Deprescribing: When to "Let it Go!"

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What is polypharmacy and why should we care about it?

A. Taking two or more medications concurrently
B. Taking five or more medications concurrently ←
C. Taking nine or more medications concurrently
D. A patient who uses two or more different pharmacies

Consequences of polypharmacy:
Frailty
Dementia
Cognitive decline
Disability
Hospitalization
Mortality

Consequences of polypharmacy at EOL:
As above, plus:
Anticholinergic burden
Sedation burden
Disease-associated and age-associated pharmacokinetic and pharmacodynamic changes

Prevalence of polypharmacy in the US:
Approximately 8.2% in 1999-2000
Approximately 15% in 2011-2012

Polypharmacy in long-term care:
91% of residents ≥ 5 medications
74% of residents ≥ 9 medications
65% of residents ≥ 10 medications

JAMA 2015;314:1818-1831; J Am Med Dir Assoc 2015;16:e1-12; J Am med Dir Assoc 2018;19:919-22; JAMA Intern Med 2015;175:827-34; Arch Intern Med 2007;167:781-7; Clin Pharm Ther 2009;85:103-7

Polypharmacy at the end of life

- How does the number of medications patients take as they near the end of life, compare with patients in a similar age bracket?
  A. The same
  B. More
  C. Less

Morin et al reconstructed the medication regimens for the previous 12 months of over 500,000 older adults who died in Sweden between 2007 and 2013.

- Average results showed during the year before death, the percentage of patients taking ≥ 10 medications increased from 30.3 to 47.2%

Retrospective study of > 500 older nursing home residents in Sydney, Australia evaluated changes in the prescribing of symptomatic and preventative medications in last year of life.

Overall medication use changed little:

- Symptom management medications increased slightly
- Disease-prevention medication use decreased slightly
- At the time of death, ~ 1/3 of patients had actively prescribed antithrombotic agents, antihypertensive medications and osteoporosis medications

179 patients in last week of life in hospital, hospice, or home in Netherlands

- Mean number of medications used per patient was nine on day 7 before death.
- 30% of patients received a preventative medication on the day of death.

Am J Med 2017;130(8):927-36;
Front Pharmacol 2018;8:990;
J Palliat Med 2018;21(2):149-55.

If polypharmacy is the problem, what's the solution?

The geriatrician's salute!

De-intensification!

Deprescribing!

- "Deprescribing" – defined as "the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes."

Goal-concordant care!

J Pharm Pract Res 2003;33:323-8; Br J Pharm Soc 2015;80:1254-68

Who's with me??

Survey says…

Survey of community-dwelling older adults living in Canada

- "I am comfortable with the number of medications that I am taking" - > 80% strong agreed/agreed
- Half thought they were taking a large number of medications
- Half stated they would like to reduce the number of medications they were taking
- ~ 75% said they would be willing to stop ≥ 1 medications if their doctor said it was possible
- ~80% said they would also they would take more medications if necessary

Survey in Australia in aged care facilities

- 40% said they wished to stop taking ≥ 1 of their medications
- This number increased to 80% if their doctor said this was appropriate

Survey of older adults admitted to a teaching hospital in Sydney, Australia

- 90% said they would be willing to stop ≥ 1 medications if their doctor was this was possible
- 95% were willing to discontinue their statin, and a similar number were concerned about statin side effects

Medicare beneficiaries in the USA surveyed about deprescribing (~ 2,000 respondents)

- "If my doctor said it was possible, I would be willing to stop one or more of my regular medicines" – 92% SA/agreed
- "I would like to reduce the number of medicines I am taking" – 2/3 SA/agreed

Res Soc Adm Pharm 2017;13:864-70; Res Soc Admin Pharm 2016;12:784-8;
Int J Clin Pharm 2015;37:949-57; JAMA Intern Med 2018;178(12)1673-80.

So what do the prescribers think about this?

Survey says…

160 physicians in Parma surveyed

- 75% reported general confidence in their ability to deprescribe, including preventative medications
- 53% were comfortable stopping guideline-recommended medications
- 40% were reluctant to discontinue a medication prescribed by another physician
- 45% felt uncomfortable stopping a medication in cases where patient/caregiver thought it was important to continue

General practitioners in Australia

- Comfortable with deprescribing and felt they had the skills to communicate this information to their patients

Primary care physicians

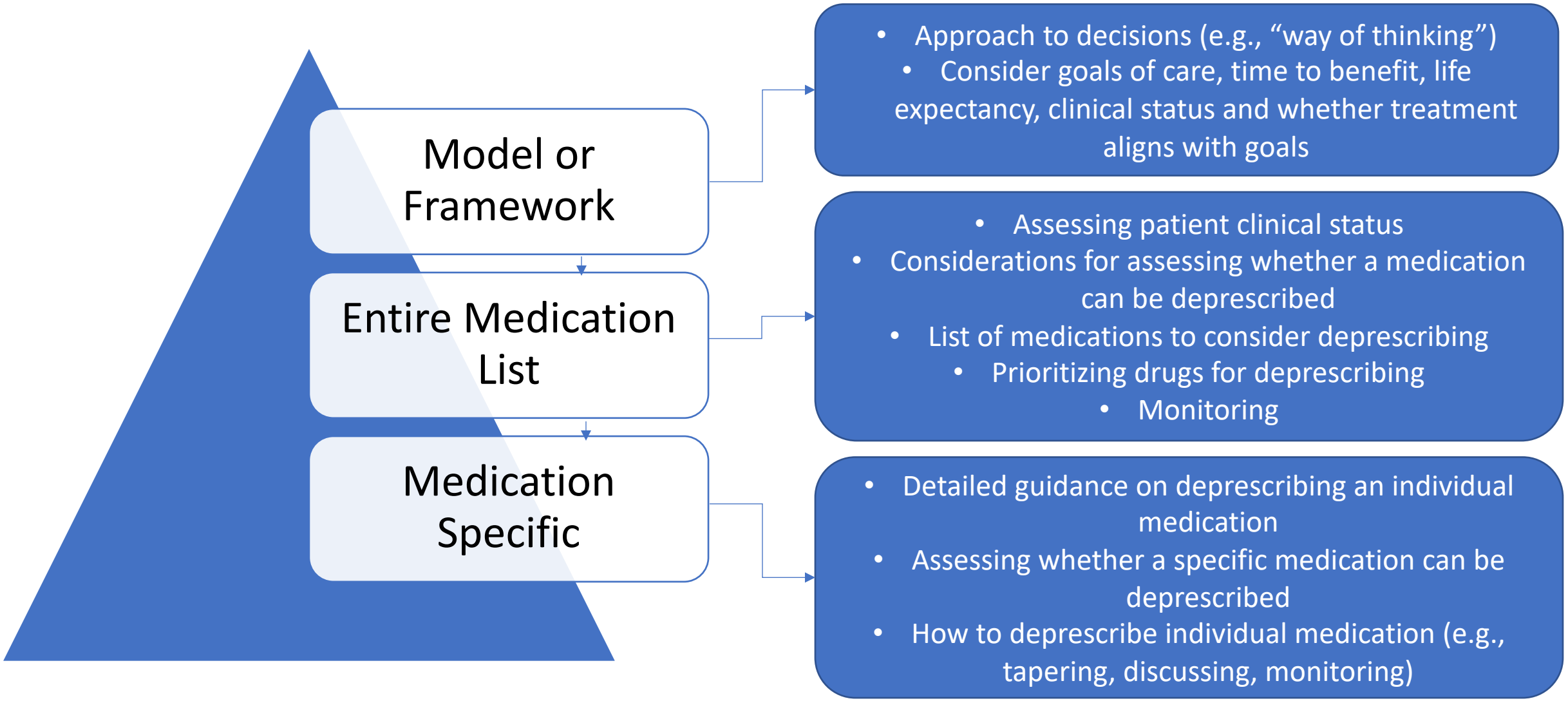
- Deprescribing feels like "swimming against the tide" due to:
  - The medical culture of prescribing (deprescribing not taught to physicians)
  - Patient expectations (prescriptions fix things, not stopping prescriptions)
  - Organizational constraints (lack of time, fragmentation of care, lack of access to expert guidance, etc.)

16 general practitioners in Denmark

- Themes of barriers to deprescribing include lack of interprofessional communication, patients not on board, culture encouraged continuing medications and not deprescribing

