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End-of-Life Deprescribing in Advanced Cancer: A Retrospective Cohort Study of Elderly Patients in Japan

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Abstract

Potentially inappropriate medications (PIMs) impose a considerable load on individuals with advanced cancer who are approaching the final stages of life. Nonetheless, the patterns of PIM prescriptions and the variables influencing their discontinuation in this patient group remain unclear. To outline the changes over time in PIM prescribing practices and to examine the elements connected with deprescribing PIMs in patients diagnosed with advanced cancer in Japan. Retrospective cohort study drawing on medical claims data. We reviewed records of patients exceeding 65 years of age who had received a cancer diagnosis 6 months before death and who died between December 2017 and August 2023 in Mito City, Ibaraki Prefecture, Japan. Sociodemographic details, clinical information, and prescription records were extracted at 6 months (M6), 3 months (M3), and 1 month (M1) before death. Assessment of PIMs followed the OncPal Deprescribing Guidelines.
In the group of 1269 patients, the average age was 80.6 years, with 62.2% male. PIMs had been prescribed to 77.0% at M6, 76.4% at M3, and 70.0% at M1 ($P < 0.001$, M6 to M1). Variables linked to the removal of at least one PIM between M6 and M1 encompassed female gender, the quantity of medications at M6, the count of coexisting conditions, admission to a palliative care unit, and admission to a standard hospital ward. For patients with advanced cancer, reliance on PIMs lessened progressively as they neared death. The practice of deprescribing PIMs proved more widespread among female patients, those experiencing polypharmacy together with multiple comorbidities, and those receiving inpatient care, most notably within palliative care units.

Keywords: Advanced cancer, Deprescribing, End-of-life care, Palliative care, Polypharmacy, Potentially inappropriate medications

Introduction

Polypharmacy is generally understood as the regular use of five or more different medicines at the same time [1]. This practice is very common in people living with advanced cancer, who often have only a short time left to live [2]. It frequently results in the continued prescribing of potentially inappropriate medications (PIMs) – treatments where the dangers are likely to outweigh any possible gains. Such use can raise the likelihood of harmful side effects, dangerous interactions between drugs, and a noticeable drop in the patient's overall quality of life [3]. Several recent investigations have found that the total count of prescribed drugs keeps climbing as death draws nearer. This increase is mainly driven by the addition of medicines intended to ease symptoms, even as drugs meant for long-term prevention are rarely stopped [4–6].
Because life expectancy is limited, continuing preventive drugs can be questionable when it may take years for any benefit to appear. At the same time, these patients become more vulnerable to drug-related problems as their body's ability to process and respond to medications steadily worsens [7]. Interestingly, certain drugs that are

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normally flagged as potentially inappropriate – including non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants, and benzodiazepines – can still play a useful role in relieving symptoms for individuals with advanced cancer [8]. For this group of patients, successful medication management means carefully adjusting both preventive and disease-treating therapies, as well as symptom-control treatments, such as pain treatments, to match each person's specific situation and needs [6].

The term "deprescribing" means the planned identification and withdrawal of medicines that are no longer providing benefit or that may actually be causing harm. This is especially relevant for patients with limited remaining life or those already experiencing unwanted effects [9]. The goal is usually to streamline treatment plans, raise the quality of life, and cut down on the problems linked to polypharmacy and PIMs. Published work indicates that the process requires detailed review by medical professionals to curb excessive medication use and improve patient outcomes [9]. In more recent years, experts have highlighted the need to separate proactive deprescribing – the thoughtful stopping of drugs to prevent future harm – from reactive deprescribing, which happens only after a clear clinical problem has already appeared [10]. Although deprescribing is now widely viewed as a valuable approach to improving medication use, it has received relatively little attention in the specific setting of end-of-life cancer care. To help guide decisions in advanced cancer, various tools and standards have been proposed to support better prescribing [11]. One example is the OncPal Deprescribing Guideline, created by Lindsay and colleagues, which provides a framework for assessing whether preventive medicines remain suitable for patients with advanced cancer and a life expectancy of less than 6 months [12].

