CONTEMPORARY CASE STUDIES TO MANAGE PAIN

INCLUDING THE UTILIZATION OF BUPRENORPHINE

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Disclosures

- No conflicts of interest to disclose
- Trade names may be used to differentiate form/routes
  - Generics are unavailable for most forms
- The information from Nathan Dewey, MD is presented through the background of a palliative medicine provider
  - It is intended to be generalizable though other prescriber practices may differ
  - The cases presented will rely on knowledge from the prior lecture
- Palliative medicine as a field treats the symptoms of serious, life-threatening illness and helps patients navigate their illness with their self, family, and medical teams
  - In treating cancer-related pain, opioid prescribing may be more aggressive than for chronic, non-malignant pain

Goals

- Review clinical examples to:
- Demonstrate the rationale for prescribing buprenorphine for chronic pain
- Practice converting to buprenorphine and between buprenorphine forms for pain
- Learn how to adjust buprenorphine dosing for pain as indicated
- Understand management principles to enhance medical documentation, communication, and coordination of care

Terms

- Oral morphine equivalents (OME) (in milligrams)
- Morphine equivalent daily dose (MEDD) = Daily OME (in milligrams)
- Buprenorphine (Bup, pronounced “bupe”)
  - If a dose of sublingual buprenorphine is mentioned, the naloxone component may be omitted
- Buprenorphine (Bup) total daily dose (TDD)
- Transdermal (TD)
- Sublingual (SL)
- Two times per day (BID), synonymous with every 12 hours (q12h)
- Three times per day (TID), synonymous with every 8 hours (q8h)
- Four times per day (QID), synonymous with every 6 hours (q6h)
- Breakthrough pain (BTP)

Case 1

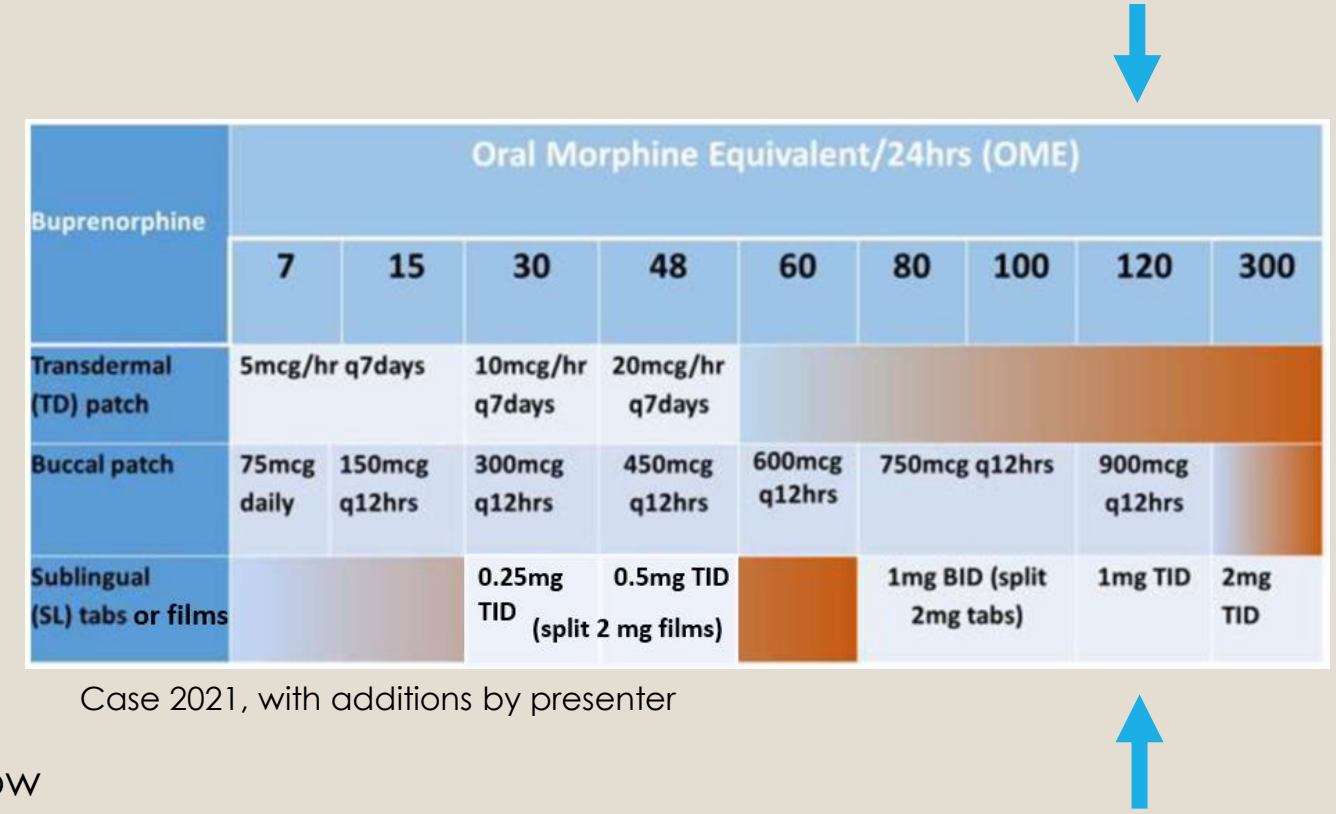
- A 68-year-old man presents with uncontrolled, acute on chronic neck pain following neck dissection for squamous cell carcinoma of the tongue
  - Has chronic neck and back pain following an MVA in the 1970s
- Pain regimen:
  - Prior chronic treatment with: Hydrocodone-Acetaminophen (Norco) 10-325 mg every 8 hours as needed
  - More recent acute treatment with: Oxycodone 15 mg every 4 hours as needed
- Other PMHx:
  - Hypertension
  - Diabetes mellitus type II
  - CAD and PAD with an MI in 2015
  - Prior tobacco use of 100-150 pack years (quit in 2015 after his MI)