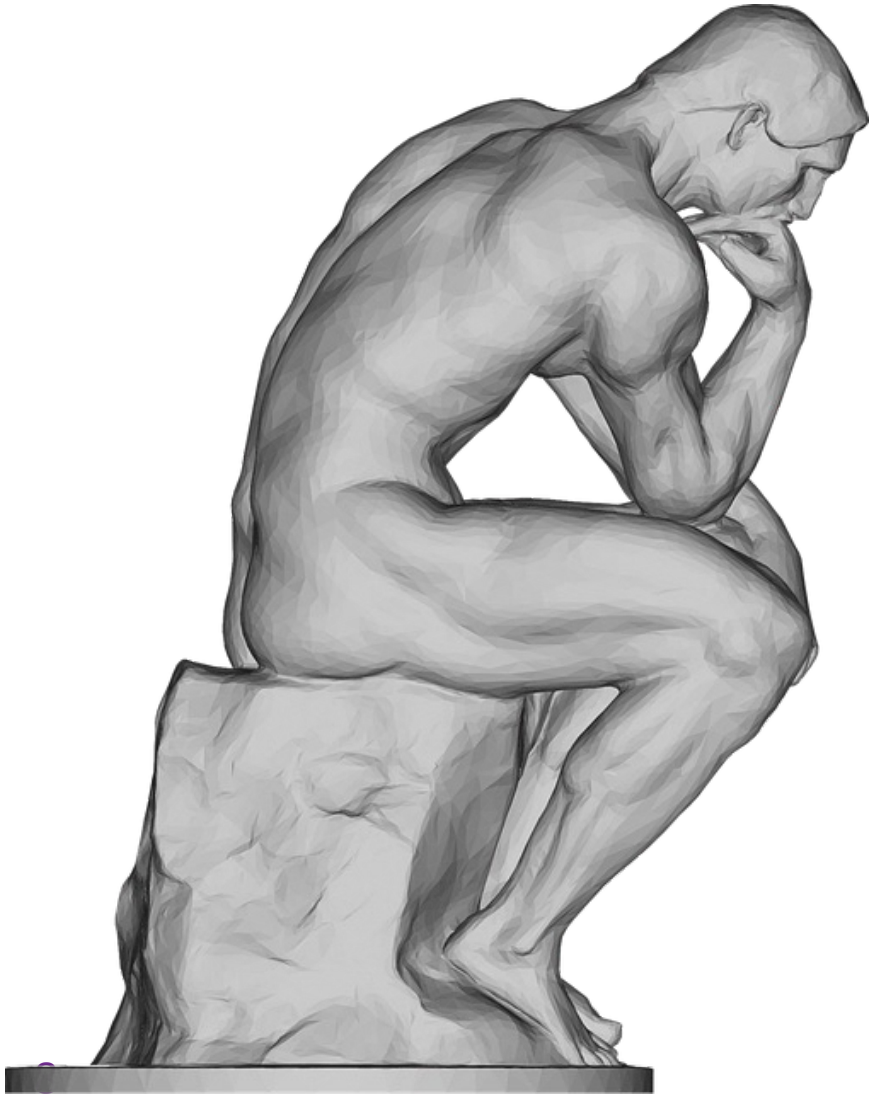
J Clin Pharm Ther 2018;43:550-5; Aust J Prim Health 2019;24:463; Res Soc Adm Pharm 2018;14:18-25;
Res Soc Adm Pharm 2016;12:438-49; Ann Fam Med 2017;15(341):346; Health Serv Res Man Epidem 2014;5:1-7

Let's DO this! Ok….how exactly do I DO this??



JAGS 2018;67(1):172-180

Model or Framework



Clipart from pixabay.com

- High-level model or framework for making medication decisions in persons with limited life expectancy
- A “way” of thinking
  - Consider time to benefit of a medication, life expectancy, goals of care, and whether a medication is likely to achieve goals or targets
  - Multiple-step, person-centered approach that includes comprehensive assessment of the individual’s clinical status, diagnosis-specific status, and medications, with goals of care and shared decision-making incorporated at every step

JAGS 2018;67(1):172-180

Approaching the Entire Medication List

- Tools that outline approaches to identify and prioritize drugs for deprescribing
- Tools include general principles to use when evaluating the whole medication list
  - Weighing the benefits and harms of the medications
  - Considering whether a medication is likely to help an individual achieve goals of care
  - Considering burden of treatment
- Tools may have a stepwise approach or algorithm process

STOPPFrail (Screening Tool of Older Persons prescriptions in Frail Adults with Limited life expectancy)

Beer's List

DE-PHARM

JAGS 2018;67(1):172-180

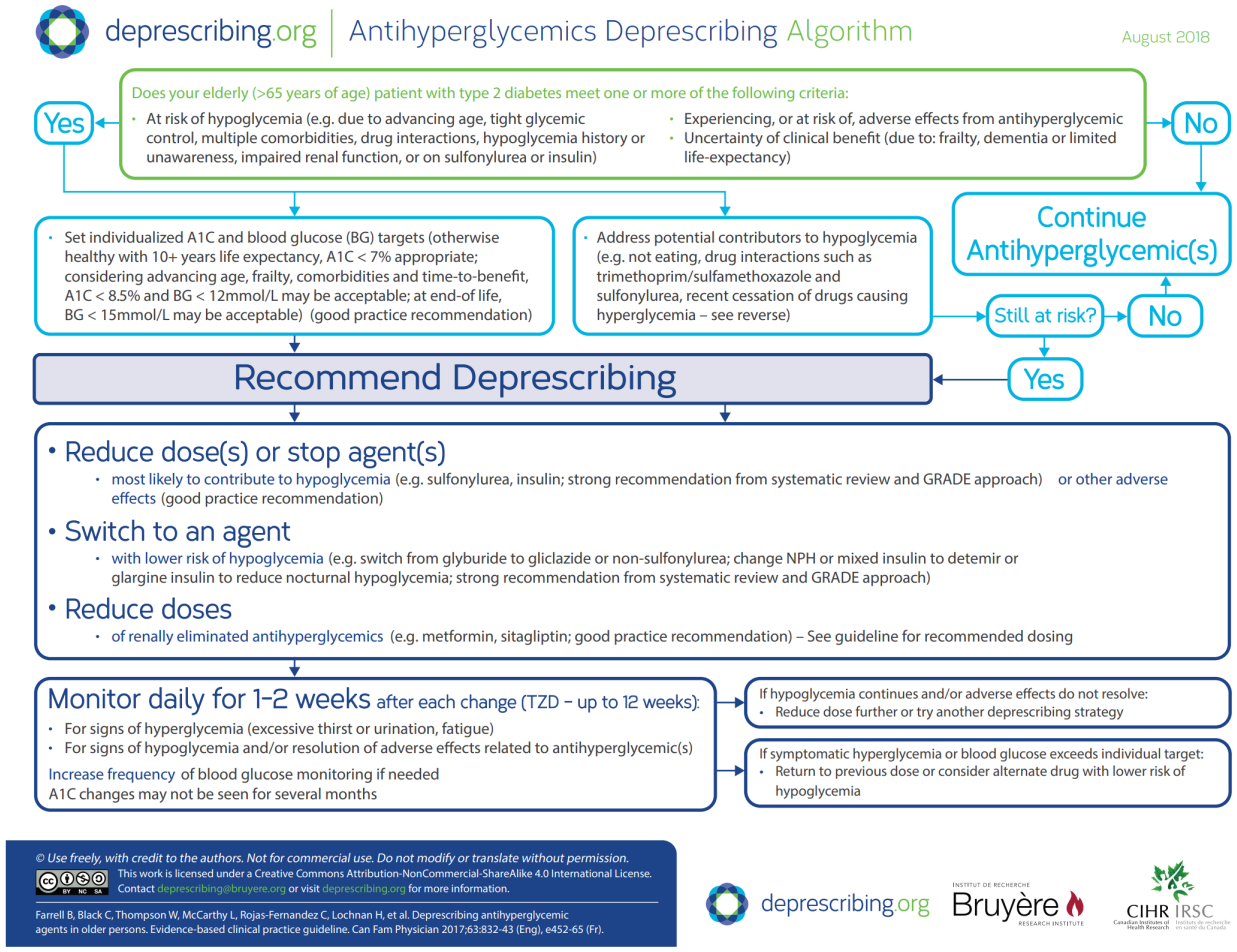
STOPPFrail v2

Section	
A: General	Any drug that the patient is not taking consistently; without a clear clinical indication; symptom now resolved
B: Cardiology	Lipid-lowering, antihypertensives, anti-anginal therapies
C: Coagulation	Anti-platelets, aspirin
D: Central nervous system	Neuroleptic antipsychotics, memantine
E: Gastrointestinal	PPIs, H2 receptor antagonists
F: Respiratory	Theophylline, leukotriene antagonists
G: Musculoskeletal	Calcium supplements, Vitamin D, anti-resorptive/bone anabolic drugs for OP, long-term oral NSAIDs, long-term oral corticosteroids
H: Urogenital	Drugs for BPH and overactive bladder
I: Endocrine	Anti-diabetic drugs
J: Miscellaneous	MVI, folic acid, nutritional supplements

Curtin D, Gallagher P, O'Mahony D. Deprescribing in older people approaching end-of-life: development and validation of STOPPFrail version 2. *Age Ageing*. 2021;50(2):465-471. doi:10.1093/ageing/afaa159

Medication-Specific Tools

- Tools in this category provide more detail on how to approach deprescribing (monitoring, tapering, benefits, harms



Proton pump inhibitors

Antihyperglycemics

Antipsychotics

Benzodiazepine receptor agonists

Cholinesterase inhibitors and memantine

Metabolic Syndrome?

- A cluster of risk factors that raise the risk of heart disease, diabetes, stroke, and other health problems
- According to the American Heart Association, about 1/3 of all adults have metabolic syndrome

Diagnosed with 3 of 5 Risk Factors

- National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III
- Metabolic syndrome is defined as:
  - Central obesity (defined by waist circumference)
  - Plus 2 of the following 4 factors:
    - Increased triglycerides, or treatment thereof
    - Reduced HDL cholesterol, or treatment thereof
    - Increased blood pressure or treatment thereof
    - Raised fasting plasma glucose or previously diagnosed diabetes

Circulation 2004;109:433-438.

