Three palliative care concepts that will reframe YOUR practice!

CSHP NS Branch Lunch and Learn – April 2019

Halifax, Nova Scotia

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Disclosures

- I have no conflicts of interest to disclose

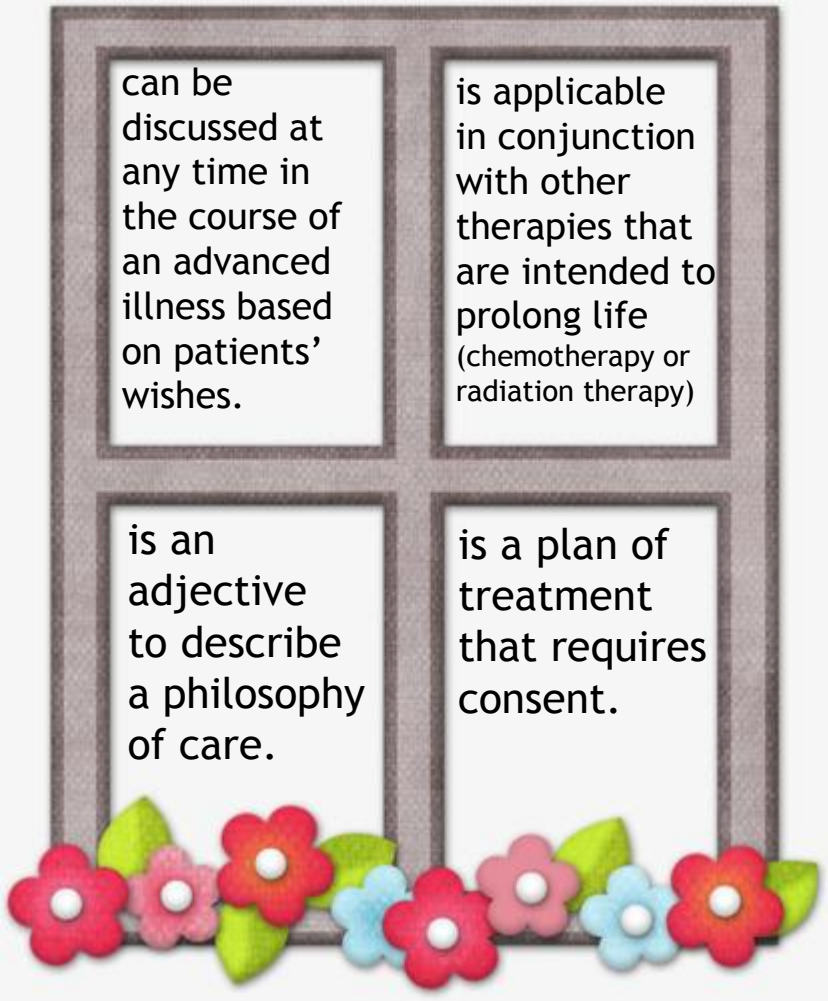
Learning Objectives:

By the end of this session you will be able to:

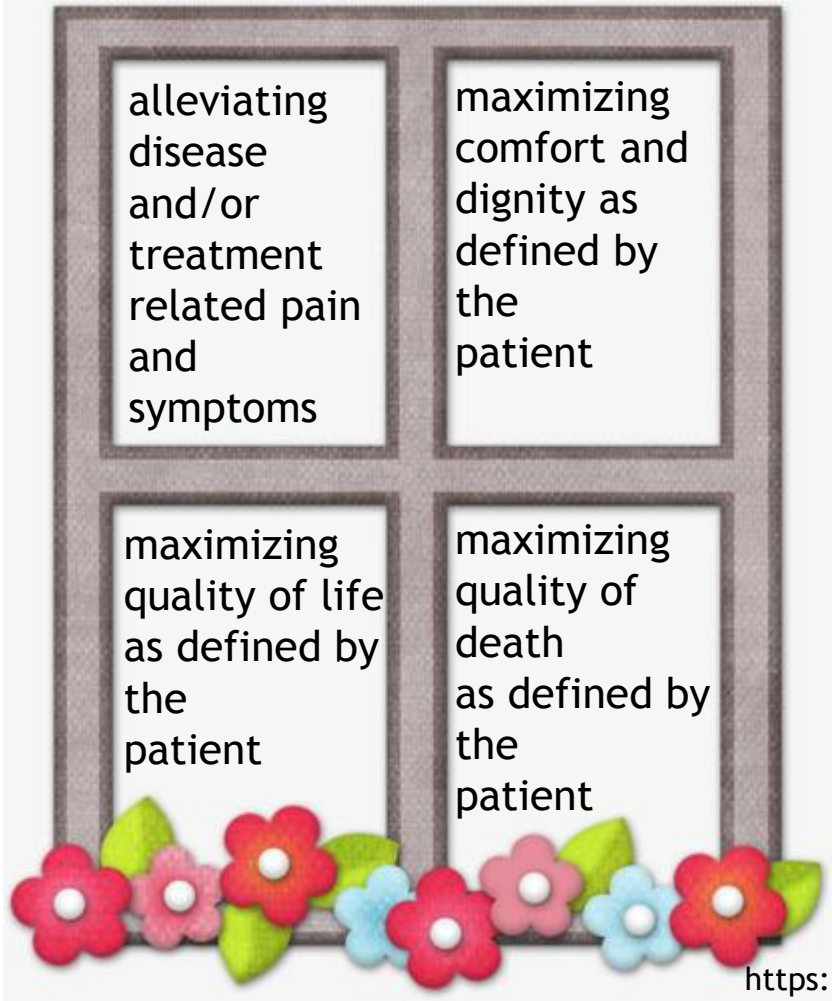
- Define the term *palliative*
- Describe the goals of *palliative care*
- Evaluate a patient's medication list for deprescribing opportunities
- List the differences between patients with cancer pain and those with non-cancer pain, receiving opioid therapy.
- Describe the role of shared decision making and directed patient autonomy in supporting a patient through a medication related decision making processes

Lets *reframe* our understanding of *"Palliative"*

Palliative care:



Goals of palliative care:



Can Fam Physician 2017;63:191-2,194
https://www.who.int/cancer/palliative/definition/en/

Case 1 - Deprescribing

- Mr SR is a 68 year old man with metastatic renal cell carcinoma (RCC). He is cared for by his medical oncologist for his chemotherapy as well as the palliative and supportive care service to optimize his symptom management. Mr SR has adopted a palliative approach to his care. His estimated overall survival prognosis is less than one year.
- Mr SR is seeing you in an ambulatory care setting to conduct a best possible medication history and provide recommendations on opportunities for deprescribing.

