COST-EFFECTIVENESS OF ROTAVIRUS VACCINATION AS PART OF THE NATIONAL IMMUNIZATION PROGRAM FOR THAI CHILDREN

Peeranath Chotivitayatarakorn[1], Pairoj Chotivitayatarakorn[2] and Yong Poovorawan[3]

[1]Faculty of Medicine, Chulalongkorn University; [2]Department of Pediatrics, Bangpakok 9 International Hospital, Bangkok, Thailand; [3]Center of Excellence in Clinical Virology, Pediatric Department, Faculty of Medicine, Chulalongkorn University and Hospital, Bangkok, Thailand

Abstract. Rotavirus infection is a common cause of gastroenteritis in infants and thus, presents an economic burden. Currently, there are effective vaccines against rotavirus licensed for use in Thailand. We evaluated the cost-effectiveness of rotavirus vaccination as part of the national immunization program for Thai children based on information derived from studies of disease burden of rotavirus infection, vaccine effectiveness, expenditure for care according to the WHO CHOICE; average GNP per capita provided by the Bank of Thailand and statistics from the Ministry of Health. The hypothesis of economic cost-effectiveness administering the vaccine along with DPT and OPV at ages 2 and 4 months was derived from a 5-year cohort study of 96% vaccinated children. Evaluation of vaccine cost-effectiveness included reduction of disease burden, cost averted, incremental cost-effectiveness ratio (ICER) to disability adjusted life year (DALY) averted and cost per life saved. Routine rotavirus immunization would prevent 109,918 visits to outpatient departments, 46,542 hospitalizations and 419 deaths in children under 5 years of age. It could reduce cost of care by USD12,066,484 or USD13 per child. As part of the national immunization program, the vaccine would be cost-effective at the direct medical break-even price of USD6.2 per dose. At a maximum vaccine price of USD6.2-10.5 per dose, the cost-effectiveness ratio is approximately USD185-759 per DALY averted. Vaccine price is greatly influenced by vaccine efficacy, mortality and G genotypes of rotavirus. Rotavirus vaccination could reduce gastroenteritis in children but the price, if used as part of the national immunization program should be below USD10 per dose.

Key words: cost-effectiveness, rotavirus vaccine, EPI, Thailand

INTRODUCTION

Rotavirus infection is the most common cause of mild and severe gastroenteritis among children under 5 years of age. It may account for 10-20% of gastroenteritis episodes, and cause 25-55% of hospitalizations due to gastroenteritis in young children (Glass *et al*, 2006; Nelson *et al*, 2008). It has been estimated 4 out of 5 children in the United States have had rotavirus gastroenteritis by the age of 5 years, one in seven required a clinic or emergency department visit, one in 70 was hospitalized, and one in 200,000 died from

Correspondence: Prof Yong Poovorawan, Center of Excellence in Clinical Virology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University and Hospital, Bangkok, Thailand.
Tel: 66 (0) 2256 4909; Fax: 66 (0) 2256 4929
E-mail: Yong.P@chula.ac.th

this disease (Cortese and Parasha, 2009). Surveillance studies in Thailand have demonstrated rotavirus infection is commonly found during October-February, and surveys from 6 general hospitals found 1 in 8 children are at risk for rotavirus infection, 1 in 36 will seek care from a clinic and 1 in 85 will be hospitalized (Jiraphongsa *et al*, 2005).

Since rotavirus infection can strike children irrespective of economic background, improved hygiene seems unlikely to be effective in reducing its incidence. Currently, vaccination against rotavirus is the principle strategy to reduce disease burden (World Health Organization, 2005; Salinas, 2005). The efficacy of the vaccine against rotavirus gastroenteritis of any severity is 75-87%, and the efficacy against severe gastroenteritis is 95% (Ruiz-Palacios *et al*, 2006; Committee on Infectious Disease, 2009). Routine immunization may decrease health care costs, both medical and non-medical, and is being considered for universal immunization in several countries (Widdowson *et al*, 2007; Linhares *et al*, 2008). For high income countries where the cost of treatment is high and deaths due to rotavirus disease are less common, the potential for avoiding health care and non-medical costs by using this intervention is an important consideration. Thailand is a middle income country with a strong public health infrastructure.

