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Founding Member, Mass General Brigham

Palliative Care in the ICU

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- Clinical focus: Critical Care
- Research focus:
  Palliative Care in Chronic Critical Illness

DISCLOSURES

No financial disclosures.

Some slides are adapted from Dr. Joshua Lakin at DFCI, to whom I am grateful – he also has no financial disclosures.

OBJECTIVES

- Define palliative care & the patients who may benefit from it
- Review palliative care communication techniques to improve goal-concordant care in the ICU
- Apply symptom management approaches to ICU patient cases

Practice Question 1

A 65-year-old woman with end-stage kidney disease on hemodialysis, peripheral artery disease, and emphysema is admitted to the intensive care unit for sepsis and acute respiratory failure due to cellulitis of her leg. After 14 days of intubation, she has not yet liberated from the ventilator or weaned off sedation. You discuss tracheostomy with her husband (who is her healthcare proxy): she had not previously stated her preferences about tracheostomy or prolonged mechanical ventilation, so her husband does not know what to decide. What is the next best step?

A. Proceed with tracheostomy as an emergency treatment to see if the patient can regain decisional capacity off sedation.
B. Do not offer tracheostomy because the patient's quality of life and prognosis are poor.
C. Transfer the decision to a court-appointed guardian.
D. Ask her husband about her values and goals and make a recommendation, which her husband can accept or decline.
E. Consult the hospital ethics team.

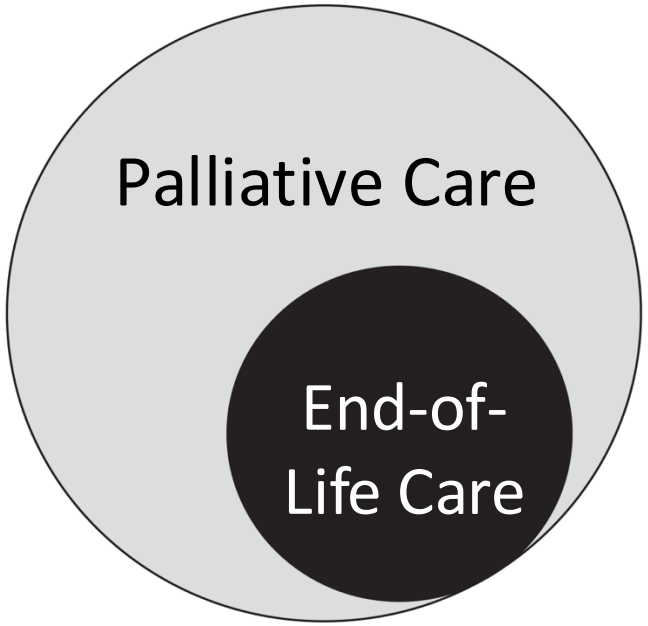
Questions adapted with permission from Dr. Joshua Lakin, DFCI

Palliative Care

Specialized medical care for patients with serious illness

Provide relief from:
- symptoms
- stress of the illness

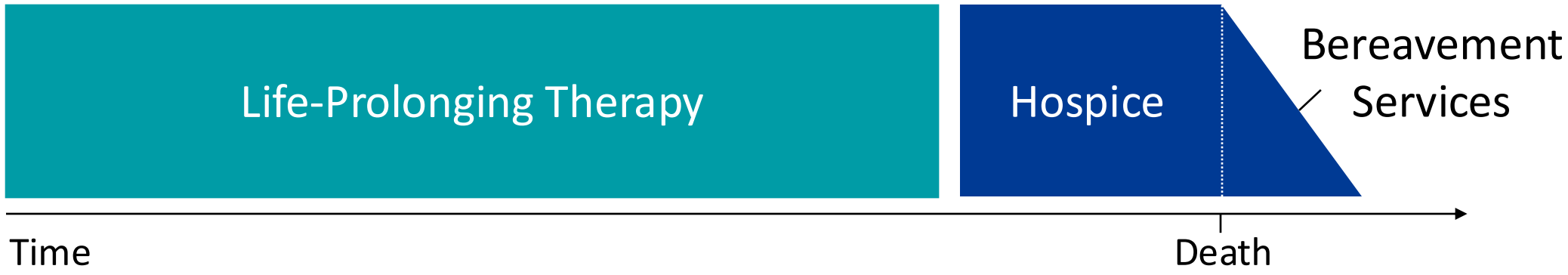
Goal: improve quality of life



Definition adapted from The Center for the Advancement of Palliative Care
Images from seriousillnessmessaging.org
Graphic adapted from J. Randall Curtis, *Eur Respir J* 2008

Palliative Care is Appropriate at Any Stage of Serious Illness

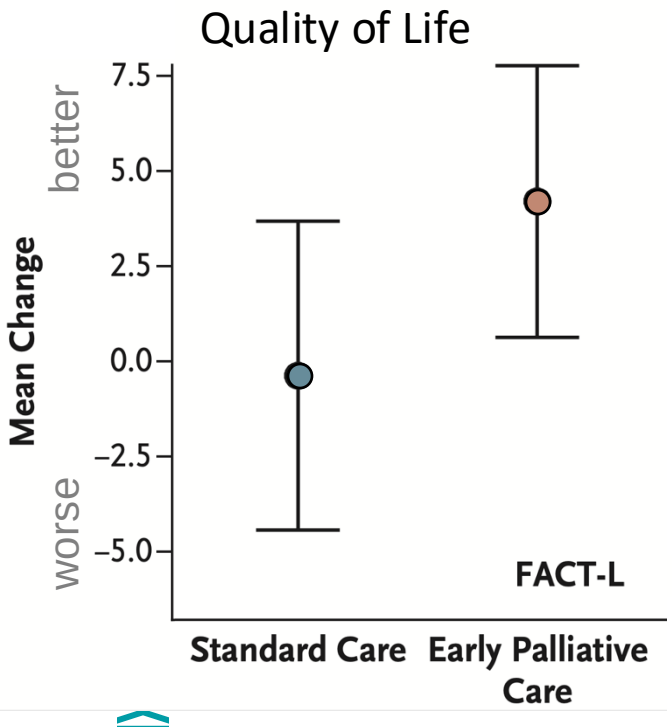
Old concept:

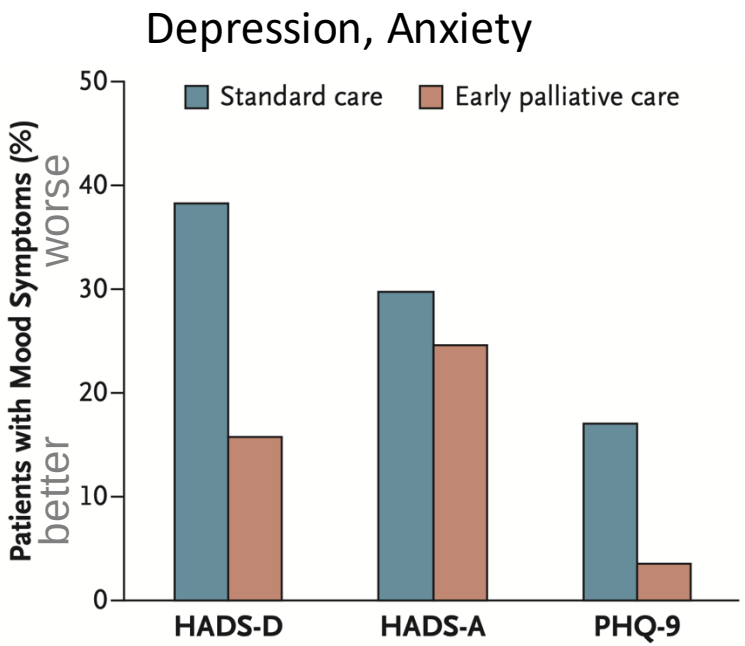


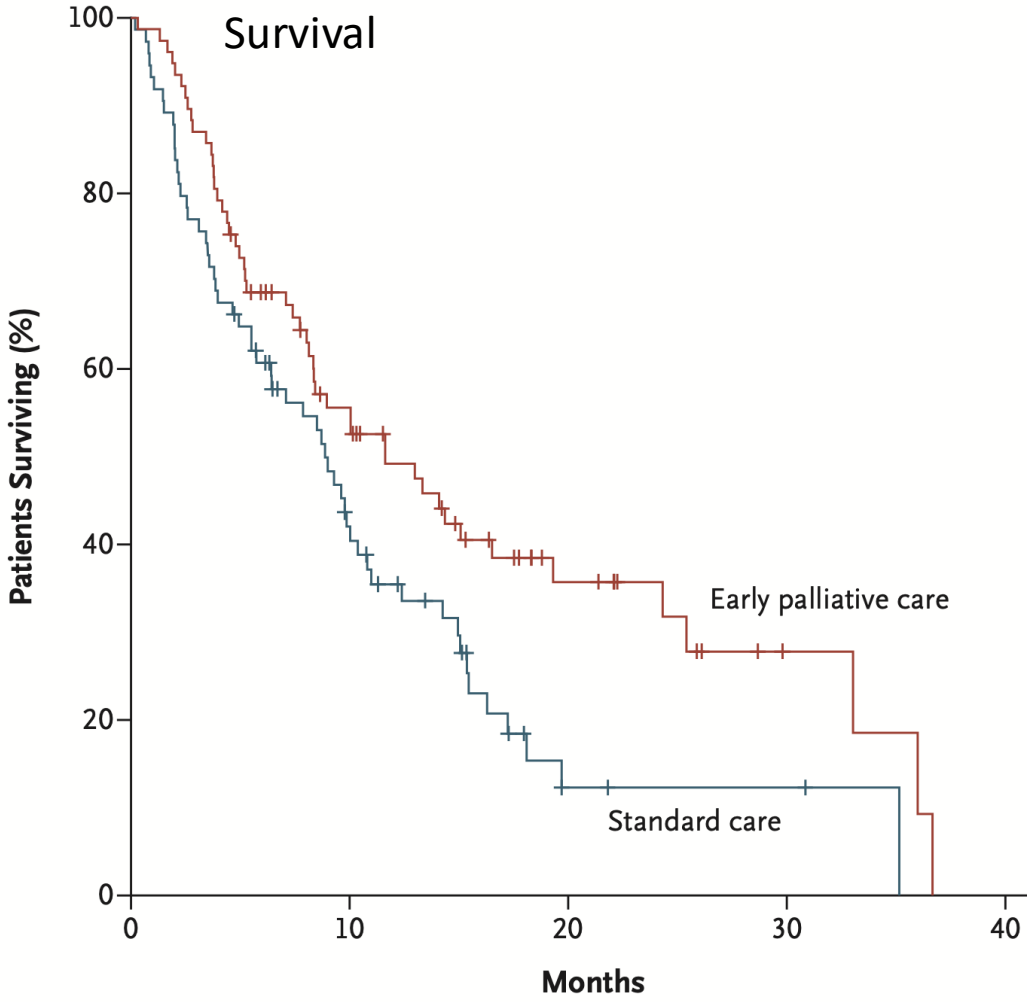
New (or not that new) concept!

