Support Care Cancer (2015) 23:71–78
DOI 10.1007/s00520-014-2322-0

ORIGINAL ARTICLE

The development and evaluation of an oncological palliative care deprescribing guideline: the 'OncPal deprescribing guideline'

Julian Lindsay · Michael Dooley · Jennifer Martin · Michael Fay · Alison Kearney · Mohsina Khatun · Michael Barras

Received: 4 March 2014 / Accepted: 11 June 2014 / Published online: 1 July 2014

Abstract
Purpose Current data suggests that potentially inappropriate medicines (PIMs) are common in palliative cancer patients; however, there is a lack of criteria to assist clinicians in identifying PIMs in these patients. The aims of this study were to design and validate a deprescribing guideline for palliative cancer patients and to undertake a descriptive analysis of the identified PIMs.
Methods This prospective, non-interventional cohort study consisted of four major stages: developing an 'OncPal Deprescribing Guideline' from current evidence, the prospective recruitment of consecutive palliative cancer inpatients with an estimated <6-month prognosis, the assessment of all medications to identify PIMs using both a panel of medical experts without access to the guideline as well as a Clinical Pharmacist independently using the OncPal Deprescribing Guideline and the evaluation of the guideline by testing concordance. Descriptive data on the incidence of PIMs identified were also assessed.
Results A total of 61 patients were recruited. The OncPal Deprescribing Guideline matched 94 % of 617 medicines to the expert panel with a Kappa value of 0.83 [95 % CI (0.76, 0.89)] demonstrating an 'outstanding' concordance. Forty-three (70 %) patients were taking at least one PIM, with 21.4 % of the total medicines assessed identified as PIMs. The medication-associated cost per patient/month was AUD$26.71.
Conclusion A guideline to assist in the de-escalation of inappropriate medications in palliative cancer patients was developed from current literature. The OncPal Deprescribing Guideline was successfully validated, demonstrating statistically significant concordance with an expert panel. We found that the incidence of PIMs was high in our patient group, demonstrating the potential benefits for the OncPal Deprescribing Guideline in clinical practice.

Keywords Deprescribing · De-prescribing · Drug therapy · Potentially inappropriate medications · Medical futility · Neoplasms · Cancer

J. Lindsay (✉)
Royal North Shore Hospital, New South Wales, Australia, Monash University, Victoria, Australia
e-mail: julianlindsay1@gmail.com

M. Dooley
Pharmacy Department, Alfred Health, Monash University, Victoria, Australia

J. Martin
Princess Alexandra Hospital, The University of Queensland Medical School, Queensland, Australia

M. Fay · A. Kearney · M. Barras
Royal Brisbane and Women's Hospital, The University of Queensland Medical School, Queensland, Australia

M. Khatun
Queensland Institute of Medical Research (QIMR), Queensland, Australia

Introduction

Cancer patients who have transitioned from curative intent chemotherapy or radiotherapy to palliative therapy often remain on medications with potentially harmful effects or no short-term benefit [1]. With estimated life expectancies commonly less than 6 months [1], when these patients transition to palliative therapy, many continue to be prescribed numerous medications for the secondary prevention of co-morbid diseases. When this transition is established, the focus of care should be on the patient's quality of life, including alleviating

suffering from cancer-related symptoms and treating short-term, acute medical illnesses [1]. In addition to a patient's potential adverse drug effects and pill burden, there are also financial impacts to patients, as well as the healthcare sector, particularly from the rising cost of preventative medicines.

Deprescribing unnecessary or 'futile' medications [2] in a palliative cancer patient can benefit the patient by reducing the associated cost, potential adverse effects and the burden of polypharmacy in the last months of life. However, the rationalization of drug therapy in this patient group is poorly established when compared to geriatric medicine. A recent literature review by our study group identified that potentially inappropriate medicines (PIMs) are common in palliative cancer patients; however, there is a lack of criteria to easily identify PIMs in this patient group [3]. Additionally, there are no studies measuring the patient outcomes of ceasing PIMs in palliative cancer patients. We concluded that further research was warranted to establish and implement clear guidelines for the identification of PIMs in palliative cancer patients.

