Primary Liver Cancer in the Philippines: Ten Year Analysis of a National Health Insurance Database

Fausto, Adrian Manuel M.; Ong, Janus P.; Co, Kim Carmela D.; De Claro, Vergil M.

Introduction

Cancer is the eighth leading cause of mortality in the Philippines with an estimate of 109,280 new cases and 66,151 cancer deaths per year [1,2]. Its increasing global disease burden is mainly attributed to the aging and growth of the world population as well as the increasing prevalence of cancer-causing behaviors including smoking, physical inactivity, and "westernized" diets. Liver cancer is the fourth most commonly diagnosed cancer in the country and is the second leading cause of cancer death[2]. It has an annual incidence rate of 10.0 per 100,000 for males, and 4.3 per 100,000 for females[3].

Twenty-six percent of Filipinos live below the poverty line[4]. Most patients will not be able to afford cancer treatment due to their low socio-economic status. To address this, the Philippines made a commitment to provide universal health insurance coverage for its citizens through the establishment of the National Health Insurance Program. By means of the Philippine Health Insurance Corporation (PhilHealth), the country provides medical assistance to 91% of the total population[5]. Its database can provide a useful estimate of the burden of hospitalization of liver cancer nationwide.

Little is known about recent national trends in liver cancer hospitalizations. This study therefore aims to evaluate hospitalizations associated with liver cancers in the Philippines from 2007 to 2016 using the national health insurance inpatient database. Specifically, the study aims to describe the characteristics of liver cancer-related hospitalizations and investigate the trends of hospitalization rates. As a secondary objective, the study seeks to estimate the annual costs for inpatient care of liver cancer and determine the proportion of the costs shouldered by PhilHealth. By analysing the trends and cost of hospitalizations, public health officials can have a measure of the accessibility and effectiveness of health care services for this disease.

Methods

Data source

All PhilHealth inpatient claims with admission dates between January 1, 2007 and December 31, 2016 were extracted electronically from the PhilHealth Claims Database processed through a cloud-based business analytics service (Microsoft Power BI). These comprised claims from all PhilHealth-accredited hospitals in the country. The following demographic and health service utilization data for each patient were obtained: age, sex, dates of admission and discharge, member type (principal member or qualified dependent), total actual charges, total amount reimbursed by PhilHealth, discharge diagnoses, type of institution in which the patient was admitted including location (region and province), ownership (private or government-owned), and functional capacity (infirmary, Level 1, 2 or 3 hospital). Personal identifiers in the data were removed and replaced with encrypted numbers, and permission to conduct the study was approved by PhilHealth.

Patient population

Adult patients aged 19 years old and above with a primary discharge diagnosis of liver cancer with codes that conform to the *International Classification of Disease*, tenth revision (ICD-10) were included: C22.0 (Liver cell carcinoma), C22.1 (Intrahepatic bile duct carcinoma), C22.3 (Angiosarcoma), C 22.4 (Other sarcomas), C22.7 (Other specified carcinomas), C22.8/9 (Unspecified as to type or as primary or

secondary)[6]. Hepatoblastoma, with ICD-10 code of C22.2, is a primary liver malignancy in early childhood and is therefore excluded from the studied population.

Patient and Institution characteristics

Patients were categorized according to their specific type of liver cancer. Characteristics such as age, sex and membership type were examined. Hospitalizations were analysed according to length of stay, location, and type of institution.

Outcome measures and Statistical analysis

Hospitalization rate

We estimated the annual incidence rate of first hospitalization for liver cancer, using the total number of first unique hospital admissions for liver cancer per year divided by the average number of PhilHealth beneficiaries, computed from the mean of the total number of beneficiaries for the given year and the previous year. For patients with multiple hospitalizations across years, only the first unique hospitalization was included. All incidence rates are reported per 100,000 person-years. To determine whether there is a linear trend in the incidence rates across years, we fitted an ordinary least squares regression model, with year as a covariate, and a Newey-West variance correction, which is robust to heteroscedasticity and first-order auto-correlations. A separate analysis of the incidence rate trends specific to hepatocellular carcinoma was also conducted. All statistical analyses were conducted in Stata/IC Version 12.

Cost of Hospitalization

The total annual cost of hospitalization and total annual reimbursements of PhilHealth of all liver cancer patients were obtained. Out-of-pocket (OOP) expenses were computed by getting the difference of the total cost of hospitalization and the total reimbursements. For this analysis, data from years 2014 to 2016 were excluded because of a major change in PhilHealth payment scheme that would have greatly affected the analysis. All costs reported were adjusted to 2010 pesos. Again, a subgroup analysis on hepatocellular carcinoma was also performed.

Results

A total of 22,742 unique liver cancer patients were hospitalized between 2007 and 2016, with majority of patients (67.37%) belonging to the hepatocellular carcinoma group (see Table 1). The second most common liver cancer was intrahepatic cholangiocarcinoma (7.27%). The rest of the liver cancers - angiosarcomas, sarcomas and other specified carcinomas - comprised only 1% of the total population. A notable percentage of the studied population belonged to the unspecified group (24.35%).

