

Costs of Breast Cancer Treatment Incurred by Women in Vietnam

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Abstract

Background: There is a paucity of research on the cost of breast cancer (BC) treatment from the patient's perspective in Vietnam.

Methods: Individual-level data about out-of-pocket (OOP) expenditures on use of services were collected from women treated for BC (n=202) using an online survey and a face-to-face interview at two tertiary hospitals in 2019. Total expenditures on diagnosis and initial BC treatment were presented in terms of the mean, standard deviation, and range for each type of service use. A generalised linear model (GLM) was used to assess the relationship between total cost and socio-demographic characteristics.

Results: 19.3% of respondents had stage 0/I BC, 68.8% had stage II, 9.4% had stage III, none had stage IV. The most expensive OOP elements were targeted therapy with mean cost equal to 649.5 million VND (\$28,025) and chemotherapy at 36.5 million VND (\$1,575). Mean total OOP cost related to diagnosis and initial BC treatment (excluding targeted therapy cost) was 61.8 million VND (\$2,667). The mean OOP costs among patients with stage II and III BC were, respectively, 66% and 148% higher than stage I.

Conclusions: BC patients in Vietnam incur significant OOP costs. The cost of BC treatment was driven by use of therapies and presentation stage at diagnosis. It is likely that OOP costs of BC patients would be reduced by earlier detection through raised awareness and screening programs and by providing a higher insurance coverage rate for targeted therapy.

Introduction

Healthcare services including cancer treatment in Vietnam are financed via three main sources: State, social health insurance, and out-of-pocket (OOP) payments [1, 2]. The largest share of total health expenditure is OOP which increased from 37% of total healthcare expenditures in 2011 to approximately 45% in 2017 [1, 3]. Vietnam was ranked 46/186 countries in terms of the share of expenditure from OOP which was higher than the 30% upper bound recommended by the World Health Organization (WHO) [2, 3]. The proportion of Vietnamese households who suffered 'catastrophic' health expenditure due to OOP payment was relatively high at 4–6% during the 2000s [2].

Previous studies showed that high OOP payment was associated with medication adherence, service utilization, and treatment outcomes [4–6]. However, the level and composition of OOP payments related to BC treatment in Vietnam and the drivers of expenditure remain largely unexamined. One study reported the majority (72%) of BC patients' households faced catastrophic health expenditure (where a household's total OOP for healthcare was equal to or exceeded 40% of a household's income) though the study did not examine the cost of BC care according to stage or use of therapies [7]. The only study to examine the cost of BC care in Vietnam assessed the direct medical cost of treatment by category and stage of cancer [8]. However, the representativeness and currency of the data which was from 2001 and 2006 for only one tertiary hospital in central Vietnam call into question its relevance. Moreover, as it is

confined to an examination of cost from the payer's perspective [8], it offers limited insight into costs incurred by patients.

The treatment and timing/dosage of drugs depend on the stage of BC cancer and the pathology type [9]. Ideally, treatment is 'personalised' so that the optimum result with the lowest toxicity and least undesirable effects is achieved [9]. Thus, using patient-level data in the calculation of costs (rather than calculating according to clinical guideline-informed treatment pathways) can reveal between-patient heterogeneity [10]. In other words, patient-level costing allows the comparison of costs between subgroups (defined by stage at diagnosis and treatment options) as well as the identification of cost drivers. The transferability of estimates from other jurisdictions are open to question [6, 10]. In this context, there is a need to gather data about current costs from a patient perspective to understand service uptake and the financial burden of care. This study sought to address this gap in the literature by using patient-level data to assess the OOP expenses regarding diagnosis and initial treatment (D&T) of Vietnamese BC patients by stage and category of treatment.

Methods

Study design and participants

We analysed data from a 2019 study of medical expenses and health-related quality of life of women with BC through an online survey and a hospital-based face-to-face survey. Respondents included both women who were receiving 'initial treatment' (defined below) and those who had finished initial treatment and were discharged from hospital. Details about study design and methodology are available elsewhere (manuscript is under review, preprint [11]). As the total OOP for direct medical costs of D&T of those were receiving treatment is unknown, only data of those had already finished the initial treatment were included in this analysis.

