CONGRÈS INTERNATIONAL DE SOINS PALLIATIFS MCGILL

MCGILL INTERNATIONAL PALLIATIVE CARE CONGRESS

October 18–21 octobre 2022

Palais des Congrès de Montréal

Quick Medication Tips, New Drugs and Updates on Pain and Symptom Management

Presented by:

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CONFLICTS OF INTEREST DECLARATION

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- None

LEARNING OBJECTIVES

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At the conclusion of this presentation, participants will be able to:

- Identify and describe emerging practices integrating into palliative care practice
  - Opioid conversion calculations
  - Goal concordant prescribing/deprescribing, use of tools
- Contemporary medication strategies in pain and symptom management
  - Secretogogues in the management of treatment-resistant constipation
  - Update on nausea management in advanced illness
  - Number needed to treat in coanalgesic therapy

CanMEDS COMPETENCY FRAMEWORK

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- Professional CanMEDS competency

- Lack of therapeutic response
- Development of adverse effects
- Change in patient status
- Other considerations
  - Opioid/formulation availability
  - Formulary issues
  - Patient/family health care beliefs

Reasons for Changing Opioids

Equianalgesic Dosing Terminology

- Opioid responsiveness
  - The degree of analgesia achieved as the dose is titrated to an endpoint defined either by intolerable side effects or the occurrence of acceptable analgesia
- Potency
  - Intensity of the analgesic effect of a given dose
  - Dependent on access to the opioid receptor and binding affinity
- Equipotent doses = equianalgesic
- Equianalgesic Opioid Dosing

Converting Among Routes: Same Opioid

- Bioavailability
  - The rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action
- Oral bioavailability
  - Morphine 30-40% (range 16-68%)
  - Hydromorphone 50% (29-95%)
  - Oxycodone 80%
  - Oxymorphone 10%

Equianalgesic Opioid Dosing

	Equianalgesic Doses (mg)	
Drug	Parenteral	Oral
Morphine	10	25
Codeine	100	200
Fentanyl	0.15	NA
Hydrocodone	NA	25
Hydromorphone	2	5
Meperidine	100	300
Oxycodone	10*	20
Oxymorphone	1	10
Tapentadol	NA	100
Tramadol	100*	120

*Not available in the US

NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

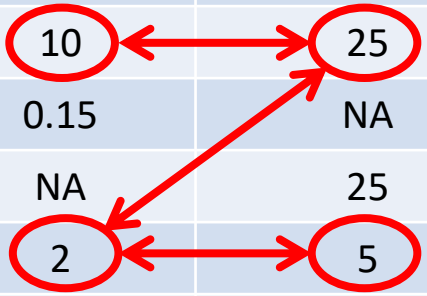
The Problem with “Those Charts”

- Source of equianalgesic data
- Patient-specific variables
- Unidirectional vs. bidirectional equivalencies

Equianalgesic Opioid Dosing

2010	Equianalgesic Doses (mg)	
Drug	Parenteral	Oral
Morphine	10	30
Fentanyl	0.1	NA
Hydrocodone	NA	30
Hydromorphone	1.5	7.5
Oxycodone	10*	20

2018	Equianalgesic Doses (mg)	
Drug	Parenteral	Oral
Morphine	10	25
Fentanyl	0.15	NA
Hydrocodone	NA	25
Hydromorphone	2	5
Oxycodone	10*	20



Reprinted with permission from McPherson ML. Demystifying opioid conversion calculations: a guide for effective dosing, 2nd ed. Bethesda: ASHP; ©2018.

NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

*Not available in the US

Parenteral to Oral Hydromorphone

- Largely determined by oral bioavailability (of oral hydromorphone)
  - Parab - 50.7 +/- 29.8%; Ritschel – 51.35 +/- 29.3%
- Do we need to evaluate conversion from oral to parenteral?
  - No, because conversion is determined primarily by BAB
  - Secondarily by pharmacogenetics
- Clinical experience in large patient populations provide average guidance
- Best data is 1:2.5 (IV:oral)

McPherson Table	Equianalgesic Doses (mg)	
Drug	Parenteral	Oral
Hydromorphone	2	5

Biopharm & Drug Dispo, 1988;9(2):187-199.
J Clin Pharm 1987;27(9):647-653.

Conversion Ratio from IV Hydromorphone to Oral Opioids in Cancer Patients

IV Hydromorphone	→	Oral Opioid
1 mg IV hydromorphone (< 30 mg/day)	→	Oral hydromorphone 2.5 mg
1 mg IV hydromorphone (≥ 30 mg/day)	→	Oral hydromorphone 2.1 mg
1 mg IV hydromorphone (< 30 mg/day)	→	Oral morphine 11.54 mg
1 mg IV hydromorphone (≥ 30 mg/day)	→	Oral morphine 9.86 mg
1 mg IV hydromorphone	→	Oral oxycodone 8.06

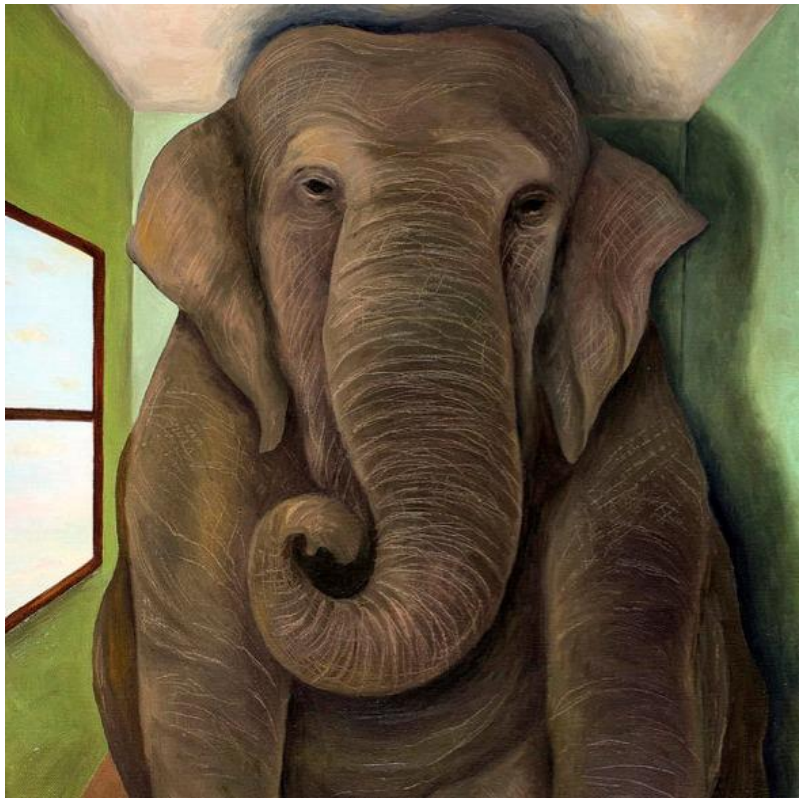
McPherson Table	Equianalgesic Doses (mg)	
Drug	Parenteral	Oral
Morphine	10	25
Hydromorphone	2	5
Oxycodone	10*	20

Reddy's bottom line:
I:2.5 (IV hydromorphone to oral hydromorphone)
1:10 (IV hydromorphone to oral morphine)
1:8 (IV hydromorphone to oral oxycodone)

Reddy, et al. J Pain Sx Manage 2017;54:280-288.

Morphine ⇌ Hydromorphone

- Is it bidirectional? (IV HM to PO MS equal to PO MS to IV HM?)
- Study by Lawlor – SQ to SQ HM/MS and PO to PO HM/MS
  - Going from morphine to hydromorphone (same route) was 5:1 (M:HM)
  - Going from hydromorphone to morphine (same route) was 3.7:1 (M:HM)
- Limitations of Lawlor study:
  - Data highly skewed and variable, not normally distributed
  - Authors stated differences in direction were clinically insignificant and called for further research...in the meantime differences in M→HM and HM→M remain speculative



Pain 1997;72(1-2):79-85.

Equianalgesic Opioid Dosing

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NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

*Not available in the US

IV to Oral Morphine – what's the dealio?

- Equianalgesic tables range from 1:2 to 1:3
- Supported by Kalso (1990)
  - 20-30 mg of morphine by mouth ~ 10 mg IV or SQ morphine
- Starlander (2011)
  - Conversion factor of 1:2 (calls for individual adjustments)
  - 11 patients, pilot study, not definitive
- Takahashi (2003)
  - Conversion factors between 1:2 and 1:3 (based on morphine and M6G in advanced cancer patients receiving chronic morphine treatment)
- Lasheen (2010) – 1:3 IV to PO confirmed

2018	Equianalgesic Doses (mg)	
Drug	Parenteral	Oral
Morphine	10	25

Case

- PR is a 58-year-old man end stage 4 lung cancer, admitted directed to the hospice inpatient unit with a complaint of uncontrolled pain.
- He is started on an IV infusion of hydromorphone at 0.2 mg/hr which was titrated up over 4 days to 0.5 mg/hour with a bolus of 0.2 mg every 15 minutes as needed.
  - PR is using the bolus about 4 times in a 24 hour period.
- It is time to discharge the patient home with hospice care, and you would like to switch him to oral morphine to maintain his current level of pain control.
- What dosage regimen do you recommend?

Case

- 0.5 mg/hr hydromorphone x 24 hours = 12 mg/day, plus four doses of the 0.2 mg IV hydromorphone bolus (0.8 mg) for a TDD of 12.8 mg IV hydromorphone

- $\frac{\text{“x” mg PO morphine}}{\text{12.8 mg IV HM}} = \frac{\text{25 mg PO morphine}}{\text{2 mg IV HM}}$

- (2)(x) = (25)(12.8)
- X = 160
- Reduce by 25% - 120 mg oral morphine a day
- LA MS – MS Contin 60 mg po q12h
- SA MS – Oral morphine 20 mg po q4h

Reddy’s bottom line:
I:2.5 (IV hydromorphone to oral hydromorphone)
1:10 (IV hydromorphone to oral morphine)
1:8 (IV hydromorphone to oral oxycodone)

Case To Go Points

- Going from one opioid to a different opioid
  - IV hydromorphone to oral morphine
- Reduce slightly for lack of cross tolerance (but our table for this conversion IS built on steady-state data)

	Equianalgesic Doses (mg)	
Drug	Parenteral	Oral
Morphine	10	25
Hydromorphone	2	5
Oxycodone	10*	20

Reddy's bottom line:
I:2.5 (IV hydromorphone to oral hydromorphone)
1:10 (IV hydromorphone to oral morphine)
1:8 (IV hydromorphone to oral oxycodone)

So for the “non-expert” or “new learner” doing opioid conversion calculations, when they access an equianalgesic chart, are they more likely to:

a. Calculate the conversion and make a well-considered decision regarding dose reduction, and to what degree?
b. Calculate the conversion and run with it?

Which is my seat?

Don’t know – I just got you in the ball park!

5-Step OCC Process

1. Globally assess pain complaint (PQRSTU)
2. Determine TDD current opioid (LA and SA)
3. Decide which opioid analgesic will be used for the new agent and consult established conversion tables to determine new dose
4. Individualize dosage based on assessment information gathered in Step 1
5. Patient follow-up and continual reassessment (7-14 days)

Gammaitoni AR, et al. Clinical J Pain 2003;19:286-297

OPIOID CONVERSION CALCULATIONS

It is often necessary to switch from one opioid to a different opioid, a different formulation, or a different route of administration.

STEPS INCLUDE:[a]

1. Assess patient's pain complaint thoroughly; is pain controlled (e.g., at goal)?
2. Determine average total daily dose of current opioid use (long- and short-acting).
3. Set up ratio using equianalgesic equivalence chart; calculate new dose.
4. Individualize calculated dose based on patient assessment in step 1.
   - **a.** Staying with same opioid, but different route of administration:
     - ▸ pain controlled, use calculated dose
     - ▸ pain not controlled, increase dose (e.g., 20-30%)
   - **b.** Switching from one opioid to another opioid:
     - ▸ pain controlled, reduce calculated dose by 30-50%
     - ▸ pain not controlled, reduce calculated dose by less (e.g., 10-20%)
5. Monitor patient closely; adjust as needed.

SELECTED EQUIVALENCIES[bc]

	Equianalgesic Equivalence (mg)	
OPIOID	PARENTERAL	ORAL
Morphine	10	25
Fentanyl	0.15	NA
Hydrocodone	NA	25
Hydromorphone	2	5
Oxycodone	10[d]	20
Oxymorphone	1	10

Example: Patient receiving long- and short-acting oral oxycodone, on average 80 mg per day. Patient can no longer swallow tablets or capsules; pain is well controlled on this regimen. Switch to oral morphine solution, dosed q4h around the clock.

$$\frac{\text{“x” mg oral morphine}}{\text{80 mg oral oxycodone}} = \frac{\text{25 mg oral morphine}}{\text{20 mg oral oxycodone}}$$

“x” = 100 mg oral morphine
Reduce by 25-50% because switching opioids and pain was controlled, to oral morphine 50-75 mg daily. Ex: morphine 10 mg po q4h.

a. Gammaitoni, et al. Clin J Pain 2003;19(5):286-297.
b. Equianalgesic data presented in this table are that which are most commonly used by healthcare practitioners, and based on best evidence available, but they are still approximate. These are NOT opioid DOSES for individual patient use; this is equivalency information. The clinician is urged to access the original work: McPherson ML. Demystifying opioid conversion calculations: A guide for effective dosing, Second edition. Bethesda, MD: American Society of Health-System Pharmacists, 2018.”

d. Not available in the US.

