Healthcare resource utilization and costs of Medicare-enrolled patients with HR+/HER2- metastatic breast cancer treated with CDK4/6i in the first-line setting

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Abstract

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Background: The introduction of cyclin-dependent kinases 4 and 6 (CDK4/6i) inhibitors (palbociclib, ribociclib, and abemaciclib) has transformed the treatment landscape for patients with hormone-receptor-positive (HR+) and human epidermal growth factor receptor 2 negative (HER2-) metastatic breast cancer (MBC). To our knowledge, no studies have quantified healthcare resource utilization (HRU) or economic burden following CDK4/6i initiation in the Medicare population.

Objective: The objective of this study is to describe HRU and quantify healthcare costs among Medicare-enrolled patients with HR+ HER2- MBC treated with CDK4/6i in the first-line setting.

Methods: We conducted a retrospective cohort study on Medicare-enrolled HR+ HER2- MBC patients who initiated a CDK4/6i in the first-line setting between February 2nd, 2016, and December 31st, 2022 using claims from the Merative MarketScan ® database. We examined all-cause healthcare resource utilization (HRU) by summarizing the number of inpatient (IP), outpatient (OP), and emergency room (ER) visits, as well as the length of stay during the six months following CDK4/6i initiation. Additionally, we assessed all-cause healthcare costs, including IP, OP, ER, and pharmacy, over the one year following CDK4/6i initiation using the Kaplan-Meier sample average (KMSA) estimator to account for censoring. We reported total healthcare costs as the sum of IP, OP, ER, and pharmacy costs, providing insights into the economic burden associated with CDK4/6i treatment in this patient population.

Results: A total of 901 patients met the inclusion criteria with a mean age of 74 years (standard deviation [SD] 6.84) and a mean Charlson Comorbidity Index (CCI) score of 0.64 (SD 0.8). Most patients initiated palbociclib (n=804 (90%)) at the index date and most had a systemic therapy (n=634 (70%)) before CDK4/6i initiation. Nearly 24% (n=214) had an inpatient admission in the six months following CDK4/6i initiation. Among patients with an inpatient admission, the mean number of admissions per patient was 1.65 (SD=0.98) with a mean length of stay per admission of 5.98 days (SD=6.25). Roughly 30% [n=271] of patients had an ER visit, with a mean of 2.1 (SD=1.54) visits per patient among those who had a visit. Most patients (n=868 (96.44%)) had an outpatient service, and among those with an OP service, the mean number of days with outpatient services was 19.96 (SD=12.29). Mean total healthcare costs over the one-year period following CDK4/6i were $62,228 (95% CI 52281, 73029) per patient with the main drivers being outpatient services ($31,686 (95% CI 27168, 36925)) and pharmacy costs ($22,727 (95% CI 19273, 25931)).

Conclusions: There are numerous sources of healthcare resource use and cost in patients following CDK4/6i initiation in the Medicare population, especially in the outpatient setting. High outpatient costs are possibly attributable to infusion therapies. Our study suggests further advancements in the treatment of HR+, HER2- MBC may have the ability to reduce economic expenditures and provide information for value assessment and healthcare decision-makers.

Table of Contents

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1. Introduction

Breast cancer (BC) is the most common cancer and the second leading cause of cancer-associated death in women in the United States.[1] In 2020 the CDC reported a total of $29.8 billion in annual medical costs for breast cancer care making it a substantial economic burden in the United States. [2] Breast cancer is divided into four subtypes based on tumor receptor status, with roughly 87.2% of new breast cancer cases representing the hormone-receptor-positive (HR+) and human epidermal growth factor receptor 2 negative (HER2-) subtype.[3] Metastatic breast cancer (MBC), breast cancer where the cancer has spread to other regions of the body, is the most expensive to treat and is expected to increase by 54.8% between 2015 and 2030.[4]

The introduction of cyclin-dependent kinases 4 and 6 (CDK4/6i) inhibitors (palbociclib, ribociclib, and abemaciclib) has transformed the treatment landscape for patients with HR+ HER2- MBC. Before the introduction of CDK4/6i, women were primarily treated with chemotherapy or endocrine therapy (ET) despite the less-than-desirable toxicity and tolerability profiles.[5] While CDK4/6i has become the standard of care in the first-line setting, patients will eventually progress due to resistance, with a median overall survival (OS) of about 5 years. [5] After progression on a CDK4/6i optimal second-line treatment has yet to be clearly defined. [6]

Real-world evidence of healthcare resource utilization (HRU) and economic burden provide important insights into the patient experience and impact on the healthcare system. Evaluation of HRU and costs via electronic claim records can help inform clinical research, value assessment, drug development, and payers, as the data gives us insight into the experience patients with HR+ HER2- MBC are having and can show how best to support patients.