Case 1 – Planning

- Patient sees me in clinic (palliative medicine)
- Complaints:
  - Roller coaster: Pain is mostly controlled with oxycodone but it as it wears off and the next dose absorbs, his pain is hard to tolerate
- Considerations:
  - Pain is nonmalignant
  - Expect improvement with healing back to chronic baseline
- Next steps?
  - Rotate to a long-acting typical/full-agonist opioid
  - Rotate to buprenorphine

Case Continued – Paper and Pens

- Conversion:
  - Calculate Daily OME
  - Choose buprenorphine product based on OME range
  - Convert using ratio (based on bioavailability)
    - TD Patch and IV
      - 100:1 ratio (100% bioavailable)
    - Buccal
      - 50:1 ratio (roughly 50% bioavailable)
    - Sublingual
      - 30:1 ratio (roughly 30% bioavailable)
  - Divide dose into appropriate frequency
  - Choose rotation method (stop/start or low dose)



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 or films			0.25mg TID	0.5mg TID (split 2 mg films)		1mg BID (split 2mg tabs)		1mg TID	2mg TID

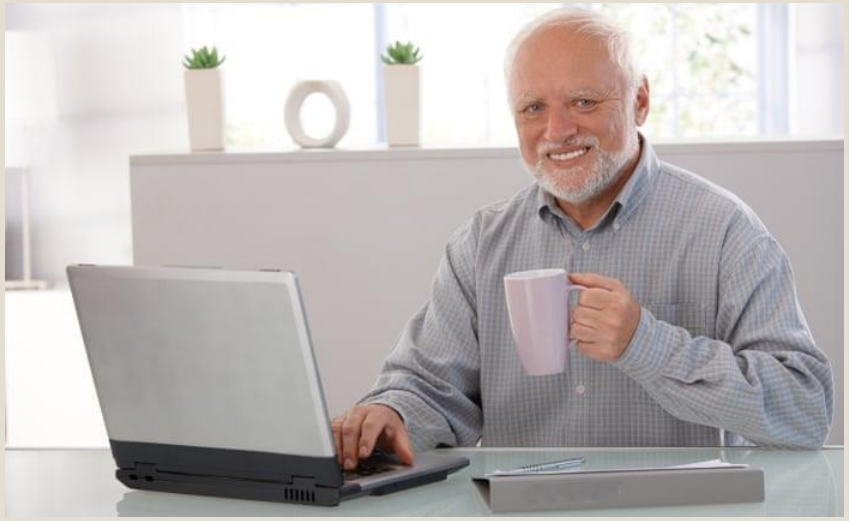
Case 2021, with additions by presenter

Case 1 Continued – Drug Math

- Oxycodone 15 mg x 1.25 (4:5 OME: oxycodone ratio) x 6 doses per day = 112.5 MEDD
- 112.5 OME is within range of buccal or SL bup
- Sublingual choice
  - 112.5 / 30 (1:30 OME: SL bup ratio) = 3.75 mg SL bup total daily dose
  - Round down to 3 mg (as mentioned in the prior lecture)
  - Divide into dosing three times per day/every 8 hours = 1 mg (1/2 of a 2-0.5 mg film) SL bup TID
- Buccal choice
  - 112.5 / 50 (1:50 OME: buccal bup ratio) = 2.25 mg = 2,250 mcg buccal bup total daily dose
  - Divide into dosing two times per day/every 12 hours = 1,125 mcg buccal bup BID
  - 1,125 mcg product does not exist and is higher than manufacturer recommended dose
  - Round down to 750 or 900 mcg buccal bup BID
- Pain Stop/Start method chosen
  - Patient is only on short-acting opioids and the starting dose of SL bup is not greater than 1 mg

Case 1 – Plan in Action

- Patient instructed:
  - Take a dose of oxycodone (his short-acting typical opioid)
  - Wait 6-8 hours without taking it again
  - Take bup 1 mg SL
  - Continue bup every 8 hours and stop oxycodone
- At follow up:
  - Patient reports some nausea during the first few days which spontaneously resolved
  - No more roller coaster of pain – analgesia is smoothed out
  - He has missed his midday dose without aggravated pain
- Next step:
  - Reduce frequency to every 12 hours/BID
- Pain remains well controlled!



Case 1 – Resolution

