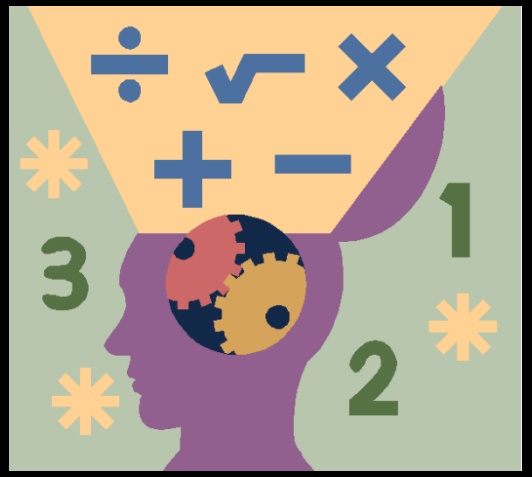
PAINWEEK®

The Wild, Wild World of MATHadone: Opioid Conversion Calculations and Methadone Dosing



Alexandra L. McPherson, PharmD, MPH
Clinical Specialist, Palliative Care
MedStar Washington Hospital Center
Alexandra.l.mcpherson@medstar.net
Mary Lynn McPherson, PharmD, MA, MDE, BCPS, CDE
Professor and Executive Director, Advanced Post-Graduate Education in Palliative Care
Program Director, Online Master of Science in Palliative Care
University of Maryland School of Pharmacy
mmcphers@rx.umaryland.edu | graduate.umaryland.edu/palliative

What hath thou to disclose?

- Nothing…..absolutely nothing…..so boring….

Objectives

- At the conclusion of this lecture, the participant will be able to:
  - Describe the rationale for rotating patients from one opioid to another when treating chronic pain.
  - Identify recent research on retrospective opioid conversions and impact on the development of an equianalgesic opioid resource.
  - Given a simulated patient, calculate a new opioid regimen using the same opioid but with a different dosage formulation or route of administration.
  - Given a simulated patient, calculate a new opioid regimen that reflects switching between opioids, dosage formulations and/or routes of administration.
  - Describe appropriate dosing strategies for dosing methadone in opioid-naïve and opioid-tolerant patients.

Reasons for Changing Opioids

- Lack of therapeutic response
- Development of adverse effects
- Change in patient status
- Other considerations
  - Opioid/formulation availability
  - Formulary issues
  - Patient/family health care beliefs

- Opioid rotation
- Opioid substitution
- Opioid switching
- Opioid Conversion Calculation!

Equianalgesic Dosing Terminology

- Opioid responsiveness
  - The degree of analgesia achieved as the dose is titrated to an endpoint defined either by intolerable side effects or the occurrence of acceptable analgesia
- Potency
  - Intensity of the analgesic effect of a given dose
  - Dependent on access to the opioid receptor and binding affinity
- Equipotent doses = equianalgesic
- Equianalgesic Opioid Dosing

Converting Among Routes: Same Opioid

- Bioavailability
  - The rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action
- Oral bioavailability
  - Morphine 30-40% (range 16-68%)
  - Hydromorphone 50% (29-95%)
  - Oxycodone 80%
  - Oxymorphone 10%

Equianalgesic Opioid Dosing

	Equianalgesic Doses (mg)	
Drug	Parenteral	Oral
Morphine	10	25
Codeine	100	200
Fentanyl	0.15	NA
Hydrocodone	NA	25
Hydromorphone	2	5
Meperidine	100	300
Oxycodone	10*	20
Oxymorphone	1	10
Tapentadol	NA	100
Tramadol	100*	120

NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

*Not available in the US

The Problem with “Those Charts”

- Source of equianalgesic data
- Patient-specific variables
- Unidirectional vs. bidirectional equivalencies

5-Step OCC Process

1. Globally assess pain complaint (PQRSTU)
2. Determine TDD current opioid (LA and SA)
3. Decide which opioid analgesic will be used for the new agent and consult established conversion tables to determine new dose
4. Individualize dosage based on assessment information gathered in Step 1
5. Patient follow-up and continual reassessment (7-14 days)

Gammaitoni AR, et al. Clinical J Pain 2003;19:286-297

Case 1

- HW is an 84 year old man in a LTC facility with general debility on oxycodone 5 mg/acetaminophen 325 mg tabs, six per day, pain well controlled.
- He can no longer swallow the tablets and his physician asks you convert him to an oral solution of oxycodone 5 mg per 5 ml.

