

Prescribing Cascades

Lisa C Hutchison, PharmD, MPH, BCPS, BCGP, FCCP

Vice-Chair and Professor

UAMS College of Pharmacy

Little Rock, AR

Objectives

- Describe the significance of prescribing cascades in older adults
- List examples of common prescribing cascades
- Given a medication list, identify an inappropriate prescribing cascade.
- Evaluate alternative medications or treatments which help avoid prescribing cascades.

A 75 year old man with knee arthritis is prescribed naproxen, a non-steroidal anti-inflammatory agent

Two months later, at next visit, patient's blood pressure is elevated. He is diagnosed with hypertension and treated with amlodipine.

At the 1-month follow-up visit, patient complains of lower extremity edema. Furosemide and a potassium supplement are prescribed.

At the next visit 2 weeks later, the patient complains of stomach upset, so esomeprazole is prescribed.

At the next visit 2 months later, which is a wellness visit, concern over increased risk for fracture and due to esomeprazole prompts the clinician to add calcium and vitamin D to the patient's regimen.

Laboratory results from the wellness visit show a decreased vitamin B-12 level. He is prescribed Vitamin B-12 injections and called to come back in 2 months for assessment of memory loss. Donepezil was added.

At the next visit 1 month later, patient's wife identifies he has problems with urinary incontinence. Tolterodine is prescribed.

Prescribing Cascade Definition

- New symptoms are interpreted as a new medical condition that requires medication therapy when symptoms are medication side effects that can be avoided by deprescribing the culprit agent, using non-pharmacologic treatment, or switching to another agent without that side effect
- Often unintentional and an underrecognized contributor to polypharmacy

- Intentional prescribing cascade if culprit agent cannot be deprescribed
  - Example: Opioids at end of life with laxatives

McCarthy LM et al. Drugs & Aging 2022; 39:829-40

Prevalence of Prescribing Cascades

- Varies with medication
  - 1.4%-4.9% for CCB with diuretic compared with 0.5%-0.7% with other antihypertensive agents
  - Often a different prescriber than the one who prescribed the CCB (64%)
- Varies with setting
  - Community-dwelling older adults for 5 medications was 0.4%-3.2%
  - Post-discharge from a hospital for 20 selected index medications was 2% out of 24,282 patients

Doherty AS et al. Ann Fam Med 2025;23:315-24;
Mohammad AK et al. Pharmacoepi Drug Safety 2026;
35:e70305

Outcomes associated with Prescribing Cascades

- Increased pill burden
- Reduced quality of life
- Additional costs
- Unnecessary risk for adverse drug events
  - Calcium channel blocker (CCB) with added diuretic or laxative
  - Gabapentinoid with added diuretic
  - Cholinesterase inhibitor with anticholinergic drug or sleep agent
  - Diuretics with potassium supplements

McCarthy LM et al. Drugs & Aging 2022; 39:829-40;

Systematic Review of Prescribing Cascades

- Community-dwelling adults over 18 years old
- Prescription of medication with potential to cause ADR resulting in prescription of further medication
- New medication to treat ADR or reduce risk of an ADR
- In primary care and community settings
- All study types except case reports
- Included 101 studies

Doherty AS et al. Pharmacol Res Perspect. 2022; 10:301008

Systematic Review

- Alimentary tract and metabolism-9 studies
  - SGLT2 inhibitors, thiazolidinediones, anti-diabetic agents, acid reducing agents, metoclopramide
- Cardiovascular system-22 studies
  - ACE inhibitors, CCBs, beta blockers, dihydropyridines, antihypertensives, statins, amiodarone
- Nervous system-29 studies
  - Neuroleptics/antipsychotics, anxiolytics, anti-Parkinson agents, SSRIs, antidepressants, lithium, gabapentinoids, anti-epileptic agents, cholinesterase inhibitors, memantine, varenicline
- Multiple medications/classes-16 studies
- Blood, Skin, GU/sex hormones, Infection, Musculoskeletal, Respiratory, Eye
  - 1-4 studies
- 7 Exploratory studies-looking for any signals

Doherty AS et al. Pharmacol Res Perspect. 2022; 10:301008

Most Common Identified in Systematic Review

Culprit Medication	Side Effect	Cascade Drug
Amiodarone	Thyroid disease	Thyroid hormone agents
Calcium Channel Blockers	Peripheral edema	Diuretics
Inhaled Corticosteroids	Oral candidiasis	Topical antifungal agents
Antipsychotic Agents	Parkinsonian symptoms	Anti-Parkinson medication
Cholinesterase Inhibitors	Urinary incontinence	Urinary anticholinergics
ACE Inhibitors	Cough	Antitussives
Metoclopramide	Parkinsonian symptoms	Anti-Parkinson medication
Non-steroidal Anti-inflammatory Drugs	GI symptoms	Anti-ulcer medication

