

# Optimizing Medication Use at End of Life: A Guide to Deprescribing

Angela House, RPh, MS, BCPS

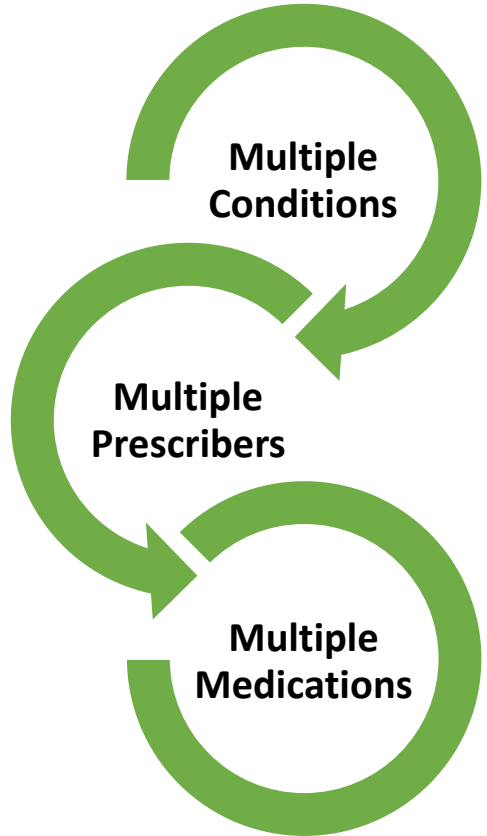
Optum Hospice Pharmacy Services

[Angela.House@Optum.com](mailto:Angela.House@Optum.com)

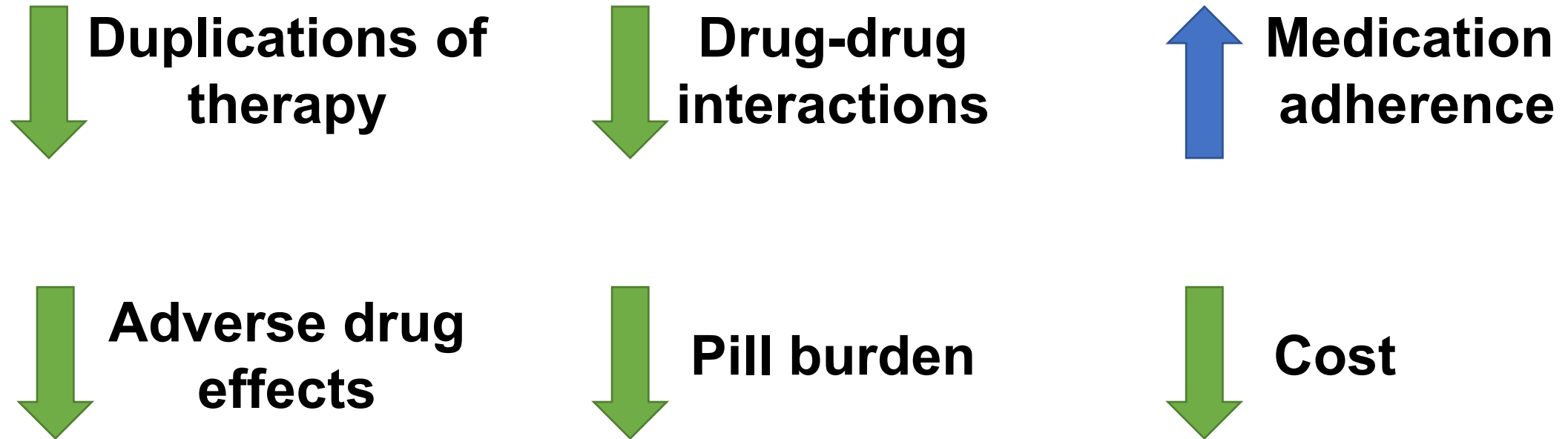
# Objectives

- Describe deprescribing barriers
- Identify medications for deprescribing
- Apply deprescribing principles to practice