Overall, the mean age of adult liver cancers hospitalized is 61.56 years old and the median age was 63. Hepatocellular carcinoma and cholangiocarcinoma patients showed comparable characteristics with a mean age of 61.66 and 62.26, respectively; and median age of 63 for both populations. Majority of adult liver cancer patients were male (68.00%), as was also observed independently in the hepatocellular carcinoma, angiosarcoma, and other sarcomas and carcinomas subgroups. Interestingly, patients with cholangiocarcinoma showed a slight female predominance at 50.88%. Most of the inpatient claims were from enrolled members (63.74%) and only 36.26% were dependents.

The total number of liver cancer-related hospitalizations for 2007 to 2016 was 33,691. Again, the bulk of hospitalizations was from patients with hepatocellular carcinoma (66.62%) or an unspecified liver malignancy (22.47%). The mean length of stay per hospitalization was 5.51 days and the median length of stay was 4 days. A great portion of hospitals providing medical care to adult liver patients were private-owned (67.80%) and only a smaller portion were government-owned (32.20%). More than 80% of hospitals (82.28%) catering to liver cancer patients were level 2 or 3 hospitals; but a noteworthy number

of hospitals (17.72%) were either level 1 hospitals or infirmaries. Hospital locations were fairly distributed in Metro Manila, Luzon, Visayas and Mindano except for hospitals in the cholangiocarcinoma, angiosarcoma and other sarcomas subgroups that were mostly situated in Metro Manila.

Table 1. Characteristics of liver cancer–related hospitalizations reimbursed by PhilHealth from 2007 to 2016

	Liver cell carcinoma (C22.0)	Intrahepatic bile duct carcinoma (C22.1)	Angio-sarcoma (C22.3)	Other sarcomas (C22.4)	Other specified carcinomas (C22.7)	Unspecified as to type or as primary or secondary (C22.8/9)	All Adult Liver Cancers (C22)
Unique patients							
Total, n	15,322	1,653	29	30	171	5,537	22,742
Percentage	67.37%	7.27%	0.13%	0.13%	0.75%	24.35%	100.00%
Age							
Mean	61.66	62.26	57.10	51.70	61.25	61.16	61.56
Median	63	63	63	55.5	62	62	63
Sex							
Male (%)	11,030 (71.99%)	812 (49.12%)	16 (55.17%)	17 (56.67%)	101 (59.06%)	3,489 (63.01%)	15,465 (68.00%)
Female (%)	4,292 (28.01%)	841 (50.88%)	13 (44.83%)	13 (43.33%)	70 (40.94%)	2,048 (36.99%)	7,277 (32.00%)
Member Status							
Member (%)	9,730 (63.50%)	1,035 (62.61%)	19 (65.52%)	21 (70.00%)	132 (77.19%)	3,558 (64.26%)	14,495 (63.74%)
Dependent (%)	5,592 (36.50%)	618 (37.39%)	10 (34.48%)	9 (30.00%)	39 (22.81%)	1,979 (35.74%)	8,247 (36.26%)
Hospitalizations							
Total	22,445	3,349	40	46	239	7,572	33,691
Percentage	66.62%	9.94%	0.12%	0.14%	0.71%	22.47%	100.00%
Length of Stay (days)							
Mean	5.67	5.70	4.78	5.41	4.72	5.16	5.51
Median	4	4	2	3.5	3	4	4
Institution Ownership							
Government (%)	7,219 (32.16%)	1,027 (30.67%)	10 (25.00%)	19 (41.30%)	88 (36.82%)	2,487 (32.84%)	10,850 (32.20%)
Private (%)	15,226 (67.84%)	2,322 (69.33%)	30 (75.00%)	27 (58.70%)	151 (63.18%)	5,085 (67.16%)	22,841 (67.80%)

Institution Class							
Infirmary	235 (1.05%)	6 (0.18%)	0 (0.00%)	0 (0.00%)	1 (0.42%)	95 (1.26%)	337 (1.00%)
Level 1 Hospital (%)	3,712 (16.54%)	252 (7.57%)	3 (7.69%)	11 (23.91%)	73 (30.54%)	1,574 (20.82%)	5,625 (16.72%)
Level 2 Hospital (%)	6,584 (29.34%)	654 (19.66%)	6 (15.38%)	8 (17.39%)	71 (29.71%)	2,817 (37.26%)	10,140 (30.13%)
Level 3 Hospital (%)	11,906 (53.06%)	2,415 (72.59%)	30 (76.92%)	27 (58.70%)	94 (39.33%)	3,075 (40.67%)	17,547 (52.15%)
Hospital Location[§]							
Metro Manila (%)	6,972 (31.06%)	1,589 (47.45%)	23 (57.50%)	22 (47.83%)	88 (36.82%)	1,727 (22.81%)	10,421 (30.93%)
Luzon (%)	4,712 (20.99%)	753 (22.48%)	5 (12.50%)	14 (30.43%)	99 (41.42%)	2,670 (35.26%)	8,253 (24.50%)
Visayas (%)	5,476 (24.40%)	672 (20.07%)	4 (10.00%)	7 (15.22%)	29 (12.13%)	1,582 (20.89%)	7,770 (23.06%)
Mindanao (%)	5,285 (23.55%)	335 (10.00%)	8 (20.00%)	3 (6.52%)	23 (9.62%)	1,593 (21.04%)	7,247 (21.51%)

