Hospice care utilisation among elderly patients who died with hepatocellular carcinoma in the United States

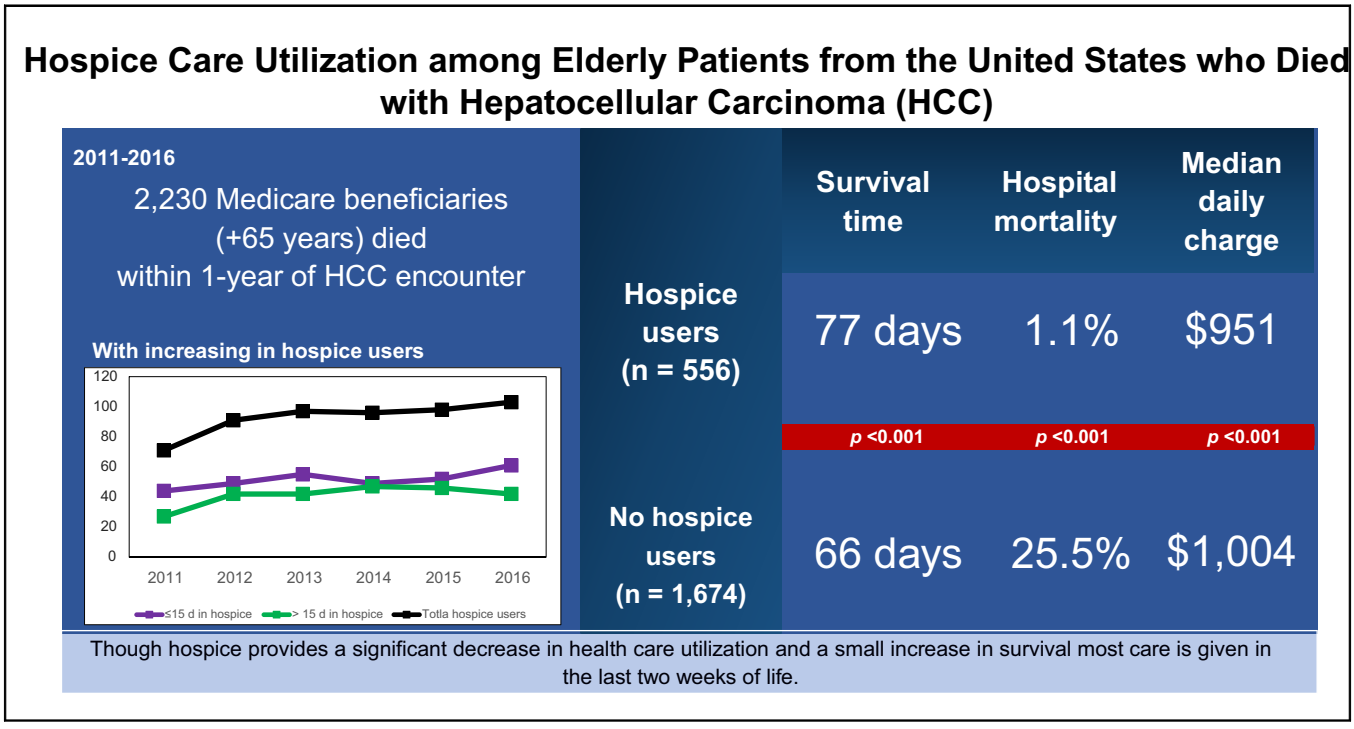
Authors

Victor de Avila, James M. Paik, Leyla de Avila, Linda Henry, Denise Mohess, Alva Roche-Green, Zobair M. Younossi

Correspondence

zobair.younossi@inova.org (Z.M. Younossi).

Graphical abstract



Highlights

- The majority of people do not want to die in the hospital.
- Hepatocellular carcinoma is lethal and rates are rising.
- Only 25% of Medicare recipients with hepatocellular carcinoma use hospice care.
- Hospice care significantly reduced the number of in-hospital deaths (1.1% *vs.* 25.5%).
- Use of hospice services produced a 48.6% reduction in daily charges.

Lay summary

The purpose of hospice care is to provide comfort and lessen suffering at the end of life. Hospice care allows one to die outside the hospital environment which is the wish of most people. However, we found that among persons aged 65 years and older who were diagnosed with liver cancer (which has a poor prognosis), only 25% were enrolled in hospice care and the majority used a hospice only in the last weeks of life. This is a disheartening finding as liver cancer patients with longer hospice enrolment had lower costs and improved survival. We suggest that healthcare practitioners consider discussion of palliative and hospice care routinely with patients suffering from liver cancer.

https://doi.org/10.1016/j.jhepr.2021.100236

Research article

JHEP|Reports

Hospice care utilisation among elderly patients who died with hepatocellular carcinoma in the United States

Victor de Avila,[1] James M. Paik,[1,3] Leyla de Avila,[1] Linda Henry,[2] Denise Mohess,[1] Alva Roche-Green,[1] Zobair M. Younossi[1,3,4,*]

[1]*Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA, USA;* [2]*Center for Outcomes Research in Liver Diseases, Washington, DC, USA;* [3]*Center for Liver Disease and Department of Medicine, Inova Fairfax Medical Campus, Falls Church, VA, USA;* 4*Inova Medicine, Inova Health Systems, Falls Church, VA, USA*

JHEP Reports **2021.** https://doi.org/10.1016/j.jhepr.2021.100236

Background & Aims: The benefits of hospice care in Medicare recipients with hepatocellular carcinoma (HCC) have not been fully evaluated, which we aimed to study.
Methods: We used nationally representative samples of the Medicare beneficiaries in the USA (2011–2016) to assess the impact of hospice care on the outcomes of patients with HCC. Hospice care benefits on the survival time, length of stay (LOS), 30-day readmissions, and daily charges during the last year and month of life were assessed by logistic regression and generalised linear regression.
Results: Among 2,230 Medicare beneficiaries with HCC (mean age, 74.9 years; non-Hispanic White 79.1%; male 66.6%), median survival from HCC diagnosis was 68 days; 556 (24.9%) received hospice services; median hospice LOS was 12 days (4–35 days). Hospice users increased from 20.1% to 31.1% over time, driven by enrolment ≤15 days (45.1–59.2%, respectively). In the last year of life, hospice users (*vs.* no hospice care) had longer median survival time (76.5 *vs.* 66 days), lower in-hospital mortality (1.1% *vs.* 25.5%) and lower median daily charges ($951 *vs.* $1,004) despite more inpatient admissions and higher comorbid diseases. Hospice enrolment was associated with 48.6% reduction in daily charges (95% CI: -54.9% to -41.5%). Longer hospice LOS was associated with lower rates of healthcare utilisation. Patients with chronic liver disease were less likely to enrol in hospice care (odds ratio = 0.18, 95% CI: 0.14–0.24).
Conclusions: Although hospice provides a significant decrease in healthcare utilisation and some benefit in survival, most care is given in the last 2 weeks of life. Efforts to encourage earlier use of hospice services must continue.
Lay summary: The purpose of hospice care is to provide comfort and lessen suffering at the end of life. Hospice care allows one to die outside the hospital environment which is the wish of most people. However, we found that among persons aged 65 years and older who were diagnosed with liver cancer (which has a poor prognosis), only 25% were enrolled in hospice care and the majority used a hospice only in the last weeks of life. This is a disheartening finding as liver cancer patients with longer hospice enrolment had lower costs and improved survival. We suggest that healthcare practitioners consider discussion of palliative and hospice care routinely with patients suffering from liver cancer.