The primary aim of this study was to develop a specialized oncological palliative deprescribing guideline that assists in identifying PIMs to aid in the rationalization of medicines in this patient group. We then aimed to validate the guideline by assessing the concordance with an expert medical panel and to undertake a descriptive analysis of identified PIMs in this cohort. The purpose of developing and validating the guideline was to assist clinicians in targeting PIMs to improve appropriate prescribing and rationalize medications. This will reduce adverse drug effects, improve quality of life and reduce medication costs. The guideline is not intended to replace or substitute the decision to prescribe, which requires complex clinical and ethical decisions in regard to each individual patient, but rather is intended to be a tool to highlight potential targets for deprescribing by the treating team. It is also imperative that a sensitive discussion should precede any deprescribing as the discontinuation of a long-standing medication may cause patient distress.

Patients and methods

Study design

This prospective, non-interventional cohort study consisted of four major stages: the development of an 'OncPal Deprescribing Guideline' from current evidence, a prospective chart review of consecutive palliative cancer inpatients with an estimated <6-month prognosis, an independent assessment of all medications to identify PIMs using both a panel of medical experts blinded to the guideline as well as a pharmacist independently using the Onc-Pal Deprescribing Guideline, and assessing the results of each patient's identified PIMs for concordance. The flow of the study is shown in Fig. 1.

Guideline development

The OncPal Deprescribing Guideline is shown in Appendix 1. The guideline was created by investigating the current literature for the de-escalation of medications by systematically reviewing each medication class according to the EphMRA (European Pharmaceutical Market Research Association) anatomical classification list [4]. As the guideline was developed as a tool to assist in the identification of medications suitable for discontinuation in palliative cancer patients, EphMRA medication classes not listed in the table have either demonstrated benefits in this population or the literature is lacking to guide a decision-making process.

Many guidelines currently in use in the geriatric population were originally developed using a Delphi consensus model, for example Beers Criteria in 1991 [5]. This study used a single-phase consensus model by sending the draft guideline to three palliative care consultants, three oncology consultants and three senior pharmacists for their feedback. Minor

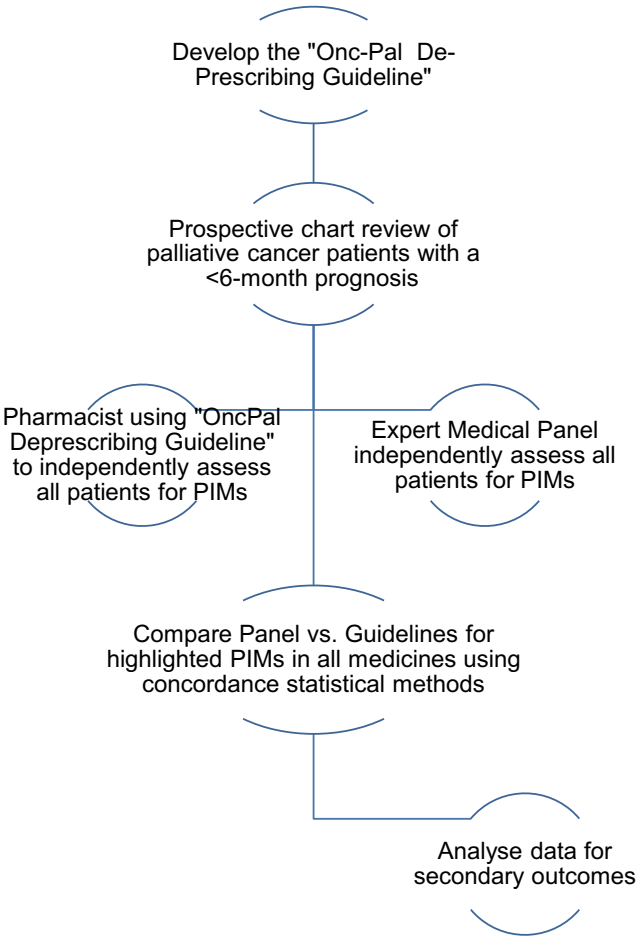

Fig. 1 Study design

adjustments to the draft were made when a suitable argument was presented.

