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RESEARCH ARTICLE

Inappropriate prescribing in patients accessing specialist palliative day care services

A. Todd · H. Nazar · S. Pearson · I. Andrew · L. Baker · A. Husband

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Abstract *Background* For patients accessing specialist palliative care day services, medication is prescribed routinely to manage acute symptoms, treat long-term conditions or prevent adverse events associated with these conditions. As such, the pharmacotherapeutic burden for these patients is high and polypharmacy is common. Consequently, the risk of these patients developing drug-related toxicities through drug–drug interactions is exacerbated. Medication use in this group should, therefore, be evaluated regularly to align with achievable therapeutic outcomes considering remaining life expectancy. *Objective* To (1) assess the prevalence of inappropriate medication use; (2) identify potential drug–drug interactions; and, (3) determine how many potential drug–drug interactions could be prevented by discontinuing inappropriate medication. *Setting* A specialist tertiary care palliative care centre in Northern England serving a population of 330,000. *Main outcome measure* Prescribing of inappropriate medication. *Method* Medication histories for patients accessing a specialist palliative day care centre were established and a modified Delphi method was used to reach consensus of medication appropriateness. The Delphi method utilized a framework considering the following factors: remaining life expectancy of the patient, time until benefit of the treatment, goals of care and treatment targets. Potential drug interactions were established using drug interaction recognition software and categorised by their ability to cause harm. *Results* A total number of 132 patients were assessed during the study period who were prescribed 1,532 (mean = 12/patient) medications; 238 (16 %) were considered inappropriate in the context of limited life expectancy. The most common class of medications considered inappropriate were the statins, observed in 35 (27 %) patients. A total of 267 potential drug–drug interactions were identified; 112 were clinically significant and 155 were not considered clinically significant. Discontinuation of inappropriate medication would reduce the total number of medications taken to 1,294 (mean = 10/patient) and prevent 31 clinically significant potential drug–drug interactions. *Conclusion* Patients accessing specialist palliative day care services take many inappropriate medications. These medications not only increase the pharmacotherapeutic burden for the patient but they also contribute to potential drug–drug interactions. These patients should have their medication reviewed in the context of life limiting illness aligned with achievable therapeutic outcomes.

Keywords Drug interactions · Inappropriate prescribing · Life expectancy · Medication review · Palliative care

A. Todd (✉) · A. Husband
Division of Pharmacy, School of Medicine, Pharmacy and Health, Durham University, Stockon-on-Tees, UK
e-mail: adam.todd@durham.ac.uk

H. Nazar
Department of Pharmacy, Health and Well-being, Faculty of Applied Science, University of Sunderland, Sunderland, UK

S. Pearson
Faculty of Pharmacy and School of Public Health, The University of Sydney, Sydney, Australia

I. Andrew · L. Baker
St Benedict's Hospice and Centre for Specialist Palliative Care, Ryhope, Sunderland, UK

Impacts on practice

- Careful therapeutic planning is essential for the management of patients with limited life expectancy in the context of original goals of treatment;

- Clear guidelines are needed on discontinuing inappropriate medication in patients with limited life expectancy; and,
- Evidence-based approaches to discontinuation of medication for patients with limited life expectancy may contribute to simpler, safer and more appropriate treatment regimens.

Introduction

Patients with limited life expectancy experience significant symptom burden associated with their disease [1]. These patients may require specialist care—including the initiation of pharmacotherapy—delivered by a palliative care team [2]. In addition to this care, patients also routinely use medication to treat long-term conditions or medication to prevent adverse events associated with these conditions. Consequently, the pharmacotherapeutic burden for these patients is high and polypharmacy common [3]. This can be problematic as the time until benefit of preventative medication (typically months to years) can extend beyond patient life expectancy, raising questions over the risk: benefit ratio; patients taking five or more medications per day are more likely to become non-adherent; [4] and, as these patients have changing pharmacodynamic and pharmacokinetic parameters, the risks of developing drug-related toxicities through drug–drug interactions is increased [5, 6]. In view of these issues, the rational use of medication in patients with incurable illness has recently been highlighted and discussed within the medical community [7, 8].

