# Palliative Care Pharmacy:
# 411 for the Interdisciplinary Team

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## Learning Objectives

- Understand the burden-to-benefit ratio of medications commonly used in caring for patients with serious illness.
- Develop best practices for transitions in care and medication management from hospital to home or facility in advanced disease processes.
- Explore strategies to increase discipline specific pharmacology knowledge among all members of the palliative care interdisciplinary team.

## Faculty Disclosures

- We have no disclosures



## Why a Pharmacist?

- Administration on Aging predicts that by the year 2030 there will be more than 72.1 million Americans over age sixty-five in the United States
  - Many of these elderly people will have at least one, if not more, chronic medical conditions
- People with chronic medical conditions are the most frequent health care utilizers accounting for 81% of all hospital admissions, and 91% of prescriptions filled
- Medications are involved in 80% of all treatments
- Drug-related morbidity and mortality in this country costs nearly $200 billion dollars annually

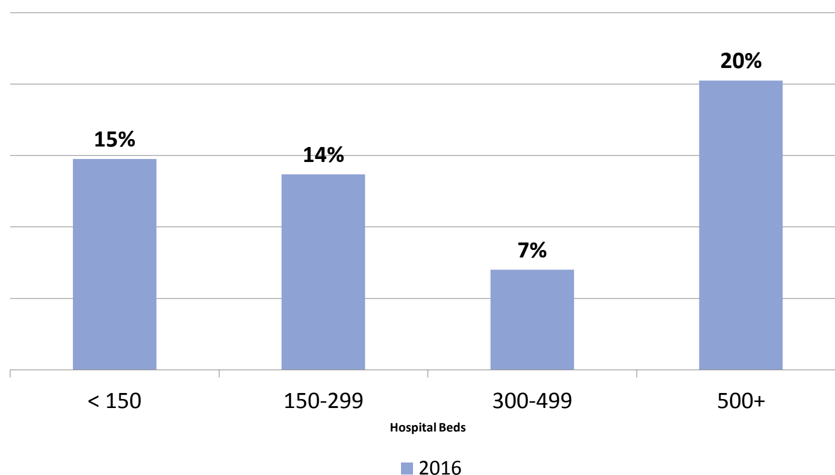
# Top Ten Medications Prescribed in Hospice

1. Acetaminophen
2. Lorazepam
3. Morphine
4. Atropine
5. Haloperidol

6. Prochlorperazine
7. Albuterol
8. Docusate
9. Bisacodyl
10. Scopolamine

Am J Hosp Palliat Care. 2014 Mar; 31(2): 126–131.

# Programs Reporting Pharmacists on PC Team




Data courtesy of National Palliative Care Registry™ survey

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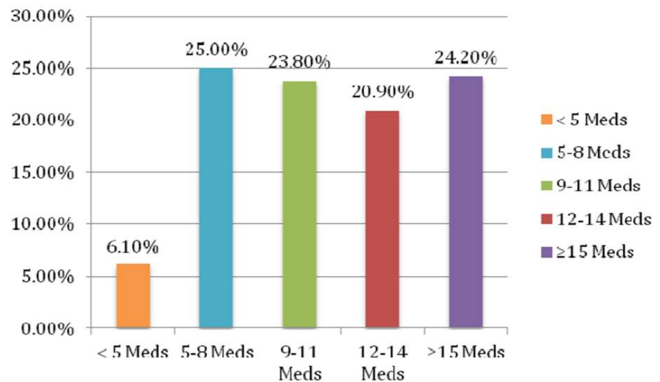
# Burden of Polypharmacy

- Adverse drug reactions
  - 4x increase in risk when 5 meds → 8 meds
- Administration
- Drug interactions
- Costs




J Pain Symptom Manage. 2016 Feb; 51(2): 178–183.e2.

# Deprescribing – The What

**Definition:**

- The systematic <u>process</u> of identifying and discontinuing drugs in instances in which **existing or potential harms outweigh existing or potential benefits** within the context of an individual *patient's care goals, current level of functioning, life expectancy, values, and preferences*.

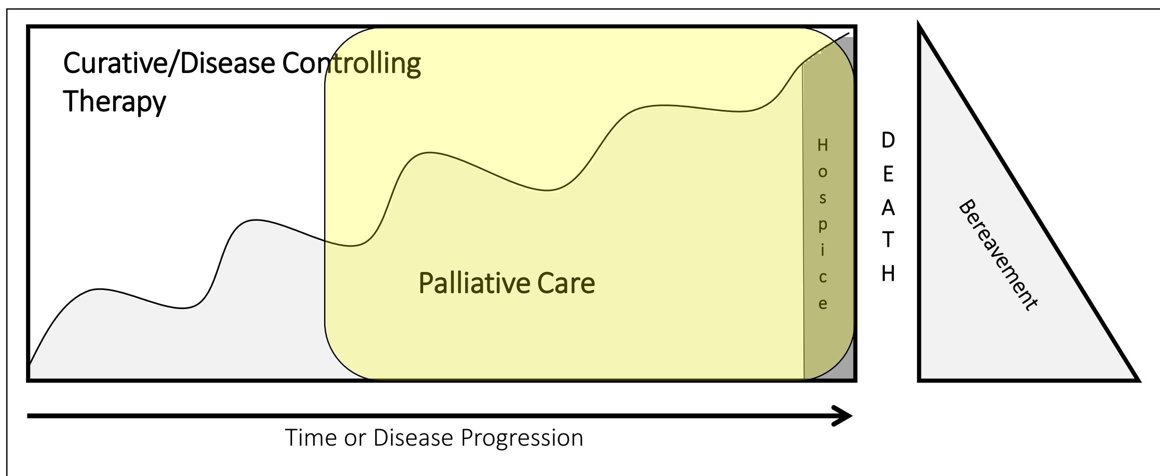
JAMA Intern Med. 2015 May;175(5):827-34.