Our earlier work conducted in the Japanese home-care setting showed that two-thirds of patients with advanced cancer near the end of life were taking five or more medications, and half of them had been prescribed at least one PIM according to the OncPal Deprescribing Guideline [13]. Even so, it is still not clear which types of PIMs are typically kept, withdrawn, or initiated in the final phase of life. In addition, only a small number of studies have examined factors influencing the decision to stop PIMs in the last 6 months for these patients.

For these reasons, the current study set out to (1) map the changes in the use of PIMs – as defined by the OncPal Deprescribing Guideline – across the final six months before death among older adults with advanced-stage cancer, and (2) pinpoint the factors linked to stopping any PIMs in this group.

The outcomes of this research should help build a clearer picture of how preventive medicines are prescribed and how their use evolves near the end of life, as well as the elements that affect their discontinuation in patients with advanced cancer. While the study does not directly measure the clinical impact of these preventive drugs, the information gathered here will serve as important groundwork for future studies exploring the value of deprescribing in this population.

Materials and Methods

Data source

Japan's healthcare system includes National Health Insurance, intended for the self-employed, retirees, and others not covered by company-based health plans. Separately, the late-stage elderly medical care system provides coverage for all individuals aged 75 or older [14]. Insurance claims data records monthly details covering diagnoses, medical services performed, and all prescribed drugs. Diagnoses in these records are originally coded using Japanese disease classification systems that correspond to the International Classification of Diseases, Tenth Revision (ICD-10).

The present analysis drew on medical and pharmacy claims records for two groups in Mito City: people covered by the National Health Insurance (self-employed individuals and retirees aged 75 years or younger) and those covered by the late-stage elderly medical care system (adults aged 75 years or older). The study period ran from April 2017 to March 2023. Mito City, the capital of Ibaraki Prefecture, had a total population of about 266,000 in 2012, of whom roughly 73,000 (27.0%) were 65 years of age or older [15].

Research design and study population

This study adopted a retrospective cohort design and drew upon medical claims records. We pulled information from the National Health Insurance database on individuals who passed away between April 2019 and June 2022, and from the late-stage medical care database on those who died between December 2017 and August 2023. Participants were included if they met the following conditions: a primary cancer diagnosis documented in the claims data within 6 months of death (defined as the index time) and age 65 years or older at that time. No formal statistical power calculation was performed to determine the sample size; instead, the analysis included all qualifying cases to provide a comprehensive view of the patterns.

Measurements

Details on patient characteristics – such as age, gender, main cancer location, and coexisting health conditions – were gathered from the medical claims documented 6 months before death. Both cancer diagnoses and comorbidities were identified through the standard Japanese disease codes that map directly to ICD-10 codes. The

various cancer sites were classified into 9 distinct groups according to the system established by the Ministry of Health and Welfare [16]. These groups consisted of: (1) oral cavity, pharynx, gastric, and esophageal; (2) colorectal; (3) liver, gallbladder, bile duct, and pancreas; (4) lung; (5) breast; (6) gynecologic; (7) urothelial (bladder, renal, and urothelial) and prostate; (8) hematologic malignancies; and (9) others. Comorbidities were selected drawing from prior multimorbidity research, while deliberately excluding any form of cancer [17]. The list included hypertension, diabetes, hyperlipidemia, cerebrovascular diseases (hemorrhagic stroke, ischemic stroke, and other cerebrovascular diseases), cardiac diseases (ischemic heart disease, heart failure, atrial fibrillation, and poor circulation in the lower limbs), chronic respiratory diseases (asthma, chronic obstructive pulmonary disease, and chronic bronchitis), digestive diseases (stomach problems, colon problems, and chronic hepatitis), kidney diseases or failure, urologic diseases (neurogenic bladder, overactive bladder, and prostatic hypertrophy), arthritis or rheumatoid arthritis, chronic musculoskeletal conditions causing pain or limitation, fractures (femur fractures and other fractures), osteoporosis, dementia, neurological diseases (Parkinson disease and epilepsy), mental disorders (depression and anxiety), and thyroid disorders.

