

Older Medicare Beneficiaries Frequently Continue Medications with Limited Benefit Following Hospice Admission



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BACKGROUND: The use of medications not relieving symptoms or maximizing quality of life should be minimized following hospice enrollment.

OBJECTIVE: To evaluate the frequency of and predictive factors for continuation of medications with limited benefit after hospice admission among those admitted for cancer- and non-cancer-related causes.

DESIGN: Cohort study using the Surveillance, Epidemiology and End Results-Medicare linked database.

PATIENTS: Medicare Part D-enrolled beneficiaries 66 years and older who were admitted to and died under hospice care between January 1, 2008, and December 31, 2013 (N = 70,035).

MAIN MEASURES: Patients were followed from hospice enrollment through death for Part D dispensing of limited benefit medications (LBMs) they had used in the 6 months prior to hospice admission, including anti-hyperlipidemics, anti-hypertensives, oral anti-diabetics, anti-platelets, anti-dementia medications, anti-osteoporotic medications, and proton pump inhibitors. The proportion of patients continuing an LBM after hospice admission was evaluated. Adjusted relative risks (RRs) were estimated for factors associated with LBM continuation.

KEY RESULTS: Overall, 29.8% and 30.5% of patients admitted to hospice for a cancer- and non-cancer-related cause, respectively, continued at least one LBM after hospice admission. Anti-dementia medications were continued most frequently (29.3%) while anti-osteoporotic medications were continued least often (14.1%). Compared to home hospice, LBM continuation was greater in hospice patients residing in skilled nursing (RR 1.25, 95% CI 1.20–1.29), non-skilled nursing (RR 1.29, 95% CI 1.25–1.32), and assisted living facilities (RR 1.28, 95% CI 1.24–1.32). Patients with hospice stays \geq 180 days were more likely to continue at least one LBM

compared to those with stays of 1 week or less (RR 13.11, 95% CI 12.25–14.02).

CONCLUSIONS: A substantial proportion of Medicare hospice beneficiaries continued to receive LBMs following hospice enrollment. Providers should evaluate the necessity of continuing non-palliative medications at the end of life through a careful, patient-centric consideration of their potential risks and benefits.

KEY WORDS: hospice; inappropriate medication use; deprescribing; Medicare Part D; end-of-life care.

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INTRODUCTION

In 2015, 46% of all Medicare decedents were enrolled in hospice care at the time of death.¹ Medicare's hospice benefit pays for enrollees' hospice-related care, including medications for palliative treatment of the terminal illness and related conditions, through Medicare Part A. Medications unrelated to the palliation of the patient's terminal illness may still be obtained through the Medicare Part D Prescription Drug Benefit for those with an active Part D plan.²

As the central purpose of hospice is to provide comfort care and support measures, medications which do not provide symptom relief or help to maximize quality of life may be unnecessary. Patients receiving hospice care are prescribed, on average, greater than 10 unique medications during their stay, including medications which are unlikely to have a palliative focus.^{3–5} The number of medications patients are prescribed as they approach the end of life has been shown to vary according to their terminal illness and associated disease trajectory, though it is unclear whether this variation is driven by changes in palliative medication prescribing only or whether differences in discontinuation of non-palliative medications also exist.^{6, 7}

In addition to limited effectiveness, continuation of these potentially unnecessary medications may increase the risk of

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medication side effects and drug-drug interactions, particularly given the high degree of polypharmacy often present in older adults as well as the physiological changes which occur as individuals approach the end of life.^{8–11} Other unintended consequences such as increased patient and healthcare system costs and burden on caregivers may also result.^{12–15} A number of barriers to routine deprescribing in the setting of limited life expectancy have been identified to date, including a reluctance among clinicians to discuss de-escalation of therapy, clinical inertia, refusal by patients and family members to stop medications, and lack of clinical consensus on what constitutes inappropriate medication use in the terminally ill.^{10, 12, 16–22}

We have previously reported the overall frequency of medication receipt, including potentially non-palliative drugs, through the Medicare Part D benefit in patients admitted to hospice.²³ However, the continued use of limited benefit medications after hospice admission in patients with a history of use prior to admission has not been quantified nor well characterized. It is unclear whether post-admission continuation may vary according to medication class, hospice admission diagnosis, or other patient and clinical factors. The goal of this research was to describe the prevalence of continuing medications with limited benefit after hospice admission among those with pre-hospice admission use, and identify factors associated with continuation in Medicare beneficiaries admitted to hospice for cancer- and non-cancer-related causes.

METHODS

Data Source and Study Population

This study used the nationally representative Surveillance, Epidemiology and End Results (SEER)-Medicare linked database and a random 5% non-cancer sample of Medicare beneficiaries residing in the SEER registry regions. Comprehensive, de-identified administrative claims were available for fee-for-service Medicare beneficiaries from January 1, 2007, to December 31, 2013. Claims contained data on sociodemographic characteristics, Medicare enrollment, healthcare utilization, diagnoses and procedures, vital status, and Medicare Part D prescription dispensing. The Medicare hospice enrollment file was used to identify individuals who enrolled and subsequently died in hospice between January 1, 2008, and December 31, 2013.

