Deprescribing at the End of Life: When Less is More

Elizabeth A. Bukowy, DO

Geriatrician

MCW Palliative Care/Hospice Fellow

Kristina Teso, PharmD, BCPS, BCOP

Clinical Oncology Pharmacist

Froedtert Hospital Clinical Cancer Center

- No financial disclosures.

Objectives

- Discuss goals of and barriers to deprescribing
- Present strategies for deprescribing medications at end of life
- Review common medication classes to target for deprescribing and pharmacological considerations
- Highlight tools and resources to aid in deprescribing

Case: Miss Mary

- 85 y/o F with coronary artery disease, Type II diabetes, atrial fibrillation with moderate dementia was discharged from hospital after a stroke to a long term care facility with hospice.

  - Has difficulty swallowing but able to tolerate modified diet and crushed pills
  - Can preform most basic activities of daily living (eating, mobility, self care)
  - Needs assistance with more advanced cares

Miss Mary's (non Hospice) Medications

- Cardiac
  - Aspirin 81 mg daily
  - Clopidogrel 75 mg daily
  - Warfarin 2 mg daily
  - Metoprolol 50 mg BID
  - Lisinopril 10 mg daily
  - Atorvastatin 20 mg nightly
- Post-stroke seizure prophylaxis
  - Levetiracetam 500 mg BID
- Gastroenterology protection
  - Pantoprazole 40 mg daily
- Dementia
  - Donepezil 10 mg daily
  - Memantine 5 mg BID
- Diabetes
  - Metformin 1000 mg BID
  - Glipizide XL 10 mg daily
- Bone Health
  - Alendronate 70 mg weekly
  - Calcium + D 600 mg/200 units BID
- Other
  - Ocuvite 1 tab daily

Starting Drug Count:
15

Pills per day:
20

- Family is interested in reducing pill burden
- They ask you to review her list and reduce or stop any medications you think appropriate
- **Where do you start???**

Discussion Road Map

- Who are we targeting?
- Why deprescribe?
- Barriers to deprescribing
- Low hanging fruit – Medications that DO NOT need to be tapered/weaned
- Medications that DO need tapering/weaning
- Common medications that need dose reductions

What population are we focusing on today?

- Focus on patients who are suspected to have long weeks to months
  - Not patients with hours to days
- Still relatively functional and able to take medications by mouth
- Patient who want to minimize their bill burden at any point in their illness

Why deprescribe? What's the harm?

- Polypharmacy correlates with increased
  - Drug interactions
  - Adverse events
  - Hospitalization and mortality
  - Medication Costs
  - Pill Burden
- Age and disease related pharmacokinetic changes = Increased drug exposure
  - Altered renal and hepatic function
  - Decreased nutritional status, altered protein binding

Masnoon N, et al. BMC geriatrics 2017
Reeve E, et al. Drugs Aging 2013

Burden of Polypharmacy Near End of Life

- Patients discharged to nursing facility average 14 +/- 4.7 medications
- Journal Pain and Symptom Management 2016:
  - 11.5 +/- 5 medications for primary disease prevention in last month-1year of life
- Retrospective review of 4252 patients enrolled in hospice in 11 US states in 2010
  - Average 7.9 PRN medications, 8.3 scheduled medications
  - Most common 6 were those prescribed upon admission in the comfort kits
    - Acetaminophen, morphine, haloperidol, lorazepam, prochlorperazine, and atropine

McNeil M, et al. J Pain Symptom Manage 2016
Saraf AA, et al. J Hosp Med 2016
Sera L, et al. Am J Hosp Palliat Care 2014

How do you identify which medications are appropriate to deprescribe?

- Benefits no longer outweigh risk of adverse effects
- Time to benefit is longer than anticipated life expectancy
- Treatment target no longer aligns with patient's goals of care

- Deprescribing is a trial – medications can be restarted!!!

But I didn't start this medication!
Common Barriers to Deprescribing

- Lack of provider confidence
- Fear of triggering psychological distress from patient
- Patient psychological attachment to chronic medications
- Patient/family not understanding their prognosis

The guidelines say my patient needs this...