# Polypharmacy



# Risk reduction via deprescribing



# Barriers to deprescribing

## Patient/Family

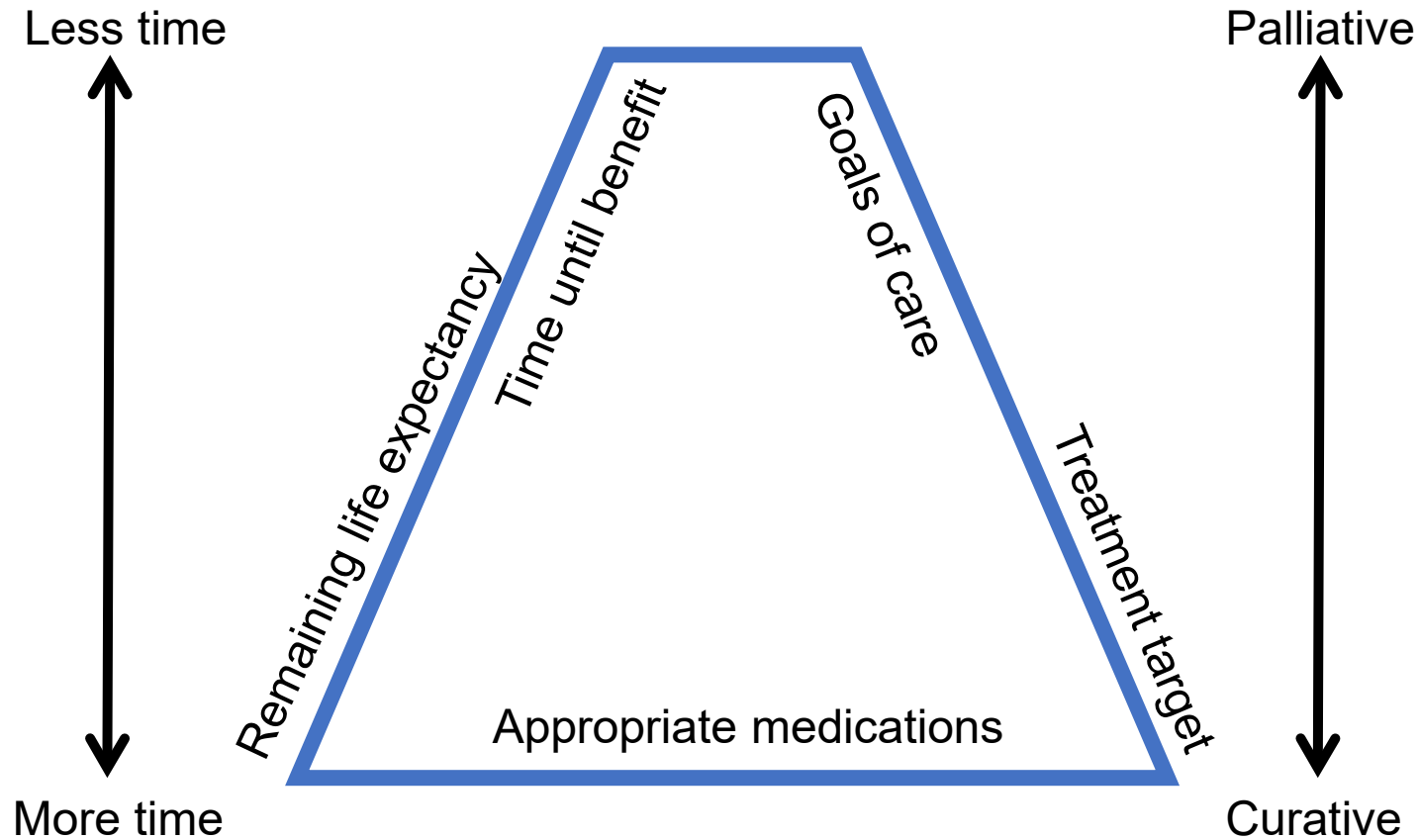
- Changing goals of care
- Attachment to medications
- Risk of abandonment
- Influential family members
- Confrontation with mortality
- Believe that medication discontinuation is suboptimal care

## 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

# Medication Appropriateness

# Medication appropriateness at end of life



# Factors to consider

## Patient factors

- Swallowing ability
- Ambulation status
- Cognitive ability
- Functional status

## Medication factors

- Time to benefit
- Medication safety profile
- Changes in effectiveness

## Environmental factors

- Caregiver ability
- Changes in goals of care



# Medications to Consider Deprescribing

# Case study – Mrs. Davis

## Patient Info

78yo F

Chief complaint:  
dyspnea

Comorbid conditions:  
fall risk, peripheral  
edema, dysphagia

PPS 30%

BP 100/58

HR 70s

## Past Medical History

Atrial fibrillation

Type 2 diabetes

Hypothyroidism

Hyperlipidemia

Renal insufficiency

Peptic ulcer disease

## Medications

Amlodipine (Norvasc®) 10mg PO QD

Carvedilol (Coreg®) 6.25mg PO BID

Furosemide (Lasix®) 40mg PO QD

Potassium chloride 20mEq PO QD

Hydralazine (Apresoline®) 25mg PO  
TID

Clopidogrel (Plavix®) 75mg PO QD

Metformin (Glucophage®) 500mg PO  
BID

Glipizide (Glucotrol®) 5mg PO QAM

Insulin glargine (Lantus®) 20 units SQ  
QHS

Levothyroxine (Synthroid®) 50mcg  
PO QD

Atorvastatin (Lipitor®) 40mg PO QHS

Omeprazole 40mg (Prilosec®) PO  
BID

Multivitamin PO QD

Calcium/vitamin D PO BID

# Mrs. Davis – Low-hanging fruit

Amlodipine (Norvasc<sup>®</sup>) 10mg PO QD  
Carvedilol (Coreg<sup>®</sup>) 6.25mg PO BID  
Furosemide (Lasix<sup>®</sup>) 40mg PO QD  
Potassium chloride 20mEq PO QD  
Hydralazine 25mg PO TID  
Clopidogrel (Plavix<sup>®</sup>) 75mg PO QD  
Metformin (Glucophage<sup>®</sup>) 500mg PO BID  
Glipizide (Glucotrol<sup>®</sup>) 5mg PO QAM  
Insulin glargine (Lantus<sup>®</sup>) 20 units SQ QHS  
Levothyroxine (Synthroid<sup>®</sup>) 50mcg PO QD  
Atorvastatin (Lipitor<sup>®</sup>) 40mg PO QHS  
Omeprazole 40mg (Prilosec<sup>®</sup>) PO BID  
Calcium/vitamin D PO BID  
Multivitamin PO QD



---

# Antihypertensives

---

# Antihypertensives: Literature

## 2017 ACC/AHA Guidelines:

Recommendations for Treatment of Hypertension in Older Persons ( $\geq 65$  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

# Antihypertensives: Risk vs. benefit



## Risks

- Syncope
- Fatigue
- Weakness
- Dizziness
- Falls

## Benefits

- Prevent symptomatic hypertension and/or tachycardia
- Manage edema (diuretics)



