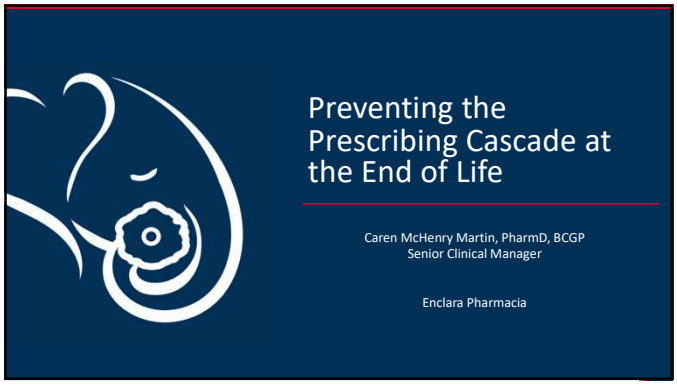


1

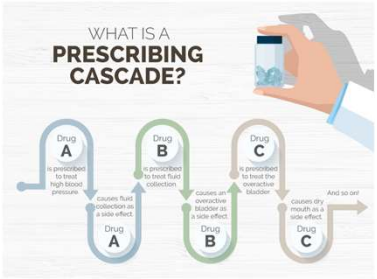
Objectives

- Discuss at least three potential benefits of deprescribing in hospice and palliative care, and the medication classes that can often be considered
- List at least five different medication adverse reactions that can be mistaken as new symptoms or conditions
- Recommend a strategy for prioritizing the medication evaluation to prevent the prescribing cascade and for deprescribing nonessential medications

2

What is the Prescribing Cascade?

- The sequence of events in which an adverse drug event is misinterpreted as a new medical condition, leading to the addition of another, potentially avoidable, medication
- Causes increased pill burden, medication costs and preventable adverse events



Rochon PA, Gurwitz JH. The prescribing cascade revisited. Lancet 2017;389:1778-80.

3

Part 1: Deprescribing

4

Polypharmacy

- Polypharmacy is associated with a 2.3-fold increase in adverse drug events
- Risk doubles if taking 9+ medications
- ADEs found in 35% of older people and 2 out of 3 nursing home residents
- 2015 survey found patients were taking an average of 10.2 medications during the last week of life

> At the time of hospice admission, Enclara's pharmacy call center sometimes receives profiles with upwards of **20 UNIQUE MEDICATIONS,** one-third of which are of questionable benefit to the patient during this phase of life."

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

5

Implications of Polypharmacy in Hospice

- Unintended Adverse Drug Events (ADEs)
- 4X increase in the risk of an ADE as medication burden increased from three medications to eight medications in hospice patients
- Cost
- Patient/Family member concerns
- Pill burden
- Medication errors
- Diversion
- Waste

6

More Medications, More Problems

- 13% risk of an interaction between TWO medications
- 82% risk of an interaction when taking >7 medications
- For every additional medication, a person's risk of harm increases by 7% to 10%
- 100% risk of an interaction when taking >10 medications

Goldberg R., Mabee J., Chan L., Wong S. (1996) Drug-drug and drug-disease interactions in the ED: analysis of a high-risk population. *Am J Emerg Med* 14: 447-450.
Working Group on Medication Overload. Brookline, MA: Lown Institute, 2020. https://lowninstitute.org/reports/eliminating-medication-overload-a-national-action-plan/. Accessed February 2, 2021.

7

Are We Paying Attention?

A study of nearly 38,000 adult patients admitted to hospice with primary diagnosis of end stage respiratory disease

- 21% of patients had claims for inhalers within last 30 days of life
- 13% of patients had claims for inhalers within last 14 days of life
- 7% of patient had claims for inhalers within last 7 days of life

Stevenson MH, Protus BM, Amanda G. Lovell AG, et al., A Pharmacoeconomic Study of Respiratory Medications for Hospice patients with End-Stage Respiratory Disease, Journal of Palliative Medicine 2022:25:12, 1782-178.