Doherty AS et al. Pharmacol Res Perspect. 2022; 10:301008

Delphi Process to Identify Prescribing Cascades

- Literature review supplemented by examples from clinicians
- Final list of 139 unique prescribing cascades underwent 3 rounds of ranking by 30-40 expert panelists from 6 countries
- Experts identified these factors as most important:
  - Severity of side effect
  - Ability of clinician to anticipate and manage the side effect
- Final list of 30 prescribing cascades; 9 were highly rated

McCarthy LM et al. Drugs & Aging 2022; 39:829-40

ThinkCascades Tool

Culprit Medication	Side Effect	Cascade Drug
Alpha-1 receptor blocker	Orthostatic hypotension, dizziness	Vestibular sedative
Antipsychotic	Extrapyramidal symptoms	Antiparkinsonian agent
Benzodiazepine	Cognitive impairment	Cholinesterase inhibitor or memantine
Benzodiazepine	Paradoxical agitation or agitation secondary to withdrawal	Antipsychotic
Calcium channel blocker	Peripheral edema	Diuretic
Diuretic	Urinary incontinence	Overactive bladder medication
NSAID	Hypertension	Antihypertensive
SSRI/SNRI	Insomnia	Sleep agent
Urinary anticholinergics	Cognitive impairment	Cholinesterase inhibitor or memantine

McCarthy LM et al. Drugs & Aging 2022; 39:829-40

Systematic Review Vs. ThinkCascades Tool

Culprit Medication	Side Effect	Cascade Drug
Alpha-1 receptor blocker	Orthostatic hypotension, dizziness	Vestibular sedative
Antipsychotic	**Extrapyramidal symptoms**	**Antiparkinsonian agent**
Benzodiazepine	Cognitive impairment	Cholinesterase inhibitor or memantine
Benzodiazepine	Paradoxical agitation or agitation secondary to withdrawal	Antipsychotic
Calcium channel blocker	**Peripheral edema**	**Diuretic**
Diuretic	Urinary incontinence	Overactive bladder medication
NSAID	Hypertension	Antihypertensive
SSRI/SNRI	Insomnia	Sleep agent
Urinary anticholinergics	Cognitive impairment	Cholinesterase inhibitor or memantine

McCarthy LM et al. Drugs & Aging 2022; 39:829-40;
Doherty AS et al. Pharmacol Res Perspect. 2022; 10:301008

Recent Studies

Received: 2 May 2025 | Revised: 20 October 2025 | Accepted: 2 December 2025

DOI: 10.1002/bcp.70425

SHORT COMMUNICATION

Prevalence and impact of prescribing cascades in community-dwelling adults: Longitudinal analysis of the Irish longitudinal study on ageing (TILDA)

Ann Sinéad Doherty[1] | Rose Anne Kenny[2,3] | Frank Moriarty[2,4] | Fiona Boland[5] | Barbara Clyne[6] | Tom Fahey[7] | Denis O' Mahony[8,9] | Emma Wallace[1]

WILEY

ORIGINAL ARTICLE OPEN ACCESS

Occurrence of Potential Prescribing Cascades After Hospital Discharge: A Cohort Study

Atiya K. Mohammad[1,2] | Johanna H. M. Driessen[3,4] | Jacqueline G. Hugtenburg[5] | Alex Marmorale[6] | Carl Siegert[7] | Patricia M. L. A. van den Bemt[2] | Petra Denig[2] | Fatma Karapinar-Çarkıt[1,3,4]

[1]Department of Clinical Pharmacy, OLVG Hospital, Amsterdam, the Netherlands | [2]Department of Clinical Pharmacy and Pharmacology, University Medical Centre Groningen, Groningen, the Netherlands | [3]Department of Clinical Pharmacy & Toxicology, Maastricht University Medical Center+,

Community-dwelling Patients

- Longitudinal aging cohort (50 YO and above) over a 9-year period in Ireland
- ThinkCascades 9 dyads evaluated in eligible sample of 1153 patients
- Overall prevalence of prescribing cascade was 2.1%
- Five of 9 dyads identified occurring 0.9%-8.3%
  - NSAID/antihypertensive 8.3%
  - CCB/diuretic 2.8%
  - Alpha-blocker/vestibular sedative 1.8%
  - Benzodiazepine/antipsychotic 1.1%
- Compared to those 50-64 years old, those over age 75 were almost 5 times more likely to experience prescribing cascade

Doherty AS et al. Ann Fam Med 2025;23:315-24

What about hospitalized patients?

