
BRIGHAM HEALTH
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WOMEN'S HOSPITAL
Palliative Care in the Intensive Care Unit
HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL
Mass General Brigham

BRIGHAM HEALTH

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DISCLOSURES

I have no conflicts of interest to disclose

OBJECTIVES

- Review opioid dosing in acute pain
- Discuss management of symptoms at the end of life
- Describe tools for serious illness communication and shared decision making in the ICU

QUESTION 1: ISSUES WITH SEVERE ACUTE COMPLEX PAIN

- A 65-year-old woman with triple negative breast cancer metastatic to numerous osseous structures is admitted to the ICU with sepsis after her most recent chemotherapy. She is now on hospital day 5 and is extubated. Her Creatinine is 0.68 mg/dL. She is now in significant pain at multiple sites in her extremities corresponding to known worsening bony metastases. She describes the pain as severe and similar in character to what she experiences at home. She has been taking time-release Oxycodone 40mg q8hrs plus a daily total of 60 mg of PRN Oxycodone (in 10 mg doses). You restart her time-release Oxycodone at her home dosing. In addition, which of the following would be the most appropriate choice for an as needed pain medication for her right now:

  a) PO Oxycodone 5 mg q6hrs
  b) IV Fentanyl 25 mcg q1 hr
  c) IV Morphine 5-8 mg q6hrs
  d) IV Hydromorphone 0.8-1.2mg q3hrs

CHOSING AN INITIAL SHORT ACTING OPIOID DOSE

- Initial Dosing – Consider Onset, Peak, and Duration of each formulation

	Onset	Peak	Duration
Oxycodone PO	15-30 min	30-60 min	4-6 hours
Morphine PO	15-60 min	90-120 min	4 hours
Morphine IV	5-10 min	10-30 min	3-5 hours
Hydromorphone PO	15-30 min	90-120 min	4-6 hours
Hydromorphone IV	5-20 min	15-30 min	3-4 hours
Fentanyl IV	1 min	5-7 min	1-2+ hours

https://pinkbook.dfci.org/assets/docs/pinkBook.pdf

CONSIDER DOSE AND FREQUENCY INDIVIDUALLY

- Think about peak and duration – they are not the same thing
  - Peak – think “Am I giving enough or too much?” ~Dose
  - Duration – think “Is it lasting long enough?” ~Frequency

OPIOID CONVERSIONS FOR PATIENTS ON EXISTING THERAPY

- Conversions/Equivalency for 20mg Oxycodone
  - Hydrocodone 30mg
  - Morphine PO 30mg
  - Morphine IV 10mg
  - Hydromorphone PO 7.5mg
  - Hydromorphone IV 1.5mg
  - Fentanyl IV Push (not patch or infusion) 100mcg
- Reduce Dose for Cross tolerance

https://pinkbook.dfci.org/assets/docs/pinkBook.pdf

OPIOID CONVERSIONS FOR PATIENTS ON EXISTING THERAPY

Start by tallying total opioids to prepare for conversion

- Combine total daily long acting and PRN usage
- For this patient, long-acting Oxycodone 80 mg (40 x 2) and short acting Oxycodone 60 mg (10 x 6) = 140 mg of Oxycodone

Then, think to yourself: where are we in treatment of her pain?

- Continue the long-acting as is at first – already done
- This is a pain crisis -> choose an IV medication to get ahead of the pain – want fast onset of action

OPIOID CONVERSIONS FOR PATIENTS ON EXISTING THERAPY

- Time to do some chemistry:

140mg ~~PO Oxycod~~ x 10mg IV Morphine = 70mg IV Morphine
20mg ~~PO Oxycodone~~

140mg ~~PO Oxycod~~ x 1.5mg IV Hydromorph = 10.5mg IV Hydromorph
20mg ~~PO Oxycodone~~