DOSING METHADONE IN ADVANCED ILLNESS

- Methadone is a very useful opioid, but requires close attention to detail in dosing and follow-up.
- Evaluate patient's risk status (e.g., QTc prolongation), prognosis, history of medication adherence, interacting medications, pain history.
- ***Opioid-naïve patients***: 2-5 mg oral methadone total daily dose (or, up to 7.5 mg per day if appropriate). Consider interacting medications.
- ***Opioid-tolerant patients***: Convert patient's current opioid regimen to oral morphine equivalents (see reserve side).

Recommended dosing is as follows:

Total Daily Dose Oral Morphine Equivalent (OME)	Conversion Ratio to Oral Methadone
0-< 60 mg	Follow opioid-naïve dosing (above)
60-199 OME *and* < 65 years old	10 mg OME : 1 mg oral methadone
≥ 200 mg OME *and/or* ≥ 65 years old	20 mg OME : 1 mg oral methadone

ADDITIONAL GUIDANCE:

- Do not increase dose before 5-7 days.
- Do not increase total daily oral methadone dose by more than 5 mg/day (can increase by up to 10 mg/day once total daily oral methadone dose is 30-40 mg/day)
- When converting to oral methadone, do not exceed 30-40 mg oral methadone per day as starting dose, regardless of previous opioid dose.
- Reduce calculated oral methadone dose by 25-30% if patient receiving known enzyme inhibitor.
- Assess patient daily for 5-14 days after methadone initiation and adjustment.

Reference: McPherson et al. *J Pain Symptom Manage, 2019;57*(3), 635–645

This is not a substitute for clinical judgment, particularly with complex comorbidities and high morphine equivalents.

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Goal Concordant Prescribing and Deprescribing

Slides courtesy of Dr. Ryan Costantino

LR’s Medication List

94 year old man with end-stage COPD recently admitted to hospice.

1. Coenzyme Q-10 Supplement, 1 capsule PO daily
2. PreserVision AREDS2, 1 tablet PO daily
3. Azithromycin 200mg/5mL, 6 mL PO daily on M/W/F
4. Levothyroxine 75mcg, 1tab PO daily in the morning
5. Ramipril 10mg, 1 capsule by mouth daily in the morning
6. Omeprazole DR 20mg, 1 capsule PO daily in the morning
7. Furosemide 20mg, 1 tablet PO daily in the morning
8. Famotidine 20mg, 1 tablet PO twice daily
9. Rosuvastatin 20mg, 1 tablet PO daily with dinner
10. Finasteride 5mg, 1 tablet PO daily with dinner
11. Amlodipine 5mg, Take 1 tablet PO with dinner
12. Warfarin 3mg, Take 1 tablet PO daily
13. Duoneb, Inhale 3 mL vial nebulizer 4 times per day as needed

Approaching a patients medication list

STEP 1: Comprehensive Medication Review or Targeted Deprescribing

STEP 2: Identify decision support tools to inform deprescribing

STEP 3: Apply the tools and prepare for deprescribing conversation

MedStopper (http://medstopper.com/)

- MedStopper is a web application, decision tool that supports deprescribing
- What evidence informs the application?
  - Beers Criteria
  - STOPP criteria
  - Edmonton Frail Scale
  - https://www.thennt.com/
- Limitations
  - Vitamins/supplements
  - Antibiotics
  - Combination products

Stopping Priority RED=Highest GREEN=Lowest	Medication/ Category/ Condition	May Improve Symptoms?	May Reduce Risk for Future Illness?	May Cause Harm?	Suggested Taper Approach	Possible Symptoms when Stopping or Tapering	Beers/STOPP Criteria
	levothyroxine (Synthroid, Levoxyl , Levothroid) / Thyroid / **prevention but no symptoms (High TSH)**				Taper based on TSH and symptoms	return of hypothyroid symptoms (tiredness, weakness, weight gain, hair loss, constipation, depression, coarse dry hair, hair loss)	None
	warfarin (Coumadin) / Warfarin / **afib/valve**		 CALC / NNT		Taper to INR targets		None
	ramipril (Altace) / ACE inhibitor / **blood pressure**		 CALC / NNT		If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	chest pain, pounding heart, heart rate, blood pressure (re-measure for up to 6 months), anxiety, tremor	None
	finasteride (Proscar) / 5-alpha reductase inhibitor / **benign prostatic hyperplasia**				Tapering not required		None
	amlodipine (Norvasc) / Calcium antagonist dihydropyridine / **blood pressure**		 CALC / NNT		If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	chest pain, pounding heart, heart rate, blood pressure (re-measure for up to 6 months), anxiety, tremor	Details
	omeprazole (Prilosec, Losec) / Proton pump inhibitor / **heartburn/GERD**				If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	return of symptoms, heartburn, reflux	Details
	famotidine (Pepcid) / H2 antagonist / **heartburn/GERD**				If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	return of symptoms, heartburn, reflux	None
	rosuvastatin (Crestor) / Statin / **previous heart attack or stroke**		 NNT		Tapering not required		None
	ipratropium (Atrovent) / Anticholinergic / **chronic obstructive lung disease**				Tapering not required		Details
	salbutamol/albuterol (Ventolin) / Beta-agonist / **chronic obstructive lung disease**				Tapering not required		None
	furosemide (Lasix) / Diuretic / **other**				If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	weight gain, swelling, shortness of breath	Details

PRINT PLAN

Arrange medications by: Stopping Priority

Stopping Priority
Medical Condition

CLEAR ALL MEDICATIONS

PRINT PLAN

Stopping Priority RED=Highest GREEN=Lowest	Medication/ Category/ Condition	May Improve Symptoms?	May Reduce Risk for Future Illness?	May Cause Harm?	Suggested Taper Approach	Possible Symptoms when Stopping or Tapering	Beers/STOPP Criteria
	levothyroxine (Synthroid, Levoxyl , Levothroid) / Thyroid / **prevention but no symptoms (High TSH)**				Taper based on TSH and symptoms	return of hypothyroid symptoms (tiredness, weakness, weight gain, hair loss, constipation, depression, coarse dry hair, hair loss)	None
	warfarin (Coumadin) / Warfarin / **afib/valve**		 CALC / NNT		Taper to INR targets		None
	ramipril (Altace) / ACE inhibitor / **blood pressure**		 CALC / NNT		If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	chest pain, pounding heart, heart rate, blood pressure (re-measure for up to 6 months), anxiety, tremor	None

STOPPFrail

- **S**creening **T**ool of **O**lder **P**ersons Prescriptions in **Frail** adults with limited life expectancy

- STOPPFrail is a list of potentially inappropriate prescribing indicators designed to assist physicians with deprescribing decisions. It is intended for older people with limited life expectancy for whom the goal of care is to optimize quality of life and minimize the risk of drug-related morbidity. Goals of care should be clearly defined, and, where possible, medication changes should be discussed and agreed with patient and/or family.

Appropriate candidates for STOPPFrail-guided deprescribing typically meet ALL of the following criteria:

1. Activities of daily living dependency (i.e. assistance with dressing, washing, transferring, walking) and/or severe chronic disease and/or terminal illness.

2. Severe irreversible frailty, i.e. high risk of acute medical complications and clinical deterioration.

3. Physician overseeing care of patient would not be surprised if the patient died in the next 12 months.

Curtin D. Age Ageing. 2021 Feb 26;50(2):465-471.

STOPPFrail

Section A: General	• Any drug that the patient persistently fails to take or tolerate despite adequate education and consideration of all appropriate formulations. • Any drug without a clear clinical indication. • Any drug for symptoms which have now resolved (e.g. pain, nausea, vertigo, pruritus)
Section B: Cardiology system	• Lipid-lowering therapies (statins, ezetimibe, bile acid sequestrants, fibrates, nicotinic acid, lomitapide and acipimox). • Antihypertensive therapies: Carefully reduce or discontinue these drugs in patients with systolic blood pressure (SBP) persistently <130 mmHg. An appropriate SBP target in frail older people is 130–160 mmHg. Before stopping, consider whether the drug is treating additional conditions (e.g. beta-blocker for rate control in atrial fibrillation, diuretics for symptomatic heart failure). • Anti-anginal therapy (specifically nitrates, nicorandil, ranolazine): None of these anti-anginal drugs have been proven to reduce cardiovascular mortality or the rate of myocardial infarction. Aim to carefully reduce and discontinue these drugs in patients who have had no reported anginal symptoms in the previous 12 months AND who have no proven or objective evidence of coronary artery disease.
Section C: Coagulation system	• Anti-platelets: No evidence of benefit for primary (as distinct from secondary) cardiovascular prevention. • Aspirin for stroke prevention in atrial fibrillation: Aspirin has little or no role for stroke prevention in frail older people who are not candidates for anticoagulation therapy and may significantly increase bleeding risk.
Section D: Central nervous system	• Neuroleptic antipsychotics in patients with dementia: Aim to reduce dose and discontinue these drugs in patients taking them for longer than 12 weeks if there are no current clinical features of behavioural and psychiatric symptoms of dementia (BPSD). • Memantine: Discontinue and monitor in patients with moderate to severe dementia, unless memantine has clearly improved BPSD.
Section E: Gastrointestinal system	• Proton pump Inhibitors: Reduce dose of proton pump inhibitors when used at full therapeutic dose ≥8 weeks, unless persistent dyspeptic symptoms at lower maintenance dose. • H2 receptor antagonist: Reduce dose of H2 receptor antagonists when used at full therapeutic dose for ≥8 weeks, unless persistent dyspeptic symptoms at lower maintenance dose.
Section F: Respiratory	• Theophylline and aminophylline: These drugs have a narrow therapeutic index, have doubtful therapeutic benefit and require monitoring of

Curtin D. Age Ageing. 2021 Feb 26;50(2):465-471.

STOPP/START

- STOPP/START criteria for potentially inappropriate prescribing in older people: version 2
  - Screening tool of older people's prescriptions (STOPP) and screening tool to alert to right treatment (START) criteria
- Aims to address potentially inappropriate medications and potential prescribing omissions

O'Mahony D et al. *Age and Ageing*, Volume 44, Issue 2, March 2015, Pages 213–218.

STOPP/START

STOPP Criteria References

- Section B: Cardiovascular System criteria
  - Loop diuretic as first-line treatment for hypertension (lack of outcome data for this indication; safer, more effective alternatives available)

START Criteria References

- Section A: Cardiovascular System criteria.
  - Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease.

Denis O'Mahony et al. *Age and Ageing*, Volume 44, Issue 2, March 2015, Pages 213–218.

AGS Beers Criteria

- The AGS Beers Criteria® is a list of medications worth discussing with health professionals because they may not be the safest or most appropriate options for older adults.
  - NOTE: AGS Beers Criteria are intended for older adults outside of hospice & palliative care settings but can still be useful in deprescribing conversations

Curtin D. Age Ageing. 2021 Feb 26;50(2):465-471.

AGS Beers Criteria

Organ System, Therapeutic Category, Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Benzodiazepines	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults. May be appropriate for seizure disorders, rapid eye movement sleep behavior disorder, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and periprocedural anesthesia	Avoid	Moderate	Strong

Curtin D et al. Age Ageing. 2021 Feb 26;50(2):465-471.

Deprescribing.org

- Evidence-based deprescribing guidelines and algorithms

Proton Pump Inhibitor

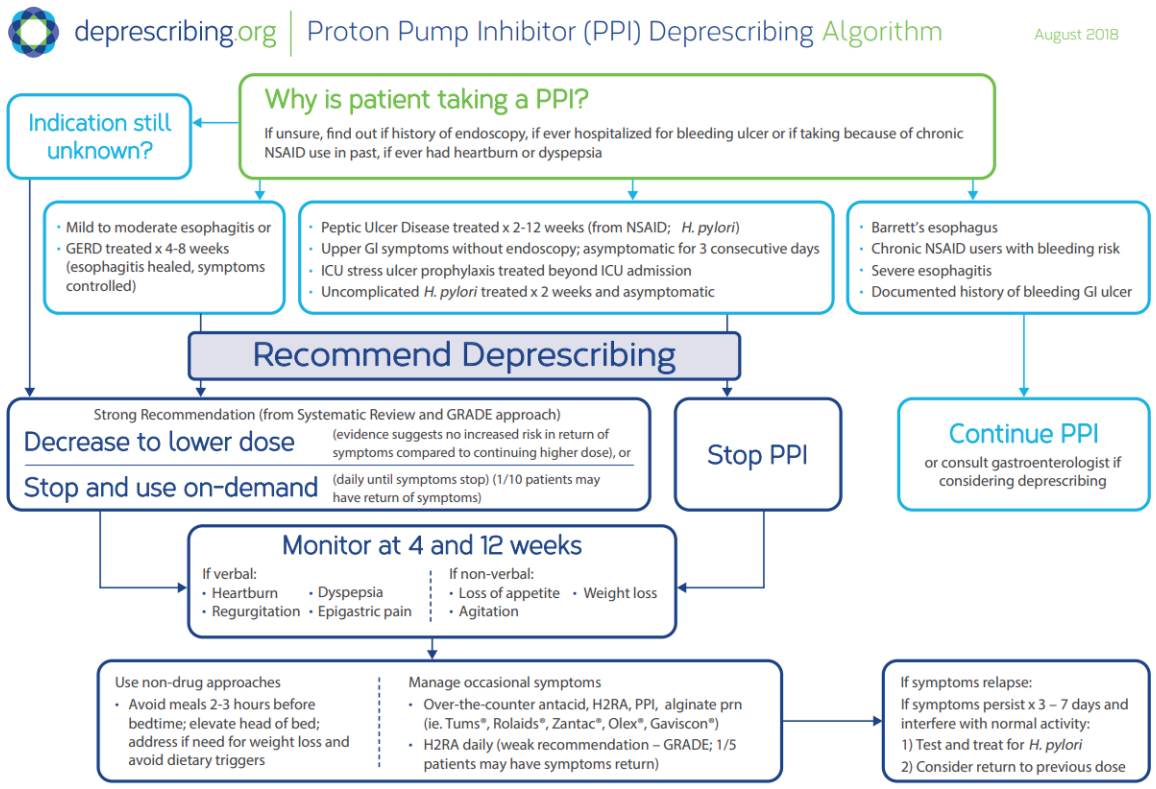
Antihyperglycemics

Antipsychotics

Benzodiazepine Receptor Agonist

Cholinesterase Inhibitors and Memantine

Deprescribing.org



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This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License.
Contact deprescribing@bruyere.org or visit deprescribing.org for more information.
Farrell B, Pottie K, Thompson W, Boghossian T, Pizzola L, Rashid FJ, et al. Deprescribing proton pump inhibitors. Evidence-based clinical practice guideline. Can Fam Physician 2017;63:354-64 (Eng), e253-65 (Fr).
deprescribing.org
Bruyère
open

deprescribing.org | Proton Pump Inhibitor (PPI) Deprescribing Notes

August 2018

PPI Availability

PPI	Standard dose (healing) (once daily)*	Low dose (maintenance) (once daily)
Omeprazole (Losec®) - Capsule	20 mg+	10 mg+
Esomeprazole (Nexium®) - Tablet	20[a] or 40[b] mg	20 mg
Lansoprazole (Prevacid®) - Capsule	30 mg+	15 mg+
Dexlansoprazole (Dexilant®) - Tablet	30[c] or 60[d] mg	30 mg
Pantoprazole (Tecta®, Pantoloc®) - Tablet	40 mg	20 mg
Rabeprazole (Pariet®) - Tablet	20 mg	10 mg