- Medications (indication):
  - Sorafenib 200 mg PO BID (RCC)
  - Dexamethasone 2 mg PO BID at 08:00 and 12:00 (Fatigue)
  - Methylphenidate 5 mg PO qAM (Fatigue)
  - Pantoprazole 40 mg PO BID (Dyspepsia)
  - Metoclopramide 5 mg PO BID PRN (Nausea/vomiting)
  - Prochlorperazine 10 mg PO q6h PRN (Nausea/vomiting)
  - Olanzapine 5 mg PO BID PRN (Nausea/vomiting)
  - Atorvastatin 20 mg PO daily qHS (Dyslipidemia)
  - Lorazepam 1 mg PO qHS PRN (Insomnia)

Hospital Pharmacy

Six Things Clinicians and Patients Should Question
by
Canadian Society of Hospital Pharmacists
Last updated: January 2019

Choosing Wisely Canada™
In partnership with the Canadian Medical Association

1. **Don't continue medications that are no longer indicated or where the risks outweigh the benefits.**
2. **Don't use a medication for long-term risk reduction if life expectancy is shorter than the time to benefit of the medication.**
3. **Don't continue a proton pump inhibitor at discharge unless there is a compelling reason to continue therapy.**
4. **Don't start or prolong broad-spectrum antibiotic treatment unless clinically indicated.**
5. **Don't routinely prescribe benzodiazepines or other sedative-hypnotics for promotion of sleep without first a trial of non-pharmacologic interventions.**
6. **Don't initiate or escalate opioid doses for chronic non-cancer pain before optimizing non-opioid pharmacotherapy and non-pharmacologic therapy.**

Discontinuation of Preventive Medicines in Older People with Limited Life Expectancy: A Systematic Review

Population	Older people with LLE; n = 26,854 participants
Intervention	Deprescribing of aspirin, clopidogrel, dipyridamole, warfarin, dabigatran, statins, and/or bisphosphonates
Outcome	Discontinuation of specific preventative medicines in the presence of a life limiting illness
Objectives	Systematically evaluate the literature to examine the discontinuation of preventive medicines in older people with LLE
Results	-The most commonly studied preventative medication deprescribed were statins. -Two studies examined the association of outcomes related to discontinuation of preventive medicines. - Warfarin deprescribing: increased risk of mortality, and ischemic and hemorrhagic events. - Statin deprescribing: improvement in quality of life, reduction in medication costs, reduction in use of other potentially inappropriate medicines. -Deprescribing of preventative medications in the context of LLE is incomplete and requires further research

LLE = limited life expectancy

Drugs Aging (2017) 34:767–776

Deprescribing Tools

Table 1. Comparison of geriatric medication screening tools

Screening tool	Advantages	Disadvantages	Level of evidence[a]	Time to administer/ medication (min)[b]
Beers 2015	Most widely used	Drug-nutrient interactions not discussed	◇◇◇◇	2
	Endorsed by the AGS	Lack of guidance for underuse, adherence, and OTC/herbal medications		
	Provides quality of evidence			
	Includes geriatric syndromes			
	Evidence in patients with cancer			
MAI	Multiple elements of drug therapy can be assessed simultaneously	Does not address drug allergies, adverse drug reactions, adherence, or medication underuse	◇◇◇	10
	Takes into account practical aspects of care	Time-consuming to administer		
	Applies to OTC or CAM therapies	Has not been extensively used for evaluation of patient outcomes		
	Inclusive of clinical judgment			
START/ STOPP	Effective at identifying "red flags" that might require intervention	Needs continuous updating as new literature is available and additional drugs come onto the market	◇◇◇◇	2–3
	Assesses drug-drug and drug-disease interactions	Does not evaluate the use of CAM, OTC therapies, or medication underuse		
	The AGS supports use in conjunction with the Beers criteria			
HEDIS DAE	Comprehensive, concise, and points out the need to evaluate combination products	Not all-inclusive, does not provide rationales for avoidance, and does not include drug-disease interactions	◇◇	2
	Medications listed on the HEDIS DAE measure are meant to *always* be avoided in the elderly	Short-acting benzodiazepines, NSAIDs, clonidine, doxepin, and other anticholinergic drugs are not listed as medications to avoid		
IPET	Quick reference for the busy clinician	Not all-inclusive and does not evaluate drug-disease interactions or drug-drug interactions	◇	2
	Studies were evaluated prospectively in acutely ill elderly patients	Recommendations are out of date based on current clinical evidence and guidelines		
Zhan	Can be quickly reviewed by the clinician	Low level of intrarater reliability	◇	2
	Effective retrospective screening tool in population-based studies of PIMs and PP	Not all-inclusive		
		Does not look at drug interactions, drug-disease interactions, underuse, and CAM		
ACOVE-3	Information assessed is comprehensive and focuses on the process of care	Need for constant up-keep and data evaluation	◇◇	15–20
	Can evaluate care at the population level and can collect a large amount of data for quality improvement purposes	Extensive document that cannot be applied to a single patient by a single clinician in a timely manner		

STOPFrail** and ***OncPal are two additional deprescribing tools not discussed in this review paper that may be appropriate to include in your deprescribing assessment for oncology patients.

TheOncologist 2016;21:723–730
Support Care Cancer (2015) 23:71–78
Age and Ageing 2017; 46: 600–607
NCCN Clinical Practice Guidelines in Oncology - Older Adult Oncology. 2015

Pharmacist-Led Medication Assessment and Deprescribing Intervention for Older Adults with Cancer and Polypharmacy: A Pilot Study

Population (setting)	Adult patients with cancer aged 65 and older, n = 26 (geriatric oncology clinic - August 1, 2015 to April 30, 2016)
Intervention	pharmacist-led polypharmacy assessment using: Beers Criteria (2012), START/STOPP, MAI
Comparator	pharmacist-led polypharmacy assessment using: Beers Criteria (2012)
Objectives	**Primary**: compare the sequential application of three geriatric medication screening tools (Beers Criteria, STOPP, and MAI) to the Beers Criteria alone for PIM quantification **Secondary (descriptive):** feasibility of a pharmacist-led deprescribing intervention in a geriatric oncology clinic, number of medications deprescribed, cost savings, and pharmacist intervention time
Results	**Primary**: Intervention = 119, Comparator = 38 **Secondary**: feasible; 87/119 medications deprescribed in real-time; potential net cost savings = $110,470 USD; intervention time average of 30 minutes (18 to 77 minutes)

START/STOP = Screening Tool to Alert doctors to Right Treatment / Screening Tool of Older Persons' Prescriptions, MAI = Medication Appropriateness Index, PIM = potentially inappropriate medication

Support Care Cancer. 2018 December; 26(12): 4105-4113.