[§] Luzon – Regions I, II, III, IVA, IVB, V and CAR; Visayas – Regions VI, VII and VIII; Mindanao – Regions ARMM, IX, X, XI, XII and CARAGA

Hospitalization rates

The adjusted rate of hospitalization for all adult liver cancers was 2.59 cases per 100,000 person-years in 2007 (see Figure 1). It increased to 4.07 cases per 100,000 person-years in 2016. The regression model result showed that every year increase from 2007 was associated with a 0.19 increase per 100,000 person-years in the incident hospitalization rate of liver cancer (β1=0.19; 95% confidence interval: 0.08-0.31, p-value=0.005). A separate analysis conducted on the hepatocellular carcinoma subgroup showed similar trends. The adjusted rate of hospitalization was 1.82 per 100,000 person-years in 2007 (see Figure 2). It increased to 2.63 per 100,000 person-years in 2016. The regression model result showed that every year increase from 2007 was associated with a 0.10 increase per 100,000 person-years in the incident hospitalization rate of hepatocellular carcinoma (β1=0.10; 95% confidence interval: 0.04-0.17, p-value=0.006).

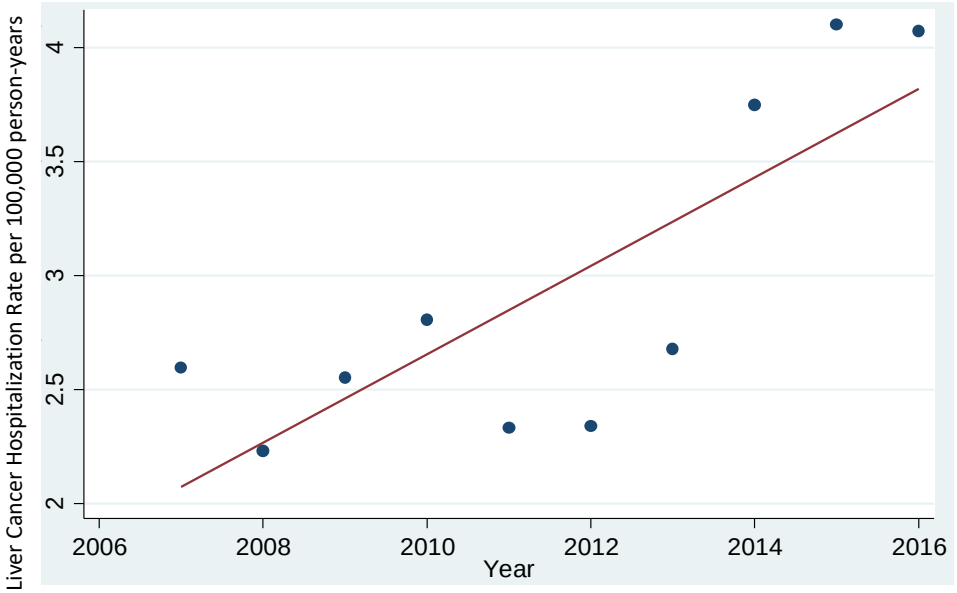

Figure 1. Adjusted incident hospitalization rate for adult liver cancer patients from 2007 to 2016; β1=0.19; 95% CI: 0.08-0.31, p-value=0.005