# Antihypertensives: Adverse Effects

Medication Class	Adverse Effects: hypotension, dizziness, fatigue
<b>ACE Inhibitors</b> (ex. lisinopril, ramipril, enalapril)	Hyperkalemia, dry cough, angioedema
<b>Angiotensin Receptor Blockers</b> (ex. losartan, irbesartan)	Hyperkalemia, angioedema, chest pain, diarrhea
<b>Alpha-1 Blockers</b> (ex. doxazosin, terazosin)	Orthostatic hypotension, edema
<b>Alpha-2 Agonist</b> (ex. clonidine)	Orthostatic hypotension, anticholinergic side effects, edema
<b>Beta-Blockers</b> (ex. metoprolol, carvedilol, atenolol)	Bradycardia, bronchospasms (non-selective), cold extremities, mask symptoms of hypoglycemia
<b>DHP Calcium Channel Blockers</b> (ex. amlodipine, nifedipine)	Edema, flushing, headache
<b>Non-DHP Calcium Channel Blockers</b> (ex. diltiazem, verapamil)	Edema, bradycardia, constipation, flushing
<b>Diuretics</b> (ex. furosemide, hydrochlorothiazide)	Electrolyte imbalance, dehydration, nocturia
<b>Direct Arterial Vasodilators</b> (ex. hydralazine)	Headache, palpitations, angina, sodium and water retention

# Antihypertensives: Deprescribing

## Opportunities to deprescribe

Symptoms of hypotension?

Adverse effects from BP meds?

Change in patient status?

Time to benefit?



# Antihypertensives: Deprescribing

## Deprescribing

How to  
discontinue?

What to discontinue first?

Abrupt  
discontinuation

Taper (ex. beta  
blockers,  
clonidine)

Medication that  
is causing  
adverse drug  
effects

Medication with  
least benefit or  
without dual  
benefit

Medication that  
is inconvenient  
for  
patient/family

Medication that  
was last started

# Antihypertensives: Beneficial agents

## Diabetes

- ACE-Inhibitors
- ARBs

## Chronic Kidney Disease

- ACE-Inhibitors
- ARBs

## Atrial fibrillation

- Beta Blockers
- Non-DHP CCB (ex. diltiazem)

## Heart Failure

### Benefit:

- ACE-Inhibitors
- ARBs
- Beta blockers
- Loop diuretics

### Possible Benefit

- Vasodilators
- Aldosterone antagonist
- Thiazide diuretics

# Mrs. Davis

## Poll Question 1

### Medication List:

- Amlodipine (Norvasc®) 10mg PO daily
- Carvedilol (Coreg®) 6.25mg PO BID
- Furosemide (Lasix®) 40mg PO daily
- Potassium chloride 20mEq PO daily
- Hydralazine 25mg PO TID
- Clopidogrel (Plavix®) 75mg daily
- Metformin (Glucophage®) 500mg PO BID
- Glipizide (Glucotrol®) 5mg PO qam
- Insulin glargine (Lantus®) 20 units QHS
- Levothyroxine (Synthroid®) 50mcg PO daily
- Atorvastatin (Lipitor®) 40mg PO qhs
- Omeprazole 40mg BID

**Which antihypertensive would you consider reducing or discontinuing FIRST?**

- A. Amlodipine (Norvasc®) 10mg PO daily
- B. Carvedilol (Coreg®) 6.25mg PO BID
- C. Furosemide (Lasix®) 40mg PO daily
- D. Hydralazine (Apresoline®) 25mg PO TID

# Mrs. Davis

## Poll Question 1

### Medication List:

- Amlodipine (Norvasc®) 10mg PO daily
- Carvedilol (Coreg®) 6.25mg PO BID
- Furosemide (Lasix®) 40mg PO daily
- Potassium chloride 20mEq PO daily
- Hydralazine 25mg PO TID
- Clopidogrel (Plavix®) 75mg daily
- Metformin (Glucophage®) 500mg PO BID
- Glipizide (Glucotrol®) 5mg PO qam
- Insulin glargine (Lantus®) 20 units QHS
- Levothyroxine (Synthroid®) 50mcg PO daily
- Atorvastatin (Lipitor®) 40mg PO qhs
- Omeprazole 40mg BID

**Which antihypertensive would you consider reducing or discontinuing FIRST?**

- A. Amlodipine (Norvasc®) 10mg PO daily**
- B. Carvedilol (Coreg®) 6.25mg PO BID
- C. Furosemide (Lasix®) 40mg PO daily
- D. Hydralazine (Apresoline®) 25mg PO TID

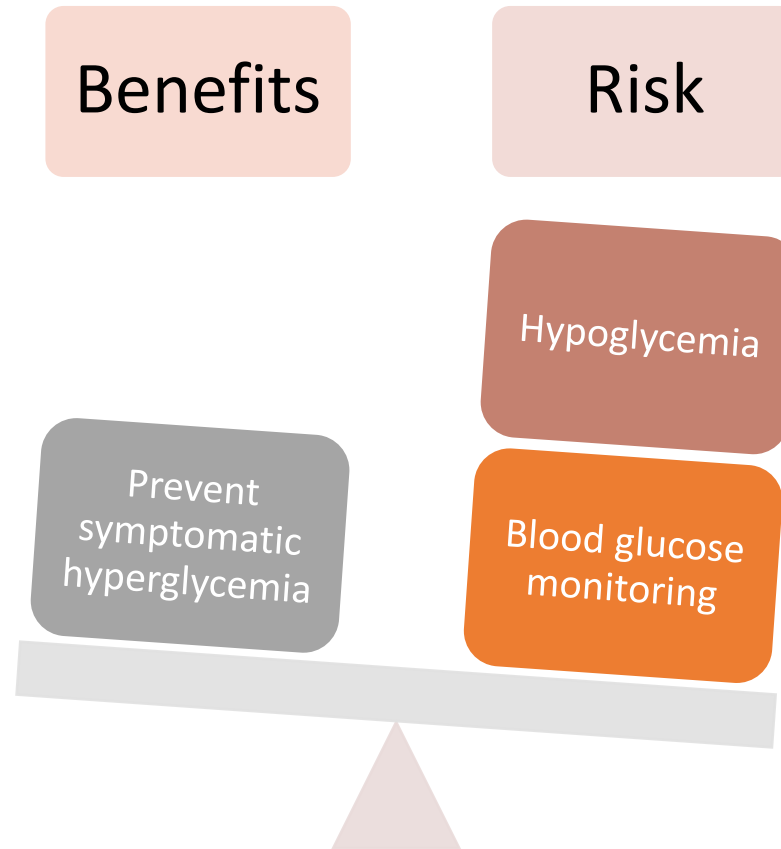
Amlodipine can cause peripheral edema that does not respond well to diuretics.

