



# Letting go of non-beneficial treatments: show me the evidence

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# Objectives

- Identify non-beneficial or equivocal palliative care treatments that are in common use
  - Describe the evidence, strengths, limitations and gaps for select palliative care treatments
- 



# Case study #1

- ▶ Thomas is in the advanced stage of un-resectable, metastatic colon cancer
  - ▶ Hospice home care
  - ▶ Partial bowel obstruction
  - ▶ Venting PEG
    - ▶ Diet and fluids ad lib for oral gratification
    - ▶ Appetite is poor, cachectic
  - ▶ Ascites, peripheral edema in legs
  - ▶ Palliative Performance Scale = 40
    - ▶ Mean survival = 40 days, median = 19 days
  - ▶ Daughter's wedding is in 6 weeks (42 days)
  - ▶ Family requests IV hydration to extend survival
    - ▶ Patient still has his port



# Clinical Considerations

- ▶ Is the family expectation realistic?
- ▶ Family training
- ▶ Home infusion team referral
- ▶ Frequent home visits to evaluate for worsening ascites, edema
- ▶ Expense exceeds hospice benefit
  - ▶ Disenrollment
  - ▶ Family out of pocket



# Reasons patient's families favor IV hydration

- Misconceptions about the value vs. burden
- Symbolism
- Doing something
- Low level of acceptance of patient's prognosis
- Religion or cultural beliefs



## Reasons nurse and/or physician providers favor IV hydration

- Inexperience with care at the end of life
- View hydration as part of routine care
- Minimum standard of care
- Acceding to patient/family preferences may be easier than explaining reasons to avoid hydration
- Religion and cultural factors



# Select religion and/or cultural beliefs (del Rio et al., Pscho-oncology, 2012)

- ▶ Hindu regard reduced consumption as a voluntary act and a sign of imminent death producing a self-controlled and dignified process
- ▶ In Buddhism, when a person dies hungry the soul becomes restless and hungry
  - ▶ Taiwanese nurses favor the use of artificial hydration
- ▶ In Judaism, human life has a positive value
  - ▶ Israeli physicians value the administration of IV hydration



# Postulated benefits for IV hydration

- Reduce symptoms of dehydration
    - Fatigue
    - Myoclonus
    - Sedation
    - Hallucinations
  - Reduce or prevent delirium
  - Reduce thirst
  - Reduce nausea
  - Improve patient-reported Quality of Life
  - Extend survival
- 



# Postulated burdens

- ▶ Increased fluid retention and worsening of
    - ▶ Airway secretions
    - ▶ Pleural effusion
    - ▶ Ascites
    - ▶ Dependent edema
  - ▶ IV therapy can be painful and intrusive
  - ▶ Maintains urine output and caregiver burden from patient incontinence
  - ▶ Extended dying
  - ▶ Cost
- 

# Evidence

- ▶ Prospective Observation (Morita et al., Ann Onc, 2005)
  - ▶ 226 patients with abdominal malignancies, 1-3 weeks before death
    - ▶ Hydration group, n = 59, 1 or more liters/day
    - ▶ No hydration, n = 167
  - ▶ Measures
    - ▶ Membranous hydration
    - ▶ Fluid retention (pleural effusion, edema, ascites)
    - ▶ Bronchial secretions
    - ▶ Agitated delirium
    - ▶ Myoclonus
  - ▶ Major results hydration vs. no hydration
    - ▶ Improvement in membranous hydration signs in hydration group
    - ▶ Worsening of fluid retention in hydration
    - ▶ No differences in bronchial secretions, delirium, or myoclonus



# Evidence (equivocal findings)

- ▶ Cochrane Review (Good et al., 2008, 2011)
  - ▶ Systematic review of relevant randomized controlled trials or prospective controlled studies of medically assisted hydration in palliative care patients
  - ▶ Five studies
    - ▶ 2 RCTs, n = 93
    - ▶ 3 CTs, n = 360
    - ▶ Meta-analysis not possible due to heterogeneity and small numbers
  - ▶ Insufficient good quality studies to inform practice
  - ▶ One ongoing high quality study is pending full enrollment (see next slide)