Introduction

There is increasing evidence that many individuals spend the last days of their lives in the ICU in pain with severely impaired quality of life, accruing medical debt without lengthening survival.[1] However, data suggest that most Americans would prefer not to die in hospital.[1] In response to these findings, hospice care was developed to provide end-of-life care for those dying with a focus on maximising patients' quality of life through palliative care.[2] Palliative care involves addressing terminally ill patients' physical, intellectual, emotional, social, and spiritual well-being while also supporting their independence, access to information, and ability to make choices about their healthcare.[3,4]

Medicare, the United States government's healthcare system for those aged 65 years and older or disabled, adopted the use of hospice care in 1982.[5] For patients to qualify for hospice under Medicare, a physician must submit a written statement acknowledging that the patient has ≤6 months to live. In this context, Medicare approves hospice care for 90 days at a time which can be renewed as needed.

In 2017, 48.2% of the Medicare beneficiaries who died had been enrolled in hospice at the time of their death; however, 40.5% of the patients received care for 14 days or less while only 14.1% received care for more than 180 days. This is most likely a result of the Medicare requirement that patients discontinue curative care before enrolling in hospice, despite evidence that demonstrates hospice improves care and shorter hospice stays are associated with lower-quality end-of-life scores.[6,7]

Keywords: Mortality; Length of stay; Costs; Chronic liver disease.
Received 4 November 2020; received in revised form 8 December 2020; accepted 28 December 2020; available online 27 January 2021
* Corresponding author. Address: Medical Service Line, Betty and Guy Beatty Center for Integrated Research, Claude Moore Health Education and Research Building, 3300 Gallows Road, Falls Church, VA, 22042, USA. Tel.: +1-703-776-2540; Fax: +1-703-776-4386.
E-mail address: zobair.younossi@inova.org (Z.M. Younossi).

In addition to impairment of quality of life, patients with terminal cancer account for $18.99 billion in homecare.[1] Given the fact that cancer is the second most common cause of death in the USA, the impact of hospice care in these patients has been a major priority. In this context, hepatocellular carcinoma (HCC) is one of the few solid cancers that has been increasing. HCC accounts for 75–85% of liver cancers, and, in 2018, was considered the fourth leading cause of cancer deaths worldwide.[8] In this context, HCC related to non-alcoholic fatty liver disease (NAFLD) is now considered to be one of the main contributors to HCC worldwide.[9,10] A global forecasting study reported that the age-standardised incidence rates per 100,000 person-years for primary liver cancer would increase for both males and females by the year 2030 with the main driver of the increase resulting from the growing prevalence of NAFLD and non-alcoholic steatohepatitis (NASH).[10] Additionally, another recent study reported the prevalence of NASH HCC cases has increased by 68% from 2010 to 2015.[11] Finally, studies from the USA and Europe have reported that NASH-related HCC has become and leading indication for liver transplantation.[12,13]

Although treatment of HCC has improved over the years, early detection and treatment is of great importance. Unfortunately, a large number of patients with HCC are diagnosed late providing only a median survival time of 3–6 months.[14] Given the increasing burden of HCC and its late presentation with a poor prognosis, hospice care may play an important role in providing end-of-life care for these patients. In fact, results from our previous study using surveillance, epidemiology, and end results (SEER) data suggested that HCC patients receiving hospice care had a mortality advantage.[15] In another study, we also demonstrated that Medicare recipients with advanced chronic liver disease (CLD) incurred higher hospital resource utilisation and shorter hospice stays as compared with those who were enrolled in hospice without CLD, suggesting that these patients could potentially benefit from early referral to hospice care.[16]

Therefore, the aim of this study was to utilise the recent Medicare dataset (2011–2016) to assess the association between enrolment in hospice and survival and healthcare utilisation in Medicare recipients with HCC. Given that HCC is a global problem, our second aim was to provide information to guide decision- and policy makers worldwide when developing optimal utilisation strategies for those with HCC who may benefit from hospice care.

Patients and methods

Data source and study population

We conducted a retrospective, serial cross-sectional analysis of Medicare beneficiaries using Medicare denominator, inpatient, outpatient, and hospice files (a random 5% sample for each of our study years) for the years 2011–2016 (https://data.cms.gov/). For each year, the denominator file reported Medicare beneficiary entitlement, enrolment, and demographic information including the date of death. The inpatient, outpatient, and hospice files contained claims for each beneficiary who received each service. We identified Medicare beneficiaries with HCC who died within the study period to ensure hospice enrolment was a reasonable consideration. To ensure that beneficiaries had Medicare coverage during their last year of life, we included only patients 65 years or older. We excluded patients with hospice claims before the diagnosis of HCC. These data are publicly available from CMS and can be obtained through a formal request and associated fees.

We determined whether patients had a diagnosis of HCC based on the International Classification of Diseases Ninth Revision (ICD-9) and ICD-10 code for HCC (155.0 in ICD-9 or C22.0 in ICD-10) in inpatient, outpatient, and hospice files, excluding outpatient rule-out codes. The date of diagnosis of HCC was obtained from the date of the first inpatient or outpatient claim with an HCC diagnosis code, whichever came first. Hospice beneficiaries were defined as patients with at least 1 claim for hospice care from the time of diagnosis to death. We assumed that patients remained in hospice after enrolment until death from enrolment (*i.e.* day of first hospice claim). Beneficiaries who did not choose hospice were considered as a control group.

To investigate the effect of early enrolment in hospice, we also grouped hospice users according to the duration of enrolment: (1) enrolled within 5 days of death, (2) enrolled 6–15 days before death; (3) enrolled 16–29 days before death, and 4 enrolled for 30 days or more before death.

For the purpose of this study, the following outcomes during the last year of life as well as the last month of life were assessed: (1) survival time – measured from date of diagnosis to death; (2) time to hospice enrolment – measured from date of diagnosis to first hospice entry; (3) patients' total annual charges/payments for inpatient, outpatient and hospice services; also, to determine patients' daily charges, patients' total annual charges were divided by the survival times (days); (4) hospital and hospice length of stay (days) were defined as the total number of days in hospital and hospice, respectively; (5) 30-day all-cause hospital readmission was identified; and (6) cirrhosis and CLD including HBV and HCV, alcoholic liver disease (ALD), NAFLD, and Charlson comorbidity index (CCI) were ascertained using the ICD-9/10 codes (Supplementary information). To reduce misclassifying NAFLD, we excluded NAFLD cases with any other liver diseases (viral hepatitis, ALD, iron overload, autoimmune disease, Wilson disease, haemochromatosis, and alpha-1-antitrypsin deficiency or alcohol abuse).[17,18] All Medicare expenditures were adjusted using the medical component of the Consumer Price Index year 2016.[19] The Inova Health System IRB provided an exempt study status.

Data analysis

We compared sociodemographic characteristics, healthcare utilisation and comorbidities of the study cohort between hospice and non-hospice beneficiaries during the last year of life as well as the last 30 days of life using a non-parametric Kruskal-Wallis test for continuous variables and Chi-square test for categorical analysis.