Case 1

1. Pain assessed; stable and controlled
2. Six tabs x 5 mg oxycodone per day = 30 mg TDD oral oxycodone
3. Switching to 5 mg oxycodone by oral solution (5 mg/5 ml). Dose is 5 mg; volume is 5 ml (5 mg oxycodone/5 ml) q4h
4. Individualization – oxycodone is oxycodone; no need to change dose
5. Monitor response

Case 1 To Go Points

- Ignore contribution of acetaminophen
- You're going from oral oxycodone tablet (as oxycodone/acetaminophen) to oral oxycodone (oral solution).
  - The only thing you have to consider is the bioavailability difference between oxycodone as a tablet, and oxycodone as an oral solution.
  - It's the same, so it's a 1:1 conversion.

Case 2

- WP is a 62 year old man with multiple myeloma and diffuse bony mets admitted to hospice.
- Current analgesic regimen extended-release oral morphine 30 mg po q12h plus oral morphine solution 10 mg prn (takes six times per day), plus dexamethasone.
- Admitted to inpatient to switch to IV morphine due to continued pain.

Case 2

- Pain assessed
- TDD oral morphine = 30 mg po q12h = 60
- Oral morphine solution 10 mg x 6 = 60 mg
- TDD = 120 mg oral morphine
- Consult equianalgesic dosing chart for equivalency

TDD – total daily dose

Case 2

$$\frac{\text{“x” mg new opioid}}{\text{mg of current opioid}} = \frac{\text{equivalent mg new opioid}}{\text{equivalent mg current opioid}}$$

$$\frac{\text{“x” mg IV morphine}}{\text{120 mg oral morphine}} = \frac{\text{10 mg (IV morphine)}}{\text{25 mg (oral morphine)}}$$

$(x)(25) = (10)(120)$

X = 48 mg IV morphine per day

25-50% increase → morphine 10 mg IV q4h (TDD 60 mg)

Case 2 To Go Points

- You're converting from morphine to morphine, BUT you're converting between routes of administration (oral to IV)
  - Morphine IV dose = ~ 1/3 of morphine PO dose
  - So, morphine IV dose is ~ 1/3 morphine PO dose (work in total daily doses for ease of calculation)

Case 2 To Go Points

- When you do a conversion calculation if you are SWITCHING from one opioid to a DIFFERENT opioid, you usually need to reduce the dose you calculated
  - This patient was going from morphine to morphine so you don't have to do that
- BUT he is in pain, so you need to increase the dose

Case 3

- Mrs. Smith is a 92 year old woman with breast cancer, currently receiving MS Contin 60 mg po q12h, plus MSIR 20 mg po q4h prn, taking on average 3 doses per day.
- She has been on this dose for about 2 weeks, and her pain is well controlled, but she has developed visual hallucinations which she finds quite frightening.
- She has significant renal impairment (serum creatinine of 2.0 mg/dl) and this adverse effect may be due to accumulation of morphine metabolites.
- Her physician would like to switch her to long-acting oxycodone.
- What are the steps necessary to make this conversion?

Setting up the Conversion Equation

1. Calculate total daily dose of current opioids.
2. Set up conversion ratio between old opioid (and route of administration) and new opioid (and route of administration) as follows:

$$\frac{\text{“x” mg new opioid}}{\text{mg of current opioid}} = \frac{\text{equivalent mg new opioid}}{\text{equivalent mg current opioid}}$$

Case 3

"x" mg new opioid = equivalent mg new opioid
mg of current opioid equivalent mg current opioid

"x" mg new opioid = 20 mg (oxycodone)
180 mg morphine 25 mg (morphine)

(x)(25) = (20)(180)
X = 144 mg oral oxycodone per day

Solving the Equation

- Cross multiply, solve for “x”
- Individualize dose for patient
  - Pain controlled; developed adverse effect
  - Reduce 25-50%
  - Calculated oxycodone 144 mg po qd
  - Reduce to 72 - 108 mg po qd

