Study of Trends and Outcomes of Prescription Medications Continued During Hospice Care (STOP Med)

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THESIS

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I led and was primarily responsible for study conceptualization and design, data analysis and interpretation, and manuscript development and submission. All committee members provided input on study conceptualization and design prior to finalization, aided in interpreting results, and provided critical review of the final manuscripts prior to journal submission. Dr. Gregory Calip provided additional guidance on study design, analytic methods, and use of the SEER-Medicare data. Dr. Holly Holmes provided key clinical and subject matter expertise which served to strengthen the validity of the study approach and frame the importance of the results when discussing implications for clinical practice and health care policy. Dr. Todd Lee, advisor and dissertation committee chair, assisted in obtaining the data and supervised all study activities. Dr. Lee provided detailed guidance at each step from study conceptualization to completion of the final manuscripts. He serves as senior author on the manuscripts resulting from this dissertation.

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**LIST OF ABBREVIATIONS**

|  |  |
| --- | --- |
| ADE | Adverse Drug Event |
| CI | Confidence Interval |
| CMS | Centers for Medicaid and Medicare Services |
| DDI | Drug-Drug Interaction |
| ED | Emergency Department |
| EOL | End of Life |
| IAHPC | International Association for Hospice and Palliative Care |
| ICD-9 | International Classification of Diseases, Ninth Revision |
| IRR | Incidence Rate Ratio |
| LBM | Limited Benefit Medication |
| MHB | Medicare Hospice Benefit |
| PIM | Potentially Inappropriate Medication |
| RR | Relative Risk |
| SEER | Surveillance, Epidemiology and End Results |
| STOPPFrail | Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy |
| US | United States |

**SUMMARY**

 In the United States (US), hospice is an increasingly utilized mode of end of life (EOL) care. Patients enrolling in hospice forego curative treatment in favor of holistic palliative care aimed at relieving symptoms and maximizing quality of life in their final weeks and days. In 2015, nearly half of older Medicare beneficiaries died in hospice. Given the widespread use of hospice services, it is of great public health importance to ensure that high-quality, ethical care is provided in a manner consistent with the hospice mission. Encompassed in this mission is the discontinuation of limited benefit medications (LBMs), those medications which no longer provide a patient benefit in the context of limited life expectancy. The continued use of LBMs contributes to overly complicated medication regimens and poor adherence, exposure to medication side effects and drug interactions, significant patient and caregiver burden, and needlessly high medications costs. Despite the hospice care treatment philosophy, there was preliminary evidence demonstrating that a substantial proportion of older hospice patients continued to receive medications that could be considered LBMs until death. However, these studies were generally small and did not specifically aim to evaluate LBM use. Much remained unknown about use of these medications among patients admitted to hospice. Further assessment of LBM use in the hospice setting was needed to inform providers and policy makers of the scope of the issue and prompt the development of interventions aimed at improving medication use at the end of life. This dissertation is comprised of five chapters and aimed to help fill the current evidence gaps by providing the first large-scale, comprehensive evaluation of LBM use in older adults who have enrolled in hospice care.

 The first chapter of this dissertation includes a review of the current state of hospice care in the US, including hospice care treatment principles, hospice utilization trends, and coverage of healthcare treatments and services under the Medicare Hospice Benefit (MHB), which covers the majority of hospice patients. A key finding of this review was that medications not

**SUMMARY (continued)**

for palliation of a hospice patient’s terminal illness are not reimbursable under the MHB as with palliative medications, but may be covered by a patient’s Medicare Part D prescription drug plan. However, the Centers for Medicare and Medicaid Services (CMS) anticipates the frequency of Part D use by hospice patients to be extremely rare given the types of medications anticipated to be used by hospice patients. Current research on polypharmacy, treatment guidelines, and prescribing patterns in elderly patients and those at the EOL was also reviewed to identify gaps in the evidence around optimal medication use in the terminally ill. Medication use in the hospice population, particularly changes in the use of non-palliative medications before and after hospice admission, was identified as a major research gap and served to inform the objectives of this dissertation. To address the identified research gaps, a series of retrospective cross-sectional and cohort studies were conducted using the Surveillance, Epidemiology and End Results (SEER)-Medicare linked database from 2008 to 2013. LBM classes identified for the purposes of this research included anti-hyperlipidemics, antihypertensives, oral antidiabetics, antiplatelets, anti-dementia and anti-osteoporotic medications, and proton pump inhibitors.

 In the second chapter, the prevalence and patterns of medication use through the Medicare Part D prescription drug benefit after patients were admitted to hospice were examined. We assessed the most common medications dispensed through Medicare Part D according to hospice admission diagnosis and evaluated the prevalence of receiving medications from pre-defined therapeutic and drug classes considered to consist of LBMs in those with limited life expectancy. Dispensing of at least one medication through the Part D benefit was common, occurring in over half of all hospice patients, and varied by hospice admission diagnosis (e.g., dementia, 62%; cancer, 54%; renal disease, 36%). The receipt of

**SUMMARY (continued)**

potential LBMs such as antihypertensives, proton pump inhibitors, and anti-hyperlipidemics was also common, with little variation by year of hospice admission diagnosis.

In chapter three, changes in LBM use before and after hospice admission were assessed. We evaluated the prevalence of and factors associated with LBM continuation once a patient enrolled in hospice. We found that 29.8% of patients who entered hospice due to cancer and 30.5% of patients who enrolled due to a non-cancer cause continued at least one LBM after hospice admission. Of the LBMs assessed, continuation was lowest for anti-osteoporotic medications and highest for anti-dementia medications. Using modified Poisson regression models with generalized estimating equations, we found that the likelihood of continuing at least one LBM after hospice admission was greater in older patients, patients admitted to hospice in a nursing or assisted-living facility, and patients with longer hospice stays.

 In chapter four, we evaluated the association between burdensome health care transitions after hospice admission and subsequent receipt of LBMs. Burdensome transitions included emergency department (ED) visits, inpatient admissions, and hospice discharges occurring after initial hospice enrollment. Patients who experienced a burdensome health care transition were 33% more likely to receive an LBM compared to non-transitioning patients. The risk of LBM receipt was further increased when considering only inpatient admissions and when shortening the follow-up window for assessment of LBM dispensing in transitioning patients and matched non-transitioning patients.

 In chapter five, a summary of the dissertation, implications for clinical practice and health care policy and recommended avenues for future research are provided. Despite hospice care principles and Medicare guidance regarding use of the Medicare Part D benefit in hospice patients, the findings of this research suggest that use of non-palliative medications after hospice admission is common. LBM use and continuation varied by LBM class, and several

**SUMMARY (continued)**

demographic and clinical factors were independently associated with continuing LBMs after hospice admission. The impact of burdensome health care transitions on LBM receipt suggests

that fragmentation in care may exacerbate the issue of sub-optimal medication prescribing in

hospice patients. A number of patient, provider, and health care system and policy-related barriers to medication discontinuation have been identified and likely contribute to the observed results. This dissertation highlights the need to explore and address these barriers with the end goal of improving quality of care in this at risk population. Additionally, this work provides critical evidence on the scope of problematic medication use in hospice patients to help inform health care providers and policy makers. Future studies should aim to confirm these findings and evaluate their impact on patients, their families, and the health care system as a whole. In the interim, a more careful review of patients’ drug regimens at the time of hospice enrollment and thoughtful consideration of the need to continue each medication in the context of the patient’s illness is warranted.

I. INTRODUCTION

1.1 Hospice Care in the United States

Hospice is a comprehensive, holistic care model for addressing the palliative care and support needs of patients with a life-limiting illness.1–3 Though palliative care and hospice care are generally considered synonymous outside of the US, hospice care in the US typically refers to care for the terminally ill while palliative care is provided to those requiring symptom control for serious, but not yet terminal, illnesses.1 The treatment philosophy in the hospice setting is one that is centered on “caring, not curing”; by electing hospice, patients have chosen to forego aggressive, life-prolonging treatment in favor of care aimed at maximizing quality of life during their final weeks and days.2 In addition to medical care and pain management for the terminally ill patient, patients and families receive emotional and spiritual support services by an interdisciplinary hospice care team.3 Core members of the care team generally consist of a hospice physician, the patient’s personal physician, a hospice nurse, a social worker, and a spiritual and bereavement counselor; pharmacists, therapists, home health aides, and trained volunteers may also be included based on the needs of the patient and family.2,3 As outlined by the National Hospice and Palliative Care Organization4, the hospice team:

* Manages the patient’s pain and other symptoms
* Assists the patient and family members with the emotional, psychosocial, and spiritual aspects of dying
* Provides medications and medical supplies and equipment
* Instructs the family on how to care for the patient
* Provides grief support and counseling
* Makes short-term inpatient care available when pain or other symptoms become too difficult to manage
* Delivers special services like speech and physical therapy when needed

The concept of hospice as specialized care for the dying was originally developed in the United Kingdom, with the first modern hospice opening in London in 1967.1 Several years later in 1973, the first hospice in the US opened in Branford, Connecticut.1 Several models of hospice care were tested and multiple attempts at introducing legislation to pay for hospice care services were introduced over the next decade. In 1983, a hospice benefit was established within Medicare, a government-administered insurance program that provides health care coverage to individuals at least 65 years old as well as individuals with certain disabilities and chronic diseases.1,5 A Medicaid hospice benefit followed shortly thereafter in 1986, and a majority of private health insurance companies now include hospice care as a covered service.6

Since its introduction as a model of care, the number of hospice programs in the US has increased dramatically. There were approximately 1,600 hospice programs in the US in 1990, increasing to 3,100 programs in 2000 and 5,150 programs in 2010.2 As of 2014, there were approximately 6,100 hospice programs in the US which served nearly 1.7 million patients annually, including more than 1.3 million Medicare beneficiaries.2,5 It is estimated that approximately 46% of all deaths among Medicare beneficiaries occur under hospice care.4 Today, hospice admission is primarily referral-based, and hospice services may be administered in a number of care settings including hospitals, nursing homes, freestanding hospice facilities and the patient’s private residence.2 The majority of hospices (59%) operate as freestanding independent agencies, while 20% are part of a hospital system, 16% are part of a home health agency, and 5% are part of a nursing home.2 In the 1980’s, nearly all hospices were not-for-profit or government-owned. However, a trend toward for-profit hospice began in the 1990’s, and today 68% of hospices hold for-profit status.2 Currently, 93% of hospice agencies are certified by the CMS and most patients electing hospice care receive healthcare benefits under Medicare. In 2014, 85.5% of patients receiving hospice care did so under the

MHB. Managed care payers or private insurance provided coverage for 6.9% of patients while the Medicaid Hospice Benefit covered 5.0% of hospice enrollees.2

Use of hospice has been associated with significantly higher levels of patient and family satisfaction with EOL care compared to the non-use of hospice services in the terminally ill.7,8 Pain and dyspnea are more likely to be adequately treated in hospice, and hospice patients and their families are more likely to report receiving sufficient emotional support.7 In addition to high patient and caregiver satisfaction with care, hospice has been associated with decreased costs, fewer hospital and intensive-care unit days, fewer 30-day hospital readmissions, and fewer in-hospital deaths compared to those receiving non-hospice EOL care.9,10

1.2 US Hospice Patient Characteristics and Utilization Trends

The large majority of patients enrolling in hospice in the United States are elderly and white. In 2014, 84% of hospice enrollees were 65 years of age or older and 41% were at least 85 years old.2 Whites made up 76% of hospice patients, while African-Americans comprised 7.6% of patients and 7.1% of patients were of Hispanic or Latino origin.2 Slightly over half of hospice enrollees were women (54%), an increase from the year 2000 when there was an equal proportion of men and women.11 In the early years of hospice, the vast majority of admissions were for terminal cancer diagnoses. Though terminal cancer is still the most common admitting diagnosis, the past several decades have seen a shift toward increases in hospice admissions for chronic diseases. In 1992, patients admitted with a primary diagnosis of cancer comprised 75% of all hospice patients.11 By 2014, only 37% of hospice admissions were for cancer diagnoses.2 Cardiovascular disease, lung disease and dementia now make up a substantial proportion of hospice admitting diagnoses (**TABLE I**).2,4,12–14

While the proportion of deaths occurring under hospice care has steadily increased, the mean and median length of stay have decreased since their peaks of 84.0 days and 27.4 days,

**TABLE I**

DISTRIBUTION OF PRIMARY HOSPICE ADMISSION DIAGNOSES, 2010-2014

|  |  |
| --- | --- |
| Primary Diagnosis | Hospice Admission Year |
| 2010 | 2011 | 2012 | 2013 | 2014 |
| Cancer | 35.6% | 37.7% | 36.9% | 36.5% | 36.6% |
| Dementia | 13.0% | 12.5% | 12.8% | 15.2% | 14.8% |
| Heart Disease | 14.3% | 11.4% | 11.2% | 13.4% | 14.7% |
| Lung Disease | 8.3% | 8.5% | 8.2% | 9.9% | 9.3% |
| Other | 5.4% | 4.8% | 5.2% | 6.9% | 8.3% |
| Stroke or Coma | 4.2% | 4.1% | 4.3% | 5.2% | 6.4% |
| Kidney Disease | 2.4% | 2.7% | 2.7% | 3.0% | 3.0% |
| Liver Disease | 1.9% | 2.1% | 2.1% | 2.1% | 2.3% |
| Non-ALS Motor Neuron | 1.2% | 1.6% | 1.6% | 1.8% | 2.1% |
| Debility Unspecifieda | 13.0% | 13.9% | 14.2% | 5.4% | 1.9% |
| Amyotrophic Lateral Sclerosis  | 0.4% | 0.4% | 0.4% | 0.4% | 0.4% |
| HIV/AIDS | 0.3% | 0.2% | 0.2% | 0.2% | 0.2% |

aIn April 2013, CMS released guidance strongly discouraging the use of debility or adult failure to thrive as a principal hospice admission diagnosis, stating that in the future most hospice claims with these conditions as a principal diagnosis will be rejected.

respectively, in the mid-1990’s.6,11 The minimum length of stay for fully effective hospice care has been cited to be between 30 and 60 days; however, the majority of patients are enrolled in hospice for shorter periods.6,11 In 2014, the average length of stay was 71.3 days while the median length of stay was 17.4 days.2 Nearly four out of 10 patients had hospice stays greater than 30 days. Several reasons have been cited for the large proportion of late referrals, including a lack of knowledge of the availability and benefits of hospice care in both the medical community and the general public, and an unwillingness of patients, caregivers, and providers to discuss EOL care until the patient is very close to death.11

Patients may receive hospice care in a variety of settings, though the majority of hospice patients receive care at their place of residence. In 2014, 35.7% of patients received care at their private residence, 14.5% received care in a nursing home, and 8.7% received care in a residential facility at the time of death.2 Other care settings include dedicated hospice inpatient units or facilities (31.8%) and acute care hospitals (9.3%). Hospice care is generally provided at four different levels: routine home care, continuous home care, general inpatient care, and inpatient respite care. Most hospice patient care days are classified as routine home care (93.8%), where the hospice team provides up to 8 hours of direct patient care in a 24-hour period at the patient’s residence. General inpatient care comprises approximately 4.8% of hospice care days and is generally reserved for cases of pain control or acute/complex symptom management that cannot be treated in other settings. Continuous care (direct patient care for >8 hours in a 24-hour period) and short-term inpatient respite care make up 1.0% and 0.4% of patient care days, respectively.2

1.3 The Medicare Hospice Benefit: Eligibility and Health Care Service Coverage

Nearly 46 million individuals over 65 years of age currently receive healthcare benefits under Medicare, of which approximately 2.8 million individuals die annually. Of these decedents, nearly half elect hospice services for some period of time near the EOL.15 From 1990 to 2010, the annual number of patients electing hospice care under the MHB has grown from 77,000 to 1.2 million.15 As of 2014, Medicare decedents who have elected hospice care represent approximately 85.5% of all patients receiving hospice care in the United States.2 The dramatic increase in hospice use in recent years has led to significant increases in Medicare spending under the MHB, from $309 million in 1990 to $2.9 billion in 2000 and $15.1 billion in 2013.5,15 In 2014, hospice care accounted for approximately 2% of total Medicare expenditures.5

The MHB is administered under Medicare Part A for all Medicare beneficiaries, regardless of whether the patient was enrolled in Original Medicare, a Medicare Advantage Plan, or another type of Medicare health plan prior to hospice enrollment.16 There are no restrictions on age or type of terminal illness in order to be eligible for hospice. Requirements that must be met in order for patients to be eligible for the MHB include:

* A certification from a hospice physician and the patient’s primary care physician (if he or she has one) of less than 6 months to live if the terminal illness runs its normal course;
* Patient waiver of non-palliative treatment options intended to cure the terminal illness and/or prolong life; and
* A signed statement from the patient choosing hospice care instead of other Medicare-covered treatments for the terminal illness and related conditions (e.g., inpatient care).

If these conditions are met and the chosen hospice is Medicare-approved, hospice care services received for the patient’s terminal illness and related conditions are covered 100% under the Part A MHB.16 A summary of healthcare service coverage for Medicare beneficiaries who have elected hospice care are shown in **TABLE II**.16,17

**TABLE II**

HEALTH CARE COVERAGE UNDER MEDICARE FOR PATIENTS ENROLLED IN HOSPICE

|  |  |
| --- | --- |
| Service | Medicare Coverage |
| All palliative care for terminal illness and related conditions | Part A, MHB |
| Medications for terminal illness and related conditions | Part A, MHB |
| Medications for conditions unrelated to terminal illness and related conditions | Part Da |
| Any treatment intended to cure the terminal illness and/or related conditions | None |
| Room and board | Noneb |
| ER visits and hospitalizations for terminal illness and related conditions | Nonec |
| ER visits and hospitalizations unrelated to terminal illness and related conditions | Part A, non-MHB |

aIf patient has active Part D coverage.

bExcept short-term inpatient or respite care arranged by the hospice team.

cUnless arranged by the hospice team.

Patients meeting hospice eligibility requirements receive hospice care in defined benefit periods, starting with two 90-day benefit periods followed by an unlimited number of 60-day benefit periods.5 There is no limit on hospice length of stay; however, a hospice physician must recertify that the patient is terminally ill with a life expectancy of less than 6 months at the beginning of each benefit period.5 Patients are free to disenroll from hospice care at any time for any reason, and they may choose to reenroll in hospice as long as Medicare’s hospice eligibility criteria are still met. During any period of disenrollment, patients will receive care under their previous Medicare benefit provided that any applicable premiums are paid.