# Eligible Patients for Deprescribing – The Who and When

- Patients with a life-limiting, or debilitating, illness and have at least one of the following:
  - Documented comfort-focused goals of care
  - Reduced functional level, or manifesting advanced or end-stage disease
  - Presentation of a new symptom or clinical syndrome suggestive of a potential adverse drug effect
  - Receiving high-risk drug combinations
  - Receiving medications for comorbid conditions for scenarios associated with no increased disease risk despite drug cessation

JAMA Intern Med. 2015 May;175(5):827-34.

## Continuum of care for a patient with a life-limiting illness.

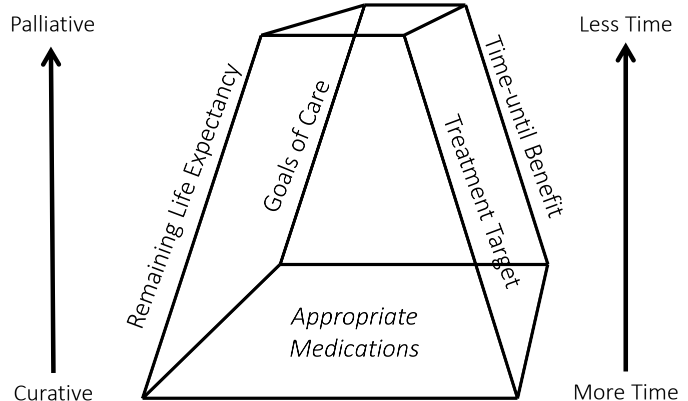


# Benefits of Deprescribing – The Why

- 1. Reduces unnecessary burden
- 2. Reduces unnecessary cost
- 3. Improves quality care

# The Process of Deprescribing – The How

- Rational prescribing for patients with a reduced life expectancy
- Note:
  - Two patient-specific factors
  - Two medication-specific factors




Clin Pharmacol Ther. 2009 Jan;85(1):103-7.

# Number needed to treat

- The NNT – average number of patients who need to be treated to prevent one bad outcome
  - Example: If I treat 1,000 patients with hypertension with Drug X for ten years, I will prevent 2 strokes compared to placebo
  - What is the NNT if the study period is 17 days instead of 3,650?
  - How many strokes can we prevent by treating patients for 17 days?

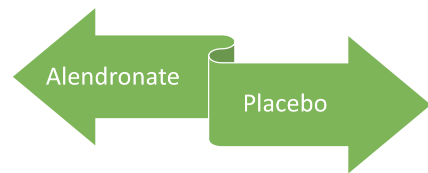
# Number needed to harm

- The NNH – average number of patients who need to be exposed to a risk factor (e.g., medication) over a specific period to cause harm in one (who would not otherwise have been harmed)
  - Example: One in 38 ambulatory patients treated with an opioid for 2 months will consistently experience nausea.
  - What is our population of patients who are close to death? Medically fragile, numerous comorbid conditions?
  - How many patients out 38 receiving an opioid will consistently experience nausea?

## Time To Benefit (TTB) / Time to Harm

- The TTB for a medication would be the time necessary for an individual patient to gain various benefits of all kinds that exceed all the potential harms.
- Similar conceptually to TTB, time to harm (TTH) is the amount of time required for a therapy to cause harm.
- Tight Blood Glucose Control
  - Time to benefit ~ 10 years
  - Time to harm ~ minutes

## Persistence of Benefit




- Patients at risk for osteoporosis received alendronate for five years, then placebo for the next five years
- No increase in fracture risk in placebo group.
- Alendronate administration instructions:
  - Administer first thing in the morning and $\geq$ 30 minutes before first food, beverage (except plain water) or other medication(s) of the day.
  - Do not take with mineral water or with any other beverages.
  - Patients should be instructed to stay upright (do NOT lie down) for at least 30 minutes AND until after first food of the day (to reduce esophageal irritation)

Black D. M. *et al* (2006) JAMA 296 (24), 2927–2938

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## The Case

Judy is a 78-year-old female

- **CC:** Repeated falls in the past 3 months
- **PMH:** Breast cancer, hypertension, dyslipidemia, nonvalvular atrial fibrillation (no h/o CVA), Alzheimer's disease (FAST 7C - > 10% weight loss, recent UTI)
- Lives with daughter, Loria, in Maryland
- Son, Frederick, is a lawyer who lives in California