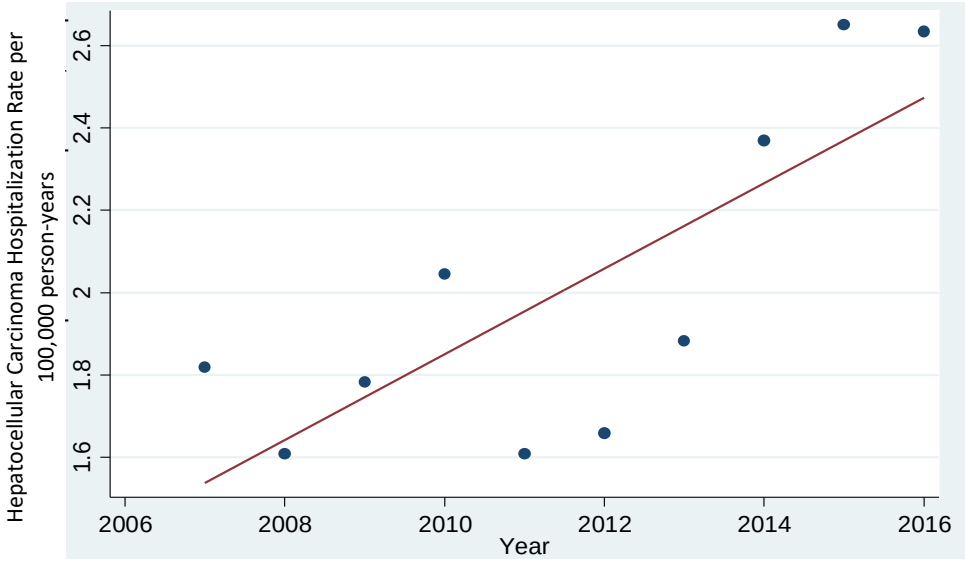

Figure 2. Adjusted incident hospitalization rates for hepatocellular carcinoma patients from 2007 to 2016; β1=0.10; 95% CI: 0.04-0.17, p-value=0.006

Cost of Hospitalization

Total nationwide cost of hospitalizations for adult liver cancers was 631.2 million pesos in 2007, and the amount steadily increased, reaching 2.04 billion pesos in 2013 (see Figure 3). The percentage of hospitalization costs shouldered by PhilHealth per year was around thirty percent (24.04% – 36.90%) (see Figure 4). A subgroup analysis on patients with hepatocellular carcinoma showed similar trends. Total nationwide cost of hospitalizations for hepatocellular carcinoma was 463.8 million pesos in 2007. The cost

increased steadily up to 1.53 billion pesos in 2013 (see Figure 5). The percentage of hospitalization costs shouldered by PhilHealth was also constant at around thirty percent (21.46% – 34.76%) (see Figure 6).

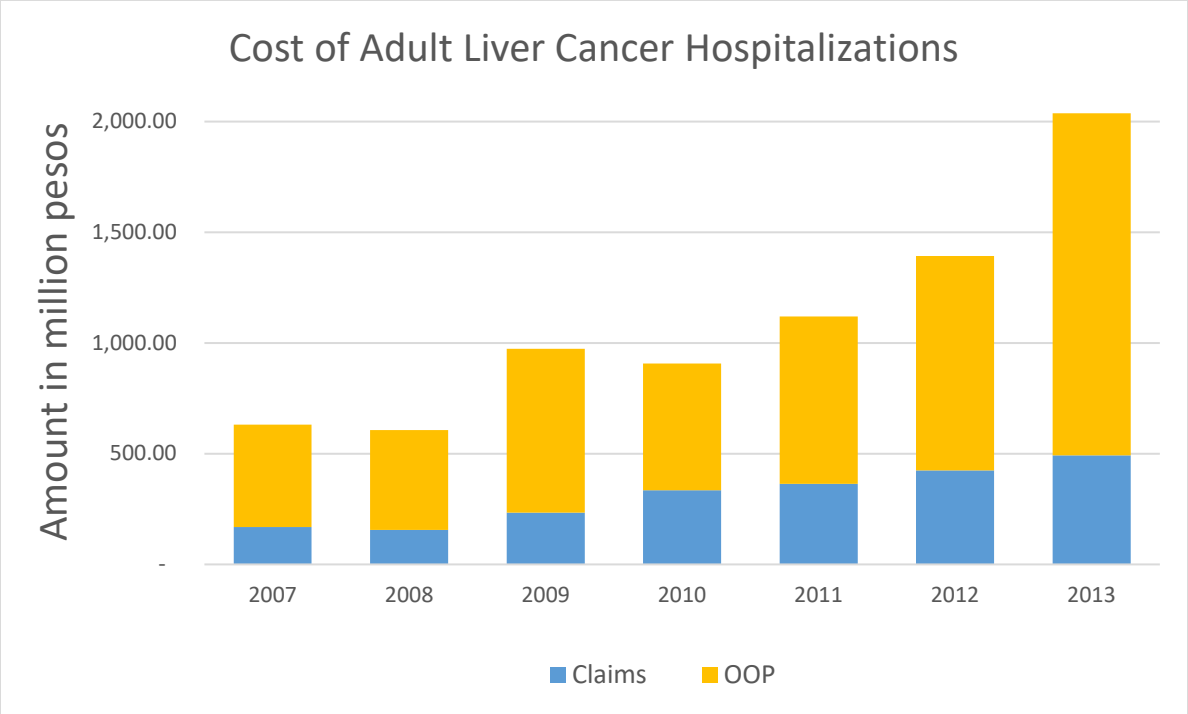

Figure 3. Total Cost of adult liver cancer hospitalizations from 2007 to 2013. Costs reported in 2010 pesos; Claims pertain to PhilHealth benefits; OOP – Out-of-pocket expenditures.

