Yuliastuti F, Andayani TM, Endarti D, Kristina SA. Cost determinant of chemotherapy in breast, cervical, and lung cancer in the era of National Health Insurance. Pharmacy Practice 2024 Apr-Jun;22(2):2957.
https://doi.org/10.18549/PharmPract.2024.2.2957

Original Research

Cost determinant of chemotherapy in breast, cervical, and lung cancer in the era of National Health Insurance

Fitriana Yuliastuti, Tri Murni Andayani, Dwi Endarti, Susi Ari Kristina

Received (first version): 21-Aug-2023 Accepted: 13-Nov-2023 Published online: 15-Apr-2024

Abstract

Introduction: This study focuses on the financial burden of treating breast, cervical, and lung cancer in Indonesia. The prevalence and mortality rates of this cancer, particularly in the context of the National Health Insurance program, are highlighted. The financial strain created by cancer treatment, its relationship to Universal Health Coverage goals, and the impact of the JKN initiative are discussed. **Novelty:** The originality of the study lies in exploring patient profiles, disease severity, and associated expenses, culminating in a comprehensive evaluation of medical expenses. Methods: This study used an analytic observational approach with a cross-sectional design, centered on the perspective of the Dharmais Cancer Center Hospital. The population consists of JKN patients diagnosed with breast, cervical and lung cancer. Data were collected retrospectively from JKN claim files and medical device records. Quantitative studies were conducted to understand the components of real costs, variations of chemotherapy, and the determinants of differences in costs. Statistical tests were used for data analysis. **Results:** This study involved 348 breast cancer patients, 306 cervical cancer patients, and 176 lung cancer patients undergoing chemotherapy in 2020. The distribution of patients by age group and cancer type was analysed, and disease characteristics were categorized by stage and severity using the Indonesian Case Base Groups (INA-CBGs) code. The cost analysis reveals the importance of accommodation, medicines, and medical equipment in terms of the overall expenditure. The cost of chemotherapy is very influential, and different treatment regimens are being explored for each type of cancer. **Conclusion:** This study underscores the important role of chemotherapy drugs, pharmaceutical costs, and medical devices in driving the overall cost of care. These insights contribute to informed decision making in healthcare policy and patient management, potentially reducing the financial burden faced by cancer patients. Recommendation: Further research and interventions can be designed based on these findings to optimize cancer treatment strategies and resource allocation.

Keywords: cancer treatment; breast cancer; cervical cancer; lung cancer; healthcare costs

INTRODUCTION

The International Agency for Research on Cancer (IARC) has indicated that breast, cervical, and lung cancer remain areas of concern. These diseases not only lead to fatalities but also fall within the government's purview for providing treatment and care. According to the IARC's 2020 report on Indonesia, among a total population of 73,523,621, there were 946,088 reported cases of cancer over a five-year period, resulting in 396,914 new cases and 234,511 fatalities.[1] The most prevalent new cancer cases in 2020, encompassing all genders and age groups, included breast cancer at 65,858 cases (16.6%), cervical cancer at 36,633 cases (9.2%), and lung cancer at 34,783 cases (8.8%). Analyzing the cases among females in 2020, the highest incidence was breast cancer at 65,858 cases (30.8%), while among males, the leading new case was lung cancer at 25,943 cases (14.1%).[1,2]

The financial burden associated with cancer treatment has reached 2nd place, accounting for 18% of overall spending among the most economically burdensome catastrophic diseases. Indonesia has taken the ambitious goal of achieving Universal Health Coverage by 2019.[3] However, as of October 2019, statistical records show that 17% of the population is not enrolled in the National Health Insurance program. This difference in participation is mainly due to financial shortfalls experienced since the program's inception. The National Health Insurance (JKN) initiative, which was introduced in 2014 in response to the alarming prevalence of chronic diseases in the community, inadvertently contributed to increasing healthcare costs, thereby increasing the fiscal pressure on the healthcare system.[4]

The economic burden associated with cancer treatment encompasses various factors, including the incidence, prevalence, and mortality of cancer, alongside advancements in medical technology.[5] This financial burden remains consistent regardless of the specific treatment modality employed or the nature of the medical procedures undertaken. This comprehensive framework is referred to as the Indonesian Case Base Groups (INA-CBGs). An alternate scenario involves an added financial load in the form of hospitalization expenses

Fitriana YULIASTUTI. Doctoral Program in Pharmaceutical Science, Faculty of Pharmacy, Universitas Gadjah Mada Yogyakarta, Department of Pharmacy, Faculty of Health Science, Universitas Muhammadiyah Magelang, Magelang, Indonesia. fitrianayuliastuti@ummgl.ac.id
Tri Murni ANDAYANI*. Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia. trimurtia@ugm.ac.id
Dwi ENDARTI. Department of Pharmaceutics, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia. endarti_apt@ugm.ac.id
Susi Ari KRISTINA. Department of Pharmaceutics, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia. susiari_k@ugm.ac.id

www.pharmacypractice.org (eISSN: 1886-3655 ISSN: 1885-642X)

incurred by cancer patients undergoing surgical interventions. For instance, in the case of breast cancer treated with hormone therapy, the cost spectrum ranges from IDR 5,436,756 to IDR 5,646,678. Among the present cost constituents, the predominant share is attributed to consumable materials for medical equipment, accounting for 28.6% of the total costs. Inpatient chemotherapy expenses span between IDR 2,546,166 and IDR 6,823,821, while pharmaceutical costs contribute significantly at 83.5%.[6]

From the available data, cancer treatment is a complex and expensive process, involving various medical interventions, therapies, and drugs.[7,8] Financing cancer treatment can be a major challenge for patients and the healthcare system. Access to care and follow-up treatment, as well as the overall quality of care, is affected by financial constraints.[9,10] In Indonesia, there is a mix of public and private health care providers,[11,12] with the government health insurance program known as BPJS playing an important role in providing coverage for various medical treatments, including cancer treatment.[13] The INA-CBGs reimbursement system is one of the methods used for reimbursement in the BPJS scheme. In INA-CBGs, each group is associated with a certain rate that determines the amount of reimbursement that healthcare providers receive for treating patients in that group.

