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Research Article

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Tables 1 to 3 are available in the Supplementary Files section.

Cardiovascular Medication Prescribing Patterns Across Hospice Care Models in Non-Cancer Patients Near the End of Life

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Abstract

Background: Cardiovascular preventive medications may provide limited benefits near the end of life. However, prescribing patterns among non-cancer patients receiving different models of hospice care remain poorly understood. This study examined the association between hospice care and cardiovascular medication prescribing during the final 14 days of life.

Methods: This retrospective study included non-cancer patients who died between 2010 and 2019. Propensity score matching (1:2) based on age and sex was performed to compare hospice and non-hospice care. Prescriptions of antithrombotic, lipid-lowering, antihypertensive, and hypoglycemic agents were assessed at five time points during the final 14 days of life. Generalized estimating equations were used to evaluate prescribing differences between groups.

Results: After matching, 1,562 hospice patients and 3,124 non-hospice patients were included. Hospice care was associated with lower odds of prescribing antithrombotic (OR, 0.60; 95% CI, 0.46-0.79), lipid-lowering (OR, 0.55; 95% CI, 0.34-0.90), antihypertensive (OR, 0.37; 95% CI, 0.21-0.66), and hypoglycemic agents (OR, 0.70; 95% CI, 0.58-0.85). Compared with hospice shared care, hospice ward care was associated with lower odds of prescribing antithrombotic (OR, 0.23), lipid-lowering (OR, 0.14), and hypoglycemic agents (OR, 0.37).

Conclusions: Hospice care was associated with lower cardiovascular medication prescribing among non-cancer patients nearing the end of life, with additional differences observed between hospice care models. These findings highlight the importance of individualized medication

management in end-of-life care.

Keywords: Cardiovascular medications, Deprescribing, End-of-life care, Hospice care

Introduction

Originated for late-stage cancer patients, hospice care focuses on a comfort-based approach with symptoms alleviation, reduced psychological distress, better satisfaction with treatment, improved quality of life, and minimized costs of medical care.[1] Better short-term and long-term outcomes were also noted in caregivers of patients who underwent hospice care than those of patients who did not.[2] The concept of hospice care was first introduced in the 1980s in Taiwan.[3] After years of advocation and promotion, the National Health Insurance system began reimbursing hospice care for non-cancer patients in 2009, leading to an increasing number of these patients receiving palliative interventions. A nationwide observational study by Lin et al. revealed a steady upward trend in palliative care consultations among terminally ill non-cancer patients from 2011 to 2019, underscoring growing clinical recognition of unmet needs in this population.[4]

When encountering terminal stage of life, a large portion of patients are concurrently comorbid with chronic diseases and prescribed multiple medications. In a nationwide cohort of more than 500,000 older adults, nearly half received 10 or more medications during the final month of life.[5] Polypharmacy has also been associated with poorer health-related quality of life in patients with chronic illnesses, including cancer survivors.[6] Although part of the purpose of those medications is to lower the risk of complications from comorbidities, the benefit was suggested to be less significant when patients approach the end of their lives.[7] Research about polypharmacy in patients near the end of life suggested that the amount of medication taken was correlated with symptom burden and worse quality of life.[8] As part of hospice care, removing futile and

58 inappropriate medication, which potentially avoids patients suffering from pill overload and
59 potential adverse effects, should be thoroughly considered in the end-of-life period.[9]

60 Among commonly prescribed drug classes, cardiovascular medications targeting dyslipidemia,
61 hypertension, and hyperglycemia are frequently used in patients with metabolic risk factors.
62 However, in the context of terminal illness, the continued use of these agents may provide limited
63 clinical benefit and is often appropriate for deprescribing.[10] A randomized controlled trial
64 investigating the effects of discontinuing statins on patients expected to live no longer than one
65 year concluded that stopping statin therapy is safe and may be beneficial, given that there is no
66 significant difference between groups continuing and discontinuing statin as well as better quality
67 of life among the group discontinuing statin.[11] Declining blood pressure is usually noticed in the
68 late stages of life. Antihypertensive therapy, therefore, may not be indicated and should be
69 withdrawn out of concern for hypotension.[12] Oral hypoglycemics for mild hyperglycemia are also
70 unnecessary, and flexible blood glucose control goals are acceptable due to the common anorexia
71 and weight loss seen in cancer patients.[13,14]

