Cost Effectiveness of both (Monovalent and Pentavalent) Rotavirus Vaccines

Her İki (Monovalan ve Pentavalan) Rotavirus Aşısının Maliyet Etkinliği

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Abstract

Objective: Rotavirus (RV) infections constitute a substantial burden in Turkey, particularly in children under 5 years of age. RV vaccines are administered to infants by payment only,and no reimbursement is available. The first aim of this study is to evaluate the cost effectiveness of implementing a national basis monovalent or pentavalent RV vaccination program in target populations.

Material and Methods: A decision tree model was employed using demographic and epidemiological input obtained from study sources conducted before in our region and international literature. Monovalent or pentavalent vaccination was assumed to protect in 83.7% or 90% of severe RV acute gastroenteritis (RVAGE) in children respectively. Costs inputs were obtained from a provincial study conducted in 2007. Univariate sensitivity analyses and Monte-Carlo simulations were performed.

Results: The vaccination program was cost effective and cost saving compared to no vaccination with 85% coverage. Monovalent and pentavalent RV vaccination led to a mean of 2,316 (95% CI: 2.240-2.392) and 2.972 (95% CI: 2.677-3.267) life-years gained (LYG) with 83.7% and 90% efficacy level respectively. Monovalent and pentavalent RV vaccinations avoided 551.820 (95% CI: 539.032; 564.609) and 683,529 (95% CI: 638.906-728.158) individuals with clinical acute gastroenteritis (AGE) cases requiring hospital visits respectively. In the simulation for monovalent and pentavalent vaccines, the cost of RVAGE was 116.1 million TL (€59.2 million) in the non-vaccinated cohort and 35 and 22.5 million TL (€17.8 and 11.5 million) in the vaccinated cohort respectively. The cost of the vaccination program was estimated to be approximately 65.6 and 83.4 million TL (€33.5 and 42.5 million) and the incremental cost was approximately-15.4 million TL (-€7.9 million) and -15.3 million TL(-€. 9.6 million) respectively.

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Özet

Amaç: Rotavirus (RV) enfeksiyonları Türkiye'de özellikle 5 yaş altında önemli bir hastalık yükü oluşturur. Ülkemizde RV aşıları bebeklere devlet katkısı olmadan ücreti ödenerek yapılmaktadır. Bu çalışmanın temel amacı ülkemizde monovalan ve pentavalan RV aşılama programının hedef gruplarda ulusal düzeyde maliyet etkinliğini araştırmaktır.

Gereç ve Yöntemler: Uluslararası literatür verileri ve bölgemizde daha önce yapılan bir çalışmadan kaynaklanan demografik ve epidemiyolojik veriler kullanılarak çalışma modeli oluşturuldu. Monovalan ve pentavalan aşılamanın çocuklardaki ciddi RV akut gastroenteritinden (RVAGE) sırasıyla %83.7 veya %90 oranında koruduğu varsayıldı. Maliyet verileri 2007 yılında yapılan bölgesel bir çalışmadan alındı. Tek değişkenli duyarlılık analizleri ve Monte-Carlo simulasyonları uygulandı.

Bulgular: Yüzde 85 aşı kapsama oranıyla yapılacak olan aşılama programı, hiç aşılamamaya kıyasla maliyet etkin (cost-effective) ve maliyet tasarruflu (cost-saving) bulundu. Monovalan ve pentavalan RV aşılaması sırasıyla RVAGE'den korunmada %83.7 ve %90 etkinlik düzeyiyle, sırasıyla ortalama 2.316 (%95 CI: 2.240-2.392) ve 2.972 (%95 CI: 2.677-3.267) kazanılmış yaşam yılı (life-years gained; LYG) sağladı. Monovalan ve pentavalan RV aşılamaları sırasıyla 551.820 (%95 CI: 539.032-564.609) ve 683.529 (%95 CI: 638.906-728.158) kişide hastane başvurusuna yol açan klinik akut gastroenterit (AGE) vakasını önledi. Monovalan ve pentavalan aşılama için yapılan simulasyon analizinde, RVAGE maliyeti aşılanmamış kohortta 116.1 milyon TL (59.2 milyon€) ve aşılanmış grupta ise sırasıyla 35 ve 22.5 milyon TL (17.8 ve 11.5 milyon€) bulundu. Aşılama programının maliyeti sırasıyla 65.6 ve 83.4 milyon TL (33.5 ve 42.5 milyon€) ve artımlı maliyet (incremental cost) gene sırasıyla yaklaşık -15.4 milyon TL ve -15.3 milyon TL (-7.9 milyon€ ve -9.6 milyon€) bulundu.

