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ARTICLE

Treatment Patterns Among De Novo Metastatic Cancer Patients Who Died Within 1 Month of Diagnosis

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Abstract

Background: Little is known about patterns of and factors associated with treatment for de novo metastatic cancer patients who die soon after diagnosis. In this study, we examine treatment patterns for patients newly diagnosed with metastatic lung, colorectal, breast, or pancreatic cancer who died within 1 month of diagnosis.
Methods: We identified 100 848 adult patients in the National Cancer Database with de novo metastatic lung, colorectal, breast, and pancreatic cancer, diagnosed between 2004 and 2014 and who died within 1 month. We performed descriptive and multivariable logistic regression analyses to examine receipt of surgery, chemotherapy, radiation, and hormonal therapy by cancer type, adjusting for sociodemographic and clinical variables.
Results: Treatment substantially varied by cancer type, over time, age, insurance, and facility type. Surgery ranged from 0.4% in pancreatic to 28.3% in colorectal cancer (CRC) patients, chemotherapy from 5.8% among CRC to 11% in lung and breast cancer patients, and radiotherapy from 1.3% in pancreatic to 18.7% in lung cancer patients. Use of some treatments (eg, surgery for CRC and breast cancer) progressively declined between 2004 and 2014. Compared with lung cancer patients treated at National Cancer Institute-designated cancer centers, those treated at community cancer centers had 48% lower odds of radiation.
Conclusions: Treatment of patients diagnosed with imminently fatal de novo metastatic cancer varied markedly by cancer type and patient/facility characteristics. These variations warrant more research to better identify patients with imminently fatal de novo metastatic cancer who may not benefit from aggressive and expensive therapies.

Lung, colorectal, breast, and pancreatic cancers are among the leading causes of cancer death in the United States (1). De novo metastatic diseases account for a substantial proportion of the deaths from these cancers (1–3). Despite advances in cancer care, many patients diagnosed with de novo metastatic cancers die soon after diagnosis, with racial minorities, the uninsured, socioeconomically disadvantaged, and older patients disproportionately represented in this group (2,4–6). Determining the appropriateness and quality of care among these patients is difficult (7), and their treatment patterns are poorly characterized to date.

In this study, we examined contemporary patterns of care and factors associated with surgery, chemotherapy, radiation, and hormonal therapy among patients with de novo metastatic lung, colorectal, pancreas, or female breast cancer who died within 1 month of diagnosis. Our goal was to provide "real-world" information on patterns of care in patients who quickly succumbed to their disease. These patients are generally not enrolled in clinical trials. This information may be useful in identifying patients who may benefit from better integration of palliative care and may be good candidates for hospice care, which cannot always be initiated concurrently with active treatments.

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Methods

Study Population

We used data from the National Cancer Database (NCDB), a national hospital-based cancer registry database jointly sponsored by the American College of Surgeons and the American Cancer Society, which captures approximately 70% of newly diagnosed cancer patients in the United States (8,9). We included patients diagnosed between 2004 and 2014 with single primary invasive cancers; primary sites for colon and rectum, lung, breast, and pancreas; histology codes (*International Classification of Diseases for Oncology*, 3rd edition) for each cancer type (Supplementary Table 1); treated at the reporting facility; American Joint Committee on Cancer clinical stage IV (at diagnosis; pathologic used if clinical stage was missing); aged 18 years and older; vital status of "dead" at last follow-up with death within 1 month of diagnosis; no duplicate data. Patients with missing/unknown values for driving distance, insurance (also excluded non-Medicaid or non-Medicare government insurance), surgery, chemotherapy, radiotherapy, or distant site surgery were excluded (n = 11 802) (Figure 1). A sensitivity analysis showed that the characteristics of the excluded 11 802 patients were generally similar to the patients in the analytic cohort (data not shown). Variables were coded according to the Facility Oncology Registry Data Standards Manual revised for 2013 (10).

Study Variables

Primary Outcome of Interest. Our main outcome of interest was receipt or initiation of first course (first line) of treatment within 1 month after diagnosis with de novo metastatic cancer and death. Because the NCDB captures first course of treatment for a year or more after diagnosis, all therapy within 1 month after diagnosis is ascertained. Initiation of first course of treatment for each treatment type was categorized as surgery of primary site (no, yes), chemotherapy (no, yes), radiation treatment (no, yes; based on radiation to primary site or other sites), hormonal therapy in female breast cancer (no, yes), and surgery of distant site (none, other site, distant site) (Supplementary Table 2).

Control Variables. We included the following sociodemographic variables as categorized in Table 1: race/ethnicity, age, sex, diagnosis year, US census division, insurance coverage categorized by age group (18–64 years: Medicare and private, private only, Medicare and/or Medicaid, uninsured; and ≥65 years: Medicare and private, Medicare and Medicaid, Medicaid only, private only, Medicare only), area-level median income quartiles, and geographic driving distance to the reporting center (calculated using the centroid of patient's ZIP code of residence at diagnosis and street address of reporting facility). Variables of clinical characteristics were grade (1, 2, 3, 4, missing/unknown; or 1, 2, 3, missing/unknown for female breast cancer) and comorbidity score (0, 1, ≥2; generated using the sum of weighted Charlson-Deyo score [11]). For institutional variables, we included facility type and facility case volume (low, medium, high; calculated using tertiles by counting the number of all de novo metastatic cancer cases reported by each facility during the study period by diagnosis year).

Statistical Analysis

We conducted descriptive analyses of patient characteristics and treatment by cancer type. We used Cochrane-Armitage trend tests to assess changes in treatment by diagnosis year and separate multivariable logistic regression analyses to assess the association between sociodemographic, clinical, and facility characteristics and treatment with surgery, radiation therapy, chemotherapy, and hormonal therapy in female breast cancer. All control variables were included in the models. Statistical significance was determined based on two-sided *P* value less than 0.05. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). Our study received exempt status from the institutional review board of the Morehouse School of Medicine, Atlanta, GA. Because patients with lung cancer included non-small cell and small cell histologic types, we

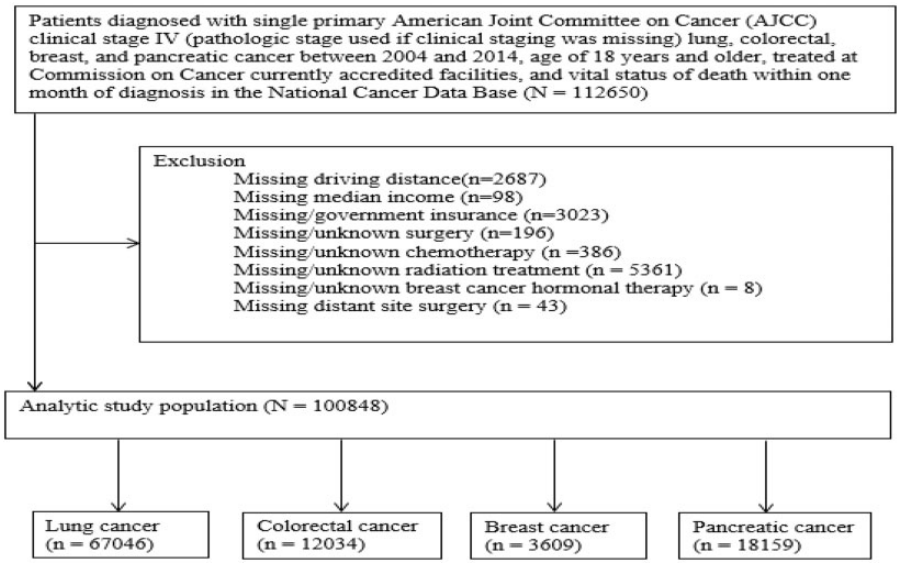

Figure 1. Cohort selection flowchart for patients diagnosed with de novo metastatic lung, colorectal, breast, or pancreatic cancer in the National Cancer Database (2004–2014).