Medication use should, therefore, be evaluated regularly to align with achievable therapeutic outcomes considering limited life expectancy. However, there is a growing body of evidence suggesting inappropriate prescribing for patients with limited life expectancy [9]. Previous work has shown that patients admitted for hospice care were using many inappropriate medications in view of their life limiting diagnosis [10] but, in order to establish the true extent of inappropriate medication use among patients accessing specialist palliative care services, it is essential to include day care patients, as the majority of such services are accessed in this way [11].

In a cohort of day care patients attending a specialist palliative care centre this study seeks to (1) assess the prevalence of inappropriate medication use; (2) identify potential drug–drug interactions using electronic drug interaction software; and, (3) determine how many potential drug interactions could be prevented by discontinuing inappropriate medication.

Methods

Setting

A specialist tertiary care palliative care centre in Northern England serving a population of 330,000. Approximately, 2,000 patients are referred for specialist palliative care each year including inpatient services, home visits from specialist palliative care community nurses, lymphoedema clinics and a day care centre. Of the patients referred to the specialist palliative care centre, around 300 patients access the day care centre per year.

Study design

This was a prospective cohort study of all day care patients attending a specialist palliative care centre in the period September 2012 until January 2013.

Inclusion criteria

Patients were included in the study if they had evidence of taking at least one prescribed medication; the study assessed both medications prescribed acutely (e.g. a course of antibiotics) and chronically (e.g. antihypertensives). The study focused exclusively on medications prescribed by healthcare practitioners. We did not explore the use of over-the-counter medication.

Data collection

As part of the normal provision for day care patients, a paper copy of their electronic medical record is obtained from their GP each time they attend the palliative care centre to ensure the most up-to-date information is used. For each day care patient, demographic details, medical history and medication lists were extracted from the paper copy of the medical record. In terms of medication, we extracted information on the type of medication, formulation, indication, dose, and how long it had been prescribed.

Study outcomes

1. Prevalence of inappropriate medications in day care patients attending a specialist palliative care centre;
2. the number of potential drug–drug interactions; and,
3. the number of potential drug–drug interactions that could be prevented by discontinuing inappropriate medication.

Medication appropriateness

We used a modified Delphi process [12] to reach consensus about medication appropriateness based on the conceptual

framework described by Holmes and colleagues for patients with limited life expectancy [13]. Our panel comprised ten clinical pharmacists and five palliative medicine consultants. All panel members were experienced practitioners in palliative care and were either working directly at the specialist palliative care centre or working in centres within the study region. Among those approached to be part of the consensus panel, 7 clinical pharmacists (mean years qualified 15 years; range 5–28) and 3 consultants in palliative medicine (mean years qualified 26 years; range 17–39) agreed to take part. Before the survey was undertaken, the panel received a recently published literature review regarding medication use in patients with limited life expectancy [9] and the Holmes and colleagues conceptual framework to guide their decision-making [13]. According to the framework, the following factors were considered when determining medication appropriateness: patients estimated life expectancy, time until benefit of treatment, goals of care and treatment targets.

Our modified Delphi process comprised of 3 stages:

1. All panel members received a structured questionnaire by e-mail containing a list of medications, alongside the specific indication for each one and were required to rank each one as inappropriate or appropriate ($n = 247$ medications).
2. Each panel member was then asked to review their choices based upon an anonymous summary of other panel members' responses.
3. A face-to-face meeting was then held with panel members to discuss the medications ranked as inappropriate from step 2. During the meeting, the patient's life limiting illness, expected remaining life expectancy, dosage of the medication and co-morbidities were considered to help determine the final decision on whether to rank the medication as inappropriate.

During the process no patient identifiable details were provided to panel members. Consensus for medication inappropriateness was defined according to agreement of seven of the ten respondents in line with previous Delphi processes [14].

Potential drug–drug interactions

For each patient, medications were manually entered into the drug interaction software, Proscript [15], which identified potential drug interactions and categorised them as either clinically significant or not. Clinically significant interactions were then manually sub-classified independently by two clinical pharmacists (AT and AH) as moderately significant or severe, based upon previous literature for categorising drug interactions that considered: if the drug interaction is likely to result in hospitalisation; if it is reversible or irreversible; and, if any treatment would be required to manage the drug interaction [16]. Stockley's drug interactions [17] and the electronic summary of product characteristics (SPCs) [18] were the data sources used. If agreement was not reached by AT and AH, a third clinical pharmacist (IA) was asked to review the data and make a final decision.