The HRU and economic burden of patients with HR+ HER2- MBC in the commercially insured population is well documented [7-11], however, exploration of HRU and costs, specifically following initiation of CDK4/6i, in the Medicare population is limited.[12-13] The Medicare population is a unique clinical subset of patients that may have different disease progression, and complications, and react differently to treatment due to older age and higher comorbidities. In this study, we aim to comprehensively assess healthcare resource use and costs associated with Medicare-enrolled patients with HR+, HER2- MBC treated in the first-line setting with a CDK4/6i.

2. Methods

2.1 Study Design and Data Source

We conducted a retrospective cohort study using health insurance claims to describe HRU and costs among Medicare-enrolled patients with HR+ HER2- MBC who initiated a CDK4/6i in the first-line setting.

Data from Merative MarketScan® Medicare Databases was used to identify patients and capture HRU and costs. The MarketScan Medicare Supplemental and Coordination of Benefits (COB) Database is created for Medicare-eligible retirees with employer-sponsored Medicare Supplemental plans. The database includes both the Medicare-paid amounts and the employer-paid supplemental insurance amounts, with only plans where both the Medicare-paid amounts and the employer-paid amounts are selected. We collected all enrollment, inpatient, outpatient, and drug claim records. [14]

The study period was from February 19th, 2015 (FDA approval of first CDK4/6i) through December 31st, 2022 (the end of available data) (Figure 7.1).

2.2 Sample Selection

We used the Medicare databases to identify patients with HR+ HER2- MBC who started a CDK4/6i in the first-line setting. We selected patients with primary breast cancer (BC) for initial study inclusion by requiring them to have ≥2 primary BC outpatient claims, dated ≥30 days apart or ≥1 inpatient claim (proxy is 174x and C50x) in any billing position during the study period. To identify patients with MBC, we looked for the presence of at least two claims with a diagnosis of a secondary malignancy on two distinct dates during the study period (proxy is 197x,198x, 199x, C77x, C78x, C79x, C80) with the first metastatic claim being after the primary breast cancer diagnosis. To avoid misclassification of diagnosis codes, the presence of 2 medical claims for secondary malignancy after the diagnosis of the primary breast was required. [15]

We required a patient with MBC to initiate a CDK4/6i in the first-line setting. We considered a CDK4/6i first line if the agent was given within 90 days of the MBC diagnosis. The date of the first claim for a CDK4/6i defined the study index date. We identified tumor HR and HER2 status using previously published algorithms.[7-11] HR+ status was confirmed by evidence of a claim for a CDK4/6i (as therapy indicates) and HER2- status by no evidence of claims for therapies targeting HER2 positivity (HER2 +). The cohort selection is depicted in Figure 7.2.

Patients had to meet the following inclusion criteria at the index date: (1) Medicare enrolled; (2) breast cancer as the first or only cancer diagnosis; and (3) 6 months of continuous Medicare enrollment before the study index date to ensure incident cancer and to calculate comorbidity index score.

We excluded patients if they met any of the following: (1) the presence of a claim for MBC diagnosis or CDK4/6i in any billing position during the washout period to ensure incident MBC CDK4/6 initiation, (2) claims for HER2+ medications anytime during the study period; (3) Diagnosis of cancer other than BC in any billing position during the study period to ensure that BC is primary cancer and that secondary malignancies are associated with BC.

We define the index period from the index date, through 1 year, the end of the patient's continuous health plan enrollment, or the end of data availability, whichever occurred first. Diagnoses and treatment codes can be found in the supplementary appendix (9.1 Appendix A and 9.2 Appendix B).

2.3 Study Measures and Outcomes

Baseline Patient Characteristics

We assessed baseline characteristics, including patient age, region, year of CDK4/6i initiation, type of CDK4/6i initiated, organ-level metastatic sites, and pre-index systemic therapies, on the index date. Using diagnosis codes from medical claims collected during the 6-month pre-index period, we calculated a modified Charlson Comorbidity Index that excluded malignancies. [16,17] We assessed metastatic sites only at baseline, defining them based on the presence of ≥1 claim with ICD-9-CM or ICD-10-CM diagnosis codes for secondary malignant neoplasm observed at the index date. A full list of codes used to define metastatic sites is provided in the supplementary appendix (9.1 Appendix A).