As shown in **TABLE II** above, Medicare regulations stipulate that medications intended for the palliation of the patient’s terminal illness and any related conditions must be provided by hospice as part of the Part A MHB. Common medications provided by hospice include those for pain, anxiety, depression, anorexia, nausea and vomiting, constipation, diarrhea, fatigue, dyspnea, respiratory secretions, insomnia and delirium.18,19 Specific medications considered essential in palliative care by the International Association for Hospice and Palliative Care (IAHPC) are listed in **TABLE III** along with their palliative indications.20 Medications for conditions completely unrelated to the patient’s terminal illness (e.g., longstanding chronic conditions) may still be covered by Medicare, but under Medicare Part D as opposed to the MHB. Though CMS has stated in guidance released in 2013 that payment for medications under Part D for Medicare beneficiaries covered by the MHB should be exceedingly rare, recent studies have shown that use of medications for unrelated conditions is common in the hospice population.17,21–23 In 2012, Medicare payments under Part D for patients currently enrolled in hospice totaled $340 million.5

**TABLE III**

IAHPC LIST OF ESSENTIAL MEDICATIONS AND INDICATIONS FOR PALLIATIVE CARE**a**

|  |  |
| --- | --- |
| Medication | Palliative Indication |
| Acetaminophen | Mild to moderate pain |
| Amitriptyline | Depression, neuropathic pain |
| Bisacodyl | Constipation |
| Carbamazepine | Neuropathic pain |
| Citalopramb | Depression |
| Codeine | Diarrhea, mild to moderate pain |
| Dexamethasone | Anorexia, nausea, vomiting, neuropathic pain |
| Diazepam | Anxiety |
| Diclofenac | Mild to moderate pain |
| Diphenhydramine | Nausea, vomiting |
| Fentanyl patch | Moderate to severe pain |
| Gabapentin | Neuropathic pain |
| Haloperidol | Delirium, nausea, vomiting, terminal restlessness |
| Hyoscine butylbromide | Nausea, vomiting, visceral pain, terminal secretions |
| Ibuprofen | Mild to moderate pain |
| Levomepromazine | Terminal restlessness |
| Loperamide | Diarrhea |
| Lorazepam | Anxiety, insomnia |
| Megestrol acetate | Anorexia |
| Methadone | Moderate to severe pain |
| Metoclopramide | Nausea, vomiting |
| Midazolam | Anxiety, terminal restlessness |
| Mirtazapine | Depression |
| Morphine | Dyspnea, moderate to severe pain |
| Octreotide | Vomiting, diarrhea |
| Oral rehydration salts | Diarrhea |
| Oxycodone | Moderate to severe pain |
| Prednisolone | Anorexia |
| Senna | Constipation |
| Tramadol | Mild to moderate pain |
| Trazodone | Insomnia |
| Zolpidem | Insomnia |

 aAdapted from Lima 201220

 bOr other selective serotonin reuptake inhibitor, except paroxetine and fluvoxamine

1.4 Polypharmacy in the Elderly and Those with Limited Life Expectancy

Adults aged 65 years or older are the fastest growing segment of the US population, and nearly 50% have two or more chronic conditions.24 Given that multiple medications are often prescribed to optimally manage common chronic conditions of older adults such as hypertension, diabetes, and heart disease, it is unsurprising that the elderly are at an increased risk of polypharmacy. 25 While there is no formal definition of polypharmacy, it is most often described as the concurrent use of a certain number of medications over a particular threshold, commonly five or more.26,27 Less frequently, it is described as the use of any medically unnecessary or inappropriate medications.26,28,29

Several studies have been conducted which assess the prevalence of polypharmacy in the elderly population across a variety of settings. Using data from the 2014 Commonwealth Fund International Health Policy Survey of Older Adults, Osborn et al. reported that 53% of US adults aged 65 years and older took 4 or more medications, more than in Canada, Australia, and 7 countries in Western Europe.30 A recent community-based study of ambulatory US adults 62 to 85 years old conducted from 2010-2011 reported the prevalence of any prescription medication use to be 87.7%, with 35.8% reporting the concurrent use of 5 or more medications.31 When including over-the-counter medications and dietary supplements, the proportion reporting concurrent use of 5 or more medications increased to 67.1%.31 The most prevalent therapeutic classes were antihypertensives (65.1%), analgesics (54.3%), antihyperlipidemics (50.1%), and anticoagulants (47.6%). In 2012, Medicare Part D enrollees were found to fill an average of 4 prescriptions per month, with 29% filling 4-7 prescriptions and 19% filling 8 or more prescriptions monthly.25 High rates of polypharmacy have also been found in other care settings. Among US nursing home residents, approximately 40% concurrently use 9 or more medications.32 The proportion of elderly adults taking 5-8 medications and 9+ medications at hospital discharge has been estimated at 41% and 37%, respectively.33

A growing body of evidence has linked the concurrent use of multiple medications with negative health outcomes in the elderly population. Patients taking multiple medications are at an increased risk of adverse drug events (ADEs) and nonadherence, both of which can lead to increased ED visits and hospitalizations.34 For patients prescribed more than seven medications, the risk of developing an ADE has been reported to be greater than 80%.24,34 One study of ambulatory care visits reported each additional medication to increase the number of ADEs per patient by 10%.35 The probability of drug-drug interactions (DDIs), a common cause of drug toxicity-related hospitalizations in the elderly, also increases with use of an increasing number of medications. A recent study reported that approximately 15% of elderly adults are using medication combinations that put them at risk for serious DDIs.31 In patients taking 8 or more medications, the presence of at least one medication combination posing a potential DDI risk has been reported to approach 100%.24,36 Polypharmacy has been associated with decreased cognitive and functional ability, decreased ability to perform activities of daily living, and increased urinary incontinence in elderly patients.37–39 In a 2005 review of 16 studies, polypharmacy was also found to be a significant predictor of nursing home placement, hypoglycemia, fractures, pneumonia and mortality.40

Elderly patients near the EOL may be at an even greater risk of polypharmacy and subsequent ADEs due to the addition of medications used to treat EOL symptoms coupled with the onset of declining organ function, malnutrition, and changes in body composition.34,41,42 In a recent analysis of patients in an HMG-CoA reductase inhibitor (i.e., statin) discontinuation trial with an estimated life expectancy of 1-12 months, 68% of patients were found to be prescribed 9 or more medications and a mean of 11.5 non-statin medications at baseline.43 Only 6% of patients were taking fewer than 5 medications and 24% of patients were taking 15 or more medications at baseline.43 Antihypertensives were the most commonly prescribed medication class, prescribed in 70% of patients and representing 9.3% of all medications prescribed in the trial population. Similar levels of polypharmacy have been found in the EOL population utilizing hospice care. Using data from the 2007 National Home and Hospice Care Survey, Dwyer et al. reported that 76.5% of hospice patients in the last week of life take 6 or more medications and 43% take between 11 and 25 medications.21 A study of 4,252 hospice patients enrolled in Seasons Hospice and Palliative Care in 2010 revealed an average number of medications during admission of 15.7, with 8.5% of patients prescribed 30 or more medications.23 The average number of medications prescribed on a “as needed” and regularly scheduled basis was 7.9 and 8.3, respectively.23

1.5 Appropriate Prescribing in End of Life and Hospice Patients

Several tools have been developed for the assessment of medication appropriateness in the elderly, such as the Medication Appropriateness Index, the STOPP criteria, and the Beers Criteria.44–47 However, to date there have been few tools developed specifically for desprescribing in the elderly EOL and hospice patient populations, where considerations for medication therapy may differ from that of the general elderly population.44,45,48,49 In a study by Bain and Weschules, the Beers criteria were applied to a hospice population and an expert panel concluded that several medications considered inappropriate according to the criteria were actually appropriate in older hospice patients and vice versa.48 Other studies have applied modified versions of the Medication Appropriateness Index to quantify reductions in potentially inappropriate medications (PIMs) following palliative care team intervention.50,51 In one of the few examples of a tool for use specifically in the palliative care setting, Lindsay and colleagues developed an “OncPal deprescribing guideline” to assist clinicians in identifying unnecessary medications in palliative care patients with cancer.52 The authors identified a high incidence of unnecessary medication use when applying the guideline and a very high level of concordance between the deprescribing guideline and an expert panel, thus demonstrating the potential usefulness of the tool in cancer patients transitioning to palliative care.

Though no clear consensus criteria is currently available regarding appropriate deprescribing practices in the EOL population, the area has received substantial research interest in recent years and several approaches have been suggested.41,45,49,53,54 Holmes et al. proposed a framework for discontinuing medications for patients late in life based on four components: remaining life expectancy of the patient, time until benefit of the medication, goals of care, and desired treatment targets. The authors suggested that as these components change over the course of the patient’s illness, so does the pool of appropriate medications for that patient.49

In a review of EOL pharmacotherapy, O’Mahoney and O’Connor55 provided several guiding principles for prescribing in EOL patients, including those receiving palliative or hospice care:

* Life-extending drugs are usually not appropriate.
* Drugs for primary prevention have, in general, no place in the treatment of end-of-life patients, since the time-to-benefit usually exceeds life expectancy.
* Drugs for secondary prevention require careful scrutiny and should be prescribed only where ongoing benefit is to be expected within a patient’s life expectancy.
* In general, prescribing more than five regular daily drugs to a patient with end-of-life status should be avoided. Six or more daily drugs heighten the risk of ADEs as well as poor medication compliance in older people.
* Defining treatment goals is of central importance and will usually direct the prescriber to the most appropriate pharmacotherapy. This process should be discussed between the physician and the patient and, where necessary the patients primary caregiver.

Three studies of terminally-ill cancer patients took a medication-specific approach, outlining specific criteria to classify individual medications and medications classes as unnecessary based on the patient’s recent medical history, prognosis, and presence of a valid indication for the medication.56–58 Other studies have used expert clinician panels to reach consensus on specific medications and medication classes deemed to be inappropriate in the EOL population.52,59,60 Based on the available evidence, prescription medications and medication-classes deemed largely to be of limited benefit in patients with limited life expectancy include lipid-lowering medications, oral hypoglycemic agents, antihypertensives (with some exceptions), bisphosphonates, antidementia medications, antiplatelet/anticoagulants, proton pump inhibitors and hormonal medications.52,56–66 Medications from most of these therapeutic classes can be stopped immediately without the concern of inducing adverse events due to drug withdrawal; however, some antihypertensives may need to be reduced gradually to prevent rebound hypertension and tachycardia.63

Clearly, the need to reduce medication burden and limit non-essential medication use in the EOL patient population is recognized. However, there continues to be a high prevalence of polypharmacy in these patients and research has suggested that a significant proportion of patients continue to take limited benefit medications LBMs at the EOL. In one study of 4,602 community-dwelling elderly adults in the US, 44% were found to take at least one inappropriate medication in the last year of life based on Beers Criteria.67 A study of 106 patients admitted to a single inpatient palliative care unit in England reported that 25% of patients were taking at least one unnecessary medication on admission.68 In ambulatory patients with advanced cancer, 24% have been reported to be taking at least one unnecessary medication, primarily those for the prevention of long-term consequences of chronic conditions.56 Silveira et al. reported that of 337 Veterans Health Administration patients receiving statins at six months prior to death, 51% still had an active statin prescription at death.69 In nursing home residents with advanced dementia, the percentage of patients taking hypoglycemic medications,

cardiovascular agents, antiplatelets/anticoagulants and lipid-lowering agents in the last week of life was estimated to be 7.3%, 43.9%, 30.5% and 7.9%, respectively.70

Several prescriber- and patient-specific barriers to medication discontinuation in the EOL population have been identified to help explain the high prevalence of inappropriate prescribing. These include a lack of prescriber training and economic incentives to promote deprescribing, clinical inertia, poor physician-patient/family communication and education, the wishes of patients and family members, the perception that discontinuation equates to “giving up hope”, and unrealistic perceived benefits of continued medication use.45,54,56,63,71–75 In addition to prescriber and patient/family factors, fragmentation in care across healthcare settings has also been suggested as a potential contributor to polypharmacy and LBM use in EOL patients.74 Patients near the EOL often experience multiple healthcare transitions, which can lead to disruptions in care planning and poor coordination of care across healthcare settings.3 Medication documentation and reconciliation during transfers between care settings has been shown to be especially poor, in part due to the “siloed” nature of individual practice settings.72,76–79 Because medication regimens frequently change based upon the stage of the patient near the EOL, hospice and palliative care patients may be at particular risk of using LBMs subsequent to healthcare transitions.72 In 2009, Medicare fee-for-service patients experienced a mean of 3.1 healthcare transitions in the last 90 days of life, with 43% experiencing a transition in their final two weeks.80 Approximately 69% of patients had at least one hospitalization in the last 90 days and 11.5% had three or more hospitalizations. A recent study among elderly Medicare beneficiaries using hospice care found that one in 10 experienced a burdensome healthcare transition (i.e., a transition likely to result in changes in the patient’s care team) following hospice enrollment, with transition to a hospital occurring in 53% of those with at least one transition.81

In addition to transitions occurring while under hospice care, an estimated 16%-18% of hospice patients experience a care transition via live hospice discharge.11,82 While the most commonly cited reason for hospice discharge is the stabilization or improvement of the patient’s terminal illness, a previous study of Medicare beneficiaries reported that patients who disenrolled from hospice died a median of 24 days after disenrollment.83,84 Additionally, approximately 25% of hospice disenrollments are followed by a hospitalization, and patients are often found to reenroll in hospice shortly after hospice disenrollment and receipt of care in non-hospice settings.82,85 Thus, care transitions after disenrollment from hospice followed shortly thereafter by death or hospice reenrollment may also represent fragmentation in care with the potential to result in LBM use.

Given hospice’s central, transparent mission of foregoing curative treatment in the terminally-ill patient to focus on holistic comfort care which maximizes patient and family quality of life, it may be reasonable to believe that many of the barriers to discontinuation of LBMs in patients receiving traditional EOL care can be mitigated in the hospice setting. However, there is evidence to suggest that these LBMs continue to be frequently prescribed in terminally-ill patients currently enrolled in palliative and hospice care programs, potentially for similar reasons as those for EOL patients not enrolled in hospice or palliative care.22,23,57 Among patients with advanced dementia enrolled in a palliative care program, Holmes et al. reported that 29% were prescribed at least one medication considered never appropriate by an expert consensus panel.59 Riechelmann et al. reported that of 372 patients with terminal cancer, 18.8% continued to receive at least one unnecessary medication after initial palliative care consultation, compared to 19.9% before initial consultation.57 Statins (56%) and multivitamins (30%) made up the majority of unnecessary medications taken by patients prior to consultation. In elderly hospice patients with a diagnosis of failure to thrive or debility, Sera et al. reported several classes of chronic disease medications to be frequently prescribed, including antihypertensives (47.1%), antiplatelet medications (30.0%), cholinesterase inhibitors (12.6%), and lipid-lowering agents (10.6%).22

A study of 4,252 hospice patients across 11 states reported that a number of medications were prescribed that are primarily used for chronic conditions or supplementation.23 These included omeprazole (14.6%), metoprolol (13.2%), multivitamins (9.5%), lisinopril (7.3%), amlodipine (6.5%), donepezil (4.9%), simvastatin (4.7%), clopidogrel (3.8%), and memantine (3.5%). Significant differences in the prevalence of chronic disease medications used among patients admitted to hospice for cancer, dementia, and lung disease were also described. Based on data from 2,623 hospice patients aged 65 years and older in the 2007 National Home and Hospice Care Survey, multiple LBM classes were found to be taken frequently by patients in the last three days of life, including antihypertensives (49.2%) and anticoagulants (25.2%).21 Similar to the study by Sera et al.23, significant differences in LBM prevalence were apparent according to primary admission diagnosis. In addition to an increased medication burden, LBM continuation in this patient population can result in an increased risk of adverse effects and drug-drug interactions, lower adherence to symptomatic medications, and needlessly high medication costs.44,45,86–88

1.6 Research Gaps

There has been increased interest in research on appropriate medication prescribing in the EOL population in recent years. Research on medication use patterns specifically in the hospice population has begun to emerge; however, it is primarily descriptive data reporting the most commonly medications used in hospice overall (including palliative medications) or use of a particular medication class. No studies have been conducted which specifically examine medication use through the Medicare Part D benefit after patients are admitted to hospice. Further, little data are available describing LBM use before admission to hospice and subsequent use and continuation of these medications after the transition to hospice care. No research has been conducted which examines the factors associated with LBM continuation among hospice patients, such as patients’ sociodemographic characteristics and pre-hospice healthcare utilization, comorbidities, primary hospice admission diagnosis and care setting, and hospice length of stay. It is also unknown whether healthcare transitions to non-hospice settings after hospice admission result in increased LBM use due to poor care coordination between hospice and non-hospice providers. Many of these factors have been shown to significantly influence treatment intensity in the EOL care setting, and further knowledge of their association with LBM continuation in the hospice setting may aid in tailoring interventions targeted at hospice providers and patients.89–93

1.7 Dissertation Objective

The purpose of this research was to help fill the identified gaps in the evidence by rigorously characterizing LBM use and continuation in a population of elderly Medicare beneficiaries who transition to hospice care. This was accomplished through a series of studies which examined medication use through Medicare Part D after hospice enrollment (Aim 1), the prevalence of and factors associated LBM continuation in hospice patients (Aim 2), and the impact of post-hospice admission burdensome health care transitions and subsequent LBM use (Aim 3). A particular emphasis is placed on identifying differences according to primary hospice admission diagnosis, especially cancer versus non-cancer diagnoses, which are hypothesized to be present due to the more rapid and predictable pattern of decline in hospice patients with terminal cancer compared to other non-cancer terminal illnesses; this may impact clinicians’ ability to predict survival and in turn affect health care delivery and medication treatment decisions. These studies are intended to help clinicians and policy makers understand the scope of LBM use in hospice patients and encourage a needed dialog among healthcare

providers, patients, and their families concerning medication management strategies that minimize burden without impacting quality of life at the EOL.

1.8 Conceptual Framework

Previously published frameworks have largely focused on the general EOL population. While informative, they may not be sufficient to describe terminally ill patients who utilize hospice services, a setting where treatment modalities and philosophy may differ substantially from the general EOL care setting. Moreover, no frameworks have been developed specifically relating to LBM use and continuation in this population.

The conceptual framework for this dissertation is presented in **FIGURE 1**. The framework takes into account the underlying concepts from the model developed by Holmes and colleagues, and is based on the assumption that as the patient’s condition progresses to the point where he or she elects hospice care, the pool of appropriate medications for that patient significantly decreases.49 The proposed conceptual framework also incorporates elements from a previously published framework by Kelley and colleagues for factors affecting treatment intensity in patients with serious illness.89 The Kelley framework separates predictors of treatment intensity into patient & family determinants and region & physician determinants. The patient and family factors are centered on financial access to care and treatment preferences while the region and physician factors focus on practice patterns and regional supply of resources.

As depicted in the left section of **FIGURE 1**, the proposed process leading to LBM continuation in the hospice setting begins when patients are diagnosed with a terminal illness which progresses to the point that they elect hospice care. Especially in the elderly population, these patients often have multiple chronic comorbid conditions and are using multiple medications to prevent long-term disease complications. By its nature, the election of hospice signals a change in treatment philosophy and goals of care, and thus many of the medications used to treat chronic conditions pre-hospice admission may no longer provide a patient benefit and would therefore be considered LBMs. Aim 1 of this research was to broadly describe medication use through Medicare Part D after admission to hospice, with a focus on use of LBMs and differences in medication use by primary hospice admission diagnosis.

A number of patient and clinical factors are anticipated to impact the magnitude of LBM use and continuation in the hospice setting. These are depicted along the path between “Terminal Illness” and “LBM Continuation” in **FIGURE 1** and form the basis of Aim 2. Specifically, this was a cohort study which described the prevalence of LBM continuation after hospice admission and evaluated factors associated with LBM continuation such as sociodemographic characteristics, hospice admission diagnosis, hospice care setting, comorbidities, and pre-hospice healthcare utilization intensity.