Mr. Herndon

- 76-year-old man admitted to hospice with stage 4 non-small cell lung cancer
- Prognosis is 4-6 weeks according to his oncologist
- He has comorbid conditions of:
  - Type 2 diabetes mellitus
  - Hypertension
  - Chronic kidney disease stage 4
  - Dyslipidemia
  - 80 pack-year history of smoking; stopped 1 year ago when diagnosed with lung CA

Medication History

Medication	Directions for Use/Indication	Date Started
Atorvastatin 40 mg (Lipitor)	Once a day for dyslipidemia	2010
Metformin ER 1,000 mg	2 tablets diabetes for T2DM	2009
Lantus insulin	20 units at bedtime daily for T2DM	2014
NovoLog insulin	Sliding scale 4 times daily for T2DM	2019
Lisinopril 10 mg	Once daily for hypertension	2015
Amlodipine 5 mg	Once daily for hypertension	2016
Multivitamin with iron	Once daily for general health	2000
Acetaminophen XR 650 mg	2 capsules every 8 hours for pain	2020
MS Contin 30 mg	Every 12 hours for pain	2021
Roxanol 10 mg	Every 2 hours as needed for pain	2021
Senna	2 tablets daily	2021

Mr. Herndon

- 5’10”
- Weighs 165 pounds at present (lost 100 pounds since diagnosis)
- Waist circumference 34
- Rarely, if ever, uses sliding scale NovoLog insulin
- Complaints of hypoglycemia symptoms occasionally
- Last A1c 6.9% six months ago
- BP about 120/70 seated, gets “woozy” when he stands

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Mr. Herndon

- When you suggest slimming down his medication regimen, he gets VERY upset and cries:

“WHAT? My heart doctor and regular doctor said I had to stay on these medications ‘til the day I die! Are you saying I’m going to die tomorrow? You young whipper-snappers always want to upset the apple cart!”

- So, young whipper-snapper, how do you respond?

Multivitamin with Iron

- If Mr. Herndon feels strongly about keeping this medication, that's fine
- The iron and vitamins/minerals are probably increasing his risk of constipation and may cause a little nausea
- The iron may also turn his stools dark, making it hard for us to determine if he's bleeding internally, but that's unlikely
- Let's throw him a bone with the MVI!

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Analgesics and Laxative

- Once someone is taking 60-70 mg a day of oral morphine, they can't tell the difference with or without acetaminophen
  - Patient's wishes? Liver disease? Alcoholism?
- Is morphine controlling the pain?
- Is Senna maintaining normal bowel function?

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Words of the day…

TIME TO BENEFIT!

- "Time to benefit" is defined as the time to significant benefit observed in trials of people treated with a drug compared with controls

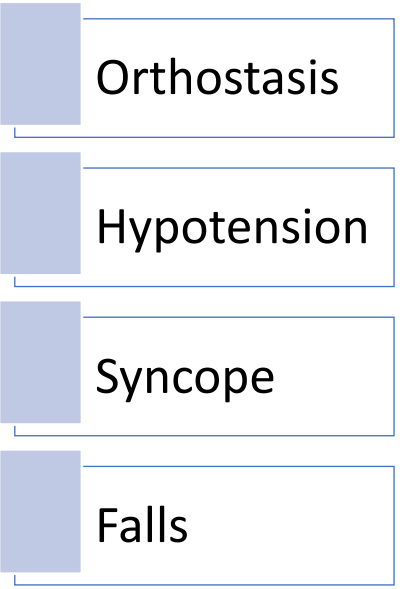
LEGACY EFFECT!

- "Legacy effects" are treatment effects that persist or emerge at some time after trial treatment ends.

Nayak A, et. al. BMJ Open. 2018; UpToDate 2022
Image purchased from canstockphoto

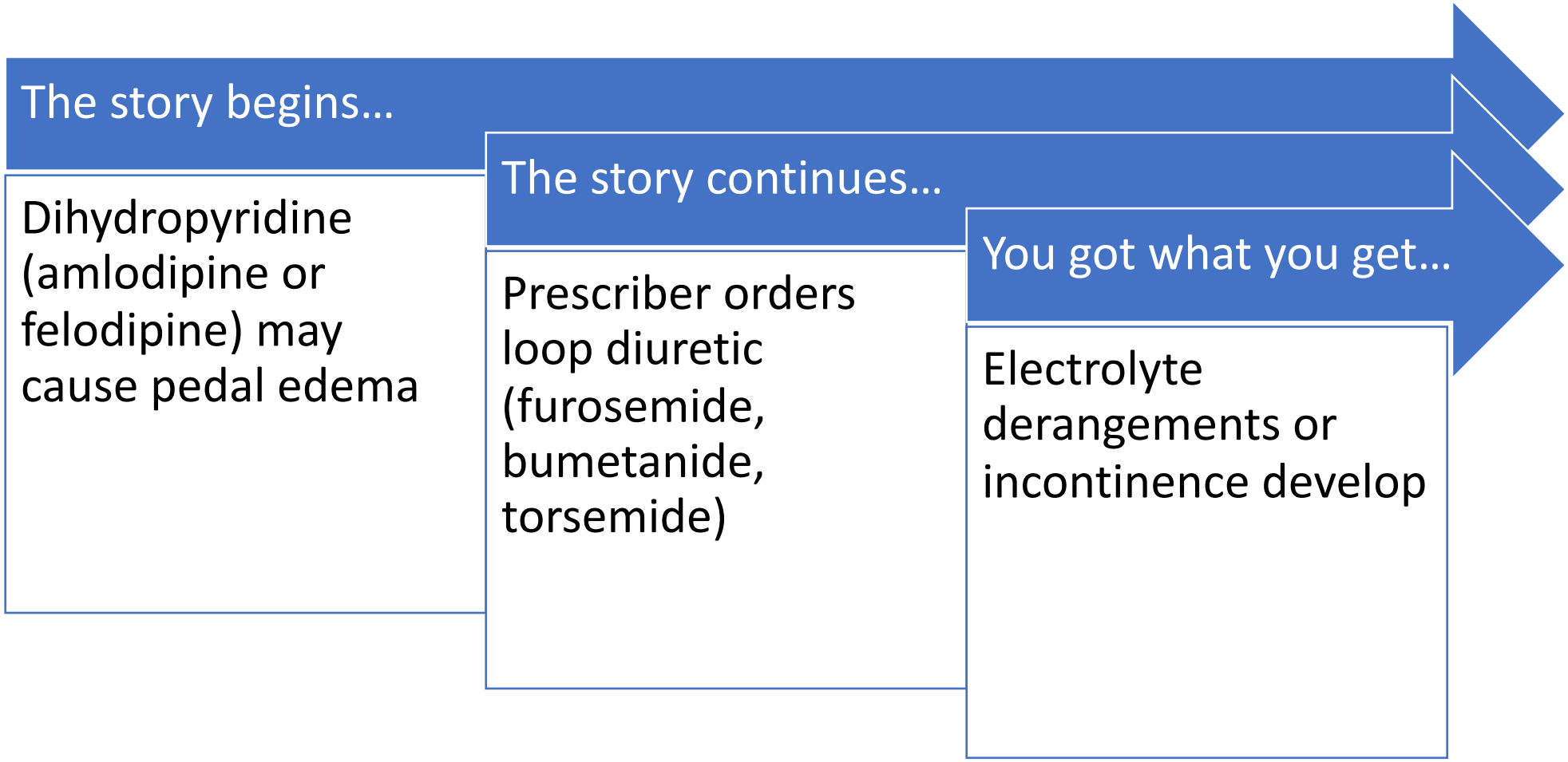
Hypertension – the “silent killer”

- So what’s a goal BP? Well…..
  - ACC/AHA 2017 guidelines say < 130/80 mmHg
    - Including > 65 yo who are ambulatory and community-dwelling
  - European Soc of Cardiology and UK NICE guidelines say < 140/90 mmHg
  - UK/NICE guidelines recommend < 150/90 mmHg for fit patients ≥ 80 yo
  - ACP/AAFP recommend SBP < 150 mmHg for adults > 60 yo (or < 140 mmHg with h/o CVA/CV risk)
- Time to benefit ranges from 2-5 years
- Legacy effect – 37% of patients remain normotensive 6 months after withdrawing therapy; effect persists in 26% of patients at 2 years
  - BP trajectories in the last 14 years of life continually decline regardless of treatment



J Hyperten 2017;35(9):1742-1749; JAMA Intern med 2018;178(1):93-99.

Be careful of prescribing cascades



And the guidelines say…

Group	Recommendation
AGS/Beers Criteria	• Recommend against use of alpha-1 blockers (doxazosin, prazosin, terazosin) • Centrally acting alpha-agonists (guanfacine, methyldopa) should be avoided • Clonidine should be avoided • Avoid immediate-release nifedipine

European Consensus	• Adults ≥ 75 yo with anticipated life expectancy ≤ 3 mo
	  • Diuretics of questionable value (excluding torsemide and furosemide)
	  • Inappropriate to initiative ACEi, ARB, peripheral vasodilator, verapamil
	  • Questionable value to continuing alpha-agonist, ACEi, ARB, CCB, non-selective BB, diuretic (except loop diuretics and spironolactone)
	  • Inappropriate to continue peripheral vasodilator
	  • No consensus re: continuing loop diuretics, spironolactone, selective BB, carvedilol, labetalol

STOPPFrail	• Recommended to carefully reduce or discontinue antihypertensive therapies with SBP persistently < 130 mmHg
Choosing Wisely/AMDA	• Do not initiate antihypertensive therapy in patients ≥ 60 for SBP < 150 mmHg or DBP < 90 mmHg

Age Ageing 2020;1-7; Choosing Wisely AMDA; JAGS 2019;67(4):674-694; Eur J Clin Pharmacol 2018;74(10):1333-1342

Pulling the trigger…

- Evaluate co-morbid conditions
  - Atrial fibrillation – beta blocker or nondihydropyridine may be beneficial for both
  - Heart failure – ACEi or loop diuretic may be beneficial for both
- Gradually withdraw beta-blockers and centrally-acting alpha-agonists
- Monitor for withdrawal effects
  - Beta-blockers – angina, anxiety, MI, palpitations
  - Centrally acting alpha-agonists – agitation, headache, palpitations
  - BP – target , 150/90 mmHg, but symptoms unlikely with BP < 180/110 mmHg (risk for target organ damage)

Antihypertensives

- “HELLO” – Mr. Herndon is experiencing side effects from his antihypertensive regimen right NOW!
- His BP is low-normal and he is complaining of orthostasis
- Minimally we should stop one (lisinopril or amlodipine) now
- He’s lost 100 pounds, so his BP has naturally declined
- Let’s stop the amlodipine and re-evaluate
- Chances are good we can reduce the lisinopril to 5 mg for a few days, then stop that as well
- Reassure the patient……

Image from pixabay.com

I don’t care about no stinkin’ cholesterol!