Patients aged less than 66 years at hospice admission and those not continuously enrolled in Medicare Parts A, B, and D from 1 year prior to hospice entry through the date of death were excluded. Patients with any enrollment in a Medicare Advantage plan were also excluded. Patients were required to have at least one Part D claim in the year prior to admission and no hospice enrollment gaps (i.e., discharges) lasting greater than 30 days after initial hospice admission.

The primary *International Classification of Diseases, Ninth Revision* (ICD-9) diagnostic code on the initial hospice claim was used to classify patients as having an admission for a

cancer or non-cancer diagnosis ([Online Supplementary Appendix](#)). SEER registry patients included in the cancer admission cohort were those admitted to hospice with a primary diagnosis of lung, colorectal, breast, pancreatic cancer, or lymphoma, which have been reported as the five most prevalent cancer-related hospice admission diagnoses among Medicare beneficiaries.²⁴ A unique patient identifier allowed for linkage of the SEER cancer cases with their respective Medicare claims. Patients admitted to hospice for a non-cancer diagnosis were identified from the random 5% non-cancer sample in addition to those in the SEER registry who ultimately entered hospice with a non-cancer-related primary admission diagnosis, despite being diagnosed with cancer in the past.

Medications with Limited Benefit Definition

Medication classes considered to be of potentially limited benefit in the end-of-life population were identified via literature review, which included primary research studies, review articles, and expert opinion pieces.^{16, 18, 25–35} Anti-hyperlipidemics, anti-hypertensives, oral antidiabetics, anti-platelets, anti-dementia medications, anti-osteoporotic medications, and proton pump inhibitors were included, with some disease-specific exceptions. Based on the aforementioned literature and expert opinion, drug classes were excluded from the analysis at the patient level if a diagnosis was present (via ICD-9 codes on two outpatient claims or one inpatient admission) in the year prior to hospice admission for a condition where the medication may provide a symptomatic benefit or decrease the short-term (e.g., < 1 year) risk of major adverse events (Table 1). Medication classes that were entirely available over-the-counter during the study period (e.g., H2 receptor antagonists) were excluded as they are not reliably captured via Medicare Part D claims. While not intended to be definitive or comprehensive, the selected medication classes are characterized by a general lack of utility in the palliation of terminal illness symptoms or in optimizing quality of life near the end of life.

Limited Benefit Medication Use

Baseline limited benefit medication use was measured in the 6 months prior to hospice admission. Patients were considered active pre-hospice admission users of a particular drug or therapeutic class if they had two or more Part D claims for any days' supply on different days for the class of interest or one Part D claim with a days' supply of at least 90 days. Patients not meeting these criteria for at least one limited benefit medication were excluded (Fig. 1).

Outcomes

The primary outcome was continuation of at least one limited benefit medication between the date of hospice admission and date of death. Pre-admission users of a particular drug class

Table 1 Medication Classes Identified as Being of Limited Benefit in Patients Receiving Hospice Care and Criteria for Exclusion from the Continuation Analysis*

Therapeutic class	Associated drug classes	Patient-specific exclusions
Anti-hyperlipidemic	HMG-CoA reductase inhibitors Fibric acid derivatives Bile acid sequestrants 2-Azetidinones (ezetimibe)	HMG-CoA reductase inhibitors excluded when used after recent myocardial infarction or ischemic stroke [†]
Anti-hypertensive	Thiazide diuretics Other non-loop diuretics [‡] ACE inhibitors ARBs DHP CCBs Non-DHP CCBs Beta-blockers Alpha-blockers Centrally acting agents Vasodilators Direct renin inhibitors	i. Diuretics, beta-adrenergic antagonists, ACE inhibitors, ARBs, and hydralazine (in combination with nitrates) excluded when used for congestive heart failure ii. Beta-adrenergic antagonists and CCBs excluded when used for angina pectoris iii. Non-DHP CCBs and beta-adrenergic antagonists excluded when used for atrial fibrillation/flutter iv. Beta-adrenergic antagonists, ACE inhibitors, and ARBs excluded when used after recent myocardial infarction [†]
Oral antidiabetic	Biguanides Sulfonylureas Dipeptidyl peptidase-4 inhibitors Meglitinides Alpha glucosidase inhibitors Thiazolidinediones	
Anti-dementia	Cholinesterase inhibitors NMDA receptor antagonists	
Anti-osteoporotic	Bisphosphonates SERMs	
Anti-platelet	P2Y ₁₂ inhibitors Aspirin-dipyridamole	i. P2Y ₁₂ inhibitors excluded when used after recent myocardial infarction or ischemic stroke [†] ii. Aspirin-dipyridamole excluded when used after recent ischemic stroke [†]
	Proton pump inhibitors	

ACE angiotensin-converting enzyme, ARB angiotensin receptor blocker, CCB calcium channel blocker, DHP dihydropyridine, SERM selective estrogen receptor modulators

*identified via published literature^{16, 18, 25-35} (medication classes and patient-specific exclusions) and expert opinion (patient-specific exclusions only)

[†]'Recent' defined as presence of a primary hospital discharge for the event in the 12 months prior to hospice admission

[‡]Includes amiloride and triamterene in combination with hydrochlorothiazide; includes all formulations of spironolactone

with at least one new Part D claim for a medication from the same class on or after the date of hospice admission were considered continuers of the class of medications. Medication class-specific continuation and post-admission continuation of all limited benefit medication classes used in the pre-hospice admission period were assessed.