For cancer treatment, the INA-CBGs system will likely categorize various types of cancer cases into appropriate groups, considering factors such as the type and stage of the cancer, the method of treatment (surgery, chemotherapy, radiation, etc.), and other medical considerations relevant. However, not all types of chemotherapy drugs are not covered by BPJS. The reimbursement amount provided to healthcare providers is intended to cover the costs associated with treating patients in each group.[14] In our previous research it was shown that there was a real difference between the INA-CBGs rates and the real costs of all breast, cervical and lung cancer patients at the Dharmais Cancer Center Hospital. The real cost component for chemotherapy patients with code Ina CBGs C-4-3 degrees of severity 1, 2 and 3 for breast, cervical and lung cancer patients but not explained by the real cost component.[15] In our recent study, we have found the overall cost of medical equipment for non-surgical procedures, surgical procedures, expert consultations, nursing, class accommodation, radiology support costs, laboratories, blood bank services, pharmaceutical costs, medical equipment, non-chemotherapeutic drugs, and chemotherapy regiments. This study also looks at the order of cost analysis by presenting the cost of chemotherapy drugs given to breast, cervical, and lung cancer patients.

Therefore, our present study addresses three different aspects (patient profiles, disease severity, and expenditures) related to the three predominant cancers in Indonesia. The current investigation evaluates the comprehensive expenses associated with treatment. This encompasses primary therapeutic interventions, encompassing expenses for chemotherapy and radiotherapy, alongside supplementary therapeutic costs encompassing pharmaceuticals, laboratory fees, blood bank charges, and medical equipment procedures involving specialist remuneration, physician or nurse fees, and consultation charges. Additionally, this study undertakes an examination of the elements influencing costs by presenting a comprehensive analysis of expenses and diverse forms of chemotherapy protocols for patients diagnosed with breast, cervical, and lung cancer. These individuals are part of the National Health Insurance program at Dharmais Cancer Center Hospital.

MATERIALS AND METHODS

This research was conducted with an analytic observational approach using a cross-sectional study design according to the hospital's perspective. The subjects used in this study were all JKN patients with a diagnosis of breast cancer, cervical cancer, and lung cancer who were treated at the Dharmais Cancer Center hospital. Data were collected retrospectively from BPJS claim files and medical equipment records of breast cancer, cervical cancer, and lung cancer patients. This research is a quantitative study with the aim of knowing the real cost components based on the level of variation of chemotherapy patients in breast, cervical, and lung cancer and knowing the determinants that affect these differences in costs. The research subjects are all the population of BPJS chemotherapy patients for breast, cervical, and lung cancer at the Dharmais Cancer Center Hospital for the 2020 period. The entire subject population was calculated using the Slovin formula with an error margin of 5%.

Analysis determinant data affecting costs was analyzed based on a nominal scale for age, sex, and type of financing or health insurance from data obtained from medical equipment records, financial data, and claims from the administration. The staging was analyzed based on the ordinal scale, while severity was analyzed by looking at the INA-CBGs code based on the nominal scale from data obtained from medical equipment records, chemotherapy regimens were analyzed based on continuous drug administration data, and doses obtained from medical equipment records. The determinant analysis measured the average cost per patient per episode over a one-year period. The real cost component is calculated from the average per patient seen from the main therapy cost components, namely chemotherapy costs, radiotherapy costs, surgery costs, and from additional therapy costs which consist of side effect drug costs, laboratory costs, doctor or nurse fees, hospital fees from financial data and claims from the administration. The relationship between the use of chemotherapeutic drug regimens and the real total costs is described.

RESULTS

This research was conducted on breast, cervical, and lung cancer patients undergoing chemotherapy at Dharmais Cancer Center Hospital in 2020. The total population in this study was 2,660 breast cancer patients, 1,305 cervical cancer patients, and 313 lung cancer patients.[6] Sampling was carried out using the Slovin formula with an error tolerance limit used 0.05 in Equation (1), where n= sample, N= population, and e= margin

of error. The results of the calculation of the sample population are then characterized and presented in Table 1.

Table 1 presents the patient distribution across various cancer types, specifically breast, cervical, and lung cancers. The calculations were derived using the Slovin formula, yielding a total of 348 patients for breast cancer, 306 patients for cervical cancer, and 176 patients for lung cancer. Notably, the highest incidence of breast cancer was observed within the 41-50 years age group, comprising 128 individuals (37%), followed by the 51-60 years age group with 100 patients (29%). This investigation aligns with the epidemiological pattern of breast cancer prevalence in the United States during 2015, which indicated a heightened occurrence of breast cancer among individuals aged 40-69 years, particularly within the 51-60 years bracket. Regarding cervical cancer, most cases occurred within the 41-50 years age category, constituting 112 patients (36%), as well as within the 51-60 years group, with 94 patients (31%). Notably, among the 176 lung cancer patients, the largest cohort, comprising 65 individuals (37%), fell within the 51-60 years age range. Conversely, a declining trend was observed in the occurrence of cervical cancer among patients aged 61-71 years. This decline might be attributed to the waning immune system efficacy associated with advanced age, rendering the patients more vulnerable to succumbing to the disease, ultimately leading to mortality.

Furthermore, this study delves into a comprehensive analysis of the distinct attributes exhibited by individuals undergoing chemotherapy due to breast, cervical, and lung cancers, as meticulously outlined in Table 2. Disease characteristics have been meticulously scrutinized with an emphasis on both the stage and severity of the conditions, employing the INA-CBGs code as a framework for classification.