Statistical analysis

This was a descriptive study. We calculated the means, standard deviations, or percentages for outcomes as appropriate using Microsoft Excel. We used forest plots to graphically represent selected outcomes using the metaphor package in the statistical programme, R.

Ethical issues

This study was certified for ethical approval by the research team (HN) in accordance with University of Sunderland Ethics Committee. The research team was advised that National Health Service (NHS) ethics approval was not required and the work was registered with the Trust as a baseline audit. All patient data used in this study were handled and processed in accordance with NHS best practice and Caldicott recommendations.

Results

Cohort characteristics

During the study period, 132 day patients accessed the specialist palliative care centre; all patients met the inclusion criteria. The mean age was 70 years (range 26–94) and 68 (52 %) were male. The most common life limiting illness was cancer (108 patients, 82 %), then, end-stage chronic obstructive pulmonary disease (COPD) (11 patients, 8 %), followed by end-stage congestive heart failure (8 patients, 6 %) and Parkinson's disease (5 patients, 4 %).

Prevalence of inappropriate medications

The total number of medications prescribed for the cohort was 1,532 (mean per patient, 12; range 1–21); the average number of prescribed medications was 10 (cancer patients), 10 (Parkinson's Disease patients), 13 (COPD patients) and 14 (end-stage heart failure patients). Of the 1,532 medicines assessed for appropriateness, 238 (16 %) were considered to be inappropriate in the context of limited life expectancy; 92 (70 %) patients were considered to be

Table 1 Inappropriate medication identified in day care patients

Medication	Number of patients
Statins	35
Mineral supplements	32
Aspirin	27
ACE inhibitors	26
Beta-blockers	25
Bisphosphonates	15
Quinine sulphate	14
Vitamins supplements	12
Calcium channel blockers	11
A2RBs	8
Clopidogrel	7
Thiazide diuretics	7
Ezetimbe	7
Betahistine	1
Colestyramine	1
Didronal PMO	1
Doxazosin	6
Fenofibrate	1
Moxonidine	1
Thiamine	1

ACE angiotensin converting enzyme, *A2RBs* angiotensin II receptor antagonists

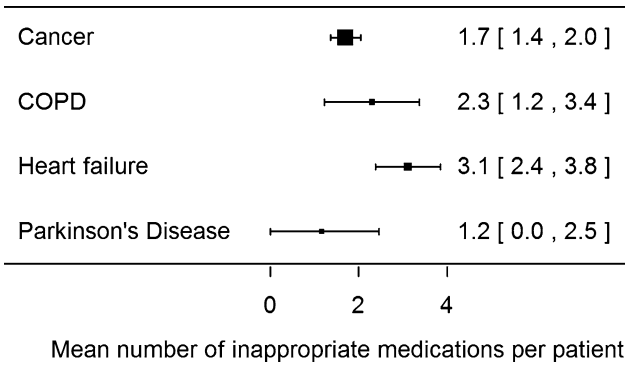

Fig. 1 Mean and confidence intervals of inappropriate medications per patient according to life limiting illness

taking at least one inappropriate medication: 30 patients (22 %) were taking one inappropriate medication; 21 patients (16 %) were taking two; 14 patients (11 %) were taking three; 14 (11 %) patients were taking four; and, 13 patients (10 %) were taking more than four. Statins were the most common 'inappropriate' therapeutic group (35 patients, 27 %) followed by mineral supplements (32 patients, 24 %) and aspirin when used for antiplatelet therapy (27 patients, 20 %), Table 1. The average number of 'inappropriate' medications ranged from 1 (patients with

Table 2 Moderately significant potential drug interactions identified in hospice day patients