In the general patient population, health care fragmentation is known to result in an increased risk of medication-related errors due to generally poor medication reconciliation and documentation practices. This may be amplified in hospice patients due to the fact that medication regimens frequently change after admission to hospice. Further, there may be poor communication between hospice and non-hospice providers. The objective of aim 3 of this dissertation was to estimate the association between burdensome health care transitions and subsequent LBM use after hospice enrollment.



**FIGURE 1.** Conceptual framework for LBM use in patients receiving hospice care

II. MEDICARE PART D USE AMONG OLDER MEDICARE BENEFICIARIES ADMITTED TO HOSPICE

2.1 Preface

 This chapter addresses Aim 1 of the dissertation and has been published online (ahead of print) in the *Journal of the American Geriatrics Society* as: Zueger PM, Holmes HM, Calip GS, Qato DM, Pickard AS, Lee TA. Medicare Part D Use of Older Medicare Beneficiaries Admitted to Hospice. J Am Geriatr Soc. 2018 Mar 6. The pre-publication version is included here. License for reuse from the *Journal* is provided in the **APPENDIX**.

2.2 Introduction

Nearly half of all deaths in the United States now occur under hospice care, with most patients covered by the Medicare Hospice Benefit under Medicare Part A.2,94 For eligible beneficiaries electing hospice, the Medicare Hospice Benefit provides a per-diem payment to the patient’s hospice program intended to cover all palliative care related to the terminal illness, including palliative prescription drugs.16,95 After hospice admission, the Medicare Part D Prescription Drug Benefit may continue to cover medications for conditions unrelated to the terminal illness. CMS has stated that because hospice programs are expected to provide nearly all medications that beneficiaries may need, payment for medications under Part D should be “extremely rare.”17 However, a 2016 Medicare Payment Advisory Commission report revealed that Part D payments for hospice patients total $340 million annually.5 Further, a recent CMS communication reported that approximately 63% of hospice patients filled at least one maintenance drug through Part D in 2016.96 Despite these reports, the specific medications driving utilization of the Part D benefit are not well understood.

The concurrent coverage of medications under the Medicare Hospice Benefit and Part D allows for medication use that may be inconsistent with both care goals and Medicare payment policies for hospice patients. For patients with a life-limiting illness and whose primary care objective is comfort and symptom control, medications used for long-term prevention are largely unnecessary and under most circumstances can be discontinued.51,53,97,98 Prior studies in hospice patients have found substantial use of medications which largely are not symptom-directed.21–23 However, the payer source (e.g., hospice/Part A, Part D, self-pay) and whether new medication supplies continued to be obtained after hospice enrollment are unclear. These studies also demonstrated some variation in medication utilization among patients admitted to hospice for cancer and non-cancer causes, which may be partly explained by differences in comorbidity burden and greater difficulty in predicting patterns of decline for non-cancer terminal conditions.99,100 Further, Medicare’s payment model requires that medications be intended for the palliation of the patient’s terminal illness in order to be covered by the hospice benefit. For cancer, these relationships may be apparent, as pain and symptom-relieving medications are more clearly related to a terminal cancer diagnosis. For non-cancer conditions, the distinction between what is covered by hospice and what should be covered by Part D may be more difficult. In conditions such as heart failure and chronic obstructive pulmonary disease, medications commonly used to prevent long-term disease outcomes may also provide varying levels of short-term symptomatic benefit, complicating coverage determinations.

The goal of this study was to describe the medications received through the Medicare Part D benefit in older adults admitted to hospice. We identify the most common medications obtained through Part D and characterize medication class-specific dispensing patterns and trends for patients admitted to hospice for cancer and non-cancer causes.

2.3 Methods

2.3.1 Data Source and Study Population

The SEER Program and Medicare linked database was used to identify patients who were admitted to hospice and died while under hospice care between January 1, 2008 and December 31, 2013. The nationally-representative, population-based SEER cancer registries cover approximately 28% of the United States population and contain more than 95% of all Medicare-eligible individuals diagnosed with a first primary cancer within the registry regions. The SEER-Medicare linked database also includes a random 5% sample of fee-for-service Medicare beneficiaries residing in the SEER registry regions and not diagnosed with cancer. We included a SEER registry-derived cohort of Medicare beneficiaries diagnosed with a first primary lung, breast, colorectal, pancreatic cancer or lymphoma between January 1, 2001 and December 31, 2011. These cancer sites represent the most common cancer-related hospice admission diagnoses among Medicare beneficiaries.101 The random 5% non-cancer sample was used to identify non-cancer patients residing in the registry regions during the same time frame. Linked Medicare claims were available through December 31, 2013.

Patients were at least 66 years of age at hospice admission, were continuously enrolled in Medicare Parts A, B and D without managed care plan enrollment starting 12 months prior to hospice admission, and had at least one Part D prescription claim in the 12-month pre-admission period. After initial admission, patients with any hospice enrollment gaps (i.e., discharges) lasting greater than 30 days were excluded. Hospice admission diagnosis was identified via the primary *International Classification of Diseases, Ninth Revision* (ICD-9) diagnostic code recorded on the first hospice claim for each patient and used to define patients as a cancer or non-cancer hospice admission. Those admitted for a non-cancer cause were further subdivided into distinct groups based on the most prevalent hospice admission diagnoses reported nationally: debility/failure to thrive, dementia, heart disease, lung disease, renal disease, and ischemic stroke.2,101 Patients with other non-cancer admission diagnoses were not grouped and analyzed as a distinct cohort, but were included when analyzing hospice patients admitted for a non-cancer cause as a whole. As not all patients diagnosed with cancer ultimately die from or enter hospice for cancer, the SEER registry-derived cohort was also used to identify patients who were previously diagnosed with cancer and later entered hospice for a non-cancer cause.

2.3.2 Medications Dispensed Through Medicare Part D

We analyzed all fully adjudicated Part D claims occurring between the date of hospice admission and date of death. The 25 most common medications obtained through Part D by hospice patients were determined along with the prevalence of post-admission receipt of opioid analgesics, preventative medications, and at least one Part D medication. Dispensing patterns were evaluated for the overall cohort and stratified by the admission diagnosis groups described above. The preventative therapeutic and drug classes assessed are provided in **TABLE IV**. These classes were chosen as representative examples of medications with potentially limited benefit in the setting of limited life expectancy based on the literature.41,52,56–61,63,66,102–104 Conversely, opioid analgesics were chosen to represent medications that are appropriate in the hospice setting, but should overwhelmingly be provided by a patient’s hospice program as opposed to through the Part D benefit. To evaluate temporal trends, the prevalence of receiving the selected drug and therapeutic classes was evaluated by year of hospice admission.

2.3.3 Statistical Analysis

Descriptive statistics were used to describe baseline characteristics and post-hospice admission Part D dispensing. Receipt of individual medications, drug classes, and therapeutic classes through Part D were expressed as the proportion of patients with at least one Part D dispensing for that medication or class after hospice admission. Baseline patient characteristics were compared using t-tests and chi-square tests, as appropriate. Absolute differences with 95% confidence intervals (CIs) were used to describe medication class-specific differences in the prevalence of Part D dispensing between patients whose hospice qualifying diagnosis was a cancer versus non-cancer cause. Statistical tests were two-sided with *p-*values <0.05 considered statistically significant. All analyses were conducted using SAS software, version 9.4 (SAS Institute Inc., Cary, NC). The institutional review board at the University of Illinois at Chicago approved this study.

**TABLE IV**

PREVENTATIVE THERAPEUTIC CLASSES AND DRUG CLASSES ASSESSED FOR RECEIPT THROUGH PART D AFTER HOSPICE ADMISSION

|  |  |
| --- | --- |
| **Therapeutic Classa** | **Associated Drug Classesa** |
| Anti-hyperlipidemic | HMG-CoA reductase inhibitors Fibric acid derivatives Bile acid sequestrants 2-azetidinones (ezetimibe) |
| Antihypertensive | Thiazide diureticsOther non-loop diureticsbACE inhibitorsARBsDHP CCBsNon-DHP CCBsBeta-blockersAlpha-blockersCentrally-acting agentsVasodilatorsDirect renin inhibitors |
| Oral Antidiabetic | BiguanidesSulfonylureasDipeptidyl peptidase-4 inhibitorsMeglitinidesAlpha glucosidase inhibitorsThiazolidinediones |
| Anti-dementia | Cholinesterase inhibitorsNMDA receptor antagonists |
| Anti-osteoporotic | BisphosphonatesSelective estrogen receptor modulators |
| Antiplatelet | P2Y12 inhibitorsCombination antiplatelets  |
| Anti-secretoryc | Proton pump inhibitors |

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; DHP: dihydropyridine

aOral and transdermal formulations only.

bIncludes all formulations of spironolactone and includes amiloride and

triamterene in combination with hydrochlorothiazide; loop diuretics excluded as use for preventative indications (e.g., essential hypertension) expected to be minimal in hospice patients.

cClass comprised only of proton pump inhibitors for this research and

therefore not evaluated as a distinct therapeutic class.

2.4 Results

A total of 88,957 Medicare beneficiaries were identified, including 57,204 patients with a cancer-related hospice admission and 31,753 patients with a non-cancer-related hospice admission (**FIGURE 2**). Compared to patients admitted to hospice for a non-cancer cause, patients admitted for cancer were younger (mean [SD], 79.0 [7.7] years vs 85.5 [7.9] years), less likely to be female (62.2% vs 73.0%), white (84.0% vs 87.7%), or receiving a Part D low-income subsidy (38.2% vs 47.3%), and more likely to be admitted to home hospice (69.3% vs 39.1%) (**TABLE V**). Patients admitted for cancer had longer hospice lengths of stay compared to non-cancer admissions (median [IQR], 17 [6-47] days vs 12 [4-49] days), and were less likely to have very short (≤7 days, 30.0% vs 39.8%) or very long (≥180 days, 4.8% vs 9.0%) hospice stays. Overall medication use in the year prior to hospice admission was similar between the two groups (**TABLE V**).

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**FIGURE 2.** Patient flow diagram for Aim 1. Application of inclusion and exclusion criteria to reach final study cohort.

**TABLE V**

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF STUDY COHORT, OVERALL AND BY CANCER AND NON-CANCER PRIMARY ADMISSION DIAGNOSIS

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **All Patients****(n=88,957)** | **Cancer** **(n=57,204)** | **Non-Cancer****(n=31,753)**  |
| Age  |  |  |  |
| Mean (SD) | 81.3 (8.4) | 79.0 (7.7) | 85.5 (7.9) |
| 66-69 years | 9.5% | 12.8% | 3.4% |
| 70-74 years | 15.7% | 20.3% | 7.4% |
| 75-79 years | 17.2% | 20.5% | 11.4% |
| 80-84 years | 19.9% | 20.5% | 18.8% |
| 85-89 years | 19.2% | 15.8% | 25.4% |
| 90+ years | 18.5% | 10.0% | 33.6% |
| Sex |  |  |  |
| Female | 66.0% | 62.2% | 73.0% |
| Race |  |  |  |
| White | 85.3% | 84.0% | 87.7% |
| Black | 8.2% | 8.7% | 7.3% |
| Other | 6.5% | 7.3% | 5.0% |
| Geographic Region |  |  |  |
| Midwest | 15.9% | 15.0% | 17.6% |
| Northeast | 20.4% | 20.4% | 20.4% |
| South | 28.4% | 28.4% | 28.4% |
| West | 35.3% | 36.2% | 33.6% |
| Hospice Length of Stay  |  |  |  |
| Median (IQR) | 15 (5-47) | 17 (6-47) | 12 (4-49) |
| ≤7 days | 33.5% | 30.0% | 39.8% |
| 8-14 days | 15.7% | 16.1% | 15.1% |
| 15-29 days | 16.0% | 17.8% | 12.7% |
| 30-89 days | 20.5% | 23.3% | 15.6% |
| 90-179 days | 7.9% | 8.0% | 7.9% |
| 180+ days | 6.3% | 4.8% | 9.0% |
| Admitting Hospice Care Setting |  |  |  |
| Private Residence | 58.5% | 69.3% | 39.1% |
| Assisted Living Facility | 4.1% | 2.4% | 7.2% |
| Nursing Facility (Skilled or Unskilled) | 19.7% | 13.0% | 31.5% |
| Hospital, Inpatient Hospice Facility | 16.4% | 14.0% | 20.7% |
| Other | 1.3% | 1.3% | 1.5% |
| Comorbidities |  |  |  |
| Hypertension | 81.0% | 78.5% | 85.4% |
| Heart Failure | 33.6% | 24.4% | 50.1% |
| Diabetes Mellitus | 37.0% | 36.0% | 39.0% |
| Chronic Obstructive Pulmonary Disease | 42.0% | 43.4% | 39.6% |
| Coronary Atherosclerosis | 34.6% | 31.0% | 41.1% |
| Renal Disease | 23.1% | 18.1% | 32.2% |
| Liver Disease | 20.3% | 25.1% | 11.6% |
| Part D Low-Income Subsidy at Admission |  |  |  |
| Yes | 41.5% | 38.2% | 47.3% |
| Unique Medications in Year Prior to Admission |  |  |  |
| Mean (SD) | 14.7 (7.2) | 14.8 (7.1) | 14.7 (7.2) |

Levothyroxine, furosemide, morphine, and omeprazole were among the most common medications obtained through Part D after hospice admission across all primary admission diagnoses (**TABLE VI, TABLE VII**). For both cancer and non-cancer hospice admissions, medication classes frequently observed among the top 25 included antihypertensives, opioid analgesics, proton pump inhibitors, anticoagulants and quinolone antibiotics. Antidepressants and anti-dementia medications were among the medications most frequently received by patients admitted for any non-cancer cause (**TABLE VI**). Receipt of disease- and symptom-directed therapy was prevalent across specific non-cancer admission diagnosis groups, including bronchodilators and steroids in patients admitted for lung disease, donepezil and memantine in patients admitted for dementia, and cardiovascular medications in patients admitted for heart disease (**TABLE VII**).

**TABLE VI**

TOP 25 MEDICATIONS RECEIVED AFTER HOSPICE ADMISSION THROUGH MEDICARE PART D, OVERALL AND BY CANCER VS NON-CANCER PRIMARY ADMISSION DIAGNOSIS

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **All Patients (n=88,957)** |  | **Cancer (n=57,204)** |  | **Non-Cancer (n=31,753)** |
| **Rank** | **Medication** | **%** |  | **Medication** | **%** |  | **Medication** | **%** |
| 1 | Levothyroxine  | 7.7 |  | Furosemide | 6.7 |  | Levothyroxine  | 9.9 |
| 2 | Furosemide | 7.7 |  | Levothyroxine  | 6.5 |  | Furosemide | 9.5 |
| 3 | Morphine  | 6.7 |  | Morphine  | 6.0 |  | Morphine  | 7.9 |
| 4 | Omeprazole | 6.0 |  | Omeprazole | 5.6 |  | Omeprazole | 6.6 |
| 5 | Potassium Chloride | 5.5 |  | Hydrocodone/APAP | 5.3 |  | Potassium Chloride | 6.5 |
| 6 | Hydrocodone/APAP | 5.1 |  | Potassium Chloride | 5.0 |  | Metoprolol Tartrate | 5.4 |
| 7 | Metoprolol Tartrate | 4.9 |  | Metoprolol Tartrate | 4.6 |  | Hydrocodone/APAP | 4.6 |
| 8 | Amlodipine  | 4.2 |  | Amlodipine  | 4.1 |  | Donepezil  | 4.5 |
| 9 | Lisinopril | 3.9 |  | Lisinopril | 3.6 |  | Lisinopril | 4.5 |
| 10 | Insulin | 3.7 |  | Oxycodone +/- APAP | 3.6 |  | Insulin | 4.4 |
| 11 | Levofloxacin | 3.4 |  | Fentanyl | 3.5 |  | Amlodipine  | 4.3 |
| 12 | Digoxin | 3.3 |  | Insulin | 3.3 |  | Levofloxacin | 4.0 |
| 13 | Fentanyl | 3.2 |  | Digoxin | 3.0 |  | Memantine  | 3.6 |
| 14 | Oxycodone +/- APAP | 3.0 |  | Megestrol  | 3.0 |  | Digoxin | 3.6 |
| 15 | Megestrol  | 3.0 |  | Levofloxacin | 3.0 |  | Ciprofloxacin | 3.6 |
| 16 | Simvastatin | 2.9 |  | Pantoprazole  | 2.7 |  | Simvastatin | 3.6 |
| 17 | Ciprofloxacin | 2.9 |  | Albuterol  | 2.7 |  | Mirtazapine | 3.3 |
| 18 | Albuterol  | 2.9 |  | Zolpidem  | 2.7 |  | Albuterol  | 3.2 |
| 19 | Warfarin  | 2.8 |  | Warfarin  | 2.6 |  | Carvedilol | 3.1 |
| 20 | Donepezil  | 2.7 |  | Diltiazem  | 2.6 |  | Clopidogrel  | 3.1 |
| 21 | Pantoprazole  | 2.7 |  | Dexamethasone | 2.6 |  | Warfarin  | 3.1 |
| 22 | Prednisone | 2.6 |  | Metoprolol Succinate | 2.6 |  | Prednisone | 3.1 |
| 23 | Diltiazem  | 2.6 |  | Simvastatin | 2.5 |  | Quetiapine  | 3.0 |
| 24 | Carvedilol | 2.5 |  | Ciprofloxacin | 2.4 |  | Nystatin | 2.9 |
| 25 | Metoprolol Succinate | 2.5 |  | Prednisone | 2.4 |  | Citalopram  | 2.8 |