Early Integrated Palliative Care Improves Outcomes

- 151 patients, new metastatic non-small cell lung cancer
- Early integrated palliative care vs standard of care
- Quality of life, anxiety, depression scores at baseline and 12 weeks

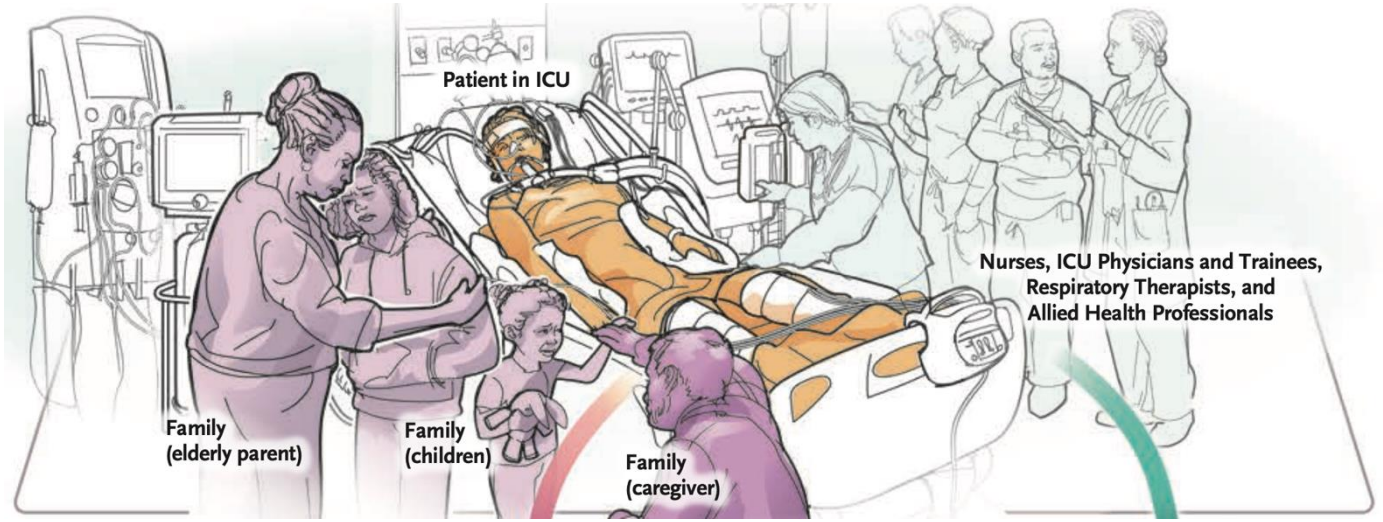






Temel et al, *New Engl J Med* 2010. Graphs annotated. FACT-L = Functional Assessment of Cancer Therapy – Lung. HADS = Hospital Anxiety and Depression Scale – Depression, – Anxiety. PHQ9 = Patient Health Questionnaire 9.

Challenges to discussing the ‘big picture’ in the ICU



Anxiety / Stress / PTSD
Setbacks & Recoveries
‘Positive Thinking’
Decision-Making Trauma
Prior discussions
– what’s different now?

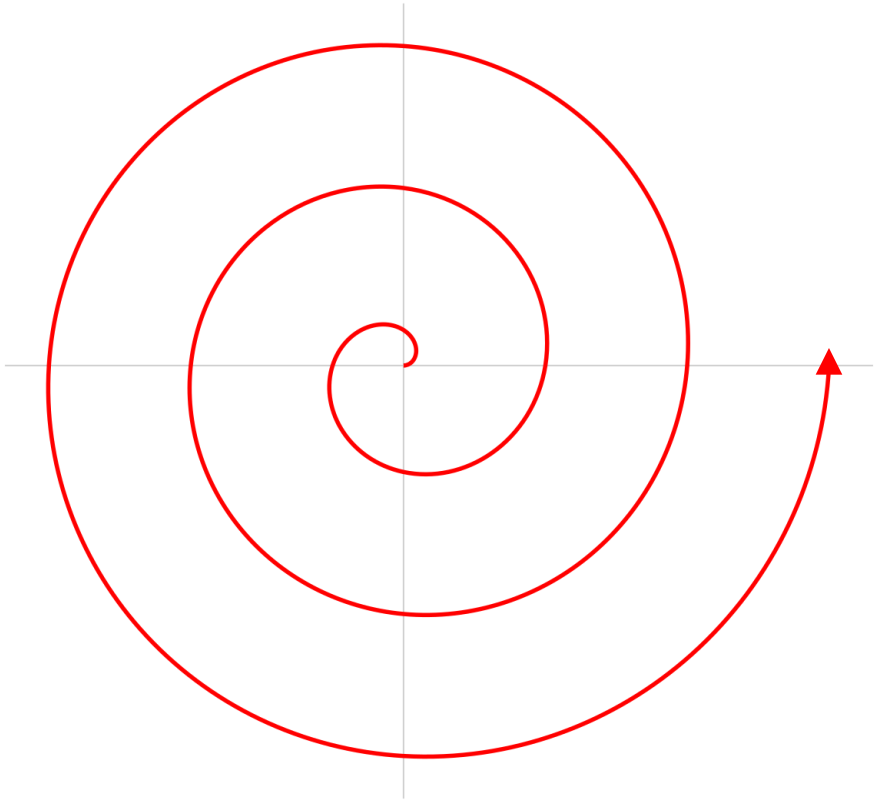
Active Symptoms
Ambivalence
History of survival

Varied trajectories
Subjectivity
Structural Racism
Therapeutic Nihilism
Moral Distress

Image from Herridge & Azoulay, *New Engl J Med* 2023

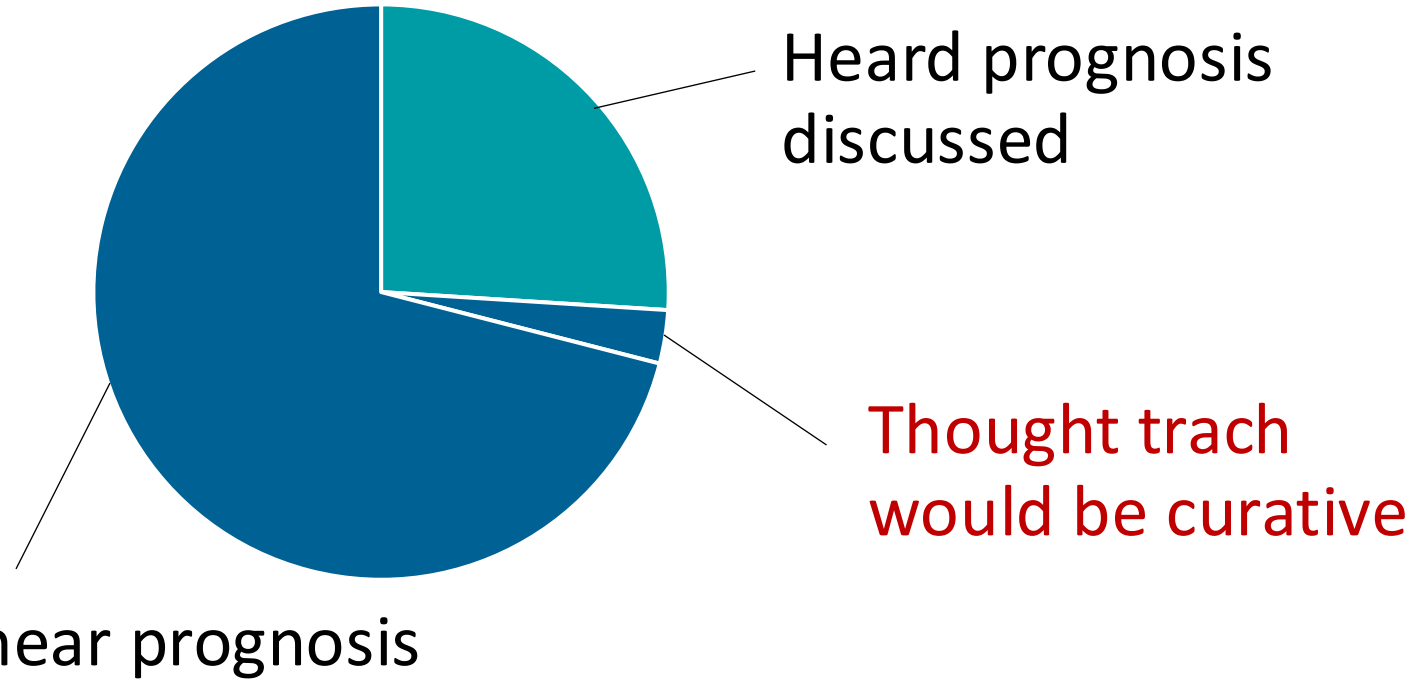
Palliative Care Techniques: Communication

- Assess Understanding
- Understand Goals & Values
- Align Hope
- Check our biases
- Offer Information
- Titrate Shared Decision-Making