Legend

a Non-erosive reflux disease

b Reflux esophagitis

c Symptomatic non-erosive gastroesophageal reflux disease

d Healing of erosive esophagitis

+ Can be sprinkled on food

* Standard dose PPI taken BID only indicated in treatment of peptic ulcer caused by *H. pylori*; PPI should generally be stopped once eradication therapy is complete unless risk factors warrant continuing PPI (see guideline for details)

Key

GERD = gastroesophageal reflux disease

NSAID = nonsteroidal anti-inflammatory drugs

H2RA = H2 receptor antagonist

SR = systematic review

GRADE = Grading of Recommendations Assessment, Development and Evaluation

Engaging patients and caregivers

Patients and/or caregivers may be more likely to engage if they understand the rationale for deprescribing (risks of continued PPI use; long-term therapy may not be necessary), and the deprescribing process

PPI side effects

- When an ongoing indication is unclear, the risk of side effects may outweigh the chance of benefit
- PPIs are associated with higher risk of fractures, *C. difficile* infections and diarrhea, community-acquired pneumonia, vitamin B12 deficiency and hypomagnesemia
- Common side effects include headache, nausea, diarrhea and rash

Tapering doses

- No evidence that one tapering approach is better than another
- Lowering the PPI dose (for example, from twice daily to once daily, or halving the dose, or taking every second day) OR stopping the PPI and using it on-demand are equally recommended strong options
- Choose what is most convenient and acceptable to the patient

On-demand definition

Daily intake of a PPI for a period sufficient to achieve resolution of the individual's reflux-related symptoms; following symptom resolution, the medication is discontinued until the individual's symptoms recur, at which point, medication is again taken daily until the symptoms resolve

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This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License.
Contact deprescribing@bruyere.org or visit deprescribing.org for more information.
Farrell B, Pottie K, Thompson W, Boghossian T, Pizzola L, Rashid FJ, et al. Deprescribing proton pump inhibitors. Evidence-based clinical practice guideline. Can Fam Physician 2017;63:354-64 (Eng), e253-65 (Fr).
deprescribing.org
Bruyère
open

LESS-CHRON

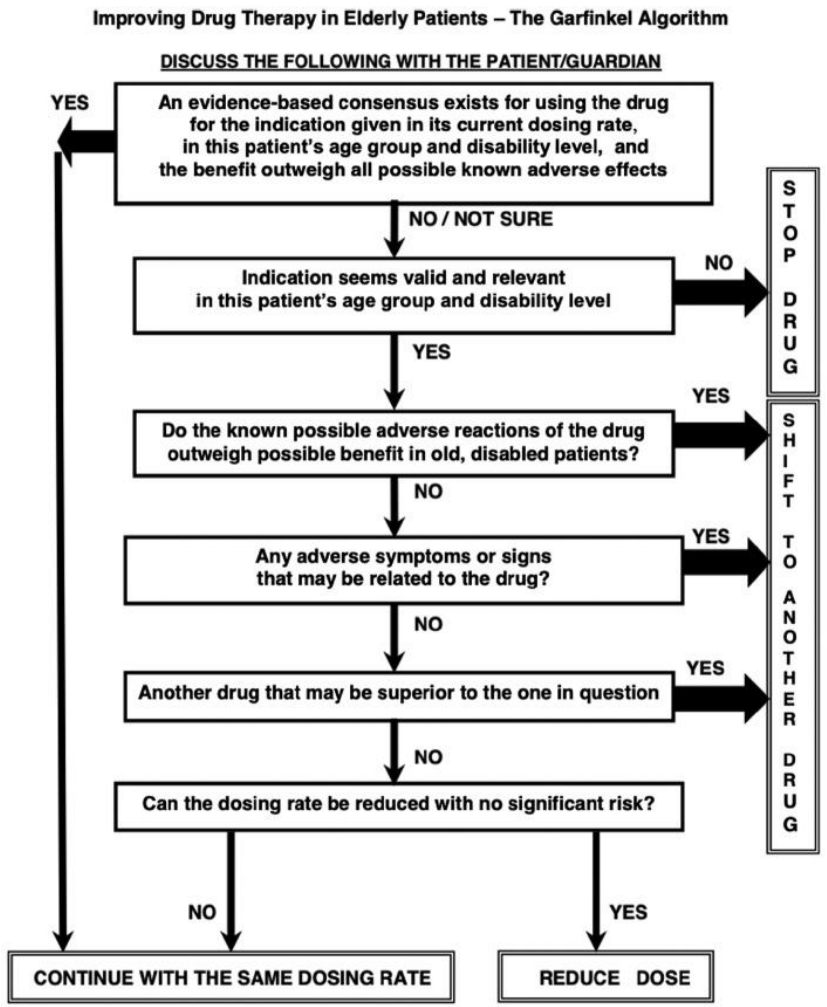
- List of Evidence-Based Deprescribing for Chronic Patients criteria
- Focuses on deprescribing in patients with multimorbidity
- 27 criteria organized by anatomical group
- Each criterion contains
  - Drug indication for which it is prescribed
  - Clinical situation that offers an opportunity to deprescribe
  - Clinical variable to be monitored
  - Minimum time to follow up the patient after deprescribing

Rodríguez-Pérez A et al. *Eur J Hosp Pharm*. 2019;26(6):334-338
Rodríguez-Pérez A et al. Geriatr Gerontol Int. 2017 Nov;17(11):2200-2207

LESS-CHRON

Drug	Indication for which it is prescribed	Deprescribing condition	Health variables to monitor	Follow up
Oral anticoagulants	Atrial fibrillation	• Pfeiffer questionnaire ≥8 points and PROFUND index ≥11 points • High risk of falls	• Not applicable • Not applicable	• Not applicable • Not applicable
Anticholinergics	Urinary incontinence	• Use of nappy. • Worsening of dementia symptoms in patients under anticholinesterase treatment.	• Urine control	1 month

The Garfinkel Good Palliative-Geriatric Practice algorithm (GPA)



Ref: Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults - Addressing Polypharmacy. ARCH INT MED 170: 1648-54, 2010.

The Garfinkel Good Palliative-Geriatric Practice algorithm (GPGP)

- Implicit judgment-based tool
  - Beer's Criteria or STOPP/START would be considered explicit tools
- Applicability to any drug in any clinical context

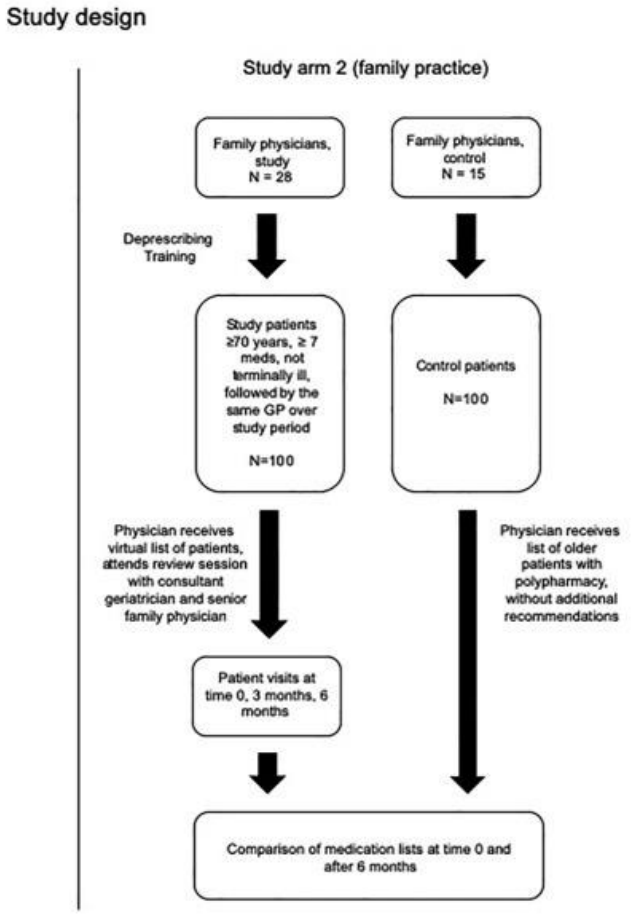


Table 3. Number of medications prescribed before and 6 months after the intervention.

	Study group ($n = 100$)	Control group ($n = 100$)	p value
Drugs at baseline (mean ± SD)	10.5 ± 2.2	10.97 ± 2.7	0.149
Drugs at 6 months (mean ± SD)	10.04 ± 2.16	11.21 ± 2.9	0.001
p value	0.005	0.062	

Bilek AJ et al. *Ther Adv Drug Saf*. 2019.

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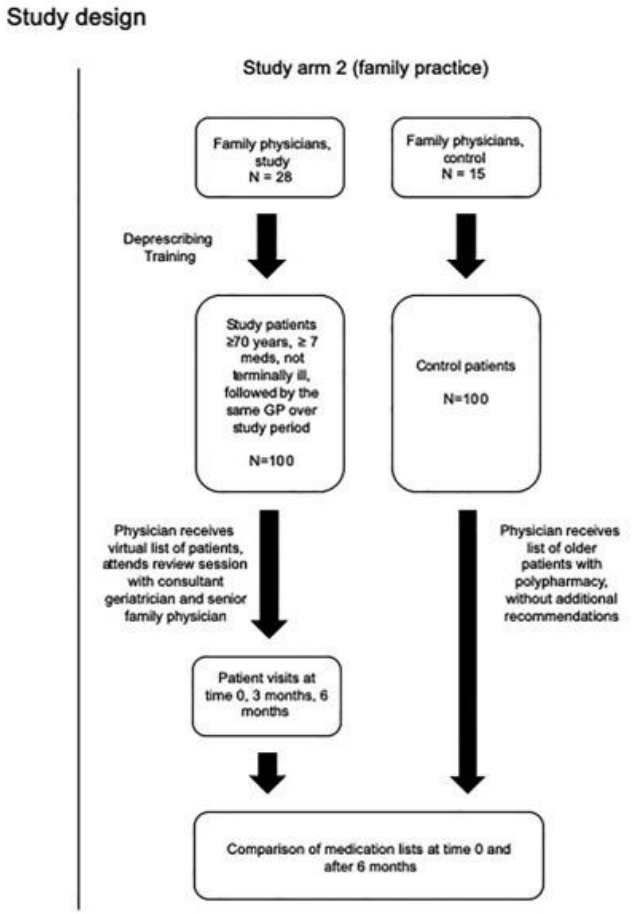

