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Cost of pneumonia in children: A systematic review

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Abstract

Childhood pneumonia is a leading cause of mortality worldwide. The estimates of the economic burden of these illnesses will be beneficial to the design of effective treatment, management of resources, and evaluation of the cost-effectiveness of health interventions. Nevertheless, a systematic review of the economic cost of treatment of pneumonia in children has not been performed. Thus, the objective of this study was to systematically review the cost of pneumonia in children.

A systematic literature search was conducted in PubMed, including journal articles reporting the cost of pneumonia in children from 2000 to 2015. Seventeen articles were selected for the review. Ten articles included only direct medical cost. One article included direct medical cost and direct non-medical cost. Six articles included all components, i.e., direct medical cost, direct non-medical cost and indirect cost. Costs were converted to 2015 US dollars. The results show a wide range of cost estimates due to study design, types of pneumonia, patient age, patient types (inpatient or outpatient), and the economic and healthcare systems in each country. Pneumonia has a substantial economic impact, and the lack of information on the cost of pneumonia in several countries highlights the need for further work in order to describe the global economic burden of pneumonia.

Keyword: cost of illness, children, pneumonia, systematic review, review

1. INTRODUCTION

Childhood pneumonia is a leading cause of mortality, resulting in 15% of deaths worldwide, with an estimated one million children dying before the age of five years in 2013[1]. In the year 2000, it represented more than 11% of all childhood deaths with 90% of deaths from pneumococcal pneumonia occurring in Africa[2]. The pathogen *Streptococcus pneumoniae* is the major cause of this disease. The estimated incidence in this age group is 0.29 episodes per child-year in developing and 0.05 episodes per child-year in developed countries, with about 151 million new episodes per year in the developing world[3]. For the general economic burden, the World Health Organization (WHO) estimated the cost of antibiotic treatment, including the antibiotics and diagnostics for pneumonia management for all children with pneumonia, at approximately US$109 million per year[4].

Pneumococcal vaccines were developed to control the serotypes most commonly related to severe pneumococcal diseases. There are three types of pneumococcal conjugate vaccines (PCV): PCV-7 valent, PCV-10 valent, and PCV-13 and 23-valent pneumococcal polysaccharide vaccine (PS23). The injection of pneumococcal vaccines can be used to prevent bacteremia, meningitis, and pneumonia caused by *S. pneumoniae*[5]. WHO has recommended the use of pneumococcal conjugate vaccines in all countries with high pneumonia and mortality rates for children less than five years old. However, PCVs are not included in the WHO Expanded Programme of Immunization (EPI)[6]. Economic information on the cost-effectiveness of the vaccines is essential to EPI policy decision making. To conduct a cost-effectiveness analysis, the cost of this illness is required. Therefore, we need to know the situation regarding the studies on the cost of the illness.

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Nevertheless, a systematic review on the economic cost of pneumonia in children has not yet been performed. Therefore, the objective of this study was to systematically review the cost of pneumonia in children.

2. METHOD

Study design

This study was conducted as a systematic review following the PRISMA guidelines[7] to explore the study methodology and the magnitude of the economic burden. The review focused on the cost of pneumonia among children aged up to 18 years old.

Search strategy

The PubMed database was searched for literature published in English from January 2000 to December 2015. The search strategy was based on a broad combined search string (economic* OR cost* OR "cost of illness"[Mesh]) AND (neonat* OR child* OR infant* OR "Infant" [Mesh] OR "Child"[Mesh] OR "Adolescent"[Mesh] OR "Pediatrics"[Mesh]) AND ("Pneumonia"[Mesh] OR Pneumonia).

Inclusion criteria

The selection of eligible articles was performed on the basis of the following inclusion criteria: the papers were original research and provided at least the direct medical cost of pneumonia in children aged up to 18 years old.

Exclusion criteria

Studies were excluded if they were not in the health sector or were not human subject research. Non-English full text or poster format, oral communications, or conference papers were not accepted in this review. The articles that show incomplete cost components (provide only drug cost and laboratory cost) or no specific cost of pneumonia (cost of a group of diseases that includes pneumonia), or are an economic evaluation study using secondary costing data were also excluded.

