

Palliative Medicine and Symptom Management for Terminally Ill Patients

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Learning Objectives

At the conclusion of the lecture, the pharmacist learner shall be able to:

- Describe the roles and responsibilities of the pharmacist in palliative care
- Describe basic principles and approach to deprescribing
- Assess and recommend treatment strategies for pain and common symptoms encountered in the palliative care setting
- Identify communication techniques for discussing serious illness and advance directives with patients and their families

Learning Objectives

At the conclusion of this lecture, the pharmacy technician learner shall be able to:

- Describe the role of palliative care in the trajectory of illness
- Identify commonly used medications and various routes of administration utilized in the palliative care setting
- Identify communication techniques for discussing serious illness and advance directives with patients and their families

Get your thinking cap on...

What is the most common symptom experienced by cancer patients in the last 1-2 weeks of life?

- A. Pain
- B. Fatigue
- C. Anxiety
- D. Constipation

What medication is the treatment of choice for severe dyspnea in a patient with end stage lung cancer?

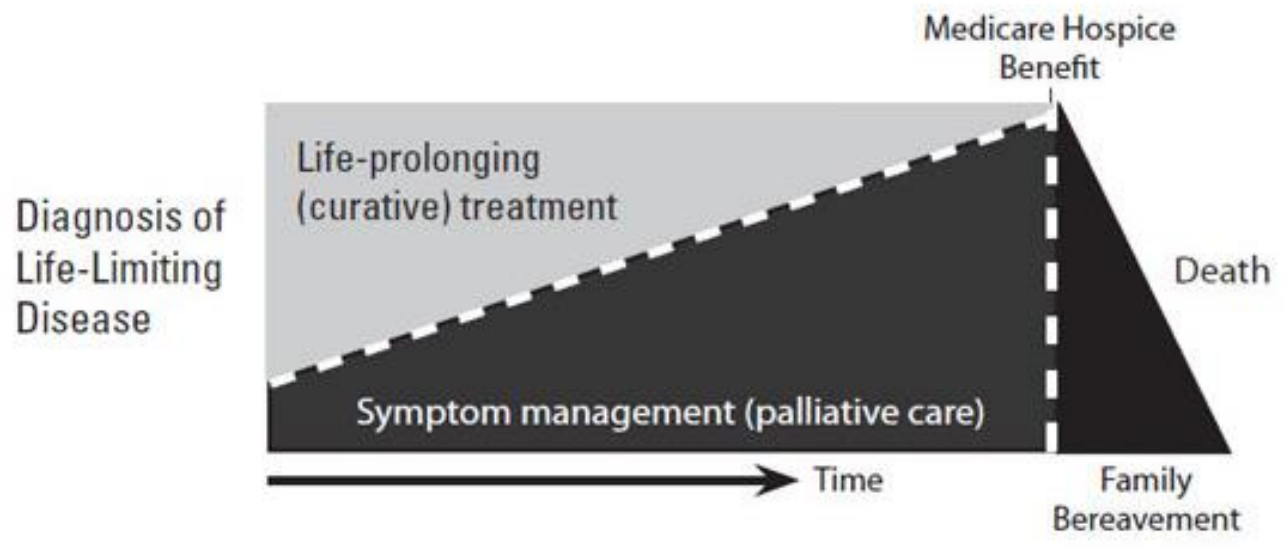
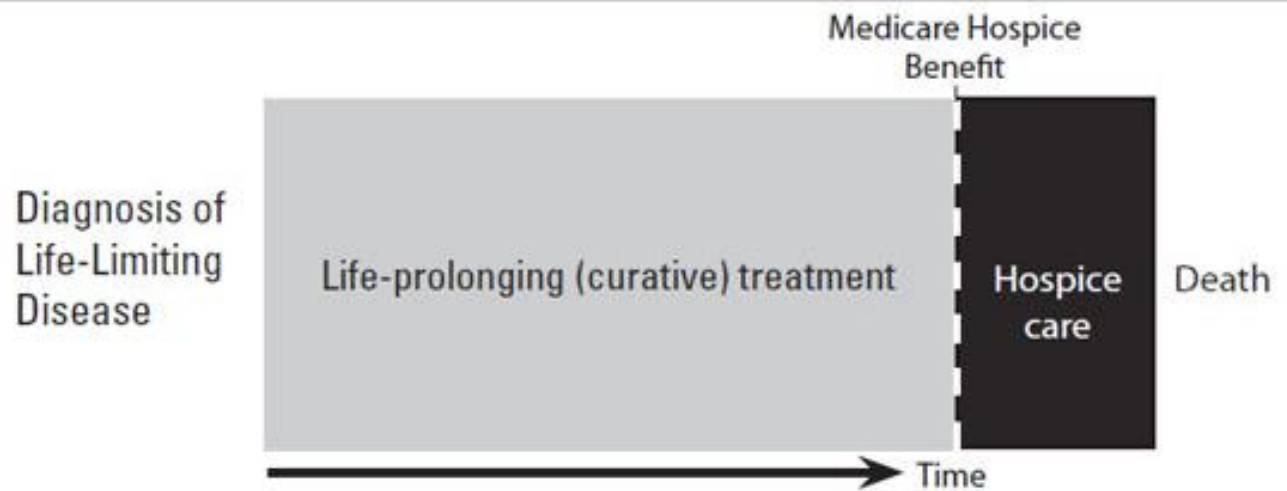
- A. Albuterol
- B. Prednisone
- C. Morphine
- D. Alprazolam