72 With growing evidence for the disadvantages of polypharmacy in terminally ill patients,
73 clinicians are increasingly encouraged to review and individualize pharmacotherapy with regard to
74 the patient's values, goals of care, and prognosis.[15] However, deprescribing decisions can be
75 complex, particularly among patients with non-cancer chronic illnesses, where disease trajectories
76 are less predictable and evidence-based guidance is limited. While hospice care has been associated
77 with improved medication appropriateness among patients with advanced cancer,[16,17] its association

with pharmacological decision-making in non-cancer populations remains insufficiently characterized. This gap is particularly salient in the context of cardiovascular medications, which are commonly maintained in terminal patients despite questionable clinical benefit. Accordingly, this study aimed to examine the association between hospice care and patterns of cardiovascular medications among non-cancer patients nearing the end of life. We examined overall prescribing patterns, assessed temporal changes in medication use during the final 14 days of life, and explored how different models of hospice care may be associated with variation in deprescribing practices.

Methods

Data Source and Population

This retrospective cross-sectional study was conducted using electronic medical records from Taichung Veterans General Hospital, a tertiary medical center in Taiwan. All data were anonymized by the Clinical Informatics Research and Development Centre (registration number: F20400). The study protocol was approved by the Institutional Review Board of Taichung Veterans General Hospital (IRB No. CE20362A, approved on December 2, 2020). Individual consent was waived due to the retrospective and anonymized nature of the data. We identified all non-cancer patients who died between January 1, 2010, and December 31, 2019. Patients were excluded if they died before the age of 20 or if they died on the same day of hospitalization. The process of patient selection, including inclusion and exclusion criteria, is illustrated in Figure 1. Baseline demographic variables, prior medication exposure (antithrombotic, lipid-lowering, antihypertensive, and hypoglycemic agents), and major comorbidities were extracted from

electronic health records covering the two years prior to death.

Hospice care interventions

Hospice care services were delivered by an interdisciplinary team comprising physicians, nurses, psychologists, spiritual care providers, social workers, and art therapists. In inpatient hospice settings, care encompassed pharmacologic symptom control (e.g., pain, dyspnea, nausea), supportive physical care (e.g., wound dressing, hygiene, and rehabilitation guidance), as well as emotional, spiritual, and communication support. Shared hospice care was defined as specialist palliative input provided upon consultation in general wards. Based on the presence of hospice care intervention, patients were initially classified into two groups: the hospice care group and the non-hospice care group. The hospice care group was further divided into two subgroups for secondary analysis: those who received inpatient hospice care (hospice ward group) and those who received hospice shared care (shared care group). Patients who initially received hospice shared care and were subsequently transferred to an inpatient hospice ward were classified into the hospice ward group.

Prescription of cardiovascular medications

Drug prescription data were extracted according to the Anatomical Therapeutic Chemical (ATC) classification system for the two years preceding death. The primary outcome was the presence of active prescriptions for cardiovascular medications during the final 14 days of life. Cardiovascular medications of interest included antithrombotic agents, lipid-lowering agents,

antihypertensive agents, and hypoglycemic agents. The prescription status of each medication class was assessed at five specific time points: the14th, 7th, 5th, and 3rd days before death, as well as the day of death.

Propensity-score matching

To reduce potential selection bias, propensity-score-matching model was applied to balance baseline characteristics between hospice care group and non-hospice care group. Propensity scores (the probabilities of patients receiving hospice care) were calculated using a logistic regression model, with gender and age included as covariates. A 1:2 nearest-neighbor propensity scores matching approach with a caliper of 0.2 were employed, leveraging the larger number pool of non-hospice care patients (n = 6,759) relative to hospice care patients (n = 1,562). For subgroup analysis, we further compared patients receiving hospice shared care with those receiving hospice ward care.

Statistical analysis

Descriptive statistics, including means with standard deviations and percentages for basic characteristics, length of stay, and the prescription status of cardiovascular medications in all matched groups were examined, and comparisons were performed using the Mann-Whitney U test, chi-square test, or Fisher's exact test. To assess differences in cardiovascular medication prescribing patterns, we used generalized estimating equations (GEE) to evaluate the associations of hospice care status (hospice vs. non-hospice), hospice care model (hospice ward vs. hospice shared care),

and time before death (14th, 7th, 5th, and 3rd days before death and the day of death) with cardiovascular medication prescribing. P value less than 0.05 was considered statistically significant. SPSS (IBM SPSS version 22.0; International Business Machines Corp., New York, NY, USA) was used to conduct all statistical estimations.