Analysis

Data from eligible studies were then independently extracted by the two authors (VS and TGV) using standardised data extraction forms. Country, currency/year of reported results, study design, patients, disease, health resources utilisation data sources, duration of study, perspective cost component, source of costing data, unit cost for valuing resource used, sensitivity analysis and cost estimates were extracted from the eligible articles.

To obtain current and comparable estimates, all costs were adjusted using a country specific Consumer Price Index (CPI) adjusted to 2015 value. The costs were then converted into US dollars using the exchange rate of 2015[8]. In cases where the year value was given in the study, we used the average annual inflation rate from that year to 2015. For studies that did not report the year value and reported data collected in a single year, we used the CPI in the year that the data was collected. For those studies that reported data collected over a range of years, we used the CPI for the midpoint of the range.

3. RESULTS

The search from PubMed found 444 potential papers. We used a filter in PubMed to exclude articles that are not written in English (45 articles), that did not mention humans (2 articles) and were not original research (3 case reports and 81 review articles) and were conducted on adults (those aged more than 18 years) (143 articles). The flow diagram describing the process of the systematic review is provided (figure 1). Of the remaining 170 papers, we excluded 47 articles after reviewing the titles because one article was a case series study, 12 articles were not conducted on pneumonia and 34 articles did not include a primary costing study (just discussion or recommendations on pneumonia and costs). Ninety-eight articles were excluded after reviewing the abstract: 43 articles did not include a primary costing study, 24 articles did not cover the complete cost components (only drug and/or investigation costs), and 31 articles did not present the specific cost of pneumonia. Following this, eight articles were excluded

after reviewing the full text; two articles were conducted on adults and six articles did not present the specific costs of pneumonia. Finally, there were 17 papers included in this review.