Moderate drug interactions identified	Description	Number of patients
ACE inhibitors and loop diuretics	Increased risk of severe hypotension (including dizziness, lightheadedness and fainting)	19
ACE inhibitors and thiazide diuretics	Increased risk of severe hypotension (including dizziness, lightheadedness and fainting)	4
Angiotensin II receptor antagonists and loop diuretics	Increased risk of severe hypotension (including dizziness, lightheadedness and fainting)	4
Angiotensin II receptor antagonists and thiazide diuretics	Increased risk of severe hypotension (including dizziness, lightheadedness and fainting)	2
Allopurinol and warfarin	Increased anticoagulant effect, possibly increasing the risk of bleeding	1
Alpha blockers and ACE inhibitors	Increased risk of severe hypotension (including dizziness, lightheadedness and fainting)	1
Alpha blockers and beta-blockers	Increased risk of severe hypotension (including dizziness, lightheadedness and fainting)	1
Alpha blockers and loop diuretics	Increased risk of severe hypotension (including dizziness, lightheadedness and fainting)	4
Amitriptyline and citalopram	Increased levels of amitriptyline	3
Amitriptyline and warfarin	Increased anticoagulant effect, possibly increasing the risk of bleeding	2
Carbamazepine and dexamethasone	Accelerated metabolism of dexamethasone	1
Chlorphenamine and morphine	Increased sedation/drowsiness	2
Citalopram and warfarin	Increased anticoagulant effect, possibly increasing the risk of bleeding	3
Clopidogrel and omeprazole	Reduced antiplatelet effect of clopidogrel	2
Clopidogrel and fluoxetine	Reduced antiplatelet effect of clopidogrel	1
Cyclizine and amitriptyline	Increased risk of sedation/ drowsiness	1
Cyclizine and clomipramine	Increased risk of sedation/ drowsiness	1
Cyclizine and opioid analgesics	Increased risk of sedation/ drowsiness	21

Table 2 continued

Moderate drug interactions identified	Description	Number of patients
Dexamethasone and warfarin	Increased anticoagulant effect, possibly increasing the risk of bleeding	1
Gabapentin and haloperidol	Increased risk of sedation/ drowsiness	1
Gabapentin and mirtazapine	Increased risk of sedation/ drowsiness	2
Gabapentin and SSRIs	Increased risk of sedation/ drowsiness	3
Gabapentin and TCAs	Increased risk of sedation/ drowsiness	3
Gabapentin and quetiapine	Increased risk of sedation/ drowsiness	1
Haloperidol and tramadol	Increased risk of convulsions	1
Lansoprazole and phenytoin	Possible increased risk of phenytoin toxicity	1
Lansoprazole and theophylline	Possible increase in theophylline metabolism reducing theophylline levels	1
Lansoprazole and warfarin	Increased anticoagulant effect, possibly increasing the risk of bleeding	1
Levothyroxine and warfarin	Increased anticoagulant effect, possibly increasing the risk of bleeding	2
Simvastatin and warfarin	Increased anticoagulant effect, possibly increasing the risk of bleeding	2

SSRIs selective serotonin re-uptake inhibitors, *TCAs* tricyclic antidepressants

Parkinson's disease) and 3 (patients with heart failure), Fig. 1. The most common 'inappropriate' medications by disease state were statins in cancer (30 patients, 28 %), calcium supplements in end-stage congestive heart failure (3 patients, 38 %), aspirin in end-stage COPD (5 patients, 45 %) and statins in Parkinson's disease (2 patients, 40 %).

Potential drug–drug interactions

The drug interaction software identified 267 potential drug interactions, categorising 112 as clinically significant and 155 as not clinically significant. Among those categorised as significant, 92 were further sub-classified as moderate (Table 2) while 20 were considered severe (Table 3); all severe drug interactions had the potential to result in hospitalisation, irreversible harm or death. At least one potential drug interaction was identified in 85 patients (64 %). The average number of potential drug interactions observed was between 1 (COPD patients) and 4 (heart failure patients), Fig. 2.

Table 3 Severe potential drug interactions identified in hospice day patients

Severe Drug Interactions Identified	Description	Number of patients
Amisulpride and furosemide	Increased risk of prolongation of the QT interval resulting in ventricular tachycardia	1
Amlodipine and simvastatin (>20 mg daily)	Increased risk of myopathy and rhabdomyolysis	4
Aspirin and ibuprofen	Increased risk of bleeding and haemorrhage	2
Candesartan and spironolactone	Increased risk of developing severe hyperkalaemia	1
Clopidogrel and warfarin	Increased risk of bleeding and haemorrhage	1
Dexamethasone and methotrexate	Increased risk of acute hepatotoxicity	1
Diclofenac and fluoxetine	Increased risk of bleeding and haemorrhage	1
Digoxin and bendroflumethiazide	Increased risk of digoxin toxicity through loss of potassium	1
Digoxin and bumetanide	Increased risk of digoxin toxicity through loss of potassium	1
Digoxin and furosemide	Increased risk of digoxin toxicity through loss of potassium	4
Fenofibrate and simvastatin	Increased risk of myopathy and rhabdomyolysis	1
Haloperidol and quinine sulphate	Increased risk of prolongation of the QT interval resulting in ventricular tachycardia	1
Lisinopril and spironolactone	Increased risk of developing severe hyperkalaemia	1

