Optum Health Education™

Deprescribing in primary care

Erin Johnson, PharmD, BCCCP

July 23, 2025

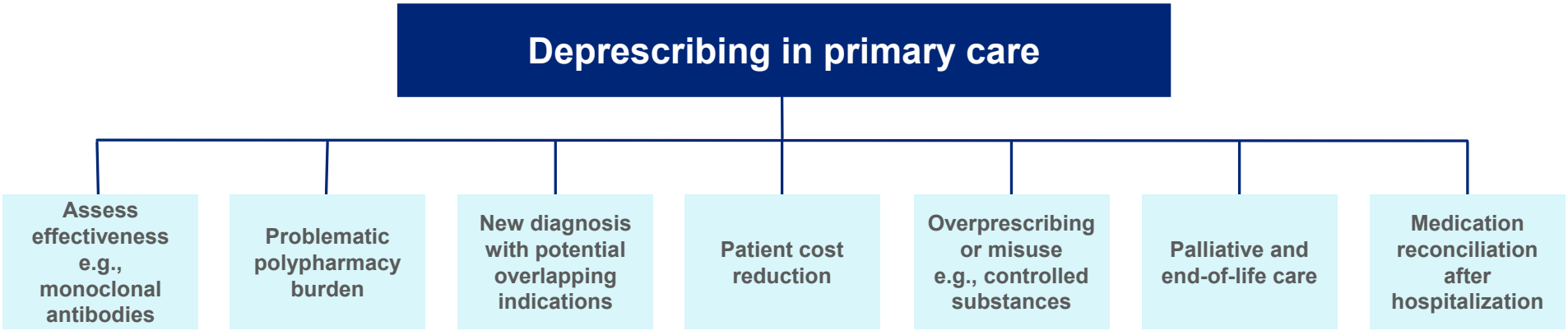
Objectives

- Explain the significance of deprescribing and associated goals for patients in primary care settings
- Recognize the challenges of problematic polypharmacy and learn how to pinpoint opportunities for deprescribing
- Describe how governance strategies can be employed to help identify and advocate for less apparent deprescribing initiatives

Agenda

1. Background
2. Considerations for deprescribing
3. Strategies to address deprescribing

Areas to consider deprescribing



The overall goal(s) of deprescribing is to improve patient outcomes by crafting a medication regimen that maintains quality of life, achieve goals, and minimize harm.

- Patient is experiencing adverse events e.g., a fall due to medication side effects
- Patient is having difficulty with medication regimen dosed multiple times per day e.g., reduce medication regimen complexity
- Problematic polypharmacy: inappropriate prescribing of multiple medications when intended benefit is unclear, prescribed to treat side effects of other medications etc.
- Medications intended for short-term use are not reassessed or stopped

Duerden & Payne, 2014, p.45) Study: Too Long a Duration Is a Type of Inappropriate Prescribing

Why deprescribing?

Deprescribing is the process of identifying and discontinuing potentially inappropriate or unnecessary medications to improve quality of life. Involves a stepwise, patient-centered process to reduce the risks and burden of taking multiple medications.

Polypharmacy is common in older adults

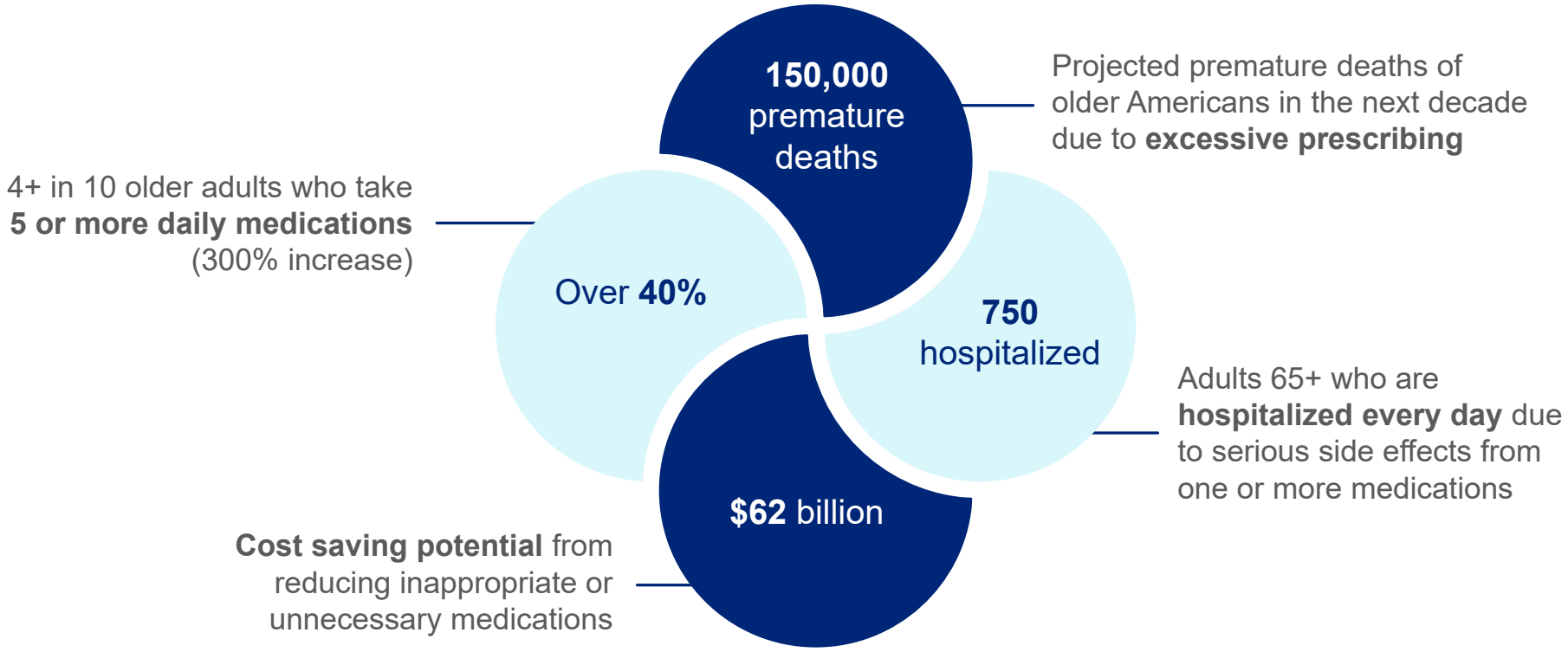
- A 2016 study, 36% of adults aged 62–85 were taking 5+ medications, up from 31% in 2005.
  - By 2030, nearly half of older adults may be affected
- Risk factors for polypharmacy include age >62, multiple health conditions, multiple prescribers/pharmacies, OTC self-treatment, and past hospitalizations.
- Poor medication tracking (e.g., outdated/inaccurate lists) increases risk.

Many clinical practice guidelines often overlook older adults with multiple comorbidities:

- ***Adherence to guidelines tends to result in increased medication burden***
- Following single-disease guidelines can increase medication burden e.g.,treating each chronic disease in isolation
- Guidelines are based on trials that typically exclude older adults with comorbidities.

1. Lindsay J, et al. 2014
2. McNeil MJ, et al. 2016
3. https://www.aafp.org/pubs/fpm/issues/2018/0500/p28.html

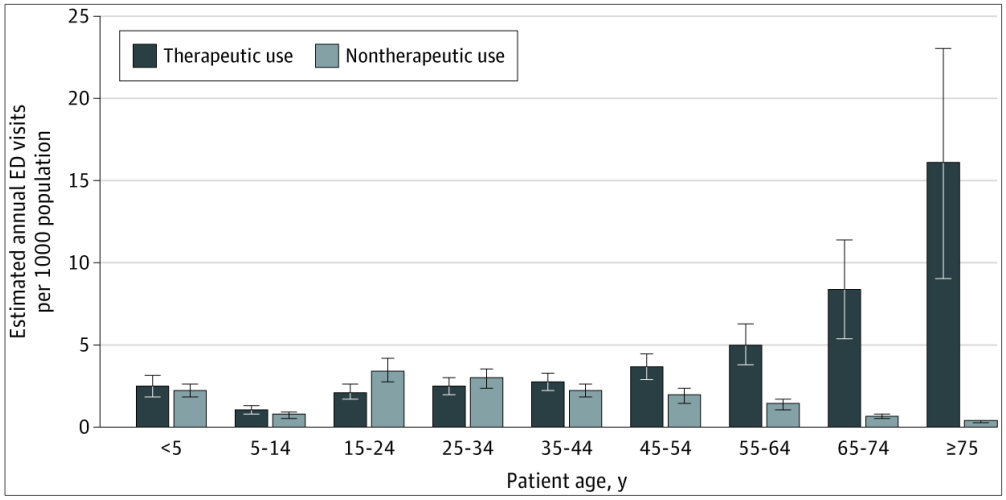
Medication Overload and Associated Outcomes



Emergency department visits related to adverse drug events

JAMA study reviewing ED visits to 60 EDs in the U.S. participating in the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance Project from 2017 to 2019

- 97000 cases reviewed
- Among patients > 65 years, ~96% of ED visits for ADEs involved therapeutic use, higher than any other age group
- In contrast, patients < 45 years had an estimated 53% of ED visits for ADEs involving nontherapeutic use of medications



Medication Safety Program CDC

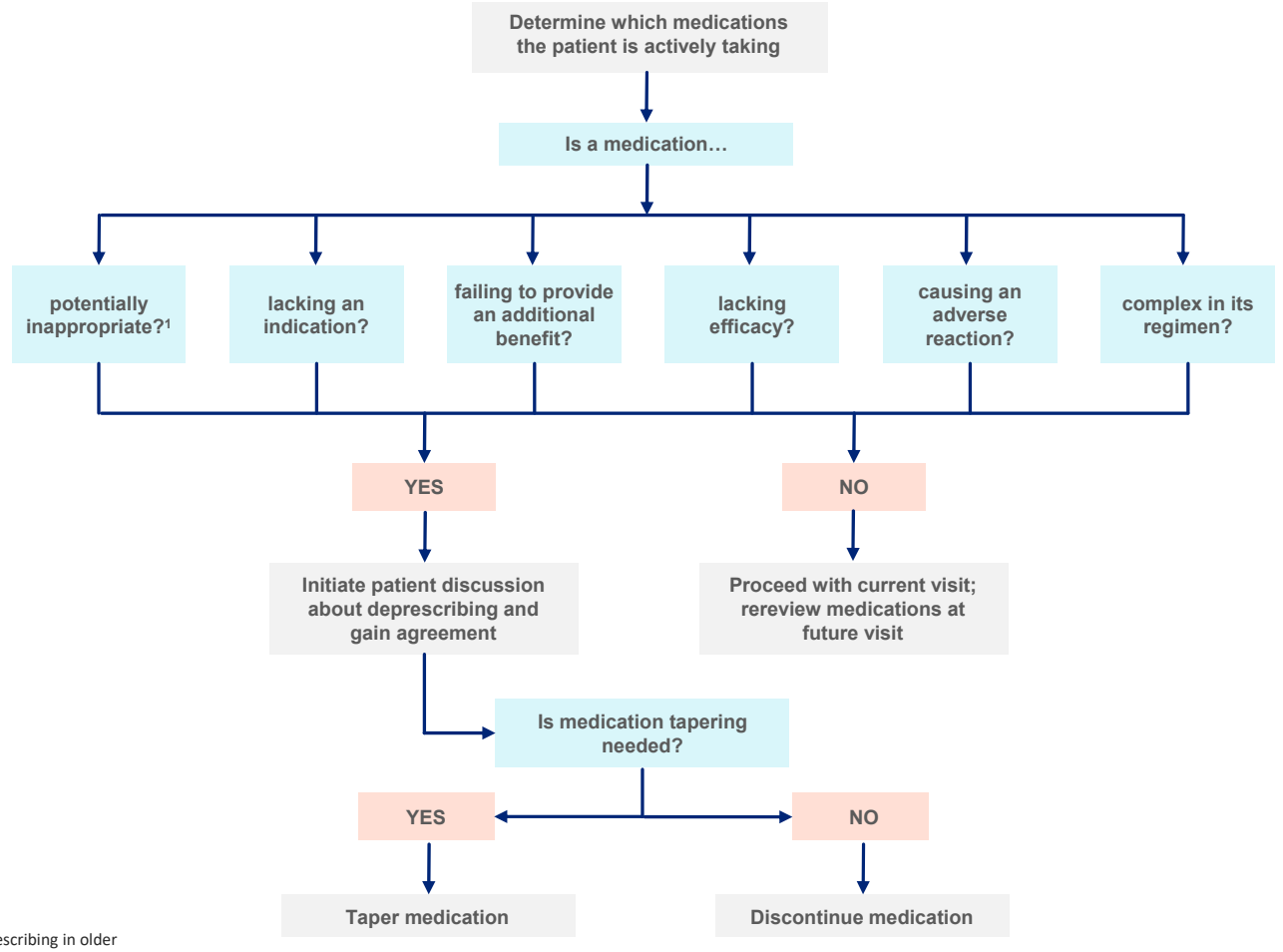
- More than 1.5 million people visit emergency departments for Adverse Drug Events (ADEs) every year, and almost 500,000 require hospitalization
- Adults ≥ 65 years visit emergency departments more than 600,000 times each year, twice as often as younger adults
- Leading causes of ED visits for ADEs for patients aged > 44
  - Anticoagulants (~1 in 5, or 21%)
  - Diabetes agents such as insulin (~1 in 7, or 14%)
- In contrast, the leading cause for ED visits related to ADE for adults aged 25-44 is nontherapeutic use of benzodiazepines and opioids

US Emergency Department Visits Attributed to Medication Harms, 2017-2019 | Emergency Medicine | JAMA | JAMA Network

A deprescribing algorithm

The deprescribing process has 4 key parts:

1. Conduct a thorough medication reconciliation through a brown bag review
2. Identify inappropriate, unnecessary, or harmful medications
   - Beers list, lack effectiveness, lack an indication, require long duration for effect
3. Plan deprescribing with the patient
   - Patients may be concerned about worsening symptoms
   - Consider tapering or discontinuing one medication at a time
4. Regularly re-review medication
   - Due to tapering or medications or withdrawal symptoms, the process should be closely monitored



1. Consider Beers list drugs, opioids, anticholinergics, NSAIDS, etc.

1. Page AT, Clifford RM, Potter K, Schwartz D, Etherton-Beer CD. The feasibility and effect of deprescribing in older adults on mortality and health: a systematic review and meta-analysis. *Br J Clin Pharmacol.* 2016;82(3):583-623.