Definitions

- **Palliative care** – specialized medical care for people with serious illness that focuses on providing relief from the pain, symptoms and distress of serious illness
- **Hospice** - type of care and a philosophy of care that focuses on the palliation of a terminally ill patient's symptoms
 - **Terminal illness** – estimated survival 6 months or less
- **ALL** hospice care is palliative but **NOT** all palliative care is hospice
- **BOTH** are team-based approaches with focus on improving quality of life including spiritual and psychosocial support

Palliative Care

- Unlike hospice, palliative care can be provided **at the same time** as curative treatments
- Appropriate at any age and at any stage of serious illness
- Supportive care – extra layer of support
 - Time devoted to intensive family meetings and patient/family counseling
 - Resolves questions and conflicts between families/patients and physicians on achievable goals of care
 - Provides expertise in pain and symptom management
- Palliative Care Bridge



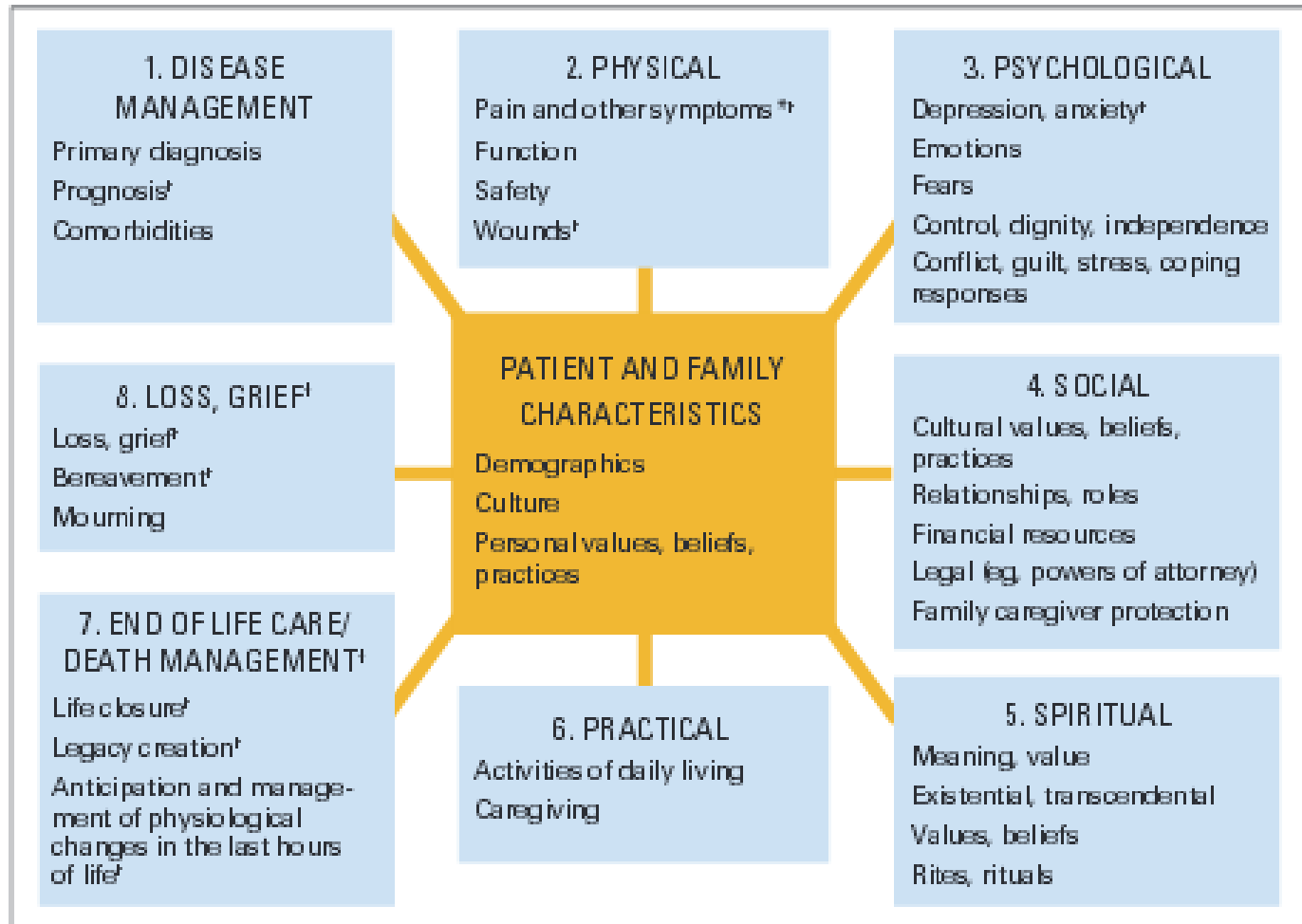
Palliative Care and Oncology

- Temel et al – NEJM 2010;363:733-42
 - Phase III randomized, controlled, single institution, non-blinded clinical trial comparing palliative care plus standard oncology care, begun at the time of diagnosis, to standard oncology care
 - 151 patients with newly-diagnosed metastatic non-small cell lung cancer
 - Intervention: a baseline evaluation and follow-up, at least once per month, by members of a multidisciplinary PC team comprised of 7 palliative care clinicians
 - Primary Outcome: QOL
 - Secondary outcomes: mood, aggressive treatment at EOL

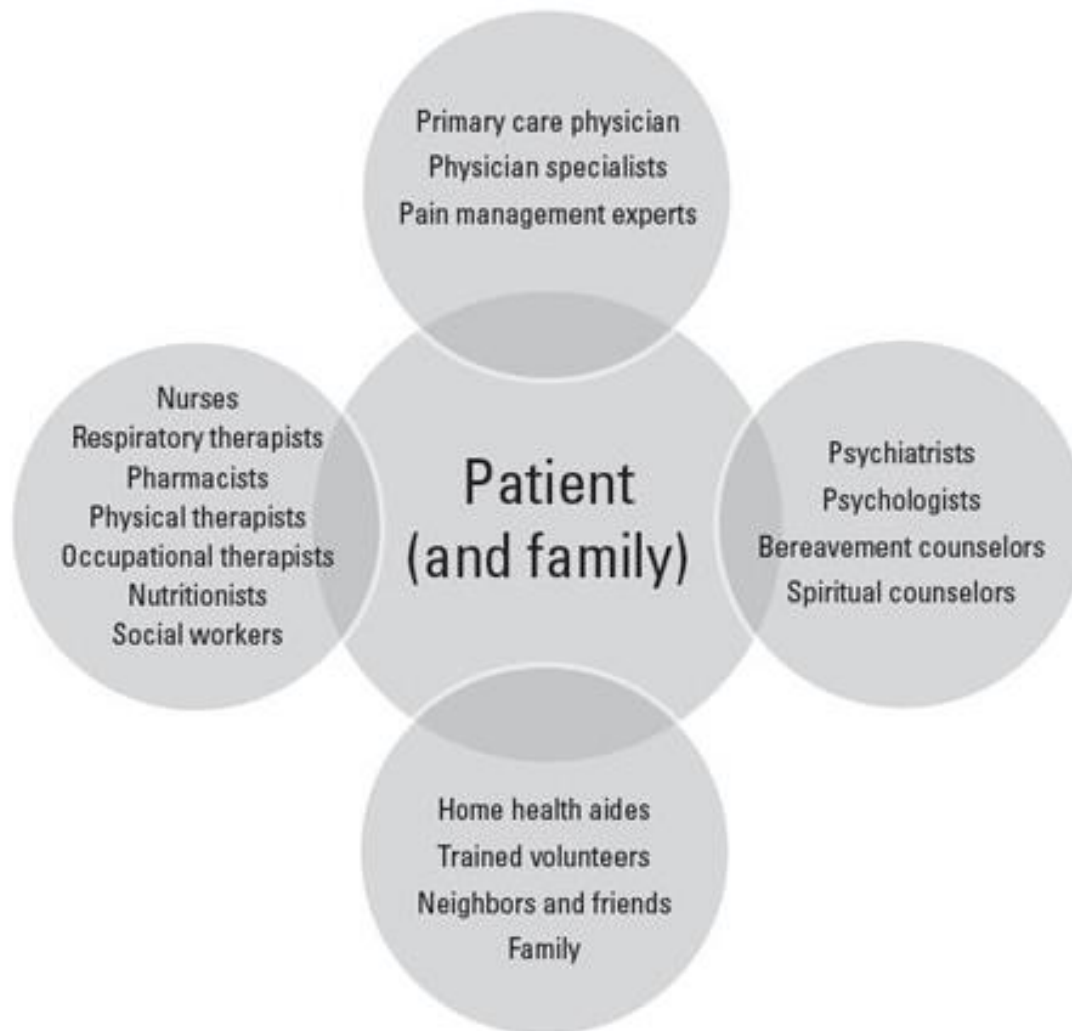
Palliative Care and Oncology

- Results in intervention arm
 - Better understanding of the disease, prognosis, and options
 - Significantly higher QOL scores ($p=0.03$)
 - Fewer depressive symptoms ($p=0.01$)
 - Less aggressive end of life care ($p=0.05$)
 - Less use of chemotherapy near end of life
 - Less hospitalization and intubation
 - More and longer use of hospice
 - **Survival 2.7 months longer ($p=0.02$)**