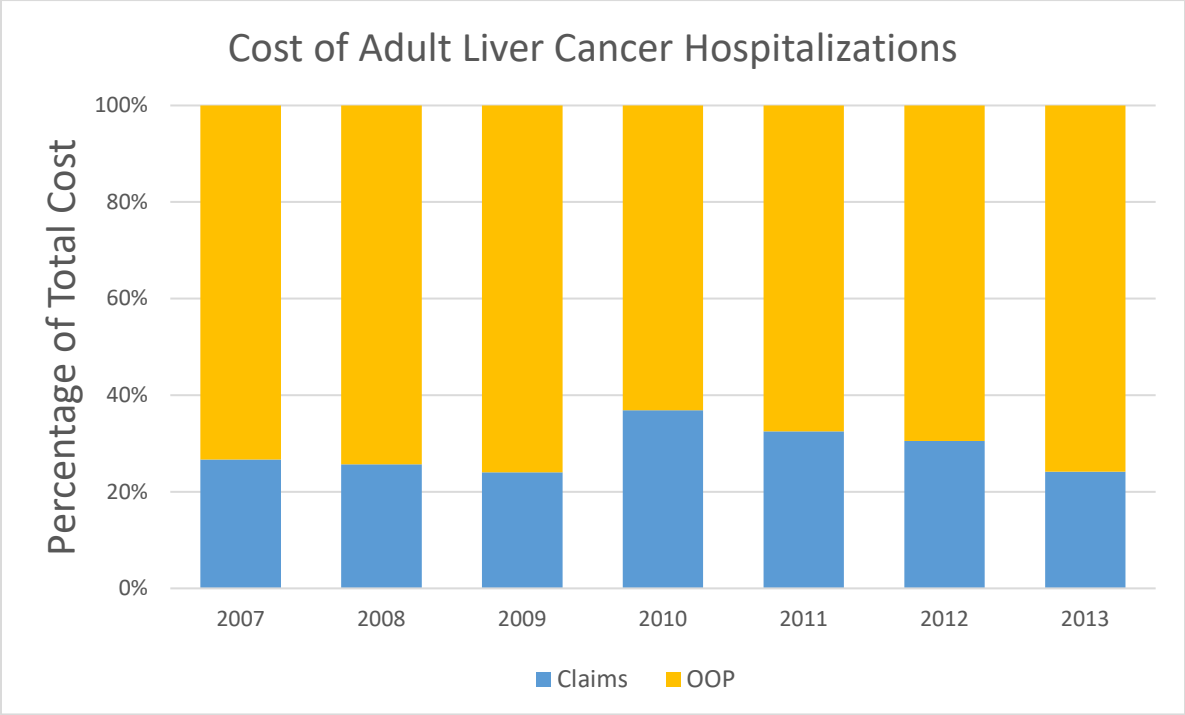

Figure 4. Total Cost of adult liver cancer hospitalizations from 2007 to 2013 expressed in percentages; Claims pertain to PhilHealth benefits; OOP – Out-of-pocket expenditures