# Evidence

- ▶ Double-blinded, placebo-controlled, randomized trial (Bruera et al. J Clin Onc, 2013)
  - ▶ 102 hospice patients with cancer with life expectancy  $\geq$  1 week randomized to 2 groups
    - ▶ Normal saline at 1 liter/day infused over 4 hours (n=49)
    - ▶ Placebo – normal saline at 100cc/day infused over 4 hours (n=53)
  - ▶ Measures
    - ▶ Dehydration symptoms (fatigue, myoclonus, sedation, hallucinations)
    - ▶ Delirium
    - ▶ Survival
  - ▶ No differences between groups, hydration did not improve symptoms, quality of life or survival compared to placebo
  - ▶ Study did not achieve planned sample size



# Evidence summary IV hydration in advanced cancer

- Largely non-beneficial in patients who are close to death (1-2 weeks)
- May improve select outcomes in patients with a better performance status, bowel obstruction, and estimated survival of several months

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## Development of a National Clinical Guideline for Artificial Hydration Therapy for Terminally Ill Patients with Cancer

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# Guidelines regarding select patient outcomes

(Morita et al., J Pall Med, 2007)

- Ascites - no benefit, worsens symptom
- Nausea – benefit if etiology is bowel obstruction
- Thirst – mouth care is more effective than hydration
- Pleural effusion – worsens symptom
- Bronchial secretions – worsens if volume  $\geq 1500\text{cc/day}$
- Delirium – equivocal, multi-factorial etiologies
- Fatigue – benefit if survival of several months
- Peripheral edema – worsens with  $>1000\text{cc/day}$



# Summary

- A very small, largely under-powered body of evidence exists to inform practice
- Patient-family values may be based on lack of knowledge, inexperience, and/or religion and culture
- IV hydration may be of value to reduce symptoms of dehydration when the patient has bowel obstruction and months to live
- IV hydration may worsen volume overload in patients in the last 1-2 weeks
- Case-by-case decision-making is indicated in the absence of a strong evidence base

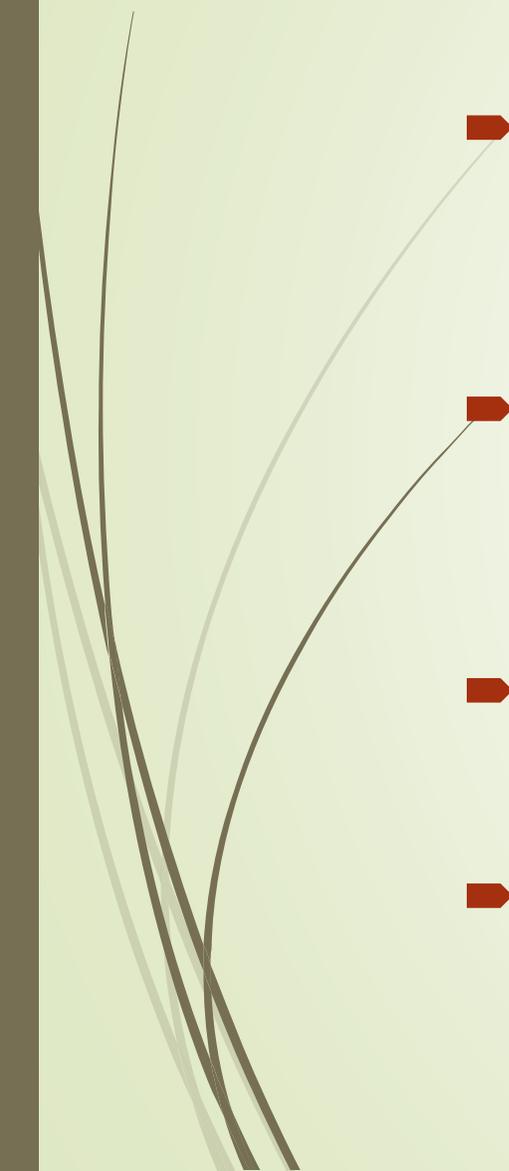


## Case study #2

- ▶ Melissa is near death following bilateral ischemic stroke. On patient rounds you note noisy upper airway sounds (death rattle). Sounds are audible at the foot of the bed. Melissa is not conscious and has no signs of distress.
  - ▶ Her family have been visiting round the clock and ask you about the noisy breathing.
- 



# Death rattle

- Naturally occurring upper airway sound from retained pharyngeal secretions
  - Patients near death become drowsy and/or unconscious and unable to clear secretions
  - Small volumes resonate in airway generating noise
  - Noise intensity varies
- 