APAP: acetaminophen, SMZ-TMP: sulfamethoxazole-trimethoprim

**TABLE VII**

TOP 25 MEDICATIONS RECEIVED THROUGH MEDICARE PART D AFTER HOSPICE ADMISSION BY NON-CANCER HOSPICE ADMISSION DIAGNOSIS

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Debility/AFT** |  | **Dementia** |  | **Lung Disease** |  | **Heart Disease** |  | **Ischemic Stroke** |  | **Renal Disease** |  |
|  | **(n=7,031)** |  | **(n=6,401)** |  | **(n=4,526)** |  | **(n=5,539)** |  | **(n=1,744)** |  | **(n=1,758)** |  |
| **Rank** | **Medication** | **%** | **Medication** | **%** | **Medication** | **%** | **Medication** | **%** | **Medication** | **%** | **Medication** | **%** |
| 1 | Levothyroxine  | 12.9 | Levothyroxine  | 11.2 | Furosemide | 11.1 | Furosemide | 14.1 | Morphine | 6.0 | Morphine  | 6.6 |
| 2 | Furosemide | 11.5 | Morphine  | 9.7 | Prednisone | 8.3 | Levothyroxine  | 11.9 | Levothyroxine  | 6.0 | Levothyroxine  | 5.1 |
| 3 | Morphine  | 10.3 | Donepezil  | 8.5 | Levothyroxine  | 7.6 | Potassium Chloride | 8.6 | Insulin | 4.1 | Furosemide | 4.4 |
| 4 | Omeprazole | 8.3 | Memantine  | 7.8 | Potassium Chloride | 7.3 | Omeprazole | 7.6 | Metoprolol Tartrate | 4.0 | Omeprazole | 4.3 |
| 5 | Potassium Chloride | 8.3 | Furosemide | 7.7 | Omeprazole | 6.8 | Morphine  | 7.2 | Furosemide | 3.6 | Amlodipine  | 4.0 |
| 6 | Metoprolol Tartrate | 7.6 | Omeprazole | 6.4 | Morphine  | 5.8 | Carvedilol | 5.8 | Potassium Chloride | 3.3 | Insulin | 3.8 |
| 7 | Hydrocodone/ APAP | 6.0 | Potassium Chloride | 6.4 | Diltiazem  | 5.7 | Insulin | 5.5 | Omeprazole | 3.2 | Metoprolol Tartrate | 3.6 |
| 8 | Donepezil  | 6.0 | Metoprolol Tartrate | 6.4 | Albuterol  | 5.5 | Warfarin  | 4.7 | Clopidogrel  | 3.2 | Carvedilol | 3.5 |
| 9 | Lisinopril | 5.8 | Amlodipine  | 5.9 | Tiotropium  | 5.3 | Clopidogrel  | 4.7 | Lisinopril | 3.1 | Hydrocodone/ APAP | 3.5 |
| 10 | Amlodipine  | 5.7 | Lisinopril | 5.3 | Digoxin | 4.8 | Digoxin | 4.7 | Simvastatin | 2.9 | Hydralazine  | 2.3 |
| 11 | Mirtazapine | 5.4 | Quetiapine  | 5.2 | Levofloxacin | 4.7 | Hydrocodone/ APAP | 4.6 | Amlodipine  | 2.8 | Isosorbide Mononitrate | 2.1 |
| 12 | Memantine  | 4.7 | Hydrocodone/ APAP | 4.9 | Hydrocodone/ APAP | 4.6 | Simvastatin | 4.6 | Digoxin | 2.8 | Simvastatin | 2.1 |
| 13 | Levofloxacin | 4.7 | Insulin | 4.7 | Amlodipine  | 4.4 | Metoprolol Tartrate | 4.5 | Hydrocodone/ APAP | 2.8 | Lisinopril | 2.0 |
| 14 | Insulin | 4.6 | Ciprofloxacin | 4.6 | Lisinopril | 4.2 | Lisinopril | 4.3 | Levofloxacin | 2.2 | Clonidine | 1.9 |
| 15 | Ciprofloxacin | 4.4 | Levofloxacin | 4.6 | Ipratropium/ Albuterol  | 4.2 | Levofloxacin | 4.2 | Warfarin  | 2.1 | Digoxin | 1.9 |
| 16 | Fentanyl | 4.2 | Megestrol  | 4.2 | Metoprolol Tartrate | 4.2 | Ciprofloxacin | 4.0 | Clonidine | 2.0 | Albuterol  | 1.8 |
| 17 | Quetiapine  | 4.1 | Mirtazapine | 4.2 | Insulin | 4.0 | Pantoprazole  | 3.7 | Mirtazapine | 1.9 | Fentanyl | 1.8 |

**TABLE VII (continued)**

Top 25 Medications Received THROUGH MEDICARE PART D After Hospice Admission By Non-Cancer HOSPICE Admission Diagnosis

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Debility/AFT** |  | **Dementia** |  | **Lung Disease** |  | **Heart Disease** |  | **Ischemic Stroke** |  | **Renal Disease** |  |
|  | **(n=7,031)** |  | **(n=6,401)** |  | **(n=4,526)** |  | **(n=5,539)** |  | **(n=1,744)** |  | **(n=1,758)** |  |
| **Rank** | **Medication** | **%** | **Medication** | **%** | **Medication** | **%** | **Medication** | **%** | **Medication** | **%** | **Medication** | **%** |
| 18 | Megestrol  | 4.1 | Simvastatin | 3.7 | Fluticasone/ Salmeterol | 3.8 | Nitroglycerin | 3.4 | Sertraline  | 1.9 | Oxycodone +/- APAP | 1.8 |
| 19 | Digoxin | 4.1 | Collagenase Clostrid. Hist. | 3.5 | Simvastatin | 3.8 | Donepezil  | 3.4 | Ciprofloxacin | 1.8 | Pantoprazole  | 1.8 |
| 20 | Nystatin | 4.0 | Risperidone | 3.4 | Warfarin  | 3.5 | Isosorbide Mononitrate | 3.4 | Donepezil  | 1.8 | Atropine  | 1.7 |
| 21 | Simvastatin | 4.0 | Fentanyl | 3.3 | Pantoprazole  | 3.2 | Albuterol  | 3.3 | Memantine  | 1.8 | Citalopram  | 1.7 |
| 22 | Citalopram  | 3.9 | SMZ-TMP | 3.3 | Azithromycin | 3.1 | Prednisone | 3.0 | Quetiapine  | 1.8 | Metoprolol Succinate | 1.6 |
| 23 | Warfarin  | 3.7 | Nystatin | 3.3 | Ciprofloxacin | 3.0 | SMZ-TMP | 2.9 | Scopolamine | 1.8 | Clopidogrel  | 1.6 |
| 24 | Risperidone | 3.5 | Albuterol  | 3.1 | Clopidogrel  | 2.9 | Sertraline  | 2.9 | Fentanyl | 1.8 | Megestrol  | 1.6 |
| 25 | Clopidogrel  | 3.4 | Digoxin | 3.1 | Citalopram  | 2.9 | Nystatin  | 2.9 | SMZ-TMP | 1.8 | Zolpidem  | 1.5 |

AFT: adult failure to thrive, APAP: acetaminophen, SMZ-TMP: sulfamethoxazole-trimethoprim

Overall, 53.5% of hospice patients admitted for cancer and 52.9% of patients admitted for a non-cancer cause obtained at least one medication through the Part D benefit after admission (**TABLE VIII)**. Antihypertensives were the most common preventative therapeutic class dispensed, received by 22.8% of cancer patients and 23.8% of non-cancer patients. The most frequently dispensed preventative drug classes for both cancer and non-cancer admissions included beta adrenergic antagonists (11.9% and 13.0%), proton pump inhibitors (10.8% and 11.2%), ACE inhibitors (6.0% and 6.7%), and statins (5.2% and 6.6%). Compared to hospice patients admitted for cancer, nearly three times as many patients admitted for a non-cancer cause received anti-dementia medications through Part D (7.4% vs 2.6%). Hospice patients admitted for cancer had a significantly lower absolute risk of receiving all of the preventative therapeutic classes assessed except oral antidiabetics. The prevalence of receiving opioid analgesics through Part D was similar for cancer (16.6%) and non-cancer (16.1%) hospice admissions (risk difference: 0.5%, 95% CI -0.04% to 1.0%; *p*=0.07).

Receipt of any Part D medication after hospice admission varied substantially among non-cancer admission diagnosis groups, with the greatest prevalence among patients admitted to hospice for debility/adult failure to thrive (63.5%) and dementia (61.5%), and the lowest prevalence among patients admitted for ischemic stroke (35.4%) and renal disease (36.0%) (**TABLE IX**). Across non-cancer diagnosis groups, the receipt of opioid analgesics and preventative medication classes generally followed similar patterns to that of any Part D use, with several notable exceptions. Patients admitted to hospice for heart disease demonstrated the highest prevalence of receiving anti-hyperlipidemic (9.7%), oral antidiabetic (5.3%), and antiplatelet agents (5.0%). The prevalence of receiving anti-dementia medications was substantially greater in hospice patients admitted for dementia (14.7%) compared to other non-cancer causes (2.2%-9.8%).

**TABLE VIII**

RECEIPT OF SELECTED DRUG AND THERAPEUTIC CLASSES THROUGH PART D AFTER HOSPICE ADMISSION, OVERALL AND BY CANCER AND NON-CANCER PRIMARY ADMISSION DIAGNOSIS

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **All Patients****(n=88,957)** | **Cancer** **(n=57,204)**  | **Non-Cancer** **(n=31,753)** | **Absolute % Difference, Cancer vs. Non-Cancer** |
| **Therapeutic or Drug Classa** | **%** | **%** | **%** | **% (95% CI)** |
| Anti-hyperlipidemic | 6.3 | 5.8 | 7.3 | -1.5 (-1.9, -1.2) |
| Statin | 5.7 | 5.2 | 6.6 | -1.4 (-1.7, -1.1) |
| Antihypertensive | 23.1 | 22.8 | 23.8 | -1.0 (-1.5, -0.4) |
| Beta adrenergic antagonist | 12.3 | 11.9 | 13.0 | -1.1 (-1.5, -0.6) |
| ACE inhibitor | 6.3 | 6.0 | 6.7 | -0.8 (-1.1, -0.4) |
| DHP calcium channel blocker | 5.1 | 5.1 | 5.1 | 0.1 (-0.2, 0.4) |
| Thiazide diuretic | 3.0 | 3.2 | 2.7 | 0.5 (0.3, 0.7) |
| ARB | 2.9 | 3.0 | 2.7 | 0.3 (0.1, 0.5) |
| Oral Antidiabetic | 4.1 | 4.4 | 3.8 | 0.6 (0.3, 0.9) |
| Biguanide | 1.9 | 2.0 | 1.6 | 0.5 (0.3, 0.6) |
| Sulfonlyurea | 2.2 | 2.3 | 2.0 | 0.3 (0.1, 0.5) |
| Anti-dementia  | 4.3 | 2.6 | 7.4 | -4.9 (-5.2, -4.5) |
| Anti-osteoporotic | 1.0 | 0.9 | 1.3 | -0.4 (-0.6, -0.3) |
| Antiplatelet | 2.6 | 2.2 | 3.5 | -1.3 (-1.5, -1.0) |
| Opioid analgesic | 16.4 | 16.6 | 16.1 | 0.5 (-0.04, 1.0) |
| Proton pump inhibitor | 10.9 | 10.8 | 11.2 | -0.5 (-0.9, -0.02) |
| Any Part D Medication | 53.3 | 53.5 | 52.9 | 0.7 (-0.03, 1.3) |

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; CI: confidence interval; DHP: dihydropyridine

aOnly selected drug classes shown within therapeutic classes; results by therapeutic class include all associated drug classes shown in **TABLE IV**.

**TABLE IX**

RECEIPT OF SELECTED DRUG AND THERAPEUTIC CLASSES THROUGH MEDICARE PART D AFTER HOSPICE ADMISSION BY NON-CANCER PRIMARY ADMISSION DIAGNOSIS

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Therapeutic or Drug Classa** | **Debility/AFT** | **Dementia** | **Lung Disease** | **Heart Disease** | **Ischemic Stroke** | **Renal Disease** |
| **(n=7,031)** | **(n=6,401)** | **(n=4,526)** | **(n=5,539)** | **(n=1,744)** | **(n=1,758)** |
| **%** | **%** | **%** | **%** | **%** | **%** |
| Anti-hyperlipidemic | 7.9 | 7.1 | 8.2 | 9.7 | 4.8 | 4.1 |
| Statin | 7.0 | 6.3 | 7.6 | 9.1 | 4.5 | 4.0 |
| Antihypertensive | 30.0 | 26.1 | 24.3 | 23.6 | 14.3 | 15.6 |
| Beta adrenergic antagonist | 17.2 | 13.7 | 10.9 | 14.3 | 7.6 | 10.0 |
| ACE inhibitor | 8.8 | 7.9 | 6.3 | 6.6 | 4.7 | 2.8 |
| DHP calcium channel blocker | 6.8 | 6.6 | 5.2 | 3.2 | 3.1 | 4.8 |
| Thiazide diuretic | 3.1 | 3.0 | 2.9 | 3.3 | 1.3 | 1.2 |
| ARB | 3.5 | 3.0 | 2.7 | 2.9 | 1.5 | 1.4 |
| Oral Antidiabetic | 3.9 | 4.3 | 3.6 | 5.3 | 2.9 | 1.6 |
| Biguanide | 1.8 | 2.1 | 1.9 | 1.9 | 1.2 | --b |
| Sulfonlyurea | 2.1 | 2.2 | 1.6 | 2.8 | 1.4 | 1.3 |
| Anti-dementia  | 9.8 | 14.7 | 3.4 | 5.0 | 3.4 | 2.2 |
| Anti-osteoporotic | 1.9 | 1.6 | 1.5 | 0.9 | --b | --b |
| Antiplatelet | 3.9 | 3.3 | 3.1 | 5.0 | 3.8 | 1.8 |
| Opioid analgesic | 21.8 | 18.6 | 12.8 | 15.2 | 10.8 | 12.0 |
| Proton pump inhibitor | 13.5 | 10.3 | 12.2 | 13.3 | 6.3 | 7.5 |
| Any Part D Medication | 63.5 | 61.5 | 48.3 | 54.7 | 35.4 | 36.0 |

AFT: adult failure to thrive; ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; DHP: dihydropyridine

aOnly selected drug classes shown within therapeutic classes; results by therapeutic class include all associated drug classes shown in **TABLE IV**.

bCell value that allows derivation of patient counts below pre-specified threshold (directly or indirectly from remaining row/column values) cannot be disclosed to preserve patient confidentiality per SEER-Medicare Data user agreement.

We observed little variation by year of hospice admission in the prevalence of Part D dispensing for the preventative drug and therapeutic classes assessed (**FIGURE 3**). However, the proportion of hospice patients receiving opioid analgesics through Part D decreased from 19.8% to 13.7% in those admitted for cancer and from 22.9% to 13.7% in those admitted for non-cancer causes between 2008 and 2012.

**(A)**

**(B)**

**FIGURE 3.** Trends in post-hospice admission Medicare Part D dispensing of selected therapeutic and drug classes by hospice admission year (2008-2012). Plotted points represent the proportion of patients first admitted to hospice in the given year with at least one dispensing after admission for the indicated therapeutic or drug class of interest. Results are stratified by patients admitted with a (A) cancer, or (B) non-cancer primary hospice admission diagnosis.

2.5 Discussion

We found that more than half of Medicare beneficiaries admitted to hospice for cancer or for any non-cancer cause obtained at least one medication through the Part D benefit after hospice admission. The receipt through Part D of medications not primarily aimed at symptom control near the end of life, particularly antihypertensives, was common. Overall and medication class-specific dispensing through Part D varied substantially among primary hospice admission diagnosis. Nearly one in six hospice patients received opioids though Part D, though the prevalence declined steadily over the study period. The prevalence of receiving preventative medication classes was relatively stable over time.

Previous research examining medication appropriateness in the end-of-life setting has described many medications typically used for preventing complications of chronic illness as being of limited benefit or even futile in those with limited life expectancy.52,57,59,104 Continuation of such medications contributes to polypharmacy in this already susceptible population, resulting in needlessly high medications costs and waste, overly complicated medication regimens, exposure to medication side effects and drug-drug interactions, lower medication adherence, and significant patient and caregiver burden.87,88,105 A lack of consensus guidelines and limited outcomes data supporting drug discontinuation have been frequently cited as contributing factors to inappropriate prescribing at the end of life, though recent research efforts have begun to bridge this evidence gap.45,106,107 Kutner and colleagues conducted a randomized, controlled trial demonstrating that statin discontinuation is safe in terminally-ill patients and may even modestly improve quality of life.108 The recently developed Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy (STOPPFrail) consensus criteria provide the first set of broadly applicable recommendations for deprescribing specific medications in frail older adults with limited life expectancy.103 Whether the frequent receipt of preventative medications observed in our study is driven by clinical uncertainty, lack of provider education, patient/family treatment preferences, poor communication and care coordination, administrative issues, or some combination of factors is currently unclear and deserves further study.

The prevalence of receiving opioid analgesics over the period of our study is similar to estimates from a previous CMS analysis, which found that 14.9% of hospice beneficiaries enrolled in Part D in 2010 received analgesics through the Part D benefit.17 A 2012 report from the Department of Health and Human Services addressed this issue, stating that Medicare may be paying twice for medications related to the palliation of a hospice patient’s terminal illness, once through the hospice benefit’s per diem payment and again through Part D.109 In 2014, CMS released guidance strongly encouraging Part D plan sponsors to place prior authorization requirements on four classes of prescription drugs almost always covered by Medicare’s hospice benefit: analgesics, antiemetics, laxatives, and anxiolytics.110 Between 2013 and 2016, CMS reported that the prevalence of Part D utilization among hospice patients for drugs in these four categories decreased by more than 75%, from 15.8% to 3.6%, with no negative impact on patient satisfaction.96 Thus, for the medications most commonly designated to be provided by hospice, the problem of inappropriate billing to beneficiaries’ Part D plans appears to have largely been eliminated. It is unknown whether this is also true for diagnosis-specific palliative therapies without prior authorization requirements. Among the top 25 medications dispensed through Part D stratified by primary admission diagnosis, we noted multiple bronchodilator medications in patients admitted for lung disease and several cardiac medications which may provide significant symptomatic benefit (e.g., ACE inhibitors and loop diuretics) in those admitted for terminal heart disease.

 Patients admitted to hospice for dementia and debility/failure to thrive exhibited substantially higher utilization of the Part D benefit compared to patients admitted for cancer, stroke, or organ failure-related illnesses. The reasons for this are unclear. Previous studies have demonstrated that hospice patients admitted for dementia and debility are significantly more likely to have longer hospice stays compared to those with other terminal admission diagnoses.111–113 We found that a primary hospice admission diagnosis of dementia or debility/failure to thrive was associated with a mean hospice stay of 76 days, compared to 44 days for cancer, 54 days for heart disease, 57 days for lung disease, 31 days for ischemic stroke, and 22 days for renal disease (data not shown). The prevalence of Part D dispensing within the admission diagnosis groups, tended to increase with increasing group length of stay. It is plausible that compared to patients with short hospice stays, those with longer stays may have simply survived long enough to be eligible for continued refills of medications used prior to admission. Further, hospice patients with dementia and debility diagnoses are more than twice as likely to reside in nursing facilities compared to other settings.113 These facilities are often serviced by long-term care pharmacies which frequently use automatic medication refill and delivery processes for the patients they serve. As hospice admission to a nursing facility often does not represent a change in physical location for many of these patients, routine refills of preventative medications may continue to be processed through Part D by the long-term care pharmacy unless explicit orders are received from a prescriber discontinuing the medication(s).

The utilization of the Part D prescription drug benefit in over half of hospice patients highlights the importance of comprehensively reviewing each patient’s medication regimen at hospice admission, including an assessment of medication appropriateness in the context of the patient’s terminal illness. A framework for discontinuing medications for patients late in life based on life expectancy, time to benefit of the medication, goals of care, and medication treatment targets could be used to reduce medicines deemed unnecessary in light of terminal illness.49,102 A mutual understanding of treatment goals among patients and families and the hospice care team upon hospice admission is critical to ensuring smooth care transition and expectations for medical care during the hospice stay. Clinical pharmacists with training in geriatrics and palliative care may be an especially valuable resource in this setting, as their ability to manage complex medication regimens has been shown to positively influence patient outcomes and prevent drug-related problems in terminally-ill patients.114,115

Several limitations of our study should be noted. Our intent was to broadly describe the medications that older Medicare fee-for-service hospice patients received through Medicare Part D. The results of our study may not be generalizable to hospice patients enrolled in other health plan types (e.g., Medicare Advantage) or those without Part D prescription coverage. Beginning in October 2014, CMS no longer allowed debility, adult failure to thrive, and certain dementias (e.g., senile, vascular, and unspecified dementias) to be listed as a patient’s primary hospice admission diagnoses.116 The observed results for these patient groups may thus be less applicable today. While the utilized data source is nationally representative, we did not attempt to account for confounding factors that may explain the observed differences across admission diagnosis cohorts.