## The Case

Judy is a 78-year-old female

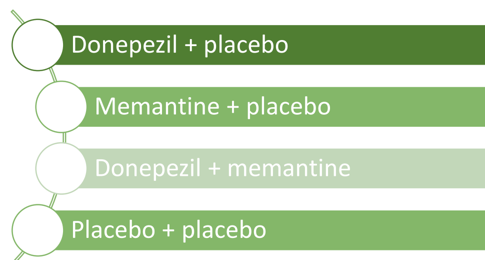
Current Medication Regimen

- Donepezil (Aricept®)
- Memantine (Namenda®)
- Lisinopril
- Atorvastatin (Lipitor®)
- Warfarin
- MVI
- Ferrex
- Calcium and Vitamin D3

- When you suggest slimming down on the medications, Lori is agreeable.
- Frederick, on the other hand, goes ballistic and angrily says, **"What's WRONG with you people – are you TRYING to kill her off?"**
- So…..any issues here?

# Donepezil and Memantine for Moderate-to-Severe AD

- 295 community-dwelling moderate-to-severe AD patients treated with donepezil for at least 3 months (MMSE 5-13); 52 weeks
- Stratified by
  - Study center
  - Duration of donepezil treatment before entry (3-6 mo vs. $\geq$ 6 mo)
  - Baseline MMSE (5-9 vs. 10-13)
  - Age (< 60; 60-74; $\geq$ 75)




Howard R, et al. NEJM 2012;366:893-903.

# Donepezil and Memantine for Moderate-to-Severe AD

- Outcomes:
  - Score on MMSE
    - Clinically important difference: **Scoring 1.4 points or higher than comparator**
  - Caregiver-rated Bristol activities of Daily Living Scale (BADLS)
    - Clinically important difference: **Scoring 3.5 points or lower than comparator**
- Baseline MMSE 9.1-9.2 in all groups
- Baseline BADLS 26.9-28.6

Howard R, et al. NEJM 2012;366:893-903.

## Donepezil and Memantine for Moderate-to-Severe AD

- Clinically important difference:
  - MMSE $\geq$ 1.4 point increase

| Treatment group | MMSE | BADLS |
|---|---|---|
| All donepezil vs. no donepezil | +1.9 | -3.0 |
| All memantine vs. no memantine | +1.2 | -1.5 |

- Effect of donepezil and memantine did not differ significantly in the presence or absence of either.
- Donepezil plus memantine showed no difference vs. donepezil alone

Howard R, et al. NEJM 2012;366:893-903.

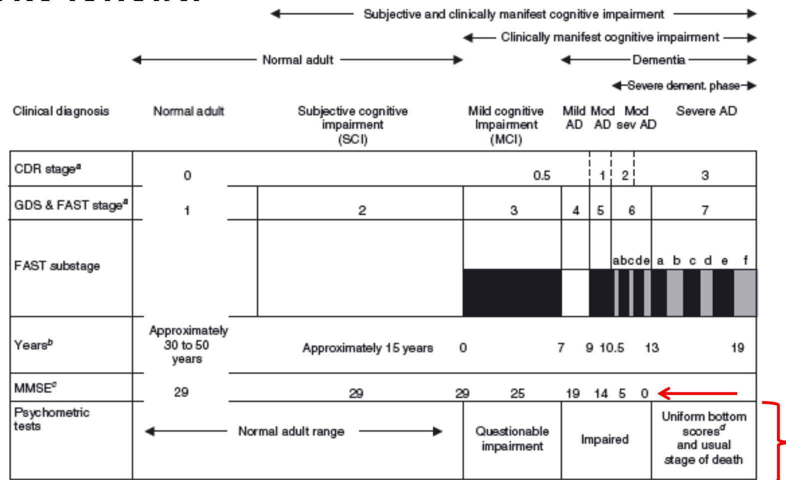
## Donepezil and Memantine for Moderate-to-Severe AD

| Baseline MMSE | Impact of donepezil therapy on MMSE |
|---|---|
| MMSE 10-13 | +2.6 |
| MMSE 5-9 | +1.3 |

Donepezil only showed clinical significance in patients with baseline MMSE $\geq$ 10

Howard R, et al. NEJM 2012;366:893-903.

# FAST and MMSE




Reisberg Prin Prac Ger Psy, 3rd ed. Used with permission, John Wiley and Sons.

