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# Prevalence, trend and disparities of palliative care utilization among hospitalized metastatic breast cancer patients who received critical care therapies

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## ARTICLE INFO

## ABSTRACT

Background: Early integration of palliative care (PC) for patients with advanced cancer has been recommended to improve quality of care. This study aims to describe prevalence, temporal trend and predictors of PC use in metastatic breast cancer (mBCa) patients receiving critical care therapies (CCT; included invasive mechanic ventilation, percutaneous endoscopic gastrostomy tube, total parenteral nutrition, tracheostomy and dialysis).

Methods: The National Inpatient Sample was queried for mBCa patients receiving CCT between 2005 and 2014. Annual percent changes (APC) were calculated for PC prevalence in the overall cohort and subgroups. Multivariable logistic analysis was used to explore predictors of PC use.

Results: Of 5833 mBCa patients receiving CCT, 880 (15.09%) received PC. Rate of PC use increased significantly from 2.53% in 2005 to 25.96% in 2014 (APC: 35.75%; p < 0.0001). Higher increase in PC use was observed in South (from 0.65% to 27.11%; APC: 59.42%; p < 0.0001), medium bedsize hospitals (from 3.75% to 26.05%; APC: 38.16%; p = 0.0006) and urban teaching hospitals (from 4.13% to 29.86%; APC: 37.33%; p = 0.0005). Multivariable analysis revealed that year interval, urban teaching hospitals, and invasive mechanical ventilation were associated with increased PC use, while primary diagnosis of gastrointestinal disorders, fractures, metastatic sites from lymph nodes and tracheostomy were associated with lower PC use.

Conclusions: PC use in mBCa patients receiving CCT increases significantly over the period. However, it still remains low. Efforts to illustrate disparities in PC use are needed to improve quality of care for mBCa patients receiving CCT, especially for those hospitalized in rural and nonteaching hospitals.

## 1. Introduction

Palliative care (PC) is an organized, structured system that delivers care to patients with life-threatening or end-stage diseases through interdisciplinary cooperation, aiming at alleviating symptom burdens and psychological sufferings in these patients and their family members [1]. The American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) has recommended early integration of inpatient and outpatient PC for patients with advanced cancer as soon as the

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diagnosis is made, usually along with active treatment [2,3]. It has been suggested that early PC use in advanced cancer could not only improve symptom management and quality of life, but also reduce mortality, hospitalization cost and length of stay [4,5]. Patients diagnosed with metastatic cancer who concurrently required critical care therapies (CCT) have higher risk of cancer-related complications and poorer outcomes, and are potential candidates for PC use [6].

Breast cancer is the most common human malignancy and the second most frequent cause of cancer-related deaths in women in the United States (US) [7,8]. It is estimated that about 5%—10% of newly diagnosed breast cancer are diagnosed with metastasis [9,10]. With the emerging and introduction of novel targeted drugs, the prognosis of metastatic breast cancer (mBCa) is expected to be improved [11,12]. Compared with other solid malignancies, patients with mBCa have more approved treatment options and less consideration for PC referral [13,14]. Virtually mBCa could involve any organ with substantial symptom burdens and unmet psychosocial needs at the end of life, among which pain management has been identified as a crucial component [15]. In addition, due to substantial heterogeneity among mBCa subtypes, the clinical course of mBCa is challenging to predict [13,14]. For some cases, end of life care is too late in the disease trajectory as the condition sharply progresses in a short time [9]. Previous publications regarding the status and features of PC use in mBCa patients are limited [6,13,14,16—18]. Shin et al. retrospectively reviewed 123 mBCa cases at a single care center from 2009 to 2010, and found that only 17% attended the outpatient PC appointment although nearly 57% were evaluated by the inpatient PC team during the last hospitalization prior to death [14]. Recently, a report focused on the integration of PC in hospitalized patients with metastatic tumor receiving CCT from California in 2010. Nonetheless, only 268 mBCa patients who received CCT were considered in the report, among whom 60 (22.39%) had PC [6].

From a national perspective, the current study aims to evaluate the prevalence, temporal trend and predictors of PC use in mBCa patients receiving specific CCT across time using the National Inpatient Sample (NIS) database. Identifying the predictors of PC use is beneficial to understand the disparities in PC use and further to improve quality of care for mBCa patients receiving CCT.

## 2. Materials and methods

### 2.1. Data source

The NIS is the largest publicly available inpatient database in the US, which represents about 20% hospitalization sample from discharged patients in community hospitals, and is created by the Healthcare Cost and Utilization Project (HCUP). It contains nearly 800 million inpatient hospitalizations annually across the US. The database was redesigned in 2012 to better represent the US population. More information could be found at the HCUP website [19]. The NIS is a publicly available, de-identified database; thus, requirements for Institutional Review Board approval and informed consent were waived. The current analysis mainly uses 2005—2014 database that includes patient characteristics, hospital characteristics, comorbidity measure, inpatient procedures, discharge status, total charges, and length of stay (LOS).