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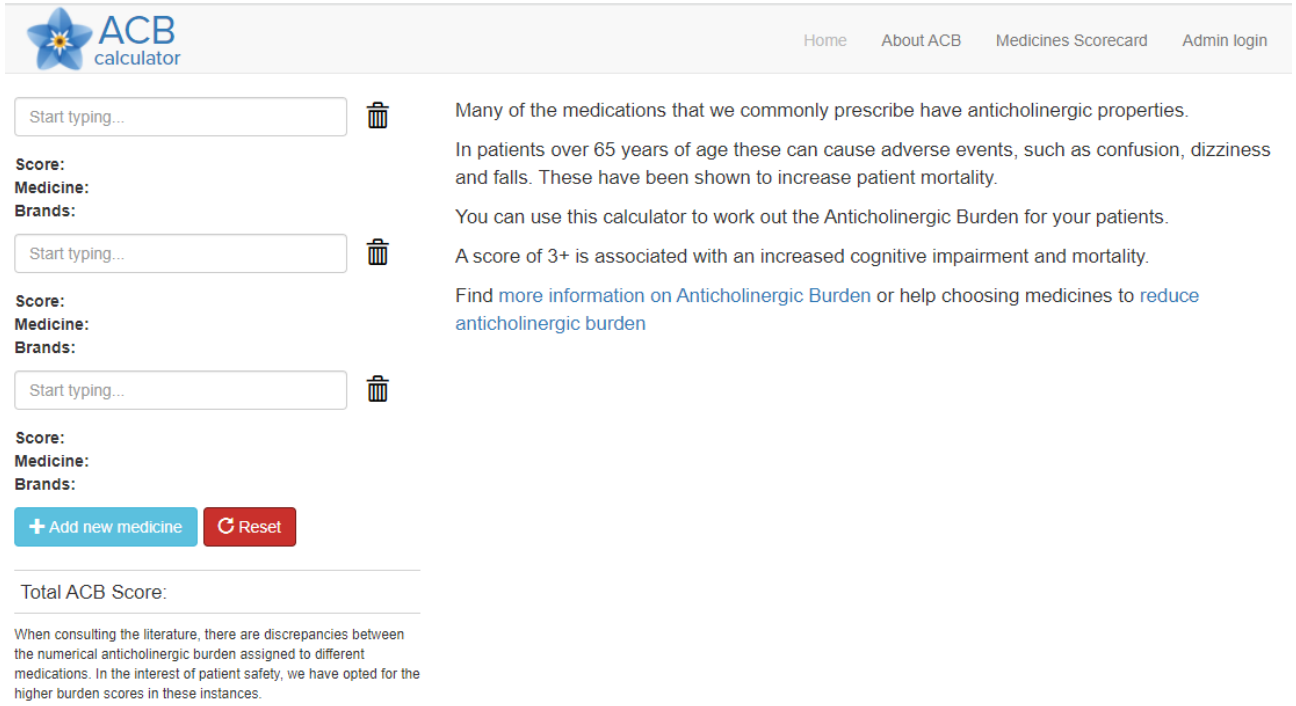
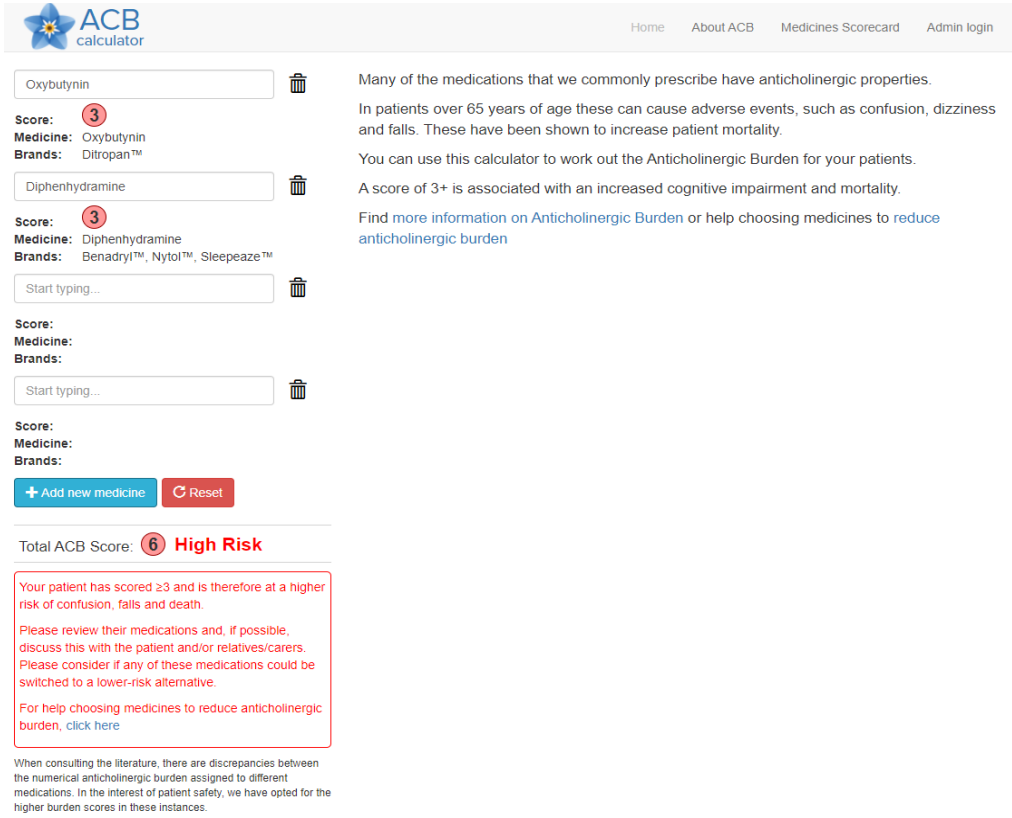
Bilek AJ et al. *Ther Adv Drug Saf*. 2019.

Anticholinergic Burden Calculator (http://www.acbcalc.com/)

- Can be used to work out the Anticholinergic Burden for your patients
- A score of 3+ is associated with an increased cognitive impairment and mortality.



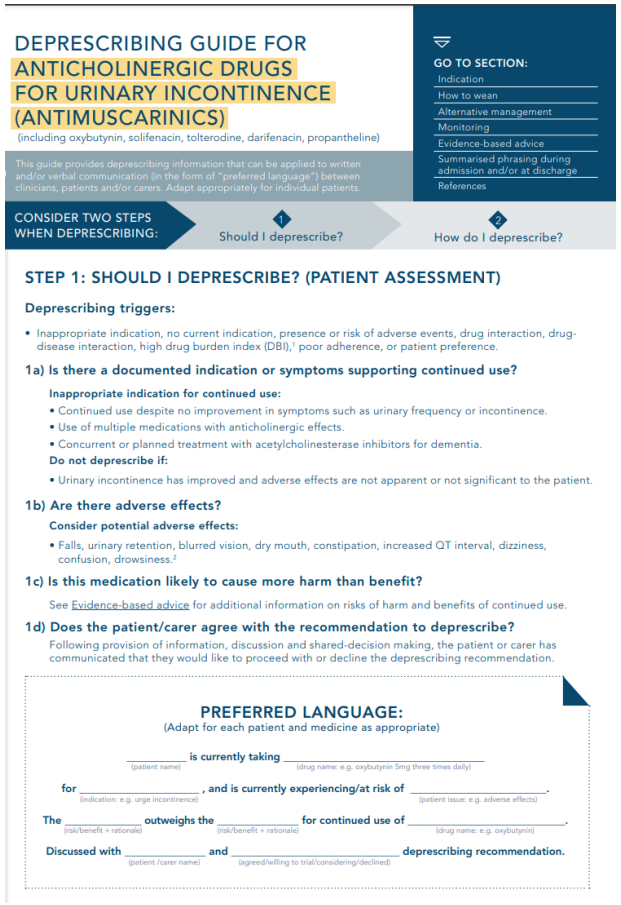


NSW TAG Deprescribing Tools

- Deprescribing resources developed by a translational research project team led by Prof Sarah Hilmer
- Deprescribing guides
- Consumer Information Leaflets

https://www.nswtag.org.au/deprescribing-tools/

Deprescribing Guide for Anticholinergic Drugs for Urinary Incontinence



DEPRESCRIBING GUIDE FOR ANTICHOLINERGIC DRUGS FOR URINARY INCONTINENCE (ANTIMUSCARINICS)

(including oxybutynin, solifenacin, tolterodine, darifenacin, propantheline)

This guide provides deprescribing information that can be applied to written and/or verbal communication (in the form of "preferred language") between clinicians, patients and/or carers. Adapt appropriately for individual patients.

GO TO SECTION:
- Indication
- How to wean
- Alternative management
- Monitoring
- Evidence-based advice
- Summarised phrasing during admission and/or at discharge
- References

CONSIDER TWO STEPS WHEN DEPRESCRIBING: 1 Should I deprescribe? 2 How do I deprescribe?

STEP 1: SHOULD I DEPRESCRIBE? (PATIENT ASSESSMENT)

Deprescribing triggers:

- Inappropriate indication, no current indication, presence or risk of adverse events, drug interaction, drug-disease interaction, high drug burden index (DBI),[1] poor adherence, or patient preference.

1a) Is there a documented indication or symptoms supporting continued use?

Inappropriate indication for continued use:
- Continued use despite no improvement in symptoms such as urinary frequency or incontinence.
- Use of multiple medications with anticholinergic effects.
- Concurrent or planned treatment with acetylcholinesterase inhibitors for dementia.

Do not deprescribe if:
- Urinary incontinence has improved and adverse effects are not apparent or not significant to the patient.

1b) Are there adverse effects?

Consider potential adverse effects:
- Falls, urinary retention, blurred vision, dry mouth, constipation, increased QT interval, dizziness, confusion, drowsiness.[2]

1c) Is this medication likely to cause more harm than benefit?

See Evidence-based advice for additional information on risks of harm and benefits of continued use.

1d) Does the patient/carer agree with the recommendation to deprescribe?

Following provision of information, discussion and shared-decision making, the patient or carer has communicated that they would like to proceed with or decline the deprescribing recommendation.

PREFERRED LANGUAGE:
(Adapt for each patient and medicine as appropriate)

_____ (patient name) **is currently taking** _____ (drug name: e.g. oxybutynin 5mg three times daily)

for _____ (indication: e.g. urge incontinence) **, and is currently experiencing/at risk of** _____ (patient issue: e.g. adverse effects).

The _____ (risk/benefit + rationale) **outweighs the** _____ (risk/benefit + rationale) **for continued use of** _____ (drug name: e.g. oxybutynin).

Discussed with _____ (patient /carer name) **and** _____ (agreed/willing to trial/considering/declined) **deprescribing recommendation.**

STEP 2: HOW DO I DEPRESCRIBE? (RECOMMENDATION AND MANAGEMENT)

2a) How to wean

Key Points
- Establish a supportive and trusting relationship with the patient to engage in complex/sensitive discussions.
- Accompany weaning with commencement of relevant non-pharmacological therapy. See Alternative management recommendations.
- In general, wean gradually by 25-50% of the daily dose every 1-4 weeks.
- If reason for deprescribing is due to serious adverse effects, consider weaning faster.
- Provide advice to patient/carer on self-monitoring and what to do if symptoms re-occur.
- Organise appropriate follow up appointments with general practitioner (GP) (frequency determined by rate of weaning).

Initiation
Reduce dose slowly by 25-50% of the daily dose each week to month.
Adjustments depend on response
Adjust according to response (see Monitoring recommendations). • If no withdrawal symptoms occur, continue to wean then stop. • In the presence of worsening confusion, cease outright. • Consider slower weaning (e.g. 12.5%) when reducing to the final lowest dose. End treatment 2 weeks after administering the lowest dose. • Consider alternate day dosing to aid with weaning if dosage forms are limited.
Adjustments in the case of recurrent symptoms
In the case of recurrent/withdrawal symptoms, revert to the previous lowest tolerated dose. Recommence weaning after 6-12 weeks at the lower weaning rate (e.g. 5-12.5% of daily dose each month) then stop.

(Based on recommendations in References[2-4])

PREFERRED LANGUAGE:
(Adapt for each patient and medicine as appropriate)

Recommend non-pharmacological replacement therapy to reduce reliance on antimuscarinics.

Recommend gradually reducing to _____ (drug: e.g. oxybutynin 5mg twice daily) **for** _____ (timeframe: e.g. 1 week) **and reassess,**

then reduce to _____ (e.g. oxybutynin 2.5mg twice daily) **for** _____ (e.g. 1 week) **and reassess,**

then reduce to _____ (e.g. oxybutynin 2.5mg daily) **for** _____ (e.g. 2 weeks) **and stop.**

Follow up with GP _____ (e.g. fortnightly) **after discharge.**

2b) Alternative management

Non-pharmacological support
Symptom diary, attention to fluid intake, avoiding constipation, bladder training, timed toileting and incontinence aids, pelvic floor exercises, toileting assistance.

Switching within drug class or consider alternative therapy
Consider changing formulation or switching to another antimuscarinic medication if anticholinergic medication is effective but cannot be tolerated due to adverse drug reactions [AMH-Anticholinergics (genitourinary)].

Mirabegron is registered for overactive bladder and is a beta3 adrenergic receptor agonist, not an antimuscarinic, with a different side effect profile. It is not currently funded by the PBS.[2]

PREFERRED LANGUAGE:

Use **symptom diary, attention to fluid intake, avoiding constipation, bladder training, timed toileting and incontinence aids, pelvic floor exercises, and toileting assistance** concurrently.

2c) Monitoring

Monitor short term (within 1-3 days)	Monitor long term (>7 days)
Monitor for withdrawal symptoms Symptoms can occur within 1-3 days of dose reduction.	**Monitor for recurrence of symptoms** Recurrence of previous or new symptoms (e.g. incontinence, urinary urgency) may occur within 1-2 weeks of dose reduction.
• Withdrawal symptoms (irritability, anxiety, insomnia, sweating and gastrointestinal effects [e.g. nausea]) are usually mild, highly variable and can last up to 6-8 weeks. • If severe symptoms (e.g. severe anxiety, tachycardia, orthostatic hypotension, severe insomnia) occur, restart at the previous lowest effective dose.	

PREFERRED LANGUAGE:

Within 1-3 days of dose reduction, monitor for **withdrawal** symptoms which can be **mild** (e.g. nausea, sweating, irritability) or **severe** (e.g. anticholinergic discontinuation syndrome including *anxiety, tachycardia, orthostatic hypotension, insomnia*).

Monitor for **recurrence** of symptoms within 1-2 weeks of dose reduction, including *incontinence or urinary urgency.*

Restart at lowest effective dose with retrial deprescribing at *6-12 weeks.*

EVIDENCE-BASED ADVICE

Effectiveness and safety

A systematic review of trials over 2-52 weeks, found antimuscarinics reduced episodes of incontinence compared to placebo by 0.4 to 1.1 incontinence episodes per day, with a pooled relative risk (RR) of 1.3-3.5 (p<0.01).[1]

The RR for any adverse event when using an antimuscarinic in comparison to placebo varied between 1.13 and 2.00. Higher doses were associated with a higher risk of withdrawal due to adverse events (oxybutynin 7.5–10 mg/day RR 1.91; 95% CI 1.18–3.10, oxybutynin 15 mg/ day RR 1.89; 95% CI, 1.23–2.90, and solifenacin 10 mg/day (RR 1.53; 95% CI, 1.02– 2.30).[7]

Over 90% of people would be willing to stop their medicines if recommended by their physician.[8]

Recommended duration of use

Limit drug treatment to short-term use. Antimuscarinics are associated with significant harm (e.g. falls, fractures), and long term use is not recommended, especially in older adults.