Data on utilization of home medical care (HMC) and inpatient stays in general hospital wards or palliative care units (PCU) were likewise retrieved from claims covering the 164 to 31 days preceding death. In Japan, HMC typically involves scheduled physician home visits – often at least once monthly – to oversee medical treatment, including the issuance of regular prescriptions reimbursed by health insurance. This service can encompass primary care, recovery support, ongoing long-term assistance, and palliative measures for advanced cancer patients in their own residences, thereby facilitating the possibility of dying at home [18].

Dependent variable

The main outcome measure was the PIM occurrence rate, as outlined in the OncPal Deprescribing Guidelines. Discontinuation of PIMs was considered to have occurred when more than one regular preventive medication was removed from the list provided in the Guidelines. Medication assessment involved collecting records of all prescriptions dispensed orally within three specific windows: 0–30 days (1 month: M1), 75–105 days (3 months: M3), and 165–195 days (6 months: M6) before death. Injectable and topical formulations, which are often used for symptom management in advanced cancer, were deliberately excluded from the evaluation, as the emphasis remained on oral preventive agents specified by the OncPal Deprescribing Guidelines. Prescription length was accounted for by calculating the end date as the issue date plus the supplied days, ensuring any medication ending within the target windows was captured. For each window, we tallied the overall medication count and checked whether each PIM listed in the OncPal Deprescribing Guidelines was present or absent. The claims database records drugs via the Ministry of Health, Labour and Welfare (MHLW) drug codes, known as YJ codes. These consist of 12-digit alphanumeric identifiers maintained by the MHLW for setting official drug prices. A corresponding list of YJ codes for the relevant PIMs was compiled to allow identification of affected patients. The application of the OncPal Deprescribing Guidelines did not include assessment of blood pressure or glucose control due to constraints in the claims data format. Additionally, details on complementary and alternative remedies were not captured in the database, even though they were mentioned in the guidelines. Polypharmacy was classified as having five or more prescriptions [19].

Statistical analysis

To begin with, we summarized the core demographic and clinical features of the study participants. We also outlined the total count of medications and PIMs recorded for these patients at the M6, M3, and M1 time points. Next, we evaluated shifts in the overall medication count using the Wilcoxon signed-rank test, and changes in the occurrence of PIMs using the McNemar test. In addition, the percentage shift in the occurrence rate of each specific PIM and its therapeutic category from M6 to M1 was computed, and these differences were tested for significance using the McNemar test. Lastly, we explored variables linked to the withdrawal of any PIMs between M6 and M1. This analysis was restricted to patients who had received at least one PIM at M6 and was conducted using a logistic regression model. In the multivariable model, the explanatory variables included age, sex, medication count at M6, comorbidity count, utilization of HMC, admission to a palliative care unit (PCU) between M6 and M1, and admission to a general hospital ward between M6 and M1.

The logistic regression results were expressed as odds ratios (ORs) with accompanying 95% confidence intervals (CIs). Every statistical computation was executed with SPSS version 27 (IBM, Armonk, NY, USA). Statistical significance was defined as a two-sided p-value below 0.05. Since the analysis relied exclusively on health insurance claims records, the dataset had no missing entries. The reporting of this research adheres to the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [20].

Ethical considerations

The study received ethical clearance from the Ethics Committee of the Institute of Medicine, University of Tsukuba (Approval Number: 1870–2). Because the data were completely de-identified, the requirement to obtain

informed consent from individual patients was waived. All procedures were carried out in keeping with the ethical standards outlined in the Declaration of Helsinki.

Results and Discussion

Characteristics of participants

Altogether, 1269 adult patients with advanced cancer — who had cancer listed as the primary diagnosis 6 months before death — were included in the final analysis. Summary of patient characteristics appears in **Table 1**. The average age was 80.6 years, and 62.2% of the cohort consisted of male patients. Cancer site distribution is presented in **Table 1**, with colorectal cancer, respiratory tract cancers, and esophagus/stomach cancers ranking as the three most frequent types, in that sequence. The leading comorbidities, ranked by prevalence, were digestive system disorders, hypertension, chronic musculoskeletal disorders, and heart conditions. The median number of comorbidities (excluding malignancy) was five per patient.

Table 1. Basic characteristics of the study population (n = 1269).