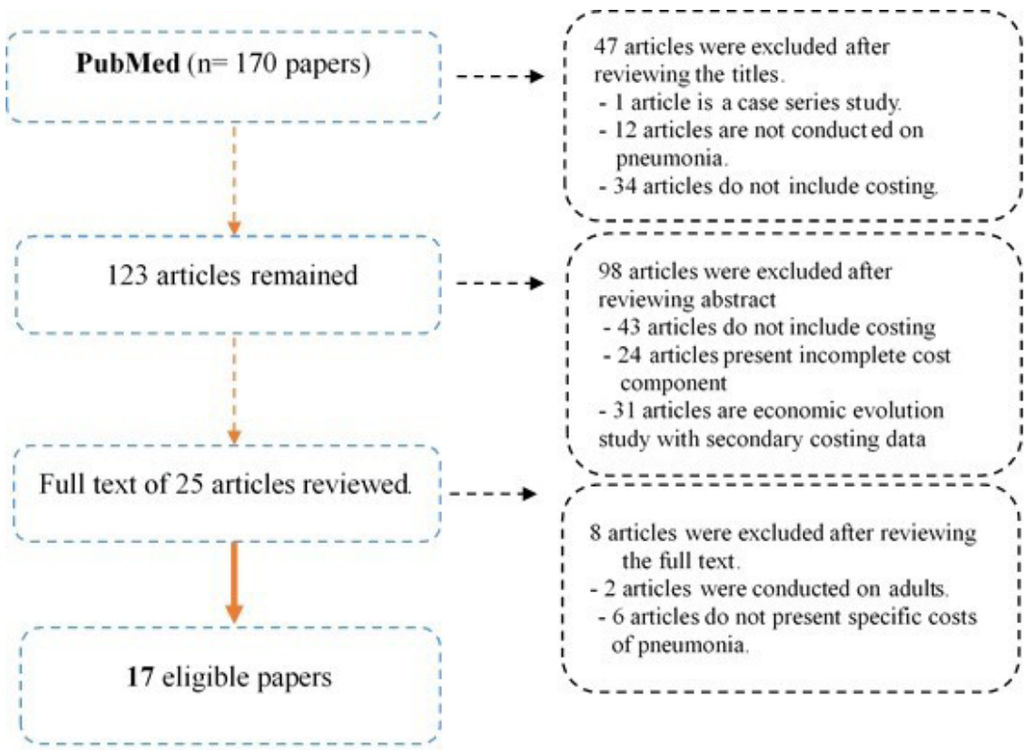

Figure 1. Flowchat of process of the systematic review

In Table 1, the main methodologies used in the study are retrospective (n=9: 52.9%) and prospective (n=8: 47.0%). Pneumonia studies were conducted in Asia (n=6: 35.3%), America (n=6: 35.3%), Europe (n=3: 17.6%), Australia (n=1: 5.9%) and Africa (n=1: 5.9%) mainly on subjects that were children from 0 to 5 years old (n=10: 58.8%). With such conditions, the results showed that all pneumonia (n=8: 47%) accounts for the highest rate followed by community-acquired pneumonia (n=4: 23.5%) severe pneumonia (n=2, 23.5%), pneumonia and severe pneumonia (n=1, 5.9%), RSV pneumonia (n=1, 5.9%) and invasive pneumococcal pneumonia (n=1, 5.9%). The 17 studies were conducted for various lengths of time. There are nine articles, which accounted for 52.9 percent, that were conducted for under one year of length. Next, the percentages of one-to-five- and five-to-ten-year studies were 35.3 and 17.6 percent, respectively. Six articles (35.3%) did not report a costing study perspective. For the healthcare system, household, societal, and societal plus household perspectives, each of them had two articles. To provide data on pneumonia's economic burden, all seventeen articles calculated the direct medical cost. Fifty-nine percent (10/17) of the articles included only direct medical cost, 5.9 percent (1/17) of the articles included both direct medical and direct non-medical cost, and 35.3 percent (6/17) included all three types of cost (direct medical, direct non-medical, and indirect). Regarding the sources of data, these included hospital electronic databases (n=8; 47%), medical records and interviews (n=4, 23.5%), interviews (n=3; 17.6%), and medical records (n=2, 11.8%). Study design and measurement of costs are shown in Table 2 and Table 3, respectively. All articles used an incidence-based approach

in the study. Regarding the cost calculation method, the bottom-up approach was used in most studies (n=11; 64.7%), and the top down approach was used in three studies. The other studies did not mention the approach. For the estimation of direct medical costs, it included personnel cost; physician, and other health care provider fee, (n=12) drug and medical supplies cost (n=12), investigation or diagnostic tests (n=11), hospital bed-day costs (n=10). The five studies did not report detail of direct medical cost components. In general, most studies (n=9) estimated the personnel cost using cost at charge, followed by direct measurement (n=6) and two studies used national reference to service valuing. Unit cost applied in the calculation of drug and medical supplies costs were cost at charge (n=7), direct measurement (n=4), wholesale drug prices (n=2), retail prices (n=1), drug price list (n=1) and national reference (n=2) as source of unit cost value. Cost at charge (n=9) was the most commonly used unit cost for investigation cost, followed by direct measurement (n=5) and national reference (n=2). One study did not report detail of unit cost for investigation cost. A total of seven studies estimated the direct non-medical cost covering meal (n=4), transportation (n=7), accommodation (n=1), under-the-table payments made for services at the health facility (n=2), childcare (n=1) and miscellaneous; lodging, soap, diapers, etc; (n=1). All studies that estimated travel and meal costs, direct measurement of actual expenditure was applied. The human capital approach was applied for indirect cost estimation covering time loss of caregivers in all six studies. These indirect costs were estimated based on real lost income (n=3), national reference (n=2) and both (n=1).

Table 1. General characteristics of studies

Characteristics	N	%	Characteristics	N	%
Study location			**Source of data**		
America	6	35.3	Electronic database	8	47.0
Asia	6	35.3	Medical record + interview	4	23.
Europe	3	17.6	Interview	3	17.6
Africa	1	5.9	Medical record	2	11.8
Australia	1	5.9	**Duration**		
Study design			≤1 year	9	52.9
Retrospective	9	52.9	1-5 years	6	35.3
Prospective	8	47.0	5-10 years	3	17.6
Disease/syndromes			**Type of cost**		
All pneumonia	8	47.0	DMC only	10	58.8
CAP	4	23.5	DMC+DNMC	1	5.9
Severe pneumonia	2	11.8	DMC+DNMC+IC	6	35.3
Pneumonia+severe pneumonia	1	5.9	**Perspective**		
RSV pneumonia	1	5.9	Healthcare system	2	11.8
Invasive pneumococcal pneumonia	1	5.9	Household	2	11.8
			Societal	2	11.8
Target population (years old)			Societal + household	2	11.8
0-5	10	58.8	Provider	1	5.9
0-16	1	5.9	Provider + household	1	5.9
0-18	4	23.5	Societal + provider + household	1	5.9
No specific age of children	2	11.8	No report	6	35.3
Sensitivity analysis					
Multi-way analysis	1	5.9			
No report	16	94.1			

