Palliative care and deprescribing

Mirjam Crul | July 2022

no conflicts of interest


Content

Background of “deprescribing”
Deprescribing of common drug classes
Rules of thumb for pharmacists
Practical aids

Definition deprescribing

Deprescribing is the process of tapering or stopping drugs, aimed at minimizing polypharmacy and improving patient outcomes

Scott IA, Hilmer Sn, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. JAMA Intern Med 2015 ;175(5):827-834.

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Palliative care = multidisciplinary care

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Palliative team - role of the pharmacist

- NL: since 2012
- Query after 196 patients - 0 patients without medicines!
- 60% pharmaceutical intervention:
  - Starting a drug for symptom relief/complaints
  - Stopping a drug that is no longer useful
  - Optimizing sedation regimens (benzodiazepine-tolerant, addiction issues)
  - Wound/ulcer treatments
  - Reimbursement issues

Crul M, Oosterhof P. International Journal of Pharmacy Practice Volume 28, Issue 1, 1 Feb 2020, 92-96

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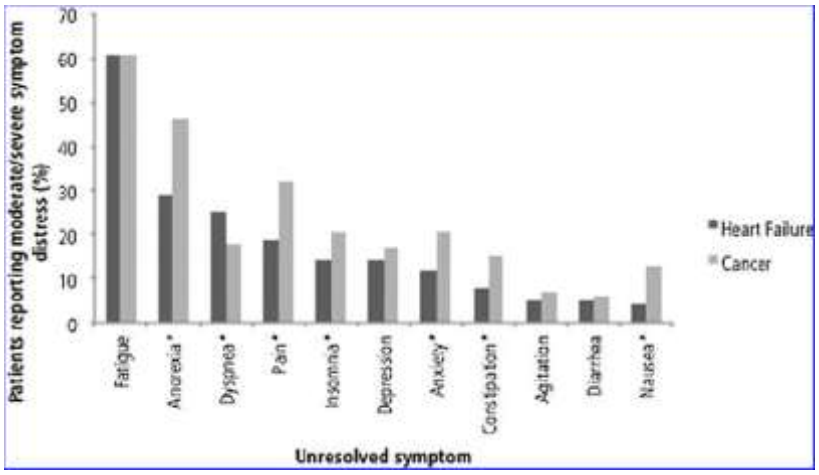
Symptoms in the palliative phase



Kavalieratos D, et al. Journal of palliative medicine. 17. 10.1089/jpm.2013.0526.

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Original Article

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

Lucas Morin, MS[1]; Adam Todd, MPharm, PhD[2]; Stephen Barclay, MA, FRCGP, MD[3]; Jonas W. Wastesson, PhD[1]; Johan Fastbom, MD, PhD[1], and Kristina Johnell, MPharm, PhD[1]

- Retrospective cohort research
- 151.201 patient >65 year who died of cancer in Sweden 2007-2013
- Drug use rises in the last year of life from average 7 to 10 drugs per patient
- Costs of prophylactic drugs in the last year of life around 10% of total drug costs (ca $220)

Morin L et al. Cancer; 125: 2309-2317

TABLE 2. Use of Preventive Drugs During the Last Year of Life Among Older Adults (Those Aged ≥65 Years) With Solid Cancers in Sweden, 2007 Through 2013

