Potentially inappropriate prescribing in older adults with cancer receiving specialist palliative care: a retrospective observational study

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Abstract
Background Older adults (≥ 65 years) with cancer receiving palliative care often have other health conditions requiring multiple medications.
Aim To describe and assess the appropriateness of prescribing for older adults with cancer in the last seven days of life in an inpatient palliative care setting.
Method Retrospective observational study of medical records for 180 patients (60.6% male; median age: 74 years; range 65–94 years) over a two-year period. Medication appropriateness was assessed using: STOPPFrail, OncPal deprescribing guideline and criteria for identifying Potentially Inappropriate Prescribing in older adults with Cancer receiving Palliative Care (PIP-CPC).
Results 94.5% of patients had at least one other health condition (median 3, IQR 2–5). The median number of medications increased from five (IQR 3–7) seven days before death, to 11 medications on the day of death (IQR 9–15). The prevalence of PIP varied depending on the tool used: STOPPFrail (version 1: 17.2%, version 2: 19.4%), OncPal (12.8%), PIP-CPC (30%). However, the retrospective nature of the study limited the applicability of the tools. Increasing number of medications had a statistically significant effect on risk of PIP across all tools (STOPPFrail (version 1: 1.29 (1.13–1.37), version 2: 1.30 (1.16–1.48)); OncPal 1.13 (1.01–1.27); PIP-CPC 0.70 (0.61–0.82)).
Conclusion This study found that the number of medications prescribed to older adults with cancer increased as time to death approached, and the prevalence of PIP varied with the application of different tools. The study also highlights the difficulties of examining PIP in this patient cohort.

Keywords Aged · Cancer · Geriatric oncology · Older adults · Palliative care · Prescribing

Impact statements
• The number of medications prescribed to older adults with cancer in the last seven days of life in an inpatient palliative care setting increased as time to death approached.
• Some older adults with cancer received medications that were potentially inappropriate during their last week of life, such as lipid-lowering therapies, alpha-blockers for hypertension, proton pump inhibitors and H2 antagonists.
• Interventions are needed to optimise medication prescribing and use in older adults with cancer in palliative care settings.
Introduction

Cancer commonly affects the older population, with almost half of all cancer diagnoses worldwide occurring in older adults (≥ 65 years) [1]. There is an ever increasing demand for palliative care services due to a multitude of factors, including global demographic ageing and improved detection and treatment of chronic illnesses, such as cancer [2]. Palliative care is an approach to care that aims to improve the quality of life for patients with life-limiting illnesses [3]. It focuses on providing comfort to patients and their families by addressing the physical, psychosocial, and spiritual needs of patients [3]. Traditionally, palliative care was synonymous with end-of-life care, whereby it was delivered to relieve symptoms at the terminal phase of illness [4]. More recently, it has been shown that early integration of palliative care in the disease course can lead to significant improvements in symptom management, quality of life and mood [5, 6].

Older adults with cancer often have other health conditions, which require management with multiple medications [7, 8]. However, polypharmacy (≥ 5 medications) is also associated with physical and functional decline in older adults with cancer [9], and an increased risk of potentially inappropriate prescribing (PIP) [10]. PIP encompasses a range of suboptimal prescribing practices, including prescribing inappropriate medications (i.e. inappropriate doses, durations, medications associated with high risks of adverse drug events (ADEs) and underprescribing (i.e. omission of medications for specific clinical indications)) [11, 12]. Optimising medication regimens requires clinicians to consider multiple factors including treatment goals and life expectancy [13–15]. As life expectancy decreases, the goal of prescribing typically moves from disease prevention and treatment, to controlling symptoms (e.g. pain), and improving an individual’s quality of life [16]. This change in the primary focus of care can lead to medications becoming potentially inappropriate as patients transition to the terminal phase of illness whereby the associated risks of the medication may outweigh the benefits.