Examples of medications to consider deprescribing – STOPPFrail criteria

- Medication that patients persistently fail to take or tolerate despite adequate education and consideration of all formulations
- Drugs without a clear clinical indication
- Drugs associated with symptoms that have resolved (e.g., pain, nausea, vertigo, pruritus)
- STOPPFrail-guided deprescribing significantly reduced polypharmacy and medication costs in frail older people

System	Drugs
Cardiology	• **Lipid-lowering therapies** • **Alpha-blockers for hypertension** • Anti-anginal therapy (nitrates, ranolazine)
Coagulation	• Anti-platelets for primary CV prevention • Aspirin for stroke prevention in atrial fibrillation
CNS	• **Neuroleptic antipsychotics in patients with dementia** • Acetylcholinesterase inhibitors and memantine
Gastrointestinal	• **PPI** and H2RA
Respiratory	• Theophylline and aminophylline • Montelukast for COPD
Musculoskeletal	• Calcium supplements/Vitamin D • Anti-resorptive/bone anabolic drugs for osteoporosis • Long-term NSAIDs • Long-term oral corticosteroids
Urogenital	• Drugs for BPH in patients with catheter • Drugs for overactive bladder
Endocrine	• **Anti-diabetic drugs – deintensify therapy**

Rationale for deprescribing

- Lipid-lowering therapies: must be prescribed for long-term to show benefit, in short term ADEs outweigh risks
- Antihypertensives: Strict blood pressure control is not required in very frail older people. Alpha blockers cause vasodilatation, leading to marked postural hypotension, falls and injuries
- Antipsychotics use in dementia: ↑ risk of somnolence and death despite modest efficacy
- PPI: Often continue to be used without an appropriate indication or for longer/higher dose than necessary
- DM meds: Avoid hypoglycemia and symptomatic hyperglycemia

Curtin D, et al. 2021.

Common inappropriate prescribing cascades

A prescribing cascade occurs when a medication is prescribed to treat or prevent the adverse effects of another medication leading to a new and unnecessary medication. Occurs when an adverse drug reaction (ADR) is misinterpreted as a new medical condition.

Examples include:

- Ibuprofen → hypertension → antihypertensive
- Metoclopramide → parkinsonism → levodopa/carbidopa
- Risperidone → parkinsonism → benztropine
- Amlodipine → edema → furosemide
- Gabapentin → edema → furosemide
- Ciprofloxacin → delirium → risperidone
- Lithium → tremor → propranolol
- Bupropion → insomnia → mirtazapine
- Donepezil → urinary incontinence → oxybutynin
- Amiodarone → tremor → lithium
- Venlafaxine → tremor → diazepam
- Beta-blocker → depression → antidepressant
- Amitriptyline → decreased cognition → donepezil
- Sennosides → diarrhea → loperamide
- Lorazepam → morning drowsiness → caffeine
- ACE inhibitors → cough → dextromethorphan
- Furosemide → hypokalemia → potassium supplement
- Nonsteroidal anti-inflammatory drug → acid reflux → H2 antagonist or PPI
- Omeprazole → low Vitamin B12 → B12 supplementation

Prescribing Cascades: How to Detect Them, Prevent Them, and Use Them Appropriately - PMC

Prudent Prescribing

Value and Therapeutics Committee

Mission

The National Value and Therapeutics Committee (V&T) serves as an advisory and governing body. It is a collaborative approach with clinicians and professionals to advance pharmaceutical care knowledge to promote clinically appropriate and value-conscious treatments, and to achieve positive patient outcomes

Roles and functions

The Committee's primary function is to review, evaluate, and approve clinical & budget impact recommendations to achieve high quality, value-focus, and improved health outcomes.

- The National Value and Therapeutics (V&T) Committee conducts cost-effective analyses for chosen topics by comparing costs and outcomes of different interventions to determine which drug provides the most value for the resources invested.
- They inform decision-makers on the efficiency of health interventions by comparing their costs to their outcomes (i.e., Is an intervention effective relative to its cost?).
  - Define the problem (Clinical Review)
  - Identify alternatives (Clinical Review)
  - Estimate costs (RWD)
  - Measure outcomes (RWD)
  - Calculate cost-effectiveness (HEOR)
  - Interpret results (HEOR)

Deprescribing in End-of-Life Care

What is palliative care?

“Beneficial **at any stage of a serious illness**, palliative care is an interdisciplinary care delivery system designed to anticipate, prevent, and manage physical, psychological, social, and spiritual suffering to optimize quality of life for patients, their families and caregivers. Palliative care can be **delivered in any care setting** through the collaboration of many types of care providers. Through early integration into the care plan of seriously ill people, palliative care **improves quality of life for both the patient and the family.”**

Per the Clinical Practice Guidelines for Quality Palliative Care 4th edition

Palliative care is a medical specialty focused on patients living with a serious illness.

Essential components of palliative include:

- Symptom management
- Alignment of care delivery with patient centered goals of care
- Care coordination

The value of palliative care

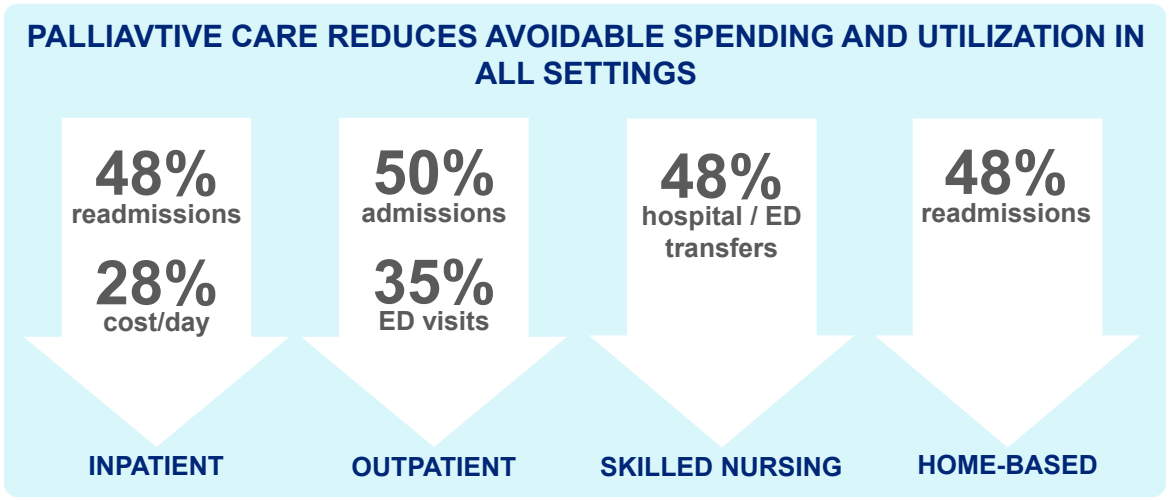
5% of Medicare beneficiaries die each year. 25% of Medicare spend occurs in the last 12 months of life.[1]

Palliative care in hospitals

- Reduce 30-day readmission rates and ICU utilization
- Save 9-25% of costs for each inpatient stay

Palliative care in home-based programs

- Save ACOs, health plans, and health systems as much as $12,000/person enrolled
- Reduce ER visits, hospital admissions, hospital readmissions, and hospital length of stay



Source: capc.org

1. Einav L, et al. 2018

Economic impact to deprescribing in Palliative Care

Medication assessment

- Cancer patients (≥ 65 yo) underwent a comprehensive geriatric assessment, using three screening tools. Mean ECOG score = 2
- The mean number of inappropriate medications = 12.5.
- 3 medications (mean) per patient were deprescribed
- 2/3 of patients reported a reduction in symptoms after deprescribing intervention.

Healthcare savings*

Avoided costs:
- $4282.27 per patient from deprescribing
- **Cost values for:**
  - Minor adverse event prevention ($220.00)
  - Major adverse event prevention ($2,200)
  - Medication teaching ($208.00)
  - Detailed medication history ($642.00)

Total intervention time:
- Approximately 30 minutes per patient (range of 18 to 77)

*The potential healthcare savings were assessed through application of University HealthSystem Consortium outcome cost data.

Commonly deprescribed medication classes

Medication class	Potential adverse events prevented
Vitamins/minerals (n=18)	Pill burden, ineffectiveness, drug interactions
Antihypertensives (n=11)	Fatigue, orthostatic hypotension, dizziness, falls
Statins (n=8)	Fatigue, myalgias, myopathies, lack of benefit
Benzodiazepines (n=7)	CNS depression, falls, delirium, somnolence
Aspirin/NSAIDS (n=6)	Gastrointestinal bleeding, lack of benefit
Proton pump inhibitors (n=6)	Hypocalcemia, hypomagnesemia, fractures, infections, chronic kidney disease, dementia
Omega-3 fatty acids (n=5)	Increase bleeding risk, pill burden
Electrolyte supplements (n=5)	Pill burden
Other (n=21)	Various adverse drug effects

Barriers to deprescribing

Patient/family

- Changing goals of care
- Attachment to medications
- Risk of abandonment
- Influential family members
- Confrontation with mortality
- Belief that medication discontinuation is suboptimal care

Prescribers

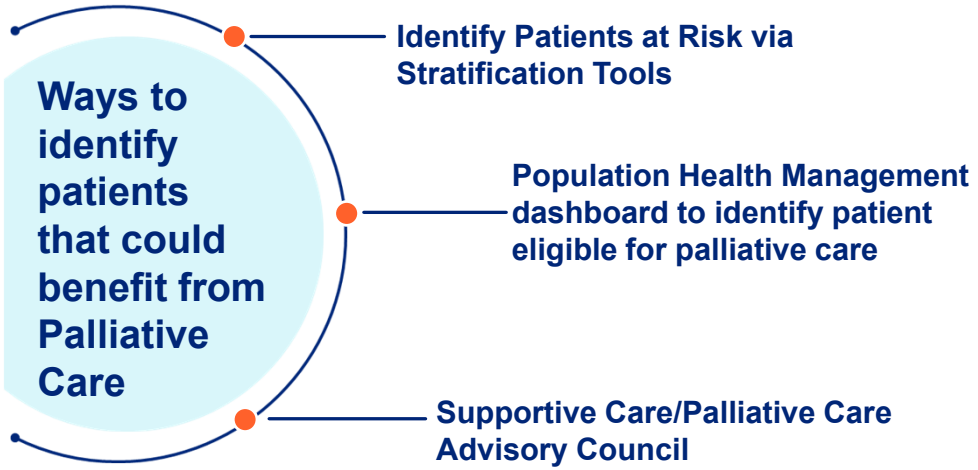
- Clinical complexity
- Multiple prescribers
- Risk of withdrawal side effects
- Risk of return of symptoms
- Limited information on harm of continuation or discontinuation
- Limited guidelines on deprescribing

Deprescribing in palliative care: general strategies

Multi-disciplinary approach to deprescribing in palliative care patients

Deprescribing is essential to optimize patient care by reducing medication burden, minimize the risk of adverse events and improve overall health outcomes for all patients, especially for frail seniors and patients with advanced illness.

1. Conduct a full medication review and consult pharmacist when available and appropriate.
2. Discuss goals of care and level of interest with deprescribing with the patient and patient's family.
3. Identify non-beneficial or inappropriate medications and consider deprescribing.
4. Conduct a specific follow-up with the clinician who initiated the deprescribing, the patient and patient's family.



Overactive Bladder Considerations

Overactive bladder treatments

Background

- The estimated U.S. prevalence of OAB (depending on the study) is **16 to 23%**.
- In 2007, the estimated economic impact of OAB both direct (medical and non-medical) and indirect (loss of productivity) was **66 billion dollars**.

Treatment:

- ***First-line is behavioral therapy***
- Second-line is medications (i.e., antimuscarinics, beta-3 adrenergic agonists)
  - Due to limited efficacy and significant side effects, bladder control symptoms should be reassessed after initiation
  - If symptoms have not improved, then the medication should be discontinued
- Third-line is Botox injections
- Fourth-line is surgical procedures.