- Over 8 months, patient heals from the surgical changes in his neck
  - Pain returns to chronic level
- Next Step:
  - Transition opioid management to PCP or chronic pain provider
- Recreational THC is decriminalized in MI; also helps the pain
- Chronic pain provider presents an ultimatum: THC or opioids
  - Patient elects THC over chronic opioid therapy, more convenient
- Next Step:
  - Buprenorphine taper and discontinuation

Case 1 – Taper

- No set guidelines for opioid tapering
  - Recommend dose reductions no sooner than two weeks apart, and up to a few months apart
  - If safety concerns are present, more rapid tapering may be chosen
- Patient preferred expedited taper
- Instructed patient:
  - Take 1/4 film (0.5 mg) of SL bup (2-0.5 mg films) BID for a week
  - Take 1/8 film (0.25 mg) of SL bup (2-0.5 mg films) BID for a week
  - Stop buprenorphine

Hypothetical – Dose-Finding

- What if you took him on to manage his chronic pain using buprenorphine long-term?
- Since pain improved, buprenorphine could be reduced
- Sublingual:
  - Take the same steps as the previous taper but hold for two weeks at a time until patient reaches the lowest dose tolerable
  - This patient is on SL dosing BID already; for other patients on TID or QID dosing, frequency of dosing can be decreased before dose strength is decreased
- Buccal:
  - Rotate to buccal and decrease film strength gradually & stepwise to reach the lowest dose tolerable
  - More dose options available thus more fine control of dosing
- Transdermal:
  - With overall reductions in total daily dose, patient may enter the range for Butrans
  - Rotate to transdermal and decrease strength gradually & stepwise to reach the lowest dose tolerable
- If any dose proves too low, increase back to the previous step and continue

Pain Interference Scoring

- To determine tolerability, use a pain interference scoring tool
- Pain, Enjoyment of Life and General Activity (PEG) Scale
  - Uses a scale of 1 to 10
  1. What number best describes your pain on average in the past week?
  2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?
  3. What number best describes how, during the past week, pain has interfered with your general activity?
- Tracks changes with time, try to find a nadir
  - If scores go up as the dose goes down, consider returning to the next highest dose

Case 1 – Hypothetical

- Consider the same patient presents with chronic neck and back pain after his prior opioid provider retires
  - He was taking Hydrocodone-Acetaminophen (Norco) 10-325 mg TID
- You take over, and choose to rotate to buprenorphine