RCT: randomized clinical trial, CAP: community -acquired pneumonia, RSV: Respiratory Syncytial Virus, DMC: direct medical cost, DNMC: direct non-medical cost, IC: indirect cost +: plus

Table 2. Study design

Country	Author, year	Study design	Disease/syndromes	Patients	Duration	Currency
Bangladesh	Alamgir et al., 2010[11]	Prospective study	All pneumonia	Inpatient: aged <5 years	2 months	2007 US dollar
Colombia	Alvis-Guzman et al., 2013[23]	Retrospective study	All pneumonia, diarrhea	Inpatient: aged <5 years	1 years	2010 US dollars
Fiji.	Temple et al., 2012[9]	Prospective study	Community -acquired pneumonia	Outpatient: aged <5 years	4 months	2008 US dollars
India	Madsen et al., 2009[16]	Prospective study	Severe pneumonia	Inpatient: aged 2–36 months	2 months	2008 US dollars and Indian Rupee (INR)
Italy	Di Ciommoet al., 2002[18]	Retrospective study	All pneumonia	Inpatient: children affected by ALRI	6 months	1999 Euros
Pakistan	Hussain et al., 2008[13]	Prospective study	Pneumonia, severe pneumonia, very severe febrile disease	Inpatient: aged < 3 years	1 years	2002 Rupees
Pakistan	Sadruddin et al., 2012[14]	Prospective study (RCT)	Severe pneumonia	Inpatient: 2–59 months of age	20 months	2009 Pakistani rupees (PKR), US dollars
South Africa	Kitchin et al., 2011[24]	Retrospective study (cross-sectional)	All pneumonia	Inpatient: children admission with pneumonia	1 years	2007 US dollars
Spain	Brotons et al., 2013[22]	Retrospective study	Invasive pneumococcal pneumonia	Inpatient: aged <18 years	10 years	2011 Euros
Switzerland	Keitel et al., 2014[15]	Prospective study (cohort)	Community -acquired pneumonia	Outpatient and inpatient: 2 months to 16 years	2 years 5 months	Swiss franc (CHF)
United States	Howard et al., 2000[17]	Retrospective study	RSV pneumonia	Inpatient: aged < 4 years	3 years	1998 US dollars
United States	Leyenaar et al., 2014[20]	Retrospective study (cohort)	All pneumonia	Inpatient: 1 to 17 years of age	3 years	US dollar
United States	Thomson et al., 2015[19]	Retrospective study (cohort)	Community -acquired pneumonia	Inpatient: aged 3 months to 18 years	1 years	US dollars
United States	Williams et al., 2013[21]	Retrospective study (cohort)	Community -acquired pneumonia	Inpatient: aged 6 months to 18 years	6 years	US dollars
United States	Zhou et al., 2007[10]	Retrospective study	Pneumonia, meningitis, septicemia	Outpatient and Inpatient: aged < 2 years	2 year and 1 years	2004 US dollars
Vietnam	Anh et al., 2010[25]	Prospective study	All pneumonia, sepsis, meningitis	Inpatient: aged <5 years	4 years	2006 US dollars
Vietnam	Le et al., 2014[12]	Prospective study	All pneumonia, meningitis	Inpatient: aged <5 years	10 months	2012 US dollars