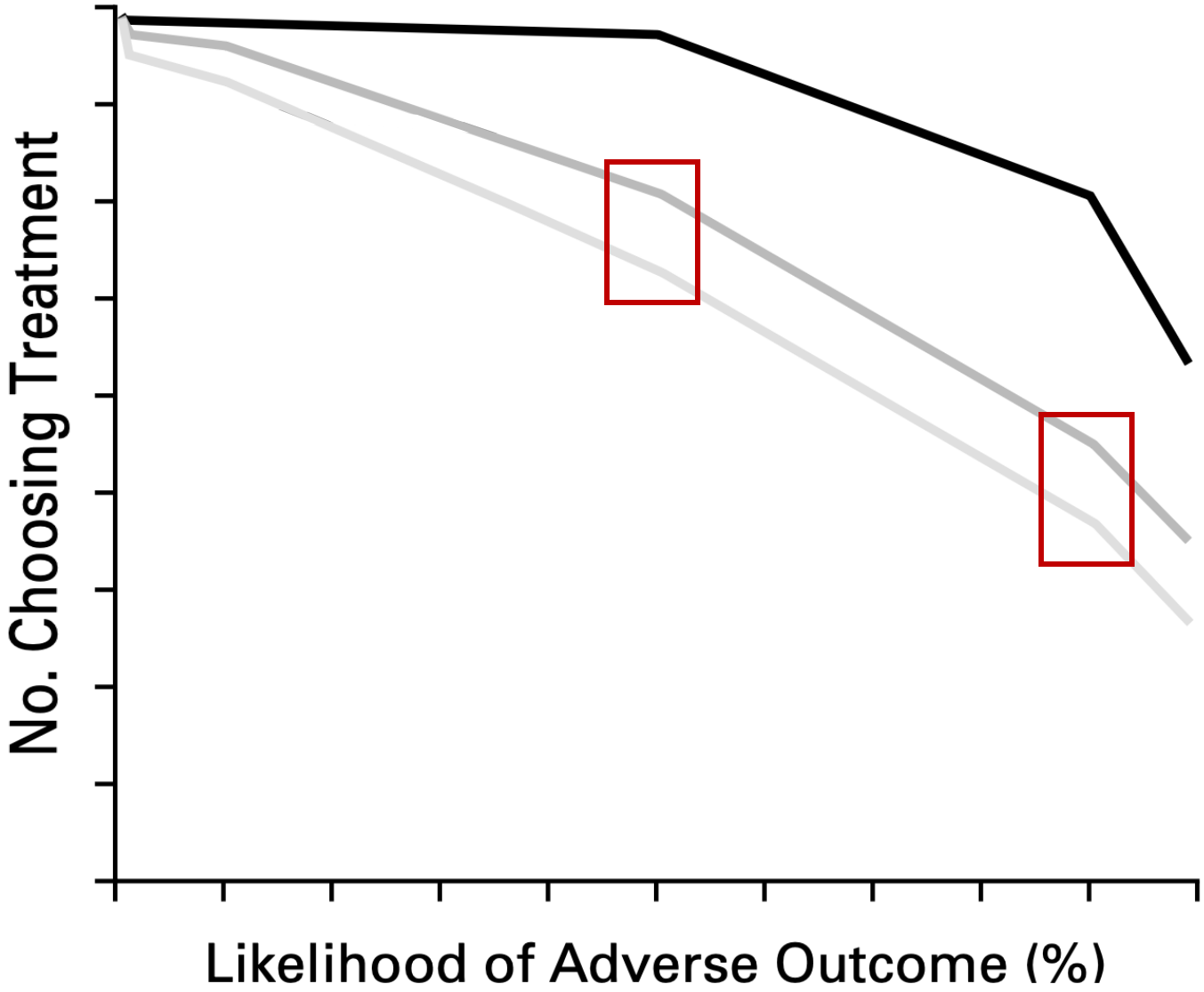
Assess Understanding: “What have you heard so far?”

Surrogates of 126 ICU patients at time of trach



adapted from Cox et al, *Crit Care Med* 2009

Understand (& Document!) Goals & Values



If the adverse outcome is:

Death

Functional Impairment

Cognitive Impairment

Figure adapted from Fried et al, *New Engl J Med* 2002

Tell Me More …

… And What Else?

What's most important to you?

To live as long as possible

And what else?

To go outside

And what else?

To be comfortable when I die

Tell me more

To spend as much time as possible with my son

Tell me more

To attend my son's graduation

Tell me more

To let my son know that I accept this

Breadth

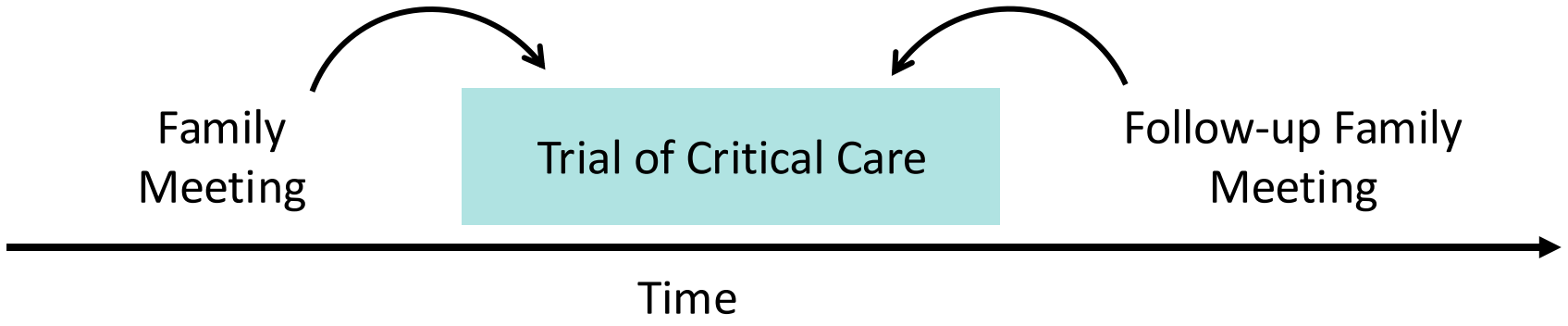
Depth

adapted from *What's in the Syringe? Principles of Early Integrated Palliative Care* by Jacobsen, Jackson, Greer & Temel

Align Hope

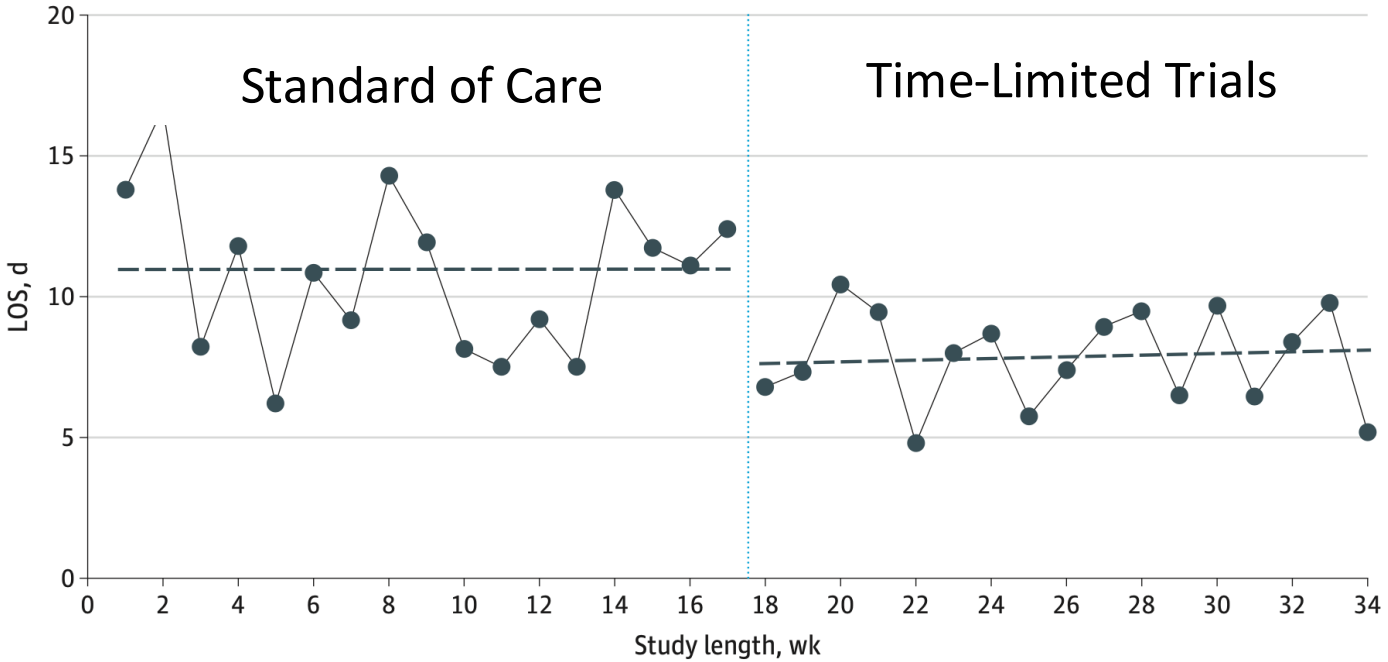
Communication

- “I hope” / “I wish”
- “I worry”



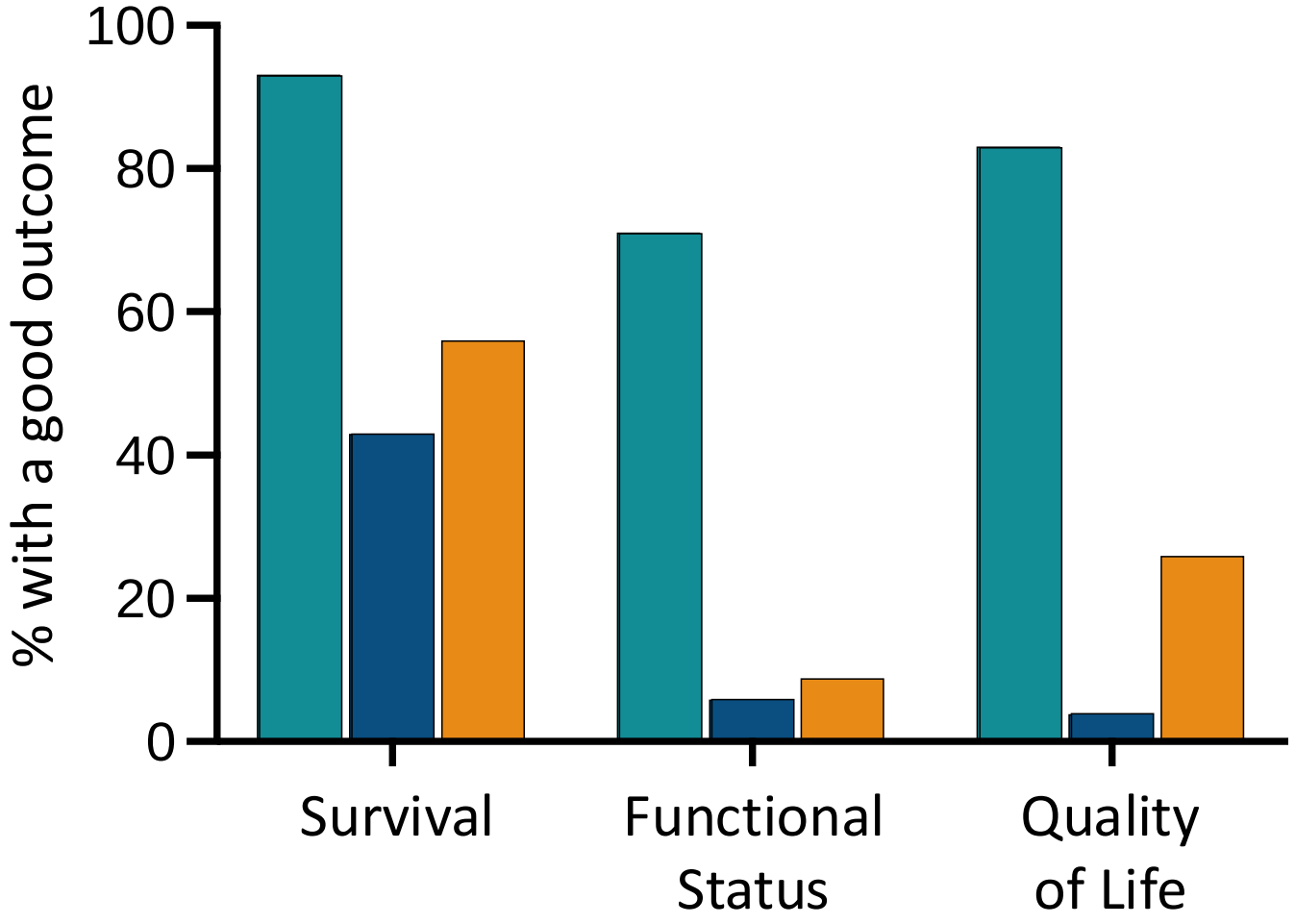
Time-Limited Trial

- Prospective
- Describe what improvement would look like
- Follow up



Chang et al, *JAMA* 2021; Leiter & Tulsky, *JAMA* 2021. Jacobsen et al, *What’s in the Syringe? Princples of Early Integrated Palliative Care* 2021