# Adverse Effects of Dementia Drugs

| Drug Category | Drug Name(s) | Adverse Effects |
|---|---|---|
| **Cholinesterase Inhibitors ($6-8/day)** | Donepezil (Aricept)<br><br>Galantamine (Razadyne, Razadyne ER)<br><br>Rivastigmine (Exelon) | Insomnia (up to 14%)<br>Nausea (up to 19%)<br>Diarrhea (up to 15%)<br>Accidents (up to 13%)<br>Infection (up to 11%)<br>Headache (10%)<br>Pain (9%)<br>Vomiting (9%)<br>Anorexia (8%)<br>Fatigue (8%)<br>Dizziness (8%)<br>Hallucinations (3%) |
| **NMDA Antagonist ($6-8/day)** | Memantine (Namenda) | Dizziness (7%), Hypertension (4%), Confusion (6%), Hallucinations (3%) Diarrhea (5%), Back pain (3%) |

## Cholinesterase Inhibitors - DFO

- CI use and syncope-related outcomes
  - 19,803 community-dwelling older adults with dementia on a CI
- Hospital visits more frequent in CI users
  - 31.5 vs. 18.6 events/1000 person-years
  - Adjusted hazard ratio 1.76
- Increased hospital visits for bradycardia, permanent pacemaker insertion, hip fracture

Gill, Arch Intern Med 2009;169(9):867-873

## Bottom Line: Dementia Drugs

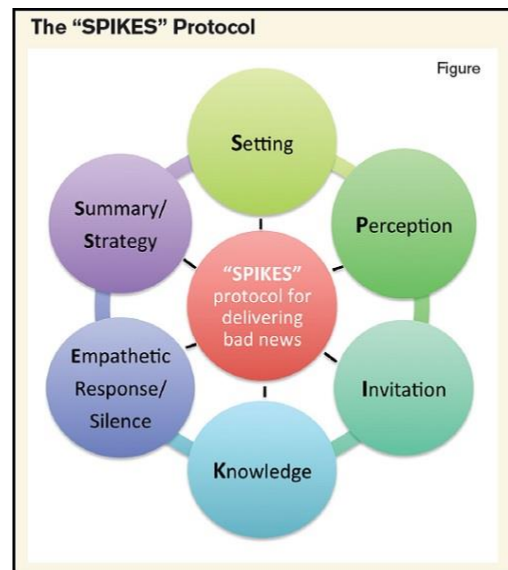
- Dementia medications are LESS HELPFUL and MORE HARMFUL in advanced disease (see adverse effects)
- NOT indicated or provided with FAST 7 without clear and ongoing benefit in managing identifiable and distressing behaviors.
- MAY be covered with FAST 6; discuss goals/outcomes with hospice physician or pharmacist
- 2 week tapering supply should be provided if medication discontinued

## But is Frederick buying what you're selling?

## SPIKES – Having those conversations

- S – setting
- P – perception
- I – invitation
- K – knowledge
- E – emotion
- S – summarize recommendation

Slides from McPherson, Walker, Pruskowski, Talebreza. "Right Sizing Medication Regimens in Serious Illness: Doing the Prescribing and Deprescribing Dance"



# Communication Models – Responding to Emotional Cues – The NURSE mneumonic

- **N – Name it**
  - "…it sounds like you've been worried about what's going on…"
- **U – Understand the core message:**
  - "…if I understand you correctly, you are worried about what to say to your family and how they will react…"
- **R – Respect/Reassurance at the right time:**
  - "…I'm really impressed that you've continued to be independent…"
- **S – Support:**
  - "…would you like me to talk to your family about this?"
- **E – Explore:**
  - "…I notice that you're upset, can you tell me what you're thinking?"

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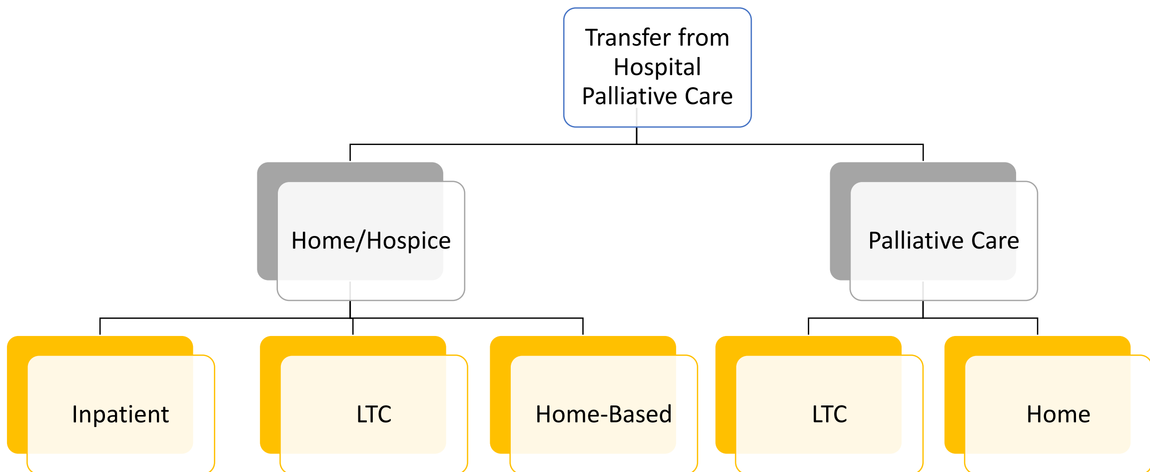
https://training.caresearch.com.au/files/file/EoLEss/NURSE.pdf

# Medication Considerations in Transitions in Care!

Include **coordinated, efficient, and interoperable information transfer** across all providers and all settings; **seamless, high-quality, integrated**, patient-centered, family-oriented, and consistently accessible around the clock.