The accurate determination of cancer staging holds paramount significance in the precise selection of appropriate treatment strategies. As illustrated in Table 2, the distribution of cancer stages unveils notable insights. Specifically, in breast cancer, Stage IVA accounts for 54%, whereas in lung cancer, it escalates to 88%. Notably, cervical cancer exhibits its highest frequency at stage IIIB, constituting 34%. The pronounced prevalence of cancer patients in stages III and IV underscores the prevailing dearth of patient awareness and timely detection, prompting treatment initiation at the incipient manifestation of symptoms or the early disease phases. Evidently, the meager percentage of patients diagnosed at stage 1, amounting to less than 0.1%, corroborates this observation. These findings resonate with parallel investigations conducted at the Dr. Moewardi Surakarta Hospital, underscoring a prevailing trend wherein a substantial portion of breast, cervical, and lung cancer patients received diagnoses during advanced stages. This is evident in the distribution of 40.35% for Stage IVA and 17.54% for Stage III.

Based on the data provided in Table 3, the analysis reveals that the mean expenses associated with chemotherapy medications for severity levels I, II, and III are IDR 3,635,191; IDR 5,872,590; and IDR 4,167,751, respectively. The cost element that predominantly contributes to the overall expenses is the

Table 1. Characteristics of patients with breast cancer, cervical cancer, and lung cancer

Category		Breast Cancer	Cervical cancer	Lung Cancer
sample (N)		348	306	176
Age	<20	0	-	7
	21-30	11	11	4
	31-40	57	42	12
	41-50	128	112	34
	51-60	100	94	65
	61-70	45	39	47
	>70	7	8	6
Gender	Female	347	306	56
	Male	1	-	120
Class in Treatment	1	143	84	85
	2	60	49	36
	3	146	173	55
Membership type in BPJS	PBI	316	88	29
	Non-PBI	28	198	76

PBI: Contribution Assistance Recipients; Non-PBI: Non-Contribution Assistance Recipients

Table 2. Staging characteristics of breast, cervical, and lung cancer stage and severity based on INA-CBGs code

Disease characteristics		Breast cancer (%)	Cervical cancer (%)	Lung cancer (%)
Stadium	1A	3	-	4
	1B	-	28	-
	1C	-	2	-
	2A	18	27	5
	2B	14	81	-
	3A	38	9	8
	3B	61	114	1
	3C	6	8	-
	3D	-	-	-
	4A	189	27	155
	4B	5	4	1
	4C	13	7	2
Severity level I C-4-13-I	1	101	86	58
	2	39	24	17
	3	81	86	26
Severity level II C-4-13-II	1	42	16	22
	2	16	8	-
	3	31	47	14
Severity level III C-4-13-III	1	15	16	18
	2	5	8	15
	3	18	16	5

https://doi.org/10.18549/PharmPract.2024.2.2957

Table 3. Components of breast cancer, cervical cancer, and lung cancer treatment costs in severity code the INA-CBGs

Breast Cancer		**C-4-13-I**			**C-4-13-II**			**C-4-13-III**		
Class in treatment		1 (N)	2 (N)	3 (N)	1 (N)	2 (N)	3 (N)	1 (N)	2 (N)	3 (N)
Cost component (IDR)		287	222	231	120	88	261	42	15	52
Medical equipment cost	Non-surgical procedure	19,264	69,135	45,807	114,458	-	61,609	192,902	-	145,216
	Surgical procedure	-	-	-	-	-	-	-	-	-
	Consultation	1,346	1,577	2,174	2,708	3,977	5,775	-	-	-
	Experts	238,279	224,505	241,609	220,717	243,455	230,184	242,341	177,429	221,882
	Nursing	7,326	5,237	3,914	9,098	-	10,063	-	-	11,213
	Accommodation class	2,282,467	1,763,957	1,260,509	2,495,102	1,834,508	1,348,529	2,854,249	1,717,531	1,472,667
Supporting cost	Radiology	578,666	41,477	25,191	159,383	10,364	355,678	89,805	250,143	125,725
	Laboratory	139,999	181,372	218,339	237,600	74,636	136,391	603,659	210,643	331,863
	Blood bank services	5,297	6,883	6,287	58,200	65,727	62,667	35,268	54,571	28,353
Pharmaceutical Cost	Medical equipment	195,319	246,659	217,401	282,048	201,976	275,511	287,824	363,618	362,263
	Non chemotherapy drug	2,159,461	2,150,565	2,126,428	2,422,283	2,161,351	2,199,595	2,709,601	2,404,214	2,168,127
	Chemotherapy regiment	1,154,269	1,895,607	1,419,242	3,402,113	5,133,153	2,299,275	3,069,468	977,77	1,174,072
Cervical Cancer		**C-4-13-I**			**C-4-13-II**			**C-4-13-III**		
Class in Treatment		1 (N)	2 (N)	3 (N)	1 (N)	2 (N)	3 (N)	1 (N)	2 (N)	3 (N)
Cost Component (IDR)		10	6	10	2	1	6	0	2	2
Medical equipment cost	Non-surgical procedure	-	-	-	-	-	-	-	537	-
	Surgical procedure	-	-	-	-	-	-	-	-	-
	Consultation	-	-	-	-	-	-	-	-	-
	Experts	331,000	252,000	252,000	184,000	184,000	230,000	-	184,000	368,000
	Nursing	-	-	-	-	-	-	-	-	-
	Accommodation class	2,616,863	1,937,491	1,937,491	2,294,698	1,664,200	1,006,000	-	1,431,517	1,606,000
Supporting cost	Radiology	-	533,600	533,600	-	-	-	-	-	-
	Laboratory	146,200	237,333	237,333	157,000	157,000	204,500	-	162,000	108,500
	Blood bank services	-	-	-	-	-	-	-	-	-
Pharmaceutical Cost	Medical equipment	182,613	146,005	146,005	228,938	228,247	259,371	-	132,466	241,66
	Non chemotherapy drug	2,368,000	2,332,667	2,332,667	2,360,000	1,990,000	1,990,000	-	2,309,500	2,146,000
	chemotherapy regiment	1,982,709	3,509,879	3,509,879	1,085,200	1,085,200	851,79	-	1,136,300	102,96
Lung Cancer		**C-4-13-I**			**C-4-13-II**			**C-4-13-III**		
Class in Treatment		1 (N)	2 (N)	3 (N)	1 (N)	2 (N)	3 (N)	1 (N)	2 (N)	3 (N)
Cost Component (IDR)		60	20	27	24	16	16	22	16	5