The proportion of patients receiving anticancer therapies including surgery, CT, ET, and other targeted therapies before the index date was assessed. We identified all anticancer treatments by using Health Care Common Procedure Coding System codes (HCPCS), ICD-9-CM procedure codes, ICD-10-CM procedure codes, and National Drug Codes/generic drug names. We identified and adapted codes for anticancer therapies using previously published papers [11,13] which can be found in the supplementary appendix (9.3 Appendix C).

Healthcare resource utilization and costs

Our primary outcomes of interest were healthcare resource utilization (HRU) in the 6 months following CDK4/6 initiation and 1-year costs following first-line CDK4/6i initiation in HR+/HER2- MBC Medicare-enrolled patients. We chose a 6-month follow-up period for HRU to ensure the analysis did not ignore censoring. For costs, we selected a 1-year follow-up period, allowing us to use the Kaplan-Meier sample average (KMSA) to account for censoring beyond 6 months.

HRU components analyzed include the following: number of inpatient [IP] admissions, IP days, length of stay per IP admission, days with emergency room [ER] services, number of outpatient [OP] services, and days with [OP] services. The MarketScan variable STDPLAC was used to define healthcare settings and service types. We adapted codes to define different care settings from previously published literature.[18,19] Codes are available in the supplementary appendix (9.4 Appendix D).

We assessed total 1-year costs, as well as costs separately by care setting/service type (inpatient (IP), emergency room (ER), outpatient services (OP), and pharmacy). Total healthcare costs are the sum of IP, ER, OP, and pharmacy costs. The cost estimates represent all payments directly by CMS Medicare according to paid amounts included in each claim, excluding employer-paid amounts and patients' deductibles and copayments. We adjusted costs to 2023 US dollars using the medical care component of the US Consumer Price Index. [20]

2.4 Statistical Analysis

We summarized baseline characteristics using descriptive characteristics. To characterize continuous variables, we used mean (standard deviation [SD]), median, and interquartile range, as appropriate. For categorical variables, we summarized frequencies.

We calculated the number of patients having ≥ 1 admission, the mean number of inpatient (IP) admissions, and among those who had IP admissions, the mean length of stay per admission. For emergency room services, we calculated the number of patients having ≥ 1 visit, and among those who had an ER visit, we calculated the mean number of visits per patient. For outpatient OP services, we calculated the number of patients having ≥ 1 service, and among those who had an OP visit, the mean number of days with OP services per patient.

The mean 1-year cumulative cost following first-line CDK4/6i initiation was estimated using the Kaplan-Meier sample average (KMSA) to account for differential follow-up due to censoring. We censored patients at discontinuation of insurance coverage or the end of the study period, whichever occurred first. We estimated the cumulative mean costs during the 1-year period by calculating the sum of the monthly mean costs among patients who remained in the health plan at the start of each month, weighted by the probability of remaining in the health plan at the start of each month. [21] Nonparametric bootstrapping with 10,000 independent samples was used to generate the 95% CIs for the KMSA estimates. We reported costs as 1-year and monthly means.

We performed cohort selection and statistical analyses using SAS version 9.4 (SAS Institute, Cary, NC).

3. Results

3.1 Baseline Characteristics

A total of 901 Medicare-enrolled patients with HR+, HER2- MBC met the study inclusion criteria. The mean age of the cohort was 74 years (standard deviation [SD] 6.8), with a mean CCI score of 0.6 (SD 0.8). Patients were more likely to reside in the North Central than any other region, and the most common CDK4/6i initiated was palbociclib (n=804 (90%)). At baseline, 651 (72%) of patients had evidence of bone metastasis, 316 (35%) had visceral disease, 160 (18%) had lung metastasis, 187 (16%) had liver metastasis, and 119 (13%) had lymph metastasis. Before CDK4/6i initiation, most patients received some form of systematic therapy. Nearly 68% (n=612) of patients received endocrine monotherapy, 2.1% (n=19) received combination endocrine and chemotherapy, 0.3% (n=3) received monotherapy with chemotherapy, and 30% (n=267) received no prior systematic treatments. Baseline characteristics are presented in Table 6.1.

3.2 Primary Outcome

Healthcare Resource Utilization:

During the 6 months following the index date 214 (23.8%) patients had ≥ 1 inpatient admission. Among those with an inpatient admission, the mean number of admissions per patient was 1.7 (SD=0.98) and the mean length of stay was 5.9 days (SD=6.3). 271 (30%) patients had an ER visit, and among those with a visit, the mean number of visits per patient was 2.1 (SD=1.5).

