

Discontinuing Medications at End of Life

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Objectives

- Identify characteristics that would enable medications to be discontinued in patients at end of life
 - Utilizing the medical literature
- Identify common medications and their characteristics that allows them to be discontinued
- Describe strategies for discontinuing the identified medications

Discontinuing Medication at End of Life

- Evaluating a model for appropriate prescribing for patients late in life

Holly M. Holmes, Reconsidering Medication Appropriateness for Patients Late in Life. ARCH INTERN MED. 2006; VOL 166, MAR 27; 605-609.

Discontinuing Medication at End of Life

- The Medication Appropriateness Index
 1. Is there an indication for the drug?
 2. Is the medication effective for the condition?
 3. Is the dosage correct?
 4. Are the directions correct?
 5. Are the directions practical?
 6. Are there clinically significant drug-drug interactions?
 7. Are there clinically significant drug-disease/condition interactions?
 8. Is there unnecessary duplication with other drugs?
 9. Is the duration of therapy acceptable?
 10. Is this drug the least expensive alternative compared with others of equal usefulness?

Holly M. Holmes, Reconsidering Medication Appropriateness for Patients Late in Life. ARCH INTERN MED. 2006; VOL 166, MAR 27; 605-609.

Discontinuing Medication at End of Life

- Prioritize based on the following information:
 - REMAINING LIFE EXPECTANCY
 - TIME UNTIL BENEFIT
 - GOALS OF CARE
 - TREATMENT TARGETS

Holly M. Holmes, Reconsidering Medication Appropriateness for Patients Late in Life. ARCH INTERN MED. 2006; VOL 166, MAR 27; 605-609.

Medication Appropriateness Cross-Walk

Holly M. Holmes, Reconsidering Medication Appropriateness for Patients Late in Life. ARCH INTERN MED. 2006; VOL 166, MAR 27; 605-609.

Example

- Case 1- From Journal Article
 - A 75-year-old woman with hypertension and osteoarthritis diagnosed as having type 2 diabetes mellitus. She is functionally independent. LE: ~17 years
 - Laboratory test results were as follows:
 - LDL: 143 mg/dL; creatinine: 1 mg/dL; Hemoglobin A1C 8.7%
 - Currently prescribed medications include
 - Lasix, Atorvastatin, Calcium, Lisinopril, and Aspirin, Plavix, Metoprolol, Spironolactone, Actonel

Example

- What do we know about medication therapies and regimens patients are on?
- Did you know that.....
 - Treatment of hyperglycemia and hypertension with a sulfonylurea and an angiotensin converting enzyme inhibitor may show benefit on average after about 10 years, which is when about 25% of patients with type 2 diabetes mellitus develop proteinuria and/or significant renal damage.
 - Treatment with a statin could reduce her risk for vascular events after about 2 years of treatment and significantly reduce cardiovascular events at 5 years.
 - Use of aspirin for primary prevention could reduce her risk of myocardial infarction at 5 years

Holly M. Holmes, Reconsidering Medication Appropriateness for Patients Late in Life. ARCH INTERN MED. 2006; VOL 166, MAR 27; 605-609.

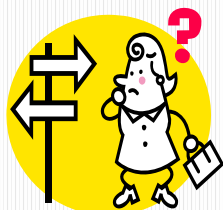
Example

- Case 2- From Journal Article
 - A 75-year-old woman with End stage CHF and osteoarthritis diagnosed as having type 2 diabetes mellitus. She is functionally independent. LE: ~<6 months
 - Laboratory test results were as follows:
 - LDL: 143 mg/dL; creatinine: 1 mg/dL; Hemoglobin A1C 8.7%
 - Currently prescribed medications include
 - Lasix, Atorvastatin, Calcium, Lisinopril, and Aspirin, Plavix, Metoprolol, Spironolactone, Actonel

Discontinuing Medication at End of Life

- Prioritize Case 2 based on the following information:
 - REMAINING LIFE EXPECTANCY
 - _____
 - TIME UNTIL BENEFIT
 - _____
 - GOALS OF CARE
 - _____
 - TREATMENT TARGETS
 - _____

So lets look at some examples!



Cardiovascular



- Cholesterol Lowering Agent
 - Burden
 - Potential side effects

Silveira, Maria J et al. Statins in the Last Six Months of Life: A Recognizable, Life-Limiting Condition Does Not Decrease their Use. Journal of Palliative Medicine 2008; Vol 11, Issue 5; 685-693.