Causes of Suffering for Patients with Advanced Cancer



Palliative Care Team



ASHP Guidelines on the Role of the Pharmacist

- Direct patient care
 - Optimal symptom management
 - Anticipate transitions of care related to pharmacotherapy plan
- Medication order review and reconciliation
 - Medication-use process
- Education
 - Medication counseling
 - Provider and nursing in-services
- Administrative
 - Ensure safe use of medications
 - Policy and procedure development
 - Algorithms and protocols for best practices

Symptom Prevalence in Cancer

Systematic review of most common symptoms in end stage cancer in last 7-14 days of life

Fatigue – 88%

Weight loss – 86%

Weakness – 70%

Appetite loss – 56%

Pain – 45%

Dyspnea – 39%

Dry mouth – 34%

Nervousness/anxiety – 30%

Constipation – 29%

Depressed mood – 19%

Nausea – 17%

Commonly Used Medications

- Analgesics (opioids and non-opioids)
- Benzodiazepines
- Corticosteroids
- Anticholinergics
- Antipsychotics
- Laxatives
- Antidepressants

Pharmacotherapy

- Medications are often cornerstone to symptom management in hospice setting
- Non-symptom based drugs may no longer be appropriate or desired
- Data often limited
 - PK/PD differences
 - Goals of treatment
- Alternative routes of administration
 - Rectal
 - Subcutaneous
 - Transdermal
 - Sublingual

Medication Review

- What is the indication?
- Is this in line with my patient's goals?
- Is there any data to support use of this medication in the disease state/age group/comorbidities?
- Do the benefits of the medication(s) outweigh the possible risks?
- Can the patient use the medication(s) appropriately and are the directions practical?
- Is there a formulary alternative or superior medication?

Deprescribing - Less is More

- Optimizing meds through targeted deprescribing is vital in managing chronic conditions to avoid adverse effects and improve outcomes
- Consider risks/benefits of each med
- Proceed with caution in stopping maintenance meds
 - Could have no effect
 - Could lead to withdrawal events/symptoms
 - Physical dependence
 - Physiologic dependence on exogenous drug (steroids)
 - Signs/symptoms of chronic disease may re-appear
- Communicating changes



Medication Classes to Assess for Discontinuation

- Supplements
- Statins
- Anticoagulants
- Antihypertensives
- Dementia medications
- Hypoglycemics
- Inhalers



Individualized Approach

- Anticipate symptoms based on disease state(s)
 - Use of standard assessments
 - Frequent evaluation and re-evaluation
- Utilize a medication that treats multiple symptoms to reduce polypharmacy
- Discontinue medications that no longer contribute to symptom management
- Anticipate and treat side effects

Pain Management

- Complete the **pain assessment**
- **Match** the appropriate drug to the pain type
- Consider potential **risks and side effects**
- Assess the safest **route of delivery**
- Consider **who** will administer the meds and in what **setting**
- Determine whether the patient can **find and afford** the medication
- Assess the **cultural, spiritual, and social** context for the pain

Medication Dosage Forms

- Liquid – PO, SL
 - Buccal absorption dependent on lipophilicity of drug
 - Fentanyl > methadone > hydromorphone > oxycodone > morphine
 - 20% avg absorption of morphine 5 mg dose after 10 minutes
- Injection – IV, SC
- Suppository – including oral formulations
- Topical gel – local absorption
- Transdermal

ROUTE	ADVANTANGES	DISADVANTAGES
Injectable – IV, SC	<ul style="list-style-type: none"> -Quick onset of action -Effective -Essential meds available 	<ul style="list-style-type: none"> -High caregiver burden -High cost -Difficulty obtaining medication/delays -Decreased peripheral circulation
Rectal	<ul style="list-style-type: none"> -Effective absorption -Versatility in medications -May be inexpensive 	<ul style="list-style-type: none"> -High caregiver burden -Discomfort for patient -May be expensive if compounded -Limited doses -Delayed onset of action
Transdermal	<ul style="list-style-type: none"> -Generally easy and comfortable for patient and caregiver 	<ul style="list-style-type: none"> -Delayed onset of action -Potential for erratic absorption -Cost -Limited medications -Lack of breakthrough med

Short-Acting Opioids

Medication	Onset	Peak Effect	Duration	Common starting doses
Morphine	PO: 20-30 min	PO: 60-90 min	PO: 3-6 hrs IV: 2-4 hrs	5 mg PO q4h PRN
Hydromorphone	IV: 1-2 min	IV: 10-15 min		1 mg PO q3-4h PRN
Oxycodone	PO: 20-30 min	PO: 60-90 min	PO: 3-6 hrs	5 mg PO q4h PRN
Hydrocodone				5 mg PO q4h PRN
Fentanyl	IV: < 1 min	IV: < 5 min	0.5-2 hrs	25 mcg IV q15min