Independent predictors of hospice enrolment were studied using multivariable logistic regression. After adjusting for calendar year, age, sex, race/ethnicity, number of 30-day readmissions and CCI, multivariable regression analyses were performed on charges and survival time (generalised linear regression model [GLM] with gamma distribution), and length of stay (GLM with Poisson distribution) to assess the effect of hospice enrolment. The adjusted relationship between factors and each outcome were estimated using coefficients from these models, which were exponentiated to yield a percentage change in the outcomes associated with each factor. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

After applying our inclusion and exclusion criteria (Fig. 1), our overall study population consisted of 2,230 Medicare beneficiaries with HCC (n = 556 [24.9%] were hospice recipients) with a mean (SD) age of 74.9 (7.2) years old and 66.6% male. A total of 79.1% were non-Hispanic White and 9.2% were non-Hispanic Black. The median survival time from HCC diagnosis was 68 days (IQR 22–158 days). Patients with CLD were significantly less likely to use hospice services (43.85% *vs.* 14.93%, p <0.0001; Table 1).

There were no demographic differences between those who received hospice care and those who did not (p >0.05). The median length of stay in hospice was 12 days (IQR: 4–35 days). Overall, 72.3% had a hospice claim within 30 days of death in which 31.7% enrolled in hospice care within 5 days of death; 24.1% within 6–15 days; 16.6% within 16–29 days; and 27.7% within 30 days or more. The median survival time from HCC diagnosis for those in hospice was 76.5 days (IQR: 29.5–154.5 days) with the median survival time of 126 days (IQR: 79–218 days) among patients who spent more than 30 days in hospice. For non-hospice users, the median survival time was 66 days (IQR: 29.5–154.5 days; Table 1). From 2011 through 2016, hospice care usage steadily increased from 20.1% to 31.1%, mainly driven by the increasing trend in the percentage of HCC patients (45.1% in 2011 to 59.2% in 2016) who stayed in hospice for ≤15 days (Fig. 2).

Although patients who received hospice care had a higher comorbid disease burden (median comorbidity index: 6.7 *vs.* 6.0), they had a lower proportion of metabolic components (hypertension, hyperlipidaemia, diabetes, and obesity), alcohol abuse (3.1% *vs.* 13.7%), cirrhosis (14.9% *vs.* 42.8%), NAFLD (6.5% *vs.* 14.9%), HCV (5.8% *vs.* 18.7%), HBV (1.1% *vs.* 2.9%), and ALD (2.3% *vs.* 11.0%). There were no differences among hospice users with different hospice lengths of stay except for patients enrolled in hospice for shorter periods where they were more likely to have a higher comorbidity index (median comorbidity index: 6.0 for >15 days *vs.* 7.0 for ≤15 days).

Results of the multivariable analysis on predictors for hospice enrolment are shown in Table 2. Higher hospice enrolment was independently associated with calendar year (OR: 1.18 [1.10–1.26], p <0.0001), being from the Midwest (OR: 2.25 [1.53–3.29], p <0.0001), South (OR: 1.94 [1.37–2.76], p = 0.0002) or West (OR: 1.94 [1.31–2.97], p = 0.0009) compared with the Northeast, comorbidity index (OR: 1.17 [95% CI: 1.13–1.21]) and, lower hospice enrolment was associated with hypertension (OR: 0.14 [0.10–0.20]), hyperlipidaemia (OR: 0.12 [0.06–0.26]), diabetes (OR: 0.23 [0.15–0.34]), NAFLD (OR: 0.30 [0.20–0.47]), HCV (OR: 0.23 [0.15–0.35]), HBV (OR: 0.29 [0.11–0.75]), and ALD (OR: 0.17 [0.09–0.32]; p <0.01).

Results of the multivariable analysis on factors associated with time to hospice enrolment indicated that there were no associations found between the studied variables and time to hospice enrolment for those with HCC who died within 1 year of their HCC diagnosis (Table S1).

Table 3 compared healthcare utilisation between hospice and non-hospice users, according to the length of hospice enrolment in the last year of life. There were no significant differences for hospital lengths of stay and 30-day readmissions between those who used hospice and those who did not. Additionally, there were no significant differences among the 4 hospice-user groups for hospital lengths of stay or 30-day readmissions although there was a higher proportion of 30-day readmissions among

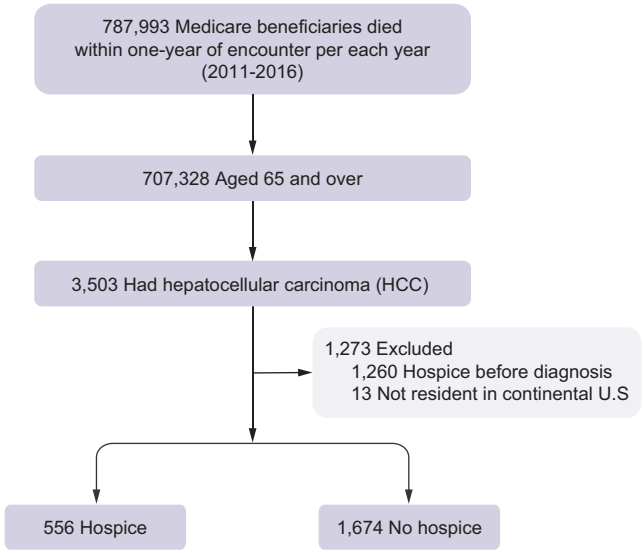


Fig. 1. Flow chart of study cohort selection.

hospice users who were grouped into ≤5 days compared with the other hospice groups (21.0% *vs.* 13.4%, 17.4%, and 12.3%, respectively). Compared with the non-hospice users, hospice beneficiaries had more claims (median: 5 *vs.* 2), more diagnoses (median: 31 *vs.* 22), higher total charges (median: $66,024 *vs.* $51,034) and higher total payment (median: $20,682 *vs.* $13,762; all p <0.05).

Hospice beneficiaries with hospice stays over 30 days had the highest median total charges of $73,764 (IQR: $42,954–125,745) with the highest median hospice charge of $17,815 (IQR: $11,719–27,516). Over the last year of life, median daily charges for hospice beneficiaries were $951 (IQR: $447–2,286) compared with $1,004 ($269–3,371) for non-hospice beneficiaries. Among hospice beneficiaries, median daily charges were lowest for those in hospice for 30 days or more ($616) and was highest for those in hospice for 15 days or fewer ($1,453–1,462), suggesting that being in hospice more than 15 days was associated with markedly lower daily charges.

Multivariable GLMs taking into account age, sex, race, region of the country, and comorbidity index demonstrated significant differences between hospice users compared with non-hospice users for daily charges, inpatient length of stay, 30-day readmissions, and survival. Hospice users incurred decreased daily charges (48.6% reduction [95% CI: -54.9 to -41.5%]) which was associated with lower daily charges among each hospice group ranging from 19.7% reduction for those in hospice for 5 days or fewer to 77.4% reduction in those for 30 days or more compared with non-hospice users (Table 4).

However, GLMs conducted among hospice patients found that hospice patients had an increased number of hospital admissions (22.11% [95% CI: 3.65–43.87]) which was driven by the increased number of hospital admissions among those who spent 5 days or less in hospice care (46.31% [95% CI: 1.24–85.75). Among those who stayed less than 5 days in hospice, patients incurred an increased length of inpatient stay (12.6% [95% CI: 6.59–18.9]) whereas those who were in hospice for 16–29 days or 30 days or more had a decreased length of an inpatient hospital stay (-16.92 [95% CI: -23.65 to -9.61] and (-6.34 [95% CI: -12.14 to -0.15]), respectively. Those who stayed less than 5 days in hospice or

Table 1. Characteristics of Medicare beneficiaries who died within 1 year of HCC encounter between 2011 and 2016.