Table 1. Characteristics of patients diagnosed with de novo metastatic cancer and died within 1 month of diagnosis in the NCDB by cancer type*

Variable	Lung cancer No. (%)	Colorectal cancer No. (%)	Breast cancer No. (%)	Pancreatic cancer No. (%)
Total	67046 (66.5)	12034 (11.9)	3609 (3.6)	18159 (18.0)
Race/ethnicity				
NH white	53 083 (79.2)	8790 (73.0)	2634 (73.0)	13 375 (73.7)
NH black	6016 (9.0)	1647 (13.7)	522 (14.5)	2262 (12.5)
Hispanic	1708 (2.5)	465 (3.9)	120 (3.3)	831 (4.6)
Other	1261 (1.9)	284 (2.4)	82 (2.3)	485 (2.7)
Unknown	4978 (7.4)	848 (7.0)	251 (7.0)	1206 (6.6)
Diagnosis age, y				
18–39	165 (0.2)	99 (0.8)	57 (1.6)	59 (0.3)
40–54	5150 (7.7)	915 (7.6)	458 (12.7)	1266 (7.0)
55–64	13 248 (19.8)	1879 (15.6)	843 (23.4)	3252 (17.9)
65–74	20 677 (30.8)	2622 (21.8)	807 (22.4)	4823 (26.6)
75–84	20 203 (30.1)	3730 (31)	871 (24.1)	5582 (30.7)
85+	7603 (11.3)	2789 (23.2)	573 (15.9)	3177 (17.5)
Sex				
Male	37 601 (56.1)	5902 (49.0)	0 (0)	9383 (51.7)
Female	29 445 (43.9)	6132 (51.0)	3609 (100)	8776 (48.3)
Diagnosis year				
2004	5197 (7.8)	1031 (8.6)	285 (7.9)	1368 (7.5)
2005	5329 (7.9)	990 (8.2)	282 (7.8)	1348 (7.4)
2006	5235 (7.8)	1036 (8.6)	281 (7.8)	1363 (7.5)
2007	5167 (7.7)	969 (8.1)	273 (7.6)	1357 (7.5)
2008	5658 (8.4)	1046 (8.7)	313 (8.7)	1621 (8.9)
2009	5860 (8.7)	1111 (9.2)	329 (9.1)	1644 (9.1)
2010	6801 (10.1)	1144 (9.5)	351 (9.7)	1727 (9.5)
2011	6904 (10.3)	1140 (9.5)	375 (10.4)	1845 (10.2)
2012	6855 (10.2)	1193 (9.9)	338 (9.4)	1919 (10.6)
2013	7045 (10.5)	1224 (10.2)	384 (10.6)	1990 (11.0)
2014	6995 (10.4)	1150 (9.6)	398 (11.0)	1977 (10.9)
Grade (non-breast cancer)				
Grade 1	525 (0.8)	350 (2.9)	107 (3.0)	182 (1.0)
Grade 2	2962 (4.4)	3197 (26.6)	713 (19.8)	922 (5.1)
Grade 3	12 842 (19.2)	2454 (20.4)	945 (26.2)	2329 (12.8)
Grade 4	3980 (5.9)	324 (2.7)	31 (0.9)	161 (0.9)
Missing/unknown	46 737 (69.7)	5709 (47.4)	1813 (50.2)	14 565 (80.2)
Grade (breast cancer)				
Grade 1			107 (3.0)	
Grade 2			713 (19.8)	
Grade 3			976 (27.0)	
Missing/unknown			1813 (50.2)	
Comorbidity score				
0	31 159 (46.5)	7340 (61.0)	2343 (64.9)	10 005 (55.1)
1	21 849 (32.6)	2956 (24.6)	781 (21.6)	5166 (28.4)
2+	14 038 (20.9)	1738 (14.4)	485 (13.4)	2988 (16.5)
US census division				
New England	3881 (5.8)	704 (5.9)	210 (5.8)	1148 (6.3)
Middle Atlantic	8964 (13.4)	1823 (15.1)	635 (17.6)	2886 (15.9)
South Atlantic	15 314 (22.8)	2718 (22.6)	786 (21.8)	3949 (21.7)
East North Central	13 118 (19.6)	2281 (19)	666 (18.5)	3381 (18.6)
East South Central	6149 (9.2)	934 (7.8)	272 (7.5)	1215 (6.7)
West North Central	5425 (8.1)	883 (7.3)	232 (6.4)	1342 (7.4)
West South Central	5244 (7.8)	978 (8.1)	296 (8.2)	1461 (8.0)
Mountain	2237 (3.3)	440 (3.7)	118 (3.3)	630 (3.5)
Pacific	6714 (10.0)	1273 (10.6)	394 (10.9)	2147 (11.8)
Facility type				
Community cancer program	9699 (14.5)	1835 (15.2)	533 (14.8)	2336 (12.9)
Comprehensive community cancer program	34 315 (51.2)	6050 (50.3)	1759 (48.7)	8968 (49.4)
Teaching/research center	13 382 (20)	2346 (19.5)	742 (20.6)	3877 (21.4)
NCI-designated center	2586 (3.9)	418 (3.5)	163 (4.5)	1068 (5.9)
Community networked program	7064 (10.5)	1385 (11.5)	412 (11.4)	1910 (10.5)

(continued)

Table 1. (continued)

Variable	Lung cancer No. (%)	Colorectal cancer No. (%)	Breast cancer No. (%)	Pancreatic cancer No. (%)
Case volume				
Low	7148 (10.7)	1482 (12.3)	414 (11.5)	1903 (10.5)
Medium	19 385 (28.9)	3589 (29.8)	1101 (30.5)	5265 (29.0)
High	40 513 (60.4)	6963 (57.9)	2094 (58)	10991 (60.5)
Insurance				
Uninsured	3240 (4.8)	578 (4.8)	298 (8.3)	610 (3.4)
Medicare with private or supplement	1077 (1.6)	128 (1.1)	39 (1.1)	219 (1.2)
Medicare and/or Medicaid	6321 (9.4)	907 (7.5)	377 (10.4)	1310 (7.2)
Private only	7925 (11.8)	1280 (10.6)	644 (17.8)	2438 (13.4)
Medicare with private or supplement	23 049 (34.4)	4319 (35.9)	1014 (28.1)	6788 (37.4)
Medicare and Medicaid	4020 (6.0)	756 (6.3)	184 (5.1)	1018 (5.6)
Medicaid only	882 (1.3)	148 (1.2)	47 (1.3)	269 (1.5)
Medicare only	15 410 (23.0)	3006 (25.0)	788 (21.8)	4022 (22.1)
Private only	5122 (7.6)	912 (7.6)	218 (6.0)	1485 (8.2)
Driving distance, miles				
<12.5	38 340 (57.2)	7618 (63.3)	2319 (64.3)	10 820 (59.6)
12.5–49.9	21 799 (32.5)	3448 (28.7)	1039 (28.8)	5455 (30.0)
≥50	6907 (10.3)	968 (8.0)	251 (7.0)	1884 (10.4)
Median income, $†				
<38 000	14 978 (22.3)	2654 (22.1)	793 (22)	3657 (20.1)
38 000–47 999	17 854 (26.6)	3061 (25.4)	848 (23.5)	4386 (24.2)
48 000–62 999	17 794 (26.5)	3066 (25.5)	894 (24.8)	4770 (26.3)
63 000+	16 420(24.5)	3253 (27.0)	1074 (29.8)	5346 (29.4)

*P values (two-sided) were calculated using χ^2 test and were statistically significant (<.05) for all variables. NCDB = National Cancer Database.; NCI = National Cancer Institute; NH = Non-Hispanic;
†Area-level median household income quartiles based on 2012 American Community Survey.

conducted a supplemental analysis to assess treatment for patients diagnosed with small-cell lung cancer.