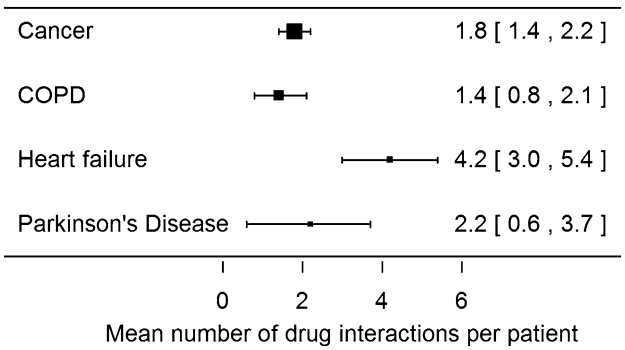

Fig. 2 Mean and confidence intervals of potential drug interactions according to life limiting illness

Drug–drug interactions prevented

Discontinuation of inappropriate medication would reduce the mean number of medications to 10 per patient and prevent 57 interactions considered not clinically significant plus 33 moderate and 12 severe drug interactions. Among patients identified as being subject to a potential drug interaction, discontinuing inappropriate medication would prevent at least one drug interaction in 46 patients, while 21 of these patients would have all potential drug interactions prevented.

Severe drug interactions that could be prevented by discontinuing inappropriate medication include:

- Simvastatin (>20 mg daily) and amlodipine,
- Haloperidol and quinine sulphate,
- Lisinopril and spironolactone,
- Ibuprofen and aspirin (<300 mg),
- Clopidogrel and warfarin,
- Simvastatin and fenofibrate,
- Candesartan and spironolactone,
- Digoxin and bendroflumethiazide.

Discussion

Our results show that the pharmacotherapeutic burden is high and polypharmacy is common amongst our cohort of patients accessing specialist palliative day care services. The majority of patients were prescribed at least one inappropriate medication, contributing to potential drug–drug interactions and increasing the risk of patients developing drug-related toxicies. Discontinuation of inappropriate medication would reduce the pharmacotherapeutic burden amongst this patient group, decrease potential drug–drug interactions and, minimise the probability of developing drug-related toxicities.

Our findings build upon our previous work that demonstrated patients with advanced lung cancer take many inappropriate medications—some of which can potentially interact with medication resulting in negative outcomes for patients [19]. Several other studies have also reported inappropriate medication use amongst patients with limited life expectancy [20, 21]. These studies, however, have focused primarily upon patients with advanced cancer; for example, Fede and colleagues accessed the medication history of 87 patients with terminal cancer and concluded that 21 were taking at least one unnecessary medication in view of their life expectancy [21]. Our data suggest that other patient groups with limited life expectancy also use inappropriate medication. Indeed, given the mean number of inappropriate medications and potential drug–drug interactions were highest in patients with end-stage heart failure, a larger study examining appropriate medication use in this patient group is warranted.