Characteristics	Total (n = 2,230)	Non-hospice users (n = 1,674)	Hospice users (n = 556)	Hospice users				*p* value*
				≤5 days (n = 176)	6–15 days (n = 134)	16–29 days (n = 92)	≥30 days (n = 154)	
Age (years) at encounter, mean ± SD	74.85 ± 7.2	74.77 ± 7.21	75.09 ± 7.17	74.72 ± 7.07	74.66 ± 7.28	74.93 ± 6.72	75.97 ± 7.46	0.2882
Age group (years)								
65–74	1,184 (53.09%)	905 (54.06%)	279 (50.18%)	96 (54.55%)	74 (55.22%)	40 (43.48%)	69 (44.81%)	0.1120
75–84	781 (35.02%)	577 (34.47%)	204 (36.69%)	56 (31.82%)	43 (32.09%)	43 (46.74%)	62 (40.26%)	0.3412
≥85	265 (11.88%)	192 (11.47%)	73 (13.13%)	24 (13.64%)	17 (12.69%)	9 (9.78%)	23 (14.94%)	0.2946
Male	1,484 (66.55%)	1,105 (66.01%)	379 (68.17%)	125 (71.02%)	98 (73.13%)	56 (60.87%)	100 (64.94%)	0.3506
Race								
White	1,763 (79.06%)	1,328 (79.33%)	435 (78.24%)	145 (82.39%)	99 (73.88%)	74 (80.43%)	117 (75.97%)	0.5830
Black	206 (9.24%)	157 (9.38%)	49 (8.81%)	13 (7.39%)	13 (9.70%)	9 (9.78%)	14 (9.09%)	0.6898
Other race	261 (11.70%)	189 (11.29%)	72 (12.95%)	18 (10.23%)	22 (16.42%)	9 (9.78%)	23 (14.94%)	0.2916
Residential region								
Northeast	404 (18.12%)	334 (19.95%)	70 (12.59%)	22 (12.50%)	16 (11.94%)	16 (17.39%)	16 (10.39%)	0.0001
South	855 (38.34%)	638 (38.11%)	217 (39.03%)	69 (39.20%)	50 (37.31%)	38 (41.30%)	60 (38.96%)	0.7002
Midwest	494 (22.15%)	353 (21.09%)	141 (25.36%)	40 (22.73%)	38 (28.36%)	19 (20.65%)	44 (28.57%)	0.0356
West	477 (21.39%)	349 (20.85%)	128 (23.02%)	45 (25.57%)	30 (22.39%)	19 (20.65%)	34 (22.08%)	0.2789
Year of death								
2011	353 (15.83%)	282 (16.85%)	71 (12.77%)	19 (10.80%)	25 (18.66%)	14 (15.22%)	13 (8.44%)	0.0225
2012	370 (16.59%)	279 (16.67%)	91 (16.37%)	35 (19.89%)	14 (10.45%)	19 (20.65%)	23 (14.94%)	0.8692
2013	394 (17.67%)	297 (17.74%)	97 (17.45%)	38 (21.59%)	17 (12.69%)	15 (16.30%)	27 (17.53%)	0.8741
2014	404 (18.12%)	308 (18.40%)	96 (17.27%)	26 (14.77%)	23 (17.16%)	14 (15.22%)	33 (21.43%)	0.5479
2015	378 (16.95%)	280 (16.73%)	98 (17.63%)	29 (16.48%)	23 (17.16%)	19 (20.65%)	27 (17.53%)	0.6243
2016	331 (14.84%)	228 (13.62%)	103 (18.53%)	29 (16.48%)	32 (23.88%)	11 (11.96%)	31 (20.13%)	0.0048
Time from diagnosis of HCC to death	68 (22–158)	66 (19–159)	76.5 (29.5–154.5)	56 (15–142)	47 (20–121)	56.5 (30.5–132.5)	126 (79–218)	0.0056
Time from diagnosis of HCC to death group								
<30 days	698 (31.30%)	559 (33.39%)	139 (25.00%)	68 (38.64%)	51 (38.06%)	20 (21.74%)	0 (0.00%)	0.0002
30–89 days	586 (26.28%)	416 (24.85%)	170 (30.58%)	45 (25.57%)	37 (27.61%)	37 (40.22%)	51 (33.12%)	0.0079
90–179 days	471 (21.12%)	342 (20.43%)	129 (23.20%)	27 (15.34%)	29 (21.64%)	19 (20.65%)	54 (35.06%)	0.1654
≥180 days	475 (21.30%)	357 (21.33%)	118 (21.22%)	36 (20.45%)	17 (12.69%)	16 (17.39%)	49 (31.82%)	0.9590
Time from diagnosis of HCC to hospice	n.a.	n.a.	43.5 (12–121.5)	53.5 (12–138)	35.5 (10–110)	38.5 (11–112)	48.5 (15–125)	
Comorbid conditions								
Hypertension	949 (42.56%)	900 (53.76%)	49 (8.81%)	11 (6.25%)	18 (13.43%)	7 (7.61%)	13 (8.44%)	<0.0001
Hyperlipidaemia	365 (16.37%)	357 (21.33%)	8 (1.44%)	2 (1.14%)	4 (2.99%)	0 (0.00%)	2 (1.30%)	<0.0001
Diabetes	635 (28.48%)	602 (35.96%)	33 (5.94%)	9 (5.11%)	10 (7.46%)	3 (3.26%)	11 (7.14%)	<0.0001
Obesity	103 (4.62%)	103 (6.15%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	<0.0001
Alcohol abuse	247 (11.08%)	230 (13.74%)	17 (3.06%)	4 (2.27%)	7 (5.22%)	4 (4.35%)	2 (1.30%)	<0.0001
Cirrhosis	799 (35.83%)	716 (42.77%)	83 (14.93%)	24 (13.64%)	28 (20.90%)	15 (16.30%)	16 (10.39%)	<0.0001
Chronic liver diseases	817 (36.64%)	734 (43.85%)	83 (14.93%)	21 (11.93%)	26 (19.40%)	16 (17.39%)	20 (12.99%)	<0.0001
NAFLD	286 (12.83%)	250 (14.93%)	36 (6.47%)	9 (5.11%)	10 (7.46%)	7 (7.61%)	10 (6.49%)	<0.0001
HCV	345 (15.47%)	313 (18.70%)	32 (5.76%)	6 (3.41%)	13 (9.70%)	5 (5.43%)	8 (5.19%)	<0.0001
HBV	55 (2.47%)	49 (2.93%)	6 (1.08%)	2 (1.14%)	2 (1.49%)	1 (1.09%)	1 (0.65%)	0.0149
ALD	197 (8.83%)	184 (10.99%)	13 (2.34%)	4 (2.27%)	5 (3.73%)	3 (3.26%)	1 (0.65%)	<0.0001
Comorbidity index, mean ± SD	6.29 ± 3.15	6.13 ± 3.13	6.77 ± 3.16	6.93 ± 3.18	6.80 ± 2.88	6.64 ± 3.21	6.64 ± 3.37	<0.0001
Comorbidity index	6.0 (3.54–8.0)	6.0 (3.2–8.0)	6.7 (4.0–9.0)	7 .0 (4.0–9.0)	7 .0 (5.0–9.0)	6.0 (4.0–9.0)	6.5 (3.0–9.0)	<0.0001

All values are displayed as count (%) except where otherwise noted. Hospice users are further grouped according to length of hospice enrolment in the last year of life. Data displayed as median (IQR) for numerical variables and count (percentage) for categorical variables.
*Comparison between hospice and non-hospice users using a non-parametric Kruskal-Wallis test for continuous variables and Chi-square test for categorical analysis.
ALD, alcoholic liver disease; HCC, hepatocellular carcinoma; n.a., not applicable; NAFLD, non-alcoholic fatty liver disease.