Preventive Drugs in the Last Year of Life of Older Adults With Cancer: Is There Room for Deprescribing?

Population	Swedish nation-wide cohort, solid tumor, age greater than 65 years who passed away between 2007 and 2013, n = 151,201
Objective	Assess the use and cost of preventive drugs during the last 12 months of life. Preventative drugs include: drugs for diabetes, vitamins, mineral supplements, antithrombotic agents, antihypertensives, statins, bisphosphonates, and medications for chronic anemia.
Results	The percentage of older adults who continued therapy until the final month of life: - 56.6% for bisphosphonates - 65% for statins and vitamins - ≥80% for insulin, ß-blockers, and vitamin B12 or folic acid.

Cancer. 2019 Mar 25. [Epub ahead of print]

Barriers and enablers to deprescribing for patients with life-limiting illnesses:

Barriers (clinician focus)	Enablers (clinician focus)
- Shortages in staff - Perceived difficulty or resistance of the nursing home resident's family – or the resident themselves - Lack of research in this area - Reluctance to deprescribe a medication not originally prescribed by the current care team - Lack of early introduction of deprescribing concept/language to patients* - Limited focus on "difficult conversation" training for pharmacy health care providers* - Difficulty in identifying which patients may benefit most from the intervention*	- Organizational support (e.g. for standardized medication review) - Involvement of multidisciplinary teams in medication review and the perception of the importance of coming to a joint decision regarding deprescribing - Interdisciplinary collaboration and involving the patient and family in the decision-making process - Expanding literature base* - Increased presence of pharmacists on inpatient teams and in ambulatory clinics*
Patient reported barriers to deprescribing: - fear of return of symptoms or worsening of underlying condition being treated - patient's need to check with their primary care provider before deprescribing - feeling of physical dependence - patient and caregiver confusion about medications	

*additional barriers/facilitators I identified during my palliative oncology practice

2019, Pall Med. Vol. 33(1) 37–48
Support Care Cancer. 2018; 26(12): 4105–4113

What can we be doing now to overcome some of these barriers?

Clinician reported barriers to deprescribing	Potential solutions
Shortages in staff	Evaluate your activities, make changes if opportunities identified, become comfortable with available tools and **prioritize** their use in your practice in a systematic, sustainable way.
-Perceived difficulty or resistance of patient or their care givers -Lack of early introduction of deprescribing concept/language to patients* -patient reported barriers to deprescribing (fear of return of symptoms or worsening of underlying condition being treated, patient's need to check with their primary care provider before deprescribing, feeling of physical dependence, patient and caregiver confusion about medications)	**Clear communication and education** for patients and their care givers at every opportunity throughout the care journey. It is critical to identify patient and/or clinician specific barriers to deprescribing based on their **personal experiences, values,** and level of **understanding of the role and value of deprescribing** and work in collaboration to work through those barriers together.
Lack of research in this area	**Be familiar** with available research. Unique opportunity to **contribute** to the body of literature!
Reluctance to deprescribe a medication not originally prescribed by the current care team	Create formal **communication templates** to inform prescribers of recommended changes and supports you are able to provide the patient.
Limited focus on "difficult conversation" training for pharmacy health care providers*	Find resources to **educate yourself (i.e. Harvard Business Review)**
Difficulty in identifying which patients may benefit most from the intervention*	Will vary by practice setting. Be empowered to work with your interprofessional team to **define which criteria you will use** to identify patients who may benefit most within your available organizational resources.

2019, Pall Med. Vol. 33(1) 37–48
Support Care Cancer. 2018; 26(12): 4105–4113

What are we already doing well?

- Acutely life-limiting/palliative care
- Patients completely cured and all/majority of anti-cancer therapy is discontinued
  - A large proportion of our patients do not fit into these categories

In what novel directions should we be challenging ourselves to integrate deprescribing into our patient care activities?

- Step 1 – integrate available literature effectively into our practices, where applicable
- Step 2 – expand the scope of medications we consider for deprescribing
- Step 3 – expand the patient population in which we actively discuss (and research) deprescribing

Why is it important for us to seek out deprescribing opportunities in non-acutely palliative oncology patients?

- Impact on adherence
- Number of medications is an independent predictor of urgent/emergent health system utilization
- Supportive care medications are not without their own risks:
  - Drug-drug interactions
  - Complex dosing instructions
  - Potential to impede early identification of worsening clinical status

NCCN: Medications commonly used for supportive care that are of concern in older adults with cancer

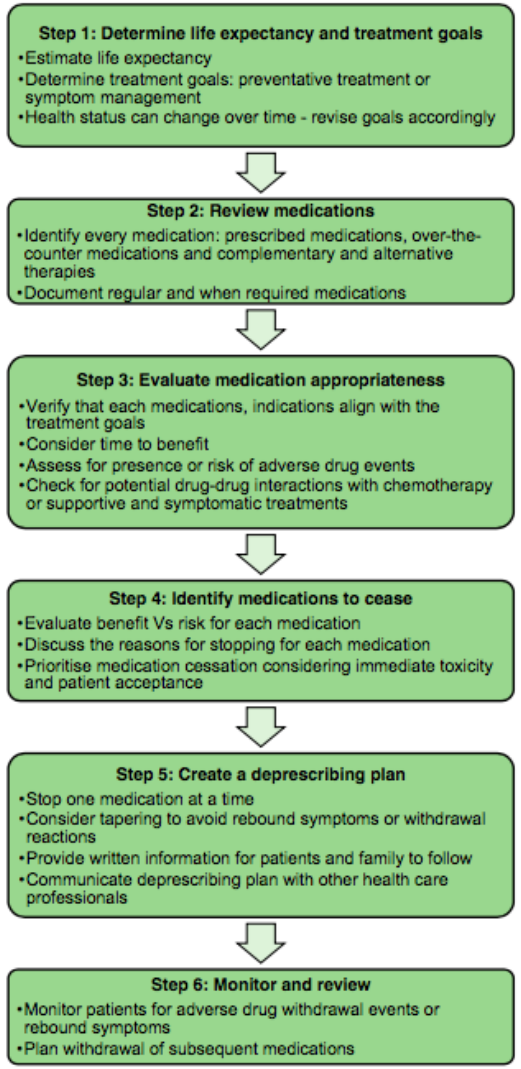
- Corticosteroids, benzodiazepines, first-generation antihistamines, antiemetic/prokinetic, histamine-2 receptor antagonists, phenothiazine antiemetics, antipsychotics, non-benzodiazepines sedative hypnotics, selective serotonin reuptake inhibitors, antiepileptic drugs

*****These medications should be systematically reassessed for deprescribing opportunities in all patients at regular intervals*****

Public Health Rep. 2011 Jul-Aug; 126(4): 460–471.
CMAJ 2008;178(12):1563-9
NCCN Clinical Practice Guidelines in Oncology - Older Adult Oncology. 2015

An approach we can extrapolate to any of our patients … applied to Mr SR

*include assessment of supportive care medication use



Mr SR is a 68 year old male with metastatic renal cell carcinoma (RCC) taking a palliative approach to his care.