- American Diabetic Association
  - Insulin, Metformin, Sulfonylureas
- JNC 8, ACC/AHA STEMI guidelines
  - Beta blockers, ACE inhibitors, diuretics, aspirin
- CHEST Guidelines for VTE
  - Warfarin, Enoxaparin, DOACs
- ATP III, ACC/AHA Guidelines for Cholesterol
  - Statins, fenofibrates, niacin
- AACE/ACE Osteoporosis and Hypothyroidism
  - Bisphosphonates, Levothyroxine
- GOLD guidelines for COPD
  - Inhaled steroids, bronchodilators, anticholinergics
- APA guidelines for Major Depressive Disorder or Agitation/Psychosis in patients with Dementia
  - Antidepressants, antipsychotics

Where are the deprescribing guidelines???

Easy targets for discontinuation

- Vitamins, Multivitamins, Antioxidants
  - Calcium and vitamin D: changes in bone mineral density and prevention of osteoporosis irrelevant at end of life
    - Continue in patients on bone modifying agents for oncology indications
- Supplements
  - Iron: anemia of chronic disease often misdiagnosed as iron deficiency
  - Complementary medicines: lack data for clinical benefit, often have interactions with other medications
- Bisphosphonates
  - Risks of esophagitis outweighs any continued benefit

Allen, R. NHPCO Newsline(2014): 5.

Easy targets for discontinuation

- Docusate
  - Poor evidence for efficacy in the management of constipation
  - 74 patients randomized to receive Docusate 200 mg BID + Senna vs Placebo + Senna in 3 Canadian inpatient hospice facilities
    - No significant differences in stool volume, frequency, or consistency between docusate and placebo
    - Additional interventions to manage constipation were required in both arm in approximately 70% of patients (no different)
    - Use may be considered on case by case basis

MacMillan TE, et al. Am J Med 2016
Tarumi Y, et al. J Pain Symptom Manage. 2013

The statin can go!

- Evaluation of risks and benefits of statin use at the end of life
- Randomized 381 patients with life expectancy 1 month to 1 year to continue vs discontinue statin therapy
  - No difference in 60 day mortality
  - No difference in cardiovascular events
  - QOL better in the discontinuation arm
  - Daily cost savings of $3.37 ($716 annually)
- Can extrapolate to other anti-lipid agents: niacin, fibrates, omega-3

Kutner JS, et al. JAMA Intern Med. 2015

What about those eye drops?

- American Glaucoma Society 2016 Annual Meeting:
  - 214 patients, primary open angle glaucoma treated with prostaglandin >6 months
  - 124 assigned to discontinue and washout
  - Average IOP at baseline 26.6mmHg (normal 12-22mmHg)
  - Average IOP with treatment 14.5mmHg
  - After 6 weeks without treatment, average IOP 20.3mmHg

- If eye pain, redness, blurry vision resume drops!!!

Benefit Persists After Prostaglandin Stopped in Glaucoma - *Medscape* - Mar 07, 2016

Antiplatelet agents

- Clopidogrel (Plavix®), Ticagrelor (Brilinta®), Prasugrel (Effient®)
  - Recommended duration of therapy only 12 months after ACS/PCI
    - Discontinuation often missed
- Aspirin
  - ACS Guidelines recommend indefinite treatment for secondary prevention
    - Assess clinical significance near end of life
  - Updated 2019 CVD primary prevention guidelines no longer recommend low dose aspirin
- Overall bleeding risks > long-term benefit, especially in elderly

Levine GN, et al. Circulation 2016
Arnett DK, et al. Journal of the American College of Cardiology. 2019

To anticoagulate...?

- No guidelines for discontinuation, but duration of therapy differs by indication
  - VTE: Chest guidelines = 3 months
  - Cancer-associated VTE: no consensus, common 3-6 months
  - Indefinite treatment for Afib and mechanical valves

- Consider alternatives to Warfarin if anticoagulation needed/desired
  - Difficult to manage with altered dietary intake and liver function at end of life, requires INR monitoring
  - Assess renal dosing needs for LMWH or direct oral anticoagulants

Kearon C, et al. Chest 2012
Lee AYY. Blood 2017
January CT, #278 Warfarin And Palliative Care. Web. 26 Feb. 2015

… Or Not?