Table 2. Factors associated with hospice enrolment among Medicare beneficiaries who died within 1 year of HCC encounter.

Factors	Odds ratio (95% CI)	*p* value
Calendar year	1.18 (1.10–1.26)	<0.0001
Age	1.00 (0.99–1.02)	0.7730
Male	1.10 (0.85–1.41)	0.4747
Race		
Non-Hispanic White	0.74 (0.50–1.08)	0.1173
Non-Hispanic Black	1.03 (0.59–1.79)	0.9201
Other race	Reference	
Residential region		
Northeast	Reference	
South	1.94 (1.37–2.76)	0.0002
Midwest	2.25 (1.53–3.29)	<0.0001
West	1.94 (1.31–2.87)	0.0009
Charlson comorbidity index	1.17 (1.13–1.21)	<0.0001
Hypertension	0.14 (0.10–0.20)	<0.0001
Hyperlipidaemia	0.12 (0.06–0.26)	<0.0001
Diabetes	0.23 (0.15–0.34)	<0.0001
NAFLD	0.30 (0.20–0.47)	<0.0001
HCV	0.23 (0.15–0.35)	<0.0001
HBV	0.29 (0.11–0.75)	0.0105
ALD	0.17 (0.09–0.32)	<0.0001

Odds ratio were computed by using logistic regression. ALD, alcoholic liver disease; HCC, hepatocellular carcinoma; NAFLD, non-alcoholic fatty liver disease.

between 16 and 29 days had an increased number of 30-day readmissions (45.06% [95% CI: 6.09–98.36%] and 52.52% [1.33–129.56]), respectively. Those who stayed in hospice for 6–15 days had a decreased survival (-21.66% [-34.96 to -5.78]) while those who stayed for 30 days or more had an increased survival (58.6% [95% CI: 33.34–88.65]). A significantly fewer number of patients died in the hospital among those who received hospice care compared with those that did not (1.1% vs. 25.5%). These data were true despite having a higher median comorbidity index and more inpatient admissions (Table 4).

Healthcare utilisations during the last year of life are shown in Table 5. In the last year of life, for Medicare patients with HCC, there were no differences between hospice users and non-hospice use for the number of inpatient admissions, hospital length of stay, inpatient charges or 30-day admissions. However, the median daily charges per hospice user was $667 (95% CI: $323–1,763) compared with $369 (95% CI: $0–1,659) per non-hospice users, but longer lengths of stay in hospice were associated with lower daily charges, especially for those in hospice for 30 days or more (≥30 days – $382 [95% CI: $292–566] *vs.* ≤ 5 days – $1,046 [$394–2,720]). Those in hospice also had higher total payments ($8,960 [$5,166–15,985] *vs.* $4,888 [$0–14,773]), higher median number of claims (2 [2–3] *vs.* 1 [0–1]) and higher median number of diagnoses (15 [5–26] *vs.* 10 [0–21]; *p* <0.0000). Together, the longer the stay in hospice the lower the charges.

Multivariable GLMs revealed that even in the last month of life, hospice enrolment was strongly associated with decreased daily charges (44.9% reduction [95% CI: -50.8 to -38.2%]). Also, longer lengths of stay in hospice was associated with lower daily charges, ranging from 31.1% reduction for those in hospice for 5 days or fewer to 67.5% reduction for those with 30 days or more of hospice care compared with non-hospice users (Table S2). Hospice enrolment was also the strongest contributor to decreased inpatient admissions (10.9% reduction [-18.9 to 02.1%]), decreased inpatient length of stay (42.9% [-45.8 to -39.9%]), and a decreased 30-day readmission (-40.5% [-58.8 to -14.1%]). Together, early enrolment in hospice leads to decreased healthcare utilisations during the last month of life (Table S2).

Discussion

Our data provides an in-depth analysis of the Medicare recipients with HCC and their use of hospice care. Our data confirm the poor prognosis of HCC diagnosis with an overall median post-diagnosis survival time of 68 days (22–158 days). Despite this poor prognosis, only 25% of Medicare recipients with HCC received hospice care. Interestingly, although HCC Medicare recipients who received hospice care had higher comorbidity scores, they experienced both longer overall survival as well as fewer inpatient deaths. In fact, it is important to note that the length of time spent under hospice care appeared to have had a positive impact on patients' survival. These data confirm our previous report for patients with CLD that suggested enrolment in hospice care could improve survival and possibly better quality of life.[15] More importantly, the use of hospice care provided the opportunity for patients to die outside the hospital environment which has been shown to be the preference for patients dying with cancer.[20,21]

In addition to improvement in survival and lower rates of in-hospital death, we found the use of hospice care to provide lower charges. In fact, those in hospice care had daily charges that were ~49% lower than those who were not receiving hospice care. These savings became even more significant the longer the time Medicare recipients with HCC spent in hospice care. In contrast, those who stayed in hospice care for a very short period of time (≤5 days), experienced a 46% increase for inpatient admissions, a 13% increase for inpatient length of stays, and a 45% increase in 30-day readmissions. These higher resource utilisations led to almost $20,000 more in total charges. These data support our previous study where we reported a potential cost advantage when using hospice care for patients with HCC.[15,16] Our findings are also similar to a study completed on Medicare patients with a poor cancer prognosis where investigators found higher healthcare utilisation and costs among non-hospice users.[22]

As previously noted, the diagnosis of HCC is increasing despite the decreasing trend in HCV-related HCC, which before the advent of the new curative HCV treatment agents in late 2013, was the main cause of HCC in the USA. Now, however, as the prevalence of NAFLD has increased, NAFLD has become an important cause of HCC and other complications of liver disease.[23,24] Therefore, the potential increase in survival, decrease for in-hospital deaths, and cost savings among Medicare patients with HCC who use hospice have important clinical and economic implications. However, there are potentially several barriers to improving the timely use of hospice care which include the inherent difficulty in determining a patient's prognosis which is made more challenging by Medicare's requirements of certifying a patient has less than 6 months to live as well as foregoing any active cancer treatment. In addition, Medicare does not reimburse physicians for the time necessary to discuss a patient's desires regarding their end-of-life care which may be a disincentive for a physician to refer a patient to hospice earlier.[5]

Fortunately, to address these barriers, Medicare in 2016 under the Affordable Care Act, implemented a pilot program, the Medicare Care Choices Model (MCCM) to allow eligible Medicare beneficiaries to receive hospice care while concurrently receiving curative treatment. The MCCM pilot program has been designed to measure whether these changes improve access to hospice

Table 3. Healthcare utilisation of Medicare beneficiaries who died within 1 year of HCC encounter during the last year of life according to length of hospice enrolment between 2011 and 2016.