RSV: Respiratory Syncytial Virus

Table 3. Measurement of costs

Author, year	Perspective	Approach	Cost component			Data collection method	Unit cost for valuing			travel, meal	Time cost
			Direct medical cost	Direct non-medical cost	Indirect cost		Personnel	Drug and medical supplies	Investigation		
Alamgir et al., 2010[11]	Household	Incidence, bottom up	P, D, I, B	M,T, Tip	-	Interview	Cost at charge	Cost at charge	Cost at charge	Direct measurement	-
Alvis-Guzman et al., 2013[23]	Healthcare system	Incidence, top down	P, D, I, B	-	-	Electronic database	Cost at charge	Cost at charge	Cost at charge	-	-
Temple et al., 2012[9]	Provider, household, societal	Incidence, bottom up	P,D	T	CT	Medical record and interview	National reference	Wholesale drug prices	No detail	Direct measurement	Real lost income
Madsen et al., 2009[16]	Provider, household	Incidence, bottom up	P, D, I, B	M,T,A	CT	Medical record and interview	Direct measurement	Wholesale drug prices	Direct measurement	Direct measurement	Real lost income and national reference
Di Ciommoet al., 2002[18]	No report	Incidence, bottom up	P, D, I	-	-	Medical record	Direct measurement	National reference	National reference	-	-
Hussain et al., 2008[13]	Societal, household	Incidence, bottom up	P, D, I, B	M,T	CT	Interviews	Cost at charge	Cost at charge	Cost at charge	Direct measurement	National reference
Sadruddin et al., 2012[14]	Household	Incidence, bottom up	P, D, I, B	M, T, Tip	CT	Medical record and interview	Cost at charge	Retail price	Cost at charge	Direct measurement	Real lost income
Kitchin et al., 2011[24]	No report	Incidence, top down	P, D, I, B	-	-	Electronic database	Cost at charge	Cost at charge	Cost at charge	-	-
Brotons et al., 2013[22]	Provider	Incidence, top down	No detail	-	-	Electronic database	National reference	National reference	National reference	-	-
Keitel et al., 2014[15]	Societal	Incidence, bottom up	P, D, I, B	T, Childcare	CT	Interview	Cost at charge	Drug price list	Cost at charge	Direct measurement	National reference
Howard et al., 2000[17]	No report	Incidence -based	No detail	-	-	Electronic database	Cost at charge	Cost at charge	Cost at charge	-	-
Leyenaar et al., 2014[20]	No report	Incidence, bottom up	P, D, I, B	-	-	Electronic database	Direct measurement	Direct measurement	Direct measurement	-	-
Thomson et al., 2015[19]	No report	Incidence -based	No detail	-	-	Electronic database	Cost at charge	Cost at charge	Cost at charge	-	-
Williams et al., 2013[21]	No report	Incidence, bottom up	No detail	-	-	Electronic database	Direct measurement	Direct measurement	Direct measurement	-	-
Zhou et al., 2007[10]	No report	Incidence -based	No detail	-	-	Electronic database	Cost at charge	Cost at charge	Cost at charge	-	-
Anh et al., 2010[25]	Healthcare system	Incidence, bottom up	P, D, I, B	-	-	Medical record	Direct measurement	Direct measurement	Direct measurement	-	-
Le et al., 2014[12]	Household, societal	Incidence, bottom up	P, D, I, B	T, Miscellaneous	CT	Medical record and interview	Direct measurement	Direct measurement	Direct measurement	Direct measurement	Real lost income

- = not included P= Personnel cost: physician, and other health care provider fee, D=Drug and medical supplies cost, I=Investigation or diagnostic tests, B=hospital bed-day costs, M=meal cost, T=transportation cost, A=accommodation cost, Tip= under-the-table payments made for services at the health facility, Miscellaneous: lodging, soap, diapers, etc, CT=caregiver time.