Check Our Biases



Surrogate – Clinician Pairs for 126 Patients with Chronic Critical Illness

Estimates at time of trach

Outcomes 1 year post discharge

Graphical representation of data from from Cox et al, *Crit Care Med* 2009

Good functional status denoted by absence of major dependencies; measured by activities of daily living instrument

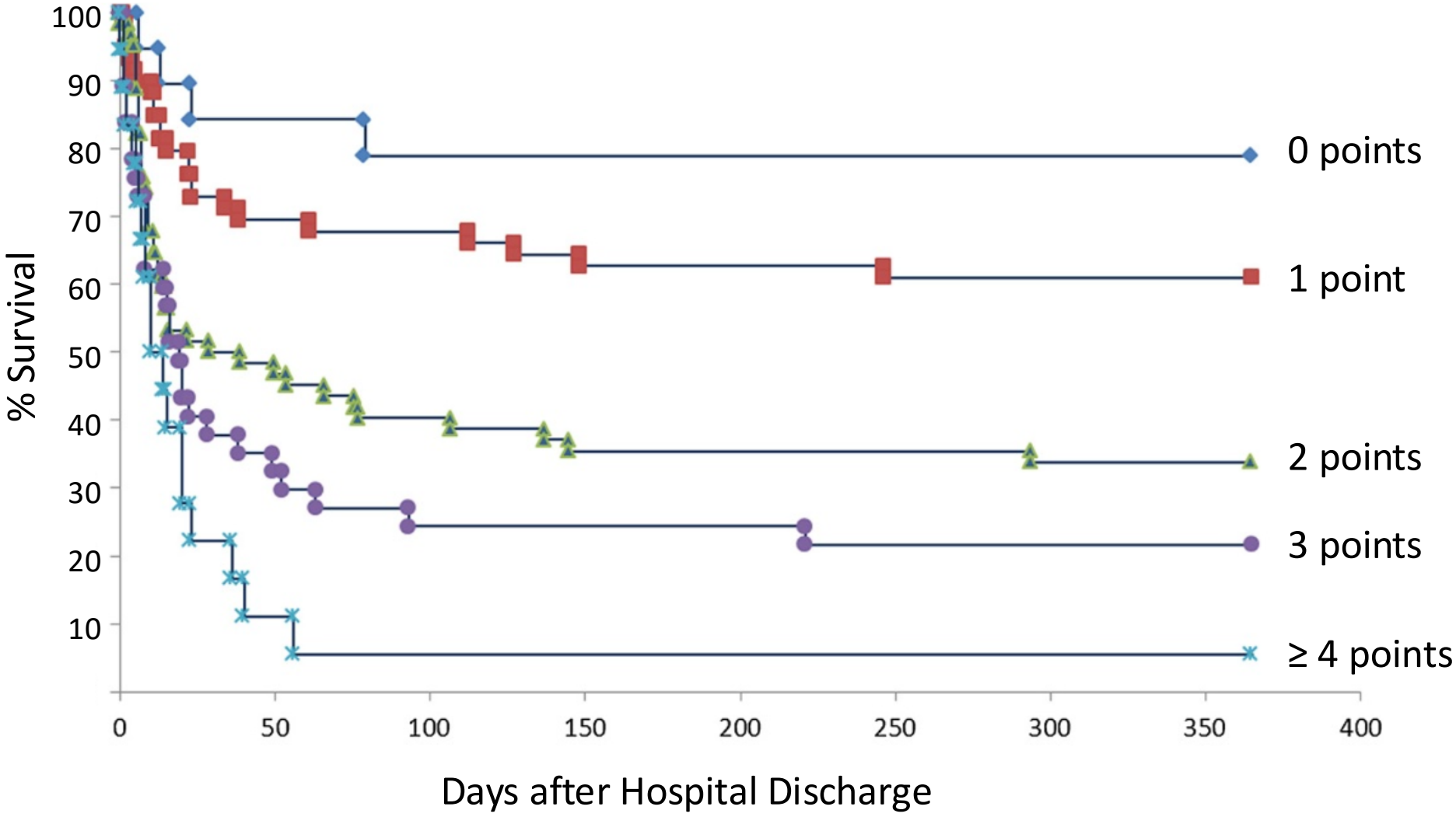
Quality of life measured by EuroQOL-5D (five-domain, preference-based tool validated among critical illness survivors / surrogates)

Offer Information to Patients & Surrogates

ProVent Score

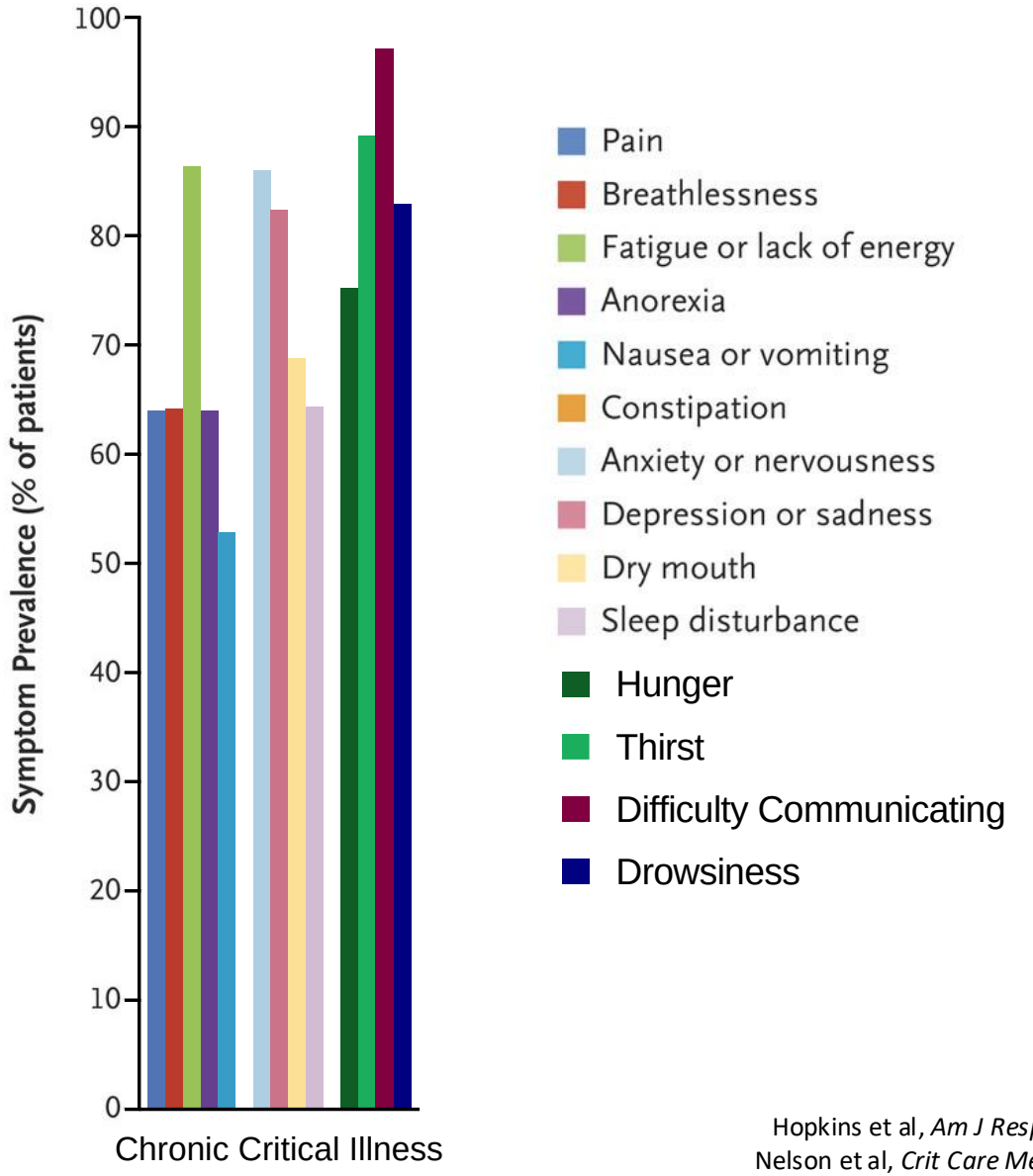
day 21 of ventilation

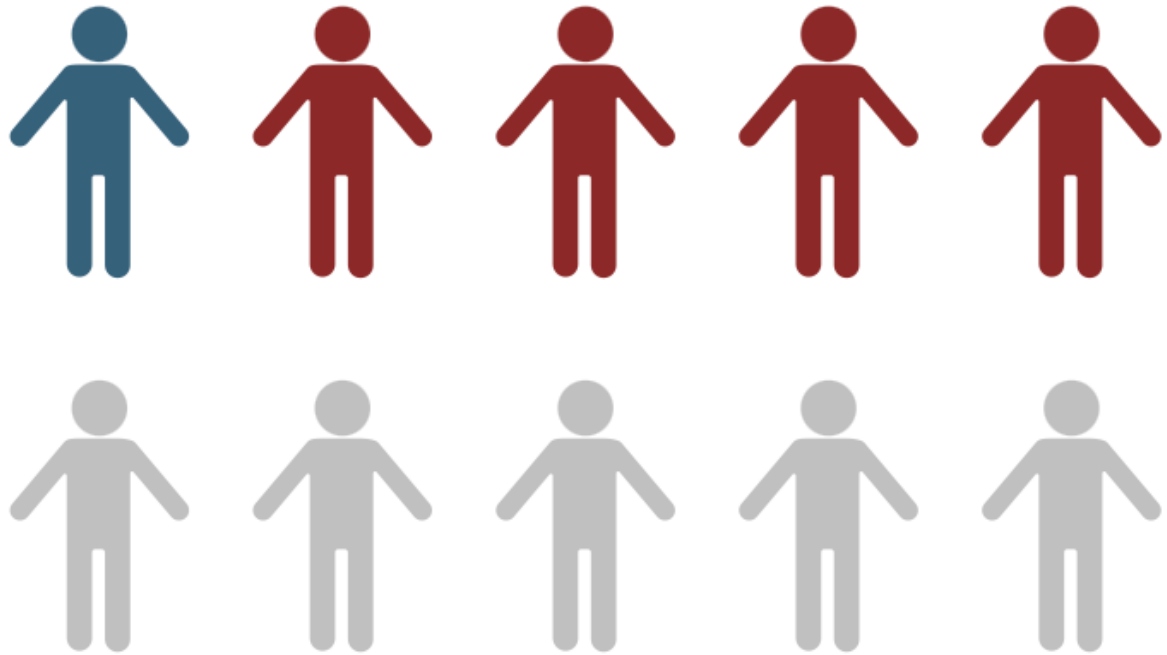
- Renal Replacement
- Vasopressors
- Age over 50
- Age over 65
- Platelets < 150k/uL