While the topic of PIP in older adults with cancer is receiving increased attention [17], there are various issues that need to be addressed. A recent scoping review found that only a minority of studies assessed PIP in patients receiving palliative care, and that the prevalence of patients receiving ≥ 1 PIP ranged from 15 to 92% [16]. The review also highlighted that several studies used tools that are not specific to palliative care populations (e.g. Beers criteria) [16]. The use of such tools outside of the intended population could result in the misclassification of medications as potentially inappropriate, where the medication may have an important role, such as managing symptoms experienced by patients towards end of life (e.g. pain, breathlessness).

Some progress has been made in recent years to develop tools that are specific to palliative care populations. Most existing tools focus specifically on medication deprescribing [18–20]. For example, STOPPFrail was developed to assist deprescribing in frail older adults with limited life expectancy [18, 20]. OncPal is a guideline that was specifically developed for deprescribing in palliative patients with cancer [19]. To ensure appropriate prescribing, it is also important to consider potential prescribing omissions (PPOs) of medications for symptom control at end of life. The PIP-CPC criteria (criteria for identifying Potentially Inappropriate Prescribing in older adults with Cancer receiving Palliative Care) were recently developed to identify PIP involving medications for symptomatic relief in older adults with cancer and limited life expectancy [21]. However, to date, the application of these tools to older adults with cancer has been lacking [16].

Aim

To describe and assess the appropriateness of prescribing for older adults with cancer in the last seven days of life in an inpatient palliative care setting. The specific objectives were to:

1. Describe the medications received during the last week of life in a cohort of older adults with cancer;
2. Identify the prevalence of PIP using three tools: STOPP-Frail (Version 1 and 2) [18, 20], OncPal [19] and PIP-CPC [21];
3. Determine the association between the presence of PIP and each of the following variables: gender, age, number of other health conditions and number of medications in the cohort of older patients with cancer.

Ethics approval

Ethical approval was granted by the University of Limerick Research Ethics Committee in December 2019 (REC reference: 143/19).

Method

Study design

A retrospective observational cohort study was conducted of medical records of older adults with cancer who received specialist palliative care in an inpatient palliative care setting.
Setting

The specialist palliative care centre served a population of 360,000 within the mid-western region of Ireland. The centre comprises a 30-bed specialist palliative care inpatient unit and also provides community services (home care service, specialist palliative care day unit and outpatient clinics).

Participants

Healthcare records of the following population were included in the analysis: older adults (≥ 65 years at time of death) with a primary diagnosis of cancer, who received inpatient specialist palliative care services through the palliative care centre in the final week of life. Participants included in this study were under the care of the inpatient palliative care unit prior to death at any time between January 1, 2017 and December 31, 2018.

Data collection

Hardcopy medical records of patients meeting the above inclusion criteria were identified and retrieved by staff members using the centre’s electronic database. A specifically designed electronic pro-forma was developed and used by the researcher (MM) to collate all necessary information relating to patient demographics [gender, age, type of cancer(s) and other health conditions coded using ICD-classification system (ICD-10 Version: 2019)] and prescribed medications (date administered, drug name, dose, route of administration, frequency and indication, where available). The researcher pseudonymised all patients meeting inclusion criteria, by assigning them with a unique study identification code (e.g. PT001). Data collection commenced in February 2020. Due to the COVID-19 pandemic, data collection was temporarily suspended and subsequently concluded in June 2020.

Assessment of potentially inappropriate prescribing

The following tools were applied to the dataset: STOPPPFrail (Version 1 [18] and 2 [20]); consists of 27 and 25 deprescribing criteria, respectively, for use in frail older adults with limited life expectancy), the OncPal deprescribing guideline [19]; consists of eight medication classes for deprescribing in palliative patients with cancer, and PIP-CPC criteria [21]; consists of 24 criteria for identifying potentially inappropriate prescribing of medications for symptomatic relief in older adults with cancer. The study was designed prior to publication of STOPPPFrail V2 and the team decided to apply both versions of STOPPPFrail in the current study. The criteria across each of the three tools were assessed for applicability to the study dataset by the research team. Some criteria could not be applied due to the absence of clinical information. For example, the STOPPPFrail criteria “any drug without clear indication” could not be applied because some medications would not have a clear indication consistently documented in the Kardexes. Other criteria were partially applicable, and required caveats. Caveats were supported by published scientific evidence and input from the palliative care clinicians. Full details on the applicability of each individual criterion can be found in Supplementary Table S1. MM applied the criteria to the data and any difficulties were resolved through discussion with the research team.