Patient identification and data collection

The inpatient medical notes of consecutive cancer patients admitted to an Australian tertiary, 900-bed hospital from 01 March 2013 to 01 September 2013 were initially screened by the ward pharmacist using criteria of predicting factors for a life expectancy of less than 6 months. This process was based on the validated method for prognosis assessment, initially screening the inpatients for widespread metastatic disease, cerebral metastases, ascites, recurrent hypercalcaemia and/or the treating team's estimated prognosis. Following the initial screening, a palliative care consultant confirmed an accurate estimated prognosis of 6 months or less of life using current validated methods including a Karnofsky performance status, lab results and type of malignancy [6–8]. All data was scanned as a secure PDF document for the evaluation stage of the study. The number of participants required for the study was calculated using a sample size with a 90 % power to detect a Kappa value significantly different to 0 [9]. We aimed for a 90 % power of a two-tailed test for a Kappa value of at least 0.6, estimating the guideline would have greater than 90 % concordance with the expert panel. The calculated value was based on the assessment of 30 medicines. As individual drug classes needed to be tested, we estimated from the literature that the most common drugs would occur in 60 % of patients [10]. Therefore, greater than 50 participants were required.

Medication assessment

Each patient's data was assessed to highlight PIMs by an expert panel comprising of a radiation oncology consultant, medical consultant and palliative care consultant who used their knowledge and expertise to identify PIMs. Independently, blinded and in parallel, the patient's data was assessed by a clinical pharmacist, instructed to systematically use the OncPal Deprescribing Guideline to identify PIMs in accordance with its considerations only. If there was any ambiguity or clinical judgement was required, the medication was deemed 'not a PIM'.

Analysis and secondary outcomes

The results from the two independent assessments were compared (OncPal Deprescribing Guideline vs. expert panel) for each patient. To allow the guideline to be accurately assessed, medicines were divided into 24 drug classes as well as duplicates. Duplicates of the same drug class for an individual patient were documented separately to eliminate bias in the analysis. The equivalence/concordance of the guideline was measured by identifying each medication as a 'PIM' or 'not PIM' with a >90 % consistency with an expert panel. Assessments of the individual medicine classes were evaluated using two methods as follows: Cohen's Kappa values were used to make the conclusion about the interrater reliability to examine the agreement between expert medical panel and the guideline for the medicines associated with PIMs, and McNemar's chi^2 values were used to assess if there was symmetry in discordance, for individual drug classes. In addition, an overall Cohen's Kappa was calculated for the concordance of all assessed medicines. Descriptive statistics [11] were used to measure proportion of palliative cancer patients taking at least one PIM, medications and medication classes most frequently identified as PIMs suitable for discontinuation, patient demographics associated with PIMs such as analysis of variance (ANOVA) testing of patient's age and total number of medicines and potential drug avoidance cost of PIMs.

Results

Demographic

There were a total of 61 patients identified (Table 1). There were a total of 617 medicines assessed with a median (range) of 10 (4–21) medicines per patient. The median (range) age of patients was 66 years old (23–93), with a relatively even distribution of genders (34 males and 27 females). The median (range) Karnofsky performance status was 50 (20–80). The primary cancer site was relatively consistent with the general population [12, 13] shown in Table 2.

Guideline concordance

The proportion of the medicines that were assessed correctly using the OncPal Deprescribing Guideline compared to the expert panel was 94 % (580/617). Using Cohen's Kappa to measure the overall agreement, the concordance was Kappa 0.83 [95 % confidence interval (0.76, 0.89)]. The strength of

Table 1 Patient demographics

	Total	Min	Max	Male	Female
Patients	61			34	27
Medicines	617				
Median medicines per patient	10	4	21		
Median age	66	23	93		
Median Karnofsky score	50	20	80		