Medications (indication):

- Sorafenib 200 mg PO BID (RCC)
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- Methylphenidate 5 mg PO qAM (Fatigue)
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- Olanzapine 5 mg PO BID PRN (Nausea/vomiting)
- Atorvastatin 20 mg PO daily qHS (Dyslipidemia)
- Lorazepam 1 mg PO qHS PRN (Insomnia)

J.P. Turner et al. / Journal of Geriatric Oncology 8 (2017) 77–81

Summary

- Deprescribing is important for all patients
- Pharmacists play a key role in assessing for deprescribing opportunities
- The best deprescribing tool is the one that fits with your practice and style
- We can do a lot to overcome perceived barriers to deprescribing
- The theories of deprescribing should be applied to all patients and all of their medications

Case 2

- Ms MP is a 54 year old female with chronic non-cancer pain related to a history of low back pain. She is followed closely by a pain specialist to support her through the process of tapering with the goal of discontinuing opioid therapy. She has signed a *treatment agreement* and receives *urine drug screens* at regular intervals as determined by the prescribing physician. Her other past medical history is significant for hypertension and type 2 diabetes mellitus.
- Medications
  - Fentanyl patch 25 mcg/hour transdermal every 72 hours (dispensed monthly)
  - Hydromorphone 2 mg PO q1h PRN pain (actual use consistently 2 to 3 x daily based on her activity level) (dispensed monthly)
  - Ramipril 5 mg PO daily
  - Metformin 1000 mg PO BID
  - Naloxone kit (including 2 x 1 mL ampules containing naloxone 0.4 mg/mL) PRN for signs or symptoms of opioid overdose

National Pain Center. Canadian Guideline for Opioids for ***Chronic Non-Cancer Pain***. 2017.
Government of Canada. National report: Apparent opioid-related deaths in Canada. 2017.

Case 2

- Ms MP is a 54 year old female with chronic ~~non-~~cancer pain related to ~~a long-standing history of low back pain~~ her bilateral mastectomy surgical site (surgery 6 years ago). [redacted] Her other past medical history is significant for history of triple negative breast cancer, hypertension, and type 2 diabetes mellitus.
- Medications
  - Fentanyl patch 25 mcg/hour transdermal every 72 hours [redacted]
  - Hydromorphone 2 mg PO q1h PRN pain (actual use consistently 2 to 3 x daily based on her activity level) [redacted]
  - Ramipril 5 mg PO daily
  - Metformin 1000 mg PO BID
  - [redacted]

National Pain Center. Canadian Guideline for Opioids for ***Chronic Non-Cancer*** Pain. 2017.
Subst Abuse Rehabil 2016 71:789-794

Opioid use in the cancer population

- Opioid use is increasing in the general population, as are opioid-related deaths.
  - Patients with cancer or a history of cancer are not immune to opioid associated risks with at least 1 in 5 patients with cancer being at risk of opioid use disorder.
- Opioids are effective in managing cancer related pain, as part of a multimodal care plan.
- Opioid prescribing rates are 1.22 times higher in cancer survivors than those who have never had cancer.
- Patients with cancer receiving opioids for pain management are continuing these therapies for an extended period of time after they have been cured of their cancer diagnoses.
- Clinicians who care for patients with cancer require:
  - Education
  - Primary literature, guidelines and support tools
  - Knowledge translation programs

Government of Canada. National report: Apparent opioid-related deaths in Canada. (2017)
Subst Abuse Rehabil 2016: 71:789-794
National Pain Center. Canadian Guideline for Opioids for ***Chronic Non-Cancer Pain*** (2017)
Cancer. 2017 Nov 1;123(21):4286-4293
Barbera L, et al. Factors associated with opioid use in long term cancer survivors., *Journal of Pain and Symptom Management* (2019)

What can we do *today* to make pain management safer for our patients using opioid therapy?

- Educate yourself and your colleagues on why it is important to talk about risk mitigation strategies with your patients!

- Know your local hospital and community resources, referral services, tools, and guidelines

- *Participate in research / Engage in knowledge translation activities*

- Be vigilant!
  - Provide education to your patients on:
    - the role of opioids in pain management as part of a multimodal strategy
    - appropriate use of PRN opioids
    - self-monitoring for benefit and risks of opioid use
    - proper storage/disposal of controlled substances
    - naloxone use in patients on opioid therapy, *even* when being taken as prescribed
    - physical dependence and addiction, as needed, based on patients/care givers voiced concerns around opioid use

- Advocate for organizational support of opioid stewardship programs.

- Don't forget to include opioids in your assessment of deprescribing opportunities!
  - Requires close collaboration with the patient and their care givers, the prescribing physician, as well as other services providing pain management care for the patient throughout and after the tapering and discontinuation process.

Participate in research; engage in knowledge translation activities

A sneak peak:

- **Managing opioids and mitigating risk: A survey of attitudes, confidence and practices of oncology health care professionals**

Summary:

- Patients with cancer (or a history of cancer), requiring opioid therapy for pain management, require the same education and risk mitigation support as patients with chronic non-cancer pain.

- Additional studies are required to close the knowledge gap in this area.
  - There is a lot of Canadian literature coming out in this area so make sure to stay tuned!

- No need to wait! There are a lot of tools we can use today to mitigate the risk of opioid use in patients with cancer (or a history of cancer)!

A closing word on shared decision making and directed patient autonomy ("palliative paternalism")

- Palliative paternalism:
  - Is an approach to communication with limited open-ended questions that uses well-informed, discrete, concrete options during medical discussions
  - Provides a communication approach that determines the appropriate level of patient autonomy.