Value & Therapeutics Committee and Optum recommends non-pharmacological behavioral therapies for treatment of overactive bladder symptoms before exposure to oral medications (i.e., anti-muscarinic agents or beta-3 adrenoceptor agonist agents)

Anticholinergics and beta agonists for treatment of overactive bladder

Table 1 – Product Summary

Medication (generic name)	Brand Name	Dose	Incidence of Side Effects (> 2%)	*Cost/Generic Available
Antimuscarinics				
Darifenacin extended-release (7.5 and 15mg tablets)	Enablex	7.5 to 15 mg once daily	dry mouth (20-35%), constipation(14-21%)	$65/yes
Fesoterodine extended-release (4 and 8mg tablets)	Toviaz	4mg to 8 mg once daily	dry mouth (19-35%), constipation (4-6%)	$39.50/yes
Oxybutynin immediate-release (5mg tablet)	Ditropan	5mg two to four times daily	dry mouth (72%), constipation (15%),UTI, insomnia, nervousness, dizziness, somnolence, headache, blurred vision, nausea, dyspepsia, urinary hesitation, urinary retention	$10/yes
Oxybutynin extended-release (4,10,15mg tablets)	Ditropan XL	5mg to 30mg once daily	dry mouth (35%), constipation (9%), diarrhea, headache, somnolence, dizziness	$17/yes
Oxybutynin transdermal (10% gel sachet [packet] or pump)	Gelnique	1 packet or pump once daily	dry mouth (7.5%), dizziness, application site reaction	$396/no
Oxybutynin transdermal 3.9mg patch	Oxytrol	1 patch twice per week	dry mouth (4-10%), constipation (3%), abnormal vision, application site pruritus	$680/no
	Oxytrol for Women			OTC $20/no
Solifenacin (5 and 10mg tablets)	Vesicare	5-10mg once daily	dry mouth (11-28%), constipation (5-13%), blurred vision	$10/yes
Tolterodine extended-release (2 and 4mg tablets)	Detrol LA	2 to 4mg once daily	dry mouth (23%), constipation (6%), somnolence	$60/yes
Tolterodine immediate-release (1 and 2mg tablets)	Detrol	1 to 2mg twice daily	dry mouth (35%), constipation (7%), dizziness, fatigue	$20/yes
Trospium extended-release (60mg tablet)	Sanctura XR	60mg once daily	dry mouth (11%), constipation (9%)	$130/yes
Trospium immediate-release (20mg tablet)	Sanctura	20mg once - twice daily	dry mouth(20%), constipation (10%)	$21/yes
Beta-3 adrenergic agonists				
Mirabegron (25 and 50 mg tablets)	Myrbetriq	25 to 50mg once daily	Hypertension (7.5-11.3%) , headache (2-3%)	$430/no
Vibegron (75mg tablets)	Gemtesa	75mg once daily	Headache (4%), diarrhea, nausea	$472/no

*Redbook WAC Pricing, accessed on 1/24/2023 (1-month supply)

- Consider dose modifications or changing to a different agent when patients experience a lack of efficacy or occurrence of side effects
- Combination therapy may increase efficacy, but will increase anticholinergic side effects
- To prevent dry mouth, consider extended-release or transdermal antimuscarinics rather than immediate-release products.
- Utilization for OAB medications exceeded $69 MIL with only 30% of data reported in 2022
- Mirabegron has the highest spend

Medications for the treatment of overactive bladder: V&T recommendation

Reassess after initiation

Non-pharmacological behavioral therapies are first-line

- Trial of pelvic floor exercises, lifestyle therapy, and behavioral changes
- Bladder training
- Add medication if initial treatments do not provide sufficient symptoms relief

Second-line treatment

- Initiate medication therapy if inadequate improvement with non-pharmacological behavioral therapies
- Current medication classes: antimuscarinics, beta-3 agonists

Limited efficacy with signification side effects

- No benefit in patients with persistent, irreversible urinary incontinence unless presence of painful detrusor hyperactivity
- Manage side effects of dry mouth, constipation, blurred vision, somnolence by adjusting the dose, increasing fluids, preventing constipation
- Medication adherence is a known issue due to side effects

Reassess after 4 to 8 weeks; if symptoms have not improved, discontinue.

Biologics for Specialty Use

Monoclonal Antibodies (mAbs): Considerations

mAbs are used for hematologic malignancies, solid tumors, immune disorders, hypercholesterolemia, asthma, osteoporosis, inflammatory bowel disease, myasthenia gravis, hemophilia, and drug reversal.

Cost and supply considerations

- High cost due to long and complex manufacturing process
- Expensive to patients
- Administration (e.g., office infusion or self-administered injection)
- Verify insurance coverage
- Biologics account for 2% of prescriptions but 37% of net drug spend

Choosing a biologic

- Requires detailed review of drug history for tried and failed past medications
- Generally, not recommended for first-line therapy
- Consider disease-drug interactions and drug-drug interactions
- Consider co-morbidities that may be treated with biologics as well

Patient-centered approach

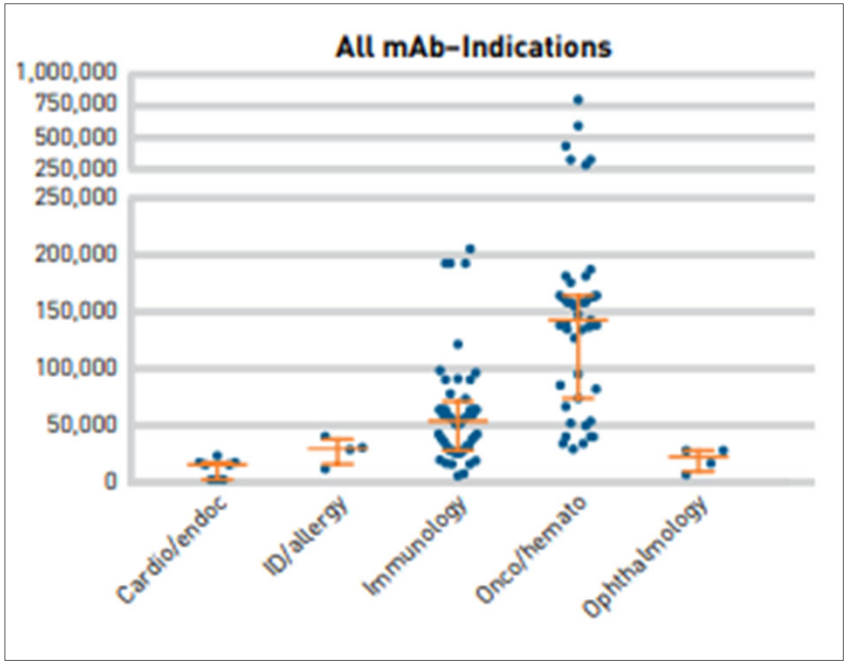
- Adherence-focused counseling
- Long-term use to see benefits
- Screening tests may be required (e.g., HIV, tuberculosis and hepatitis B and C) and any other required tests before starting biologic (e.g., bloods and x-rays)
- Increased risk of infection due to immunosuppression
- Use of biosimilars

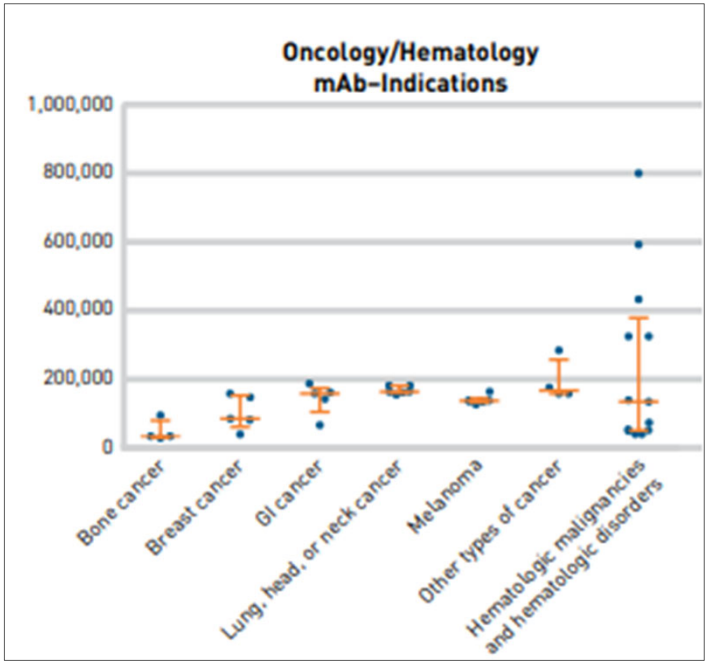
General principle: Reassess after 4 months; if symptoms have not improved, after 6 months, discontinue.

Full article: Cost and supply considerations for antibody therapeutics
Initiating biologics and biosimilars in practice: approach and consultation guidance - The Pharmaceutical Journal
https://meridian.allenpress.com/innovationsjournals-JQSH/article/1/1/4/434796/Pricing-of-Monoclonal-Antibodies-in-the-United

Cost Ranges for Monoclonal Antibodies

Annual Price of Treatment for mAb- FDA approved 1997-2016





In 2017, the average annual price of mAb was $96,731 with the annual price exceeding $100,000 for 32% of available mAbs.

Examples of cost-effectiveness reviews from ICER

The Institute of Clinical and Economic Review (ICER) has reviewed many biologic therapies, and few have been found to be cost-effective at current prices.

Drug	Indication	ICER Finding Related to Cost-Effectiveness
Dupilumab (Dupixent) 2021	Asthma, Atopic Dermatitis	Not cost-effective at current prices, price discount of at least 50% to reach cost-effectiveness
Omalizumab (Xolair) 2021	Severe Asthma	Not cost-effective at current prices, price discount of at least 50% to reach cost-effectiveness
Mepolizumab (Nucala) 2021	Severe Asthma	Not cost-effective at current prices, price discount of at least 50% to reach cost-effectiveness
Benralizumab (Fasenra) 2021	Severe Asthma	Not cost-effective at current prices, price discount of at least 50% to reach cost-effectiveness
Tezepelumab (Tezspire) 2021	Severe Asthma	Not cost-effective at current prices, price discount of at least 50% to reach cost-effectiveness
Adalimumab (Humira) 2017	RA, PsA, Crohn's	Not cost-effective at list price, price discount of 50-69% to reach cost-effectiveness thresholds
Ustekinumab (Stelara) 2020	Crohn's, UC	Not cost-effective at list price, price discount of 82% required to reach cost-effectiveness thresholds
Belimumab (Benlysta) 2021	Lupus nephritis	Cost-effective at list price
Inclisiran (Leqvio)	Hypercholesterolemia	Cost-effective at list price
Eculizumab (Soliris)	Myasthenia gravis	Not cost-effective at list price, price discount of 98% to reach cost-effectiveness thresholds
Lecanemab (Leqembi) 2023	Alzheimer's mild, Mild Cognitive Impairment	Not cost-effective due to limited net health benefits
Tocilizumab (Actemra)	RA	Cost-effective vs lower-cost alternatives (adalimumab)
Ocrelizumab (Ocrevus)	MS	Not cost-effective at current prices, price discount of 50% to reach cost-effectiveness
ofatumumab (Kesimpta)	MS	Not cost-effective at current prices, price discount of at least 70% to reach cost-effectiveness
Ublituximab (Briumvi)	MS	Not cost-effective at current prices, price discount of at least 40% to reach cost-effectiveness

Cost-effective in the right patient population

Unsupported price increases

Top 10 drugs with largest increases in net price

Drug (Generic)	Manufacturer	2022 too 2023 Percentage Change*		Increase in Drug Spending Due to Net Price Change (in Millions)
		WAC	Net price	
Drugs with Price Increases Unsupported by New Clinical Evidence				
Biktarvy (Bictegravir, Emtricitanine, and Tenofovir Alafenimide)	Gilead	5.9%	3.8%	$359
Darzalex (Daratumumab)	Johnson & Johnson	7.6%	3.7%	$190
Entresto (Sacubitril/Valsartan)	Novartis	6.2%	3.6%	$108
Cabometyx (Cabozantinib)	Exelixis	7.5%	5.9%	$86
Xeljanz (Tofacitinib)	Pfizer	6.0%	6.7%	$72
Drugs with Price Increases with New Clinical Evidence**				
Keytruda (Pembrolizumab)	Merck	4.1%	2.8%	$364
Imfinizi (Durvalumab)	AstraZeneca	3.0%	9.9%	$203
Opdivo (Nivolumab)	Bristol Myers Squibb	4.0%	3.8%	$194
Tagrisso (Osimertinib)	AstraZeneca	3.7%	6.6%	$137
Prolia (Denosumab)	Amgen	9.9%	4.5%	$113

**Year-over-year percentage changes were estimated by averaging over the four quarterly changes in price (i.e., Q1 2022 to Q1 2023; Q2 2022 too Q2 2023; Q3 2022 to Q3 2023 and; Q4 2022 to Q4 2023)*
***This is not a determination that the new evidence necessarily justified these price increases*

- Continued price increases that are far above the rate of inflation for many of the costliest drugs
- Price hikes resulted in over $800 million in excess costs to the U.S. healthcare system in one year (2023)
- ICER's determination that new evidence exists for treatments should not be interpreted to mean that the new evidence justifies the level of price increase (a full cost-effectiveness assessment was not conducted to determine the comparative value)

Monoclonal Antibodies: General side effects

mAbs are made using recombinant biotechnology and may elicit immune-mediated reactions. While many side effects are mild and manageable, some can be serious.

Infusion-related reactions

- Usually occur in first 1-2 hours of starting an infusion
- IgG or IgE-mediated
- Fever, Flushing, Shortness of breath, hypotension, urticaria, hives
- May be managed with pre-treatment medications

Undesired effects related to target antigen

- Bleeding: abciximab block platelet aggregation and can cause bleeding
- Skin reactions: cetuximab inhibits epidermal growth factor receptor and can cause dermatological toxicity
- Immune suppression: drugs that target immune cells, cytokines, complement pathways

Immune system effects

- Can suppress or over-activate the immune system
- Increased risk of infections requiring baseline testing for latent infections (e.g., tuberculosis, HCV, HBV, herpes zoster)
- May require routine and additional vaccinations at least 2-4 weeks prior to initiation
- Antibody development

Resistance can occur due to altered biology of disease e.g., mutations in cancer cells or viral variants, or by neutralizing antibodies generated by the immune system.