Results

Patient Characteristics

We included 100 848 patients diagnosed with de novo metastatic lung, colorectal, female breast, and pancreatic cancer who died within 1 month of diagnosis. Of these patients, 66.5% were lung, 18% pancreatic, 12% colorectal (CRC), and 3.6% female breast cancer patients (Table 1). Overall, most patients were non-Hispanic white (77%), though the proportions of non-Hispanic blacks were relatively higher among patients with colorectal, breast, and pancreatic cancer. Almost one-half of all patients (44%) were 75 years and older with some variation by cancer type. A large proportion of patients (60%) received treatment at a high de novo metastatic case volume treatment facility. Lung cancer had the highest percentage (21%) of patients with a comorbidity score of 2 or higher.

Treatment Patterns and Trends by Cancer Type

Overall, 12.5%, 29%, 34.9%, and 37.2% of patients with pancreatic, lung, breast, and CRC received at least one treatment modality, respectively. Figure 2 illustrates percentage of patients who received surgery, radiation, chemotherapy, or multiple treatments by cancer type. Overall, 72.6% of patients did not receive any type of cancer-directed treatment. Surgery of the primary tumor was least common among pancreatic cancer patients (0.4%) and most common among CRC (28.3%) patients. Chemotherapy use ranged from 5.8% for colorectal to 11.3% for lung or breast cancer. Radiotherapy ranged from 1.3% among patients with pancreatic cancer to 18.7% among patients with lung cancer. In the supplemental analysis, chemotherapy was relatively common among patients diagnosed with small-cell lung cancer (27%) (Supplementary Table 3). Among women with hormone receptor-positive breast cancer, 23.9% received hormonal therapy. Among women with hormone receptor-negative and Human Epidermal Growth Factor Receptor 2-positive breast cancer diagnosed between 2010 and 2014, 33% received chemotherapy (data not shown). Surgery to a distant (metastatic) site was highest in patients with CRC (4.6%).

Over the study period, surgery of primary tumor for CRC and breast cancer, chemotherapy and radiation treatment for lung cancer and breast, and chemotherapy for pancreatic cancer steadily declined ($P_{trend} < .01$ for all) (Table 2).

Factors Associated with Receipt or Initiation of Treatment

Table 3 shows adjusted odds ratios for selected factors associated with treatment by cancer type. Compared with patients aged 18–39 years, patients aged 75 years and older had 46–70% lower odds of initiating radiation treatment and 77–92% lower odds of initiating chemotherapy for lung cancer. Older patients had 65–99% lower odds of initiating chemotherapy for breast cancer compared with patients aged 18–39 years. Patients with higher Charlson-Deyo comorbidity score (2+) had lower odds of initiating chemotherapy among pancreatic cancer patients (25% lower odds) and radiation among lung cancer patients (33% lower odds) compared with those with no comorbid conditions.

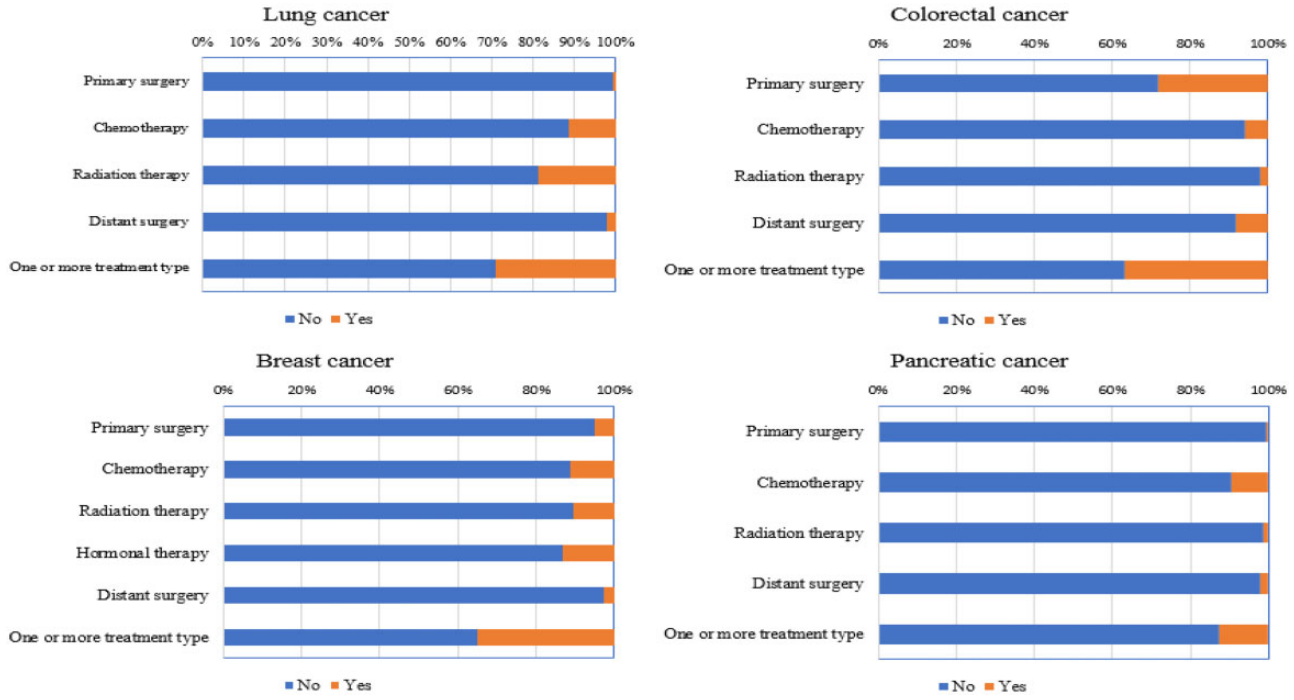

Figure 2. Percentage of patients who received treatment among those diagnosed with de novo metastatic cancer and died within 1 month of diagnosis.

Table 2. Trends in receipt/initiation of treatment in patients with de novo metastatic lung, colorectal, breast, and pancreas cancer who died within 1 month of diagnosis