Carson et al, *Crit Care Med* 2012; Leroy et al. *Critical Care* 2014

Offer Information to Patients & Surrogates

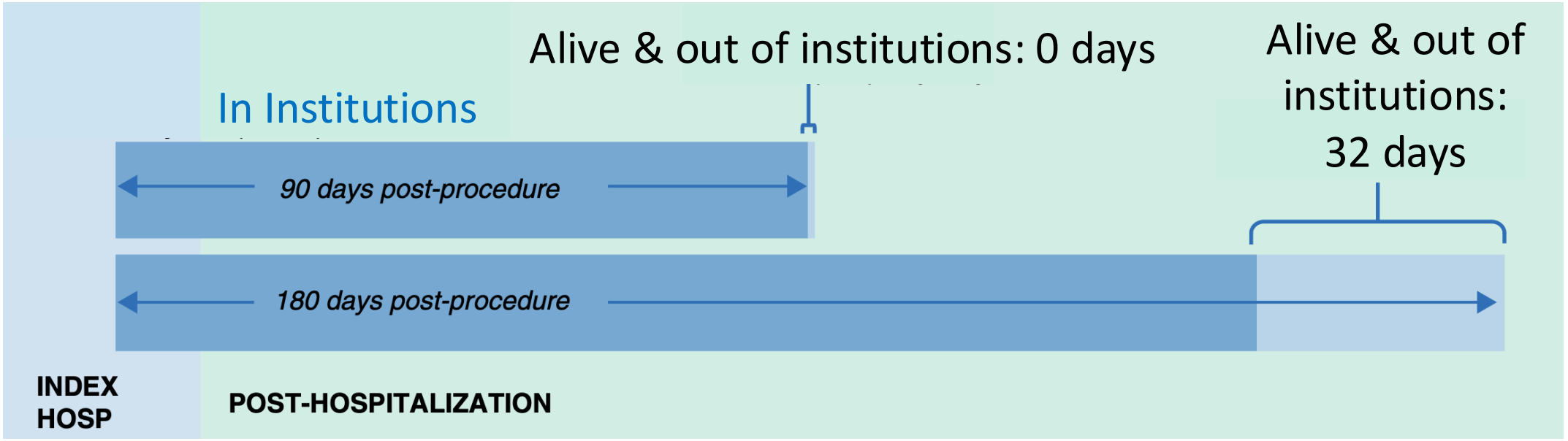




Graphical overview of collated data from
Hopkins et al, *Am J Respir Crit Care Med* 1999; Enogren et al, *Chest* 2004; Lamas, *Crit Care Med* 2017; Kelley & Morrison, *New Engl J Med* 2015; Nelson et al, *Crit Care Med* 2004 Mehta et al, *Crit Care Med* 2019; Law et al, *Ann Am Thorac Soc.* 2022; Herridge & Azoulay *New Engl J Med* 2023

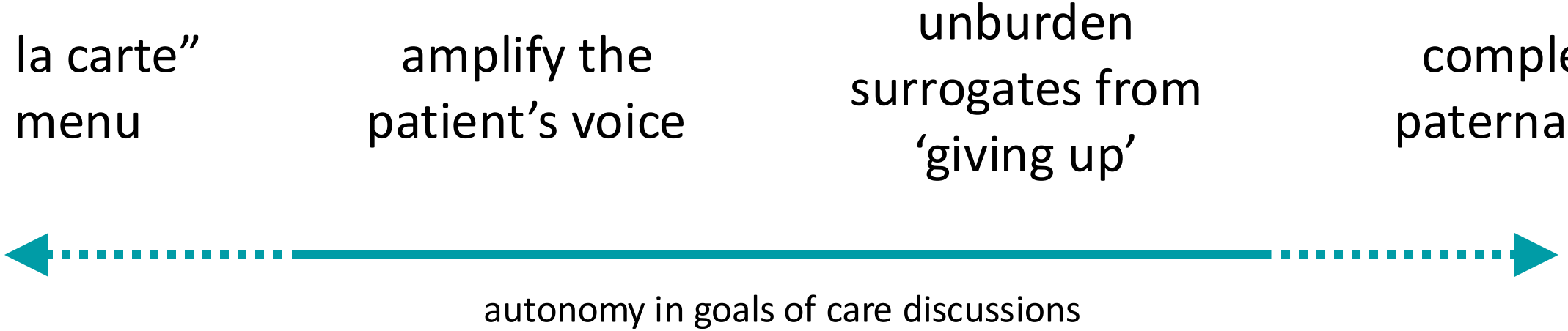
Offer Information to Patients & Surrogates: Older Patients Spend ~5 Months in Facilities after ICU

- Retrospective cohort
- 3,504 Medicare Beneficiaries
- s/p trach/PEG in ICU
- 90% of discharged patients → SNF or LTAC



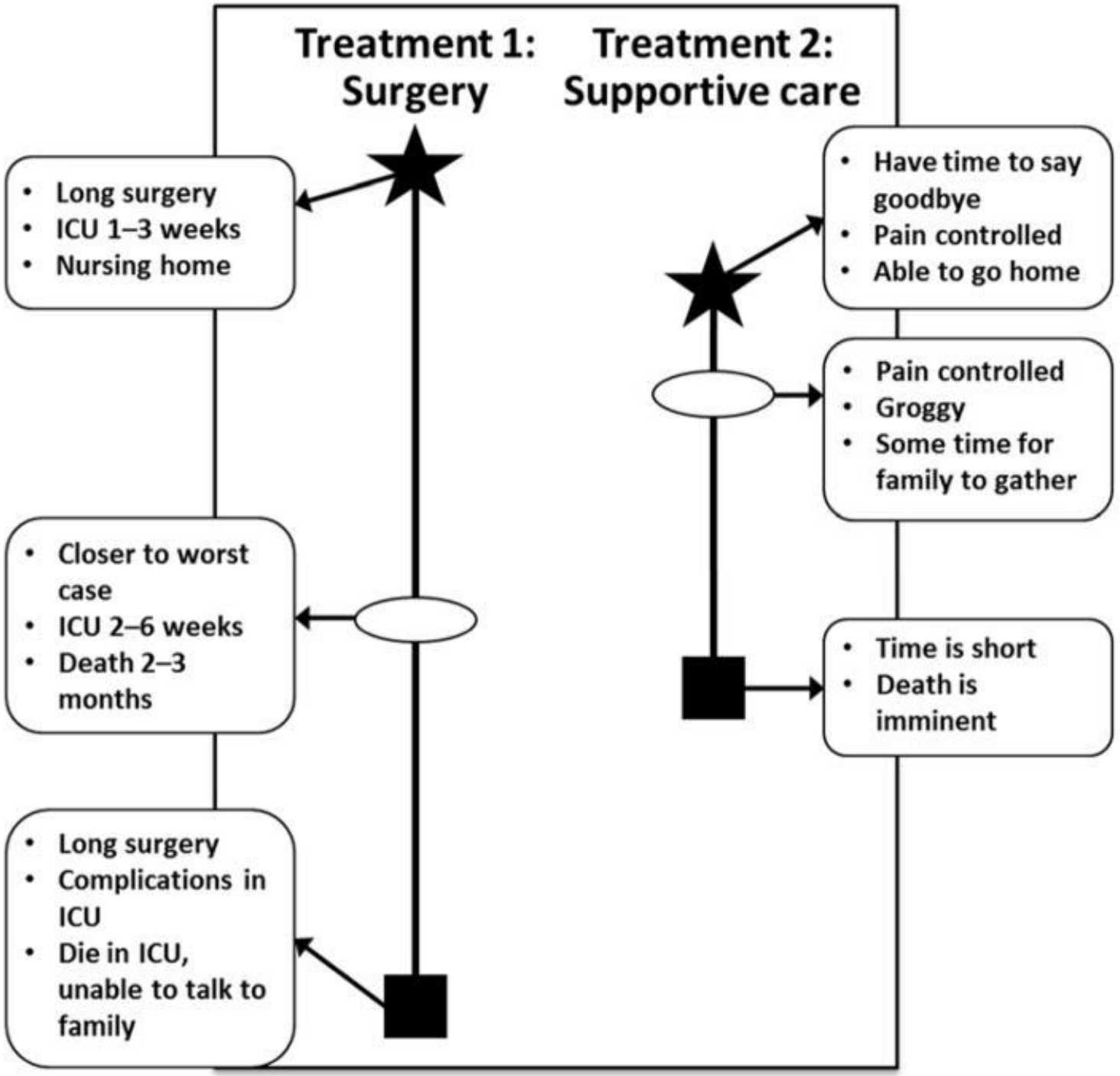
Annotated graphic from Law et al, *Annals ATS* 2022; numbers represent median values of the population