Cardiovascular-Statins

- Reduce 5 major cardiovascular incidence per 100 patients treated for 5 yrs
- Reduce 5 yr mortality by 20 % in patient who have taken statins for atleast 1-2 years
- 1 stroke prevented for every 100 patients treated for 5 years

Vollrath Annette, et al. Discontinuing Cardiovascular Medications at the End of Life: Lipid-Lowering Agents JOURNAL OF PALLIATIVE MEDICINE 2005; Vol 8, Issue 4; 876-881.

Heart Failure



- Medications slow, block, or reverse cardiac remodeling, inotropes, reduce fluid overload, preload and afterload
- Beta blockers
- ACEI, ARB's
- Diuretics, aldosterone antagonists
- Hydralazine/nitrates
- Digoxin, amiodarone

Mary Lynn McPherson, Palliative and Appropriate Medication Use in End Stage Heart Failure, May 9 2007, Medscape

Heart Failure

- Digoxin toxicity
- Symptomatic hypotension: reduce dose of:
 - ACE inhibitor (or ARB)
 - beta-adrenergic blocker. (must taper depending on dose)
- Renal function deteriorates
 - discontinue ACE inhibitor (or ARB).
- ACEI or beta blockers
- CCB's

Mary Lynn McPherson, Palliative and Appropriate Medication Use in End Stage Heart Failure, May 9 2007, Medscape

Heart Failure

- M.L. 98 yr, F, EF 10-15%
- She complains of severe dyspnea and poor quality of life and wants to discontinue all medications. Serum Creatinine 2.2 mg/dl
- Aspirin 81 mg qd
- Simvastatin 20 mg qd
- Carvedilol 3.125 mg bid
- Lisinopril 5 mg qd
- Digoxin 0.125 mg qd
- Morphine 5-10 mg q 1 hr prn dyspnea
- Furosemide 80 mg qd

ICD

- Implanted cardioverter-defibrillators (ICDs)
- Have plan to discuss deactivation of device at end of life
- ICD activation from arrhythmias
 - Increased anxiety
 - Lowered quality of life
 - Increased mortality

Goldfinger, A.D., Adler, E.D. End of Life Options For Patients with Heart Failure. Curr Heart Fail Rep (2010) 7:140-147

ALS

- Riluzole
- To Continue or Not to Continue?



S. Zoccollella, et al. Riluzole and amyotrophic lateral sclerosis survival: a population-based study in southern Italy. European Journal of Neurology 2007, 14: 262-268.

Miller R.G, Mitchell J.D, Lyon M, Moore D.H. Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND). Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.:

CD001447. DOI: 10.1002/14651858.CD001447.pub2.

ALS

- Riluzole Guidelines:

- _____
- _____
- _____

Multiple Sclerosis

- Fingolimod
 - Reduce MS attacks
- Dalfampridine
 - Increased walking speed over 25 feet

Pulmonary Arterial Hypertension

- Sildenafil
- Double blind, placebo-controlled trial¹
 - Placebo vs sildenafil 20, 40, or 80mg po tid for 12 weeks
 - 6MW (six minute walking test) distance increased by 45m, 46m and 50m respectively
 - 222/278 patients completed 1 full year of monotherapy with sildenafil resulting in a 6MW walking distance of 51m
- Evidence level A for class II/III PAH*
- Evidence level C for class IV*

Galie N, Ghofrani HA, Torbick A, et al. Sildenafil citrate therapy for pulmonary arterial hypertension. *N Engl J Med* 2009;353:2149-2157

Pulmonary Arterial Hypertension

- Bosentan
- Double-blinded, placebo controlled trial
 - 213 patients with class III/IV PAH for 16 weeks
 - Improvement in 6MW walking distance of 36m
- Long term outcomes
 - First line therapy with bosentan followed by adding or transitioning therapy as necessary resulted in Kaplan-Meier survival estimates of 96% at 12 months and 89% at 24 months
 - At end of 12 months and 24 months, 85% and 75% of patients were still alive and on bosentan monotherapy

Rubin LJ, Badesch DB, Barst RJ, et al. Bosentan therapy for pulmonary arterial hypertension. *N Engl J Med* 2002;346:896-903.
McLaughlin VV, Sitbon O, Badesch DB, et al. Survival with first-line bosentan in patients with primary pulmonary hypertension. *Eur Respir J* 2005;25:244-249.

