Managing Complex Pharmacological Scenarios: Deprescribing and Polypharmacy

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Disclosures

I have no actual or potential conflicts of interest in relation to this presentation

Learning Objectives

1. Describe how problematic polypharmacy and prescribing cascades can lead to adverse outcomes

2. Identify opportunities to optimize and deprescribe medications in older adults living with frailty

3. Apply deprescribing and geriatric principles to older adults with type 2 diabetes mellitus

Differentiating Polypharmacy

APPROPRIATE *POLYPHARMACY*

"Prescribing for an individual for complex conditions or multiple conditions in circumstances where medicines use has been optimised and where medicines are prescribed according to best evidence"

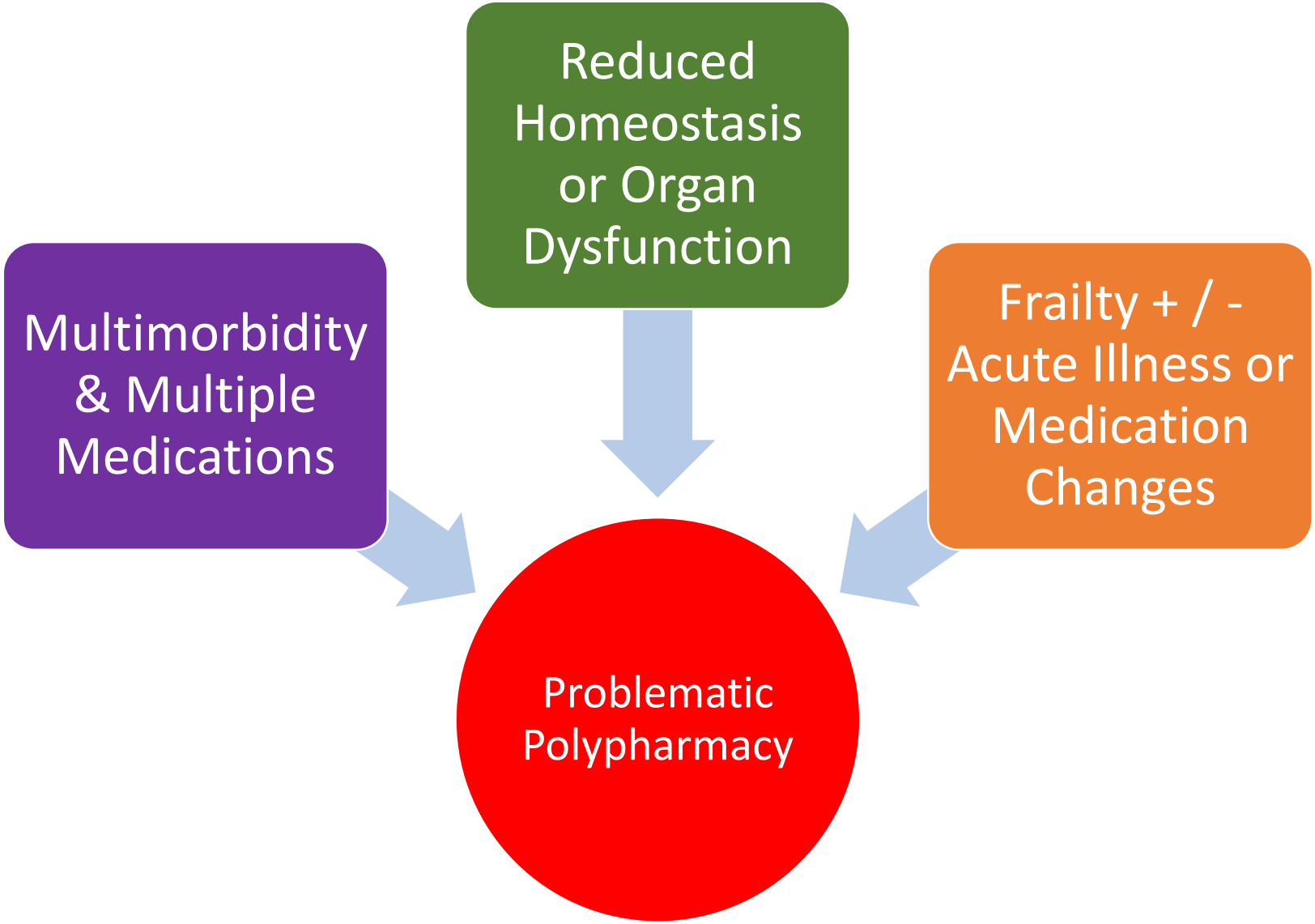
PROBLEMATIC *POLYPHARMACY*

"Prescribing of multiple medicines inappropriately, or where the intended benefits of medications are not realized"

Duerden M, et al. *Prescriber* 2014;25:44-47.

www.kingsfund.org.uk

Polypharmacy Risk Factors



Decreased Homeostasis and Organ Dysfunction

Pharmacokinetics Changes

Absorption

Distribution

Metabolism (CYP P450)

Excretion

Age-Related Physiological Changes

↑ Adipose tissue

↓ Body water

↓ Albumin

↓ Hepatic metabolism

↓ Renal function

Pharmacodynamic Changes

Changes in receptor binding

↓ # of receptors and receptor activity

↑or↓ Drug efficacy

↑ Toxicity

Adverse Outcomes Associated with Polypharmacy

↑ Risk Adverse Drug Events

- ❑ 2 medications: 13%
- ❑ 5 medications: 58%
- ❑ >7 medications: 82%

Prescribing cascade

Unnecessary drug expenses

ED visits

↓ Adherence

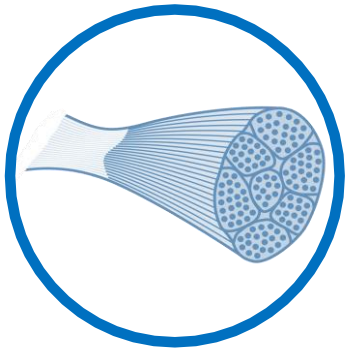
↓ QOL

Functional decline

↑ Mortality risk

Zed et al. *CMAJ* 2008;178:1563-1569; Bourgeois et al. *Pharmacoepidemiol Drug Saf* 2010;19:901-910; Gnjidic D et al. *J Clin Epidemiol* 2012;65(9):989-95; Maher RL, et al. *Expert Opin Drug Saf* 2014;13(1):57-65; Patterson SM et al. *Cochrane Database Syst Rev* 2014;(10): CD008165; Johansson T et al. *Br J Clin Pharmacol 2016;*82:532–548

Frailty and Geriatric Syndromes



Sarcopenia

Falls

Functional decline
& Immobility

Delirium

Malnutrition &
Dehydration

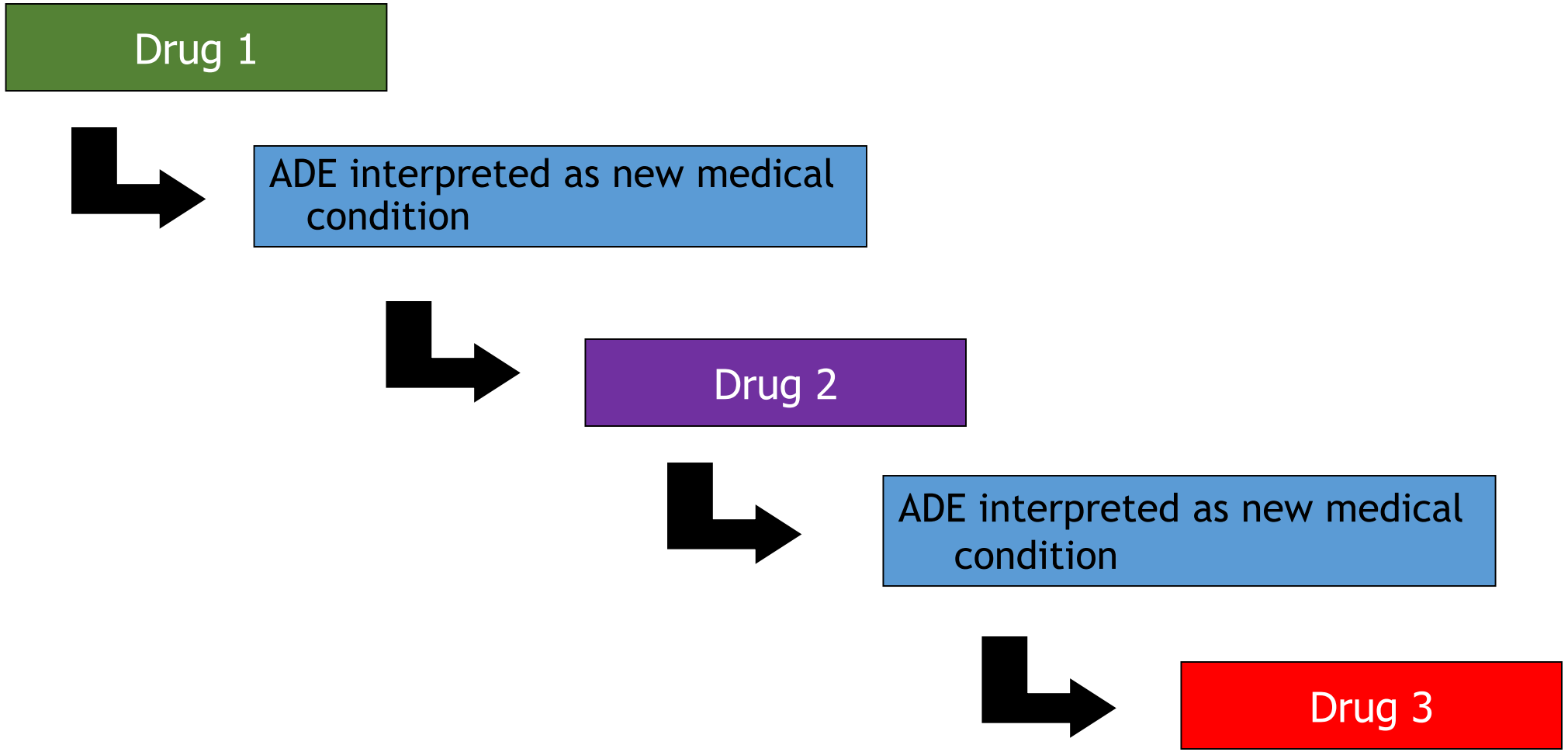
Polypharmacy

Incontinence

Inouye SK et al. *J Am Geriatr Soc* 2007;55(5):780-91.