Case Continued – Paper and Pens

- Conversion:
  - Calculate Daily OME
  - Choose buprenorphine product based on OME range
  - Convert using ratio (based on bioavailability)
    - TD Patch and IV
      - 100:1 ratio (100% bioavailable)
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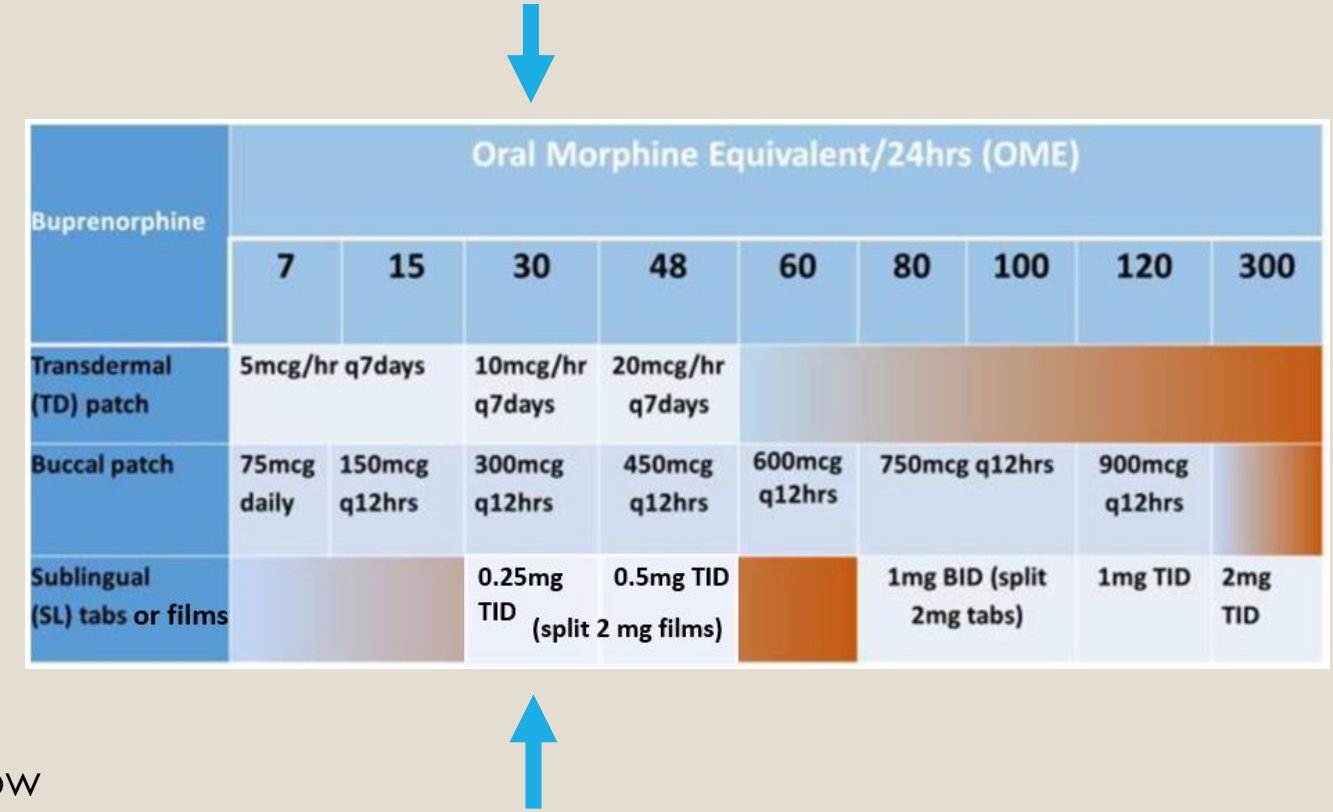

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Buccal patch	75mcg daily	150mcg q12hrs	300mcg q12hrs	450mcg q12hrs	600mcg q12hrs	750mcg q12hrs		900mcg q12hrs	
Sublingual (SL) tabs or films			0.25mg TID	0.5mg TID (split 2 mg films)		1mg BID (split 2mg tabs)		1mg TID	2mg TID

Case 1 Hypothetical – Drug Math

- Hydrocodone 10 mg (1:1 OME: hydrocodone ratio) x 3 doses per day = 30 MEDD
- 30 OME is within range of all bup forms
- Transdermal choice
  - 30 OME / 100 (1:30 OME: TD bup ratio) = 0.30 mg buprenorphine total daily dose
  - 0.30 mg / 24 hours = 0.013 mg/hour = 13 mcg/h
  - Round down to 10 mcg/h patch
- Sublingual choice
  - 30 / 30 (1:30 OME: SL bup ratio) = 1 mg SL bup total daily dose
  - Divide into dosing three times per day/every 8 hours = 0.33 mg SL bup TID
  - Round down to 0.25 mg (1/8 of a 2-0.5 mg film) SL bup TID
- Buccal choice
  - 30 / 50 (1:30 OME: buccal bup ratio) = 0.6 mg = 600 mcg buccal bup total daily dose
  - Divide into dosing two times per day/every 12 hours = 300 mcg buccal bup BID