- Open-ended questions and unlimited care options may cause more harm or suffering in some patients and/or surrogates.

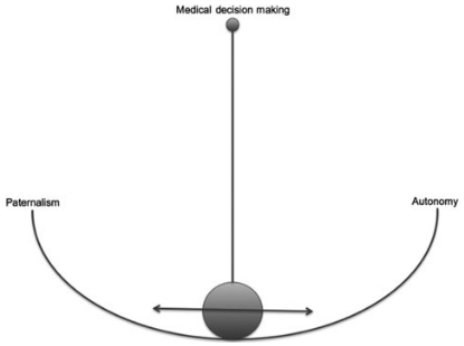

FIG. 1. The medical decision making pendulum.

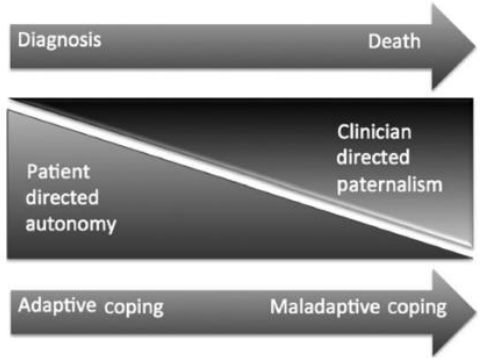

FIG. 2. The illness communication continuum.

J Palliat Med. 2014 Apr;17(4):415-20.

A closing word on palliative paternalism…

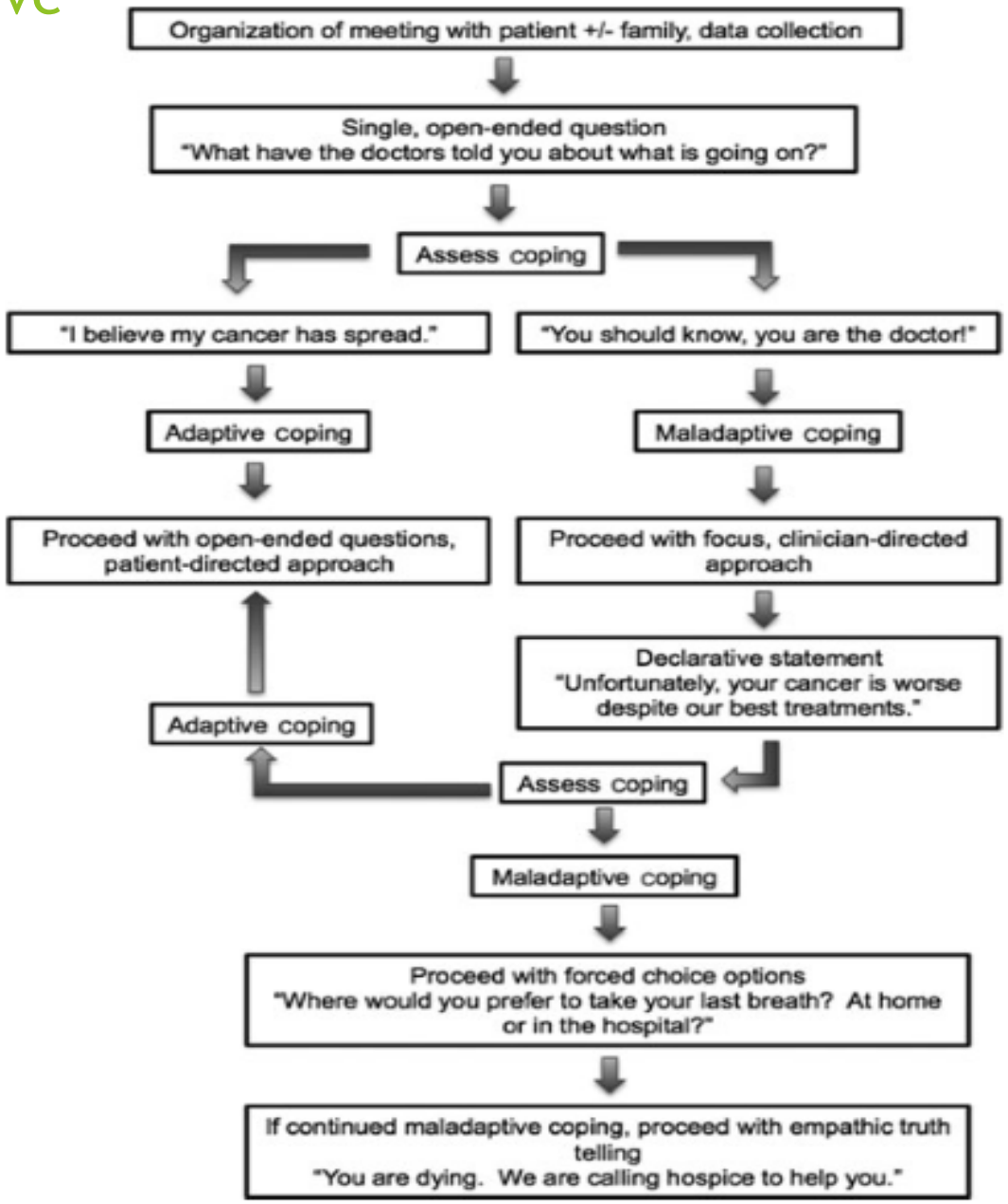

FIG. 3. Approach to medical discussions based on assessment of patient coping.

J Palliat Med. 2014 Apr;17(4):415-20.

Learning Objectives revisited:
By the end of this session you will be able to…

Learning objectives	Reflection
▪Define the term *palliative*	An adjective to describe a philosophy of care.
▪Describe the goals of *palliative care*	Diverse, based on patient values and goals.
▪Evaluate a patient's medication list for deprescribing opportunities	It is important to integrate simple, systematic deprescribing assessments into the care of all patients you see.
▪List the differences between patients with cancer pain and those with non-cancer pain, receiving opioid therapy.	No differences! Patients with cancer require the same risk mitigations supports as those with non-cancer pain.
▪Describe the role of shared decision making and directed patient autonomy in supporting a patient through a medication related decision making processes	There is a role for palliative paternalism in any patient care practice. Ask open-ended questions to gauge coping skills and practice patient-centered shared decision making.