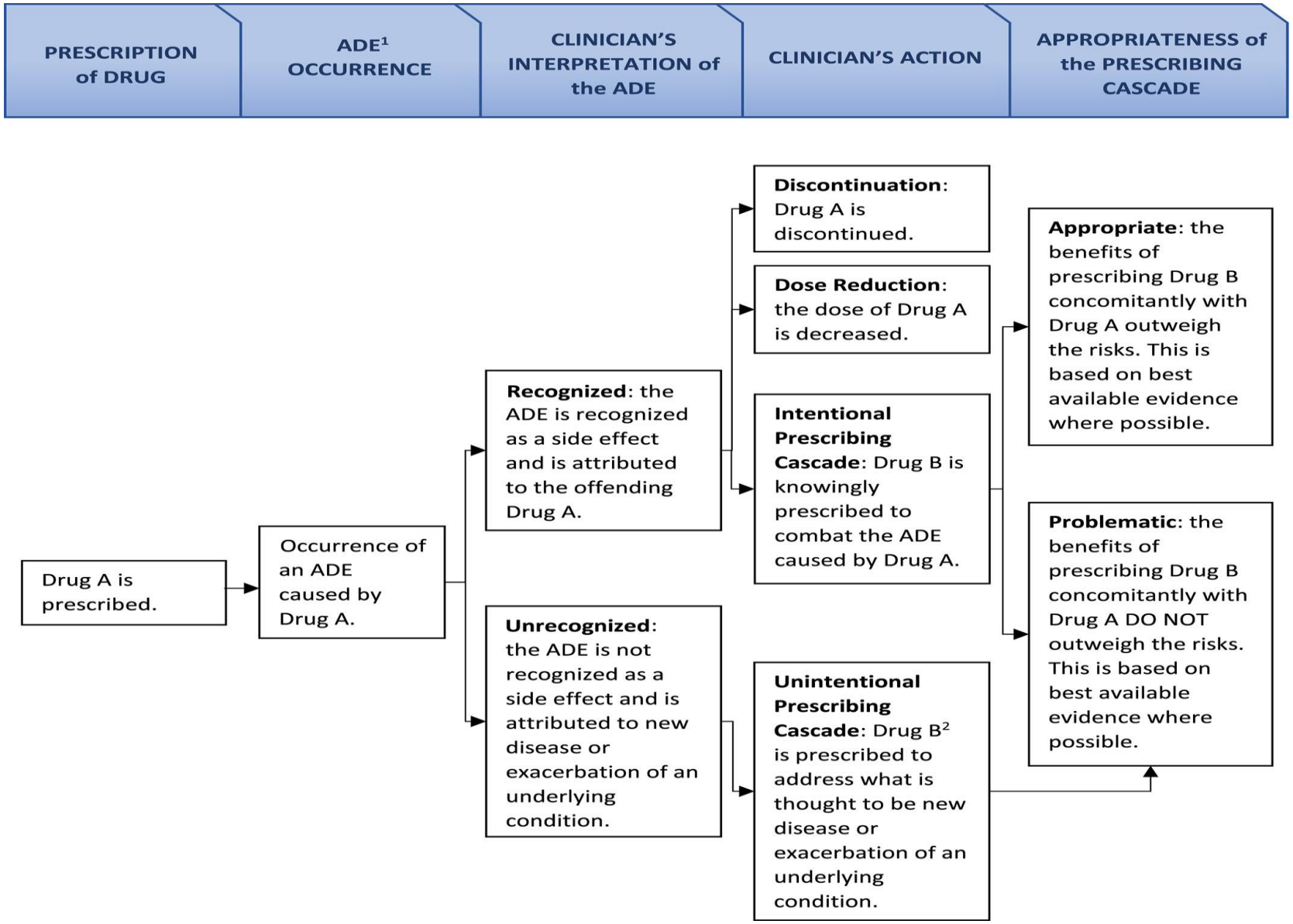
Icons from Noun Project and Sinai Geriatrics

Prescribing Cascades



Rochon PA, Gurwitz JH. *BMJ* 1997;315:1097.

Appropriate and Problematic Prescribing Cascades



McCarthy LM, et al. *J Am Geriatr Soc* 2019; 67: 1023-1026.

ThinkCascades: Clinically Important Prescribing Cascades

Drug A	Side effect	Drug B
Cardiovascular System (n=2)		
Calcium Channel Blocker →	Peripheral edema →	Diuretic
Diuretic →	Urinary incontinence →	Overactive bladder medication
Central Nervous System (n=4)		
Antipsychotic →	Extrapyramidal symptoms →	Antiparkinsonian agent
Benzodiazepine →	Cognitive impairment →	Cholinesterase Inhibitor or memantine
Benzodiazepine →	Paradoxical agitation or agitation secondary to withdrawal →	Antipsychotic
Selective Serotonin Reuptake Inhibitor (SSRI) / Serotonin-norepinephrine Reuptake Inhibitor (SNRI) →	Insomnia →	Sleep agent (e.g., Benzodiazepines, Benzodiazepine Receptor Agonists, Sedating antidepressant, Melatonin)
Musculoskeletal System (n=1)		
NSAID →	Hypertension →	Antihypertensive
Urogenital System (n=2)		
Urinary Anticholinergics →	Cognitive impairment →	Cholinesterase inhibitor or memantine
Alpha-1 Receptor Blocker →	Orthostatic hypotension, dizziness →	Vestibular sedative (e.g., betahistine, Antihistamines, Benzodiazepines)

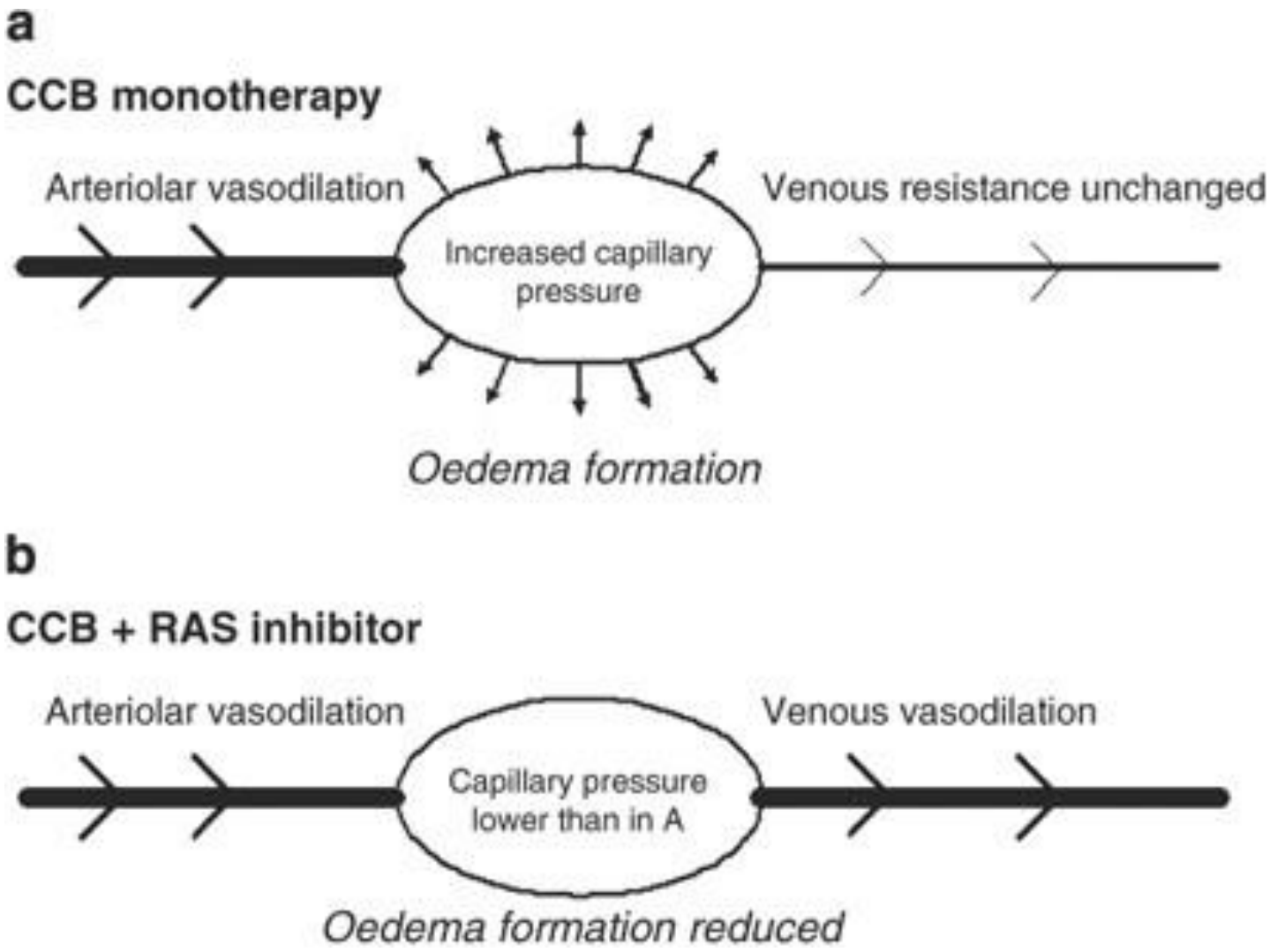
McCarthy LM et al. *Drugs Aging* 2022; 39(10):829-840.

Question 1

Which of the following is an example of a problematic prescribing cascade?

A. Amlodipine – Peripheral edema – Furosemide
B. Morphine – Constipation – Senna
C. Furosemide – Hypokalemia – Potassium Chloride
D. Methotrexate – Liver toxicity – Folic acid

Effect of CCBs + / - RAS inhibition on Capillary Pressure



de la Sierra A. *J Hum Hypertens* 2009; 23: 503–511.

Learning Objectives

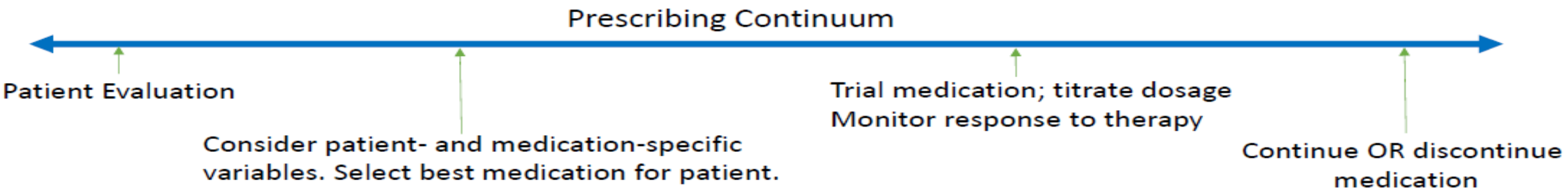
1. Describe how problematic polypharmacy and prescribing cascades can lead to adverse outcomes

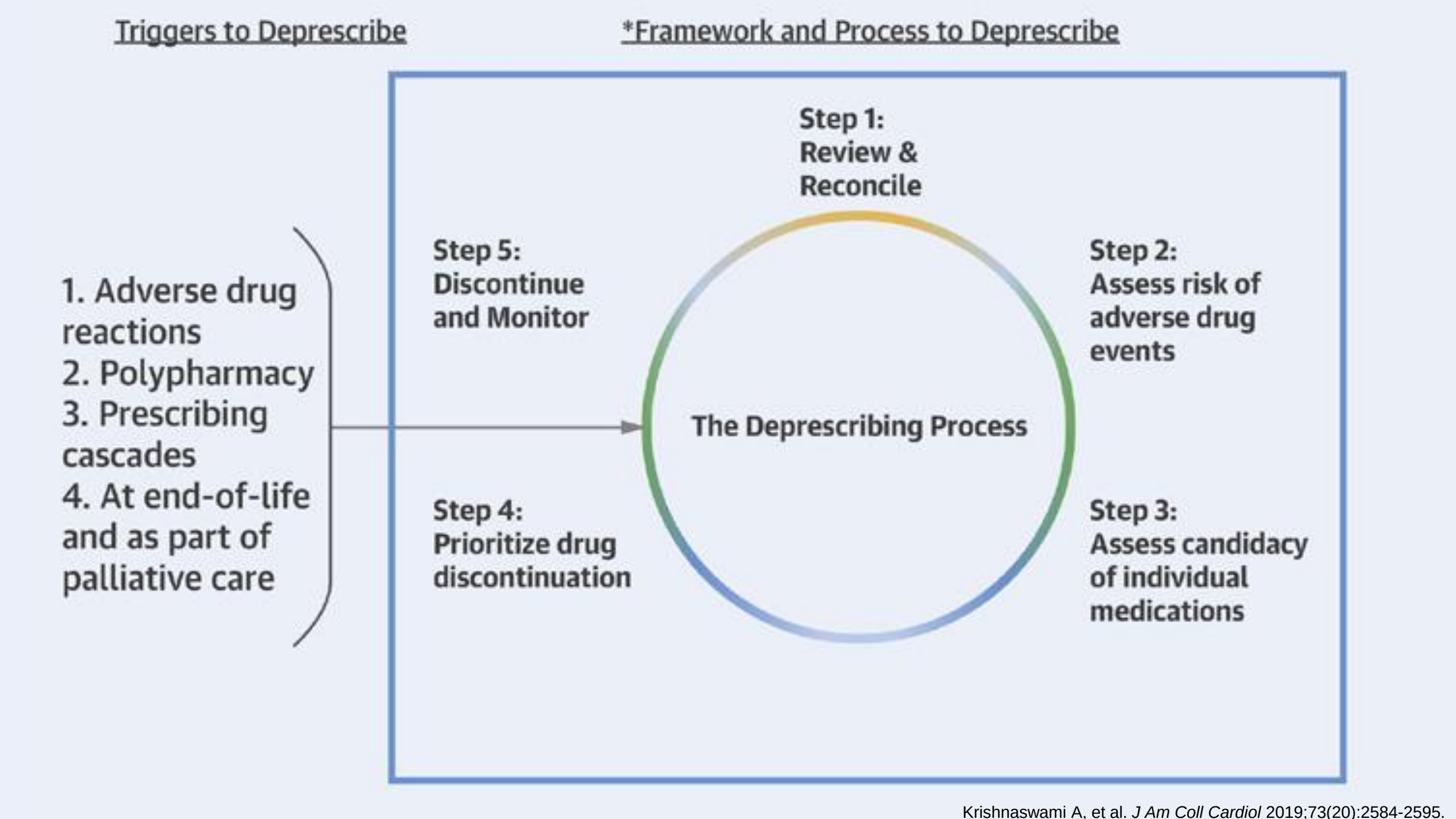
2. Identify opportunities to optimize and deprescribe medications in older adults living with frailty

3. Apply deprescribing and geriatric principles to older adults with type 2 diabetes mellitus

Deprescribing

"The process of ***reducing***,***discontinuing*** or ***substituting*** medications to manage polypharmacy, adverse drug effects and inappropriate or ineffective medication use."