8

Important Deprescribing Concepts

Time to Benefit

Legacy Effect

9

Time to Benefit

Eprognosis.ucsf.edu

10

Legacy Effect

- Legacy effect refers to long-term sustained benefits after a period of intensive treatment intervention, even after the intervention is stopped
- First studied in diabetes, with the results of the DCCT and UKPDS trials
  - The benefits of good glycemic control (microvascular and macrovascular) persisted even when the intervention was stopped
- Also seen in trials of lipid therapies and antihypertensives
- The bottom line: when there has been early intervention and good control, effects linger after medications are stopped
- Duration, intensity, and initial timing are important (before damage is done)

11

Deprescribing Tools

Tool	Description
Beers criteria[6]	An evidence-based list of potentially inappropriate medications that are best avoided, prescribed at reduced dosage or with caution, or carefully monitored in older adults and in those with certain diseases or syndromes
STOPP/START criteria[4]	A Screening Tool of Older People's Prescriptions (STOPP) and Screening Tool to Alert to Right Treatment (START)
Deprescribing.org	4 evidence-based guidelines to support clinicians in safely reducing or stopping medication in 4 specific drug classes: proton pump inhibitors, benzodiazepine-receptor agonists, antipsychotics, and antihyperglycemics
Medication Management Instrument for Deficiencies in the Elderly (MedMaIDE)[27]	Addresses issues surrounding medication compliance and management in the home setting
Medi-Cog[28]	A 7-minute tool designed to assess cognitive literacy and pillbox skills in order to optimize medication safety. It is a combination of the Mini-Cog, a validated cognitive screen, and the Medication Transfer Screen (MTS), a pillbox skills test.
Appropriate Medications for Older people (AMO)–Tool[29]	Composed of 8 open-ended questions. Developed for the long-term care setting, the tool does not provide specific, rigid prescribing criteria, but asks open-ended questions and, therefore, relies strongly on interpretation by the prescriber.
Good Palliative-Geriatric Practice Algorithm[30]	Assists with drug discontinuation in the outpatient setting. Asks the prescriber to consider drug indication, dose, benefits, and potential adverse effects.

McGrath K, Hajjar ER, Kumar C, et al. Deprescribing: A simple method for reducing polypharmacy. The J of Fam Practice. 2017; 66(7): 436-445.

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Deprescribing Tool: STOPPFRAIL v. 2

Screening **T**ool of **O**lder **P**ersons **P**rescriptions in **Frail** adults with limited life expectancy

System	Medications to Consider Deprescribing
A. General	Any drug the patient is not taking consistently, or which is lacking clear clinical indication, or for which symptom is resolved
B. Cardiology	Lipid-lowering, antihypertensives, anti-anginal therapies
C. Coagulation	Anticoagulants, anti-platelets, aspirin
D. Central Nervous System	Neuroleptic antipsychotics, memantine
E. Gastrointestinal	PPIs, H2 receptor antagonists
F. Respiratory	Theophylline, leukotriene antagonists
G. Musculoskeletal	Calcium, vit D, osteoporosis medications, long-term oral NSAIDs, long term oral corticosteroids
H. Urogenital	BPH and OAB medications
I. Endocrine	Diabetes medications
J. Miscellaneous	Vitamins and supplements

Approaching end of life: development and validation of STOPPFRAIL Version 2 Age Ageing 2021

13

Dementia Medications

14

FAST Criteria

Stage	Stage Name	Characteristic	Expected Untreated AD Duration (months)	Mental Age (years)	MMSE (score)
1	Normal Aging	No deficits whatsoever	--	Adult	29-30
2	Possible Mild Cognitive Impairment	Subjective functional deficit	--		28-29
3	Mild Cognitive Impairment	Objective functional deficit interferes with a person's most complex tasks	84	12+	24-28
4	Mild Dementia	IADLs become affected, such as bill paying, cooking, cleaning, traveling	24	8-12	19-20
5	Moderate Dementia	Needs help selecting proper attire	18	5-7	15
6a	Moderately Severe Dementia	Needs help putting on clothes	4.8	5	9
6b	Moderately Severe Dementia	Needs help bathing	4.8	4	8
6c	Moderately Severe Dementia	Needs help toileting	4.8	4	5
6d	Moderately Severe Dementia	Urinary incontinence	3.6	3-4	3
6e	Moderately Severe Dementia	Fecal incontinence	9.6	2-3	1
7a	Severe Dementia	Speaks 5-6 words during day	12	1.25	0
7b	Severe Dementia	Speaks only 1 word clearly	18	1	0
7c	Severe Dementia	Can no longer walk	12	1	0
7d	Severe Dementia	Can no longer sit up	12	0.5-0.8	0
7e	Severe Dementia	Can no longer smile	18	0.2-0.4	0
7f	Severe Dementia	Can no longer hold up head	12+	0-0.2	0