Image from pixabay.com

Dyslipidemia

- Increases risk for ASCVD → cardiovascular events, cerebrovascular events, peripheral vascular disease
- Statin therapy/other medications can slow or prevent atherosclerotic disease by reducing progression or formation of atherosclerotic lesions in artery walls
- Goal of therapy is to prevent morbidity/mortality associated with ASCVD
  - MI, ischemic stroke, angina, need for revascularization procedures, peripheral artery disease, arrhythmias, heart failure, sudden death
- Time to benefit – one year or longer (much shorter following an acute coronary event)
  - Usually 2-5 years for MI protection; 2 years to impact all-cause mortality; 4-5 years for CVA/TIA protection
- A recent meta-analysis showed a legacy effect on all-cause mortality and CVD mortality in those taking a statin for **primary prevention**.

Nayak A, et. al. BMJ Open. 2018.

Atorvastatin

- Kutner, et al. evaluated 381 patients within 1 year of death, taking a statin
  - Randomized to continue or stop statin therapy
  - Primary outcome – rate of death at 60 days
  - No statistically significant difference

Discontinued Statin	20.3% died by 60 days	Median time to death 229 days
Continued Statin	23.8% died by 60 days	Median time to death 190 days

- Anglo-Scandinavian Cardiac Outcomes Trial:
  8 years AFTER study completed evaluating atorvastatin impact, patients who HAD been taking atorvastatin had fewer deaths from CV and non-CV disease!

Sever, Dahlöf, Poulter, et al. *Lancet*. 2003;361(9364):1149-1158. doi:10.1016/S0140-6736(03)12948-0.
Kutner J, et al. JAMA Int Med 2015;175(5):691-700.

Guidelines say what…

Organization	Recommendation
STOPP/START Criteria	• No recommendation for primary prevention • START statin for patients with h/o coronary, cerebral or PVD, unless patient's status is EOL and age is > 85 yo
STOPPFrail	• Risks > benefits for patients with life-expectancy < 1 year • No differentiation between primary and secondary prevention
ACC/AHA 2018 Cholesterol Guidelines	• Primary prevention in patients > 75 yo WITH diabetes – may be reasonable to continue statin • Primary prevention in patients > 75 yo WITHOUT diabetes and LDL-C ≥ 70 mg/dl, may be reasonable to start statin therapy • In patients > 75 yo may be reasonable to stop statin with functional decline, multimorbidity, frailty, reduced life expectancy
Nat'l Lipid Association	• Patients 65-79 yo who are statin eligible should be managed similarly to younger patients • Older patients – have discussion with provider re: primary prevention • For patients 65-80 yo with clinical ASCVD or diabetes, consider statin (evaluate risk/benefit) • For patients ≥ 80 yo statins for secondary prevention should be considered after discussion with provider

J Am Coll Cardiol 2019;73(24):e285-e350; J Clin Lipiol 2015;9(65):S1-S122; Age Ageing 2015;44:213-218; Age and Ageing 2017;46:600-607.

Bring it on home…

- Primary prevention
  - Conflicting information for patients ≥ 75 yo
  - Generally speaking, ok to discontinue lipid-lowering therapy in patients with life expectancy < 1-2 years
- Secondary prevention
  - Evidence supports time to benefit is earlier in lipid-lowering therapy
  - Continue statin therapy if recent acute coronary syndrome, recent stroke or TIA, or if patient has unstable, symptomatic disease (e.g., recurrent angina)
- Statins/lipid-lowering therapies may be stopped abruptly!

Statin Chat…

- “Mr. Herndon, kudos to you for taking atorvastatin all these years.
- Clearly, it’s been providing you benefit because you’ve not had a heart attack or stroke.
- But the good news is that research has shown that the benefit you accrued from taking atorvastatin all those years was like putting money in the bank, and even if we discontinue the atorvastatin now, you will continue to reap the benefits.
- Research has further shown there is not an increased risk of a heart attack or stroke for people clinically similar to you.
- While statins do not cause major side effects, it would be one less tablet you have to take, and you’d have less risk of side effects such as muscle weakness.”

Go get the donuts and sweet tea!

- Prevalence of diabetes mellitus
  - 2019 – 37.3 million Americans (11.3% of population)
  - Of these, 28.7 million were diagnosed, 8.5 million were undiagnosed
- Prevalence in seniors
  - The percentage of Americans aged 65 and older remains high, at 29.2%, or 15.9 million seniors (diagnosed and undiagnosed)

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DCCT Trial – Early 1990s

- Patients with T1DM divided into 2 groups – tight BG control and usual BG control
  - Half had no complications of DM; half had early complications
- Those who achieved tight BG control had a 40%-60% reduction in development of complications; and those with complications had much slower progression.
- Fast forward to 17 years after STARTING the DCCT trial
  - Those who had been in the tight glycemic arm had:
    - 42% risk reduction in any cardiovascular event
    - 57% risk reduction in risk of nonfatal MI, stroke, or death from CV disease

Mazze, Bergenstal, Ginsberg. *Int J Clin Pharmacol Ther*. 1995;33(1):43-51.

American Diabetes Association

- Healthy (few coexisting chronic illnesses, intact cognitive and functional status)
  - A1c <7.0-7.5%; FBG 80-130 mg/dl
- Complex/intermediate (multiple coexisting chronic illnesses or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)
  - A1c < 8.0%; FBG 90-150 mg/dl
- Very complex/poor health (LTC or end-stage chronic illnesses, or moderate-to-severe cognitive impairment or 2+ ADL impairments)
  - Avoid reliance on A1c; base decisions on avoiding hypoglycemia and symptomatic hyperglycemia
  - FBG 100-180 mg/dl

Diabetes Care 2022;45(Supplement 1):S195-S207.