Titrate Shared Decision-Making



Amplify the Patient's Voice

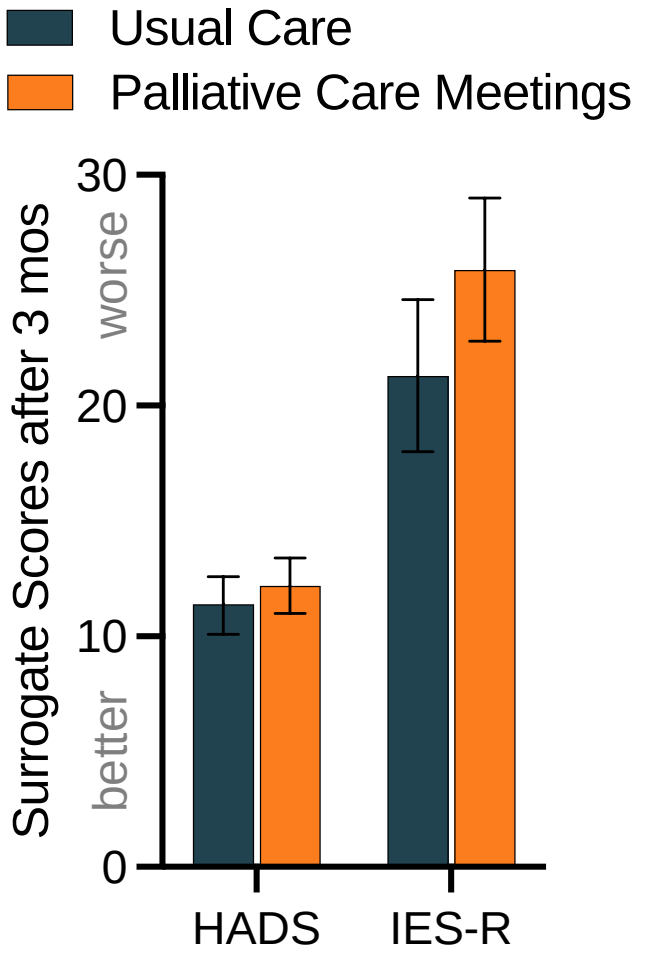
- Best case
- Worst case
- Most likely outcome

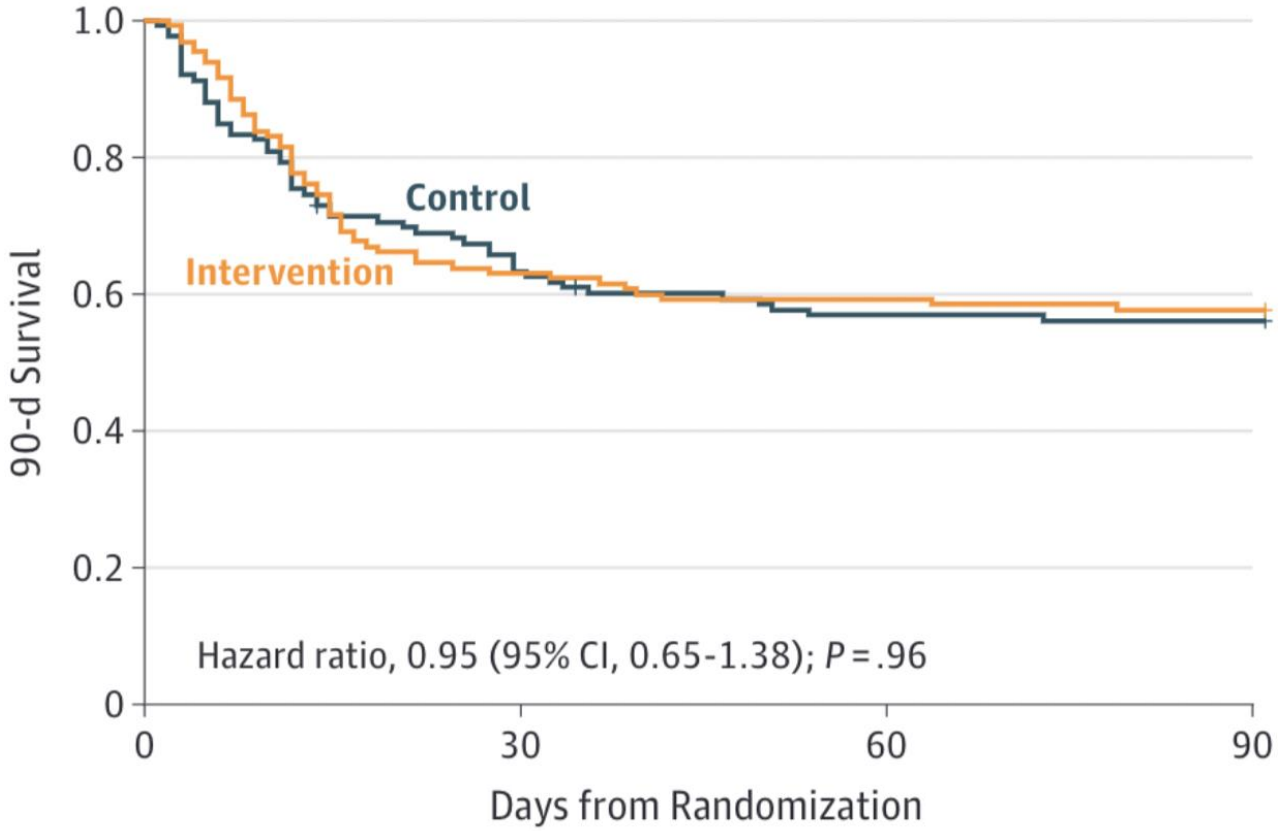


Kruser et al. *J Am Geriatr Soc*. 2015

Unburden Surrogates: ICU Decision-Making is Traumatizing

- Intervention for surrogate decision-makers for 256 patients ventilated > 7 days
- ≥ 2 family meetings by Palliative Care team (w/o ICU team) vs Usual care + brochure

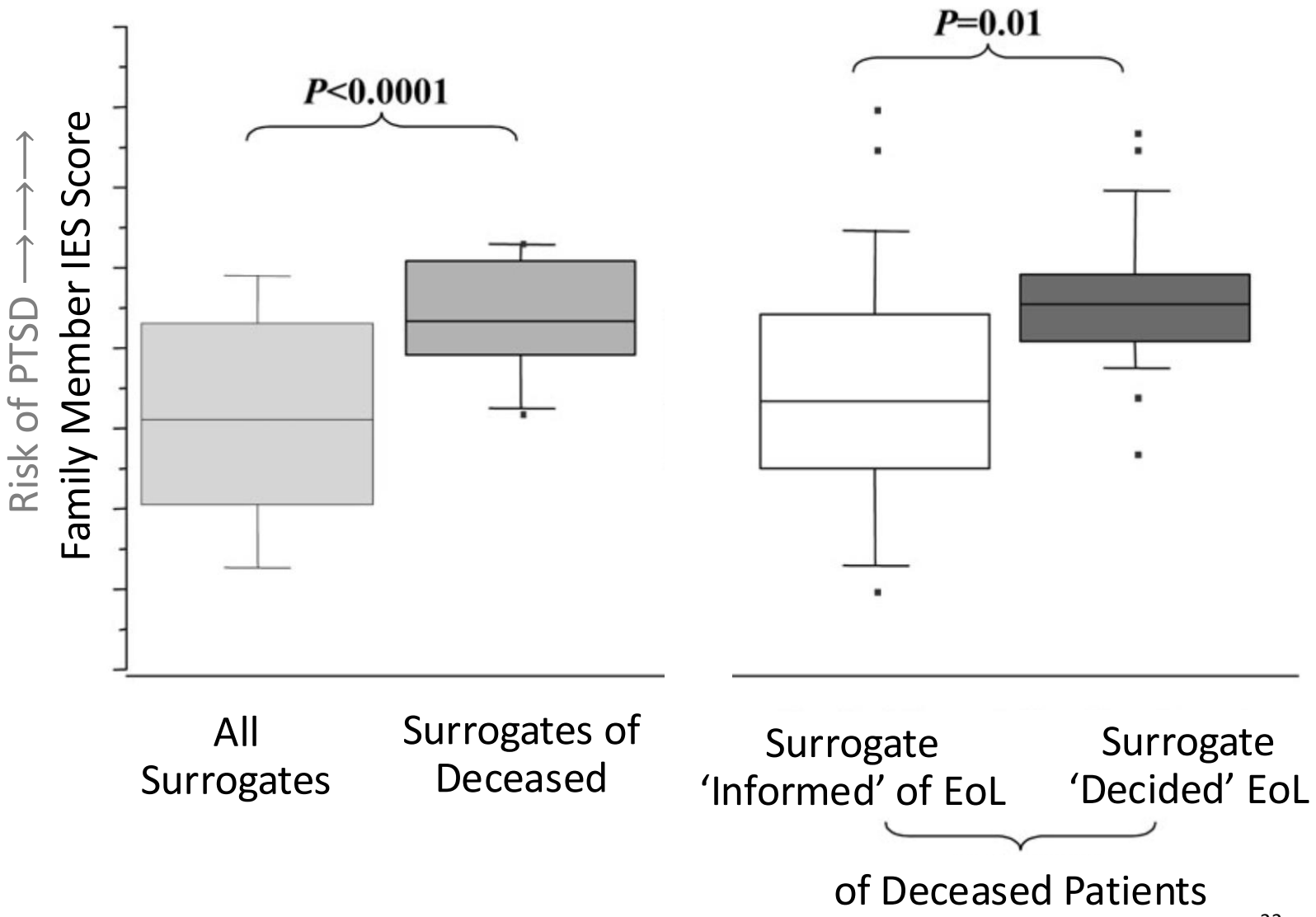




Carson et al, *JAMA* 2016; with additional graph of data therein. IES-R: Impact of Events Scale-Revised

Unburden Surrogates: ICU Decision-Making is Traumatizing

- 281 surrogates of ICU patients
- Interviewed 90 days after ICU discharge or death
- Impact of Events Scale: severity of post traumatic stress reactions
- Identified patient & surrogate risk factors for PTSD



Azoulay et al, *Am J Respir Crit Care Med* 2005. EoL = End of Life.

Unburden Surrogates

1. Open the conversation
2. Assess Understanding
3. Share hope/worry
4. Align
5. Understand goals & values
6. **Ask permission**
7. **Make a recommendation**

Open the conversation
"I'd like to talk about what is ahead with your illness. Would that be ok?"

Assess prognostic awareness
"What is your **understanding** of your illness?
"Looking to the future, what are your **hopes** about your health?" "What are your **worries**?"

Share hope and worry
"Would it be ok if we talked more about what lies ahead?"
Function: "I hear you're **hoping** for _____ **and I worry** the decline we've seen is going to continue."
Time: "I hear you're **hoping** for _____**and I worry** something serious may happen in the next few (wks/mths/yrs)."

Align
"**I wish** we didn't have to worry about this."

Explore what's important
"If your health worsens, what is most important to you?"
"How much do your family or friends know about your priorities and wishes?"