Following diagnosis BC treatment in Vietnam has two main courses including the 'initial treatment' and the 'follow-up treatment' [8, 9]. The former starts right after the diagnosis and often lasts up to 9 months. It includes surgery (e.g., lumpectomy, mastectomy, breast reconstruction surgery), radiotherapy, and systemic therapies (e.g., chemotherapy, hormone therapy, targeted therapy) [8, 9]. After initial treatment, follow-up treatment including hormone therapy (for those are eligible to prevent recurrence of BC) and periodic check-up may last 5–10 years with outpatient appointments every 3–6 months [8, 9]. Given recall bias and unknown compliance, it is difficult to precisely estimate the costs for follow-up treatment [8]. Therefore, this report contains the results of the analysis of the costs of initial treatment for BC along with diagnostic costs.

Assessment of costs

This study presents patient-reported direct payment to health care providers at time-of-service use (excluding the amount covered by health insurance, if any) which is the costs of BC D&T from a patient perspective. Mean costs for each healthcare service were calculated among those who utilised that

corresponding service. All costs were converted to 2019 prices using a Gross Domestic Product deflator index for Vietnam [12]. Costs were presented in Vietnamese Dong (VND) and US dollars (USD) for comparative purposes. The exchange rate used was 1 USD = 23,176 VND recorded on November 12, 2020.

Cost of diagnosis

Health services related to diagnosis included clinical diagnosis (e.g. clinical breast examination and medical history asking), laboratory diagnosis (e.g. mammography, ultrasound, magnetic resonance imaging-MRI, nuclear medicine imaging), and histopathological diagnosis (e.g. fine needle aspiration-FNA, core needle biopsy, vacuum-assisted breast biopsy-VABB) [9]. Patients may use these services several times at different hospitals before starting the treatment [13]. Therefore, respondents reported the lump sum of all health services related to diagnosis that they received rather than the cost of each individual service.

Cost of initial treatment

Respondents identified the treatments that they received from a list including lumpectomy, mastectomy, breast reconstruction surgery, chemotherapy, radiotherapy, hormone therapy, and targeted therapy and then reported how much they paid for each received treatment. Cost of treatments which respondents reported not receiving were recorded as zero.

Covariates

The choice of covariates that were used to explain variation in costs was based on previous studies [8, 10]: stage of cancer at diagnosis, health insurance (HI) coverage rate, age, household monthly income, and education level.

Respondents were asked 'What was their stage of cancer at diagnosis' with simplified options of 'stage 0', 'stage I', 'stage II', 'stage III', 'stage IV', and 'do not know/do not remember' to minimise recall bias. Age of respondents was recorded in years. Respondents were asked to state the total monthly income (both formal and informal) of their households using five categories ' $\leq 3,000,000$ VND', ' $3,000,001-6,000,000$ VND', ' $6,000,001-9,000,000$ VND', ' $9,000,001-12,000,000$ VND', and ' $>12,000,000$ VND'. The coverage rate of HI in Vietnam can be 100%, 95%, and 80% meaning patients pay coinsurance at 0%, 5%, and 20% respectively for covered healthcare services (there are no deductibles and out-of-pocket maximum/limit) [14]. The respondents were asked which level of HI coverage they received.

Data analysis

Descriptive statistics (mean and standard deviation-SD for continuous variables, percentages for discrete variables) were used to describe the sociodemographic and clinical-related characteristics of respondents. Costs were presented with and without outliers. Outliers were defined as values which fell more than 1.5 times the interquartile range (IQR) above the third quartile (Q3) or below the first quartile (Q1) (outliers if value $> Q3 + 1.5IQR$ or $< Q1 - 1.5IQR$).

Apart from cost analysis by type of treatment, total cost of D&T of BC was analysed by respondent key characteristics using a generalised linear model (GLM). Total cost was calculated by summing diagnosis and treatment costs excluding the cost of targeted therapy. In Vietnam, targeted therapy is optional and patients choose between usual chemotherapy or targeted therapy based on their perceived need and ability to pay. Due to its extremely high cost and low coverage rate from HI (60% for Trastuzumab, 0% for Pertuzumab [15]), the cost of targeted therapy alone was more than ten times higher than the total cost of diagnosis and all other treatment types. Therefore, targeted therapy cost was excluded in the modelling of the associated factors of total cost.