Cancer type	Treatment type, %	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	P_{trend}
Lung cancer	Primary surgery	0.7	0.9	0.8	0.7	0.7	0.6	0.6	0.6	0.7	0.5	0.5	.0017
	Chemotherapy	14.7	13.2	13.3	12.3	12.3	11.9	10.4	10.9	9.5	9.5	9.3	<.0001
	Radiation	24.0	22.3	22.0	21.6	20.4	18.4	16.4	16.9	16.2	15.6	16.1	<.0001
	Distant site surgery	1.4	1.3	1.3	1.4	1.7	1.5	1.2	1.4	1.2	1.3	1.5	.7474
Colorectal cancer	Primary surgery	35.4	34.8	36.0	35.6	28.8	29.1	28.2	23.8	21.4	22.7	19.9	<.0001
	Chemotherapy	5.1	5.2	5.9	6.2	5.6	6.7	5.2	4.7	6.5	5.3	7.1	.2269
	Radiation	2.3	1.4	2.0	1.2	2.3	1.9	2.0	1.5	2.4	1.8	1.8	.9842
	Distant site surgery	5.3	5.7	7.1	4.9	4.7	4.4	3.3	4.8	3.2	3.5	3.4	<.0001
Breast cancer	Primary surgery	8.8	8.5	8.2	6.6	4.5	5.2	3.7	4.0	3.9	2.6	1.8	<.0001
	Chemotherapy	12.3	14.5	12.8	13.6	12.8	11.6	14.0	8.8	8.0	8.6	10.1	.0016
	Radiation	10.5	14.9	11.4	13.2	9.3	10.3	11.7	9.3	8.9	9.9	7.5	.0069
	Hormonal therapy*	28.6	23.5	24.3	27.3	20.7	19.2	21.6	21.4	26.7	30.1	20.0	.6880
	Distant site surgery	1.1	2.8	2.5	2.2	1.6	2.1	2.9	2.7	2.1	1.6	1.3	.6179
Pancreatic cancer	Primary surgery	0.7	0.7	0.3	0.7	0.4	0.2	0.3	0.3	0.3	0.2	0.2	.0016
	Chemotherapy	10.1	10.0	11.2	10.2	10.1	9.2	9.4	8.9	8.4	8.8	7.9	.0002
	Radiation	1.1	1.3	1.2	1.4	2.0	1.0	1.5	1.1	1.1	1.2	1.1	.4397
	Distant site surgery	0.9	1.4	1.0	0.8	1.2	1.0	1.1	1.0	1.0	0.7	0.5	.0358

*For hormone receptor-positive breast cancer. P_{trend} values (two-sided) were calculated using Cochrane-Armitage trend test.

Compared with privately insured patients, uninsured patients had 47% lower odds of surgery of primary tumor for CRC and 14% lower odds of radiotherapy for lung cancer. Uninsured patients had 35–56% lower odds of initiating chemotherapy for each cancer type compared with their privately insured counterparts.

Compared with patients treated at National Cancer Institute (NCI)-designated cancer centers, those treated at community cancer centers had 40% lower odds of surgery on the primary tumor and 48% lower odds for radiation for lung cancer. However, CRC patients treated at community cancer centers and comprehensive community cancer centers (vs NCI-designated cancer centers) had more than twofold higher odds of surgical resection of their primary tumor. Patients with CRC treated at teaching/research cancer centers (vs NCI-designated cancer centers) had 2.4 times higher odds of receiving radiation. Compared with CRC patients treated at NCI-designated cancer centers, those treated at comprehensive community and community

Table 3. Adjusted odds ratios predicting receipt of treatment among patients with de novo metastatic cancer who died within 1 month of diagnosis by cancer type and treatment modality

Treatment modality	Lung cancer OR (95% CI)	Colorectal cancer OR (95% CI)	Breast cancer OR (95% CI)	Pancreatic cancer OR (95% CI)
Primary surgery				
Grade				
1 (ref)	1.00	1.00	1.00	1.00
2	0.35 (0.23 to 0.53)	1.28 (1.01 to 1.63)	1.93 (0.66 to 5.65)	2.53 (0.51 to 12.45)
3	0.19 (0.13 to 0.27)	1.30 (1.02 to 1.67)	4.44 (1.55 to 12.70)	1.46 (0.31 to 7.00)
4	0.07 (0.04 to 0.12)	3.57 (2.52 to 5.06)	—*	5.70 (1.00 to 32.37)
Missing/unknown	0.03 (0.02 to 0.05)	0.03 (0.02 to 0.04)	0.22 (0.07 to 0.71)†	0.10 (0.02 to 0.53)
US census division				
East North Central (ref)	1.00	1.00	1.00	1.00
East South Central	1.55 (1.05 to 2.27)	1.31 (1.05 to 1.63)	1.47 (0.74 to 2.95)	2.88 (1.06 to 7.82)
Middle Atlantic	2.03 (1.45 to 2.84)	0.84 (0.70 to 1.00)	0.91 (0.52 to 1.61)	1.82 (0.67 to 4.92)
Mountain	1.01 (0.55 to 1.86)	1.31 (0.98 to 1.74)	1.73 (0.69 to 4.38)	0.21 (0.03 to 1.76)‡
New England	1.23 (0.74 to 2.04)	0.88 (0.68 to 1.14)	0.49 (0.18 to 1.33)	0.21 (0.03 to 1.76)
Pacific	1.43 (0.96 to 2.12)	0.94 (0.76 to 1.15)	0.86 (0.42 to 1.76)	1.61 (0.53 to 4.89)‡
South Atlantic	1.21 (0.87 to 1.66)	1.15 (0.98 to 1.35)	1.36 (0.83 to 2.23)	1.74 (0.72 to 4.22)
West North Central	1.23 (0.81 to 1.88)	1.04 (0.84 to 1.30)	0.66 (0.29 to 1.48)	0.74 (0.20 to 2.72)
West South Central	0.91 (0.57 to 1.45)	1.29 (1.04 to 1.60)	1.19 (0.59 to 2.39)	1.61 (0.55 to 4.72)
Facility type				
NCI-designated center (ref)	1.00	1.00	1.00§	1.00
Community cancer program	0.60 (0.36 to 1.00)	2.34 (1.63 to 3.35)	3.44 (1.83 to 6.47)	1.60 (0.45 to 5.64)
Community networked program	0.99 (0.61 to 1.61)	1.99 (1.38 to 2.85)	2.00 (1.00 to 4.02)	0.96 (0.26 to 3.62)
Comprehensive community cancer program	0.61 (0.39 to 0.93)	2.56 (1.83 to 3.57)	2.56 (1.53 to 4.28)	0.94 (0.31 to 2.83)
Teaching/research center	0.76 (0.49 to 1.18)	1.80 (1.28 to 2.54)	—§	1.38 (0.44 to 4.32)
Insurance‖				
Private (ref)	1.00	1.00	1.00	1.00
Medicare	0.58 (0.38 to 0.90)	0.70 (0.54 to 0.91)	0.73 (0.38 to 1.42)	0.89 (0.44 to 1.82)
Medicaid	0.80 (0.61 to 1.05)	0.96 (0.82 to 1.13)	0.77 (0.47 to 1.28)	0.18 (0.04 to 0.81)¶
Uninsured	0.90 (0.59 to 1.38)	0.53 (0.40 to 0.71)	0.46 (0.22 to 0.97)	—¶
Chemotherapy				
Diagnosis age, y				
18–39 (ref)	1.00	1.00	1.00	1.00
40–54	0.56 (0.39 to 0.81)	0.64 (0.36 to 1.14)	0.34 (0.18 to 0.63)	0.48 (0.26 to 0.89)
55–64	0.47 (0.33 to 0.67)	0.47 (0.27 to 0.82)	0.24 (0.13 to 0.44)	0.42 (0.23 to 0.76)
65–74	0.40 (0.28 to 0.57)	0.33 (0.18 to 0.59)	0.12 (0.06 to 0.25)	0.32 (0.17 to 0.59)
75–84	0.23 (0.16 to 0.32)	0.17 (0.10 to 0.32)	0.05 (0.02 to 0.09)	0.18 (0.10 to 0.33)
85+	0.08 (0.06 to 0.12)	0.05 (0.03 to 0.10)	0.01 (0.01 to 0.03)	0.04 (0.02 to 0.09)
Grade				
Grade 1 (ref)	1.00	1.00	1.00	1.00
Grade 2	0.66 (0.49 to 0.88)	1.41 (0.84 to 2.38)	1.54 (0.66 to 3.57)	0.98 (0.59 to 1.61)
Grade 3	0.75 (0.57 to 0.98)	1.40 (0.83 to 2.37)	2.82 (1.24 to 6.46)	0.97 (0.60 to 1.56)
Grade 4	2.08 (1.58 to 2.73)	1.57 (0.77 to 3.20)	—*	0.67 (0.33 to 1.36)
Missing/unknown	0.85 (0.65 to 1.10)	0.81 (0.48 to 1.35)	1.06 (0.47 to 2.43)†	0.74 (0.47 to 1.18)
Comorbidity score				
0 (ref)	1.00	1.00	1.00	1.00
1	1.01 (0.95 to 1.06)	0.85 (0.69 to 1.04)	0.94 (0.70 to 1.26)	0.96 (0.85 to 1.08)
2+	0.93 (0.87 to 0.99)	0.84 (0.66 to 1.07)	0.88 (0.62 to 1.25)	0.75 (0.64 to 0.87)
US census division				
East North Central (ref)	1.00	1.00	1.00	1.00
East South Central	0.98 (0.89 to 1.08)	1.15 (0.83 to 1.60)	1.55 (0.97 to 2.46)	1.06 (0.84 to 1.33)
Middle Atlantic	0.84 (0.77 to 0.92)	0.83 (0.62 to 1.11)	0.65 (0.43 to 0.98)	0.80 (0.67 to 0.95)
Mountain	0.98 (0.85 to 1.12)	0.74 (0.45 to 1.19)	1.21 (0.65 to 2.27)	0.83 (0.62 to 1.12)
New England	0.70 (0.62 to 0.80)	0.77 (0.50 to 1.17)	0.71 (0.40 to 1.26)	0.83 (0.66 to 1.06)
Pacific	0.69 (0.62 to 0.76)	0.59 (0.41 to 0.84)	0.97 (0.62 to 1.50)	0.69 (0.56 to 0.84)
South Atlantic	0.83 (0.77 to 0.90)	1.04 (0.81 to 1.33)	0.97 (0.68 to 1.40)	0.82 (0.70 to 0.97)
West North Central	0.98 (0.89 to 1.08)	1.21 (0.87 to 1.67)	0.86 (0.52 to 1.43)	1.17 (0.95 to 1.44)
West South Central	0.94 (0.85 to 1.04)	0.94 (0.67 to 1.31)	1.00 (0.63 to 1.59)	0.85 (0.68 to 1.06)
Insurance‖				
Private (ref)	1.00	1.00	1.00	1.00
Medicaid	0.73 (0.65 to 0.81)	0.59 (0.43 to 0.81)	0.51 (0.35 to 0.76)	0.58 (0.46 to 0.74)