Medical equipment cost	Non-surgical procedure	29,433	119,333	110,296	164,739	58,357	-	194,737	296,000	191,000
	Surgical procedure	-	-	-	-	-	-	-	-	-
	Consultation	-	-	-	-	-	-	-	-	-
	Experts	210,733	184,000	202,519	192,000	177,429	184,000	197,158	197,158	197,158
	Nursing	-	-	-	12,430	-	-	-	-	-
	Accommodation class	2,452,501	1,703,542	1,278,889	2,366,866	1,728,253	1,206,000	2,878,864	2,878,864	2,878,864
Supporting cost	Radiology	10,100	105,556	48,667	29,652	188,571	10,714	23,684	23,684	23,684
	Laboratory	83,033	72,500	208,593	117,261	181,286	401,000	451,316	451,316	451,316
	Blood bank services	36,833	-	-	62,870	67,214	-	152,211	152,211	152,211
Pharmaceutical Cost	Medical equipment	130,469	140,252	191,327	105,565	362,487	143,809	227,007	227,007	227,007
	Non chemotherapy drug	2,360,500	2,389,500	2,367,407	2,373,044	2,451,964	2,508,571	2,743,684	2,743,684	2,743,684
	chemotherapy regiment	3,621,029	3,534,704	3,351,069	4,992,639	4,524,627	4,251,321	3,915,002	3,915,002	3,915,002

expenditure on chemotherapy drugs due to their substantial pricing. This observation aligns with the findings of Harianto's investigation in 2015 at Dr. Sardjito Hospital, Yogyakarta, where chemotherapy drug costs constituted 61.93% of expenses for breast cancer treatment.[16] Examining Table 3, it becomes evident that the most substantial medical equipment expenditures encompass accommodations and specialist consultation charges. The principal ancillary expense arises from radiological procedure, as regular assessments of cancer progression necessitate routine radiology examinations for cancer patients. For individuals with cervical cancer, the highest supplementary expenses pertain to laboratory tests.

The costs associated with pharmaceutical interventions, particularly those related to chemotherapy for various types of cancer, are herein discussed in the context of medical expenditures. The pertinent details are catalogued in Table 4 for breast cancer, Table 5 for cervical cancer, and Table 6 for lung cancer. Among patients diagnosed with breast cancer, specifically, those undergoing treatment with trastuzumab, it is noteworthy that this therapeutic regimen incurs the highest average cost in comparison to alternative regimens devoid of trastuzumab. In the domain of combined therapy regimens, the amalgamation of Cyclophosphamide, Doxorubicin, and Fluorouracil emerges as the costliest among its counterparts. This combination is characterized by a median cost of 940.46 in class I, 768.391 in class II, and 781.110 in class III. It is imperative to highlight that the selection of this therapeutic blend is congruent with the guidelines stipulating first-line treatments for breast cancer control.[17]

Cisplatin remains the foremost single modality employed in the treatment of cervical cancer, with comparability in costs being evident across the three delineated classes that utilize these combination treatments. The combination boasting the highest cost involves the utilization of Doxorubicin, Ifosfamide, and Uromitexan within class 1, which carries an expense of IDR 6,691,800. Turning to the sphere of lung cancer management, the predominant solitary agent employed is Paclitaxel, incurring a cost of IDR 325,750. For combined therapeutic interventions, the most frequent pairing entails Cisplatin and Pemetrexed. This composite regimen commands a relatively elevated cost, spanning a range of 5,381,572 to 6,397,587. Notably, the most fiscally demanding combined therapy for lung cancer comprises Bleocin HCl, Carboplatin, and Pemetrexed, bearing a cost of IDR 6,053,526.

DISCUSSION

The findings of this investigation pertaining to gender stratification (male and female) have elucidated distinct patterns concerning cancer prevalence. Amongst female patients, an overwhelming 99.9% were afflicted with breast cancer, whereas the incidence of cervical cancer in women reached a complete 100%. Conversely, lung cancer predominantly manifested within the male demographic, accounting for 76% of cases. It is noteworthy that individuals affected by breast and cervical cancer consistently belonged to