Component costs contained outliers and missing data (6–66% depending on the specific treatment concerned). To avoid biased parameter estimates if applying listwise deletion or complete-case analysis for this large number of missing observations [16, 17], we used a multiple imputation technique to impute missing values. Prior to the modelling, outliers were recoded as missing and then all missing data was imputed using the multivariate imputation by chained equations (MICE) method where all component costs are imputed sequentially [16, 17]. While a number of imputations (M) = 5 often deemed sufficient [17, 18] we chose $M = 20$ to increase the stability of the results. As the cost data was skewed and bounded by specific value (cost = 0 if the service were not used and no cost could be negative), we used the recommended method: predictive mean matching (PMM) with condition to predict the imputed value [16, 17, 19]. PMM randomly draws an imputed value from a set in the donor pool (observations with the closest value predicted by linear regression model for the missing one) [16, 17, 19]. The condition was that imputed values would be given only for those who used the treatment type; otherwise, missing values would be replaced with zero. The total cost was calculated after this imputation procedure.

Results

Respondent characteristics are presented in Table 1. The mean age (SD) of respondents was 48.4 (10.1) years, 78% were married, 70% were working full-time or self-employed, and 87% completed at least high school education; 88% were diagnosed at early stage (stage 0/I/II), 10% were diagnosed at stage III and none at stage IV; all respondents possessed HI and 82% had HI with 80% coverage rate.

Table 1
Characteristics of sample

Characteristics (n = 202)	Number	Percentage
Age (in years), mean (SD)	48.4 (10.1)	
Education level		
Completed at least secondary education	27	13.4
Completed high school education	38	18.9
Completed undergraduate	122	60.7
Completed graduate	14	7.0
Marital status		
Single/separated/divorce/widow	44	22.0
Married	156	78.0
Occupation		
Unemployed/Student/Homemaker	23	11.6
Full-time employee	96	48.2
Self-employed	44	22.1
Retired	36	18.1
Household income (in Vietnamese Dong – VND)		
≤ 3 000 000 VND (~\$129)	18	9.2
3 000 001–6 000 000 VND (\$130–259)	33	16.9
6 000 001–9 000 000 VND (\$260–389)	20	10.3
9 000 001–12 000 000 VND (\$390–519)	55	28.2
>12 000 000 VND (\$519)	69	35.4
Stage of cancer at diagnosis		
Stage 0/I	39	19.3
Stage II	139	68.8
Stage III	19	9.4
Don't know/Don't remember	5	2.5
Coverage rate of health insurance		
80%	160	81.6

Characteristics (n = 202)	Number	Percentage
95%	15	7.7
100%	21	10.7
<i>VND: Vietnamese Dong (the currency of Vietnam) \$: United States Dollar (USD)</i>		
<i>Exchange rate in November 2020: 1 USD = 23,176 VND</i>		

Healthcare service utilisation (related to breast cancer) and the corresponding utilisation of HI to pay for any part of the cost, among respondents who used such services are presented in Fig. 1. The most used treatment therapies were chemotherapy (88%), mastectomy (85%), and radiotherapy (60%). Only 10–12% of respondents had breast reconstruction surgery and targeted therapy, respectively. The use of HI was higher than 80% for all types of services. The lowest utilisation of HI was for breast reconstruction surgery (80%) and mastectomy (88%). All respondents (100%) used HI to pay for targeted therapy cost. Compared to stage I, the proportion of patients in stage II/III that utilised mastectomy, chemotherapy, and radiotherapy was significantly higher (Fig. 1b; chi-square test, $p < 0.001$; test not shown).

Figure 2 shows variation in costs for each category of BC D&T among those who used the corresponding services. The costliest service was targeted therapy with mean cost at 649.5 million VND (~\$28,025). Diagnostic costs had the widest range from 0.03 to 824 million VND (\$1.3–35,554) due to the highest number of outliers (17 outliers). When the outliers were removed, diagnosis was the cheapest health care service with mean cost at 2.6 million VND (\$112). The second most costly and skewed cost was chemotherapy with range from 0.2 to 371.2 million VND (\$8.6–16,017) and mean (without outliers) at 36.5 million VND (\$1,575).

Figure 3 shows the costs of each BC type in relation to other services' cost and the total cost, with and without targeted therapy (Fig. 3a and 3b, respectively). When targeted therapy was not included, chemotherapy and breast reconstruction surgery made up of approximately half the total cost (33% and 23%, respectively). The cost of lumpectomy, mastectomy, and radiotherapy shared 12–15% of the total cost while diagnosis cost only accounted for 2%. When targeted therapy was included into the treatment regime, it made up the majority of treatment cost (85.5%).