Characteristics	**N = 1269**
Age, mean (SD)	80.6 (7.3)
Sex, n (%)	
Male	789 (62.2)
Female	480 (37.8)
Type of cancer, n (%)	
Respiratory organs (incl. lung and bronchus)	239 (18.8)
Esophagus and stomach	184 (14.5)
Colorectal	261 (20.6)
Liver and intrahepatic bile duct	58 (4.6)
Pancreas	86 (6.8)
Other digestives	39 (3.1)
Breast	73 (5.8)
Urinary tract (bladder, renal, urothelial)	88 (6.9)
Female genital	22 (1.7)
Male genital	137 (10.8)
Melanoma	0 (0.0)
Brain	6 (0.5)
Unknown	6 (0.5)
Others	152 (12.0)
Lymphoma, blood	108 (8.5)
Multiple	0 (0.0)
Comorbidity, n (%)	
Hypertension	884 (69.7)
Diabetes	476 (37.5)
Hyperlipidemia	435 (34.3)
Cerebrovascular diseases	249 (19.6)
Cardiac diseases	539 (42.5)
Chronic respiratory diseases	343 (27.0)
Digestive diseases	1033 (81.4)
Kidney diseases or failure	129 (10.2)
Chronic urinary problem (urologic diseases)	347 (27.3)
Arthritis or rheumatoid arthritis	140 (11.0)
Chronic musculoskeletal conditions causing pain or limitation	759 (59.8)
Fractures	119 (9.4)
Osteoporosis	241 (19.0)
Dementia	118 (9.3)
Neurological diseases	70 (5.5)
Mental disorders	48 (3.8)
Thyroid disorder	112 (8.8)
Number of comorbidities, median [IQR]	5 [3–6]
Use of HMC between M6 and M1, n (%)	220 (17.3)

Admission to general ward between M6 and M1, n (%)	620 (48.9)
Admission to PCU between M6 and M1, n (%)	166 (13.1)

Abbreviations: SD = standard deviation; IQR = interquartile range; HMC = home medical care; PCU = palliative care unit.

Trends in PIMs during the last 6 months of life in patients with advanced cancer

Mean medication counts at M6, M3, and M1 were 7.0 (4.3), 7.3 (4.5), and 7.3 (5.2), respectively **(Table 2)**. The proportion of patients prescribed at least one PIM according to the OncPal Deprescribing Guidelines was 77.0% at M6, 76.4% at M3, and 70.0% at M1, showing a statistically meaningful reduction from M6 to M1 ($P < 0.001$).

Table 2. Trends in prescribed medications during the last 6 months of life in elderly patients with advanced cancer (n = 1269).