# Potential Transfer Plans of Care




# Case

- Mrs. Smith is a 72 year old patient with an end stage diagnosis. She is being followed in the hospital by the palliative care team. As she prepares for discharge, you consider the medications she is receiving for pain and symptom relief.
- What are some of the medication management issues you must consider during this transition?
- How does the service/or facility she is transferring to affect your comfort level?

# Degree of Concern
(High, Moderate, Low)

| Discharge to: | Issue 1 | Issue 2 | Issue 3 | Issue 4 |
|---|---|---|---|---|
| Inpatient hospice | | | | |
| Home-based/ hospice | | | | |
| LTC/hospice | | | | |
| Pall Care LTC | | | | |
| Pall Care home | | | | |

# Identified Issues

- Formulary (related/unrelated)
- Familial attachment to medications/monitoring
- Thinking ahead/availability of medications (delivery/logistics)
  - Changing routes of administration needs / parenteral / compounded
- Misuse/abuse/diversion of medications
- Facility CRAZY regulations (opioids, antipsychotics)
- Goals of care / levels of care
- Communication issues and barriers
- Medication myths, misconceptions, beliefs (opioids)
- Cost of medications / copays
- Cultural beliefs / values / healthcare beliefs
- Medication titration and monitoring (time needed for titration)

## Four Critical Medication issues in Transitions in Care

1. **Medication titration and monitoring**
2. Formulary issues
3. Prioritizing medications based on benefit/burden and goals of care
4. Thinking ahead

## Degree of Concern

| Discharge to: | Med Titration | Formulary / Insurance Considerations | Prioritizing Meds | Thinking Ahead |
|---|---|---|---|---|
| Inpatient hospice | Low | High | High | Low |
| Home-based hospice | Moderate | High | High | Moderate |
| LTC hospice | Moderate | High | High | Moderate |
| Pall Care LTC | High | Moderate | High | High |
| Pall Care home | High | Moderate | High | High |

## Assess Level of Concern

- Influencing Factors
  - Patient acuity
  - Prognosis
  - Risk of medications
  - Family support
  - Hand off site experience with specific situation of patient

## High Risk Medications

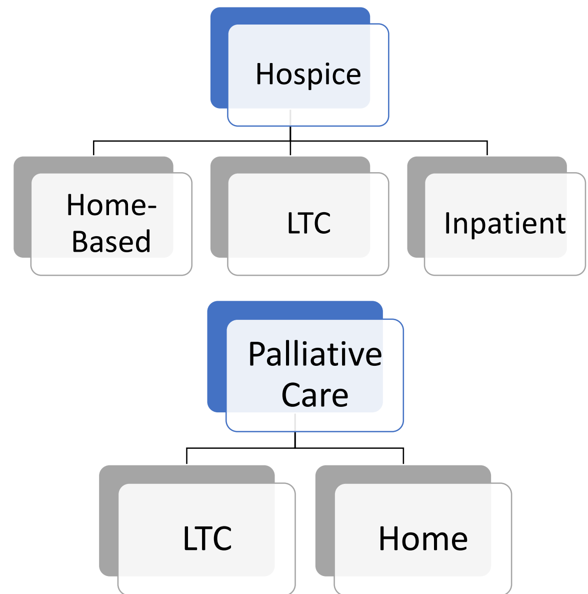
- 67 year old female with an advanced illness (COPD)
- Admitted with fractured hip; s/p total hip replacement, now in ICU
- PMH: advanced COPD (extubated 2 days ago), DM with severe neuropathy
- Team is worried about her depression and pain, patient is writhing in pain most of the day
  - Started methadone 2.5 mg BID
  - Started Ritalin 2.5 mg am/noon and Effexor
- Disposition in am…

*not actual pt

# Heading to Where?!

**Considerations:**

- Experience with methadone
  - Protocol
  - Pharmacy support
- Support services for counseling and assessment of depression




# Heading to Where?!

**Actions:**

- Specific timeframes and dosing recommendations for titrations
- Follow up phone calls to monitor
- Family education

**Methadone Recommendations:**

Converted from low dose opioids (<60 mg/d of PO morphine):

- No more than 2.5 mg TID initial dose
- Do not increase more than 5 mg/d every 5-7 days

Converted from higher dose opioids:

- No more than 30-40 mg/d initial dose
- Do not increase more than 5 mg/d every 5-7 days

Assessment during 3-5 day window after initiation or dose increase.

Chou R, et al. J of Pain. 2014. 15 (4); 321-337.

## Four Critical Medication issues in Transitions in Care

1. Medication titration and monitoring
2. **Formulary issues**
3. Prioritizing medications based on benefit/burden and goals of care
4. Thinking ahead

## Degree of Concern

| Discharge to: | Med Titration | Formulary / Insurance Considerations | Prioritizing Meds | Thinking Ahead |
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| Pall Care home | High | Moderate | High | High |

## Making the Case for Formulary Issues

- Mr. C is a 49 year old man with end-stage lung cancer discharged from the hospital to home.
- His analgesic regimen is as follows:
  - OxyContin 20 mg po q12h
  - Fentora 800 mcg four times daily
  - Morphine 10 mg po q2h as needed for additional pain
  - Zofran 8 mg q8h prn nausea
- He has not been on any additional medications.
- He is concerned about his insurance covering his medications.