### 2.2. Patient selection

Firstly, all adult patients (≥18 years) with a diagnosis of mBCa were included through International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic code 174.x. Then, we selected patients with a secondary diagnosis of metastatic disease based on ICD-9-CM codes 196.x, 197.x and 198.x (Supplementary table 1) [20]. Lastly, among patients diagnosed with mBCa, CCT was defined through ICD-9-CM procedure codes. CCT involved commonly used aggressive procedures at the end of life, including invasive mechanic ventilation (IMV, ICD-9-CM code 96.70—96.72), percutaneous endoscopic gastrostomy (PEG, ICD-9-CM code 43.11) tube, total parenteral nutrition (TPN, ICD-9-CM code 99.15), tracheostomy (ICD-9-CM code 31.1, 31.21, 31.29) and dialysis for acute kidney failure (AKF, ICD-9-CM code both 584.5—585.9 and 39.95 to preclude patients on chronic dialysis) [6,21,22].

### 2.3. Covariates and outcome measures

Patient characteristics included age, race (White, Black, Hispanic, Other and Unknown), year of admission (2005—2009 and 2010—2014), type of insurance (Medicare, Medicaid, private and self-pay/other) and income quartile. Hospital characteristics were hospital bedsize (small, medium and large), hospital type (rural, urban non-teaching and urban teaching) and hospital region (Northeast, Midwest, South and West). Bedsize categories were based on hospital beds, and were specific to the hospital's location and teaching status [19]. For example, in the Northeast region, large bedsize indicated a number of beds of more than 100 beds in rural hospitals, 200 beds in urban nonteaching hospitals and 425 beds in urban teaching hospitals. Elixhauser comorbidity score consisted of 29 common comorbidities that could reflect the severity of disease burdens (excluded cancer) [23]. The principal diagnosis was categorized through the Clinical Classifications Software (CCS) for ICD-9-CM, which was a scheme that collapsed diagnoses and procedures into clinically meaningful categories (Supplementary table 1). Discharge status for patients who survived was grouped into home or home healthcare, short term hospital, intermediate facilities and other. Total charges were transformed into total cost using the cost-to-charge ratios and were further adjusted for inflation.

The primary outcome was the temporal trend of inpatient PC use in mBCa patients who received CCT. The secondary outcome was the predictors of PC use in mBCa patients who received CCT. PC use was determined by the ICD-9-CM diagnostic code V66.7. This code was previously used and validated in metastatic disease with moderate sensitivity (ranges from 66.3 to 84.0%) and high specificity (ranges from 95.0 to 99.1%) [24,25]. Additionally, hospitals that had not ever provided one PC service were excluded from the analysis.

### 2.4. Statistical analysis

We derived the national estimates using complex survey methods incorporating stratas, clusters and sampling weights in the analysis recommended by the HCUP. For continuous variables such as age and LOS, we used mean (standard derivation) or median (interquartile range) according to the distributions. Comparison of characteristics between patients with and without PC use was conducted using $t$-test or Kruskal—Wallis tests. Categorical variables were expressed as proportions and compared using chi-square tests. Annual percentage change (APC) was calculated in the overall population and subgroups by race, hospital region, hospital bedsize and teaching status.

To explore the potential predictors and disparities of PC use in mBCa patients receiving CCT, we preformed multivariable logistic regression analysis accounting for patients clustered in the same hospitals. Variables entered into the model included age, year interval, race, type of insurance, income quartile, hospital bedsize, hospital region, hospital type, Elixhauser comorbidity score, primary diagnosis, metastatic sites, number of metastatic sites, type of

CCT and Do Not Resuscitate status. We further repeated the multivariable analysis restricted to admissions in which mBCa patients received IMV.

Two-sided p value ≤ 0.05 was considered significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, US).

## 3. Results

### 3.1. Patient characteristics

From 2005 to 2014, 379,947 patients were diagnosed with breast cancer, among which 146,693 (38.61%) were diagnosed with mBCa. We further identified 6050 (4.12%) mBCa patients who received CCT during hospitalization. Then, 217 (3.59%) patients admitted to hospitals that had no access to PC service were excluded. Finally, this study identified 5833 (weighted 28,858 patients) mBCa patients who received CCT. Of these patients, 3793 (65.03%) received IMV, 629 (10.78%) received PEG, 1465 (25.12%) received TPN, 277 (4.75%) received tracheostomy and 446 (7.65%) received dialysis for AKF.

There were 880 (15.09%) patients who received inpatient PC. As shown in Fig. 1, PC use rates in patients receiving IMV, PEG, TPN, tracheostomy and dialysis for AKF were 18.09%, 10.65%, 10.72%, 10.11% and 12.11%, respectively. Compared with patients without PC, those received PC were frequently observed during 2010−2014 (82.84% vs. 52.90%; p < 0.0001) and in urban teaching hospitals (62.50% vs. 52.59%; p < 0.0001; Table 1). In addition, patients receiving PC were more likely to metastasize to brain & spinal cord, liver, respiratory organs, adrenal glands, and were less likely to metastasize to lymph nodes, and had more metastatic sites. Do Not Resuscitate was more likely to occur in patients receiving PC (35.91% vs. 7.29%; p < 0.0001). Patients with PC had higher in-hospital mortality (64.89% vs 38.22%; p < 0.0001), lower cost (24801$ vs 24957$; p < 0.0001) and shorter LOS (8 days vs. 10 days; p = 0.0105). Among survivors, patients with PC had similar total cost but slightly higher LOS (p = 0.0468). Patients who received PC and survived the hospitalization were less likely to discharge to home or home healthcare and short term hospitals, and more likely to be discharged to intermediate facilities. Characteristics between patients with and without PC in mBCa patients receiving IMV were summarized in Supplementary table 2.