Avalonmemorycare.com/the-seven-stages-of-dementia-understanding-the-fast-scale/
https://www.gwpmed.com/image/631/stage-fast-hospice-score-assessment-72

15

Donepezil and Memantine for Moderate to Severe AD

- Study done by Howard, et al of 295 community-dwelling moderate-to-severe AD patients already treated with donepezil for at least 3 months (MMSE 5-13)
- Treatment groups – (1) donepezil + placebo, (2) memantine + placebo, (3) donepezil + memantine, (4) placebo + placebo; followed for a year
- Two outcomes
  - Score on MMSE (baseline MMSE was 9.1 to 9.2)
  - Caregiver-rated Bristol Activities of Daily Living Scale (BADLS) – Baseline was 26.9-28.6
- Clinically significant difference was defined as MMSE ≥ 1.4 point increase or greater and BADLS ≥ 3.5 point decrease or greater
- Donepezil + memantine showed no clinically significant difference than donepezil alone; and donepezil only showed clinical significance in patients with baseline MMSE ≥ 10
- No clinically significant difference on BADLS

Howard, McShane, Lindesay, et al. *N Engl J Med.* 2012;366(10):893-903.

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Guidelines for Deprescribing Dementia Medications

- STOPPFRAIL v2: discontinue memantine in patients with moderate to severe dementia, unless it has clearly improved BPSD; no consensus on ChEIs
- Deprescribing.org: discontinue if significant cognitive/functional decline over the past six months in patients who have taken for more than 1 year; also discontinue if no noticeable benefit or severe disease
- Beers list: CHEIs (donepezil, rivastigmine, galantamine) can cause bradycardia; avoid in patients with syncope due to bradycardia
- European Consensus 2018: for patients with prognosis $\leq$ 3 months, use of drugs for Alzheimer's dementia "inadequate"

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Adverse Effects and Bottom Line

- Memantine – dizziness, headache, confusion, constipation
- ChEIs – nausea, vomiting, diarrhea, anorexia, insomnia, fatigue, muscle cramps, bradycardia, syncope
- Bottom line:
  - Dementia medications are less helpful and potentially more harmful in advanced disease (FAST 7) based on adverse effects, unless there is a clear benefit with distressing behaviors (memantine only)
  - Might have value in patients admitted for other primary diagnosis with a comorbid diagnosis of dementia/Alzheimer's Disease (FAST 6 or less)
- Taper over 2 weeks to discontinue

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Conversation Starters

One of the things we try to do in hospice care is decrease the amount of pills the patient has to take. This also makes things easier for the caregiver.

Research shows there's not really any evidence that says the dementia medications provide any benefit at the end of life. And sometimes they can cause side effects like decreasing appetite or causing problems with sleep.

What do you think about changing this medication to every other night for a week and then stopping it if we don't see any changes?

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Cardiovascular Medications

20

Lipid Lowering Medications

- Time to Benefit: One year or longer (exception: following acute coronary event)
  - Treating 100 adults (aged 50-75 years) without known cardiovascular disease with a statin for 2.5 years prevented 1 MACE in 1 adult. There is no evidence of a mortality benefit.
- Recent meta-analysis showed LEGACY effect on all cause mortality and CVD mortality in those taking statin for primary prevention
- Not much impact in last year of life:
  - Kutner, et al - 381 patients within 1 year of death, taking a statin
  - 20.3% of those who discontinued a statin died by 60 days (median 229 days)
  - 23.8% of those who continued statin died by 60 days (median 190 days)
- Lipid lowering medications can be stopped without tapering

Yourman LC, Cenzer IS, Boscardin WJ, Nguyen BT, Smith AK, Schonberg MA, Schoenborn NL, Widera EW, Orkaby A, Rodriguez A, Lee SJ. Evaluation of Time to Benefit of Statins for the Primary Prevention of Cardiovascular Events in Adults Aged 50 to 75 Years: A Meta-analysis. JAMA Intern Med. 2021 Feb 1;181(2):179-185.
Nayak A, Hayen A, Zhu L, *et al* Legacy effects of statins on cardiovascular and all-cause mortality: a meta-analysis *BMJ Open* 2018;8:e020584. doi: 10.1136/bmjopen-2017-020584
Kutner JS, Blatchford PJ, Taylor DH Jr, Ritchie CS, Bull JH, Fairclough DL, Hanson LC, LeBlanc TW, Samsa GP, Wolf S, Aziz NM, Currow DC, Ferrell B, Wagner-Johnston N, Zafar SY, Cleary JF, Dev S, Goode PS, Kamal AH, Kassner C, Kvale EA, McCallum JG, Ogunseitan AB, Pantilat SZ, Portenoy RK, Prince-Paul M, Sloan JA, Swetz KM, Von Gunten CF, Abernethy AP. Safety and benefit of discontinuing statin therapy in the setting of advanced, life-limiting illness: a randomized clinical trial. JAMA Intern Med. 2015 May;175(5):691-700. doi: 10.1001/jamainternmed.2015.0289. Erratum in: JAMA Intern Med. 2015 May;175(5):869.