- Discontinue anticoagulation if
  - Recommended duration of treatment has been met
  - Risk of bleed, falls outweighs risk of thrombosis

- Consider patient and family wishes

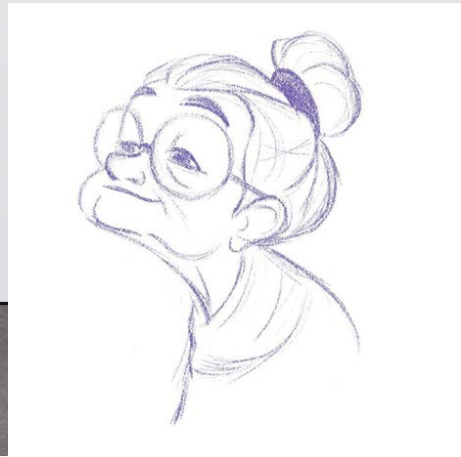
Kearon C, et al. Chest. 2012
Lee AYY. Blood 2017
January CT, #278 Warfarin And Palliative Care. Web. 26 Feb. 2015

Miss Mary's Updated Medication List

- Cardiac
  - ~~Aspirin 81 mg daily~~
  - ~~Clopidogrel 75 mg daily~~
  - ~~Warfarin 2 mg daily~~
  - Metoprolol 50 mg BID
  - Lisinopril 10 mg daily
  - ~~Atorvastatin 20 mg nightly~~
- Post stroke seizure prophylaxis
  - Levetiracetam 500 mg BID
- Gastroenterology protection
  - Pantoprazole 40 mg daily
- Dementia
  - Donepezil 10 mg daily
  - Memantine 5 mg BID
- Diabetes
  - Metformin 1000 mg BID
  - Glipizide XL 10 mg daily
- Bone Health
  - ~~Alendronate 70 mg weekly~~
  - ~~Calcium + D 600 mg/200 units BID~~
- Other
  - ~~Ocuvite 1 tab daily~~

Drug Count:
~~15~~ 8

Pills per day:
~~20~~ 12



Drugs requiring tapering

Drug Class	Disease Recurrence	Withdrawal	Rebound	Clinical Observations
Alpha Blockers		✓	✓	Agitation, headache, hypertension, palpitations
ACE Inhibitors/ARBs	✓			Heart failure, hypertension
Antianginals	✓			Angina
Anticonvulsants	✓	✓		Anxiety, depression, seizures
Antidepressants	✓	✓		Anxiety, chills, depression, GI disturbance, headache, insomnia, irritability, malaise, myalgia
Antiparkinsons	✓	✓	✓	Hypotension, psychosis, rigidity, tremor
Antipsychotics		✓		Dyskinesias, insomnia, nausea, restlessness
Anticholinergics		✓		Anxiety, nausea, headache, dizziness
Baclofen		✓	✓	Agitation, anxiety, confusion, depression, hallucinations, hypertonia, mania, nightmares, paranoia, seizures
Benzodiazepines		✓		Agitation, anxiety, confusion, delirium, insomnia, seizures
Beta Blockers	✓	✓		Angina, anxiety, hypertension, ACS, tachycardia
Corticosteroids	✓	✓	✓	Anorexia, hypotension, nausea, weakness, adrenal insufficiency, inflammatory response
Digoxin	✓			Heart failure, palpitations
Diuretics	✓			Heart failure, hypertension
NSAIDs	✓			Pain recurrence
Opioids		✓		Abdominal cramping, agitation, anger, anxiety, chills, diaphoresis, diarrhea, insomnia

Adapted from: Scott IA, et al. Evid Based Med 2013

Diabetes and end of life goals: ADA guidance

- Stable patients: continue current regimen with less stringent glucose control
- Promote comfort and quality of life
  - Discontinue A1C monitoring and minimize finger sticks
- Patients with organ failure: avoid hypoglycemia
  - Type II: taper or discontinue agents likely to cause hypoglycemia
  - Type I: adjust insulin according to food intake
- Dying patients: minimize acute complications
  - Type II: discontinuation of all agents reasonable
  - Type I: consider low dose basal insulin

American Diabetes Association. Diabetes Care 2018

Adjusting and stopping hypoglycemic agents

- Drugs most likely to cause hypoglycemia: stop or reduce dose
  - Sulfonylureas: long acting agents (glimepiride, glyburide, glipizide XL) increase risk over shorter acting agents (glipizide)
  - Meglitinides: nateglinide or repaglinide
  - Insulin: short acting (aspart, regular, and NPH)

- Switch to agents with lesser hypoglycemia potential if benefits > risks in continuing antihyperglycemic agents
  - Metformin, alpha-glucosidase inhibitors, DPP-4 inhibitors, GLP-1 agonists, SGLT2 inhibitors
  - Avoid TZDs due cardiac and stroke risks(pioglitazone)

