

The Economic Evaluation in Vaccines - A Systematic Review in Vietnam Situation

Nam Xuan Vo^{1,2*}, Trung Quang Vo^{2,3}, Ha Thi Song Nguyen⁴, Thuy Van Ha⁵

¹Department of Social, Economic and Administrative Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok 10400, THAILAND.

²Professional Healthcare Management, Education and Research center (ProHES), Ho Chi Minh City 700000, VIETNAM.

³Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy, Ho Chi Minh City 700000, VIETNAM.

⁴Department of Postgraduate, Hanoi University of Pharmacy, Hanoi 100000, VIETNAM.

⁵Department of Health Insurance, Ministry of Health, Hanoi 100000, VIETNAM.

ABSTRACT

Background: Along with economic crisis, the budget for research is also affected. Systematic review of outcome measurement instrument is a method for choosing researches and articles for our research and practice. It provides evidences to make sure that our research will useful. Besides that, economic evaluation is a new approach to help policy maker giving affordable decision to invest in health sector. Our purpose was defined and summarize the status of economic evaluations of vaccines and to find out the new trend in economic evaluation of vaccines in the future in Vietnam.

Method: A systematic literature search was conducted in some database such as MEDLINE, SCOPUS, COCHRANCE and GOOGLE SCHOLAR between May 26th, 2016 and June 16th, 2016. The quality of reviews was assessed by using a specific checklist. Abstracts and titles are read firstly to eliminate articles are not related with our topic. **Results:** A total of six articles were included. These articles focus on three vaccines: rotavirus, typhoid VI and human papillomavirus vaccine. In there, only rotavirus vaccine is cost-effectiveness. The target population is children and women. These articles using mathematic model based on decision tree and Markov model

are the method to approach. **Conclusion:** Economic evaluation is a new area in Vietnam, it need to pay attention to research and develop to control the investment effectively. It is important to be aware of methodology and interpretation of results because of affecting to decision of policy maker and also affecting in national expanded program in immunization on adding new good vaccines.

Key words: Cost-effectiveness, Economic evaluation, Immunization, Expanded Immunization Program (EPI), Systematic review, Vaccine(s), Vietnam.

Correspondence:

Mr. Nam Xuan Vo

Department of Social, Economic and Administrative Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok 10400, THAILAND.

Phone no: +84(0)988490098

E-mail id: vonamlx@yahoo.com

DOI : 10.5530/srp.2018.1.1

INTRODUCTION

A good deal of the substantial progress seen in global health over the past several decades can be ascribed to the beneficial impacts of various vaccines and immunization programs on the control of serious disease among both individuals and populations.¹⁻³ In just the first decade of the 21st century, an estimated 2.5 million deaths of children younger than five were prevented worldwide by vaccines. The population coverage of many childhood vaccines has risen sharply in recent years, along with the number of countries using the more recently arrived vaccines.⁴⁻⁷ Based on the report of the World Bank, the vaccines covered by Expanded Program on Immunization (EPI) is one of the available measures most cost-effective interventions, with measles immunization estimated \$10 per year of life with disabilities (DALY) prevented, and the Diphtheria-Pertussis-Tetanus (DPT) vaccinations \$25 per DALY prevented.⁸⁻¹⁰ One recent analysis showed that the incremental cost per death averted of EPI is about \$478 in East Asia and Pacific, \$274 in South Asia, and \$1754 in Central Asia and Europe in 2001.^{6,11-13}

EPI was first mentioned in Vietnam in 1981, and became one of six health plans national target program in 1985. The initial immunization vaccinated against six diseases of children (tuberculosis, polio, diphtheria, pertussis, tetanus and measles). By 2009, 96% of children under 1 year of age was recorded as received three doses of DPT. The success of EPI include eliminating polio in 2000 and tetanus for mothers and newborns in 2005.¹⁴⁻¹⁶ Vietnam is the support of GAVI for the introduction of vaccines and strengthen health systems, but the conditions to support these funds may end when Vietnam is a middle-income country. Therefore, the current EPI program as well as introducing new vaccines will increasingly be funded by Vietnamese national budget. However, there are competing priorities for public investments in Vietnam both within

and outside the health sector. As the government plans to invest in the future, it is difficult to assess the impact and value of Vietnam's EPI.^{15, 17,18,19}