Conclusion: This analysis suggests that both monovalent and pentavalent RV vaccinations of children are very cost effective and also cost saving. Therefore, RV vaccination is associated with a positive return on investment from a public payers' perspective and supports the continued recommendation of RV vaccines as well as their full funding in Turkey.
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Key words: Cost effectiveness, rotavirus, vaccine

Sonuç: Verilerimiz Türkiye'de her iki (monovalan ve pentavalan) RV aşılamasının çocuklarda çok maliyet etkin ve aynı zamanda maliyet tasarruflu olduğunu göstermiştir. Bu nedenle RV aşılaması toplumsal bakış açısıyla ekonomik olarak pozitif bir geri dönüş tablosu sunar. Bu çalışmanın sonuçları Türkiye'de rutin RV aşılamasının maliyet etkinlik açısından da uygun olacağını desteklemektedir.
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Anahtar kelimeler: Maliyet etkinlik, rotavirus, aşı

Introduction

Rotavirus (RV) is the leading cause of severe acute gastroenteritis (AGE) in infants and young children worldwide. It has been calculated that there are on average 700000 cases of RV related outpatient AGE cases and 87000 hospitalized cases in Europe and there are nearly 500000 RV related outpatient cases annually in the United States (1). It is possible that there are some differences in these figures with respect to the level of development of the countries. Nearly 170000 children under five years in the United States were hospitalized due to diarrhea in the last two years and this figure has been constant for the last twenty years. RVAGE constitute nearly one third of the diarrhea-related hospitalizations and 55000 annual hospitalizations are estimated due to RVAGE (2, 3). In a study done in the United States, 4.9% of the hospitalized children under five years old are hospitalized with AGE. Moreover, all the RVAGE related hospitalizations may comprise 2.5% of the pediatric hospitalizations (3, 4). The rate of RV positivity in AGE may vary according to the age of the patient, the season in which the study is conducted as well as the severity of the AGE (hospitalized or outpatient basis). Vaccination is thought to be the most effective approach to reduce the worldwide burden associated with RVAGE and the development of a safe effective vaccine has been given priority by WHO (5, 6).

There are many studies on cost effectiveness on RV vaccines (7-10). However, after reviewing the literature, we could not find any cost effectiveness study comparing both (monovalent and pentavalent) vaccines (or vaccination schedules) simultaneously in a single study. This cost-effectiveness study aims to evaluate the economic burden of RV infections among children in Turkey and to assess the public health and economic benefits of integrating monovalent or pentavalent RV vaccines into national vaccination program.

Material and Methods

This study was carried out on a multi-centered basis with the participation of the four largest pediatric hospitals in Bursa city where these hospitals dealt with nearly 90% of the population (especially on the outpatient basis) in the city.

Since only the children between the ages of 0 to 14 years could legally be admitted to these hospitals during this study, all data were assessed as the age group of 0 to 14. The study lasted for one year. An informed consent was taken from the legal guardians of the children. The study was approved by the Research Ethics Committee of the Medical Faculty, Uludağ University (23 June, 2009, 2009-12/32). The children were diagnosed with RVAGE by detecting RV antigens in their fresh stool samples by using RV monoclonal antibody test kits (Biomerineux, France). The children who had received RV vaccines before were excluded from the study. Clinical and other laboratory findings were also studied, but not included in this study.

Model specification and parameters used for the analysis

A decision-analytic model was developed to estimate the effectiveness and cost-effectiveness of a RV vaccination program in the childhood population (<59 months old) with the opportunity to focus the analysis on a risk-based vaccination program. Each hypothetical cohort, vaccinated or non-vaccinated, was designed to reflect the Turkish children population (0-59 months of age). Herd immunity of RV vaccines was not taken into account in the model.