Farrell B, et al. Can Fam Physician 2017

Adjusting and stopping hypoglycemic agents

- Reduce doses or stop when renal function is impaired
  - Metformin: contraindicated in eGFR <30 mL/minute/1.73 m^2
  - "Gliptins": varying dose reductions for decreased renal function (eGFR 15-60 ml/minute/1.73 m^2)
  - "Gliflozins": contraindicated in eGFR < 30 mL/minute/1.73 m^2

- Evaluate for possible drug-drug interactions which can affect hypoglycemia agents or cause additive hypoglycemia
  - Quinolones, beta-blockers, trimethoprim/sulfamethoxazole, salicylates

Farrell B, et al. Can Fam Physician 2017

When to taper: antihypertensives

- Optimal duration of treatment unknown
  - JNC 8 guidelines: Goal BP < 140/90 based on risk factors/age
  - ACS and HF guidelines recommend indefinite use
  - ADA suggests less strict BP goal at end of life: < 150/100

- Evaluate risk of hypotension and adverse events vs recurrence of disease or symptoms
  - Afib, heart failure symptoms, rebound hypertension/tachycardia, angina, AMI

James PA, et al. *JAMA.* 2014

How to taper: antihypertensives

- Beta blockers should not be abruptly stopped!!
  - Ventricular arrhythmias, severe angina, and myocardial infarction have been reported
  - Gradually taper over minimum of 1-2 weeks to decrease risk for rebound symptoms
- Clonidine also requires gradual taper over days to weeks
  - Abrupt withdrawal = rapid BP rise and sympathetic overload symptoms
- ACE Inhibitors/ARBs offer decreased risks of withdrawal or rebound symptoms = safer to discontinue without taper

Podrid PJ. Major side effects of beta blockers Post TW, ed. UpToDate.
Frank C, Weir E. *CMAJ.* 2014;186(18):1369–1376.

When to taper: Proton pump inhibitors

- Long term use of PPIs is associated with increased risk of fracture, C. Diff infection, CAP, diarrhea, vitamin and electrolyte deficiencies

- Stopping PPIs abruptly may cause rebound reflux symptoms

- Not all patients are candidates for deprescribing
  - Continue: Barrett's esophagus, GI ulceration, severe esophagitis, chronic NSAID/steroid use
  - Insufficient treatment duration: peptic ulcer, H.Pylori, GERD with mild-moderate esophagitis

Farrell B, et al. Can Fam Physician 2017

How to taper: Proton pump inhibitors

- Tapering approaches equally recommended
  - 50% dose daily vs alternate day dosing
  - Stop and use on-demand dosing
  - Twice daily to once daily frequency
    - Assess BID indication: H.Pylori or hypersecretory disease - do not deprescribe

- Use on-demand dosing if symptoms return after discontinuation
  - Resume at low daily dosing until resolution then stop again
  - Manage occasional symptoms with as needed OTC antacids

Farrell B, et al. Can Fam Physician 2017

Cognitive Enhancers: Cholinesterase Inhibitors (CHEI)
Aricept, Galantamine or Rivastigmine

- When:
  - Cognitive +/- functional decline over past 6 months
  - No noticeable benefit
  - Severe dementia (near total dependence for activities of daily living)
- How:
  - Reduce dose 25-50% every 1-2 weeks
- Withdrawal:
  - Reduced ability to concentrate, labile mood, hallucinations/delusions, agitation

Reeve E, et al. University of Sydney 2018
Liao P, Perri G. J Pall Med 2018

Cognitive Enhancers: NMDA Receptor Antagonists
Memantine

- When:
  - Cognitive +/- functional decline over past 6 months or near total dependence
  - No noticeable benefit
  - If eGFR< 30: max daily dose of 5mg twice per day
- How: (limited/no RCT for guidance)
  - Immediate release: reduce by 5mg weekly
  - Extended release: reduce by 7mg weekly
- Monitor:
  - Cognitive dysfunction, behavioral changes, insomnia(?)

Parsons C. Drugs & aging 2016
Kwak YT, et al. Geriatr Gerontol Int 2009

Does anyone have an answer about seizure prophylaxis???