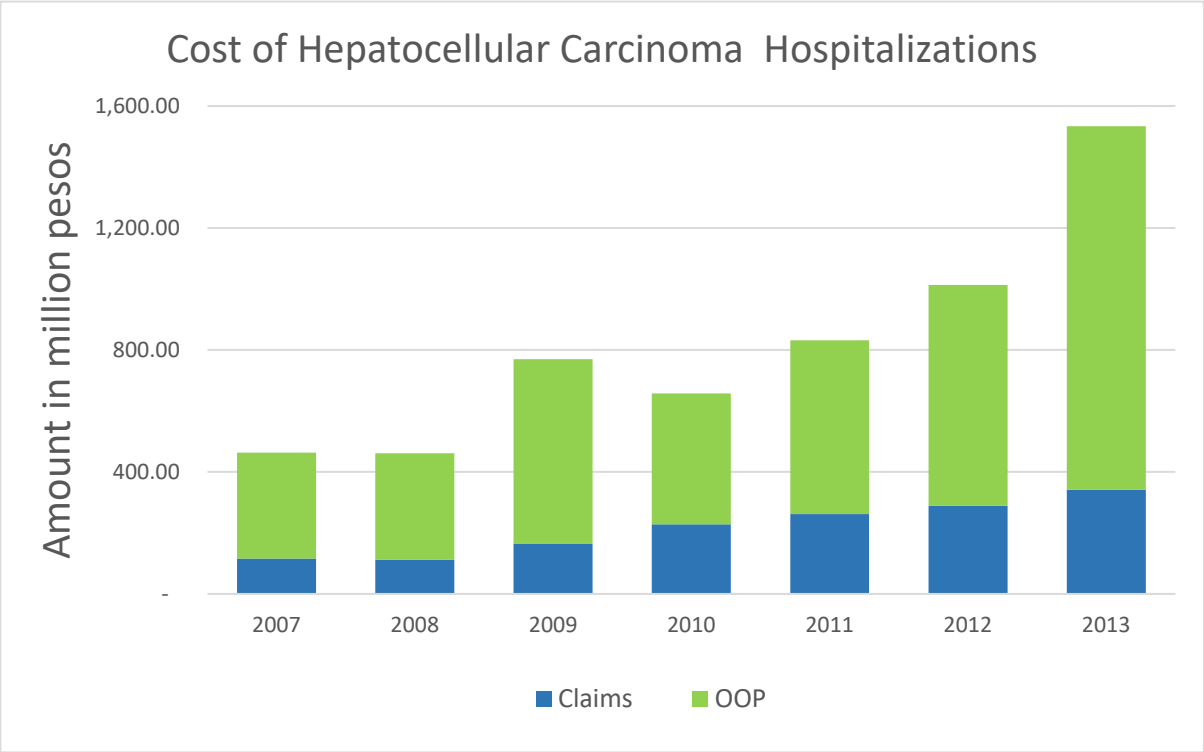

Figure 5. Total Cost of hepatocellular carcinoma hospitalizations from 2007 to 2013. Costs reported in 2010 pesos; Claims pertain to PhilHealth benefits; OOP – Out-of-pocket expenditures.

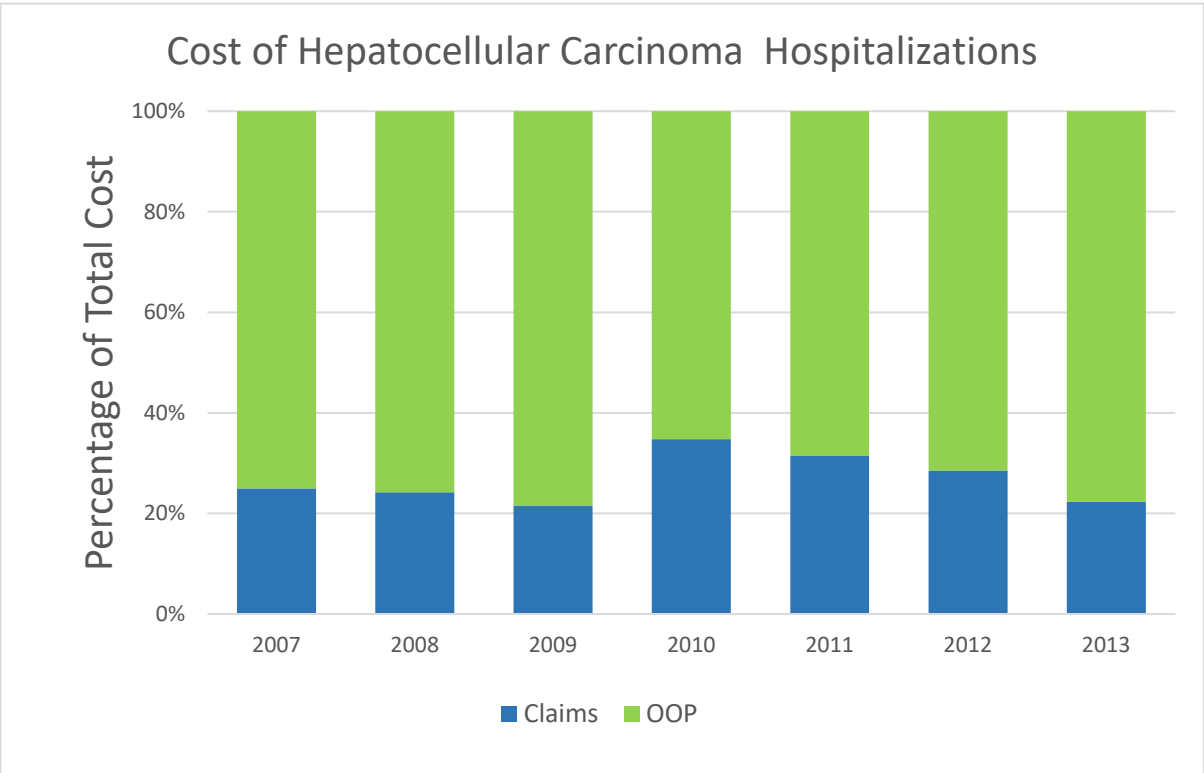

Figure 6 Total Cost of hepatocellular carcinoma hospitalizations from 2007 to 2013 expressed in percentages; Claims pertain to PhilHealth benefits; OOP – Out-of-pocket expenditures

Discussion

The most common tumor occurring in the liver is metastatic[8]. This was not reflected in the observed population because of limitations of ICD-10 coding. Liver metastases were classified under the ICD-10 code of the primary site of malignancy and would therefore be not included in the studied population. It is, however, possible that some of the patients categorized under unspecified (24.35% of the total) had liver metastasis from unknown primary malignancies. Hepatocellular carcinoma was the most commonly observed type of primary liver cancer in hospitalized patients in the Philippines. This observation was consistent with previous studies that reported that 80% of all primary liver cancers are hepatocellular carcinoma[8]. The observed average age of hospitalized hepatocellular carcinoma (mean = 61.66, median = 63) was slightly lower than the estimated average age of diagnosis for hepatocellular carcinoma (65 years old)[9]. Majority of hospitalized hepatocellular carcinoma patients were male, which was consistent with latest estimates in the country[10]. The second most common type of primary liver cancer observed in hospitalized patients was intrahepatic cholangiocarcinoma. This was also consistent with previous literature[8]. The observed median age of hospitalization is 63 - lower than the reported average age of diagnosis seen in other studies[11,12]. Interestingly, there was a slightly higher female predominance of 51% in the cholangiocarcinoma subgroup. This contradicts with previous studies on intrahepatic cholangiocarcinoma populations in South East Asia that estimated higher rates of cancer among men than women (male-to-female sex ratio of approximately two)[10].