Biologics for Severe Asthma

Asthma background

Definition:

- **Uncontrolled asthma** includes one or both of the following:
  - Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma)
  - Frequent exacerbations (≥ 2/year) requiring OCS, or (≥ 1/year) serious exacerbations requiring hospitalization
- **Difficult-to-treat asthma** is uncontrolled despite prescribing medium or high dose ICS with a LABA or with maintenance OCS or requires high dose ICS to maintain control. These patients may be difficult to treat because of modifiable risk factors such as incorrect inhaler technique, poor adherence, smoking or comorbidities
- **Severe asthma** is a subset of difficult-to treat that is uncontrolled and modifiable risk factors have been addressed

Prevalence:

- ***CDC estimates 25 MIL adults in the U.S. have asthma. Severe asthma < 5-10% cases.***
- A study in the Netherlands estimated that around 3.7% of asthma patients have severe asthma, based on the number of patients prescribed high-dose ICS-LABA, or medium or high-dose ICS-LABA plus long-term OCS, who had poor symptom control (by Asthma Control Questionnaire) and had good adherence and inhaler technique.

Dutch Population with Asthma	Definition
24% on high intensity treatment	High dose ICS-LABA or medium dose ICS-LABA + OCS (pharmacy claims database)
17% difficult- to-treat	High intensity treatment + poor symptom control
3.7% severe asthma	High intensity treatment + poor symptom control + good adherence and inhaler technique

Hekking., et. al. J Allergy Clin Immunol. 2015;135(4):896-902
GINA 2023

Asthma inhalers: Appropriate use

Key treatment insights

- Checking and correcting inhaler technique at each office visit leads to improved asthma control
- Low-dose ICS-formoterol (e.g., Symbicort) as needed is the preferred reliever medication for mild asthma
- Generic inhalers are likely the most affordable option for your patient

Asthma inhaler medications fall into two categories

Controllers that prevent acute exacerbation	Relievers that treat acute exacerbation
• Inhaled corticosteroids (ICS) • ICS + Long-Acting Beta2 Agonist (LABA) • ICS + LABA + Long-Acting Muscarinic Agonist (LAMA) • Combinations (ICS-LABA, ICS-LAMA-LABA)	• Short-Acting Beta2 Agonist (SABA) • ICS-formoterol • ICS-SABA

Choice of inhaler type and using the inhaler correctly are essential. GINA 2024 states “Most patients (up to 70-80%) are unable to use their inhaler correctly. Checking and correcting inhaler technique using a standardized checklist only takes 2-3 minutes and leads to improved asthma control.”

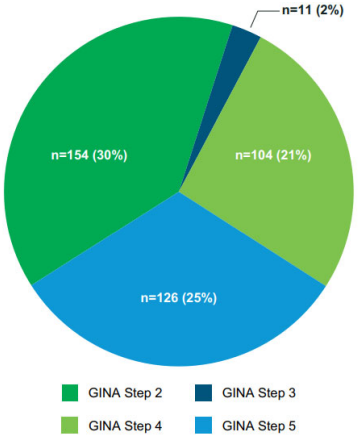
Key updates from GINA 2024 about asthma inhalers

- Patients with infrequent or mild asthma symptoms are still at risk of a severe exacerbation requiring an ED visit (up to 30% of people with asthma exacerbations and death have infrequent symptoms)
- Low-dose ICS-formoterol PRN reliever is preferred over SABA PRN reliever because of the following:
  - Reduction in severe exacerbations compared with SABA alone
  - Similar risk of severe exacerbations as with daily ICS + PRN SABA
- LAMAs should not be used as monotherapy and patients should receive medium dose ICS-LABA before considering add-on LAMA
- LABA without ICS is strongly discouraged because of risk of exacerbations

Asthma inhalers: Appropriate use

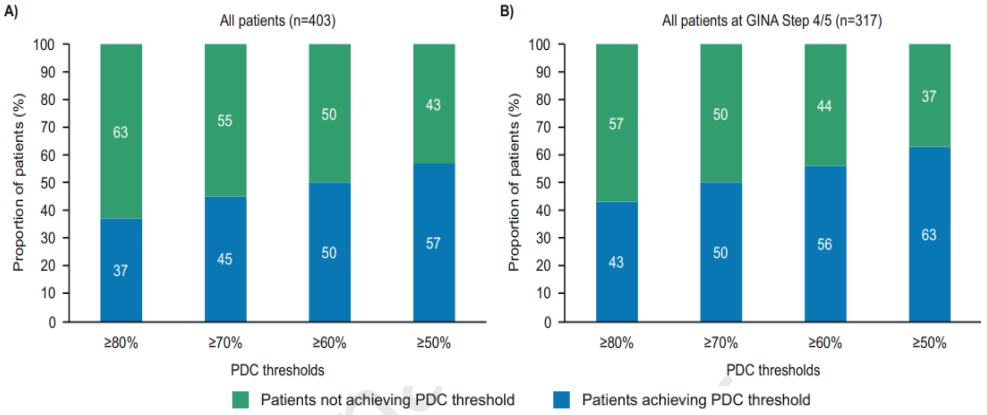
- Short acting beta-agonists (albuterol/levalbuterol) SABA as monotherapy should not be prescribed for persistent asthma and discouraged for intermittent asthma.
- Combination ICS-formoterol PRN should be used first line to manage acute symptoms of mild asthma because prn albuterol alone has been shown to increase risk of acute exacerbations requiring oral steroids .
- Single maintenance and reliver therapy (SMART) is preferred= Inhaled Corticosteroid AND SABA (e.g., Symbicort).
- Inhaled triple therapy (ICS-LAMA-LABA) has proven to have modest benefit and may be tried in patients who failed on moderate dose (ICS-LABA) before trying a biologic agent.
- Check to make sure patients are using their inhaler correctly at each appointment.
- **Deprescribing opportunity: SABA as monotherapy.**

Additional considerations prior to treating with biologics



1/3 of patients escalated to biologics were considered “mild”

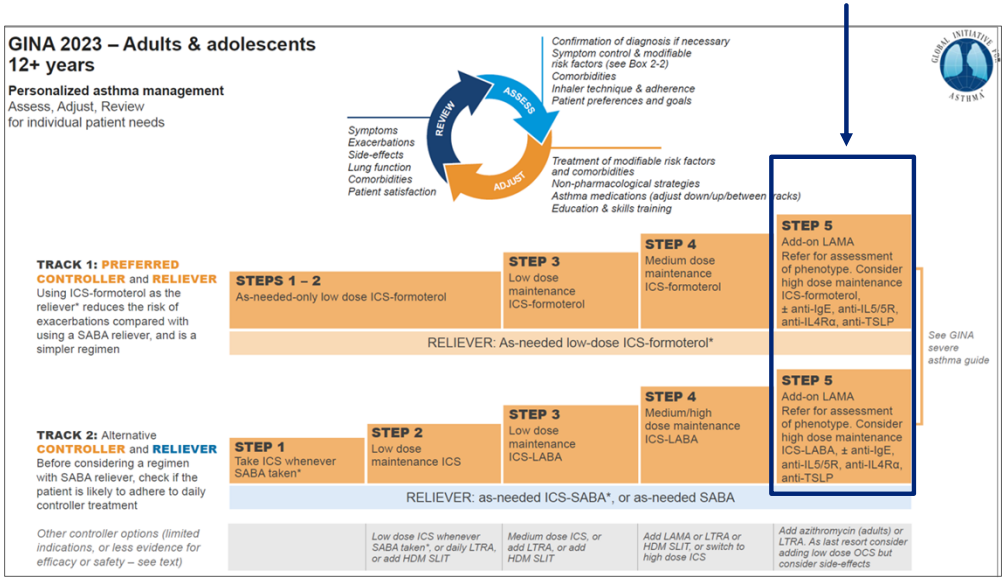
2/3 of patients had ***suboptimal adherence*** to therapy within the 12 months prior to escalation to biologic treatment

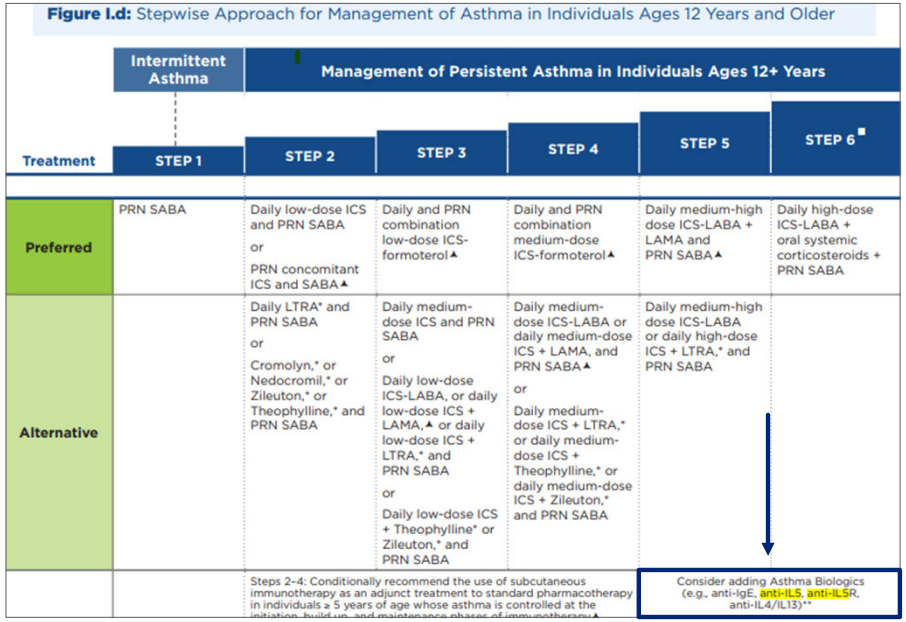


Retrospective Claims Database Analysis, N=506

GINA 2023 recommendations / NAEPPCC 2020 Guidelines

Biologics are considered at step 5





"*Regardless of regulatory approvals, GINA recommends biologic therapy for asthma **only** if asthma is severe, and **only** if treatment has been optimized*"

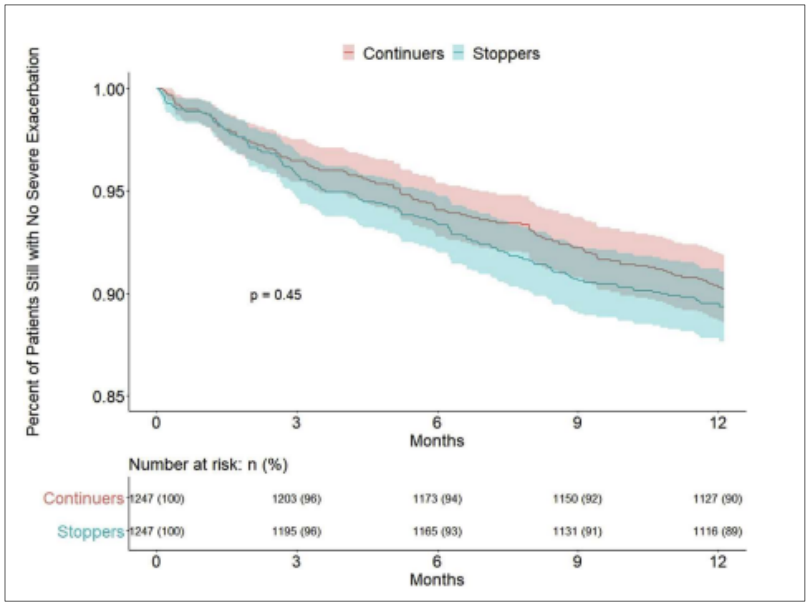
2023 GINA Main Report - Global Initiative for Asthma - GINA (ginasthma.org)

2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group | NHLBI, NIH

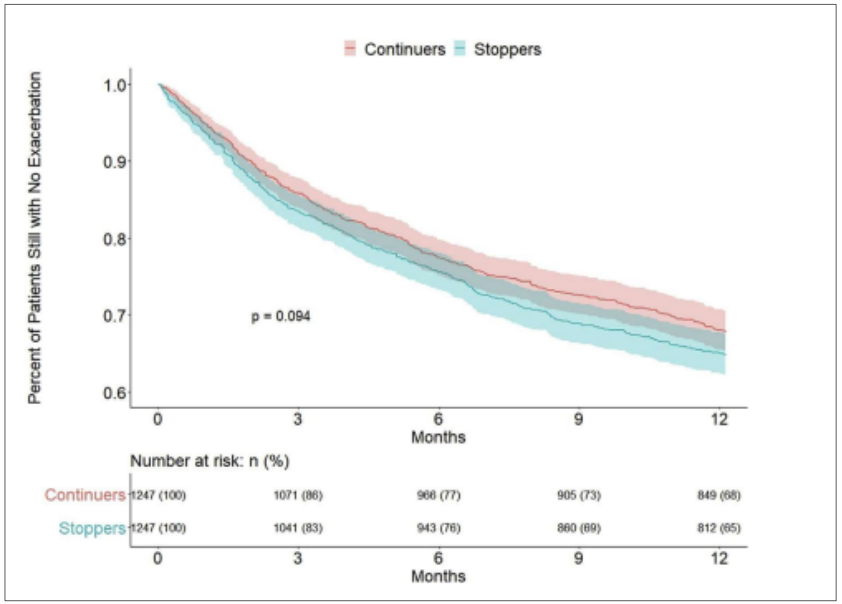
Additional considerations prior to treating with biologics

Matched cohort study of patients who **stopped vs continued** a biologic.