Table 2 Distribution of different cancers among the palliative cancer patients

Primary Cancer	Frequency	Proportion (%)	United States rate 2012 (%) [12]	Australia Rate 2010 (%) [13]
Breast	2	3	5	7
Colorectal	8	13	25	10
Endocrine	1	2	0.5	5
Gynae	10	16	5	N/A
Head and neck	9	15	1.5	N/A
Lung	16	26	28	18
Prostate	5	8	5	7
Sarcoma	1	2	0.2	N/A
Skin	6	10	2	5
Urothelial	3	5	5	N/A
Total	61	100.0		

this agreement is considered to be 'outstanding' (values of Kappa from 0.40 to 0.59 are considered moderate agreement, 0.60 to 0.79 substantial, and >0.80 outstanding agreement) [14]. Individual drug classes and the associated results are shown in Table 3.

Secondary outcomes

There were 132 PIMs identified by the expert panel, 70 % (43/61) of patients were found to have at least one PIM, with 21.4 % (132/617) of total medication found to be a PIM by the

Table 3 Concordance of medicines assessed by Guideline vs. Expert Panel

Medicine class	Total medicines (excluding duplicates)	Guideline accuracy (%)	Overall Kappa	Individual Kappa	Individual McNemar's test (p value)
Aspirin/anticoagulants	15	66.7	0.83	0.40	0.063
Dyslipidaemia	19	100.0		N/A	N/A
Antihypertensives	30	90.0		0.52	1.0
Oesteoporosis	4	100.0		N/A	N/A
Peptic ulcer prophylaxis	38	78.9		0.45	0.008
Oral hypoglycaemics	3	100.0		N/A	N/A
CAMs	20	95.0		0.64	1.0
Opioid analgesics	42	100.0			
Non-opioid analgesics	39	100.0			
Steroids	30	100.0			
NSAIDs	5	100.0			
Laxatives	35	100.0			
Benzodiazepines	21	100.0			
Nausea	33	100.0			
Antihistamines	2	100.0			
Antiepileptics/nerve pain	14	100.0			
Anti-infectives	11	100.0			
Antiarrhythmics	4	50.0			
Insulins	1	100.0			
Eye prep	4	100.0			
Prostate hyperplasia	5	100.0			
Neoplastic/immunomodulators	9	44.4			
Psycotropic drugs	25	100.0			
Inhaled respiratory	21	95.2			
Other	18	77.78			

CAMs complementary alternative medicines, *NSAIDs* non-steroidal anti-inflammatory drugs

expert panel. Medication classes most frequently identified as PIMs and suitable targets for discontinuation include antihypertensives (44 %, 27 patients), dyslipidaemic agents (31 %, 19 patients), and CAMs (complementary alternative medicines) (31 %, 19 patients). Table 4 shows the total and proportion of PIMs in each different drug class with 'duplicates' excluded for drugs in the same class per patient. For example, we found that there were 30 patients taking at least one antihypertensive, and 27 of these were assessed as PIMs.

We did not find any patient-specific factors associated with the incidence of PIMs. The results of the ANOVA showed that there were no significant differences (p value 0.316) in mean age of the patients who used more than 10 medicines and 10 or less medicines.

Potential drug avoidance cost of PIMs was calculated at AUD$26.71 per month per patient for the full cost value of medicines sourced from the Pharmaceutical Benefits Scheme (PBS) DPMQ section (Dispensed Price for Maximum Quantity) [15].

Table 4 Proportion of PIMs per drug class

Medicine class	Total medicines (excluding duplicates)	Total PIMs by panel (excluding duplicates)	Proportion of medicines assessed as PIM (excluding duplicates) (%)
Aspirin/anticoagulants	15	10	66.7
Dyslipidaemia	19	19	100.0
Antihypertensives	30	27	90.0
Osteoporosis	4	4	100.0
Peptic ulcer prophylaxis	38	5	13.2
Oral hypoglycaemics	3	3	100.0
CAMs	20	19	95.0
Opioid analgesics	42	0	0.0
Non-opioid analgesics	39	0	0.0
Steroids	30	0	0.0
NSAIDs	5	0	0.0
Laxatives	35	0	0.0
Benzodiazepines	21	0	0.0
Nausea	33	0	0.0
Antihistamines	2	0	0.0
Antiepileptics/nerve pain	14	0	0.0
Anti-infectives	11	0	0.0
Antiarrhythmics	4	2	50.0
Insulins	1	0	0.0
Eye Prep	4	0	0.0
Prostate hyperplasia	5	0	0.0
Neoplastic/ immunomodulators	9	5	55.6
Psychotropic drugs	25	0	0.0
Inhaled respiratory	21	1	4.8
Other	18	4	22.0