- 10% of this would be 7 mg IV morphine or 1 mg of IV Hydromorphone
- Dose reduce by 25-50%
- Give IV medications frequently, on the shorter end of the interval

https://pinkbook.dfci.org/assets/docs/pinkBook.pdf

CONSIDERATIONS IN LIVER AND RENAL IMPAIRMENT

Morphine

- Hepatically generated metabolites including ones that are stronger analgesics as well as excitatory neurotoxins
- Renal clearance of both parent and metabolites
- Least amount of parent drug effect, slow to cross blood-brain barrier
- Most likely to cause toxicity in renal failure

Oxycodone and Hydromorphone

- Metabolized by liver – Oxycodone some active metabolites, Hydromorphone inactive metabolites
- Renal clearance of both parent and metabolites

https://pinkbook.dfci.org/assets/docs/pinkBook.pdf

CONSIDERATIONS IN LIVER AND RENAL IMPAIRMENT

Fentanyl

- Highly lipophilic – responsible for rapid onset/offset
- Results in variable late duration due to redistribution in tissues
- Almost completely hepatically cleared – considered safe in renal failure, we use in dialysis patients

Methadone

- Primarily CYP inactivation in the liver – also considered safe in renal failure

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QUESTION 1: ISSUES WITH SEVERE ACUTE COMPLEX PAIN

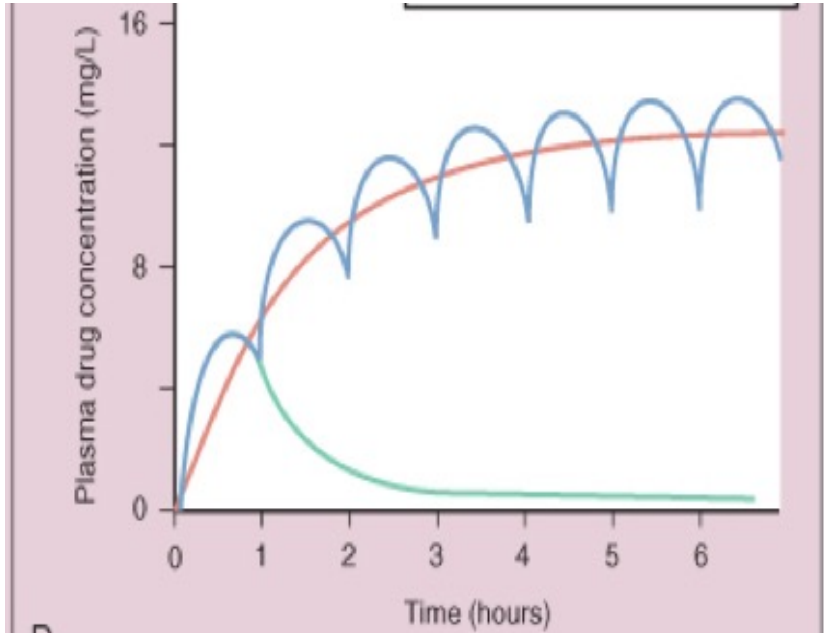
- A 65-year-old woman with triple negative breast cancer metastatic to numerous osseous structures is admitted to the ICU with sepsis after her most recent chemotherapy. She is now on hospital day 5 and is extubated. Her Creatinine is 0.68 mg/dL. She is now in significant pain at multiple sites in her extremities corresponding to known worsening bony metastases. She describes the pain as severe and similar in character to what she experiences at home. She has been taking time-release Oxycodone 40mg q8hrs plus a daily total of 60 mg of PRN Oxycodone (in 10 mg doses). You restart her time-release Oxycodone at her home dosing. In addition, which of the following would be the most appropriate choice for an as needed pain medication for her right now:

  a) PO Oxycodone 5 mg q6hrs – too low, lower than home dose
  b) IV Fentanyl 25 mcg q1 hr – lower than home dosing, requires frequent dosing
  c) IV Morphine 5-8 mg q6hrs – good dosing, given too infrequently
  d) IV Hydromorphone 0.8-1.2mg q3hrs – best choice here