Results: At 6 months post stop with an increase in asthma exacerbations: 10.2% vs 9.5% **OR** 1.085 95%CI (NS)



Time to exacerbation after stopping date



Time to severe exacerbation after stopping date

How to prescribe and reassess asthma biologics appropriately

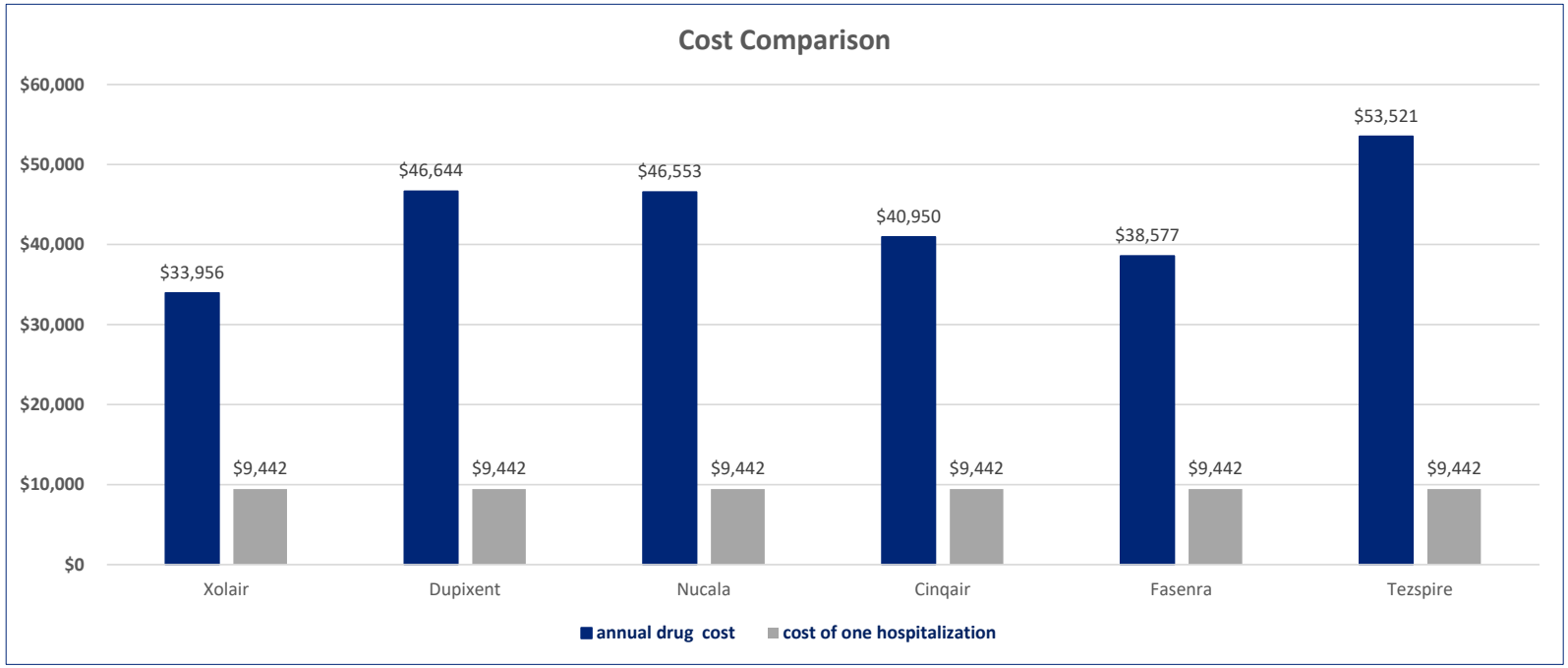
1. **Patient has confirmed diagnosis of severe asthma** that includes:
   a. Asthma that is uncontrolled (persistent symptoms, frequent exacerbations) on high-dose ICS+LABA therapy
   b. All treatable factors have been addressed: adherence, inhaler technique, comorbidities, risk factors/triggers
2. Referral to or consult with pulmonary or asthma specialist before initiation of biologic medication
3. **Assess predictors of response to biologic agent prior to initiation of biologic and use biomarkers to guide selection of biologic agent** (e.g., Xolair, Nucala, Fasenra, Cinqair, and Dupixent)
   a. Biomarkers: (e.g., blood eosinophil count [BEC] and fractional concentration of exhaled nitric oxide [FeNO])
      – BEC ≥ 150mcL and ≤ 1500mcL; (oral corticosteroids (OCS) suppress biomarkers, measure BEC 1-2 weeks after course of OCS or on lowest dose)
      – FeNO ≥ 20ppb
   b. Oral corticosteroids (OCS) dependent
4. **Assess response to treatment after trial of 4 months on biologic.** A positive response is represented by an improvement in exacerbation rate [e.g., decrease in oral corticosteroid use (frequency or dose), decrease in hospitalization rate]
   a. If no positive response, discontinue.
   b. If partial response, continue trial 6-12 months and reassess.
5. **Consider self-administration for agents administered by SC route (e.g., Xolair, Nucala, Fasenra, Dupixent and Tezspire) where appropriate**

A positive response is an improvement in exacerbations (e.g., decrease in oral corticosteroid use, decrease in hospitalization) → continue

No response → discontinue

Partial response → continue trial for 6-12 months and then reassess

Annual cost of treatment vs cost of exacerbation leading to hospitalization



Copays for a patient on asthma biologics can be substantial: up to $3000-$5000 per year

ICER: All asthma biologic treatments would need price discounts of at least 50% to reach commonly cited thresholds for cost-effectiveness, and each of these therapies therefore is deemed to be "low value" based on ICER's value assessment framework.

"While all five biologics modestly reduce asthma exacerbations and improve daily quality of life, the pricing of this entire therapy class is far out of alignment with the treatments' incremental benefits," said David Rind, MD, ICER's Chief Medical Officer.

Redbook; Micromedex accessed 8/14/2023, WAC (wholesale acquisition cost)
https://icer.org/wp-content/uploads/2021/05/ICER_Severe-Asthma_Final-Report_12-Month-Check-Up_021323.pdf

Annualized drug cost to prevent one asthma exacerbation

Event Type	Brand	Ingredient	NNT	Cost to Prevent Event
AAER	FASENRA	BENRALIZUMAB	4 - 9	$154,308 - $347,193
AAER	CINQAIR	RESLIZUMAB	4	$163,800
AAER	NUCALA	MEPOLIZUMAB	4	$186,212
AAER	TEZSPIRE	TEZEPELUMAB-EKKO (CHO)	4	$200,044
AAER	DUPIXENT	DUPILUMAB	5	$233,220
AAER	XOLAIR	OMALIZUMAB	10	$339,560
AAER_ED	TEZSPIRE	TEZEPELUMAB-EKKO (CHO)	6	$300,066
AAER_ED	FASENRA	BENRALIZUMAB	9	$347,193
AAER_ED	XOLAIR	OMALIZUMAB	13	$441,428
AAER_ED	NUCALA	MEPOLIZUMAB	10	$465,530
AAER_ED	CINQAIR	RESLIZUMAB	26	$1,064,700
AAER_ED	DUPIXENT	DUPILUMAB	35	$1,632,540

NNT (number needed to treat), AAER (annualized asthma exacerbation rate leading to course of oral corticosteroids and/or hospitalization), AAER_ED (annualized asthma exacerbation rate leading to emergency department visit or hospitalization), WAC (wholesale acquisition cost)

*treatment of exacerbation does not include indirect costs of healthcare utilization (e.g., recurrent ED/hospitalization admissions, office visits, other outpatient costs (labs, home health)

Annual cost of treatment to prevent an exacerbation with a biologic agent far exceeds *annual cost of treating an exacerbation.

Table E2.5. Health Care Utilization Cost Inputs

Health Care Cost Category	Unit Cost	Source
Exacerbation-Related Steroid Burst (SD)	$1,604 ($2,738)	Suruki et al. 2017[99]
Exacerbation-Related ED Visit (SD)	$2,161 ($2,869)	Suruki et al. 2017[99]
Exacerbation-Related Hospitalization (SD)	$9,442 ($7,568)	Suruki et al. 2017[99]
Annual Cost for SoC (95% interval)	$6,494 ($5,297, $7,827)	Whittington et al. 2018[49]
Annual Cost of Long-Term Oral Corticosteroid Use with Adverse Events (SD assumed)	$8,326 ($8,326)	Lefebvre et al. 2017[46]
Office Visit Treatment Administration for Subcutaneous Office-Administered Tezepelumab (assumed to be self-administered after loading dose)	$74	Physicians' Fee and Coding Guide (HCPCS code 99213)[100]

https://icer.org/wp-content/uploads/2021/05/ICER_Severe-Asthma_Final-Report_12-Month-Check-Up_021323.pdf

Use of Biologics in COPD

Background COPD

"**Heterogeneous** lung condition characterized by chronic respiratory symptoms (dyspnea, cough, expectoration and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction."
POCKET-GUIDE-GOLD-2024-ver-1.2-11Jan2024_WMV.pdf (goldcopd.org)

Epidemiology

- In the U.S., COPD affects more than 15 million adults, and many more do not know they have it[2]
- COPD is a major cause of disability, and it is the fourth leading cause of death in the U.S. according to the Centers for Disease Control and Prevention (CDC).

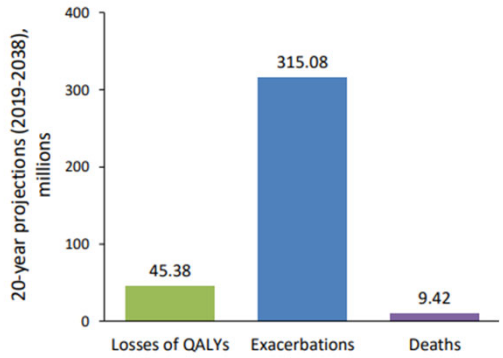
Etiotypes

Classification and description	
G	genetic - mutations in SERPINA1 gene, α1-antitrypsin deficiency
D	abnormal lung development
C	exposure to tobacco smoke, vaping/e-cigarette use, cannabis
P	biomass and pollution exposure
I	infections
A	COPD and asthma
U	unknown cause

Adapted from Global Initiative for Chronic Obstructive Lung Disease, 2024 Teaching slide set

Costs

Direct U.S. medical costs from (1) maintenance treatment (inhalers) and (2) treatment of acute exacerbations[3] projected to increase and reach $800.90 billion by 2038[1]



1. Zafari Z, Li S, Eakin MN, Bellanger M, Reed RM. Projecting Long-term Health and economic burden of CPD in the United States. Chest 2021; 159(4):1400-10
2. https://www.nhlbi.nih.gov/health/copd Accessed 4/19/2023.
3. May SM, Li JT. Burden of chronic obstructive pulmonary disease: healthcare costs and beyond. Allergy Asthma Proc. 2015;36(1):4-10. doi:10.2500/aap.2015.36.3812

COPD pharmacotherapy

The airflow limitation and structural changes in COPD is not reversible

- Current options for COPD only manage symptoms and may slow disease progression when initiated ***early*** in the disease process
- Primary goal for hospice patients is to ***reduce symptoms***

Three medication classes are used via inhalation to provide bronchodilation and reduce inflammation.

Other medications and palliative measures work as “add-ons” to inhalers/nebulizers.

Bronchodilators

- $Beta_2$ agonists
  - Long-acting beta-agonists (LABA)
  - Short-acting beta-agonists (SABA)
- Anticholinergics
  - Long-acting anticholinergics (LAMA)
  - Short-acting anticholinergics (SAMA)
- Combination (e.g., LABA + LAMA)
- Theophylline (TheoDur®)

Anti-Inflammatory

- Inhaled Corticosteroids (ICS)
- Oral Corticosteroids (OCS)
- Roflumilast (Daliresp®)

Monoclonal Antibodies

- Nucala (mepolizumab)
- Dupixent (dupilumab)

Best practices for inhaler therapy in COPD

Chronic Obstructive Pulmonary Disease

1. **Assess the correct inhaler, dose, and technique for every patient.**
2. Patients who are symptomatic should be prescribed dual therapy, LAMA + LABA.
3. LAMA + LABA inhaler therapy should be prescribed for all patients with COPD diagnosis with a history of 2 or more moderate exacerbations or 1 or more exacerbations leading to a hospitalization within a calendar year.
4. a. Addition of Inhaled Corticosteroids (ICS) for COPD in patients with ≥ 1 exacerbation leading to hospitalization or ≥ 2 moderate exacerbations requiring oral corticosteroids (OCS) in the past year and currently taking LAMA+LABA and BEC ≥ 100**.

   b. Do not generally prescribe ICS in patients with BEC < 100 because the likelihood of harm exceeds the benefit.
5. Use of single combination inhaler over individual inhalers is preferred for better adherence.

***Several well-designed studies have used a consistent range of BEC cut-off between 100 - 300 as a decision point for adding ICS therapy to LAMA-LABA. Given the ideal BEC for initiation of ICS is currently unclear*, a BEC ≥ 100 allows for individualized decision making (check eosinophil before starting and ensure this count has been consistent).

Common inhaler use errors

DPI	
Error	**Estimated frequency**
No full expiration before inhalation	46%
No post-inhalation breath-hold	37%
Incorrect device preparation	29%
Lack of brisk, accelerated deep breath	22%
Not inhaling with lips on mouthpiece	18%

MDI	
Error	**Estimated frequency**
No full expiration before inhalation	48%
No post-inhalation breath-hold	46%
Incorrect coordination of device activation with inhalation	45%
Not taking slow, deep breath	44%
Incorrect device preparation	30%

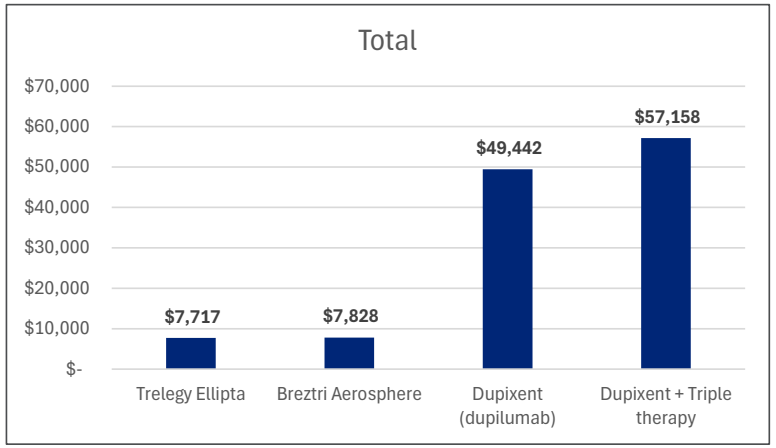
Overall inhaler technique

Correct	Acceptable, but Suboptimal	Poor
31%	41%	31%

Sanchis et al, 2016

Annual cost comparison per patient

Annual WAC based drug cost of dupilumab add-on to the triple therapy (LAMA+LABA+ICS) is approximately $57k per patient.