CAMs complementary alternative medicines, *NSAIDs* non-steroidal anti-inflammatory drugs

Discussion

Guideline validity

Deprescribing has potential benefits in patients who are taking medicines which have no benefit in regard to their prognosis [2]. We developed the OncPal Deprescribing Guideline as a tool to improve the rationalization of medicines in palliative cancer patients, with the aim to reduce adverse drug effects, pill burden and medicine-associated costs. We then tested the guidelines' validity, measuring its concordance with an expert panel.

The OncPal Deprescribing Guideline demonstrated its validity, correctly assessing 94 % of 617 medicines with an overall Kappa value of 0.83, an 'outstanding agreement'. For a more accurate assessment of the guideline, we demonstrated the concordance of each individual medicine class, using the proportion of accuracy and Kappa values, as well as McNemar values for the symmetry of discordance in medicine classes included in the guideline. When the guideline assessed the medicines with 100 % accuracy, it was not possible to use these tests.

All medicine classes in the guideline demonstrated a Kappa value of either 'moderate' or 'substantial' agreement. Aspirin/anticoagulation was the weakest class for the guideline, assessing medication accuracy 66.7 % of the time, with a Kappa value of 0.40. The McNemar values for anticoagulants and antihypertensives of 0.063 and 1.00 respectively, demonstrate that that there was symmetry in the discordance (>0.5). Analyzing this symmetry, we found that when the guideline incorrectly assessed this medicine class, the guideline evaluated the medicine as 'Not a PIM' and the Expert Panel as a 'PIM'. Therefore, on the 34 % of occasions that the guideline was incorrect, it never recommended ceasing anticoagulation when the expert panel thought it was necessary. This is a favourable result as it demonstrates a superior safety for the patient. Symmetry was also evident in the CAMs, as the guideline recommended to cease one medicine that the expert panel did not, as the patient was taking zinc for taste disturbances.

The only medicine class that was assessed incorrectly by the guideline in a majority of cases was neoplastic/immunomodulator oral anticancer treatments that were being administered to 9 patients (15 %). As this class of drug requires a complex, patient specific decision to evaluate the benefit of its continuation, it is a class that could not be included in the OncPal Deprescribing Guideline. The decision to de-escalate this medicine class needs to be evaluated on an individual basis by the treating physician.

Incidence of PIMs

Seventy percent of all patients in the study were found to be taking at least one PIM. This result was consistent with results from other studies, which ranged from 22–95 % [3]. This broad variance appears to be highly dependent on patient specific factors. The study with 95 % of patients, for example, was all lung cancer patients who potentially had more co-morbidities throughout their treatment and more PIMs in the late stages of their disease [16]. We identified a high proportion of patients taking at least one PIM, which could be attributed to the complexities of patients we identified. As we recruited only inpatients rather than ambulatory care patients seen in some trials, it is possible that our population had more co-morbidities that were being treated for secondary prevention.

The proportion of total medications that were identified as a PIM has not been previously described in the literature. Our finding of 21.4 % demonstrates the potential for the use of the guideline in this population, particularly as we found that this patient group takes an average of 10 medications, a pill burden figure consistent with the literature [16].

We found that the medications most frequently identified as PIMs by the expert panel included antihypertensives, dyslipidaemics and CAMs. This is partially consistent with the literature where 'statins' (a member of the dyslipidaemic drugs) and antihypertensives are commonly described, although proton pump inhibitors (PPIs) and antidiabetic medications have also been described [3]. A possible explanation for this discrepancy is that our study was at a single site, which showed a trend in some prescribing habits. We found a large proportion of patients taking corticosteroids, in which prophylactic PPIs were necessary. Also, the relatively small number of participants may contribute to the discrepancy as well.