Statistical Analysis

Descriptive statistics were used to evaluate baseline characteristics, pre-hospice admission limited benefit medication use, and post-admission continuation overall and stratified by cancer versus non-cancer hospice admission diagnosis. Drug and therapeutic class-specific continuation prevalence for patients admitted to hospice for a cancer versus non-cancer diagnosis were compared using absolute risk differences with 95% confidence intervals (CIs).

Modified Poisson regression with generalized estimating equations was used to generate adjusted relative risks (RRs) and 95% CIs for the association between patient factors and the continuation of at least one drug or therapeutic class with limited benefit after hospice admission, accounting for anticipated clustering of responses at the hospice facility level.^{36, 37} An exchangeable correlation structure with robust variance estimation was used to allow for valid standard error estimates.

A separate model was fit for each factor of interest.³⁸ Fractional polynomials were used to allow for non-linear exposure-outcome relationships. A manual backwards selection approach was used to identify potential confounders using a change in estimate criterion of 5%, as simulations have found the commonly used 10% change in estimate criterion to be too conservative for large sample sizes.³⁹ Age, gender, and race were treated as a priori confounders and forced into all models, regardless of empirical evidence of confounding. All statistical tests were two-sided with *p* values < 0.05 considered statistically significant. Analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC) and STATA 14.0 (StataCorp, College Station, TX). The institutional review board at the University of Illinois at Chicago approved this study. Informed consent was not obtained as this study was determined by the institutional review board to not constitute human subjects research.

RESULTS

Of 88,957 patients initially identified, 70,035 patients (78.7%) had active use of at least one limited benefit medication prior to hospice admission; 44,218 (63.1%) patients were admitted to hospice for cancer and 25,817 (36.9%) patients were