	Prevalence (N = 151,201)				
	12th Month Before Death	Last Month Before Death	Absolute Change	Continuation[b] Until the Final Month of Life	Initiation[c] During the Last Year of Life
	Percent	Percent	Percentage points (95% CI)[a]	Percent (95% CI)	Percent (95% CI)
Drugs used in diabetes	14.0%	14.9%	+0.9 (0.6 to 1.2)	87.3 (86.8 to 87.7)	3.6 (3.5 to 3.7)
Insulin and analogues	7.6%	10.0%	+2.4 (2.2 to 2.6)	89.3 (88.8 to 89.9)	4.0 (3.9 to 4.1)
Blood glucose-lowering drugs	8.7%	7.1%	-1.6 (-1.8 to -1.4)	68.2 (67.4 to 69.0)	1.8 (1.7 to 1.9)
Vitamins	8.2%	9.2%	+1.0 (0.8 to 1.2)	64.9 (64.1 to 65.7)	6.7 (6.6 to 6.8)
Mineral supplements	14.7%	19.2%	+4.5 (4.2 to 4.8)	68.4 (67.7 to 69.9)	14.2 (14.0 to 14.4)
Calcium	10.5%	11.1%	+0.6 (0.4 to 0.8)	65.7 (64.9 to 66.4)	6.5 (6.4 to 6.7)
Potassium	4.6%	7.8%	+3.2 (3.0 to 3.4)	64.5 (63.3 to 65.6)	6.8 (6.6 to 6.9)
Antithrombotic agents	46.6%	48.1%	+1.5 (1.1 to 1.9)	79.2 (78.9 to 79.5)	28.2 (27.9 to 28.5)
Vitamin K antagonists	7.7%	5.6%	-2.1 (-2.3 to -1.9)	47.6 (46.7 to 48.5)	3.8 (3.7 to 3.9)
Heparin group	2.7%	10.0%	+7.3 (7.1 to 7.5)	49.3 (47.8 to 51.9)	14.9 (14.6 to 15.9)
Platelet aggregation inhibitors	37.7%	36.2%	-1.5 (-1.8 to -1.2)	77.4 (77.1 to 77.8)	13.4 (13.2 to 13.6)
Drugs used in the treatment of hypertension	60.4%	60.1%	-0.3 (-0.6 to 0.0)	86.4 (86.2 to 86.7)	23.2 (22.9 to 23.6)
Low-ceiling diuretics	6.3%	5.2%	-1.1 (-1.3 to -0.9)	61.2 (60.2 to 62.1)	1.9 (1.8 to 1.9)
Potassium-sparing agents	7.3%	11.2%	+3.9 (3.7 to 4.1)	69.0 (68.1 to 69.9)	7.6 (7.5 to 7.8)
β-blocking agents	37.5%	38.2%	+0.7 (0.4 to 1.0)	82.9 (82.6 to 83.3)	13.3 (13.1 to 13.6)
Calcium channel blockers[d]	18.9%	15.9%	-3.0 (-3.3 to -2.7)	68.8 (68.2 to 69.3)	4.9 (4.7 to 5.7)
ACE inhibitors	20.3%	18.5%	-1.8 (-2.1 to -1.5)	71.8 (71.3 to 72.3)	6.6 (6.4 to 6.7)
Angiotensin II antagonists	11.7%	9.9%	-1.8 (-2.0 to -1.6)	71.3 (70.6 to 71.9)	2.4 (2.3 to 2.4)
Lipid modifying agents	21.5%	16.8%	-4.7 (-5.0 to -4.4)	65.0 (64.4 to 65.5)	5.4 (5.3 to 5.5)
HMG CoA reductase inhibitors	21.0%	16.3%	-4.7 (-5.0 to -4.4)	64.9 (64.4 to 65.4)	4.9 (4.7 to 5.6)
Bisphosphonates	4.2%	3.9%	-0.3 (-0.4 to -0.2)	56.6 (55.3 to 57.8)	2.8 (2.7 to 2.9)
Antianemic preparations	25.7%	30.4%	+4.7 (4.4 to 5.0)	79.7 (79.3 to 82.1)	17.6 (17.4 to 17.8)
Iron preparations	7.4%	11.0%	+3.6 (3.4 to 3.8)	55.8 (54.9 to 56.8)	11.1 (11.0 to 11.3)
Vitamin B12 and folic acid	21.0%	23.2%	+2.2 (1.9 to 2.5)	82.4 (82.0 to 82.8)	8.9 (8.7 to 9.1)