(continued)

Table 3. (continued)

Treatment modality	Lung cancer OR (95% CI)	Colorectal cancer OR (95% CI)	Breast cancer OR (95% CI)	Pancreatic cancer OR (95% CI)
Medicare	0.85 (0.79 to 0.91)	0.66 (0.52 to 0.82)	0.86 (0.60 to 1.23)	0.78 (0.67 to 0.90)
Uninsured	0.65 (0.58 to 0.73)	0.44 (0.32 to 0.62)	0.52 (0.36 to 0.77)	0.50 (0.37 to 0.66)
Median income, $**				
63 000+ (ref)	1.00	1.00	1.00	1.00
<38 000	0.81 (0.75 to 0.87)	0.73 (0.56 to 0.94)	0.68 (0.48 to 0.96)	0.66 (0.56 to 0.77)
38 000–47 999	0.84 (0.78 to 0.90)	0.88 (0.70 to 1.11)	0.70 (0.51 to 0.97)	0.64 (0.55 to 0.75)
48 000–62 999	0.91 (0.85 to 0.98)	0.83 (0.66 to 1.04)	0.72 (0.53 to 0.99)	0.78 (0.68 to 0.89)
Radiation				
Diagnosis age, y				
18–39 (ref)	1.00	1.00	1.00	1.00
40–54	1.01 (0.71 to 1.44)	0.81 (0.27 to 2.41)	2.24 (0.76 to 6.55)	1.82 (0.24 to 13.72)
55–64	0.89 (0.63 to 1.26)	0.71 (0.25 to 2.07)	2.00 (0.69 to 5.81)	1.07 (0.14 to 7.98)
65–74	0.77 (0.54 to 1.09)	0.73 (0.24 to 2.23)	1.61 (0.53 to 4.89)	0.76 (0.10 to 5.74)
75–84	0.54 (0.38 to 0.76)	0.54 (0.18 to 1.67)	1.23 (0.40 to 3.77)	0.63 (0.08 to 4.79)
85+	0.30 (0.21 to 0.43)	0.25 (0.08 to 0.84)	0.98 (0.31 to 3.09)	0.20 (0.02 to 1.66)
Grade				
Grade 1 (ref)	1.00	1.00	1.00	1.00
Grade 2	1.65 (1.29 to 2.11)	0.77 (0.36 to 1.65)	0.89 (0.48 to 1.65)	1.51 (0.34 to 6.70)
Grade 3	1.54 (1.22 to 1.95)	0.98 (0.46 to 2.11)	0.97 (0.52 to 1.78)	1.52 (0.36 to 6.37)
Grade 4	0.89 (0.70 to 1.14)	1.08 (0.36 to 3.24)	—*	1.57 (0.25 to 9.65)
Missing/unknown	0.92 (0.73 to 1.17)	0.53 (0.25 to 1.12)	0.63 (0.35 to 1.14)†	1.15 (0.28 to 4.71)
Comorbidity score				
0 (ref)	1.00	1.00	1.00	1.00
1	0.83 (0.79 to 0.86)	0.92 (0.66 to 1.28)	0.83 (0.62 to 1.10)	0.78 (0.57 to 1.06)
2+	0.67 (0.64 to 0.71)	0.93 (0.63 to 1.39)	0.90 (0.65 to 1.26)	0.64 (0.42 to 0.97)
US census division				
East North Central (ref)	1.00	1.00	1.00	1.00
East South Central	0.89 (0.82 to 0.96)	0.77 (0.44 to 1.35)	2.05 (1.30 to 3.21)	1.18 (0.66 to 2.08)
Middle Atlantic	0.97 (0.90 to 1.04)	0.58 (0.36 to 0.94)	1.15 (0.79 to 1.67)	0.92 (0.57 to 1.50)
Mountain	0.77 (0.68 to 0.87)	0.52 (0.22 to 1.24)	1.00 (0.51 to 1.97)	0.59 (0.23 to 1.51)
New England	1.03 (0.94 to 1.14)	0.76 (0.40 to 1.42)	1.07 (0.63 to 1.82)	0.81 (0.41 to 1.60)
Pacific	0.72 (0.67 to 0.79)	0.66 (0.38 to 1.13)	1.03 (0.66 to 1.60)	0.86 (0.50 to 1.49)
South Atlantic	0.86 (0.81 to 0.92)	0.60 (0.39 to 0.90)	1.09 (0.76 to 1.57)	1.33 (0.88 to 1.99)
West North Central	0.88 (0.81 to 0.96)	1.03 (0.61 to 1.73)	0.74 (0.42 to 1.29)	1.21 (0.70 to 2.09)
West South Central	0.82 (0.76 to 0.90)	0.86 (0.51 to 1.45)	0.85 (0.51 to 1.42)	0.75 (0.41 to 1.39)
Facility type				
NCI-designated center (ref)	1.00	1.00	1.00	1.00
Community cancer program	0.52 (0.47 to 0.58)	1.34 (0.51 to 3.48)	0.61 (0.33 to 1.13)	1.24 (0.57 to 2.72)
Community networked program	0.72 (0.64 to 0.80)	2.18 (0.87 to 5.41)	0.84 (0.46 to 1.52)	1.19 (0.54 to 2.62)
Comprehensive community cancer program	0.68 (0.62 to 0.75)	1.88 (0.80 to 4.41)	0.85 (0.51 to 1.42)	1.78 (0.91 to 3.47)
Teaching/research center	0.72 (0.65 to 0.80)	2.39 (1.00 to 5.67)	0.86 (0.50 to 1.48)	1.55 (0.77 to 3.12)
Case volume				
Low (ref)	1.00	1.00	1.00	1.00
Medium	1.04 (0.96 to 1.12)	0.98 (0.59 to 1.63)	0.93 (0.63 to 1.37)	0.75 (0.47 to 1.18)
High	0.91 (0.85 to 0.98)	1.16 (0.71 to 1.89)	0.79 (0.54 to 1.17)	0.68 (0.44 to 1.08)
Insurance‖				
Private (ref)	1.00	1.00	1.00	1.00
Medicaid	0.87 (0.80 to 0.95)	0.86 (0.49 to 1.51)	1.11 (0.74 to 1.67)	0.60 (0.32 to 1.12)
Medicare	0.88 (0.83 to 0.93)	0.75 (0.51 to 1.12)	0.96 (0.66 to 1.37)	0.96 (0.65 to 1.41)
Uninsured	0.86 (0.79 to 0.95)	1.35 (0.81 to 2.27)	0.83 (0.53 to 1.28)	0.80 (0.43 to 1.50)
Distant surgery				
Facility type				
NCI-designated center (ref)	1.00	1.00	1.00	1.00
Community cancer program	0.27 (0.19 to 0.38)	0.43 (0.25 to 0.75)	1.46 (0.37 to 5.68)	0.62 (0.25 to 1.54)
Community networked program	0.59 (0.44 to 0.79)	0.91 (0.54 to 1.54)	1.60 (0.43 to 6.00)	1.76 (0.81 to 3.81)
Comprehensive community cancer program	0.42 (0.33 to 0.54)	0.52 (0.32 to 0.84)	0.74 (0.21 to 2.60)	1.25 (0.63 to 2.51)
Teaching/research center	0.66 (0.51 to 0.85)	0.60 (0.36 to 0.99)	1.26 (0.35 to 4.54)	0.84 (0.39 to 1.79)
Insurance‖				
Private (ref)	1.00	1.00	1.00	1.00
Medicaid	0.89 (0.68 to 1.15)	0.69 (0.42 to 1.12)	0.78 (0.27 to 2.27)	0.94 (0.44 to 1.97)
Medicare	0.82 (0.68 to 1.00)	1.04 (0.78 to 1.37)	1.15 (0.53 to 2.47)	1.16 (0.74 to 1.83)
Uninsured	0.99 (0.74 to 1.31)	0.48 (0.25 to 0.89)	0.45 (0.12 to 1.64)	0.56 (0.20 to 1.64)