Nearly 97% of patients had ≥ 1 outpatient service with the mean number of days with outpatient services among those patients per patient being 19.9 (SD=12.3). (Table 6.2.)

Healthcare Costs:

The mean total 1-year healthcare costs per patient following CDK4/6i initiation were $62,229 (95% CI 52281, 73029), which was a sum of IP, OP, ER, and pharmacy costs. The main driver of costs was outpatient services, with a mean of $31,686 (95% CI: (27168, 36925)) per patient, which represented approximately 50% of the mean total 1-year healthcare costs. Following outpatient services, pharmacy costs were the next driver of costs with a mean of $22,727 (95% CI: (19273, 25931)) per patient. All-cause inpatient services and ER visits were $68,78 (95% CI: (5132, 8979)) and $937.58 (95% CI: (708, 1193)) respectively. (Table 6.3)

4. Discussion

We conducted a retrospective cohort study using MarketScan claims data to describe HRU and costs of Medicare-enrolled HR+, HER2- MBC patients who initiated a CDK4/6i in the first-line setting. We found a mean Medicare per patient 1-year all-cause expenditure of $62,229 (95% CI 52281, 73030) following CDK4/6i initiation. Nearly 50% of the overall expenditure, was due to outpatient services with a mean total cost of $31,686 per patient (95% CI 27168, 36925), which can be attributed to 96.4% of the cohort having ≥ 1 outpatient service in the first 6 months following therapy start. After further investigation, the high outpatient costs may be attributable to infusion therapies. The next cost driver was pharmacy costs, followed by inpatient services and ER visits. Lower costs associated with inpatient services and ER care in the total health care expenditure may be attributed to only 23.8% (N=214) of patients having an inpatient admission and 30% (N=271) having a visit to the ER.

To our knowledge, this is the first study offering a comprehensive assessment of real-world economic outcomes of Medicare-enrolled patients with HR+/HER2- MBC who started a CDK4/6i in the first-line setting. A previous study by Burne et al. (N=4,320) assessed the mean 6-month HRU and mean monthly economic impact during CDK4/6i therapy in a privately insured population [7] and found similar results. They assessed HRU and costs during treatment for the three CDK4/6i (abemaciclib, palbociclib, and ribociclib) and found, like our study, outpatient services followed by pharmacy to be the main

drivers of costs in all three cohorts. In the abemaciclib, palbociclib, and ribociclib cohort, they found patients had an average of 0.7, 0.4, and 0.5 inpatient admissions respectively. They found the abemaciclib, palbociclib, and ribociclib cohorts to have a mean number of ER service days of 0.9, 0.6, and 1.1 respectively, and a mean number of OP service days of 26.9, 23.7, and 24.4 respectively. They reported no difference in HRU between the three agents, but lower overall per-patient mean monthly costs in the ribociclib cohort (abemaciclib ($12,378), palbociclib ($7,928), ribociclib ($7,136)).

There are several limitations to our study. First, verification of HR+, HER2- MBC patients who initiated a CDK4/6i in the first line setting is not directly identifiable in Marketscan, due to the unavailability of biomarkers. The patient's HR+, and HER2- status was identified following a previously published algorithm where evidence of treatment with endocrine therapy and absence of evidence of treatment with an HER2-targeted therapy were needed. Due to the lack of biomarkers in the database, it is possible misclassification occurred. Metastatic status was identified using secondary malignant codes, which are subject to misclassification. The line of therapy is additionally difficult to determine using claims data. To ensure incident CDK4/6i use in the first-line setting we required patients to receive the index agent within 90 days of MBC diagnosis. There may be a portion of patients who initiated a CDK4/6i in the first line setting more than 90-day days after their MBC diagnosis that we missed. By implementing this restriction, we may select patients who are healthier and more motivated to receive care or have better access to care. Additionally, the duration of follow-up differed among the patients. To account for differential follow-up, outcomes were analyzed using the KMSA estimator. We assumed all censoring was noninformative and that patients whose costs were observed were representative of patients whose costs were not observed, and this assumption may be violated. Furthermore, we assumed that most costs incurred are attributed to MBC itself; however, since we analyzed all-cause costs, it is possible that costs not related to MBC itself were captured. It is also important to note that these results may not apply to younger populations with MBC, and only represent individuals who receive commercial insurance in addition to Medicare. Lastly, this study was susceptible to other inherent issues with retrospective cohort studies using claims data, such as coding errors or differences in billing practices.