21

Cardiovascular: STOPPFrail v2

Antihypertensives:

- Carefully reduce or discontinue these drugs in patients with persistent systolic blood pressure (SBP) <130 mmHg.
  - An appropriate SBP target in frail older people is 130–160 mmHg
  - Before stopping, consider whether the drug is treating additional conditions (e.g., beta-blocker for rate control in atrial fibrillation, diuretics for symptomatic heart failure).

Anti-anginal therapy (specifically nitrates, ranolazine):

- None of these anti-anginal drugs have been proven to reduce cardiovascular mortality or the rate of myocardial infarction.
- Aim to carefully reduce and discontinue these drugs in patients who have had no reported anginal symptoms in the previous 12 months AND who have no proven or objective evidence of coronary artery disease.

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Legacy Effect: Antihypertensive Medications

In a systematic review of mostly middle aged and early older people without history of cerebrovascular or cardiovascular events

- 37% of patients remained normotensive six months after withdrawing therapy; 40% at one year; 26% at 2 years or longer
- One in four people can be successfully withdrawn from antihypertensive therapy for 2 years or longer
- Monotherapy, lower blood pressure before withdrawal, and body weight were predictors of successful withdrawal
- BP trajectories continually decline in the last 14 years of life regardless of treatment

Delgado J, Bowman K, Ble A, Masoli J, Han Y, Henley W, Welsh S, Kuchel GA, Ferrucci L, Melzer D. Blood Pressure Trajectories in the 20 Years Before Death. JAMA Intern Med. 2018 Jan 1;178(1):93-99.
Van der Wardt V, Harrison JK, Welsh T, Conroy S, Gladman J. Withdrawal of antihypertensive medication: a systematic review. J Hypertens. 2017 Sep;35(9):1742-1749.

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Deprescribing Antihypertensive Medications

- Evaluate co-morbid conditions
  - Atrial fibrillation (beta blocker, nondihydropyridine)
  - Heart failure (ACEi/ARB, loop diuretic)
- GRADUALLY withdraw if possible (especially beta blockers, alpha agonists)
- Monitor for angina, anxiety, headache, palpitations
- Symptoms are unlikely with BP <180/110 mmHg

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Conversation Starters - Statins

It's really great that you have taken that cholesterol medication all these years and you never had a heart attack!

Research shows that since you've been so good about taking it, we can actually stop the medicine now and you will continue to have all the good effects from it for quite some time.

Sometimes people complain of getting more muscle aches from these medicines, and we definitely want to avoid that. What do you think about stopping this medication now?

25

Conversation Starters – Blood Pressure Medications

Your blood pressure is really well controlled, and seems to be running at about 110/70.

You've done a great job of taking your medications and you've done such a great job that I think we could actually back off on them now.

We have research that has shown that a lot of people in hospice care can taper off these medications and their blood pressure stays controlled.

This has the added benefit of making sure you don't get effects from your blood pressure being too low, which might make you dizzy or even make you fall.

What do you think about cutting the dose of this in half for a week or so and see how you do?

Then we can decide if we want to keep decreasing it or keep it as is.