Table 4. Average cost of pneumonia

Author, year	Group in study	Direct medical cost	Direct non-medical cost	Indirect cost	Total cost/case	Total cost/case in 2015 US$	Sensitivity analysis
Alamgir et al., 2010[11]	All case	$75	$36	N/A	H:$110	H:$199	No report
Alvis-Guzman et al., 2013[23]	All case	$263	N/A	N/A	$263	$309	No report
Temple et al., 2012[9]	3st level	$14.66	$7.86	$1.15	P:$13.13 H:$10.54 S:$23.67	P:$16.7 H:$13.4 S:$30	No report
	Primary care	$10.89	$3.04	$0.40	P:$10.12 H:$4.22 S:$14.33	P:$12.8 H:$5.4 S:$18.2	
Madsen et al., 2009[16]	2rd level	$83.89	$8.35	$4.88	P:$83.89 H:$41.35	P:$149 H:$73	No report
	3st level	$146.59	$21.54	$5.88	P:$146.59 H:$134.62	P:$260 H:$239	
Di Ciommo et al., 2002[18]	All case	€1,435	N/A	N/A	€1,435	$2,200	No report
	SWT	€1,066	N/A	N/A	€1,066	$1,634	
	Not SWT	€2,554	N/A	N/A	€2,554	$3,915	
Hussain et al., 2008[13]	Pneumonia	$17.77	$3.70	N/A	H:$3.70 S:$22.62	H:$11.5 S:$70	No report
	Severe pneumonia	$125.29	$11	$4.63	H:$11.13 S:$142.90	H:$32.6 S:$444	
Sadruddin et al., 2012[14]	Intervention	PKR 110.7	PKR 112	PKR 10.73	H: PKR 124.17	H: $2.5	No report
	Control	PKR 408.6	PKR 528	PKR 120	H:PKR 648.07	H:$12.9	
Kitchin et al., 2011[24]	General ward	$435.12	N/A	N/A	$435.12	$705	Multi-way (Best-worst case scenario)
	PICU	$795.81	N/A	N/A	$795.81	$1290	
Brotons. et al., 2013[22]	All case	€4,533	N/A	N/A	€4,533	$5,189	No report
Keitel et al., 2014[15]	All case	CHF 10,867	CHF 232	CHF 159	S:CHF 11,258	S:$10,639	No report
	Outpatient	CHF 618	N/A	N/A	S:CHF 1,009	S:$954	
	Inpatient	CHF 23,481	N/A	N/A	S:CHF 23,872	S:$22,560	
Howard et al., 2000[17]	All case	$91,316	N/A	N/A	$91,316	$132,763	No report
	from 1993	$80,672	N/A	N/A	$80,672	$117,288	
	from 1994	$107,244	N/A	N/A	$107,244	$155,921	
	from 1995	$74,924	N/A	N/A	$74,924	$108,931	
Leyenaar et al., 2014[20]	Direct admission	$3,685	N/A	N/A	$3,685	$4,070	No report
	Emergency departments admission	$4,380	N/A	N/A	$4380	$4,838	
Thomson et al., 2015[19]	All case	$4,097	N/A	N/A	$4,097	$4,525	No report
	Guideline	$4,118	N/A	N/A	$4,118	$4,548	
	Non-guideline	$4045	N/A	N/A	$4,045	$4,468	
Williams et al., 2013[21]	Broad-spectrum	$3,992	N/A	N/A	$3,992	$4,206	No report
	Narrow-spectrum	$4,375	N/A	N/A	$4,375	$4,610	
Zhou et al., 2007[10]	Hospitalization in 1997-1999	$6,296	N/A	N/A	$6,296	$7,899	No report
	Hospitalization in 2004	$6,392	N/A	N/A	$6,392	$8,019	
	Ambulatory in 1997-1999	$175	N/A	N/A	$175	$220	
	Ambulatory in 2004	$201	N/A	N/A	$201	$252	
Anh et al., 2010[25]	All case	$31	N/A	N/A	$31	$70	No report
Le et al., 2014[12]	All case	$180	$51	$60	H:$272 S:$318	H:$304 S $355	No report

P: provider cost H: household cost, S: societal cost, SWT: switch therapy, PICU: pediatric intensive care unit, $: United States Dollar, €: Euros, PKR: Pakistani rupees , CHF: Swiss franc