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Additional slides

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Table 8. Medications/Criteria Removed Since 2015 American Geriatrics Society Beers Criteria®

Medication/Criterion	Reason for Removal
Independent of Diagnosis or Condition (Table 2)	
Ticlopidine	No longer on US market; low use
Pentazocine	Oral no longer on US market
Considering Disease and Syndrome Interactions (Table 3)	
Chronic seizures or epilepsy Bupropion Chlorpromazine Clozapine Maprotiline Olanzapine Thioridazine Thiothixene Tramadol	Not unique to older adults
Dementia H2-receptor antagonists	Weak evidence and to avoid overly restricting therapeutic options for older adults with dementia who have gastroesophageal reflux or similar issues (given a coexisting criterion advising against chronic use of PPIs except in specific circumstances)
Insomnia *Oral decongestants* Phenylephrine Pseudoephedrine *Stimulants* Amphetamine Armodafinil Methylphenidate Modafinil *Theobromines* Theophylline Caffeine	Not unique to older adults
Parkinson disease Aripiprazole	Removed as a preferred antipsychotic in older adults with Parkinson disease because of safety and efficacy concerns
Use With Caution (Table 4)	
SIADH/hyponatremia Carboplatin Cyclophosphamide Cisplatin Vincristine	Highly specialized drugs that fell outside the scope of the criteria
Syncope Vasodilators	Not unique to older adults

Table 9. Medications/Criteria Added Since 2015 American Geriatrics Society Beers Criteria®

Medication/Criterion	Reason for Addition
Independent of Diagnosis or Condition (Table 2)	
Glimepiride	Severe, prolonged hypoglycemia in older adults
Methscopolamine Pyrilamine	Strong anticholinergic
Considering Disease and Syndrome Interactions (Table 3)	
History of falls or fractures SNRI	Associated with increased risk in older adults
Parkinson disease Pimavanserin	Unlike most other antipsychotics, the revised criteria consider pimavanserin acceptable for treatment of psychosis in Parkinson disease
Use With Caution (Table 4)	
Rivaroxaban	Emerging evidence of increased risk of serious bleeding compared with other anticoagulant options
Tramadol	Risk of SIADH/hyponatremia
Dextromethorphan/quinidine	Limited efficacy in treating patients with dementia symptoms disorder in absence of pseudobulbar affect while potentially increasing risk of falls and drug-drug interactions
TMP-SMX	Increased risk of hyperkalemia in combination with ACEIs and ARBs in patients with reduced kidney function
Clinically Important Drug-Drug Interactions (Table 5)	
Opioids + benzodiazepines	Increased risk of overdose
Opioids + gabapentin/pregabalin	Increased risk of overdose
Phenytoin + TMP-SMX	Increased risk of phenytoin toxicity
Theophylline + ciprofloxacin	Increased risk of theophylline toxicity
Warfarin + ciprofloxacin	Increased risk of bleeding
Warfarin + macrolides (excluding azithromycin)	Increased risk of bleeding
Warfarin + TMP-SMX	Increased risk of bleeding
Medications That Should Be Avoided or Have Their Dosage Reduced With Decreased Kidney Function (Table 6)	
Ciprofloxacin	Increased risk of CNS effects
TMP-SMX	Increased risk of worsening of renal function and hyperkalemia

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CNS, central nervous system; SIADH, syndrome of inappropriate antidiuretic hormone secretion;

BEERS 2019

Table 10. Medications/Criterion Modified Since 2015 American Geriatrics Society Beers Criteria®

Medication/Criterion	Modification
Independent of Diagnosis or Condition (Table 2)	
Peripheral α-1 blockers	For treatment of hypertension
Digoxin for atrial fibrillation and heart failure	Added wording to Drug column; modified rationale; QE for atrial fibrillation changed to Low
Estrogen with or without progestin	Added "recurrent" urinary tract infections
Sliding-scale insulin	Clarified definition of sliding-scale insulin
Metoclopramide	Added duration of use to recommendation
Meperidine	Removed caveat from recommendation
Considering Disease and Syndrome Interactions (Table 3)	
Heart failure	Reorganized recommendations; separated COX-2 inhibitors from other NSAIDs; added QE and SR for COX-2 inhibitors; changed recommendation for NSAIDs, COX-2 inhibitors, and thiazolidinediones to use with caution in asymptomatic heart failure and to avoid in symptomatic heart failure; modified rationale
Syncope	Specified "nonselective peripheral α-1 blockers"; separated rationales, QE, and SR for AChEIs and nonselective peripheral alpha-1 blockers; modified QE for ACHEIs and antipsychotics
Delirium	Changed "Sedative/hypnotics" to Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics; changed QE of H2-receptor antagonists to low
History of fractures and falls	Changed SR of opioids to strong
Parkinson disease	Added rationale for quetiapine, clozapine, and pimavanserin
Chronic kidney disease and NSAIDs	Changed wording (minor) of criterion title
Use With Caution (Table 4)	
Aspirin as primary prevention	Modified age, indication, rationale, and QE
Dabigatran	Modified rationale and recommendation
Prasugrel	Modified rationale
Clinically Important Drug-Drug Interactions (Table 5)	
The table title	Dropped "Non–anti-infective"
ACEIs/ARBs and hyperkalemia	Changed to renin-angiotensin system inhibitors
Combination of three or more CNS agents (antidepressants, antiepileptics, antipsychotics, benzodiazepines, and opioids)	Replaced individual criteria with a single criterion
Medications That Should Be Avoided or Have Their Dosage Reduced With Decreased Kidney Function (Table 6)	
Apixaban, dabigatran, edoxaban, and rivaroxaban	Revised CrCl at which action is required, rationale and recommendations to reflect current labeling, and CrCl exclusion parameters in clinical trials

Support Care Cancer. 2016 Apr;24(4):1831-40. doi: 10.1007/s00520-015-2970-8. Epub 2015 Oct 9.

Polypharmacy cut-points in older people with cancer: how many medications are too many?

Turner JP[1,2,3], Jamsen KM[4,5], Shakib S[6], Singhal N[7,8], Prowse R[9], Bell JS[4,10,5].

Author information

Abstract

PURPOSE: Polypharmacy is often defined as use of 'five-or-more-medications'. However, the optimal polypharmacy cut-point for predicting clinically important adverse events in older people with cancer is unclear. The aim was to determine the sensitivities and specificities of a range of polypharmacy cut-points in relation to a variety of adverse events in older people with cancer.

METHODS: Data on medication use, falls and frailty criteria were collected from 385 patients aged ≥70 years presenting to a medical oncology outpatient clinic. Receiver operating characteristic (ROC) curves were produced to examine sensitivities and specificities for varying definitions of polypharmacy in relation to exhaustion, falls, physical function, Karnofsky Performance Scale (KPS) and frailty. Sub-analyses were performed when stratifying by age, sex, comorbidity status and analgesic use.