### 3.2. Temporal trend of PC use in mBCa patients receiving CCT

Rate of PC use in mBCa patients receiving CCT increased significantly from 2.53% in 2005 to 25.96% in 2014 (APC: 35.75%; p < 0.0001; Fig. 2). According to stratified analyses by race, rate of PC use increased from 2.1% to 24.33% (APC: 35.07%; p < 0.0001) in White and from 4.28% to 31.76% (APC: 35.71%; p = 0.0003) in Black (Fig. 3).

According to stratified analyses by bedsize, rate of PC use increased from 0 to 26.13% (APC: 31.25%; p = 0.0014) in small bedsize hospitals, from 3.75% to 26.05% (APC: 38.16%; p = 0.0006) in medium bedsize hospitals, and from 2.48% to 25.87% (APC: 37.75%; p = 0.0026) in large bedsize hospitals. According to stratified analyses by hospital type, PC rate increased from 0 to 14.29% (APC: 20.97%; p = 0.0107) in rural hospitals, from 1.48% to 17.28% in urban non-teaching hospitals (APC: 33.24%; p = 0.0003) and from 4.13% to 29.86% (APC: 37.33%; p = 0.0005) in urban teaching hospitals. According to stratified analyses by hospital region, PC rate increased from 2.34% to 28.46% (APC: 29.35%; p < 0.0001) in the Northeast, from 6.53% to 24.54% (APC: 23.87%; p = 0.0141) in the Midwest, from 0.65% to 27.11% (APC: 59.42%; p < 0.0001) in the South and from 2.22% to 23.18% (APC: 32.90%; p = 0.0012) in the West.

PC use rates were 23.17% and 9.17% among patients dying in hospitals and survivors, respectively. Between 2005 and 2014, rate of PC use increased from 5.06% to 38.87% (APC: 32.21%; p = 0.0001) in patients dying in hospitals and from 0.49% to 15.89% (APC: 48.20%; p < 0.0001) in survivors.

### 3.3. Predictors of PC use in mBCa patients receiving CCT

Multivariable analysis revealed that year interval (odds ratio [OR]: 2.98, 95% confidence interval [CI]: 2.33−3.80; p < 0.0001), urban teaching status (OR: 1.68, 95%CI: 1.10−2.56; p = 0.0156), IMV (OR: 2.03, 95%CI: 1.48−2.77; p < 0.0001) and Do Not Resuscitate (OR: 4.44, 95%CI: 3.64−5.40; p < 0.0001) were associated with increased PC use, while primary diagnosis related to gastrointestinal disorders (OR: 0.66, 95%CI: 0.47−0.92; p = 0.0140), fractures (OR: 0.32, 95%CI: 0.13−0.80; p = 0.0153), complications of device or surgery (OR: 0.53, 95%CI: 0.29−0.97; p = 0.0397), metastatic sites from lymph nodes (OR: 0.67, 95%CI: 0.54−0.85; p = 0.0007) and tracheostomy (OR: 0.60, 95%CI: 0.39−0.94; p = 0.0238) were associated with lower PC use (Table 2).
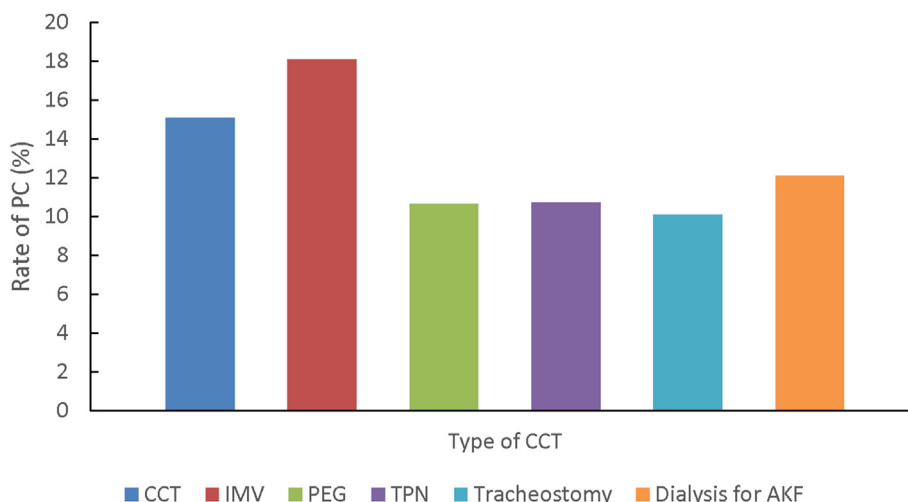