For each cohort, the number of life years experienced and the costs of RV infections were calculated and compared. To compare the costs and health consequences of vaccination versus non-vaccination, an incremental cost-effectiveness ratio (ICER) was estimated as the incremental cost per life year gained (LYG). Since there are no health utility data available in Turkey, the quality of life gained due to vaccination has not been evaluated. As recommended by the WHO health economic guidelines on vaccination, a discounted rate of 3% on costs and lives was applied in the base case analysis. The base case was conducted from a public payer perspective, i.e. all costs collected and used in the model were those borne by the government.

Demographic and epidemiological model inputs

Representative demographic data on the Turkish population was based on the national statistics data from June 2008 (11). It was assumed that all the children (0-59 months old) were at risk from RV infection (12). The all-cause mortality rate was obtained from national data (13, 14). International RV incidence rates and case-fatality rates were used as there were no sufficient Turkish data available (Table 1). However, the proportion of RV gastroenteritis (RVAGE) conducted in various part of Turkey were consistent with these international data (15). Incidence rates and case-fatality rates related to RVAGE were assumed to be similar between both developed and developing countries. Hospitalization rates were calculated as 28% children, based on the total RV gastroenteritis cases from a study conducted by the Uludağ University, Faculty of Medicine, Department of Pediatrics (Table 1) (16).

Vaccination model inputs

A two-dose vaccination program for monovalent RV vaccine and three doses vaccination program for pentavalent RV vaccine were simulated in both populations. Vaccination coverage was assumed to be 85% in the target population.

In our analyses, the values for vaccine effectiveness were based on previous studies. In a cohort study from Latin American countries, monovalent RV vaccine afforded sustained high protection (80.5%; 95% CI: 71.3-87.1) against severe RVAGE during the first 2 years of life (17). In six industrialized European countries, protective efficacy rates were in general greater than those in the Latin American trial (18). Vaccine efficacy against any RVAGE until the end of the first RV season was 87.1% (95% CI: 80-92) and protection against severe RVAGE was 95.8% (95% CI: 89.6-98.7). Monovalent RV vaccine also reduced hospitalizations of all-cause gastroenteritis by 75%. In this trial, monovalent RV vaccine demonstrated a significant cross-protection (86%) against G2P RV strains, while efficacy against the G2P serotype was 38.6% in Latin America (19). In the stochastic analysis for monovalent and pentavalent vaccines, we used an efficacy range of 76.8-88.9% (average 83.7%) and 74.0-96.0% (average 90%), respectively for children (7, 18, 20). The efficacy of pentavalent vaccine was evaluated against severe RVAGE and against RVAGE-associated hospitalization but also against RVAGE of any severity. We have assumed that efficacy of the pentavalent vaccine is 90% for reduction in hospitalizations and emergency visits and 85% for reduction in at-home visits (7).

The total duration of effectiveness was fixed conservatively at 10 years (8). Vaccination costs included the vaccine price and the procedure fees for vaccine administration were borne by the Ministry of Health. Taking into consideration this local regulation, the total public vaccination's presumed cost used was 30 TL per dose (€15.3, mean exchange rate 2010: 1.96), and the total cost of monovalent and pentavalent vaccine per child was 60 TL (€30.6, for two doses) and 90 TL (€45.9, for three doses) per child respectively. According to the expectations of the Ministry of Health, we assumed that the Ministry of Health can provide the rotavirus vaccines with considerable cost reduction on the national population basis. The cost of one dose rotavirus vaccine (both monovalent or pentavalent vaccines) would be 1/5 to1/8 of market prices (in Turkey, the marketing prices were 114 TL per dose for pentavalent vaccines and 142 TL per dose for monovalent vaccines) in regard of previous practices of other vaccines, such as, MMR, prevenar-7 and prevenar-13. These vaccines were recently included into the Turkish National Vaccination Schedule. Therefore, in our economic model, we accepted the cost of each vaccine dose as 30 TL (total vaccination costs were accepted as 60 TL for monovalent two vaccines and 120 TL for pentavalent three vaccines). The other costs, such as physician visiting costs were not included in the evaluation.

All vaccine inputs used in the modeling are presented in Table 1.