---

# Diabetic Medications

---

# Diabetic medications: Risk vs. benefit



# Diabetes: Hyperglycemia vs. hypoglycemia

## Hyperglycemia Symptoms

- Blurred vision
- Difficulty concentrating
- Dry mouth
- Fatigue
- Headaches
- Polydipsia
- Polyphagia
- Polyuria
- Weight loss

## Hypoglycemia Symptoms

- Clumsy or jerky movements
- Confusion
- Difficult concentrating
- Dizziness
- Falls
- Headache
- Hunger
- Lethargy
- Mental or behavior changes
- Pale skin
- Palpitations
- Seizures
- Shakiness
- Sweating

# Diabetic medications: Literature

## ADA Guideline Summary

- “For patients with advanced diabetes complications, life-limiting comorbid illness, or substantial cognitive or functional impairment, it is reasonable to set less intensive glycemic target goals”
- “Providers should be vigilant in preventing severe hypoglycemia in patients with advanced disease and should not aggressively attempt to achieve near-normal A1C levels in patients in whom such targets cannot be safely and reasonably achieved”

American Diabetes Association. 2020; Farrell B, 2017

## Canadian guidelines

- Deprescribe antihyperglycemic agents that cause hypoglycemia
- Deprescribe antihyperglycemic agents in patients experiencing or at risk of adverse effects
- Individual glycemic targets to goal of care for terminally ill patients



# Diabetic medications: Literature

Patient characteristics/ health status	Rationale	Reasonable A1c goal	Fasting or pre-prandial glucose	Bedtime glucose
Healthy	Longer life expectancy	< 7.5%	90-130mg/dL	90-150 mg/dL
Complex/ intermediate	Intermediate life expectancy	< 8%	90-150mg/dL	100-180 mg/dL
Very complex/ poor health	Limited life expectancy	< 8.5%	100-180 mg/dL	110-200 mg/dL
Patients at end of life		Avoid hypoglycemia		

# Diabetic medications: Literature

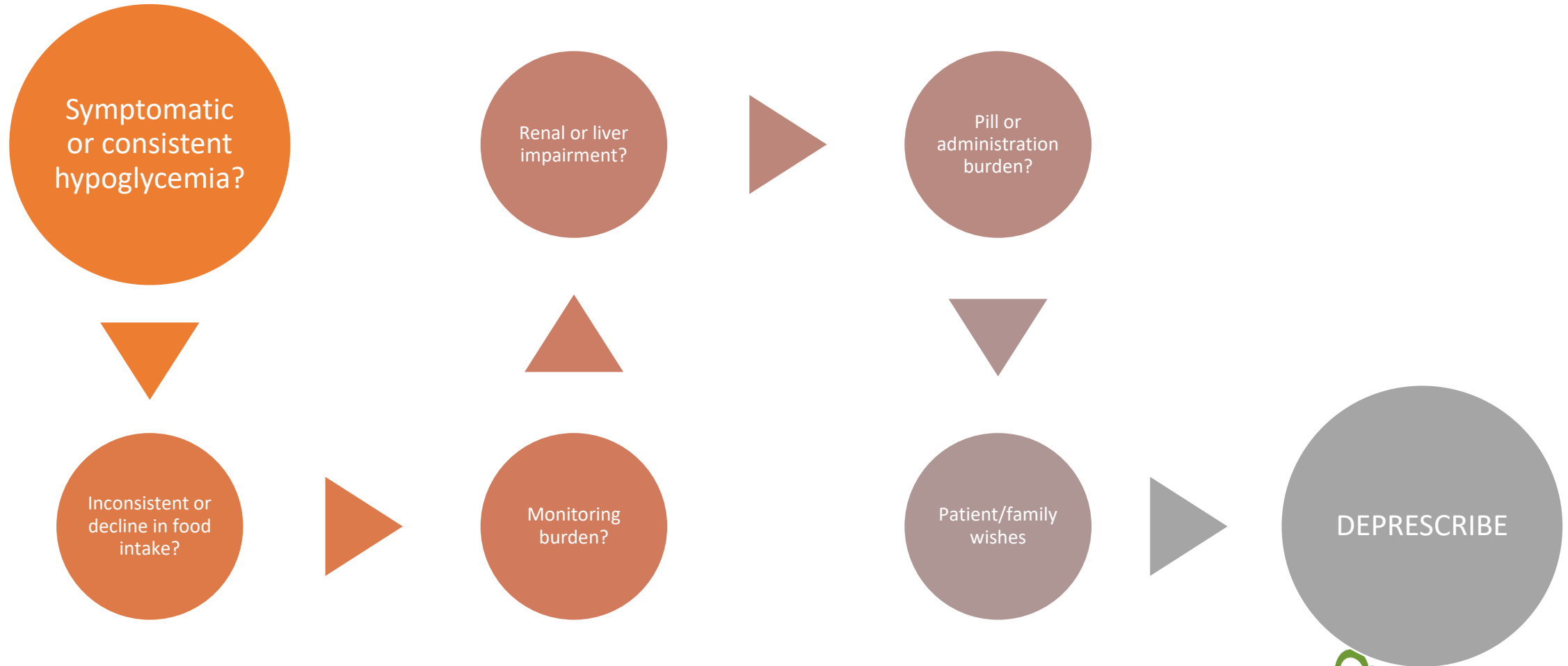
Patient Categories	Life Expectancy	Enteral Intake	Treatment Approach
Active Disease but Relatively Stable	Months to < 1 year	Fair with sporadic improvements or worsening	<p>Goal: prevent hypoglycemia and symptomatic hyperglycemia</p> <p>Management:</p> <ul style="list-style-type: none"> <li>• Adjust medication doses for nausea/vomiting, hepatic/renal impairment, decreased oral intake, weight loss, hypoglycemia</li> </ul>
Impending Death or Organ or System Failure	Days to weeks	Declining calorie intake with anorexia	<p>Goal: Prevent hypoglycemia</p> <p>Management:</p> <ul style="list-style-type: none"> <li>• Adjust medication doses for nausea/vomiting, hepatic/renal impairment, decreased oral intake, weight loss, hypoglycemia</li> <li>• T2DM: Discontinue finger-stick glucose checks</li> <li>• T1DM: May continue for insulin needs.</li> </ul>
Actively Dying	Hours to days	None	<p>Goal: Patient comfort</p> <p>Medications:</p> <ul style="list-style-type: none"> <li>• Consensus is lacking for patients in this stage.</li> <li>• Most prescribers recommend to DC medications</li> <li>• T1DM: May be reasonable to continue insulin with liberal BG targets</li> </ul>

