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Review Article

# A LITERATURE REVIEW ON INFLUENZA TREATMENT COSTING STUDIES

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**ABSTRACT**

Many researches were conducted about the burden created by influenza from an economic point of view, but they haven't yet to be specifically systematically reviewed. Our aim was to review the literature on economic burden studies of influenza focusing on direct cost (treatment cost) and indirect cost (related to school or workplace absenteeism). We conducted a systematic literature search mainly on three databases (PubMed, Science Direct and Cochrane database) on the economic burden of influenza till the end of November 2015. the publications have been carefully selected to shed light on direct and indirect costs of influenza, influenza-like-illness and pandemic influenza. There were 48 studies in 15 countries across five continents that can satisfy such criteria and those were used for in-depth statistic in our systematic review. The number of articles, which is conducted in America or using US dollar, were 19 and 37 out of 48, respectively. It can be noticed that most of the studies (27 researches , an equivalent to 56.3 percentages) discussed both direct and indirect cost whereas direct cost and indirect cost studies were 15 (29.2%) and 2 (4.2 %). There were differences between results (in direct and indirect cost) of studies due to dissimilarity in researched country, targeted population or reported year. This review will help us to have an overview on influenza economic burden. Otherwise, it also provides necessary statistic about current status in cost of influenza studies over the world. From that, investigator who want to research on this field, can follow the previous studies for building their own working.

**Keywords:** literature review, cost, treatment, influenza, economic analysis.

## INTRODUCTION

Influenza is a seasonal infectious disease caused by a virus that attacks mainly the upper respiratory tract – the nose, throat, bronchi and the lungs. It is characterized by sudden onset of high fever, myalgia, headache, severe malaise, non-productive cough, sore throat and rhinitis. Influenza epidemics can seriously affect all populations, but the highest risk of complications occur among children younger than age two years, adults aged 65 years or older, pregnant women and people of any age with certain medical conditions such as chronic heart, lung, kidney, liver, blood, metabolic diseases (such as diabetes) or weakened immune systems. Influenza viruses evolve continuously, which means that people can get infected multiple times throughout their lives [1, 2].

Influenza is an acute viral infection that spreads easily from person to person. At present, The World Health Organization (WHO) estimate that each year approximately 5 to 10% in adults and 20 to 30% in children will be infected, the annual epidemics are thought to result in about 3-5 million cases of severe illness and about 250 000 - 500 000 deaths every year around the world [1].

Influenza spreads rapidly around the world and creates a considerable macroeconomic impact include healthcare and social burden. Influenza causes not only substantial morbidity and mortality but also high economic burden in worldwide. In Europe, Italy reported cost of seasonal influenza epidemics in the period between 1999 and 2008 ranged from 15 to 20 billion Euros; the yearly average was 1.4 billion Euros[3]. The economic burden of influenza B during 2010 to 2011 for the French Health Insurance was estimated to be 145 million Euros, and the mean cost associated with influenza B was 72 Euros per patient[4]. 16.8 billion British Pound (1% of gross domestic product of 2004 –United Kingdom economy) were lost due to influenza-related expenses.

In Asia, where average gross domestic product was lower than Europe, influenza also cause a massive social burden. For instance, the annual socioeconomic costs of the 2009 pandemic H1N1 influenza were estimated at 1.09 billion US dollars (USD) (0.14% of the national GDP) in Korea[5]. Moreover, burden of influenza in Thailand was estimated to cause about 23.4 to 62.9 million USD in economic loss with lost productivity accounting for 56% of all costs between September 2003 and August 2004 [6]. During the period of time from 2009 to 2011, Zhou et al. reported that 1,797 USD has spent for direct medical cost of influenza-related hospitalizations in three provinces in China[7]. These medical and social cost imposes a huge burden not only on patient and their family but also on whole nation.