Long-Acting Opioids

- Oral agents
 - Morphine ER (MS Contin®), oxycodone ER (Oxycontin®), hydromorphone ER (Exalgo®), oxymorphone ER (Opana SR®)
 - Onset of action 1-2 hrs
 - Plateau effect 3-8 hrs, duration 8-12 hrs
 - Can dose escalate q24 hrs
- Transdermal
 - Fentanyl (Duragesic®)
 - Slow onset of action – 12-24 hrs
 - Duration of action – 48-72 hrs
 - Should only dose escalate q72 hrs
 - Fentanyl stays in circulation for up to 24 hrs after patch removal

Methadone

- Should only be prescribed/adjusted by provider with adequate training and experience
- Complex PK properties
 - Basic, lipophilic drug – onset 15-45 minutes after oral
 - Oral bioavailability: 70-80%
 - Widely distributed, retained in tissues
 - Extensively metabolized (3A4, 2B6, 2C8, 2C9, 2C19, 2D6; many drug interactions)
 - Elimination half-life: 5-130 hours (avg 20-35 hours)
 - Takes 4-10 days to achieve steady-state
 - When initiating therapy and with dosage changes
- Advantages:
 - Rapid onset of analgesia
 - Effective for neuropathic pain
 - Chemically unrelated to other opioids
 - No active or toxic metabolites
 - Available in many dosage forms
 - Lower incidence of neurotoxic adverse effects

Pain Assessment

- P = palliating/provoking
- Q = quality
- R = region/radiation
- S = severity
- T = timing (onset, duration, frequency)
- U = YOU (goals, activity level, QOL)