Close the conversation
"It sounds like _____ **is very important to you.**"
"Given what's important to you, **I would recommend…**"

Serious Illness Conversation Guide available from Ariadne Labs at https://www.ariadnelabs.org
Another conversation framework is available from Vital Talk at *https://www.vitaltalk.org/guides/transitionsgoals-of-care/*

Practice Question 2

An 87-year-old man is admitted to the intensive care unit with septic shock and liver failure from new biliary obstruction. A time-limited trial of fluid resuscitation, vasopressor support, and antibiotics does not improve his clinical status. He does not want further invasive interventions and his goals of care shift to focusing on comfort only. On exam, he is lethargic, unable to follow commands, continuously moving in bed and moaning. In addition to optimizing non-pharmacologic end-of-life care, you would like to start an opioid medication for pain. He has not taken opioids before.

What should you order first for this patient?

A. Fentanyl 25 mcg/min IV continuous infusion
B. Hydromorphone 1 mg/hr IV continuous infusion
C. Morphine 2 mg IV every 20 min as needed for signs of discomfort
D. Hydromorphone 2 mg IV every 3 hr as needed for signs of discomfort
E. Hydromorphone 0.3 mg IV every 20 min as needed for signs of discomfort

Beware of Active Opioid Metabolites that are Not Cleared

Legend:

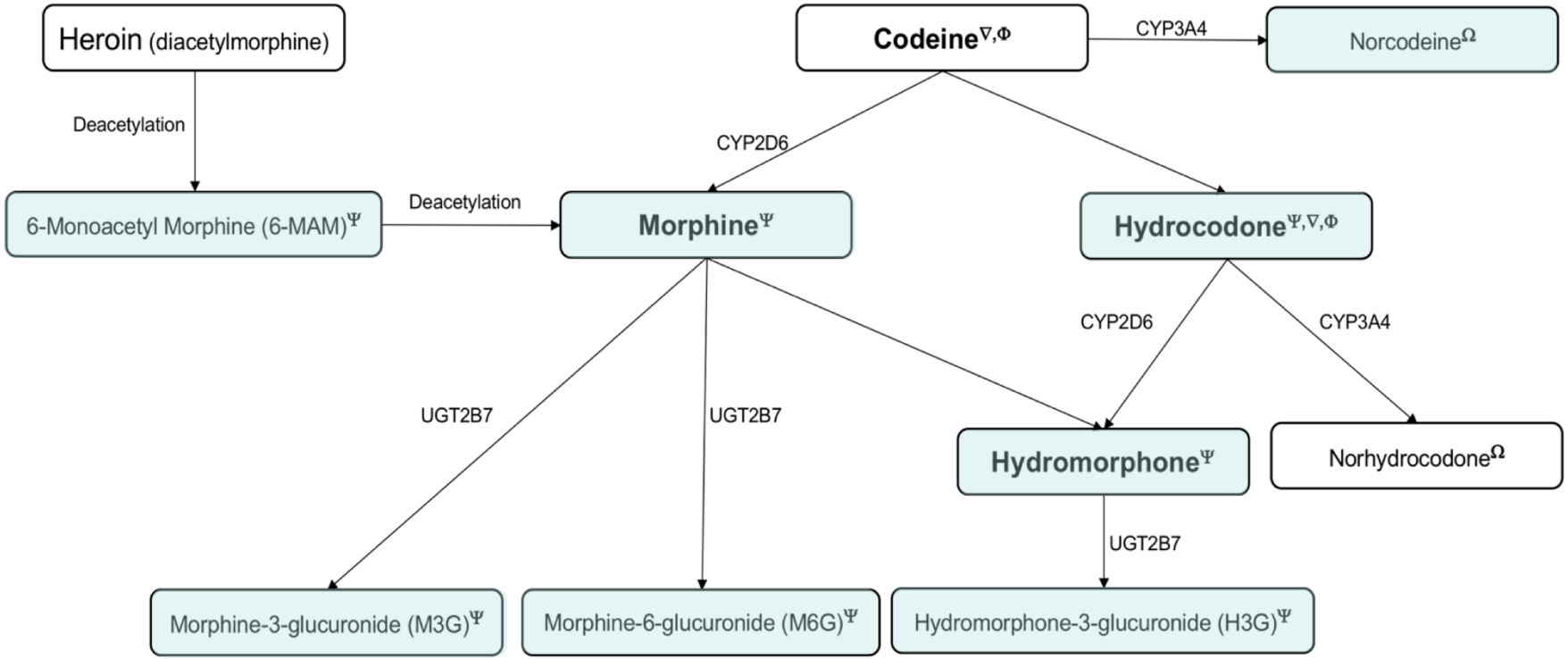
Bold = parent drug (commercially available)

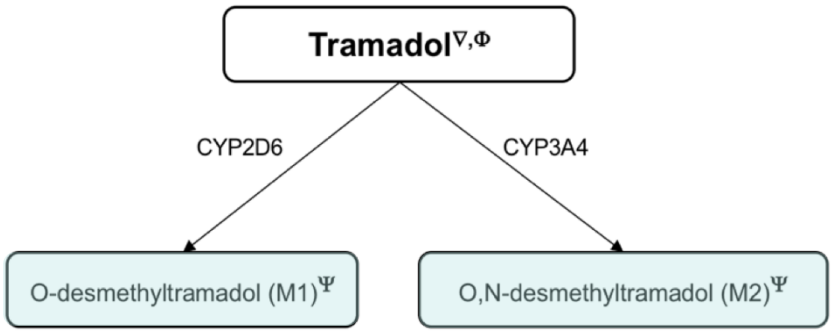
Ψ = active metabolite

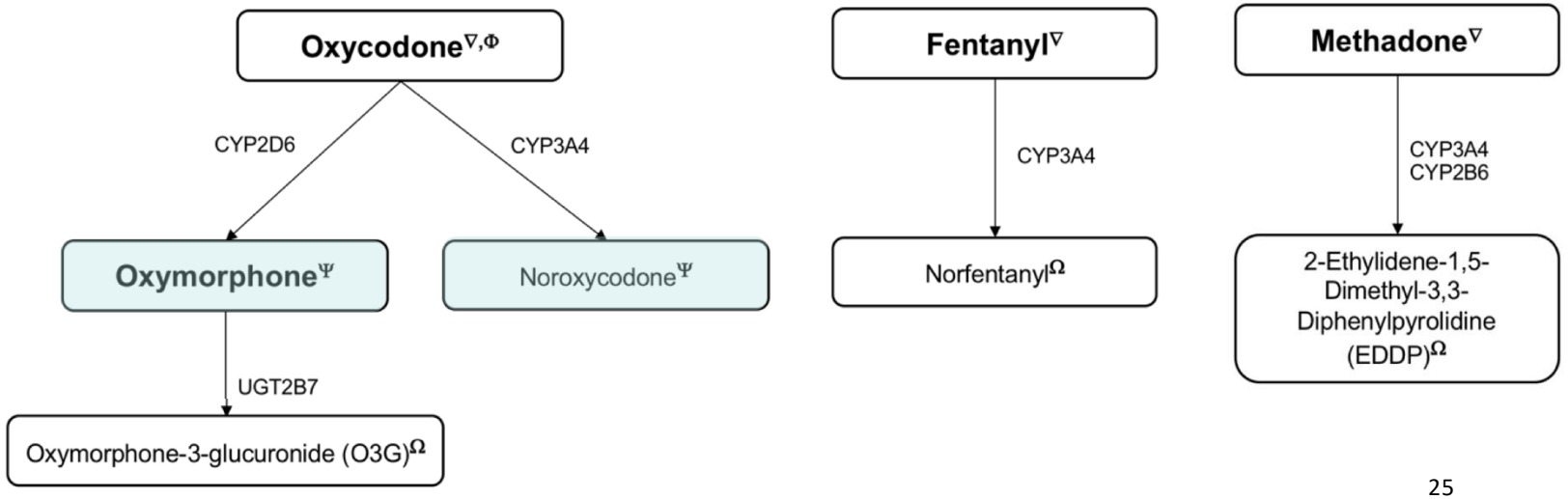
Ω = inactive metabolite

∇ = CYP3A4 drug interaction caution

Φ = CYP2D6 drug interaction caution







Adapted from "The Pink Book" : *Pain Management Tables and Guidelines*, Dana Farber Cancer Institute, 2024; https://pinkbook.dfci.org

Opioids Have Differing Safety in Liver and Renal Impairment

Liver Impairment:

Opioid Dosing in Hepatic Impairment

Agent	Degree of Hepatic Impairment			Comments
	Mild	Moderate	Severe	
Codeine	Avoid use			**Avoid Use**
Morphine	Prolong dosage interval or reduce doses, titrate slowly		Avoid use	**Avoid Use** ↑ bioavailability, ↑ T ½, ↓ clearance
OxyCODONE	Reduce dose by 25-50%, prolong dosage interval		Avoid use	**Less Safe** ↑ T ½, ↓ clearance Unpredictable serum levels
HYDROcodone	No adjustment required		Initiate at 50% dose	**Less Safe**
HYDROmorphone*	No adjustment required	Reduce dose by 25-50%	Reduce dose by 50%, prolong dosage interval	**Most Safe**
Methadone*	No adjustment required	No adjustment required	Avoid use – if needed, careful titration	**Safety considerations vary** Low 1st pass metabolism → significant absorption from GI tract ↑ T ½, ↓ clearance
Buprenorphine	TD: Start with lowest dose (5 mcg/hr) SL: No adjustment required		TD: Avoid use SL: Reduce dose by 50%	**Less Safe** Acute hepatitis has been reported with buprenorphine
FentaNYL*	TD: Reduce dose by 50% IV bolus: No dose adjustments required		TD: Use with caution IV bolus: No dose adjustments required	**Most Safe via IV bolus** **Less Safe via IV infusion** IV infusion: ↑T ½ due to lipophilicity & ↑ active drug due to decreased metabolism to inactive drug