Krishnaswami A, et al. *J Am Coll Cardiol* 2019;73(20):2584-2595.

Tools to Identify Potentially Inappropriate Medications

STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria

PAUL GALLAGHER, DENIS O'MAHONY

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CLINICAL INVESTIGATIONS

American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults

*By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel**

START (screening tool to alert doctors to the right treatment)—an evidence-based screening tool to detect prescribing omissions in elderly patients

P. J. BARRY[1], P. GALLAGHER[1], C. RYAN[2], D. O'MAHONY[1]

[1]Cork University Hospital, Department of Geriatric Medicine, Ireland
[2]University College Cork, School of Pharmacy, Ireland

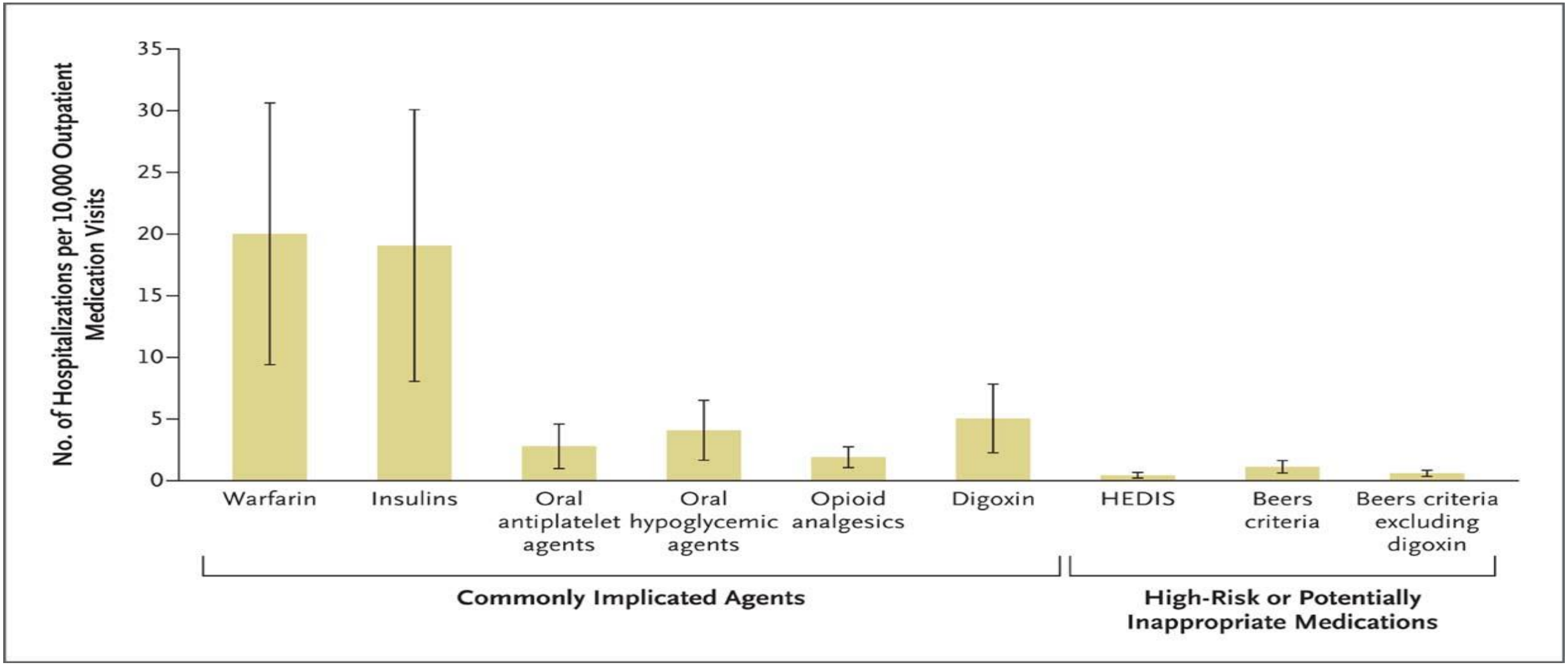
Table 1. Medication Appropriateness Index[6]

Question	score[a]
1. Is there an indication for the drug?	3
2. Is the medication effective for the condition?	3
3. Is the dosage correct?	2
4. Are the directions correct?	2
5. Are the directions practical?	2
6. Are there clinically significant drug-drug interactions?	2
7. Are there clinically significant drug-disease/condition interactions?	1
8. Is there unnecessary duplication with other drug(s)?	1
9. Is the duration of therapy acceptable?	1
10. Is this drug the least expensive alternative compared with others of equal utility?	1
Maximal score of inappropriateness	18

[a]A weight of three is given for indication and effectiveness. A weight of two is assigned to dosage, correct directions, practical directions and drug-drug interactions. A weight of one is assigned to drug-disease interactions, expense, duplication and duration.[9] These results in a total combined score of 0 to 18 (0 meaning the drug is appropriate and 18 representing maximal inappropriateness).

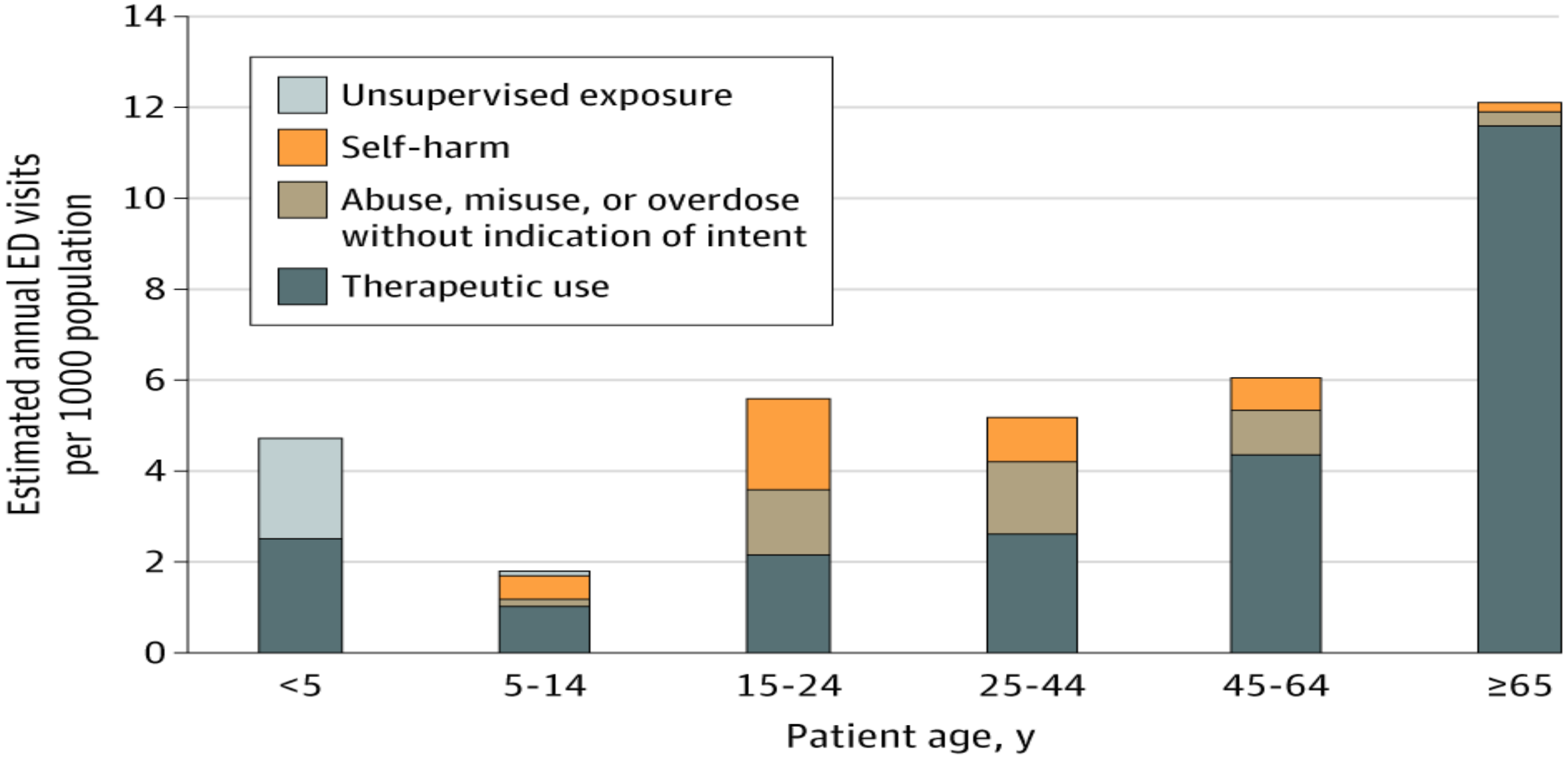
2019 American Geriatrics Society Beers Criteria Update Expert Panel. *J Am Geriatr Soc* 2019;67:674-694; Gallagher P et al. *Int J Clin Pharm Ther* 2008;46:72-83; Barry PJ et al. *Age Ageing* 2007;36:632-8; Hanlon JT et al. *J Clin Epidemiol* 1992;45(10):1045-1051.

Estimated Rates of Emergency Hospitalizations for ADEs in Older US Adults, 2007-2009



Budnitz DS et al. *N Engl J Med* 2011;365:2002-2012.