GLM results showed that later stage of cancer diagnosis and higher education level of respondents were associated with the higher total cost for breast cancer (Table 2). Respondents diagnosed at stage II and stage III spent 24.5 and 54.8 million VND (\$1,057 – 2,365) more, respectively, for D&T of BC compared to those diagnosed at stage 0/I. Likewise, respondents with a graduate degree had a total cost of treatment 62.4 million VND (\$2,692) higher than those who completed at least secondary education. The completed-data estimations for total cost (pooled-estimations from 20 imputation sets) were 61.8 million VND (\$2,667) with a wide range from 9.6 to 149.9 million VND (\$414–6,468).

Table 2

Generalised linear model (GLM) analysis of associated factors with total cost of breast cancer care.

	Coefficient	95% CI
Stage of cancer at diagnosis ^a		
Stage 0/I ^{ref}	1.0	-
Stage II	24.5	1.2–47.9*
Stage III	54.8	20.0–89.6*
Don't know/Don't remember	26.3	-31.4–84.1
Household monthly income (in Vietnamese Dong - VND)		
≤ 3 000 000 VND (\$129) ^{ref}	1.0	-
3 000 001–6 000 000 VND (\$130–259)	8.0	-40.4–56.5
6 000 001–9 000 000 VND (\$260–389)	-11.4	-44.0–21.2
9 000 001–12 000 000 VND (\$390–519)	9.0	-22.5–40.4
>12 000 000 VND (\$519)	6.5	-22.1–35.1
Coverage rate of health insurance		
80% ^{ref}	1.0	-
95%	-8.2	-33.3–16.9
100%	10.3	-19.0–39.7
Age	-0.3	-1.0–0.4
Education level		
Completed at least secondary education	1.0	-
Completed high school education	15.0	-20.2–50.1
Completed undergraduate	6.4	-21.4–34.2
Completed graduate	62.4	23.6–101.2*
<i>ref: Reference group \$: United States Dollar (USD) VND: Vietnamese Dong (currency of Viet Nam)</i>		
<i>Exchange rate in November 2020: 1 USD = 23,176 VND</i>		
<i>^aNo respondents were diagnosed at stage IV of breast cancer</i>		
<i>* p < 0.05</i>		

Discussion

The results of this study indicate that BC patients in Vietnam incurred significant OOP costs and the cost of BC treatment was driven by use of therapies and presentation stage at diagnosis. It is important to note that the analysis was based on a sample in which the proportion of patients diagnosed at early stage (0/I/II) was much higher than the national average of 50.5% [20] though the age of respondents was consistent with other studies [21, 22].

The mean total OOP cost of D&T for BC in Vietnam, excluding the cost of targeted therapy, was 61.8 million VND (\$2,667) (range: 9.6 to 149.9 million VND (\$414-6,468) - approximately five times higher than the mean cost of 11.7 million VND (\$633) reported in the only other study about costs of BC in Vietnam [8]. This difference in estimates may be due to several reasons. The former study used 2001–2006 patient data when medical equipment and medications were less advanced and their use was more restricted. Secondly, costs were calculated from the healthcare payer's perspective using unit costs which, in Vietnam, are much lower than the real cost of the resources used due to underestimation of health workforce remuneration and capital depreciation [8, 23]. From the patient's perspective, our study reported the OOP cost which reflected the cost borne by patients and reveal the financial burden they faced. For example, the unit cost of mastectomy regulated by the Ministry of Health in 2018 was 4.7 million VND (\$204) [15]. In our study, the cost borne by the patients were reported at 18.4 million VND (\$794) which was almost four times higher.

Although the costs reported in this study were much higher than the previous study, it seems much lower than the neighbouring country China or high-income countries like the US (3 and 5–15 times lower, respectively) [24–26]. Comparison of treatment costs in Vietnam with other low- and middle-income countries is not feasible due to the absence of studies with comparable methods (i.e., time horizons of costs, source of data, costing perspective). Moreover, comparison should be used with great caution as between-country differences in treatment costs are likely to be influenced by the variation in treatment guidelines, availability of treatment therapy, stage at diagnosis, and access to healthcare services [10].