In the absence of a scientific basis for the cost effectiveness of vaccines, the policy makers in Vietnam may depend heavily on the research is published and available presentations unpublished real by industry or academic researchers.²⁰⁻²² With unfiltered potential impact of literature on decision making, we set out to implement a system of economic assessment is published in the vaccine in Vietnam. Our objective is critically comprehensive review on vaccine research, funding, quality of research, changes over time, and a summary of their main findings.

METHODS

The systematic searching was conducted on June 16th, 2016, in MEDLINE (using PubMed), Scopus (using www.scopus.com), Google Scholar (using www.scholar.google.com) and Cochrance (using www.cochrance.org) to identify all articles of health-related quality of life outcome published from previous to June 16th, 2016. We aimed to identify all articles having economic evaluation in vaccines in their researches to make a comparison these studies together.

The search method consisted of search terms for systematic reviews, search terms for measurement instrument, and a validated methodological search filter for measurement properties.²³ References of included articles were checked again for additional relevant studies in case they are necessary. The Boolean word (AND, OR), field specification (Title, Abstract, All fields), checking duplication, comparison between articles and criteria also were used as technique in searching progress. The full syntax was used in this study is: ((*Economic Evaluation [MeSH Terms]*)

AND (*Vaccine** [MeSH Terms]) AND (*Viet**[Title/Abstract])).

The following inclusion criteria were used in studies on economic evaluation area were conducted in vaccine in Vietnam population. These studies were health technology assessment as a method in their researches. On the other hand, the exclusion criteria were used: (1) the studies were conducted in Vietnamese population but they are costing studies; (2) the economic evaluation of vaccines was conducted on Vietnamese population living overseas were not excepted; (3) the publications were published on non-English journals also were not included. The quality of articles were evaluated based on the same method of Quang *et al.* article²⁴ and Nam *et al.* research.²⁵

The results of the study were compared together, which used the health technology assessment as the same method. We concern about the in incremental cost-effectiveness ratio; what instrument is used; when the study was conducted; and what function the authors were mentioned. The searching progress based on the abstracts and article selection is provided in **Figure 1**.

RESULTS

The review was conducted on 16th June 2016. Through the searching syntax as above, we apply it into searching progress in the databases. 13 articles were identified from PubMed database and 9 articles were identified from Scopus by search terms. Besides that, 11 articles in Cochrance and 32 articles in Google Scholar also were found.

When we combine these studies together, 16 articles were duplicated. In there, 15 articles were excluded because of criteria selection. They are

not related in vaccine area (three articles); six studies are not in economic evaluation area. Besides that, they did not conduct in Vietnam (two articles) and four articles only have abstract. In conclusion, six articles were reviewed.²⁶⁻³¹

The procedure of review is summary as **Figure 1** as above.

In these articles, three of them using Markov model are the approach in their studies,²⁷⁻²⁹ the others used mathematic model to simulate expected costs and benefits through decision tree as the model in these articles.^{26,30,31} Almost articles had used incremental cost-effectiveness ratio (ICER) per DALY as a standard of effective, one of them used ICER per QALY.²⁸ As the summary in **Table 1** and **Figure 1**, it is very less of economic evaluation in vaccine was conducted (three articles in 2008, and one article in 2005, 2009 and 2012) in Vietnam and the most of articles was taken based on supporting by GAVI projects.

Among these economic evaluation articles in vaccine in Vietnam, they only focus on three type of vaccine, such as rotavirus vaccine,²⁶⁻²⁸ typhoid Vi²⁹ and human papillomavirus (HPV),^{30,31} as summary on **Table 2**. These vaccines are very important for children and women to avert diseases. They had calculated to define they should be available in list of EPI or not. That is why the main target population in these studies are children (four articles) and women (2 articles).