Estimated Annual ED Visits for Medication Harms, 2017-2019

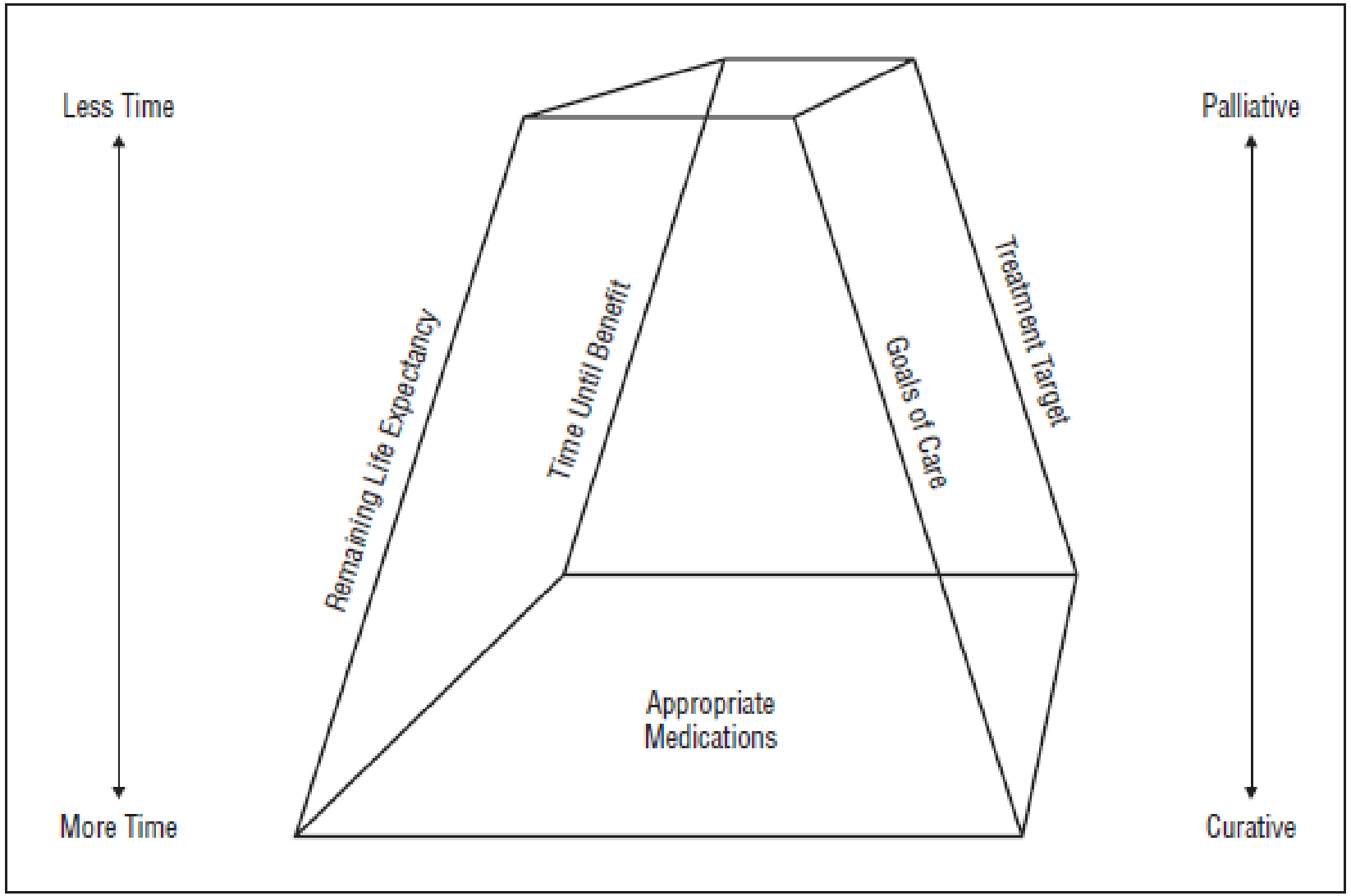


Budnitz DS et al. *JAMA* 2021;326(13):1299–1309.

Tailor Treatments in the Context of an Older Person's Life Course and Goals

Image by *Felix Mittermeier* from Pixabay

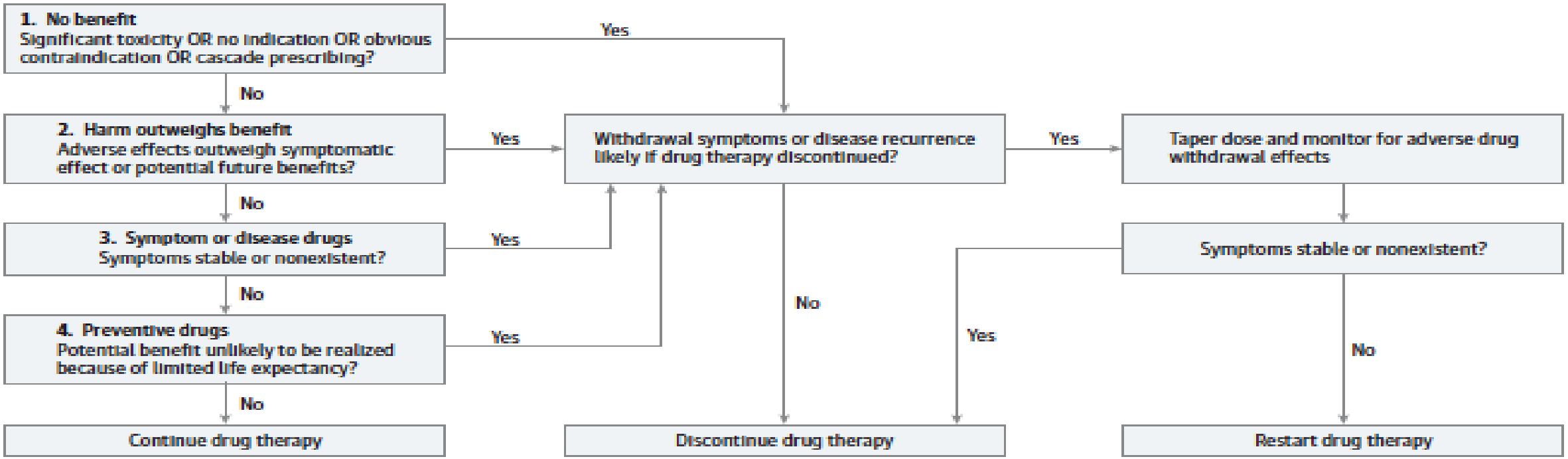
Framework for Making Medication Decisions



Holmes HM et al. *Arch Intern Med* 2006;166:605-9.

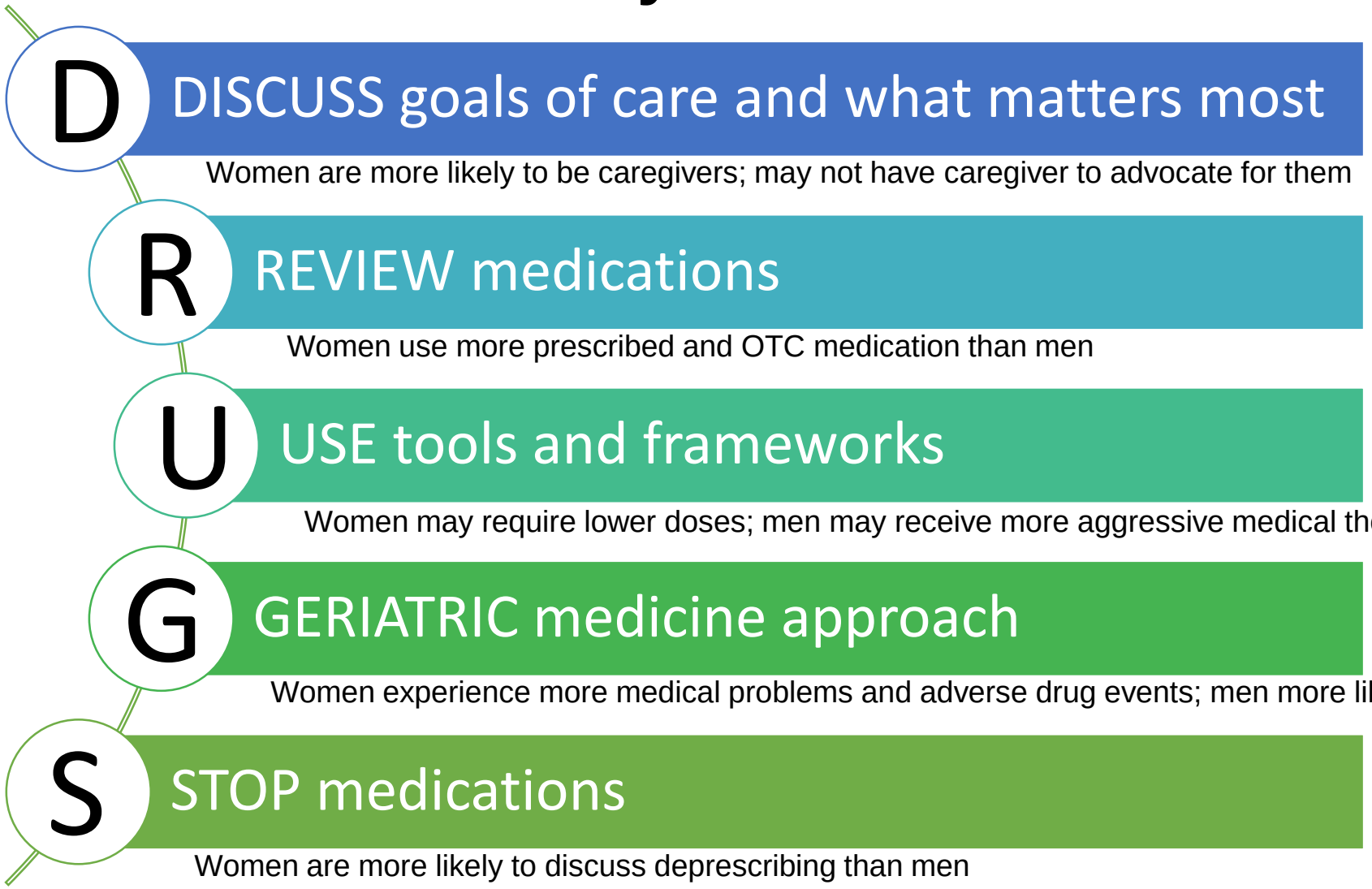
5 Step Deprescribing Protocol

Figure. Algorithm for Deciding Order and Mode in Which Drug Use Could Be Discontinued



Scott IA et al. *JAMA Intern Med 2015;*175(5):827–834.

DRUGS Guide to Optimising Medication Safety for Older Adults



Rochon PA et al. *Lancet Healthy Longev* 2021;2(5):e290-e300.

Question 2

Medication deprescribing may occur by:

A. Stopping a medication
B. Reducing or tapering the dose of a medication
C. Switching to another medication with lower risk profile and equivalent or better efficacy
D. All of the above
E. None of the above

Learning Objectives

Participants will be able to:

1. Describe how problematic polypharmacy and prescribing cascades can lead to adverse outcomes

2. Identify opportunities to optimize and deprescribe medications in older adults living with frailty

3. Apply deprescribing and geriatric principles to older adults with type 2 diabetes mellitus

Clinical Frailty Scale

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

3 Managing Well – People whose medical problems are well controlled, but are not regularly active beyond routine walking.

4 Vulnerable – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 Terminally Ill – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia,** recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia,** they cannot do personal care without help.

Moorhouse P, Rockwood K. *J R Coll Physicians Edinb* 2012;42:333-340.

Glycemic Targets in Older People with Diabetes

Status	Functionally independent	Functionally dependent	Frail and/or with dementia	End of life
Clinical Frailty Index*	1-3	4-5	6-8	9
A1C target *Low risk hypoglycemia (ie. therapy does not include insulin or SU)*	≤7.0%	<8.0%	<8.5%	A1C measurement not recommended. Avoid symptomatic hyperglycemia or any hypoglycemia
A1C target *Higher risk hypoglycemia (ie. therapy includes insulin or SU)*		7.1-8.0%	7.1-8.5%	
CBGM Preprandial: Postprandial:	4-7 mmol/L 5-10 mmol/L	5-8 mmol/L <12 mmol/L	6-9 mmol/L <14 mmol/L	Individualized

Diabetes Canada Clinical Practice Guidelines Expert Committee. *Can J Diabetes* 2018;42(Suppl 1):S1-S325.

Question 3

Lana is a 72 yo woman with DM2 x 10 yrs. She lives with her husband and provides care for him in their apartment. She had a MI 8 years ago and had a stent inserted. She is functionally independent and active, participating in water aerobics twice a week, and walking 30 minutes every day. Medications: Metformin 1000mg + Sitagliptin 50mg BID; ramipril 10 mg daily; hydrochlorothiazide 25 mg daily; ASA 81 mg daily; rosuvastatin 10 mg once daily

Labs: HbA1c is 7.3%; electrolytes WNL, Cr 76, eGFR 71 mL/min/1.73m^2

BP 122/74, HR 88. Wt 73 kg

What would be the most appropriate HbA1c target for Lana?