SUMMARISED PHRASING DURING HOSPITAL ADMISSION AND/OR AT DISCHARGE

When communicating deprescribing decisions to GPs at discharge, written and verbal communication should include information in the sequence of:

"Medicine, Intention, Rationale. Clear Plan (dose change, duration, follow up). Patient agreement"

PREFERRED LANGUAGE
(write in GP follow up plan and medication list):

_____ (current medication (e.g. oxybutynin)) : _____ (stopped/reduced with aim of stopping) **due to** _____ (specific rationale (e.g. constipation)) **outweighing effects** _____ (of/on current indication (e.g. on urinary incontinence)).

_____ (If weaning, old dose changed to new dose (e.g. oxybutynin 5mg TDS reduced to oxybutynin 5mg BD)) **reduced to** _____ **for** _____ (If weaning, time frame (e.g. 2 weeks)), **then** _____ (follow-up action (e.g. GP to follow up 2 weeks, monitor for increased urinary symptoms)). **Patient/Carer agreed.**

Refer to www.nswtag.org.au/deprescribing-tools/

Example:
Oxybutynin: reduced with aim of stopping due to constipation outweighing effects on urinary incontinence. Oxybutynin 5mg TDS reduced to oxybutynin 5mg BD for 2 weeks then GP to follow up 2 weeks, monitor for increased urinary symptoms. Patient agreed.
Refer to www.nswtag.org.au/deprescribing-tools/

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Version 1_October 2018

1. Hilmer SN, Mager DE, Simonsick EM, et al. A drug burden index to define the functional burden of medications in older people. Arch Intern Med. 2007; 167(8):781-787. Available at https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/412262 2. Australian Medicines Handbook (AMH): Anticholinergics (genitourinary). 2018. 3. NPS Medicinewise. Anticholinergic drugs for overactive bladder. Aust Prescr. 2006; 29:22-4. 4. Therapeutic Guidelines Limited. eTG complete: Anticholinergic Toxidrome. 2018. 5. Medstopper. Available at http://medstopper.com 6. Kouladjian O'Donnell L, Gnjidic D, Nahas R, et al. Anticholinergic burden: considerations for older adults. J Pharm Pract Res. 2017; 47(1): 67-77. 7. Chapple CR, Khullar V, Gabriel Z, et al. The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. Eur Urol. 2008; 54(3):543-62. 8. Reeve E, Wiese MD, Hendrix I, et al. People's attitudes, beliefs, and experiences regarding polypharmacy and willingness to deprescribe. J Am Geriatr Soc. 2013; 61(9): 1508-1514.

GO TO SECTION:
- Indication
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- References

NHPCO Hospice Medication Deprescribing Toolkit

- A companion resource
- Decision trees in the flow chart describe opportunities for deprescribing
- medications at the end of life

Table of Contents

https://www.nhpco.org/wp-content/uploads/NHPCO_Deprescribing_Toolkit.pdf

Antiplatelet & Anticoagulant Medications

Antiplatelet & Anticoagulant Medications

NHPCO Leading Person-Centered Care

DEPRESCRIBING GUIDANCE

Background

Many patients are admitted to hospice services already taking an antiplatelet or anticoagulant medication, especially if they have cardiovascular disease or a history of blood clots due to cancer. A recent study reported the prevalence of antithrombotic therapy at the time of hospice enrollment at nearly 7% of patients, with about 57% of those patients on aspirin therapy and over 18% on multiple antithrombotic medications.[1]

Antiplatelet medications prevent blood clots by inhibiting platelet aggregation and are used to decrease the risk of death from cardiovascular events such as myocardial infarction (MI), ischemic stroke, angina, or peripheral arterial disease.[2] Aspirin is the original antiplatelet medication, and is available over-the-counter (OTC); patients may choose to take aspirin without prescriber advice. Non-aspirin antiplatelet medications are also used off-label for secondary prevention of cardiovascular disease in patients with diabetes or aspirin allergy, and in some patients with atrial fibrillation to prevent thromboembolism.[2] Additionally, clopidogrel or prasugrel may be used in dual antiplatelet therapy (DAPT) in combination with aspirin for patients with acute coronary syndrome (ACS) or following stent placement.[2]

Anticoagulant medications also prevent blood clots but instead of inhibiting platelets, they prevent blood coagulation by reducing the action of clotting factors directly or indirectly. Anticoagulants are also used to prevent clotting in patients with atrial fibrillation, thromboembolic disease, and artificial heart valves.[2]

TABLE 1 – ANTIPLATELET AND ANTICOAGULANT MEDICATIONS

Antiplatelet Medications					
Aspirin	Clopidogrel (Plavix®)	Tiagrelor (Brilinta®)	Prasugrel (Effient®)	Aspirin-Dipyridamole (Aggrenox®)	
Anticoagulant Medications					
Warfarin (Coumadin®)	Apixaban (Eliquis®)	Rivaroxaban (Xarelto®)	Dabigatran (Pradaxa®)	Enoxaparin (Lovenox®)	Edoxaban (Savaysa®)

The decision to discontinue antiplatelet and anticoagulant medications should always be an individualized approach, weighing the risks vs benefits, and the patient and family's goals of care. Discontinuing these medications is generally considered acceptable in any patient with a life-limiting illness, especially when adverse effects are possible.[3] The information below is based on literature review in the primary care and hospitalized patient population; there are no studies determining risk vs benefit of aspirin, other anti-platelet therapies, or anticoagulants for patients in hospice or palliative care. Due to the likelihood of drug interactions, consulting with a pharmacist when adding or discontinuing any medication is recommended.

Why Deprescribe?

CONSIDER DEPRESCRIBING IF ANY OF THE FOLLOWING FACTORS IS PRESENT:	
❒ **Patient at risk for bleeding**	▮ Increased risk for major hemorrhage or bleeding complications present in patients on anticoagulation therapy with advanced age, CHF, CVD, hypertension, liver or renal disease, diabetes, history of or recent GI bleed, anemia, concomitant use of antiplatelets or NSAIDs.[4,8,11,12] ▮ HAS-BLED score tool can be used to assist clinicians in identifying patients at high risk for bleeding.[7] ▮ When bleeding does occur, lack of access to reversal agents other than vitamin K (phytonadione) can be difficult. Hospitalization is required for patients to use the reversal agents for dabigatran, apixaban, and rivaroxaban to manage bleeding.[2]
❒ **Medication may no longer be indicated**	▮ No palliative benefit present or clinical signs of impending death ▮ Antiplatelet or anticoagulant medications may have been started with time-limited intent after a procedure or event. Evaluate continued need and potential to de-escalate to aspirin monotherapy or deprescribe entirely. ▮ Benefits of multiple antiplatelet or anticoagulation combination therapy is generally limited to 3-12 months of therapy; likely no additional benefit to longer therapy, only increased risk of bleeding, especially in the hospice population.[4]
❒ **Patient at risk for falls**	▮ Hospice patients, young and old, have an increased risk of falling, and potential for internal or external bleeds. ▮ Risk of an intracranial hemorrhage in a debilitated ambulatory patient who may fall is greater than the benefit in preventing a stroke.[5]
❒ **Patient at risk for drug-drug interactions**	▮ Drug interactions are common with these classes of medications (especially warfarin) increasing bleeding risk or increased clot formation.[2] ▮ Review medication profile with a pharmacist when adding or discontinuing any medications.
❒ **Decreased renal or hepatic function**	▮ Many of antiplatelet and anticoagulant medications rely on liver metabolism and renal clearance.[2] Bleeding increases with kidney or liver impairment, especially in elderly patients. ▮ Avoid warfarin in patients with liver failure.[5]
❒ **Decreased nutritional intake**	▮ Hospice patients may have fluctuating nutritional intake, impacting vitamin K intake and affecting the therapeutic risk/benefit associated with warfarin. ▮ Warfarin, rivaroxaban, and apixaban are highly protein bound anticoagulants. Malnourished patients with low albumin are at an increased risk of bleeding due to higher than usual exposure to circulating active drug.[2]
❒ **Difficulty swallowing**	▮ Dabigatran must be swallowed whole; crushing results in excessive absorption and toxicity.[2] Deprescribe if patient cannot swallow intact tablets.
❒ **Increase in pill burden and frequent monitoring**	▮ Antiplatelet and anticoagulant medications contribute to polypharmacy and pill burden. ▮ Warfarin requires routine PT/INR testing. Patients may wish to avoid finger sticks or blood draws. If routine bloodwork or INR testing is refused by patient/family, discontinue warfarin.[5]
❒ **Continued use is outside the goals of care**	▮ Continuing medications that are not relieving any symptoms (i.e. not palliative), may be outside the goals of care (exception may be treatment of DVT).

Patient & Caregiver Talking Points

The BUILD Model provides a structured process to discuss deprescribing with patients, family, and caregivers.[9] The basics of the BUILD mnemonic and sample conversational phrases for family and caregiver discussions are below.

BUILD	UNDERSTAND	INFORM	LISTEN	DEVELOP
A foundation of trust and respect	What the family knows about the device	The family about clinical evidence	To the family's goals and expectations	A plan of care in collaboration with family

▮ Acknowledge that patient and family concern about medication changes, especially stopping medications is common response.

▮ Provide reassurance that all medication changes are made in consultation with the patient's doctors. The decision to stop antiplatelet and anticoagulant medications is always an individualized approach.

▮ Ask the patient and family questions to bring them into the shared decision-making process. Use open ended questions that lead into conversations about stopping medications.

— "Do you know why you are taking this medication? Is it hard to take all these pills every day? Do you ever feel worse after taking this pill? Have you noticed your wife is eating less than she used to? Have you felt unsteady when walking lately? Are you worried about your mom falling? What are your goals now that your dad is on hospice?"

▮ Explain that as patients age or diseases progress, certain medications that were once helpful can become harmful. The hospice team's role is to enhance comfort and quality of life by providing effective and safe medications, treating physical and emotional symptoms, and minimizing adverse events.

— "Dr. Jones would like to discuss stopping your wife's warfarin. Since you shared that she is no longer eating much and has fallen a few times over the past month, he is concerned the medication is no longer safe for her to take. The risk of her developing a bleed in her brain or stomach is greater than the risk of her having a stroke over that same time frame.

▮ Remind the patient and family that the hospice team will regularly reassess the patient's condition and medications

— If the patient has a relatively good prognosis, has a symptomatic DVT or is at high risk for thromboembolism, is still ambulatory, adherent to their prescribed medication regimen, and at low risk for bleeding, the patient may benefit from continued anticoagulation. Reassess at each visit, change in condition, or change in location of care to determine continued need for the medication.

— For some patients following ischemic stroke, MI, stents, or other cardiovascular event, the risk of a second event may outweigh the risk of a GI bleed, indicating that continuing the medication is reasonable.

▮ Sometimes changing to an alternative, potentially safer medication is an option to meet the patient and family halfway

— For example, aspirin seems to be similar in effectiveness to clopidogrel for patients with a history of cardiovascular or stroke; for patients wanting to continue some antiplatelet therapy, a change to aspirin can be considered. DAPT does not have significant benefit over aspirin alone for secondary prevention of MI or stroke.[4]

How to Deprescribe

▮ Once the decision has been made to discontinue antiplatelet or anticoagulant medications, they may be stopped without a taper.

▮ If family or patient is hesitant to discontinue, consider a trial discontinuation for a limited period of time (e.g., 2 weeks or 1 month) and offer to re-evaluate once that trial is completed. Often, the family or patient needs this time as an "adjustment period" to accept the possibility of discontinuation, understand the medication is not helping, and realize that continuation is not necessary.