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Diabetes

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Deprescribing for Diabetes

STOPPFrail v2:

- De-intensify therapy
- Avoid HbA1c targets (HbA1C <7.5% [58 mmol/mol] associated with net harm in this population)
- The goal of care is to minimize symptoms related to hyperglycemia (e.g., excessive thirst, polyuria) and reduce chance of hypoglycemia

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Deprescribing For Diabetes

Think about what the medication actually does

- All non-insulin diabetes medications are known to individually lower hemoglobin A1c (HbA1c) by approximately 0.5-1.5%
- A 1% difference in HbA1c translates to an average blood glucose change of about **30 mg/dl**
- Impaired renal function limits the use of most oral diabetes meds
- Evidence suggests that the majority of hospice patients will be asymptomatic with glucose levels in the 200-300s mg/dl
- Other factors that can cause/worsen hypoglycemia include inconsistent diet, lack of appetite, liver mets, GI tumors, bowel obstruction, renal insufficiency

HbA1c (%)	Glucose (mg/dl)
5	97 (76-120)
6	126 (100-152)
7	154 (123-185)
8	183 (147-217)
9	212 (170-249)
10	240 (193-282)
11	269 (217-314)
12	298 (240-347)

American Diabetes Association; 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2021. Diabetes Care 1 January 2021; 44 (Supplement 1): S73–S84.

29

Diabetes Deprescribing: Legacy Effects

What about preventing micro- and macrovascular damage?

- Seventeen years after starting the DCCT trial, those in the tight glycemic control arm had 42% risk reduction for any CV event and 57% risk reduction for nonfatal MI, stroke, or death from CV disease
- Twenty years after starting the UKPDS trial, the risk of MI and death from any cause decreased by 12-32% in the various treatment subgroups

Nada Lakhenpaung, Sandra A. Ham, Yue Gao, Howard H. Moffet, Jennifer Y. Liu, Elbert S. Huang, Andrew J. Karter; The Legacy Effect in Type 2 Diabetes: Impact of Early Glycemic Control on Future Complications (The Diabetes & Aging Study). Diabetes Care 1 March 2019; 42 (3): 416–426.

30

Conversation Starters

Now that you're in hospice care, one of our goals is to focus on your quality of life and not worry so much about things like keeping your blood sugars so tightly controlled.

Since you've done such a great job controlling your sugars up until now, we have research that has proven you will continue to reap the benefits of those efforts for quite a while, even if you start having sugars that are higher.

What do you think about stopping some of these diabetes medications and we can even stop checking your sugars unless you are feeling like they are running too high?

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Antithrombotics

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Deprescribing Antithrombotics: Quantifying the Risk

Concern	Annual Risk % (without tx)	Recommended discontinuation of therapy
Stroke from mechanical heart valve	10-91%	
Stroke from nonvalvular atrial fib	**Average 5% ;** Up to 17% based on risk factors (but probably more like 3-10%)	
Stroke from PAF	Depends on burden (**average 5%;** up to 17% but probably more like 3-10%)	
Recurrent VTE non-cancer	5-9%	
VTE in active cancer	0.5%	
VTE recurrence in cancer	15%	
Ischemic event post Acute Coronary Syndrome	10%	6-12 months?
Recurrent Stroke	11-15% within first year	
Thrombus After PCI	6-12%	12 months

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Deprescribing in Atrial Fibrillation: Quantifying Risk with CHA_2DS_2-VASc

Risk Factor	Score
C – Congestive Heart Failure	1
H – Hypertension history	1
A –Age 75 years	2
D – diabetes mellitus	1
S_2 – Prior stroke or TIA	2
V – vascular disease	1
A – age 65-74	1
Sc –Sex category (female)	1

Score	Absolute Risk per Year
0	0.2%
1	0.6%
2	2.2%
3	3.2%
4	4.8%
5	7.2%
6	9.7%
7	11.2%
8	10.8%
9	12.2%

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Deprescribing Antithrombotics: Assessing Bleeding Risk with HAS-BLED

- Uncontrolled hypertension
- Renal disease (Cr >2.26)
- Liver disease
- Hx Stroke
- Prior bleeding
- Unstable INR on warfarin
- Age >65 years
- Other anticoag meds (ASA, NSAID, antiplatelet)
- Alcohol use (>8 drinks per week)

# risk factors	Annual bleeding risk
1	3.4
2	4.1
3	5.8
4	8.9
5	Probably 10% or greater "Very high risk"

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Bleeding Risk

Age > 65 years	Previous bleeding	Conditions: Cancer (especially metastatic), kidney failure, liver failure, thrombocytopenia, previous stroke, diabetes, anemia
Medications: Antiplatelet therapy, NSAID therapy	Poor anticoagulant control	Comorbidity and reduced functional capacity
Recent surgery	Frequent falls	Alcohol misuse

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What About Aspirin Alone?