At present, researchers have started to study more about the economic aspects of influenza burden, and in order to evaluate this issue they have used many methods such as cost of illness (COI) analysis, assessing the monetary economic burden on region (cities, provinces, nations, areas…), using mathematical modelling to predict assumed pandemic scenarios. The macroeconomic burden of influenza, which is statistic in many country, are varied

which can range from millions to billions USD[3, 7]. For instance, United States of America (USA), which is the most developed country, spent 26.8 to 87.1 billion USD in 2003 for influenza-related cases treatment and their social burden[8]. That is a huge burden when compared with many developing countries all over the world. Although influenza burden has been researched in many countries, the overall view about cost of illness related to influenza has not been performed. The aim of this study is to review the literature on economic burden studies of influenza. This review focuses on treatment cost of influenza including direct costs, such as costs for consultation, medications, hospitalization, laboratory tests and indirect costs related to school or workplace absenteeism.

## MATERIALS AND METHODS

### Search strategy

We conducted a systematic review of articles on the economic burden of influenza till the end of November 2015 by using PubMed, Science Direct, Cochrane and other database (related to references in studies). The keywords were used: (influenza* OR flu OR grippe* OR pandemic*) AND (economic* OR cost* OR socioeconomic* OR socio-economic* OR expenditure* OR burden* OR fee* OR charge* OR budget impact*). To minimize publication bias, we only use articles related with human subjects, had the keywords in title or abstract and wrote in English. We followed PRISMA guidelines for this systematic review[9].

### Inclusion and exclusion criteria

Firstly, publications related to pharmacoeconomic were selected if the outcomes included seasonal influenza infection, influenza like illnesses and pandemic influenza, and it explored direct costs (medical and non - medical) and indirect costs of influenza clearly. The studies that did not discuss influenza - related diseases, that either focused on epidemiological and clinical aspects or did not mention costs of influenza, were not selected.

### Selection of eligible articles and data abstraction

Two reviewers independently screened titles and abstracts and selected all potentially eligible studies. Complete versions of these articles were independently assessed according to inclusion and exclusion criteria described above. Disagreements were solved by consensus in both phases.

