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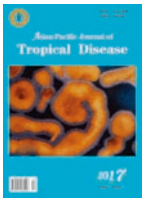

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Economic burden of influenza at a tertiary hospital in Vietnam

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ABSTRACT

Objective: To estimate cost of illness based on provider perspective of influenza treatment at Hospital of Tropical Diseases, Ho Chi Minh city.
Methods: A retrospective study was conducted between January 2013 and December 2015 at Hospital of Tropical Diseases, Ho Chi Minh City. Demographic and clinical information was collected from medical records. Treatment cost was composed of cost of hospital bed, diagnosis test, X-ray/imaging, operation, pharmaceuticals and consumable materials.
Results: Average cost per episode of all aged group was (112.58 ± 239.60) USD, the highest cost was contributed by adults group [(313.28 ± 560.5) USD],whereas the lowest cost was children group [(80.62 ± 120.80) USD]. According to high risk factor group, the average cost per day is 42.14 USD for any cardiovascular disorders group; diabetes-cardiovascular patient (41.15 USD), and elderly patient groups (48.52 USD).
Conclusions: Direct medical cost of influenza-related hospitalizations imposes a heavy burden on patients and their families in Vietnam. Further study is needed to provide more comprehensive evidence on the economic burden of influenza.

1. Introduction

Influenza is a vaccine-preventable infectious disease that causes morbidity in all age groups and appreciable mortality by its viral infection[1]. Thus, influenza viral infection are responsible for respiration illnesses resulting in substantial morbidity and increased health care utilization and cost[2]; and the illness is known to display common symptoms including fever with temperature higher than 38 ℃, sore throat, cough and runny nose, muscle and body aches, fatigue, *etc*.[3]. Although most patients are recorded to recover without medical treatment, influenza can lead to many complications which may require emergency or inpatient treatment. Southeast Asia region has been identified by the World Health Organization (WHO) as being at risk of emerging diseases including the avian influenza[4]. Even though the mounting evidence of prevalence and excessive mortality caused by influenza are approximate to those seen in temperate countries, no influenza burden in subtropics and tropics has yet been well-defined[5,6]. As the global estimating report of WHO in 2014 revealed that there were 3–5 million cases of severe illness and about 250 000–500 000 deaths due to influenza annual epidemics[7]. Consequently, not only substantial morbidity and mortality, but also worldwide serious economic burden are possible outcomes of influenza. Therefore, the treatment cost of influenza needs to be investigated in order to successfully manage cost efficiency.

During the period of time from 2003 to 2008, Vietnam had to incur five waves of avian influenza and almost every province was reported with infected poultry outbreaks. It is shown that 36 out of 63 provinces had 106 cases of infection on human, of which 56 cases were certified as mortality[8]. Such influenza epidemic is believed to thrive in Southeast Asia due to the region's vulnerability caused by population growth and movement, urbanization, environment factors such as agriculture, land use, water use, sanitation, health system factors and the development of drug resistance. WHO has showed their concern towards the inadequacy in each region's preparedness for influenza pandemic[9]. As many

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other developing countries, Vietnam shows a limited and likely insufficient level of readiness to deal with a highly pathogenic and transmissible strain of influenza outbreak[9-13]. However, when compared to other Southeast Asian countries such as Indonesia, Taiwan, Thailand and Cambodia, Vietnam has met the requirement density of health professional per capita in the region; sufficient healthcare facilities with surge capacity; equipment shortages including mechanical ventilators; and only 7.9% of provinces with gap national stock of anti-viral tablets[14].

Despite intensive researches in developing countries, the treatment cost of laboratory-confirmed influenza (LCI) in Southeast Asia, especially Vietnam, has not been well-described. In Cambodia, patient or family costs of influenza, were 45 USD per patient (15%) of total economic cost from 2005 to 2011[14]. On the other hand, during the period of time from 2009 to 2011, the treatment cost for influenza-related inpatients in three hospitals located in different Chinese provinces was funded with nearly 1 800 USD, which increased due to the annual influenza epidemic outbreaks[15]. Moreover, researchers have started to carry out further studies about the economic aspects of influenza burden, in which the equality and genuineness of statistics are ensured by taking several factors account into the perspective of patients, hospitals, and the governments. Compared to outpatients, it is clear that inpatients are to pay more money due to hospital services and workday lost[15].

In order to gain an insight into the direct medical cost of influenza hospitalization applied to different age groups in Vietnam and to provide evidence for the development of recommendations for policies and plans which are designed to ease the mitigation of pandemic, this study was conducted to estimate cost of illness based on provider perspective of influenza treatment at Hospital of Tropical Diseases (HTD), Ho Chi Minh city.

2. Materials and methods

2.1. Study design

This study employed a retrospective cost of illness study, which measured the direct medical costs in specific cases with diagnosis or influenza-like-illness (ILI) symptoms during the 2013–2015 period. This study was analyzed based on provider perspective, in which direct medical costs were collected from all cases that met the selection criteria.