(continued)

Table 3. (continued)

Treatment modality	Lung cancer OR (95% CI)	Colorectal cancer OR (95% CI)	Breast cancer OR (95% CI)	Pancreatic cancer OR (95% CI)
Driving distance, miles				
<12.5 (ref)	1.00	1.00	1.00	1.00
12.5–49.9	1.39 (1.19 to 1.61)	1.01 (0.82 to 1.24)	1.33 (0.79 to 2.24)	1.09 (0.76 to 1.54)
≥50	2.12 (1.74 to 2.58)	1.33 (0.95 to 1.86)	2.39 (1.05 to 5.46)	1.35 (0.83 to 2.22)
Median income, $**				
63 000+ (ref)	1.00	1.00	1.00	1.00
<38 000	0.84 (0.69 to 1.04)	0.86 (0.65 to 1.15)	0.41 (0.18 to 0.94)	0.81 (0.49 to 1.32)
38 000–47 999	0.83 (0.69 to 1.01)	0.93 (0.72 to 1.20)	0.71 (0.37 to 1.37)	0.72 (0.45 to 1.15)
48 000–62 999	0.78 (0.64 to 0.94)	0.96 (0.75 to 1.23)	0.83 (0.45 to 1.54)	1.00 (0.67 to 1.52)

*Not applicable; CI, confidence interval; NCI, National Cancer Institute; OR, odds ratio; ref, reference.
†Missing/unknown.
‡Mountain and New England combined.
§Reference is NCI/teaching/research center.
‖Uninsured, Medicaid, Medicare, and private were categorized regardless of age.
¶Combined Medicaid and uninsured.
**Area-level median household income quartiles based on 2012 American Community Survey.

cancer centers had 48–57% lower odds of distant site surgery. Patients treated at community cancer centers, community networked centers, and comprehensive community cancer centers had higher odds of surgery to the primary tumor for breast cancer compared with those treated at NCI-designated/teaching/research centers.

Discussion

Using a large national database, we documented marked variations in treatment by cancer type as well as patient and facility characteristics among patients with de novo metastatic cancer who died within 1 month of diagnosis. Specifically, we identified lower odds of chemotherapy for all cancer types and radiation for lung cancer among older patients, lower odds of chemotherapy and radiation for lung and pancreatic cancer among patients with higher comorbidity score, and lower odds of chemotherapy for lung and breast cancer among uninsured patients. Further, treatment modalities varied remarkably by facility type. Our results also revealed declining trends for most treatment modalities by cancer type over the study period.

Treatment planning for patients diagnosed with imminently fatal cancer is complex. Physicians and patients and their families are faced with fundamental decisions about cancer-directed treatment (12). These decisions are influenced by patient/physician preferences, goals of care, treatment response, psychological status, support systems, symptom and disease burden, access to care, cost, organ function, and performance status (13,14). Patients diagnosed with de novo metastatic cancer generally are urged to make decisions about treatment soon after diagnosis. Although recent innovations in treatment and better access to care are improving survival and quality of life among patients with de novo metastatic cancer, these survival benefits may not apply to patients who are extremely ill at the time of diagnosis.

Our findings of variations in treatment among patients with de novo metastatic cancer who died within 1 month of diagnosis suggest that some of these patients received ineffective treatment. Such treatment at the end of life could also contribute to higher cost of care (15). Although no previous studies specifically report on rates of treatment among patients with de novo metastatic cancer who died within 1 month of diagnosis by cancer type, a number of studies have reported variations in overall rates of treatment among patients diagnosed with metastatic cancer (16–19). For example, some studies reported that about 40–60% of women with de novo metastatic breast cancer received surgical treatment of the primary tumor (17,20,21). High rates of chemotherapy among patients with metastatic breast cancer have also been reported (20–22). Differences in study population selection such as restriction to those who died soon after diagnosis with de novo metastatic cancer, performance status, use of contemporary and larger sample size data, and other unmeasured factors likely explain the differences in rates of treatment between our study and the previous studies. Overestimation of survival of terminally ill cancer patients by clinicians and patients' misunderstanding of the palliative nature of treatment for metastatic cancer could also contribute to variations in planning of aggressive treatment (23,24). For example, Weeks et al. (24) reported that 69% of de novo metastatic lung cancer and 81% of de novo metastatic CRC patients did not understand that chemotherapy was not at all likely to cure their cancer.