Table 4. Characteristics for chemotherapy regimens in breast cancer

Class treatment	**1**		**2**		**3**	
Regiment Therapy	**Cost (IDR)**	**N**	**Cost (IDR)**	**N**	**Cost (IDR)**	**N**
Paclitaxel	-	7	390,500	1	260,000	5
Trastuzumab	6,598,680	-	6,598,680	1	-	-
Docetaxel + Cyclophospamide	1,552,975	24	1,622,687	5	1,499,924	5
Cyclophosphamide + Paclitaxel	805,770	7	554,695	1	-	-
Fluorouracil + Oxaliplatin	1,229,596	3	-		-	
Paclitaxel + Trastuzumab	6,989,180	-	6,989,180	1	3,020,000	3
Cyclophosphamide + Doxorubicin	727,313	-	800,779	3	559,936	7
Carboplatin + Docetaxel	1,118,225	-	1,125,104	2	1,271,664	3
Docetaxel + Trastuzumab	-	-	10,794,035	2	-	-
Docetaxel + Doxorubicin	1,000,149	-	1,000,149	1	-	
Doxorubicin + Fluorouracil	-	-	-	-	751,116	3
Cyclophosphamide + Methotrexate + Fluorouracil	1,045,649	7	364,734	2	365,096	5
Cyclophosphamide + Doxorubicin + Fluorouracil	940,465	54	768,391	36	781,110	82
Cyclophosphamide + Epirubicin + Fluorouracil	-	-	1,068,035	2	1,098,660	7
Cyclophosphamide + Doxorubicin + Paclitaxel	610,933	7	610,933	2	1,499,500	2
Cyclophosphamide + Doxorubicin + Docetaxel	1,205,582	17	787,508	2	1,094,247	19
Cyclophosphamide + Docetaxel + Rituximab	747,670	3	-	-	-	-
Ferron + Navelbin + Vinorelbine	1,283,724	3	-	-	-	-
Cyclophosphamide + Doxorubicin, + Epirubicin, Fluorouracil	-	-	1,145,377	1	-	-
Cyclophosphamide + Doxorubicin + Fluorouracil + Leucogen	-	3	-	-	1,057,355	2
Cyclophosphamide + Doxorubicin + Docetaxel + Trastuzumab	20,059,270	3	-	-	-	-
Cyclophosphamide + Docetaxel + Trastuzumab	-	-	-	-	10,807,184	-
Doxorubicin + Ifosfamide + Uromitexan + Doxorubicin	-	-	-	-	8,941,627	3

Table 5. Characteristics cost dan chemotherapy regimens in cervical cancer

Class treatment	**1**		**2**		**3**	
Regiment Therapy	**Cost (IDR)**	**N**	**Cost (IDR)**	**N**	**Cost (IDR)**	**N**
Bleomycin HCl	-	-	-	-	-	27
Carboplatin	-	-	-	-	-	13
Cisplatin	1,331,494	36	6,304,600	22	205,920	53
Paclitaxel	-	4	-	-	-	-
Cisplatin + Carboplatin	-	4	265,540	6	-	13
Carboplatin + Paclitaxel	1,085,200	18	1,085,200	16	1,102,500	67
Carboplatin + Etoposide	-	4	-	-	-	-
Cisplatin + carboplatin + Etoposide	-	4	-	-	-	-
Cyclophosphamide + Doxorubicin + Fluorourasil	7,999,950	9	-	-	-	-
Doxorubicin + Iphosphamide + Uromitexan	6,691,800	4	-	4	-	-

Table 6. Characteristics cost dan chemotherapy regimens in lung cancer

Class treatment	**1**		**2**		**3**	
Regiment Therapy	**Cost (IDR)**	**N**	**Cost (IDR)**	**N**	**Cost (IDR)**	**N**
Bleocin HCl	-	2		-		2
Paclitaxel	-	-	325,750	4		-
Carboplatin + Docetaxel	1,550,638	2	1,720,880	4	1,627,136	7
Carboplatin + Etopuside	1,089,512	3		-	557,706	2
Carboplatin + Gemcitabin	2,920,538	7	2,820,636	2	1,805,300	4
Carboplatin + Paclitaxel	2,287,409	5	1,805,377	2	1,071,985	2
Carboplatin + Pemetrexed	6,474,099	17	6,473,879	10	1,627,136	13
Cisplatin + Doxorubicin	-	-		-	5,851,946	2
Cisplatin + Gemcitabin	1,622,040	7	2,820,636	2	1,575,257	7
Cisplatin + Paclitaxel	-	-	1,805,377	2	1,808,380	2
Cisplatin + Pemetrexed	5,381,572	22	6,397,587	8	6,016,566	13
Doxorubicin + Fluorouracil	-	2	-	-	-	-
Gemcitabin + Vinorelbin	3,702,448	2	-	-	-	-
Bleocin HCl + Carboplatin + Pemetrexed	6,053,526	2	-	-	-	-
Bleocin HCl + Cisplatin + Pemetrexed	5,946,482	2	-	-	-	-
Carboplatin + Cisplatin + Etopuside	-	2	-	-	-	-
Carboplatin + Gemcitabin + Docetaxel	1,561,160	2	-	-	-	-
Cisplatin + Docetaxel + Pemetrexed	1,531,454	3	-	-	-	-
Cisplatin + Gemcitabin + Paclitaxel	-	-	1,705,420	2	-	-
Bleocin HCl + Carboplatin + Docetaxel + Pemetrexed	6,001,326	3	-	-	-	-
Bleocin HCl + Dacarbazin + Doxorubicin + Vincristin	1,697,010	2	-	-	-	-

the female gender. This phenomenon can be attributed to the heightened development and increased tissue density within female breast structures, resulting in a risk factor that surpasses that of males by a factor of 100. Male breast tissue does not undergo analogous proliferation to that observed in females. Furthermore, the endocrine milieu of women, characterized by elevated levels of estrogen, progesterone, and testosterone in comparison to men, serves as an imperative contributor. An elevation of these hormones beyond normal thresholds has been correlated with an augmented susceptibility to both breast and cervical malignancies. The augmented incidence of lung cancer in the male cohort can be traced to the heightened prevalence of smoking, a well-recognized risk factor. This is compounded by the greater prevalence of male smokers in comparison to their female counterparts.

The allocation of patient accommodations adheres to the guidelines stipulated in Regulation Number 52 of 2016 by the Minister of Health of the Republic of Indonesia, which pertains to the Standards for Health Service Costs within the framework of the Health Insurance Program. Within this framework, treatment rooms are categorized into three distinct classes, namely Class I, Class II, and Class III. The equitable distribution of patients across these treatment classes is substantiated by the information presented in Table 1, which illustrates the allocation of patient care categories. Notably, patients undergoing chemotherapy for breast, cervical, and lung cancers are evenly distributed across all three accommodation treatment classes. This distribution has a direct correlation with the financing modalities tied to national health insurance contributions, known as National Health Insurance (BPJS). Both general patients and patients with BPJS coverage play a role in this context, with the INA-CBGs rates determining the financing magnitude. Significantly, Class III represents the patient care category experiencing the highest influx of cases, particularly in the context of breast and cervical cancer. Moreover, for Class III patient care, the inpatient rates are notably lower when compared to treatment classes I and II. This financial distinction renders Class III care more economically feasible for patients enrolled in BPJS. The BPJS membership framework further segments patients into two discernible categories: Contribution Assistance Recipients (PBI), and Non-Contribution Assistance Recipients (Non-PBI), encompassing individuals not included in the PBI category. PBI beneficiaries are eligible for Class III inpatient services as part of their accommodation benefits. In contrast, non-PBI beneficiaries avail themselves of inpatient services commensurate with their respective contributions to BPJS.