Solving the Equation

- Reduce to 72 - 108 mg po oxycodone qd
- Decide how many times per day you're going to dose the new opioid; divided by the appropriate dosing interval, and select a dosage that is available in that strength.
- Oxycodone extended-release 30 mg po q12h (or 40 mg po q12h) with oxycodone IR 10 mg po q2h prn

Case 3 To Go Points

- In this case you are switching from one opioid to a DIFFERENT opioid
- Set up your ratio, calculate total daily dose of NEW opioid
  - If patient's pain was well controlled, REDUCE your calculated dose by 25-50%
  - If patient was in pain at the time of the switch, go with calculated dose (or round down a little)
- Make sure you can GIVE the dose you recommend
  - With available tablets, capsules or oral solution

Switching

From one formulation or route to another of the SAME opioid

- Account for bioavailability
- Increase if patient in pain

From one opioid to another opioid

- Use ratios from equianalgesic chart
- If pain controlled, REDUCE calculated dose by 25-50%
- If patient in pain, use calculated dose, or a little less.

Case 4

- Mrs. Claytor is a 62 year old woman with pancreatic cancer.
- Her pain is well controlled, but she is unable to swallow the MS Contin tablets (200 mg po q12h) or even the oral morphine solution (40 mg q3h prn breakthrough pain, she uses about one dose per day).
- Her physician would like to switch her to a parenteral SQ morphine infusion. Recommendation?

Case 4

$$\frac{\text{“x” mg SQ morphine}}{\text{440 mg oral morphine}} = \frac{\text{10 mg SQ morphine}}{\text{25 mg oral morphine}}$$

- Cross multiply and solve for “x” as follows:
  - (25)(x) = (10)(440)
  - 25x = 4400
  - x = 176 mg SQ morphine per day
  - 176 / 24 hours = 7.3 mg/hour
  - Recommend 7 mg/hour

Case 4

- Bolus dose?
  - 50-100% of hourly infusion rate
  - 3.5 - 7 mg every 30 minutes SQ (could extend dosing interval once stable)
- When should the continuous infusion start relative to the last dose of MS Contin?

Case 4 To Go Points

- You are switching from oral morphine to IV morphine
  - But you've been asked to calculate a continuous infusion
- No need to dose reduce due to lack of cross-tolerance (morphine to morphine)
- No need to change dose you calculate (no mention of uncontrolled pain)
- Calculate infusion rate, AND bolus dose

Case 5

- MJ is a 68 year old man admitted for total hip replacement.
- He was started on a PCA pump, hydromorphone 0.2 mg IV q10min.
- From hours 48-60 he used a total of 7.2 mg IV hydromorphone
- Convert to short-acting AND long-acting oral morphine (at 50% of IV requirements).

Case 5

- 7.2 mg IV hydromorphone over 12 hours = 14.4 mg IV hydromorphone over 24 hours

$$\frac{\text{“x” mg PO morphine}}{\text{14.4 mg IV HM}} = \frac{\text{25 mg PO morphine}}{\text{2 mg IV HM}}$$

- (2)(x) = (25)(14.4)
- X = 180
- Reduce by 50% - 90 mg oral morphine a day
- 90 mg/6 = 15 mg → MSIR 15 mg po q4h
- LA MS
  - 108 mg → MS Contin 45 mg po q12h
  - 108 mg/2 → Kadian 50 mg po q12h
  - 108 mg/3 → Oramorph SR 30 mg po q8h

Case 5 To Go Points

- Going from IV to oral opioid
- This is ACUTE pain – should be getting better every day
- Consider giving as short-acting opioid
  - Unless pain expected to last a good while, then consider long-acting opioid

Case 6

- Mrs. Hendricks is a 54 year old woman with end-stage esophageal cancer.
- She is receiving TDF 75 mcg, every 72 hours for persistent pain.
- You would like to use morphine oral solution (20 mg/ml) for breakthrough pain. What does do you recommend?