Brand name	Active ingredient	Strength	Package size	# of doses per pack	WAC package price (accessed 7/5/24)	Dose	Annual doses	Annual cost (52 weeks)
Breztri Aerosphere	budesonide/formoterol fumarate/glycopyrrolate	160 mcg-4.8 mcg-9 mcg/1	10.7 gm (120)	120	$ 645.14	2 inhalations twice daily	1456	$ 7,828
Trelegy Ellipta	fluticasone furoate/umeclidinium/vilanterol	100 mcg/1 actuation-62.5	60	60	$ 657.68	1 inhalation twice daily	704	$ 7,717
Trelegy Ellipta	fluticasone furoate/umeclidinium/vilanterol	200 mcg/1 actuation-62.5	60	60	$ 657.68	1 inhalation twice daily	704	$ 7,717
Dupixent	Dupilumab	300 mg/2ml			$ 3803.20	300 mg q2w	26	$ 49,442
Dupixent + Triple therapy	-	-	-		-	-	-	$ 57,158

Value of preventing exacerbations

- **There is not a clear data** on impact of preventing moderate exacerbations. ***However,*** the clinical consensus is that decreasing moderate exacerbations are important for QOL and future exacerbations.
- **Preventing** moderate exacerbations **adds** to prevention of more severe disease.

Goals for treatment of stable COPD

- **Relieve Symptoms**
- **Improve Exercise Tolerance**
- **Improve Health Status**

→ **REDUCE SYMPTOMS**

AND

- **Prevent Disease Progression**
- **Prevent and Treat Exacerbations**
- **Reduce Mortality**

→ **REDUCE RISK**

Treatment effect based on BOREAS and NOTUS

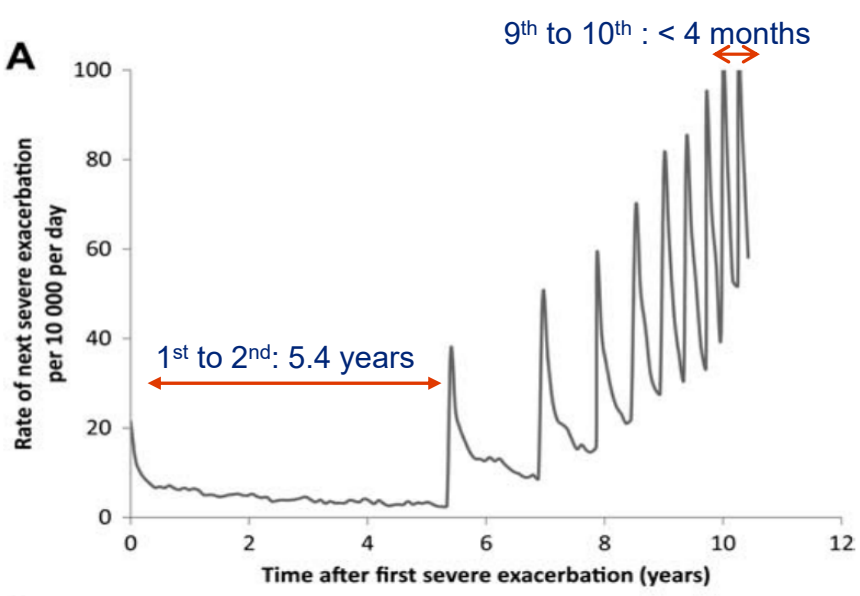
Based on BOREAS and NOTUS trials, the treatment of dupilumab add-on appears to be driven by reduction in rate of moderate exacerbations.

The treatment effect on reductions in severe exacerbations requires further confirmation.

The long-term cost-effectiveness is unknown due to short-term trial duration, i.e., 52 weeks.

The treatment effect on mortality is unknown.

Severe exacerbations and rate of subsequent exacerbations



- Baseline rate of severe exacerbations of COPD increases with each new severe exacerbations.
- Severe exacerbations were defined as hospitalizations with a primary discharge diagnosis of COPD.
- Source: Suissa S e al. Thorax 2012;67:957–63 thoraxjnl-2011-201518 1..7 (bmj.com)

Use of biologics in COPD

Reassess after 4 months. Deprescribe after 6 months if no response.

Diagnosis of moderate to severe COPD receiving triple therapy

- Recommended for COPD that is uncontrolled on LABA+LAMA+ICS or LABA+LAMA if ICS is contraindicated
- Adherence, inhaler technique, comorbidities, and triggers have been identified prior to initiation of biologics

Type 2 inflammation and high exacerbation risk

- Presence of blood eosinophils (BEC) ≥ 300 cells/microL
- ≥ 2 moderate exacerbations (e.g., requiring oral ICS and/or antibiotics) or ≥ 1 severe exacerbation leading to a hospitalization
- Insufficient evidence if BEC can predict future exacerbation risk in COPD patients

Referral or consult with a specialist

- Prior to initiation of biologics, consult with a specialist

A positive response is an improvement in exacerbations (e.g., decrease in oral corticosteroid use, decrease in hospitalization) → continue

No response → discontinue

Partial response → continue trial for 6-12 months and then reassess

Optum Health Education™

Data as of Q1 2024 Source of Truth documents

Best practice recommendation for the use of biologics in COPD

Optum Care recommends Dupixent (dupilumab) in COPD when following conditions are met:

- **Diagnosis of moderate or severe COPD** (post-bronchodilator (BD) FEV1/forced vital capacity (FVC) ratio < 0.70 and post-BD FEV1 % predicted > 30% and ≤ 70%)
- **Evidence of type 2 inflammation** (blood eosinophils ≥ 300 cells/μL at screening)
- **Receiving triple inhaler therapy** (LABA+LAMA+ICS or LABA + LAMA if ICS is contraindicated or not appropriate) at maximum tolerated dose for at least 3 months and adherent
- **High exacerbation risk**: ≥ 2 moderate (requiring oral ICS and/or antibiotics) or ≥ 1 severe exacerbation (leading to hospitalization) in the past year while on triple inhaler therapy)

AND

- Prescribed by or in consultation with a pulmonologist.

AND

- **Patient is assessed regularly for correct inhaler, dose, technique, and adherence.**
- **Reassess response after 4 months. If no response, discontinue. If partial response, continue trial for 6-12 months and then reassess.**

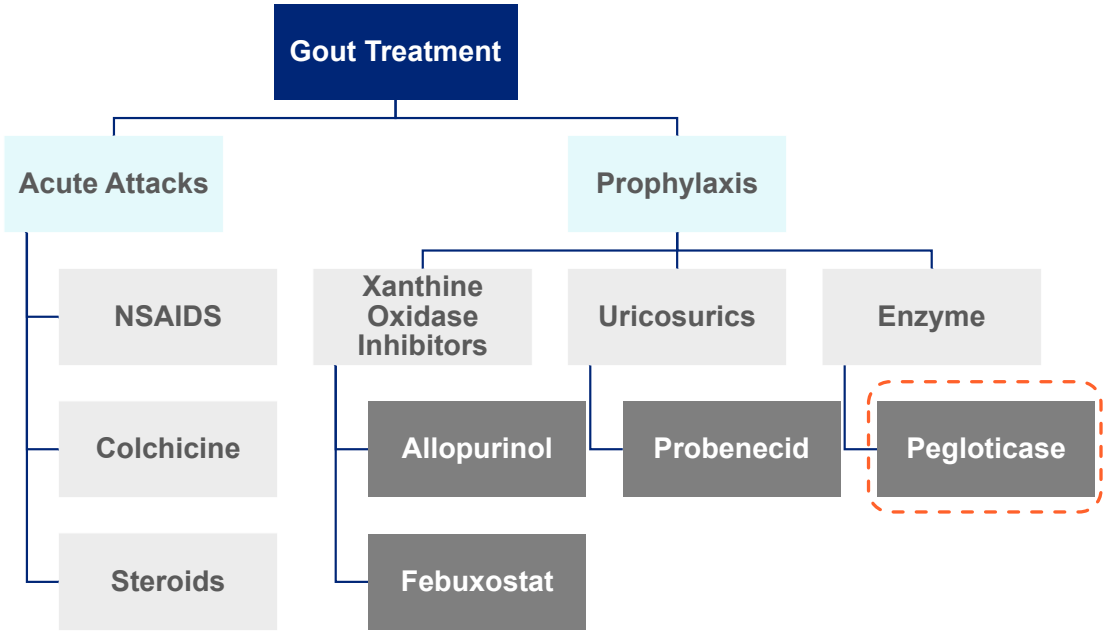
PLEASE NOTE: Treatment effect is primarily driven by reduction in moderate exacerbations. Further evidence is required to confirm the effect of dupilumab on exacerbations leading hospitalizations and mortality.

Treatment of Gout

Overview of gout treatment

General management of Urate Lowering Therapy per Gout Clinical Practice Guidelines

- For all patients (including those with CKD ≥ 3), allopurinol is the preferred first-line therapy.
- Xanthine Oxidase Inhibitors are preferred over probenecid.
- Pegloticase should NOT be used first-line!



Gout Clinical Practice Guidelines

Prophylaxis for adults

		Xanthine Oxidase Inhibitors (XOI)		Uricosurics	Enzyme
		Allopurinol (Zyloprim)	**Febuxostat (Uloric)**	**Probenecid**	**Pegloticase (Kyrstexxa)**
Place in Thx		1st line	2nd line. Use in only patients who Ø tolerate allopurinol	3rd line. Alternative to allopurinol & febuxostat	Last resort. Failure on max doses of XOI & uricosuric
↓ Serum uric acid		2 – 3.5 mg/dL at 300 mg dose	4.5 mg/dL at80 mg dose	2.9 mg/dL at 1.6 g/day	6.8 mg/dL
Dosing	Initial	100 mg QD	40 mg QD	250 mg BID X 1 week then 500 mg BID	8 mg IV Q 2 weeks + methotrexate 15 mg po Q week + folic acid (start these ≥ 4 weeks prior)
	Maximum	800 mg/day in divided doses	80 mg/day label; 120 mg/day clinical studies	120 mg/day	
	Renal Dosage Adjustment	CrCl 10 – 20 mL/min – Ø exceed 200 mg/day; < 10 mL/min – Ø exceed 100 mg/day; < 3 mL/min – lengthen dosing interval	CrCl 15 – 29 mg/dL – 40 mg/day	Efficacy lost at CrCl < 8 mL/min. Avoid if CrCl < 50 mL/min (lack safety/efficacy)	--
	Titration	↑ by 100 mg at weekly intervals until serum uric acid (SUA) level < 6 mg/dL w/o exceeding max daily dose	If SUA is still > 6 mg/dL after 2 weeks - ↑ to 80 mg/day	↑ by 500 mg Q 4-week intervals	--
Safety		Rare but severe hypersensitivity. HLA-B*5801 testing in high-risk pts (Han Chinese, Thai, Korean, Black), rare ↑ LFT, GI intolerance	Risk of CV death, ↑ LFT, liver failure	GI (N/V, ↓ appetite) Risk of nephrolithiasis	Anaphylaxis, infusion reaction, exacerbation of HF
Cost/Month		300 mg QD: $3 - $90	80 mg QD: $16 - $300	500 mg BID: $27 - $120	$37,166 for 28-day supply

Appropriate use of pegloticase (Krystexxa)

Key considerations:

- **Maximize conventional urate lowering therapy before considering pegloticase**
  - Failure of maximal doses of xanthine oxidase inhibitor (XOI) + probenecid if tolerated
- **Case management for patients using pegloticase**
  - Premedicate with antihistamines & corticosteroids; monitor for anaphylaxis
  - Pegloticase should be used concurrently with immunosuppressant such as methotrexate or mycophenolate to maximize response rate & minimize the risk of anti-drug antibodies, infusion reactions, or anaphylaxis
  - Monitor serum urate (sU) levels (2 sU > 6.0 mg/dL) as potential indicator for infusion reaction & pegloticase non-responder. Discontinue therapy as appropriate
  - For patients responding to pegloticase – evaluate if patient can be converted back to traditional urate lowering therapies after 6 months. If so, re-initiate urate lowering therapies within 1 month
- **Maximize therapy of comorbid conditions (hypertension, diabetes)**
  - Avoid agents w/ adverse profile on serum urate when possible
  - Consider alternatives with favorable profiles on serum urate

Thank you!