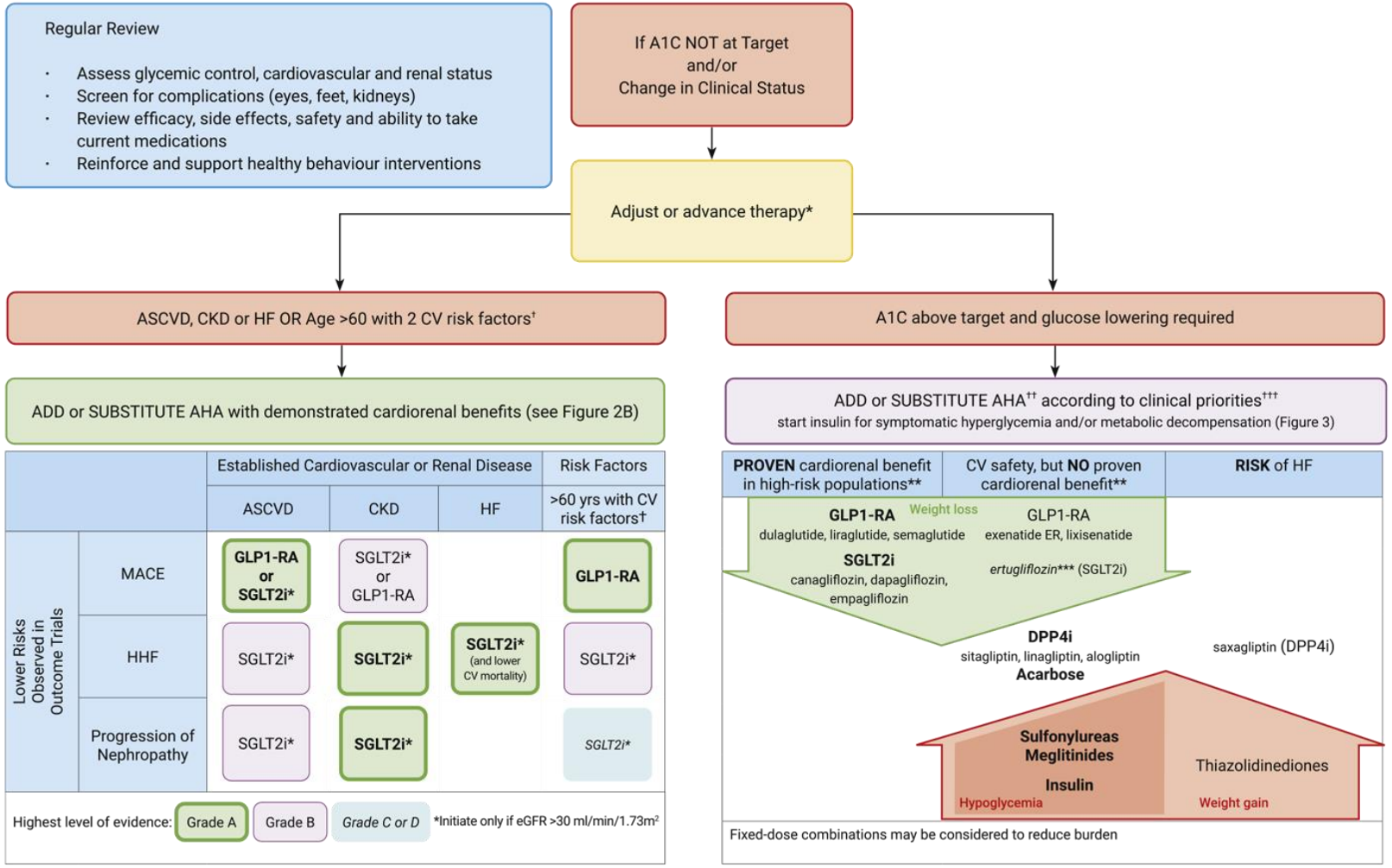
A. ≤6.5%

B. ≤7%

C. 7.1 to 8.0%

D. 7.1 to 8.5%

Adjusting Therapy in Type 2 Diabetes

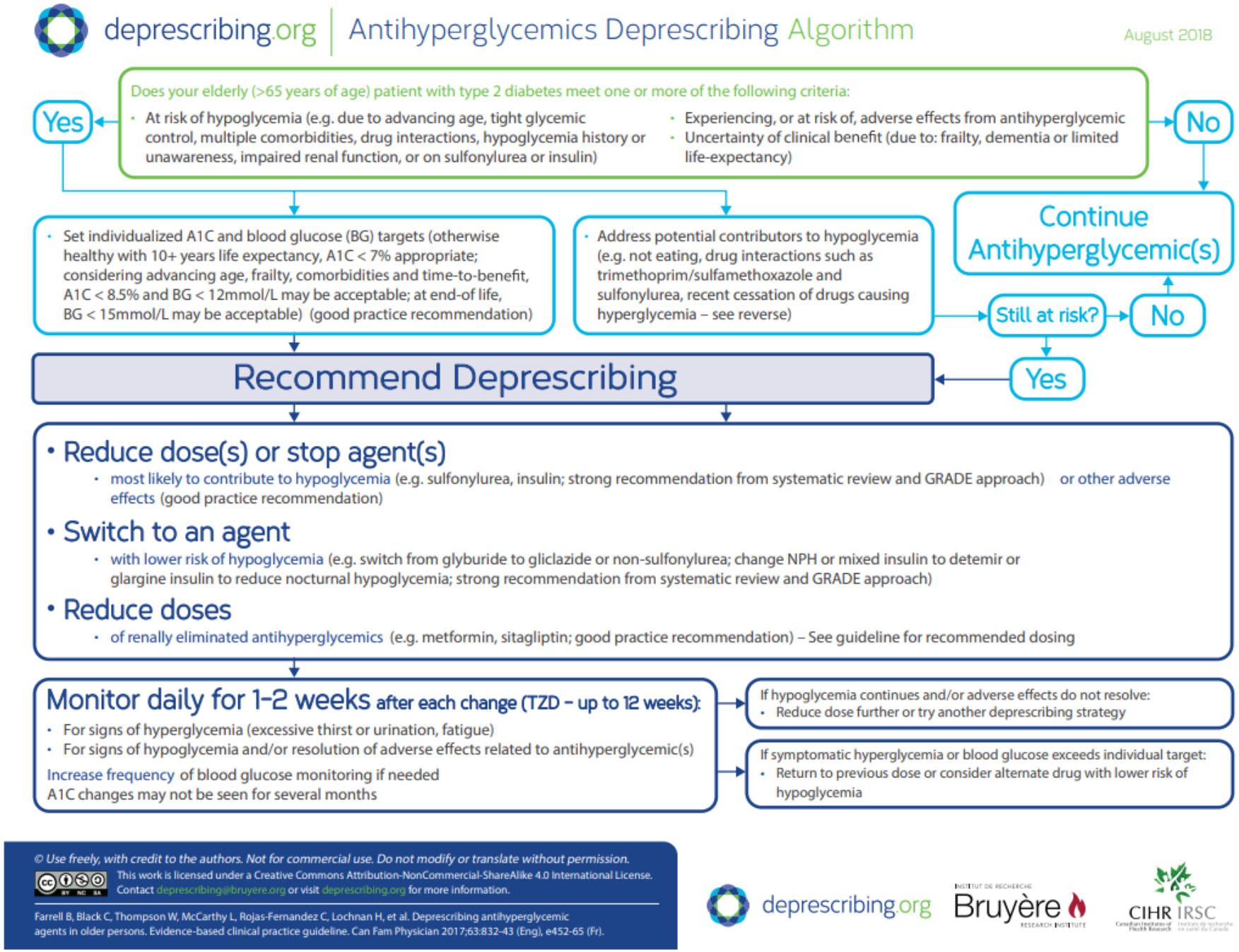


* Changes in clinical status may necessitate adjustment of glycemic targets and/or deprescribing.

† Tobacco use; dyslipidemia (use of lipid-modifying therapy or a documented untreated low-density lipoprotein (LDL) ≥3.4 mmol/L, or high-density lipoprotein-cholesterol (HDL-C) <1.0 mmol/L for men and <1.3 mmol/L for women, or triglycerides ≥2.3 mmol/L); or hypertension (use of blood pressure drug or untreated systolic blood pressure [SBP] ≥140 mmHg or diastolic blood pressure [DBP] ≥95 mmHg).

†† All antihyperglycemic agents (AHAs) have Grade A evidence for effectiveness to reduce blood glucose levels.

Lipsombe L et al. *Can J Diabetes* 2018;42(Suppl 1):S88-S103.



Farrell B et al. *Can Fam Physician* 2017;63:832-43.
Deprescribing.org

Diabetes type 2 Non-insulin Pharmacotherapy

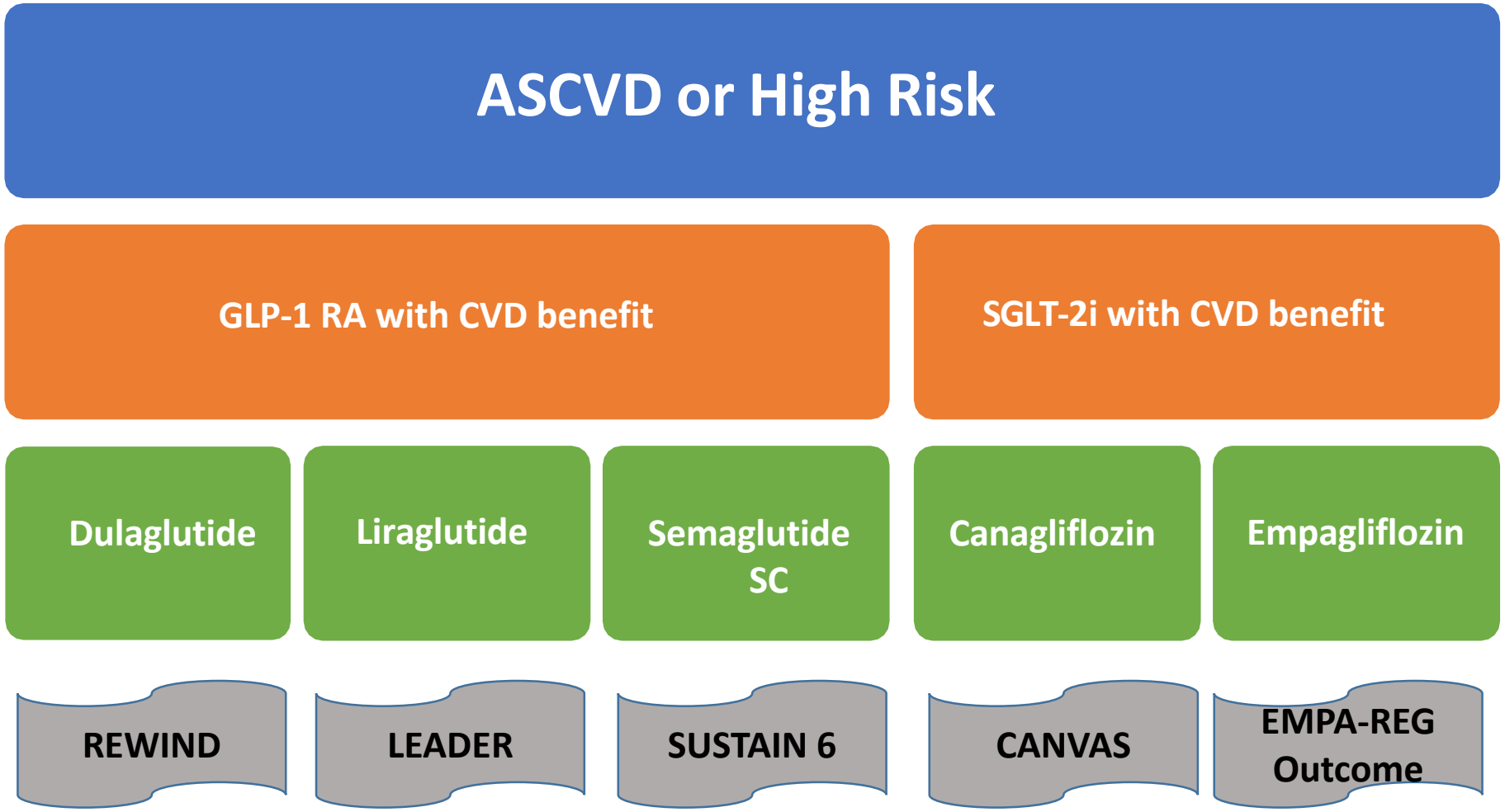
Class/Drug	Hypoglycemia	Weight	A1C ↓	Therapeutic considerations	Cost
Metformin	Rare	↓ (up to 2.9kg)	1	85% of max glucose lowering seen at 1500 mg daily; Titrate up every 1–2 weeks to avoid GI SE; Caution in pts with risk for lactic acidosis Monitor: hemoglobin and vitamin B12 (annually), SCr (baseline and periodically) **Avoid** with eGFR < 30 mL/min** **Sometimes used at low dose when eGFR between 15-30 mL/min in renally stable pts	$ **ODB** ☑
Insulin Secretagogues **Meglitinides** Repaglinide	**Yes**	↑ (1.4-3.3kg)	0.7 to 1	Rapid BG-lowering response; reduced postprandial hyperglycemia; requires TID dosing; Dose given within 30 minutes of meal Monitor: SCr and LFTs (baseline and periodically) **Caution with eGFR <30 mL/min**	$$ ODB ☒ **EAP** ☑
Sulfonylureas Gliclazide, Glimepiride, Glyburide	**Yes**	↑ (1.2-3.2kg)	0.6 – 1.2	Poor durability Risk of hypoglycemia: gliclazide < glimepiride < glyburide **Contraindicated with eGFR <30 mL/min**	$ **ODB** ☑ Glimepiride not on ODB
Acarbose	Rare	Neutral	0.7	GI side-effects common; TID dosing **Contraindicated with eGFR <25 mL/min**	$$ **ODB** ☑ (LU Code)
Thiazolidinediones Rosiglitazone Pioglitazone	Rare	↑ (2-5kg)	0.7 to 0.9	4-12 weeks for max effect **Caution: CHF, edema, fractures, possible bladder cancer (pioglitazone), CV risk (rosiglitazone)** **Caution with eGFR <60 mL/min**	$$ ODB ☒ **EAP** ☑
DPP-4 Inhibitors Alogliptin, Linagliptin, Saxagliptin, Sitagliptin	Rare	Neutral	0.5 to 0.7	**Caution: saxagliptin, alogliptin and potential risk CHF** Rare: Severe joint pain; Bullous pemphigoid; Pancreatitis; ? pancreatic cancer Alogliptin: may ↑ LFTs Linagliptin: no dosage adjustment in renal impairment	$$$ **ODB** ☑ Alogliptin not on ODB