Medication-related variables	**P-value**	**M1**	**M3**	**M6**
Number of medications, median [IQR]		7.3 (5.2)	7.3 (4.5)	7.0 (4.3)
Polypharmacy, n (%) (number of medications ≧5)		870 (68.6)	921 (72.6)	889 (70.1)
Any PIMs, n (%)	< 0.001[a]	888 (70.0)	969 (76.4)	977 (77.0)
PIMs count, median [IQR]	< 0.001[b]	1 [0–3]	2 [1–3]	2 [1–3]
Drug class	**% change from M6 to M1**	**Prevalence, n (%)**		
		M1	**M3**	**M6**
Antiplatelet	−19.8*	146 (11.5)	164 (12.9)	182 (14.3)
Antihypertensives*	−20.9*	465 (36.6)	540 (42.6)	588 (46.3)
Calcium channel blockers	−31.2*	295 (23.2)	382 (30.1)	429 (33.8)
Beta-blockers	+7.6	142 (11.2)	126 (9.9)	132 (10.4)
ACE inhibitors	−15.0	17 (1.3)	16 (1.3)	20 (1.6)
Angiotensin II receptor blockers	−36.8*	194 (15.3)	275 (21.7)	307 (24.2)
Diuretic	−36.0*	32 (2.5)	42 (3.3)	50 (3.9)
Dyslipidemia medications	−49.5*	108 (8.5)	179 (14.1)	214 (16.9)
Statin	−50.0*	88 (6.9)	146 (11.5)	176 (13.9)
Fibrates	−50.0*	12 (0.9)	20 (1.6)	24 (1.9)
Ezetimibe	−46.9*	17 (1.3)	28 (2.2)	32 (2.5)
Oral hypoglycemics	−31.9*	130 (10.2)	167 (13.2)	191 (15.1)
Sulfonylureas	−50.0*	19 (1.5)	32 (2.5)	38 (3.0)
Metformin	−52.3*	21 (1.7)	30 (2.4)	44 (3.5)
DPP-4 inhibitors	−29.8*	106 (8.4)	132 (10.4)	151 (11.9)
SGLT-2 inhibitors	0.0	27 (2.1)	29 (2.3)	27 (2.1)
Glinides	−58.8*	7 (0.6)	11 (0.9)	17 (1.3)
α-Glucosidase inhibitors	−71.1*	11 (0.9)	29 (2.3)	38 (3.0)
GLP-1 analogs	−100.0	0	1 (0.1)	2 (0.2)
Thiazolidinediones	−33.3	6 (0.5)	7 (0.6)	9 (0.7)
Imeglimin	−100.0	0	0	1 (0.1)
Peptic ulcer prophylaxis	+2.0	679 (53.5)	688 (54.2)	666 (52.5)
H2 antagonists	−18.6	57 (4.5)	62 (4.9)	70 (5.5)
Proton pump inhibitors	+4.4	493 (38.8)	493 (38.8)	472 (37.2)
Potassium-competitive acid blockers	+7.6	156 (12.3)	147 (11.6)	145 (11.4)
Osteoporosis medications	−25.9*	60 (4.7)	87 (6.9)	81 (6.4)
Bisphosphonates	−24.3	28 (2.2)	43 (3.4)	37 (2.9)
Denosumab	−19.4	29 (2.3)	37 (2.9)	36 (2.8)
Raloxifene	−50.5	4 (0.3)	8 (0.6)	8 (0.6)
Vitamin and mineral	−15.0*	187 (14.7)	215 (16.9)	220 (17.3)
Vitamin	−19.7*	147 (11.6)	174 (13.7)	183 (14.4)
Mineral	+11.8	57 (4.5)	55 (4.3)	51 (4.0)
CAM		n.a	n.a	n.a

Abbreviations: M6 = 6 months before death; M3 = 3 months before death; M1 = 1 month before death; IQR = interquartile range; PIM = potentially inappropriate medication; DPP-4 = Dipeptidyl Peptidase-4; SGLT-2 = Sodium-Glucose Co-Transporter-2; GLP-1 = Glucagon-Like Peptide-1; CAM = complementary and alternative medicine.
a McNemar test between M6 and M1.
b Wilcoxon test between M6 and M1.
* $P < 0.05$.

Discontinuation and change in prescriptions of PIMs at the end of life in patients with advanced cancer

The PIMs most commonly withdrawn between M6 and M1 were antiplatelets (−19.8%, P < 0.001), antihypertensives (−20.9%, P < 0.001), treatments for dyslipidemia (−49.5%, P < 0.001), oral blood sugar-lowering agents (−31.9%, P < 0.001), drugs for osteoporosis (−25.9%, P = 0.018), and supplements containing vitamins and minerals (−15.0%, P = 0.016). By comparison, the frequency of peptic ulcer preventive therapy showed almost no change from M6 to M1 (+2.0%, P = 0.534).

Logistic regression analysis found that female patients (adjusted odds ratio (aOR) 1.35, 95% CI: 1.02–1.79), a higher total number of medications at M6 (aOR 1.08, 95% CI: 1.04–1.13), a greater number of coexisting illnesses (aOR 1.08, 95% CI: 1.01–1.16), admission to a palliative care unit (PCU) between M6 and M1 (aOR 11.63, 95% CI: 6.60–20.48), and admission to regular hospital wards between M6 and M1 (aOR 1.54, 95% CI: 1.14–2.06) were all independently linked to the stopping of any PIMs over this timeframe **(Table 3)**.

Table 3. Factors associated with deprescribing of any PIMs from M6 to M1 using logistic regression analysis (n = 977).