5. Conclusion

This retrospective real-world study described and assessed HRU and costs in Medicare-enrolled HR+, HER2- MBC patients who initiated a CDK4/6i in the first-line setting. There are numerous sources of

healthcare resource use and cost in patients following CDK4/6i initiation in the Medicare population, especially in the outpatient setting. High outpatient costs are possibly attributable to infusion therapies. Our study suggests further advancements in the treatment of HR+ HER2- MBC may have the ability to reduce economic expenditures and provide information for value assessment and healthcare decision-makers.

6. Tables

6.1 Baseline characteristics of cohort

Table 6.1: Baseline Characteristics

Characteristic	Total Study Population (N=901)
Age (years) – mean (SD)	74.1 (6.9)
Year of CDK4/6i initiation– n (%)	
2015	85 (9.4)
2016	190 (21.1)
2017	151 (16.8)
2018	107 (11.8)
2019	99 (11.0)
2020	123 (13.9)
2021	123 (13.7)
2022	23 (2.6)
Type of CDK4/6i initiated first line – n (%)	
Palbociclib	804 (89.2)
Ribociclib	36 (4.0)
Abemaciclib	61 (6.8)
Region – n (%)	
Northeast (1)	226 (25.1)
North Central (2)	376 (41.7)
South (3)	219 (24.1)
West (4)	80 (8.9)
Charlson Comorbidity Index	
Mean (SD)	0.64 (0.8)
0– n (%)	457 (50.7)
1– n (%)	316 (35.1)

2– n (%)	94 (10.4)
≥ 3– n (%)	34 (3.8)
Site of metastasis [a] – n (%)	
Bone	651 (72.6)
Brain	53 (5.8)
Liver	137 (15.8)
Lung	160 (18.1)
Lymph	119 (13.2)
Kidney	3 (0.4)
Other	237 (25.8)
Ovary	3 (0.2)
Visceral	316 (35.4)
Pre-index cancer treatments	
Endocrine therapy only	612 (68.0)
Chemotherapy only	3 (0.3)
Endocrine therapy and Chemotherapy	19 (2.1)
No Endocrine therapy or Chemotherapy	267 (30)
Surgery	7 (0.8)

[a] Categories are not mutually exclusive

6.2 Healthcare Resource Utilization

Table 6.2: Healthcare Resource Utilization [a]

Characteristic	Total Study Population (N=901)
Inpatient Admissions	
Had ≥ 1 admission (n, %)	214 (23.8)
Number of admissions among patients with ≥ 1 admission (mean, SD) [b]	1.7 (1.0)
Median (IQR)	1 (1,3)
Min	1
Max	5
Length of stay per admission among patients with ≥ 1 admission, days (mean, SD) [b]	5.9 (6.3)

Median (IQR)	4 (3,7)
Min	1
Max	44
Emergency Room Visits	
Had ≥ 1 visit	271 (30%)
Number of visits per patient among patients with ≥ 1 visit (mean, SD) [b]	2.1 (1.5)
Median (IQR)	2 (1,2)
Min	1
Max	10
Outpatient Services	
Had ≥ 1 service	868 (96.4%)
Days with outpatient services, among patients with ≥ 1 service (mean, SD) [b]	19.96 (12.3)
Median (IQR)	18 (11,26)
Min	1
Max	110

[a] Healthcare resource utilization was calculated during the 6 months following the index date
[b] The denominator includes only those with 1≥ service