## Who provides what if it's Hospice?

| Scenario | | Who provides medication |
|---|---|---|
| Related to terminal diagnosis | → | Hospice |
| Unrelated, Part D eligible | → | Part D process for payment (no hospice PA process) |
| Unrelated in 4 categories; may be Part D eligible | → | Part D hospice submits PA process for payment |
| Related but no longer medically necessary | → | Patient |
| Related and medically necessary, but not formulary and patient refuses formulary therapeutic alternative | → | Patient |
| Unrelated but no longer medically necessary | → | Patient |

## Making the Case for Formulary Issues

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- He is concerned about his insurance covering his medications.

## Thinking Ahead

| Original Order | Amended Order |
|---|---|
| OxyContin 20 mg po q12h | MS Contin 30 mg po q12h (or patient must pay for OxyContin) |
| Fentora 800 mcg four times daily | Increase morphine oral solution |
| Ondansetron 8 mg | Haloperidol, prochlorperazine |

## Cost Effective Medications

- Ondansetron vs. haloperidol
- Tiotropium vs. ipratropium
- Methadone vs. branded LA opioid
- Citalopram vs. escitalopram
- Esomeprazole vs. omeprazole

## Four Critical Medication issues in Transitions in Care

1. Medication titration and monitoring
2. Formulary issues
3. **Prioritizing medications based on benefit/burden and goals of care**
4. Thinking ahead

## Degree of Concern

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## Goals of Care/ Benefits and Burdens

- Mrs. J is a 58 year old woman diagnosed two years ago with ALS.
- At the time of diagnosis she was started on riluzole 50 mg po q12h.
- On admission to hospice the admission nurse questions the utility of riluzole. The patient gets quite upset and cries “Are you crazy? That’s the drug that slows this awful disease from progressing!”

# Riluzole

- Study in Austria; Jan 08 – June 12; 911 patients
- Incidence, prevalence, patients' survival in dependence of age, gender and riluzole treatment

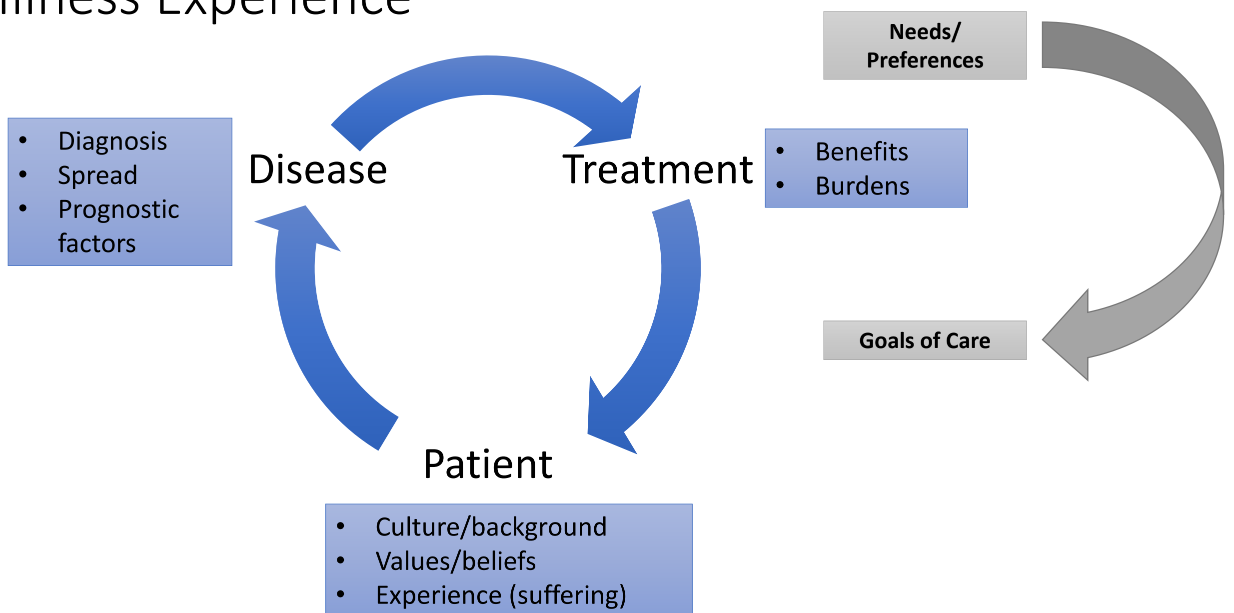
**Methods**: Stratified patients into five groups defined by their therapy ratios

  - Duration of riluzole therapy divided by their survival time

**Results:**

- Significant correlation between therapy ratios and duration of riluzole therapy.
  - 15% reduction in mortality at 6 months.
- Lower therapy ratios (shorter riluzole treatment periods) were associated with longer survival times.
  - At 18 months post-diagnosis (and start of therapy), survival curves of riluzole-treated and untreated patients crossed; untreated patients showed a better survival thereafter.