DISCUSSIONS

Vietnam just join in middle-income countries, the social – economic conditions still lack of more necessary resources, especially in health sector. It leads to Vietnam does not have strength and resources to col-

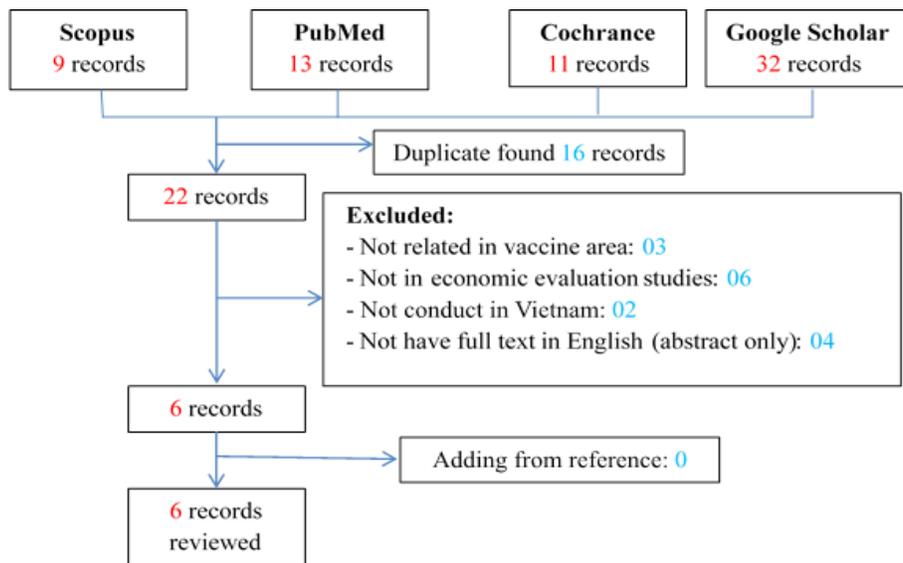


Figure 1: Flow chart of abstract and article selection.

Table 1: Summary the articles through year by year.

Years	2005	2008	2009	2012
Number of publications	1	3	1	1
Vaccine	Rotavirus	Typhoid Vi		HPV vaccine
Number of publications	3		1	2
Target samples	Children		Women	
Number of publications	4		2	

Table 2: Summary the results of articles.

No	Authors	Year	Target populations	Intervention vs comparator	Perspective	Method	Cost		Outcome	Types of model	Time horizon	Discount	Sensitivity analysis	Result
							Direct	Indirect						
1	Thea K. Fischer, Dang Duc Anh, Lynn Antil, N. D. L. Cat, Paul E. Kilgore, Vu D. Thiem, Rick Rheingans, Le H. Tho, Roger I. Glass, and Joseph S. Bresee	2005	Young children less than 5 years old	Rotavirus vaccination compared to no intervention	Societal perspectives	-	-\$3.1 million Medical direct cost \$685,000 non-medical direct cost	\$1.5 million	Incremental cost-effectiveness ratio (ICER) per DALY	Mathematic model - Decision tree	5 yrs	3 %	Monte Carlo simulations	It is cost-effectiveness intervention. \$140/DALY
2	Sun-Young Kim, Sue J Goldie and Joshua A Salomon	2009	Young children less than 5 years old	Rotavirus vaccination compared to no intervention	Societal perspectives and health care system perspectives	CEA	Social perspective: \$19.0 million; Healthcare perspective: \$18.6 million	Social perspective: \$2.0 million; Healthcare perspective: \$1.2 million	Incremental cost-effectiveness ratio (ICER) per DALY	Markov	5 yrs	3 %	Univariate sensitivity analyses and Monte Carlo simulations	It is cost-effectiveness intervention. Under base-case assumptions (94% coverage and \$5 per dose), the incremental cost per DALY averted from vaccination compared to no accination would be \$540 from the societal perspective and \$550 from the health care system perspective
3	Hong-Anh T. Tu, Mark H. Rozenbaum, Peter C. Coyte, Shu Chuen Li, Herman J. Woerdenbag, Maarten J. Postma	2012	Young children less than 1 years old	Rotavirus vaccination compared to no intervention	Societal perspectives and health care system perspectives	CEA	Mild: \$4.64; Moderate: \$5.07; Severe: \$35.28	Mild: \$4.01; Moderate: \$5.61; Severe: \$8.76	Incremental cost-effectiveness ratio (ICER) per QALY	CoRoVa model (the Concensus Model on Rotavirus Vaccination)	5 yrs	3 %	Monte Carlo simulations	It is cost-effectiveness intervention. The incremental cost per quality-adjusted-life-year (QALY) was US\$ 665 from the health system perspective, much lower than per-capita GDP of ~US\$ 1150 in 2009