The subjects under investigation in this study comprised patients undergoing chemotherapy for breast, cervical, and lung cancers. These patients were categorized within the INA-CBGs system, based on the gravity of their respective conditions, resulting in the formation of three distinct code groups denoted as C-4-13-I, C-4-13-II, and C-4-13-III. The Roman numeral annotation in the INA-CBGs code delineated the degree of disease severity. Among the cohort of chemotherapy recipients addressing breast, cervical, and lung malignancies, over 50% exhibited a distribution across varying severity tiers. Specifically, 26% of patients underwent severity level II chemotherapy for breast cancer, 23% for cervical cancer, and 20% for lung cancer, as documented.[18] It is noteworthy that severity levels I, II, and III exhibited notably elevated cost spectra. This investigation delineated three distinct dimensions of cost constituents: namely, expenditures associated with medical apparatus utilization, ancillary expenditures, and pharmaceutical outlays. Table 3 subsequently illustrates the stratification of cost components pertinent to breast, cervical, and lung cancers. Remarkably, accommodation and pharmaceutical expenses emerged as the principal constituents of medical apparatus costs across all severity classifications, encompassing breast, cervical, and lung cancers.

Aligned with antecedent inquiries, hospitalizations necessitating inpatient care emerged as the most significant contributor to aggregate expenses, except in the context of adjuvant breast cancer. These hospitalizations were not linked to admissions for chemotherapy administration, but rather to the management of chemotherapy-induced side effects and aggressive cancer treatment protocols. This discernment underscores the substantial escalation in the financial outlay for cancer treatment concomitant with the initiation of chemotherapy, transcending the expenditures incurred for anti-neoplastic medications and their delivery. Thus, there exists an imperative exigency for amassing empirical data from real-world scenarios concerning the probability and expected duration of hospital sojourns associated with diverse chemotherapy interventions. Such insights are pivotal in facilitating judicious therapeutic decisions for both medical practitioners and patients alike.[19] In accordance with empirical investigation, the utilization of a solitary pharmacological agent within the realm of cancer therapeutics in the Indonesian context remains extensively prevalent. In the context of metastatic phases, treatment protocols involving triplet chemotherapy regimens have been demonstrated to yield superior rates of patient response in comparison to both doublet regimens and monotherapeutic approaches. However, it is imperative to note that the available data concerning survival outcomes are presently inadequate to facilitate the formulation of definitive and pertinent deductions.[20]

The escalation in treatment costs is directly proportional to the number of administered cancer drugs. Across severity levels I, II, and III within all therapeutic categories, the most substantial expenditures are attributed to pharmaceutical outlays, trailed by expenses for medical equipment and ancillary medical device support. Notably, severity I exhibits the most extensive cumulative cost element in comparison to severity II and III within the identical treatment category. This disparity can be attributed to the burgeoning expenses incurred in addressing the adverse effects of chemotherapy medications in patients. This outcome aligns harmoniously with Kusnanto's empirical investigation conducted at Dr. Sardjito, which scrutinized the ramifications of genuine costs exclusive of chemotherapy on the INA-CBGs cost differential. Kusnanto's findings underscored that the expenses linked to drug procurement, medical equipment service, and treatment duration exert discernible influence on the differential rate.[21] The amplified pharmaceutical costs can

also be attributed to a multitude of side effects resulting from the administration of cytostatic agents, which subsequently necessitate augmented employment of pharmaceutical agents and medical apparatus, thereby culminating in escalated pharmacy expenses. In comparison to adjunctive therapy, elevated costs encountered by patients undergoing metastatic treatment across all tumor classifications predominantly emanate from heightened inpatient expenditures, conceivably attributed to the management of cancer progression and its sequelae. Existing research consistently demonstrates that the initial year following a cancer diagnosis and the terminal year of life are characterized by the most substantial net outlays for cancer care.[22–24]

Trastuzumab is used in cancer therapy in breast cancer patients by some patients but the number of patients with this therapy is only 0.1%. the use of this drug causes a very large increase in chemotherapy costs when compared to other therapy regimens. Trastuzumab is considered less effective in breast cancer chemotherapy. Combination therapy Cyclophosphamide, Doxorubicin, and Fluorouracil is a suitable choice for first-line therapy in the management of breast cancer control.[17,25] In this study, patients under the age of 50 years made up most breast cancer survivors, and the decision on combination therapy was related to known pathological risk factors and the patient.