- Prophylactic use of antiepileptic drug (AED) is not recommended in patients with intracranial hemorrhage
  - Subarachnoid hemorrhage controversial with limited trials

- Neurocritical Care Society and 2012 American Heart Association/American Stroke Association Guidelines
  - Short course is preferable (3-7) days if prophylaxis needed
  - Long term use if known risk factors:
    - Delayed seizure disorder (prior seizure), intracerebral hematoma, intractable HTN, CVA or aneurysm of MCA

Morgenstern LB, et al. Stroke 2010
Yerram S, et al. J Intensive Care. 2018

But my patient has a brain cancer!

- American Academy of Neurology Practice Parameters
  - AED prophylaxis had no significant preventive effect on seizure incidence or seizure free survival in patients with brain neoplasms
  - AED prophylaxis associated with significant side effects:
    - Rash, nausea, vomiting, confusion

- Does this apply to brain metastasis?
  - Randomized control trials: no significant difference in seizure incidence
    - Similar findings with short 7 day course but increase in side effects

Yerram S, et al. J Intensive Care. 2018

My patient had brain surgery!

- Current guidelines for post-op patients who have never had seizure
  - Discontinue or taper after first week post-op
  - Especially in those with medication side effects

Komotar R, et al. J Neurosurg 2011
Pulman J, et al. Cochrane Database Syst Rev. 2013

Who has highest risk of seizures and may benefit from short course AED?

Table 6

Seizure prophylaxis protocol in neuro-ICU

Seizure prophylaxis	Conditions
Definitive prophylaxis	• Severe TBI (7 days)
Probable prophylaxis	• Unsecured aneurysm in SAH
	• Elevated intracranial pressure (ICP) and concern for poor compliance
Possible/no prophylaxis	• ICH
	• AVM
	• Cavernoma
	• Brain neoplasm
	• Malignant ischemic stroke
	• Postoperative craniotomy
	• Meningitis
	• Cerebral venous sinus thrombosis (CVST)
	• PRES

Yerram S, et al. J Intensive Care. 2018

Who Gets to Stop Seizure Prophylaxis?

- If your patient has been on AED for >1week
- Has side effects from medication
- Trouble with swallowing pills

- Have benzodiazepines on board just in case!!!

Yerram S, et al. J Intensive Care. 2018

Consider Renal Dosing of Medications

- Gabapentin
- Pregabalin
- Venlafaxine
- Duloxetine
- Methadone

Gabapentin

- When:
  - eGFR >30-59 mL/minute/1.73 m^2: 200 -700 mg twice daily
  - eGFR >15-29 mL/minute/1.73 m^2: 200 - 700 mg once daily
  - eGFR <15 mL/minute/1.73 m^2: use with caution

- If discontinuing: taper gradually over ≥1 week

- Monitor:
  - Increased seizure frequency (in patients with epilepsy)
  - Confusion, irritability, tachycardia or diaphoresis

Norton 2001; Tran 2005

Pregabalin

- When:
  - eGFR 30-60 mL/minute/1.73 m2 : reduce daily dose by 50% BID/TID
  - eGFR 15-30 mL/minute/1.73 m2 : reduce by 50-75% pending on start dose, single daily dose
  - Caution with extended release and ESRD
- If discontinuing: taper gradually over ≥1 week
- Monitor:
  - Increased seizure frequency (in patients with epilepsy)
  - Agitation, delirium, delusions, GI symptoms, mood changes or diaphoresis

Bonnet 2017; "Gabapentin and Pregabalin" 2012

Venlafaxine

- When:
  - Mild to severe renal impairment: reduce dose by 25-50%
  - Mild to severe hepatic impairment: reduce dose by 50%

- If discontinuing: taper gradually over 2-4 weeks

- Monitor:
  - Re-emerging original symptoms

APA 2010; WFSBP [Bauer 2015]

Duloxetine

- When:
  - eGFR <30 mL/minute/1.73 m2 and ESRD: avoid use
  - Hepatic impairment: avoid use
- If discontinuing: taper gradually over 2-4 weeks
- Monitor:
  - Re-emerging original symptoms

APA 2010; WFSBP [Bauer 2015]

Methadone

- When:
  - eGFR <10 mL/minute/1.73 m^2 : Administer 50% to 75% of normal dose
  - Hemodialysis or peritoneal dialysis does not increase elimination of methadone
  - On other QTc prolonging or cytochrome p450 medications
- If discontinuing: taper gradually over weeks
- Monitor:
  - Opioid withdrawal – GI upset, sweating, yawning, goose bumps