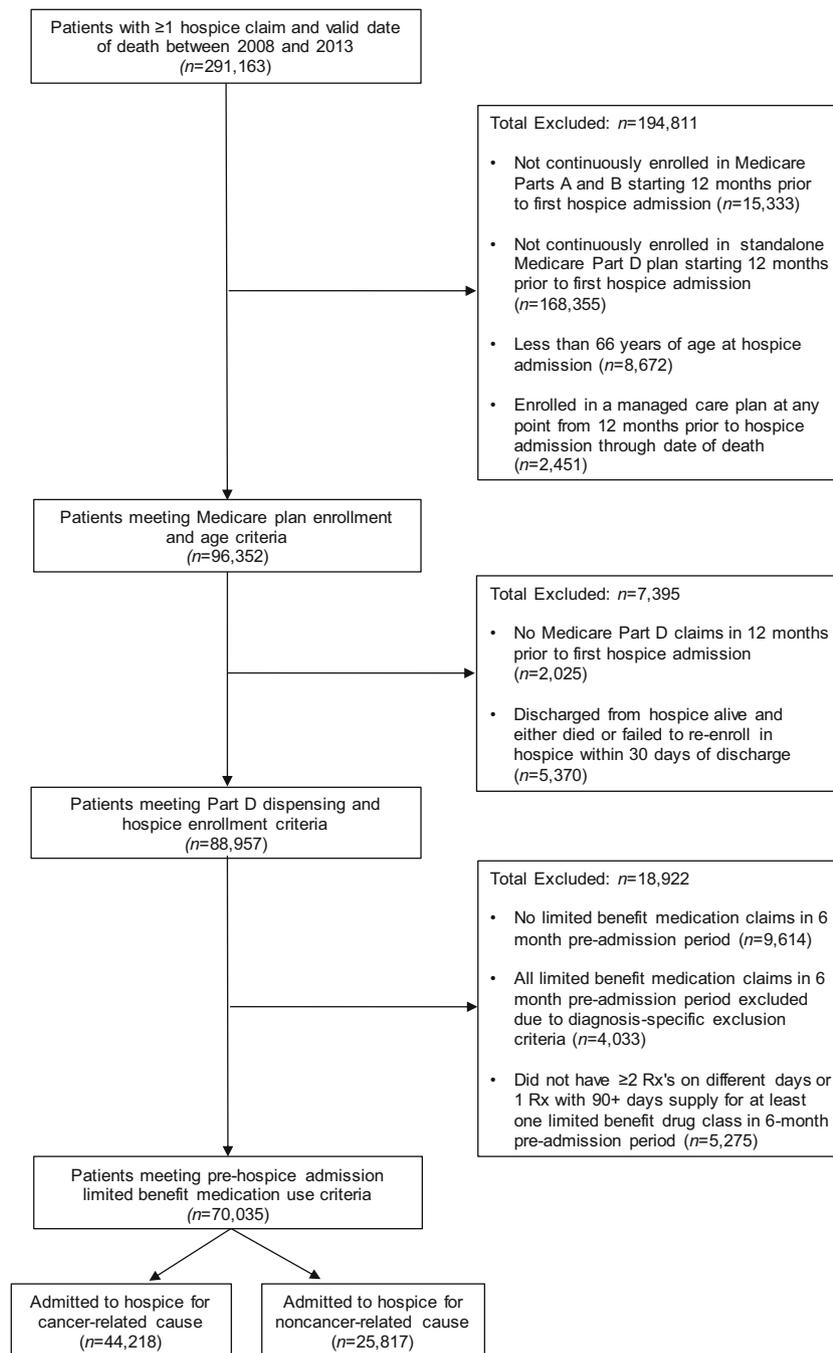


Figure 1 Patient flow diagram

admitted for a non-cancer diagnosis (Fig. 1). Most patients were white (85.2%) and female (67.3%) (Table 2). The median (interquartile range [IQR]) hospice length of stay was 15 (5–48) days, 65% of patients had hospice stays of less than 30 days, and the mean (standard deviation [SD]) number of unique medications used through the Part D benefit prior to hospice admission was 15.7 (7.0). Compared to patients admitted for a non-cancer diagnosis, patients admitted to hospice for cancer were younger (mean (SD), 79.2 (7.7) years vs. 85.5 (7.8) years, $p < 0.001$), were more likely to be admitted to hospice in a private home (68.7% vs. 38.2%, $p < 0.001$), and

had fewer very short (≤ 7 days, 29.9% vs. 39.1%, $p < 0.001$) or very long (≥ 180 days, 4.9% vs. 9.2%, $p < 0.001$) hospice stays (Table 2). The most common admission diagnoses in the non-cancer cohort were debility/failure to thrive (22.3%), dementia (21.0%), and heart disease (16.9%).

The primary outcome, continuation of at least one limited benefit medication after hospice admission among those with active pre-admission use of at least one of these medications, occurred in 29.8% of patients admitted for cancer and 30.5% of patients admitted for a non-cancer diagnosis. For both cancer and non-cancer patients, anti-dementia medications

Table 2 Demographic and Clinical Characteristics of Study Cohort

Characteristic	All patients (n = 70,035)	Cancer (n = 44,218)	Non-cancer (n = 25,817)
Female sex	67.3%	63.5%	73.8%
Age (years)			
Mean (SD)	81.5 (8.3)	79.2 (7.7)	85.5 (7.8)
66–69	8.7%	12.0%	3.2%
70–74	15.1%	19.7%	7.2%
75–79	17.2%	20.5%	11.4%
80–84	20.3%	21.0%	19.1%
85–89	20.0%	16.4%	26.0%
≥ 90	18.8%	10.5%	33.1%
Race			
White	85.2%	83.8%	87.5%
Black	8.3%	8.8%	7.5%
Hispanic	2.0%	2.0%	1.9%
Asian	2.9%	3.4%	1.8%
Other or missing	1.7%	1.9%	1.3%
Geographic region			
Midwest	16.1%	15.1%	17.8%
Northeast	20.5%	20.6%	20.3%
South	29.0%	29.0%	29.0%
West	34.4%	35.3%	32.8%
Hospice admission year			
2008	16.6%	18.2%	13.9%
2009	18.0%	19.5%	15.5%
2010	18.8%	20.0%	16.9%
2011	19.4%	19.8%	18.7%
2012	15.4%	13.4%	18.8%
2013	11.8%	9.2%	16.3%
Hospice admission setting			
Private home	57.5%	68.7%	38.2%
Assisted living facility	4.4%	2.6%	7.6%
Non-skilled nursing facility	12.3%	7.8%	20.0%
Skilled nursing facility	8.3%	5.8%	12.5%
Inpatient (acute care) hospital	8.2%	6.6%	10.8%
Inpatient hospice facility	8.1%	7.3%	9.4%
Other or missing	1.3%	1.3%	1.4%
Primary hospice admission diagnosis			
Cancer	63.1%	100.0%	0%
Debility or failure to thrive	8.2%	0%	22.3%
Dementia	7.8%	0%	21.0%
Lung disease	5.1%	0%	13.8%
Heart disease	6.2%	0%	16.9%
Ischemic stroke	2.0%	0%	5.4%
Renal disease	2.2%	0%	5.9%
Other non-cancer	5.4%	0%	14.7%
Hospice length of stay (days)			
Median (IQR)	15 (5–48)	17 (6–47)	12 (4–50)
≤ 7	33.3%	29.9%	39.1%
8–14	15.7%	16.0%	15.2%
15–29	15.9%	17.8%	12.7%
30–89	20.5%	23.3%	15.6%
90–179	8.1%	8.1%	8.0%
≥ 180	6.5%	4.9%	9.2%
Comorbidity			
Hypertension	86.4%	85.5%	88.0%
Heart failure	33.5%	24.6%	48.8%
Diabetes mellitus	40.9%	40.4%	41.8%
COPD	41.7%	43.3%	39.0%
Recent ischemic stroke	5.9%	3.9%	9.5%
Recent myocardial infarction	4.6%	3.0%	7.2%
Coronary atherosclerosis	36.9%	34.0%	41.9%
Cardiac dysrhythmia	43.3%	38.2%	51.9%
Renal disease	24.5%	19.6%	33.0%
Liver disease	20.2%	25.4%	11.4%
Swallowing difficulty	24.0%	17.4%	35.5%
Hospitalizations in year prior to admission			
0	18.0%	17.5%	18.9%
1	29.0%	29.8%	27.8%
2	21.5%	22.2%	20.2%
3 or 4	21.4%	21.4%	21.4%