PIM = potentially inappropriate medication

Potentially inappropriate medication discontinued or changed based on pharmacists' recommendations in older end-stage cancer patients receiving palliative care: a cross-sectional study

- 50.9% of patients had 1 or more PIMs
- 28% discontinuation/change upon pharmacists intervention

Takahashi M et al. Annals Pall Med 2021; 10: 11301-11307

The potential for deprescribing in a palliative oncology patient population: a cross-sectional study

- 56% of patients had 1 or more PIMs
- Most common PIMs: antihypertensive drugs, PPIs, statins

Merendonk L et al. EJHP 2022; doi: 10.1136/ejhpharm-2021-003143.

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Effect of PIMs

Journal of the American Medical Directors Association

The Association of Potentially Inappropriate Medication at Older Age With Cardiovascular Events and Overall Mortality: A Systematic Review and Meta-Analysis of Cohort Studies

- Meta analysis including 13 trials
- Not specific for palliative setting
- Patients >60 years with ≥ 1 PIM: 1.6 fold chance of death

Muhlack et al. J Am Med Dir Assoc 2017; 18: 211-220

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Case -1-

Mr R, 66 years, 1.68 m, 45 kg

History

- 2019 T2N0 tongue base carcinoma RTx with curative intent until 7-2019; suspected relaps spring 2020 post-radiation effects
- Hypertension
- Diabetes mellitus type 2, not insulin dependent
- Diabetic retinopathy
- **Since 2015 3x per week haemodialysis** (complete anuria) result of acute tubular necrosis from Salmonella-enteritis

Consult question to palliative multidisciplinary team

Chronic haemodialysis patient with deteriorating performance status due to very poor nutritional state. Lack of energy, very poor QOL, wants to stop dialysis. Prognosis 6-12 months with dialysis. **Possible interventions to increase energy/appetite/independence?**

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Case -2-

- **Physical:** Fatigued, tired man. Complaints of fatigue alternating, good days manage to cook, to clean. Changing intake, is quickly full, food is becoming more and more difficult, but satisfied with dietary advice. The slow decline and less self-sufficiency is physically the biggest problem.
- **Psychological:** Realistic. Knows that stopping dialysis will mean a rapid decline, says not to be afraid of this.
- **Social:** Lives alone, twice a day home care to help with medication intake, does the general daily care himself. A lot of (telephone) contact with mother, she still lives independently, turns 92 at the end of the month. Also good contact with siblings, experiences a lot of support from them. No contact with a general practitioner, says he had little need for this.
- **Spiritual:** Roman Catholic, now no need for spiritual caregiver, knows that one can come by on dialysis, should he need it.

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Case -3-

Current medication

- amLODIPine 10 mg TABLET, 10 mg, oraal, 1dd
- buprenorfine (BUPRENORFINE) 20 mcg/uur pleister, 1 pleister, transdermaal, 1x per 3 dagen
- carbomeer (VIDISIC) 2 mg/g ooggel, 1 druppel, Beide ogen, 1dd AN
- epoetine beta injv wsp 10000ie=0,6ml (16.667ie/ml) neorecormon, 10.000 E, parenteraal, 1x per week maandag
- HYALURONZUUR/CARBOMEER (HYLAN) 0,15/0,15 mg/ml OOGDRUPPELS, 1 druppel, oculair, 6dd ZN
- ibuprofen 400 mg tablet, 400 mg, oraal, 3dd ZN
- IRON(III)OXIDEHYDROXIDESACCHAROSEZETMEELCOMPLEX (VELPHORO) 500 mg KAUWTABLET, 500 mg, oraal, 1dd
- lidocaïne/prilocaïne 25/25 mg/g crème, 100 g, cutaan, 3x per week
- LORAzepam 1 mg tablet, 1 mg, oraal, 1dd AN
- multivitamin voor dialyse (MULTIVITAMINE) capsule, 1 capsule, oraal, 1dd
- oxaZEPAM 10 mg tablet, 10 mg, oraal, 1dd ZN AN
- pantoprazol 40 mg tablet MSR, 40 mg, oraal, 1dd
- paracetamol 500 mg tablet, 1.000 mg, oraal, 3dd
- thiaMINE 25 mg tablet, 50 mg, oraal, 2dd bij de maaltijd