The most widely used chemotherapy therapy for cervical cancer is using a single drug cisplatin. Cisplatin is the most effective alkaline antineoplastic agent for the treatment of cervical cancer, both locally advanced and metastatic and cisplatin resistance is a significant contributor to recurrence and death.[26,27] Cisplatin is the most effective medication for the treatment of cervical cancer, both for locally advanced and metastatic stages and cisplatin resistance is a significant contributor to relapse and mortality. The combination of carboplatin and paclitaxel is a combination that is often used in cervical cancer. Carboplatin and paclitaxel combination drug therapy is a combination that is often used in cervical cancer. Cisplatin-paclitaxel chemotherapy led to significantly longer free survival time for postmenopausal women with previously untreated advanced cervical cancer, resulting in significantly longer overall survival than those who received cisplatin-paclitaxel chemotherapy.[28]

In lung cancer, the use of pemetrexed therapy can also increase costs quite high because the price tends to be expensive. Even so, the two drugs are still covered by BPJS. For lung cancer, the single drug that is often used is paclitaxel at a cost of IDR 325,750. The combination of two drugs that is often used is a combination of cisplatin and Pemetrexed. The combination of pemetrexed-carboplatin could be a valuable treatment option in elderly patients, this is in line with the results of age characteristics in lung cancer patients aged more than 51 years old.[29] In cost effectiveness studies platinum based chemotherapy with paclitaxel, including pemetrexed, are the most widely used treatment regimens used in standard treatment for metastatic non-small cell lung cancer.[30] This second combination has a fairly high cost, namely in the range of IDR 5,381,572 to IDR 6,397,587. In lung cancer, the most expensive combination is the combination of Bleocin HCl, Carboplatin and Pemetrexed at a cost of IDR 6,053,526.

Finally, the outcomes derived from our investigation possess the potential to contribute substantively to the enhancement of population health management strategies. The identification of pivotal factors influencing elevated expenditures among cancer patients serves to offer invaluable insights to policy framers, enabling the formulation of precision-targeted interventions meticulously attuned to the specific requirements of these high-cost individuals, thereby effecting a diminution in the overall financial burden associated with cancer care. Notwithstanding these contributions, it is imperative to acknowledge several inherent constraints within this study. Principally, the observed associations between clinical and health attributes and the costs associated with medical equipment cannot be imbued with a causal connotation, primarily due to the inherent nature of the cross-sectional dataset employed in our analysis.

CONCLUSION

Our comprehensive investigation of gender-specific cancer prevalence and treatment costs has uncovered complex patterns that offer important insights for clinical practice and health policy development. The stark differences in cancer prevalence between the sexes underscore the important role of biological and hormonal factors in shaping cancer susceptibility. The differing prevalence rates of breast, cervical, and lung cancer among the female and male populations reflect the complex interplay between hormonal environment and behavioural factors, such as smoking.

The careful allocation of patients across different treatment classes as guided by the regulatory framework, together with the correlation between these classes and health insurance contributions, has the potential to ease the financial burden for patients, especially those enrolled in the BPJS. These findings emphasize the importance of adapting healthcare delivery and financing models to accommodate the varying needs of patients and socioeconomic backgrounds. The financial dimensions of cancer treatment revealed by our study explain the multifaceted nature of healthcare costs, with accommodation and drug costs emerging as major contributors. In particular, the impact of hospitalization on overall costs, particularly in addressing the side effects of chemotherapy, highlights the need for a holistic approach to cancer care that includes medical interventions and supportive measures. Our investigation also underscores the complexities associated with treatment decisions, highlighting the role of therapeutic regimens in shaping patient costs and outcomes. Variations in chemotherapy strategies and their financial implications highlight the importance of evidence-based treatment options, while also requiring further research to optimize the balance between clinical effectiveness and economic feasibility.

As a recommendation, this study serves as an important foundation for advancing public health management approaches, offering valuable insights into the factors driving

the cost and prevalence of cancer treatment. While the study findings provide a sound basis for decision-making, the inherent limitations of the cross-sectional dataset remind us of the need for continued research, combining longitudinal and prospective analyses, to unravel the complex dynamics of cancer care costs and patient outcomes. Ultimately, our collective efforts to understand and address these challenges will play a critical role in enhancing the quality of care and overall well-being of cancer patients.

AUTHORS CONTRIBUTION STATEMENT

Conceptualization: FY, TMA; Data curation: FY, DE, SAK; Formal analysis: FY, SAK; Methodology: FY, DE, TMA, SAK; Supervision: TMA; Writing –original draft: FY, DE, TMA, SAK; Writing –review & editing: FY, DE, TMA, SAK.

CONFLICTS OF INTEREST

The authors have no conflicts of interest regarding this research.

FUNDING

This research was funded by The Ministry of Education and Culture, research, and Technology, Republic of Indonesia through the Doctoral Research Grant in 2023.