Previous work has demonstrated that the prevalence of potential drug–drug interactions is high among cancer patients [16, 22]. Our work supports these findings and shows potential drug–drug interactions are common amongst other patients with life limiting illness. We acknowledge that many of the potential drug–drug interactions identified in this study are based on drug combinations frequently used in the management of long-term conditions (e.g. angiotensin II receptor antagonists and spironolactone in heart failure) or are routinely encountered in palliative care (e.g. a strong opioid and cyclizine) but we believe that, due to the unique and dynamic pharmacokinetic parameters of our patient cohort (e.g. declining renal function), the risk of developing toxicity from drug–drug interactions is heightened. As such, we believe that potential drug–drug interactions should always be considered in the decision making as part of the wider prescribing process—especially in patients with limited life expectancy. The two most commonly identified severe potential drug interactions in our study were simvastatin (>20 mg) and amlodipine; and, digoxin and furosemide. The interaction between simvastatin and amlodipine increases the peak concentration (C_{max}) and the area under the curve (AUC) of simvastatin and, consequently, increases the risk of developing myopathy and rhabdomyolysis [23]; recent recommendations suggest to limit the dose of simvastatin to 20 mg/day when co-prescribed with amlodipine [24]. The interaction identified between digoxin and furosemide is, in comparison to the simvastatin and amlodipine interaction, more established. Indeed, furosemide can cause hypokalamia, which, in turn, increases the toxicity of digoxin. The mechanism of action is still being debated but, it is believed that furosemide exacerbates the loss of potassium ions from cardiac cells and, as digoxin inhibits the sodium–potassium ATP-ase in cardiac tissue, it increases the activity of digoxin [25]. This drug interaction is well documented and, consequently, patients are often given a reduced dose of digoxin to account for the effect of furosemide (or indeed any other potassium-depleting diuretic) [26]. However, as patients with limited life expectancy have constantly changing pharmacokinetic and pharmacodynamic parameters—with particular emphasis on declining renal function [27]—it is very difficult to accurately and continually account for these changes when calculating doses for such patients. As digoxin is predominantly excreted unchanged by the renal system, its use should always be closely monitored in patients with limited life expectancy—especially if used in combination with a potassium depleting diuretic such as furosemide.

To minimise inappropriate prescribing and polypharmacy, a number of tools have been developed to assist

clinicans in their decision-making [28]. For example, the Beers criteria [29], the Medication Appropriateness Index [30] and the Screening Tool of Older Persons' Potentially Inappropriate (STOPP) criteria [31] are all used in clinical practice to identify inappropriate medication, with a view to minimising polypharmacy. One limitation of these criteria is that they focus entirely on elderly patients and not necessarily those who have a limited life expectancy. This is problematic for several reasons; firstly, not every patient with limited life expectancy is elderly; this was observed in our study with several patients <65 years old (the youngest patient in our cohort was 26 years old). Secondly, many medications commonly used in a palliative care setting to treat acute symptoms associated with the life limiting illness are considered inappropriate according to these criteria e.g. lorazepam, frequently used to treat anxiety and breathlessness, is, according to the Beers criteria, inappropriate. In view of these limitations, Holmes and colleagues have developed a conceptual framework that is specific to patients with limited life expectancy [13]. This framework was successfully employed in this study but, is highly conceptual and does not necessarily lend itself to application within a busy clinical environment. Further guidance is thus required to assist prescribers with their decision-making for reviewing the medications of patients with limited life expectancy.

Within our cohort of patients, statins were the most commonly prescribed medications considered inappropriate. Statins are indicated for primary and secondary prevention of cardio- and cerebrovascular events and are used extensively throughout the world. Indeed, their efficacy in reducing cardiovascular events and mortality after an acute coronary syndrome, as well as the reduction of major cardiovascular events in people with established risk factors is well documented [32–34]. The time until benefit of the statins is variable depending on type and dose, but ranges from 6 months to 2 years for prevention of cardiovascular events and approximately 2–3 years for the prevention of cerebrovascular events [35]. Similarly, other common medication identified as inappropriate in this project, such as aspirin and calcium supplements, also have time until benefit of several years [36, 37]. Previous studies have explored statin use in limited life expectancy and have shown that, despite having questionable clinical benefit, they continue to be prescribed [38–40]. For example, Pearson and colleagues explored statin use among cancer patients and showed that more than 30 % of patients who died were dispensed statins within 30 days of death—adding unnecessary therapeutic burden to patients [40]; our results appear to support these data.

The reasons for the high use of inappropriate medications among patients with limited life expectancy are unclear and there is a dearth of studies exploring the qualitative aspects of these challenges. One plausable explanation is that there are no clear guidelines available for reviewing and discontinuing medications in this group. It is not clear who should instigate a medication review or where and when is the most appropriate setting to undertake it. Recent work suggests that GPs would welcome training in shared care decision-making in relation to discontinuing inappropriate medication for elderly patients [41]. Interestingly, the same study showed that GPs perceive stopping preventative medication as being more difficult when compared with medication used to treat symptomatic conditions. One small-scale study demonstrated that hospice patients do not object to having medications discontinued provided the reasons for doing so are properly explained [10]. It is possible that the difficulties perceived by healthcare professionals in regard of speaking to patients with limited life expectancy may act as a barrier toward discontinuing medication. A robust qualitative study exploring patient, carer and prescriber experiences of medication use in limited life expectancy is warranted; this may identify challenges associated with medication review and discontinuation.