 We also did not attempt to assess appropriateness of the medications dispensed based on indication. For example, the use of certain antihypertensives in patients with terminal congestive heart failure may confer a symptomatic benefit, and thus be reasonable to continue after hospice admission. However, in such a scenario, we would anticipate that the medication is provided by hospice, and not through the Part D benefit. Medicare Part D claims do not allow a determination of whether medications dispensed are actually taken by the patient, though Part D dispensing in the hospice population is problematic on its own from a policy and systems perspective. Finally, we did not assess the proportion of pre-hospice admission users of a particular medication class who subsequently continued the medication after admission, which may serve as a proxy for hospice provider deprescribing. Further research is needed to contextualize the observed Part D utilization patterns and determine the magnitude and determinants of non-palliative, preventative medication continuation after admission to hospice.

2.6 Conclusion

In summary, we assessed the medications obtained through Medicare Part D in patients admitted to hospice and found that more than half of patients continued to receive Part D medications after admission. Preventative medications with potentially limited benefit were regularly dispensed through Part D and utilization varied widely by primary hospice admission diagnosis. The clinical and economic implications of potential misuse or overprescribing in dying patients are non-trivial. A more critical evaluation of each patient’s medication list and subsequent deprescribing of those treatments which may not be relevant in the context of terminal illness is needed. Identification of patient, provider, and healthcare system-related contributors to non-palliative medication use may help to improve medication-related quality of care in this vulnerable population.

III. Continuation of Medications with Limited Benefit in Older Hospice Patients

3.1 Preface

This chapter addresses Aim 2 of the dissertation. It is being considered for publication in the *Journal of the American Medical Association* as an article titled “Continuation of Medications with Limited Benefit in Older Hospice Patients”. The submitted version is presented here.

3.2 Introduction

Hospice utilization has increased dramatically in recent years such that nearly half of all deaths in the United States now occur under hospice care.2,94 The Medicare Hospice Benefit, administered under Part A and covering >85% of all hospice patients nationwide, provides per diem payments to hospice programs to cover all treatment for the palliation of the patient’s terminal illness and related conditions, including medications. Medications for conditions unrelated to the patient’s terminal illness are typically not provided by hospice but may be obtained through the Medicare Part D Prescription Drug Benefit. Medicare has stated that the use of medications through the Part D benefit by hospice patients should be minimal.17 However, recent reports have shown that overall Part D use among hospice patients is common, costing Medicare approximately $340 million annually.5,96

As hospice’s central focus is on providing comfort care and support measures, medications that do not deliver pain relief, provide symptom control, or improve or maintain quality of life may be largely unnecessary. Prior research has demonstrated that hospice patients use, on average, 10-16 medications during their stay, including medications which may not be directed at relieving symptoms or improving quality of life.21–23 These studies also note differences in medication use between patients admitted to hospice for cancer versus those admitted for non-cancer causes. This may be due to the more rapid and predictable pattern of decline in hospice patients with terminal cancer compared to other non-cancer terminal illnesses, impacting clinicians’ ability to predict survival and in turn affecting health care delivery and medication treatment decisions.117,118 For medications aimed at preventing or slowing the development of chronic disease sequelae with little impact on symptoms or quality of life in the short term, there may be significant discord between remaining life expectancy and the medication’s time until benefit.49,119 Continued use in this already vulnerable population increases the risk of medication side effects and drug-drug interactions, and can lead to increased patient and healthcare system costs, unnecessarily complex drug regimens, and substantial patient and caregiver burden.45,71,87

We aimed to describe the prevalence of continuing preventative medications with limited benefit after hospice admission and identify factors associated with continuation in older Medicare beneficiaries admitted to hospice for cancer and non-cancer causes.

3.3 Methods

3.3.1 Data Source and Study Population

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

 Patients aged less than 66 years at hospice admission and those not continuously enrolled in Medicare Parts A, B and D from one year prior to hospice entry through the date of death were excluded. We also excluded patients with any enrollment in a Medicare Advantage plan. 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) after initial admission lasting greater than 30 days.

The primary ICD-9 diagnostic code on the initial hospice claim was used to classify patients as a cancer or non-cancer admission. Patients admitted to hospice for cancer were identified from a SEER registry-derived cohort of patients diagnosed with a first primary lung, colorectal, breast, pancreatic cancer or lymphoma. These cancer sites have been reported as the five most prevalent cancer-related hospice admission diagnoses among Medicare beneficiaries.101 Patients admitted to hospice for a non-cancer cause were identified from the random 5% non-cancer sample in addition to those in the SEER registry-based cohort who ultimately entered hospice for a non-cancer cause.

3.3.2 Preventative Medications with Limited Benefit Definition

Preventative medication classes considered to be of limited benefit in the end-of-life population were identified via literature review, including primary research studies, review articles, and expert opinion pieces.41,52,56,57,59–61,63,65,66,103,104 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. Anti-hyperlipidemics, antihypertensives, oral antidiabetics, antiplatelets, anti-dementia medications, anti-osteoporotic medications, and proton pump inhibitors were included, with some disease-specific exceptions: Drug classes were excluded from the analysis at the patient level if a diagnosis was present in the year prior to hospice admission for a condition where the medication may have provided a symptomatic or quality of life benefit, or decreased the short-term (e.g. <1 year) risk of major adverse events (**TABLE X**). Prior studies have cited additional medication classes (e.g., leukotriene receptor antagonists, hormonal medications, antimicrobial agents) as being of questionable benefit at the end of life.59,63,103 However, for this research we

**TABLE X**

MEDICATION CLASSES IDENTIFIED AS BEING OF LIMITED BENEFIT IN HOSPICE PATIENTS AND CRITERIA FOR EXCLUSION FROM THE CONTINUATION ANALYSIS

|  |  |  |
| --- | --- | --- |
| **Therapeutic Class** | **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**a** |
| Antihypertensive | Thiazide diureticsOther non-loop diureticsbACE inhibitorsARBsDHP CCBsNon-DHP CCBsBeta-blockersAlpha-blockersCentrally-acting agentsVasodilatorsDirect 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 pectorisiii. Non-DHP CCBs and beta-adrenergic antagonists excluded when used for atrial fibrillation/flutteriv. Beta-adrenergic antagonists, ACE inhibitors, and ARBs excluded when used after recent myocardial infarction**a** |
| Oral Antidiabetic | BiguanidesSulfonylureasDipeptidyl peptidase-4 inhibitorsMeglitinidesAlpha glucosidase inhibitorsThiazolidinediones |   |
| Anti-dementia | Cholinesterase inhibitorsNMDA receptor antagonists |   |
| Anti-osteoporotic | BisphosphonatesSERMs |   |
| Antiplatelet | P2Y12 inhibitorsCombination antiplatelets  | i. P2Y12 inhibitors excluded when used after recent myocardial infarction or ischemic stroke**a**ii. Combination antiplatelets excluded when used after recent ischemic stroke**a** |
| Anti-secretoryc | Proton pump inhibitors |   |

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

**a**Recent defined as presence of a primary hospital discharge for the event in the 12 months prior to hospice admission.

bIncludes amiloride and triamterene in combination with hydrochlorothiazide; includes all formulations of spironolactone.

cClass comprised only of proton pump inhibitors for this research and therefore not evaluated as a distinct therapeutic class.

focused on medication classes which are both broadly used in the older adult population and were most consistently identified throughout the literature as being of limited benefit in the late stages of terminal illness. 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.

3.3.3 Limited Benefit Medication Use

Baseline limited benefit medication use was measured in the six 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.

Continuation of preventative medications with limited benefit was measured from the date of hospice admission through the date of death. Pre-admission users of a particular drug class 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. In addition to measuring class-specific continuation, we also assessed continuation of at least one drug or therapeutic class and post-admission continuation of all limited benefit medication classes used in the pre-hospice admission period.

3.3.4 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 cancer versus non-cancer admissions were compared using absolute risk differences with 95% CIs.

We used modified Poisson regression with generalized estimating equations 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 clustering of responses at the hospice facility level.120,121 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.122 We used fractional polynomials to allow for non-linear exposure-outcome relationships. 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).

3.4 Results

We identified 70,035 patients with active use of at least one preventative medication of limited benefit prior to hospice admission, including 44,218 patients admitted to hospice for cancer and 25,817 patients admitted for a non-cancer cause (**FIGURE 4**). Overall, 9,614 patients (10.8%) and 4,033 patients (4.5%) were excluded due to having no limited benefit medication use or only limited benefit medication use with a possible palliative benefit, respectively, in the 6 months prior to hospice admission. Most patients were white and female, had hospice stays of less than one month, and used more than 15 unique medications on average through the Part D benefit prior to hospice admission (**TABLE XI**). Compared to patients admitted for a non-cancer cause, patients admitted to hospice for cancer were younger (mean [SD], 79.2 [7.7] years vs. 85.5 [7.8] years, p<0.001), 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, had fewer cardiovascular comorbidities (p<0.001), and were more likely to be admitted to hospice in a private home (68.7% vs. 38.2%, p<0.001) (**TABLE XI**). The most common



**FIGURE 4.** Patient flow diagram for Aim 2. Application of inclusion and exclusion criteria to reach final

study cohort.

**TABLE XI**

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF STUDY COHORT

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **All Patients (n=70,035)** | **Cancer\***  **(n=44,218)** | **Non-Cancer\* (n=25,817)** |
| 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% |
| Female Sex | 67.3% | 63.5% | 73.8% |
|  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 | 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 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% |
| Primary Hospice Admission Diagnosis |  |  |   |
| Cancer | 63.1% | 100.0% | 0% |
| Debility/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% |
| Admitting Hospice Care 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 | 1.3% | 1.3% | 1.4% |
| Comorbidity |  |  |   |
| Hypertension | 86.4% | 85.5% | 88.0% |
| Heart Failure | 33.5% | 24.6% | 48.8% |
| Diabetes Mellitus | 40.9% | 40.4% | 41.8% |

**TABLE XI (continued)**

Demographic and Clinical Characteristics of Study Cohort

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **All Patients (n=70,035)** | **Cancer\***  **(n=44,218)** | **Non-Cancer\* (n=25,817)** |
| 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% |
| Number of Outpatient Providers in Year Prior to Admissiona |  |  |  |
| 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) |
| Part D Low-Income Subsidy Recipient | 42.9% | 39.5% | 48.7% |

SD: standard deviation, 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.

aExcludes provider claims generated in EDs, outpatient hospitals, and surgery centers; includes physicians, physician’s assistants, and nurse practitioners as providers.

admission diagnoses in the non-cancer cohort were debility/failure to thrive (22.3%), dementia (21.0%), and heart disease (16.9%).

Antihypertensives and anti-hyperlipidemics were the most common limited benefit therapeutic classes actively used prior to admission (**TABLE XII**). Proton pump inhibitors were used by approximately 40% of patients prior to admission. Of those with active use of one or more limited benefit medication classes at baseline, 29.8% of patients admitted for cancer and 30.5% of patients admitted for a non-cancer cause continued at least one of the limited benefit medications through Part D after hospice admission. For both cancer and non-cancer patients, anti-dementia medications (33.4% and 27.3%) and antihypertensives (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 non-cancer admissions, 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 XII**).

**TABLE XII**

PRE-HOSPICE ADMISSION LIMITED BENEFIT MEDICATION USE AND POST-ADMISSION CONTINUATION AMONG PRE-ADMISSION USERS, OVERALL AND BY CANCER VERSUS NON-CANCER HOSPICE ADMISSION DIAGNOSIS

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Pre-Hospice Admission Use** | **Proportion of Users Continuing After Admissiona** | **Pre-Hospice Admission Use** | **Proportion of Users Continuing After Admissiona** | **Risk Difference, Cancer vs. Non-Cancerb** |
| **All Patients** **(n=70,035)** | **Cancer** **(n=44,218)** | **Non-Cancer** **(n=25,817)** | **Cancer**  | **Non-Cancer**  |  |
| **Therapeutic or Drug Classc** | **n (%)** | **%** | **n (%)** | **n (%)** | **%** | **%** | **% (95% CI)** |
| Anti-Hyperlipidemic | 26,559 (37.9%) | 16.4% | 17,760 (40.2%) | 8799 (34.1%) | 15.1% | 19.0% | -3.9 (-4.9, -2.9) |
| Statin | 24,387 (34.8%) | 16.4% | 16,411 (37.1%) | 7976 (30.9%) | 15.0% | 19.2% | -4.2 (-5.3, -3.2) |
| Antihypertensive | 45,068 (64.4%) | 26.5% | 30,015 (67.9%) | 15,053 (58.3%) | 26.7% | 26.0% | 0.8 (-0.1, 1.6) |
| Beta-Blocker | 15,999 (22.8%) | 28.5% | 11,255 (25.5%) | 4744 (18.4%) | 27.9% | 29.8% | -1.8 (-3.4, -0.3) |
| ACE Inhibitor | 12,674 (18.1%) | 23.2% | 9211 (20.8%) | 3463 (13.4%) | 22.0% | 26.3% | -4.3 (-6.0, -2.6) |
| DHP CCB | 15,732 (22.5%) | 22.8% | 9943 (22.5%) | 5789 (22.4%) |  23.4% | 21.8% | 1.6 (0.3, 3.0) |
| ARB | 6535 (9.3%) | 22.2% | 4969 (11.2%) | 1566 (6.1%) | 22.0% | 22.6% | -0.6 (-3.0, 1.8) |
| Thiazide Diuretic | 12,589 (18.0%) | 15.8% | 8769 (19.8%) | 3820 (14.8%) | 16.0% | 15.3% | 0.7 (-0.7, 2.0) |
| Oral Anti-diabetic | 13,662 (19.5%) | 23.0% | 9082 (20.5%) | 4580 (17.7%) | 23.3% | 22.4% | 1.0 (-0.5, 2.4) |
| Sulfonylurea | 7589 (10.8%) | 21.4% | 4985 (11.3%) | 2604 (10.1%) | 21.8% | 20.5% | 1.2 (-0.7, 3.2) |
| Biguanide  | 6953 (9.9%) | 20.5% | 5015 (11.3%) | 1938 (7.5%) | 20.0% | 21.6% | -1.6 (-3.8, 0.5) |
| Antiplatelet | 6868 (9.8%) | 22.8% | 4040 (9.1%) | 2828 (11.0%) | 22.2% | 23.7% | -1.5 (-3.6, 0.5) |
| Anti-dementia  | 11,622 (16.6%) | 29.3% | 3861 (8.7%) | 7761 (30.1%) | 33.4% | 27.3% | 6.0 (4.2, 7.8) |
| Anti-osteoporotic | 5679 (8.1%) | 14.1% | 3309 (7.5%) | 2370 (9.2%) | 13.2% | 15.4% | -2.1 (-4.0, -0.3) |
| Proton Pump Inhibitor | 27,693 (39.5%) | 24.6% | 17,480 (39.5%) | 10,213 (39.6%) | 23.9% | 25.8% | -1.8 (-2.9, -0.8) |
|   |  |  |  |  |  |  |  |
| At Least One Limited Benefit Medication  | 70,035 (100.0%) | 30.1% | 44,218 (100.0%) | 25,817 (100.0%) | 29.8% | 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

aPatients 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.

bDifference in proportion of pre-hospice admission users with at least one Part D dispensing for the class of interest after hospice admission.

cSelected drug classes only; results by therapeutic class include all associated drug classes in **TABLE X**

In adjusted analyses, the likelihood of continuing at least one preventative 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 XIII**). Compared to those admitted to hospice in a private home, patients admitted to hospice in nursing and assisted living facilities had at least a 25% greater risk of continuing one or more limited benefit medications (assisted living facility: RR 1.28; 95% CI, 1.24-1.32; non-skilled nursing facility: RR 1.29; 95% CI, 1.25-1.32; skilled nursing facility: RR 1.25; 95% CI, 1.20-1.29). Conversely, those admitted to hospice in acute care hospitals or inpatient hospice facilities were less than half as likely to continue at least one limited benefit medication compared to private home admission. As compared to patients using only one class

prior to admission, those using two limited benefit drug classes were 39% more likely to continue at least one or more classes after admission (RR 1.39, 95% CI 1.35-1.44) while those using six or more classes prior to admission were twice as likely to continue at least one class after admission (RR 2.00, 95% CI 1.93-2.08) (Table 4). By hospice length of stay, the likelihood of receiving at least one limited benefit medication after admission was 2.6 times greater (RR 2.59, 95% CI 2.41-2.79) for those with stays of 8-14 days compared to those with stays ≤7 days, increasing to more than nine times greater (RR 9.39, 95% CI 8.80-10.02) and 13 times greater (RR 13.11, 95% CI 12.25-14.02) for those with hospice stays of 30-89 days and 180 or more days, respectively (**TABLE XIII**).

Continuation of all limited benefit medication classes used prior to hospice enrollment was observed for 12.5% of patients admitted for cancer and 13.9% of those admitted for non-cancer causes (**TABLE XIV**). With the exception of the number of limited benefit drug classes used prior to hospice admission which showed an opposite trend, variations in continuation by sociodemographic and clinical characteristics were generally similar to those observed in the analysis for continuation of at least one limited benefit medication.

**TABLE XIII**

FACTORS ASSOCIATED WITH CONTINUATION OF ≥1 LIMITED BENEFIT MEDICATION AFTER HOSPICE ADMISSION

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **≥1 Limited Benefit Medication After Hospice Admission** | **All Patients** | **Cancer Admission Diagnosis** | **Non-Cancer Admission Diagnosis** |
| **Factor** | **n/N** | **%** | **Adjusted RR (95% CI)a** |
| Sex |  |  |  |  |  |
| Male | 6198/22,883 | 27.1 | Refb | Refb | Refb |
| 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 | Refc | Refc | Refc |
| 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 | Refd | Refd | Refd |
| Black | 1,955/5,825 | 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) |
| Other | 305/1176 | 25.9 | 0.85 (0.79-0.92) | 0.85 (0.78-0.93) | 0.83 (0.73-0.96) |
| Hospice Admission Setting |  |  |  |  |  |
| Private Home | 12,992/40,241 | 32.3 | Refe | Refe | Refe |
| 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) |
| Other | 157/939 | 16.7 | 0.91 (0.79-1.05) | 0.86 (0.71-1.06) | 0.96 (0.80-1.17) |
| Hospice Admission Diagnosis |  |  |  |  |  |
| Cancer | 13,191/44,218 | 29.8 | Reff |  |  |
| Debility/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) |

**TABLE XIII (continued)**

Factors Associated With Continuation of ≥1 Limited Benefit Medication After Hospice Admission

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **≥1 Limited Benefit Medication After Hospice Admission** | **All Patients** | **Cancer Admission Diagnosis** | **Non-Cancer Admission Diagnosis** |
| **Factor** | **n/N** | **%** | **Adjusted RR (95% CI)a** |
| Hospice Length of Stay (days) |  |  |  |  |  |
| ≤7  | 1122/23,339 | 4.8 | Refg | Refg | Refg |
| 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 Providers in Year Prior to Admission |  |  |  |  |  |
| 1-3 | 6735/20,253 | 33.3 | Reff | Reff | Reff |
| 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 | Refh | Refh | Refh |
| 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 Prior to Admission |  |  |  |  |  |
| 1 | 4128/20,591 | 20.1 | Refi | Refi | Refi |
| 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

aPotential adjustment variables included all variables listed in **TABLE XI** in addition to hospice admission year, intensive care unit stay in the 90 days prior to hospice admission, hospital discharge in the 3 days prior to hospice admission, feeding tube use, number of hospitalizations in year prior to hospice admission, and number of limited benefit drug classes used prior to hospice admission.

bAdjusted for age, race and hospice length of stay.

cAdjusted for sex, race, hospice length of stay, Part D low-income subsidy and limited benefit medication classes used prior to hospice admission.

dAdjusted for age, sex, hospice length of stay and Part D low-income subsidy.

eAdjusted for age, sex, race, hospice length of stay, Part D low-income subsidy and primary hospice admission diagnosis.

fAdjusted for age, sex, race and hospice length of stay.

gAdjusted 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.

hAdjusted 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.

iAdjusted for age, sex, race, hospice length of stay and Part D low-income subsidy.