**Fig. 1.** Rate of inpatient PC in patients with mBCa who received CCT by type of CCT.

**Table 1**
Basic characteristics between mBCa patients receiving CCT with and without PC.

| Variables | No PC (N = 4953, %) | PC (N = 880, %) | P-value |
|---|---|---|---|
| **Mean age (SD)** | 61.57(12.93) | 60.68(12.84) | 0.0585 |
| **Year interval** | | | <0.0001 |
| 2005−2009 | 2333(47.10) | 151(17.16) | |
| 2010−2014 | 2620(52.90) | 729(82.84) | |
| **Race** | | | 0.0036 |
| White | 2744(55.40) | 505(57.39) | |
| Black | 1007(20.33) | 190(21.59) | |
| Hispanic | 352(7.11) | 72(8.18) | |
| Other | 298(6.02) | 53(6.02) | |
| Unknown | 552(11.14) | 60(6.82) | |
| **Type of insurance** | | | 0.3086 |
| Medicare | 2258(45.59) | 383(43.53) | |
| Medicaid | 727(14.68) | 136(15.45) | |
| Private | 1759(35.51) | 313(35.57) | |
| Self-pay/other | 209(4.22) | 48(5.45) | |
| **Income quartile** | | | 0.4322 |
| 0−25th Percentile | 1332(26.89) | 221(25.11) | |
| 25th-50th Percentile | 1255(25.34) | 213(24.20) | |
| 50th-75th Percentile | 1170(23.62) | 216(24.55) | |
| 75th-100th Percentile | 1196(24.15) | 230(26.14) | |
| **Hospital bedsize** | | | 0.9905 |
| Small | 516(10.42) | 93(10.57) | |
| Medium | 1266(25.56) | 225(25.57) | |
| Large | 3171(64.02) | 562(63.86) | |
| **Hospital type** | | | <0.0001 |
| Rural | 316(6.38) | 36(4.09) | |
| Urban non-teaching | 2032(41.03) | 294(33.41) | |
| Urban teaching | 2605(52.59) | 550(62.50) | |
| **Hospital region** | | | 0.1974 |
| Northeast | 953(19.24) | 168(19.09) | |
| Midwest | 1052(21.24) | 188(21.36) | |
| South | 1862(37.59) | 305(34.66) | |
| West | 1086(21.93) | 219(24.89) | |
| **Elixhauser comorbidity score** | 3.03(1.87) | 3.10(1.88) | 0.3211 |
| **Primary diagnosis** | | | <0.0001 |
| Cancer-related disorders | 1368(27.62) | 256(29.09) | |
| Infections | 798(16.11) | 191(21.71) | |
| Genitourinary disorders | 227(4.58) | 34(3.86) | |
| Cardiovascular disorders | 359(7.25) | 67(7.62) | |
| Pulmonary disorders | 964(19.46) | 180(20.45) | |
| Gastrointestinal disorders | 511(10.32) | 56(6.36) | |
| Fractures | 67(1.35) | a | |
| Fluid/Electrolyte disorders | 96(1.94) | a | |
| Neurologic disorders | 86(1.74) | 20(2.27) | |
| Complications of device or surgery | 141(2.85) | 17(1.93) | |
| Other disorders | 336(6.78) | 45(5.12) | |
| **Metastatic sites** | | | |
| Bone & bone marrow | 2613(52.76) | 492(55.91) | 0.0841 |
| Brain & spinal cord | 907(18.31) | 210(23.86) | 0.0001 |
| Lymph nodes | 1040(21.00) | 130(14.77) | <0.0001 |
| Liver | 1577(31.84) | 327(37.16) | 0.0019 |
| Respiratory organs | 1830(36.95) | 390(44.32) | <0.0001 |
| Adrenal glands | 71(1.43) | 21(2.39) | 0.0366 |
| Gastrointestinal organs | 302(6.10) | 60(6.82) | 0.4141 |
| Other organs | 629(12.70) | 129(14.66) | 0.1111 |
| **Number of metastatic sites (≥2)** | 2523(50.94) | 523(59.43) | <0.0001 |
| **Type of CCT** | | | |
| IMV | 3107(62.73) | 686(77.95) | <0.0001 |
| PEG tube | 562(11.35) | 67(7.61) | 0.0010 |
| TPN | 1308(26.41) | 157(17.84) | <0.0001 |
| Tracheostomy | 249(5.03) | 28(3.18) | 0.0177 |
| AKI requiring dialysis | 392(7.91) | 54(6.14) | 0.0674 |
| **Do Not Resuscitate** | 361(7.29) | 316(35.91) | <0.0001 |
| **In-hospital mortality** | 1893(38.22) | 571(64.89) | <0.0001 |
| **Discharge disposition (alive)** | | | <0.0001 |
| Home or home healthcare | 1717(56.11) | 132(42.72) | |
| Short term hospitals | 146(4.77) | a | |
| Intermediate facilities | 1183(38.66) | 165(53.40) | |
| Other | 14(0.46) | a | |
| **LOS (days, median [Q1-Q3[)** | 10(5−17) | 8(4−14) | <0.0001 |
| **Total cost (days, median [Q1-Q3[)** | 24957(14270−44386) | 24801(13342−39961) | 0.0105 |
| **LOS (days, median [Q1-Q3[) in survivors** | 11(7−18) | 11(6−17) | 0.0468 |
| **Total cost (days, median [Q1-Q3[) in survivors** | 25382(16181−45939) | 24957(14454−42065) | 0.0909 |