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Table 2. (continued)

Characteristic	All patients (n = 70,035)	Cancer (n = 44,218)	Non-cancer (n = 25,817)
5 or more	10.1%	9.1%	11.7%
ICU stay in 90 days prior to admission	26.5%	23.8%	31.2%
Hospital discharge to hospice [†]	43.1%	41.7%	45.7%
Number of outpatient clinicians in year prior to admission [‡]			
Median (IQR)	5 (3–8)	6 (4–9)	4 (3–7)
Unique Part D medications in year prior to admission			
Mean (SD)	15.7 (7.0)	15.8 (7.0)	15.5 (7.1)
Limited benefit drug classes used in 6 months prior to admission			
Mean (SD)	2.6 (1.5)	2.6 (1.5)	2.5 (1.5)
Part D low-income subsidy recipient	42.9%	39.5%	48.7%

SD standard deviation, ICU intensive care unit, IQR interquartile range, COPD chronic obstructive pulmonary disease

$p < 0.001$ for all cancer versus non-cancer group comparisons using t tests for continuous variables and Pearson's chi-square tests for categorical variables

[†]Hospital discharge occurring in the 3 days prior to hospice admission

[‡]Excludes claims generated in emergency departments, outpatient hospitals, and surgery centers; includes physicians, physician's assistants, and nurse practitioners as clinicians

(33.4% and 27.3%) and anti-hypertensives (26.7% and 26.0%) were the most frequently continued therapeutic classes while anti-osteoporotic medications (13.2% and 15.4%) and anti-hyperlipidemic medications (15.1% and 19.0%) were continued least often (Table 3). Compared to admission for a non-cancer diagnosis, patients admitted to hospice for cancer had a lower absolute risk of continuing anti-hyperlipidemic (−3.9%; 95% CI, −4.9 to −2.9%) and anti-osteoporotic medications (−2.1%; 95% CI, −4.0 to −0.3%), but a higher risk of continuing anti-dementia medications (6.0%; 95% CI, 4.2 to 7.8%) (Table 3).

In adjusted analyses, the likelihood of continuing at least one medication with limited benefit after hospice admission increased with age and was lower for Asian (RR 0.85; 95% CI, 0.80–0.91) and Hispanic patients (RR 0.88; 95% CI, 0.82–0.94) compared to White patients (Table 4). The risk of continuing one or more limited benefit medications was 1.28 (95% CI, 1.24–1.32) among those in assisted living facilities, 1.29 (95% CI, 1.25–1.32) among those in non-skilled nursing facilities, and 1.25 (95% CI, 1.20–1.29) among those in skilled nursing facilities compared to those admitted to hospice in a private home. Conversely, the risk of continuing one or more limited benefit medications was 0.45 (95% CI, 0.40–0.51) among those in acute care hospitals and 0.46 (95% CI, 0.40–0.52) among those in inpatient hospice facilities compared to private home admission. By hospice length of stay, the likelihood of receiving at least one limited benefit medication after admission was 2.59 times greater (95% CI 2.41–2.79) for those with stays of 8–14 days compared to those with stays ≤ 7 days, increasing to 9.39 (95% CI 8.80–10.02) and 13.11 (95% CI 12.25–14.02) for those with hospice stays of 30–89 days and 180 or more days, respectively (Table 4).

Table 3 Pre-hospice Admission Limited Benefit Medication Use and Post-admission Continuation Among Pre-admission Users by Cancer Versus Non-cancer Hospice Admission Diagnosis