Result

Clinical Characteristics of Hospice and Non-Hospice Patients After Matching

After excluding patients younger than 20 years old or those died on the same day of hospitalization, 8,321 non-cancer patients were included. Using a 1:2 nearest-neighbor propensity score matching with a caliper width of 0.2, 1,562 patients who received hospice care were matched with 3,124 non-hospice patients. As summarized in Table 1, the matched hospice and non-hospice cohorts were comparable in age, sex distribution, and the proportion of documented do-not-resuscitate (DNR) declarations. Differences were observed between the hospice and non-hospice groups in prior cardiovascular medication use and the prevalence of several comorbidities. Mean length of stay was longer among hospice patients (24.6 vs. 19.4 days).

Temporal Trends in Cardiovascular Medication Prescription During the Last 14 Days of Life

Figure 2 presents similar temporal prescribing patterns across all four classes of cardiovascular medications during the last 14 days of life. Prescription proportions exhibited a non-linear pattern, increasing in the days preceding death, peaking approximately 3–5 days before death, and subsequently declining near the time of death. At corresponding time points, prescription

proportions were consistently lower in patients receiving hospice care than in those receiving non-hospice care.

Association Between Hospice Care and Cardiovascular Medications Prescription

In Table 2, the GEE analysis showed a significant association between hospice care and lower odds of cardiovascular medication prescribing during the last 14 days of life. Specifically, hospice care was associated with lower odds of prescribing antithrombotic agents (OR = 0.60, 95% CI = 0.46-0.79), lipid-lowering agents (OR = 0.55, 95% CI = 0.34-0.90), antihypertensive agents (OR = 0.37, 95% CI = 0.21-0.66), and hypoglycemic agents (OR = 0.70, 95% CI = 0.58-0.85) within 14 days of death.

Subgroup Analysis: Inpatient Hospice Care Versus Shared Hospice Care

In the subgroup analysis, 741 patients received inpatient hospice care and 821 patients received hospice shared care. As illustrated in Figure 2, compared to the shared care group, cardiovascular medication prescription rates within the 14 days preceding death were consistently lower in the hospice ward group, specifically for anti-thrombotic, lipid-lowering, and hypoglycemic agents. GEE analysis in Table 3 further demonstrated that, using hospice shared care as the reference group, inpatient hospice ward care was associated with lower odds of cardiovascular medications prescription. Within the last 14 days of life, hospice ward care was associated with significantly lower odds of prescribing anti-thrombotic agents (OR 0.23; 95% CI, 0.15-0.36), lipid-lowering agents (OR 0.14; 95% CI, 0.06-0.31), and hypoglycemic agents (OR

0.37; 95% CI, 0.29-0.49), using hospice shared care as the reference group. The association between hospice ward care and antihypertensive agent prescribing did not reach statistical significance (OR 0.49; 95% CI, 0.20-1.20).

Discussion

In this retrospective cross-sectional study of non-cancer patients approaching the end of life, hospice care was associated with lower odds of cardiovascular medication prescriptions during the final 14 days of life. This association was observed across all four medication classes, with consistently lower prescription proportions among patients receiving hospice care. Notably, cardiovascular medication prescribing patterns also differed between hospice care models. Patients admitted to inpatient hospice wards had lower odds of being prescribed antithrombotic, lipid-lowering, and hypoglycemic agents than those receiving hospice shared care, suggesting variation in prescribing patterns across care settings.

Our findings are consistent with prior studies demonstrating differences in medication use between hospice and non-hospice settings near the end of life. An Italian retrospective study reported a higher prevalence of potentially inappropriate medication use among terminal cancer patients in general hospital wards than among those in hospice units.[18] Specifically, 75.0% of patients in general hospital wards were prescribed three or more PIMs during their final three days of life, compared with 42.6% of patients in hospice units. In an international expert survey and retrospective chart review, over 90% of experts considered 12 medications unlikely to be appropriate for patients nearing death, and these medications were more frequently prescribed in

hospitals than in hospice settings.[19] Temporal changes in medication prescribing have also been reported in palliative care settings. A Dutch multicenter observational study reported a decrease in the mean number of prescribed medications from 6.1 at admission to 4.6 on the day of death, including changes in the prescribing of anticoagulants, beta-blockers, hypoglycemic agents, and lipid-modifying agents.[20] Similarly, in a Portuguese observational study conducted in a palliative care unit, documented decreases in prescriptions for chronic conditions, including statins, antihypertensives, antithrombotics, and insulin, as death approached.[21] Our findings also demonstrated temporal variation in cardiovascular medication prescribing during the final 14 days of life, with prescription proportions across all four medication classes declining to levels below those at the beginning of the observation period.