**TABLE XIV**

POST-HOSPICE ADMISSION CONTINUATION OF ALL LIMITED BENEFIT MEDICATIONS AMONG PRE-ADMISSION USERS, CANCER VERSUS NON-CANCER HOSPICE ADMISSION DIAGNOSIS

|  |  |  |
| --- | --- | --- |
|   | **Cancer\*** **(n=44,218)** | **Non-Cancer\*****(n=25,817)** |
| **Characteristic** | **%** | **%** |
| Overall | 12.5% | 13.9% |
| Sex |  |  |
| Male | 11.1% | 13.1% |
| Female | 13.4% | 14.2% |
| Age (years) |  |  |
| 66-69 | 10.7% | 15.9% |
| 70-74 | 10.6% | 12.4% |
| 75-79 | 10.9% | 13.1% |
| 80-84 | 12.9% | 13.6% |
| 85-89 | 14.5% | 13.2% |
| ≥90 | 17.7% | 15.0% |
| Race |  |  |
| White | 12.6% | 14.0% |
| Black | 13.6% | 13.7% |
| Asian | 9.7% | 13.1% |
| Hispanic | 11.1% | 11.7% |
| Other/Unknown | 12.6% | 12.1% |
| Hospice Admission Setting |  |  |
| Home/Private Residence | 13.3% | 15.6% |
| Assisted Living Facility | 20.9% | 25.3% |
| Non-Skilled Nursing Facility | 21.0% | 19.1% |
| Skilled Nursing Facility | 14.9% | 14.4% |
| Inpatient (Acute Care) Hospital | 1.9% | 1.3% |
| Inpatient Hospice Facility | 2.9% | 1.5% |
| Other/Unknown | 4.1% | 8.6% |
| Hospice Length of Stay (days) |  |  |
| ≤7  | 1.1% | 1.3% |
| 8-14  | 3.6% | 4.3% |
| 15-29 | 7.2% | 10.3% |
| 30-89  | 21.2% | 26.4% |
| 90-179 | 36.6% | 38.4% |
| ≥180 | 49.2% | 45.5% |
| Outpatient Providers in Year Prior to Admission |  |  |
| 1-3 | 15.6% | 16.1% |
| 4-6 | 13.1% | 13.9% |
| 7-9 | 11.4% | 11.7% |
| ≥10 | 9.0% | 10.1% |
| Unique Part D Medications in Year Prior to Admission |  |  |
| 1-4 | 18.2% | 19.5% |
| 5-9 | 16.0% | 16.1% |
| 10-19 | 12.7% | 13.7% |
| 20-29 | 9.6% | 12.4% |
| ≥30 | 9.6% | 11.7% |

**TABLE XIV (continued)**

Post-Hospice Admission Continuation of All Limited Benefit Medications Among Pre-Admission Users, Cancer Versus Non-Cancer Hospice Admission Diagnosis

|  |  |  |
| --- | --- | --- |
|  | **Cancer\*** **(n=44,218)** | **Non-Cancer\*** **(n=25,817)** |
| **Characteristic** | **%** | **%** |
| Limited Benefit Drug Classes Used Prior to Admission |  |  |
| 1 | 19.5% | 21.0% |
| 2 | 12.3% | 13.5% |
| 3 | 9.4% | 10.6% |
| 4-5 | 7.4% | 7.8% |
| 6+ | 5.3% | 8.2% |

\*p <0.001 for all cancer versus non-cancer group comparisons.

3.5 Discussion

In this study of over 70,000 Medicare beneficiaries who died in hospice, nearly one in three patients with active limited benefit medication use prior to hospice admission continued to receive at least one of these medications after hospice enrollment. Continuation varied by medication class while factors such as age, race, hospice care setting, and length of hospice stay were independently associated with continuing one or more limited benefit medications after hospice admission.

The relatively high prevalence of limited benefit medication continuation despite hospice goals of care highlights what is likely a complex, multifactorial problem. Previously identified barriers to routine deprescribing in the setting of limited life expectancy include a reluctance among providers to discuss de-escalation of therapy, clinical inertia, lack of provider training, and refusal by patients and family members to stop medications.45,54,56,63,71–73,123,124 Further, systems-level measures curtailing non-palliative medication use in the hospice setting are lacking. In December 2013, Medicare strongly advised Part D plan sponsors to place prior authorization requirements on all medications for hospice enrollees; however, this guidance was later revised to only include four classes of medications which are typically provided by hospice: analgesics, antiemetics, laxatives, and anxiolytics.17,110 While the resulting decreases in Part D utilization for these four drug classes has been dramatic, use of maintenance medications remains high.96 Our results may prompt further development of Medicare Part D policies aimed at more closely monitoring the reimbursement of non-essential medications at the end of life without compromising quality of care.

A lack of outcomes data or guidelines supporting discontinuation of specific medication classes in the palliative care setting introduces further uncertainty into the deprescribing process. This may be illustrated in our results, where therapeutic classes more unanimously cited by geriatric and palliative care experts as providing little benefit at the end of life (e.g., lipid-lowering medications) were continued substantially less frequently than classes associated with more uncertainty (e.g., antihypertensives). However, recent efforts have been made to address this evidence gap. A randomized, controlled trial among patients with a life expectancy of one year or less found that statin discontinuation at the end of life was safe and did not diminish quality of life.108 The recently introduced STOPPFrail consensus criteria provide the first explicit, medication-specific recommendations for deprescribing in older adults with limited life expectancy, regardless of healthcare setting or terminal illness.103

The increased risk of continuation associated with hospice admission in nursing and assisted-living facilities may have a basis in the prescription processing practices of long-term care pharmacies. These pharmacies may process medication refills automatically and indefinitely for their facility residents unless a provider (or provider’s agent) explicitly notifies the pharmacy of a change in therapy.125 Given that initiation of hospice care in these facilities often does not represent a change in a patient’s care setting, standing orders for preventative medications used prior to hospice enrollment may continue to be automatically dispensed by the facility-associated pharmacy after a patient’s hospice election.

Explanations for the dramatic, positive trend of limited benefit medication continuation with increasing hospice length of stay are not immediately clear. While prescribers may be more likely to discontinue such medications in patients with a poorer prognosis, patients with longer hospice stays may simply be living long enough to be eligible for routine refills of the medications that they were taking prior to admission.126 Further research is needed elucidating the patterns of medication discontinuation at the point of hospice admission and the mechanisms by which medications with potentially limited benefit are continued after enrollment. Regardless, periodic reviews of non-palliative medication use after hospice admission seem warranted to ensure that patients’ medication regimens continue to appropriately align with their goals of care.

This is the first study to identify a cohort of medication users prior to hospice enrollment and follow them through their hospice stay until death to assess longitudinal changes in medication use. The large, nationally representative population and use of adjudicated Part D claims serve as strengths of our study. However, several limitations should be noted. First, we were unable to measure 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. Second, as we measured continuation via new Part D dispensings after hospice admission, the true prevalence of medication continuation is likely underestimated. 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. Third, medication dispensing via claims is an imperfect proxy for medication use, particularly in the terminally-ill population. Fourth, as our study took place largely before the Medicare program began issuing guidance on Part D reimbursement in hospice, providers may now be more cognizant of non-essential medication use in hospice patients. Further research is needed comparing current medication use trends in the hospice population to those observed in our study. Finally, the medication classes chosen for this study are exploratory and largely based on expert opinion. Thus, it is not intended to be a definitive or complete list of non-essential medications in the hospice population. Given the complexity of individual patient treatment decisions at the end of life, our approach and that of others should not be interpreted as a substitute for clinical judgement.

3.6 Conclusion

Despite Medicare guidance and the stated mission of hospice care, we found that nearly one-third of older hospice patients who were users of preventative medications with potentially limited benefit prior to hospice enrollment continued to receive at least one of these medications through Medicare Part D after admission. Our results highlight the need for additional research clarifying and targeting patient, provider, pharmacy, and healthcare system-level barriers which prevent the discontinuation of limited benefit medications at the point of hospice enrollment. Further, there is a significant need to understand the benefits and risks of discontinuing preventative medications in hospice care. The development and incorporation of evidence-based recommendations into palliative care guidelines will be integral to encouraging a more critical evaluation of medication appropriateness in this clinically complex population. Further development of Medicare policies for medication coverage in hospice and the introduction of strategies to promote high-quality pharmaceutical care at the end of life are warranted.

IV. Use of Non-Palliative Medications Following Burdensome Health Care Transitions in Hospice Patients: A Matched Cohort Analysis

4.1 Preface

This chapter addresses Aim 3 of the dissertation. It has been submitted for publication consideration to the journal *Medical Care* as an article titled “Use of Non-Palliative Medications Following Burdensome Health Care Transitions in Hospice Patients: A Matched Cohort Analysis”. The submitted version is presented here.

4.2 Introduction

 The 2015 Institute of Medicine Report *Dying in America* highlights the significant burden associated with transfers between health care settings at the end of life.127 These transitions are often overwhelming for patients and families, and can result in poor continuity of care among the patient’s care team.79,128 Despite the preference of most patients to spend their final weeks and days at home or in hospice care, health care transitions at the end of life are increasingly common.129–131 From 2000 to 2009, the mean number of transitions in the last 90 days of life among older Medicare beneficiaries increased from 2.1 to 3.1 while the proportion experiencing a transition in the last three days of life increased from 10.3% to 14.2%. 80 In 2011, nearly one in three Medicare decedents experienced at least four health care transitions in the six months prior to death.132

Hospice is generally associated with less aggressive end of life care than other care modalities for the terminally ill due to its emphasis on foregoing curative measures in favor of treatment focused on symptom and quality of life improvement.1 Specifically, hospice has been associated with substantial reductions in hospital admissions, ED visits, intensive-care unit stays, and overall health care costs.10,133 Despite the palliative treatment philosophy, hospice patients still experience transitions between health care settings prior to death. Wang and colleagues recently reported that 10% of older fee-for-service Medicare beneficiaries admitted to hospice experienced at least one transition to a non-hospice setting prior to death while 5% experienced a hospitalization after hospice enrollment.81 Additionally, an estimated 16%-18% of hospice patients are discharged from hospice alive, with many receiving care in other settings and reenrolling in hospice shortly thereafter.11,82,85

Given hospice’s orientation toward comfort care, most medications that no longer provide a symptomatic or quality of life benefit in the context of limited life expectancy may be discontinued upon hospice admission.87,134 However, studies have demonstrated that hospice patients continue to receive medications with potentially questionable benefit until death.21,23,135 While the exact cause for this is not well understood, poor coordination of care among providers and poor communication between providers and patients have been suggested as significant contributing factors.72,73,87 Transitions in care may exacerbate this problem. Medication reconciliation and documentation practices following care transfers in the general population have been shown to be poor, and may be further magnified in end of life populations as a result of complex and rapidly changing medication regimens.72,76,136,137 The goal of this study was to characterize the impact of burdensome health care transitions on subsequent receipt of LBMs among older Medicare beneficiaries admitted to hospice.

4.3 Methods

4.3.1 Data Source and Study Population

We conducted a matched cohort study using the SEER-Medicare linked database. We included fee-for-service Medicare beneficiaries who entered hospice and died while under hospice care between January 1, 2008 and December 31, 2013. The SEER-Medicare data obtained for this study consisted of two populations: 1) Patients diagnosed with a first primary lung, colorectal, breast, pancreatic cancer or lymphoma and 2) a random 5% sample of Medicare beneficiaries residing in the SEER registry regions and not diagnosed with cancer. De-identified data were available on patient demographics, Medicare enrollment, health care utilization measures, medical diagnoses, and Medicare Part D prescription dispensing.

We included patients aged at least 66 years at hospice admission who were continuously enrolled in Medicare Parts A, B and D starting one year prior to hospice admission (i.e., baseline) and continuing through the date of death. We excluded patients with any enrollment in a managed care plan, those without at least one Part D claim during the baseline period, and those who were discharged from hospice and subsequently died in a non-hospice care setting.

4.3.2 Measures

 Burdensome health care transitions were defined as transitions between health care settings that were likely to result in discontinuity in the patient’s health care team, namely*,* transitions from ahospice to non-hospicecare setting. This consisted of hospitalizations from hospice, ED visits from hospice without subsequent hospitalization (i.e., standalone ED visits), hospice discharges, and hospice discharges immediately followed (≤1 day) by a hospitalization or standalone ED visit. Transitions were excluded from the analysis if the patient did not have at least 1 day of valid post-transition follow-up (e.g., in-hospital death). For patients with multiple qualifying transitions after hospice admission, only the first transition was evaluated for this study. Transitions involving a hospice discharge were included only if the patient re-enrolled in hospice within 90 days of discharge. This was intended to limit hospice discharges that may have occurred due to disease remission.

Medication classes that were consistently identified as being of questionable benefit in the context of limited life expectancy were selected based on a review of the literature. We specifically focused on medication classes which are primarily used to prevent or delay long-term consequences of chronic conditions: anti-hyperlipidemics, antihypertensives (excluding loop diuretics), oral antidiabetics, anti-dementia and oral anti-osteoporotic agents, antiplatelets, and proton pump inhibitors. We also identified conditions in which these medications may positively impact quality of life or prevent serious adverse outcomes in the short-term. In these cases, the medications were excluded from the analysis at the patient level. Exclusions included: 1) Diuretics, beta-blockers, ACE inhibitors, angiotensin receptor blockers, and hydralazine (in combination with nitrates) in patients with congestive heart failure, 2) beta-blockers, ACE inhibitors, angiotensin receptor blockers, HMG-CoA reductase inhibitors (statins), and P2Y12 inhibitors in patients with a recent myocardial infarction, 3) statins, P2Y12 inhibitors, and combination antiplatelets in patients with a recent ischemic stroke, 4) beta-blockers and calcium channel blockers in patients with angina, and 5) non-dihydropyridine calcium channel blockers and beta blockers in patients with atrial fibrillation/flutter.

4.3.3 Study Cohort

Patients with at least one valid health care transition after hospice admission were matched to up to five control patients (replacement) on age category (66-69 years, 70-74 years, 75-79 years, 80-84 years, 85-89 years, 90+ years), sex, hospice admission year and time from initial hospice enrollment to transition (i.e., index date). We used an incidence density sampling approach whereby pre-transition person-time from patients with a future transition was available for selection as follow-up time for matched controls (**FIGURE 5**).

4.3.4 Outcomes

The primary outcome was the presence of a new dispensing for at least one LBM during follow-up. For hospitalizations and ED transitions, follow-up began on the day of the hospital or ED discharge. For hospice discharges not immediately followed by an ED visit or hospitalization, follow-up began the day after discharge. For both transitioners and controls,



**FIGURE 5.** Matching diagram for transitioners and non-transitioning controls. Time point t1 for each patient is the index date representing the start of follow-up for receipt of LBMs. For transitioners, t1 is the day of hospital or ED discharge or day after hospice discharge, depending on first transition type. For controls, this is a time point matched to the elapsed time (in days) between the transitioning patient’s hospice admission date and transition date. Both transitioner and control patients were followed for 7 days (Transitioner; Controls 1, 2 and 5 in diagram), until the patient’s death (Control 3), or until a non-index burdensome transition (Control 4), whichever came first.

follow-up continued for seven days, until a subsequent transition, or until the patient’s death, whichever came first (**FIGURE 5**). LBM dispensing during follow-up was assessed for the overall cohort and restricted to patients with active use of the medication class of interest in the six months prior to hospice admission. Active use was defined as two or more Part D claims (on separate days) for a drug class (e.g., ACE inhibitors) within the therapeutic class of interest (e.g., antihypertensives) or one Part D claim with a days’ supply of at least 90 days.

4.3.5 Statistical Analysis

Baseline characteristics were described using means, medians and proportions, and were compared using t-tests, Mann-Whitney U tests and chi-square tests, as appropriate. The frequency of receiving LBMs during follow-up was calculated using proportions with 95% binomial CIs. Conditional Poisson regression was used to generate adjusted incidence rate ratios (IRRs) and 95% CIs for the association between transitions and receipt of LBMs.138,139 Separate models were developed for each transition type (any transition, hospitalizations, hospice discharges) and for each LBM class within each transition type. A manual backwards selection approach was used to select potential confounders using a change in estimates criterion of 10%. Race and primary hospice admission diagnosis were treated as *a priori* confounders and forced into all models. Results for receipt of any LBM were further stratified by time from hospice admission to index date. 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).

4.3.6 Sensitivity Analysis

Two sensitivity analyses were conducted to evaluate elements of our study design. First, we varied the follow-up window after the index date between 3 and 14 days. Second, we

conducted analyses where 1) patients with hospice discharges lasting as many as 180 days were included and 2) only patients with discharges lasting 30 days or fewer were included.

4.4 Results

A total of 89,269 patients met the study inclusion criteria; 7064 patients with at least one valid transition were matched to 35,189 controls. The most common transition type was a standalone ED visit from hospice (43.7%). Other transition types included hospice discharges (21.6%), hospitalization from hospice (16.4%), and hospice discharges followed immediately by a hospitalization (15.8%) or standalone ED visit (2.6%).Transitioners and matched controls were a mean age of 81.2 years and primarily female and white (**TABLE XV**). Compared to matched controls, transitioners had shorter hospice stays (median: 102 days vs 117 days, p<0.001) and were more likely to have received hospice care in an inpatient setting prior to index (18.7% vs 9.0%, p<0.001)**.** The median time from hospice admission to burdensome transition was 37 days (IQR: 14-93 days).

Transitioners had a higher prevalence of receiving any LBM during the follow-up period compared to matched controls (17.9% vs. 13.9%; p<0.001) (**TABLE XVI**). Prevalence was significantly greater among transitioners for all medication classes assessed except anti-osteoporotic medications (0.5% vs. 0.4%; p=0.42). When restricting the cohorts to patients with recent pre-hospice admission use of the LBM class of interest, a greater proportion of transitioners compared to controls received a dispensing for an antihyperlipidemic (7.0% vs. 5.2%; p<0.001), antihypertensive (11.2% vs. 9.6%; p<0.001), proton pump inhibitor (10.8% vs. 8.5%; p<0.001), and any LBM (19.2% vs. 15.6%; p<0.001) during follow-up (**TABLE XVI**).