## RESULTS AND DISCUSSION

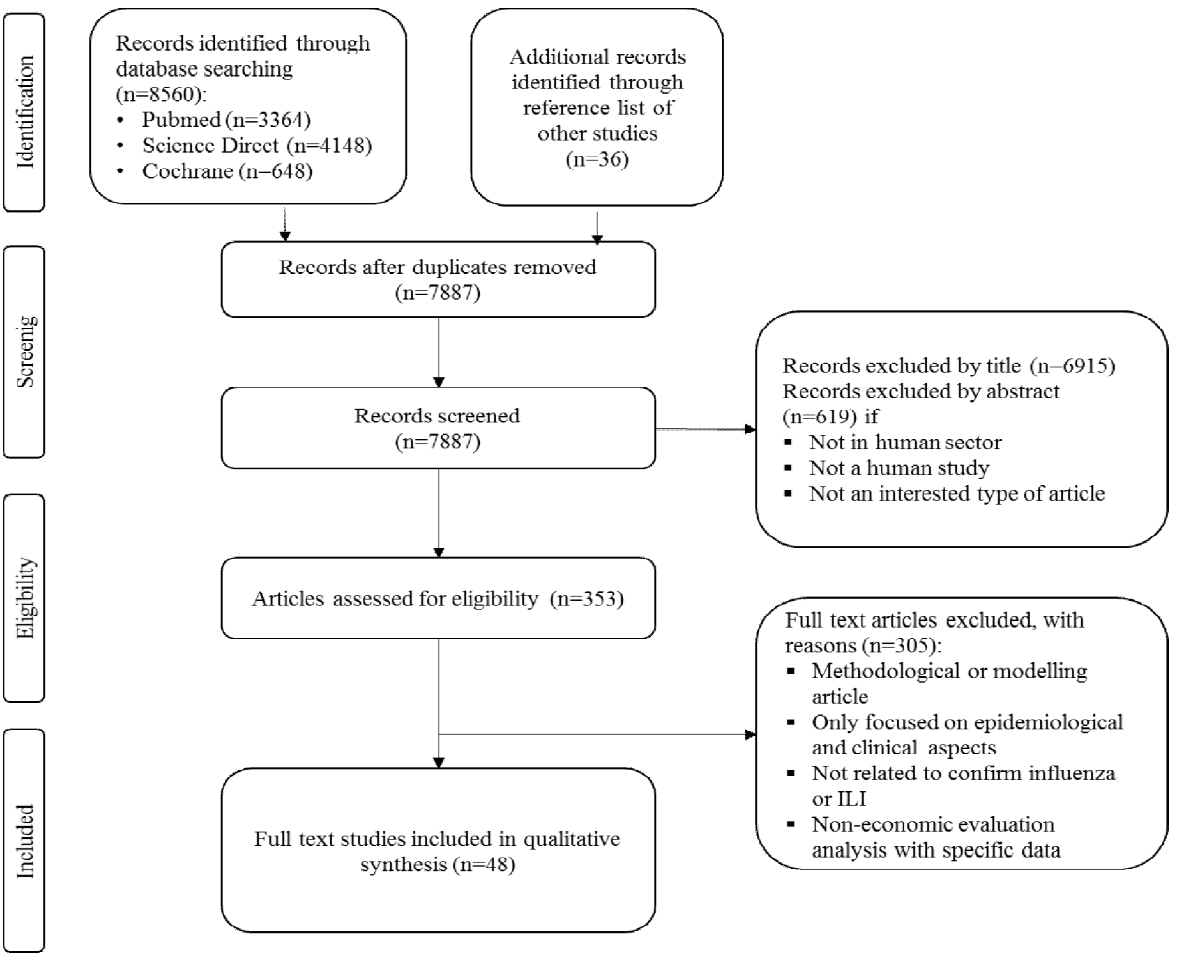


**Figure 1: PRISMA flow diagram of literature review**

As can be seen from the Figure 1; 7,887 citations were identified from both original database and other sources after removing duplicates. To measure the eligibility of these studies, checking in title and abstract are needed resulting in 6,915, 619 records excluded by title and abstract, respectively. Of 353 remaining suitable articles, full-text the whole content was checked. In the end, there were 48 full-text studies that can satisfy the criteria and those were used for in-depth statistic in this systematic review.