Abbreviation: CCT, critical care therapies; mBCa, metastatic breast cancer; PC, palliative care; SD, standard deviation; IMV, invasive mechanic ventilation; PEG, percutaneous endoscopic gastrostomy; TPN, total parenteral nutrition; AKF, acute kidney failure; LOS, length of stay; Q1, the first quantile; Q3, the third quantile.

[a] Small numbers of observations (<10) are at risk of identification of persons according to the HUCP and we replaced the number with an asterisk.
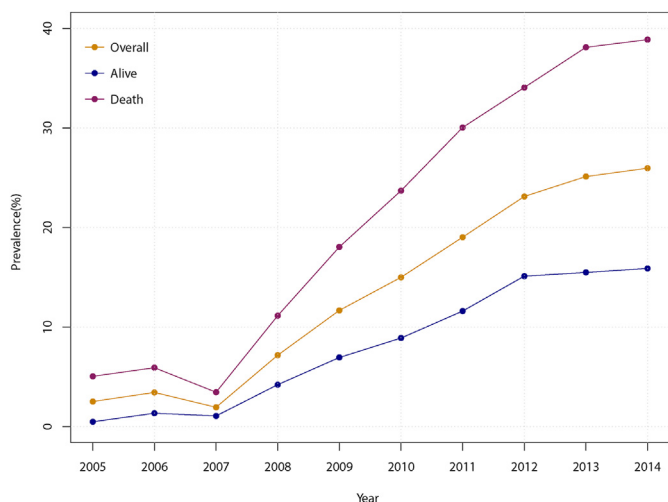
**Fig. 2.** Annual rates of inpatient PC in patients with mBCa who received CCT according to discharge status.

In mBCa patients receiving IMV, year interval (OR: 3.04, 95%CI: 2.3—4.01; p < 0.0001), urban teaching status (OR: 2.14, 95%CI: 1.28—3.56; p = 0.0035), primary diagnosis of fractures (OR: 0.38, 95%CI: 0.15—0.96; p = 0.0410), metastatic sites from lymph nodes (OR: 0.68, 95%CI: 0.52—0.88; p = 0.0035) and Do Not Resuscitate (OR: 4.22, 95%CI: 3.38—5.28; p < 0.0001) were predictors of PC use (Supplementary table 3).

## 4. Discussion

Early integration of PC for patients with advanced cancer has been recommended by the ASCO and the NCCN guidelines to improve quality of care [2,3,12]. However, timely PC use in mBCa patients was not commonplace and the existing evidence was limited by small sample size or single center design [6,13,14,17,18]. This study described the prevalence, temporal trend and predictors of PC use in mBCa patients who received CCT from a nationally representative cohort. We found that rate of PC use increased significantly from 2005 to 2014. Year interval, urban teaching status, invasive mechanical ventilation and Do Not Resuscitate were associated with increased PC use, while primary diagnosis related to gastrointestinal disorders, fractures, metastatic sites from lymph nodes and tracheostomy were associated with lower PC use.