# Diabetic medications: Causing hypoglycemia

Drug	Likely to cause hypoglycemia?
Alpha-glucosidase inhibitor (ex. acarbose, miglitol)	No
Dipeptidyl peptidase 4 (DPP-4) Inhibitors (ex. sitagliptin, saxagliptin, linagliptin)	No
Glucagon-like peptide-1 (GLP-1) agonists (ex. dulaglutide, liraglutide )	No
Insulins	Yes; Highest risk with regular and NPH insulin
Meglitinides (ex. repaglinide, nateglinide)	Yes (low risk)
Biguanides (ex. metformin)	No
Sodium-glucose linked transporter 2 (SGLT <sub>2</sub> ) inhibitors (ex. canagliflozin, dapagliflozin, empagliflozin)	No
Sulfonylureas (ex. glipizide, glyburide, glimepiride)	Yes; Highest risk with glyburide
Thiazolidinediones (TZDs)(ex: pioglitazone, rosiglitazone)	No

\*Not a complete list

# Diabetic medications: Deprescribe



# Case study – Mrs. Davis

## Patient Info

78yo F

Chief complaint:  
dyspnea

Comorbid conditions:  
fall risk, peripheral  
edema, dysphagia

PPS 30%

BP 100/58

HR 70s

## Past Medical History

Atrial fibrillation

Type 2 diabetes

Hypothyroidism

Hyperlipidemia

Renal insufficiency

Peptic ulcer disease

## Medications

Carvedilol (Coreg®) 6.25mg PO BID

Furosemide (Lasix®) 40mg PO QD

Potassium chloride 20mEq PO QD

Hydralazine (Apresoline®) 25mg PO  
TID

Clopidogrel (Plavix®) 75mg PO QD

Metformin (Glucophage®) 500mg PO  
BID

Glipizide (Glucotrol®) 5mg PO QAM

Insulin glargine (Lantus®) 20 units SQ  
QHS

Levothyroxine (Synthroid®) 50mcg  
PO QD

Atorvastatin (Lipitor®) 40mg PO QHS

Omeprazole 40mg (Prilosec®) PO  
BID

# Mrs. Davis

## Poll Question 2

### Diabetic medications:

- Metformin (Glucophage®) 500mg PO BID
- Glipizide (Glucotrol®) 5mg PO qam
- Insulin glargine (Lantus®) 20 units QHS

**Which diabetic medication would you consider reducing or discontinuing due to Mrs. Davis's renal insufficiency and increased risk for lactic acidosis?**

- A. Metformin (Glucophage®) 500mg PO BID
- B. Glipizide (Glucotrol®) 5mg PO qam
- C. Insulin glargine (Lantus®) 20 units QHS

# Mrs. Davis

## Poll Question 2

### Diabetic medications:

- Metformin (Glucophage®) 500mg PO BID
- Glipizide (Glucotrol®) 5mg PO qam
- Insulin glargine (Lantus®) 20 units QHS

Renal impairment and age >65 puts Mrs. Davis at increased risk for developing lactic acidosis.