Data analysis

Sample size calculations were conducted using an estimate of 50% prevalence of PIP in this patient cohort. To yield data with 7.5% precision, 171 patient records were required.

Demographic data were presented using descriptive statistics. Means (standard deviations) or medians (inter-quartile range, IQR and range) were used for continuous data and frequency (proportions) for categorical data. The prevalence of each individual criterion within each tool was calculated as a proportion of all eligible persons in the dataset, and reported as percentage estimates. The association between the presence of PIP (any vs. no PIP) and gender (male vs female), age (continuous variable), number of other health conditions (continuous variable), and number of medications (continuous variable) was examined using logistic regression presenting adjusted odds ratios (OR) and associated 95% confidence intervals (CI). There were no missing data for the main variables of interest. Analysis was performed using Stata software (version 15) and significance at p < 0.05 is assumed.

Results

Study population

One hundred and eighty older adults were included (Table 1), 60.6% (n = 109) of whom were male. The median age at time of death was 74 years (range 65–94 years). Cancer of the digestive organs was the most common primary cancer diagnosis (n = 57, 31.7%). Almost all patients (n = 170, 94.5%) had at least one other health condition (median 3, IQR 2–5).

Patients received a median of nine medications (IQR 7–12) over the last seven days of life. In general, patients received more medications as time to death approached (Table 2). The median number of medications prescribed seven days before death was five (IQR 3–7) compared to 11 medications on the day of death (IQR 9–15).
Table 3 provides an overview of the drug classes that patients received in the last week of life (full table can be found in Supplementary Table S2). The most frequently prescribed drug classes were: opioids (n = 180, 100%), antipsychotics (n = 173, 96.1%), antispasmodics (n = 156, 86.7%), benzodiazepines (n = 172, 85.6%) and paracetamol (n = 143, 79.4%). Drugs for other health conditions were also observed in this patient cohort: including β-blockers (n = 37, 20.6%), α-blockers (n = 29, 16.1%), antiplatelets (n = 19, 10.6%), antidiabetic agents (8.3%), calcium channel blocker (6.7%) and cholesterol lowering agents (4.4%).

### Prevalence of PIP

The different tools comprised 85 criteria in total. Thirty-four criteria (40%) across these tools were applicable to the dataset based on available clinical information. The prevalence of PIP ranged from 12.8% (23/180 patients) to 30% (54/180 patients) of the population, depending on which tool was used to identify PIP. A further breakdown of the identified PIPs is provided under each tool below.

#### STOPP Frail (V1 and V2)

The prevalence of PIP could be calculated for 16 of 27 STOPP Frail V1 criteria (59.3%) (Supplementary Table S1). Based on these criteria, 31 patients (17.2%) were found to have received at least one potentially
inappropriate prescription. One potentially inappropriate prescription was identified in 22 patients (12.2%), two potentially inappropriate prescriptions in eight patients (4.4%) and three potentially inappropriate prescriptions in two patients (1.1%). The most prevalent potentially inappropriate prescription identified was α-blockers for hypertension, with nine patients (5%) continuing to receive this medication in the last week of life. Eight patients (4.4%) received a statin, five patients (2.8%) received an anti-platelet agent and five patients (2.8%) received calcium supplementation in the final week of life.

The prevalence of PIP could be calculated for 10 of 25 STOPPFrail V2 criteria (40%) (Supplementary Table S1). Using these criteria, 35 patients (19.4%) were found to have received at least one potentially inappropriate prescription. One potentially inappropriate prescription was identified in 25 patients (13.9%) and two potentially inappropriate prescriptions in 10 patients (5.5%). The most commonly identified potentially inappropriate prescription was lipid-lowering therapies, with eight patients (4.4%) continuing to receive a lipid-lowering therapy in the last week of life. Anti-platelets, calcium and vitamin D were prescribed to five patients (2.8%). The prevalence of PIP identified by the STOPPFrail criteria V1 and V2 are detailed in Table 4.