Variables	P-value	Adjusted OR (95% CI)
Age	0.742	1.00 (0.98–1.02)
Sex: female (vs male)	0.036	1.35 (1.02–1.79)
Number of medications at M6	< 0.001**	1.08 (1.04–1.13)
Number of comorbidities	0.027*	1.08 (1.01–1.16)
Use of HMC between M6 and M1	0.830	0.96 (0.67–1.38)
Admission to PCU between M6 and M1	< 0.001**	11.63 (6.60–20.48)
Admission to the general ward between M6 and M1	0.004**	1.54 (1.14–2.06)

Abbreviations: M6 = 6 months before death; M1 = 1 month before death; PIM = potentially inappropriate medication; OR = odds ratio; 95% CI = 95% confidence interval; HMC = home medical care; PCU = palliative care unit.
* P < 0.05. **P < 0.01.

The present findings indicate that the prescribing of PIMs in patients with advanced cancer generally declined in the period leading up to death. However, the overall reduction was modest. Several patient- and care-related factors were also found to be connected with the decision to discontinue these medications. To our knowledge, this is the first investigation in any Asian country to use nationwide claims data to chart the trajectory of PIMs across the final 6 months of life in this population, while simultaneously examining predictors of medication withdrawal.

Roughly three out of every four patients with advanced cancer near the end of life were receiving at least one long-term preventive drug for chronic conditions that appear on the OncPal Deprescribing Guideline. Given that all participants survived for no more than 6 months after the index point, such continued use may often be questionable. Earlier palliative care studies have reported PIM prevalence rates spanning from 22% to 95%, with the wide range attributable to differences in patient groups and evaluation tools [21]. At the M6 mark in our cohort, the leading PIM categories were: (1) peptic ulcer prophylaxis, (2) blood pressure-lowering agents, (3) vitamins and minerals, (4) lipid-lowering drugs, and (5) oral antidiabetic medicines — a pattern largely consistent with previous observations [22]. When no clear ongoing indication or symptom exists, these agents represent logical candidates for dose tapering or complete cessation [12].

Preventive therapies aimed at managing chronic conditions — such as antihypertensives, statins, and glucose-control drugs—were progressively discontinued as death neared. In sharp contrast, peptic ulcer prophylaxis remained essentially stable. This pattern mirrors results from an earlier Swedish investigation, although the reductions observed there for antihypertensives, vitamins/minerals, and bisphosphonates failed to reach statistical significance [5]. Such discrepancies likely arise from differing healthcare customs, cultural expectations, and regional practices. Taken together, the data suggest that clinicians frequently elect to halt preventive regimens once the limited remaining lifespan of patients with advanced cancer becomes evident. It is important to note, however, that our operational definition of deprescribing was based solely on recorded discontinuations and may not always reflect intentional, forward-looking clinical decisions. Furthermore, no direct assessment of clinical benefits, harms, or patient-reported outcomes was performed. Therefore, any conclusions regarding prescribing appropriateness drawn solely from drug class or guideline lists should be interpreted with caution.

Of particular interest, the rate of peptic ulcer prophylaxis remained relatively constant throughout the final months, consistent with one earlier report [23], whereas other studies have documented a clear downward trend [22, 24]. A likely contributing factor is the frequent concurrent use of corticosteroids or NSAIDs in advanced cancer for symptom relief — agents well known to heighten the danger of stomach and intestinal complications. Consequently, physicians may prefer to maintain gastroprotective therapy even while reducing other preventive drugs. Habitual prescribing patterns and the belief that these agents pose little additional risk may further encourage their ongoing use.

In the present study, among patients with advanced cancer nearing the end of life, women (compared with men), individuals taking a larger number of medications, those with a greater burden of comorbidities, and those who required hospital admission (including both palliative care units and regular wards) showed stronger associations with the discontinuation of PIMs. A separate Japanese investigation found that factors linked to reduced use of cardiovascular preventive drugs among patients receiving home-based care included older age, longer duration of home visits, presence of cancer, dementia, and Parkinson's disease [25].