4	Joseph Cook, Marc Jeuland, Dale Whittington, Christine Poulos, John Clemens, Dipika Sur, Dang Duc Anh, Magdarina Agtini, Zulfiqar Bhutta, DOMI Typhoid Economics Study Group	2008	Children (2-14.9 aged)	Typhoid 6 vaccination compared to no intervention	Societal perspectives and health care system perspectives	CEA	-	-	-	Incremental cost-effectiveness ratio (ICER) per DALY	Markov	3 yrs	3 %	Monte Carlo simulations	It is not cost-effectiveness. Cost is \$3779 per DALY
5	Sue J. Goldie, Mireia Diaz, Sun-Young Kim, Carol E. Levin, Hoang Van Minh, Jane J. Kim	2008	Women (9-12 aged) and Women (30-35)	HPV vaccination compared to no intervention	Societal perspectives	-	-	-	Incremental cost-effectiveness ratio (ICER) per DALY	Mathematic model - Decision tree	5 yrs	3 %	Individual-based Monte Carlo simulation	It is not cost-effectiveness	
6	Jane J. Kim, Katie E. Kobus, Mireia Diaz, Meredith O'Shea, Hoang Van Minh, Sue J. Goldie	2008	Women (9-12 aged) and Women (30-35)	HPV vaccination compared to no intervention	Societal perspectives	-	-	-	Incremental cost-effectiveness ratio (ICER) per DALY	Mathematic model - Decision tree	5 yrs	3 %	Individual-based Monte Carlo simulation	It is not cost-effectiveness the cost per vaccinated girl was low (i.e., <\$25) was vaccination combined with screening (three times per lifetime or every 5 years) favored in both regions; at high costs per vaccinated girl (i.e., >\$100), screening alone was most cost-effective.	

lecting data. Many parameters do not have real data, so that, they almost use mathematic model to estimate, to predict expected costs and benefits through decision tree analysis or they assume that parameters in the Markov model as summarize in **Table 2**. Despite facing to many difficulties, Vietnam Government try to take these vaccines into National expanded program on Immunization, and all of studies had researched in social perspective. Besides that, half of articles also had done in health care provider perspective.

With Rotavirus vaccine, three researches were conducted in 2005, 2009 and 2012. The article published later improved the previous research. In 2005, Fischer *et al.*²⁶ had published original articles to make background not only in rotavirus vaccine but also in economic evaluation vaccine in Vietnam. In this article, ICER equal US \$140 per DALY and it was cost-effectiveness to launch into list of Vietnam's EPI. After that, in 2009, Sun-Young Kim *et al.*²⁷ had improved by included healthcare provider perspective and applied Markov model to calculate again. The result of this study also show that rotavirus vaccine still cost-effectiveness with US \$540 per DALY in social perspective and US \$550 per DALY in healthcare provider perspective. Three year later, in 2012, Hong-Anh T. Tu *et al.*²⁸ had improved one more time when they use new model – CoRoVa

model to calculate ICER and had used QALY replacing DALY. One more time, rotavirus vaccine was cost-effectiveness with ICER equal US \$1150 in 2009. It is easily to see that rotavirus was effective enough to put into EPI.