### OncPal

The prevalence of PIP could be calculated for four of nine OncPal criteria (44%) (Supplementary Table S1). Based on these criteria, 23 patients (12.8%) were found to have received at least one potentially inappropriate prescription. Nineteen patients (10.5%) received one potentially inappropriate prescription and four patients (2.2%) received two potentially inappropriate prescriptions, as identified by OncPal.

The most prevalent potentially inappropriate prescription identified by OncPal was the prescription of gastroprotective drugs without any medical history of gastrointestinal bleeding, peptic ulcer, gastritis, GORD or the concomitant use of anti-inflammatory agents including NSAIDs and steroids (n = 14, 7.8%), followed by statins (n = 8, 4.4%), aspirin (n = 3, 1.7%) and osteoporosis medications (n = 2, 1.1%) (Table 5).

### PIP-CPC

The prevalence of PIP could be calculated for four of 24 criteria (16.7%) (Supplementary Table S1). Only one of the four applicable PIP-CPC criteria (Table 5) identified PIP amongst the cohort.

### Table 4 Prevalence of PIP identified by STOPPFrail V1 and V2 in the study population (n = 180) in the last 7 days of life

| Section                      | Criteria                                                                 | Prevalence of PIP N (%) | STOPPFrail V1 | STOPPFrail V2 |
|------------------------------|--------------------------------------------------------------------------|-------------------------|---------------|---------------|
| Cardiovascular system        | Lipid lowering therapies                                                | 8 (4.4)                 | 8 (4.4)       |               |
| Cardiovascular system        | Alpha blockers for hypertension                                          | 9 (5)                   | N/A           |               |
| Coagulation system           | Anti-platelets                                                          | 5 (2.8)                 | 5 (2.8)       |               |
| Coagulation system           | Aspirin for stroke prevention in atrial fibrillation                    | N/A                     | 1 (0.6)       |               |
| Respiratory system           | Theophylline [and aminophylline (Version 2)]                           | 2 (1.1)                 | 2 (1.1)       |               |
| Respiratory system           | Leukotriene antagonists                                                 | 0 (0)                   | 0 (0)         |               |
| Musculoskeletal system       | Calcium supplementation                                                 | 5 (2.8)                 | 5 (2.8)       |               |
| Musculoskeletal system       | Vitamin D                                                               | N/A                     | 5 (2.8)       |               |
| Musculoskeletal system       | Anti-resorptive / bone anabolic drugs for osteoporosis                  | 2 (1.1)                 | 2 (1.1)       |               |
| Musculoskeletal system       | Selective Oestrogen Receptor Modulators (SORMs) for osteoporosis         | 0 (0)                   | N/A           |               |
| Urogenital system            | 5-Alpha reductase inhibitors                                            | 2 (1.1)                 | 3 (1.7)       | (Version 2 merges 5-alpha reductase inhibitors and alpha blockers) |
| Urogenital system            | Alpha blockers                                                          | 1 (0.6)                 |               |               |
| Urogenital system            | Muscarinic antagonists                                                  | 0 (0)                   | N/A           |               |
| Endocrine system             | Diabetic oral agents                                                    | 3 (1.7)                 | 3 (1.7)       |               |
| Endocrine system             | Angiotensin-Converting Enzyme (ACE) inhibitors for diabetes             | 3 (1.7)                 | N/A           |               |
| Endocrine system             | Angiotensin Receptor Blockers (ARBs) for diabetes                       | 0 (0)                   | N/A           |               |
| Endocrine system             | Systemic oestrogens for menopausal symptoms                             | 0 (0)                   | N/A           |               |
| Miscellaneous                | Prophylactic antibiotics to prevent recurrent cellulitis or urinary tract infections (UTIs) | 3 (1.7)                 | N/A           |               |

N/A: criterion not included in this version of STOPPFrail
The PIP-CPC criteria identified that 54 patients (30%) received an opioid without a concomitant laxative. Three criteria were applicable to the dataset, but were not prevalent within the dataset; no patient received oral liquid paraffin, a monoamine oxidase inhibitor, or concurrently used NSAIDs and corticosteroids.