2.2. Study population and site

In this study, all influenza inpatients at HTD, Ho Chi Minh city in a period of 3-fiscal years from 2013 to 2015 were included. They were identified by their primary discharged diagnosis by using the International Code of Disease 10th Revision (ICD 10^{TM}) including J10, J11[16]. However, if the selected subjects have any types of discharges due to insubordination, attempt at escaping or transfer, they are to be eliminated from the survey in the study. HTD in Ho Chi Minh City is located on an area of nearly 4.6 hectares area in Southern Vietnam with a crew of 650 staffs working in 26 departments.

2.3. Data collection

All collected cases were divided into two groups labeled as ILI and LCI. The data were extracted from hospital electronic database after ethical approval of the hospital. The case identification was based on WHO case definitions for influenza disease by ILI case definition and laboratory confirmed test for the influenza virus using the PCR test by laboratories of HTD (Figure 1).

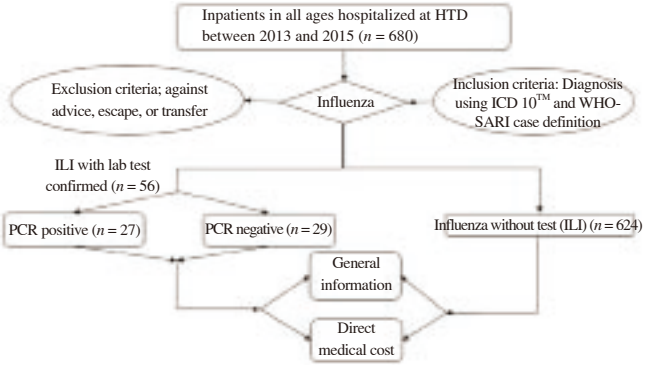

Figure 1. Selection and classification of studied patients.

The hospital database was divided into three general categories including demographic characteristics (gender, age, insurance reimbursement and payment scheme), clinical status (discharge status, number of comorbidities and number of complications and resource utilization (pharmaceuticals and supplies, laboratories, diagnostic examinations, hospitalization, surgery, procedures and hospital charges). Medical services were classified into six groups including cost of hospital bed, cost of diagnosis tests, cost of X-ray/imaging, cost of operation, cost of pharmaceuticals and cost of consumable materials.

2.4. Cost analysis

A number of each medical services received by patients were multiplied by reference unit cost of medical services[17] resulting in its cost of services. In term of cost of pharmaceuticals, patients incur the cost of drug equivalence to purchase price from the hospital. All costs were in 2015 Vietnam Dong value, and then were converted to 2015 USD values using the exchange rate of 1 USD for 21.621 Vietnam Dong[17,18].

2.5. Statistical analysis

Descriptive statistics were employed to present the costs. which were classified by independent variables and tested for statistical difference. One-way sensitivity analyses were conducted.

2.6. Ethics statement

The review and approval of this study was given by the Biomedical Research Ethics Council and HTD (IORG0007145). Due to the study's feature of running on a medical record data without patient contact, the written informed consent from the patients was waived.

3. Results

3.1. General characteristic information

It could be seen in Table 1 that the number of patients diagnosed with LCI reached its highest value of 36 cases in 2013 and bottomed out at 9 cases in 2014. In contrast, the number of patients diagnosed with ILI peaked at 267 cases in 2014 and fell to a low point of 170 cases in 2013.

Table 1
Demographics, clinical characteristics and service utilization of all patients.

Parameter		2013 (n = 206)	2014 (n = 276)	2015 (n = 198)	Total (n = 680)
Age (years)	Mean ± SD	18.7 ± 19	8.8 ± 12.1	7.9 ± 13.4	11.5 ± 15.6
	Range	4–68	3–91	2–88	2–91
	0–14	130 (63.0)	249 (90.2)	181 (91.5)	560 (82.3)
	15–24	15 (7.3)	10 (3.6)	4 (2.0)	29 (4.3)
	25–64	58 (28.2)	14 (5.1)	9 (4.5)	81 (11.9)
	> 64	3 (1.5)	3 (1.1)	4 (2.0)	10 (1.5)
Gender	Female	88 (42.7)	127 (46.0)	72 (36.4)	287 (42.2)
	Male	118 (57.3)	149 (54.0)	126 (63.6)	393 (57.8)
Health insurance	0%	89 (43.2)	116 (42.0)	81 (40.9)	286 (42.1)
	30%	56 (27.2)	68 (24.6)	-	124 (18.2)
	40%	-	1 (0.4)	52 (26.3)	53 (7.8)
	80%	9 (4.4)	1 (0.4)	-	10 (1.5)
	100%	52 (25.2)	90 (32.6)	65 (32.8)	207 (30.4)
ICD 10-code	J10.8	69 (33.5)	12 (4.3)	32 (16.2)	113 (16.6)
	J11.1	137 (66.5)	263 (95.3)	166 (83.8)	566 (83.2)
	J11	-	1 (0.4)	-	1 (0.1)
Location	Urban	160 (78.0)	213 (77.0)	127 (64.0)	500 (74.0)
	Rural	46 (22.0)	63 (23.0)	71 (36.0)	180 (26.0)
Drugs	Antiviral	34 (17.0)	8 (3.0)	11 (11.0)	53 (8.0)
	Antibiotic	59 (28.6)	43 (15.6)	48 (49.0)	150 (22.1)
Length of stay (days)	Mean ± SD	4.9 ± 2.5	3.8 ± 1.8	4.4 ± 2.6	4.3 ± 2.3
	Range	1–16	1–14	1–21	1–21
Relevant pre-period risk factors	CD[a]	4 (1.9)	-	1 (1)	5 (0.7)
	DM[b]	1 (0.5)	-	-	1 (0.1)
	Age > 64	3 (1.5)	3 (1.1)	4 (2.0)	10 (1.5)