**Which diabetic medication would you consider reducing or discontinuing due to Mrs. Davis's renal insufficiency and increased risk for lactic acidosis?**

- A. Metformin (Glucophage®) 500mg PO BID**
- B. Glipizide (Glucotrol®) 5mg PO qam**
- C. Insulin glargine (Lantus®) 20 units QHS**

# Mrs. Davis: What is the best plan?

## Medications in question:

- Metformin (Glucophage®) 500mg PO BID
- Glipizide (Glucotrol®) 5mg PO qam
- Insulin glargine (Lantus®) 20 units QHS

## Associated risks:

- Metformin: renally cleared and has risk of lactic acidosis
- Glipizide: risk of hypoglycemia
- Insulin glargine: risk of hypoglycemia and burden of injections

## What are our options?

- Discontinue one agent
- Reduce doses

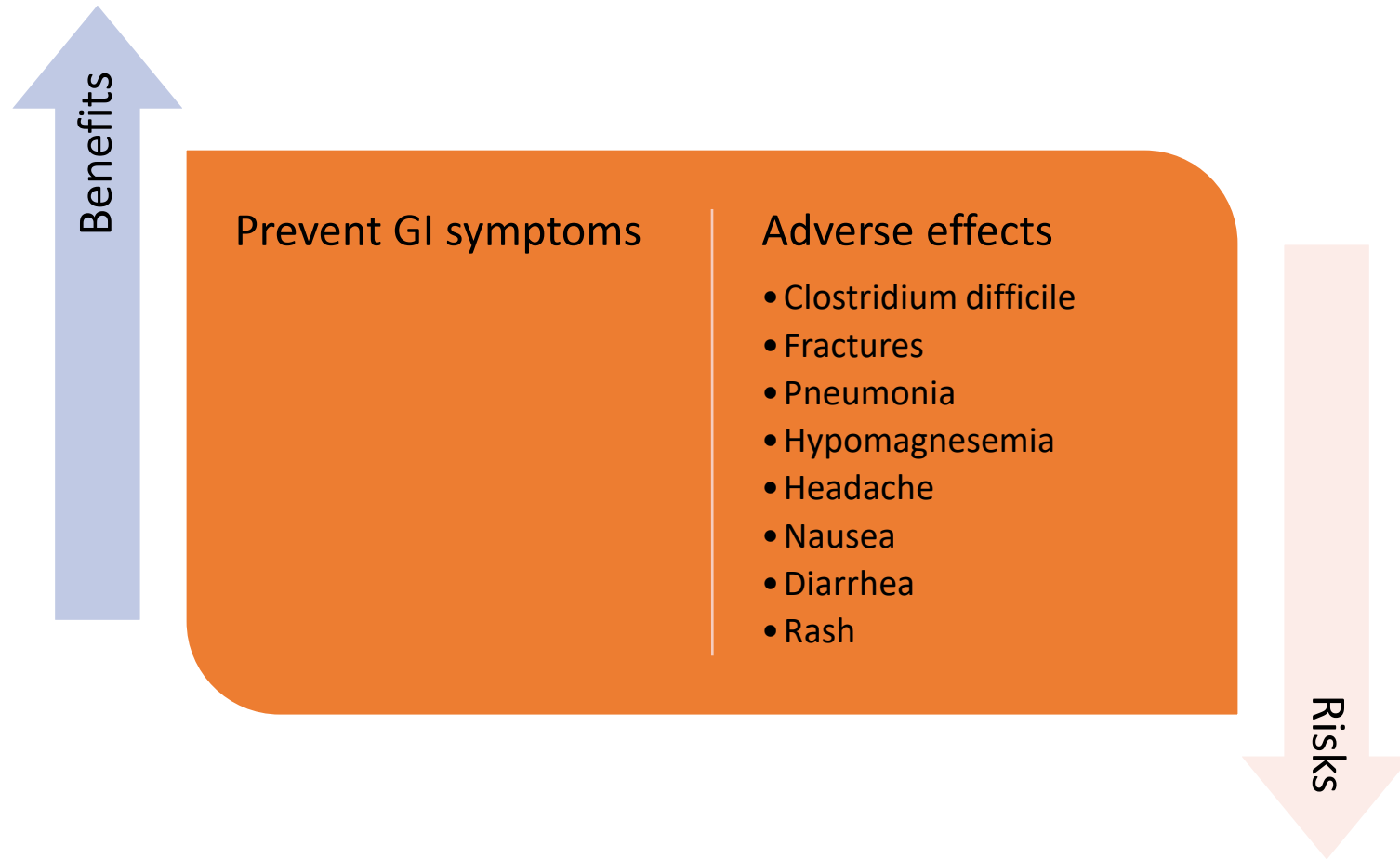


---

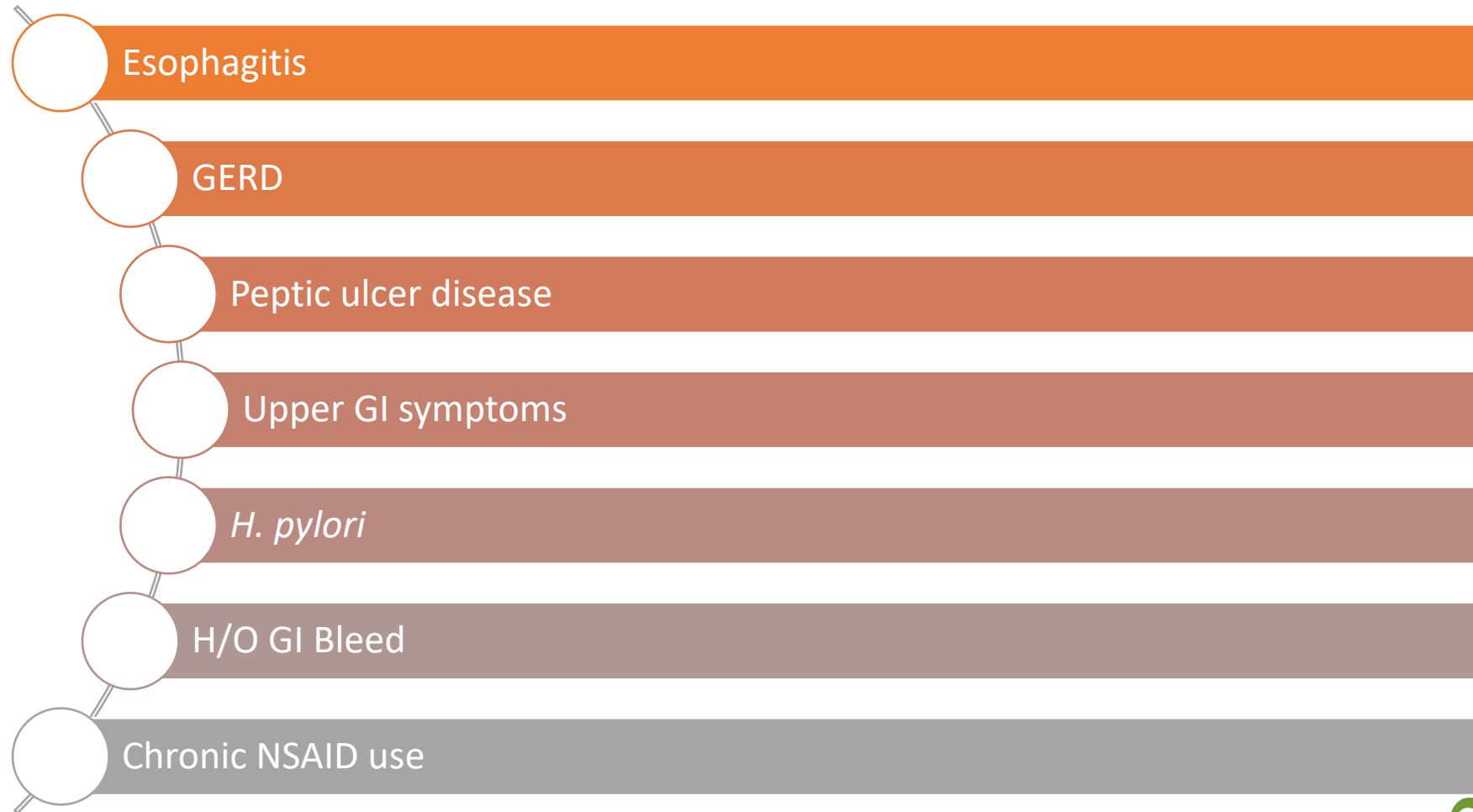
# Proton Pump Inhibitors (PPIs)

---

# PPIs: Risk vs. benefit



# PPIs: Appropriate indications



# PPIs: Literature

## American College of Gastroenterologists guidelines

- 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/continued therapy is warranted for a compelling indication such as erosive esophagitis or Barrett's esophagus.
    - If continued, use at lowest dose or changing to on-demand or intermittent PPI use

# PPIs: Deprescribe

## Discontinuation options:

- Taper dose of PPI
  - Not many indications warrant BID dosing
- Stop abruptly
- Change PPI to an H2 antagonist (ex. famotidine) as an alternative.

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

# Mrs. Davis

## Poll Question 3

### PMH:

- Atrial fibrillation
- Type 2 diabetes
- Hypothyroidism
- Hyperlipidemia
- Renal insufficiency
- Peptic ulcer disease

**Mrs. Davis takes omeprazole for peptic ulcer disease. What is the recommended duration of therapy?**

- A. 2 to 12 weeks
- B. 8 to 16 weeks
- C. Indefinitely
- D. There are no recommendations on duration of therapy.

# Mrs. Davis

## Poll Question 3

### PMH:

- Atrial fibrillation
- Type 2 diabetes
- Hypothyroidism
- Hyperlipidemia
- Renal insufficiency
- Peptic ulcer disease

Guidelines suggest that a short-term PPI treatment of 2 to 12 weeks in duration is appropriate for most patients with peptic ulcer disease. Long term PPI use increases a patient's risk of developing adverse effects.