Factors associated with PIP

Female gender was significantly associated with a decreased risk of PIP as identified by STOPPFrail V2 (OR 0.42, \( p = 0.03 \)), but was not a statistically significant predictor of PIP as identified by the other tools (Table 6). Age and increased number of health conditions were not identified as statistically significant predictors of PIP based on any of the tools (Table 6). Increased number of medications contributed to an increased risk of PIP as identified by STOPPFrail V1 (OR = 1.29, \( p < 0.01 \)), STOPPFrail V2 (OR = 1.30, \( p < 0.01 \)) and OncPal (OR = 1.13, \( p = 0.03 \)), however it contributed to a decreased risk of PIP as identified by the PIP-CPC tool based on the application of 4/24 criteria (OR = 0.70, \( p < 0.01 \)).
Discussion

Statement of key findings

This study found that the median number of medications prescribed for older adults with cancer in an inpatient palliative care setting in Ireland increased during the last week of life. The prevalence of PIP ranged from 12.8% to 30%, depending on which tool was used to identify PIP. The main factor associated with predicting PIP was the number of medications.

Strengths and limitations

This study sought to address recognised gaps with previous observational research examining prescribing practices in palliative care settings by using tools (STOPPFrail (V1 and V2), OncPal, PIP-CPC) that have been specifically developed to examine the prevalence of PIP in adults with life-limiting illness [16]. Several previous studies have examined the appropriateness of prescribing in this cohort using tools, such as Beers criteria [22], which are not intended for patients in hospice or palliative care settings [23, 24]. Moreover, previous studies in palliative care settings have tended to overlook the underprescribing of necessary medications [16]. The current study sought to address this by applying the PIP-CPC criteria. This is the first known attempt at applying these criteria.

The main limitation of this study relates to its retrospective design. Due to the reliance on chart records, detailed information regarding the real-time clinical decision-making was not consistently available. As data were only included for the final seven days of life, several criteria relating to long-term prescribing were not applicable. Although the most common primary cancer diagnoses among the study population reflect those associated with most common cancer deaths in Ireland [25], this study cannot claim to be representative of the entire population of older adults with cancer, as it was localised to one study site and participants were predominantly male.

Interpretation

The observed increase in the median number of medications per patient during the last week of life is consistent with previous related research, whereby drugs for symptomatic relief are increasingly prescribed, and there is typically a reduction in the number of medications for other health conditions [23, 26–28]. Although the current study did not differentiate between medications according to treatment intention (i.e. preventative versus symptomatic relief), it was evident from the most frequently prescribed drug classes that the medications were primarily prescribed for symptom control (e.g. opioids, antipsychotics, antispasmodics, benzodiazepines).

It is difficult to make direct comparisons between the assessments of prescribing appropriateness and those of previous studies due to the challenges in applying the full set of criteria for each of the tools. For example, previous studies involving the application of STOPPFrail V1 have reported a prevalence of PIP ranging from 67.2 to 91.2% [29, 30]. In both studies, the STOPPFrail criterion relating to ‘any drug without clear indication’ accounted for 47% and 43.8%, respectively. This criterion was not applicable to our dataset due to the reliance on information contained within Kardexes, which could have contributed to an underestimation of PIP in the current study.

To a large extent, the medications identified as potentially inappropriate by STOPPFrail and OncPal involved preventative medications. These findings mirror those of a systematic review that reported that the most common classes of inappropriate medication identified in patients with life-limiting illnesses were: statins, vitamins and mineral supplements, antidiabetic agents, antihypertensives, antiplatelets, and anti-ulcer medications [31]. Cholesterol-lowering agents are one of the few therapeutic groups that are widely deemed futile towards the end of life, because the time to risk reduction is a minimum of 1.9 years [32–34]. Moreover, clinical trial evidence has shown that these medications can be safely and effectively discontinued in advanced life-limiting illness [34].