The immunization program in Thailand, commenced in 1980 by the Ministry of Public Health, currently provides vaccines to protect against 10 childhood diseases. The immunization program is sustainable. Surveys conducted in 2008 indicate the coverage by vaccines for infants is >90% (Thailand Department of Disease Control, 2008). The government, which is the major health care provider in Thailand, is trying to decide whether to include this new and expensive vaccine into the national immunization program. In order to decide whether to add a rotavirus vaccine to the national immunization program, national estimates of disease burden, economic burden, and the cost-effectiveness of immunization are required. The economic impact and cost-effectiveness of immunization have been assessed in many countries (Isakbaeva *et al*, 2007; Linhares *et al*, 2008; Kim *et al*, 2009; Wu *et al*, 2009), but data available for Thailand has not been assessed. The purpose of this study was to estimate the disease burden, the impact of vaccination, and perform a preliminary cost-effectiveness analysis of universal rotavirus vaccination as part of the national immunization program for Thai children.

MATERIALS AND METHODS

Model design

We developed a decision model to examine the potential impact of rotavirus immunization administered orally during the first 6 months of life as part of the national immunizations program. The total health care costs, disease burden associated with rotavirus gastroenteritis and the cost-effectiveness of vaccination for Thai children were estimated. The model was applied to the 2007 annual birth cohort (N=932,000) (World Health Organization, 2008) and followed through to age 5 to estimate various health associated outcomes, including deaths, hospitalizations (IPD) and outpatient visits (OPD) in the subject group. Estimation of events and costs provides a baseline estimate of rotavirus disease burden without vaccination, followed by assessing the number of rotavirus disease-associated events and costs that would occur after the introduction of a rotavirus vaccine into the immunization program schedule. The total

health care costs associated with rotavirus disease are based on standardized cost estimates. Employing data regarding surveillance of rotavirus gastroenteritis in Thailand, vaccine efficacy, coverage, and medical costs from the WHO (WHO CHOICE for unit cost for patients service), economic data from the Bank of Thailand (GNP per capita in 2007), and health statistics from the Ministry of Public Health, the model was able to predict the cost-effectiveness of the vaccine. The exchange rate during the study period was estimated at 36 baht per US dollar and the GNP per capita was USD 3,050 per year (Bank of Thailand; WHO, 2008).

Burden of rotavirus infection

We were particularly interested in the number of incidents of rotavirus associated gastroenteritis in four different settings: patients who required only homecare, an OPD visit, an IPD visit, and fatalities. We used a surveillance survey conducted by the Thai Department of Disease Control during 2001-2002. The incidence of acute gastroenteritis in children under five years of age was 0.93-1.35 cases/person-year, and the proportion of cases due to rotavirus disease in the community was 12.2% (95% CI 7.9-18.3). The rate of hospitalization associated with rotavirus infection was 11.28 admissions/1,000 individuals. For all children 0-5 years of age with gastroenteritis, the risks of having rotavirus associated gastroenteritis, of requiring a health care visit, and of requiring hospitalization were 1 in 8, 1 in 36, and 1 in 85, respectively (Jiraphongsa *et al*, 2005). The estimated rate of rotavirus gastroenteritis associated mortality was 0.1 death/1,000 live births by the age of 5 years (Parashar *et al*, 2003).

The health burden of rotavirus gastroenteritis was estimated in terms of disability-adjusted life years (DALYs). The calculation of DALY lost as a result of death was performed on the basis of the standardized life expectancy at age 1. The DALY loss from all symptomatic cases of rotavirus was calculated on the basis of default disability weights and an estimated duration of rotavirus illness of 6 days (Shepard *et al*, 1995). Costs and benefits of the vaccine were adjusted for inflation with a standard annual rate of 3%, consistent with previous analyses (Podewils *et al*, 2005, Isakbaeva *et al*, 2007).

Vaccine characteristics

There are two oral rotavirus vaccines available in Thailand. The efficacy of both vaccines seems to be equivalent. We focused on the live attenuated human rotavirus vaccine (Rotarix®) because a larger number of children were tested and fewer doses of the vaccine are required (Glass *et al*, 2006; Committee on Infectious Disease, 2009; Cortese and Parasha, 2009). The effectiveness of vaccination on disease burden was estimated by combining information regarding vaccine efficacy and coverage.

Vaccine efficacy. Clinical trials regarding vaccine efficacy have demonstrated an efficacy of 70-85% against any rotavirus associated gastroenteritis and 85-93% against severe disease (Glass *et al*, 2006; Committee on Infectious Disease, 2009; Cortese and Parasha, 2009). Additional results from clinical trials conducted in 11 Latin American countries and Finland demonstrated 85% (69.6-93.5) efficacy for prevention of rotavirus disease-associated hospitalizations, and 100% against more severe rotavirus associated gastroenteritis (Ruiz-Palacios *et al*, 2006). A phase III study in Latin American infants has established vaccine efficacy for prevention of hospitalization due to rotavirus gastroenteritis

at 83% (73.1-89.7) (Linhares *et al*, 2008). Data regarding specific efficacy are not available for outpatient visits. With reference to clinical trials of the rotavirus vaccine, we used an average of 90% efficacy for prevention of rotavirus disease-associated deaths and 85% efficacy for prevention of hospitalization. Vaccine efficacy for preventing outpatient visits was estimated as the average of estimates of efficacy against any rotavirus event (85%). The vaccine efficacy arrived at in this study did not discriminate among infections by different rotavirus genotypes.