In our analysis, female patients had a higher likelihood of having PIMs stopped. A prior systematic review concluded that sex did not influence older adults' general attitudes toward deprescribing [26]. However, another study identified female sex as a strong predictor of willingness to stop medications, with the odds rising threefold among women [27]. The researchers proposed that this link could stem partly from differences in how faithfully patients take their medicines. In addition, variations between men and women in actively participating in deprescribing discussions may play a role. Women appeared more conscious of the potential harms of certain drugs and were more inclined than men to start conversations about stopping medications or to report side effects they attributed to treatment [28]. Additional research is required to clarify the connection between sex and deprescribing decisions in this specific patient group.

Logically, deprescribing occurred more often among patients already experiencing polypharmacy and multiple health conditions, since individuals with several coexisting illnesses and high medication loads are generally open to reducing their drug regimens [29]. Deprescribing was also more common following admission to either general hospital wards or palliative care units. This pattern may indicate reactive deprescribing triggered by a noticeable worsening of the patient's overall health at the time of hospitalization. Furthermore, the involvement of multidisciplinary teams in medication reviews upon admission could have facilitated the process. Our results showed that deprescribing occurred more frequently during palliative care unit stays than during general ward admissions. Earlier work has suggested that specialist palliative care input is linked to better overall medication management [30]. These observations imply that palliative care specialists tend to adopt a more deliberate approach to deprescribing as part of a broader focus on improving quality of life and minimizing treatment burden near the end of life. The characteristics identified here cannot be altered directly, which limits opportunities for targeted intervention. Nevertheless, awareness of these features may help clinicians identify suitable candidates for deprescribing when conducting medication reviews. On the other hand, developing effective strategies for patients who are less likely to have medications stopped remains an important area for future investigation.

This study had several limitations. First, because the analysis relied on claims data, there is a possibility of recording inaccuracies or incomplete information, which could result in either overestimation or underestimation of comorbidity prevalence. However, the medication data encompassed prescriptions from multiple physicians, which strengthens confidence in the prescription-related findings. Second, the study included only patients who had received a cancer diagnosis at least 6 months before death; therefore, individuals with a shorter time between diagnosis and death were not represented. Third, the absence of blood pressure readings in the claims data meant that antihypertensive medications may have been classified as PIMs more often than warranted by clinical indications. Fourth, the evaluation was restricted to drugs listed in the OncPal Deprescribing Guidelines; other agents, including symptom-relief medications such as opioids and laxatives that are commonly added in the final 6 months, were not examined. Fifth, because the data came from a single city, generalizability to other regions or countries may be limited. Japan's healthcare environment — featuring universal coverage, high levels of physician trust, and a strong cultural focus on medication adherence — differs markedly from systems elsewhere [31]. Caution is therefore advised when applying these results to different cultural or healthcare contexts. Sixth, the study could not capture the actual process of deprescribing, including how doctors discussed stopping medications with patients and families or how those discussions were received. Future work should investigate the perspectives of physicians, patients, and caregivers regarding deprescribing in this population, along with its potential physical and psychological effects. Seventh, as this was a retrospective observational study, causal inferences cannot be drawn, and the findings must be interpreted carefully. The lack of clinical measures, such as performance status or symptom severity, also leaves open the possibility of unmeasured confounding. Eighth, the nature of claims data made it impossible to determine the clinical reasoning behind each medication change or to separate proactive deprescribing from reactive discontinuation clearly. Consequently, the observed patterns may partly reflect patients' worsening health or shifts in care settings rather than deliberate, structured deprescribing efforts.

Conclusion

The analysis revealed that prescriptions of PIMs among elderly patients with advanced cancer generally declined as death approached, although considerable scope for further deprescribing remains, given their short life expectancy. Female sex, higher medication burden, greater number of comorbidities, and hospital admission (including palliative care units) were all associated with the discontinuation of PIMs in this population. Awareness of these characteristics may help healthcare professionals identify opportunities for deprescribing during routine medication reviews. At the same time, efforts to promote proactive rather than reactive deprescribing should be

strengthened as part of a wider strategy to optimize medication use. Evaluating the actual effects of deprescribing in patients with advanced cancer and developing approaches for those in whom deprescribing is less common continue to represent key challenges for future research.

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The requirement for consent from individual participants was waived owing to the data's anonymity.

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