Proactive deprescribing (described as “discontinuing a medicine if future gains are unlikely to outweigh future harms” [35]) is an essential aspect of combatting PIP, although it is only accountable for approximately 14% of deprescribing activities in clinical practice [35, 36]. Reactive deprescribing (described as “discontinuing a medicine in response to an adverse clinical trigger” [35]) is more commonly seen in clinical practice, whereby failure to deprescribe would likely lead to definite patient harm [37]. The hesitancy to deprescribe medications proactively has been associated with uncertainties regarding the likely benefits and potential harms [38]. Other factors that contribute to health care professionals’ decisions to engage in deprescribing in this patient cohort include: involvement of patients and relatives in treatment decisions, communication between healthcare professionals (e.g. communication between the general practitioner, oncology and palliative care) and organisational factors (e.g. workload) [39]. Deprescribing is a complex process, and it is important to note that while patients with advanced cancer generally show predictable decline in the terminal phase [40], in some instances, rapid deterioration and subsequent death could have been sudden or earlier than expected [41].
The application of the PIP-CPC criteria in this study highlighted potential underprescribing of laxative treatment in patients receiving opioid analgesics. As the data collection in this study only documented drugs that were administered, and did not account for anticipatory prescribing, there is the possibility that the prevalence of PIP related to this criterion is overestimated. Furthermore, the prescription of oral laxatives may not always be appropriate in the last week of life, as some patients may be nil by mouth. Potential pre-oral laxatives may not always be appropriate in the last week.

The inverse was found for PIP-CPC, whereby an increased number of medications was associated with decreased odds of PIP, however, this may be due to the fact this tool has a focus on PPOs and, therefore, should be interpreted with some caution due to possible bias. While this is the first known study to examine factors associated with PIP specific to older adults with cancer receiving palliative care, it should be interpreted with caution as only a limited number of criteria within each tool were applicable to the dataset. However, an association between PIP and multiple medications has also been demonstrated in other studies in the general older adult population [43–48].

**Conclusion**

This study highlights that some older adults with cancer received medications that were potentially inappropriate during their last week of life and the prevalence of PIP ranged from 12.8% to 30%, depending on which tool was used. The main factor associated with predicting PIP was the number of medications. Interventions are needed to optimise medication prescribing and use in older adults with cancer in palliative care settings. Further research is required to determine the most appropriate study design and methodology for collecting information on prescribing in older adults with cancer in a palliative care setting, in an ethically sound, practical and efficient manner.