Given the differences in care delivery between inpatient hospice care and hospice shared care, medication prescribing patterns may also vary across these settings. In our study, patients receiving inpatient hospice care had lower odds of being prescribed antithrombotic, lipid-lowering, and hypoglycemic agents than those receiving hospice shared care. Similar differences in medication use were observed in our previous study of patients with advanced cancer, in which excessive medication administration was less prevalent in inpatient hospice care than in hospice shared care.[16] A subsequent study of the same cancer population reported lower rates of newly initiated hypoglycemic, lipid-lowering, and antithrombotic agents in inpatient hospice care compared with hospice shared care.[17] These differences may reflect several aspects of hospice care delivery. First, differences in care priorities may influence prescribing decisions, as inpatient hospice care places

greater emphasis on symptom palliation, whereas clinicians providing shared care may need to balance disease-directed treatment with comfort-focused care. Second, differences in clinician expertise and involvement in medication review may contribute to variations in prescribing practices. Third, communication among healthcare professionals, patients, and families may influence goals-of-care discussions and decisions regarding medication continuation or discontinuation.[22] The dedicated multidisciplinary approach in inpatient hospice wards may facilitate coordinated decision-making regarding medication management, whereas hospice shared care requires coordination between palliative care specialists and primary medical teams, potentially adding complexity to these decisions. Supporting the relevance of care transitions, a study reported decreased prescribing of antihypertensive and lipid-lowering medications as patients transitioned from palliative care consultation to an inpatient palliative care unit.[23] Furthermore, highlighting the potential role of medication review within consultation-based care, a Korean study found that pharmacist-led deprescribing was associated with a higher deprescribing rate of preventive medications than usual consultation care.[24]

To further support medication review and deprescribing decisions near the end of life, the OncPal Deprescribing Guideline was developed to facilitate the identification of potentially inappropriate medications in patients with advanced cancer and an estimated life expectancy of less than six months.[25] The guideline recommends discontinuing lipid-lowering agents in patients with limited life expectancy, regardless of their original indications. Regarding antihypertensive medications, the guideline recommends considering discontinuation in patients with mild-to-

moderate hypertension or stable coronary artery disease, including those receiving treatment for secondary cardiovascular prevention. Furthermore, the guideline recommends discontinuing oral hypoglycemic agents in patients with mild hyperglycemia, reflecting a shift in clinical priorities from long-term prevention of diabetic complications toward symptom management near the end of life. Although the OncPal Deprescribing Guideline was developed through a literature review and expert consensus, its applicability to non-cancer patients with life-limiting illnesses remains uncertain. In addition, although the guideline provides recommendations for identifying medications suitable for discontinuation, individualized deprescribing decisions also require consideration of patient preferences, goals of care, and potential withdrawal-related risks.[26]

This study has several strengths. Evidence regarding medication prescribing near the end of life in non-cancer patients remains relatively limited. By including a large cohort of more than 8,000 non-cancer patients before propensity score matching, our study contributes additional evidence for this understudied population. Furthermore, comparing inpatient hospice care with hospice shared care provides insights into prescribing differences across hospice care models. Nevertheless, our study has several limitations. First, the retrospective design limited access to information regarding patient and family preferences, goals of care, and quality-of-life outcomes. The reasons underlying differences in medication prescribing, including potential changes in clinical indications, intentional deprescribing, or factors such as dysphagia, could not be determined. Second, although propensity score matching was performed based on age and sex, residual confounding remains possible. Unmeasured variables, particularly baseline functional

status and frailty, as well as other clinical differences between groups, may have influenced the observed associations. Third, this study was conducted at a single tertiary medical center, which may limit the generalizability of the findings to other healthcare settings with different hospice care models or prescribing practices.

Conclusion

In this retrospective study of non-cancer patients nearing the end of life, hospice care was associated with lower odds of cardiovascular medication prescribing, with further differences observed between inpatient hospice care and hospice shared care. These findings extend current evidence on end-of-life medication use beyond cancer populations and highlight variations in prescribing practices across hospice care models. Further research is warranted to determine how these prescribing patterns relate to individualized treatment goals, medication appropriateness, and patient-centered outcomes.