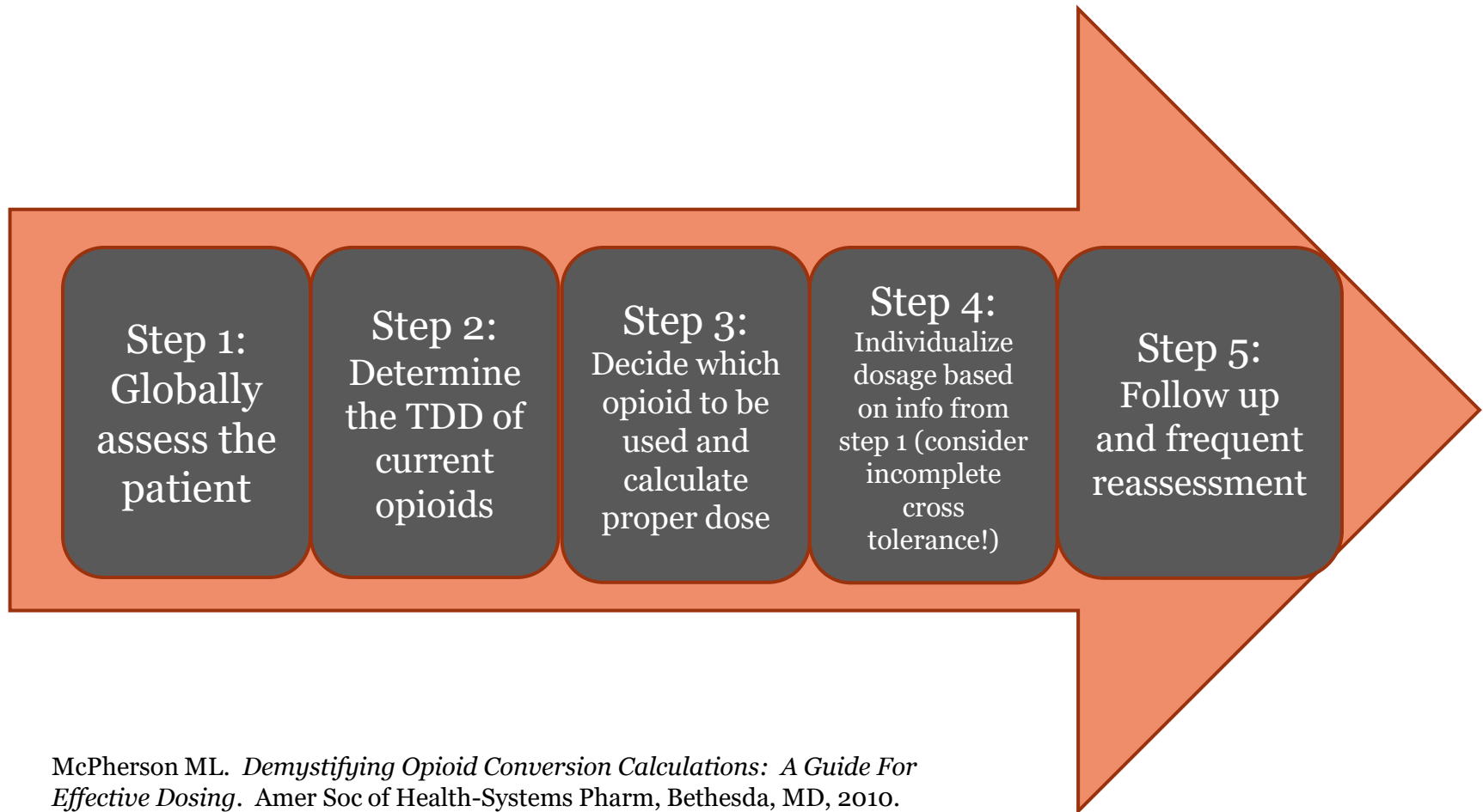
Dose Adjustments

- Educate for good record keeping of PRN doses
- “How many tablets per day do you need to stay comfortable?”
- Make the dosage increases count!
 - Increase the total daily dose of opioid by 25-50% for mild to moderate pain
 - Increase the total daily dose of opioid by 50-100% for moderate to severe pain
- Long-acting, sustained-release opioids can be increased every 24 hours (with the exception of transdermal fentanyl and methadone)

Opioid Rotation

- Lack of therapeutic response
- Development of adverse effects
 - GI effects
 - Autonomic
 - Cutaneous
 - CNS
 - True opioid allergy
- Change in patient status

5 Step Approach



McPherson ML. *Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing*. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010.

Equianalgesic Opioid Dosing

DRUG	EQUIANALGESIC DOSES (MG)	
	PARENTERAL	ORAL
Morphine	10	30
Buprenorphine	0.3	0.4 (SL)
Codeine	100	200
Fentanyl	0.1	N/A
Hydrocodone	N/A	30
Hydromorphone	1.5	7.5
Meperidine	100	300
Oxycodone	10*	20
Oxymorphone	1	10
Tramadol	100*	120

Setting Up the Conversion Calculation

1. Calculate the 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:

$$\frac{\text{"x" mg new opioid/route}}{\text{mg of current opioid/route}} = \frac{\text{equivalent mg new opioid/route}}{\text{equivalent mg current opioid/route}}$$

$$\frac{\text{"x" mg oral oxycodone}}{180 \text{ mg oral morphine}} = \frac{20 \text{ mg oral oxycodone}}{30 \text{ mg oral morphine}}$$

$$30x = (20)(180)$$

$$x = 120 \text{ mg oral oxycodone per day}$$

Patient Case

- MK is a 72 yo female with metastatic breast cancer admitted to hospice care who is now too weak to swallow her oral medications. She is currently receiving hydromorphone ER 16mg PO daily and averages 2 breakthrough doses of hydromorphone 2mg per day. Her pain has been managed with this regimen. The hospice nurse consults you for a recommendation in converting her to liquid morphine (20mg/mL concentration). What do you recommend?
 - A. Morphine 80mg PO q4 hrs
 - B. Morphine 10mg PO q4 hrs
 - C. Morphine 20mg PO q6 hrs
 - D. Morphine 30mg PO q12 hrs

Dyspnea

- Definition: a subjective sensation of difficulty breathing or an abnormally uncomfortable awareness of breathing
- Causes:
 - Obstructive airway process – tracheal obstruction, asthma, COPD
 - Parenchymal/pleural disease – aspiration, diffuse primary or metastatic cancer, lymphangitic metastases, pneumonia, pleural effusion, pulmonary drug reaction, radiation pneumonitis
 - Vascular disease - PE, SVC obstruction, pulmonary vascular tumor emboli
 - Cardiac disease – CHF, pericardial effusion, arrhythmia, myocardial ischemia
 - Chest wall/respiratory muscles – primary neurologic disease, malnutrition
 - Other – anxiety, anemia, constipation

Dyspnea - Assessment

- Patient rating: Numeric scale (1-10)
- Physical signs: Sitting up, accessory muscles, nasal flaring
- ADLs: Impairment of eating, talking, exercise tolerance
- Lab/X-Ray:
 - Assess the overall goals of care
 - No or minimal diagnostics is reasonable if focus on symptoms