References & Additional Resources

Additional Resources

▮ Primary Health Tasmania. A guide to deprescribing aspirin. May 2019. https://www.primaryhealthtas.com.au/wp-content/uploads/2018/09/A-Guide-to-Deprescribing-Aspirin-2019.pdf

References

The Process of Deprescribing

- It's as easy as: "123-ABC"

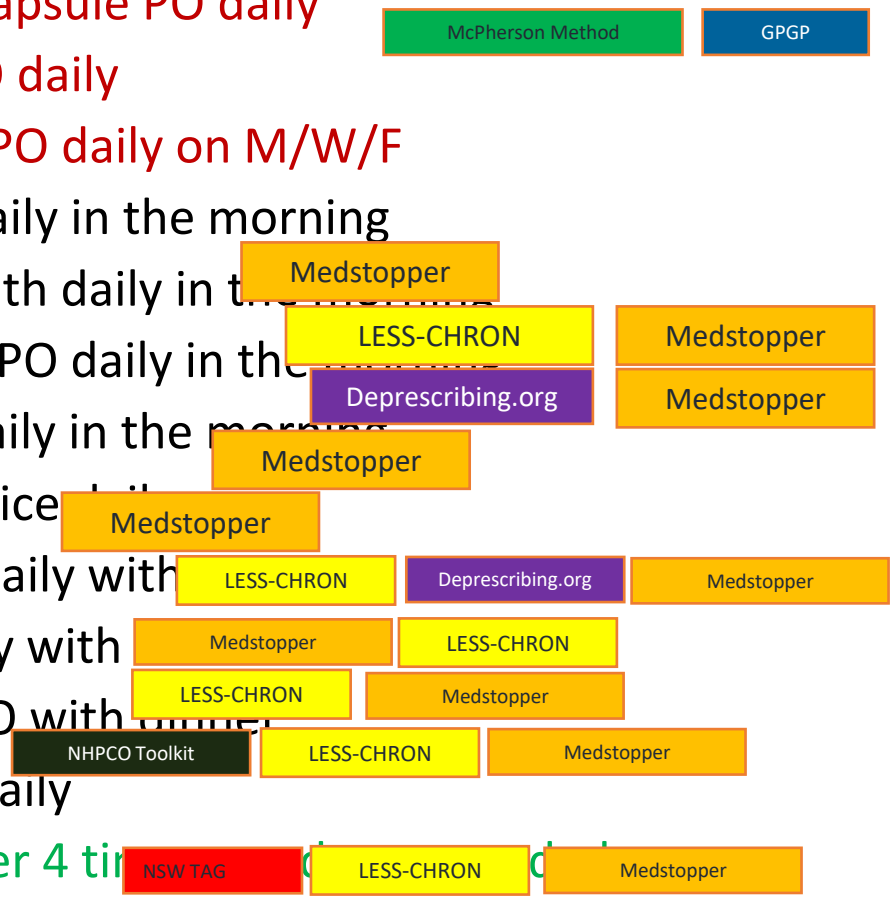
1. **Purpose** of each medication
2. How is the patient **using** medication
3. **"How's that working for you?"**

A. **A**dverse effects
B. **B**enefits/burdens of drug therapy
C. **C**onversations

LR's Medication List

94 year old man with end-stage COPD recently admitted to hospice.

1. Coenzyme Q-10 Supplement, 1 capsule PO daily
2. PreserVision AREDS2, 1 tablet PO daily
3. Azithromycin 200mg/5mL, 6 mL PO daily on M/W/F
4. Levothyroxine 75mcg, 1tab PO daily in the morning
5. Ramipril 10mg, 1 capsule by mouth daily in t
6. Omeprazole DR 20mg, 1 capsule PO daily in th
7. Furosemide 20mg, 1 tablet PO daily in the m
8. Famotidine 20mg, 1 tablet PO twice
9. Rosuvastatin 20mg, 1 tablet PO daily with
10. Finasteride 5mg, 1 tablet PO daily with
11. Amlodipine 5mg, Take 1 tablet PO with
12. Warfarin 3mg, Take 1 tablet PO daily
13. Duoneb, Inhale 3 mL vial nebulizer 4 ti
14. Oxybutynin ER 10mg, Take 1 tablet PO daily



Key Session Takeaways

1. There are several different deprescribing tools that can support evidence based deprescribing

2. Beer's lists and START/STOPP criteria represent **explicit** tools whereas the Garfinkel Good Palliative-Geriatric Practice algorithm and McPherson Method represent an **implicit** approach

3. Deprescribing.org or NHPCO's Deprescribing toolkit can be useful resources when a specific class or medication is identified for deprescribing

References

1. MedStopper. Available at: http://medstopper.com/. Accessed March 1, 2022.

2. 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 Feb 26;50(2):465-471. doi: 10.1093/ageing/afaa159. PMID: 32997135.

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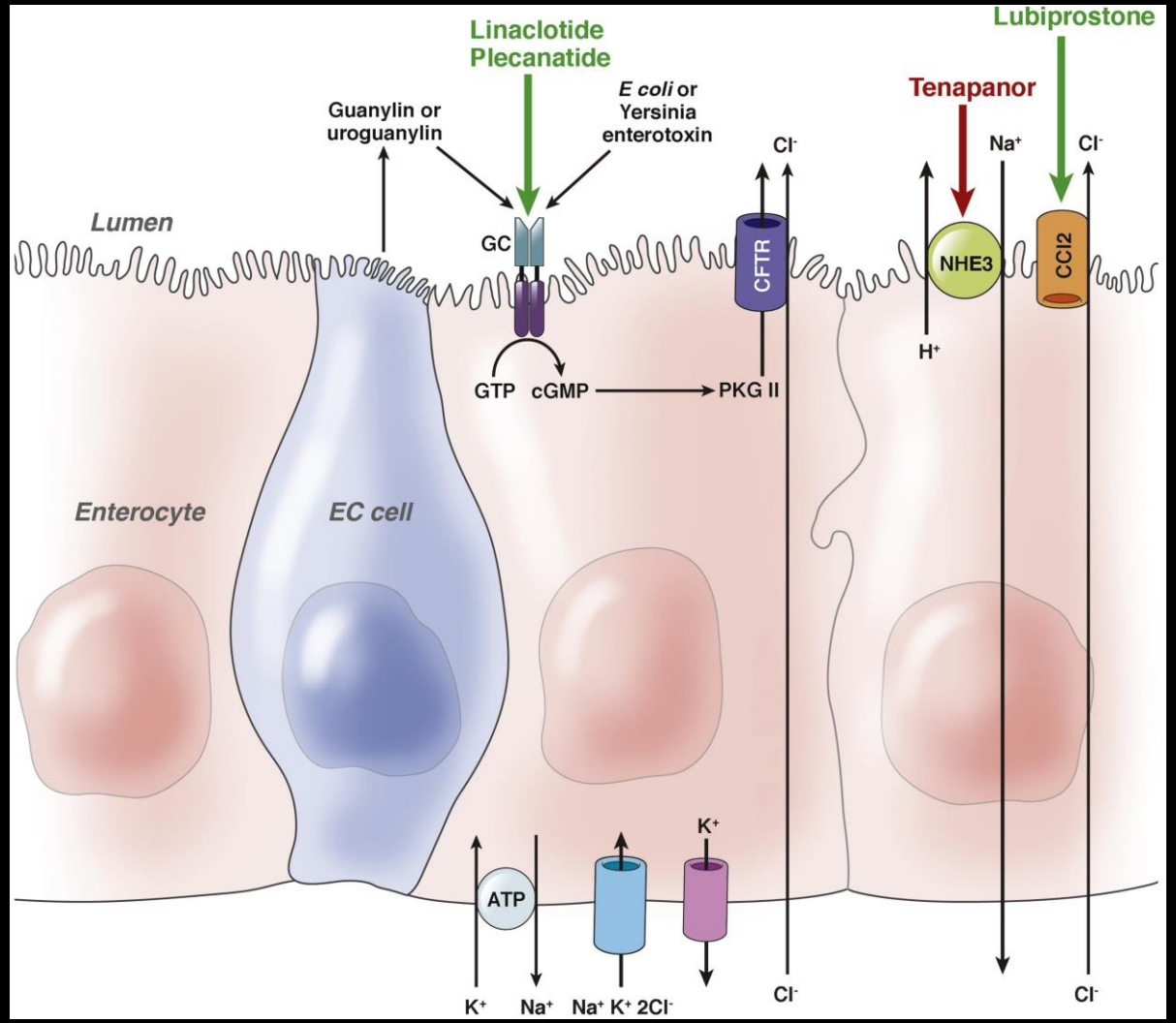
Constipation (not always a moving experience!)

- Tried and true
  - Osmotic laxatives
  - Stimulant laxatives
  - Detergents/enemas
- Ok, that didn’t work
  - PAMORAs
    - Naldemedine (Symproic)
    - Naloxegol (Movantik)
    - Methylnaltrexone (Relistor)
  - Selective 5-HT agonists
    - Prucalopride (Motegrity)
- Secretogogues
  - Lubiprostone (Amitizaa)
  - Linaclotide (Linzess)
  - Plecanatide (Trulance)
  - Tenapanor (Ibsrela)

IBS-C:
Polyethylene glycol
Antispasmodics
Peppermint oil
Tricyclic antidepressants
Rifaximin
SSRIs

Figure 1



Gastroenterology 2018 1551677-1679DOI: (10.1053/j.gastro.2018.11.005)

Secretogogues

Lubiprostone (Amitiza)	24 mcg by mouth twice daily	$450
Linaclotide (Linzess)	145-290 mcg by mouth once daily	$600-1,200
Plecanatide (Trulance)	2 mg by mouth once daily	$600
Tenapanor (Ibsrela)	50 mg by mouth twice daily	$1,800

Number Needed to Treat

- NNT – the number of patients who need to be treated to obtain one patient with more than 50% pain relief.

Analgesic	NNT
Carbamazepine	1.4
Lamotrigine	2.1-5.4
Gabapentin	3.3-3.8
Valproate	6.2-10
Topiramate	7.4

Analgesic	NNT
TCAs	1.7-3.4
Venlafaxine	4.6
SSRIs	6.8
Oxycodone	2.8
Pregabalin	3.4
Gabapentin	3.2
Imipramine	2.4

Number needed to harm:

TCAs – 13.6
SSRIs - 19
SNRIs and bupropion – 21.5

https://www.sciencedirect.com/topics/nursing-and-health-professions/numbers-needed-to-treat
Katz N, et al. J Pain 2015;16(2):116-123

What about topical compounds for pain management

Annals of Internal Medicine

ORIGINAL RESEARCH

Compounded Topical Pain Creams to Treat Localized Chronic Pain

A Randomized Controlled Trial

Robert E. Brutcher, PharmD, PhD; Connie Kurihara, RN; Mark C. Bicket, MD; Parvaneh Moussavian-Yousefi, PharmD; David E. Reece, MD; Lisa M. Solomon, BS; Scott R. Griffith, MD; David E. Jamison, MD; and Steven P. Cohen, MD

Background: The use of compounded topical pain creams has increased dramatically, yet their effectiveness has not been well evaluated.

Objective: To determine the efficacy of compounded creams for chronic pain.

Design: Randomized controlled trials of 3 interventions. (ClinicalTrials.gov: NCT02497066)

Setting: Military treatment facility.

Participants: 399 patients with localized pain classified by each patient's treating physician as neuropathic (*n* = 133), nociceptive (*n* = 133), or mixed (*n* = 133).

Intervention: Pain creams compounded for neuropathic pain (ketamine, gabapentin, clonidine, and lidocaine), nociceptive pain (ketoprofen, baclofen, cyclobenzaprine, and lidocaine), or mixed pain (ketamine, gabapentin, diclofenac, baclofen, cyclobenzaprine, and lidocaine), or placebo.

Measurements: The primary outcome measure was average pain score 1 month after treatment. A positive categorical response was a reduction in pain score of 2 or more points coupled with a score above 3 on a 5-point satisfaction scale. Secondary outcomes included Short Form-36 Health Survey scores, satisfaction, and categorical response. Participants with a positive outcome were followed through 3 months.

Results: For the primary outcome, no differences were found in the mean reduction in average pain scores between the treatment and control groups for patients with neuropathic pain (−0.1 points [95% CI, −0.8 to 0.5 points]), nociceptive pain (−0.3 points [CI, −0.9 to 0.2 points]), or mixed pain (−0.3 points [CI, −0.9 to 0.2 points]), or for all patients (−0.3 points [CI, −0.6 to 0.1 points]). At 1 month, 72 participants (36%) in the treatment groups and 54 (28%) in the control group had a positive outcome (risk difference, 8% [CI, −1% to 17%]).

Limitations: Generalizability is limited by heterogeneity among pain conditions and formulations of the study interventions. Randomized follow-up was only 1 month.

Conclusion: Compounded pain creams were not better than placebo creams, and their higher costs compared with approved compounds should curtail routine use.

Primary Funding Source: Centers for Rehabilitation Sciences Research, Defense Health Agency, U.S. Department of Defense.

Ann Intern Med. 2019;170:309-318. doi:10.7326/M18-2736 **Annals.org**

For author affiliations, see end of text.

This article was published at Annals.org on 5 February 2019.

Compounded Topical Pain Creams

- Military treatment facility
- 399 patients with localized pain classified by their MD as neuropathic, nociceptive or mixed (back/butt; neck; limb; other location)

Group	Compounded Product
1 – Neuropathic pain	Ketamine, gabapentin, clonidine, lidocaine
2 – Nociceptive pain	Ketoprofen, baclofen, cyclobenzaprine, lidocaine
3 – Mixed neuropathic/nociceptive	Ketamine, gabapentin, diclofenac, baclofen, cyclobenzaprine, lidocaine
4 – Placebo	Placebo

Concentrations of ingredients

- Ketamine 10%
- Gabapentin 6%
- Clonidine 0.2%
- Lidocaine 2%
- Ketoprofen 10%
- Baclofen 2%
- Cyclobenzaprine 2%
- Diclofenac 3%
- Lipophilic base carrier

Apply to affected area 3 times per day.

Amount applied determined by size of the area (set by investigators – 4 rotations of container for 5x5 area)

So WILL a little dab do ya?

- Primary outcome – average pain score 1 month after treatment
  - Positive categorical response was a reduction in pain score by $\geq$ 2 points (0-10) WITH a satisfaction score of $\geq$ 3 on a 5-point satisfaction scale
- Data collected by phone by a trained, blinded investigator not involved in patient care
  - 1 month (24-40 days)
  - 3 months (75-110 days)
- 399 started trial, 390 completed
  - 202 assigned to a study drug, 197 to placebo

Drum roll please….