**References**

1. Pilleron S, Sarfati D, Jansen-Heijnen M, et al. Global cancer incidence in older adults, 2012 and 2035: A population-based study. Int J Cancer. 2019;144:49–58.
2. Etkind SN, Bone AE, Gomes B, et al. How many people will need palliative care in 2040? Past trends, future projections and implications for services. BMC Med. 2017;15:102.
3. World Health Organisation. WHO Definition of Palliative Care. https://www.who.int/cancer/palliative/definition/en/. Accessed 03 Sep 2022
4. Ryan S, Wong J, Chow R, et al. Evolving definitions of palliative care: upstream migration or confusion? Curr Treat Options Oncol. 2020;21:20.
5. McDonald J, Swami N, Hannon B, et al. Impact of early palliative care on caregivers of patients with advanced cancer: cluster randomised trial. Annals Oncol. 2017;28:163–8.
6. Zimmermann C, Swami N, Krzyzanowska M, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. Lancet. 2014;383:1721–30.
7. Deliens C, Deliens G, Filleul O, et al. Drugs prescribed for patients hospitalized in a geriatric oncology unit: potentially inappropriate medications and impact of a clinical pharmacist. J Geriatr Oncol. 2016;7:463–70.
8. Sharma M, Loh KP, Nightingale G, et al. Polypharmacy and potentially inappropriate medication use in geriatric oncology. J Geriatr Oncol. 2016;7:346–53.
9. Mohamed MR, Ramsdale E, Loh KP, et al. Associations of polypharmacy and inappropriate medications with adverse outcomes in older adults with cancer: a systematic review and meta-analysis. Oncologist. 2020;25(1):e94–108.
10. Shah BM, Hajjar ER. Polypharmacy, adverse drug reactions, and geriatric syndromes. Clin Geriatr Med. 2012;28:173–86.
11. Clyne B, Fitzgerald C, Quinlan A, et al. Interventions to address potentially inappropriate prescribing in community-dwelling older adults: a systematic review of randomized controlled trials. J Am Geriatr Soc. 2016;64:1210–22.
12. O’Connor MN, Gallagher P, O’Mahony D. Inappropriate prescribing: criteria, detection and prevention. Drugs Aging. 2012;29:437–52.
13. Turner JP, Shakib S, Bell JS. Is my older cancer patient on too many medications? J Geriatr Oncol. 2017;8:77–81.
14. Todd A, Jansen J, Colvin J, et al. The deprescribing rainbow: a conceptual framework highlighting the importance of patient context when stopping medication in older people. BMC Geriatr. 2018;18:295.
15. Holmes HM, Hayley DC, Alexander GC, et al. Reconsidering medication appropriateness for patients late in life. Arch Inter Med. 2006;166:605–9.
16. Cadogan CA, Murphy M, Boland M, et al. Prescribing practices, patterns, and potential harms in patients receiving palliative care: A systematic scoping review. Explor Res Clin Soc Pharmacol. 2021;3:100050.
17. Nightingale G, Mohamed MR, Holmes HM, et al. Research priorities to address polypharmacy in older adults with cancer. J Geriatr Oncol. 2021;12:964–70.
18. Lavan AH, Gallagher P, Parsons C, et al. STOPPFrail (screening tool of older persons prescriptions in frail adults with limited life expectancy): consensus validation. Age Ageing. 2017;46:600–7.
19. 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(1):71–8.
20. Curtin D, Gallagher P, O’Mahony D. Deprescribing in older people approaching end-of-life: development and validation of STOPPFrail version 2. Age Ageing. 2020;50:465–71.
21. Cadogan CA, Murphy M, McLean S, et al. Development of criteria for identifying potentially inappropriate prescribing in older adults with cancer receiving palliative care (PIP-CPC). J Geriatr Oncol. 2021;12(8):1193–9.
22. American Geriatrics Society 2019 Updated AGS Beers Criteria(R) for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2019;67(4):674–94.
23. Currow DC, Stevenson JP, Abernethy AP, et al. Prescribing in palliative care as death approaches. J Amer Geriat Soc. 2007;55:590–5.
24. Russell BJ, Rowett D, Currow DC. Pro re nata prescribing in a population receiving palliative care: a prospective consecutive case note review. J Am Geriatr Soc. 2014;62(9):1736–40.
25. National Cancer Registry Ireland. Cancer in Ireland 1994–2019: Annual report of the National Cancer Registry, NCRI. Cork, Ireland. 2021. https://www.ncr ire.ie/sites/ncr/files/pubs/NCRI_Annual%20Report_2021.pdf. Accessed 26 Aug 2022.
26. Morin L, Vetrano DL, Rizzato D, et al. Choosing wisely? Measuring the burden of medications in older adults near the end of life: nationwide, longitudinal cohort study. Am Journal Med. 2017;130:927-936.e929.
27. Paque K, Elseviers M, Vander Stichele R, et al. Changes in medication use in a cohort of patients with advanced cancer: the international multicentre prospective European Palliative Care Cancer Symptom study. Palliat Med. 2018;32:775–85.