Resources for deprescribing

- The Anticholinergic Burden Calculator can help you evaluate a patient's potential for serious anticholinergic effects. In the geriatric population, this is a great tool to start with, as reducing or eliminating medications with high anticholinergic burdens can often improve patients' overall function and quality of life. Start with deprescribing those medications in the highest (level 3) category.
- The Beers List from the American Geriatric Society lists medications that pose the highest risk to older patients, along with alternatives. There are numerous versions of this list, but one of the better configured lists is found here: https://bit.ly/2GQhM2Y.
- Deprescribing.org: developed by a team of physicians and pharmacists, provides deprescribing guidelines and algorithms, patient decision aids, and an up-to-date resource list of evidence and research.
- MedStopper is an online tool that allows you to enter a drug list for a specific patient and receive recommendations regarding which medications might be discontinued or switched
- STOPPFrail (Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy): consensus validation | Age and Ageing | Oxford Academic
- STOPP/START criteria for potentially inappropriate prescribing in older people: version 2 – PubMed: STOPP/START version 2 criteria have been expanded and updated for the purpose of minimizing inappropriate prescribing in older people.

Data as of Q1 2024 Source of Truth documents

Deprescribing Unnecessary Medications: A Four-Part Process | AAFP

Appendix

Deprescribing in Primary Care Examples

Deprescribing Anticoagulants

Deprescribing anticoagulants

Considerations to continue

- Symptomatic
- High risk for thromboembolism
- Higher functioning status
- Low bleeding risk
- Medication compliance
- Patient/family preference

Considerations to discontinue

- Lack of indication
- High bleeding risk or bleeding complications
- Increased monitoring
- Negative impact on quality of life
- Variable or decreased nutritional status
- Poor medication compliance
- Frequent medication changes
- Liver or renal impairment
- Drug-drug interactions
- Reduce cost of care
- No longer part of goals of care
- Family or patient decision to discontinue

Communicate risks and benefits with patient and family to develop a collaborative plan of care

Why is deprescribing anticoagulants important?

- Anticoagulants are generally considered high risk medications
  - 2023 American Geriatric Society Beers Criteria
  - Institute for Safe Medication Practices (ISMP) High-Alert Medications in Long-Term Care (LTC) Settings
  - CMS State Operations Manual (Form CMS 20082 [5/2017])
- Antithrombotic therapy is present in up to 7% of patients at time of hospice admission
- A 2021 retrospective review of 180 patients found that 76% had their antithrombotic medications continued until the last week of life

Kowalewska et al, 2017
Huisman et al, 2021

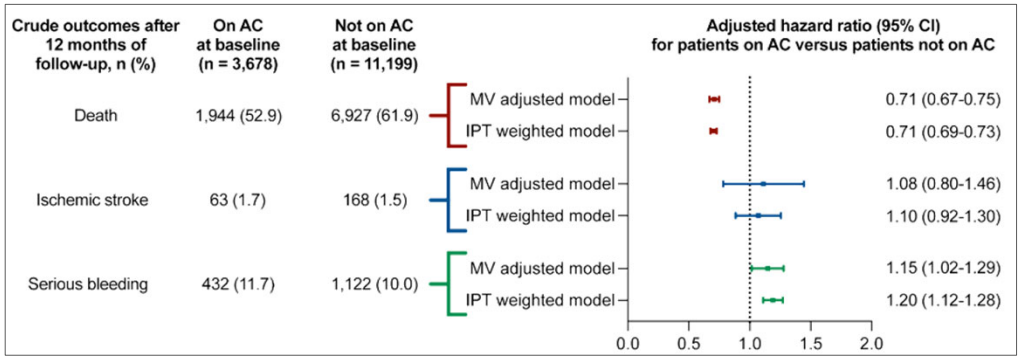
Anticoagulant use for atrial fibrillation with advanced dementia

Anticoagulation was associated with ↓ mortality, but ↑ risk of bleeding.

No association with risk of stroke.

Retrospective cohort study with 14,877 nursing home residents aged ≥ 66 between 2013 – 2018

- Primary outcome: All-cause mortality
- Secondary outcomes ischemic stroke and serious bleeding
- **Results:**
  - 72.0% were female, 82.7% were aged ≥ 80 years
  - Mean CHA_2DS_2VASC score = 6.19 ± 1.58
  - > 50% of patients in both groups died within a year. Median weighted survival was 76 days longer for anticoagulated individuals.

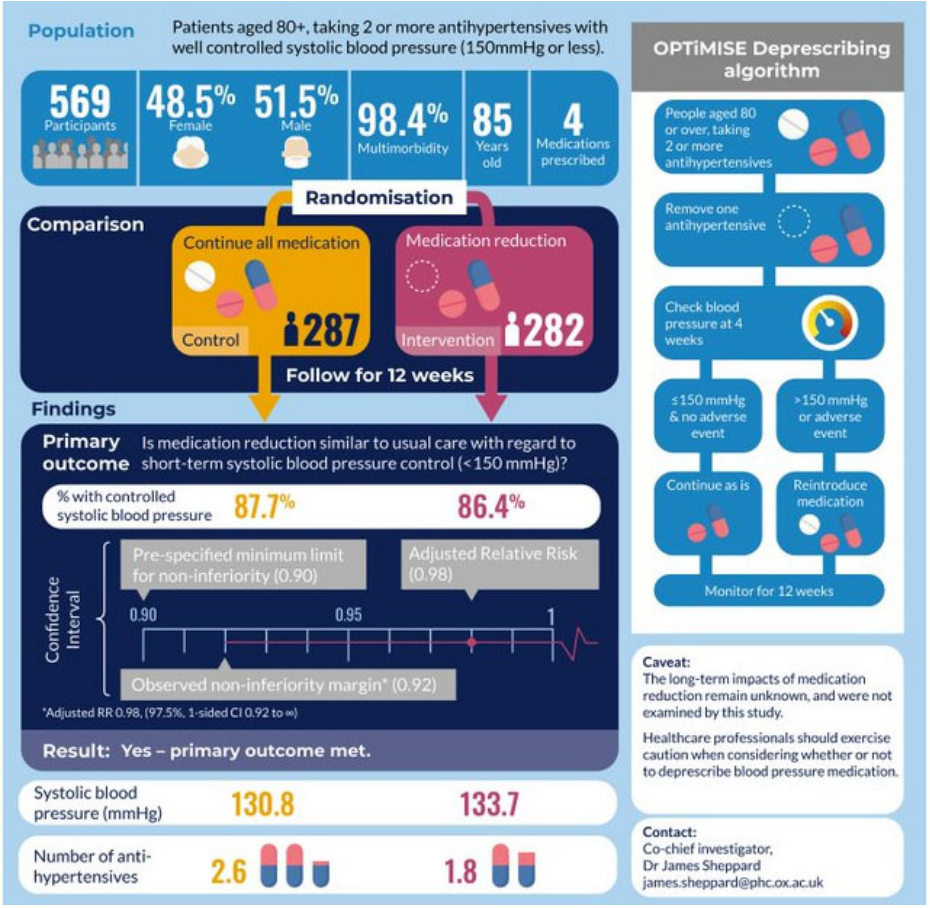


Ouellet GM, et al. 2023

Deprescribing Antihypertensives

Deprescribing antihypertensive

- Antihypertensives **may be an option** for deprescription, particularly for primary prevention
  - At risk of hypotension, dizziness and falls
- If used to improve symptoms for CV conditions, antihypertensive should be continued as long as patients tolerates.
- **The DANTE study[1]**
  - Participants: Mild cognitive impairment
  - At baseline, 11.2% had CVD, 45.8% had orthostatic hypotension, and 61.5% took at least 2 antihypertensives.
  - Physicians withdrew antihypertensives until a mx of 20-mmHg increase in SBP
  - Deprescribing did not improve cognitive, psychological, or general daily functioning at 16-week follow-up, but did not increase adverse events.
- **The OPTiMISE trial[2]**
  - Participants: Aged 80+, taking 2 or more antihypertensives



Antihypertensives: Literature

2017 ACC/AHA Guidelines:

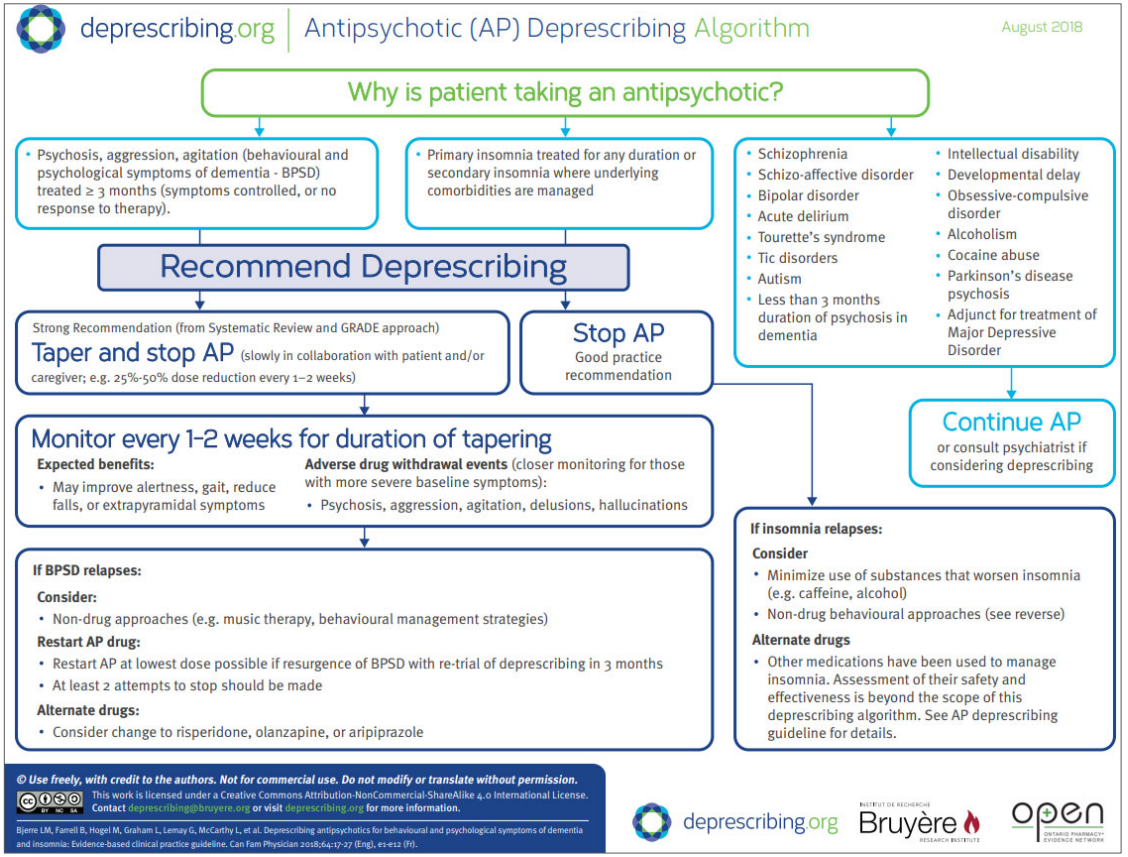
- Recommendations for treatment of hypertension in older persons (> 65 years of age)
  - For noninstitutionalized ambulatory community-dwelling adults:
    - Treatment of hypertension with a SBP treatment goal of < 130 mmHg is recommended
  - For older adults with hypertension and high burden of comorbidity and limited life expectancy:
    - Clinical judgement, patient preference, and team-based approach to assess risk/benefit is appropriate for decisions regarding BP lowering and choice of antihypertensive medications

Other guidelines recommend a more conservative goal of < 150/90 mmHg in older adults

Deprescribing in Dementia

Deprescribing: Antipsychotics for behavioral and psychological symptoms of dementia

Canadian guideline recommends deprescribing antipsychotics for adults with behavioral and psychological symptoms of dementia treated for at least for at least three months.



Deprescribing: Medications for dementia

- The benefits of acetylcholinesterase inhibitors (AChEIs) are likely mild and may not be clinically significant.[1]
- The harms from AChEI *may be greater than benefits*. Adverse reactions of AChEIs include;[2]
  - GI adverse effects – nausea, vomiting, diarrhea, and poor appetite. Concurrent use of AChEIs and NSAIDs can increase the risk of GI ulceration and bleeding.
  - Neurological and psychological adverse effects – result from excess activation of nicotinic receptors. Common neurological side effects are dizziness, dyskinesia, convulsion, muscle cramps, insomnia and vivid dream. Psychiatric adverse outcomes are usually presented in patients treated with high dose of AChEIs. These side effects include worsening hallucination, anxiety, aggression, and confusion.
  - Cardiovascular adverse effects – AChEIs increase the availability of choline in the heart and vagotonic effects through muscarinic receptors. Increased risk of SA and AV block, sinus bradycardia and QT prolongation
  - Urology adverse effects: A retrospective cohort study has shown that AChEIs are associated with overactive bladder[3].
- Patients who do not have an appropriate indication, have never experienced a benefit, are no longer benefiting, or have advanced dementia may be suitable for a trial of deprescribing ChEIs.