The wide range of initial treatment cost is similar with the previous study [8]. Variation in costs may be influenced by types of healthcare services related to BC D&T and the utilisation of HI for each service. All respondents in the study had HI and the majority (82%) used their HI to pay 20% of healthcare services cost (coinsurance = 20%). However, possession of HI did not mean respondents could utilize their HI for every service related to BC D&T. There were two possible scenarios: 1) patients chose intentionally not to use HI and opted to access 'services on demand' at public hospitals or services at private hospitals (patients pay 100% OOP) which tended to be viewed as providing better quality healthcare; 2) patients could not use HI for services which were not covered. The lowest utilisation level of HI was for breast reconstruction surgery and mastectomy (80–88%). With 'service on demand', patients receive premium service with privileges (i.e., the right to choose a surgeon, time of operation, hospital room, and level of care) which might partly explain why patients chose this option instead of using standard service covered by the HI.

The analysis showed the overwhelming dominance of targeted therapy cost in relation to total cost of care for patient with HER2+ (patients eligible for targeted therapy). The mean cost of targeted therapy was 649.5 million VND (\$28,025) - tenfold higher than the total cost of all other healthcare services related to BC D&T. The share of targeted therapy would be 86% if it was included in the total cost. A study in Portugal found that systemic therapy (targeted therapy + chemotherapy) accounted for 69.2% of the total treatment cost of HER2+ patients which, in turn, was four times higher than patients with other BC subtype [27]. Although 100% of respondents used HI for targeted therapy, the cost borne by patients was still much higher compared to other service costs due to the high-cost nature of targeted therapy and low HI coverage (e.g., HI covered 60% of the cost of Trastuzumab meaning patients paid 40% of the total cost by OOP plus 20% coinsurance of the part covered by HI [15]). Targeted therapy for HER2+ patients does not tend to be prescribed in Vietnam when it is known that patients cannot afford the treatment (personal communication). The effect of cost on doctor's prescribing behaviour and patient treatment decisions were documented elsewhere [28–30] and need further research in Vietnam. Policies involving higher HI coverage rate for targeted therapy and/or an OOP maximum (a cap on the amount of money that a patient pays for covered healthcare services plan/year) is likely to impact positively on access by patients to appropriate BC treatment.

When targeted therapy was excluded from total cost, the largest share of cost belonged to chemotherapy (33%) with a mean cost of 36.5 million VND (\$1,575). Diagnosis accounted for the smallest share in total cost (2%) with a mean cost of 2.6 million VND (\$112). This cost composition is consistent with the previously noted study in Vietnam [8]. Cost of diagnosis contained the highest number of extreme outliers. The maximum value with and without outliers was 824 million VND (\$35,554) and 17 million VND (\$734), respectively. The outliers likely reflect patients having to go through multiple tests at different hospitals before reaching the definitive diagnosis of BC [13].

Multivariate analysis revealed that later stage at diagnosis and higher education level of respondents were associated with higher total OOP cost of D&T for BC. Age, household monthly income, and coverage rate of HI were not significantly associated with costs, similar to the previous study in Vietnam [8]. The mean OOP costs of BC D&T at stage II and III were, respectively, 66% and 148% higher than stage I. The trend is similar though higher than the pooled result from a systematic review of global treatment costs of BC by stage in which the rate was 32% and 95% respectively [10]. Higher costs borne by patients in stage II/III is understandable as their utilisation of mastectomy, chemotherapy, and radiotherapy, which accounted for nearly two-third of the total cost, was significantly higher than stage I patients. The higher costs of later cancer stage emphasise the importance of early detection through screening programs. Policies that help downstaging BC at diagnosis will lessen the costs of treatment borne by the patients and their financial toxicity as well as increase the access to care and outcomes of treatment.

This study provides updated and detailed OOP costs for BC D&T in Vietnam as well as associated factors, using patient-level data. This is only the second study on the subject about costs related to BC and the first study in the country that analysed data from the patient's perspective. Apart from complementing the previous study which looked at costs from healthcare payer's perspective, the study

provides novel and valuable insights that will facilitate the evaluation of novel therapies in terms of cost-effectiveness in Vietnam including early detection. In turn, the results will help decision-making by policymakers regarding health system financing and service delivery. The sample consisted of patients who were treated in main public hospitals from all three regions of Vietnam (the North, the Central, and the South). It is important to note that the study has some limitations. All costs were self-reported by respondents and were subject to recall bias though by cross-checking information with service price lists in hospitals or regulated by government and market price of drugs, no unreasonable or inconsistent data were flagged. Due to risk of recall bias and difficulties in measurement, we could not collect the costs of follow-up treatment, direct non-medical costs (i.e., transportation, meal, accommodation), and indirect costs (i.e., lost income, premature death) were also not gathered. There were no patients diagnosed with stage IV in the sample and this fact affected cost comparisons. We applied a multiple imputation technique to deal with missing data. Although the method used for imputation was technically sound and several pre-cautionary steps were taken to obtain the best reliable imputed values, there remains a possibility of bias.