RESULTS: Patients had a mean age of 76.7 years. Using Youden's index, the optimal polypharmacy cut-point was 6.5 medications for predicting frailty (specificity 67.0 %, sensitivity 70.0 %), physical function (80.2 %, 49.3 %) and KPS (69.8 %, 52.1 %), 5.5 for falls (59.2 %, 73.0 %) and 3.5 for exhaustion (43.4 %, 74.5 %). For polypharmacy defined as five-or-more-medications, the specificities and sensitivities were frailty (44.9 %, 77.5 %), physical function (58.0 %, 69.7 %), KPS (47.7 %, 69.4 %), falls (44.5 %, 75.7 %) and exhaustion (52.6 %, 64.1 %). The optimal polypharmacy cut-points were similar when the sample was stratified by age, sex, comorbidity status and analgesic use.

CONCLUSIONS: Our results suggest that no single polypharmacy cut-point is optimal for predicting multiple adverse events in older people with cancer. In this population, the common definition of five-or-more-medications is reasonable for identifying 'at-risk' patients for medication review.

10 steps for coping with a chronic condition

It pays to organize your approach to heart disease or any chronic medical problem.

Updated: March 16, 20

- **Manage your medications.** Remembering to take one pill a day is tough; managing 10 or more is daunting. Knowing about the drugs you take — why you take them, how best to take them, and what problems to watch out for — is as important as learning about your condition. Talking with your doctor, nurse, or a pharmacist can put drug information into perspective.

https://www.health.harvard.edu/staying-healthy/10-steps-for-coping-with-a-chronic-condition

Pharmacist-Led Medication Assessment and Deprescribing Intervention for Older Adults with Cancer and Polypharmacy: A Pilot Study

Of patient reported barriers to deprescribing, the most common concern was fear of return of symptoms or worsening of underlying condition being treated (60%). Other barriers included the patient's need to check with their primary care provider before deprescribing, feeling of physical dependence, and patient and caregiver confusion about medications.

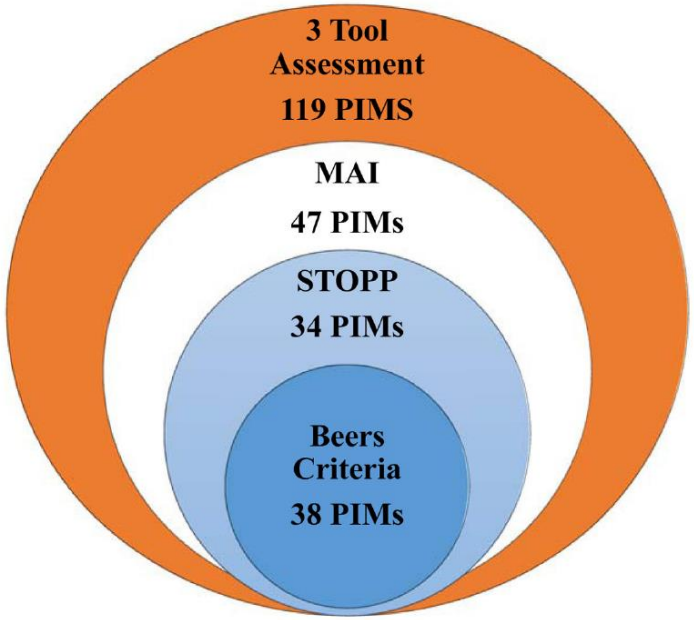

Fig 2.
Incidence of PIMs Identified by the Beers Criteria Compared With the 3 Tool Assessment

Characteristic	N=26
Age, mean years (range)	81 (65–92)
Distribution, years – n (%)	
• 65–74	9 (35)
• 75–84	7 (27)
• ≥85	10 (38)
Male, n (%)	14 (54)
Number of medications, mean (range)	12 (5–24)
ECOG score, mean (range)	2 (0–3)
Pharmacist time spent on intervention, mean (range)	30 (18–77)
Reason for referral to geriatric oncology clinic, n (%)	
• Decision for systemic cancer therapy	13 (50)
• Preoperative clearance	4 (15)
• Initial decision for surgery	4 (15)
• Goals of care assessment	3 (12)
• Cognitive impairment	2 (8)
Cancer type, n (%)	
• Colon	8 (31)
• Pancreatic	6 (23)
• Cholangiocarcinoma	3 (12)
• Leukemia/Myelodysplastic Syndrome	3 (12)
• Melanoma	2 (8)
• Lymphoma	2 (8)
• Multiple Myeloma	1 (4)
• Gastric	1 (4)

Table 3

Commonly Deprescribed Medication Classes

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

STOPP/START: version 2 (2015)

Medication Appropriate Index (MAI)

Medication Appropriateness Index

Checklist to aid prescribing in an elderly patient

- Is there a need for pharmacotherapy in this patient?
- Is this the optimal medicine for the specific clinical diagnosis in this patient?
- Will the medicine introduce unnecessary duplication with existing medicines in this patient?
- Is the dosage correct?
- Is the formulation suitable?
- Is the duration of therapy acceptable?
- Is the medicine likely to interact with existing medication?
- Is the medicine likely to affect, or be affected by, concurrent disease?
- Are the directions for use correct and feasible for this patient?

Rules for safe and effective prescribing in older patients

- Prescribe cautiously: your patient's symptoms may be amenable to non-pharmacological therapy
- Prescribe appropriately: use a checklist (see above) to make sure that the chosen medicine is appropriate for the individual patient under your care
- Start low, go slow: age-related changes may have affected your patient's ability to handle the medicine
- Review regularly: newly prescribed medicines may not be working; longterm medicines may no longer be safe or effective
- Limit the range of medicines you use in the older patient: this enables you to develop expertise in their usage
- Remember the risky medicines: e.g. diuretics, digoxin, anti-thrombotics, NSAIDs, CNS medicines, thyroxine

STOPFrail

Table 1. Final STOPPFrail criteria

STOPPFrail is a list of potentially inappropriate prescribing indicators designed to assist physicians with stopping such medications in older patients (≥65 years) who meet ALL of the criteria listed below:

(1) End-stage irreversible pathology
(2) Poor one year survival prognosis
(3) Severe functional impairment or severe cognitive impairment or both
(4) Symptom control is the priority rather than prevention of disease progression

The decision to prescribe/not prescribe medications to the patient, should also be influenced by the following issues:

(1) Risk of the medication outweighing the benefit
(2) Administration of the medication is challenging
(3) Monitoring of the medication effect is challenging
(4) Drug adherence/compliance is difficult

Section A: General

A1: Any drug that the patient persistently fails to take or tolerate despite adequate education and consideration of all appropriate formulations.
A2. Any drug without clear clinical indication.