Megestrol Acetate



- What's the benefit?
 - Increase in appetite in patients with cancer and HIV/AIDs
- What's the risk?
 - Increase in weight appears to be fat vs. lean muscle
 - Increase risk of thrombosis

Kropsky Benjamin, et al. Incidence of Deep-Venous Thrombosis in Nursing Home Residents Using Megestrol Acetate. *J Am Med Dir Assoc* 2003; 4: 255-256.
Bodemer Donaldi, et al. A Retrospective Study of the Association Between Megestrol Acetate Administration and Mortality Among Nursing Home Residents With Clinically Significant Weight Loss. *Am J Geriatr Pharmacother*. 2007; 5: 137-146.

Megestrol Acetate

- Incidence of DVT in the community is approximately 0.1%
- The incidence of DVT in this study was 4.9%
 - Conclusion: "There is a six-fold higher incidence of deep venous thrombosis among megestrol users in this population than in the general population of elderly"

Kropsky Benjamin, et al. Incidence of Deep-Venous Thrombosis in Nursing Home Residents Using Megestrol Acetate. *J Am Med Dir Assoc* 2003; 4: 255-256.

Megestrol Acetate

- Case-Control Cohort of 17,328 nursing home patients who within the last 30 days lost either 5% of TBW in the previous 3 months or 10% of TBW in the previous 6 months who received Megestrol therapy
- These patients were matched (1:2) with non-megestrol users

Megestrol Acetate

- The median survival of megestrol treated patients (23.9 months) was significantly less than the untreated group (31.2 months) ($p < 0.001$). Median weight and median of weight differences were unchanged after 6 months of treatment between groups.
- Conclusions: "Megestrol treated patients with significant weight loss were associated with a significant increase in all-cause mortality without any effect on weight."

Bokenner Donald, et al. A Retrospective Study of the Association Between Megestrol Acetate Administration and Mortality Among Nursing Home Residents With Clinically Significant Weight Loss. Am J Geriatr Pharmacother. 2007; 5: 137-146.

Diabetes

- Blood Glucose Control
 - Target: _____?
- In hospice patients, the goals change!
- What are the goals?



Diabetes Hospice and Palliative Care

- Prognosis based triage
 - Advanced disease, relatively stable
 - Impending death or organ or system failure
 - Actively dying

Angelo Mark et al. An Approach to Diabetes Mellitus in Hospice and Palliative Medicine. JOURNAL OF PALLIATIVE MEDICINE. 2011;14: Number 1.

Diabetes Advanced disease-relatively stable

- Begin education:
 - Reduce intensity of glycemic control
 - No A1C
 - Prevent hypoglycemia
 - Blood glucose less than renal threshold
- Prevent acute risks of hyperglycemia (hyperosmolar state)
 - Osmotic diuresis
 - Recurrent infection
 - Poor wound healing

Angelo Mark et al. An Approach to Diabetes Mellitus in Hospice and Palliative Medicine. JOURNAL OF PALLIATIVE MEDICINE. 2011;14: Number 1.

Diabetes Advanced underlying disease or organ failure

- Prevention of hypoglycemia
- Patient/caregiver education
- Type I diabetes
- Type II diabetes

Diabetes Actively Dying

- Comfort
- Stop insulin and oral hypoglycemics

Management of diabetes at end of life

- Management of oral and injectable diabetic medications?
- Why is this important?
 - Remember S&S of Hypoglycemia...
 - Diaphoresis, anxiety, tremors, weakness, palpitations, and, in extreme situations, seizure.
 - In hospice patients, this often resembles agitation/restlessness/delirium...
 - More susceptible

Angelo Mark et al. An Approach to Diabetes Mellitus in Hospice and Palliative Medicine. JOURNAL OF PALLIATIVE MEDICINE. 2011;14: Number 1.