QUESTION 2: ICU CARE AT THE END OF LIFE

- An 80-year-old man with idiopathic pulmonary fibrosis is initially admitted for hypoxemic respiratory failure and has been extubated and transitioning to comfort oriented care. He has confirmed his preferences to focus on his comfort and avoid re-intubation and resuscitation. He is on a morphine infusion (current rate of 1mg/hr) with PRN morphine boluses of 0.5 mg q1 hour as needed PRN pain, dyspnea, or discomfort. He has received one PRN dose in the past 8 hours without notable effect. In general, he has remained peaceful but with repositioning, his respiratory rate climbs from 8/min to 22/min. Family at beside is anxious, saying “we know he wouldn’t want to be like this for long” asking “what can you do?” Which of the following would be the most appropriate adjustment:
    a) Increase morphine infusion to 2 mg/hr to address his discomfort
    b) Increase PRN bolus dose morphine to 1-2mg q1hr and adjust infusion after 6-8 hours
    c) Decrease IV Morphine infusion to 0.8 mg/hr given low respiratory rate and mostly appearing comfortable.
    d) No change at this time

OPIOID INFUSIONS



- Infusions require ~4-5 half lives to fully reach steady state
- Morphine ½ life 2-4h
- Can take hours to take effect
- Recalling the onset/peak/duration characteristics, use bolus dosing for current or intermittent symptoms
- Adjust drip rate every 6-8 hours based on PRN usage
- Think of opioid infusions as long acting & poorly titratable
- Pharmacokinetics are more like time-released formulations than IV push

Zheng H. Intravenous Infusion. In: Shargel L, Yu AC. eds. *Applied Biopharmaceutics & Pharmacokinetics, 7e*. McGraw Hill; 2016. Accessed August 31, 2023.

IPF PATIENT EXAMPLE

- For this man, you increase the bolus and ask the nurse to give it as frequently as needed for symptoms, pre-medicating for turning
- It takes 6 more boluses of 2 mg of morphine over 6 hours to keep him comfortable
- At this time, you increase the drip rate by 2mg/hr (12mg total PRN IV morphine over 6 hours) – drip adjusts from 1 mg/hr to 3 mg/hr
- To adjust PRN dosing, I consider:
  - -10% of long-acting needs: 7 mg
  - -Same as drip rate: 3mg
- You choose 3-5mg IV Morphine q1hr
- He remains comfortable with infrequent IV PRN doses until he dies peacefully 1 day later

PRINCIPLE OF DOUBLE EFFECT

- How to consider the side effects of morphine when treating symptoms at the end of life?
- Akin to nausea and vomiting with chemotherapy for reduction of cancer burden
- Double effect – when offering a treatment, the therapeutic intention dictates its ethical definition and implications
  - Intent is pain and dyspnea relief, this is our typical approach to symptoms at the end of life and we ethically tolerate sedation, respiratory depression
  - Intent is sedation, this is ethically termed “Palliative Sedation”
  - Intent is to hasten death, this would be ethically considered physician assisted death or euthanasia

https://www.mypcnow.org/fast-fact/morphine-and-hastened-death/

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  b) Increase PRN bolus dose morphine to 1-2mg q1hr, adjust infusion after 6-8 hours

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  d) No change at this time

QUESTION 3: SERIOUS ILLNESS COMMUNICATION IN THE ICU

- An 80-year-old woman with end-stage kidney disease on hemodialysis, peripheral artery disease, type 2 diabetes mellitus, and hypertension is hospitalized for sepsis related to a gangrenous left foot. You are having trouble weaning her ventilator after 14 days of intubation. You are considering a tracheostomy to allow weaning of sedation. She has not previously stated her preferences for tracheostomy through an advance directive, Physician's Orders for Life Sustaining Treatment form, or conversations with her outpatient clinicians. She has named her husband as her designated health care proxy on a legal state form. Her husband says that they have not discussed her wishes for tracheostomy and asks for you to make the decision for her through him as the proxy. What is the best initial response?
    a) Proceed with tracheostomy as an emergency treatment to see if the patient can regain decisional capacity off sedation
    b) If the husband is uncomfortable with the decision, see if there is a secondary decision maker named who can make the decision about tracheostomy
    c) Assess the patient's values and goals and make a recommendation, providing your rationale and an opportunity for the husband to decline your recommendation
    d) Consult the hospital ethics team