Buprenorphine	Oral Morphine Equivalent/24hrs (OME)								
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Rotation Methods – TD & Buccal

- Opioid-naïve patients
  - TD and buccal bup can be started at the lowest doses
- Opioid-tolerant patients
  - Stop long-acting, scheduled full opioids. Short-acting, as-needed full opioids can be continued
  - Start TD or buccal bup at appropriate initial dose and titrate to effect
    - Official prescriber information recommends starting no higher than 10 mcg/h or 300 mcg bid, respectively
  - Once the analgesic goal is attained, short-acting full opioids can be stopped. In some cases, there is a role to continue them for breakthrough pain

Case 2

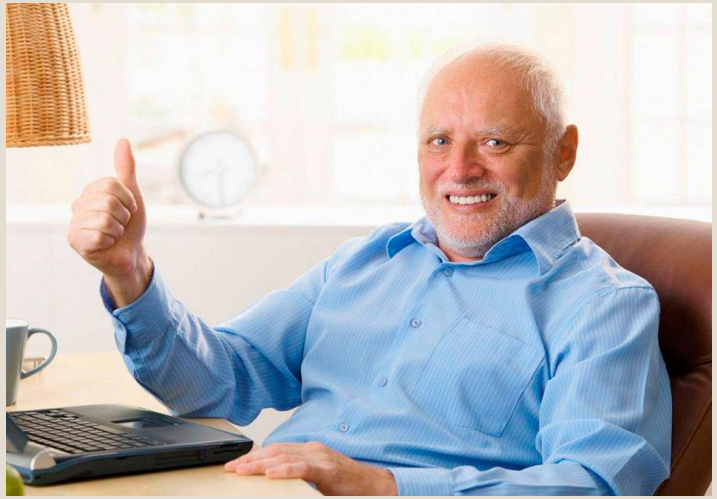
- A 65-year-old, 120 lb woman presents with falls and worsening back pain
- Pertinent Hx:
  - Breast cancer, limited stage
  - Parkinsonism (possible progressive supranuclear palsy)
  - Chronic neck pain and spasms s/p C4-C7 ACDF
  - Chronic low back pain s/p L4-S1 fusion and facet denervations
- Pain Regimen:
  - Clonazepam 1 mg BID for neck spasms
  - Ibuprofen - effective but only when she was taking higher doses than safe
  - Naproxen - not effective at a maximum safe dose
  - Diclofenac patches daily on the low back; no longer effective

Case 2 - Planning

- Considerations:
  - Pain is nonmalignant (expect stability)
  - Older age with frailty and comorbidities which reduce mobility
  - Failed conservative options
- Next steps?
  - Trial another NSAID
  - Prefer to avoid tramadol (anticholinergic effects)
  - Trial transdermal or buccal buprenorphine (no increased fracture risk in older adults)
  - Prefer to avoid a typical/full opioid even at low dose (bradykinetic with falls)