- Cohort study followed hospitalized adult patients prescribed 1 of 20 medications for 12 months for initiation of a marker medication often used for ADRs associated with the index drug
- Mean age 68.9 years, 45.1% female
- Potential prescribing cascade in 502 out of 24,292 index users
- Antibiotics prescribed for ACE inhibitor-associated cough and UTIs in 4.0% and 12.3% of ACE inhibitor users respectively
- Antihistamines and antitussives prescribed for ACE inhibitor-associated cough in 2.9% and 5.4% of ACE inhibitor users respectively

Mohammad AK et al. Pharmacoepi Drug Safety 2026; 35:e70305

Prescribing Cascades at Transitions of Care

- For cascades seen in 10+ patients (12 out of 20 medications), 31.8%-92.8% were prescribed outside the hospital
  - Multiple healthcare providers frequently involved in prescribing cascades
  - Transitions of care as a place to identify and resolve prescribing cascades
  - May underestimate some prescribing cascades because symptoms/side effects treated with OTC agents

Mohammad AK et al. Pharmacoepi Drug Safety 2026; 35:e70305

Always Ask:
Could this Symptom be a Side Effect?

Choosing Wisely®
An initiative of the ABIM Foundation

American Geriatrics Society
AGS Geriatrics Healthcare Professionals
Leading Change. Improving Care for Older Adults.

Ten Things Clinicians and Patients Should Question

9

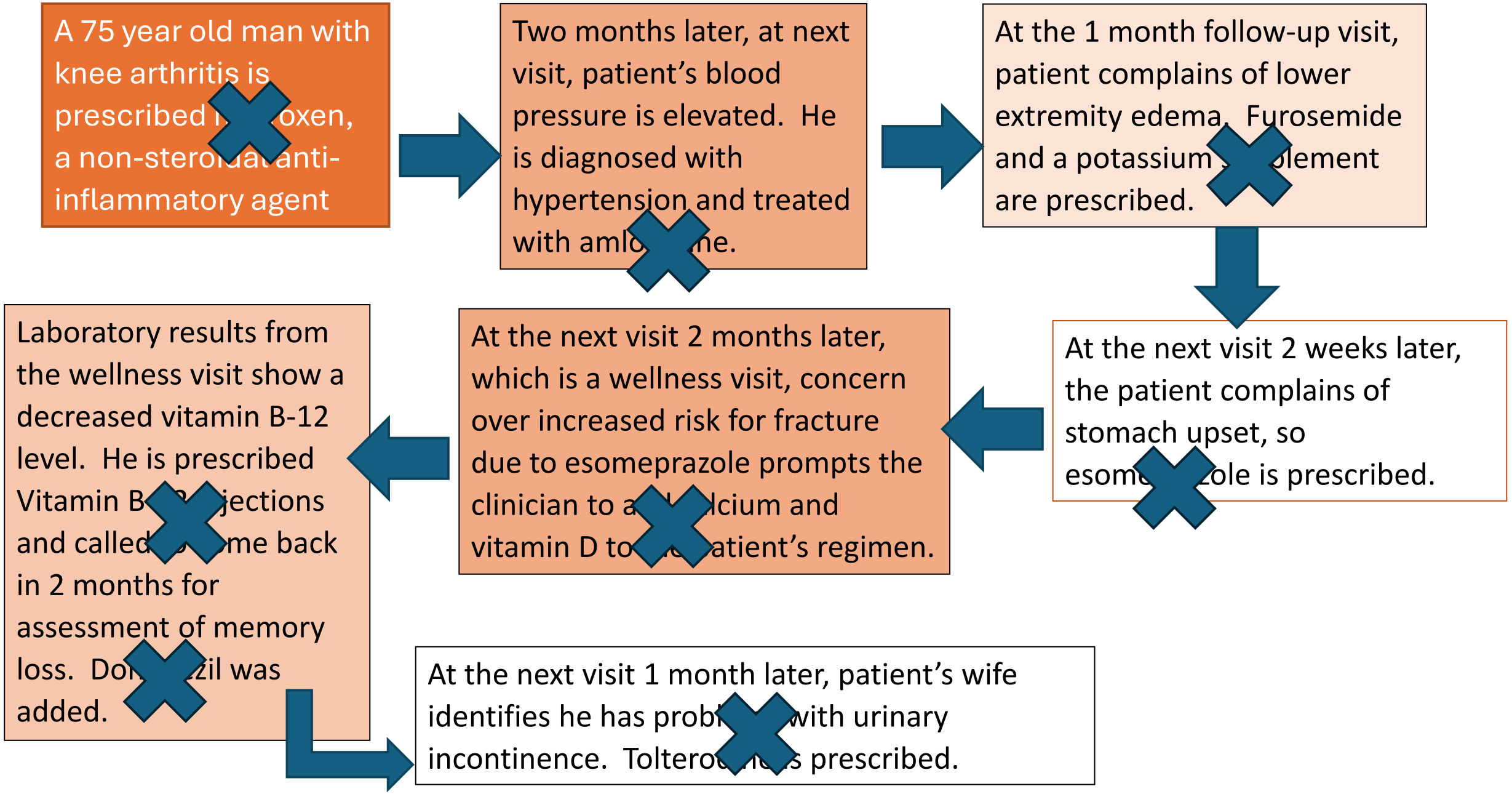
Don't prescribe a medication without conducting a drug regimen review.