[a]: Any cardiovascular disorders (I10-15, I20-25, I26-I28, I30-I52, Z99-Z99.1); [b]: Diabetes and other metabolic diseases (E10-E14). CD: Cardiovascular disorders; DM: Diabetes mellitus and other metabolic diseases.

In LCI group, the total mean age was (36.8 ± 22.6) years in the period of from 2013 to 2015. The adult age group (25–64 years) accounted for the highest value in the overall number of patients in the period from 2013 to 2015 (37 cases; 66.1%). Throughout the survey, even though the number of adult cases was recorded at 24 cases (66.7%) in 2013, 8 cases (88.9%) in 2014 and 5 cases (45.5%) in 2015, it maintained to be the most significant components that made up the final overall statistics of mean age. Following the adult age group was the children group with its entire figures of 13 cases (23.1%) being the second greatest. The youth and elderly groups were shown to share the similar statistics of 3 cases (5.4%) during three consecutive years of investigation. In consideration of the ILI group, the total mean age was (9.2 ± 12.5) years in the period from 2013 to 2015. As the figures were clearly displayed, it was the children group that took the main role in contributing to the total number of cases with its figures of 547 cases (87.6%) in three successive years followed by the adult group with 44 cases (7.1%), youth group with 26 cases (4.2%) and elderly group with only 7 cases (1.1%).

In total, the mean age of patients diagnosed with influenza was (11.5 ± 15.6) years in the period 2013–2015 with the data showing that children (0–14 years) had the highest percentage (82.3%), the adults (25–64 years) with medium percentage (11.9%) , the youth (15–24 years) with 29 cases (4.3%) and the elderly (> 64 years) with the lowest statistics of 10 cases (1.5%). Clearly, the percentage of children patients was 55 times greater than that of elderly patients. Furthermore, it was noticeable that the percentage of influenza patients dropped significantly among the age bracket from 0–14 and 15–24 from 82.3% to 4.3% and then rose lightly between the age groups of 15–24 and 25–64 (4.3% and 11.9%, respectively) and finally decreased insignificantly at the elderly age group (> 64 years).

In this study, ICD-10™ was used during the classification of diseases. Moreover, ICD-10, J10.8 "influenza with other manifestations, influenza virus identified" and ICD-J11.1 "influenza with other manifestations, virus not identified" were also applied in order to classify specific cases. The result of the research showed that cases diagnosed with influenza and LCI test were mostly classified as J10.8 (98%). On the other hand, a majority of cases with ILI were classified as J11.1 (90.5%). Conclusively, influenza cases were majorly classified as J11.1 (83.0%). In the laboratory-tested group, the number of negative and positive cases was almost equal. In 2013, there were 17 positive cases during three years between 2013 and 2015.

According to Table 2, relevant pre-period risk factors include cardiovascular disorders (CD), diabetes mellitus (DM) and other metabolic diseases and age over 64, which appears to be the most affective factor with its total figure of 10 cases (1.5%) doubling of the others (5 cases in CD – 0.7% ; only one case in DM – 0.1%). The percentage of elderly patients (64 years) was double than that of CD patients and 15 times greater than that of DM patients.

The insurance reimbursement of patients was divided into five levels of 0%, 30%, 40%, 80%, and 100%, in which 0% (out-of-pocket) was shown to be the section with the highest statistics of 286 cases (42%) and 80% section was on the other end with the lowest statistics of 10 cases (2.0%). With further investigation, it seemed that the total proportion of 0% had a slight decrease from 2013 to 2015 (from 43.0% to 41.0%). Regarding LCI test cases, the highest figure of 24 cases (42.8%) belonged to the 0% level, whereas the lowest went to the 40% level with 2 cases (3.6%). Furthermore, in 2014 there were available the figures of the 0% and 30% level, in which the proportion of the latter (33.3%) was just half of that of the former (66.7%). Later on, in 2015, two out of five levels were absent including 30% and 80% level. The 100% level accounted for nearly half of the total proportion with 5 cases (46.65%). On the other hand, the ILI cases had the highest proportion of 262 cases (42.0%) in 0% level and the lower of 2 cases (0.3%) in 80% level. And the statistics of 30% and 100% level shared the same value of 47 cases (27.6%). Specifically, there was a significant rise of 49 cases (27.3%) in the 2014 and 2015 statistics of 40% level, where it shifted from 1 case (0.4%) to 50 cases (27.7%). It is also noticeable that the figures of 40% and 80% level had the same value of one case (0.4%).