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Case -4-

- What would you suggest?
  - Start megestrol
  - Start dexamethasone
  - Start methylphenidate
  - Repeat dietetician consult

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Case -5-

MDT advice:

- Start methylphenidate 2 dd 5 mg
- Buddy from hospice for home consults
- Start ergotherapy/physiotherapy

One week later

- Methylphenidate had no effect (not even after dose increase to 3 dd 10 mg)
- Physio/ergo: hasn't had the energy to start that yet
- Now try Dexamethasone 1 dd 4 mg (effect should be noticeable after max 5 days)
- Has decided to postpone stopping dialysis, but says he does not want to make it to his next birthday, which is in 7 months time
- If stop dialysis – admission into hospice possible? Acquaintance and tours of hospices planned
- Can we decrease pill burden?
  - Prognosis when continuing dialysis: >6 months
  - Prognosis when stopping dialysis: 2-3 weeks

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Case-7-

Current medication

- amLODIPine 10 mg TABLET, 10 mg, oraal, 1dd
- buprenorfine (BUPRENORFINE) 20 mcg/uur pleister, 1 pleister, transdermaal, 1x per 3 dagen
- carbomeer (VIDISIC) 2 mg/g ooggel, 1 druppel, Beide ogen, 1dd AN
- epoetine beta injv wsp 10000ie=0,6ml (16.667ie/ml) neorecormon, 10.000 E, parenteraal, 1x per week maandag
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- multivitamine voor dialyse (MULTIVITAMINE) capsule, 1 capsule, oraal, 1dd
- oxaZEPAM 10 mg tablet, 10 mg, oraal, 1dd ZN AN
- pantoprazol 40 mg tablet MSR, 40 mg, oraal, 1dd
- paracetamol 500 mg tablet, 1.000 mg, oraal, 3dd
- thiaMINE 25 mg tablet, 50 mg, oraal, 2dd bij de maaltijd

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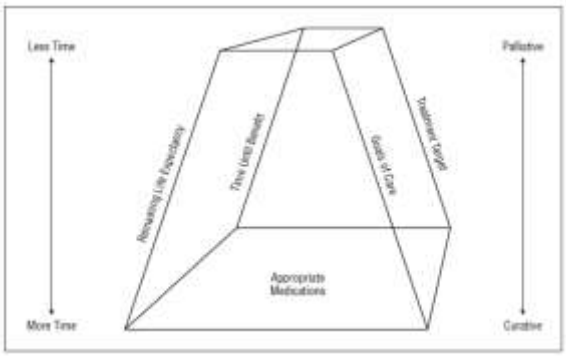
Deprescribing in practice

- Option 1: Holmes et al (Arch Intern Med 2006; 166: 605-609)
- Remaining life expectancy versus time to benefit
- Benefit versus risk



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Deprescribing in practice

Option 2 = Simple Rules of thumb

1. Reconsider primary prophylaxis at life expectancy <1 year
2. Reconsider secondary prophylaxis at life expectancy < 6 months
3. Medicines with potential side effects that lower QOL (e.g.: anticholinergic medicines in patients at high risk of delirium): risk-benefit assessment

Anti-thrombotics = exception

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Deprescribing example: statins

- The only prospective randomised clinical trial into deprescribing with hard outcome measures
- Patients with a life expectancy of 1 month to 1 year who have been taking a statin for at least 3 months
- Randomised into stopping versus continuing the statin
- Outcomes: death and QOL
- 381 patients
- No statistically significant difference in death rate after 60 days
- QOL stopping > continuing (7,11 versus 6,85 mcGill score)

Kutner JS. et al. JAMA Intern Med 2015 May;175(5):691-700.