Vaccine coverage. The model assumed that the rotavirus vaccine will be incorporated into the universal immunization program schedule. Routine vaccination with two oral doses of vaccine is recommended for infants at ages 2 and 4 months. Rotavirus vaccine can be administered together with the diphtheria-tetanus toxoid-pertussis (DTP)-1 and DTP-2 vaccines at 2 and 4 months of age, respectively. In Thailand, the WHO-UNICEF estimates the DTP coverage is 99% for DTP-1 and 96% for DTP-3 (World Health Organization, 2008). We used 96% for rotavirus vaccine coverage, and assumed no risk for serious adverse events from receiving the vaccine.

Cost estimates

Medical costs included costs for inpatient, outpatient, and health care costs per visit, as well as the cost associated with vaccination. We compared the cost proposed by the WHO-CHOICE data with that of inpatient expenses reimbursed by Buri Ram Provincial Hospital in 2005 (Sungkapalee *et al*, 2006). Hospital costs for the care of a rotavirus infected child according to WHO-CHOICE estimation at a tertiary care hospital average USD 48, which is similar to the average cost at Buri Ram Hospital of USD 46.13 (38.7-56.6). The costs of hospitalization and outpatient visits were estimated using a standardized approach developed by the WHO for its WHO-CHOICE project (Adam *et al*, 2003; World Health Organization, 2008), and the type of institution. The distribution of cases found in health care facilities at primary, secondary, and tertiary levels were 25, 45 and 30%, respectively (World Health Organization, 2008; Bureau of Epidemiology, 2007). The costs of drug and laboratory investigations were estimated at 33% and 65% for the medical costs for hospitalizations and outpatient visits, respectively (World Health Organization, 2008). Medical cost was calculated as cost per patient per day for each type of health care facility multiplied by the distribution of the health care institution type. Estimates of costs provided by WHO-CHOICE were expressed in 2005 US dollars and local currency rate. All costs were converted to 2007 US dollars applying the purchasing power parity conversion factors and official exchange rates.

The average duration of hospitalization due to rotavirus associated gastroenteritis was calculated using the results from studies conducted in Thailand and in Asia and yielded a mean duration of 3.0 days (Podewils *et al*, 2005; Sungkapalee *et al*, 2006; Widdowson *et al*, 2007; Kim *et al*, 2009). The medical cost of an outpatient visit was calculated based on an assumption the patient would consume patient care time equivalent to 1.5 days of outpatient care.

The non-medical costs of an episode of rotavirus gastroenteritis included costs for transportation and costs accrued by the caregiver due to loss of work. Lost earnings of a parent included 3 days for hospitalizations and 1.5 days for outpatient visits. The transportation cost to reach

Table 1
Variables applied for analysis of cost effectiveness.

Variable	Baseline estimate	Source
Demographic		
Birth cohort	932,000	Ministry of Health; World Health Organization, 2008
Life expectancy (year)	70	The World Bank, 2006
Incidence of gastroenteritis	0.93-1.3/person/year1/8	Bureau of Epidemiology, 2006; Jiraphongsa *et al*, 2005 Jiraphongsa *et al*, 2005
Proportion of rotavirus associated gastroenteritis among total gastroenteritis cases	1/36 1/85 0.1/1000 live births by 5 years of age	
Total		
Out patient visit		
Hospitalization	96%	Parashar *et al*, 2003
Mortality	65%	
Vaccine characteristics	85%	WHO, 2008
Coverage	85%	Salinas *et al*, 2005; WHO, 2008; Adam *et al*, 2003
Efficacy	90%	
Home care	THB 36 = USD 1	
Out patient visit	USD 3,050	
Hospitalization		
Mortality	25%	Bank of Thailand
Exchange rate	45%	Bank of Thailand
GNP per capita	30%	Bureau of Epidemiology, 2006
Institution type for medical care	3.0 days	
Primary hospital	1.5 days	
Secondary hospital		
Tertiary hospital		
Average duration of hospitalization		
Outpatient stay at the clinic		

medical service averaged USD1.60 per visit (Simmerman *et al*, 2006). The cost accrued by the caregiver due to loss of work was calculated based on a national average daily salary of USD16 and amounted to approximately 1.5 times the average daily per capita income (National Statistical Office of Thailand, 2008) (Tables 1, 2).