Cost of illness data

Since data on the cost of RV infections in Turkey were not available in the literature, they were collected from a

Table 1. Epidemiological inputs used in the model

Item	Base case	Source/comment
Estimated annual incidence rate of RVAGE by age group	1-11 months 9.18%	25
	12-23 months 9.16%	
	24-35 months 3.96%	
	36-47 months 1.05%	
	48-59 months 1.05%	
Hospitalization rates	28 per 100 children under fifteen years of age with gastroenteritis	16
RVAGE case fatality rate	0.0034	12

prospective study about confirmed RV gastroenteritis in Bursa. The perspective was from that of the public payers. Direct outpatient and inpatient costs were the costs of laboratory tests, medical examinations and treatments as well as the costs associated with the length of stay in the general ward.

Variables were retrieved from face-to-face discussions in the study. Costs were calculated based on fiscal control formal health institution price tariff.

Sensitivity analyses

Under base-case assumptions, parameter values were varied individually in a one-way sensitivity analysis to identify whether those variables with a mean value had a major impact on the cost-effectiveness results. All inputs were tested and their values are shown in Table 1 and 2. Concerning the discount rate on lives, 0% and 5% were used respectively for the low and high value.

In addition, parameters listed in Tables 1 and 2 (RV incidence, RVAGE case fatality rate, vaccine efficacy against RVAGE for children under five) were varied simultaneously in probabilistic sensitivity analyses, where random draws from each parameter's distribution were performed and the effectiveness and cost-effectiveness calculated.

Univariate sensitivity analyses and Monte-Carlo simulations were performed (21). This procedure was repeated 1000 times. Parameter distributions were chosen based on the parameter type and level of certainty. Those parameters whose distributions were least certain (epidemiological data from international literature) were assigned uniform distributions, where all values in a range were equally likely to be chosen. Parameters whose distributions were most certain (cost data from a local cost of illness study) were assigned log-normal distributions.

Results

A total of 5988 children with AGE visited the hospital on an outpatient basis. This comprised 1.1% of the whole outpatient visits. Annual AGE incidence in the 0-14 age group was found to be 1.7%. The hospitalization rate of <5 years AGE was found as 100/10 000. The AGE related hospitalizations comprised 5.7% of all hospitalizations.

RVAGE comprised 21% of the outpatient AGE cases. The rate of RV positivity in the outpatient AGE was found to be 27.7%, 25%, 22.9% and 15.8% in <1 year, <2 years,<5 years and 5-14 years, respectively.

The hospitalization rates of RVAGE cases were estimated as 22.5% in <1year, 27% in <2 years, 20.5% in <5 years. The general RV positivity rate of hospitalized AGE was 28.5%. Considering the age groups in hospitalized AGE, the RV positivity rate was found to be 29.7%, 30.7%, 29.4% and 23% in <1 year, <2 years, <5 years, respectively. The annual incidence of RVAGE related hospitalization was found as 629/100 000 in <1 year, 553/100 000 in <2 years, 293/100 000 in <5 years. The 41% of the hospitalized RVAGE cases were <1 year, 73% <2 years and 88% <5 years.

Cost of RV Infections

In the study, a total of 105 outpatient and 368 inpatient gastroenteritis cases with confirmed RV infection were included from January 2007 to December 2007. The hospital costs of the patients were calculated taking into account of official hospital bills. The hospitalized RV infection cases have a sharp decrease in Summer months (Figure 1). However, mean costs of inpatient cases were similar although the mean cost slightly

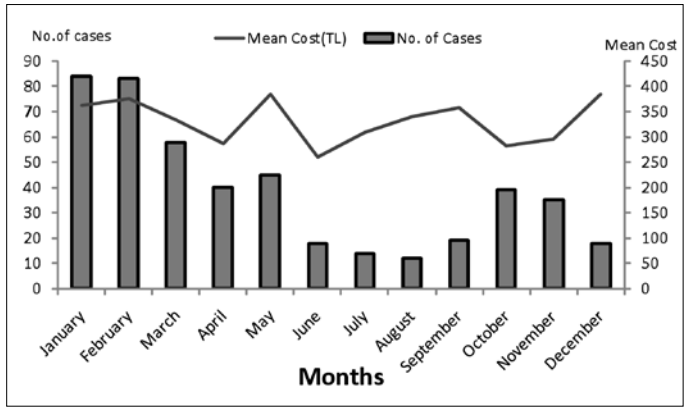

Figure 1. Distribution of number of cases in hospital by months and the mean cost per patient of hospitalized cases (TL)