An interesting and unexpected observation from the type of institutions providing medical care to hospitalized liver cancer patients was the considerable proportion of infirmaries and level 1 hospitals. These smaller facilities lack specialists - hepatologists, oncologists, and interventional radiologists - who are adept at managing and providing active therapy for liver cancer patients. In a systematic review that assessed the impact of specialization on processes and outcomes for cancer patients, it was shown that institutions with specialized centers and clinicians were associated with better outcomes and reduced incidence of mortality[13]. A study that investigated provider and health system factors in hepatocellular carcinoma patients also demonstrated that admission at an academically-affiliated hospital (corresponding to level 3 hospitals using PhilHealth's classification) and evaluation by multiple specialists were associated with higher likelihood of receiving definitive liver cancer therapy such as transplantation, resection, ablative or transarterial therapy[14]. The study also showed that subspecialty care by a hepatologist, medical oncologist or a surgeon within thirty days of admission was associated with reduced mortality[14]. This implies that liver cancer patients hospitalized in infirmaries and level 1 hospitals may have received subpar medical care which may have lead to worse patient outcomes. Possible explanations for admission to smaller facilities include the lack of patient access to appropriate subspecialist care in their region and the failure of admitting physicians to transfer patients to appropriate specialist centers or institutions.

The Philippine Cancer Society has estimated based on its 1980 to 2007 data that the trend of liver cancer incidence rate is decreasing - with an annual change of -0.5% among males and -0.5% among females[2]. This was contrary to our observed significant upward trend in incidence of hospitalization rates among adult liver cancer patients, even in the hepatocellular carcinoma group, which suggested an increasing trend in incidence of liver cancer patients in the country. We only analysed the trend in annual incidence rates in the last 10 years. Given the few number of data points, the significance of the linear time trend should still be interpreted with caution. Nevertheless, the data highlights the need to investigate the root causes of liver cancer in the country and provide concrete steps towards its prevention. In the Philippines, 86 percent of patients with hepatocellular carcinoma are positive for Hepatitis B surface antigen[15]. Controlling hepatitis B will be an effective strategy to significantly lower the incidence of liver cancer in the country[16]. Stricter implementation of existing laws such as the Republic

Act No. 7846, the bill that provides compulsory Hepatitis B immunization among infants and children less than 8 years old, and Republic Act No. 10152, the bill that provides for all infants to be given the birth dose of the Hepatitis-B vaccine within 24 hours of birth, is necessary. Providing timely initiation of safe and effective antiviral therapy and ensuring affordability of these antiviral drugs will also mean more patients benefitting from the treatment and more liver cancers prevented.

The Philippines, along with other members of the Association of Southeast Asian Nations (ASEAN), strives to achieve universal health coverage (UHC). Aside from the beneficiary (population coverage) and scope (service coverage), an important key aspect in achieving this goal is the level of financial contribution (financial coverage) [17]. Compared to other Southeast Asian countries, we have one of the lowest percentage of government expenditure on total health expenditures, higher only to Cambodia and Myanmar. Brunei and Thailand had the highest percentage - with 91.8% and 76.4% of total health expenditures shouldered by the government, respectively[17]. The World Health Organization in 2014 estimated that the Philippine government shoulders only 37.7% of total expenditures on health and that 52.0% of total expenditures are from out-of-pocket (OOP) sources[17]. This was comparable with the results of our study that showed only about thirty percent of total hospitalization costs of liver cancer were shouldered by the national health insurance, and about seventy percent of total expenditures were from OOP sources. Our study also showed that the total cost of hospitalization for adult liver cancer was increasing in the past years but the percentage of costs covered or reimbursed by PhilHealth has remained consistently low, resulting to increasing OOP expenditures for its beneficiaries. This heavy reliance on OOP expenditures may cause liver cancer patients to decline care, or worse, lead them to impoverishment. The high level of OOP health expenditures could also be an important indicator of the need to improve the current health care system. PhilHealth's high population coverage of 91% is already acceptable and adequate. The government's next important task is to increase its financial contribution to be able to move towards universal health coverage and to improve support for liver cancer patients.