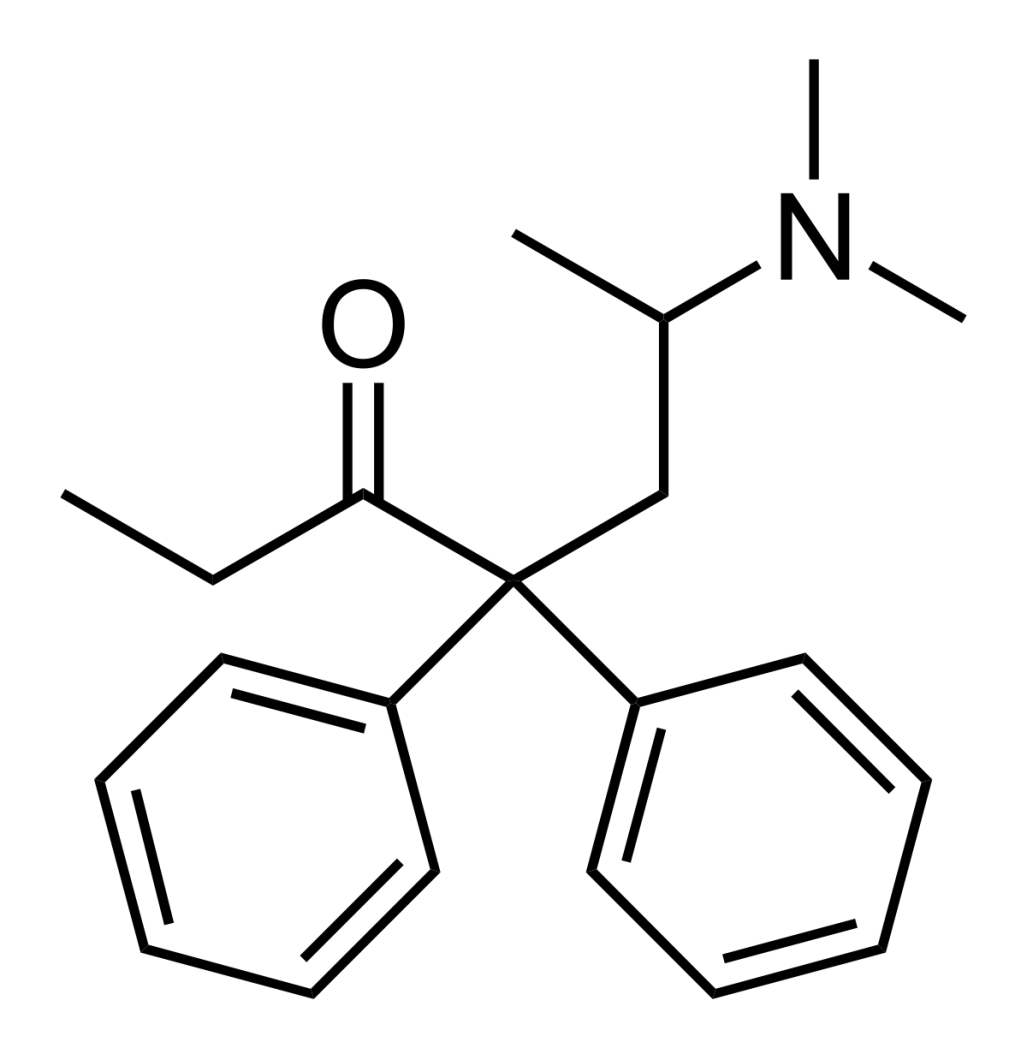
Case 6

- TDF 75 mcg ~ 150 mg TDD oral morphine
  - 10% = 15 mg
  - 15% = 22.5 mg
- Morphine oral solution, 20 mg every 2 hours as needed for breakthrough pain
- Keep a pain diary, rate pain before and after rescue opioid

Case 6 To Go Points

- TDF mcg/h x 2 ~ total daily dose oral morphine
- Apply 10-15% rule (10-15% of total daily oral morphine dose = ONE dose of breakthrough short-acting opioid)

Methadone



Case 1

- BL is a 54 year old woman with a 10 year history of low back pain, now failed back.
  - Did not respond to acetaminophen, NSAID
  - Adverse effects to gabapentin and duloxetine
- Not taking any medications that interact with methadone, and is opioid-naïve.
- Doesn't want a short-acting opioid because she works in an office and is afraid of "peak" effect.
- PCP asks for dosing recommendation.