Though not specified by initiation time of within 1 month between diagnosis and death, rates of primary tumor resection and chemotherapy are reportedly high among patients with metastatic CRC (19,25,26). Our finding of relatively higher rates of primary and distant site surgery among patients with de novo metastatic CRC were also consistent with previous studies (27), likely because of the palliation often provided by primary site surgery in CRC and the value of metastasectomy in selected patients with CRC. Using Medicare (65 years and older) patients with stage IIIB and IV non-small cell lung cancer and without defining time for receipt of treatment, Ramsey et al. (28) reported that in 1994–1999, 31% received chemotherapy, 8% surgery, and 53% radiation treatment. Furthermore, Potosky et al. (29) reported that in 1996 rates of treatment for stage IV non-small cell lung cancer patients were 41% for chemotherapy and 31% for radiation treatment. The near-zero rates of surgery and very low rates of chemotherapy among patients with de novo stage IV pancreatic cancer in our study were similar to other reports and reflect guideline adherence, baseline poor performance status, high comorbidity, and/or symptom burden (30,31). Whether the patients who received various types of

treatments in our study were in fact receiving ineffective treatments still needs further research.

Our finding of marked variation in treatment by age, comorbidity, insurance status, and facility characteristics suggests the presence both of appropriate and inappropriate decision making. Although the elderly and relatively infirm may appropriately be excluded from toxic or high-risk treatment, variation in care by insurance status or environment of care delivery may reflect problematic barriers to care. Previous studies reported disproportionate representation of higher comorbid conditions, minorities, uninsured, socioeconomically disadvantaged, or older age patients among those who died early after diagnosis of cancer (2,4–6,26,29,32). This may contribute to higher rates of early death reported in these patients (33). Differences in aggressiveness of treatments by cancer type were also reported (15,34), which could be explained by differences in aggressiveness of each cancer type, prediction of expected survival, patient/physician preferences, and prevalence of poor performance status (12,35–37). For instance, patients who expected to live at least 6 months had more that twofold higher odds of favoring life-extending therapy over comfort care compared with patients who thought there was at least a 10% probability that they would not live 6 months (12). Furthermore, higher odds of treatment among patients with younger age, lower comorbidity score, and private insurance were in line with previous studies that reported on treatment patterns in the last month of life (32), suggesting more liberty toward aggressive treatment among physicians and/or patients.

We found decreases in surgical resection between 2004 and 2014 for all four de novo metastatic cancer types, which is consistent with other studies (17,19,25,38,39), suggesting evolving preferences and recognition of the limited value of surgery in this setting. The National Comprehensive Cancer Network guidelines do not recommend surgical resection of primary tumor for most patients with de novo metastatic cancers, except for very few patients with specific characteristics such as resectable metastatic CRC (40,41). Improved systemic treatments, such as targeted therapies, and greater acceptance and awareness of benefits of hospice care may contribute to this declining rate of resection of primary tumors (18,19).

We also identified trends in chemotherapy for lung, breast, and pancreatic cancer that are inconsistent with studies that reported increasing trends in chemotherapy among patients diagnosed with de novo metastatic cancers (16,18,28,42). Differences are likely because our sample was restricted to patients who died within 1 month of diagnosis, whereas the other study samples were not similarly restricted. Previous studies also revealed high rates of treatment at the end of life among patients diagnosed with metastatic cancers (15,16,43,44). However, there were also reports of decreasing trends in chemotherapy and radiation treatment among lung cancer patients at the end of life (15,45). Declining trends in use of chemotherapy and radiation treatment may suggest increasing recognition of the importance of quality of life, cost vs benefit of care in decision making, and greater integration of patient preferences (14). Patients diagnosed with de novo metastatic cancer who die soon after diagnosis are a unique population, for whom better prognostication is clearly needed to guide care decisions.

A strength of our study is the use of a large contemporary nationwide oncologic outcomes database (9). The NCDB also implements stringent data quality and ascertainment methods. However, we acknowledge some limitations. First, there could be residual differences in ascertainment of treatment information by reporting facility. Although patients in the NCDB had similar characteristics with those patients in the population-based Surveillance, Epidemiology, and End Results database (46), the NCDB is a hospital-based registry database and results may not be generalizable to the US population. For example, because the requirement for Commission on Cancer-accreditation effectively places the quality of care at NCDB institutions at a somewhat higher level than nonaccredited institutions, it is likely that the patterns of care variation we identified are even greater in the general US population. Second, there was no information on cancer-specific cause of death, and our selection was based on all-cause mortality within 1 month of diagnosis. However, the vast majority of patients with metastatic cancer die of their disease (47). Third, there was also no information on multiple relevant factors such as the use of oral targeted therapy for lung cancer, immunotherapy, incorporation of palliative care team consultations, the location of death, or treatment-related toxicity. Fourth, we used first-course treatment information in the NCDB, which includes both curative or palliative treatments. Because of the limitations of our dataset and the inherent selection bias for who is treated (and not treated) at the end of life, we could not readily compare patients who received treatment and then lived longer because of that treatment. However, excluding patients who received treatment specifically documented as palliation did not change our results (data not shown). We were also unable to account for performance status, symptoms, or patient preferences that may influence treatment decision, because the NCDB does not capture these variables. Although lack of information on these variables may limit the direct applicability of our findings for the general oncology practice, our findings highlight important research gaps.

In conclusion, our study provides important insights about patterns of treatment initiated within a relatively short period among patients with imminently fatal de novo metastatic cancers. Treatment of patients diagnosed with imminently fatal de novo metastatic cancer varied markedly by cancer type and patient/facility characteristics. Although treatment decisions for patients with imminently fatal metastatic cancer are complex and most patients did not receive active treatment in the last month of life, some patients may have received ineffective surgery, chemotherapy, radiation, and hormonal therapy. More research is needed to specifically identify patients with imminently fatal metastatic cancer who will not benefit from attempted life-prolonging treatment who should instead be referred for end-of-life care.