The total proportion of antibiotic drugs prescribed in three years (150 cases; 22.1%) was shown to be triple of that of antiviral drug in the same period of time (53 cases; 8.0%). In comparison with the

Table 2

Demographics, clinical characteristics and service utilization of patients classified by laboratory confirmation [*n* (%)].

Parameter	Influenza with PCR lab test							ILI			
	2013		2014		2015		Total	2013	2014	2015	Total
	Positive *n* = 17	Negative *n* = 19	Positive *n* = 4	Negative *n* = 5	Positive *n* = 6	Negative *n* = 5	*n* = 56	*n* = 170	*n* = 267	*n* = 187	*n* = 624
Age											
Mean ± SD	29.94 ± 23.98	40.95 ± 17.60	48.50 ± 23.27	47.80 ± 13.01	23.67 ± 24.06	40.20 ± 35.34	36.8 ± 22.6	15.1 ± 16.4	7.4 ± 9.4	6.6 ± 10.5	9.2 ± 12.5
Range	5-67	6-64	29-77	28-60	3-61	5-88	3-88	4-68	3-91	2-80	2-91
0–14	6 (35.3)	2 (10.5)	-	-	3 (50.0)	2 (40.0)	13 (23.1)	122 (71.7)	249 (93.3)	176 (94.1)	547 (87.6)
15–24	3 (17.6)	-	-	-	-	-	3 (5.4)	12 (7.1)	10 (3.7)	4 (2.1)	26 (4.2)
25–64	7 (41.2)	17 (89.5)	3 (75.0)	5 (100.0)	3 (50.0)	2 (40.0)	37 (66.1)	34 (20.0)	6 (2.3)	4 (2.1)	44 (7.1)
> 64	1 (5.9)	-	1 (25.0)	-	-	1 (20.0)	3 (5.4)	2 (1.2)	2 (0.7)	3 (1.7)	7 (1.1)
Gender											
Female	8 (47.1)	11 (57.9)	2 (50.0)	2 (40.0)	4 (66.7)	3 (60.0)	26 (46.4)	71 (41.8)	122 (45.7)	69 (36.9)	262 (42.0)
Male	9 (52.9)	8 (42.1)	2 (50.0)	3 (60.0)	2 (33.3)	2 (40.0)	30 (53.6)	99 (58.2)	145 (54.3)	118 (63.1)	362 (58.0)
Insurance reimbursement of patients (%)											
0%	4 (23.5)	10 (52.6)	3 (75.0)	3 (60.0)	2 (33.3)	2 (40.0)	24 (42.8)	75 (44.1)	110 (41.2)	77 (41.2)	262 (42.0)
30%	3 (17.6)	6 (31.6)	1 (25.0)	2 (40.0)	-	-	12 (21.4)	47 (27.6)	65 (24.3)	-	112 (17.9)
40%	-	-	-	-	2 (33.3)	-	2 (3.6)	-	1 (0.4)	50 (27.7)	51 (8.2)
80%	5 (29.4)	3 (15.8)	-	-		-	8 (14.3)	1 (0.7)	1 (0.4)	-	2 (0.3)
100%	5 (29.4)	-	-	-	2 (33.3)	3 (60.0)	10 (17.9)	47 (27.6)	90 (33.7)	60 (32.1)	197 (31.6)
ICD-10 code											
J10.8	16 (94.1)	19 (100.0)	4 (100.0)	5 (100.0)	6 (100.0)	5 (100.0)	55 (98.0)	34 (20.0)	3 (1.1)	21 (11.0)	58 (9.3)
J11.1	1 (5.9)	-	-	-	-	-	1 (2.0)	136 (80.0)	263 (98.5)	166 (89.0)	565 (90.5)
J11	-	-	-	-	-	-	-	-	1 (0.4)	-	1 (0.2)
Location											
Urban	11 (64.7)	9 (47.4)	4 (100.0)	3 (60.0)	2 (33.3)	2 (40.0)	31 (55.4)	140 (82.4)	206 (77.2)	123 (65.8)	469 (75.0)
Rural	6 (35.3)	10 (52.6)	-	2 (40.0)	4 (66.7)	3 (60.0)	25 (44.6)	30 (17.6)	61 (22.8)	64 (34.2)	155 (25.0)
Drugs											
Antiviral	17 (100.0)	17 (89.7)	4 (100.0)	4 (80.0)	6 (100.0)	5 (100.0)	53 (95.0)	-	-	-	-
Antibiotic	12 (70.6)	12 (63.2)	3 (75.0)	-	6 (100.0)	5 (100.0)	38 (68.0)	34 (20.0)	40 (15.0)	38 (43.7)	112 (18)
Length of stay (days)											
Medium	9.00	6.00	6.50	6.00	10.00	7.00	7	4	5	4	4
Mean ± SD	9.76 ± 2.80	5.37 ± 1.71	8.25 ± 3.86	5.00 ± 1.73	11.67 ± 4.63	7.40 ± 1.14	7.7 ± 3.5	4.4 ± 2.0	3.7 ± 1.7	4.0 ± 2.1	4.0 ± 1.9
Range	7-16	1-7	6-14	2-6	9-21	6-9	1 – 21	1 – 12	1 – 13	1 – 10	1 – 13
Relevant pre-period risk factors[a,b] (as defined by STIKO)											
CD[a]	1 (5.9)	1 (5.3)	-	-	1 (16.7)	-	3 (5.0)	2 (1.2)	-	-	2 (0.3)
DM[b]	-	1 (5.3)	-	-	-	-	1 (2.0)	-	-	-	-
Age > 64	1 (5.9)	-	1 (25.0)	-	-	1 (20.0)	3 (5.0)	2 (1.2)	2 (0.8)	3 (1.7)	7 (1.1)