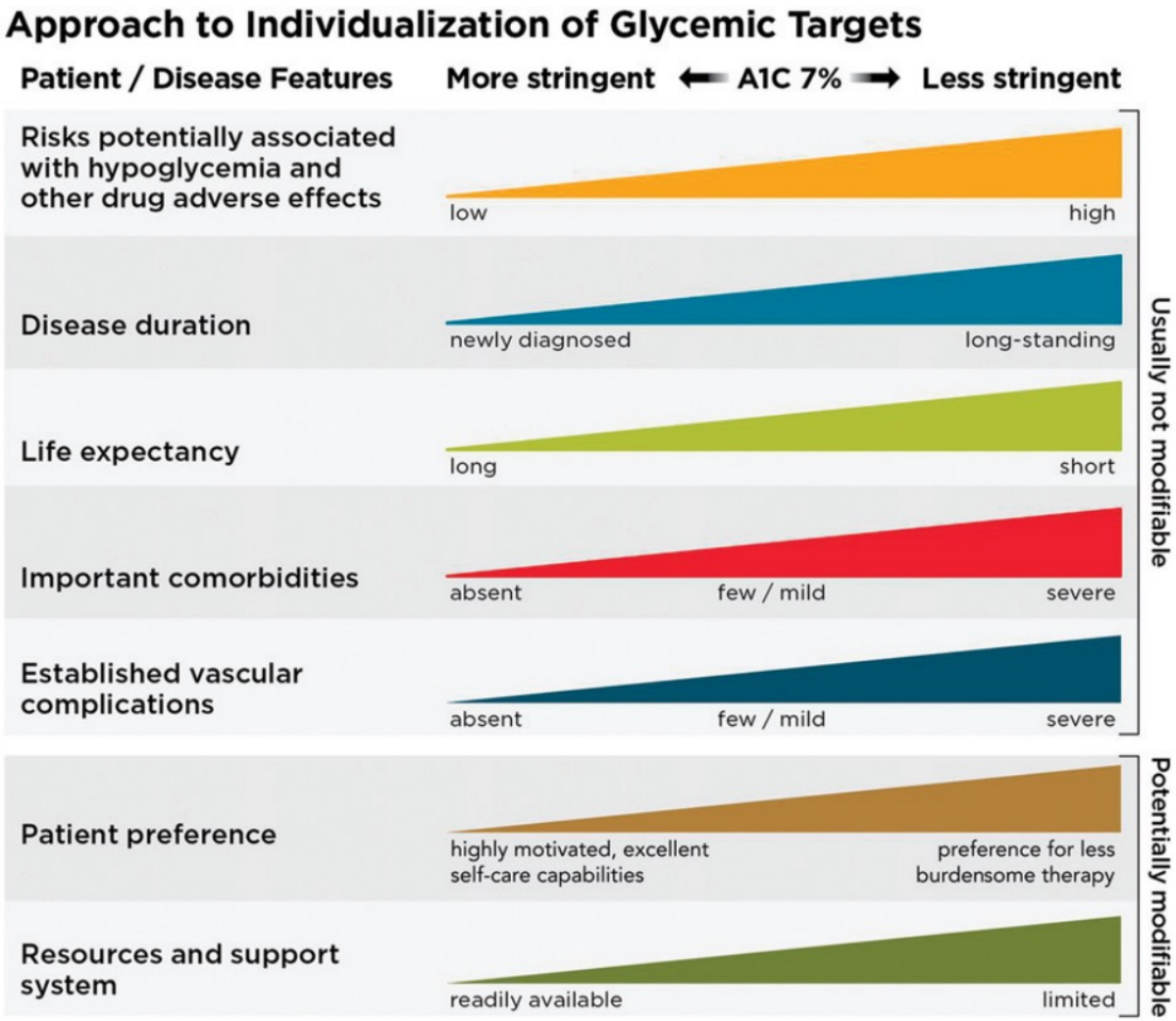
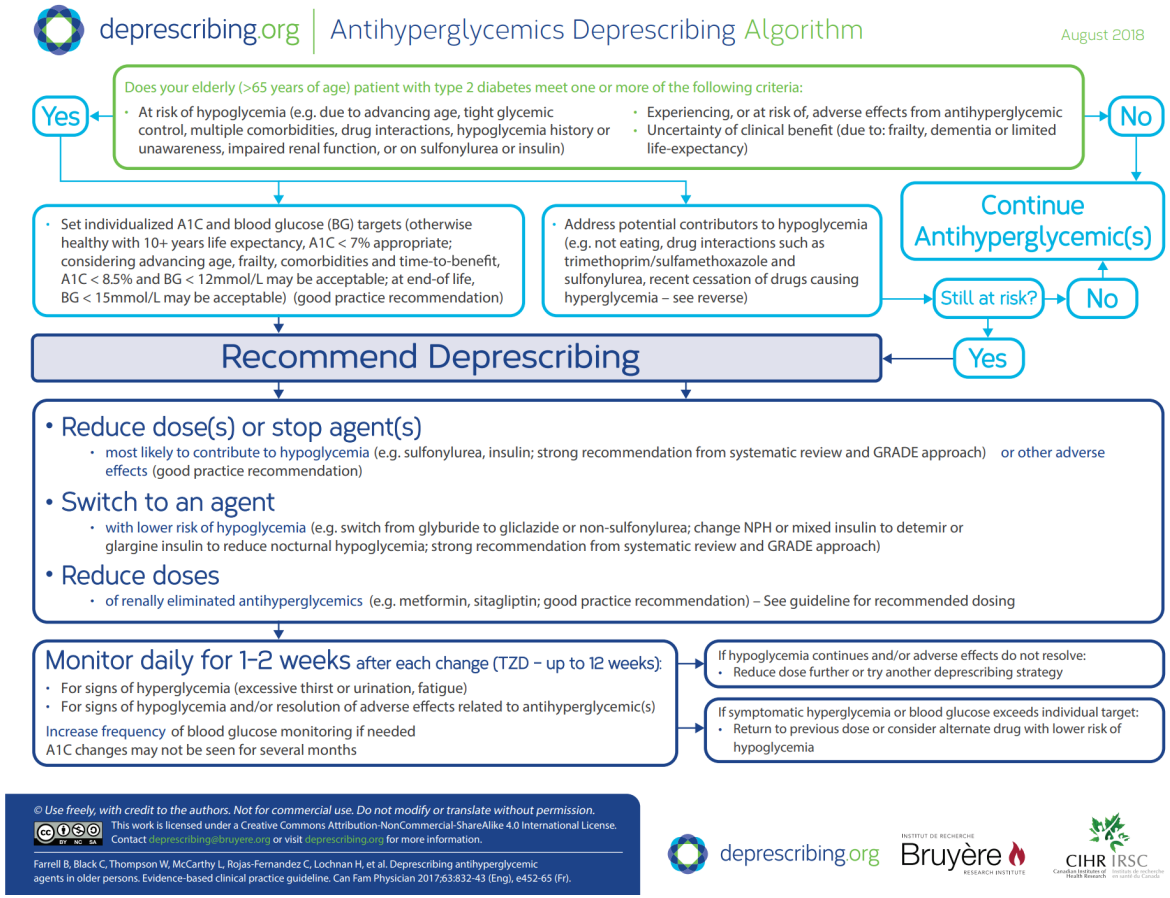
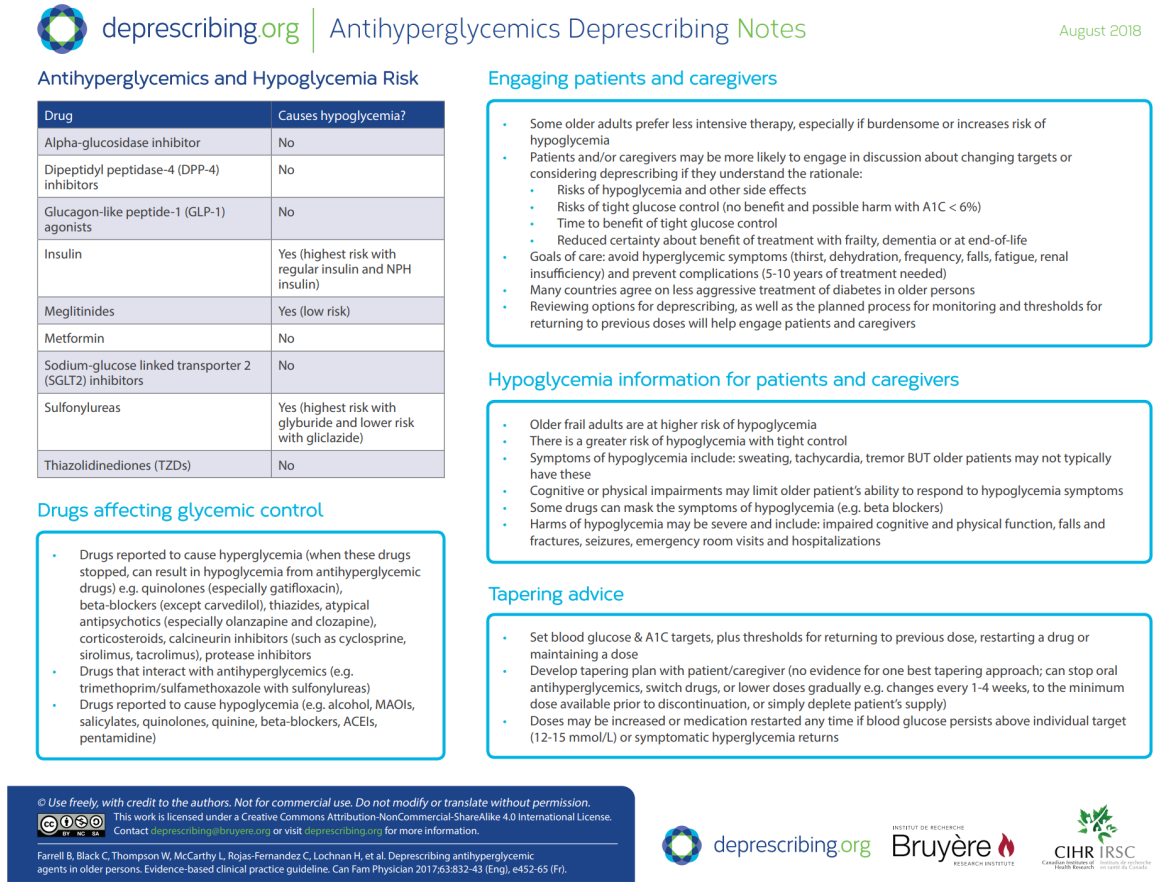


Figure 6.2—Patient and disease factors used to determine optimal glycemic targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. A1C 7% = 53 mmol/mol. Adapted with permission from Inzucchi et al. (68).

American Diabetes Association; Diabetes Care 2022; 45(Supplement 1):S83-S96.

Deprescribing.org





Antihyperglycemics

Mr. Herndon has had diabetes for many years and is on:	Metformin	NovoLog sliding scale insulin	Lantus? First…
• Metformin XR 1000 mg, 2 tablets per day • Lantus insulin 20 units at bedtime • NovoLog insulin sliding scale 4 times daily	• Patient has chronic kidney disease, stage 4, CLcr 15-30 ml/min; contraindicated	• Not requiring; increases risk of hypoglycemia	• Let's consider what we know about diabetes and glucose control first before we address the Lantus

Image from pixabay.com

What does this mean for Mr. Herndon?

- All those years he watched his diet, took his medications, monitored his BG – it was like putting money in the bank!
- Now we can loosen the reins a bit and he can "draw his dividends," secure in the knowledge that his risk of diabetes-related complications is extremely low
- We will monitor him for symptoms suggestive of hyperglycemia

So, what about the Lantus?

- Let's stop the metformin and NovoLog insulin now
- Let's check the fasting BG 3 times in the next week
- Even if his BG is up to 200 mg/dl, it's probably ok
- We may be able to reduce the Lantus, or even stop it at some point
- STOP checking his BG 4 times a day – that's NOT very palliative!

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Diabetes Convo…

- “Mr. Herndon, you deserve an ENORMOUS amount of credit for following your diet and your diabetes medication regimen for all these years.
- And like the statins, research has shown that tighter blood glucose control starting at the time of diabetes diagnosis leads to an accrued benefit in reduction of complications later in life.
- You’re not even using the NovoLog insulin because your blood glucose isn’t getting high enough to warrant it.
- You’ve lost a lot of weight and you’re not eating like you used to.

Image from pixabay.com

Diabetes Convo…

- “Given your kidney disease, we really should stop the metformin so you won’t have any side effects.
- Let’s stop the metformin and the NovoLog insulin.
- Let’s follow your blood glucose over the next week or so and make a decision about whether or not to continue the Lantus at your current dose, or to reduce it.
- In the meantime, we can liberalize your meal plan, and stop checking your blood glucose so frequently, you’ve earned it!”