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Deprescribing antihypertensive drugs

- Depending on indication?
- Mild hypertension
- Heart failure
- Rhythm disorders
  - Symptomatic versus Asymptomatic
- Depending on side effects?
  - Fatigue in beta-blockers
  - Hydration status in diuretics

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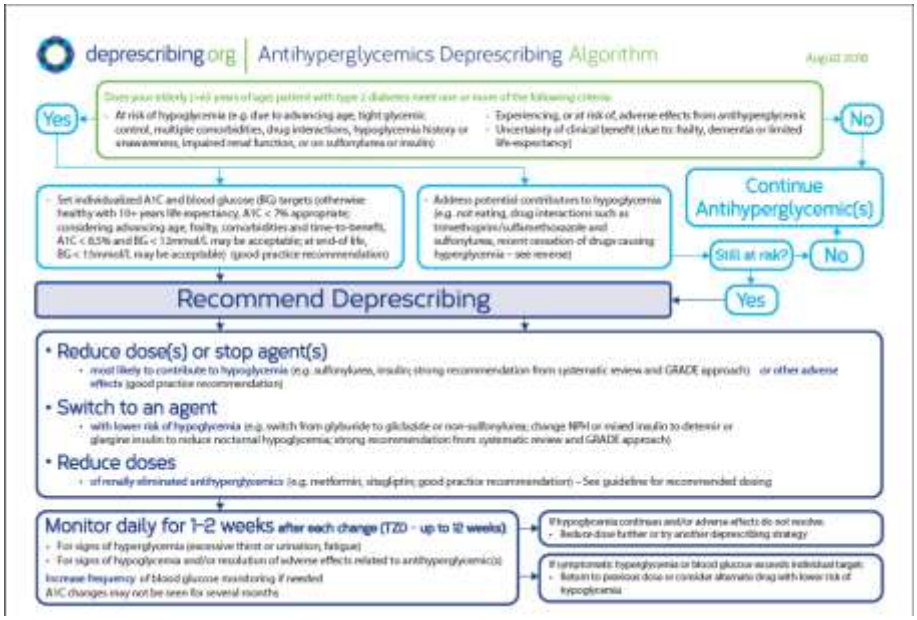
Deprescribing glucose lowering drugs



Deprescribing and antithrombotics

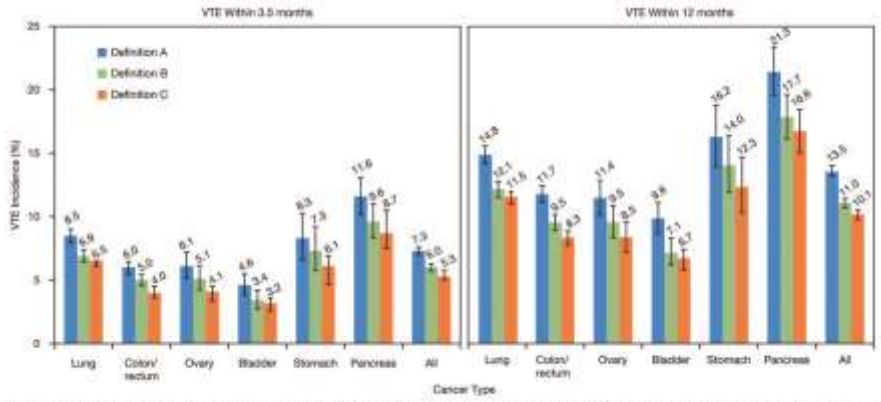


Figure 1. VTE incidence (95% confidence interval) by cancer site and VTE definition (see text) (A, B, and C) at 3.5 months and 12 months post-index. Data labels indicate point estimates. Abbreviation: VTE, venous thromboembolism.