Aronoff 2007
Lexicomp Drugs: Methadone

Miss Mary's Updated Medication List

- Cardiac
  - ~~Aspirin 81 mg daily~~
  - ~~Clopidogrel 75 mg daily~~
  - ~~Warfarin 2 mg daily~~
  - Metoprolol 50 mg ~~BID~~ daily
  - ~~Lisinopril 10 mg daily~~
  - ~~Atorvastatin 20 mg nightly~~
- Post stroke seizure prophylaxis
  - ~~Levetiracetam 500 mg BID~~
- Gastroenterology protection
  - Pantoprazole ~~40~~ 20 mg daily
- Dementia
  - ~~Donepezil 10 mg daily~~
  - Memantine 5 mg ~~BID~~ daily
- Diabetes
  - Metformin 1000 mg BID
  - ~~Glipizide XL 10 mg daily~~
- Bone Health
  - ~~Alendronate 70 mg weekly~~
  - ~~Calcium + D 600 mg/200 units BID~~
- Other
  - ~~Ocuvite 1 tab daily~~

Drug Count:
~~15~~ ~~8~~ 4

Pills per day:
~~20~~ ~~12~~ 5

Online Resources

- AGS Beers Criteria resources
  - Alternative Medications List
  - Criteria and evidence table
- Deprescribing.org Guidelines and Algorithms
- Canadian Deprescribing Network (CaDeN)
  - Patient resources and brochures
- Polypharmacy Guidance, NHS of Scotland
- OncPal Deprescribing Guideline


KEEP
CALM
it's
QUESTION
TIME

References

- Allen, Richard. 10 Drugs to Reconsider When a Patient Enrolls in Hospice. NHPCO Newsline 2014: 5.
- American Diabetes Association. 11. Older adults: Standards of Medical Care in Diabetes 2018. *Diabetes Care* 2018;41(Suppl. 1): S119–S125
- American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Peripheral Vascular Disease; Council on Clinical Cardiology Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2013
- Farrell B, Black C, Thompson W, McCarthy L, Rojas-Fernandez C, Lochnan H, et al. Deprescribing antihyperglycemic agents in older persons. Evidence-based clinical practice guideline. *Can Fam Physician* 2017;63:832-43.
- Farrell B, Pottie K, Thompson W, Boghossian T, Pizzola L, Rashid J, Rojas-Fernandez C, Walsh K, Welch V, Moayyedi P. Evidence-based clinical practice guideline for deprescribing proton pump inhibitors. *Can Fam Physician* 2017;63:354-64.
- James PA, Oparil S, Carter BL, et al. 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507–520. doi:10.1001/jama.2013.284427
- January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. *Journal of the American College of Cardiology* Dec 2014, 64 (21) e1-e76; DOI: 10.1016/j.jacc.2014.03.022
- Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e419S-e494S.
- Komotar RJ, Raper DS, Starke R, Iorgulescu JBS, Gutin PH. Prophylactic antiepileptic drug therapy in patients undergoing supratentorial meningioma resection: a systematic analysis of efficacy: A review. *Journal of neurosurgery* 2011: 483-490.
- Kutner JS, Blatchford PJ, Taylor DH, et al. Safety and Benefit of Discontinuing Statin Therapy in the Setting of Advanced, Life-Limiting Illness: A Randomized Clinical Trial. *JAMA Intern Med.* 2015;175(5):691–700.
- Kwak YT, Han IW, Suk SH, Koo MS. Two cases of discontinuation syndrome following cessation of memantine. *Geriatr Gerontol Int.* 2009 Jun;9(2):203-5.
- Lee AYY. When can we stop anticoagulation in patients with cancer-associated thrombosis? *Blood* 2017; 130(23): 2484-2490. DOI: 10.1182/blood-2017-05-787929
- Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, Granger CB, Lange RA, Mack MJ, Mauri L, Mehran R, Mukherjee D, Newby LK, O'Gara PT, Sabatine MS, Smith PK, Smith SC Jr. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 ACC/AHA guideline for the management of patients with non–ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation*. 2016;134:e123–e155. DOI: 10.1161/CIR.0000000000000404.
- Liao P, Perri GA. Deprescribing Cholinesterase Inhibitors at the End of Life #354. *Journal of Palliative Medicine*. Jul 2018.ahead of print http://doi.org/10.1089/jpm.2018.0220.
- Lowry F. Benefit Persists After Prostaglandin Stopped in Glaucoma. Medscape - Mar 07, 2016.