Lipscombe L et al. *Can J Diabetes* 2020;44(7):575-591; RxFiles Anti-hyperglycemic type 2 diabetes agents: Drug comparison chart. www.rxfiles.ca;
Centre for Effective Practice. Type 2 diabetes: Non-insulin pharmacotherapy: Ontario. Toronto. https://.cep.health

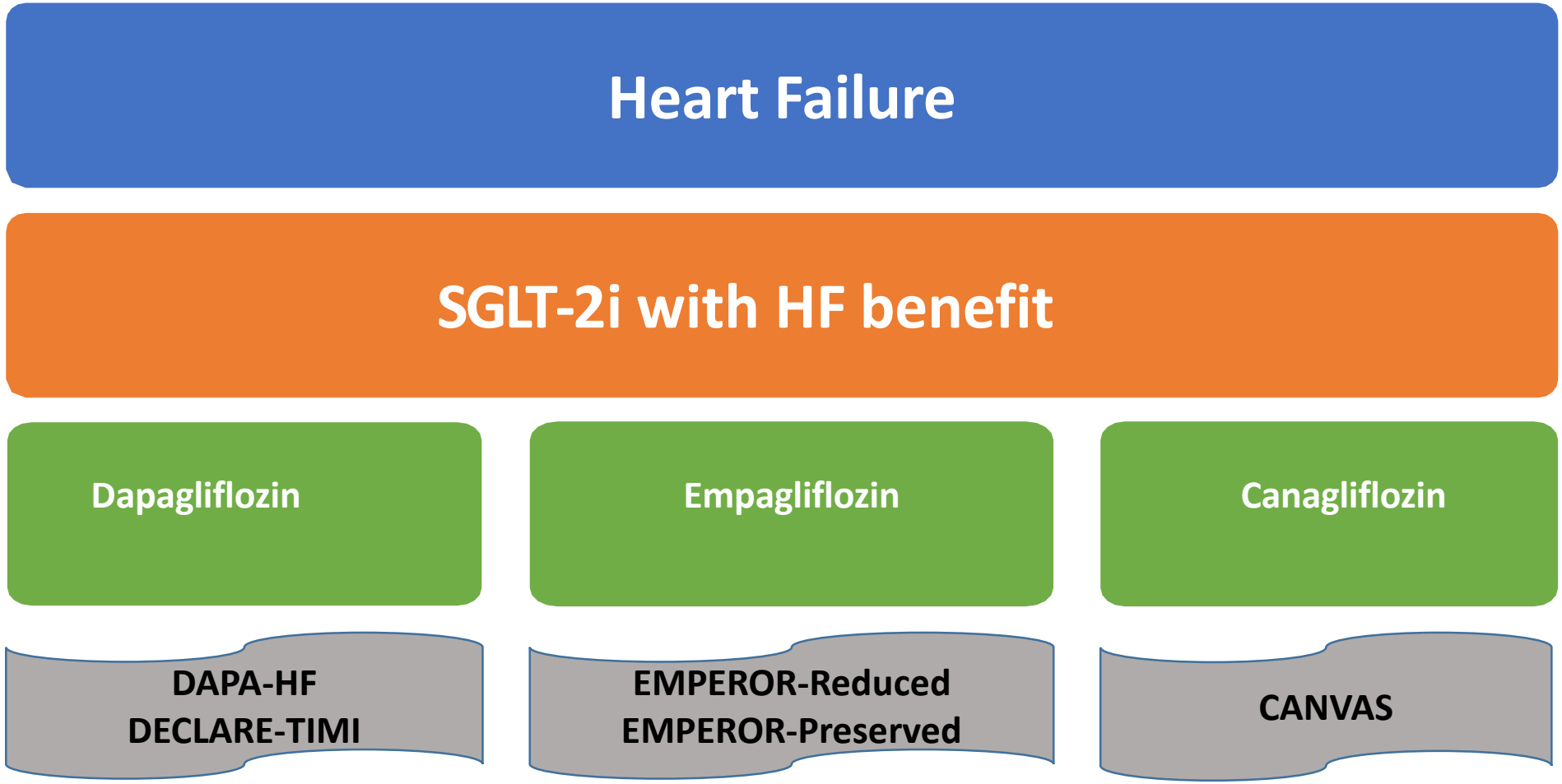
Diabetes type 2 Non-insulin Pharmacotherapy

Class/Drug	Hypoglycemia	Wt	A1C ↓	Considerations	Cost
GLP-1R agonists **Short acting:** Exenatide Lixisenatide **Long acting:** **Dulaglutide** Exenatide **Liraglutide** **Semaglutide**	Rare	↓ (1.6-4kg)	0.6 to 1.4	Mechanism of action: 1. stimulates glucose- dependent insulin release by pancreatic beta cells 2. decreases post-prandial glucagon secretion 3. **slows gastric emptying** **Weight loss: 1.6-4 kg. CAUTION** Requires SC injection (except semaglutide PO) GI side-effects : N/V/diarrhea/constipation **Avoid combining DPP4i with GLP1-RA** **Cautions: pts with history of cholelithiasis or pancreatitis; diabetic retinopathy (semaglutide SUSTAIN trial)** **Contraindicated with personal / family history of medullary thyroid cancer or MEN type 2**	$$$$ **ODB ☑** **Lisixenatide** **Semaglutide** **SC**
SGLT2 inhibitors **Canaglflozin** **Dapagliflozin** **Empagliflozin**	Rare	↓ (2-3kg)	0.5 to 0.7	Side effects: **Genital fungal infections, hypotension, volume depletion, urinary frequency; renal dysfunction** **Caution: dapagliflozin and bladder cancer; Euglycemia diabetic ketoacidosis (rare).** Increased risk of fractures and amputations with canagliflozin.	$$$ **ODB ☑**

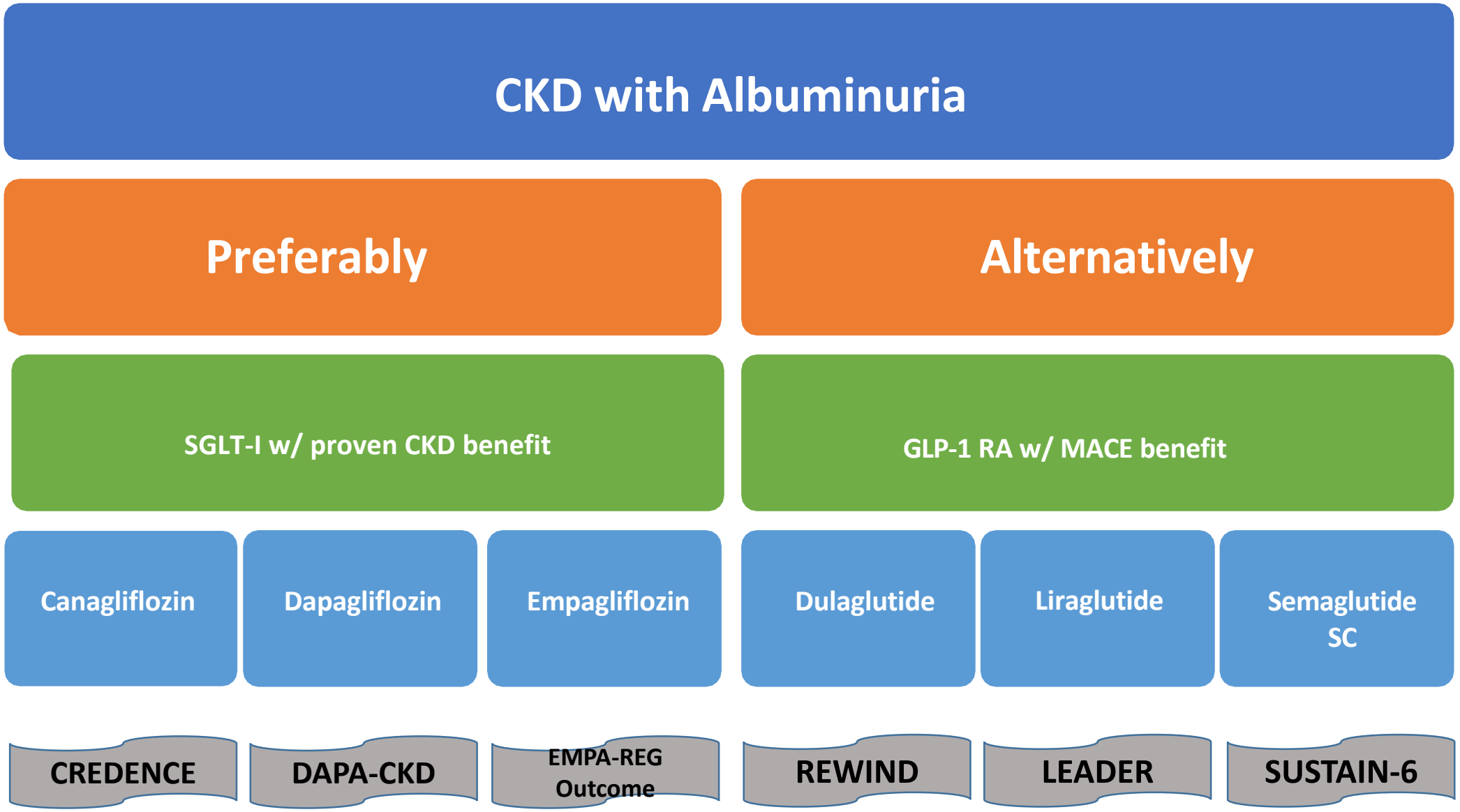
Lipscombe L et al. *Can J Diabetes* 2020;44(7):575-591; RxFiles Anti-hyperglycemic type 2 diabetes agents: Drug comparison chart. www.rxfiles.ca;
Centre for Effective Practice. Type 2 diabetes: Non-insulin pharmacotherapy: Ontario. Toronto. https://.cep.health



Gerstein HC et al; *Lancet* 2019;394:121-130; Marso SP et al. *N Engl J Med* 2016;375(4):311-22; Marso SP et al. *N Engl J Med* 2016;375:1834-44; Neal B et al. *N Engl J Med* 2017;377:644-57; Wanner C et al. *N Engl J Med* 2016;375:323-34.