**General characteristics of included studies**

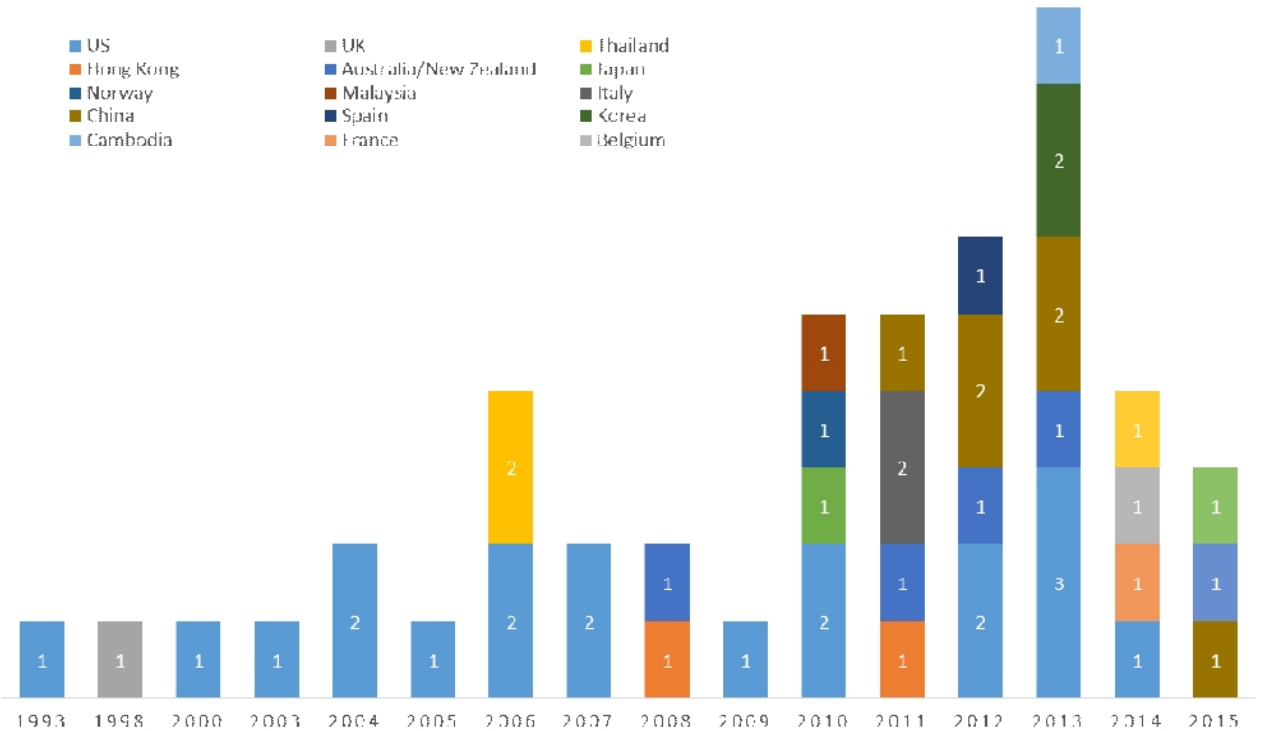


**Figure 2: Included studies by country and publication year**

A quick overview of all reviewed publications (Figure 1), we identified with only one article in the year of 1993, 1998, 2000, 2003, 2005 and 2008, two in the year of 2004, 2007 and 2008, three in the year of 2015, four in the year of 2006 and 2014, five in the year of 2010 and 2011, six in the year of 2012 and nine - the largest number of publications in 2013. Only 48 studies with various methodology and the subject of evaluation during 22 years, the average of number publications per year was 2.18 (range 0-9). The number of studies increased slightly through years and peak in the year of 2013 (with 9 studies) before decreasing to three studies in 2015. There can be seen that the studies was conducted in many country spreading from the Eastern to the Western. Of that, USA have the highest number of studies with 19 out of 48 total studies.

**Table 1: The characteristic of economic evaluation on influenza studies (n=48)**

| Characteristics of Included Studies | N | % | | Characteristics of Included Studies | N | % |
|---|---|---|---|---|---|---|
| **Currency of reported results** | | | | **Type of data used** | | |
| Euro | 6 | 12.5 | | Primary data | 23 | 47.9 |
| US Dollar | 37 | 77.1 | | Secondary data | 18 | 37.5 |
| Other | 5 | 10.4 | | N/a | 7 | 14.6 |
| **Study design** | | | | **Type of cost included** | | |
| Retrospective | 15 | 31.3 | | Direct medical costs | 15 | 29.2 |
| Prospective | 11 | 22.9 | | Indirect costs | 2 | 4.2 |
| Both | 3 | 6.3 | | Mix | 27 | 56.3 |
| N/a | 19 | 39.6 | | N/a | 4 | 8.3 |
| **Target population** | | | | **Type of perspective** | | |
| Adults | 2 | 4.3 | | Healthcare system | 3 | 6.3 |
| Children | 12 | 25.0 | | Patient | 9 | 18.8 |
| Elderly | 5 | 10.4 | | Societal | 5 | 10.4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Worker | 3 | 6.3 | | Payer (Ex: health insurance…) | 2 | 4.2 |
| Other | 2 | 4.2 | | Provider (Ex: hospital…) | 9 | 18.8 |
| All | 11 | 22.9 | | Mix | 5 | 10.4 |
| N/a | 13 | 27.1 | | N/a | 15 | 31.3 |
| **Disease outcomes /syndromes considered** | | | | **Type of sensitivity analysis** | | |
| ILI | 16 | 33.3 | | One-way analysis | 13 | 27.1 |
| SARI | 3 | 6.3 | | Multi-way analysis | 4 | 8.3 |
| ICD-9 | 12 | 25.0 | | Univariate/multivariate regression | 8 | 16.7 |
| ICD-10 | 1 | 2.1 | | Probabilistic analysis | 2 | 4.2 |
| Mixed | 3 | 6.3 | | Mix | 2 | 4.2 |
| N/a | 13 | 27.1 | | N/a | 19 | 39.6 |
| **Health resources utilization data sources** | | | | **Methodological approach** | | |
| Hospital discharge database | 9 | 18.8 | | Prevalence-based approach | 10 | 20.8 |
| Others (direct cost) | 7 | 14.6 | | Incidence-based approach | 3 | 6.3 |
| Indirect cost: Interview | 1 | 2.1 | | N/a | 35 | 72.9 |
| Others (indirect cost) | 1 | 2.1 | | **Discount rate** | | |
| Mix | 26 | 54.2 | | ……. (%) | 6 | 12.5 |
| N/a | 4 | 8.3 | | N/a | 42 | 87.5 |