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Mr. Herndon

A. Sir, you are a few weeks away from death; does it really matter what your cholesterol, blood pressure, and blood glucose are?

B. You aren't dying TODAY but within a month or so, and it's really unlikely you'll have a heart attack or stroke, so I feel lucky!

C. Clearly you aren't dying today, but all medications have risks and benefits, and no medication is meant to be continued FOREVER (and you start humming "Let It Go" under your breath)

D. We'll take a look at each of your medications, and you and I and your family will discuss this with your doctor and make decisions that give you the most benefit from your medications and cause the least harm. Sound good?

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Alzheimer's Disease

- Most common cause of dementia (60-70% of 50 million affected worldwide)
- Relentlessly progressive neurodegenerative disease; average age > 75 years old
- Worsening memory; declines in language, visuospatial, and executive functioning
- Behavioral and psychological symptoms (depression, anxiety, agitation, psychosis, wandering)
- Survival after diagnosis is approximately 4-8 years on average
- Goals of care – slow functional and cognitive decline; maximize symptom control and QOL

WHO 2020l Dementia Facts; Continuum 2019;25(1):14-33
Alzheimers Dement 2016;12(3):216-224; Alzheimers Dement 2011;7(5):532-539

Treatment of Alzheimer's Disease

- **Non-pharmacologic**
  - Physical activity
  - Cognitive training/rehabilitation
- **Management of co-morbid conditions**

5	3			7				
6			1	9	5			
	9	8					6	
8				6				3
4			8		3			1
7				2				6
	6					2	8	
			4	1	9			5
				8			7	9

- **Cholinesterase Inhibitors**
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine (Razadyne)
- **NMDA Antagonist**
  - Memantine (Namenda)
- **Combination**
  - Donepezil/memantine (Namzaric)
- **Aducanumab (Aduhelm)**

The Case of Miss Judy

Judy is a 78-year-old female

- **CC:** Repeated falls in the past 3 months
- **PMH:** Breast cancer, hypertension, dyslipidemia, nonvalvular atrial fibrillation (no h/o CVA), Alzheimer's disease (FAST 7C - > 10% weight loss, recent UTI)
- Lives with daughter, Laura, in Maryland
- Son, Frederick, is a lawyer who lives in California

The Case of Miss Judy

Judy is a 78-year-old female

Current Medication Regimen

- Donepezil (Aricept®)
- Memantine (Namenda®)
- Lisinopril
- Atorvastatin (Lipitor®)
- Warfarin
- MVI
- Ferrex
- Calcium and vitamin D3

- When you suggest slimming down on the medications, Laura is agreeable.
- Frederick, on the other hand, goes ballistic and angrily says, **“What’s WRONG with you people – are you TRYING to kill her off?”**
- So…..any issues here?

“Cognitive Enhancers”

Drug Category	Drug Name(s)	Indication(s)
Cholinesterase Inhibitors	Donepezil	Treatment of dementia of the Alzheimer’s type. Efficacy has been demonstrated in patients with mild, moderate and severe Alzheimer’s dementia.
	Galantamine	Treatment of mild and moderate dementia of the Alzheimer’s type.
	Rivastigmine	Treatment of mild, moderate and severe dementia of the Alzheimer’s type. Treatment of mild to moderate dementia associated with Parkinson’s disease.
NMDA Antagonist	Memantine	Treatment of moderate to severe dementia of the Alzheimer’s type.

FAST Criteria

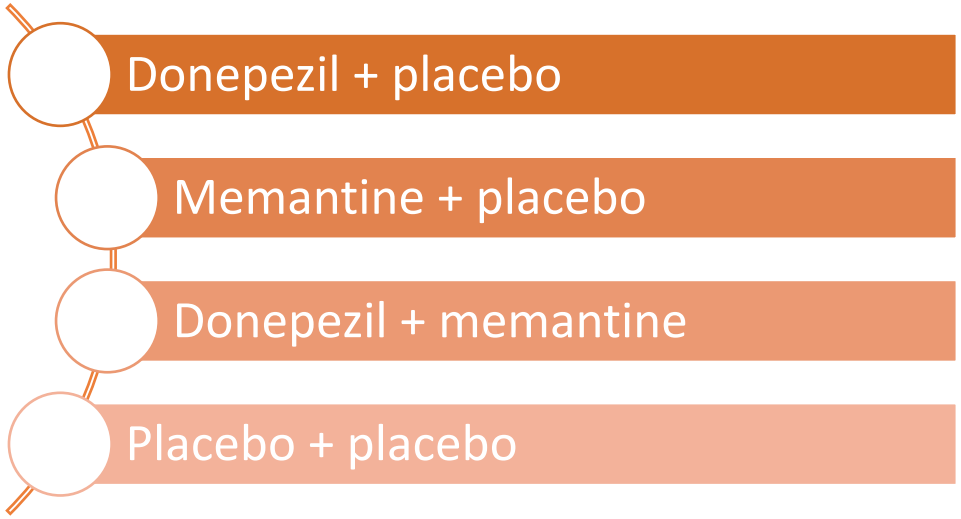
1. Normal adult
2. Normal older adult
3. Early dementia
4. Mild dementia
5. Moderate dementia
6. Moderately severe dementia
7. Severe dementia

- 7a. Ability to speak limited to approximately a half dozen different words or fewer, in the course of an average day or in the course of an intensive interview.
- 7b. Speech ability limited to the use of a single intelligent word in an average day or in the course of an interview (the person may repeat the word over and over).
- 7c. Ambulatory ability lost (cannot walk without personal assistance)
- 7d. Ability to sit up without assistance lost (e.g., the individual will fall over if there are no lateral rests [arms] on the chair)
- 7e. Loss of the ability to smile

avalonmemorycare.com/the-seven-stages-of-dementia-understanding-the-fast-scale/.

Donepezil and Memantine for Moderate-to-Severe AD

- 295 community-dwelling moderate-to-severe AD patients treated with donepezil for at least 3 months (MMSE 5-13); 52 weeks
- Stratified by
  - Study center
  - Duration of donepezil treatment before entry (3-6 mo vs ≥ 6 mo)
  - Baseline MMSE (5-9 vs 10-13)
  - Age (< 60; 60-74; ≥75)



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

Donepezil and Memantine for Moderate-to-Severe AD

- Outcomes:
  - Score on MMSE - Clinically important difference:
    - **Scoring 1.4 points or greater higher than comparator**
  - Caregiver-rated Bristol activities of Daily Living Scale (BADLS): Clinically important difference:
    - **Scoring 3.5 points or greater lower than comparator**
- Baseline MMSE 9.1-9.2 in all groups
- Baseline BADLS 26.9-28.6

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

Donepezil and Memantine for Moderate-to-Severe AD

- Clinically important difference:
  - MMSE ≥ 1.4 point increase or greater
  - BADLS ≥ 3.5 point decrease or greater

Treatment group	MMSE	BADLS
All donepezil vs no donepezil	**+1.9**	-3.0
All memantine vs no memantine	+1.2	-1.5

- Effect of donepezil and memantine did not differ significantly in the presence or absence of either
- Donepezil plus memantine showed no difference vs donepezil alone

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

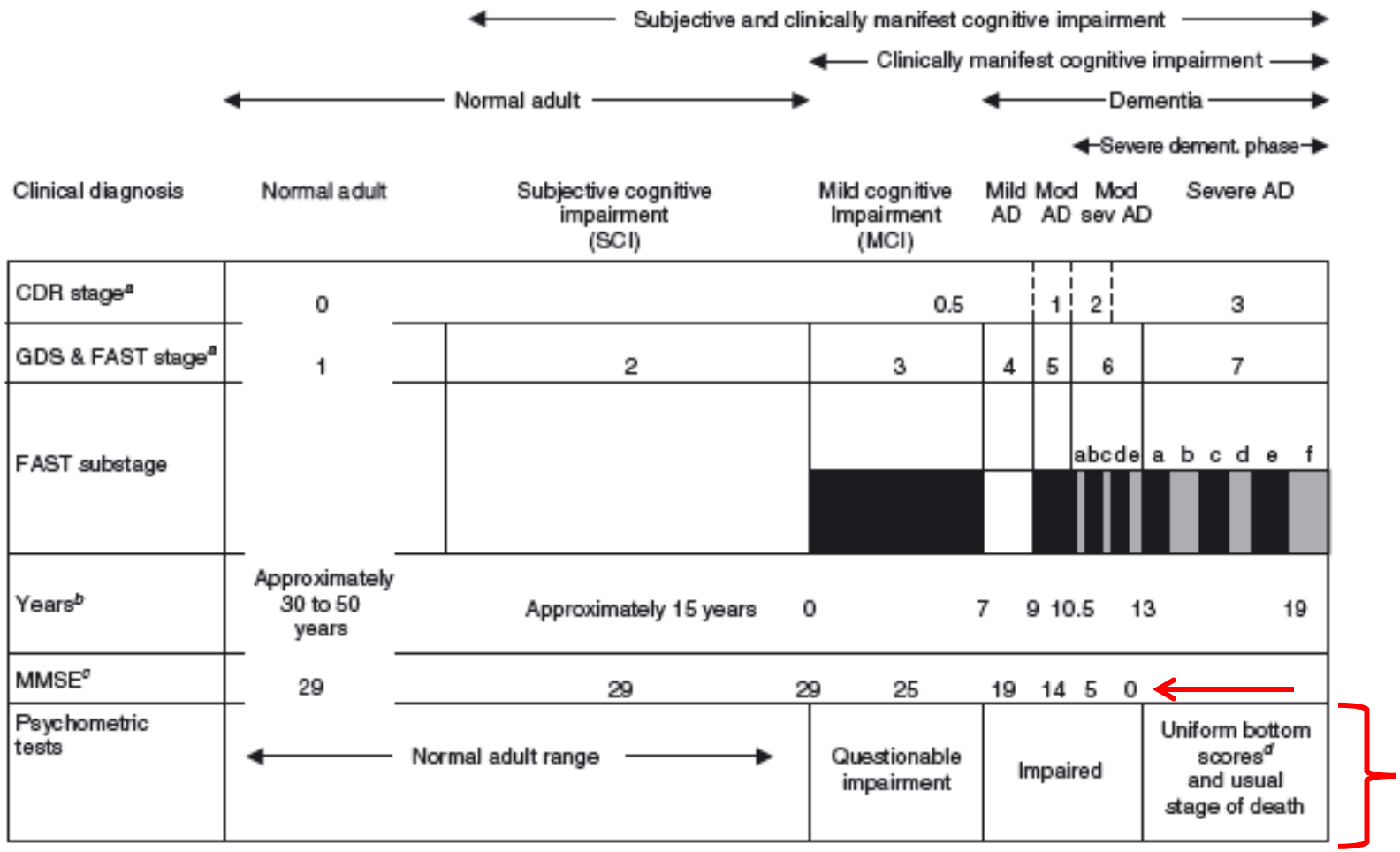
Donepezil and Memantine for Moderate-to-Severe AD