Deprescribing dementia medications

Clinical significance in end-stage dementia is unknown

- No curative therapies exist
- Patients in clinical trials would not be considered hospice eligible
- Burdens of adverse effects, polypharmacy, and cost likely outweigh potential benefit in end-stage dementia

Adverse effects

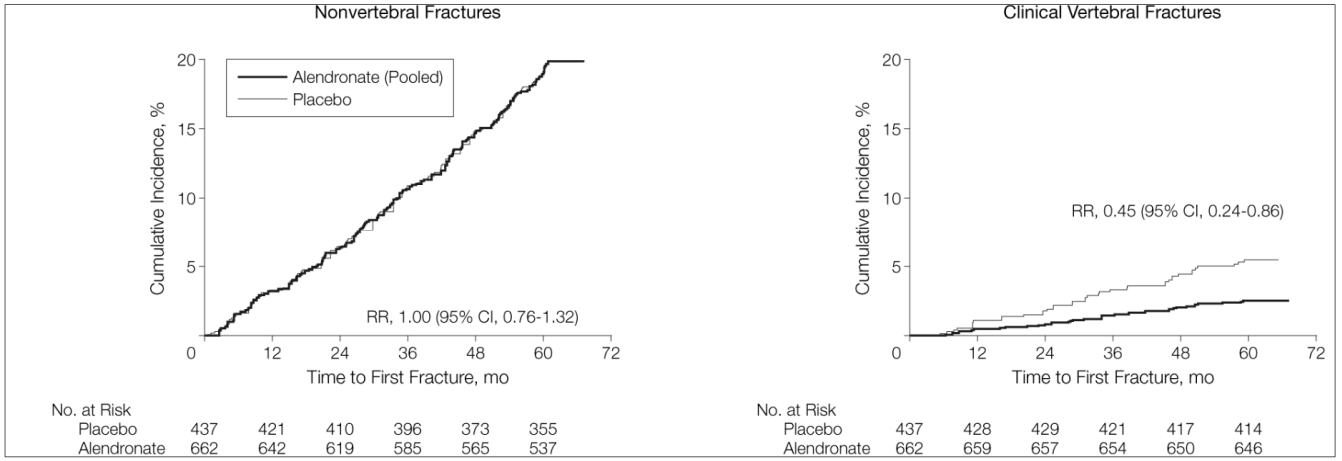
- Decreased appetite
- Gastrointestinal effects: nausea, vomiting, diarrhea, dyspepsia
- CNS effects: confusion, hallucinations, agitation
- CV effects: bradycardia, hypotension, orthostasis, syncope

- Acetylcholinesterase Inhibitors (AChEI)
  - Donepezil (Aricept®)
  - Rivastigmine (Exelon®)
  - Galantamine (Razadyne®)
- NMDA Receptor Antagonist
  - Memantine (Namenda®)
- Combination
  - Memantine + Donepezil (Namzaric®)

Deprescribing Bisphosphonates

Deprescribing: Bisphosphonate

- **Not for cancer patients** who are on bisphosphonate
- A retrospective cohort study[1] showed deprescribing of bisphosphonate only occurred for ~ 20% among the nursing home residents with dementia, and many residents continued to take bisphosphonates despite a lack of strong evidence to support continued treatment.
- Duration of bisphosphonate therapy is typically 5 years for patients taking alendronate and 3 years for patients receiving zolendronic acid yearly.
- FLEX trial[2] investigated the effects of discontinuing alendronate treatment after 5 years vs continuing for 10 years. The result showed no difference in the risk of non-vertebral fracture who continued alendronate therapy for additional 5 years, compared to individuals who took placebo.



Deprescribing in Diabetes

Deprescribing: Diabetic medications

2024 Diabetes Care 13: Older Adults

American Diabetes Association (ADA) recommends to avoid hypoglycemia and symptomatic hyperglycemia while reducing the burdens of glycemic management for people with diabetes receiving palliative care and end-of-life care. When an organ failure develops, ADA recommends to de-intensify or discontinue several agents.

Table 13.2—Considerations for treatment plan simplification and deintensification/deprescribing in older adults with diabetes

Characteristics and health status of person with diabetes	Reasonable A1C/ treatment goal	Rationale/considerations	When may medication plan simplification be required?	When may treatment deintensification/ deprescribing be required?
Very complex/poor health (LTC or end-stage chronic illnesses or moderate to severe cognitive impairment or two or more ADL impairments)	Avoid reliance on A1C and avoid hypoglycemia and symptomatic hyperglycemia	• No benefits of tight glycemic management in this population • Hypoglycemia should be avoided • Most important outcomes are maintenance of cognitive and functional status	• If on an insulin plan and the individual would like to decrease the number of injections and finger-stick blood glucose monitoring events each day • If the individual has an inconsistent eating pattern	• If on noninsulin agents with a high hypoglycemia risk in the context of cognitive dysfunction, depression, anorexia, or inconsistent eating pattern • If taking any medications without clear benefits
At the end of life	Avoid hypoglycemia and symptomatic hyperglycemia	• Goal is to provide comfort and avoid tasks or interventions that cause pain or discomfort • Caregivers are important in providing medical care and maintaining quality of life	• If there is pain or discomfort caused by treatment (e.g., injections or finger sticks) • If there is excessive caregiver stress due to treatment complexity	• If taking any medications without clear benefits in improving symptoms and/or comfort

Table 13.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Characteristics and health status of person with diabetes	Rationale	Reasonable A1C goal*	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Very complex/poor health (LTC or end-stage chronic illnesses‡ or moderate to severe cognitive impairment or two or more ADL impairments)	Limited remaining life expectancy makes benefit minimal	Avoid reliance on A1C; glucose control decisions should be based on avoiding hypoglycemia and symptomatic hyperglycemia	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<140/90 mmHg	Consider likelihood of benefit with statin

Diabetes management: Treatment considerations

- Goals shift from long-term control to short-term benefit and safety
- Aggressive glycemic control not warranted
- Blood glucose goal < 200-250mg/dl to limit symptoms of hypoglycemia and hyperglycemia
- Consolidate or discontinue medications to reduce med burden, adverse events, and medication costs without affecting symptom management or quality of life

Type 1 diabetes

- Continue insulin to prevent diabetic ketoacidosis
- Dose reduction and consolidation may be appropriate, especially in last days to weeks

Type 2 diabetes

- Dose reduction and consolidation of regimen to allow for less tight BG control
- Discontinuation of all antihyperglycemic medications may be appropriate

Deprescribing – The Beers criteria

- Consider deprescribing anticholinergics if possible
- Use ACB calculator https://www.acbcalc.com/ to estimate anticholinergic burden

Potentially inappropriate medication use in older adults*

- **Aspirin:** Consider deprescribing aspirin already taken.
- **Non-selective peripheral alpha-1 blockers for the treatment of hypertension:** Avoid use as an antihypertensive.
- **Antipsychotics, first- and second- generation:** Avoid, except in FDA-approved indications.
- **Megestrol:** Avoid due to minimal effect on weight.
- **PPI:** Avoid scheduled use for > 8 weeks unless for high-risk patients due to risk of C difficile infection, pneumonia, GI malignancies, bone loss, and fractures.
- **GI antispasmodics with strong anticholinergic activities:** Avoid due to highly anticholinergic burden and uncertain effectiveness.

*Refer to 2023 updated AGS criteria Table 2 for complete list

Potentially inappropriate medication use in older adults due to drug-disease interactions**

- **Heart failure:** Avoid cilostazol, dextromethorphan-quinidine and nondihydropyridine calcium channel blockers in HFrEF.
- **Dementia or cognitive impairment:** Avoid anticholinergics, antipsychotics (chronic use or persistent as-needed use), benzodiazepine, “Z-drug”.
- **Parkinson disease:** Avoid metoclopramide, prochlorperazine, promethazine and antipsychotics ***except*** clozapine, pimavasnserin, and quetiapine.

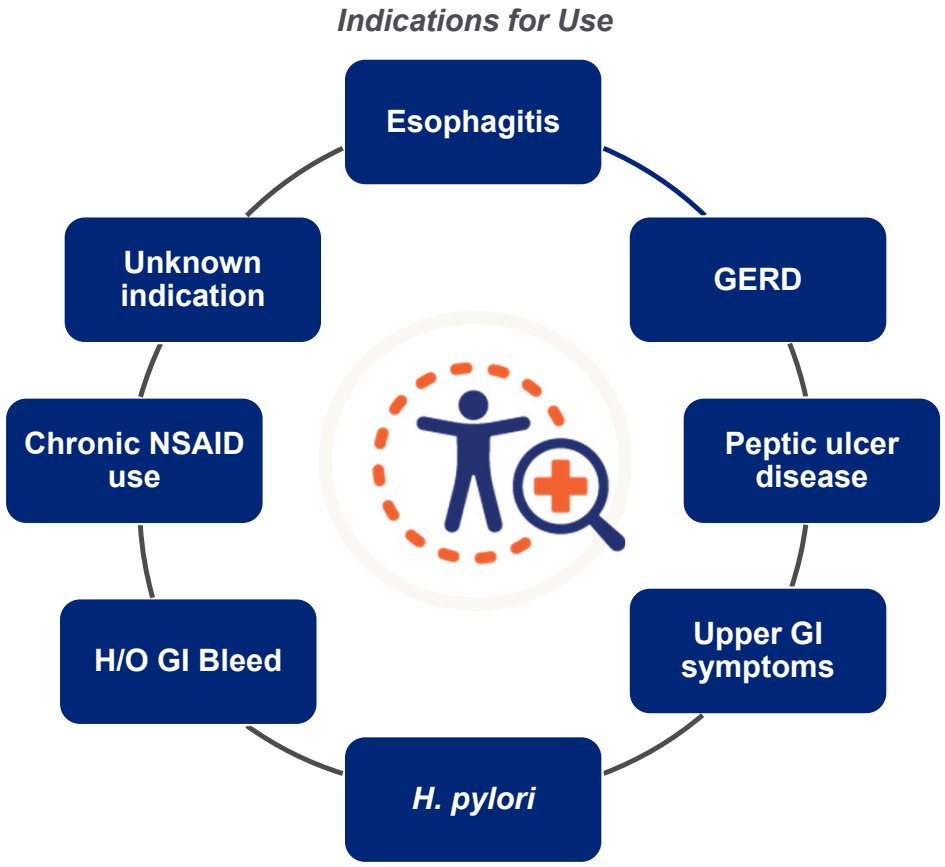
**Refer to Table 3 for complete list

Deprescribing Proton Pump Inhibitors

Proton pump inhibitors

Benefits of therapy:
- Prevent GI Symptoms

Risks of therapy:
- Clostridium difficile infection
- Fractures
- Hypomagnesemia
- Pneumonia
- Headache
- Nausea
- Inappropriate indication and/or duration of therapy



Proton pump inhibitors: Literature

American College of Gastroenterologists guideline:

- Management of GERD and peptic ulcer disease
  - Suggest short-term treatment (2-12 weeks) for most patients
  - GERD 4-8 weeks
  - Peptic ulcer disease 2-12 weeks
- Recommendations are to discontinue PPI after recommended duration of therapy
- Maintenance therapy is warranted for a compelling indication
  - Erosive esophagitis or Barrett esophagus
  - GI bleed
  - Chronic NSAID use
  - If continued, use at lowest dose or changing to on-demand or intermittent PPI use

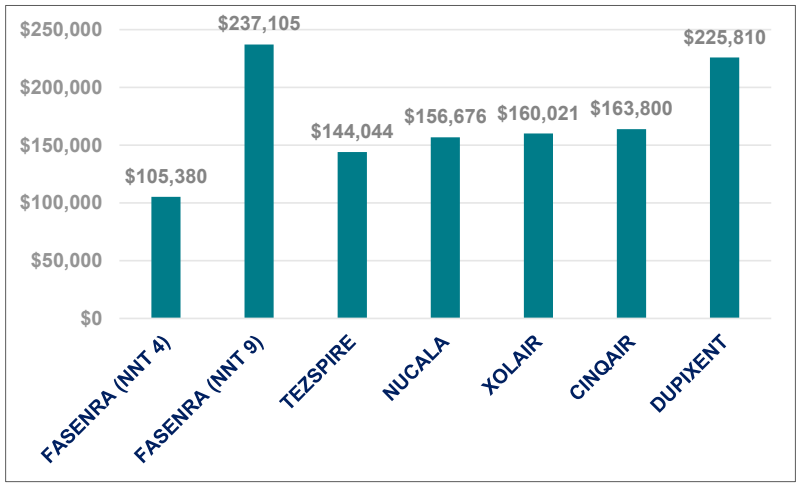
Discontinuation options:

- Taper dose of PPI over 2-4 weeks by reducing the dose, then extending the dosing interval
  - Not many indications warrant BID dosing
- Stop abruptly
  - Avoid if patient has been using longer than 2 months
- Change PPI to an H2R antagonist (ex. famotidine) for 2-3 weeks, then taper H2RA to PRN only

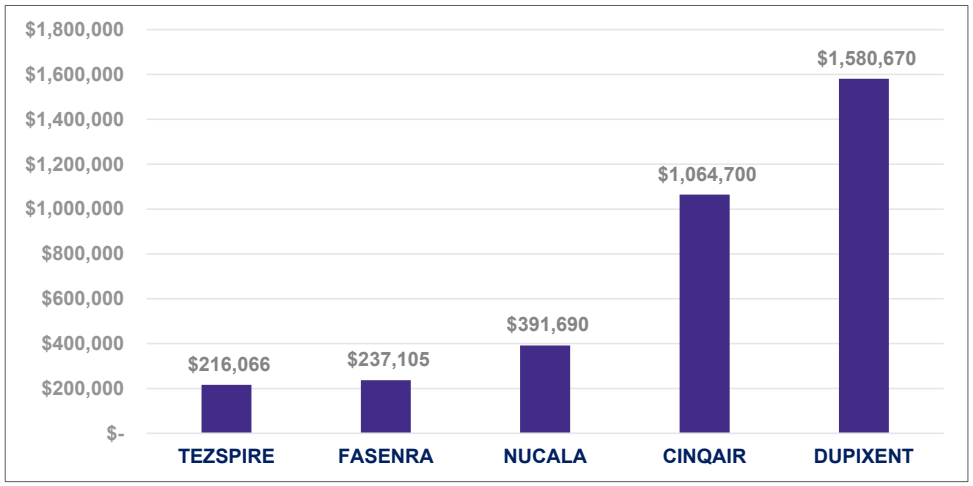
Monitor for heartburn, dyspepsia, regurgitation, epigastric pain, decreased appetite, weight loss

Cost to prevent an asthma exacerbation, hospitalization or ED visit

Annualized Asthma Exacerbation Rate (AAER)



AAER leading to ED visit or hospitalization



AAER leading to hospitalization