Notes: N/a = Not available; ILI = Influenza-like illnesses; SARI = severe acute respiratory infections; ICD-9 = International classification of disease, 9th revision; ICD 10 = International classification of disease, 10th revision

As can be seen from Table 1, from a total of 48 articles were surveyed, the methodology commonly used were retrospective (n = 15: 31.3%) and prospective (n = 11: 22.9%), a few articles were combined two methods above (n = 3: 6.3%). Besides, there are some articles without available research method (n = 19: 39.6%). The number of articles using USD as currency were the most common type with 37 studies, and only a few articles using the Euro (n = 6: 12.5%) or other currency (n = 5: 10.4%). The majority of articles were conducted on patients who had ILI (n = 16: 33.3%) and ICD-9 (n = 12: 25.0%). Besides, there are some other symptoms related influenza were surveyed like SARI (n=3: 6.3%), ICD-10 (n=1: 2.1%), mixed (n=3: 6.3%) and not available outcome (n=13: 27.1%). When researching the cost of influenza, children was the most common targeted population, with 25 percentages.

Table 1 revealed that nearly half of surveyed articles using primary data (n=23: 47.9%) while the majority of remaining using secondary data (n=18: 37.5%) and a few articles were not clearly stated (n=7: 14.6%). From health resources utilization data sources, mix data sources accounting for more than half of the total number of articles (n=26: 54.2%). Meanwhile, the hospital discharge database was 18.8 percent (n = 9) and interview was only 2.1 percent (n = 1). Almost of 48 articles referred to both direct cost and indirect cost (n = 27). Besides, the articles referred to only direct cost were 15 (29.2%) and 2 articles mentioned indirect cost only. The assessment of costs was based on multiple perspective, including the viewpoint of healthcare system, payer, provider, society, patient, mix and not available. The proportion of those perspectives were 6.3 percent, 18.8 percent, 10.4 percent, 4.2 percent, 18.8 percent, 10.4 percent and 31.3 percent, respectively. Among the methodological approach, there are two method consisted of prevalence-based approach (n=10: 20.8%) and the incidence-based approach (n=3: 6.3%). In the other hand, the articles with unclear methodological approach accounting for superior percentage (72.9%), with n = 35. Only 6 articles (12.5%) had discount rate. Of the total 48 articles surveyed, many types of sensitivity analysis were used, including one-way analysis (n=13: 27.2%), multi-way analysis (n=4: 8.3%), univariate / multivariate regression (n=8: 16.7%), probabilistic analysis (n=2: 4.2%), mixed (n=2: 4.2%) and not available (n=19: 39.6%).

**Cost of influenza**

We divided 48 articles into four types of cost for further examination, which is divided into two tables. It is separated to include studies which is focusing only direct cost (n=14); only indirect cost (n=2); both direct and indirect cost (n=27); or not available (not clearly stated whether direct or indirect cost but mention about economic burden of influenza; n=4).