Besides rotavirus vaccine, in 2008, two other kind of vaccine also had been researched. Joseph Cook *et al.*²⁹ Had mentioned typhoid Vi vaccine in economic evaluation research. Through this study, they showed that this vaccine is not cost-effectiveness, the cost to pay was too high (US \$3,779 per DALY). It was not appropriated to add into list of vaccine covered by national budget. In the same year, 2008, human papillomavirus vaccine also was concerned. Because of high vaccine price, it is also not cost-effectiveness.

CONCLUSIONS

We observed diverse approached to evaluate vaccine economics in Vietnam. Because economic evaluation analysis may influence policy maker decision about national EPI, it is important to be aware of methodology and interpretation of results. Vietnam need more research, review, and assess not only the findings but also the risk of the economic evaluations

of vaccines before applying new vaccine into national expanded program in immunization.

ABBREVIATION

DALY: Disability-Adjusted Life Year; **DPT:** Diphtheria-Pertussis-Tetanus; **EPI:** Expanded Program on Immunization; **ICER:** Incremental cost-effectiveness ratio; **GAVI:** Global Alliance for Vaccines and Immunization; **QALY:** Quality-Adjusted Life Year.

COMPLIANCE WITH ETHICAL STANDARDS

CONFLICT OF INTEREST

All authors of this study participated in this study had done searching filter separately with high agreement. None of author and co-authors on any of the included articles in this systematic review.

ETHICAL APPROVAL

This research does not contain any studies with human participants conducted by any of the authors.