Table 2. Vaccination inputs used in the model*

Item	Base case	Range	Source/comment
Vaccine efficacy against RVAGE			
For monovalent vaccine	83.7%	76.8-88.9%	18
For pentavalent vaccine	90%	74.0-96.0%	7
Vaccination coverage rate assumed	85%	85%	13
Vaccination cost	TL 30 (€15.3)/per dose	TL 30 (€15.3)/per dose	
*The mean exchange rate 2010 was used: 1€=1.96 TL			

decreased from 384 TL (€195.9) in May to 261 (€133.2) in June. There was no significant difference between mean costs of hospitalized cases on a monthly basis, after performing the Kruskal Wallis test.

Cost Effectiveness Analyses

In regard to the base case scenario, direct medical costs with and without hospitalization are shown in Table 3. In the base case scenario where a routine RV vaccination program is implemented in Turkey for children, vaccination markedly reduced the number of episodes of RV disease (Tables 3, 4): In the 0-14 age group, the estimated number of RVAGE cases avoided due to monovalent RV vaccination would be a population of 551.820 (95% CI: 539.032; 564.609). They would be clinical RVAGE cases and would require a visit to the hospital, if they weren't

Table 3. Direct medical inpatient and outpatient costs and combined values

	No. of cases	Direct medical mean cost±Standard deviation (TL)
Without hospitalization (outpatient)	819,753	72.9 ±26.1 per case
With hospitalization (inpatient)	2,401	287.7±183.1 per case
* The mean exchange rate 2010 was used: 1 =1.96 TL		

Table 4. Base case results of the cost-effectiveness analysis of RV vaccination in children (target coverage rate assumed to be 85%)*

	Non-vaccinated (95%CI)	Vaccinated (95%CI)
Number of episodes		
For monovalent vaccine	802,142 (783.548; 820.737)	250,322 (244.516; 256.128)
For pentavalent vaccine	802,142 (783.548; 820.737)	144,642 (73.990; 168.191)
Number of LYG	--	
For monovalent vaccine	--	2,316 (2.240; 2.392)
For pentavalent vaccine	--	2,972 (2.677; 3.267)
Costs, in TL		
Cost of RV infections		
For monovalent vaccine	116,074,218 (111.648.483; 120.499.954)	35,033,493 (33.700.919; 36.366.0684)
For pentavalent vaccine	116,074,218 (111.648.483; 120.499.954)	22,582,796 (20.026.477; 25.139.116)
Vaccination		
For monovalent vaccine	-	65,659,383 (65.659.383; 65.659.558)
For pentavalent vaccine	--	83,427,266 (83.426.457; 83.428.076)
Cost reduction thanks to vaccination, in TL*		
Incremental costs		
For monovalent vaccine	-15,381,499 (-18.475.514; -12.287.484)	
For pentavalent vaccine	-15,255,788 (-26.413.569; -4.098.006)	
Cost effectiveness analysis		
ICER (TL/LYG)		
For monovalent vaccine	ICER = 3,248 TL/Life Year Gained (CI 95% = 1,648 ; 4,847)	
For pentavalent vaccine	ICER = 2,350 TL/Life Year Gained (CI 95% = 1,191; 3,662)	
*The mean 2010 exchange rate was used: 1 =1.96 TL		

vaccinated. Similarly, the number of episodes avoided by pentavalent RV vaccine was 683.529 (95% 638.906-728.158). The number of life years gained (LYG) by monovalent vaccination was 2.316 (95% CI: 2.240-2.392) and 2.972 (95% CI: 2.677-3.267) in children with the pentavalent vaccine.