[a]: Any cardiovascular disorders (I10-15,I20-25, I26-I28, I30-I52, Z99-Z99.1). [b]: Diabetes and other metabolic diseases (E10-E14). ILI: Influenza-like-illness; STIKO: Standing Committee on Vaccination in German; CD: Cardiovascular disorders; DM: Diabetes mellitus and other metabolic diseases.

percentage of drug usage in 2013 including both aforementioned two drugs with their values being 34 cases (17.0 %) for antiviral and 59 cases (28.6%) for antibiotic drug, the 2014 intakes appeared to be lower with 8 cases (3.0%) for antiviral and 43 cases (15.6%) in antibiotic. Nevertheless, there were increases in usage, where the use of antiviral and antibiotic both rose 11 cases (11.0%) and 48 cases (49.0%). With further investigation into LCI and ILI groups, it was shown that all of the drug prescription for LCI in 2015 was antiviral drugs (100%). Moreover, back in 2014 the figures for antibiotic drug was just only 3 cases (33.3%). The average of the length of stay for the LCI cases (7.7 ± 3.5) was nearly double that of ILI cases (4.0 ± 1.9). The length of stay in 2014 had the shortest time (3.7 ± 1.7). Significantly, in 2015, the longest stay in the LCI group was 11.67 ± 4.63 in 6 cases and 7.40 ± 1.14 in 5 cases. For the influenza with PCR (-) laboratory test, the proportion of elderly and CD patients was equal to each other at 5% and the percentage of DM patients was 2%. For the ILI cases, there were only figures of 1.1% for elderly patients and 0.3% for CD patient.

3.2. Treatment cost of influenza

Table 3 shows the results of the total cost of influenza/ILI per episode during the period of time from 2013 to 2015 at Hospital for Tropical Disease, Ho Chi Minh City based on four age groups. The total cost of ILI cases had the lowest value of (78.60 ± 117.50) USD. By contrast, PCR (+) case had the highest total cost of (697.69 ± 792.50) USD. Meanwhile, the total cost of PCR (-) was (298.98 ± 331.30) USD. Of total ILI cases, the children (0–14) and youth (14–25) age groups had approximate total costs of (76.47 ± 118.30) USD and (73.59 ± 87.50) USD, respectively.

The mean total cost of 25–64 and > 64 age group was more than 100 USD higher than that of other groups with (100.04 ± 128.70) USD and (128.50 ± 49.80) USD, respectively. The total cost of PCR positive cases was (697.69 ± 792.50) USD, which was much greater than that of PCR negative [(298.98 ± 331.30) USD].

As to age groups, both PCR (+) and PCR (-) had the highest cost in adult patients (25–64 years) with the values of (1 020.36 ± 1 037.80) USD and (321.21 ± 361.00) USD, respectively. In PCR (+), the average cost was higher in the cost of drug [(264.80 ± 362.80) USD] and was considerably lower in the cost of X-ray/imaging [(46.51 ± 48.60) USD]. Moreover, there were no significant differences among the cost of hospital bed [(97.63 ± 57.90) USD], cost of laboratory test [(85.89 ± 47.04) USD] and the cost of consumed material [(71.12 ± 72.20) USD].

Table 3

Average cost of influenza/ILI patients between 2013 and 2015 (USD in 2015).