# Death rattle prevalence

- 44% of inpatient palliative care unit patients (Heisler, et al. J Pain Symptom Manage, 2013)
  - 45% of inpatient palliative care/hospice patients (Campbell, et al. J Pall Med, 2013)
- 

# Distress

- Bereaved relatives – semi-structured interviews (Wee, et al., Palliative Med, 2006)
  - n = 27; 12 had experienced death rattle
  - 50% were distressed by the sound
    - *“It was soul-destroying to see her there....she was lying there in a sort of daze but all she was doing was like this horrible noise from her mouth”*
  - 50% were neutral or found it a helpful signal of impending death
    - *“I wasn’t distressed by it. I had heard that people who were near the end did breathe a bit oddly”*



# Distress

- ▶ Hospice staff and volunteers – focus group (Wee, et al., Palliative Med, 2008)
  - ▶ Seven meetings with 41 total participants (nursing, medical, chaplaincy, housekeeping, and volunteers)
  - ▶ Some were matter-of-fact
    - ▶ *“I think it’s kind of a natural progression... deep down they’re quite comfortable, aren’t they?”*
  - ▶ Most reported negative responses
    - ▶ *“I can’t imagine that if that was present at death, you won’t continue to hear that because it’s such a horrible noise....I think I would because it’s so horrible”*



# Distress

- ▶ Patients – prospective observation (Campbell, et al., J Pall Med, 2013)
  - ▶ 71 patients who were near death
    - ▶ Karmanos inpatient hospice
    - ▶ VAMC inpatient hospice
    - ▶ DRH inpatient palliative care
  - ▶ Measures
    - ▶ Death rattle intensity
    - ▶ Respiratory Distress Observation Scale

# Results

Variable	No death rattle	Death rattle	p
	n = 39	n = 32	
Age, mean (S.D.)	69.7 (17.4)	71.4 (12.6)	NS
Gender	22 men 17 women	19 men 13 women	NS
Ethnicity	11 Caucasian 28 African-American	10 Caucasian 22 African-American	NS
Diagnoses	Cancer 16 Unconscious 4 Dementia 5 Pulmonary 4 Cardiac 3 Other 7	Cancer 12 Unconscious 8 Dementia 3 Pulmonary 2 Cardiac 2 Other 5	NS
DRIS, mean (S.D.)	0 (0)	1.8 (.82)	<.01
RDOS, mean (S.D.)	2.8 (2.1)	3.5 (1.9)	NS



# Treatment

- Cochrane review: Interventions for noisy breathing in patients near to death (Wee et al., 2012)
- Selection criteria
  - Randomized controlled trials
  - Controlled before-after studies
  - Interventions – atropine, hyoscine, glycopyrrolate
- Results – n = 4 studies
  - No evidence that any intervention is superior to placebo



# Medication alternatives

- ▶ Side-lying positioning
- ▶ No treatment
  - ▶ Advise listeners about “naturalness” of the sounds
  - ▶ Advise listeners about “no patient distress”
  - ▶ Advise listeners about limited/no medication benefit
    - ▶ Medications have adverse effects but patient cannot report them
  - ▶ Consider that medicating patient to soothe family (or staff) is ethically problematic