Healthcare utilisation	Total sample (n = 2,230)	Non-hospice users (n = 1,674)	Hospice users (n = 556)	Hospice users				p value*
				≤5 days (n = 176)	6–15 days (n = 134)	16–29 days (n = 92)	≥30 days (n = 154)	
Inpatient admissions								
0	1,732 (77.67%)	1,317 (78.67%)	415 (74.64%)	124 (70.45%)	103 (76.87%)	69 (75.00%)	119 (77.27%)	0.0479
1	360 (16.14%)	261 (15.59%)	99 (17.81%)	33 (18.75%)	23 (17.16%)	16 (17.39%)	27 (17.53%)	0.2189
2	86 (3.86%)	61 (3.64%)	25 (4.50%)	12 (6.82%)	3 (2.24%)	4 (4.35%)	6 (3.90%)	0.3658
≥3	52 (2.33%)	35 (2.09%)	17 (3.06%)	7 (3.98%)	5 (3.73%)	3 (3.26%)	2 (1.30%)	0.1906
Hospital length of stay	5 (1–9)	5 (1–9)	4 (2–10)	5 (2–11.5)	4.5 (2–9)	4 (1–7.5)	4 (1–9)	
Total charge, $	55,206 (23,916–119,539)	51,034 (20,897–115,799)	66,024 (33,580–125,692)	69,271 (28,049–137,813)	60,122 (34,448–118,632)	56,173 (31,117–108,712)	73,764 (42,954–125,745)	<0.0001
Inpatient charge, $	35,756 (8,252–86,038)	36,668 (6,567–89,167)	33,385 (12,325–82,583)	48,310 (14,321–105,946)	34,805 (17,983–75,754)	25,719 (9,005–71,687)	32,283 (4,212–70,054)	0.1001
Outpatient charge, $	0 (0–15,324)	0 (0–14,553)	1,176 (0–20,147)	2,403 (0–18,111)	0 (0–22,402)	320 (0–19,244)	1,550 (0–23,118)	0.0557
Hospice charge, $	0 (0–0)	n.a.	6,416 (2,925–14,863)	2,404 (1,426–4,973)	4,725 (3,284–8,443)	7,477 (5,623–11,116)	17,815 (11,719–27,516)	<0.0001
Total payment, $	15,527 (8,445–29,903)	13,762 (7,436–28,321)	20,682 (12,714–35,004)	18,645 (9,992–33,128)	17,855 (12,226–31,349)	20,659 (13,466–27,910)	26,604 (16,513–41,145)	<0.0001
Daily charge, $	991 (317–2972)	1,004 (269–3,371)	951 (447–2,286)	1,453 (585–4,236)	1,462 (631–3,010)	906 (414–1,611)	616 (327–1,008)	<0.0001
No. of claims	3 (1–5)	2 (1–4)	5 (3–8)	4 (3–7)	4 (2–8)	4 (3–9)	6.5 (4–10)	<0.0001
No. of diagnoses	31 (20–49.5)	22 (13–36)	31 (20–49.5)	33 (19–50.5)	29 (19–45)	34 (21–58)	15 (14–51)	<0.0001
No. of 30-day readmissions								
0	1,904 (85.38%)	1,438 (85.90%)	466 (83.81%)	139 (78.98%)	116 (86.57%)	76 (82.61%)	135 (87.66%)	0.2270
1	265 (11.88%)	195 (11.65%)	70 (12.59%)	30 (17.05%)	13 (9.70%)	10 (10.87%)	17 (11.04%)	0.5524
≥2	61 (2.74%)	41 (2.45%)	20 (3.60%)	7 (3.98%)	5 (3.73%)	6 (6.52%)	2 (1.30%)	0.1505
30-day readmission	326 (14.62%)	236 (14.10%)	90 (16.19%)	37 (21.02%)	18 (13.43%)	16 (17.39%)	19 (12.34%)	0.2270
Death in hospital	333 (19.12%)	328 (25.49%)	5 (1.10%)	2 (1.37%)	1 (0.85%)	1 (1.33%)	1 (0.85%)	<0.0001

All values were displayed as count (%) except where otherwise noted. Hospice users are further grouped according to length of hospice enrolment in the last year of life. Data displayed as median (IQR) for numerical variables and count (percentage) for categorical variables.
*Comparison between hospice and non-hospice users using a non-parametric Kruskal-Wallis test for continuous variables and Chi-square test for categorical analysis.
HCC, hepatocellular carcinoma; n.a., not applicable.

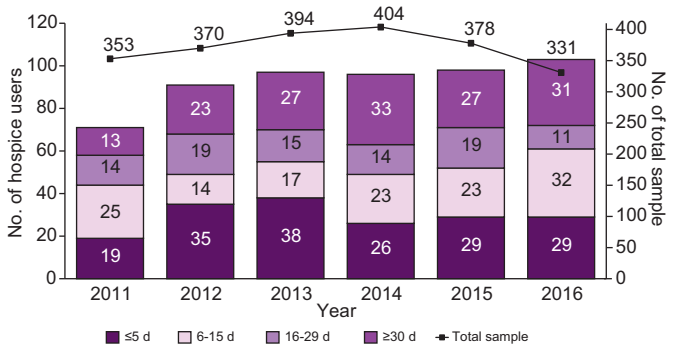


Fig. 2. Hospice use among patients who died with HCC according to the number of days in hospice. HCC, hepatocellular carcinoma.

supportive care services, improves patients' quality of life, improves patient/family satisfaction while at the same time reducing Medicare's expenditures. As such, we suggest that the findings from our studies on the benefits obtained when using hospice services among those with HCC should be considered in addition to the MCCM outcomes to inform the policy makers when making their final determination on how hospice services should be provided.[25]

An intriguing finding of this study is the regional variation in the use of hospice care. The highest use was noted to be in the South where approximately 40% of those who died within a year after HCC diagnosis were enrolled in hospice care whereas only 13% from the Northeast were enrolled in this care. There are a few other potential explanations for this variation. One previous study has noted that the higher the intensity of end-of-life care (hospitalisation, ICU use), the lower the use of hospice care.[26] In this context, the very short enrolment in hospice care has been considered as a 'spillover care' for those receiving care in the ICU or other critical clinical care settings.[26] This spillover pattern has been more commonly seen in areas with low volume of health maintenance organisations as well as for non-Whites and those with comorbidity.[27] Our data support some of these previous reports. Nevertheless, future research is needed to better explain the differences in the use of hospice care and provide barriers for most optimal utilisation of palliative and hospice care for patients with HCC.

It is important to note that the suboptimal use of hospice care is not unique to the Medicare population of the USA. Despite being recognised as a medical subspecialty in the USA, Canada, England, Ireland, Australia, New Zealand, and a number of other European countries, the suboptimal use in patients with different types of cancer remains a global challenge.[28] In fact, recent global statistics show that 86% of those who most need palliative care do not receive it. Additionally, 80% of patients who died with serious health-related suffering were seen in the developing regions of the world without access to palliative care. In fact, 83% of those who were in need of pain relief with opioids did not have access to such medication.[29,30] Both the World Health Assembly (2014) and the World Health Organization (2013) have taken steps to provide such services to everyone through a resolution calling for their members to incorporate palliative care into their mainstream health systems and including palliative care medications in their essential medications list.[31,32] As such, our findings can assist country and regional health policy makers in developing policies and

Table 4. Adjusted comparisons in daily charge, inpatients admissions and length of stay, 30-day readmission, and survival time among Medicare beneficiaries who died with HCC in the last year of life according to length of hospice enrolment.