Diabetes Medications

Medication	Comments	Dose considerations
Long and short acting insulin	Short acting: missed meals, erratic appetites Long acting: zless hypoglycemia	Reduce dose in renal and liver dysfunction. Stop if organ failure.
Sulfonylureas	Use shorter acting agents	Reduce dose in renal and liver dysfunction. Stop if organ failure.
Repaglinide, Nateglinide	Adjust according to food intake	Dose should be adjusted in patients with renal and/or liver dysfunction and stopped altogether if organ failure.
Metformin	High GI side effects Low hypoglycemia	Discontinue in hepatic or renal failure

Diabetes Medications

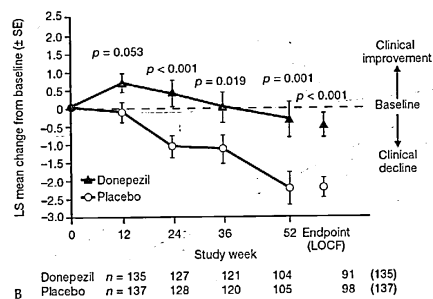
Medication	Comment	Dose considerations
Pioglitazone, rosiglitazone	Low hypoglycemia risk Edema	Discontinue in liver failure and cardiac compromised
Acarbose, miglitol		Do not take if miss meal
Exenatide, liraglutide, pramlintide,	Nausea common adverse effect	Dose adjust in renal failure
Staglipitin, saxagliptin	Nausea common adverse effect	Dose adjust in renal and liver failure

Dementia Medications

- Donepezil, Galantamine, Rivastigmine
- Improve cognition, function, behavioral
- Statistical significance was seen for the following types of measures:
 - Language; Visuospatial; bowel and bladder; Getting Dressed; Turning off the water

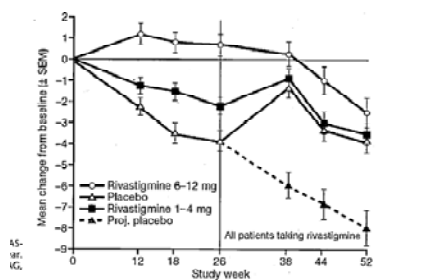
Bengt Winblad, et al. Donepezil in patients with severe Alzheimer's disease: double-blind, parallel-group, placebo-controlled study. *Lancet* 2006; 367: 1057-65.
Herman Nathan. Garthie Serge. Diagnosis and Treatment of dementia: Management of Severe Alzheimer's disease. *CMAJ* 2008;179(12):1279-1287.

Donepezil



Winblad, Bengt. Alzheimers Disease and Disorders. Long Term treatment of Alzheimers Disease 16.1:51-58

Rivastigmine



Winblad, Bengt. Alzheimers Disease and Disorders. Long Term treatment of Alzheimers Disease.10,1:51-58

Memantine

Improve cognition and function, (?)behavioral

Herman Nathan, Garthie Serge. Diagnosis and Treatment of dementia: Management of Severe Alzheimer's disease. CMAJ2008;179(12):1279-1287

Antiplatelets

- CVA's? Acute MI? Recent Cardiac Stents?
- Aspirin + Plavix + Aggrenox
 - When is the bleed risk greater than the clot risk?

Antiplatelets- Chest Guidelines

- Combination therapy w/ASA and Plavix not recommended, *unless recent acute MI, acute coronary syndrome, or recent coronary stent placement: 30 days (MI); up to 1 year (ACS, stent)*
- 1st CVA- ASA or plavix or Aggrenox
- 2nd CVA- either Aggrenox or Plavix
- Typically Antiplatelet therapy rule of thumb:
 - Continue indefinitely, with monthly re-assessment of risk-benefit ratio*.

Risk of bleeding and recurrent clot is highest in Hospice and Palliative Care Patients