Conclusion

The average OOP for D&T of BC in Vietnam was 61.8 million VND (\$2,667) which is substantially higher than previous estimates based on costs incurred by government and indicates the considerable financial burden associated with BC to the patients and their families. The costs generally increase with the advancement of the stage of cancer at diagnosis. Stage as a significant driver of cost suggests there exists scope for policies aim at early detection to reduce both the health and economic impacts of BC.

List Of Abbreviations

BC: Breast cancer

D&T: Diagnosis and initial treatment

GLM: Generalised linear model

HI: Health insurance

IQR: Interquartile range

OOP: Out-of-pocket payment

PMM: Predictive mean matching

Q1: First quartile

Q3: Third quartile

SD: Standard deviation

US: The United States of America

VND: Vietnamese Dong

Declarations

Ethics approval and consent to participate: The study was carried out in accordance with the Declaration of Helsinki. It was approved by the Ethics Committee of Hanoi University of Public Health (No. 265/2019/YTCC-HD3 dated 25th April 2019) and by each participating hospital. Informed consent was obtained from all individual participants included in the study. Participants were assured of the confidential nature of the information gathered. All data collected were anonymized using unique study identifiers.

Consent for publication: Not applicable.

Availability of data and materials: All data generated or analysed during this study are included in this published article.

Competing interests: *The authors declare that they have no competing interests.*

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Authors' contributions: TTN, MD, and CON contributed to the study conception and design. Data collection were conducted by TTN and NBN. Data analysis were performed by TTN and CON. All authors contributed to the interpretation of the findings. The first draft of the manuscript was written by TTN. CON, MD, and HVM provided supervisory support and reviewed this paper. All authors contributed to the revision of the manuscript and approved the final manuscript.

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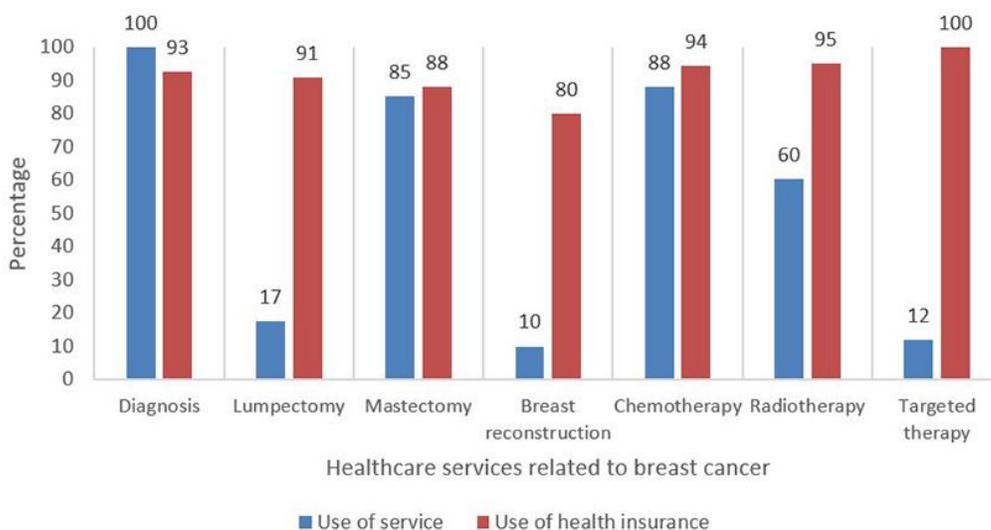
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Figures

1a. Utilisation of healthcare service and health insurance*



* Utilisation of health insurance for each service was among those utilised such service (instead of the entire sample). Utilisation of health insurance was defined as when the patients used health insurance to pay for any part of the service cost.