**Table 2: Articles evaluated in this review (direct cost, indirect cost, not available)**

| No. | Reference | Country | Currency | Year cost value | Aged | Direct cost | Direct-medical cost | Indirect cost | LOS | Cost per episode |
|---|---|---|---|---|---|---|---|---|---|---|
| **Direct cost** | | | | | | | | | | |
| 1 | Mei Poh Ong et al., 2010 [34] | Malaysia | USD | 2009 | N/a | 94,357; 510* | | | 4.6 | |
| 2 | Diana J Jeffery et al., 2013[14] | US | USD | 2009 | All | 156,7 million | | | | |
| 3 | Bruce Stuart et al., 2010[35] | US | USD | 2005 | Elderly | 1956* | | | | |
| 4 | A. T.Newall et al, 2008 [16] | Australia | USD | 2005 | All | 115 million | | | | |
| 5 | A.H.Higgins et al, 2011 [17] | Australia | AUD | 2009 | N/a | 85,395 | | | | |
| 6 | Joke Bilcke et al., 2014, [21] | Belgium | USD | 2012 | All | | 51-53* | | 4 | |
| 7 | Tao Zhang et al., 2012, [20] | China | USD | 2009 | Children | | 624* | | 7 | |
| 8 | Gerry Fairbrother et al., 2010[13] | US | USD | 2006 | Children | | 5,402* | | | |
| 9 | Ron Keren, et al., 2006, [12] | US | USD | 2004 | Children | | 13,159* | | 2 | |
| 10 | Fred M.Cox et al., 2000, [11] | US | USD | 1998 | Unknown | | | | 4.3 | 3251.04 |
| 11 | Jichui Kevin Yin et al.,2013 [18] | Australia | AUD | 2010 | Children | | | | 9 | 626 (484-768) |
| 12 | Sudeep Karre et al., 2013, [15] | US | USD | 2009 | Other | | | | 0.38 | 2608 |
| 13 | A.M. McBean et al., 2004, [10] | US | USD | 1996 | Elderly | | | | | 7009 |
| 14 | Kenji Kawakami et al., 2010 [19] | Japan | USD | 2007 | Elderly | | | | | 310 |
| **Indirect cost** | | | | | | | | | | |
| 1 | M. Akazawa et al., 2003 [22] | US | USD | 1996 | Worker | | | 137 USD | 1 | |
| 2 | Kenneth Lee et al., 2008, [23] | Hong Kong | HKD | 2008 | Worker | | | | | 833 |
| **Not available** | | | | | | | | | | |
| 1 | A. M. McBeen et al., 1993 [26] | US | USD | 1991 | Elderly | | | | | 1989-1990: >1billion<br>1990-1991: 750 million |
| 2 | Jason Matheny et al., 2007 [27] | US | USD | 2005 | N/a | | | | | Net LOSs: 3.9 billion;<br>784,592 per hospital) |
| 3 | R.N.Guo et al., 2011 [36] | China | USD | 2007 | All | | | | | Urban: 40,12<br>Rural: 15.65 |
| 4 | Piero Luigi Lai et al., 2011, [3] | Italy | Euro | 2010 | Unknown | | | | | 1999-2008:15-20 billion.<br>H1N1 pandemic: 1.3-2.3 billion |
| 5 | Wilson,N et al., 2012, [25] | New Zealand | NZD | 2009 | Other | | | | 12.41± 14.8 | 7.1*<br>30,5million |

*: cost per case; USD = United States Dollar; AUD = Australia Dollar; HKD = Hong Kong Dollar; NZD = New Zealand Dollar; N/a: Not available

**Direct cost**

From 14 articles referred to direct cost only, seven reported results in USA. For example, in 1996, total cost per episode in this country was 7009 USD[10] and this number in 1998 was 3251.04 USD with 4.3 days for the length of stay[11]. In 2006, according to Ron Keren et al., direct-medical cost in USA was 13,159 USD per case[12] and this figure in 2010 according to Gerry Fairbrother et al. was 5,402 USD[13]. In 2013, two surveyed studies concerned to direct cost were published in USA and used the same currency (2009 USD). The first study by Diana J Jeffery et al. referred that the direct cost in the US of the total population was 156.7 million USD[14]. And the second study by Sudeep et al. estimated that the total direct cost per episode was 2608 USD[15]. As can be seen from Table 2, there are three articles reported direct cost in Australia. In 2008, there was study indicated that the direct cost caused by influenza per year was 115 million USD[16]. Others articles published in 2011 indicated that the direct cost of influenza was 85,395 Australian dollar (AUD)[17]. According to Jichui Kevin Yin et al. total cost per influenza episode was 626 (484-768) AUD with 9 days for the length of stay[18]. In addition, direct cost of some other Asian countries had also been reported. For example in Japan, the total cost per episode was 310 USD[19] and in China, Tao Zhang et al. estimated that the direct-medical cost was 624 USD per case[20]. And from all of articles reported direct cost only, the newest research is in Belgium. Direct-medical cost is estimated 51-53 Euros per episode[21].