References

1. IARC. Indonesia - Global Cancer Observatory. Globocan. 2020;858:1-2.
2. Fatonah S, Yulandari A, Wibowo FW. A Review of E-Payment System in E-Commerce. Journal of Physics: Conference Series. 2018;1140(1).
3. Dewi BA, Oetari O, Andayani TM. Cost Compliance Analysis of Real Therapy and INA-CBG's of Chemotherapy Breast Cancer Inpatien At 2017 Dr. Moewardi Surakarta Hospital. STRADA Jurnal Ilmiah Kesehatan. 2021;10(1):1234-41.
4. Utami M. Upaya Indonesia Capai Universal Health Coverage di Tahun 2019. sehatnegeriku.kemkes. 2018.
5. Hofmarcher T, Lindgren P, Wilking N, et al. The cost of cancer in Europe 2018. European Journal of Cancer. 2020;129:41-9. https://doi.org/10.1016/j.ejca.2020.01.011
6. Oktafiani E, Herowati R, Andayani TM. Analisis Biaya Riil Dan Kesesuaian Dengan Tarif INA-CBGs Pada Pasien Kanker Ovarium RS Di Kota Surakarta Tahun 2018 Analysis Real Cost And Compatibility With INA-CBGs Tariff Ovarian Cancer Patient In General Hospital Surakarta 2018 Kanker ovarium menurut . 2020;17(02):156-65.
7. Senapati S, Mahanta AK, Kumar S, et al. Controlled drug delivery vehicles for cancer treatment and their performance. Signal transduction and targeted therapy. 2018;3:7. https://doi.org/10.1038/s41392-017-0004-3
8. Dolgin E. Bringing down the cost of cancer treatment. Nature [Internet]. 2018 Aug 20;555:S26+. Available from: https://link.gale.com/apps/doc/A649098746/HRCA?u=anon~b80240d5&sid=googleScholar&xid=107d3b83
9. Riera R, Bagattini ÂM, Pacheco RL, et al. Delays and disruptions in cancer health care due to COVID-19 pandemic: systematic review. JCO Global Oncology. 2021;7(1):311-23. https://doi.org/10.1200/go.20.00639
10. Solikhah S, Matahari R, Utami FP, et al. Breast cancer stigma among Indonesian women: A case study of breast cancer patients. BMC Women's Health. 2020;20(1):1-5. https://doi.org/10.1186/s12905-020-00983-x
11. Stallworthy G, Dias HM, Pai M. Quality of tuberculosis care in the private health sector. Journal of clinical tuberculosis and other mycobacterial diseases. 2020;20:100171. https://doi.org/10.1016/j.jctube.2020.100171
12. Mulyanto J, Kringos DS, Kunst AE. Socioeconomic inequalities in healthcare utilisation in Indonesia: a comprehensive survey-based overview. BMJ open. 2019;9(7):e026164. https://doi.org/10.1136/bmjopen-2018-026164
13. Arini M, Sugiyo D, Permana I. Challenges, opportunities, and potential roles of the private primary care providers in tuberculosis and diabetes mellitus collaborative care and control: a qualitative study. BMC Health Services Research. 2022;22(1):215. https://doi.org/10.1186/s12913-022-07612-3
14. Satibi dkk. Analisis of Factors Influencing the Availability of Medicine During JKN Era. 2018;29(1):37-43.
15. Yuliastuti F, Andayani TM, Endarti D, et al. Breast, cervical, and lung cancer: A comparison of real healthcare costs and INA-CBGs rates in the era of national health insurance. Pharmacy Practice. 2023;21(1):1-7. https://doi.org/10.18549/pharmpract.2023.1.2768
16. Fathoni MIA, Gunardi, Adi-Kusumo F, et al. Characteristics of breast cancer patients at dr. Sardjito Hospital for early anticipation of neutropenia: Cross-sectional study. Annals of Medicine and Surgery. 2022;73:103189. https://doi.org/10.1016/j.amsu.2021.103189
17. Kementerian Kesehatan RI. Pedoman Nasional Pelayanan Kedokteran : Kanker payudara. 2017;
18. Kementerian Kesehatan Republik Indonesia. Profil Kesehatan Indonesia 2016. Profil Kesehatan Provinsi Bali. 2016. 1-220 p.
19. Mostert S, Njuguna F, van de Ven PM, et al. Influence of health-insurance access and hospital retention policies on childhood cancer treatment in Kenya. Pediatric Blood and Cancer. 2014;61(5):913-8. https://doi.org/10.1002/pbc.24896
20. Nguyen VT, Winterman S, Playe M, et al. Dose-Intense Cisplatin-Based Neoadjuvant Chemotherapy Increases Survival in Advanced Cervical Cancer: An Up-to-Date Meta-Analysis. Cancers. 2022;14(3). https://doi.org/10.3390/cancers14030842
21. Indriani D, Kusnanto H, Ghufron Mukti A, et al. The Effect of Laboratory Cost to Gap Price Between INA-CBGs Reimbursement

and Itemized Bill in Leukemia Diagnosis. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal). 2013;7(10):440-6.
22. Hu L, Li L, Ji J, et al. Identifying and understanding determinants of high healthcare costs for breast cancer: a quantile regression machine learning approach. BMC health services research. 2020;20(1):1-10. https://doi.org/10.1186/s12913-020-05936-6
23. Al. LHwClL et. Cost Efectiveness of PD-L1-Based Test-and-Treat Strategy with Pembrolizumab as the First-Line Treatment for Metastatic NSCLC in Hong Kong. Hong Kong: PharmacoEconomics; 2019. p. 235-46. https://doi.org/10.1007/s41669-019-00178-7
24. Ward RL, Laaksonen MA, van Gool K, et al. Cost of cancer care for patients undergoing chemotherapy: The Elements of Cancer Care study. Asia-Pacific journal of clinical oncology. 2015;11(2):178-86. https://doi.org/10.1111/ajco.12354
25. Martin M, Pienkowski T, Mackey J, et al. Adjuvant docetaxel for node-positive breast cancer. The New England journal of medicine. 2005;352(22):2302-13.
26. Federico C, Sun J, Muz B, et al. Localized Delivery of Cisplatin to Cervical Cancer Improves Its Therapeutic Efficacy and Minimizes Its Side Effect Profile. International journal of radiation oncology, biology, physics. 2021;109(5):1483-94. https://doi.org/10.1016/j.ijrobp.2020.11.052
27. Joerger M, Ess S, Dehler S, et al. A population-based study on the patterns of use of different chemotherapy regimens in Swiss patients with early breast cancer. Swiss medical weekly. 2012;142:w13571. https://doi.org/10.4414/smw.2012.13571
28. Chu G, Liu X, Yu W, et al. Cisplatin plus paclitaxel chemotherapy with or without bevacizumab in postmenopausal women with previously untreated advanced cervical cancer: a retrospective study. BMC cancer. 2021;21(1):133. https://doi.org/10.1186/s12885-021-07869-7
29. Gervais R, Robinet G, Clément-Duchêne C, et al. Pemetrexed and carboplatin, an active option in first-line treatment of elderly patients with advanced non-small cell lung cancer (NSCLC): a phase II trial. Lung cancer (Amsterdam, Netherlands). 2013;80(2):185-90. https://doi.org/10.1016/j.lungcan.2013.01.008
30. Yuliastuti F, Kristina SARI, Endarti DWI, et al. A Systematic Review of Cost Effectiveness of Pembrolizumab Versus Standard Treatment for Metastatic Non-Small Cell Lung Cancer. International Journal of Pharmaceutical Research. 2021;13(02). https://doi.org/10.1371/journal.pone.0238536