Cetin H et al. Neuroepidemiology 2015;44:6-15.



## Goals of Care Change Over Time

- Maintaining and improving function
- Staying in control
- Relief of suffering (pain and symptom management)
- Prolonging life for as long as possible or until a specific event (time limited trials of care)
- Quality of life/ living well
- Relieving burden for family members
- Strengthening relationships
- Preferences for location of care or death
- Life closure/ dying well
- Personal wishes for management of dying

**Goals of Care Reconciliation**

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## Four Critical Medication issues in Transitions in Care

1. Medication titration and monitoring
2. Formulary issues
3. Prioritizing medications based on benefit/burden and goals of care
4. **Thinking ahead**

Cetin H et al. Neuroepidemiology 2015;44:6-15.

## Degree of Concern

| Discharge to: | Med Titration | Formulary / Insurance Considerations | Prioritizing Meds | Thinking Ahead |
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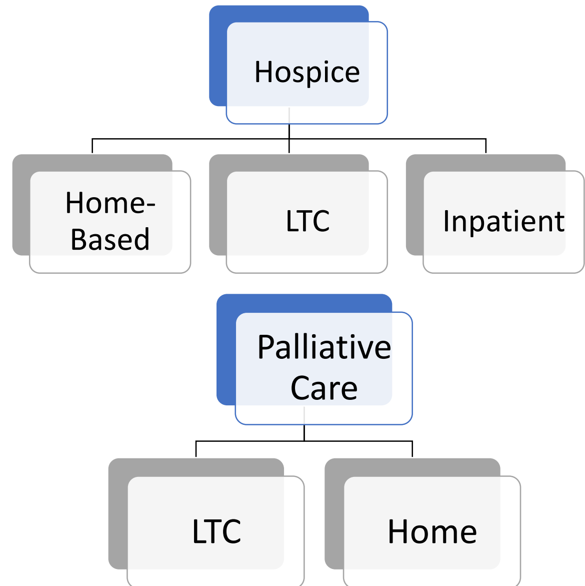
## Making the Case to Think Ahead

- Patient leaving hospital s/p extubation with stage IV lung ca (mets to bone, brain, liver)
- Comfortable on BiPAP currently but planning to discharge in the next day
- Patient has been bed bound for 3 months
- Current meds:
  - Morphine 10 mg q4h prn (x4-6/day) for SOB
  - Ativan 0.5 mg q6h prn (x3-4/day)
- Family afraid morphine will kill him and wants it stopped, nurse feels “on the spot” for every dose

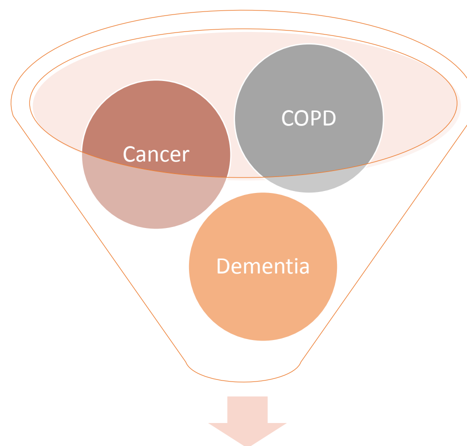
# Heading to Where?!

**Considerations:**

- Common symptoms for EOL picture for this patient
- Response time for quickly emerging symptoms
- Prognosis/ symptom burden




# Common EOL Clinical Pathways




SOB, secretions, decreased intake, N/V, pain, fatigue, agitation, delirium, bedridden (ulcers)

## Predictable Challenges in the Final Days

**What is happening to patient**

- Functional decline- transfers, toileting, fall risk
- Can't swallow meds- route of administration
- Terminal pneumonia
  - Dyspnea
  - Congestion
  - *Delirium > 80%* (+ agitation)
- Concerns of family and friends

**Approach to Care**

- Prepare caregivers with proactive" communication
  - Anticipate questions and concerns
  - Be available
  - Don't present "non-choices" as choices
- Aggressive pursuit of comfort
- ***Try to anticipate predictable problems***

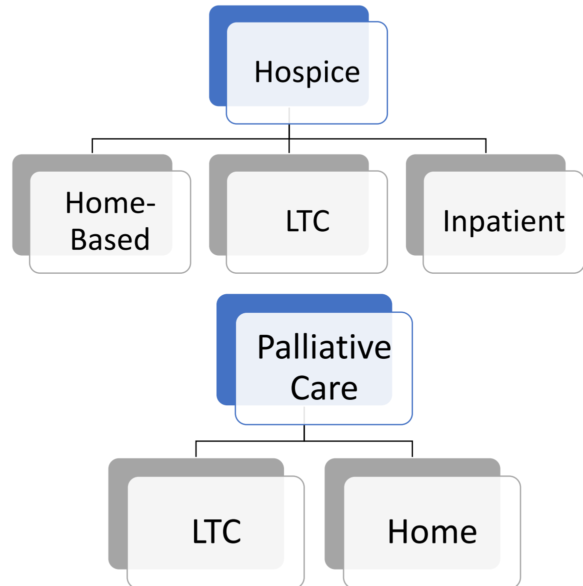
## Basic Medication Toolkit

- Opioids
  - Pain, SOB
- Anticholinergic
  - Secretions
- Benzodiazepine
  - Agitation, Seizures
- Antipsychotic
  - Delirium, N/V