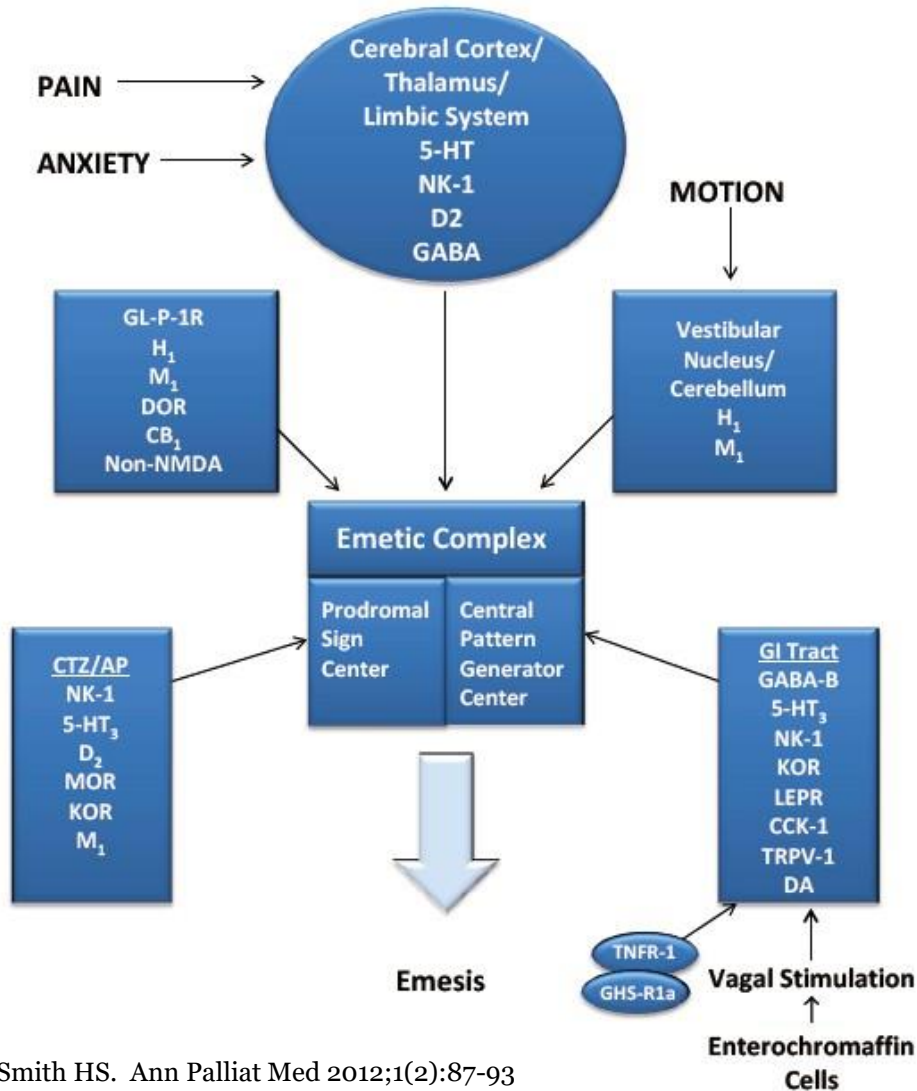
Dyspnea - Management

- Non-pharmacologic
 - Re-positioning (avoid lying flat), maintain cool room temps, relaxation exercises, acupuncture, minimal exertion
- Pharmacologic
 - Oxygen therapy for documented hypoxia esp. COPD
 - Opioids – first-line treatment
 - No optimal agent or dose although nebulized route not shown to be superior; consider opioid naïve vs. opioid-tolerant patient
 - Morphine most commonly used
 - Rescue doses at 30-50% of scheduled dose typically effective
 - Anxiolytics
 - Benzodiazepines reserved for breakthrough or refractory dyspnea compounded by anxiety or when ADRs limit titration of opioids to efficacy

Nausea/Vomiting

- Self-report is gold standard for nausea
 - Associated symptoms, triggers, duration, severity
- Documentation of vomiting and retching
- Other monitoring parameters:
 - Food intake
 - Hydration status
 - Bowel movements
- Documentation of relief from medication

Nausea/Vomiting Assessment



- Sensation of vertigo
 - Vestibular irritation
- Abdominal pain/ache
 - GERD/ulcer
- Early satiety or anorexia
 - Compressed stomach
 - Liver metastases
- Headache with nausea
 - Brain tumor
- Positional vomiting or vomiting with no nausea
 - Reflux

Nausea/Vomiting - Management

- Match the cause of nausea with the most appropriate drug class
 - Stimulation of CTZ (drugs, uremia) – dopamine or serotonin antagonist
 - Haloperidol 1-2 mg PO/IV/subQ q4h PRN
 - Movement-related nausea – antihistamine
 - Anxiety – benzodiazepine
 - Elevated intracranial pressure – glucocorticoid (dexamethasone preferred)
 - Constipation – laxative
 - GERD – proton pump inhibitor

Medical Cannabis

- NM Medical Program includes 21 approved conditions
 - Hospice
 - Severe chronic pain
 - Painful peripheral neuropathy
 - Intractable nausea/vomiting
 - Severe anorexia/cachexia
- Survey sent to 400 clinical hospice staff
 - Majority of respondents (90%) felt cannabis should be legalized to palliate symptoms
 - Almost half had experience with patients asking about or using cannabis for symptom control
 - Identified appropriate uses and side effects
 - Respondents over the age of 50 were significantly more likely than younger respondents to disagree that smoked cannabis is addictive

Delirium

- Most common neuropsychiatric complication in patients with advanced cancer
- Disturbance in attention and awareness
- Changes in cognition not explained by a pre-existing condition
- Pathophysiology
 - Medication-induced – opioids, anticholinergics, benzodiazepines, corticosteroids
 - Infection
 - Urinary retention, fecal impaction, dehydration
 - Brain tumor/metastases
 - Metabolic disorders – hypercalcemia, hyponatremia, liver/renal failure
 - Other brain disorders – stroke, dementia