Older patients disproportionately use more prescription and non-prescription drugs than other populations, increasing the risk for side effects and inappropriate prescribing. Polypharmacy may lead to diminished adherence, adverse drug reactions and increased risk of cognitive impairment, falls and functional decline. Medication review identifies high-risk medications, drug interactions and those continued beyond their indication. Additionally, medication review elucidates unnecessary medications and underuse of medications, and may reduce medication burden. Annual review of medications is an indicator for quality prescribing in vulnerable elderly.

https://www.americangeriatrics.org/sites/default/files/inline-files/AGS%20Choosing%20Wisely%20Poster.pdf/

Let’s Revisit our prescribing cascade




A 75 year old man with knee arthritis is prescribed naproxen, a non-steroidal anti-inflammatory agent
Two months later, at next visit, patient's blood pressure is elevated. He is diagnosed with hypertension and treated with amlodipine.
At the 1 month follow-up visit, patient complains of lower extremity edema. Furosemide and a potassium supplement are prescribed.
At the next visit 2 weeks later, the patient complains of stomach upset, so esomeprazole is prescribed.
At the next visit 2 months later, which is a wellness visit, concern over increased risk for fracture due to esomeprazole prompts the clinician to add calcium and vitamin D to the patient's regimen.
Laboratory results from the wellness visit show a decreased vitamin B-12 level. He is prescribed Vitamin B12 injections and called to come back in 2 months for assessment of memory loss. Donepezil was added.
At the next visit 1 month later, patient's wife identifies he has problems with urinary incontinence. Tolterodine is prescribed.

Alternatives to Consider

A 75 year old man with knee arthritis is prescribed naproxen, a non-steroidal anti-inflammatory agent

Physical therapy
Exercise

Topicals with Menthol

Topical Diclofenac

Two months later, at next visit, patient's blood pressure is elevated. He is diagnosed with hypertension and treated with amlodipine.

Stop naproxen
Weight loss
Low sodium diet
ACE inhibitor,
Thiazide diuretic

At the 1-month follow-up visit, patient complains of lower extremity edema. Furosemide and a potassium supplement are prescribed.

Replace amlodipine with ACE inhibitor
Replace furosemide with elevation, compression, exercise, sodium reduction, massage or spironolactone

American Geriatrics Society Beers Criteria® Alternatives Panel. Am Geriatr Soc. 2025; 73:2657-77; 2023

Alternatives to Consider

At the next visit 2 weeks later, the patient complains of stomach upset, so esomeprazole is prescribed.

Stop potassium.
Non-pharmacologic options: raise HOB, avoid trigger foods, avoid eating late in evening, (if obese, lose weight); OTC antacids;
H2 blockers

At the next visit 2 months later, which is a wellness visit, concern over increased risk for fracture due to esomeprazole prompts the clinician to add calcium and vitamin D to the patient's regimen.

Stop esomeprazole.
Non-pharmacologic options: Weight-bearing exercise; High calcium/vitamin D foods

Laboratory results from the wellness visit show a decreased vitamin B-12 level. He is prescribed Vitamin B-12 injections and called to come back in 2 months for assessment of memory loss. Donepezil was added.

