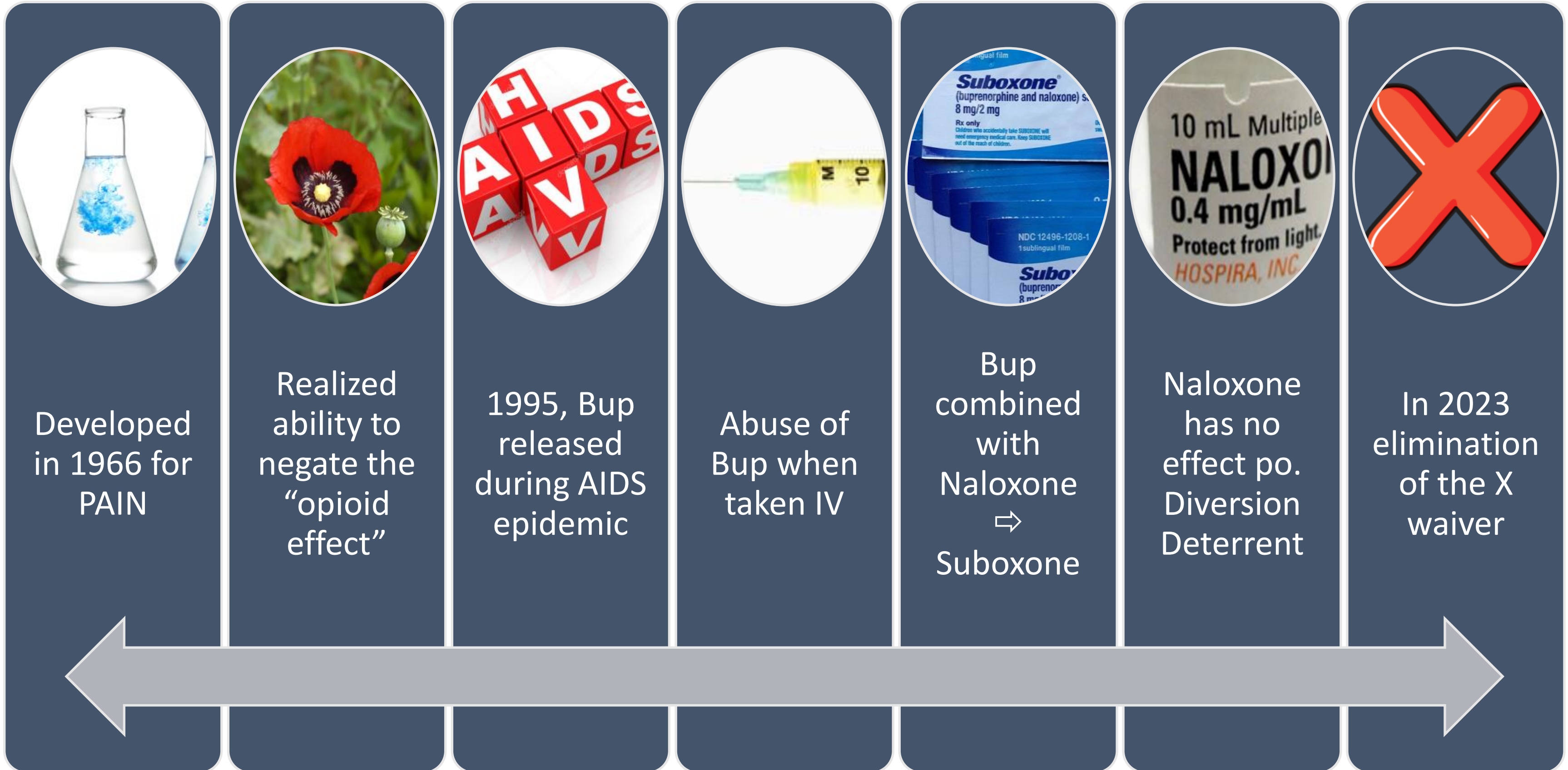
Ketamine

Research findings:

- Peri-operative, associated with decreased morphine consumption and better symptom control
- Improved efficacy of opioid treatment in patients with cancer associated pain
- Interacts with opioids additively or synergistically
- NMDAR antagonists prevent development of opioid induced hyperalgesia

Jouguelet-Lacoste J, La Colla L, Schilling D, Chelly JE. The use of intravenous infusion or single dose of low-dose ketamine for postoperative analgesia: a review of the current literature. *Pain Med*. 2015;16(2):383-403. doi:10.1111/pme.12619
Lossignol DA, Obiols-Portis M, Body JJ. Successful use of ketamine for intractable cancer pain. *Support Care Cancer*. 2005;13(3):188-193. doi:10.1007/s00520-004-0684-4

Buprenorphine



Sivils A, Lyell P, Wang JQ, Chu XP. Suboxone: History, controversy, and open questions. Front Psychiatry. 2022 Oct 28;13:1046648. doi: 10.3389/fpsyt.2022.1046648. PMID: 36386988; PMCID: PMC9664560.