Vaccination costs

Vaccination costs include the cost of administration, the price per dose, and the number of doses given. Based on the assumption the rotavirus vaccine would be administered along with the DPT vaccine, we stipulated an administration cost of USD0.50 per dose of vaccine.

Cost-effectiveness analysis

We calculated the incremental cost-effectiveness ratio expressed as the cost per DALY averted and as the cost per life

Table 2
Cost estimate for cost effectiveness analysis in US dollars.

Variable	Primary	Secondary	Tertiary	Estimate	Source
Medical cost/patient/day					WHO, 2005
Outpatient	8.6	12.1	17.8	13.53	
Hospitalized patient	27	35.3	48.0	38.38	
Health care cost/service	-			3.2	WHO, 2005
Non medical cost/patient/day					
Transportation cost/day				1.6	Simmerman *et al*, 2006
Loss of earnings/day				16	National Statistical Office of Thailand, 2008
Vaccine administration				0.5	Shepard *et al*, 1995

saved. The incremental cost-effectiveness ratio (ICER) was calculated based on the health care cost with and without vaccine per DALY or death averted with and without vaccine [ICER = (intervention cost – total health care cost averted)/DALY or death averted]. The WHO World Health Report states interventions with an ICER in USD/DALY averted of less than the per capita GNP should be considered "very cost-effective", and those with an ICER less than three times the GNP should be considered "cost-effective" (Guilbert, 2003). In "Investing in Health", the World Bank states interventions with an ICER/DALY averted of USD 185-759 are highly cost-effective in developing and middle income countries (The World Bank, 1993). The vaccine prices were calculated applying these criteria. The market price of vaccine (Rotarix) was about USD38-40 per dose during the study period, but the price for national immunization has not yet been set in our country. A recent report from Brazil gave a cost of USD7-8 per dose as a cost effective level for the vaccine (Parashar *et al*, 2003). The cost of the vaccine, DALY loss, ICER/DALY averted and life saved were added into this vaccine price. Sensitivity analysis was conducted to assess the impact of vaccine efficacy, prevalence of rotavirus associated gastroenteritis, mortality, hospitalization rate, outpatient visit rate, and vaccine prices into the cost-effectiveness ratio.

RESULTS

National disease and economic burden

Based on a birth rate in Thailand of 932,000 births per year, we estimated approximately 582,500 cases of gastroenteritis, 466 deaths, 54,755 hospitalizations, and 129,315 outpatient visits attributable to rotavirus infection would occur before a child reaches 5 years of age, resulting in a net loss of 14,940 DALY. Under the assumption rotavirus vaccine coverage would be similar to DTP-1 and DTP-2 coverage, rotavirus vaccination would prevent annually 82% (475,251) of rotavirus gastroenteritis cases, and prevent approximately 419 deaths, 46,542 hospitalizations, and 109,918 outpatient visits (Table 3).

We estimated the annual costs of rotavirus associated gastroenteritis at USD16,954,060, with USD10,206,982 (60%) as medical costs and USD6,747,078 (40%)

Table 3
Estimate of rotavirus burden, economic burden, and cost averted by vaccination.

Variable	Without vaccine	With vaccine	Averted by immunization	Percent
Number of events				
Rotavirus gastroenteritis	582,000	106,749	475,251	82
Death				
Hospitalization	466	47	419	90
Outpatient visit	54,755	8,213	46,542	85
DALY Number	129,315	19,397	109,918	85
Costs (USD)	14,940	1,599	13,341	89
Medical cost	10,206,982	3,855,616	6,351,366	62
Non-medical cost	6,747,078	1,031,960	5,715,118	85
Transportation cost	617,315	92,597	524,718	
Cost lost workday	6,129,763	939,363	5,190,400	
Total	16,954,060	4,887,576	12,066,484	72
Cost per child (USD)	17.8	4.9	12.9	72

Table 4
Estimate of cost, net benefit and cost effectiveness at a vaccine price of USD7/dose.

	Amount (USD)
Vaccine cost	13,420,000
Total medical and non medical cost averted	12,066,484
DALY No. averted	13,341
Incremental cost effectiveness ratio (ICER) per	
DALY averted	370
Life saved	11,800

as non-medical costs, and a cost per child of USD17.80. Based on the above assumption, an immunization program would save USD12,066,484, USD6,351,366 and USD5,715,118 of total costs, medical costs, and non-medical costs, respectively. Costs per child would decrease by 72% or a savings of USD12.90.