What do YOU think?

- 54 years old, ambulatory, opioid-naïve
- Starting dose of methadone?
  - A. 1 mg by mouth every 12 hours
  - B. 2.5 mg by mouth every 12 hours
  - C. 2.5 mg by mouth every 8 hours
  - D. 5 mg by mouth every 12 hours
  - E. 5 mg by mouth every 8 hours

Case 1

- No interacting medications, and she is younger (54 years old)
- Possible recommendations:
  - 2.5 mg by mouth q12h (half of a 5 mg tablet)
  - 2.5 mg by mouth q8h (possibly switch to q12h dosing later)
- Rescue opioid?
  - If appropriate, morphine or oxycodone 5 mg by mouth every 4 or 6 hours as needed for additional pain

Case 2

- FA is an 89 year old man admitted to hospice with a diagnosis of protein-calorie malnutrition, complaining of generalized aches and pains.
- Patient is ambulatory and frail.
- Has a history of bleeding ulcer, PCP does not want to prescribe a NSAID. Did not respond to acetaminophen.
- PCP would like you to recommend a methadone dose.
- No interacting medications.

Case 2

- No interacting medications, but he is elderly and frail.
- Possible recommendations:
  - 1 mg by mouth qam or qhs
  - 1 mg by mouth q12h
  - 2.5 mg by mouth qam or qhs
- Rescue opioid?
  - Morphine or oxycodone 2.5 to 5 mg by mouth every 2, 3 or 4 hours as needed for additional pain

Initiating Methadone (Chou,APS)

- Start at low dose
  - In opioid-naïve patients, or converting from low doses of other opioids (e.g., < 40-60 mg OME/day) – do not exceed methadone 2.5 mg by mouth every 8 hours
    - Dose increases no more than 5 mg/day every 5-7 days
  - Converting from higher doses of other opioids, start methadone at 75-90% less than calculated equianalgesic dose
    - Do not exceed methadone 30-40 mg by mouth qd
    - Dose increases no more than 10 mg/day every 5-7 days

OME – oral morphine equivalent

Initiating Methadone (HPM)

- In opioid-naïve patients, or ≥ 40-60 mg OME/day – do not exceed methadone 2-7.5 mg by mouth per day in 2-3 divided doses
  - 1 mg by mouth q12h (oral solution)
  - 2 mg by mouth q12h (oral solution)
  - 2.5 mg by mouth q12h (tablet or oral solution)
  - 2.5 mg by mouth q8h (tablet or oral solution)
- Reduce calculated dose by 25-33% if enzyme inhibiting medication on board
- Dose increase no more than 5 mg/day every 5-7 days

OME – oral morphine equivalent

Case 3

- AO is a 64 year old woman with end-stage breast cancer. She is taking extended-release morphine 60 mg by mouth q12h with morphine oral solution 20 mg by mouth q2h prn breakthrough pain (using about 2 doses qd).
- The morphine makes her itch, and diphenhydramine makes her too sleepy. Her physician would like to switch her to methadone. AO not taking any interacting medications.
- Step 1 - PQRST
- Pain is nociceptive and neuropathic; pain in chest area, numbness and tingling from axilla, down arm

Case 3 – Step 2 (TDD Opioid)

- She is taking extended-release morphine 60 mg by mouth q12h with morphine oral solution 20 mg by mouth q2h prn breakthrough pain (using about 2 doses qd).
- TDD = 60 mg x 2 = 120 mg PLUS 20 x 2 = 40 mg for a TDD of 160 mg oral morphine
- If patient is not already taking oral morphine, convert to oral morphine
  - Refer to equianalgesic dosing chart
  - Consider LA and SA opioid use
  - Do not reduce for lack of complete cross-tolerance

	Equianalgesic Equivalence (mg)	
Opioid	Parenteral	Opioid
Morphine	10	25
Fentanyl	0.15	NA
Hydrocodone	NA	25
Hydromorphone	2	5
Oxycodone	10 (not in US)	20
Oxymorphone	1	10

NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

Case 3 – Step 3 – Conversion

- Patient's TDD oral morphine is 160 mg; < 65 years old
- Use 10:1 conversion
  - Methadone 16 mg TDD
  - Recommendation: 8 mg po q12h (or 5 mg po q8h)
- No interacting medications
  - No need to reduce methadone dose
- What to do for rescue medication?
  - Methadone?
  - Morphine or oxycodone – 10-15% TDD
    - Morphine (MSIR) 15 mg by mouth q4h prn breakthrough pain
- Rapid switch or gradual?