In the simulation for monovalent vaccine, the cost of RVAGE was 116.1 million TL (€59.2 million) in the non-vaccinated cohort and 35 million TL (€17.8 million) in the vaccinated cohort. The cost of the vaccination program was estimated to be approximately 65.6 million TL (€33.5 million). The incremental cost was approximately -15.4 million TL (-€7.9 million). While we carried out simulation for pentavalent vaccine, the cost of vaccination and incremental cost were found 83.4 million TL (€42.5 million) and -15.3 million TL (-€.9.6 million) respectively. The strategy of 'vaccinate all children' using both monovalent and pentavalent was cost saving compared with the non-vaccination strategy. In child populations, the overall cost of RV infections avoided was therefore greater than the overall cost of a vaccination program. The vaccination program was found cost saving in the case of a routine vaccination in children in Turkey.

Sensitivity Analyses

In the univariate sensitivity analysis, we evaluated the individual effects of epidemiological and vaccination parameters on the effectiveness of the vaccination strategy using the minimum and maximum of the input ranges. These analyses suggested that the factors having the greatest impact on effectiveness results were the case-fatality rate, the incidence rates and vaccine effectiveness of RV infection. Moreover, the influence of costs discounting was also evaluated.

Since the costs incurred from the prospective study were realistic, we also ran the model using the optimal cost of illness. The incremental cost for monovalent and pentavalent vaccines were estimated at 15.4 and 15.3 million TL (€7.9 and 7.8 million) respectively. In this case, the cost effectiveness ratio for monovalent vaccine was ICER=3.248 TL (€1.657)/Life Year Gained and for pentavalent vaccine ICER was calculated 2.350 TL (€1.199)/ Life Year Gain. Both of them are lower than the national GDP per capita in Turkey (10.436 USD per capita in 2008 i.e. around 15.800 TL or €8.061 (22). Therefore, a vaccination program can be considered as very cost-effective.

Discussion

In this simulation, the costs of RV disease that were avoided by vaccination were greater than the cost of a vaccination program, thus indicating that both RV vaccination strategies were very cost effective and cost saving as well. Cost saving is generally defined as a concept when any implementation results in a cost lower than the historical cost or the projected cost. On the other hand, cost-effectiveness analysis is a kind of economic analysis that compares the outcome of two or more implementations in terms of cost and desired effects. Cost effectiveness studies constitute valuable data for the decision-makers in how to manage the limited healthcare sources. It is sometimes observed that the terms *cost-saving* and *cost-effective* are mistakenly used interchangeably. Preventive care services decrease costs and therefore, are cost-saving. When we assess benefit-cost comparison, if the benefits are sufficiently large compared to the costs, the implementation will be cost-effective, despite no reasonable money saving. In this context, something that is cost-effective is not necessarily cost-saving. For example, many childhood vaccinations are the rare examples that are essentially cost-saving. In contrast to the studies carried out previously on this issue, we evaluated both monovalent and pentavalent vaccination schedules in the same period and they had comparable figures in this regard. The results of our analyses are consistent with other analyses performed on RV monovalent or pentavalent vaccines, which demonstrated that a RV vaccination program is likely to be cost effective (9). RV vaccinations were previously reported to be cost-effective across various European countries (7). In addition, a cost-effectiveness analysis for RV vaccination in England and Wales showed that routine vaccination of all children appeared to be cost effective. However, their results were dependent on the uncertainties around vaccine effectiveness estimates and the number of hospitalizations and deaths attributable to RVAGE (10).

The present study does have limitations, including the large standard deviation associated with the costing data. The data should accurately represent the situation in clinical practice as they were obtained from resources consumed throughout the year in which the study was conducted. In comparison of RVAGE costs of several studies, the costs of illness found in our study have turned out to be less. With regards to the rules and regulations in effect in Turkey, the public payer is responsible for nearly 90% of population-based health costs, and the public payer cost is usually cheaper than the private hospitals in Turkey. Indeed, they are similar to Mexico cost data (23). In that study, univariate sensitivity analyses were performed to evaluate the impact of cost data on the cost-effectiveness results. With much lower costs for RVAGE, RV vaccination was not found to be cost-saving; however, it turned out to be a very cost-effective strategy, as mentioned above (23).