Cost-effectiveness analysis

At the rotavirus vaccine price of USD27.50 per dose, a vaccine program would come under cost-effective interventions (cost per DALY averted less than GNP per capita), and the vaccine would be cost-effective even at vaccine prices up to USD73 per dose. The direct medical break-even price was USD6.2 per dose. At a vaccine price of USD7 per dose, the rotavirus vaccine and administration cost would be USD13.5 million and total costs averted would be USD12 million. From a public health perspective, the incremental cost-effectiveness per DALY averted would be USD 370 and per life saved would be USD11,800 (Table 4). The maxi-

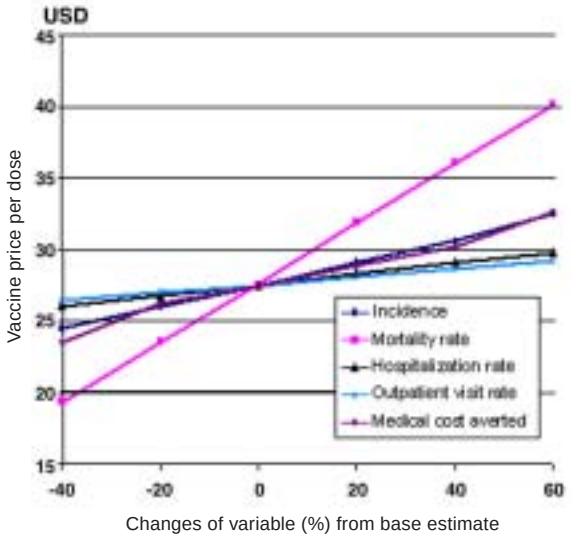

Fig 1–Effect of variations in percentage of incidence of rotavirus gastroenteritis, mortality rate, rate of hospitalization, rate of outpatient visits and costs of treatment on the price of rotavirus vaccine.

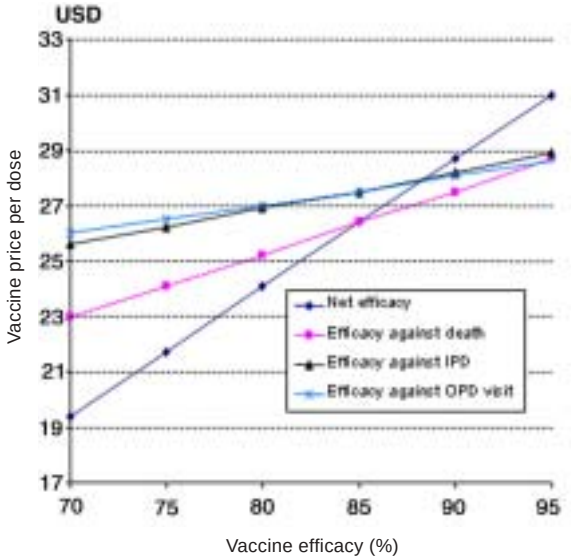

Fig 2–Price of rotavirus vaccine (USD) according to efficacy of vaccine.

mum vaccine price of USD6.2-10.5 per dose meets the World Bank criterion for high cost-effectiveness with an ICER/DALY averted of USD185-759.

Sensitivity analysis

The sensitivity analysis determined which variables have the largest influence on the vaccine price. As shown in Figs 1 and 2, the variables that affected the estimated price of vaccine per dose were the incidence of rotavirus gastroenteritis, mortality rate and efficacy of vaccine. The mortality rate had the largest impact on vaccine price; a 20% change in the mortality rate from the estimated baseline provided a USD4 per dose change in price of vaccine. A 20% change in the incidence of rotavirus gastroenteritis resulted in a USD1.60 (5%) change in the price of vaccine. If the incidence of rotavirus gastroenteritis was up to 20%, the price of vaccine would be USD32.50. Changes in the efficacy of vaccine also influence the price of vaccine. If the overall efficacy was less than 80%, the price of the vaccine should be less than USD24 per dose.