- There is some proven benefit for stroke prevention in atrial fib and recurrent stroke (approx. 30% ASA vs 60% DOAC/warfarin)
- Per 2021 CHEST update
  - *In patients with an unprovoked proximal DVT or PE who are stopping anticoagulant therapy and do not have a contraindication to aspirin, we suggest aspirin over no aspirin to prevent recurrent VTE (weak recommendation, low-certainty evidence)*
- There is still a bleed risk (the risk is similar to the DOACs)
  - Consider adding PPI for GI protection

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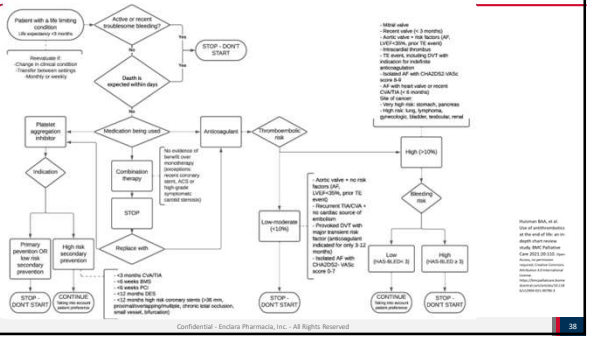
Antithrombotic Deprescribing Decision Tool



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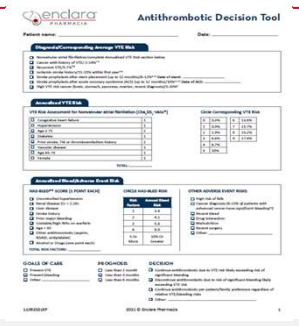
Enclara Antithrombotic Decision Tool



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Conversation Starters

It's really important to think about both the risks and benefits of the anticoagulant (antiplatelet) medication you're taking. Your primary care doctor has been doing that all these years, and up until now, the benefit of you taking the medication was big enough that it outweighed the risk of bleeding that it can cause.

Now that you're in hospice care, however, we know that your risks for having a pretty significant bleed while taking these medications is higher. It's likely that your risk of bleeding is actually HIGHER than any benefit the medication can provide as far as lowering your risk of a blood clot or stroke. And the bleeding that might occur can be pretty devastating and probably not something we can reverse. We sometimes actually have patients who die from the bleeding.

With that in mind, I wonder what you think about stopping this anticoagulant (antiplatelet) medication now?

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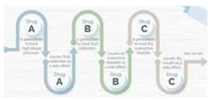
Part 2: Symptom or Side Effect?



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Medication AE #1: Opioid-Induced Neurotoxicity

Symptoms	Contributing Factors
Severe sedation	High dose
Delirium	Rapid dose escalation
Hallucinations	Dehydration
Myoclonus, tremors, seizures	Impaired renal function
Hyperalgesia	Concomitant infection
Allodynia	Other psychoactive/sedating medications

⚠

Muscle relaxants
Benzodiazepines
Seizure medications
Antipsychotics

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Medication AE #2: Anticholinergic Effects

Dry mouth	Swallowing difficulty	Constipation	Paralytic ileus	Nausea or vomiting
Increased heart rate	Urinary retention	**Difficulty in urinating**	**Blurred vision**	Dry eyes
Exacerbation or precipitation of acute angle-closure glaucoma	Decreased sweating	Drowsiness or sedation	**Dizziness**	Hallucinations
Delirium	Restlessness	Irritability	Nervousness	Slurred speech
	Impaired concentration	Confusion	Memory impairment	

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Medication AE #2: Anticholinergic Effects

Dry mouth	Swallowing difficulty	Constipation	Paralytic ileus	Nausea or vomiting
Increased heart rate	Urinary retention	Difficulty in urinating	Blurred vision	Dry eyes
Exacerbation or precipitation of acute angle-closure glaucoma	Decreased sweating	Drowsiness or sedation	Dizziness	Hallucinations
Delirium	Restlessness	Irritability	Nervousness	Slurred speech
	Impaired concentration	Confusion	Memory impairment	