References

- MacMillan, TE, Kamali, R, Cavalcanti, RB. Missed opportunity to deprescribe: docusate for constipation in medical inpatients. *Am J Med* 2016; 129(9): 1001.e1–01.e7.
- Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr*. 2017;17(1):230. Published 2017 Oct 10. doi:10.1186/s12877-017-0621-2
- McNeil MJ, Kamal AH, Kutner JS, Ritchie CS, Abernethy AP. The Burden of Polypharmacy in Patients Near the End of Life. *J Pain Symptom Manage*. 2015;51(2):178–83.e2. doi:10.1016/j.jpainsymman.2015.09.003
- Morgenstern LB, Hemphill JC, III, Anderson C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: aguideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2010
- Parsons, Carole. Withdrawal of antidementia drugs in older people: who, when and how? *Drugs & aging* 2016; 33 (8): 545-556.
- Podrid PJ. Major side effects of beta blockers Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com (Accessed on April 7, 2019.)
- Pulman J, Greenhalgh J, Marson AG. Antiepileptic drugs as prophylaxis for post-craniotomy seizures. *Cochrane Database of Systematic Reviews* 2013, Issue 2. Art. No.: CD007286. DOI: 10.1002/14651858.CD007286.pub2.
- Reeve E, Farrell B, Thompson W, Herrmann N, Sketris I, Magin P, Chenoweth L, Gorman M, Quirke L, Bethune G, Forbes F, Hilmer S. Evidence-based Clinical Practice Guideline for Deprescribing Cholinesterase Inhibitors and Memantine. Sydney: The University of Sydney; 2018. ISBN-13: 978-0-6482658-0-1 Available from: http://sydney.edu.au/medicine/cdpc/resources/deprescribing-guidelines.php
- Reeve E, To J, Hendrix I, Shakib S, Roberts MS, Wiese MD. Patient barriers to and enablers of deprescribing: a systematic review. *Drugs Aging* 2013; 30: 793–807
- Saraf AA, Petersen AW, Simmons SF, Schnelle JF, Bell SP, Kripalani S, Vasilevskis EE. Medications associated with geriatric syndromes and their prevalence in older hospitalized adults discharged to skilled nursing facilities. *Journal of hospital medicine* 2016;11(10):694-700.
- Schenker Y, Park SY, Jeong K, Pruskowski J, Kavalieratos D, Resick J, Abernethy A, Kutner JS. Associations Between Polypharmacy, Symptom Burden, and Quality of Life in Patients with Advanced, Life-Limiting Illness. *J Gen Intern Med*. 2019 Apr; 34(4): 559–566. Published online 2019 Feb 4. doi: 10.1007/s11606-019-04837-7
- Scott IA, Gray LC, Martin JH, Pillans PI, Mitchell CA. Deciding when to stop: towards evidence based deprescribing of drugs in older populations. *Evid Based Med*. 2013;18:121-124.
- Tarumi Y, Wilson MP, Szafran O, Spooner GR. Randomized, double-blind, placebo-controlled trial of oral docusate in the management of constipation in hospice patients. *J Pain Symptom Manage,* 2013; 45: 2-13.
- Von Gunten, Charles, David Weissman, and Janet Abraham. Fast Fact #278 Warfarin and Palliative Care. Web. 26 Feb 2015.
- WRITING COMMITTEE MEMBERS, Arnett DK, Blumenthal RS, Albert MA, Michos ED, Buroker AB, Miedema MD, Goldberger ZD, Muñoz D, Hahn EJ, Smith Jr SC, Himmelfarb CD, Virani SS, Khera A, Williams Sr KA, Lloyd-Jones D, Yeboah J, McEvoy JW, Ziaeian B, ACC/ AHA TASK FORCE MEMBERS, O'Gara PT, Beckman JA, Levine GN, Chair IP, Al-Khatib SM, Hlatky MA, Birtcher KK, Ikonomidis J, Cigarroa JE, Joglar JA, Deswal A, Mauri L, Fleisher LA, Piano MR, Gentile F, Riegel B, Goldberger ZD, Wijeysundera DN, 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease, Journal of the American College of Cardiology (2019), doi: https://doi.org/10.1016/j.jacc.2019.03.010.
- Yerram S, Katyal N, Premkumar K, Nattanmai P, Newey CR. Seizure prophylaxis in the neuroscience intensive care unit. *J Intensive Care*. 2018;6:17. Published 2018 Mar 5. doi:10.1186/s40560-018-0288-6