Section B: Cardiovascular system

B1. Lipid lowering therapies (statins, ezetimibe, bile acid sequestrants, fibrates, nicotinic acid and acipimox)
These medications need to be prescribed for a long duration to be of benefit. For short-term use, the risk of ADEs outweighs the potential benefits [43–45]
B2. Alpha-blockers for hypertension
Stringent blood pressure control is not required in very frail older people. Alpha blockers in particular can cause marked vasodilatation, which can result in marked postural hypotension, falls and injuries [46]

Section C: Coagulation system

C1: Anti-platelets
Avoid anti-platelet agents for primary (as distinct from secondary) cardiovascular prevention (no evidence of benefit) [47]

Section D: Central Nervous System

D1. Neuroleptic antipsychotics
Aim to reduce dose and gradually 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) [48–52]
D2: Memantine
Discontinue and monitor in patients with moderate to severe dementia, unless memantine has clearly improved BPSD (specifically in frail patients who meet the criteria above) [53–56]

Section E: Gastrointestinal system

E1. Proton Pump Inhibitors
Proton Pump Inhibitors at full therapeutic dose ≥8/52, unless persistent dyspeptic symptoms at lower maintenance dose [57]
E2: H2 receptor antagonist
H2 receptor antagonist at full therapeutic dose for ≥8/52, unless persistent dyspeptic symptoms at lower maintenance dose [57]
E3. Gastrointestinal antispasmodics
Regular daily prescription of gastrointestinal antispasmodics agents unless the patient has frequent relapse of colic symptoms because of high risk of anti-cholinergic side effects [57]

Section F: Respiratory system

F1. Theophylline.
This drug has a narrow therapeutic index, requires monitoring of serum levels and interacts with other commonly prescribed drugs putting patients at an increased risk of ADEs [58–60]
F2. Leukotriene antagonists (Montelukast, Zafirlukast)
These drugs have no proven role in COPD, they are indicated only in asthma [61]

Section G: Musculoskeletal system

G1: Calcium supplementation
Unlikely to be of any benefit in the short term
G2: Anti-resorptive/bone anabolic drugs *FOR OSTEOPOROSIS* **(bisphosphonates, strontium, teriparatide, denosumab)**
Unlikely to be of any benefit in the short term
G3. SORMs for osteoporosis
Benefits unlikely to be achieved within 1 year, increased short–intermediate term risk of associated ADEs particularly venous thromboembolism and stroke [57]
G4. Long-term oral NSAIDs
Increased risk of side effects (peptic ulcer disease, bleeding, worsening heart failure, etc.) when taken regularly for ≥2 months [62–64]
G5. Long-term oral steroids
Increased risk of side effects (peptic ulcer disease, etc.) when taken regularly for ≥2 months. Consider careful dose reduction and gradual discontinuation [65]

Section H: Urogenital system

H1. 5-Alpha reductase inhibitors
No benefit with long-term urinary bladder catheterisation [66, 67]
H2. Alpha blockers
No benefit with long-term urinary bladder catheterisation [66, 67]
H3. Muscarinic antagonists
No benefit with long-term urinary bladder catheterisation, unless clear history of painful detrusor hyperactivity [66, 67]

Section I: Endocrine system

I1. Diabetic oral agents
Aim for monotherapy. Target of HbA1c < 8%/64 mmol/mol. Stringent glycaemic control is unnecessary [68]
I2. ACE-inhibitors for diabetes
Stop where prescribed only for prevention and treatment of diabetic nephropathy. There is no clear benefit in older people with advanced frailty with poor survival prognosis [69]
I3. Angiotensin receptor blockers
Stop where prescribed only for prevention and treatment of diabetic nephropathy. There is no clear benefit in older people with advanced frailty with poor survival prognosis [69]
I4. Systemic oestrogens for menopausal symptoms
Increases risk of stroke and VTE disease. Discontinue and only consider recommencing if recurrence of symptoms [57]

Section J: Miscellaneous

J1. Multi-vitamin combination supplements
Discontinue when prescribed for prophylaxis rather than treatment
J2. Nutritional supplements (other than vitamins)
Discontinue when prescribed for prophylaxis rather than treatment [70]
J3: Prophylactic antibiotics
No firm evidence for prophylactic antibiotics to prevent recurrent cellulitis or UTIs [71–73]

OncPal

Medication class	Medication	Considerations for limited benefit	Explanation
Blood and blood-forming organs	Aspirin	For primary prevention only.	Long-term benefits at population level. Little short or intermediate term risk of stopping (1). Drugs for primary prevention have, in general, no place in the treatment of end-of-life patients since the time-to-benefit usually exceeds life expectancy (2).
Cardiovascular system	Dyslipidaemia medications Statins Fibrates Ezetimibe	All indications.	Long-term benefits at population level. Little short or intermediate term risk of stopping (1).
	Antihypertensives ACE inhibitors Sartans Beta blockers Calcium channel blockers Thiazide Diuretics	If sole use is to reduce mild to moderate hypertension for secondary prevention of cardiovascular events or as management of stable coronary artery disease.[ab]	Long-term benefits at population level. Ongoing therapy unnecessary in most shortened life expectancy (1).
Musculo-skeletal system	Osteoporosis medications Bisphosphonates Raloxifene Strontium Denosumab	Except if used for the treatment of hypercalcaemia secondary to bone metastases.	Except if used for the treatment of hypercalcaemia secondary to bone metastases. Long-term benefits at population level. Little short or intermediate term risk of stopping (1).
Alimentary tract and metabolism	Peptic ulcer prophylaxis Proton pump inhibitors H2 antagonists	Lack of any medical history of gastrointestinal bleeding, peptic ulcer, gastritis, GORD or the concomitant use of anti-inflammatory agents including NSAIDs and steroids (3).	Ongoing therapy unnecessary in most shortened life expectancy (1).
Oral Hypoglycaemics Metformin Sulfonylureas Thiazolidinediones DPP-4 inhibitors GLP-1 analogues Acarbose	If sole use is to reduce mild hyperglycaemia for secondary prevention of diabetic associated events.[c]	Potential short-term complications outweigh benefit (1).	
Vitamins Minerals Complementary—alternative medicines	If not indicated to treat a low blood plasma concentration.	No evidence for effectiveness (4, 5).[d]	

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