With the emerging and introduction of novel targeted drugs, several optional therapies were available for mBCa patients, possibly causing lateness or absence of PC referrals and impeding clinically significant improvements in symptoms and quality of life [13,14]. Additionally, when the disease progressed or the symptoms were out of control, lack of PC use often caused crisis interventions and emergency admissions with intensive care therapies [26]. Thus, focusing on PC use in mBCa patients who received CCT was of practical clinical significance. Although early integration of PC has been increasingly recognized as the standard of care in advanced cancer, mBCa patients failed to have adequate knowledge towards the concepts and benefits of PC use according to Rabow et al. [17]. Among patients enrolled in the specialty PC program, most thought that the ideal time for PC referral was when the symptoms became uncontrolled and seriously affected their quality of life. Some even
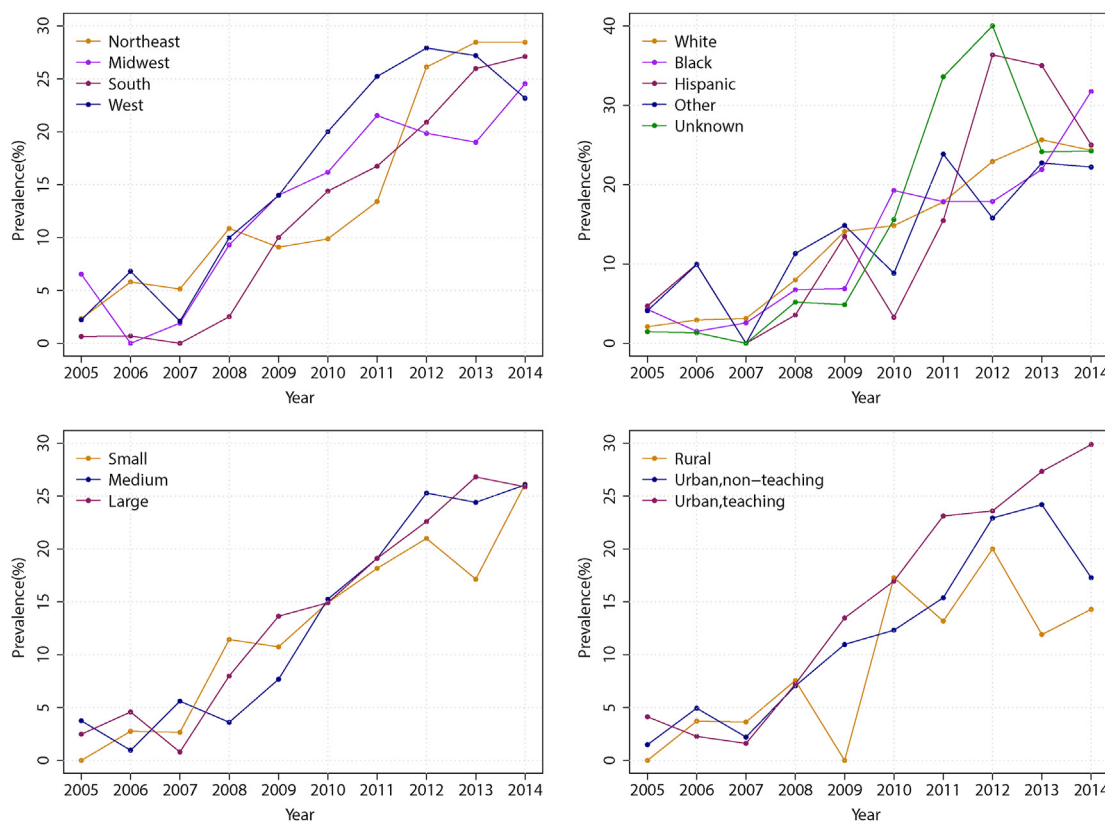


**Fig. 3.** Annual rates of inpatient PC in patients with mBCa who received CCT stratified by hospital region, race, hospital bedsize and hospital teaching status.