**Indirect cost**

Out of 48 studies**,** there are two studies researching only in indirect cost of influenza. It can be seen that, those studies were conducted in workers who has lost productivity due to working day lost. It resulted in 137 USD lost in USA in 1996[22] and 833 Hong Kong dollar (HKD) lost per influenza case in Hong Kong in 2008[23].

**Not available**

Multiple studies reported direct cost, indirect cost or mix of two cost, but only five reported results without information about direct cost or indirect cost. In China, R. N. Guo et al. reported that the total cost per episode in urban was 40.12 USD while this figure in rural was 15.65 USD (2009 USD)[24]. Meanwhile, at the same time, Wilson. N et al. estimated the total cost per case in New Zealand was 7.1 New Zealand Dollar (NZD), and the cost per year in this country was 30.5 million NZD, with length of stay was 12.41±14.8 days[25], highest among 48 surveyed articles. In the study of A. Marshall McBeen et al. the total cost of influenza in USA was estimated at over one billion USD (1989-1990) and 750 million USD (1990-1991)[26]. According to Jason Matheny et al. the cost of influenza in 2005 rose up to net loss 3.9 Billion USD[27]. The last study, which is conducted in Italy, estimated that the total cost of influenza during the period 1999 to 2008 was 15-20 billion Euros (2010 Euro)[3]. Besides, H1N1 pandemic has caused an economic burden of influenza, estimated 1.3-2.3 Billion Euros[3]. Actually, this is not a small number.

**Direct and indirect cost**

Most of articles (27 out of 48) researched about both direct and indirect cost related to influenza. Each studies had different results because of various in conducted country, currency and targeted population. Mejbah U.Bhuiyan et al.[28] estimated in Bangladesh, direct cost, indirect cost of influenza were 109.4 and 59.4 million USD, respectively while Liang Mao et al. did the same research in USA indicated that direct and indirect cost of flu were 10.2 billion USD and 18.9 billion USD, respectively (2010 USD)[29]. There are the difference in country's level of economic development that can be results in unequal results between two studies. Derek Weycker et al. doing the research in 2004 among children who had influenza estimated that direct and indirect cost was 2.2 and 8.8 billion USD (2000 USD)[30]. Using the CPI of 2000 and 2010[31], we can calculated the direct and indirect cost of Derek's study in 2010 were 2.8 and 11.1 billion USD, respectively. When compare with Liang Mao's study, there was lower due to the difference in targeted population. In Korea, there are two studies working on the same year, using the same 2010 USD resulting in nearly equal direct and indirect cost[32, 33].