Baseline MMSE	Impact of donepezil therapy on MMSE
MMSE 10-13	**+2.6**
MMSE 5-9	+1.3

Donepezil only showed clinical significance in patients with baseline MMSE ≥ 10

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

FAST and MMSE



Reisberg. *Prin Prac Ger* Psy, 3rd ed. Used with permission, John Wiley and Sons.

Adverse Effects

- Memantine
  - Dizziness, headache, confusion, constipation
- ChEIs
  - Nausea, vomiting, diarrhea, anorexia, insomnia, fatigue, muscle cramps
  - Warning: “Cholinesterase inhibitors may have vagotonic effects on the sinoatrial and atrioventricular nodes manifesting as bradycardia or heart block”

Outcome Measure	ChEI recipients	Controls
Hospital visits for syncope	31.5/1000 person-years (HR 1.76)	18.6/1000 person-years
Hospital visits for bradycardia	6.9/1000 person years (HR 1.69)	4.4/1000 person-years
Permanent pacemaker insertion	4.7/1000 person-years (HR 1.49)	3.3/1000 person-years
Hip fracture	22/4.1000 person-years (HR 1.18)	19.8/1000 person-years

Prescribing information; Arch Intern Med 2009;169(9):867-873

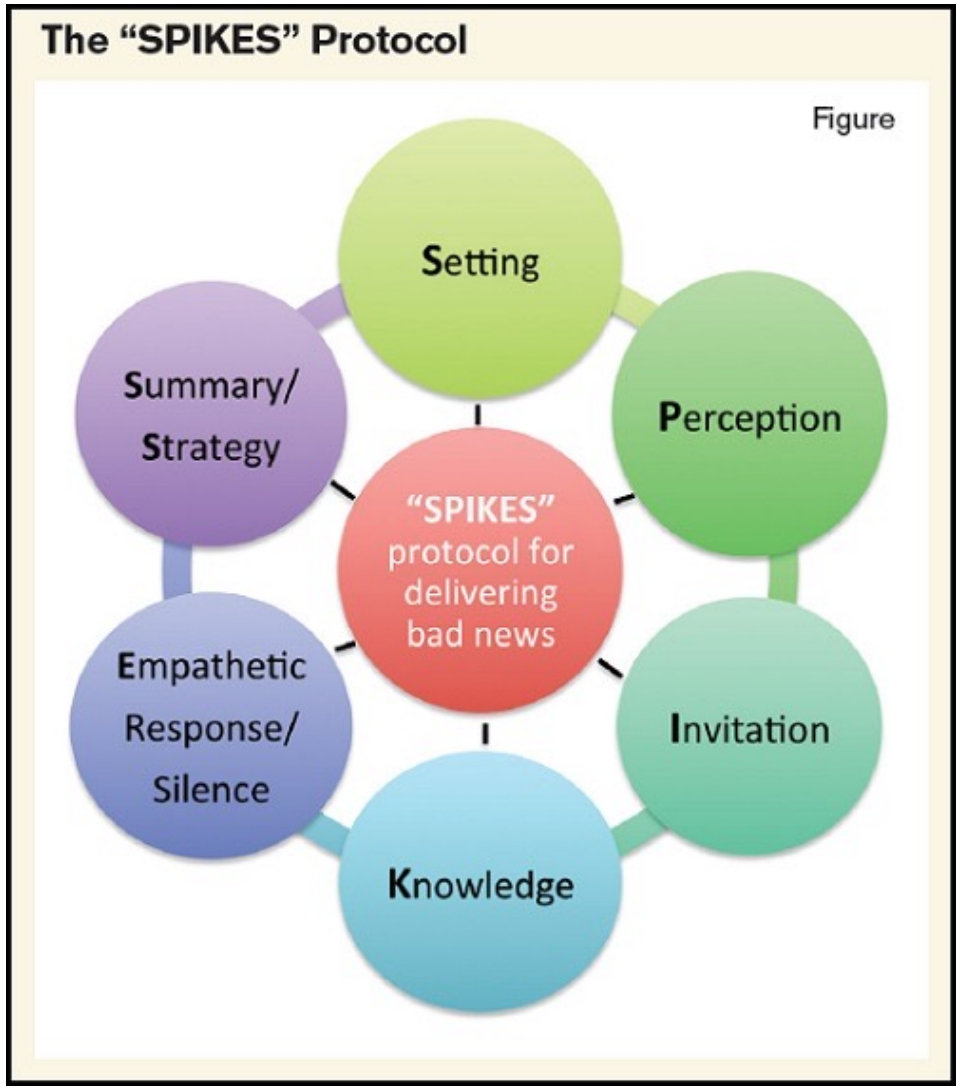
Bottom Line: Dementia Drugs

- Dementia medications are LESS HELPFUL and MORE HARMFUL in advanced disease (see adverse effects)
- NOT indicated or provided with FAST 7 without clear and ongoing benefit in managing identifiable and distressing behaviors
- MAY be covered with FAST 6; discuss goals/outcomes with hospice team leadership
- 2 week tapering supply should be provided if medication discontinued

But is Frederick buying what you're selling?

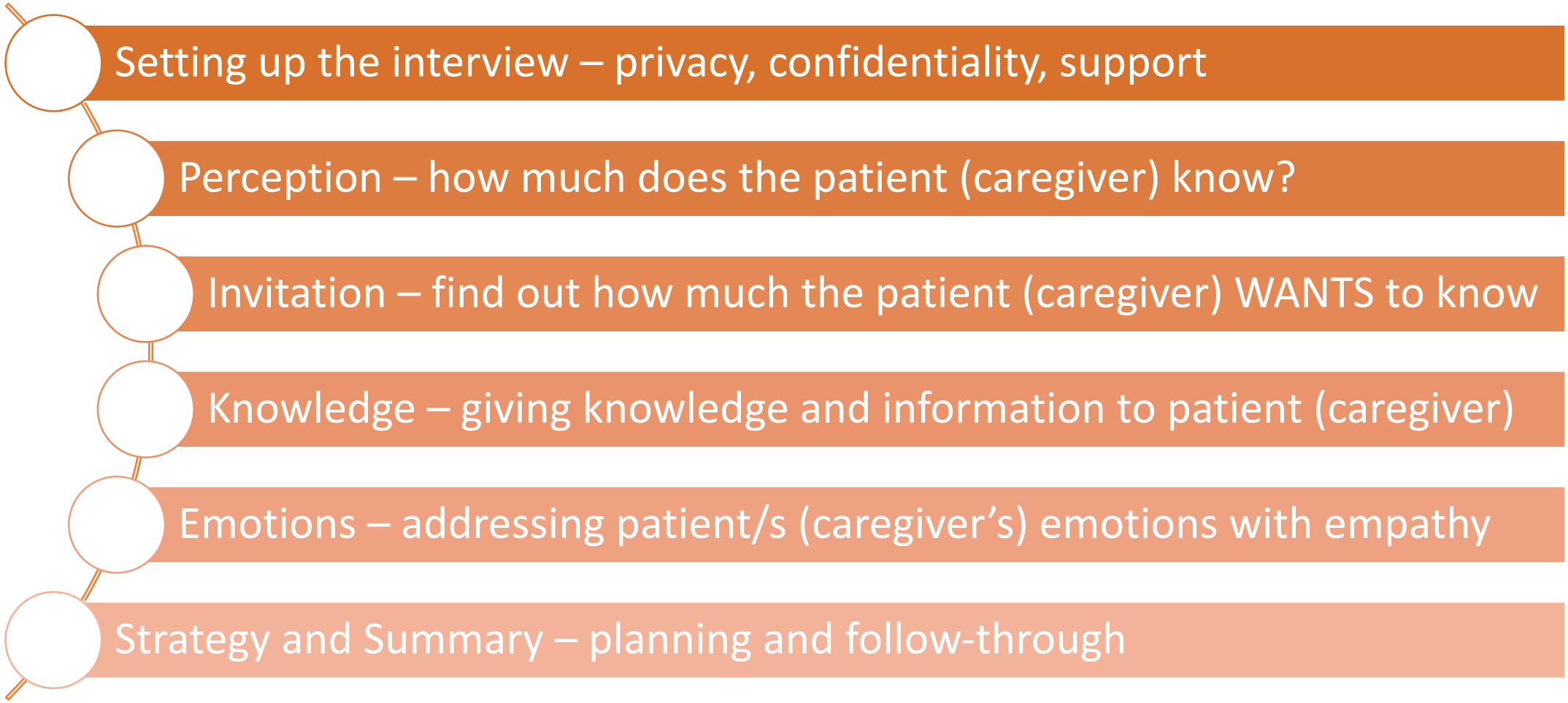
SPIKES – Having those Conversations

- S – setting
- P – perception
- I – invitation
- K – knowledge
- E – emotion
- S – summarize recommendation



Slide from McPherson, Walker, Pruskowski, Talebreza. "Right Sizing Medication Regimens in Serious Illness: Doing the Prescribing and Deprescribing Dance"

Having the Conversation: Breaking “Bad” News: SPIKES



www.cetl.org.uk/learning/feedback_opportunities/data/downloads/breaking_bad_news.pdf.