TDD – total daily dose

Case 3 – Step 5: Patient Monitoring

- Ask AO's husband to observe AO several times a day for changes in her respirations (depth, rhythm, rate), difficulty awakening her, snoring, and other signs of opioid overdose.
- We will see or speak to AO/husband daily over the next week.
- Do not adjust therapy before 5-7 days.

Case 4

- Mrs. Juniper is an 84 year old woman residing in a long-term care facility, admitted to hospice with a diagnosis of Alzheimer's dementia.
- She also has a long history of chronic low back pain (spinal stenosis) and osteoarthritis of both knees and hips.
- She is bedbound for much of the day, and shifts about restlessly. The nurse case manager believes this is due to physical discomfort.
- The patient was admitted to hospice on OxyContin 20 mg by mouth every 12 hours, and oxycodone oral solution 5 mg every 2 hours as needed for additional pain (not receiving).
- You decide to switch her to methadone. Not receiving any interacting drugs.

Case 4

- The patient was admitted to hospice on OxyContin 20 mg by mouth every 12 hours, and oxycodone oral solution 5 mg every 2 hours as needed for additional pain (not receiving).
- Her total daily dose of oral oxycodone is 40 mg
- How do you convert this to oral morphine equivalents per day?

Opioid Conversion Calculations

1. Assess patient's pain complaint thoroughly; is pain controlled (at goal?).
2. Determine average total daily dose of current opioid use (long- and short-acting).
3. Set up ratio using equianalgesic equivalence chart; calculate new dose.
4. Individualize calculated dose based on patient assessment in step 1.
5. Monitor patient closely; adjust as needed.

	Equianalgesic Equivalence (mg)	
Opioid	Parenteral	Opioid
Morphine	10	25
Fentanyl	0.15	NA
Hydrocodone	NA	25
Hydromorphone	2	5
Oxycodone	10 (not in US)	20
Oxymorphone	1	10

Reprinted with permission from ML McPherson, Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing, Second Ed. ASHP. ©2018 in press.
NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

Case 4

- Total daily dose of oxycodone is 40 mg

- $\frac{\text{“x” mg oral morphine}}{\text{40 mg oral oxycodone}} = \frac{\text{25 mg oral morphine}}{\text{20 mg oral oxycodone}}$

- (20)(x) = (25)(40)
- X = 50 mg oral morphine
- Because you are using this number to convert to methadone, no need to adjust

Case 4

- 84 years old (> 65 years old)
- Receiving 50 mg OME per day
- Defaults to opioid naïve dosing
- Methadone 1 mg by mouth every 8 OR 12 hours
- Methadone 2 mg by mouth every 12 hours
- Oral morphine solution 5 mg by mouth as needed for additional pain every 2 hours

OME – oral morphine equivalent

Case 5

- Mr. J. is a 62 year old man admitted to home-based hospice with a diagnosis of end-stage prostate cancer, with widespread metastases to the bone.
- He is 5'8" and weighs 165 pounds (normal body habitus)
- Mr. J. is on a transdermal fentanyl patch 75 mcg/h, changed every 72 hours.
- He also has an order for oral morphine solution 20 mg every 2 hours as needed for additional pain (about 5 doses/day).
- His pain is not well managed on this regimen and he wants to switch to a different opioid. Not on any interacting medications.

Case 5

- You decide to switch him from transdermal fentanyl to methadone, and to add dexamethasone for the metastatic bone pain (no history of diabetes or serious gastrointestinal issues)
- How do you determine the oral morphine equivalent of his current regimen?
- What dose of methadone do you recommend starting?
- How would you time removing the transdermal fentanyl patch and starting oral methadone?
- All EXCELLENT questions!