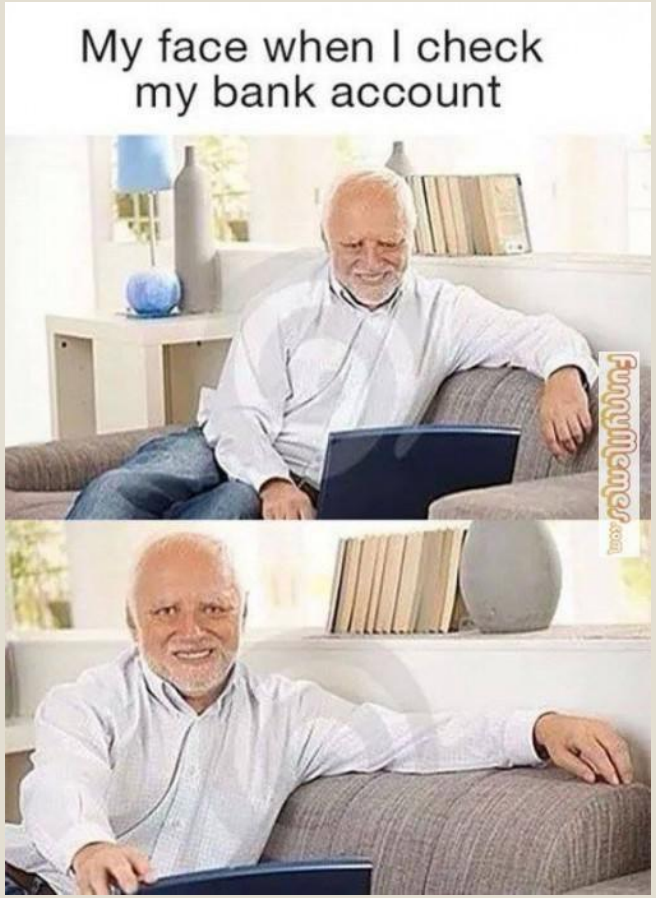
Case 2 Continued

- Initiation
  - Patient is opioid naïve (also frail), so we start at the lowest dose
    - Butrans was prescribed at 5 mcg/h
  - Prior authorization denied
  - Letter of medical necessity sent (with info to avoid tramadol ER), accepted!
  - Also started celecoxib
- Follow Up
  - Celecoxib caused speech garbling but helped
    - Chose to discontinue
  - Buprenorphine had a partial effect
    - Increased to 10 mcg/h
- Pain is well controlled!



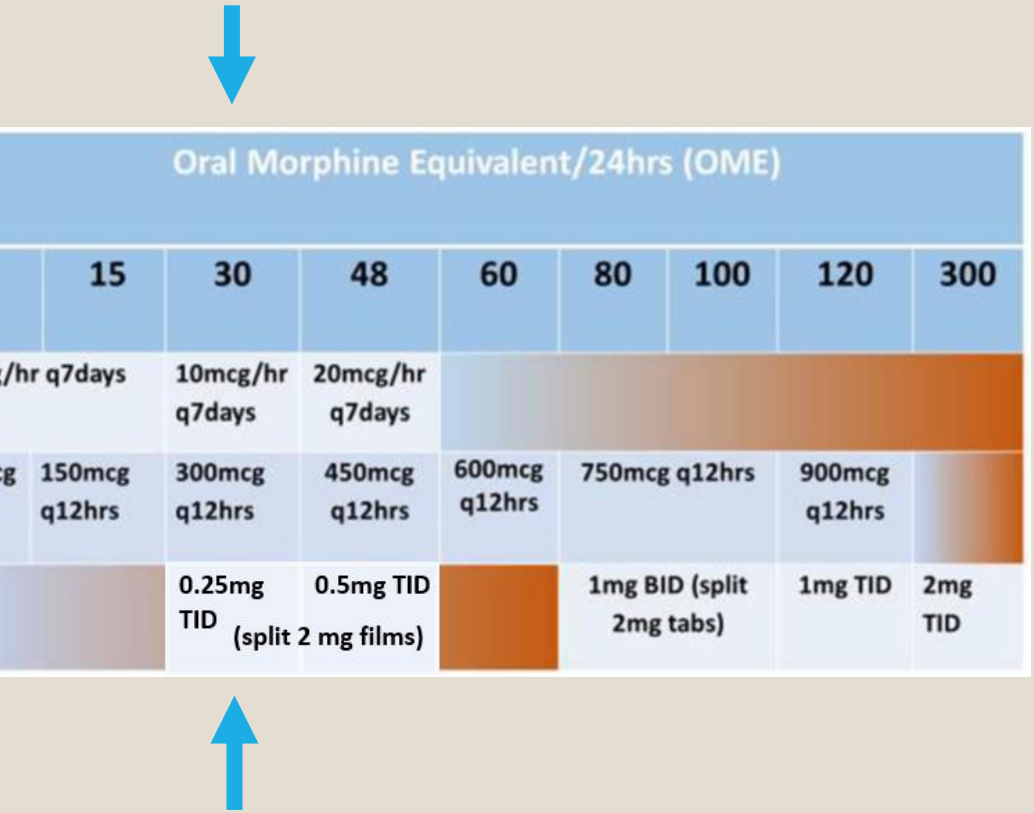
Case 2 – A New Year!