Limitations

While we believe our work is robust and has important implications in the review and discontinuation of inappropriate medication in patients with limited life expectancy, we acknowledge that a limitation of this work is that the majority of our patient cohort were cancer patients, with only a minority having other life-limiting illnesses, such as end-stage heart failure. In addition, only patients from one specialist palliative care centre were accessed. Generalisation of this work to other centres in the UK and more widely should, therefore, be made carefully. We also acknowledge that the drug interaction software used throughout the study has not been validated in the literature. We do, however, believe Proscript is robust in terms of predicting the sensitivity and specificity of potential drug–drug interactions, as it is routinely used in clinical practice throughout the UK; all predicted drug–drug interactions were also independently checked with two experienced clinical pharmacists.

Conclusions

Patients who access specialist palliative day care services take many inappropriate medication for the treatment or prevention of long-term conditions. These medications not only increase the pharmacotherapeutic burden for the patient but they also contribute to potential drug–drug interactions, which can increase the risk of patients

developing drug-related toxicies. These patients should have their medication reviewed in the context of their original therapeutic goals.

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Conflicts of interest The author(s) declare that they have no competing interests.

References

1. Potter J, Hami F, Bryan T, Quigley C. Symptoms in 400 patients referred to palliative care services: prevalence and patterns. Palliat Med. 2003;17:310–4.
2. Sera L, McPherson ML, Holmes HM. Commonly prescribed medications in a population of hospice patients. Am J Hosp Palliat Care. 2013; Feb 12 (Epub ahead of print).
3. Koh NY, Koo WH. Polypharmacy in palliative care: can it be reduced? Singap Med J. 2002;43(6):279–83.
4. Rottlaender D, Scherner M, Schneider T, Erdmann E. Polypharmacy, compliance and non-prescription medication in patients with cardiovascular disease in Germany. Dtsch Med Wochenschr. 2007;132(4):139–44.
5. Riechelmann RP, Zimmermann C, Chin SN, Wang L, O'Carroll A, Zarinehbaf S, et al. Potential drug interactions in cancer patients receiving supportive care exclusively. J Pain Symptom Manag. 2008;35:535–43.
6. Girre V, Arkoub H, Puts MT, Vantelon C, Blanchard F, Droz JP, et al. Potential drug interactions in elderly cancer patients. Crit Rev Oncol Hematol. 2011;78:220–6.
7. Currow DC, Abernethy AP. Frameworks for approaching prescribing at the end of life. Arch Intern Med. 2006;166(21):2404.
8. Hall PS, Lord SR, El-Laboudi A, Seymour MT. Non-cancer medications for patients with incurable cancer: time to stop and think? Br J Gen Pract. 2010;60(573):243–4.
9. Maddison AR, Fisher J, Johnston G. Preventive medication use among persons with limited life expectancy. Prog Palliat Care. 2011;19(1):15–21.
10. Nicholson A, Andrew I, Etherington R, Gamlin R, Lovel T, Lloyd J. Futile and inappropriate prescribing: an assessment of the issue in a series of patients admitted to a specialist palliative care unit. Int J Pharm Pract. 2001;9(S1):72.
11. The end of life care. The national audit office, 2008. http://www.nao.org.uk/wp-content/uploads/2008/11/07081043.pdf. Accessed 10 Oct 2013.
12. Boulkedid R, Abdoul H, Loustau M, Sibony O, Alberti C. Using and reporting the Delphi method for selecting healthcare quality indicators: a systematic review. PLoS ONE. 2011;6(6):e20476.
13. Holmes HM, Hayley DC, Alexander GC, Sachs GA. Reconsidering medication appropriateness for patients late in life. Arch Intern Med. 2006;166(6):605–9.
14. Hsu CC, Sandford BA. The Delphi technique: making sense of consensus. Pract Assess Res Eval. 2007;12(10):1–8.
15. Rx systems. Proscript. http://rxsystems.co.uk/products. Accessed 10 Oct 2013.