28. McLean S, Sheehy-Skeffington B, O’Leary N, et al. Pharmacological management of co-morbid conditions at the end of life: is less more? J Med Sci. 2013;182(1):107–12.
29. Sevilla-Sánchez D, Molist-Brunet N, Espaullera-Panicot J, et al. Potentially inappropriate medication in palliative care patients according to STOPP-Frail criteria. Eur Geriatr Med. 2018;9:543–50.
30. Lavan AH, O’Mahony D, Gallagher P. STOPPFrail (Screening Tool of Older Persons’ Prescriptions in Frail adults with a limited life expectancy) criteria: application to a representative population awaiting long-term nursing care. Eur J Clin Pharmacol. 2019;75:723–31.
31. Todd A, Husband A, Andrew I, et al. Inappropriate prescribing of preventative medication in patients with life-limiting illness: a systematic review. BMJ Support Palliat Care. 2017;7:113–21.
32. Amareno P, Labreuche J, Lavallée P, et al. Statins in stroke prevention and carotid atherosclerosis: systematic review and up-to-date meta-analysis. Stroke. 2004;35:2902–9.
33. Thavendiranathan P, Bagai A, Brookhart MA, et al. Primary prevention of cardiovascular diseases with statin therapy: a meta-analysis of randomized controlled trials. Arch Intern Med. 2006;166:2307–13.
34. Kutner JS, Blatchford PJ, Taylor DH Jr, et al. Safety and benefit of discontinuing statin therapy in the setting of advanced, life-limiting illness: a randomized clinical trial. JAMA Intern Med. 2015;175:691–700.
35. Scott S, Clark A, Farrow C, et al. Deprescribing admission medication at a UK teaching hospital: a report on quantity and nature of activity. Int J Clin Pharm. 2018;40:991–6.
36. Scott S, Wright DJ, Bhattacharya D. The role of behavioural science in changing deprescribing practice. Br J Clin Pharm. 2021;87:39–41.
37. Anderson K, Stowasser D, Freeman C, et al. Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: a systematic review and thematic synthesis. BMJ Open. 2014;4:e006544.
38. Scott S, Twigg MJ, Clark A, et al. Development of a hospital deprescribing implementation framework: a focus group study with geriatricians and pharmacists. Age Ageing. 2019;49:102–10.
39. Lundby C, Graabaek T, Ryg J, et al. Health care professionals’ attitudes towards deprescribing in older patients with limited life expectancy: a systematic review. Br J Clin Pharm. 2019;85:868–92.
40. Seow H, Barbera L, Sutradhar R, et al. Trajectory of performance status and symptom scores for patients with cancer during the last six months of life. J Clin Oncol. 2011;29:1151–8.
41. Ito S, Morita T, Uneno Y, et al. Incidence and associated factors of sudden unexpected death in advanced cancer patients: a multicenter prospective cohort study. Cancer Med. 2021;10:4939–47.
42. Moriarty F, Bennett K, Cahir C, et al. Potentially inappropriate prescribing according to STOPP and START and adverse outcomes in community-dwelling older people: a prospective cohort study. Br J Clin Pharm. 2016;82:589–57.
43. Bradley MC, Fahey T, Cahir C, et al. Potentially inappropriate prescribing and cost outcomes for older people: a cross-sectional study using the Northern Ireland Enhanced Prescribing Database. Eur J Clin Pharmacol. 2012;68:1425–33.
44. Cahir C, Fahey T, Teeling M, et al. Potentially inappropriate prescribing and cost outcomes for older people: a national population study. BR J Clin Pharmacol. 2010;69:543–52.
45. Cooper JA, Moriarty F, Ryan C, et al. Potentially inappropriate prescribing in two populations with differing socio-economic profiles: a cross-sectional database study using the PROMPT criteria. Eur J Clin Pharmacol. 2016;72:583–91.
46. Thiruchelvam K, Byles J, Hasan S, et al. Frailty and potentially inappropriate medications using the 2019 Beers Criteria: findings from the Australian Longitudinal Study on Women’s Health (ALSWH). Aging Clin Exp Res. 2021;33:2499–509.

47. Thiruchelvam K, Byles J, Hasan S, et al. Prevalence and association of continuous polypharmacy and frailty among older women: a longitudinal analysis over 15 years. Maturitas. 2021;146:18–25.

48. Lim LM, McStea M, Chung W, et al. Prevalence, risk factors and health outcomes associated with polypharmacy among urban community-dwelling older adults in multi-ethnic Malaysia. PLoS ONE. 2017;12: e0173466.

49. Murphy M, Bennett K, Hughes CM, et al. Interventions to optimise medication prescribing and adherence in older people with cancer: a systematic scoping review. Res Social Adm Pharm. 2022;18(3):2392–402.

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