<u>Pharmacokinetics</u>

Ceiling effect

High affinity

<u>Pharmacodynamics</u>

Treats Pain

Reduces W/D

Reduces craving

Blunt other opioids

Perioperative or Acute Pain Tx when on Bup

CONTINUE, CONTINUE, CONTINUE

- Opioids that can out compete μ receptor affinity: fentanyl, hydromorphone
- If you are using oxycodone – must use a higher dose
- Can use PRN Bup (1/6 of TDD. If on 24mg Suboxone, use 4mg Suboxone q6 hours PRN)

Transdermal Buprenorphine Patch

Table 1. Initial Buprenorphine Transdermal Patch Dose Recommendations

Previous Total Daily Opioid Dosage[a]	Initial Transdermal Dosage
Opioid-naïve	5 mcg/h
<30 mg	5 mcg/h
30-80 mg	10 mcg/h (must taper previous opioid for up to 7 days to no more than 30 mg of oral morphine [or its equivalent] per day prior to initiating patch)
>80 mg	Consider an alternative analgesic

[a] *In oral morphine-equivalents. Source: Reference 1.*

Vartan, C. M. (2014, October 16). *Buprenorphine transdermal patch: An overview for use in chronic pain*. U.S. Pharmacist. https://www.uspharmacist.com/article/buprenorphine-transdermal-patch-an-overview-for-use-in-chronic-pain

Buprenorphine Patch

Pros

- Convenience
- Route
- Consistent blood levels
- Less constipation
- Good in renal dx/dialyzable

Cons

- Slow onset
- Long elimination period
- Not good for acute pain

Transdermal Patch

- Potential to ↑ QTc interval by up to 9.2ms
- In the US, dosages >20 should not be used
- Outside US, patches available in 35, 52.5, 79 mcg/h
- If discontinuing, dose should be tapered down every 7 days to avoid w/d
- No dose adjustment for renal or hepatic impairment or for elderly

Race and Pain Management

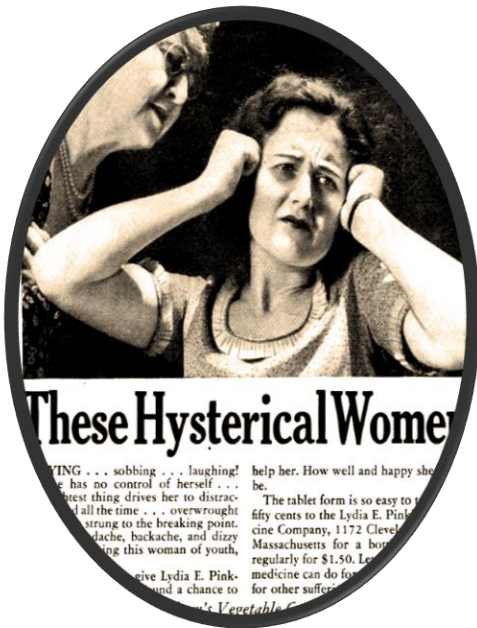
Multiple research studies have revealed that minority patients more likely have their pain underestimated and be undertreated for their pain

Hypothesized reasons:

1) Recognition of pain, but do not treat – concern for noncompliance, limited access to health care

2) Pain is not recognized (not believed?)

Hoffman KM, Trawalter S, Axt JR, Oliver MN. Racial bias in pain assessment and treatment recommendations, and false beliefs about biological differences between blacks and whites. *Proc Natl Acad Sci U S A*. 2016;113(16):4296-4301. doi:10.1073/pnas.1516047113



“Brave Men” vs “Emotional Women”

One recent study, looking at renal colic in the ED

- Men were more likely to receive analgesic medication as compared with women
- Opioids significantly more likely to be used in men
- More analgesic medications (by number) were used in men (significant result)

Samulowitz A, Gremyr I, Eriksson E, Hensing G. "Brave Men" and "Emotional Women": A Theory-Guided Literature Review on Gender Bias in Health Care and Gendered Norms towards Patients with Chronic Pain. *Pain Res Manag*. 2018;2018:6358624. Published 2018 Feb 25. doi:10.1155/2018/6358624

Naamany E, Reis D, Zuker-Herman R, Drescher M, Glezerman M, Shiber S. Is There Gender Discrimination in Acute Renal Colic Pain Management? A Retrospective Analysis in an Emergency Department Setting. *Pain Manag Nurs*. 2019;20(6):633-638. doi:10.1016/j.pmn.2019.03.004

Key Takeaways

Opioids are not equivalent

- Differences between route of administration
- Differences across type of opioid

Opioids are DANGEROUS when math is ignored

When in doubt, reach out!

Good resource:

https://opioidcalculator.practicalpainmanagement.com/

References

- American Academy of Hospice and Palliative Medicine (AAHPM), Equinalgesic Guide for Adults and Children with Communication Tool (Chicago: AAHPM, 2014).
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