1b. Utilisation of healthcare services, by stage at diagnosis

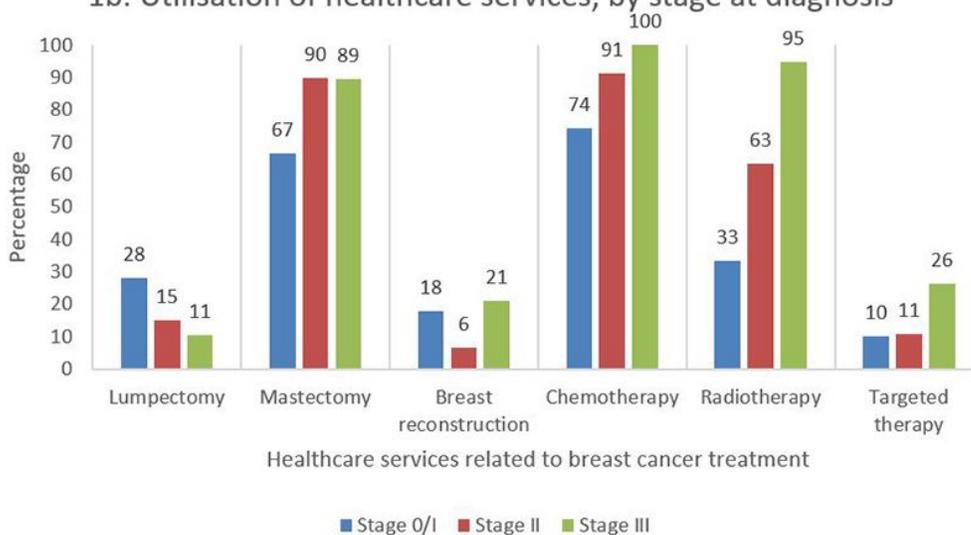
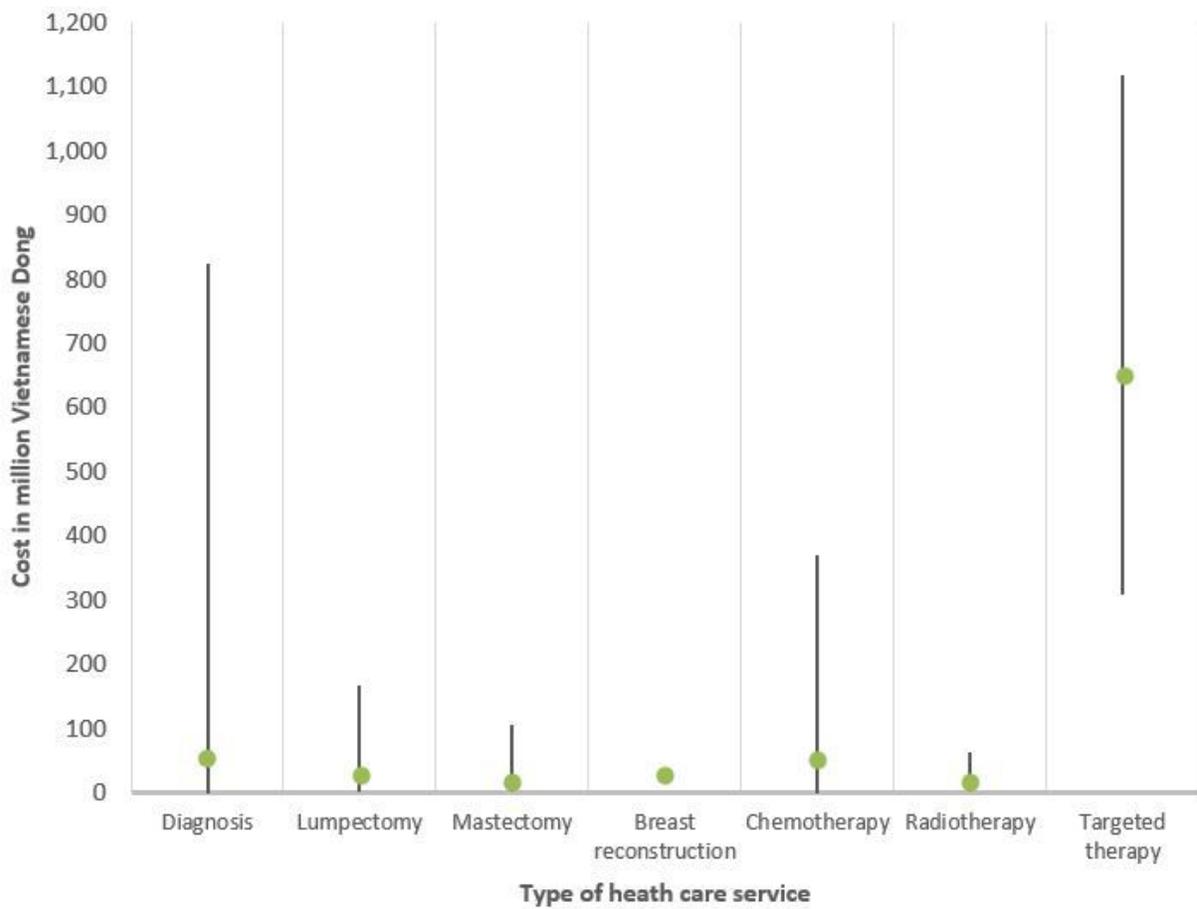