16. Riechelmann RP, Tannock IF, Wang L, Saad ED, Taback NA, et al. Potential drug interactions and duplicate prescriptions among cancer patients. J Natl Cancer Inst. 2007;99(8):592–600.
17. Baxter K, Preston CL. Stockley's drug interactions. 10th ed. UK: Pharmaceutical Press; 2013. ISBN 978 0 85711 061 9.
18. Electronic Medicines Compendium. http://www.medicines.org.uk/emc/. Last accessed 10 Oct 2013.
19. Todd A, Williamson S, Husband A, Baqir W, Mahony M. Patients with advanced lung cancer: is there scope to discontinue inappropriate medication? Int J Clin Pharm. 2013;35:181–4.
20. Riechelmann RP, Krzyzanowska MK, Zimmermann C. Futile medication use in terminally ill cancer patients. Support Care Cancer. 2009;17(6):745–8.
21. 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. Support Care Cancer. 2011;19:1313–8.
22. van Leeuwen RW, Swart EL, Boven E, Boom FA, Schuitenmaker MG, Hugtenburg JG. Potential drug interactions in cancer therapy: a prevalence study using an advanced screening method. Ann Oncol. 2011;22(10):2334–41.
23. Nishio S, Watanabe H, Kosuge K, Uchida S, Hayashi H, Ohashi K. Interaction between amlodipine and simvastatin in patients with hypercholesterolemia and hypertension. Hypertens Res. 2005;28(3):223–7.
24. Drug Safety Update. Simvastatin: evidence supporting recent advice on dose limitations with concomitant amlodipine or diltiazem. Med Healthc Regul Agency. http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON199561. Accessed 10 Oct 2013.
25. Steiness E. Diuretics, digitalis and arrhythmias. Acta Med Scand Suppl. 1981;647:75–8.
26. British National Formulary 64, September 2012. UK: Pharmaceutical Press. ISBN 978-0857110657.
27. Launay-Vacher V, Oudard S, Janus N, Gligorov J, Pourrat X, Rixe O, et al. Renal Insufficiency and Cancer Medications (IRMA) Study Group: prevalence of Renal Insufficiency in cancer patients and implications for anticancer drug management: the renal insufficiency and anticancer medications (IRMA) study. Cancer. 2007;110(6):1376–84.
28. Gokula M, Holmes HM. Tools to reduce polypharmacy. Clin Geriatr Med. 2012;28(2):323–41.
29. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med. 2003;163:2716–24.
30. Hanlon JT, Schmader KE, Samsa GP. A method for assessing drug therapy appropriateness. J Clin Epidemiol. 1992;45:1045–51.
31. Gallagher P, Ryan C, Byrne S. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert Doctors To Right Treatment). Consensus validation. Int J Clin Pharmacol Ther. 2008;46:72–83.
32. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet. 1994;344(8934):1383–9.
33. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM. PROSPER study group. PROspective Study of Pravastatin in the Elderly at Risk: pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet. 2002;360:1623.
34. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet. 2002;360(9326):7–22.
35. Callahan AS. Vascular pleiotropy of statins: clinical evidence and biochemical mechanisms. Curr Atheroscler Rep. 2003;5(1):33–7.
36. Weisman SM, Graham DY. Evaluation of the benefits and risks of low-dose aspirin in the secondary prevention of cardiovascular and cerebrovascular events. Arch Intern Med. 2002;162(19):2197–202.

37. Nordin BEC. Calcium and osteoporosis. Nutrition. 1997;13(7/8):664–86.
38. Bayliss EA, Bronsert MR, Reifler LM, Ellis JL, Steiner JF, McQuillen DB, et al. Statin prescribing patterns in a cohort of cancer patients with poor prognosis. J Palliat Med. 2013;16(4):412–8.
39. Tanvetyanon T, Choudhury AM. Physician practice in the discontinuation of statins among patients with advanced lung cancer. J Palliat Care. 2006;22(4):281–5.
40. Stavrou EP, Buckley N, Olivier J, Pearson SA. Discontinuation of statin therapy in older people: does a cancer diagnosis make a difference? An observational cohort study using data linkage. BMJ Open. 2012;2:e000880.
41. Schuling J, Gebben H, Veehof LJ, Haaijer-Ruskamp FM. Deprescribing medication in very elderly patients with multimorbidity: the view of Dutch GPs. A qualitative study. BMC Fam Pract. 2012;13:56.