Delirium - Symptoms

- Agitation
- Restlessness
- Altered perceptions
- Difficulty forming thoughts and incoherent speech
- Disorientation to time, place, person
- Sleep disturbances and nightmares
- Sundowning
- Changes in consciousness level

Delirium - Treatment

- Hyperactive (agitation), hypoactive (lethargy), or mixed
- Non-pharmacologic
 - Provide calm environment, music, aromatherapy, spiritual counselor
 - Identify any reversible causes (i.e. medications, constipation, urinary retention)
- Pharmacologic
 - Antipsychotics considered 1st line
 - Most evidence with haloperidol and chlorpromazine given in low doses PRN; once total dose required to manage symptoms is identified, then given on scheduled bases and adjust accordingly
 - Haloperidol 0.5-1mg PO/SL every hour PRN – schedule every 4-8 hours
 - Chlorpromazine 10-25mg PO every hour PRN – schedule every 4-8 hours
 - Quetiapine 25mg PO BID
 - Benzodiazepines useful for sedation when agitation is prominent feature and antipsychotics ineffective (use with caution as may worsen delirium)

Anticholinergic Effects

- Peripheral
 - Dry eyes
 - Urinary retention
 - Dry mouth
 - Constipation
 - Heat intolerance
 - Tachycardia
 - Decreased sweating
- Central
 - Forgetfulness
 - Agitation/
confusion
 - Delirium
 - Paranoia
 - Dizziness
 - Drowsiness
 - Falls

Drugs that Cause Anticholinergic Effects*

- Oxybutynin
- Benztropine
- Scopolamine
- Diphenoxylate
- Hyoscyamine
- Atropine
- Ipratropium
- Diphenhydramine
- Tricyclic antidepressants
- Chlorpromazine
- Prochlorperazine
- Promethazine
- Cyclobenzaprine

*List not all-inclusive

Opioid Adverse Effects and Management

Adverse Effect	Duration	Treatment
Constipation	Chronic – will NOT develop tolerance to	stimulant (senna +/- osmotic agent)
Nausea/vomiting	3-7 days	Dopamine antagonists (prochlorperazine, promethazine), metoclopramide, ondansetron
Sedation	2-3 days	Decrease opioid dose, consider other causes
Confusion/hallucinations	< 2 days	Opioid rotation, lower dose, antipsychotic
Pruritis/itching	< 5 days	Antihistamines, steroids
Respiratory depression		Naloxone if non-responsive and decreased respirations

Terminal Secretions

- Known as the “death rattle”
 - Mean time from onset to death ~16 hrs
 - Type 1 – predominately salivary secretions
 - Type 2 – predominately bronchial secretions
- Treatment
 - Discontinue artificial nutrition/hydration
 - Repositioning
 - Oropharyngeal suctioning – use only if necessary
 - Anticholinergic meds to dry secretions
 - Atropine, scopolamine, glycopyrrolate, hyoscyamine

Advance Directives

- Substantive directives – allow patient to specify wishes for future care; may include a section to designate proxy decision maker
 - Living will
 - Five Wishes
 - Personal wishes statement
- Process directives – designates decision maker; does not specify wishes for care
 - Healthcare power of attorney (POA)
 - Healthcare proxy
 - Durable power of attorney for healthcare
- Physician Orders for Life Sustaining Treatment (POLST)
 - Orders for CPR, antibiotics, artificial nutrition/hydration
 - Travels with patient and is legally valid as order in transit
- Code status
 - Specifies whether to perform CPR

Having the Conversation

- **SPIKES**
 - S = Setup
 - P = Perception
 - I = Invitation
 - K = Knowledge
 - E = Empathize
 - S = Summarize and Strategize
- **NURSE (empathy)**
 - N = Naming
 - U = Understanding
 - R = Respecting
 - S = Supporting
 - E = Exploring
- **Ask-Tell-Ask**

Pearls in the Retail Pharmacy Setting

- Can accept a faxed CII for original if noted for terminal or hospice patient
 - Partial fills cannot exceed 60 days from original RX
- Can accept **emergency** CII order via phone
 - Immediate administration is necessary
 - No alternative available, amount limited to emergent need
 - Not reasonably possible for prescriber to provide written prescription
 - Pharmacist reduces oral RX to written form
 - Prescriber provides written RX within 7 days
- Billing via hospice formulary – CMS advises hospices responsible for analgesics, anxiolytics, laxatives, antiemetics



maslin

"You've got one foot in the grave. Further testing will determine if it's your left or your right."

Selected Resources

- Provider education
 - Center to Advance Palliative Care
 - www.capc.org
 - American Academy of Hospice and Palliative Medicine
 - www.aahpm.org
 - Education in Palliative and End-of-Life Care
 - www.epec.net
 - Palliative Care Fast Facts
 - www.mypcnow.org
- Patient education
 - www.getpalliativecare.org
 - www.theconversationproject.org