Declarations

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Author Contributions

The authors' responsibilities were as follows—JYS (Jhen-Yu Shih) and CLW (Chun-Li Wang): designed the research; JYS, CLW and Lung-Chun Lee: conducted the research; Chiann-Yi Hsu:

analyzed the data; JYS, and CLW: wrote the article; CLW: had primary responsibility for the final content; and all authors: read and approved the final manuscript.

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Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to institution's policy but will be available through contacts with the corresponding author on reasonable requests.

Ethical approval and consent to participate

The study protocol was approved by the Institutional Review Board of Taichung Veterans General Hospital (IRB No. CE20362A, approved on December 2, 2020)

Competing interests

The authors declare no conflict of interest.

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Figure Legends

Figure 1. Flowchart of eligible patients for the study

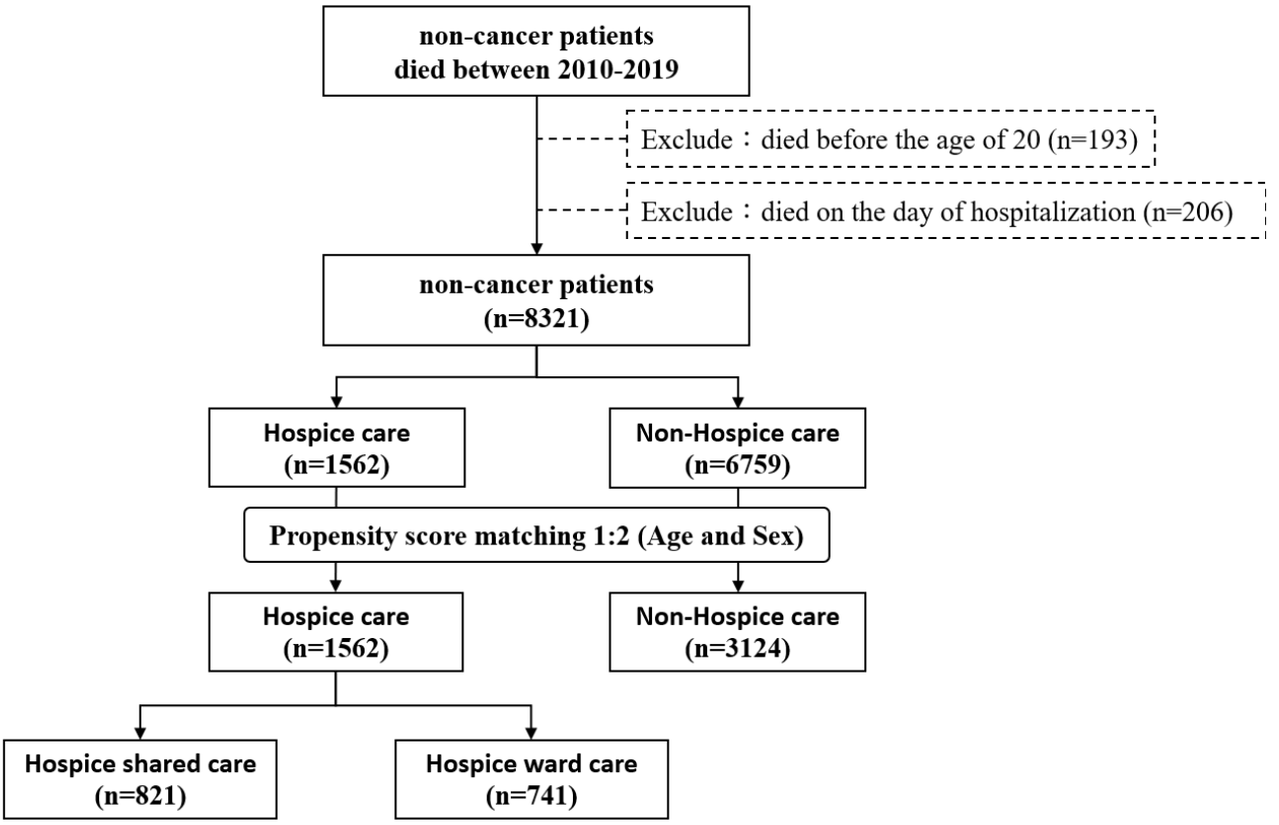
Non-cancer patients who died between 2010 and 2019 were initially identified. After excluding patients who died before the age of 20 (n = 193) and those who died on the day of hospitalization (n = 206), a total of 8,321 patients were eligible for the study. Of these, 1,562 received hospice care and 6,759 received non-hospice care. Following 1:2 propensity score matching based on age and sex, 1,562 patients in the hospice care group were matched with 3,124 patients in the non-hospice care group. The hospice care group was further categorized into hospice shared care (n = 821) and hospice ward care (n = 741).