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Anticholinergic Medications

Table 4. Anticholinergic Risk Scale*

3 Points	2 Points	1 Point
Amitriptyline hydrochloride	Amantadine hydrochloride	Carbidopa-levodopa
Atropine products	Baclofen	Entacapone
Benztropine mesylate	Cetirizine hydrochloride	Haloperidol
Carisoprodol	Cimetidine	Methocarbamol
Chlorpheniramine maleate	Clozapine	Metoclopramide hydrochloride
Chlorpromazine hydrochloride	Cyclobenzaprine hydrochloride	Mirtazapine
Cyproheptadine hydrochloride	Desipramine hydrochloride	Paroxetine hydrochloride
Dicyclomine hydrochloride	Loperamide hydrochloride	Pramipexole dihydrochloride
Diphenhydramine hydrochloride	Loratadine	Quetiapine fumarate
Fluphenazine hydrochloride	Nortriptyline hydrochloride	Ranitidine hydrochloride
Hydroxyzine hydrochloride and hydroxyzine pamoate	Olanzapine	Risperidone
Hyoscyamine products	Prochlorperazine maleate	Selegiline hydrochloride
Imipramine hydrochloride	Pseudoephedrine hydrochloride–triprolidine hydrochloride	Trazodone hydrochloride
Meclizine hydrochloride	Tolterodine tartrate	Ziprasidone hydrochloride
Oxybutynin chloride		
Perphenazine		
Promethazine hydrochloride		
Thioridazine hydrochloride		
Thiothixene		
Tizanidine hydrochloride		
Trifluoperazine hydrochloride		

*To calculate the Anticholinergic Risk Scale score for a patient, identify medications the patient is taking and add the total points for each medication.

Medication Type	Examples
Anti-nausea medications	Hydroxyzine, meclizine, promethazine, scopolamine, prochlorperazine
Parkinson's medications	Benztropine, trihexyphenidyl
Antispasmodics	Hyoscyamine, glycopyrrolate, homatropine, scopolamine, atropine, belladonna
Urinary meds	Oxybutynin, tolterodine, trospium, darifenacin, solifenacin
Antipsychotics	Chlorpromazine, fluphenazine, loxapine, thioridazine, clozapine, olanzapine
Antihistamines	Diphenhydramine, doxepin, hydroxyzine, meclizine, chlorpheniramine
Muscle relaxants	Tizanidine, orphenadrine
Antidepressants	Amitriptyline, desipramine, doxepin, imipramine, nortriptyline, paroxetine

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Anticholinergic Burden

ACBCalc.com

Sialogogues
Laxatives
Artificial tears
Antiemetics
Antipsychotics
Anxiolytics

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Medication AE #3: Serotonin Toxicity/Withdrawal

Toxicity	Withdrawal
Agitation/anxiety/restlessness	Anxiety
Disorientation	Insomnia or vivid dreams
Tremors/hyperreflexia/ muscle rigidity	Flu-like symptoms, including achy muscles and chills
Increased BP	Headaches
Tachycardia/cardiac arrhythmias	Dizziness
Increased body temp	Tiredness
Flushed skin/shivering/diaphoresis	Irritability
Vomiting/diarrhea	Nausea
Tachypnea	
Dry mucous membranes	Electric shock sensations

Medications

Antidepressants
Tramadol
Buspirone
Migraine medications
Ondansetron/metoclopramide
Cyclobenzaprine
Opioids
Antipsychotics
Dextromethorphan
Levodopa

Anxiolytics
Sedative/hypnotics
Muscle relaxants
Antiemetics

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Medication AE #4: Edema

Calcium channel blockers (amlodipine, felodipine, nifedipine)	NSAIDs	Steroids
Pioglitazone (Actos®)	Hormonal therapy: estrogen, testosterone	Pramipexole (Mirapex®)
Gabapentin (>1800 mg/day)	Pregabalin	Rare: omeprazole, lansoprazole, pantoprazole

Diuretics

Evidence of a gabapentinoid and diuretic prescribing cascade among older adults with lower back pain. J Am Geriatr Soc 2021 Oct; 69:2842. (https://doi.org/10.1111/jgs.17312).

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Medication AE #5: Sedation/Fatigue

- Antihistamines
- Antidepressants (TCAs, SSRIs, mirtazapine)
- BP meds (beta blockers, clonidine)
- Muscle relaxants
- Opioids
- Anticonvulsants (gabapentin, pregabalin)

steroids
methylphenidate

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Medication AE #6: Constipation

Opioids	Anticholinergics (ipratropium, tiotropium)	Anti-Parkinsonian drugs (benztropine)	Anti-psychotics (chlorpromazine)
Antihistamine (diphenhydramine)	Tricyclic antidepressants (amitriptyline)	Calcium channel blockers (verapamil, diltiazem)	Clonidine
	Iron, calcium	Diuretics	

Laxatives

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So Now What Do We Do?