Non-pharmacologic options: Mediterranean diet, Exercise, oral Vitamin B-12 tablets; Wait for memory loss assessment after B-12 replacement to start a medication

At the next visit 1 month later, patient's wife identifies he has problems with urinary incontinence. Tolterodine is prescribed.

Stop donepezil.
Manage fluids,
Bladder training;
Beta-3 agonist

American Geriatrics Society Beers Criteria® Alternatives Panel. Am Geriatr Soc. 2025; 73:2657-77; 2023

Deprescribing

- Not just “discontinuing medications”
- Identify, taper, discontinue medications whose harms outweigh benefits for an individual
- Tailored to patient’s care goals, level of functioning, life expectancy, values and preferences
- Reducing the dose of a medication with a high risk to benefit ratio is a success because the risk is lowered!
- Deprescribing studies support reduction in inappropriate medications, adverse effects, re-hospitalization and death.

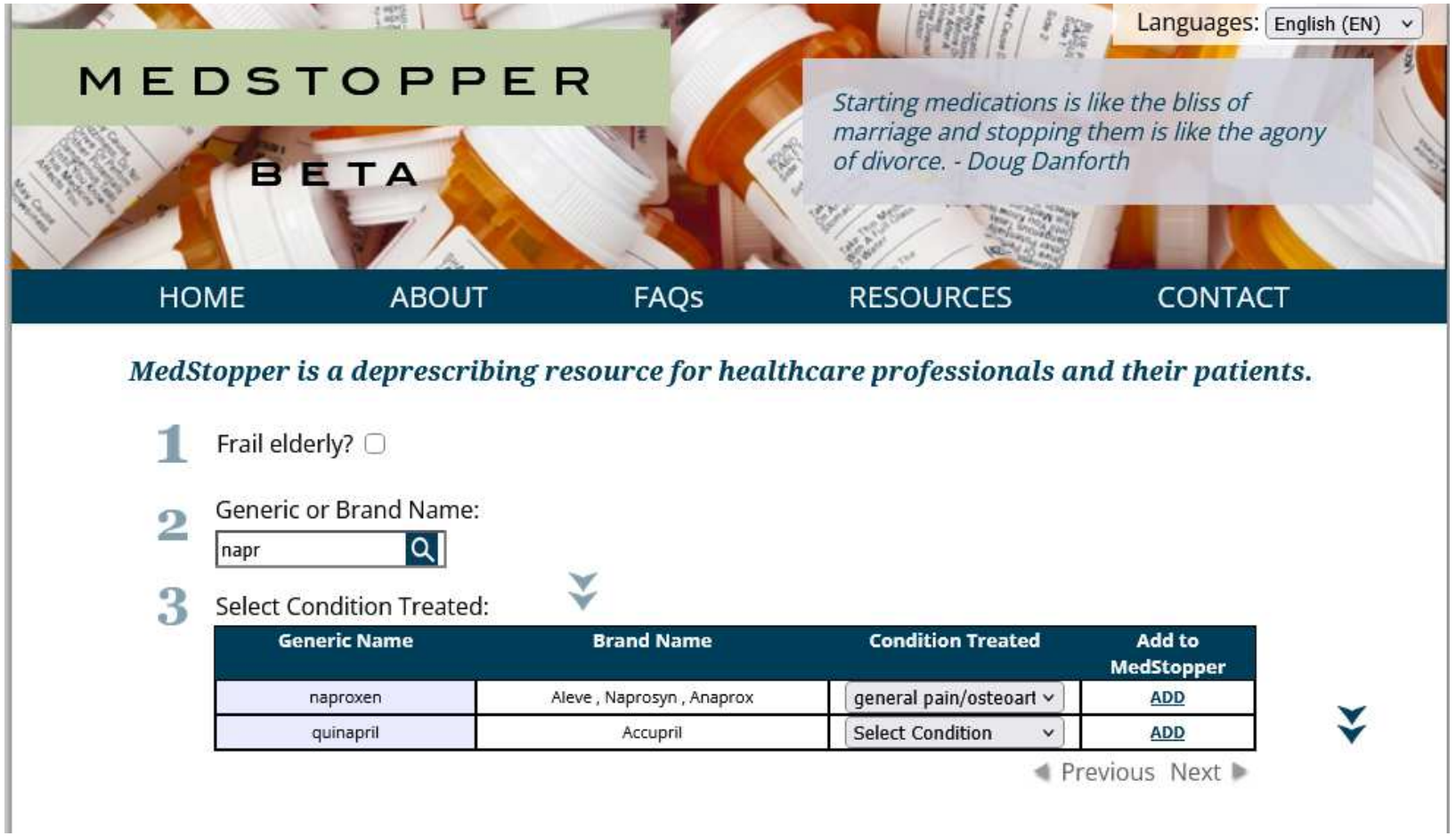
Scott IA. JAMA Intern Med. 2015;175:827-34; Carollo M, Crisafulli S, Vitturi G et al. J Amer Geriatr Soc 2024;72:3219-38.