SERIOUS ILLNESS COMMUNICATION IN THE ICU

- Setup
- Explore Illness Understanding & Information Preferences
- Deliver a Prognosis
- Explore what is most important to patients
- Summarize and make recommendations

Bernacki Block JAMA Internal Medicine 2014
Lakin Jacobsen JAMA Internal Medicine 2018
Paladino Lakin Sanders JAMA 2019
Lakin Tulsky Bernacki Ann Intern Medicine 2020

ORDERS FOR LIFE SUSTAINING TREATMENTS

- What are they? What are they not?

MASSACHUSETTS MEDICAL ORDERS
for LIFE-SUSTAINING TREATMENT

(MOLST) www.molst-ma.org

Patient's Name _____
Date of Birth _____
Medical Record Number if applicable: _____

INSTRUCTIONS: *Every patient should receive full attention to comfort.*

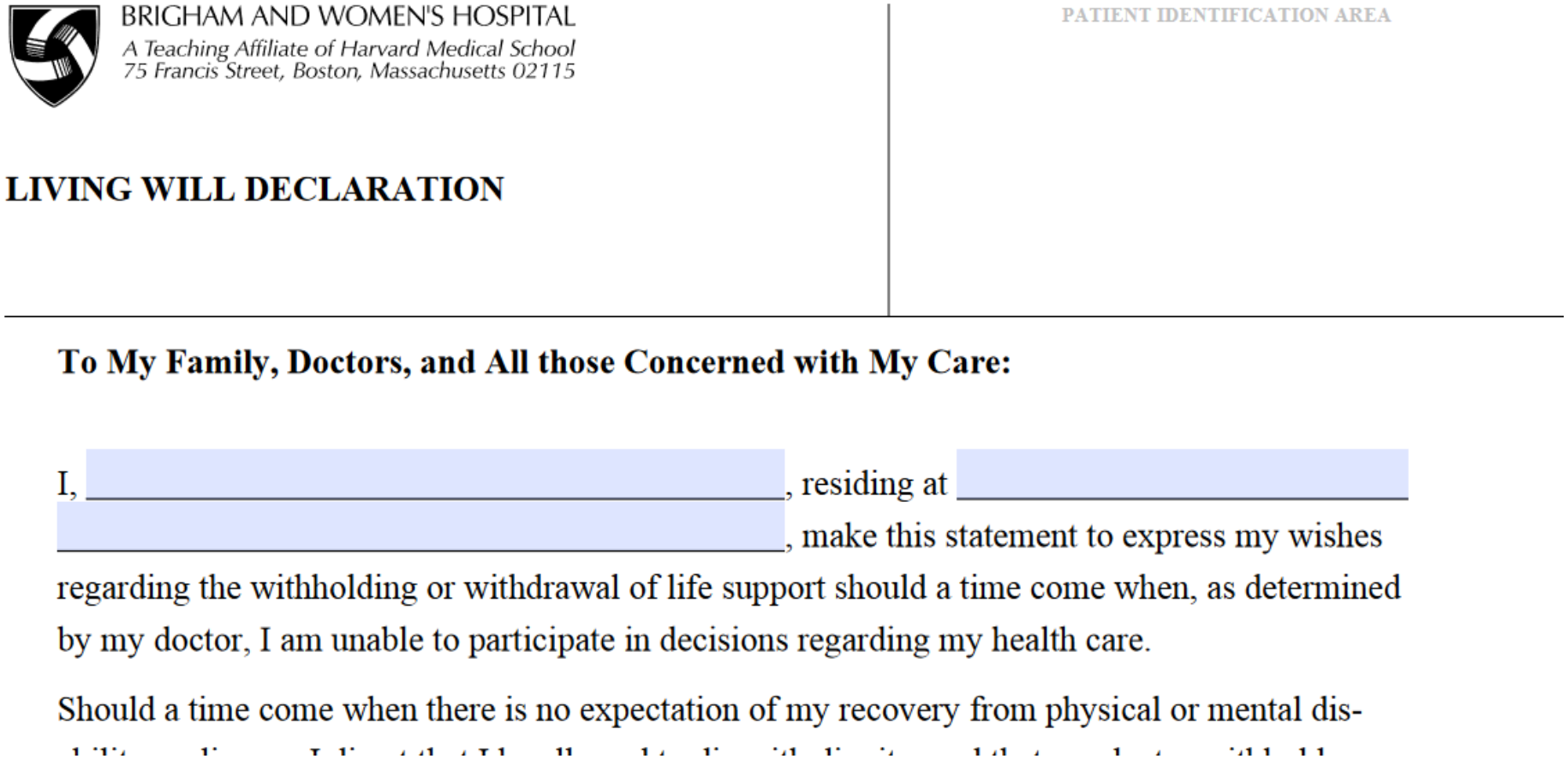
→ This form should be signed based on goals of care discussions between the patient (or patient's representative signing below) and the signing clinician.
→ Sections A–C are valid orders only if Sections D and E are complete. Section F is valid only if Sections G and H are complete.
→ If any section is not completed, there is no limitation on the treatment indicated in that section.
→ The form is effective immediately upon signature. Photocopy, fax or electronic copies of properly signed MOLST forms are valid.