According to the principle of reimbursement system in Turkey, ill patients should first go to the public facility or

family practitioners unless they have severe or emergency illnesses. If the costs of RV infection are retrieved from a university hospital, costs are expected likely to be higher than in a public hospital due to relatively higher prices, the availability of a greater number of procedures and more advanced technology. Our study was carried out not only at an university hospital but included two state hospitals and one private hospital as well. Thus, this study covered three types of hospital (university, state and private hospitals) costs available in Turkey and represented an average cost of gastroenteritis due to RV. However, it could have been better adjusted according to the distribution of cases in Turkey by private, state and university hospitals. This can be one of the limitations of our study.

In the present cost-effectiveness analysis, only RV related AGE cases were considered. As RV can be also responsible for other clinical conditions such as serious complication with hepatic transaminase elevation, bleeding disorders with prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT) and cerebral hemorrhagic infarct, which have an important social and economic burden, this calculation produces a conservative estimate of the cost of RV infection (24). Furthermore, outpatient costs after hospitalization to monitor malnutrition or secondary bacterial infection were not available for gastroenteritis. Inclusion of outpatient costs would probably have increased the overall cost of RV infection, and thus, the benefits of vaccination.

It should be noted that the simulations were two doses for monovalent vaccine, and three doses for pentavalent vaccine. In addition, the simulation assumed that an age-based vaccination policy resulted in a higher vaccine coverage rate. Indeed, an age-based strategy was shown to be easier to implement than a risk-based strategy (such as implementation in squatter area in big cities) for the vaccination program.

Our model did not take into account the protective effect (i.e., herd immunity). However, there may be an increase of the incidence of serotypes not covered by the already-in-use vaccines in children. At present, Turkey has not undertaken universal immunization of infants with RV, although it is considering the implementation of such a program. The future effect of a RV vaccination program in Turkey will depend on the Vaccine Coverage Rate (VCR) and serotype prevalence and their clinical importance.

In regard of the costs obtained from the study, we also ran the model using the most conservative cost of illness. In this conservative case, the cost effectiveness ratio was 3.248 TL (€1.657)/LYG for monovalent vaccine and 2.350 TL (€1.199)/LYG for pentavalent vaccine, which is largely lower than the national GDP (gross domestic product) per capita in Turkey (10.436 USD per capita in 2008 i.e. around 15.800 TL or €8.061 in December 2009 exchange rate) and therefore cost-effective. These results have showed that vaccination remains economically attractive and cost-effective even if the incidence of RV disease has decreased among children. Indeed, the lower RVAGE incidence in vaccinated children simply means that the Cost Effectiveness (CE) ratio must increase.

The current VCR of RV vaccines in Turkey is unknown. The reasons for this may involve factors involving intervention by public health organizations or the perspective of physicians and the general public on RV vaccination. Physicians and the general public may have a low awareness of the risks of RV disease or the benefits of vaccination. Data from the active promotion of the benefits of RV vaccination were not included in this study since the results were difficult to evaluate. However, costs saved by a RV vaccination program could be reinvested in the education of physicians and the public on the benefits of vaccination.

The indirect medical and/or non-medical costs for the RVAGEs were not included in this study. These indirect costs can be other indirect medical costs (such as secondary nosocomial infections, antipyretics, antiemetics, probiotics, etc) or indirect non-medical costs (costs of baby nappies, specific infant formula milks for gastroenteritis, transportation costs, loss of work-days of parents, etc.). They may even exceed the direct medical costs of RVAGE and may add extra beneficial and positive effects on cost effectiveness of RV vaccination.

Conclusion

This model has suggested that a RV vaccination program in Turkey will be cost saving and very cost-effective. Ithas also been shown to be the case for both RV vaccines (monovalent vaccine for 2 doses and pentavalent vaccine for 3 doses). These results are consistent with the previous studies conducted on RV vaccines. Vaccination of the children with RV is not publicly funded in Turkey. Because of this, the VCR of RV vaccines in Turkey has been minimal and its increase is to improve the public health. In addition, an awareness campaign to promote the benefits of RV vaccination in the children should be undertaken on a nation-wide basis in Turkey, mainly targeting parents and the medical community. The cost saved as a result of RV vaccination can be appropriately used to promote the benefits of vaccination and thereby raise the VCR and utilize the available health resources more productively.

Conflict of Interest
No conflicts of interest were declared by the authors.

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