Figure 2. Comparison of Cardiovascular medications prescription at five time points during the final 14 days of life

Across all four medication classes, prescription rates were consistently higher in the non-hospice care group than in the hospice care group, with statistically significant differences at all assessed time points. Within the hospice care group, patients receiving hospice shared care generally had higher prescription rates than those

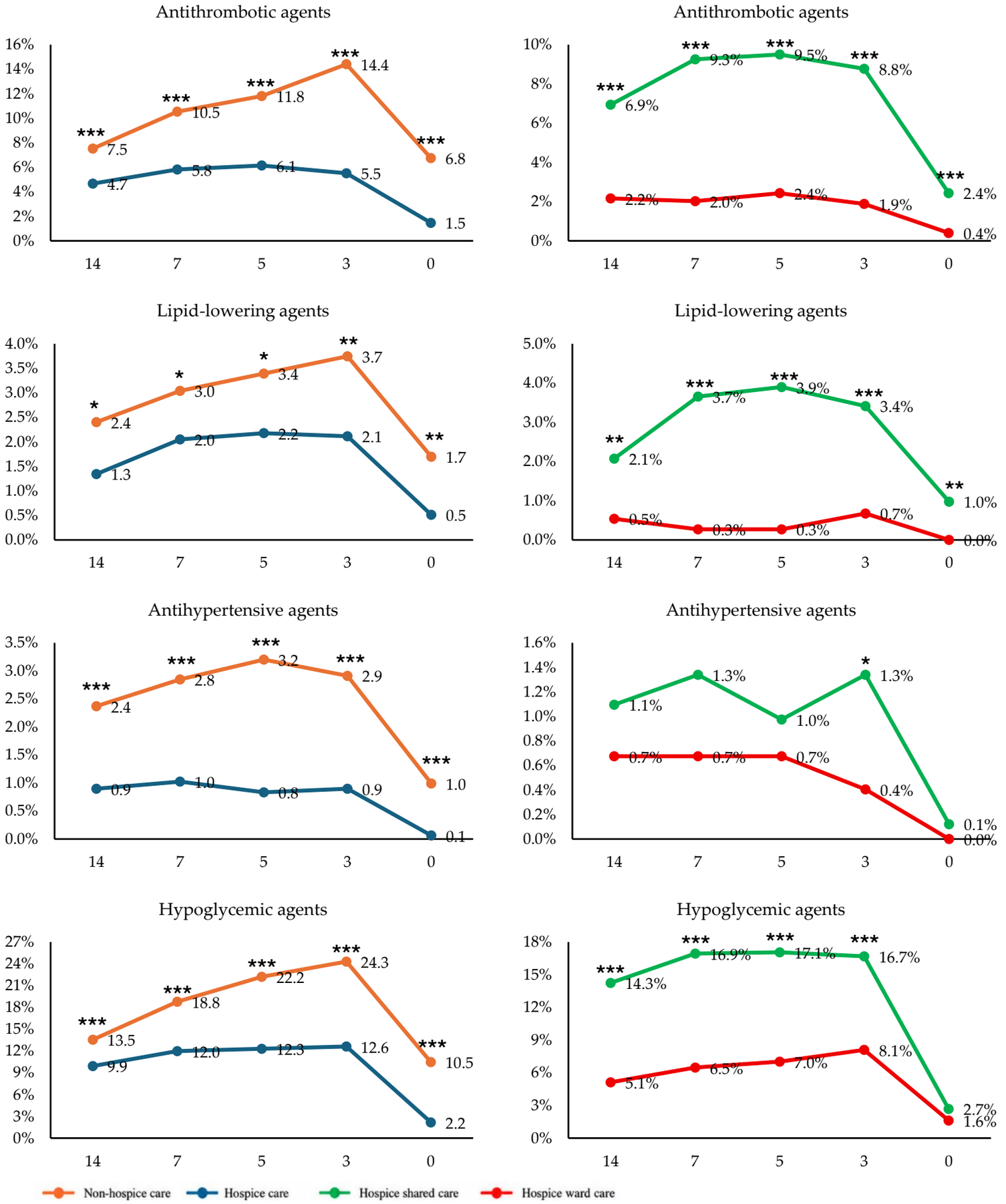
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*p<0.05, **p<0.01, ***p<0.001.

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