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References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics. *CA Cancer J Clin*. 2018;68(1):7–30.
2. Vaz-Luis I, Lin NU, Keating NL, Barry WT, Winer EP, Freedman RA. Factors associated with early mortality among patients with de novo metastatic breast cancer: a population-based study. *Oncologist*. 2017;22(4):386–393.
3. Robbins AS, Siegel RL, Jemal A. Racial disparities in stage-specific colorectal cancer mortality rates from 1985 to 2008. *J Clin Oncol*. 2012;30(4):401–405.
4. Brewster DH, Clark DI, Stockton DL, Munro AJ, Steele RJ. Characteristics of patients dying within 30 days of diagnosis of breast or colorectal cancer in Scotland, 2003-2007. *Br J Cancer*. 2011;104(1):60–67.
5. O'Dowd EL, McKeever TM, Baldwin DR. What characteristics of primary care and patients are associated with early death in patients with lung cancer in the UK? *Thorax*. 2015;70(2):161–168.
6. Downing A, Aravani A, Macleod U, et al. Early mortality from colorectal cancer in England: a retrospective observational study of the factors associated with death in the first year after diagnosis. *Br J Cancer*. 2013;108(3):681–685.
7. Kahn KL, Malin JL, Adams J, Ganz PA. Developing a reliable, valid, and feasible plan for quality-of-care measurement for cancer: how should we measure? *Med Care*. 2002;40(suppl 6):Iii73–Iii85.
8. Lerro CC, Robbins AS, Phillips JL, Stewart AK. Comparison of cases captured in the National Cancer Data Base with those in population-based central cancer registries. *Ann Surg Oncol*. 2013;20(6):1759–1765.
9. American College of Surgeons: National Cancer Database: 2017 update. http://www.facs.org/cancer/ncdb/. Accessed March 26, 2018.
10. Commission on Cancer: FORDS: Facility Oncology Registry Data Standards—Revised for 2013. https://www.facs.org/~/media/files/quality%20programs/cancer/coc/fords/fords%20manual%202013.ashx. Accessed March 15, 2018.
11. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45(6):613–619.
12. Weeks JC, Cook EF, O'Day SJ, et al. Relationship between cancer patients' predictions of prognosis and their treatment preferences. *JAMA*. 1998;279(21):1709–1714.
13. Steinhauser KE, Christakis NA, Clipp EC, McNeilly M, McIntyre L, Tulsky JA. Factors considered important at the end of life by patients, family, physicians, and other care providers. *JAMA*. 2000;284(19):2476–2482.
14. Neumann PJ, Palmer JA, Nadler E, Fang C, Ubel P. Cancer therapy costs influence treatment: a national survey of oncologists. *Health Aff*. 2010;29(1):196–202.
15. Guadagnolo BA, Liao KP, Elting L, Giordano S, Buchholz TA, Shih YT. Use of radiation therapy in the last 30 days of life among a large population-based cohort of elderly patients in the United States. *J Clin Oncol*. 2013;31(1):80.
16. Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC. Trends in the aggressiveness of cancer care near the end of life. *J Clin Oncol*. 2004;22(2):315–321.
17. Gnerlich J, Jeffe DB, Deshpande AD, Beers C, Zander C, Margenthaler JA. Surgical removal of the primary tumor increases overall survival in patients with metastatic breast cancer: analysis of the 1988-2003 SEER data. *Ann Surg Oncol*. 2007;14(8):2187–2194.
18. Sacher AG, Le LW, Lau A, Earle CC, Leighl NB. Real-world chemotherapy treatment patterns in metastatic non–small cell lung cancer: are patients undertreated? *Cancer*. 2015;121(15):2562–2569.
19. Vargas GM, Sheffield KM, Parmar AD, et al. Trends in treatment and survival in older patients presenting with stage IV colorectal cancer. *J Gastrointest Surg*. 2014;18(2):369–377.
20. Neuman HB, Morrogh M, Gonen M, Van Zee KJ, Morrow M, King TA. Stage IV breast cancer in the era of targeted therapy: does surgery of the primary tumor matter? *Cancer*. 2010;116(5):1226–1233.
21. Khan SA, Stewart AK, Morrow M. Does aggressive local therapy improve survival in metastatic breast cancer? *Surgery*. 2002;132(4):620–626; discussion 626–627.
22. Bafford AC, Burstein HJ, Barkley CR, et al. Breast surgery in stage IV breast cancer: impact of staging and patient selection on overall survival. *Breast Cancer Res Treat*. 2009;115(1):7–12.
23. Vigan A, Dorgan M, Bruera E, Suarez-Almazor ME. The relative accuracy of the clinical estimation of the duration of life for patients with end of life cancer. *Cancer*. 1999;86(1):170–176.
24. Weeks JC, Catalano PJ, Cronin A, et al. Patients' expectations about effects of chemotherapy for advanced cancer. *N Engl J Med*. 2012;367(17):1616–1625.
25. Shapiro M, Rashid NU, Whang EE, et al. Trends and predictors of resection of the primary tumor for patients with stage IV colorectal cancer. *J Surg Oncol*. 2015;111(7):911–916.
26. Temple LK, Hsieh L, Wong WD, Saltz L, Schrag D. Use of surgery among elderly patients with stage IV colorectal cancer. *J Clin Oncol*. 2004;22(17):3475–3484.
27. Bartlett EK, Simmons KD, Wachtel H, et al. The rise in metastasectomy across cancer types over the past decade. *Cancer*. 2015;121(5):747–757.
28. Ramsey SD, Howlader N, Etzioni RD, Donato B. Chemotherapy use, outcomes, and costs for older persons with advanced non–small-cell lung cancer: evidence from Surveillance, Epidemiology and End Results–Medicare. *J Clin Oncol*. 2004;22(24):4971–4978.
29. Potosky AL, Saxman S, Wallace RB, Lynch CF. Population variations in the initial treatment of non–small-cell lung cancer. *J Clin Oncol*. 2004;22(16):3261–3268.
30. National Comprehensive Cancer Network: NCCN guidelines for breast cancer (version 2.2018). https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed February 27, 2018.
31. Sener SF, Fremgen A, Menck HR, Winchester DP. Pancreatic cancer: a report of treatment and survival trends for 100, 313 patients diagnosed from 1985-1995, using the National Cancer Database. *J Am Coll Surg*. 1999;189(1):1–7.
32. Earle CC, Venditti LN, Neumann PJ, et al. Who gets chemotherapy for metastatic lung cancer? *Chest*. 2000;117(5):1239–1246.
33. Allard P, Dionne A, Potvin D. Factors associated with length of survival among 1081terminally ill cancer patients. *J Palliat Care*. 1995;11(3):20–24.
34. Earle CC, Landrum MB, Souza JM, Neville BA, Weeks JC, Ayanian JZ. Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? *J Clin Oncol*. 2008;26(23):3860–3866.
35. Lilenbaum RC, Cashy J, Hensing TA, Young S, Cella D. Prevalence of poor performance status in lung cancer patients: implications for research. *J Thorac Oncol*. 2008;3(2):125–129.
36. Ngeow J, Leong SS, Gao F, et al. Impact of comorbidities on clinical outcomes in non-small cell lung cancer patients who are elderly and/or have poor performance status. *Crit Rev Oncol Hematol*. 2010;76(1):53–60.
37. Temel JS, McCannon J, Greer JA, et al. Aggressiveness of care in a prospective cohort of patients with advanced NSCLC. *Cancer*. 2008;113(4):826–833.
38. Hu CY, Bailey CE, You YN, et al. Time trend analysis of primary tumor resection for stage IV colorectal cancer: less surgery, improved survival. *JAMA Surg*. 2015;150(3):245–251.
39. Thomas A, Khan SA, Chrischilles EA, Schroeder MC. Initial surgery and survival in stage IV breast cancer in the United States, 1988-2011. *JAMA Surg*. 2016;151(5):424–431.
40. National Comprehensive Cancer Network: NCCN guidelines for breast cancer (version 1.2018). https://www.nccn.org/professionals/physician_gls/default.aspx#site. Accessed May 16, 2018.
41. National Comprehensive Cancer Network: NCCN guidelines for colon cancer (version 2.2018). https://www.nccn.org/professionals/physician_gls/default.aspx#site. Accessed May 16, 2018.
42. Lang K, Marciniak MD, Faries D, et al. Trends and predictors of first-line chemotherapy use among elderly patients with advanced non-small cell lung cancer in the United States. *Lung Cancer*. 2009;63(2):264–270.
43. Emanuel EJ, Young-Xu Y, Levinsky NG, Gazelle G, Saynina O, Ash AS. Chemotherapy use among Medicare beneficiaries at the end of life. *Ann Intern Med*. 2003;138(8):639–643.
44. Falchook AD, Dusetzina SB, Tian F, Basak R, Selvam N, Chen RC. Aggressive end-of-life care for metastatic cancer patients younger than age 65 years. *J Natl Cancer Inst*. 2017;109(9):djx028.
45. Green JB, Shapiro MF, Ettner SL, Malin J, Ang A, Wong MD. Physician variation in lung cancer treatment at the end of life. *Am J Manag Care*. 2017;23(4):216.
46. Mettlin CJ, Menck HR, Winchester DP, Murphy GP. A comparison of breast, colorectal, lung, and prostate cancers reported to the National Cancer Data Base and the Surveillance, Epidemiology, and End Results Program. *Cancer*. 1997;79(10):2052–2061.
47. Wei S, Tian J, Song X, Wu B, Liu L. Causes of death and competing risk analysis of the associated factors for non-small cell lung cancer using the Surveillance, Epidemiology, and End Results database. *J Cancer Res Clin Oncol*. 2018;144(1):145–155.