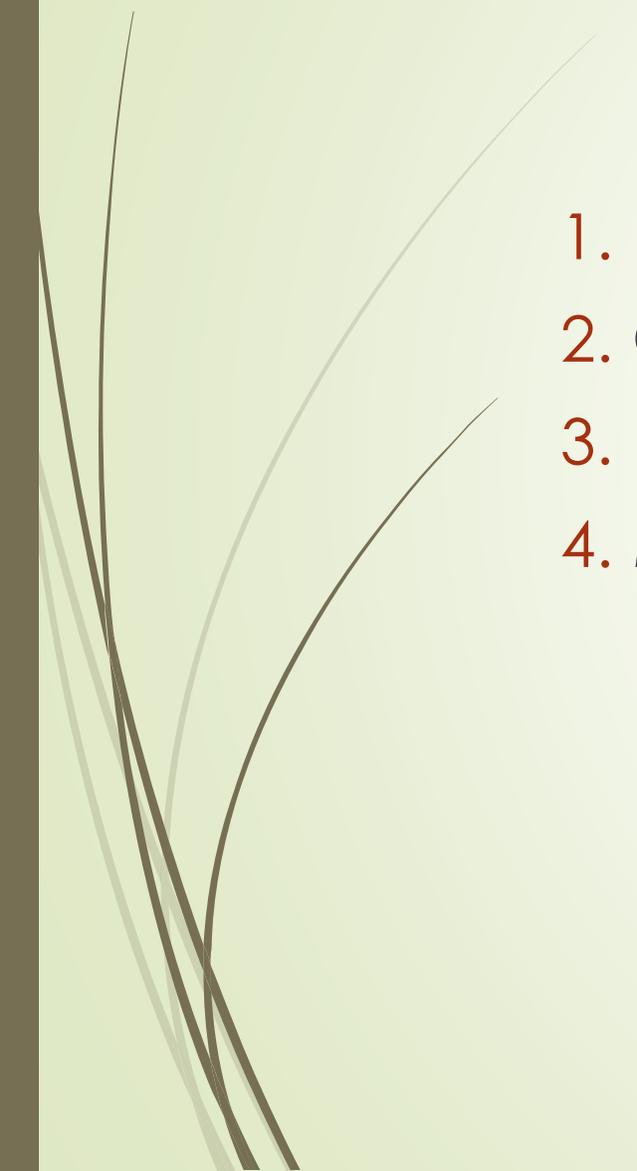


# Case study #3

- ▶ Howard is dying from advanced COPD and lung cancer. He is hypersomnolent, rouses briefly to touch, breathing 12-14 breaths/minute, with no signs of respiratory distress. He uses oxygen by nasal cannula at 3 l/min. He can no longer use his metered-dose inhalers. He can no longer swallow.
- ▶ On home visit his wife reports no recent use of prn morphine and nothing to eat or drink. You conclude that death is imminent is comfortable.
- ▶ His wife asks if the oxygen can be discontinued?



# How will you respond?

1. Discontinue the oxygen
  2. Continue the oxygen
  3. Decrease the oxygen flow rate
  4. Measure the peripheral oxygen saturation
- 



# Your response is based on

1. Experience
  2. Evidence
  3. Institutional policy
  4. Finance
- 



# Oxygen benefits

- Correct hypoxemia
  - Reduce dyspnea
  - Prolong life
- 



# Oxygen burdens

- Decreased mobility
- Nasal drying
  - Nosebleed
- Feeling of suffocation
- Prolongs dying
  - Extends caregiver days
  - Increases health care costs
- Flammability risks around open flame



# Oxygen therapy for dyspnea in adults

- ▶ Cochrane review (Cranston et al., 2009)
  - ▶ Eight RCTs with 144 participants
    - ▶ Cancer n = 97
    - ▶ Heart failure n = 35
    - ▶ Kyphoscoliosis n = 12
  - ▶ No consistent beneficial effect of oxygen inhalation over air inhalation



Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnea: a double-blind, randomized controlled trial (Abernethy et al., 2010)

- 239 terminally ill patients with refractory dyspnea,  $\text{PaO}_2 > 55$  mm Hg
- Random assignment to oxygen or air via nasal cannula for 7 days for at least 15 hours/day
- Dyspnea by NRS (0-10) morning and evening
- Oxygen provided no additional symptomatic benefit in non-hypoxemic, dyspneic patients



# Symptomatic oxygen for non-hypoxemic COPD

- ▶ Cochrane review (Uronis, et al., 2011)
- ▶ RCTs comparing oxygen to air in mildly or non-hypoxemic patients with COPD
  - ▶ 28 studies with 702 patients
- ▶ Slight improvement in dyspnea with oxygen



# Oxygen is non-beneficial for most patients who are near death (Campbell, et al., 2013)

- ▶ Repeated measures, double – blinded, randomized cross-over, using the patient as his/her own control
- ▶ 32 inpatient palliative care patients and inpatient hospice patients near death with one or more of COPD, heart failure, lung cancer or pneumonia; comfortable at baseline
- ▶ Random application of oxygen, medical air, or no flow via nasal cannula every 10 minutes with respiratory distress measurement
  - ▶ 27 (84%) had oxygen flowing at baseline
- ▶ 91% patients experienced no distress during the protocol
- ▶ No differences in patient comfort were seen across gas and flow conditions ( $F = 0.55$ ,  $p = 0.74$ )
- ▶ 3 patients were restored to baseline oxygen



# Conclusions

- Declining oxygen saturation is naturally occurring and expected
  - Declining oxygen saturation may predict but does not signify respiratory distress
  - The routine application of oxygen to most patients who are near death is not supported
  - An n of 1 trial of oxygen is appropriate in the face of respiratory distress
- 