- Deductible reset, patient responsible for Butrans copay
  - $0 becomes $250
- Next step:
  - Rotation in form for cost challenges



Case Continued – Paper and Pens

- Rotation:
  - Calculate Total Daily Dose of Bup
  - Convert using ratio (based on bioavailability)
    - TD Patch:Buccal
      - 1:2 ratio (100%:50% bioavailable)
    - TD Patch:Sublingual
      - 1:3 ratio (100%:30% bioavailable)
    - Buccal:Sublingual
      - 0.6:1 ratio (50%:30% bioavailable)
  - Divide dose into appropriate frequency
  - Alternatively, choose the product in the same column of the table for an equianalgesic dose



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Sublingual (SL) tabs or films			0.25mg TID (split 2 mg films)	0.5mg TID		1mg BID (split 2mg tabs)		1mg TID	2mg TID

Case 2 Continued – Drug Math

- Butrans 10 mcg/h x 24 hours = 0.24 mg daily
- TD Patch: Sublingual bup has a 1:3 ratio
- 0.24 mg x 3 = 0.72 mg SL bup total daily dose; round to 0.75 mg
- 0.75 mg / 3 (for TID dosing) = 0.25 mg (1/8 of a 2-0.5 mg film) bup SL TID

Case 2 – A New Year!

- In practice, next step chosen:
  - Bup 0.25 mg SL (1/8 of a 2 mg SL film) nightly
    - Once daily dosing chosen due to opioid sensitivity, also the first patient we made this rotation on
    - Husband to cut films due to patient's motor difficulty
- Terminal dose failure with qHS dosing
  - Increased frequency to q8h
  - Pain well controlled
  - 12 films lasts 30 days and were covered by insurance

Case 3

- A 67-year-old man presents to the hospital with a massive liver mass, unintentional weight loss of 20-30 lbs. in 2-3 months, and RUQ abdominal pain
- Pertinent Hx:
  - Heroin and alcohol abuse, sober since 2014
  - Chronic hepatitis C infection
- Hospital course:
  - Functional status and kidney function rapidly declined
  - Not well enough to receive treatment for his new presumed HCC
  - Enrolled in hospice
- Discharge pain regimen:
  - Hydromorphone 2-4 mg q4h as needed

Case 3 Continued

- Patient's sister serves as caretaker and gives him medications
- Patient is taking hydromorphone 4 mg 7 times daily
  - Pain control reported as adequate with this dose
  - Duration is variable, from only about 2 hours up to greater than 4 hours
  - Pain wakes him at night and he requires nighttime doses
- Fentanyl 50 mcg/h patch started
- Sister notes after less than a month that hydromorphone use did not decrease
  - Cannot tell if early (before 4 hours) requests are for pain or possible euphoric effects
- Team visit:
  - Patient describes returning feelings of opioid cravings since starting hydromorphone

Case 3 - Planning

- Next step:
  - Rotation to buprenorphine
- Buprenorphine chosen due to:
  - History of SUD with OUD
  - Appropriate opioid use though concern for returning cravings and potential for opioid misuse

Case Continued – Paper and Pens

- Conversion:
  - Calculate Daily OME
  - Choose buprenorphine product based on OME range
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Sublingual (SL) tabs or films			0.25mg TID	0.5mg TID (split 2 mg films)		1mg BID (split 2mg tabs)		1mg TID	2mg TID

Case Continued – Drug Math

- Hydromorphone 4 mg x 5 (1:5 OME: hydromorphone ratio) x 7 doses per day = 140 OMEs
- Fentanyl 50 mcg/h patch = 100 OMEs per day
- Total MEDD = 240 OMEs
- 240 OME / 30 (1:30 OME: SL bup ratio) = 8 mg bup SL total daily dose
- 8 mg / 3 (TID dosing) = 2-3 mg TID (could choose 2 mg QID to be precise)

- However…

Case 3 – Induction Planning

- Goal chosen: 3 mg total daily dose
  - This is often all patients need for pain even with moderately high MEDD (200s, 300s)
- Contingencies included:
  - After initiation, increase buprenorphine to 2 mg (1 full film) SL every 8 hours
  - Continue hydromorphone 4 mg every 2 hours PRN for BTP
  - Add bup SL 1 mg TID PRN for BTP
- For BTP dosing utilizing bup
  - Can use about half or equal to the scheduled bup dose
  - Can allow for use once daily or up to the scheduled frequency
  - Not usually needed
- Low-dose initiation method chosen
  - Patient with high MEDD and on a long-acting opioid