6.3 Healthcare Costs

Table 6.3: Healthcare costs

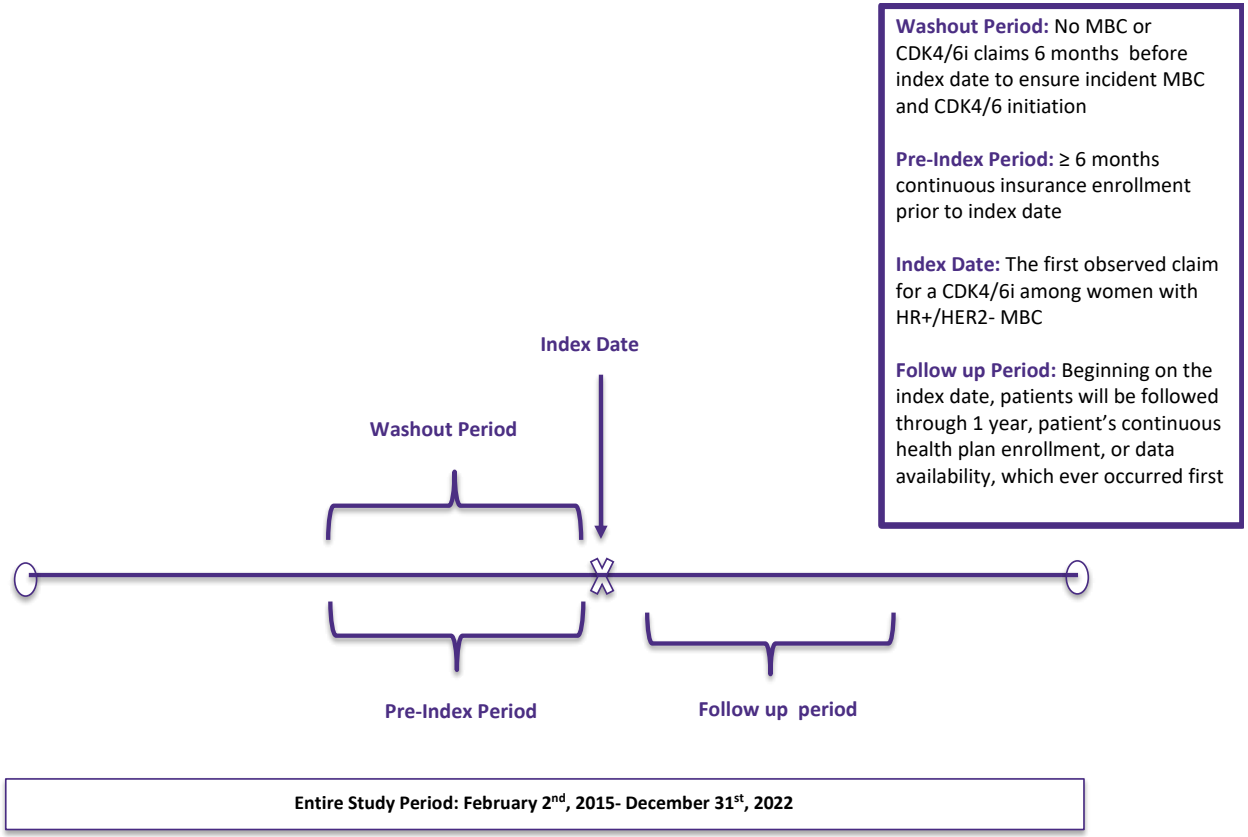
	Month											
Setting	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Inpatient Services												
Mean monthly costs	$1,584	$755	$341	$916	$419	$4345	$479	$407	$662	$465	$227	$189
Mean total IP costs [a]	$6,878 **(**95%CI 5132, 8979)											
ER Visits												
Mean monthly costs	$170	$101	$159	$86	$74	$24	$64	$71	$40	$49	$39	$60
Mean total ER costs [a]	$938 (95% CI 708, 1194)											
Outpatient Services												
Mean monthly costs	$4,272	$2,507	$2,855	$3,013	$2,806	$2,659	$2,636	$2,278	$2,072	$2,663	$1,970	$1,955
Mean total OP costs [a]	$31,686 (95% CI 27168, 36925)											
Pharmacy Costs												

Mean monthly costs	$4,396	$1,924	$2,313	$2,119	$1,941	$1,799	$1,696	$1,412	$1,399	$1,261	$1,249	$1,218
Mean total pharmacy costs [a]	$22,727 (95% CI 19273 , 25932)											
Mean Total Costs												
Mean total monthly costs	$10,423	$5,287	$5,668	$6,134	$5,241	$4,917	$4,874	$4,167	$4,174	$4,439	$3,485	$3,422
Mean total annual healthcare costs	$62,229 (95% CI 52281, 73030)											