Case 5

- How do you determine the oral morphine equivalent of his current regimen?
  - TDF in mcg/h ~ 50% of total daily dose oral morphine
  - TDF 75 mcg/h ~ 150 mg oral morphine
  - Plus five doses of morphine 20 mg a day = 100 mg
  - TDD oral morphine ~ 250 mg

Case 5

- What dose of methadone do you recommend starting?
  - 62 years old
  - > 200 mg oral morphine per day (he's receiving 250 mg oral morphine)
  - 20:1 (20 mg OME:1 mg oral methadone) → 12.5 mg oral methadone per day
- Considerations
  - He's not that much > 200 mg oral morphine a day
  - Is he a "young" 62 year old or an "old" 62 year old?
  - But you're adding a co-analgesic which COULD give you a significant opioid-sparing effect
  - Be conservative with scheduled methadone, but generous with breakthrough

Case 5

- Recommendation:
  - Methadone 7 mg by mouth every 12 hours (methadone 10 mg/ml)
  - Patient tells you a 20 mg dose of oral morphine brings pain down about 2 points
  - Morphine solution 20 mg by mouth every 2 hours as needed for moderate pain, OR
  - Morphine solution 30 mg by mouth every 2 hours as needed for severe pain
- How would you time removing the transdermal fentanyl patch and starting oral methadone?

Case 5

- How would you time removing the transdermal fentanyl patch and starting oral methadone?
- Once the oral methadone solution is IN THE HOME, remove the transdermal fentanyl patch
- Start methadone 8 hours later
- Use oral morphine solution (at 20 or 30 mg q2h prn)

Case 5

- Patient's opioid log

Day	Methadone	Morphine	Avg Pain Rating
1	Removed TDF at 8 am, one dose methadone 7 mg at 8 pm	4 doses x 30 mg 2 doses x 20 mg = 160 mg OME	8
2	Methadone 7 mg at 8 am and 8 pm	5 doses x 30 mg 2 doses x 20 mg = 190 mg OME	7
3	Methadone 7 mg at 8 am and 8 pm	3 doses x 30 mg 3 doses x 20 mg = 150 mg OME	7
4	Methadone 7 mg at 8 am and 8 pm	2 doses x 30 mg 2 doses x 20 mg = 100 mg OME	6
5	Methadone 7 mg at 8 am and 8 pm	4 doses x 20 mg = 80 mg OME	5
6	Methadone 7 mg at 8 am and 8 pm	4 doses x 20 mg = 80 mg OME	4-5

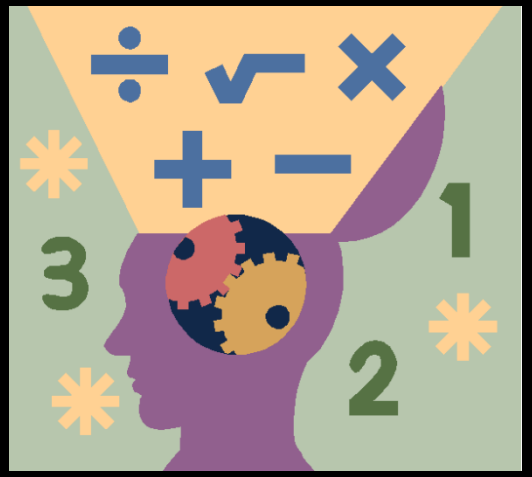
- What would you like to do at this time? Pain goal ≤ 3.

Case 5

- Do not increase methadone before 5 days
- Do not increase by more than 5 mg/day (until TDD methadone > 30 mg)
- Patient currently on methadone 7 mg by mouth every 12 hours
- Increase methadone to 9 mg (or even 10 mg) by mouth every 12 hours
- Maintain oral morphine as prescribed for breakthrough pain

PAINWEEK®

The Wild, Wild World of MATHadone: Opioid Conversion Calculations and Methadone Dosing



Alexandra L. McPherson, PharmD, MPH
Clinical Specialist, Palliative Care
MedStar Washington Hospital Center
Alexandra.l.mcpherson@medstar.net
Mary Lynn McPherson, PharmD, MA, MDE, BCPS, CDE
Professor and Executive Director, Advanced Post-Graduate Education in Palliative Care
Program Director, Online Master of Science in Palliative Care
University of Maryland School of Pharmacy
mmcphers@rx.umaryland.edu | graduate.umaryland.edu/palliative