Although the primary concern with PIMs is the pill burden and associated potential adverse drug effects the patients may experience, we demonstrated that there is also an associated cost to the patient and/or healthcare facility, often without benefit in efficacy, which also needs to be considered. This is a particularly import finding for healthcare facilities that specialize or have a large cohort of palliative cancer patients.

Challenges

During the assessment stage of the study, the expert panel encountered one particular challenge where an agreement could not be made on the assessment of particular medication classes. In this circumstance, the medicines involved were documented as 'not a PIM', for the purpose of the study. The classes included antidepressants, eye preparations and, when multiple opioids were presented, for example, oxycodone and methadone. To assist in the decision, the expert panel investigated the literature as this was their common practice in these scenarios. Unfortunately, there was no evidence found to support the decision. This challenge indicates a gap in knowledge, which we believe warrants future research.

Limitations

We have identified three limitations of this study: the population size, that it was conducted at a single centre and the theoretical nature of the assessment (non-interventional design).

Due to limited resources, it was only possible to collect data for 6 months. Although this was sufficient to assess the guideline's overall validity, a number of individual medication classes had too few examples to statistically analyse concordance. For example, although the guideline correctly assessed oral hypoglycaemics 100 % of the time, there were only three examples, and therefore, we were unable to test statistically.

As the study was conducted at a single centre, the secondary outcomes, such as the incidence of PIMs, may differ to other centres due to prescribing habits and cancer types treated by particular specialists.

Lastly, the study was only able to validate the guideline against expert clinical practice; however, further interventional studies are required to assess patient outcomes after the guideline is used to modify prescribing habits in these patients.

Conclusion

A contemporary deprescribing guideline to highlight medications as potential targets for discontinuation was developed from current literature and consensus from palliative care specialists. The 'OncPal Deprescribing Guideline' was successfully validated, demonstrating a statistically significant 'outstanding' concordance with an expert panel. The incidence of PIMs in palliative cancer patients was high, with 70 % taking at least one PIM, demonstrating the potential benefits for guidelines in clinical practice.

Conflict of interest The authors had no financial relationship with the organization in which the research was conducted and have full control of all primary data. We agree to allow the journal to review the data if requested.

Appendix 1 OncPal De-prescribing guideline

This guideline has been developed to assist in highlighting medications with a limited benefit that are suitable targets for discontinuation in palliative cancer patients. Medication classes not listed below have demonstrated benefits in this population or the literature is lacking to guide a decision-making process. If the foreseeable benefits of any medications do NOT outweigh the adverse

effects and/or associated risks, it is recommended to consider appropriate de-escalation

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]	

[a]Some short-term benefits need consideration—recommended to monitor blood pressure after discontinuation for symptomatic hypertension

[b]The use of these agents in symptom management for an underlying disease should be continued. For example, antihypertensives in heart failure or rate control in irregular heart rhythm (6)

[c]Some short-term benefits need consideration—recommended to monitor blood sugar levels infrequently after discontinuation for symptomatic hyperglycaemia. Aim for blood sugar levels below 20mmols/L (7)

[d]Some topical preparations may provide some benefits (5)

1. Stevenson J, Abernethy AP, Miller C, Currow DC. Managing co-morbidities in patients at the end of life. BMJ. 2004;329 (7471):909–12

2. Holmes HM, Hayley DC, Alexander GC, Sachs GA. Reconsidering medication appropriateness for patients late in life. Archives of internal medicine. 2006;166 (6):605–9

3. Fede A, Miranda M, Antonangelo D, Trevizan L, Schaffhausser H, Hamermesz B, et al. Use of unnecessary medications by patients with advanced cancer: cross-sectional survey. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2011;19 (9):1313–8

4. Macpherson H, Pipingas A, Pase MP. Multivitamin-multimineral supplementation and mortality: a meta-analysis of randomized controlled trials. The American journal of clinical nutrition. 2013;97 (2):437–44