There were several limitations to this study which may lead to the underestimation of reported hospitalization rates and costs. First is the reliance on the billing hospitals for encoding. The inpatient claims database of PhilHealth relies heavily on the ICD-10 classification entered at the billing hospital. This may not accurately reveal the condition a patient was treated during hospitalization. This is especially true beginning 2014, when the case rate payment scheme was implemented. In this scheme, only the highest case rate – either an ICD code of the discharge diagnosis or a procedure code - is encoded. These means that hospitalized patients with liver cancer encoded under a specific procedure code such as hepatectomy, transarterial chemoembolization, or radiofrequency ablation will not be included in the study population. Second, only patients with primary discharge diagnosis of liver cancer were included in the study. Other patients that were primarily admitted due to other causes, such as variceal bleeding, hepatic encephalopathy or other complications of liver cirrhosis and liver cancer, are coded under a different classification and will also be not included in the studied population. Third, the data used for this study came from the PhilHealth claims database, and would exclude cases of liver cancer that were admitted in non-PhilHealth accredited institutions; and those that were not PhilHealth beneficiaries. Lastly, the out-of-pocket costs of hospitalizations may be underestimated in cases when patients are asked to buy medicines and items outside the hospital because these expenses are not reflected in the final hospital bill. Charity cases that have no or minimal out-of-pocket expenses also underestimates the out-of-pocket costs of private patients. These limitations could be expected when analysing administrative databases that were not primarily purposed for epidemiologic or economic research. Despite having possible underestimates, this study was able to demonstrate important recent trends in hospitalization and costs of liver cancer-related hospitalizations in the Philippines in the last ten years.

Conclusion

Liver cancer continues to carry a high burden to Filipinos with its increasing rate of hospitalization in the last ten years. This is associated with a substantial economic burden caused by the increasing total cost of hospitalization, majority of which are out-of-pocket. These results highlight the need for concrete steps towards prevention of liver cancer in the country.

References:

1 Department of Health Statistics 2013. Retrieved from: https://www.doh.gov.ph

2 Laudico, A.V. et al. 2015 Philippine Cancer Facts and Estimates. Retrieved from: https:// www.philcancer.org.ph

3 Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R et al (2017). Cancer Incidence in Five Continents, Vol. XI (electronic version). Lyon: International Agency for Research on Cancer, 2017. Retrieved from: http://ci5.iarc.fr

4 Bersales, L.S. Poverty incidence among Filipinos registered at 26.3%, as of first semester of 2015 – PSA. Retrieved from: https://psa.gov.ph

5 2007-2016 PhilHealth Stats and Charts; 2003 – 2016 Annual report. Retrieved from: https://www.philhealth.gov.ph

6 International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Version for 2010 Retrieved from: http://apps.who.int

7 Philippines Statistics Authority. Retrieved from: http://psa.gov.ph

8 Stewart BW, Wild CP. World cancer report 2014. Lyon: IARC Press, 2014.

9 Waghray A, Murali AR, and Narayanan Menon KV. Hepatocellular carcinoma: From diagnosis to treatment. World J Hepatol. 2015; 7(8): 1020–1029.

10 Shin H, Oh J, Masuyer E, Curado M, Bouvard V, Fang Y et al. Comparison of Incidence of Intrahepatic and Extrahepatic Cholangiocarcinoma - Focus on East and South-eastern Asia. Asian Pacific Journal of Cancer Prevention. 2010; 11: 1159-66.

11 Saha SK, Zhu AX, Fuchs CS and Brooks GA. Forty-Year Trends in Cholangiocarcinoma Incidence in the U.S.: Intrahepatic Disease on the Rise. The Oncologist. 2016; 21(5): 594-599.

12 Jarnagin W, Winston C. Hilar cholangiocarcinoma: diagnosis and staging. HPB (Oxford). 2005; 7(4): 244–251.

13 Grilli R, Minozzi S, Tinazzi A, Labianca R, Sheldon TA, Liberati A. Do specialists do it better? The impact of specialization on the processes and outcomes of care for cancer patients. Ann Oncol. 1998; 9(4):365-74.

14 Serper M, Taddei TH, Mehta R, D'Addeo K, Dai F, Aytaman A, et al. Association of Provider Specialty and Multidisciplinary Care With Hepatocellular Carcinoma Treatment and Mortality. Gastroenterology. 2017; 152(8):1954-1964.

15 Merican I, Guan R, Amarapuka D, Alexander MJ, Chutaputti A, Chien RN, et al. Chronic hepatitis B virus infection in Asian countries. J Gastroenterol Hepatol. 2000; 15(12):1356-61.

16 Lok AS. Does antiviral therapy for hepatitis B and C prevent hepatocellular carcinoma? J Gastroenterol Hepatol. 2011 ;26(2):221-7.

17 Minh HV, Pocock NS, Chaiyakunapruk N, Chhorvann C, Duc HA, Hanvoravongchai P et al. Progress toward universal health coverage in ASEAN. Glob Health Action. 2014; 7: 10.3402/gha.v7.25856. Published online 2014 Dec 3.