Guideline Consensus

Guideline	Opinion
Beers List	ChEIs cause bradycardia; avoid in older adults with syncope due to bradycardia
STOPPFrail*	ChEIs – no consensus Memantine – recommended to discontinue with moderate to severe dementia, unless clearly shows improvement of BPSD
European Consensus 2018	Prognosis ≤ 3 months – use of drugs for AD "inadequate"; "special circumstances" may warrant consideration
Australian Guidelines	Recommend a trial of discontinuation of ChEIs and memantine if receiving ≥ 12 months and have worsening of disease, or no benefit noted, or have end-stage disease. Can resume if behavior worsens with discontinuation
Deprescribing.org	Trial discontinuation if taking > 12 months and significant cognitive/functional decline over past 6 months, or no benefit seen, or severe disease
Choosing Wisely/AGS	ChEIs – long term use > 1 year not studied sufficiently; if improvement not seen within 12 weeks, consider discontinuing

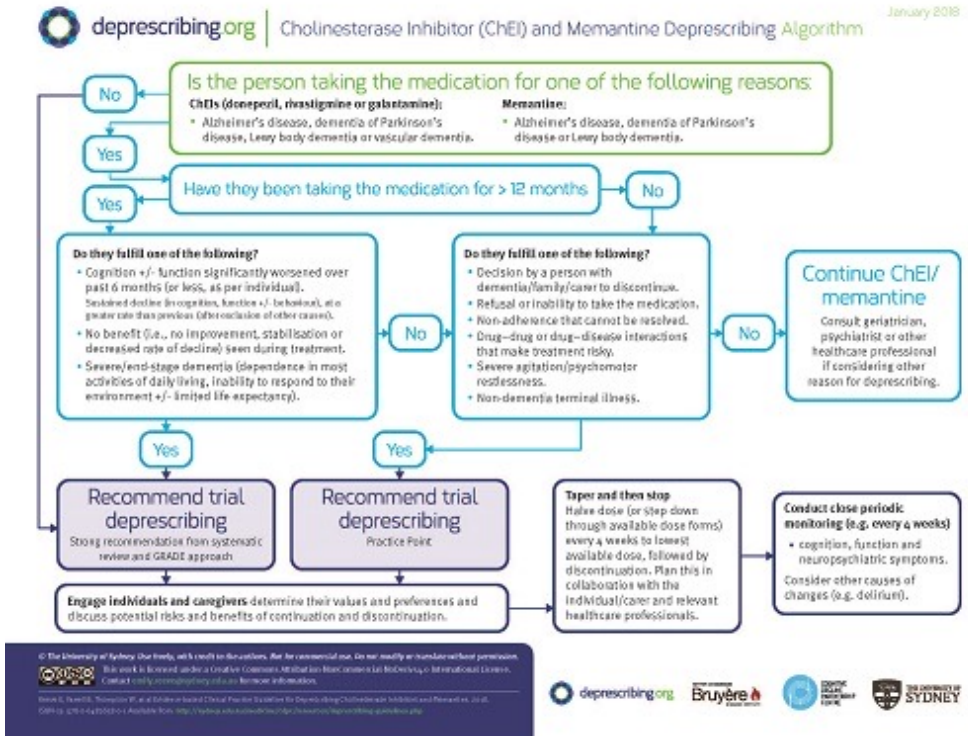
* - STOPPFrail criteria include end-stage irreversible pathology, poor 1 year survival prognosis, severe functional or cognitive impairment, symptom control is priority)

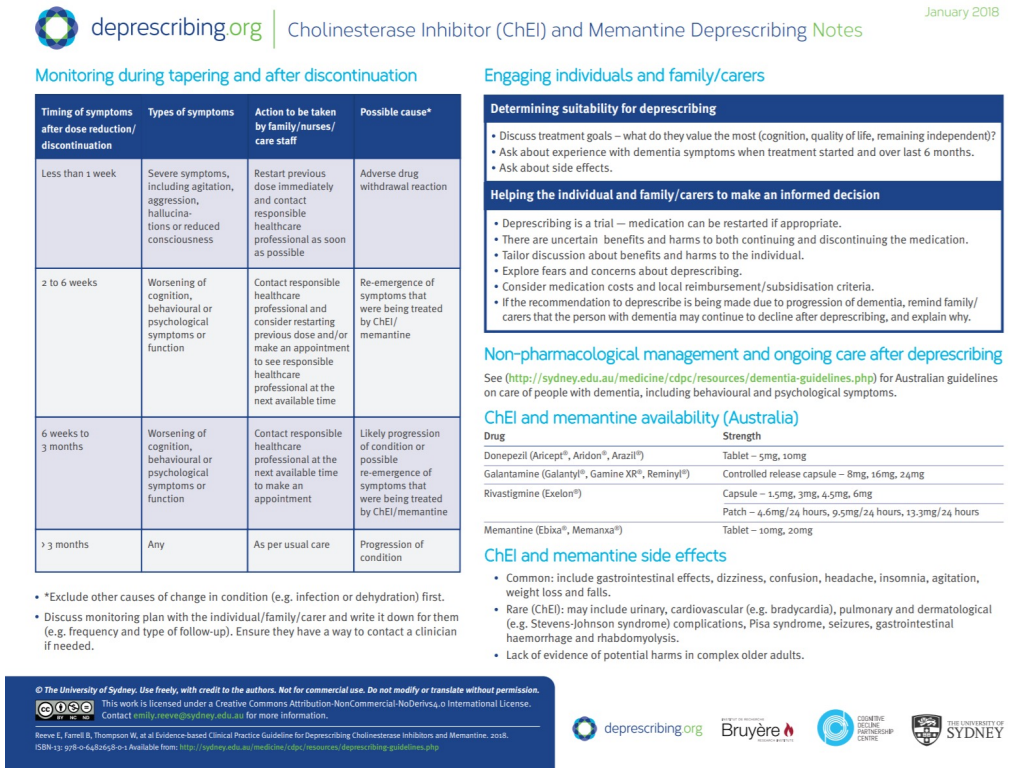
JAGS 2019;67(4):674-694; Age Ageing 2017;46(4):600-607; Eur J Clin Pharmacol 2018;74:1333-1342
Deprescribing.org; AAFG online

Deprescribing Cholinesterase Inhibitors/Memantine

- Developing organizations:
  - The University of Sydney
  - NHMPRC Partnership Centre: Dealing with Cognitive and Related Functional Decline in Older People (Cognitive Decline Partnership Centre)
  - Bruyere Research Institute, Deprescribing Guidelines in the Elderly Project

- sydney.edu.au/medicine/cdpc/resources/deprescribing-guidelines.php
- EBR – evidence-based recommendations
- CBR – consensus-based recommendations
- PP – practice points



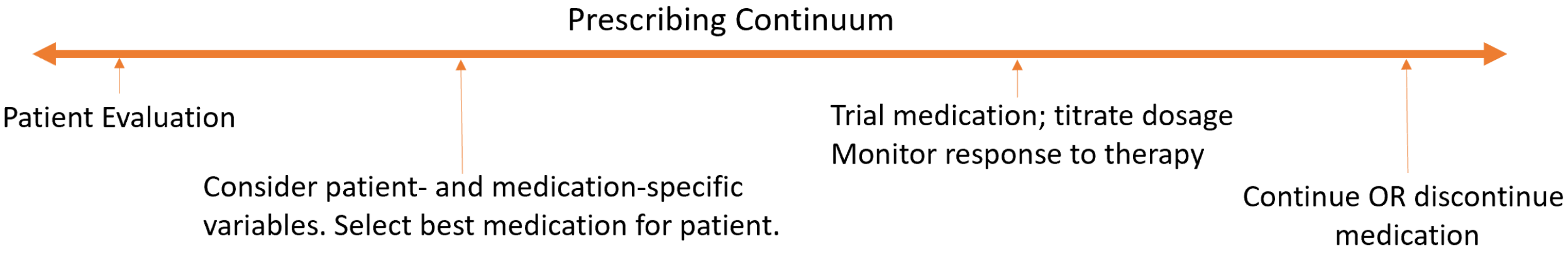


Proton pump inhibitors; antihyperglycemics; antipsychotics; benzodiazepine receptor antagonists

Deprescribing.org; specifically: cdpc.sydney.edu.au/wp-content/uploads/2019/06/algorithm-for-deprescribing.pdf.

Conclusion

- Deprescribing is part of the prescribing continuum



- Practitioners must weigh the benefits and burdens of drug therapy in all patients, but especially in advanced or serious illness
- Conversations with patients, families and other healthcare providers are VERY important

Deprescribing: When to "Let it Go!"

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