Assessing Medications for Deprescribing

- Obtain a full medication history and then assess for:
  - Current valid indication
  - Duplication of therapy
  - Part of a prescribing cascade
  - Harm outweighs benefit
  - Ineffective or symptoms have resolved
  - Preventive medication vs. life expectancy and treatment goals
  - Unacceptable treatment burden; consider cost burden

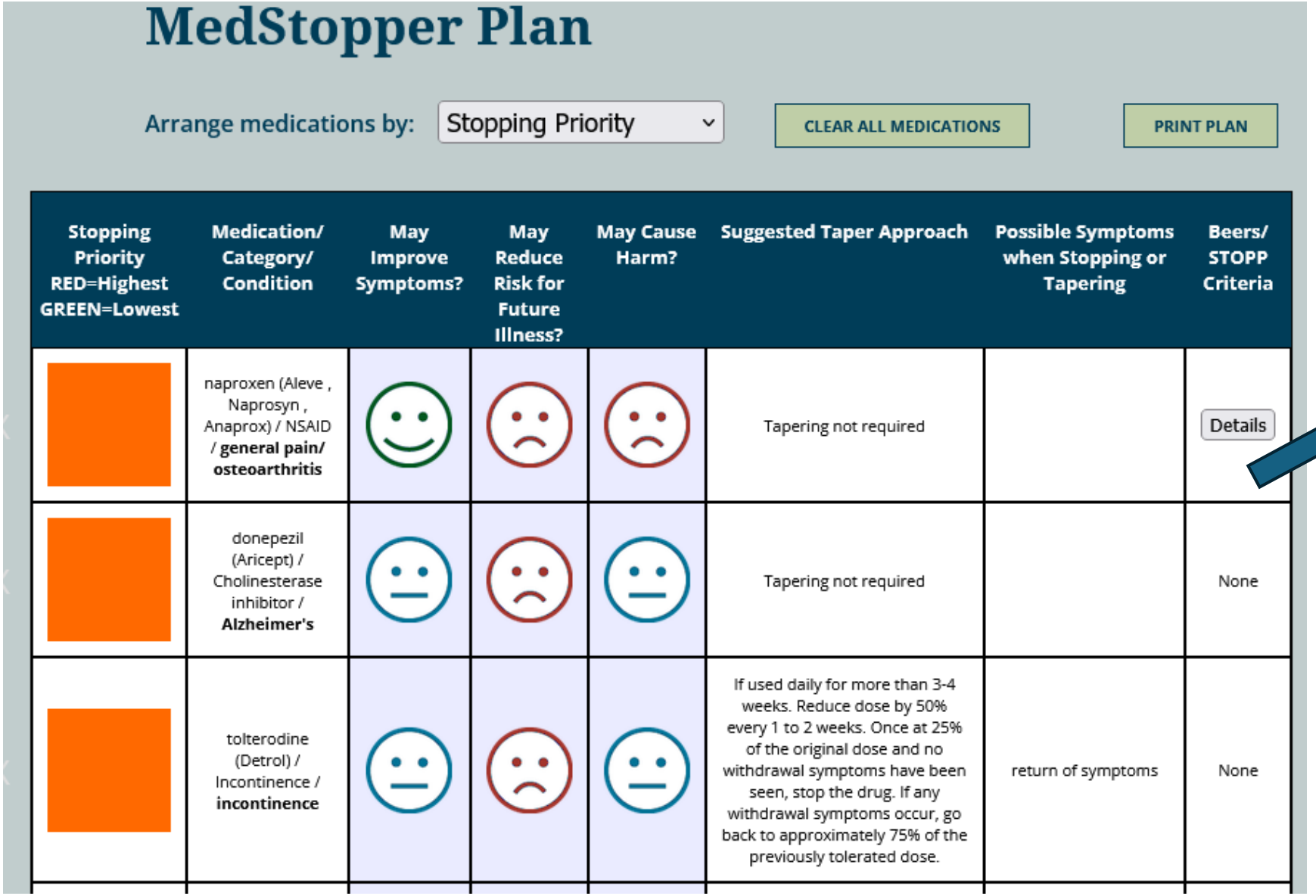
Halli-Tierney, et al. *Am Fam Physician*. 2019 Jul 1;100(1):32-38; Scott IA. JAMA Intern Med. 2015;175:827-34