**Mrs. Davis takes omeprazole for peptic ulcer disease. What is the recommended duration of therapy?**

- A. 2 to 12 weeks**
- B. 8 to 16 weeks
- C. Indefinitely
- D. There are no recommendations on duration of therapy.

# Communication Techniques



# Deprescribing Process

Step 1: Obtain a comprehensive medication history



Step 2: Identify potentially inappropriate medications



Step 3: Determine priority of medications to be stopped



Step 4: Plan and initiate medication discontinuation



Step 5: Monitor, support, and document

# End of life communication

Study findings:

- Avoiding discussions can lead to poor patient satisfaction and psychological morbidity

Key areas of patient satisfaction include:

- Talking honestly and straightforward
- Talking about dying
- Providing information in a sensitive manner
- Listening and encouraging questions
- Being considerate with timing of discussions

# The BUILD Model



# The BUILD Model

- **Build** a foundation of trust and respect.
- **Understand** what the patient and caregiver know about the medication and disease progression.
- **Inform** the patient and caregiver of evidence-based information.
- **Listen** to the patient's and caregiver's goals and expectations.
- **Develop** a plan of care in collaboration with the patient and caregiver.

# The BUILD Model: Key Phrases

## Building a foundation of trust and respect:

- “I appreciate you sitting down to talk with me today.”
- “Your dad is really lucky to have you looking out for him.”

## Understanding what the patient and caregiver know about the medication and disease:

- “How is this medication supposed to help you?”
- “When will you know that the medication is no longer working like it’s supposed to?”

## Informing the patient and caregiver about appropriateness of medications:

- “We know that this drug works well in milder disease, but it doesn’t help as much in advanced disease.”
- “We’ll need to keep making adjustments to your medications as things change.”

# The BUILD Model: Key Phrases

Listening to the patient and caregiver as they share goals and expectations:

- “What other information can I provide to help you decide what is best?”
- “Did you and the patient ever talk about what they would want if they couldn’t make their own medical decisions?”