5. Kassab S, Cummings M, Berkovitz S, van Haselen R, Fisher P. Homeopathic medicines for adverse effects of cancer treatments. The Cochrane database of systematic reviews. 2009 (2):CD004845

6. Goodlin SJ, Hauptman PJ, Arnold R, Grady K, Hershberger RE, Kutner J, et al. Consensus statement: palliative and supportive care in advanced heart failure. Journal of cardiac failure. 2004;10 (3):200–9

7. McCoubrie R, Jeffrey D, Paton C, Dawes L. Managing diabetes mellitus in patients with advanced cancer: a case note audit and guidelines. European journal of cancer care. 2005;14 (3):244–8

References

1. Fede A, Miranda M, Antonangelo D, Trevizan L, Schaffhausser H, Hamermesz B, Zimmermann C, Del Giglio A, Riechelmann RP (2011) Use of unnecessary medications by patients with advanced cancer: cross-sectional survey. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 19(9):1313–1318. doi:10.1007/s00520-010-0947-1
2. Jecker NS, Schneiderman LJ (1992) Futility and rationing. The American journal of medicine 92(2):189–196
3. Lindsay J, Dooley M, Martin J, Fay M, Kearney A, Barras M (2013) Reducing potentially inappropriate medications in palliative cancer patients: evidence to support deprescribing approaches. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. doi:10.1007/s00520-013-2098-7
4. Tollier C, Fusier I, Husson MC (2005) ATC and EphMRA classifications: evolution from 1996 to 2003 and comparative analysis. Therapie 60(1):47–56
5. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC (1991) Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine Archives of internal medicine 151(9):1825–1832
6. Hwang SS, Scott CB, Chang VT, Cogswell J, Srinivas S, Kasimis B (2004) Prediction of survival for advanced cancer patients by recursive partitioning analysis: role of Karnofsky performance status, quality of life, and symptom distress. Cancer Investig 22(5):678–687
7. Gwilliam B, Keeley V, Todd C, Gittins M, Roberts C, Kelly L, Barclay S, Stone PC (2011) Development of prognosis in palliative care study (PiPS) predictor models to improve prognostication in advanced cancer: prospective cohort study. Bmj 343:d4920. doi:10.1136/bmj.d4920
8. Tredan O, Ray-Coquard I, Chvetzoff G, Rebattu P, Bajard A, Chabaud S, Perol D, Saba C, Quiblier F, Blay JY, Bachelot T (2011) Validation of prognostic scores for survival in cancer patients beyond first-line therapy. BMC Cancer 11:95. doi:10.1186/1471-2407-11-95
9. Sim J, Wright C (2005) The Kappa statistic in reliability studies: use, interpretation, and sample size requirements. Phys Ther 85(3):257–268
10. Riechelmann RP, Krzyzanowska MK, Zimmermann C (2009) Futile medication use in terminally ill cancer patients. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 17(6):745–748. doi:10.1007/s00520-008-0541-y
11. De Muth JE (2009) Overview of biostatistics used in clinical research. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists 66(1):70–81. doi:10.2146/ajhp070006
12. Siegel R, Naishadham D, Jemal A (2013) Cancer statistics, 2013. CA: a cancer journal for clinicians 63(1):11–30. doi:10.3322/caac.21166
13. AIHW & AACR (2012) Cancer in Australia: an overview. Cancer series Canberra: AIHW 74 (70)
14. Landis JR, Koch GG (1977) The measurement of observer agreement for categorical data. Biometrics 33(1):159–174
15. Australian Government Department of Health (2013) Pharmaceutical benefits scheme. Commonwealth of Australia. http://www.pbs.gov.au/pbs/home. Accessed 12/10/2013
16. Todd A, Williamson S, Husband A, Baqir W, Mahony M (2013) Patients with advanced lung cancer: is there scope to discontinue inappropriate medication? Int J Clin Pharm 35(2):181–184. doi:10.1007/s11096-012-9731-2