## Heading to Where?!

**Actions:**

- Addition of prn meds for symptoms that may emerge
- Optimize dosing for current medications
- Follow up phone calls to monitor
- Family education




## Family Education

- Prioritized medication list
- External teamwork: Starting the conversation early
- Symptoms to expect
- Anticipate barriers

**Common Family Concerns:**

- How could this be happening so fast?
- What about food & fluids?
- Things were fine until that medicine was started!
- Isn't the medicine speeding this up?
- Too drowsy! Too restless!
- Confusion… he's not himself, lost him already
- What will it be like? How will we know?
- We've missed the chance to say goodbye

## From the Patient's Point of View

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## Skills Required for Team Members

- Complex medical evaluation
- Expert pain and symptom management
- Professional-to-patient and family communications
- Ability to address decisions about goals of care
- Sophisticated discharge planning
- An ability to deliver continuity of care and reliable access to services

http://www.capc.org/building-a-hospital-based-palliative-care-program/implementation/staffing

## Skills Required for Team Members

- Complex medical evaluation **& medication evaluation**
- Expert pain and symptom management **& medication evaluation**
- Professional-to-patient and family communications **about medications**
- Ability to address decisions about goals of care **and adjust medications**
- Sophisticated discharge planning **including medications**
- An ability to deliver continuity of care and reliable access to services **and medications**

http://www.capc.org/building-a-hospital-based-palliative-care-program/implementation/staffing

## Pharmacologic Competencies for all Disciplines

- Pain Management:
  - Onset/duration of opioids
  - Bowel regimen
  - Educate on how to take prn pain medications
  - Assess and monitor for opioid risk
- Assess for medication adherence/beliefs, issues with access
- Medication reconciliation
- Deprescribing
  - After goals of care conversations
  - Questioning key medications

| **OPIOIDS →** | ONSET | DURATION |
|---|---|---|
| IV | **5-15 min** | **3- 4 hr**<br>***fent: 2 hr** |
| PO | **30-60 min** | **3-4 hr** |

# Homework

**Palliative Care Fast Facts** 17+
HAIPENG ZHANG
Free

1. Read pharmacy journals and medication related Fast Facts
   - American J Health Sys Pharmacy, Pharmacotherapy

Pharmacotherapy. 2016 Jul;36(7):774-80. doi: 10.1002/phar.1776. Epub 2016 Jul 5.

**Deprescribing: An Application to Medication Management in Older Adults.**

Bemben NM[1].

⊕ **Author information**

**Abstract**

Polyphramacy has been found to have potentially negative ... well as increased risk of drug interactions and adverse effe... throughout a patient's course of care. This article reviews th... commonly encountered by clinical pharmacists. This review...

Am J Health Syst Pharm. 2017 Jul 15;74(14):1053-1061. doi: 10.2146/ajhp150893.

**Nebulized opioids for the palliation of dyspnea in terminally ill patients.**

Afolabi TM[1], Nahata MC[1], Pai V[2].

⊕ **Author information**

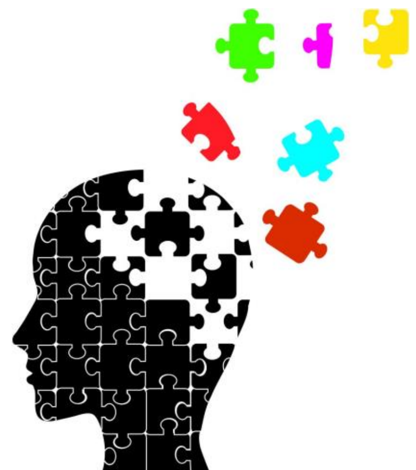
**Abstract**

**PURPOSE:** The use of nebulized opioids for the palliation of dyspnea in terminally ill patients is reviewed.

**SUMMARY:** More than 50% of patients with advanced diseases experience dyspnea during their final stages of life. Systemically administered opioids are recommended for the management of dyspnea in these patients, but adverse effects may limit their use. Nebulization offers an alternative route for administering opioids, providing relief of dyspnea while minimizing adverse events. An extensive literature search was conducted to identify publications evaluating nebulized opioids for the palliation of dyspnea in patients at end-of-life. ...

# Homework

2. Befriend a pharmacist (or a few)
   - Offer to give talks to your local pharmacy department
   - Offer to have pharmacy learners (i.e., students, residents)
   - Invite them to come along on rounds or goals of care meetings
3. Download a good drug information source
   - Epocrates (free version available), Lexicomp, Micromedex
   - Good Rx for pricing, availability
4. Participate in P&T process



# *Discussion*

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