Group	Age	Cost of hospital bed		Cost of lab test		Cost of x-ray/imaging		Cost of operation		Cost of drug		Cost of consumable material		Total cost of episode
		Cost	%	Cost	%	Cost	%	Cost	%	Cost	%	Cost	%	Cost
ILI	0-14	55.82 ± 108.9	73.0	1.30 ± 3.00	1.7	1.37 ± 2.80	1.8	6.74 ± 31.0	8.8	2.35 ± 4.40	3.1	8.90 ± 12.40	11.6	76.47 ± 118.30
	15-24	36.06 ± 91.70	49.0	5.01 ± 6.80	6.8	11.46 ± 7.70	15.6	1.33 ± 4.90	1.8	3.20 ± 2.40	4.3	4.33 ± 6.50	22.5	73.59 ± 87.58
	25-64	58.56 ± 109.50	58.5	5.76 ± 7.40	5.8	17.30 ± 11.90	17.3	0.57 ± 3.80	0.6	9.72 ± 17.90	9.7	8.13 ± 16.10	8.1	100.04 ± 128.70
	> 64	56.87 ± 35.40	44.3	10.17 ± 9.60	7.9	40.25 ± 19.00	31.3	-	-	18.32 ± 25.10	14.3	2.89 ± 5.10	2.2	128.50 ± 49.80
	Total cost	55.86 ± 107.50	71.1	1.82 ± 4.10	2.3	3.24 ± 7.50	4.1	5.99 ± 29.10	7.6	3.06 ± 7.24	3.9	8.63 ± 12.50	11.0	78.60 ± 117.50
PCR (+)	0-14	85.30 ± 28.80	29.7	71.28 ± 15.20	24.8	14.97 ± 4.80	5.2	52.65 ± 76.50	18.3	33.19 ± 17.90	11.5	30.00 ± 37.20	10.4	287.40 ± 96.90
	15-24	102.35 ± 81.40	17.6	66.81 ± 4.30	11.5	23.86 ± 31.80	4.1	26.75 ± 46.30	4.6	266.90 ± 377.20	45.8	96.30 ± 22.50	16.5	582.97 ± 452.50
	25-64	96.50 ± 67.20	9.5	98.83 ± 63.70	9.7	63.91 ± 47.30	6.3	227.12 ± 531.20	22.3	439.44 ± 431.70	43.1	94.58 ± 90.10	9.3	1 020.36 ± 1 037.80
	> 64	153.34 ± 73.70	24.8	96.18 ± 37.30	15.5	109.30 ± 100.70	17.7	25.20 ± 35.60	4.1	168.68 ± 73.70	27.3	65.93 ± 42.70	10.7	618.65 ± 11.30
	Total cost	97.63 ± 57.90	14.0	85.89 ± 47.00	12.3	46.51 ± 48.60	6.7	131.74 ± 375.60	18.9	264.80 ± 362.80	38.0	71.12 ± 72.20	10.2	697.69 ± 792.50
PCR (-)	0-14	71.26 ± 53.57	39.0	61.35 ± 1.10	33.6	9.56 ± 6.90	5.2	-	0.0	19.64 ± 7.60	10.8	20.82 ± 37.10	11.4	182.63 ± 46.90
	15-24	-	-	-	-	-	-	-	-	-	-	-	-	-
	25-64	66.49 ± 71.90	20.7	65.50 ± 7.40	20.4	16.36 ± 10.20	5.1	79.31 ± 351.20	24.7	51.26 ± 50.30	16.0	42.29 ± 20.60	13.2	321.21 ± 361.00
	> 64	53.79	23.3	68.88	29.9	31.05	13.5	25.20	10.9	45.85	19.9	5.91	2.6	230.68
	Total cost	66.71 ± 67.60	22.3	65.05 ± 6.90	21.8	15.93 ± 10.30	5.3	66.50 ± 319.60	22.2	46.72 ± 47.00	15.6	38.07 ± 24.30	12.7	298.98 ± 331.30
Total	0-14	56.40 ± 107.80	70.0	2.85 ± 10.70	3.5	1.65 ± 3.40	2.0	7.43 ± 32.50	9.2	2.97 ± 6.40	3.7	9.32 ± 13.60	11.6	80.62 ± 120.80
	15-24	57.23 ± 90.70	45.3	10.40 ± 20.50	8.2	10.30 ± 12.10	8.2	3.64 ± 15.40	2.9	30.01 ± 129.90	23.8	14.70 ± 29.50	11.6	126.28 ± 215.40
	25-64	67.00 ± 93.70	21.4	38.40 ± 45.30	12.3	24.50 ± 27.20	7.8	60.26 ± 290.50	19.2	91.00 ± 229.50	29.0	32.12 ± 49.60	10.3	313.28 ± 560.50
	> 64	75.86 ± 55.70	32.0	33.24 ± 40.60	14.0	53.14 ± 47.40	22.4	7.56 ± 17.00	3.2	51.15 ± 67.50	21.6	15.80 ± 30.30	6.7	236.75 ± 207.80
	Total cost	57.98 ± 104.90	51.5	7.86 ± 22.70	7.0	5.50 ± 14.90	4.9	13.56 ± 105.40	12.0	15.32 ± 88.50	13.6	12.36 ± 23.30	11.0	112.58 ± 239.60