Low-Dose Induction, Outpatient

Day #	Bup dose and schedule	Suboxone film size	Bup total daily dose	Full mu-opioid agonists
Day 0	No Bup	No Suboxone	0 mg	Continue full mu-opioid agonists at the original dose
Day 1	0.5 mg SL BID	1/4 film (2-0.5 mg)	1 mg	
Day 2	0.5 mg SL TID	1/4 film (2-0.5 mg)	1.5 mg	
Day 3	1 mg SL BID	1/2 film (2-0.5 mg)	2 mg	
Day 4 *	1 mg SL TID	1/2 film (2-0.5 mg)	3 mg	Stop full mu-opioid agonists on Day 4 (or later as below) for pain only or Day 8 for at-risk patients
Day 5	2 mg SL BID	Full film (2-0.5 mg)	4 mg	
Day 6	2 mg SL TID	Full film (2-0.5 mg)	6 mg	
Day 7	4 mg SL BID	2 full films (2-0.5 mg)	8 mg	
Day 8	4 mg SL TID	2 full films (2-0.5 mg)	12 mg	
Optional titration	4 mg QID to 8 mg TID or QID	Full film (4-1 mg or 8-2 mg)	16 to 32 mg	

* Consider holding at Suboxone 1 mg TID for several days before increasing

Case 3 – Induction "Hiccups"

- During initiation, developed nausea, vomiting, and looser stools than normal
- Concern for withdrawal present, though symptoms seemed coincidental
- Out of caution:
  - Started clonidine 0.1 mg TID and taper down every 2 days (to BID then Daily then stop)

- Patient taking buprenorphine as prescribed (1 mg TID and taking each PRN 1 mg TID)
- Patient also continued to use the hydromorphone 2 hours apart with regularity
  - Patient reported inadequately controlled pain from bup alone and ongoing cravings
- Next step:
  - Discontinue hydromorphone and rely only on buprenorphine

Case 3 - Titration

- After cessation of hydromorphone, Sister reports patient is able to sleep through the night, not asking for breakthrough medication
- Patient reports same level of pain control (inadequate with bup alone)
- Plan:
  - Uptitrate buprenorphine
- Drug math:
  - Current bup total daily dose is 6 mg SL
  - A conservative increase is 33%, to 8 mg total daily dose
  - Divided dosing yields 2 mg SL QID

Case 3 - Titration

- On reassessment 2 days later, patient reports same level of pain control (inadequate)
  - Increase total daily dose more aggressively, 50%
  - 8 mg to 12 mg total
  - Divided dosing yields 4 mg SL TID
- Reassessed again a few days later, patient notes some improvement but still inadequate control
  - Conservative increase of 33%, from 12 to 16 mg per day
  - Divided dosing yields 4 mg QID
- Pain control improved with 4 mg QID
  - Opioid cravings also controlled

Case 3 – Down the Road

- 2 weeks later, RUQ pain worsened
  - Increase total daily dose more aggressively, 50%
  - 16 mg to 24 mg bup total daily dose
  - Divided dosing yields 6 mg bup SL QID; also allowed for 4 mg SL BID PRN
- Patient used all breakthrough doses, with decent control
  - Add this dosing, 8 mg total, to the scheduled regimen of 24 mg
  - 24 mg to 32 mg total (a 33% increase)
  - Divided dosing yields 8 mg bup SL QID; continued 4 mg BID PRN
- Patient had pain and opioid cravings well controlled for the last month of his life

Hypothetical

- How does this apply to other cases?
  - Patients may have severe, nonmalignant chronic pain and may be on high doses of opioids
  - A similar approach with buprenorphine induction and titration can be used
  - As-needed doses of bup are not necessary, especially with a conservative approach
    - (this patient was on hospice and we used an aggressive approach)

Hypothetical

- What if OUD/SUD was uncontrolled or overdose has occurred with opioids?
  - Avoid typical/full-agonist opioids
  - Initiate buprenorphine upfront
- What if buprenorphine is poorly tolerated AND OUD was uncontrolled?
  - Shared approach with addiction specialists
  - Typical/full-agonist opioids are risky and are not recommended in the setting of OUD/SUD
  - If there is uncontrolled OUD/SUD or high overdose risk, administration of methadone via an addiction provider is preferred
  - In palliative and hospice settings we may cautiously utilize methadone or morphine as these are less commonly misused; though they certainly can be
  - If typical opioids are prescribed, it would be done so in small amounts (1- or 2-week prescriptions) with close follow up
- CAPC (Center to Advance Palliative Care)
  - Resource with modules to learn more about palliative care including managing pain in patients with OUD
- MAPPIT (Managing Addiction in Pain in the Palliative Interdisciplinary Team)
  - Resource for discussing challenging cases

MAPPIT
MANAGING ADDICTION AND PAIN IN THE PALLIATIVE INTERDISCIPLINARY TEAM

capc

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