Medstopper On-line Tool



https://medstopper.com/

Medstopper Plan



MedStopper Plan

Arrange medications by: Stopping Priority

CLEAR ALL MEDICATIONS

PRINT PLAN

Stopping Priority RED=Highest GREEN=Lowest	Medication/ Category/ Condition	May Improve Symptoms?	May Reduce Risk for Future Illness?	May Cause Harm?	Suggested Taper Approach	Possible Symptoms when Stopping or Tapering	Beers/ STOPP Criteria
	naproxen (Aleve , Naprosyn , Anaprox) / NSAID / **general pain/ osteoarthritis**				Tapering not required		Details
	donepezil (Aricept) / Cholinesterase inhibitor / **Alzheimer's**				Tapering not required		None
	tolterodine (Detrol) / Incontinence / **incontinence**				If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	return of symptoms	None

Naproxen-
Beers Criteria:
Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent (proton pump inhibitor or misoprostol)

https://medstopper.com/

	amlodipine (Norvasc) / Calcium antagonist dihydropyridine / **blood pressure**		 CALC / NNT		If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	chest pain, pounding heart, heart rate, blood pressure (re-measure for up to 6 months), anxiety, tremor	Details
	esomeprazole (Nexium) / Proton pump inhibitor / **heartburn/ GERD**				If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	return of symptoms, heartburn, reflux	Details
	vitamin B12 (cyanocobolamin) (multiple brands) / Vitamin B / **actual deficiency**				Tapering not required		None
	furosemide (Lasix) / Diuretic / **other**				If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	weight gain, swelling, shortness of breath	Details

Possible Deprescribing Plan

Medication	More Info, Taper or Alternatives	Priority	Ease
Naproxen	Alternatives	1	3
Amlodipine	Alternatives; taper	1	3
Furosemide	Taper	2	3
Potassium	Serum potassium?	2	1
Esomeprazole	Taper; bleeding risk-NSAID?	2	3
Calcium	Osteoporosis risk?	3	1
Vitamin D	Osteoporosis risk?	3	1
Vitamin B-12	Vitamin B-12 level after 3-6 mo	3	2
Donepezil	Risk; benefit after 3 months	2	2
Tolterodine	Taper	1	2

Most Patients Want Fewer Medications

- 80% of patients age 50-80 years would stop prescription medications if recommended by health care professional
  - Prefer to stop drugs for cardiac > arthritis > diabetes > psychiatric > lung
- Patients who disagree with deprescribing
  - Had doubts (condition would worsen, not sure of harms, general concern)
  - Valued medication as important/necessary
  - Avoided change (satisfied with current use or had long-term use)