McMurray JJV et al; *N Engl J Med* 2019;381:1995-2008; Wiviott SD et al; *N Engl J Med* 2019;380: 347-57; Packer M et al. *N Engl J Med* 2020; 383:1413-1424; Anker SD et al; *N Engl J Med* 2021; 385:1451-1461;Neal B et al. *N Engl J Med* 2017;377:644-57;



Perkovic V et al; *N Engl J Med* 2019; 380(24):2295-306; Heerspink HJL et al. *N Engl J Med* 2020; 383:1436-1446; Wanner C et al. *N Engl J Med* 2016;375:323-34; Gerstein HC et al; *Lancet* 2019;394:121-130; Marso SP et al. *N Engl J Med* 2016;375(4):311-22; Marso SP et al. *N Engl J Med* 2016;375:1834-44

Question 4

Mel is a 71 yo musician with T2DM, HTN, dyslipidemia. Married, functionally independent. Recent Dx CHF.

Labs: HbA1c 7.5%; SCr 113; eGFR 56
P/E: BP 129/88 mmHg; HR 88
No orthostatic BP↓. Euvolemic.

Current Medications:
Saxagliptin 5 mg daily; Metformin 1 g BID; Ramipril 10 mg qhs; Furosemide 40 mg BID; Atorvastatin 40 mg daily; ASA 81 mg daily

Image by Leroy Skalstad from Pixabay

Question 4

What medication change would you recommend for Mel?

Saxagliptin 5 mg daily; Metformin 1 g BID; Ramipril 10 mg qhs
Furosemide 40 mg BID; Atorvastatin 40 mg daily; ASA 81 mg daily

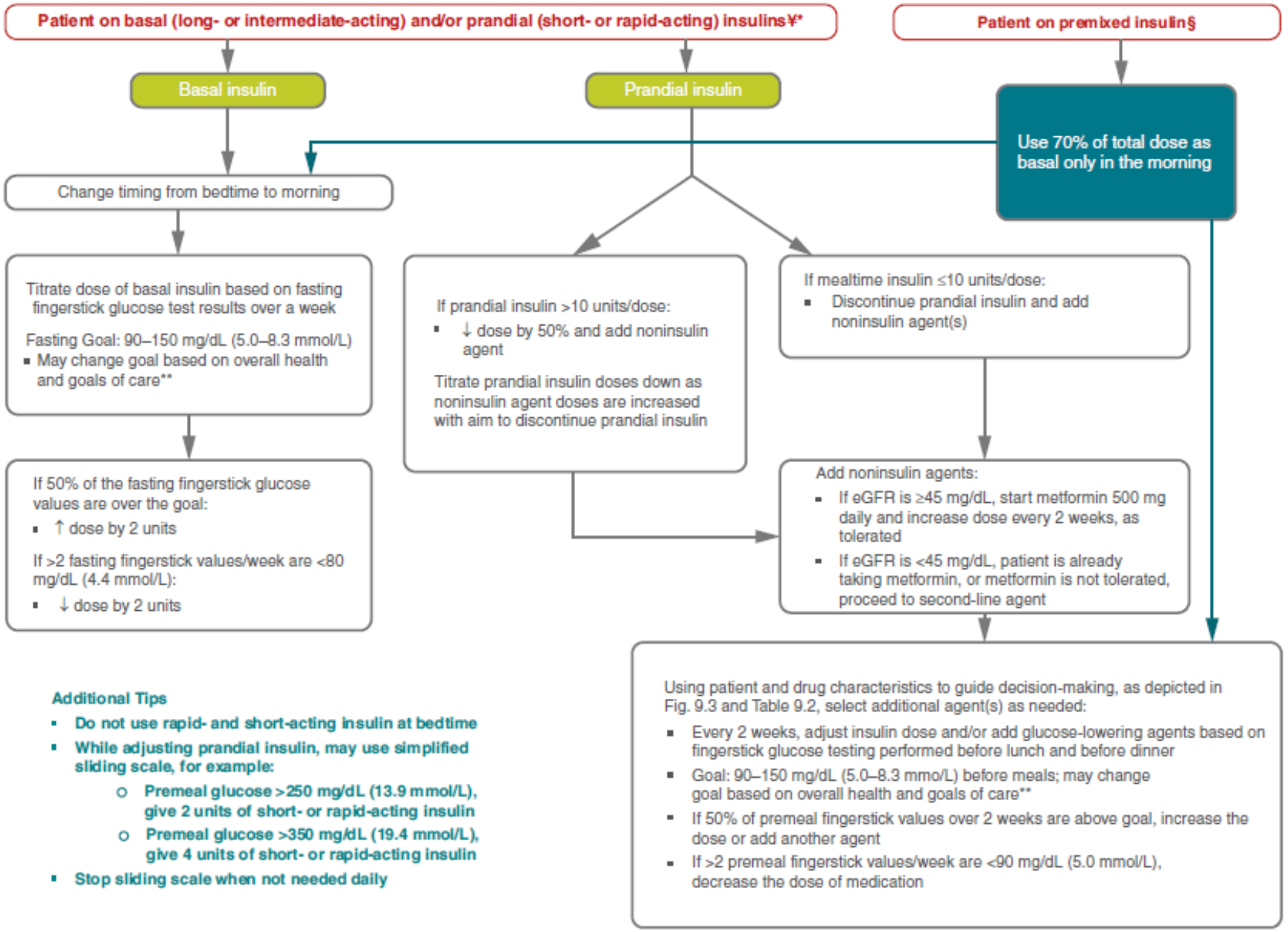
A. Discontinue saxagliptin; start insulin glargine
B. Discontinue saxagliptin; start dapagliflozin; consider ↓ diuretic
C. Discontinue metformin; start dapagliflozin; consider ↓ diuretic
D. Add dapagliflozin to current regimen; consider ↓ diuretic

When to Deintensify Diabetes Pharmacotherapy

- Frailty
- Short life expectancy
- Cognitive impairment
- Low functional status
- Patient preference for less intensive care
- Severe or high number of comorbidities
- Disease duration
- Vascular complications
- **Hypoglycaemia and other drug-related adverse events**
- Low level of resources and support

Aubert CE et al. *BMJ* 2021; 375:e066061.

Simplification of Complex Insulin Therapy



American Diabetes Association Professional Practice Committee. *Diabetes Care* 2022;45(Suppl 1):S195-S207.

Antihyperglycemic Agents and Kidney Function

		DRUG CLASS						
		Metformin (max daily dose)	**SGLT2i** (Recommended daily dose*)	**GLP1-RA**	**DPP4i** (max daily dose)	**All Insulins**	**Secretagogues**	
							Glyburide	**Others**
eGFR (mL/min/1.73m²)	45 – 59	2 g	No dose change	No dose change	No dose change	No dose change	Avoid Glyburide	No dose change
	30 – 44	1 g	Canagliflozin 100 mg Dapagliflozin 10 mg Empagliflozin 10 or 25 mg	No dose change	Linagliptin 5 mg Sitagliptin 50 mg (Saxagliptin 2.5 mg**)	No dose change		Gliclazide or Repaglinide preferred Dose reduction may be needed
	15 – 29	500 mg			Linagliptin 5 mg Sitagliptin 25 mg	Dose reduction may be needed		
	<15 or on dialysis	Avoid	Stop on dialysis	Limited data available				
	Risk related to low GFR	Lactic acidosis	Cardiorenal protection preserved but less reduction in A1C with low GFR		Accumulation***	Accumulation and hypoglycemia	Prolonged and severe hypoglycemia	Hypoglycemia

*listed alphabetically, **increased risk for heart failure, ***except linagliptin

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DIABETES CANADA

Question 5

Leslie is a 74 yo woman with T2DM x12 yrs, HTN, OA and stage 3 CKD. She lives at home alone and receives help for some IADLs. Recently she has been experiencing hypoglycemic episodes around 10 am.

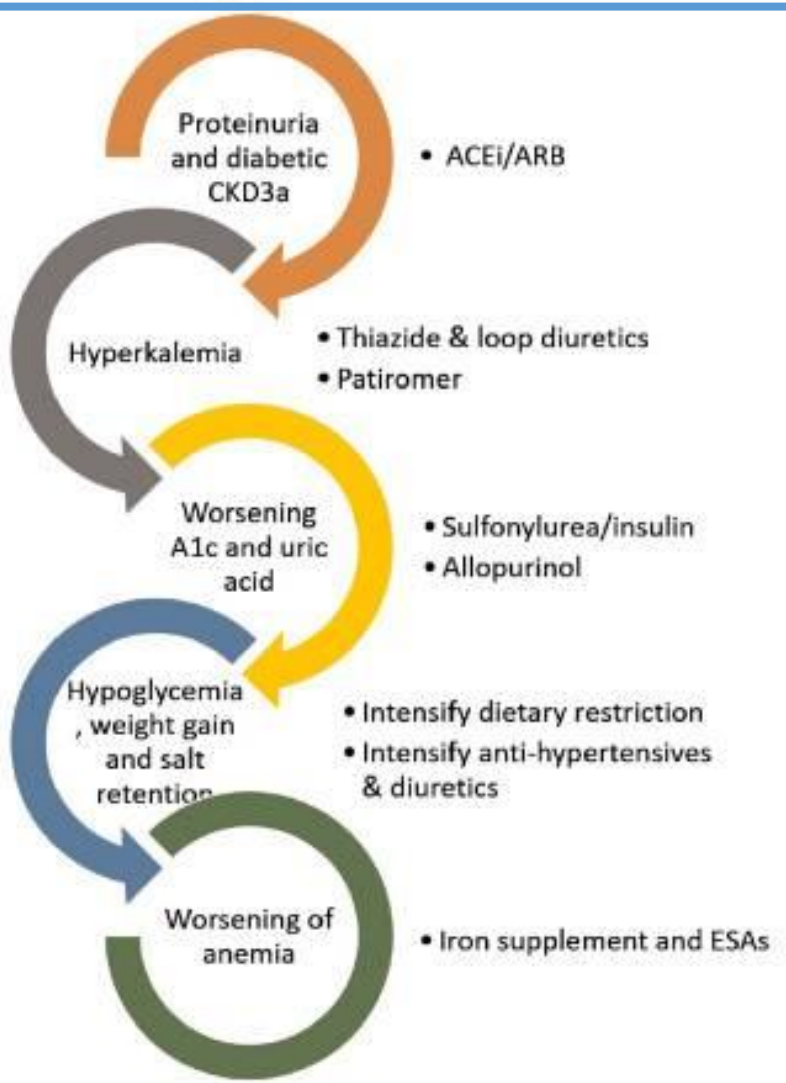
SCr 102; eGFR 50 mL/min/1.73m² ;A1c 7.3%; ACR 15 mg/mmol; BMI 29 kg/m²
BP 147/76; HR 84; no orthostasis
Medications: Metformin 1 g BID; Gliclazide 30 mg daily; Perindopril 8 mg daily; Atorvastatin 20 mg daily; Acetaminophen 650 mg TID; Vitamin D 1000 units daily

Which of the following would be the most appropriate medication to replace her gliclazide at this time?

A. Dulaglutide 0.75 mg SC once weekly
B. Semaglutide 3 mg PO once daily
C. Canagliflozin 100 mg PO once daily
D. Repaglinide 0.5 mg PO TID AC

Deprescribing When Using SGLT-2is

Prescribing cascade leads to polypharmacy



SGLT2 inhibitors for deprescribing

- Lower risk of hyperkalemia
- Improve anemia (instead of worsening)

- Improve glycemic control and lower uric acid (instead of worsening)
- Dual benefit of renal protection and neutral effect on potassium

- Glycemic control without weight gain
- Avoid side effects of allopurinol

- Lower risk of hypoglycemia
- Diuretics-sparing

- Increase endogenous EPO production

Li J et al. *Clin Kidney J* 2019;12(5):620-628.