Developing a plan of care in collaboration with the patient and caregiver:

- “I can’t tell you what to do or make the choice for you, but I can provide you with tools so you can make an informed decision.”
- “We have some options: we can stop the medication now, we can reduce the dose and follow-up next week, or we can leave everything the same for now.”

# Planning discussions

---

At time of admission

---

Prior to recertification

---

During a family or facility care conference

---

When it is time to re-order a potentially disease-delaying medication

---

When filling the patient's pillbox or ordering refills

---

Change in location or level of care

---

Change in patient condition

---

# Key Points

---

Continuously reevaluate medication appropriateness at end of life.

---

Deprescribing guidelines are lacking and though some clinical guidelines mention medication use at end of life, recommendations are not specific. Clinical judgement is required.

---

Medication use of end of life should be prioritized based on the patient's preferences, functional status, goals of care, and prognosis.

---

Practicing effective communication leads to increased patient satisfaction, better understanding, and improved clinical outcomes.

---



# Thank you.

Angela House, RPh, MS, BCPS

Clinical Pharmacist, Manager of Formulary Development

[angela.house@optum.com](mailto:angela.house@optum.com)



# References

1. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018;71(19):e127-e248. <https://doi.org/10.1016/j.jacc.2017.11.006>
2. American Diabetes Association. Standards of medical care in diabetes—2020. *Diabetes Care* 2020;43(Suppl. 1):S152-S162 [https://care.diabetesjournals.org/content/43/Supplement\\_1/S152](https://care.diabetesjournals.org/content/43/Supplement_1/S152)
3. Angelo M, Ruchalski C, Sproge BJ. An approach to diabetes mellitus in hospice and palliative medicine. *Journal of Palliative Medicine*. 2011;14(1):83-87.
4. Boghossian TA, Rashid FJ, Thompson Q, et al. Deprescribing versus continuation of chronic proton pump inhibitor use in adults (Review). *Cochrane Database of Systematic Reviews*. 2017(3). DOI: 10.1002/14651858.CD011969.pub2.
5. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Diabetes in the Elderly. *Can J Diabetes* 37 (2013) S184-S190.
6. Collier KS, Kimbrel J, Protus BM. Medication Appropriateness at End of Life: A New Tool for Balancing Medicine and Communication for Optimal Outcomes – the BUILD Model. *Home Healthcare Nurse* 2013;31(9):518-524.
7. Farrell B, Black C, Thompson W, McCarthy L, Rojas-Fernandez C, Lochnan H, et al. Deprescribing antihyperglycemic agents in older persons. Evidence-based clinical practice guideline. *Can Fam Physician* 2017;63:832-43 (Eng), e452-65 (Fr).
8. Farrell B, Pottie K, Thompson W, et al. Deprescribing proton pump inhibitors. *Canadian Family Physician*. May 2017(63):354-364.
9. Holmes HM. Reconsidering medication appropriateness for patients late in life. *Arch Intern Med* 2006;166:605-9
10. Kutner JS, Blatchford PJ, Taylor DH, et al. Safety and Benefit of Discontinuation Statin Therapy in the Setting of Advanced, Life-Limiting Illness. *JAMA Intern Med*. 2015;175(5):691-700.

# References

11. Lee SJ, Jacobson MA, Johnston CB. Improving Diabetes Care for Hospice Patients. *American Journal of Hospice & Palliative Medicine* 2015.
12. Lexicomp. Lexi-Drugs [database online]. Wolters Kluwer Health, Inc. <http://online.lexi.com/lco/action/home>. Accessed December, 2019.
13. Linsky A, Simon S, Bokhour B. Patient perceptions of proactive medication discontinuation. *Patient Educ Couns* 98 2015;220-225.
14. Lipska KJ, Krumholz H, Soones T, Lee SJ. Polypharmacy in the Aging Patient: A Review of Glycemic Control in Older Adults With Type 2 Diabetes. *JAMA*. 2016 Mar;315(10):1034-45.
15. Morley JE. Hypertension: Is It Overtreated in the Elderly? *Journal of the American Medical Directors Association*. 2010; 11(3):147-152. doi:10.1016/J.JAMDA.2009.12.081
16. Morley JE. Systolic Hypertension Should Not Be Treated in Persons Aged 80 and Older Until Blood Pressure Is Greater than 160 mmHg. *Journal of the American Geriatrics Society*. 2013; 61(7):1197-1198. doi:10.1111/JGS.12322\_1
17. Parekh N, Page A, Ali K, Davies K, Rajkumar C. A practical approach to the pharmacological management of hypertension in older people. *Therapeutic Advances in Drug Safety*. 2017; 8(4):117-132. doi:10.1177/2042098616682721
18. Protus BMC, Kimbrel JM, Grauer PA. End Stage Heart Disease: Table 1. Medication Considerations in End Stage Heart Failure In: *Palliative care consultant: a reference guide for palliative care: guidelines for effective management of symptoms*. 4th ed. Montgomery, AL: Hospiscript Services; 2015:222.
19. Reeve E, Shakib S, Hendrix I, et al. Review of deprescribing processes and development of an evidence-based, patient-centered deprescribing process. *Br J Clin Pharmacol* 2014;78(4):738-747
20. Ren D, Gurney E, Hornecker JR. *US Pharmacist*. 2019;44(12):25-31. [https://www.medscape.com/viewarticle/923739\\_6](https://www.medscape.com/viewarticle/923739_6)
21. Stuart B. Palliative Care and Hospice in Advanced Heart Failure. *J Palliat Med* 2007;10:210-228.
22. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *European Heart Journal*. 2018; 39: 3021-3104. doi:10.1093/eurheartj/ehy339