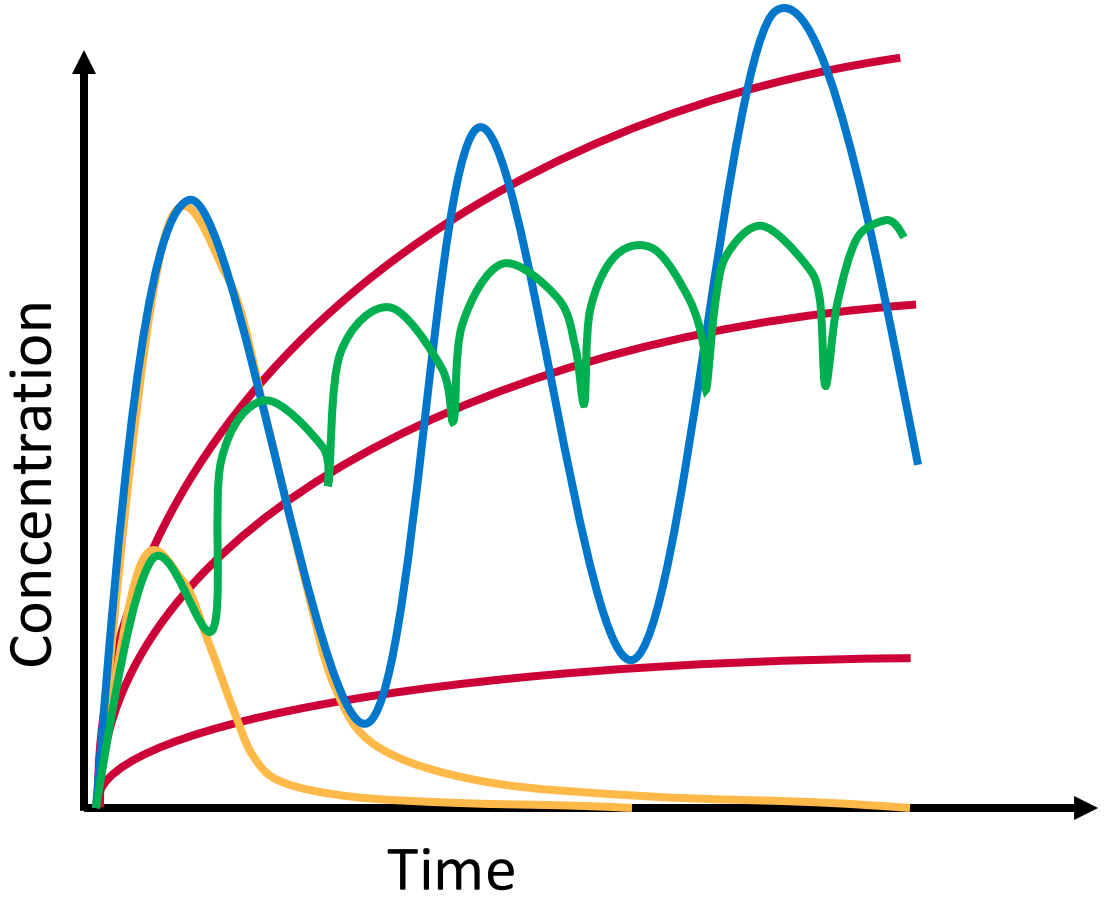
Kidney Impairment:

Opioid Dosing in Renal Impairment

Agent	Renal Impairment		Dialysis	Renal Excretion Percentage	Comments
	GFR 10 – 50 mL/min*	GFR < 10 mL/min*			
Codeine	Do not use				**Do Not Use**
Morphine	Reduce dose by 25 – 50% if used	Avoid use; reduce dose by 50 – 75% if necessary	Use cautiously Dialyzable	~ 90% Not recommended in ESRD due to accumulation of drug & metabolites	**Avoid Use** If must be used, monitor closely for side effects and neurotoxicity
HYDROmorphone	Reduce dose by 25 – 50% if used; prolong dosage interval	Reduce dose by 50% if used; prolong dosage interval	Use cautiously	Hydromorphone:75% Hydrocodone: 6.5% Inactive metabolites may accumulate in renal insufficiency	**Less Safe** IV hydromorphone is **commonly used** in renal insufficiency in clinical practice Side effects typically occur over prolonged exposure
HYDROcodone					
OxyCODONE	Reduce dose by 50% if used	Use cautiously & prolong dosing interval	Use cautiously & prolong dosing interval Partially dialyzable	75 – 85% ↓ excretion of metabolites & ↑ T ½ in uremia	**Less Safe** Insufficient evidence for safety in renal impairment
FentaNYL	May reduce dose by 25%	Reduce dose by 50%	Overall not dialyzable May be dialyzable by some filters	75 % No clinically active metabolites	**Most Safe**

"The Pink Book" : *Pain Management Tables and Guidelines*, Dana Farber Cancer Institute, 2024; https://pinkbook.dfci.org

IV Opioid Boluses Control Acute Pain Better than a Continuous Infusion



Continuous Infusions

Single Dose

Less frequent, high doses

More frequent, low doses

Figure adapted from *Applied Biopharmaceutics & Pharmacokinetics, 7e*. 2016; slide adapted with permission from Dr. Joshua Lakin

Symptom Management: Start with PRN in nearly all cases

- Pain / Agitation*
  - Mild → Acetaminophen (unless liver failure), often scheduled Q8h
  - Severe → Opioid, start with PRN based on symptoms

Once you have use data (6-12 h of 'comfort maintenance') → calculate a scheduled regimen or infusion that is ~2/3 total use

- Anxiety / Agitation* → anxiolytic (often benzodiazepines)
- Delirium / Agitation* → antipsychotic (i.e. haloperidol)
- Secretions → anti-muscarinic (i.e. glycopyrrolate, scopolamine)

* It's sometimes hard to know what is causing agitation!

Take-Home Points

- Palliative Care (specialized medical care for patients with serious illness, at any stage of illness, to improve quality of life by reducing symptoms and stress of illness) can improve outcomes

- Palliative Care communication includes:
  - Assess Understanding
  - Understand Goals & Values
  - Align Hope
  - Check our biases
  - Offer Information
  - Titrate Shared Decision-Making

- Symptom management includes careful selection of medication, route, dose, and frequency – all adjusted for the patient's organ failure(s) – and most commonly starts with frequent PRN dosing

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Additional Slides

Palliative Care as an Umbrella: The Umbrella Doesn't Cause The Rain

A Late palliative care referral

B Early palliative care referral

C. Zimmermann & J. Mathews, *JAMA Oncology* 2022; 8(5):681-682

Opioid Dosing in Renal Impairment

- The degree to which renal impairment affects analgesia, side effects, and toxicity of opioids is not well understood due to the lack of sufficient evidence.
- Glomerular filtration rate (GFR) recommendations have been provided to correlate with literature; however, creatinine clearance (CrCl) should also be assessed for dose adjustments.

Opioid Dosing in Renal Impairment

Agent	Renal Impairment		Dialysis	Renal Excretion Percentage	Comments
	GFR 10 – 50 mL/min*	GFR < 10 mL/min*			
Codeine	Do not use				**Do Not Use**
Morphine	Reduce dose by 25 – 50% if used	Avoid use; reduce dose by 50 – 75% if necessary	Use cautiously Dialyzable	~ 90% Not recommended in ESRD due to accumulation of drug & metabolites	**Avoid Use** If must be used, monitor closely for side effects and neurotoxicity
HYDROmorphone HYDROcodone	Reduce dose by 25 – 50% if used; prolong dosage interval	Reduce dose by 50% if used; prolong dosage interval	Dialyzable Use cautiously	Hydromorphone:75% Hydrocodone: 6.5% Inactive metabolites may accumulate in renal insufficiency	**Less Safe** IV hydromorphone is **commonly used** in renal insufficiency in clinical practice Side effects typically occur over prolonged exposure
OxyCODONE	Reduce dose by 50% if used	Use cautiously & prolong dosing interval	Use cautiously & prolong dosing interval Partially dialyzable	75 – 85% ↓ excretion of metabolites & ↑ T ½ in uremia	**Less Safe** Insufficient evidence for safety in renal impairment
FentaNYL	May reduce dose by 25%	Reduce dose by 50%	Overall not dialyzable May be dialyzable by some filters	75 % No clinically active metabolites	**Most Safe**
Meperidine	Do not use (see page 6)				**Do Not Use**
Methadone	Dose reduction may be required alongside clinical assessment.		Not dialyzable	21% as unmetabolized No clinically active metabolites	**Safety considerations vary** Methadone is commonly used in renal insufficiency in clinical practice
Buprenorphine	Insufficient evidence for recommendations in renal insufficiency		Not dialyzable	27 – 30%	**Less Safe** Eliminated through the biliary system
Tapentadol	No dose adjustment	Do not use	Partially dialyzable		**Less Safe**
TraMADol	Reduce initial dose; prolong dosage interval to Q12H; max 200 mg/day	Do not use in GFR < 30 mL/min	7% of drug and active metabolite removed by dialysis	90% (30% as unmetabolized) ↑ T ½ in renal insufficiency	**Less Safe** Do not use long-acting tramadol Risk for seizures high with ↑↑ uremia & drugs that ↓ seizure threshold

*Glomerular filtration rate (GFR) recommendation interpretation should be coupled with evaluating the degree and duration of renal dysfunction, such as AKI, CKD, vs. acute on chronic CKD.

Opioid Dosing in Hepatic Impairment

Agent	Degree of Hepatic Impairment			Comments
	Mild	Moderate	Severe	
Codeine	Avoid use			**Avoid Use**
Morphine	Prolong dosage interval or reduce doses, titrate slowly		Avoid use	**Avoid Use** ↑ bioavailability, ↑ T ½, ↓ clearance
OxyCODONE	Reduce dose by 25-50%, prolong dosage interval		Avoid use	**Less Safe** ↑ T ½, ↓ clearance Unpredictable serum levels
HYDROcodone	No adjustment required		Initiate at 50% dose	**Less Safe**
HYDROmorphone*	No adjustment required	Reduce dose by 25-50%	Reduce dose by 50%, prolong dosage interval	**Most Safe**
Methadone*	No adjustment required	No adjustment required	Avoid use – if needed, careful titration	**Safety considerations vary** Low 1st pass metabolism → significant absorption from GI tract ↑ T ½, ↓ clearance
Buprenorphine	TD: Start with lowest dose (5 mcg/hr) SL: No adjustment required		TD: Avoid use SL: Reduce dose by 50%	**Less Safe** Acute hepatitis has been reported with buprenorphine
FentaNYL*	TD: Reduce dose by 50% IV bolus: No dose adjustments required		TD: Use with caution IV bolus: No dose adjustments required	**Most Safe via IV bolus** **Less Safe via IV infusion** IV infusion: ↑T ½ due to lipophilicity & ↑ active drug due to decreased metabolism to inactive drug
Meperidine*	Do not use (see page #6)			**Do Not Use**
Tapentadol	No adjustment required	Reduce doses	Avoid use	**Less Safe** Extensive 1st pass metabolism (32% bioavailability)
TraMADol	Prolong dosage interval to Q12H		Avoid long-acting tramadol	**Less Safe** 3.2-fold ↑ AUC, 2.6-fold ↑ T ½

* Heavily protein bound (>70%); serum levels may be increased in low albumin states.