Lyman et al. The Oncologist, 2013

Deprescribing and antithrombotics

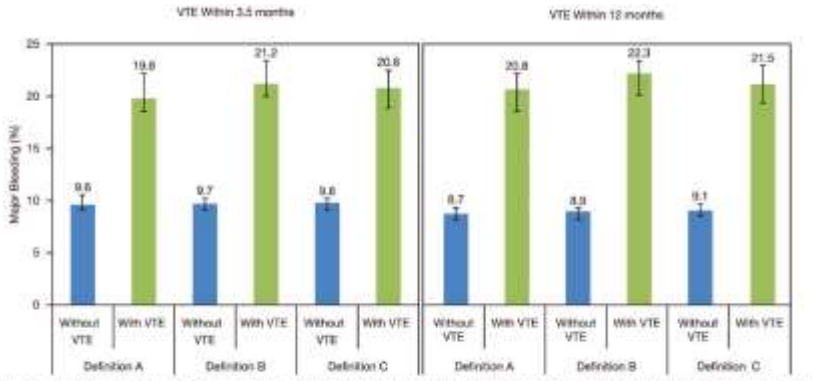


Figure 4. Incidence (95% confidence interval) of major bleeding (using the expanded International Society on Thrombosis and Haemostasis definition) within 12 months after starting chemotherapy (for definitions of VTE A, B, and C) in patients with and without VTE within 3.5 months and 12 months post-index. Data labels indicate point estimates. Abbreviation: VTE, venous thromboembolism.

Lyman et al. The Oncologist, 2013

Khorana score

Table 1. Khorana risk score

Patient characteristics	Risk score
Site of cancer	
Very high risk (stomach, pancreas)	2
High risk (lung, lymphoma, gynecologic, bladder, or testicular)	1
Prechemotherapy platelet count ≥350 x 10^9/L	1
Prechemotherapy hemoglobin level <100 g/L or use of red cell growth factors	1
Prechemotherapy leukocyte count >11 x 10^9/L	1
Body mass index ≥35 kg/m^2	1

- ≥ 2 means >9.6% probability of VTE within the first 6 months of chemotherapy
- Mobility not included….

Deprescribing and antithrombotics

- Until some years ago: cumarines/LMWH
- Now also DOACs
  - No regular blood monitoring of INR
- Risk of DVT versus bleeding should be made for each patient
- Take risk factors such as artificial valves, MI < 3month into account

Rule of thumb

If no recent DVT/PE/MI: stopping is possible with life expectancy <3 months

Huisman BAA, Semin Thromb Hemost. 2021; 47: 735-744

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Deprescribing – caveats

- Beers criteria do not always work in palliative patients
- Anticoagulation is a fine balance
- Life expectancy sometimes difficult to estimate (end stage COPD)
- Approach to patients in the processing phase or using an avoidance coping strategy

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Deprescribing - tools

- http://deprescribing.org
- http://medstopper.com
- http://rxisk.org
- https://www.primaryhealthtas.com.au/resources/deprescribing
- https://bpac.org.nz/BPJ/2010/April/stopguide.aspx
- Oncpal: Lindsay et al, J Support Care Cancer 2015; 23: 71-78

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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
	calcium (multiple brands) / Calcium / **prevention of deficiency**				Tapering not required		None
	metformin (Glucophage) / Metformin / **type 2 diabetes**		CALC / NNT		Tapering not required	symptoms of increased thirst/increased urination, re-measure A1c in 3 months, measure blood glucose only if high glucose symptoms occur/return	None
	pantoprazole (Protonix, Pantoloc) / 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