**TABLE XV**

BASELINE CHARACTERISTICS OF HOSPICE PATIENTS EXPERIENCING ONE OR MORE HEALTHCARE TRANSITION AFTER HOSPICE ADMISSION AND MATCHED CONTROLS

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **Transitioners****No. (%)** | **Controls****No. (%)** | **p-value** |
| No. of patients | 7064 | 35189 |  |
| Age (years)a |  |  |  |
| Mean (SD) | 81.2 (8.4) | 81.2 (8.4) | 0.70 |
| 66-69 years | 693 (9.8%) | 3441 (9.8%) | 1.00 |
| 70-74 years | 1093 (15.5%) | 5441 (15.5%) |
| 75-79 years | 1255 (17.8%) | 6247 (17.8%) |
| 80-84 years | 1432 (20.3%) | 7134 (20.3%) |
| 85-89 years | 1353 (19.2%) | 6748 (19.2%) |
| 90+ years | 1238 (17.5%) | 6178 (17.6%) |
| Hospice Length of Stay (days) |  |  |  |
| Median (IQR) | 102 (45-242) | 117 (47-275) | <0.001 |
| ≤14 | 374 (5.3%) | 2298 (6.5%) | <0.001 |
| 15-29  | 704 (10.0%) | 3131 (8.9%) |
| 30-89  | 2159 (30.6%) | 9351 (26.6%) |
| 90-179  | 1497 (21.2%) | 7344 (20.9%) |
| 180+  | 2330 (33.0%) | 13065 (37.1%) |
| Sexa |  |  |  |
| Male | 2327 (32.9%) | 11568 (32.9%) | 0.91 |
| Female | 4737 (67.1%) | 23621 (67.1%) |
| Race |  |  |  |
| White | 5753 (81.4%) | 30094 (85.5%) | <0.001 |
| Black | 847 (12.0%) | 3008 (8.5%) |
| Hispanic | 210 (3.0%) | 935 (2.7%) |
| Asian | 150 (2.1%) | 567 (1.6%) |
| Other/Unknown | 104 (1.5%) | 585 (1.7%) |
| Hospice Admission Yeara |  |  |  |
| 2008 | 1264 (17.9%) | 6280 (17.8%) | 1.00 |
| 2009 | 1370 (19.4%) | 6824 (19.4%) |
| 2010 | 1429 (20.2%) | 7128 (20.3%) |
| 2011 | 1432 (20.3%) | 7142 (20.3%) |
| 2012 | 1026 (14.5%) | 5109 (14.5%) |
| 2013 | 543 (7.7%) | 2706 (7.7%) |
| Geographic Region |  |  |  |
| Midwest | 972 (13.8%) | 5352 (15.2%) | <0.001 |
| Northeast | 1284 (18.2%) | 6167 (17.5%) |
| Southeast | 2461 (34.8%) | 11214 (31.9%) |
| West | 2347 (33.2%) | 12456 (35.4%) |
| Primary Hospice Admission Diagnosis |  |  |  |
| Cancer | 4428 (62.7%) | 21732 (61.8%) | <0.001 |
| Debility/Failure to Thrive | 743 (10.5%) | 3829 (10.9%) |
| Dementia | 542 (7.7%) | 3512 (10.0%) |
| Lung Disease | 420 (5.9%) | 1744 (5.0%) |
| Heart Disease | 520 (7.4%) | 2199 (6.2%) |
| Ischemic Stroke | 90 (1.3%) | 400 (1.1%) |
| Renal Disease | 74 (1.0%) | 297 (0.8%) |
| Other Non-Cancer | 247 (3.5%) | 1476 (4.2%) |
|  |
| **TABLE XV (continued)**Baseline Characteristics of Hospice Patients Experiencing One or More Healthcare Transition After Hospice Admission and Matched Controls |
| **Characteristic** | **Transitioners****No. (%)** | **Controls****No. (%)** | **p-value** |
| Comorbidity |  |  |  |
| Hypertension | 5765 (81.6%) | 27387 (77.8%)  | <0.001 |
| Heart Failure | 2277 (32.2%)  | 10102 (28.7%) | <0.001 |
| Diabetes Mellitus | 2701 (38.2%)  | 11884 (33.8%)  | <0.001 |
| COPD | 3092 (43.8%)  | 14068 (40.0%)  | <0.001 |
| Recent Ischemic Strokeb | 324 (4.6%)  | 1634 (4.6%)  | 0.84 |
| Recent Myocardial Infarctionb | 321 (4.5%)  | 1340 (3.8%)  | 0.004 |
| Coronary Atherosclerosis | 2508 (35.5%)  | 10933 (31.1%)  | <0.001 |
| Renal Disease | 1471 (20.8%)  | 6438 (18.3%)  | <0.001 |
| Liver Disease | 1158 (16.4%)  | 5181 (14.7%)  | <0.001 |
| Depression | 1604 (22.7%) | 7871 (22.4%) | 0.53 |
| Most Recent Hospice Care Setting |  |  |  |
| Home/Private Residence | 4335 (61.4%) | 22869 (65.0%) | <0.001 |
| Assisted Living Facility | 470 (6.7%) | 2315 (6.6%) |
| Non-Skilled Nursing Facility | 878 (12.4%) | 5274 (15.0%) |
| Skilled Nursing Facility | 518 (7.3%) | 2861 (8.1%) |
| Inpatient (Acute Care) Hospital | 401 (5.7%) | 448 (1.3%) |
| Inpatient Hospice Facility | 359 (5.1%) | 966 (2.7%) |
| Other/Unknown | 103 (1.5%) | 456 (1.3%) |
| Hospitalizations in Year Prior to Hospice Admission |  |  |  |
| 0 | 1651 (23.4%) | 9594 (27.3%) | <0.001 |
| 1 | 1950 (27.6%) | 10413 (29.6%) |
| 2 | 1377 (19.5%) | 6634 (18.9%) |
| 3-4 | 1358 (19.2%) | 6102 (17.3%) |
| 5 or more | 728 (10.3%) | 2446 (7.0%) |
| Any Prior Use of Inpatient Hospice | 1322 (18.7%) | 3151 (9.0%) | <0.001 |
| Part D Low-Income Subsidy Recipient | 3444 (48.8%) | 15457 (43.9%) | <0.001 |
| Unique Part D Medications in Year Prior to Hospice Admission |  |  |  |
| Mean (SD) | 15.4 (7.6) | 14.2 (7.1) | <0.001 |
| Time from Hospice Admission to Index Date (days)a |  |  |  |
| Median (IQR) | 37 (14-93) | 37 (14-93) | 0.63 |
| Post-index Follow-up (days) |  |  |  |
| <7 | 1404 (19.9%) | 50532 (14.4%) | <0.001 |
| 7 | 5660 (80.1%)  | 30136 (85.6%) |

IQR: interquartile range, SD: standard deviation

aMatching variable.

bPrimary hospital discharge occurring in the 12 months prior to hospice admission.

**TABLE XVI**

PREVALENCE OF LIMITED BENEFIT MEDICATION DISPENSING FOLLOWING BURDENSOME HEALTH CARE TRANSITIONS

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **All Patients** |  | **Patients with Pre-Hospice Admission Use of Medication Class** |  |
|  | **Transitioners** **(N=7064)** | **Controls (N=35189)** |  | **Transitioners** | **Controls** |  |
| **Medication Class** | **% (95% CI)** | **% (95% CI)** | **p-value** | **n/N** | **% (95% CI)** | **n/N** | **% (95% CI)** | **p-value** |
| Any LBM | 17.9 (17.0-18.8) | 13.9 (13.6-14.3) | <0.001 | 1220/6352 | 19.2 (18.2-20.2) | 4828/31020 | 15.6 (15.2-16.0) | <0.001 |
| Antihyperlipidemic | 2.9 (2.6-3.4) | 2.0 (1.9-2.1) | <0.001 | 194/2768 | 7.0 (6.1-8.0) | 671/12804 | 5.2 (4.9-5.6) | <0.001 |
| Antihypertensive | 8.9 (8.3-9.6) | 7.1 (6.8-7.4) | <0.001 | 588/5264 | 11.2 (10.3-12.1) | 2418/25213 | 9.6 (9.2-10.0) | <0.001 |
| Oral Antidiabetic | 2.2 (1.9-2.6) | 1.8 (1.6-1.9) | 0.01 | 143/1302 | 11.0 (9.3-12.8) | 598/5593 | 10.7 (9.9-11.5) | 0.76 |
| Antiplatelet | 1.2 (0.9-1.4) | 0.9 (0.8-1.1) | 0.09 | 68/892 | 7.6 (6.0-9.6) | 313/4108 | 7.6 (6.8-8.5) | 1.00 |
| Anti-Dementia | 2.6 (2.2-3.0) | 2.1 (2.0-2.3) | 0.02 | 169/1190 | 14.2 (12.3-16.3) | 721/6341 | 11.4 (10.6-12.2) | 0.006 |
| Oral Anti-Osteoporotic | 0.5 (0.3-0.6) | 0.4 (0.3-0.5) | 0.42 | 32/573 | 5.6 (3.9-7.8) | 135/2920 | 4.6 (3.9-5.4) | 0.32 |
| Proton Pump Inhibitor | 5.8 (5.3-6.4) | 3.7 (3.5-3.9) | <0.001 | 314/2918 | 10.8 (9.7-11.9) | 1124/13208 | 8.5 (8.0-9.0) | <0.001 |

n: number of patients in stratum who received a medication dispensing from the class of interest during follow-up; N: total number of patients in stratum; CI: confidence interval

In multivariable regression, transitioners were 33% more likely to receive any LBM during follow-up compared to controls (IRR: 1.33, 95% CI: 1.25-1.42) (**TABLE XVII**). Transitioners were also more likely than controls to receive antihyperlipidemics (IRR: 1.38, 95% CI: 1.13-1.70), antihypertensives (IRR: 1.28, 95% CI: 1.16-1.40) and proton pump inhibitors (IRR: 1.40, 95% CI: 1.20-1.63) during follow-up. When restricting transitioners to those whose first transition was a hospitalization from hospice or immediately following a hospice discharge, transitioners were 56% more likely to receive any LBM compared to matched controls (IRR 1.56, 95% CI: 1.39-1.76) (**TABLE XVII**). Similar patterns to that for all transition types were observed for specific medication classes. Compared to controls, patients experiencing a standalone live hospice discharge were significantly more likely to receive antihypertensives (IRR 1.25, 95% CI: 1.01-1.55), proton pump inhibitors (IRR 1.69, 95% CI: 1.22-2.34), and any LBM (IRR 1.32, 95% CI: 1.15-1.52) (**TABLE XVII**).

In sensitivity analysis, decreasing the post-index follow-up window from 7 days to 3 days resulted in increased effect sizes for the receipt of any LBM across transition types (**TABLE XVIII**). Using a 3-day follow-up window, transitioners whose first transition was a hospitalization were over twice as likely to receive any LBM during follow-up compared to controls (IRR 2.11, 95% CI: 1.84-2.41). Conversely, risk estimates decreased when increasing the follow-up window to 14 days. When considering only transitioners with a live hospice discharge as their first health care transition, limiting the allowable hospice enrollment gap to 30 days resulted in no increased risk of receiving a LBM compared to controls (IRR 1.06, 95% CI: 0.89-1.28). The number of days elapsed between hospice admission and the index date appeared to have little impact on the likelihood of subsequently receiving an LBM across all transition types (**TABLE XVIII**). Final adjustment variables for each model assessing the association between specific transition type and specific LBM class are presented in **TABLE XIX.**

**TABLE XVII**

ASSOCIATION BETWEEN BURDENSOME HEALTH CARE TRANSITIONS AFTER HOSPICE ADMISSION AND DISPENSING OF LIMITED BENEFIT MEDICATIONSa

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Any Transition** | **Hospitalization** | **Hospice Discharge** |
| **Medication Class** | **Adjusted IRR (95% CI)** |
| Any LBM | 1.33 (1.25-1.42) | 1.56 (1.39-1.76) | 1.32 (1.15-1.52) |
| Antihyperlipidemic | 1.38 (1.13-1.70) | 1.57 (1.11-2.22) | 0.98 (0.61-1.57) |
| Antihypertensive | 1.28 (1.16-1.40) | 1.61 (1.36-1.90) | 1.25 (1.01-1.55) |
| Oral Antidiabetic | 1.02 (0.75-1.40) | 1.34 (0.68-2.61) | 0.83 (0.37-1.89) |
| Antiplatelet | 1.30 (0.77-2.20) | 1.22 (0.34-4.39) | 1.36 (0.26-7.19) |
| Anti-Dementia | 1.24 (0.97-1.59) | 0.82 (0.51-1.33) | 1.55 (0.90-2.66) |
| Oral Anti-Osteoporotic | 1.46 (0.62-3.42) | 1.55 (0.10-22.9) | 2.50 (0.23-27.2) |
| Proton Pump Inhibitor | 1.40 (1.20-1.63) | 1.63 (1.25-2.13) | 1.69 (1.22-2.34) |

CI: confidence interval; IRR: incidence rate ratio

aAmong patients with pre-hospice admission use of medication class of interest.

bSee **TABLE XIX** for final model adjustment variables.

**TABLE XVIII**

SENSITIVITY ANALYSES AND STRATIFICATION BY TIME FROM HOSPICE ADMISSION TO INDEX DATE FOR THE ASSOCIATION BETWEEN BURDENSOME HEALTH CARE TRANSITIONS AND DISPENSING OF ONE OR MORE LIMITED BENEFIT MEDICATIONS

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Any Transition** | **Hospitalization** | **Hospice Discharge** |
| **Analysis** | **Adjusted IRR (95% CI)** |
| Base Case | 1.33 (1.25-1.42) | 1.56 (1.39-1.76) | 1.32 (1.15-1.52) |
| Varied Allowable Discharge Gap (≤30d) | 1.34 (1.25-1.44) | NA | 1.06 (0.89-1.28) |
| Varied Allowable Discharge Gap (≤180d) | 1.39 (1.30-1.47) | NA | 1.41 (1.25-1.59) |
| Varied Follow-up (3d) | 1.55 (1.43-1.68) | 2.11 (1.84-2.41) | 1.40 (1.17-1.66) |
| Varied Follow-up (14d) | 1.22 (1.16-1.29) | 1.39 (1.26-1.54) | 1.17 (1.04-1.31) |
| Time to Index <14d | 1.26 (1.09-1.45) | 1.39 (1.04-1.86) | 1.26 (0.96-1.65) |
| Time to Index 15-29d | 1.32 (1.13-1.55) | 1.77 (1.36-2.30) | 1.47 (1.01-2.13) |
| Time to Index 30-89d | 1.37 (1.22-1.54) | 1.64 (1.35-2.00) | 1.25 (0.92-1.69) |
| Time to Index 90-179d | 1.27 (1.07-1.49) | 1.35 (1.00-1.83) | 1.25 (0.89-1.77) |
| Time to Index 180d+ | 1.44 (1.21-1.72) | 1.60 (1.16-2.21) | 1.33 (0.93-1.90) |

CI: confidence interval; IRR: incidence rate ratio; NA: not applicable

aModels adjusted for same confounders as in base case analysis for association between transitions and subsequent receipt of any limited benefit medication. See **TABLE XIX.**

**TABLE XIX**

MODEL ADJUSTMENT VARIABLES FOR ASSOCIATIONS BETWEEN BURDENSOME HEALTH CARE TRANSITIONS AFTER HOSPICE ADMISSION AND DISPENSING OF LIMITED BENEFIT MEDICATIONS

|  |  |  |
| --- | --- | --- |
|  | **Any Transition** | **Model Adjustment Variablesa** |
| **Medication Class** | **Adjusted IRR (95% CI)** |  |
| Any LBM | 1.33 (1.25-1.42) | any prior use of inpatient hospice, post-index follow-up |
| Antihyperlipidemic | 1.38 (1.13-1.70) | any prior use of inpatient hospice, post-index follow-up, coronary atherosclerosis |
| Antihypertensive | 1.28 (1.16-1.40) | any prior use of inpatient hospice, post-index follow-up |
| Oral Antidiabetic | 1.02 (0.75-1.40) | any prior use of inpatient hospice, post-index follow-up, diabetes |
| Antiplatelet | 1.30 (0.77-2.20) | any prior use of inpatient hospice, post-index follow-up, coronary atherosclerosis, diabetes, hypertension |
| Anti-Dementia | 1.24 (0.97-1.59) | any prior use of inpatient hospice, post-index follow-up, number of LBM classes used prior to hospice |
| Oral Anti-Osteoporotic | 1.46 (0.62-3.42) | any prior use of inpatient hospice, post-index follow-up, liver disease, recent myocardial infarction |
| Proton Pump Inhibitor | 1.40 (1.20-1.63) | any prior use of inpatient hospice |
|  | **Hospitalization** | **Model Adjustment Variablesa** |
| **Medication Class** | **Adjusted IRR (95% CI)** |  |
| Any LBM | 1.56 (1.39-1.76) | any prior use of inpatient hospice, post-index follow-up |
| Antihyperlipidemic | 1.57 (1.11-2.22) | any prior use of inpatient hospice, post-index follow-up, coronary atherosclerosis |
| Antihypertensive | 1.61 (1.36-1.90) | any prior use of inpatient hospice, post-index follow-up |
| Oral Antidiabetic | 1.34 (0.68-2.61) | any prior use of inpatient hospice, post-index follow-up, number of LBM classes used prior to hospice, diabetes, recent ischemic stroke, hospitalizations in year prior to hospice admission |
| Antiplatelet | 1.22 (0.34-4.39) | any prior use of inpatient hospice, post-index follow-up, number of LBM classes used prior to hospice, most recent hospice care setting |
| Anti-Dementia | 0.82 (0.51-1.33) | any prior use of inpatient hospice, number of LBM classes used prior to hospice |
| Oral Anti-Osteoporotic | 1.55 (0.10-22.9) | any prior use of inpatient hospice, post-index follow-up, number of LBM classes used prior to hospice, depression, Part D low-income subsidy recipient |
| Proton Pump Inhibitor | 1.63 (1.25-2.13) | any prior use of inpatient hospice |
|  | **Hospice Discharge** | **Model Adjustment Variablesa** |
| **Medication Class** | **Adjusted IRR (95% CI)** |  |
| Any LBM | 1.32 (1.15-1.52) | -- |
| Antihyperlipidemic | 0.98 (0.61-1.57) | post-index follow-up |
| Antihypertensive | 1.25 (1.01-1.55) | post-index follow-up, hypertension |
| Oral Antidiabetic | 0.83 (0.37-1.89) | post-index follow-up, diabetes |
| Antiplatelet | 1.36 (0.26-7.19) | any prior use of inpatient hospice, COPD, recent myocardial infarction, coronary atherosclerosis |
| Anti-Dementia | 1.55 (0.90-2.66) | any prior use of inpatient hospice, most recent hospice care setting |
| Oral Anti-Osteoporotic | 2.50 (0.23-27.2) | any prior use of inpatient hospice, post-index follow-up, renal disease |
| Proton Pump Inhibitor | 1.69 (1.22-2.34) | post-index follow-up |

CI: confidence interval; IRR: incidence rate ratio

aAll models additionally adjusted for race and primary hospice admission diagnosis.

4.5 Discussion

In this cohort of older Medicare patients admitted to hospice, nearly one in five received at least one LBM following a burdensome health care transition. Transitions were significantly associated with subsequent receipt of at least one LBM as well as with receipt of antihyperlipidemics, antihypertensives, and proton pump inhibitors. The risk of receiving one or more LBMs following a transition was further increased when evaluating only hospitalization transitions. Patients who used at least one LBM prior to hospice admission were more than twice as likely to receive an LBM in the three days following a hospital discharge compared to matched controls. Conversely, the risk of LBM receipt was attenuated when extending the post-transition follow-up window to 14 days.