Factors	Daily charge		Inpatient admissions		Inpatient length of stay		Survival time		30-Day readmission	
	% Change (95% CI)	*p* value	% Change (95% CI)	*p* value	% Change (95% CI)	*p* value	% Change (95% CI)	*p* value	% Change (95% CI)	*p* value
Hospice users*	-48.61 (-54.88 to -41.47)	<0.0001	22.11 (3.65–43.87)	0.0169	-1.69 (-5.19 to 1.94)	0.3566	8.08 (-2.47 to 19.77)	0.1380	18.13 (-4.89 to 46.72)	0.1320
Length of hospice enrolment†										
≤5 days	-19.78 (-34.84 to -1.23)	0.0379	46.31 (15.24–85.75)	0.0018	12.57 (6.59–18.9)	<0.0001	-7.49 (-21.44 to 8.93)	0.3504	45.06 (6.09–98.36)	0.0198
6–15 days	-44.81 (-56.38 to -30.18)	<0.0001	11.16 (-17.95 to 50.58)	0.4947	-4.71 (-10.9 to 1.9)	0.1587	-21.66 (-34.86 to -5.78)	0.0096	2.5 (-32.01 to 54.53)	0.9061
16–29 days	-60.61 (-70.23 to -47.87)	<0.0001	23.95 (-12.04 to 74.67)	0.2198	-16.92 (-23.65 to -9.61)	<0.0001	-1.83 (-21.15 to 22.22)	0.8688	52.52 (1.33–129.56)	0.0430
≥30 days	-77.42 (-81.9 to -71.83)	<0.0001	1.71 (-24.95 to 37.85)	0.9128	-6.34 (-12.14 to -0.15)	0.0448	58.6 (33.34–88.65)	<0.0001	-21.6 (-49.77 to 22.37)	0.2840

The coefficients from GLMs were exponentiated to yield a percentage change.
GLMs adjusted for calendar year, age, sex, race, regions, and comorbidity index.
*Comparison between no hospice users and hospice users by using GLMs.
†Comparisons between no hospice users with different length of hospice enrolment by using GLMs.
GLM, generalised linear regression model; HCC, hepatocellular carcinoma.

Table 5. Healthcare utilisation of Medicare beneficiaries who died within 1 year of HCC encounter during the last month of life according to length of hospice enrolment.

				Hospice users				
Healthcare utilisation	**Total sample (n = 2,230)**	**Non-hospice users (n = 1,674)**	**Hospice users (n = 556)**	**≤5 days (n = 176)**	**6–15 days (n = 134)**	**16–29 days (n = 92)**	**≥30 days (n = 154)**	***p* value***
Inpatient admissions								
0	2,076 (93.09%)	1,556 (92.95%)	520 (93.53%)	156 (88.64%)	124 (92.54%)	87 (94.57%)	153 (99.35%)	0.6436
1	143 (6.41%)	109 (6.51%)	34 (6.12%)	19 (10.80%)	9 (6.72%)	5 (5.43%)	1 (0.65%)	0.7411
2	9 (0.40%)	7 (0.42%)	2 (0.36%)	1 (0.57%)	1 (0.75%)	0 (0.00%)	0 (0.00%)	0.8506
≥3	2 (0.09%)	2 (0.12%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0.4148
Hospital length of stay	1 (0–6)	1 (0–6)	1 (0–5)	3 (0–9)	3 (0–6)	1 (0–5)	0 (0–0)	0.3290
Total charge, $	14,670 (0–51,102)	11,073 (0–49,770)	20,010 (9,686–52,900)	31,366 (11,812–81,609)	34,489 (14,570–59,533)	22,772 (8,190–38,797)	11,468 (8,768–16,977)	<0.0001
Inpatient charge, $	5,057 (0–45,721)	5,355 (0–47,052)	4,358 (0–41,459)	22,959 (0–68,394)	25,682 (0–48,891)	8335 (0–29,316)	0 (0–0)	0.1745
Outpatient charge, $	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–912)	0 (0–329)	0 (0–0)	0 (0–0)	0.0008
Hospice charge, $	0 (0–0)	n.a.	5,869 (2,650–11,070)	2,404 (1,426–4,973)	4,725 (3,284–8,443)	7,384 (5,519–10,924)	11,207 (8,192–16,329)	
Total payment, $	7,138 (0–15,140)	4,888 (0–14,773)	8,960 (5,166–15,985)	11,845 (3,117–19,281)	12,876 (6260–19,471)	10,844 (4,298– 19,105)	6,810 (5,548–8,514)	<0.0001
Daily charge, $	489 (0–1,703)	369 (0–1,659)	667 (323–1,763)	1,046 (394–2,720)	1,150 (486–1,984)	759 (273–1293)	382 (292–566)	<0.0001
No. of claims	1 (0–2)	1 (0–1)	2 (2–3)	2 (2–3)	3 (2–3)	3 (2–3)	2 (2–2)	<0.0001
No. of diagnoses	12 (0–22)	10 (0–21)	15 (5–26)	20 (13–28)	20 (11–27)	17 (7–25)	4 (2–10)	0.0009
No. of 30-day readmissions								
0	2,076 (93.09%)	1,556 (92.95%)	520 (93.53%)	156 (88.64%)	124 (92.54%)	87 (94.57%)	153 (99.35%)	0.6436
1	143 (6.41%)	109 (6.51%)	34 (6.12%)	19 (10.80%)	9 (6.72%)	5 (5.43%)	1 (0.65%)	0.7411
≥2	11 (0.49%)	9 (0.54%)	2 (0.36%)	1 (0.57%)	1 (0.75%)	0 (0.00%)	0 (0.00%)	0.6039
30-day readmission	154 (6.91%)	118 (7.05%)	36 (6.47%)	20 (11.36%)	10 (7.46%)	5 (5.43%)	1 (0.65%)	0.6381

All values were displayed as count (%) except where otherwise noted. Hospice users are further grouped according to length of hospice enrolment in the last month of life. Data displayed as median (IQR) for numerical variables and count (percentage) for categorical variables.
*Comparison between hospice and non-hospice users using a non-parametric Kruskal-Wallis test for continuous variables and Chi-square test for categorical analysis.
HCC, hepatocellular carcinoma; n.a., not applicable

strategies to meet the palliative care needs of their patients with HCC. We, therefore, suggest further research in clinical, economic, and patient-reported outcomes benefit of palliative and hospice care for HCC patients across different countries. Finally, research is needed to better understand barriers to hospice and palliative care including the stigma and culturally related perceptions of opioids, death, and end-of-life care as well as lack of awareness about the value of palliative care to the patients, their families and society.

This study is not without its limitations. We relied on electronic medical record ICD codes to identify HCC and other comorbid diseases, but claims-based diagnoses can be suboptimal. However, owing to our large sample size, we feel any discrepancies would be balanced. We assumed that Medicare beneficiaries who died within 1 year of their HCC encounter would have been eligible for hospice which is a reasonable assumption given the current Medicare guidelines. In addition, we were unable to measure the influence of patient preferences on the selection to use hospice or not. It is also necessary to examine cultural norms to better understand why some patients elect to use or not use hospice services.

Conclusions

In summary, our data show that only 25% of Medicare beneficiaries with HCC used hospice services in their last year of life with approximately 30% of these patients enrolling less than 5 days before their death. In contrast, we found that those who used hospice care for longer periods of time survived longer, used fewer hospital-based services, and incurred significant cost savings. These findings add to the increasing evidence that the use of early hospice care should be considered for advanced HCC. Finally, we suggest that the benefits of hospice care we report should be considered in addition to the MCCM outcomes to inform policy makers when making their final determination on how hospice services should be provided to Medicare beneficiaries who suffer from terminal illness.

Abbreviations

ALD, alcoholic liver disease; CCI, Charlson comorbidity index; CLD, chronic liver disease; GLM, generalised linear regression model; HCC, hepatocellular carcinoma; MCCM, Medicare Care Choices Model; NAFLD, non–alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis.