Therapeutic or drug class [‡]	Pre-hospice admission use		Proportion of users continuing after admission*		Risk difference, cancer versus non-cancer [†]
	Cancer (n = 44,218)	Non-cancer (n = 25,817)	Cancer	Non-cancer	
	No. (%)	No. (%)	No. (%)	No. (%)	% (95% CI)
Anti-hyperlipidemic	17,760 (40.2%)	8799 (34.1%)	2682 (15.1%)	1671 (19.0%)	-3.9 (-4.9, -2.9)
Statin	16,411 (37.1%)	7976 (30.9%)	2457 (15.0%)	1532 (19.2%)	-4.2 (-5.3, -3.2)
Anti-hypertensive	30,015 (67.9%)	15,053 (58.3%)	8026 (26.7%)	3909 (26.0%)	+0.8 (-0.1, 1.6)
Beta-Blocker	11,255 (25.5%)	4744 (18.4%)	3145 (27.9%)	1412 (29.8%)	-1.8 (-3.4, -0.3)
ACE inhibitor	9211 (20.8%)	3463 (13.4%)	2030 (22.0%)	911 (26.3%)	-4.3 (-6.0, -2.6)
DHP CCB	9943 (22.5%)	5789 (22.4%)	2323 (23.4%)	1260 (21.8%)	+1.6 (0.3, 3.0)
ARB	4969 (11.2%)	1566 (6.1%)	1094 (22.0%)	354 (22.6%)	-0.6 (-3.0, 1.8)
Thiazide diuretic	8769 (19.8%)	3820 (14.8%)	1402 (16.0%)	586 (15.3%)	+0.7 (-0.7, 2.0)
Oral anti-diabetic	9082 (20.5%)	4580 (17.7%)	2117 (23.3%)	1024 (22.4%)	+1.0 (-0.5, 2.4)
Sulfonylurea	4985 (11.3%)	2604 (10.1%)	1086 (21.8%)	535 (20.5%)	+1.2 (-0.7, 3.2)
Biguanide	5015 (11.3%)	1938 (7.5%)	1003 (20.0%)	419 (21.6%)	-1.6 (-3.8, 0.5)
Antiplatelet	4040 (9.1%)	2828 (11.0%)	897 (22.2%)	671 (23.7%)	-1.5 (-3.6, 0.5)
Anti-dementia	3861 (8.7%)	7761 (30.1%)	1288 (33.4%)	2121 (27.3%)	+6.0 (4.2, 7.8)
Anti-osteoporotic	3309 (7.5%)	2370 (9.2%)	438 (13.2%)	364 (15.4%)	-2.1 (-4.0, -0.3)
Proton pump inhibitor	17,480 (39.5%)	10,213 (39.6%)	4186 (23.9%)	2634 (25.8%)	-1.8 (-2.9, -0.8)
At least one limited benefit medication	44,218 (100.0%)	25,817 (100.0%)	13,191 (29.8%)	7862 (30.5%)	-0.7 (-1.5, 0.1)

ACE angiotensin-converting enzyme, ARB angiotensin receptor blocker, DHP CCB dihydropyridine calcium channel blocker, CI confidence interval
 *Patients with at least one dispensing for the class of interest through the Part D benefit after hospice admission among those with active use of that class in the 6 months prior to hospice admission

[†]Difference in proportion of pre-hospice admission users with at least one Part D dispensing for the class of interest after hospice admission

[‡]Selected drug classes only; results by therapeutic class include all associated drug classes in Table 1

Compared to patients using only one class prior to admission, the risk of continuing at least one limited benefit medication class after admission was 1.39 (95% CI 1.35–1.44) among those using two limited benefit drug classes prior to admission and 2.00 (95% CI 1.93–2.08) in those using six or more classes prior to admission (Table 4).

DISCUSSION

This is the first study to evaluate the continuation of limited benefit medications after admission to hospice. We accomplished this by identifying a cohort of patients with limited benefit medication use prior to hospice enrollment and following them through their hospice stay until death to assess continued dispensing of these medications through the Medicare Part D benefit. Among 70,035 Medicare beneficiaries who died in hospice and had active use of at least one limited benefit medication prior to hospice admission, 29.8% of patients admitted to hospice for a cancer diagnosis and 30.5% of those admitted for a non-cancer diagnosis continued to receive at least one of these medications after hospice enrollment. Continuation varied by medication class while factors such as age, hospice care setting, and length of hospice stay were independently associated with continuing one or more limited benefit medications after hospice admission.

Our results appear to align with current expert opinion and consensus surveys. Therapeutic classes more uniformly cited by geriatric and palliative care experts as providing minimal or no benefit at the end of life, such as anti-hyperlipidemic and anti-osteoporotic medications, were generally continued less

frequently than classes associated with a more uncertain benefit.^{25, 40} If a medication has the potential to provide a symptomatic benefit, even if modest or only realized in a small proportion of total patients using the medication (e.g., oral anti-diabetics for treating symptomatic hyperglycemia), clinicians may elect to continue the medication as a conservative measure for the majority of their patients. This may help to explain the relatively frequent continuation of anti-dementia medications in our study, particularly among those admitted to hospice for cancer. While there is a growing consensus for anti-dementia medications' lack of benefit in terminal dementia, these medications could still be perceived to have therapeutic value in patients with terminal cancer (or other non-dementia terminal illnesses) where mild or moderate comorbid dementia is present.^{26, 30, 41}

Recent studies have emerged which may help address the evidence gap concerning deprescribing outcomes in the hospice and palliative care setting. A large, epidemiologic study found that blood pressure values decreased progressively for the 14 to 18 years prior to death, with the steepest decreases among those dying at older ages and those being treated for hypertension; this may support a more judicious use of anti-hypertensive medications in the end of life setting.⁴² A randomized, controlled trial among patients with a life expectancy of 1 year or less found that statin discontinuation at the end of life was safe and did not diminish quality of life.⁴³ In a small, interventional trial among frail older adults (mean age = 84.3 years), patients discontinuing inappropriate medications and medications with no further symptomatic benefit did not experience an increase in mortality or reduction in quality of life after 12 months of follow-up.⁴⁴

Table 4 Factors Associated with Continuation of ≥ 1 Limited Benefit Medication After Hospice Admission