**Table 3: Articles evaluated in this review on both direct cost and indirect cost**

| No. | Reference. Author-year | Country | Currency | Year cost value | Aged | Direct cost | Direct-medical cost | Direct non-medical cost | Indirect cost | LOS | TOTAL Cost per episode |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M. U.Bhuiyan et al., 2014 [28] | Bangladesh | USD | 2010 | All | 109.4 million | | | 59.4 million | | Outpatient: 4.8 Inpatient: 82.2 |
| 2 | Yting Xue et al., 2010 [37] | Norway | USD | 2005 | All | 22 million | | | 793000 Days (231 million) | | |
| 3 | Derek Weycker et al., 2004 [30] | US | USD | 2000 | Children | 2.2 billion | | | 8,8 billion | | 351.4 |
| 4 | Liang Mao et al., 2012 [29] | US | USD | 2010 | All | 10,2 billion | | | 18,9 billion | | |
| 5 | Fauziya Hassan et al., 2009 [38] | US | USD | 2003 | Children | 76,5 million | 2785-7774* | | | 2.8 | |
| 6 | Krow Ampofo, et al., 2006 [39] | US | USD | 2001 | Children | 8414* | 2 million | | | 3.83 | |
| 7 | James. M. Simmerman et al., 2006 [6] | Thailand | USD | 2004 | All | 23.4- 62.9 million | 3.8-6.4million | | 0.5-8.7million 11.1-24.9 million | 6.6 | |
| 8 | Birgit Ehlken et al., 2015 [40] | Germany | Euro | 2012 | All | Adults:90* Child:105 * | | | Adults: 424±566* Children: 1±62* | | Adults:514±609 Children:105±224 |
| 9 | Susan S. Chiu et al., 2011 [41] | Hong Kong | USD | 2006 | Children | 1217.82* | | | 1328.33* | | |
| 10 | K. Humphries-Waa et al., 2013[42] | Cambodia | USD | 2011 | All | 276,16* | 254,87* | 21,29* | 23,54* | | 299,69 |
| 11 | Ru-ning Guo et al., 2012 [24] | China | USD | 2009 | All | 26-34.9* | 17.4-25.5* | 6-34.9* | | 1-2 | |
| 12 | Lei Zhou et al., 2013 [7] | China | USD | 2010 | All | | 1797* | | | 6 | |
| 13 | Dan Wang et al., 2013 [43] | China | USD | 2012 | Children | | 63.1* | 88.2* | 38.7* | | Outpatient: 123,4 ED: 134,6 \ |
| 14 | Yang-Woo Kim et al., 2013 [32] | Korea | USD | 2009 | All | | 322.6 million | 105.4 million | 622.5 million | | |
| 15 | Mina Suh et al., 2013 [33] | Korea | USD | 2009 | All | | 337,07million | 73,51million annual | 899,32million | | Inpatient(625.8±800.81) Outpatient(16.6±56.32) |
| 16 | Maria L. Silva et al., 2014 [44] | France | Euro | 2011 | All | | 50.6 ±184.7* | | 21.2 ± 91.4* | | 71.8 ± 205.1* |
| 17 | M. Keech et al., 1998 [45] | UK | Pound | 1995 | Worker | | 1756* | | 116,464* | 2.8±2 | |
| 18 | M. Galante et al., 2012 [46] | Spain | Euro | 2009 | All | | Inpatient:4687,5* Outpatient:167,3* | | Inpatient:1383* Outpatient:582* | 5 | Inpatient: 6028 Outpatient:749.2 |
| 19 | Birgit Clague et al., 2006 [47] | Thailand | USD | 2003 | All | | 2.33* | 2.24* | 11.21* | | 15.78 |
| 20 | Ismael R.Ortega-Sanchez, Noelle-Angelique M.Molinari et al, 2012 [48] | US | USD | 2003 | Adults | | Inpatient:3990* ED: 730* | Inpatien:178 * Ed patient:125* Outpatient:52 * | Inpatient:1456* ED patient:383 * outpatient:222 * | | |
| 21 | M. E. Klepser et al 2014 [49] | US | USD | 2003 | Adults | | 10,4billion | | 76,7 billion | | 92-299 |
| 22 | Sudeep Karve et al., 2013 [50] | US | USD | 2009 | All | | 296* | | 279.5-226.3* | 1 | |
| 23 | N. A. Molinari et al. 2007 [8] | US | USD | 2009 | Children | | 10,4 billion | | 76,7 billion | | |
| 24 | S. Esposito et al., 2011 [51] | Italy | Euro | 2008 | Children | | | | | | 131.7±71.4 |
| 25 | Jennifer L. Hall et al., 2005 [52] | US | USD | 2002 | Children | | | | | 5.1 | 384.2 |
| 26 | Jian Chen et al., 2015 [53] | China | USD | 2009 | Elderly | | | | | 17 | 1651 |
| 27 | Pratyush Kumar et al., 2015 [54] | India | USD | 2015 | All | | | | | 6-10 | 3326 |

*: cost per case; USD = United States Dollar

## CONCLUSIONS

Although there are some gaps in existing data, we hope this review will helps to shed light on the current situation and the urgent need for development of national methodological guideline for conducting and reporting health cost of influenza. It also help researcher in understanding current report about influenza for their future research. Besides that, summaries of the data may provide important information for policy maker in building both preventing influenza policies for limiting the burden of influenza not only in direct healthcare cost but also in productivity lost.

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