A Mark one circle →	**CARDIOPULMONARY RESUSCITATION: for a patient in cardiac or respiratory arrest**	
	O Do Not Resuscitate	O Attempt Resuscitation
B Mark one circle →	**VENTILATION: for a patient in respiratory distress**	
	O Do Not Intubate and Ventilate	O Intubate and Ventilate
Mark one circle →	O Do Not Use Non-invasive Ventilation (e.g. CPAP)	O Use Non-invasive Ventilation (e.g. CPAP)

https://www.molst-ma.org/

ADVANCE DIRECTIVES

- What are they? What are they not?



BRIGHAM AND WOMEN'S HOSPITAL
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PATIENT IDENTIFICATION AREA

LIVING WILL DECLARATION

To My Family, Doctors, and All those Concerned with My Care:

I, _____, residing at _____
_____, make this statement to express my wishes regarding the withholding or withdrawal of life support should a time come when, as determined by my doctor, I am unable to participate in decisions regarding my health care.

Should a time come when there is no expectation of my recovery from physical or mental dis-

https://www.mass.gov/info-details/massachusetts-law-about-health-care-proxies-and-living-wills

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TAKE HOME MESSAGES

- When dealing with opioid tolerant patients, do dose conversion calculations and perform dose reduction for cross tolerance at opioid receptors
- Careful with morphine in renal failure and all opioids in hepatic failure
- At end of life, bolus dosing is key first line action for achieving immediate comfort
- Think of opioid infusions as akin to long-acting pain medications and act accordingly
- The intention of your therapy at the end of life is critical – focusing on treating symptoms while accepting side effects is considered ethical in the theory of double effect
- Evidence supports conversations about goals and values between you and your seriously ill patients for decision making near the end of life (and earlier)
- Focus first on prognostic awareness, goals, and values – not CPR and feeding tubes – then make recommendations about medical care and employ forms in a targeted manner after discussion
- Certain forms (such as Health Care Proxies and POLST forms) have clear legal roles, others, such as Living Wills seem to have less effect and may cause some unanticipated harms