In contrast, the total cost of PCR (-) (298.98 ± 331.3) was four-times fewer than PCR due to the cost of hospital bed [(66.71 ± 67.60) USD], the cost of operation [(66.50 ± 319.60) USD] and the cost of X-ray/imaging [(15.93 ± 10.30) USD]. Especially, there was no record of adult patients (25–64 years) but only elderly patients (≥ 64 years) with the highest cost of lab test being 68.88 USD. On the other hand, the total cost of hospital bed represented the largest proportion in three out of four surveyed categories, except PCR (+). Moreover, both of the PCR groups had their lowest statistics in the same category of cost of X-ray/imaging with their values being (46.51 ± 48.60) USD and (15.93±10.30) USD respectively. Meanwhile, the smallest figures of ILI belonged to the cost of lab test with (1.82 ± 4.10) USD.

The total average cost was (112.58 ± 239.60) USD per case of which the adult age group contributed the highest proportion with (313.28 ± 560.50) USD. Meanwhile, the lowest cost of (80.62 ± 120.85) USD belonged to the children age group. Moreover, it is recognizable that the cost of hospital bed contributed the greatest proportion of 57.98 ± 104.90 to the total cost of ILI cases with the value being (57.98 ± 104.90) USD.

As it is shown in Table 3, the total cost of ILI in Vietnam was constituted from 6 components including cost of hospital bed (71.1%), cost of pharmaceuticals (3.9%), cost of operation (7.6%), cost of laboratory test (2.3%), cost of X-ray/imaging (4.1%) and cost of consumable material (11.0%). As regards components of hospitalization costs of 680 cases between 2013 and 2015, the percentage of cost of hospital bed (51.5%), cost of pharmaceuticals (13.6%), cost of operation (12.0%) was recorded, whereas cost of laboratory test, cost of X-ray/imaging, and cost of consumable material accounted for 7.0%, 4.9%,11.0%, respectively.

Sensitivity analysis for influenza treatment to change the percentage of total cost (Figure 2) in LCI group confirmed that the cost of illness (COI) for influenza related to hospitalization fell dramatically to 8% of the average cost considering the fact that cost of hospital bed decreased by 50%. On the other hand, the figure was likely to decrease greatly to 7% if cost of PCR-test in laboratory test decreased by 50%. This result may probably be the consequence caused by the percentage of cost of PCR-test in laboratory test cost was 86%, considering reduction in the cost of PCR-test in order to improve outcomes and total treatment cost. The reduction in cost of antiviral oseltamivir 75 mg, was almost insignificant in determining the cost of influenza treatment.

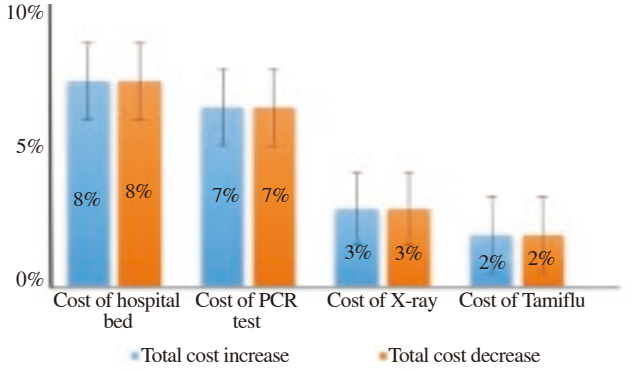

Figure 2. Sensitivity analysis exploring effect of variables on the direct medical cost.

4. Discussion

This study presents a better perspective on the administration of ILI cases and its economic impact on patient of all ages in Vietnam. Overall, the initial discovery of this study was the proportion of LCI cases among all ILI symptoms which was 8% (56/680) lower than the range from 14% to 23% when compared to other studies in other Asian countries, which have reported proportions of LCI over ILI cases[19,20]. Length of stay of hospitalization period of LCI test was seven days, which approximated to that of other Asian countries such as Cambodia (7 days)[14], Thailand (5 days)[21], Indonesia (6 days)[22], and China (6 days)[15]. The mean hospitalization days of this study was four days, which was correlative to ILI cases, and more than twice as long for LCI cases and high-risk cases (eight days).