DISCUSSION

We examined cost of rotavirus gastroenteritis from a health care perspective (medical and non-medical) and projected the cost-effectiveness of the rotavirus vaccine. This represents the first evaluation of the impact of a national rotavirus immunization program in Thailand in economic terms. Vaccination provides an effective opportunity for improving children's health. We estimate vaccination would prevent more than 80% of all cases of rotavirus associated gastroenteritis. A universal rotavirus immunization program in Thailand would prevent 109,917 outpatient visits, 46,542 hospitalizations and 419 deaths, respectively. It would also reduce the cost of care by USD12,066,484 or USD13 per child. Our analysis demonstrated, with a vaccine price of less than USD27 per dose, vaccination would be cost-effective from the perspective of the

health care provider based on WHO benchmarks for cost-effectiveness. At a vaccine price of USD7 per dose of Rotarix® vaccine, the immunization program would produce an ICER at USD370 per DALY averted. The vaccine costs and total costs averted were estiemated to be USD13.4 million and USD12.1 million, respectively. Hence, routine rotavirus vaccinations are likely to be cost-effective but not cost-saving in Thailand. Due to high morbidity of rotavirus gastroenteritis, rotavirus vaccine is a potential vaccine inclusion in the EPI in the future. The main challenge needed to be overcome is the cost of the vaccine. The immunization program would be considered cost-saving at a vaccine price <USD6.2-10.5 per dose.

In the course of this analysis, our group also found a number of important factors in considering the introduction of a rotavirus vaccine. The incidence of rotavirus associated gastroenteritis, mortality rate, hospitalization rate, and vaccine efficacy were significant contributors to the price of vaccine. With a decrease in vaccine price the immunization program would become more cost-effective. With a gradual decline in mortality and hospitalization rates associated with rotavirus gastroenteritis, the value of a rotavirus vaccine will decrease as well.

The limitations of this preliminary cost-effectiveness analysis of rotavirus vaccination are that we made several assumptions that could affect the results of the analysis. For example, uncertainties with respect to the epidemiology of gastroenteritis due to rotavirus in Thailand, mortality rate, health care costs and efficacy of vaccine. Moreover, the actual proportion of gastroenteritis-related deaths due to rotavirus is unknown. We estimated the mortality rate at 0.1/1,000 live births, which was lower than the WHO estimation, with rotavirus-related deaths < 5 years = total deaths < 5 years (17/1,000 live births) x proportion with diarrhea (16%) x the proportion with rotavirus infection (12%) (World Health Organization, 2005, 2006). If the mortality rate due to rotavirus infection was 1,520 cases, the vaccine price per dose should be <USD75, or 2.7 times the estimation. Efforts should be made to ascertain the incidence of death due to rotavirus infection using active surveillance studies.

Another limitation is related to the coverage rate for vaccination. The coverage is based on the coverage for other vaccines, which may not be an accurate estimation of coverage for the current rotavirus vaccine. If vaccinations were missed or delayed, the effectiveness would be reduced. Since rotavirus associated gastroenteritis occurs in young children and protection is conferred by the first dose of vaccine and reinforced by the second booster dose, future considerations should be made to account for the fact that not all children will receive the vaccine at the time recommended.

We also made assumptions regarding the efficacy of the rotavirus vaccine. The issue of serotype coverage is an area of some uncertainty. The efficacy trial in Latin America showed an efficacy of the Rotarix® vaccine of 80.5 to 82.1% against wild-type G1 rotavirus, 77.5% against pooled non-G1 strains, and 80.5% against pooled G1P [8] strains. For serotype G2P [4], the vaccine efficacy was only 41% (Linhares *et al*, 2008). The vaccine label indicates immunization against rotavirus gastroenteritis caused by strains G1, G3, G4 and G9 (Committee on Infectious Disease, 2009). In Thailand, variations among G genotypes have been prevalent during the last ten years. From 2002 to 2004, the G2 strain was highly prevalent (69.4%)

followed by G9 (Theamboonlers *et al*, 2005); G1 was the most common strain from 2004 to 2006 (Theamboonlers *et al*, 2008) and from 2007 to early 2009 G2 has tended to increase (Center for Excellence in Clinical Virology, Chulalongkorn University, unpublished data). Moreover, in Brazil, after universal rotavirus vaccination, the prevalence of G2 increased (Carvalho-Costa *et al*, 2009). Vaccine efficacy may be lower than assumed. The high uncertainty about vaccine efficacy affected by diverse genotypes of rotavirus warrants a national surveillance study (World Health Organization, 2005).

We used the standard WHO-CHOICE project estimates for costs/bed/day. Yet, the economic burden of rotavirus hospitalization costs might be greater, making rotavirus vaccination slightly more cost-effective. However, country specific estimates may be more precise than estimates obtained by WHO-CHOICE, and therefore may be closer to the true costs.

According to various studies conducted regarding cost-effectiveness of rotavirus vaccine as part of the national immunization for children in Asia, such as in Vietnam, universal vaccination of infants at a cost of USD7.26 or less per vaccine dose would be a cost effective public health intervention (Fischer *et al*, 2005), and in Uzbekistan vaccination per course would be USD8 (Isakbaeva *et al*, 2007). A national immunization program for Brazilian children would be cost saving at a price <USD 2.2 per dose (Constenla *et al*, 2008). Currently, the price of the vaccine (Rotarix®) has not yet been set for Thailand. With the recently quoted price of USD7 per dose in Brazil (Constenla *et al*, 2008), a middle income country with a GNP per capita of about USD8,000, there is a possibility the vaccine price per dose might be set lower than USD7 for Thailand.