REFERENCES

- Disease Control and Prevention Center. Ten Great Public Health Achievements. Morbidity Mortality Weekly Report 2011 Contract No.: 24.
- De Moerloose J. The role of immunization in communicable disease control. Compulsory or voluntary vaccination. Public Health Papers. 1961;8:85-100.
- Cruickshank R. The role of immunization in communicable disease control. The background to immunization. Public Health Papers. 1961;8:19-50.
- Nieburg P, McLaren NM. Role(s) of Vaccines and Immunization Programs in Global Disease Control. Center for Strategic and International Studies: 2011.
- Afzal S, Naeem A, Shahid U, Noor Syed W, Khan U, Misal Zaidi N. Effective role of lady health workers in immunization of children in Pakistan. Pakistan Journal of Medical Sciences. 2016;32(6):1500-5.
- Sharma B, Mahajan H, Velhal GD. Immunization coverage: role of sociodemographic variables. Advances in Preventive Medicine. 2013;2013:607935.
- Shen AK, Spinner JR, Salmon DA, Gellin BG. Strengthening the U.S. vaccine and immunization enterprise: the role of the National Vaccine Advisory Committee. Public Health Reports. 2011;126(1):4-8.
- Bank W. The World Bank World Development report 1993. New York: 1993.
- Yamashiro H, Cutcliffe N, Dobson S, Fisman D, Gold R. The role of pediatricians as key stakeholders in influencing immunization policy decisions for the introduction of meningitis B vaccine in Canada: The Ontario perspective. The Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicale. 2015;26(4):183-90.
- Virdi V, Depicker A. Role of plant expression systems in antibody production for passive immunization. The International journal of developmental biology. 2013;57(6-8):587-93.
- Brenzel L, Wolfson LJ, Fox-Rushby J, Miller M, Halsey NA. Vaccine-preventable diseases. Washington, DC: 2006.
- Nohynek H, Wichmann O, D'Ancona F, Gatekeepers VN. National Advisory Groups and their role in immunization policy-making processes in European countries. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2013;19(12):1096-105.
- Joint Ministry of Health/UNICEF/WHO Review of the Expanded Program on Immunization in the Socialist Republic of Vietnam. 4-22 May 1992. Summary report of findings and recommendations. Asia-Pacific Journal of Public Health. 1994;7(1):60-9.
- Vietnam TEPI-M. 25 years of National Expanded Program in Immunization Report. Ha Noi: 2012.
- Jit M, Dang TT, Friberg I, Hoang VM, Pham Huy TK, *et al.* Thirty years of vaccination in Vietnam: Impact and cost-effectiveness of the national Expanded Programme on Immunization. Vaccine. 2015;33(Suppl 1):A233-9.
- Le Dien H. The expanded program on immunization in Vietnam. Asia-Pacific journal of public health. 1990;4(2-3):125-7.
- Nguyen TD, Dang AD, Van Damme P, Nguyen CV, Duong HT, Goossens H, *et al.* Coverage of the expanded program on immunization in Vietnam: Results from 2 cluster surveys and routine reports. Human Vaccines & Immunotherapeutics. 2015;11(6):1526-33.
- Minh-Thang N, Bhushan I, Bloom E, Bonu S. Child immunization in Vietnam: situation and barriers to coverage. Journal of Biosocial Science. 2007;39(1):41-58.
- An DT, Lee JK, Minh HV, Trang NT, Huong NT, Nam YS, *et al.* Timely immunization completion among children in Vietnam from 2000 to 2011: a multilevel analysis of individual and contextual factors. Global health action. 2016;9(1):29189.
- Maertens K, Hoang TT, Nguyen TD, Cabore RN, Duong TH, Huygen K, *et al.* The Effect of Maternal Pertussis Immunization on Infant Vaccine Responses to a Booster Pertussis-Containing Vaccine in Vietnam. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2016;63(suppl 4):S197-S204.
- An PN, Huong TT. Etiological structure of acute encephalitis in children and immunization program concerns at The National Hospital of Paediatrics in Vietnam. The Southeast Asian Journal of Tropical Medicine and Public Health. 2014;45(Suppl1):37-9.
- Hipgrave DB, Nguyen TV, Vu MH, Hoang TL, Do TD, *et al.* Hepatitis B infection in rural Vietnam and the implications for a national program of infant immunization. The American Journal of Tropical Medicine and Hygiene. 2003;69(3):288-94.
- Terwee CB, Jansma EP, Riphagen II, de Vet HC. Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. Quality of life research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation. 2009;18(8):1115-23.
- Tran QV, Le PH, Vo TQ. Quality Assessment in Systematic Reviews: A Literature Review of Health Economic Evaluation of Hepatitis Studies. Systematic Reviews in Pharmacy. 2017;8(1):52-61.
- Vo NX, Ha TV, Chaikledkaew U. The Quality of Life - A Systematic Review Orientation to Establish Utility Score in Vietnam. Systematic Reviews in Pharmacy. 2017;8(1):92-6.
- Fischer TK, Anh DD, Antil L, Cat ND, Kilgore PE, Thiem VD, *et al.* Health care costs of diarrheal disease and estimates of the cost-effectiveness of rotavirus vaccination in Vietnam. The Journal of Infectious Diseases. 2005;192(10):1720-6.
- Kim SY, Goldie SJ, Salomon JA. Cost-effectiveness of Rotavirus vaccination in Vietnam. BMC Public Health. 2009;9(1):29.
- Tu HA, Rozenbaum MH, Coyte PC, Li SC, Woerdenbag HJ, Postma MJ. Health economics of rotavirus immunization in Vietnam: potentials for favorable cost-effectiveness in developing countries. Vaccine. 2012;30(8):1521-8.
- Cook J, Jeuland M, Whittington D, Poulos C, Clemens J, Sur D, *et al.* The cost-effectiveness of typhoid Vi vaccination programs: calculations for four urban sites in four Asian countries. Vaccine. 2008;26(50):6305-16.
- Goldie SJ, Diaz M, Kim SY, Levin CE, Van Minh H, Kim JJ. Mathematical models of cervical cancer prevention in the Asia Pacific region. Vaccine. 2008;26(Suppl 12):M17-29.
- Kim JJ, Kobus KE, Diaz M, O'Shea M, Van Minh H, Goldie SJ. Exploring the cost-effectiveness of HPV vaccination in Vietnam: insights for evidence-based cervical cancer prevention policy. Vaccine. 2008;26(32):4015-24.