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Deprescribing in oncology

Table 1. The OncPal deprescribing guideline

Class of medication	Medication	Situations of limited benefit
Aspirin	Aspirin	Primary prevention
Lipid lowering medications	Statins	All indications
	Fibrates	
	Ezetimibe	
Blood pressure lowering medications	ACE inhibitors	Mild to moderate hypertension
	Sartans	Secondary prevention of cardiovascular events
	Beta blockers	Management of stable coronary artery disease
	Calcium channel blockers	
	Thiazide	
	Diuretics	
Anti-ulcer medications	Proton pump inhibitors	All indications unless recent history of gastrointestinal bleeding, peptic ulcer, gastritis, GORD, or the concomitant use of NSAIDs and steroids
	H2 antagonists	
Oral hypoglycaemics	Metformin	Mild hyperglycaemia (prevention of diabetic complications)
	Sulfonylureas	
	Thiazolidinediones	
	DPP-4 inhibitors	
	GLP-1 analogues	
	Acarbose	
Osteoporosis medications	Bisphosphonates	All indications except hypercalcaemia
	Raloxifene	
	Strontium	
	Denosumab	
Vitamins	n/a	All except treatment of low serum concentrations
Minerals	n/a	All except treatment of low serum concentrations
Complementary therapies	n/a	All indications

Adapted with permission from Lindsay J, Dooley M, Martin J, et al. The development and evaluation of an oncological palliative care deprescribing guideline: the 'OncPal deprescribing guideline'. Support Care Cancer 2015;23:71–8.

ACE = angiotensin converting enzyme; DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1; GORD = gastro-oesophageal reflux disease; NSAIDs = non-steroidal anti-inflammatory drugs; n/a = not applicable.

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The future?

Randomized Controlled Trial > JAMA Intern Med. 2022 Mar 1;182(3):265-273. doi: 10.1001/jamainternmed.2021.7425.

The MedSafer Study-Electronic Decision Support for Deprescribing in Hospitalized Older Adults: A Cluster Randomized Clinical Trial

Emily G McDonald [1 2 3], Peter E Wu [4], Babak Rashidi [5], Mamie Goodwin Wilson [6], Émilie Bortolussi-Courval [3], Anika Afique [7], Kiran Battu [8], Andre Bonnici [8], Sarah Elsayed [2], Allison Goodwin Wilson [10], Louise Papillon-Ferland [11], Louise Pilote [1 12], Sandra Porter [8], Johanna Murphy [13], Sydney B Ross [3 7], Jennifer Shiu [14], Robyn Tamblyn [12], Rachel Whitty [15], Jieqing Xu [16], Gabriel Fabreau [17], Taleem Haddad [18], Anita Palepu [6], Nadia Khan [6], Finlay A McAlister [19], James Downar [20], Allen R Huang [21], Thomas E MacMillan [22], ... Todd C Lee [2 3 24]

> Lancet Reg Health Eur. 2022 Apr 21;18:100390. doi: 10.1016/j.lanepe.2022.100390. eCollection 2022 Jul.

Efficacy of the eHealth application Oncokompas, facilitating incurably ill cancer patients to self-manage their palliative care needs: A randomized controlled trial

Anouk S Schuit [1 2], Karen Holtmaat [1 2], Birgit I Lissenberg-Witte [3], Simone E J Eerenstein [4], Josée M Zijlstra [5], Corien Eeltink [5], Annemarie Becker-Commissaris [6], Lia van Zuylen [7], Myra E van Linde [7], C Willemien Menke-van der Houven van Oordt [7], Dirkje W Sommeijer [7 8], Neil Verbeek [9], Koop Bosscha [10], Rishi Nandoe Tewarie [11], Robert-Jan Sedee [12], Remco de Bree [13], Alexander de Graeff [14], Filip de Vos [14], Pim Cuijpers [1], Irma M Verdonck-de Leeuw [1 2 4]

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Take home messages

- Palliative care should be multidisciplinary care with involvement of pharmacists
- Symptoms and complaints are often multifactorial and require a combined approach
- Deprescribing deserves attention
- Make time for the palliative patient