**Table 2**
Predictors of PC use in mBCa patients receiving CCT and IMV.

| Variables | CCT | | IMV | |
|---|---|---|---|---|
| | OR(95%CI) | P-value | OR(95%CI) | P-value |
| **Age** | 1.00(0.99,1.01) | 0.4937 | 0.99(0.99,1.00) | 0.2666 |
| **Year interval** | | | | |
| 2005—2009 | Ref | | Ref | |
| 2010—2014 | 2.98(2.33,3.80) | <0.0001 | 3.04(2.31,4.01) | <0.0001 |
| **Race** | | | | |
| White | Ref | | Ref | |
| Black | 0.89(0.72,1.10) | 0.2717 | 0.87(0.69,1.10) | 0.2526 |
| Hispanic | 0.96(0.71,1.31) | 0.8079 | 1.01(0.71,1.43) | 0.9490 |
| Other | 0.72(0.51,1.03) | 0.0735 | 0.67(0.45,1.00) | 0.0523 |
| Unknown | 0.88(0.62,1.26) | 0.4922 | 0.97(0.66,1.43) | 0.8737 |
| **Type of insurance** | | | | |
| Medicare | Ref | | Ref | |
| Medicaid | 0.89(0.67,1.19) | 0.4434 | 0.90(0.66,1.23) | 0.5065 |
| Private | 1.07(0.85,1.34) | 0.5602 | 1.07(0.83,1.38) | 0.6075 |
| Self-pay/other | 1.37(0.93,2.03) | 0.1116 | 1.26(0.82,1.93) | 0.2945 |
| **Income quartile** | | | | |
| 0—25th Percentile | Ref | | Ref | |
| 25th-50th Percentile | 0.99(0.79,1.25) | 0.9598 | 0.95(0.74,1.23) | 0.7117 |
| 50th-75th Percentile | 1.10(0.86,1.39) | 0.4564 | 1.11(0.84,1.45) | 0.4606 |
| 75th-100th Percentile | 1.06(0.83,1.35) | 0.6524 | 1.08(0.82,1.43) | 0.5696 |
| **Hospital bedsize** | | | | |
| Small | Ref | | Ref | |
| Medium | 1.13(0.83,1.53) | 0.4420 | 1.08(0.75,1.54) | 0.6844 |
| Large | 1.27(0.96,1.68) | 0.0984 | 1.29(0.93,1.78) | 0.1292 |
| **Hospital type** | | | | |
| Rural | Ref | | Ref | |
| Urban non-teaching | 1.23(0.80,1.90) | 0.3427 | 1.42(0.84,2.40) | 0.1892 |
| Urban teaching | 1.68(1.10,2.56) | 0.0156 | 2.14(1.28,3.56) | 0.0035 |
| **Hospital region** | | | | |
| Northeast | Ref | | Ref | |
| Midwest | 1.08(0.82,1.42) | 0.6047 | 1.09(0.80,1.49) | 0.5692 |
| South | 0.94(0.73,1.21) | 0.6213 | 0.95(0.72,1.26) | 0.7367 |
| West | 1.29(0.97,1.71) | 0.0750 | 1.26(0.91,1.73) | 0.1579 |
| **Elixhauser comorbidity score** | 0.98(0.93,1.02) | 0.3007 | 0.98(0.93,1.04) | 0.5829 |
| **Primary diagnosis** | | | | |
| Cancer-related disorders | Ref | | Ref | |
| Infections | 0.90(0.71,1.14) | 0.3882 | 0.95(0.73,1.25) | 0.7352 |
| Genitourinary disorders | 1.06(0.68,1.64) | 0.8035 | 1.19(0.59,2.39) | 0.6208 |
| Cardiovascular disorders | 0.76(0.55,1.06) | 0.1063 | 0.91(0.64,1.29) | 0.5962 |
| Pulmonary disorders | 0.83(0.66,1.05) | 0.1229 | 0.91(0.71,1.18) | 0.4880 |
| Gastrointestinal disorders | 0.66(0.47,0.92) | 0.0140 | 0.92(0.58,1.47) | 0.7272 |
| Fractures | 0.32(0.13,0.80) | 0.0153 | 0.38(0.15,0.96) | 0.0410 |
| Fluid/Electrolyte disorders | 0.63(0.31,1.26) | 0.1917 | 0.97(0.39,2.39) | 0.9474 |
| Neurologic disorders | 0.87(0.51,1.47) | 0.5934 | 0.85(0.46,1.55) | 0.5947 |
| Complications of device or surgery | 0.53(0.29,0.97) | 0.0397 | 0.48(0.22,1.05) | 0.0673 |
| Other disorders | 0.79(0.56,1.12) | 0.1819 | 0.82(0.52,1.29) | 0.3839 |
| **Metastatic sites** | | | | |
| Bone & bone marrow | 1.04(0.85,1.26) | 0.7201 | 1.07(0.85,1.34) | 0.5759 |
| Brain & spinal cord | 1.20(0.97,1.49) | 0.0965 | 1.12(0.87,1.43) | 0.3765 |
| Lymph nodes | 0.67(0.54,0.85) | 0.0007 | 0.68(0.52,0.88) | 0.0035 |
| Liver | 1.10(0.90,1.34) | 0.3465 | 1.03(0.82,1.29) | 0.8091 |
| Respiratory organs | 1.19(0.98,1.44) | 0.0776 | 1.20(0.96,1.49) | 0.1137 |
| Adrenal glands | 1.64(0.96,2.82) | 0.0697 | 1.76(0.94,3.28) | 0.0754 |
| Gastrointestinal organs | 1.19(0.85,1.67) | 0.3181 | 1.43(0.91,2.24) | 0.1206 |
| Other organs | 1.17(0.91,1.49) | 0.2186 | 1.14(0.85,1.53) | 0.3741 |
| **Number of metastatic sites (≥2)** | 1.09(0.84,1.43) | 0.5114 | 1.03(0.75,1.41) | 0.8629 |
| **Type of CCT** | | | | |
| IMV | 2.03(1.48,2.77) | <0.0001 | – | – |
| PEG tube | 1.09(0.78,1.53) | 0.6016 | 0.79(0.45,1.40) | 0.4212 |
| TPN | 1.19(0.86,1.64) | 0.3062 | 1.49(0.97,2.30) | 0.0718 |
| Tracheostomy | 0.60(0.39,0.94) | 0.0238 | 0.73(0.44,1.19) | 0.2083 |
| AKI requiring dialysis | 1.00(0.70,1.43) | 0.9852 | 0.76(0.46,1.27) | 0.2961 |
| **Do Not Resuscitate** | 4.44(3.64,5.40) | <0.0001 | 4.22(3.38,5.28) | <0.0001 |

Abbreviation: CCT, critical care therapies; mBCa, metastatic breast cancer; PC, palliative care; IMV, invasive mechanic ventilation; PEG, percutaneous endoscopic gastrostomy; TPN, total parenteral nutrition; AKF, acute kidney failure.

hold the views that the oncologist treated them as dying patients. Fortunately, it should be noted that the concerns above were alleviated after the first PC visit with doctors in the PC program. PC care providers should educate patients and emphasize the need for early and actively continued assessments to improve PC care in mBCa patients who received CCT through interdisciplinary care teams including medical oncologists, PC specialists, psychologists, nurses and social workers [27—29].