Variable	≥ 1 limited benefit medication after hospice admission		Adjusted association		
			All patients	Cancer admission diagnosis	Non-cancer admission diagnosis
	n/N	%	RR (95% CI)	RR (95% CI)	RR (95% CI)
Sex					
Male	6198/22,883	27.1	Ref*	Ref*	Ref*
Female	14,855/47,152	31.5	1.01 (0.99–1.03)	1.02 (0.99–1.05)	0.99 (0.96–1.02)
Age (years)					
66–69	1553/6117	25.4	Ref [†]	Ref [†]	Ref [†]
70–74	2807/10,580	26.5	1.04 (0.99–1.08)	1.05 (1.00–1.10)	1.00 (0.90–1.10)
75–79	3393/12,010	28.3	1.06 (1.02–1.10)	1.08 (1.03–1.13)	1.00 (0.91–1.09)
80–84	4379/14,196	30.9	1.11 (1.07–1.16)	1.13 (1.08–1.18)	1.01 (0.92–1.10)
85–89	4537/13,972	32.5	1.14 (1.10–1.18)	1.17 (1.12–1.22)	0.99 (0.91–1.08)
≥ 90	4381/13,160	33.3	1.17 (1.13–1.22)	1.19 (1.14–1.25)	0.99 (0.91–1.08)
Race					
White	17,832/59,664	29.9	Ref [‡]	Ref [‡]	Ref [‡]
Black	1,955/5825	33.6	0.97 (0.94–1.01)	0.98 (0.94–1.03)	0.95 (0.90–1.01)
Asian	568/1996	28.5	0.85 (0.80–0.91)	0.81 (0.75–0.88)	0.95 (0.95–1.07)
Hispanic	393/1374	28.6	0.88 (0.82–0.94)	0.86 (0.79–0.93)	0.89 (0.80–0.99)
Hospice admission setting					
Private home	12,992/40,241	32.3	Ref [§]	Ref [§]	Ref [§]
Assisted living facility	1496/3103	48.2	1.28 (1.24–1.32)	1.24 (1.18–1.30)	1.28 (1.22–1.34)
Non-skilled nursing facility	3812/8601	44.3	1.29 (1.25–1.32)	1.35 (1.30–1.40)	1.26 (1.21–1.32)
Skilled nursing facility	2012/5778	34.8	1.25 (1.20–1.29)	1.29 (1.23–1.36)	1.21 (1.15–1.27)
Inpatient (acute care) hospital	239/5718	4.2	0.45 (0.40–0.51)	0.49 (0.42–0.56)	0.38 (0.31–0.47)
Inpatient hospice facility	345/5655	6.1	0.46 (0.40–0.52)	0.51 (0.44–0.60)	0.35 (0.29–0.43)
Primary hospice admission diagnosis					
Cancer	13,191/44,218	29.8	Ref		
Debility or adult failure to thrive	2190/5757	38.0	1.05 (1.02–1.09)		
Dementia	2025/5425	37.3	1.06 (1.03–1.10)		
Lung disease	1024/3568	28.7	1.11 (1.07–1.16)		
Heart disease	1286/4368	29.4	0.97 (0.93–1.01)		
Ischemic stroke	244/1389	17.6	0.89 (0.81–0.98)		
Renal disease	253/1512	16.7	1.03 (0.94–1.13)		
Other non-cancer	840/3798	22.2	0.98 (0.93–1.03)		
Hospice length of stay (days)					
≤ 7	1122/23,339	4.8	Ref	Ref	Ref
8–14	1498/10,994	13.6	2.59 (2.41–2.79)	2.43 (2.22–2.66)	2.93 (2.61–3.30)
15–29	3072/11,155	27.5	4.95 (4.62–5.30)	4.60 (4.21–5.02)	5.85 (5.26–6.51)
30–89	7686/14,347	53.6	9.39 (8.80–10.02)	8.82 (8.11–9.59)	10.87 (9.86–11.98)
90–179	4033/5650	71.4	12.11 (11.33–12.95)	11.81 (10.85–12.86)	12.92 (11.69–14.29)
≥ 180	3642/4550	80.0	13.11 (12.25–14.02)	12.86 (11.79–14.03)	14.04 (12.71–15.51)
Number of outpatient clinicians in year prior to admission					
1–3	6735/20,253	33.3	Ref	Ref	Ref
4–6	7170/23,122	31.0	0.99 (0.96–1.01)	0.97 (0.95–1.00)	0.99 (0.96–1.03)
7–9	4352/15,353	28.4	0.96 (0.94–0.98)	0.95 (0.92–0.98)	0.97 (0.93–1.01)
≥ 10	2796/11,307	24.7	0.91 (0.89–0.94)	0.90 (0.86–0.93)	0.95 (0.90–1.00)
Unique Part D medications in year prior to admission					
1–4	399/1628	24.5	Ref [#]	Ref [#]	Ref [#]
5–9	3330/11,769	28.3	1.08 (1.01–1.16)	1.09 (0.99–1.19)	1.07 (0.96–1.20)
10–19	11,514/38,072	30.2	1.11 (1.03–1.18)	1.10 (1.01–1.20)	1.14 (1.02–1.28)
20–29	4859/15,716	30.9	1.13 (1.06–1.22)	1.12 (1.02–1.22)	1.20 (1.07–1.34)
≥ 30	951/2850	33.4	1.18 (1.09–1.28)	1.13 (1.02–1.25)	1.33 (1.16–1.51)
Limited benefit drug classes used in 6 months prior to admission					
1	4128/20,591	20.1	Ref ^{**}	Ref ^{**}	Ref ^{**}
2	5398/18,817	28.7	1.39 (1.35–1.44)	1.41 (1.36–1.47)	1.37 (1.31–1.43)
3	4868/14,260	34.1	1.61 (1.56–1.66)	1.64 (1.57–1.70)	1.57 (1.50–1.65)
4–5	5158/13,035	39.6	1.81 (1.75–1.86)	1.86 (1.79–1.94)	1.71 (1.64–1.79)
≥ 6	1501/3332	45.1	2.00 (1.93–2.08)	2.08 (1.98–2.18)	1.87 (1.76–1.98)