- No change in pain score at 1 month between drug and placebo for any group
  - Neuropathic pain – 0.1 point reduction in pain
  - Nociceptive pain – 0.3 point reduction in pain
  - Mixed pain – 0.3 point reduction in pain
- SF-36 measures did not differ between the groups

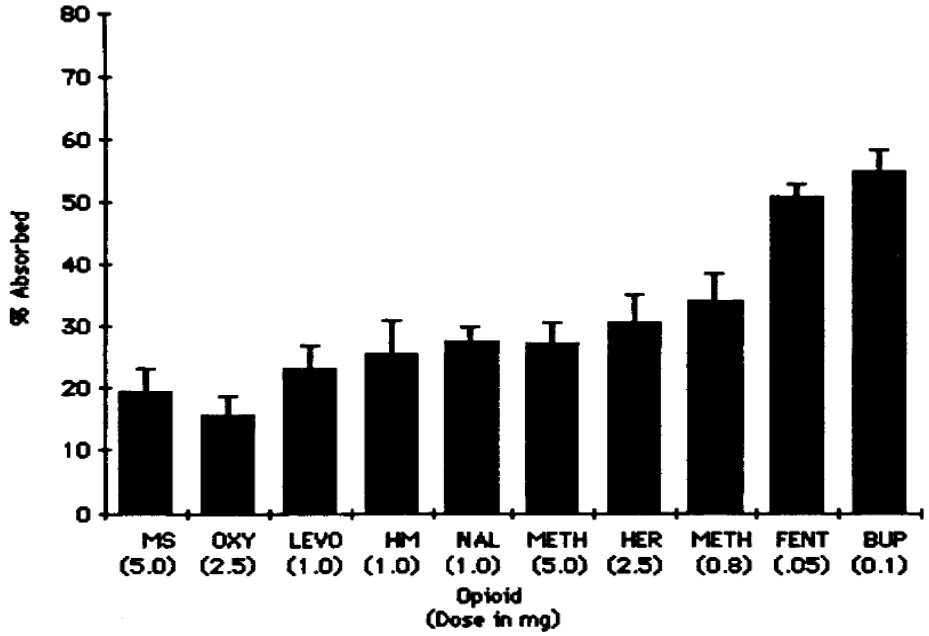
Whoa – that's intense. No, it's an INTENSOL!

- Mr. Jones is a 58-year-old man with lung cancer, who was admitted to the inpatient hospice unit for pain out of control.
- His pain was eventually controlled on an IV PCA infusion of morphine 2 mg/h with a 1 mg bolus every 15 minutes prn.
- He is very weak and has a hard time swallowing, but he wants to go HOME.
- Do we have to send him home on the IV morphine?

- 54 mg/day IV morphine ~ 162 mg oral morphine/day
- ~ 16 mg a day oral methadone
- Breakthrough oral morphine is 10-15% TDD, so 16-24 mg oral morphine
- Order:
  - Methadone 10 mg/ml oral solution, 8 mg po q12h
  - Morphine 20 mg/ml oral solution, 20 mg po q2h prn additional pain

Intensols

- Alprazolam 1 mg/ml
- Dexamethasone 1 mg/ml
- Diazepam 5 mg/ml
- Lorazepam 2 mg/ml
- Methadone 10 mg/ml
- Morphine 20 mg/ml
- Oxycodone 20 mg/ml
- Prednisone 5 mg/ml



- Prop upper body up 30°
- Instill up to 1.5 ml in buccal cavity

Clin Pharmacol Ther 1988;44:335-342

Use of Pregabalin in the Management of Chronic Uremic Pruritus

- CKD patients with severe intractable pruritus
- 12 patients; average dose 25 mg po qd

Time Point	Pain Rating
Baseline	9.7 +/- 0.9
One week	3.7 +/- 2.35
Four weeks	3.2 +/- 1.75
24 weeks	3 +/- 1.5

STOP! Before you stop that medication!

- ISMP reports on drug withdrawal symptoms
  - At least 10 reported cases of withdrawal effect
  - Twice as many as expected given the total number of adverse events for the drug
  - 95% probability that withdrawal symptoms was not due to chance
- Consider alternate delivery systems
- Taper doses down
- Anticipate swallowing difficulties

Class	Drug
Effects on serotonin	Duloxetine Paroxetine Venlafaxine
Effects on GABA	Pregabalin Vigabatrin Gabapentin
Effects on opioid receptors	Buprenorphine/naloxone Oxycodone Gabapentin
Effects on dopamine	Quetiapine Olanzapine Methylphenidate
Other mechanisms	Baclofen Cetirizine Ziconotide

Pharmacy Today October 2017

Olanzapine

Navari RM et al. Olanzapine for the treatment of advanced cancer-related Chronic nausea and/or vomiting. JAMA Oncology 2020;6(6):895-899.

- 30 patients (16 women, 14 men) ages 39-79 (average 63 yo)
- Nausea, unrelated to chemotherapy with advanced cancer
- Chronic nausea present for at least one week; severity $\geq$ 3 on a 0-10 scale)
- Patients receive olanzapine 5 mg or a placebo, by mouth, qd x 7 days
- Patient-reported outcomes used for study end points
  - Baseline, and daily x 7 days; primary outcome was change in nausea numeric rating
- Baseline median nausea scores were 9/10
- Placebo (after one week and one day) – 9/10
- Olanzapine (day 1) – 2/10; (after one week) – 1/10
  - Less emesis, antiemetic drug use, better appetite, les sedation, less fatigue, better well-being

Mirtazapine

Hunter CN, et al. Mirtazapine in cancer-associated anorexia and cachexia: A double-blind placebo-controlled randomized trial. JPSM 2021;62(6):1207-15.

- 120 cancer patients with anorexia (appetite loss $\geq$ 4 on a 0-10 scale), cachexia (> 5% body weight loss over 6 months or > 2% plus BMI > 20) and depression score $\leq$ 3 n a 0-6 scale).
- Randomized 1:1 to mirtazapine 15 mg qhs or placebo, for 8 weeks
- Primary endpoint was change in appetite from baseline to day 28
  - QOL, fatigue, depressive symptoms body weight, lean body mass, handgrip strength, inflammatory markers, adverse events and survival
- Mirtazapine associated with significantly less increase in depressive symptoms and higher prevalence of somnolence.
- No difference in other outcomes including appetite score

Anticoagulation

Why do we anticoagulate hospice patients?

- *Venous thromboembolism*
- *Atrial fibrillation*
- Acute coronary syndrome / percutaneous coronary intervention
- Atherosclerotic cardiovascular disease
- Valvular heart disease

What are these anticoagulants/antiplatelets of which you speak?

Pharmacologic Category	Examples
Vitamin K antagonists	Warfarin (Coumadin, Jantoven)
Direct acting oral anticoagulants (DOACs) Direct thrombin inhibitor Factor Xa inhibitors	 Dagibatran (Pradaxa) Apixaban (Eliquis) Edoxaban (Savaysa) Rivaroxaban (Xarelto)
Other anticoagulants	Heparin (IV and SQ) Low molecular weight heparins (e.g., daltaparin, enoxaparin, etc.) Fondaparinux (Arixtra)
Antiplatelets Aspirin P2Y12 inhibitors Other	 Aspirin; aspirin + dipyridamole Clopidogrel (Plavix), prasugrel (Effient), ticagrelor (Brilinta) Cilostazol, dipyridamole, vorapaxar (cangrelor, eptifibatide, tirofiban)

How common is antithrombotic use at the end of life?

- Antithrombotics are frequently prescribed for patients with limited life expectancy
- Chart review of 180 patients who died of malignant or non-malignant disease in the Netherlands
  - At home, in hospice, or hospital; reviewed last three months of life
- 108/180 (60%) of patients had used antithrombotics in the last three months of life
  - 33% died at home; 21.3% died in a hospice; 45.4% died in a hospital
- 157 antithrombotic prescriptions among the 108 patients
  - 30/157 warfarin; 60/157 heparin; 66/157 platelet aggregation inhibitors
  - Of 51 patients using heparins, 32 only received a prophylactic dose
  - 75.9% of antithrombotics were continued until the last week before death

Huisman et al. BMC Palliative Care 2021;20:110.

Venous Thromboembolism

- VTE – deep vein thrombosis (DVT) and pulmonary embolus (PE) – occurs in 1 in 1,000 adults
- Increases with age, reduced mobility and concurrent chronic illness including cancer
- Treatment approach has changed from a nihilistic point of view, to more individualized care
- "*a large PE might be a nice way to go*" - **NOT!**
  - Asymptomatic in about 10% of patients. Majority suffer a prolonged symptomatic death averaging 2 hours (dyspnea, tachycardia, distress)
- Likely underdiagnosed in hospice and palliative care
  - PE - Dyspnea, anemia, pulmonary edema, infection, pleural effusion – seen in advanced illness
  - DVT – Swollen legs (r/t hypoalbuminemia), left ventricular failure or pelvic lymphadenopathy - seen in advanced illness

Noble S. Clinical Medicine 2019;19(4):315-8.

Venous Thromboembolism

- Treatment for CAT (cancer-associated thrombosis) is low-molecular weight heparin
  - Superior to warfarin in preventing recurrent VTE, without an increase in bleeding complications
  - LMWH has fewer drug-drug interactions and rarely requires monitoring
    - Trials excluded patients with < 3 mo prognosis, poor performance status, increased bleeding risk, renal impairment, weight < 40 kg, thrombocytopenia, other comorbidities associated with palliative patients
    - Daily SQ injection(s) may reduce QOL and be less acceptable than an oral equivalent
- Guidelines recommend indefinite anticoagulation for patients with ongoing active cancer
  - None address management of anticoagulation at the end of life

Noble S. Clinical Medicine 2019;19(4):315-8.

Venous Thromboembolism

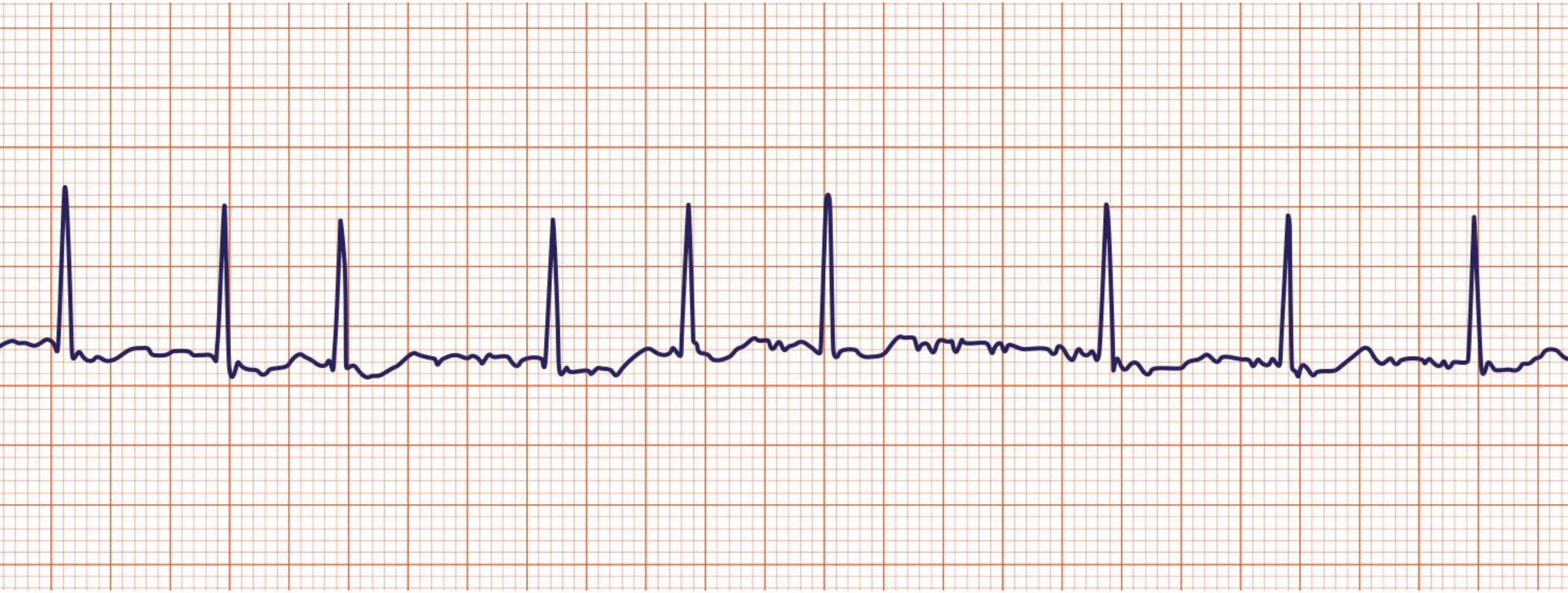
- Recent study of 1,199 patients admitted to 22 hospices/palliative care units (90% cancer patients) (Tardy)
  - Low incidence VTE, but a high incidence of clinically relevant bleeding (9.8%)
  - Analysis showed bleeding was associated with thromboprophylaxis
  - Concluded risks of bleeding may outweigh benefits in this population
- Hospice inpatient Deep Vein Thrombosis Detection study (White)
  - Prospective, longitudinal observational study
  - 343 cancer patients underwent bilateral femoral vein ultrasonography on admission and weekly until death or discharge (prognosis > 5 days)
  - Patients had an AKPS of 49 and survival of 44 days
  - Femoral DVT observed in 28% of participants with minimal symptoms; no difference in survival with/without DVT

Tardy B, et al. J Thromb Haemost 2017;15:420-428.
White C, et al. Lancet Haematol 2019;6:e79-88.

This is a tough one…

- No clear clinical guidance…limited outcomes data
- Risks vs. benefits
  - Shared decision-making
  - Symptoms, morbidity, mortality
  - Monitoring
- Location of VTE
  - Proximal vs. distal
  - Upper vs. lower
- Any risk factors or reversible causes?
- Patient's prognosis?
- Adherence? History of INR values?