Practical approach to SGLT2 inhibitors for treatment of cardiovascular disease

Indications

Patients with Type 2 DM[1]

or

Patients with chronic kidney disease (eGFR 25-90, UACR> 200 mg/g)[2]

or

Patients with chronic HFrEF[3]

Contraindications

- CLI[3]
- eGFR<25[4]
- Allergy or intolerance to SGLT2i[5]

→ Do not initiate SGLT2i

Caution

- Volume depletion[5]
- Active GMI[6]
- Hypotension (Blood pressure<95 mmHg)[*,7]
- Prior CLI
- DKA[5] [specific to DM]
- History of severe hypoglycemia[†] [specific to DM]

→ Delay initiation of SGLT2i until condition resolved/ therapies modified to reduce risk

Outpatient Initiation

Start 10 mg od qam:
- Dapagliflozin[5]
- Empagliflozin[8]

Start 100 mg od qam:
- Canagliflozin[9]

Special Considerations

- Monitor for GMIs, counsel on proper hygiene[6]
- Concomitant dehydrating illness (SADMANS)[‡,10]
- Borderline renal function[§,5,6]
- Volume depletion[‖,5]

Potential drug-drug effects with:

Loop diuretics

- Optional dose reduction[¶] if euvolemic; 30–50% dose reduction if volume depletion occurs[3]

Insulin or SU

- If DM w/A1C<7.5, consider dose reduction (i.e., 10–20% insulin, and/or 50% SU)[11]
- If episodes of hypoglycemia[#], stop SU and dose reduce insulin[11]

Follow-up

Follow up routine as per underlying condition:
- Weight[6]
- Symptoms of hypotension[6]
- Adherence[6]
- Renal function (eGFR)[**,††,6]
- Blood glucose[6] [specific to DM]

Abbreviations:

CLI: critical limb ischemia; **DKA:** diabetic ketoacidosis; **DM:** diabetes mellitus; **eGFR:** estimated glomerular filtration rate; **GMI:** genital mycotic infections; **HFrEF:** heart failure with reduced ejection fraction; **SGLT2i:** SGLT2 inhibitors; **SU:** sulfonylurea; **UACR:** urine albumin to creatinine ratio

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CHFS SCIC
Canadian Heart Failure Society
Société canadienne d'insuffisance cardiaque

Practical Considerations to Defer or Withhold SGLT-2is

Condition	Clinical Concern
Dynamic volume status (poor oral intake, diarrhea) or labile blood pressure	Dehydration and hypotension
Urinary incontinence	Increased urinary frequency and volume
Cognitive impairment	Unable to follow instructions for monitoring or sick day protocol; at risk for dehydration
Poorly controlled hyperglycemia and a history of diabetic ketoacidosis	Poor adherence; risk of hyperglycemia-induced dehydration; risk of ketoacidosis
Frequent candida infections or unable to maintain genital hygiene for medical/social reasons	Risk of genital mycotic infections Risk of Fourniere's gangrene (rare)
Unhealed diabetic foot wound Peripheral vascular disease	Risk of amputation (CANVAS)

Li J et al. *Clin Kidney J* 2019;12(5):620-628; Li J et al. *Clin J Am Soc Nephrol* 2020;15(11):1678-1688; Engelhardt K et al. *Ann Pharmacother* 2021;55(4):543-548.

Question 6 – Lana 2 Years Later

Lana is a 74 yo woman with DM2. She lives with her husband and provides care for him in their apartment. Past history of MI with stent inserted. She is still functioning well without assistance. She walks daily and exercises 2x/wk.

Medications: Metformin 1000 mg + Sitagliptin 50 mg BID; ramipril 10 mg daily; hydrochlorothiazide 25 mg daily; ASA 81 mg daily; rosuvastatin 10 mg once daily

Labs: HbA1c is 7.7%, electrolytes WNL, Cr 103, eGFR 49 mL/min/1.73m^2

BP 136/82, HR 74. No orthostasis. Wt 76 kg

Lana had trialled empagliflozin a few months ago but had to stop it as she was bothered by the frequent urination and some dizzy spells.

Question 6 – Lana 2 Years Later

You discuss her preferences and she is willing to try an injection medication to help keep her diabetes under control and protect her heart and kidneys. You decide together to trial her on semaglutide subcut once weekly.

Medications: Metformin 1000 mg + Sitagliptin 50 mg BID; ramipril 10 mg daily; hydrochlorothiazide 25 mg daily; ASA 81 mg daily; rosuvastatin 10 mg once daily

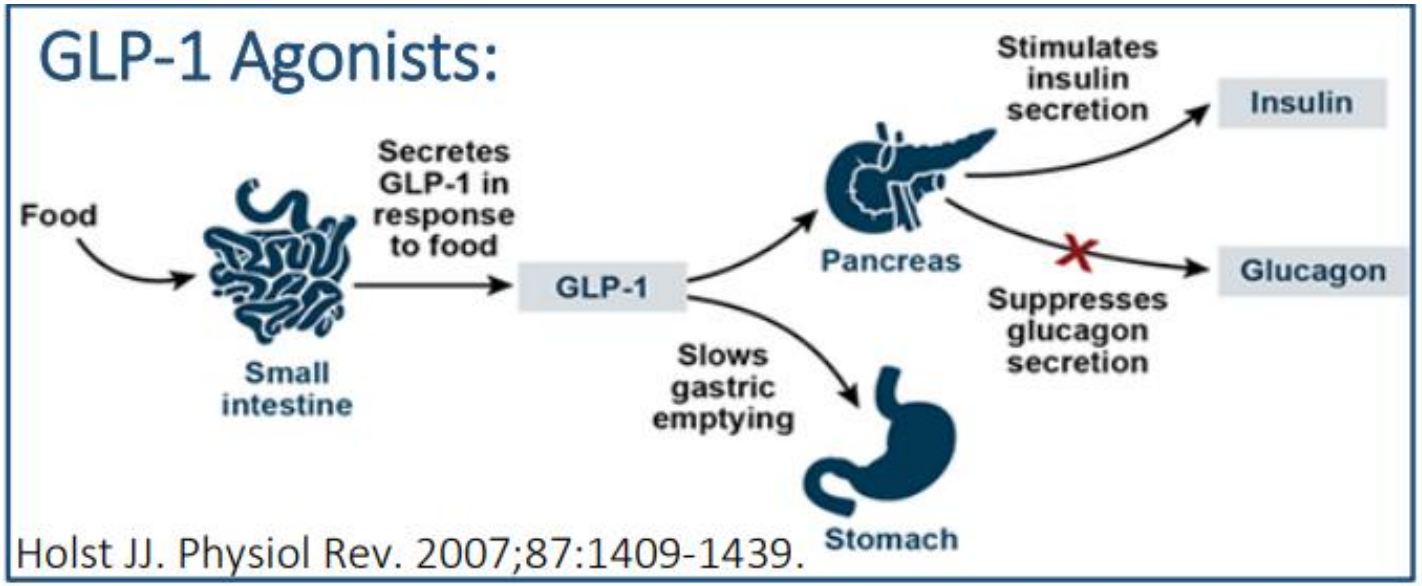
Labs: HbA1c is 7.7%, electrolytes WNL, Cr 103, eGFR 49 mL/min/1.73m^2

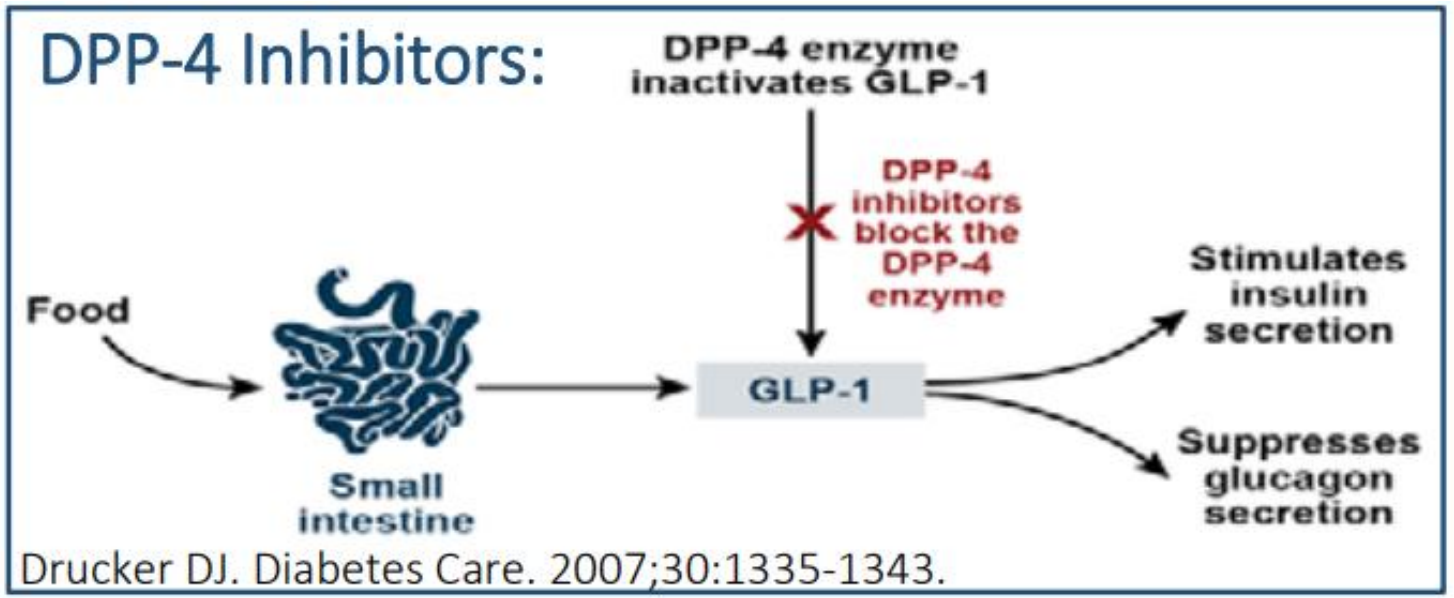
BP 136/82, HR 74. No orthostasis. Wt 76 kg

Which medication would you deprescribe?

A. Hydrochlorothiazide
B. Ramipril
C. Sitagliptin
D. Metformin
E. None of the above

Combining GLP-1 Agonists + DPP-4 Inhibitors?





What to do if your patient is on a DPP-4 inhibitor and GLP-1 agonist?

Preferred Option	Alternative Option
Continue GLP-1 agonist and Discontinue DPP-4 inhibitor	Continue DPP-4 inhibitor and Discontinue GLP-1 agonist

A taper is not needed when discontinuing either medication

Nauck MA et al. *Diabetes Obes Metab* 2017;19(2):200-207; Lipscombe L et al. *Can J Diabetes* 2020;44(7):575-591; American Diabetes Association Professional Practice Committee. *Diabetes Care* 2022; 45 (Supplement_1): S125–S143.

Deintensification of Insulin with GLP-1 agonists

Glycemic control at Baseline	Basal Insulin Dose Reduction	Bolus Insulin Dose Reduction
A1C <7% (or average FPG < 7.2 mmol/L)	20%	50%
A1C 7.1 – 8 % (or average FPG 7.2 – 11.1 mmol/L)	10 – 20 %	25%
A1C > 8 % (or average FPG > 11.1 mmol/L) with glycemic variability, hypoglycemia unawareness or severe hypoglycemic events	10%	25%
A1C > 8 % (or average FPG > 11.1 mmol/L) without glycemic variability, hypoglycemia unawareness or severe hypoglycemic events	-	10 – 20%

Van Dril E et al. *Am Heart J Plus* 2022;17: 100163.

Gastric Emptying: Medication Considerations

Delay Gastric Emptying	Increase Gastric Emptying
Anti-muscarinics / Anticholinergics	Macrolides
Opioids	Prokinetics
Tricyclic antidepressants	β receptor antagonists
Calcium channel blockers	
Proton pump inhibitors	
Octreotide	
Progesterone	
Levodopa	
Aluminum hydroxide antacids	
Calcineurin Immunosuppressants	
Alcohol	
Tobacco / nicotine	

Krishnasamy S, Abell TL. *Diabetes Ther* 2018;9 (Suppl 1),1–42.

Summary

- Polypharmacy is common and increases the risk of inappropriate prescribing
- Adverse drug effects are important contributors to harm and prescribing cascades
- Prescribing cascade framework can identify medications used in potentially inappropriate ways
- Deprescribing is an iterative process to stop, reduce or switch medications that may be inappropriate for a person's clinical status and prognosis
- Use of frameworks and tools can aid clinicians to deprescribe
- Individualized treatment goals are needed to avoid overtreatment of frail older adults with DM2
- GLP-1 and SGLT2i agents with cardiorenal benefit may be options for carefully selected patients
    - Monitoring is crucial
    - Deprescribing opportunities


thank you
danke
謝謝
рахмат
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شكراً جزيلاً
teşekkür ederim
Баярлалаа
спасибо
faafetai lava
vinaka
спасибі
blagodaram
dank je
misaotra
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