Most of LCI cases in Vietnam (95%) received antiviral treatment with oseltamivir 75 mg in 7 days, compared to those studies in Indonesia (69%; 9 days), Thailand (57%–71%; 9 days), and

Cambodia (28%; 7 days). Turning to cases which were treated with the antiviral, the treatment time appeared to be longer than that for the Vietnam group on a scale of medium nine days versus seven days except for the Cambodia group which shared the similarity with Vietnam[21,22]. Comparing the medium hospitalization period among inpatients with antiviral treatment, it was clear that children and clearly group had the longest length of hospital stay (7 days) in all of the LCI cases due to the disability of using oral solution and parenteral oseltamivir as it was difficult to adjust doses of these medicine. Thus, the imparity is in hospitalization period among LCI cases. The study found that 68% of LCI cases (38 in total of 56 cases) were prescribed antibiotics, which may cause antibiotic resistance and worsen influenza complications if used excessively. Nevertheless, only two of 56 LCI cases were found treated with corticosteroids, which was recommended by WHO[23].

This is the first study about direct medical cost of influenza inpatients in Vietnam. It was found out that the mean cost of influenza inpatient cases with the medium 4 days of treatment was (112.58 ± 239.61) USD per cases, which was not as great as its corresponding cost in Cambodia (299.69 USD per patient in 2011) [14], and China (1 797 USD per episode in 2012)[15]. Such contrast is likely to result from the different levels of medical care system, economic development and medical health system. Between 2005 and 2011, the report in Cambodia showed that cost of influenza was 299.96 USD per case (334.08 USD in 2015)[14]. Otherwise, in Thailand Lee *et al.* estimated the cost of influenza was 1024.06 USD in 2004 per case (1367.08 USD in 2016)[20]. Also finding in Singapore was 437.05 USD for per influenza case in 2009 (397.32 USD in 2015)[24].

In comparison to cost per day, that of LCI case (70 USD) was much higher than the cost of ILI case (20 USD). This gives out a hint that the direct medical costs of LCI case might possibly be a more significant reason that leads to financial burden to patients and their families than that of ILI case. In this study, the average direct medical cost of influenza for children was 80.62 USD, which was not as great in value as the corresponding cost in China (624 USD, data from 2005 to 2009)[15] and the United States (3 366–19 444 USD) [25-28]. Nevertheless, it should be considered that surveyed children in different studies did not share the same state of health and many of them were likely to require more intensive medical treatment than the others. While compared to LCI cases, the study found differences between using of antiviral and not using antiviral in influenza treatment. For antiviral and not using antiviral cases, their average length of stay was 8.92 days and 2.33 days respectively. Furthermore, direct medical cost for treatment was 564.51 USD and 120.78 USD respectively. The costs of major components in antiviral group were the cost of pharmaceuticals (27%) and cost of operation (25%). Meanwhile, the costs of diagnosis (51%) were the major component in not using antiviral group.

In comparison with the average cost per day among the high risk factor group, any CD group was similar to diabetes-cardiovascular patient and elderly patient groups with 42.14 USD, 41.15 USD, and 48.52 USD respectively. Nevertheless, only one case was reported with treatment of pneumonia with the enormously average cost with 280.01 USD per day, which is much higher than any individual case in this study. Although cases might not be the representative for the whole population, this case suggests that pneumonia treatment was the highest risk which had effect on treatment cost. As regards components of hospitalization costs of ILI, the given features are far from similarity to results achieved from findings in China and Cambodia, in which the greater percentage of the total medical costs was diagnosis test (23% and 41.2% respectively). However, the majority component of the direct medical cost was in agreement with study in the US, where the greatest component of hospitalization cost is from the cost hospital bed (64%)[29]. In LCI cases, the main component of direct medical cost was due to cost of pharmaceuticals (31%).

The main concentration of this study was inpatients diagnosed with influenza among ILI and LCI cases. The study is now the foundation for future research of direct non-medical cost and indirect costs including loss of productivity and transportation. In order to thoroughly estimate the annual social, economic burden and impact attributed to influenza infections in Vietnam, further studies about the cost of influenza-related outpatient treatment are required. The limitation of this part is not to cover all three areas in Vietnam so the results may not a representative of the national situation of influenza.

Some limitations of this study should be noted. Firstly, physicians would be identified correctness and completeness of ICD code classification in practice; for instance, the number of cases with risk factor may be underestimated when compared with Ehlken *et al.* study[16] and correctness and completeness of a number of services utilized. The unit cost applied is not from HTD but from the reference list. The cost does not reflect the HTD but would be applied for modeling economic evaluation of the country. Finally, the results are from only one tertiary hospital at Ho Chi Minh City in Southern Vietnam, which may not be representative of the entire Vietnam. Patients who visit tertiary hospitals are usually more severely ill than those who visit other pharmacies, outpatient clinics or outpatient departments of hospital.

Direct medical cost of hospitalization in Vietnam indicates that patients and their family may have to suffer from a hefty economic burden, which is likely to increase if the patient's health requires special medical treatment. Consequently, it is important that further researches are conducted in an attempt to yield more comprehensive evidences on social and economic burden. This study emphasizes the demand to enhance the aimed strategies of development in order to cut down the economic burden, and to evaluate health economic model in Vietnam.

Conflict of interest statement

We declare that we have no conflict of interest.

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