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Preventing the Prescribing Cascade

- ✓ **Inquiry:** *"Could my patient's new symptom be caused by a drug they are taking rather than a new medical condition?"*
- ✓ **Medication review**: *"What's new or changed in how my patient is taking medications?*
  - Pill count
  - PRN use pattern
  - Indications still relevant?

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Is This An Opportunity for Deprescribing?

- Difficulty Swallowing
  - *"This might be a good time to look at the medications the patient is taking to see if we can decrease or stop any of them"*
- Functional Decline
  - *"When we see declines like this, we always want to look at the medications to see if they are all still beneficial"*
- Unclear Goals of Care
  - *"It sounds like you are frustrated with all the medications, so let's talk about whether we could decrease or stop some of them."*
- Adverse Reaction from Medication
  - *"I'm worried that this symptom might actually be an adverse reaction to a medication, so let's talk about whether we might want to change or stop the medication."*
- Lack of Medication Benefit
  - *"It's possible that these medications might actually be causing more problems than they are fixing (e.g., hypoglycemia, hypotension, dizziness) so let's look at tapering them off and seeing how things go."*

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Medication AE	Medication(s)
Neurotoxicity (Severe sedation, delirium/hallucinations, tremor, seizure, myoclonus, hyperalgesia/allodynia)	Opioids
Anticholinergic Effects (dry mouth, sedation, blurred vision, difficulty urinating, constipation, others) *(can't see can't pee can't poop, can't spit)*	Antihistamines, scopolamine, promethazine, prochlorperazine, hyoscyamine, atropine, olanzapine, doxepin, meclizine, amitriptyline, paroxetine, others
Serotonin Effects (Mental status changes, cardiac changes, nausea/vomiting/diarrhea, others)	Antidepressants, tramadol, buspirone, migraine medications, ondansetron, metoclopramide, cyclobenzaprine, opioids, antipsychotics, dextromethorphan, levodopa
Edema	Amlodipine, NSAIDs, steroids, hormones, pramipexole, higher dose gabapentin, pregabalin, PPIs
Nausea	All meds; great time to deprescribe!
Sedation/Fatigue	Antihistamines, antidepressants (TCAs, SSRIs, mirtazapine), BP meds (beta blockers, clonidine), muscle relaxants, opioids, anticonvulsants (gabapentin, pregabalin)
Movement Disorders	Antipsychotics, metoclopramide, SSRIs, antiepileptics, tricyclic antidepressants, bronchodilators, amiodarone, opioids, methylphenidate, rivastigmine, gabapentin
Constipation	Opioids, anticholinergics, Parkinson's meds, antipsychotics, antihistamines, tricyclic antidepressants, calcium channel blockers (amlodipine, diltiazem), clonidine, iron, calcium, diuretics
Dyspnea	ACE inhibitors, NSAIDs, anticonvulsants, beta blockers, dementia meds, antihypertensives, antibiotics, antifungals, antiretrovirals, digoxin, opioids, chemo agents
Agitation/Delirium	Any medication affecting the brain or mood; anticholinergics, BP meds, antibiotics, steroids

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Deprescribing: Medications to Taper

Drug Class	Recurrence	Withdrawal	Rebound	Symptoms
Alpha blockers		X	x	Agitation, headache, hypertension, palpitations
ACEi/ARB	X			Heart failure, hypertension
Antianginals	x			Angina
Anticonvulsants	x	x		Anxiety, depression, seizures
Antidepressants	x	x		Anxiety, chills, depression, GI disturbance, headache, insomnia, irritability, myalgia, malaise
Antiparkinsons	x	x	x	Hypotension, psychosis, rigidity, tremor
Antipsychotics		x		Dyskinesia, insomnia, nausea, restlessness
Anticholinergics		x		Anxiety, nausea, headache, dizziness
Baclofen		x	x	Anxiety, agitation, confusion, depression, hallucinations, hypertonia, mania, nightmares, paranoia, seizures
Benzodiazepine		x		Agitation, anxiety, confusion, delirium, insomnia, seizures
Beta blockers	x	x		Angina, anxiety, hypertension, acute coronary syndrome, tachycardia
Corticosteroids	x	x	x	Anorexia hypotension nausea weakness, adrenal insufficiency, inflammatory response
Digoxin	x			Heart failure, palpitations
NSAIDs	x			Heart failure, hypertension
Opioids		x		Abdominal cramping, agitation, anger anxiety chills diaphoresis, diarrhea, insomnia

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.

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Questions?

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