Overall, we found that only 15.09% of mBCa patients with CCT received inpatient PC. Fortunately, it is encouraging that PC use rate has clinically meaningfully increased from 2.53% in 2005 to 25.96% in 2014 (APC: 35.75%; p < 0.0001). This might be a result of the widely acceptance of PC use in mBCa patients and the improved adherence of related guidelines. Loh et al. previously reported a PC use rate of 22.4% in California in 2010, higher than the national estimate of 15.09% in our study [6]. Actually, in subgroup analyses stratified according to the hospital region, the highest overall PC use rate was observed in the West (16.78%) which included California. Meanwhile, the rate of PC use in the West in 2010 was 20.01%, which was similar to 22.4% in California in 2010. The maximum rate of PC use in mBCa receiving CCT from the national perspective was 25.96% in 2014, which was still lower than the rate reported for metastatic lung cancer receiving CCT (28.3%) in California in 2010. This might suggest inadequate PC use and possibly suboptimal quality of care in the study population. As a consequence, more work are needed to identify the nationwide barriers towards the underuse of PC in critical care of patients with mBCa.

For geographical differences among the four regions, we examined the overall PC use rate and changes in PC use rate over the study period, and found that hospitals from the West had the highest rate of PC use (16.78%), followed by Midwest (15.16%), Northeast (14.99%) and South (14.07%). Although the lowest PC use rate was observed in the South, PC use has dramatically increased in recent years in this region, accompanied by the highest APC (59.42%; p < 0.0001). Similar phenomenon has been reported in publication focusing on metastatic prostate cancer receiving CCT [21]. Future researches are required to expound this disparities in regional differences and reinforce PC delivery in the Midwest with relatively unmet PC use throughout the whole period.

For type of hospital, we found that urban teaching hospitals had higher rate of PC use in both univariate (17.43% vs. 10.23%; p < 0.0001) and multivariable analysis (OR: 1.68, 95%CI: 1.10−2.56; p = 0.0156). Urban centers may have more dedicated PC specialists who are routinely involved in end-of-life decision-making and could provide more PC services [30]. In detail, higher PC rate in urban teaching hospitals was consistent over 2005 to 2014. More importantly, the maximum change in PC use was also observed in urban teaching hospitals (APC: 37.33%; p = 0.0005). It should be noted that such results were consistent with previous publications that studied PC use in metastatic genitourinary cancers receiving CCT, reflecting the fact that disparities of PC use in hospital type was pronounced from the national perspective [21,22]. Type of insurance was not a statistically significant predictor for inpatient PC use in the study. Specifically, Medicaid, Private and Self-pay/other were not associated with PC use compared with Medicare in mBCa patients undergoing CCT. Additionally, multivariable logistic regression analysis indicated that Black race was not associated with PC use in mBCa patients compared with the White race.

In view of discharge disposition, in-hospital mortality was significantly higher in patients who received PC (64.89% vs. 38.22%; p < 0.0001). However, this did not mean that PC use could increase odds of death. On the contrary, higher mortality in the PC group indicated more severe illness and thus prompted more PC use. Despite this, the majority of patients (76.83%) who died in hospitals did not receive any PC services. Rabow et al. found that 20.4% mBCa patients were referred to PC before death, consistent with our result (23.17%) [17]. Shin et al. reported a higher in-hospital mortality of approximately 50% in 123 mB C patients and concluded that hospitalization should be treated as a trigger for clinicians to discuss end-of-life care goals with the patients [14]. For those discharged alive, patients with PC were frequently discharged to intermediate facilities, which mainly referred to nursing facilities, or facilities that provided supportive care and hospice care.

The present study using national-level large sample identified an increasing trend of PC use rate in both overall and subgroup populations, reported disparities in PC use and illustrated potential predictors of PC use in mBCa patients who received CCT. Despite the above strengths, several limitations should also be acknowledged. First, PC was defined through ICD-9-CM code V66.7. Although this code had been widely used in publications, its sensitivity for identifying PC in metastatic disease ranged from 66.3 to 84.0%, resulting in possibly underestimation of actual number of PC cases [24,25]. Second, CCT in the study included frequently used therapies. Thus, the results could be only generalized to settings involved these specific CCTs. Third, as an administrative database, several characteristics were not available, such as performance status, laboratory values, chemotherapy regimens and quality of PC service. Lack of patient-reported outcomes including quality of life limited effect assessment after PC initiation. Fourth, post-discharge outcomes or outpatient PC use was not available. The NIS database was an inpatient database so only inpatient PC during the admission associated with the provision of CCT was considered. Although PC use in the outpatient setting was not captured in this study, previous publications had highlighted the underutilized status of PC in outpatient patients for mBCa patients, even in hospitals with well-established outpatient PC program [14,31]. Therefore, more prospective studies are needed to describe the trends, predictors and barriers of outpatient PC in mBCa patients.

## 5. Conclusions

PC use in mBCa patients receiving CCT increases significantly from 2005 to 2014. Given high risk of mortality among these patients, the rate still remains low. This study highlights the underutilized PC in mBCa patients receiving CCT. Future efforts to illustrate disparities in PC use are needed to improve quality of care for mBCa patients receiving CCT, especially for those hospitalized in rural and nonteaching hospitals.

## Declaration of competing interest

None.

## Details of ethics approval

The study was exempt from ethics approval as the NIS is a publicly available, de-identified database.

## Acknowledgements

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2020.11.001.

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