Although a rotavirus vaccine has the potential to be cost-effective, the interpretation of cost-effectiveness will ultimately depend on country-specific comparisons with other strategies for improving the health of children. The ability of a country to introduce the vaccine and sustain its use will be more influenced by price than merely by cost-effectiveness estimates. A study, similar to ours, conducted in Vietnam concluded the introduction of rotavirus vaccine to the immunization program of the country would be cost-effective if the cost of the vaccine is USD5 per dose (Sun-Young Kim). To better define the disease and economic burden of rotavirus, reliable information regarding local disease burden is essential to formulate a rational decision about the introduction of a vaccine into the national immunization program. Even an intervention that provides good value for resources invested may have prohibitive financial requirements that could not be accommodated by the health care system in Thailand.

Distribution of the rotavirus vaccine can reduce both disease and economic burden of rotavirus associated gastroenteritis, but the price, if used as part of the national immunization program, should be less than USD10 per dose. Routine rotavirus vaccination is potentially cost-effective but not cost saving for Thailand. Even with steeply tiered pricing, the vaccine is most likely unaffordable. Based on the vaccine price of USD7-8 per dose, we project the national rotavirus immunization program would cost the National Health Society Fund USD14-16 million annually or approximately 7% of its budget. However, decisions regarding the adoption of rotavirus vaccines will rely not only on considerations of economic savings but also on their value in preventing mortality and morbidity associated with rotavirus gastroenteritis.

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REFERENCES

Adam T, Evans DB, Murray CJL. Econometric estimation of country-specific hospital costs. *Cost Eff Resour Alloc* 2003; 1: 3.

Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand. Annual epidemiology surveillance report 2006. Nonthaburi: Ministry of Public Health, 2006. (Cited 2009 Apr 1). Available from: UR: http://203.157.15.4/ (in Thai).

Carvalho-Costa FA, Ara˙jo IT, Santos de Assis RM, *et al*. Rotavirus genotype distribution after vaccine introduction, Rio de Janeiro, Brazil. *Emerg Infect Dis* 2009; 15: 95-7.

Committee on Infectious Diseases. Prevention of rotavirus disease: updated guideline for use of rotavirus vaccine. *Pediatrics* 2009. (Epub ahead of print).

Constenla DO, Linhares AC, Rheingans RD, Antil LR, Waldman EA, da Silva LJ. Economic impact of a rotavirus vaccine in Brazil. *J Health Popul Nutr* 2008; 26: 388-96.

Cortese MM, Parasha UD, Center for Disease Control and Prevention (CDC). Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practice (ACIP). *MMWR Recomm Rep* 2009; 58: 1-25.

Fischer TK, Anh DD, Antil L, *et al*. Health care costs of diarrheal disease and estimates of the cost-effectiveness of rotavirus vaccination in Vietnam. *J Infect Dis* 2005; 192: 1720-6.

Glass RI, Parashar UD, Bresee JS, *et al*. Rotavirus vaccines: current prospects and future challenges. *Lancet* 2006; 368: 323-32.

Guilbert JJ. The world health report 2002 - reducing risks, promoting healthy life. *Educ Health* (Abingdon) 2003; 16: 230.

Isakbaeva ET, Musabaev E, Antil L, *et al*. Rotavirus in Uzbekistan: cost-effectiveness of a new vaccine. *Vaccine* 2007; 25: 373-80.

Jiraphongsa C, Bresee JS, Pongsuwanna Y, *et al*. Epidemiology and burden of rotavirus diarrhea in Thailand: results of sentinel surveillance. *J Infect Dis* 2005; 192: S87-93.

Kim SY, Goldie SJ, Salomon JA. Cost-effectiveness of rotavirus vaccination in Vietnam. *BMC Public Health* 2009; 9: 29-40.

Linhares AC, Velázquez FR, Pérez-Schael I, *et al*. Efficacy and safety of an oral live attenuated human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in Latin American infants: a randomized, double-blind, placebo-controlled phase III study. *Lancet* 2008; 371: 1181-9.

National Statistical Office of Thailand. Wages and salary, Thailand. Bangkok:National Statistical Office, 2008. (Cited 2009 Apr 2). Available from: URL: http://service.nso.go.th/nso/nsopublish/indicator/indEco51.pdf (in Thai).