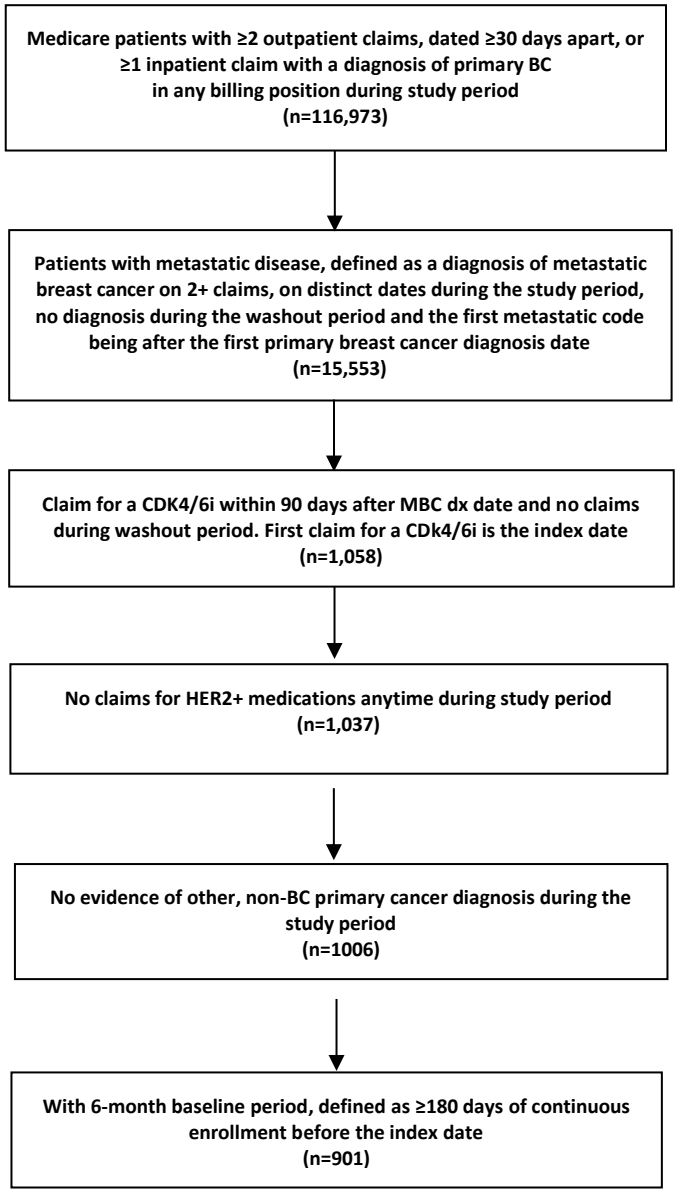
[a] Mean 1-year total costs following CDK4/6i initiation, calculated using the KSMA

7. Figures

7.1 Study design



7.2 Cohort Selection Process



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9. Appendices

9.1 Appendix A –ICD-9CM and ICD-10-CM diagnosis codes

Table 9.1 Appendix A ICD-10-CM and ICD-9CM Diagnoses Codes
*Adapted from Smyth et al.

Type of Cancer	**ICD-10-CM**	**ICD-9-CM**	**Notes**

Breast cancer	C50x	*174x,*	*To identify primary BC cases*
Secondary malignancy	C77x – C80x	197x-199x	*To identify MBC cases*
	C78.7	197.7	Secondary liver metastases
	C78.00, C78.01, C78.02	197.0	Secondary lung metastases
	C77.0, C77.1, C77.2, C77.4, C77.8, C77.9	196.0, 196.1, 196.2, 196.5,196.6,196.8, 196.9	Secondary lymph metastases
	C78.30, C78.39, C78.4, C78.5, C78.89, C79.10, C79.11, C79.19, C79.2, C79.31, C79.32, C79.40, C79.49, C79.52, C79.70,C79.71, C79.72, C79.82, C79.89, C79.9, C80.0	*197.4, 197.5, 198.1, 198.2, 198.4, 198.7, 198.82, 198.89, 199.0*	Secondary other metastases
	C79.00, C79.01, C79.01, C79.02,	*197.8 198.0*	Secondary kidney metastases
	C7800, C78.01, C78.02, C78.2, C78.6, C78.7	197.0, 197.2, 197.6, 197.7	Secondary visceral metastases
	C79.31	*198.3,*	Secondary brain metastases

	C79.60, C79.61, C79.62	*198.6*	Secondary ovary metastases
	C79.51	*198.5*	Secondary bone metastases
Presence of another primary malignancy	C00 – C49, C60 – C97	*140x-173x, 175x-194x*	*To ensure incident BC cases*

9.2 Appendix B –Codes for HER2+ Medications

Table 9.2 Appendix B Codes for HER2+ Médications
*Adapted from Smyth et al.