Journal of Palliative Medicine
2009 Jan;12(1):83-7

Arguments for comfort and against anticoagulation

Journal of Thrombolysis 2009 27:335-339

Factors that increase bleeding risk

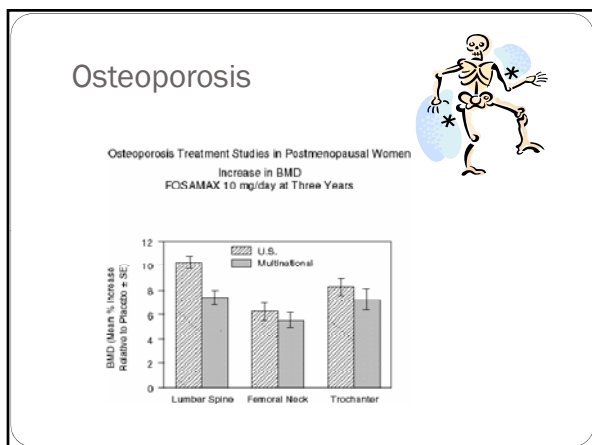
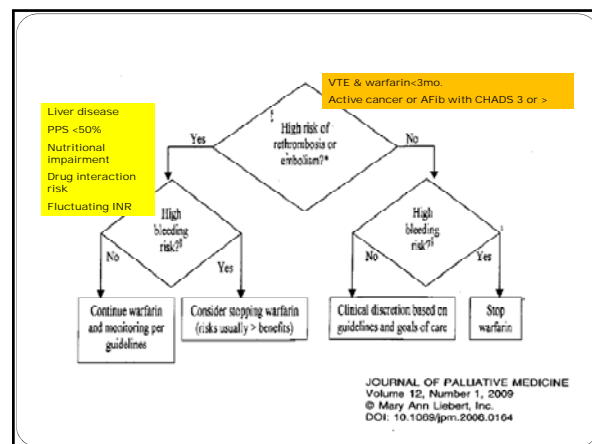
- Advanced age (>75 yrs)
- History of falls, or high fall risk (dementia, orthostatic hypotension, meds -antipsychotics, anticholinergics, opiates, a-blockers)
- History of peptic ulcers/ GI bleeds
- Poor nutritional status
- Variable appetite and nutrition intake (specific to warfarin use)
- Liver disease
- Concurrent aspirin, antiplatelets, nsaid, antibiotic therapy
- Leukemia, multiple myeloma, other myelodysplasias

Table 2. CHADS₂ Risk Stratification to Assess Risk in Patients with Atrial Fibrillation¹⁹

CHADS ₂ Scoring System		Stroke Risk	
Risk Factor	Points	CHADS ₂ Score	Adjusted Stroke Rate (per 100 pt. years)
Congestive heart failure	1	0	1.9
Hypertension	1	1	2.8
Age, >75 y	1	2	4.0
Diabetes	1	3	5.9
Stroke	2	4	8.5
		5	12.5
		6	18.2

CHADS = congestive heart failure, age, diabetes, stroke.

The Journal of Pharmacology • 2008 April, Volume 17 • 527



Osteoporosis

- Stopping alendronate after 5 yrs of treatment led to a decline BMD of 2.4 % in hip and 3.7% in spine over 5 years.

Black DM et al. "Effects of Continuing or Stopping Alendronate After 5 Years of Treatment: The Fracture Intervention Trial Long-term Extension (FLEX): A Randomized Trial." JAMA. 2006;296:2927-2938

Supplements: Vitamin C and Zn

- No effect on prevention or treatment of pressure ulcers, based on the literature.
- Adverse effects Vit C:
 - Nausea and diarrhea
- Adverse effects of zinc excess:
 - 7.8 times greater risk of antibiotic requirement for infections
 - 12.5 times more likely to have gastrointestinal side effect
 - zinc supplementation in patients without a deficiency is not recommended.

Jamshed, N., Schneider E. Is the Use of Supplemental Vitamin C and Zinc for the Prevention & Treatment of Pressure Ulcers Evidence-Based? Annals of Long Term Care; March 2010; 18: 28-32.

Supplements

- Evidence based studies show that antioxidants such as vitamin C, or E do not prevent CV disease.

Clinical Review: the adult vitamin and mineral supplement maze. The Consultant Pharmacist, April 2010:25.

Supplements

- Vit B6, B12, FA do no improve homocysteine blood levels or provide any protective effect.

Clinical Review: the adult vitamin and mineral supplement maze. The Consultant Pharmacist. April 2010:25.

Supplements

- Ferrous sulfate:
 - Anemia increased the risk of injurious falls by 1.66 times compared with no anemia
 - Incidence of injurious falls increased from 6.5 to 15.8 per 1,000 person-years when Hb levels decreased from 13 g/dl to less than 10 g/dl

Cooper, J.W., Burfield A.H. Medication intervention for fall prevention in the older adult. J Am Pharm Assoc. 2009;49:e70-e84

Discontinuing of Medications

- Abrupt stop/withdrawal of medication
- Taper of medications
 - Adrenergic, Cholinergic, and Histamine Drugs
 - Antidepressants
 - Antipsychotic, Dopaminergic, and Mood-stabilizing Drugs
 - Benzodiazepine, Opioid, and Stimulant Drugs
 - Beta blockers
 - Seizure medications
- Monitor and develop plan of care

Howland, RH. Potential Adverse Effects of Discontinuing Psychotropic Drugs. Journal of Psychosocial Nursing and Mental Health Services 2010;48(6-9): Parts 1,2,3,4