To our knowledge, this is the only study to measure non-palliative medication use among terminally-ill patients subsequent to burdensome health care transitions. Prior studies examining medication use following care transitions among the general geriatric population have primarily focused on adverse drug events and medication discrepancies after hospitalizations.76,140–142 Poor communication between providers at the time of hospital admission and between providers and patients/families at the time of discharge have been identified as significant contributors to these medication-related problems.77–79,143,144 Direct communication between hospital and primary care providers at hospital discharge, for example, may only occur in 3%-20% of cases.77 Sinvani and colleagues followed geriatric patients longitudinally across three separate transitions in care and reported that patients experienced an average of at least seven medication discrepancies across each transition: hospital admission to discharge, hospital discharge to skilled nursing facility admission, and skilled nursing facility admission to home or long-term care.145

Older patients, those at the end of life, and those taking at least five daily medications have previously been identified as populations at an increased risk of medication-related problems following health care transitions.79,137 As patients entering hospice typically comprise all three of these high-risk populations, it is not surprising that we observed suboptimal medication use following transitions in care for a substantial proportion of our cohort. Further, uncertainty still exists over which medications should be discontinued at hospice admission, and guidelines assisting clinicians in the deprescribing process are currently lacking. While it is generally agreed that medication classes such as antihyperlipidemics have little to no place in the treatment of the dying patient, the appropriateness of other medication classes is less clear.52,56,57,63,103 A lack of provider education, misunderstanding of hospice care goals, and refusal by patients and families to discontinue medications may also contribute to the continuation of LBMs in hospice patients.22,104,146 If not discontinued at hospice admission and these medications still appear on the patient’s profile during the course of a care transition, the receiving providers may renew the medications per the usual course of clinical practice, regardless of the patient’s hospice status.

Given that presentations to the ED and hospital by hospice patients are typically unplanned and not coordinated by the patient’s hospice care team, providers in these settings may not be aware of a patient’s status as a hospice patient or their plan of care.Olsen and colleagues found that in these unplanned inpatient admissions by hospice patients, 25% of admissions resulted in care that was not concordant with the patient’s documented goals while 39% had no documentation regarding patient wishes for treatment.147 Even in cases where non-palliative medications may have been discontinued at hospice admission, the lack of care continuity may result in counterproductive medication reconciliation practices, whereby previously discontinued medications are re-activated in the patient’s record due to poor documentation of the change in regimen. The general orientation toward aggressive and curative care in acute care hospitals may have also contributed to the observed results. We found that restricting follow-up to the three days after transition resulted in an increase in the risk of LBM receipt, which may strengthen the argument that the observed results are directly a result of the fragmented care that frequently occurs during care transitions.127 The consistent risk of post-transition LBM receipt regardless of time since hospice admission further points to a broader care continuity problem as opposed to isolated issues immediately following the initial transition to hospice care.

Our study is subject to several limitations. While allowing for a broad and nationally representative population in our analysis, the use of administrative claims data limits the ability to collect important information such as patient treatment preferences, quality of life data, and functional or physical impairment. Relatedly, we were not able to determine the causes for the observed health care transitions, which may impact subsequent receipt of an LBM. Transitions occurring directly from hospice may be more indicative of a health system failure given the mission of hospice while hospice discharges and transitions occurring immediately after discharge may more likely be due to patient and family preference.81 We did not evaluate specific discharge location for live hospice discharges. Patients discharged from hospice to settings typically associated with greater health care system contact (e.g., long-term care) may have experienced different subsequent LBM use compared to patients discharged to less resource-intensive settings (e.g., home).This study also relies on Medicare Part D dispensing data to assess LBM use. It is possible that patients received LBMs through other sources (e.g., self-pay); however, for the medication classes assessed we would not expect differential use outside of Part D between transitioning and non-transitioning patients. Finally, while attempts were made to exclude medications at the patient level where use may have been appropriate (e.g. ACE inhibitors in patients diagnosed with heart failure), we were not able to definitively determine the indications for specific medications. It is possible that some medications were

classified as being of limited benefit when in fact their use may have had an appreciable symptom relief of quality of life benefit.

4.6 Conclusion

We found that older hospice patients who experienced a burdensome health care transition after hospice admission were significantly more likely to subsequently receive medications with potentially limited benefit compared to those without such transitions. The risk was further increased for patients with a hospitalization and when limiting follow-up to the three days after the transition in care. Medication classes more unanimously considered to be of limited benefit in the context of limited life expectancy were more likely to be continued after a post-hospice admission transition, suggesting the presence of poor care continuity for patients moving from hospice to non-hospice settings. Further research determining the underlying causes of health care transitions in patients admitted to hospice is needed. Providers should critically evaluate each patient's medication regimen for appropriateness at hospice admission. A better understanding of the care processes and medication documentation practices leading to the continuation of non-palliative medications subsequent to health care transitions will help to improve quality of care in the hospice population.

V. CONCLUSIONS

As the United States population continues to age, the need for high-quality end of life care will continue to grow. The holistic and comfort-focused care associated with hospice has grown in popularity as an alternative to the aggressive care that terminally ill older adults frequently receive; in 2015, nearly half of all Medicare beneficiaries in the United States died in hospice. Given the mission of hospice, most ongoing treatments that do not provide symptom relief or improve patients’ quality of life can be discontinued upon hospice admission. In the context of very limited life expectancy, many medication therapies for chronic illness may no longer be appropriate. These treatments put patients at unnecessary risk of drug-drug interactions and adverse drug events and increases healthcare costs and patient/caregiver burden. Despite this, previous cross-sectional studies have shown that patients enrolled in hospice may continue to use non-palliative medications.

The structure of medication coverage among Medicare hospice beneficiaries allows for a unique opportunity to examine potentially unnecessary medication use. Under the Medicare Hospice Benefit, medications used for palliation of the patient’s terminal illness or related conditions should be covered by the patient’s hospice program. For these drugs, the hospice is indirectly reimbursed through the per diem payment provided by Medicare for all hospice beneficiary treatment. Medications not used for palliative treatment of the patient’s terminal illness may be covered by the patient’s prescription drug benefit, which frequently consists of a Medicare Part D plan. Even for hospice patients who have this drug coverage available, CMS has stated that it should be used infrequently given hospice care goals.17 Nevertheless, a recent analysis found that nearly two-thirds of Medicare hospice patients with concurrent Part D coverage used their Part D plan to obtain at least one maintenance medication in 2016.96

 While there is general agreement among providers that certain classes of medications are no longer useful and should be stopped when life expectancy is limited, little objective evidence existed which evaluated the landscape of LBM use in the hospice population. Of particular importance was the lack of evidence evaluating changes in LBM use longitudinally before and after admission to hospice. This dissertation research helped to fill these evidence gaps by comprehensively evaluating LBM use in older patients who entered hospice and died while under hospice care. A series of cross-sectional and cohort studies were conducted using the SEER-Medicare linked database to estimate the frequency of medication use through Medicare Part D after hospice admission and evaluate the prevalence and predictors of post-admission use and continuation of a pre-defined set of LBM classes. Given hospice’s palliative care focus and requirement for admission of a six month or shorter life expectancy, the date of hospice admission presented a defined and objective time point at which LBMs used prior to hospice were assumed to be appropriate to discontinue. Further, in cases where LBMs were continued after hospice admission, they were expected to be obtained through the patient’s Part D plan. Due to anticipated differences in end of life disease trajectories and healthcare utilization, particular emphasis was placed on differences in LBM use and continuation by admission to hospice for cancer vs. non-cancer causes.

 The first research aim assessed Medicare Part D medication use prevalence and patterns after hospice admission, both generally and for a pre-defined set of therapeutic and drug classes. Despite Medicare guidance, this study corroborated a recent report of high overall use of the Part D benefit among Medicare beneficiaries admitted to hospice.96 Over half of patients admitted for cancer used the Part D benefit after hospice admission. Among non-cancer admissions, post-admission Part D use was substantially more common among patients admitted for debility/failure to thrive (63.5%) or dementia (61.5%) compared to ischemic stroke (35.4%) or renal disease (36.0%). Overall, nearly one in four patients received an antihypertensive, one in ten received a proton pump inhibitor, and one in six received an opioid (though prevalence decreased over the study period) through Part D after admission to hospice. Though drug indication was not assessed for this study, Part D use of medications likely considered to be LBMs in the context of hospice was frequent and consistent over the study period. This suggests that there is still substantial uncertainty among providers concerning the appropriateness of deprescribing medications for chronic conditions in the terminally ill. While recent medication coverage changes instituted by CMS have dramatically curtailed the receipt through Part D of medications that are primarily the responsibility of hospice (e.g., opioids), no guidance currently exists for Part D use of non-palliative medications in hospice. Thus, use of LBMs through Part D in hospice is still expected to be highly prevalent today.

 While the first dissertation aim highlighted the magnitude of Medicare Part D and potential LBM use in hospice patients broadly and in a cross-sectional manner, it did not provide information on whether the observed results represented a substantial deviation from pre-hospice admission use or whether they could be explained by patient and clinical factors. The second aim of this dissertation examined medication use longitudinally, starting with patients who were users of at least one LBM prior to hospice admission and following them through the date of death for evidence of LBM continuation. In total, 29.8% of patients admitted to hospice for cancer and 30.5% admitted for a non-cancer cause continued at least one LBM after hospice admission. Continuation varied by LBM class and was more likely among older patients, patients admitted to hospice in a nursing or assisted-living facility, and those with longer hospice stays. The high prevalence of LBM continuation observed in this study provides further evidence of potentially problematic medication use in the hospice population and suggests that further research efforts and guidance are needed to elucidate the risk-benefit profile of these medications at the end of life. The importance of this issue is magnified by the fact that our results are likely underestimates, as only new Part D prescription dispensings were captured. An additional proportion of patients likely continued to use medication supplies obtained prior to hospice admission or obtain new supplies through their hospice program, both of which were unobservable in these studies. The observed differences in continuation rates by hospice care setting and length of stay may be indicative of failures at the health care system level. Further assessment of physician and patient/family barriers to medication discontinuation at the point of hospice admission are needed to clarify the underlying causes of the observed results.

 The final aim of this dissertation evaluated the impact of burdensome health care transitions on subsequent LBM use in hospice patients. Older patients at the end of life typically have more complex health care needs and experience more care transfers than those in the general geriatric population. These care transitions often result in poor care continuity and were hypothesized to impact the subsequent receipt of LBMs. In total, 7064 patients with at least one burdensome health care transition after hospice admission were identified, with 17.9% receiving one or more LBMs in the seven days following the first transition. Patients with any transition were 33% more likely to receive an LBM compared to matched controls during follow-up (IRR 1.33, 95% CI: 1.25-1.42), while a hospitalization after hospice admission was associated with a 56% risk increase (IRR 1.56, 95% CI: 1.39-1.76). The increase in risk of LBM receipt when shortening the follow-up window and consistent risk regardless of time since hospice admission further strengthens the link between health care transitions and subsequent LBM use in hospice patients. The impact of poor communication and health care fragmentation on receipt of LBMs may be amplified in older patients at the end of life given rapidly changing medication regimens and other complex treatment needs.79,137 However, the specific provider, patient and health care system-related factors leading to up to the observed results are unclear and deserve further study.

 Research to date examining medication use in the hospice population has primarily been limited to cross-sectional studies, with no information on medication use in the pre-hospice admission period.21–23,135,148–151 This dissertation research consists of the largest published studies of medication use in hospice patients to date, and the first to examine longitudinal changes in drug use before and after hospice admission. Overall, the results suggest that medication use is suboptimal in older hospice patients and, in many cases, may directly conflict with hospice care principles. The prevalence of LBM dispensings after hospice admission was surprisingly common, and contrary to initial hypotheses, the patient’s primary hospice admission diagnosis does not appear to be a major independent predictor of continuing LBMs after hospice admission.

Though the exact factors leading to this potentially unnecessary medication use are unclear, the published literature and the study findings presented here provide potential explanations that warrant further exploration and confirmation. Perhaps most importantly, there are few guidelines currently available which aid clinicians in determining the specific medications that may be appropriate to deprescribe in the context of limited life expectancy. Such guideline creation is particularly difficult for this patient population given that evidence generation via clinical trials may be unethical or unfeasible, and there is little real-world outcomes data available demonstrating the benefits and risks of medication discontinuation at the end of life. Still, the uncertainty surrounding deprescribing in the terminally ill has gained increasing attention in recent years and efforts are being made to address this issue. The recently published STOPPFrail criteria provide 27 explicit criteria for deprescribing specific classes of commonly used medications in older patients with limited life expectancy.103 Though the most comprehensive and broadly applicable set of deprescribing guidelines in terminal illness developed to date, further testing and validation outside of the country of origin (i.e. Ireland) are needed to enhance generalizability and widespread adoption in clinical practice. A recent randomized, controlled trial demonstrating that stopping statins is safe at the end of life further aids in filling the evidence gap and should prompt further research in this area.108 Until this body of evidence is developed, the results of this dissertation suggest that a more

thoughtful and careful review of hospice patients’ medication regimens at hospice enrollment is needed to ensure that the medications they continue to receive fully align with their care goals.

This research identified factors such as hospice care setting, hospice length of stay, and burdensome health care transitions as contributing to LBM use in the hospice population. However, the underlying events and processes leading to these observations are likely complex. Apart from the uncertainty over the risk-benefit balance of medications at the end of life as described above, poor communication among providers during care handoffs and between patients/families and providers during the transition to hospice likely plays a role in LBM use and continuation in hospice patients. Patients in this research used an average of approximately 15 unique medications in the year prior to hospice admission. Without careful communication and documentation of medication regimens in patients with this drug burden, medication-related problems are likely. Further, terminally ill patients are often seeing multiple providers due to the complexity of their conditions, each of which may be prescribing and adjusting different medications. If plans of care are poorly communicated during the transition to hospice and any future transitions to non-hospice settings, hospice providers may simply not be aware of all of the medications that a patient is taking. This may make other efforts to curb LBM use at the patient and provider level futile. Other breakdowns and barriers to communication preventing deprescribing may include a lack of education and reluctance among providers to discuss de-escalation of therapy with patients, and the refusal of patients and families to stop medications. There is a significant need to quantify the frequency with which such problems are present at hospice enrollment and develop interventions targeting them, for example, by the implementation of standardized care processes aimed at facilitating better communication throughout patients’ transition to hospice.

Finally, the way in which health care policies might influence LBM use in hospice patients is not well understood. However, the key to widespread change may lie in revisiting the medication coverage policies under Medicare’s hospice benefit, by far the single largest financier of hospice care in the US. Despite the assumption by CMS that the Part D benefit would be rarely used in the hospice population, Part D costs to Medicare among patients using the hospice benefit were most recently estimated to total $340 million annually.5 While previous attempts to place prior authorization requirements on all medications submitted for Part D reimbursement in hospice patients were short-lived, a more gradual and targeted approach may find more success within the payer, patient, and hospice provider community. CMS could start by limiting reimbursement through Part D for medications with strong consensus and objective evidence for a lack of benefit in terminal illness, such as lipid-lowering medications. As the body of evidence continues to grow, this could be expanded to other medication classes in the future.

Given the dissertation findings, a reassessment of the originally proposed conceptual framework is warranted. Patient cohorts defined by primary hospice admission diagnosis experienced differences in the prevalence of LBM use and continuation. However, contrary to initial hypotheses, admission diagnosis does not appear to play a significant role as an independent predictor, with variations in use largely explained by hospice length of stay. While the demographic characteristics measured in this study (e.g., age, sex, race, geographic region) did not play a major role in LBM continuation overall, characteristics unobservable within our data such as socioeconomic status, marital status, and family support should be evaluated. We attempted to control for differences in treatment patterns at the hospice facility level in our analysis as previous research suggests that hospice program characteristics (e.g., profit status, staffing levels) are important factors influencing the intensity of care received by hospice patients. Further research is needed to determine if these theoretical predictors are indeed influential empirical determinants of LBM continuation. We found differences in LBM continuation by medication class; classes with more objective evidence and consensus supporting discontinuation were continued less frequently. This suggests that the potential for benefit, either real or perceived, may be a relevant addition to the framework for medication continuation in the hospice setting. Components of the original framework which are preliminarily validated as factors affecting LBM continuation based on our research include hospice care setting and post-hospice admission health care fragmentation. The specific results for these factors, along with hospice length of stay, suggest that more broad and systemic health care system-level processes may be to blame, and should encompass these factors within the framework. Treatment preferences (provider and patient/family), while not measurable in this research, remain a strong theoretical determinant of LBM continuation and warrant future assessment. This updated framework may serve as a starting point for future studies examining medication use in hospice and be subsequently refined based on the results.

At a minimum, the results of this research are intended to provide much needed evidence for policy makers and healthcare providers to better understand the magnitude of LBM use in hospice patients as well as differences in use by medication class and patient and clinical characteristics. Ideally, this research will also encourage a critical dialog among healthcare providers and patients/families to promote the development of tailored medication management strategies that minimize burden without impacting quality of life during the patient’s final weeks and months. Additional research is needed clarifying the risks and benefits of LBM discontinuation in the hospice setting and evaluating interventions aimed at limiting problematic medication use at the end of life.

VI. CITED LITERATURE

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VII. APPENDIX

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VIII. VITA

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| PUBLICATIONS | Zueger PM, Kumar VM, Harrington RL, Rigoni GC, Atwood A, DiDomenico RJ, Touchette DR. Cost-Effectiveness Analysis of Sacubitril-Valsartan for the Treatment of Heart Failure with Reduced Ejection Fraction in the United States. *Pharmacotherapy (In Press).*Zueger PM, Holmes HM, Calip GS, Qato DM, Pickard AS, Lee TA. Medicare Part D Use of Older Medicare Beneficiaries Admitted to Hospice. *J Am Geriatr Soc.* 2018 Mar 6. Epub ahead of print.Han MK, Martinez C, Au DH, Bourbeau J, Boyd C, Branson R, Criner G, Kalhan R, Kallstrom T, King A, Krishnan J, Lareau SC, Lee TA, Lindell K, Mannino DM, Martinez FJ, Meldrum C, Press V, Thomashow B, Tycon L, Sullivan JL, Walsh J, Wilson K, Wright J, Yawn B, Zueger PM, Bhatt S, Dransfield MT. Meeting the Challenge of COPD Care Delivery in the USA: A Multiprovider Perspective. *Lancet Respir Med*. 2016 Jun;4(6):473-526 Kim S, Martin MT, Pierce AL**,** Zueger PM.Satisfaction with Medication Therapy Management Services at a University Ambulatory Care Clinic. *J Pharm Pract*. 2016 Jun; 29(3):199-205.Zueger PM, Schultz NM, Lee TA. Cost Effectiveness of Liraglutide in Type II Diabetes: A Systematic Review. *Pharmacoeconomics*. 2014 Nov; 32(11):1079-91.Zueger PM, Katz NL, Popovich NG. Assessing Outcomes and Perceived Benefits of a Professional Development Seminar Series. *Am J Pharm Educ*. 2014 Oct 15;78(8):150.Patel H, Ursan I, Zueger PM, Pickard AS. Stakeholder Views on Pharmacogenomic Testing. *Pharmacotherapy*. 2014Feb; 34(2): 151-165 |
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