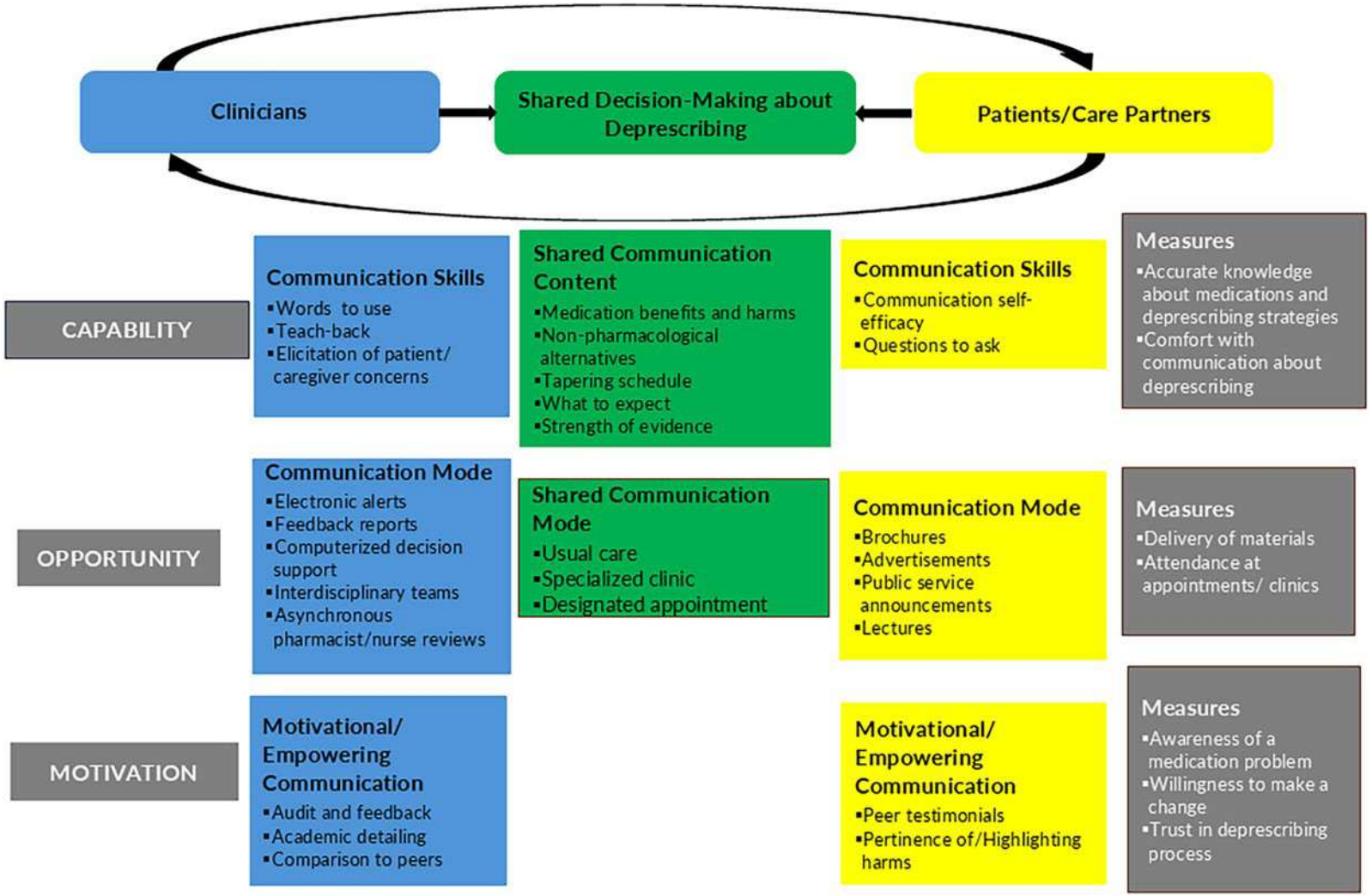
Vordenburg SE et al. J Gen Intern Med. 2024; 39:2631-3; Weir KR et al. JAMA Netw Open. 2023;6: 1-13

Communication with Patients

- FRAME Acronym
  - Fortify trust
  - Recognize patient willingness or barriers
    - Incorporate motivational interviewing
  - Align recommendations to goals of care
  - Manage cognitive dissonance
    - Address patient beliefs, concerns
  - Empower self-efficacy

Felton M, et al. J Palliat Med. 2019; 22:335-6.

Figure 1: Application of the COM-B Model to Deprescribing Communication



Fried T, Gnjidic D, Goyal P, et al. J Amer Geriatr Soc. 2026; 74:2059-63

Key Takeaways

- Prescribing cascades cause significant pill burden, cost burden, decreased quality of life and increased adverse drug effects
- Common prescribing cascades have been identified through consensus and systematic reviews.
- Review of a patient's medication list can reveal prescribing cascades ripe for intervention
- Alternatives include non-pharmacologic treatments or switching to a different medication

Questions?

HutchisonLisaC@uams.edu



Question 1

True or false:

The definition of a prescribing cascade is when new symptoms are interpreted as a new medical condition that requires medication therapy when symptoms are medication side effects.



Question 2

According to a survey of patients age 50-80 years, what percentage would be willing to stop prescription medications if recommended by a health care professional?

a. 20%

b. 50%

c. 80%

d. 100%



Question 3

True or false:

Prescribers should conduct a drug regimen review before prescribing a new medication.



Question 4

Which of the following is more likely associated with a prescribing cascade?

a. A patient requests a prescription for a new drug they saw on television

b. Multiple healthcare providers are prescribing medications

c. Patients that are 50-64 years old.

d. Patients in the hospital or nursing home



Question 5

A patient is started on lisinopril, an ACE inhibitor, for hypertension. About a week later he notices a cough.

What is the best plan for treating his cough?

a. Mucinex DM (guaifenesin and dextromethorphan)

b. Loratadine 10 mg

c. Sugar-free menthol cough drops

d. Change his hypertension medication



Thanks for your participation!

hutchisonlisac@uams.edu