Description	**HCPCS code**	**NDC code**
Ado-trastuzumab emtansine		
Injection, ado-trastuzumab emtansine, 1 mg	C9131	
Injection, ado-trastuzumab emtansine, 1 mg	J9354	
Kadcyla		50242008701
Kadcyla		50242008801
Trastuzumab		
Injection, trastuzumab, excludes biosimilar, 10 mg	J9355	
Injection, trastuzumab, 10 mg and hyaluronidase-oysk	J9356	
Injection, trastuzumab-dttb, biosimilar, (ontruzant), 10 mg	Q5112	
Injection, trastuzumab-pkrb, biosimilar, (herzuma), 10 mg	Q5113	

Injection, trastuzumab-dkst, biosimilar, (ogivri), 10 mg	Q5114	
Injection, trastuzumab-qyyp, biosimilar, (trazimera), 10 mg	Q5116	
Injection, trastuzumab-anns, biosimilar, (kanjinti), 10 mg	Q5117	
		05024213460
		50242005656
Herceptin Hylecta		50242007701
Herceptin		50242013201
Herceptin		50242013210
Herceptin		50242013460
Herceptin		50242013468
		50242033301
Kanjinti		55513013201
Kanjinti		55513014101
		63459030547
		63552047001
Enhertu		65597040601
		67457084550
Ogivri		67457084744
Ogivri		67457099115
Pertuzumab		
Injection, pertuzumab, 10 mg	C9292	
Injection, pertuzumab, 1 mg	J9306	
Perjeta		50242014501
Lapatinib		
Tykerb		00078067119
Tykerb		00173075200
		51947075200
		51947075201
		51947075202
		51947075203

Neratinib		
Nerlynx		70437024018
		70437024026

9.3 Appendix C – Codes used to define anticancer agents

Table 9.3 Appendix C Codes used to define anticancer agents
*Adapted from Smyth et al. and Gopal et al.

Description	HCPCS/CPT code	NDC code
Aromatase inhibitors , everolimus, fulvestrant, olaparib, tamoxifen, doxorubicin, paclitaxel, cyclophosphamide, carboplatin, docetaxel, cisplatin, epirubicin, ixabepilone, capecitabine, gemcitabine, flurouracil, eribulin, vinorelbine, palbociclib, ribociclib, abemaciclib, surgery, nonspecific chemotherapy	Available upon request	Available upon request

9.4 Appendix D – Codes and description of each place of service variables for health care settings

The components and descriptions of health care setting

*Adapted from Yang et al. and Chua et al.

Claim type	Definition
Inpatient Setting	1. SVCSCAT not ending with "20" (emergency services) 2. STDPLAC = 21 (inpatient hospital) or SVCSCAT equal to one of the following: - 10xxx (facility inpatient) - 20xxx (physician inpatient) - 301xx, 302xx, 303xx (mental health inpatient) - 311xx, 312xx, 313xx (substance abuse inpatient) - 22130, 22131, 22132, 22135, 22136, 22137, 22140,

	22115, 22120, 22126, 22141, 22151, 22152, 22153, 22154, 22155, 22156, 22159, 22161, 22162, 22163, 22164, 22165, 22166, 22167, 22168, 22169, 22199 (inpatient professional services)
Institution Setting	1. STDPLC= 31 (skilled nursing facility), 32 (nursing facility), 34 (hospice) , 35(Adult Living Care Facility), 13 (Assisted Living)
Emergency Department	1. STDPLAC = 23 (emergency room – hospital) or SVCSCAT ending with "20" (emergency services)
Outpatient/Ambulatory Setting **Exclude** SVCSCAT not ending with "20" (emergency services)	
Office Visit	1. STDPLAC = 11 (office), 18 (place of employment), 49 (independent clinic), 50 (federally qualified health center), 71 (state or local public health clinic), 72 (rural health clinic), 95 (outpatient not elsewhere classified), 65 (ESRD Treatment Facility) or 99 (other)
Hospital outpatient department	1. STDPLAC = 19 or 22 (on-campus or off-campus outpatient hospital)
Urgent care center	1. STDPLAC = 20 (urgent care center), 41 (ambulance-land), 42 (ambulance-Air or water)
Retail clinic	1. STDPLAC = 17 (walk-in retail clinic)
Outpatient surgery	1. STDPLAC = 11 (office), 19 or 22 (on-campus or off-campus outpatient hospital), or 24 (ambulatory surgery center)
Mobile Unit	1. STDPLAC=15

Home visit	1. STDPLAC = 12 (patient home)
Behavioral Health Care	1. STDPLAC = 53 (community mental health center), 62 (comprehensive outpatient rehabilitation facility) , 57(non-rsidential substance abuse treatment facility), 55 (residential substance abuse treatment facility) , 56 (psychiatric residential treatment center)