Table 4 show average cost of pneumonia. All studies provided the value of direct medical cost. The costs were in range of $10.89 (13.8 USD 2014 value) in Fiji[9] and $6,392 (8,019 USD 2015 value) in United States[10]. In addition, the direct non-medical cost was included in six studies with the value of $36 (65 USD 2015 value) in Bangladesh[11] and $51 (59 USD 2015 value) in Vietnam[12], for example. The indirect cost was also an interesting issue in Pakistan[13-14], Switzerland[15], Vietnam[12], India[16], and Fiji[9], in which the cost in Pakistan[13] was $4.63 for severe pneumonia in 2008 ($14.4 for severe pneumonia in 2015 value). Four studies in Pakistan[13], Switzerland[15], Vietnam[12] and Fiji[9] mentioned the societal cost, in which the value in 2015 USD ranged from $18 to $22,560. Regarding the household perspective, five studies in developing countries estimated the cost of inpatients accounted for a range of $2.5 to 304 US dollars[11-14,16].

4. DISCUSSION AND CONCLUSION

By searching with keywords in the PubMed database, we found many studies, but only 10**%** of the articles met the selection criteria. Although many studies used the keywords "cost" or "economic" in the discussion or recommendations, they were not primary economic research. Thus, these studies were excluded.

Most of the papers did not provide information on sensitivity analysis and the perspective of the costing study that are essential in an economic study. This affects the quality of the studies. In cost of illness studies, the cost components are the direct medical cost, direct non-medical cost and indirect cost. However, most studies covered only the direct medical cost. Therefore, there is a limitation to the demonstrating of the economic burden incurred by society. This is because of the difficulty of collecting direct non-medical costs and indirect costs from patient or caregiver interviews.

This study has reviewed articles published during the years 2000 – 2015, of which only three articles were published during 2000-2007 and were conducted in America[10,17] and Europe[18]. The majority of the articles were published during 2008 – 2015 and conducted in Asia[11,12,14,13,16,19]. This reflects the development of health economics in developing countries in recent years.

The results show a wide range of cost estimates due to country-specific differences in disease management, hospital admission criteria, types of pneumonia, patient age, patient types (inpatient or outpatient), and the economic and healthcare systems in each country. For example, the costs of inpatients conducted in developed countries (five studies in America[10,17,19-21] and three studies in Europe[15,18,22]) were higher than those of developing countries. For the societal perspective, the costs in Switzerland[15] were 10 times higher than those of Fiji[9], Vietnam[12], and Pakistan[13]. This is most likely due to the higher GDP in Switzerland.

The review shows that the economic burden of pneumonia among children worldwide is high. The results from this study should be used to forecast the cost of treatment, improve budget management and evaluate the cost-effectiveness of related vaccines such as pneumococcal conjugate vaccines (PCV) and the *H. influenzae* type B vaccine (Hib). These vaccines may help to alleviate a substantial proportion of the overall burden of pneumonia.

Pneumonia has a significant economic impact because of its high prevalence and association with multiple chronic complications. The lack of recent direct or indirect cost estimates in several countries highlights the need for further work in examining the global economic burden of pneumonia.

REFERENCES

1. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet. 2015;385(9966):430-40.
2. O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet. 2009;374(9693): 893-902.

3. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. Bull World Health Organ. 2008;86(5):408-16.
4. World Health Organization. Pneumonia [document on the Internet]. Geneva: World Health Organization; 2015 [updated 2015 November; cited 2016 May 1]. Available from: http://www.who.int/mediacentre/factsheets/fs331/en/.
5. Brady MT, Byington CL, Davies HD, Edwards KM, Glode MP, Jackson MA, et al. Recommendations for Prevention and Control of Influenza in Children, 2012–2013. Pediatrics. 2012;130(4):780-92.
6. World Health Organization. Pneumococcal disease [document on the Internet]. Geneva: World Health Organization; 2005 [updated 2011 October 11; cited 2016 March 15]. Available from: http://www.who.int/immunization/topics/pneumococcal_disease/en/.
7. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4:1.
8. International Monetary Fund. World Economic Outlook Database April 2016 [Internet database]. Washington, D.C.: International Monetary Fund; 2016 [update 2016 April; cited 2016 April 18] Available from: https://www.imf.org/external/pubs/ft/weo/2016/01/weodata/index.aspx.
9. Temple B, Griffiths UK, Mulholland EK, Ratu FT, Tikoduadua L, Russell FM. The cost of outpatient pneumonia in children <5 years of age in Fiji. Trop Med Int Health. 2012;17(2):197-203.
10. Zhou F, Kyaw MH, Shefer A, Winston CA, Nuorti JP. Health care utilization for pneumonia in young children after routine pneumococcal conjugate vaccine use in the United States. Arch Pediatr Adolesc Med. 2007;161(12):1162-8.
11. Alamgir NI, Naheed A, Luby SP. Coping strategies for financial burdens in families with childhood pneumonia in Bangladesh. BMC public health. 2010;10:622.
12. Le P, Griffiths UK, Anh DD, Franzini L, Chan W, Pham H, et al. The economic burden of pneumonia and meningitis among children less than five years old in Hanoi, Vietnam. Trop Med Int Health. 2014;19 (11):1321-7.
13. Hussain H, Waters H, Khan AJ, Omer SB, Halsey NA. Economic analysis of childhood pneumonia in Northern Pakistan. Health Policy Plan. 2008;23(6):438-42.
14. Sadruddin S, Shehzad S, Bari A, Khan A, Ibad ul H, Khan A, et al. Household costs for treatment of severe pneumonia in Pakistan. Am J Trop Med Hyg. 2012;87(5 Suppl):137-43.
15. Keitel K, Alcoba G, Lacroix L, Manzano S, Galetto-Lacour A, Gervaix A. Observed costs and health care use of children in a prospective cohort study on community-acquired pneumonia in Geneva, Switzerland. Swiss Med Wkly. 2014;144:w13925.
16. Madsen HO, Hanehoj M, Das AR, Moses PD, Rose W, Puliyel M, et al. Costing of severe pneumonia in hospitalized infants and children aged 2-36 months, at a secondary and tertiary level hospital of a not-for-profit organization. Trop Med Int Health. 2009;14(10):1315-22.
17. Howard TS, Hoffman LH, Stang PE, Simoes EA. Respiratory syncytial virus pneumonia in the hospital setting: length of stay, charges, and mortality. J Pediatr. 2000;137(2):227-32.
18. Di Ciommo V, Russo P, Attanasio E, Di Liso G, Graziani C, Caprino L. Clinical and economic outcomes of pneumonia in children: a longitudinal observational study in an Italian paediatric hospital. J Eval Clin Pract. 2002;8(3):341-8.
19. Thomson J, Ambroggio L, Murtagh Kurowski E, Statile A, Graham C, Courter JD, et al. Hospital outcomes associated with guideline-recommended antibiotic therapy for pediatric pneumonia. J Hosp Med. 2015;10(1):13-8.
20. Leyenaar JK, Shieh MS, Lagu T, Pekow PS, Lindenauer PK. Variation and outcomes associated with direct hospital admission among children with pneumonia in the United States. JAMA Pediatr. 2014;168 (9):829-36.

21. Williams DJ, Hall M, Shah SS, Parikh K, Tyler A, Neuman MI, et al. Narrow vs broad-spectrum antimicrobial therapy for children hospitalized with pneumonia. Pediatrics. 2013;132(5):e1141-8.
22. Brotons P, Gelabert G, Launes C, Sicuri E, Pallares R, Munoz-Almagro C. Cost of hospitalizing children with invasive pneumococcal pneumonia. Vaccine. 2013; 31(7):1117-22.
23. Alvis-Guzman N, Orozco-Africano J, Paternina-Caicedo A, Coronell-Rodriguez W, Alvis-Estrada L, Jervis-Jalabe D, et al. Treatment costs of diarrheal disease and all-cause pneumonia among children under-5 years of age in Colombia. Vaccine. 2013;31 Suppl 3:C58-62.
24. Kitchin OP, Wessels F, Masekela R, Becker P, Green RJ. Costs of admission for paediatric pneumonia in a setting of human immuno-deficiency virus infection. Int J Tuberc Lung Dis. 2011;15(12):1702-7.
25. Anh DD, Riewpaiboon A, Tho le H, Kim SA, Nyambat B, Kilgore P. Treatment costs of pneumonia, meningitis, sepsis, and other diseases among hospitalized children in Viet Nam. J Health Popul Nutr. 2010;28(5):436-42.