Figure 1

Title: Utilisation of healthcare services (related to breast cancer) and health insurance. Legend: * Utilisation of health insurance for each service was among those utilised such service (instead of the entire sample). Utilisation of health insurance was defined as when the patients used health insurance to pay for any part of the service cost.

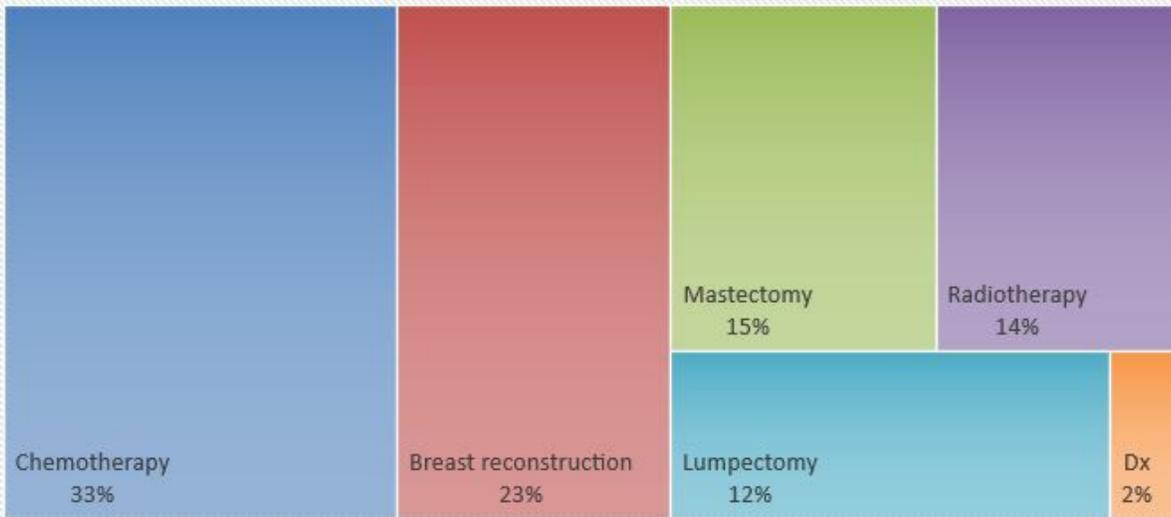


● Mean (with outliers)	55.2	28.8	18.4	25.7	53.1	18.4	649.5
Min	0.03	0.8	1.1	15.5	0.2	2.0	309.0
Max	824	168	106	40	371.2	63.6	1117.6
Upper boundary for outliers (=Q3+1.5IQR)	17.7	46.7	56.3	55.0	135.6	40.1	1588.6
No of outliers	17	2	1	0	3	2	0
Mean (without outliers)	2.6	13.7	16.5	25.7	36.5	15.2	649.5

Figure 2

Variation of costs in breast cancer diagnosis and initial treatment.

3a. Distribution of diagnosis and treatment costs, excluded targeted therapy



3b. Distribution of diagnosis and treatment costs, included targeted therapy



*Brs: Breast reconstruction surgery | Ct: Chemotherapy | Dx: Diagnosis
Lx: Lumpectomy | Mx: Mastectomy | Rt: Radiotherapy*

Figure 3

Distribution of breast cancer diagnosis and initial treatment costs.