What about…



CHA_2-DS_2-VASc Risk Stratification Score for Stroke Risk for Nonvalvular Atrial Fibrillation

Criteria		Poss. Point
Congestive heart failure Signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction	Yes / No	+1
Hypertension Resting BP > 140/90 mmHg on at least 2 occasions or current antihypertensive pharmacologic treatment	Yes / No	+1
Age 75 years or older	Yes / No	+2
Diabetes mellitus Fasting glucose > 125 mg/dL or treatment with oral hypoglycemic agent and/or insulin	Yes / No	+1
Stroke, TIA, or TE Includes any history of cerebral ischemia	Yes / No	+2
Vascular disease Prior MI, peripheral arterial disease, or aortic plaque	Yes / No	+1
Age 65 to 74 years	Yes / No	+1
Sex **C**ategory (female) Female gender confers higher risk	Yes / No	+1

Points	Absolute Risk per Year
0	0.2%
1	0.6%
2	2.2%
3	3.2%
4	4.8%
5	7.2%
6	9.7%
7	11.2%
8	10.8%
9	12.2%

Ref: https://clincalc.com/Cardiology/Stroke/CHADSVASC.aspx

CHA_2-DS_2-VASc Risk Stratification

Points	Absolute Risk per Year	Risk While Anticoagulated per year	Absolute Risk for Mean Hospice LOS (92.6 days)	Risk While Anticoagulated for Mean Hospice LOS (92.6 days)	Absolute Risk for Median Hospice LOS (18 days)	Risk While Anticoagulated for Median Hospice LOS (18 days)
0	0.2%	0.07%	0.05%	0.02%	0.01%	0.0035%
1	0.6%	0.20%	0.15%	0.05%	0.03%	0.01%
2	2.2%	0.73%	0.55%	0.18%	0.11%	0.04%
3	3.2%	1.06%	0.8%	0.27%	0.16%	0.05%
4	4.8%	1.58%	1.20%	0.40%	0.24%	0.08%
5	7.2%	2.38%	1.80%	0.60%	0.36%	0.12%
6	9.7%	3.20%	2.43%	0.8%	0.485%	0.16%
7	11.2%	3.70%	2.80%	0.93%	0.56%	0.19%
8	10.8%	3.56%	2.70%	0.89%	0.54%	0.18%
9	12.2%	4.03%	3.05%	1.01%	0.61%	0.20%

NHPCO Facts and Figures, file:///C:/Users/MLM/Downloads/NHPCO-Facts-Figures-2021.pdf

Risk of Bleeding – HAS-BLED

- HAS-BLED stands for hypertension, abnormal renal and liver function, stroke, bleeding, labile INR, elderly, drugs or alcohol

Criteria	Points
Hypertension (uncontrolled hypertension (SBP > 160 mmHg))	+1
Abnormal renal function (chronic dialysis, renal transplant, serum creatinine ≥ 2.3 mg/dl)	+1
Abnormal liver function (cirrhosis, bilirubin > 2 x UNL with AST/ALT/AP > 3 x UNL)	+1
Stroke	+1
Bleeding (bleeding history or predisposition (anemia))	+1
Labile INR (therapeutic time in range < 60%)	+1
Elderly (greater than 65 years old)	+1
Drugs (receiving other antiplatelet agents or NSAIDs)	+1
Alcohol (more than 8 drinks per week)	+1
TOTAL	

HAS-BLED Score and Recommended Action

HAS-BLED Score	Risk Group	Risk of Major Bleeding	Bleeds/100 patient-years	Recommendation
0	Relatively low	0.9%	1.13	Anticoagulation should be considered
1		3.4%	1.02	
2	Moderate	4.1%	1.88	Anticoagulation can be considered
3		5.8%	3.72	Alternatives to anticoagulation should be considered
4	High	8.9%	8.70	
5		9.1%	12.50	
> 5	Very high	-	-	

https://www.mdcalc.com/has-bled-score-major-bleeding-risk#evidence

Scores greater than 5 were too rare to determine risk, but are likely over 10%

Let’s consider a case…

- Mr. Jones is a 76-year-old man admitted to hospice with a diagnosis of advanced Alzheimer’s disease.
- He lives in an assisted living facility, although his medical needs are becoming more complicated and he may need to be transferred to a long-term care facility.
- He has comorbidities of hypertension (BP usually 140/90 – 150/95 mmHg), type 2 diabetes, nonvalvular atrial fibrillation, and a stroke 3 years ago.
- Medications include:
  - Metoprolol 50 mg po twice daily
  - Metformin 1000 mg po twice daily
  - Glipizide 10 mg po once daily
  - Warfarin 5 mg po once daily
  - Clopidogrel 75 mg once daily
  - Aspirin 81 mg once daily

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HAS-BLED

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Labile INR (therapeutic time in range < 60%)	★ +1
Elderly (greater than 65 years old)	★ +1
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TOTAL	

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4	High	8.9%	8.70	
5		9.1%	12.50	
> 5	Very high	-	-	

Ref: https://www.mdcalc.com/has-bled-score-major-bleeding-risk#evidence

Mr. Jones…

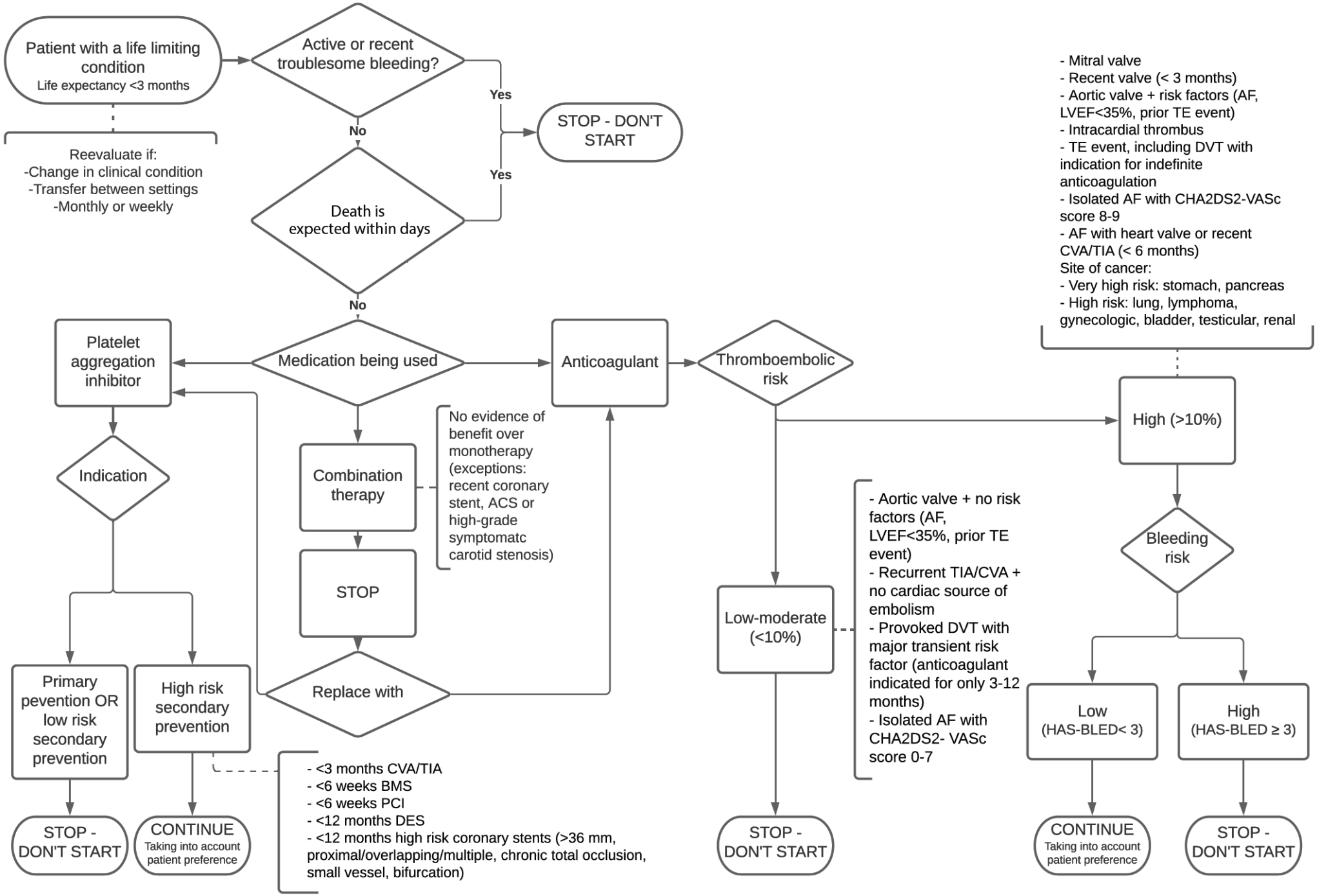
- Annual risk of having a stroke is a little less than 10% (9.7%)
  - Assume length of stay of 18 days, risk is about 0.485%
- Annual risk of major bleeding is 8.9%
- Alternatives to anticoagulation recommended
- Attending physician agrees to discontinue warfarin therapy

Shared Decision Making

https://uxdesign.cc/decision-making-for-product-managers-7fef3292cb65

Huisman BAA, et al. Use of antithrombotics at the end of life: an in-depth chart review study. BMC Palliative Care 2021:20:110. Open Access, no permission required; Creative Commons Attribution 4.0 International License. https://bmcpalliatcare.biomedcentral.com/articles/10.1186/s12904-021-00786-3

ACS – acute coronary syndrome
AF – atrial fibrillation
BMS – bare metal stent
CVA – cerebrovascular accident
DES – drug-eluting stent
DVT – deep venous thrombosis
LVEF – left-ventricular ejection fraction
PCI – percutaneous coronary intervention
TE – thromboembolic
TIA – transient ischemic attac



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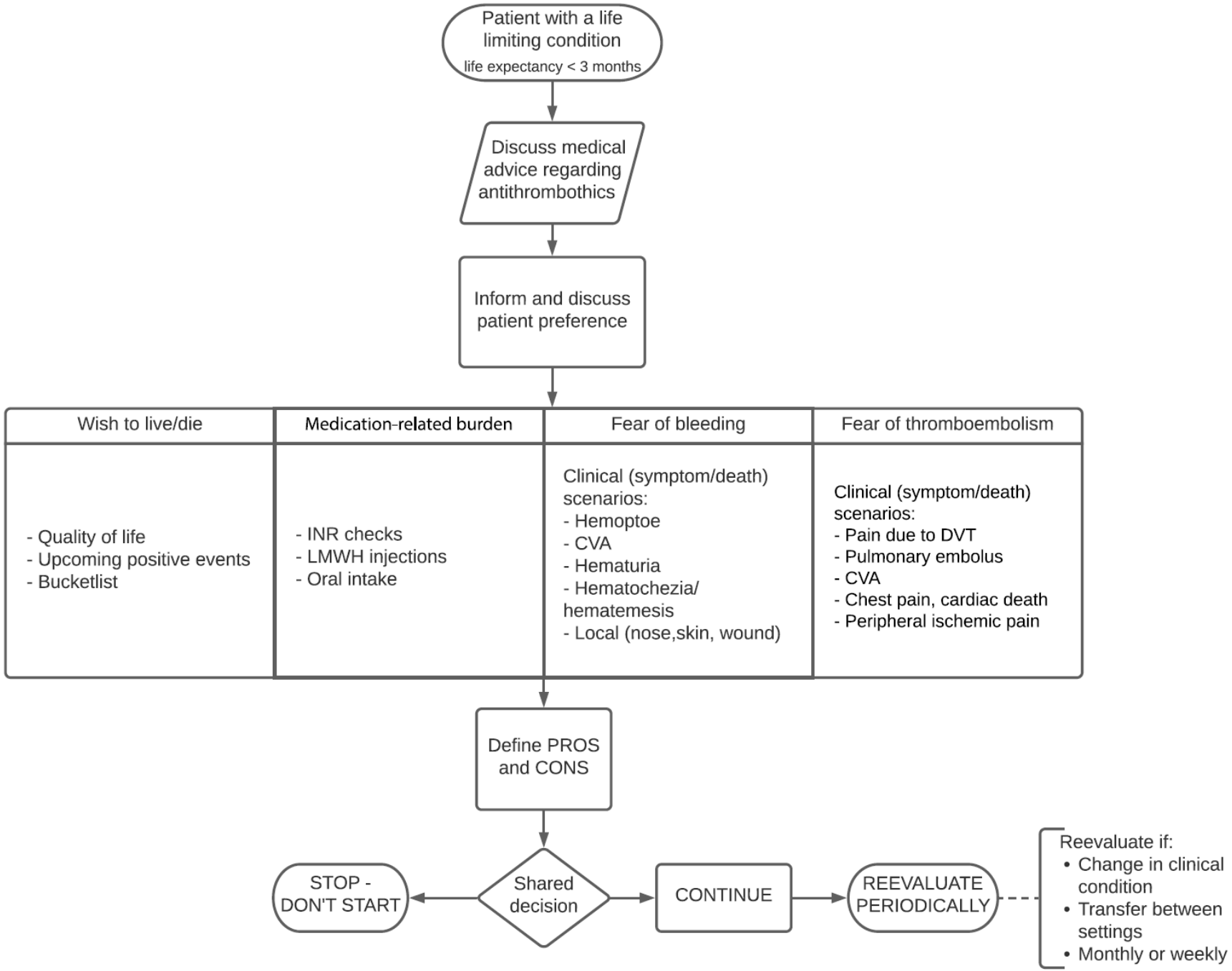

CONGRÈS INTERNATIONAL DE SOINS PALLIATIFS MCGILL

MCGILL INTERNATIONAL PALLIATIVE CARE CONGRESS

October 18–21 octobre 2022

Palais des Congrès de Montréal

Quick Medication Tips, New Drugs and Updates on Pain and Symptom Management

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