n number of patients in stratum using at least one limited benefit medication after hospice admission, N total number of patients in stratum, RR relative risk, CI confidence interval

*Adjusted for age, race, and hospice length of stay

[†]Adjusted for sex, race, hospice length of stay, Part D low-income subsidy, and limited benefit medication classes used prior to hospice admission

[‡]Adjusted for age, sex, hospice length of stay, and Part D low-income subsidy

[§]Adjusted for age, sex, race, hospice length of stay, Part D low-income subsidy, and primary hospice admission diagnosis

^{||}Adjusted for age, sex, race, and hospice length of stay

[#]Adjusted for age, sex, race, hospice length of stay, Part D low-income subsidy, limited benefit medication classes used prior to hospice, hospice admission setting, and hospital discharge to hospice

^{*}Adjusted for age, sex, race, hospice length of stay, Part D low-income subsidy, limited benefit medication classes used prior to hospice, heart failure diagnosis, and COPD diagnosis

^{**}Adjusted for age, sex, race, hospice length of stay, and Part D low-income subsidy

The increased risk of continuation with hospice admission in nursing and assisted living facilities may have a basis in the prescription processing practices of long-term care pharmacies associated with these facilities. Given that initiation of hospice care in these settings often does not represent a change in where a patient is receiving care, standing orders for non-palliative medications used prior to hospice enrollment may continue to be automatically dispensed by the facility-associated pharmacy after a patient's hospice election.⁴⁵ Explanations for higher rates of limited benefit medication continuation with increasing hospice length of stay are not immediately clear. Prescribers may be more likely to discontinue such medications in patients with a poorer prognosis and shorter anticipated life expectancy.⁴⁶ Alternatively, this result may reflect the increased likelihood of receiving a prescription refill as patient survival, and therefore, time since the last medication fill, also increases. Further research is needed elucidating the patterns of medication discontinuation at the point of hospice admission and the mechanisms by which medications that are characterized by a lack of utility for symptom management are continued. Until then, periodic reviews of non-palliative medication use after hospice admission are warranted to ensure that patients' medication regimens continue to appropriately align with their goals of care.

Limitations

This study has several limitations. First and most importantly, the medication classes and disease-specific exclusions chosen for this study are exploratory and largely based on expert opinion. Thus, it is not intended to be a definitive or complete representation of non-essential medications in the hospice population, an area that is in great need of further research. Given the complexity of individual patient treatment decisions at the end of life, this approach and that of others should not be interpreted as a substitute for clinical judgement. Second, potentially influential factors such as hospice profit status and staffing levels, hospice program age, patient and family treatment preferences or perceived treatment benefits, level of cognitive and functional impairment, and family support were unable to be measured. Third, the true prevalence of medication continuation is likely underestimated as continuation was measured via new Part D dispensings after hospice admission. Patients without a new Part D dispensing may have continued using medication supplies obtained prior to admission during their hospice stay or obtained medication refills outside of their Part D plan. Certain medications with questionable palliative benefit may nevertheless have been provided by the patient's hospice program as related to palliation of the patient's terminal illness, resulting in outcome misclassification and further underestimation of continuation. Fourth, medication dispensing via claims is an imperfect proxy for medication use, particularly in the terminally ill population. Fifth, this study took place largely before the Medicare program began issuing guidance on Part D reimbursement in hospice, and

clinicians may now be more cognizant of non-essential medication use in patients enrolled in hospice care.

CONCLUSIONS

Among Medicare beneficiaries who were admitted to and subsequently died in hospice, approximately 30% continued to receive medications which may have limited use in the palliation of terminal illness symptoms or quality of life improvement. Providers caring for patients admitted to hospice, particularly those admitted to hospice in nursing or assisted living facilities and those with a substantial non-palliative medication burden at admission, should carefully consider the burden versus benefit of medication continuation given the expectation of limited life expectancy. Our results highlight the need for the development of interventions targeting the discontinuation of limited benefit medications at the point of hospice enrollment.

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Data Availability The SEER-Medicare data that support the findings of this study are available from the National Cancer Institute, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Compliance with Ethical Standards:

The institutional review board at the University of Illinois at Chicago approved this study. Informed consent was not obtained as this study was determined by the institutional review board to not constitute human subjects research.

Conflict of Interest: PMZ was a doctoral candidate in the Department of Pharmacy Systems, Outcomes and Policy at the University of Illinois at Chicago when the study was conducted and is a current employee of AbbVie Inc. All remaining authors declare that they do not have a conflict of interest.

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