Financial support

The authors received no financial support to produce this manuscript.

Conflicts of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Guarantor of the article (*i.e.* the person who takes responsibility for the integrity of the work as a whole, from inception to published article): ZMY. Study design: VdA, JMP, ZMY. Data interpretation: JMP, LH, ZMY. Statistical analysis: JMP. Manuscript writing: VdA, JMP, LH, ZMY. Critical review of the manuscript: VdA, JMP, LdA, LH, DM, AR-G, ZMY. Approval of the final version of the manuscript: all authors.

Data availability

These data are publicly available from CMS and can be obtained through a formal request and associated fees.

Supplementary data

Supplementary data to this article can be found at https://doi.org/10.1016/j.jhepr.2021.100236.

References

[1] Institute of Medicine. Dying in America: improving quality and honoring individual preferences near the end of life. http://www.nap.edu/openbook.php?record_id=18748. [Accessed 8 September 2020].
[2] National Hospice Palliative Care Organization (NHPCO). History of hospice. https://www.nhpco.org/hospice-care-overview/history-of-hospice/. [Accessed 8 September 2020].
[3] NHPCO hospice care overview. https://www.nhpco.org/hospice-care-overview/. [Accessed 8 September 2020].
[4] Palliative Care Organization. What is palliative care. https://getpalliativecare.org/whatis/. [Accessed 8 September 2020].
[5] Centers for Medicare and Medicaid Services (CMS). Use of hospice. https://www.cms.gov/Center/Provider–Type/Hospice–Center. [Accessed 8 September 2020].
[6] Schockett ER, Teno JM, Miller SC, Stuart B. Late referral to hospice and bereaved family member perception of quality of end-of-life care. J Pain Symptom Manage 2005;30:400–407.
[7] Wachterman MW, Hailpern SM, Keating NL, Tamura MK, O'Hare AM. Association between hospice length of stay, health care utilization, and Medicare costs at the end of life among patients who received maintenance hemodialysis. JAMA Intern Med 2018;178:792–799.
[8] World Health Organization. Cancer. https://www.who.int/news-room/fact-sheets/detail/cancer. [Accessed 22 June 2020].
[9] Hashimoto E, Yatsuji S, Tobari M, Taniai M, Torii N, Tokushige K, et al. Hepatocellular carcinoma in patients with nonalcoholic steatohepatitis. J Gastroenterol 2009;44(Suppl 19):89–95.
[10] Valery PC, Laversanne M, Clark PJ, Petrick JL, McGlynn KA, Bray F. Projections of primary liver cancer to 2030 in 30 countries worldwide. Hepatology 2018;67:600–611.
[11] Kim NG, Nguyen PP, Dang H, Kumari R, Garcia G, Esquivel CO, et al. Temporal trends in disease presentation and survival of patients with hepatocellular carcinoma: a real-world experience from 1998 to 2015. Cancer 2018;124:2588–2598.
[12] Said A, Ghufran A. Epidemic of non-alcoholic fatty liver disease and hepatocellular carcinoma. World J Clin Oncol 2017;8:429–436.
[13] Golabi P, Bush H, Stepanova M, Locklear CT, Jacobson IM, Mishra A, et al. Liver transplantation (LT) for cryptogenic cirrhosis (CC) and nonalcoholic steatohepatitis (NASH) cirrhosis: data from the Scientific Registry of Transplant Recipients (SRTR): 1994 to 2016. Medicine (Baltimore) 2018;97:e11518.
[14] Khalaf N, Ying J, Mittal S, Temple S, Kanwal F, Davila J, et al. Natural history of untreated hepatocellular carcinoma in a US cohort and the role of cancer surveillance. Clin Gastroenterol Hepatol 2017;15:273–281. e1.
[15] Fukui N, Golabi P, Otgonsuren M, de Avila L, Bush H, Younossi ZM. Hospice care in Medicare patients with primary liver cancer: the impact on resource utilisation and mortality. Aliment Pharmacol Ther 2018;47:680–688.
[16] Fukui N, Golabi P, Otgonsuren M, Mishra A, Venkatesan C, Younossi ZM. Demographics, resource utilization, and outcomes of elderly patients with chronic liver disease receiving hospice care in the United States. Am J Gastroenterol 2017;112:1700–1708.
[17] Paik JM, Henry L, Golabi P, Alqahtani SA, Trimble G, Younossi ZM. Presumed nonalcoholic fatty liver disease among Medicare beneficiaries with HIV, 2006–2016. Open Forum Infectious Diseases 2020;7(No. 1):509. New York: Oxford University Press.
[18] Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43:1130–1139.
[19] Consumer price index. https://www.bls.gov/cpi/. [Accessed 11 September 2020].
[20] Woodrell CD, Hansen L, Schiano TD, Goldstein NE. Palliative care for people with hepatocellular carcinoma, and specific benefits for older adults. Clin Ther 2018;40:512–525.

[21] National Hospice and Palliative Care Organization (NHPCO). Releases updated edition of Hospice Facts and Figures Report 2018. https://www.nhpco.org/nhpco-releases-updated-edition-of-hospice-facts-and-figures-report/. [Accessed 8 September 2020].
[22] Obermeyer Z, Makar M, Abujaber S, Dominici F, Block S, Cutler DM. Association between the Medicare hospice benefit and health care utilization and costs for patients with poor-prognosis cancer. JAMA 2014;312:1888–1896.
[23] Younossi Z, Stepanova M, Ong JP, Jacobson IM, Bugianesi E, Duseja A, et al. Nonalcoholic steatohepatitis is the fastest growing cause of hepatocellular carcinoma in liver transplant candidates. Clin Gastroenterol Hepatol 2019;17:748–755. e3.
[24] Noureddin M, Vipani A, Bresee C, Todo T, Kim IK, Alkhouri N, et al. NASH leading cause of liver transplant in women: updated analysis of indications for liver transplant and ethnic and gender variances. Am J Gastroenterol 2018;113:1649–1659.
[25] CMS. Medicare care choices model. https://innovation.cms.gov/files/reports/mccm-firstannrpt.pdf. [Accessed 8 September 2020].
[26] Wang SY, Aldridge MD, Gross CP, Canavan M, Cherlin E, Johnson-Hurzeler R, et al. End-of-life care intensity and hospice use: a regional-level analysis. Med Care 2016;54:672–678.
[27] Wang SY, Hall J, Pollack CE, Adelson K, Bradley EH, Long JB, et al. Trends in end-of-life cancer care in the Medicare program. J Geriatr Oncol 2016;7:116–125.
[28] Powell RA, Mwangi-Powell FN, Radbruch L, Yamey G, Krakauer EL, Spence D, et al. Putting palliative care on the global health agenda. Lancet Oncol 2015;16:131.
[29] World Health Organization. Palliative care. http://www.who.int/ncds/management/palliative-care/pc-infographics/en/. [Accessed 1 December 2020].
[30] Knaul FM, Farmer PE, Krakauer EL, De Lima L, Bhadelia A, Jiang Kwete X, et al. Alleviating the access abyss in palliative care and pain relief–an imperative of universal health coverage: the Lancet Commission report. Lancet 2018;391:1391.
[31] World Health Organization. Global atlas of palliative care at the end of life. http://www.who.int/cancer/publications/palliative-care-atlas/en/. [Accessed 1 December 2020].
[32] Sixty–seventh World Health Assembly. Strengthening of palliative care as a component of comprehensive care throughout the life course. http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R19-en.pdf. [Accessed 1 December 2020].