Nelson EA, Bresee JS, Parashar UD, Widdowson MA, Glass RI. Asian Rotavirus Surveillance Network. Rotavirus epidemiology: The Asian Rotavirus Surveillance Network. *Vaccine* 2008; 26: 3192-6.

Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. Global illness and deaths caused by rotavirus disease in children. *Emerg Infect Dis* 2003; 9: 565-72.

Podewils LJ, Antil L, Hummelman E, Bresee J, Parashar UD, Rheingans R. Projected cost-effectiveness of rotavirus vaccination for children in Asia. *J Infect Dis* 2005; 192: S133-45.

Ruiz-Palacios GM, Pérez-Schael I, Velázquez

FR, *et al*. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *N Eng J Med* 2006; 354: 11-22.

Salinas B, PÈrez SI, Linhares AC, *et al*. Evaluation of safety, immunogenicity and efficacy of an attenuated rotavirus vaccine, RIX4414: A randomized, placebo-controlled trial in Latin American infants. *Pediatr Infect Dis J* 2005; 24: 807-16.

Shepard DS, Walsh JA, Kleinau E, Stansfield S, Bhalotra S. Setting priorities for the Children's Vaccine Initiative: a cost-effectiveness approach. *Vaccine* 1995; 13: 707-14.

Simmerman JM, Lertiendumrong J, Dowell SF, *et al*. The cost of influenza in Thailand. *Vaccine* 2006; 24: 4417-26.

Sungkapalee T, Puntukosit P, Eunsuwan O, Theamboonlers A, Chongsrisawat V, Poovorawan Y. Incidence and clinical manifestations of rotavirus infection among children with acute diarrhea admitted at Buri Ram Hospital, Thailand. *Southeast Asian J Trop Med Public Health* 2006; 37: 1125-31.

Thailand Department of Disease Control. Bureau of General Communicable Diseases. Vaccine coverage. Nonthaburi: Thailand Department of Diseases Control, 2008. (Cited 2009 Oct 13). Available from: URL: http://thaigcd.ddc.moph.go.th/

The World Bank. World Development Report 1993: Investing in Health. 2006. (Cited 2009 Apr 2). Available from: URL: http://www-wds.worldbank.org/external/_default/WDSContentServer/WDSP/IB/1993/06/01/000009265_3970716142319/Rendered/PDF/multi0page.pdf

Theamboonlers A, Bhattarakosol P, Chongsrisawat V, Sungkapalee T, Wutthirattanakowit N, Poovorawan Y. Molecular characterization of group A human rotaviruses in Bangkok and Buriram, Thailand during 2004-2006 reveals the predominance of G1P[8], G9P[8] and a rare G3P[19] strain. *Virus Genes* 2008; 36: 289-98.

Theamboonlers A, Veravigrom M, Yambangyang O, Trairatvorakul P, Chongsrisawat V, Poovorawan Y. The incidence of rotavirus isolates of G genotype in Thailand in 2002-2004. *Acta Virol* 2005; 49: 111-5.

Widdowson MA, Meltzer MI, Zhang X, Bresee JS, Parashar UD, Glass RI. Cost-effectiveness and potential impact of rotavirus vaccination in the United States. *Pediatrics* 2007; 119: 684-97.

World Health Organization (WHO). Choosing interventions that are cost effective: results of cost effectiveness analysis (WHO-CHOICE). Estimates of unit costs for patient services for Thailand. Geneva:WHO, 2008. (Cited 2009 Apr 1). Available from: URL: http://www.who.int/choice/country/tha/cost/en/index.html

World Health Organization (WHO). External review of burden of disease attributable to Rotavirus. 30 November to 1 December 2005. Geneva:WHO, 2005. (Cited 2009 Apr 1). Available from: URL: http://www.who.int/immunization_monitoring/burden/ Rota_virus_Q5_mortality_ estimates_ external_review_report_2006_may.pdf

World Health Organization (WHO). Mortality country fact sheet 2006. Geneva:WHO, 2008. (Cited 2009 Apr 2). Available from: URL: http://www. who.int/whosis/mort/profiles/mort_searo_tha_thailand.pdf

World Health Organization (WHO). WHO-UNICEF estimates of immunization coverage: Thailand. Geneva:WHO, 2008. (Cite 2009 Apr 1). Available from: URL: http://www.who.int/vaccines/globalsummary/immunization/timeseries/tswucoveragebycountry.cfm?country=THA

Wu CL, Yang YC, Huang LM, Chen KT. Cost-effectiveness of childhood rotavirus vaccination in Taiwan. *Vaccine* 2009; 27: 1492-9.