

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/jval

On Discounting of Health Gains from Human Papillomavirus Vaccination: Effects of Different Approaches

Tjalke A. Westra, MSc^{1,*}, Mehraj Parouty, MSc², Werner B. Brouwer, PhD³, Philippe H. Beutels, PhD⁴, Raina M. Rogoza, MSc⁵, Mark H. Rozenbaum, MSc², Toos Daemen, PhD¹, Jan C. Wilschut, PhD¹, Cornelis Boersma, PhD², Maarten J. Postma, PhD^{2,6}

¹Department of Medical Microbiology, Molecular Virology Section, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; ²Unit of PharmacoEpidemiology and PharmacoEconomics (PE²), Department of Pharmacy, University of Groningen, Groningen, The Netherlands; ³Department of Health Policy and Management, Institute for Medical Technology Assessment, Erasmus University Rotterdam, Rotterdam, The Netherlands; ⁴Centre for Health Economics Research and Modeling Infectious Diseases (CHERMID), Vaccine and Infectious Disease Institute (VAXINFECTIO), University of Antwerp, Antwerp, Belgium; ⁵Market Access, Reimbursement and Pricing, Optum Insight, Burlington, Ontario, Canada; ⁶Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

ABSTRACT

Objectives: Discounting has long been a matter of controversy in the field of health economic evaluations. How to weigh future health effects has resulted in ongoing discussions. These discussions are imminently relevant for health care interventions with current costs but future benefits. Different approaches to discount health effects have been proposed. In this study, we estimated the impact of different approaches for discounting health benefits of human papillomavirus (HPV) vaccination. **Methods:** An HPV model was used to estimate the impact of different discounting approaches on the present value of health effects. For the constant discount approaches, we varied the discount rate for health effects ranging from 0% to 4%. Next, the impact of relevant alternative discounting approaches was estimated, including hyperbolic, proportional, stepwise, and time-shifted discounting. **Results:** The present value of health effects gained through HPV vaccination varied strongly when varying discount rates and approaches. The application of the current Dutch guidelines resulted in a present

value of health effects that was eight or two times higher than that produced when using the proportional discounting approach or when using the internationally more common 4% discount rate for health effects, respectively. Obviously, such differences translate into large variations in corresponding incremental cost-effectiveness ratios.

Conclusion: The exact discount rate and approach chosen in an economic evaluation importantly impact the projected value of health benefits of HPV vaccination. Investigating alternative discounting approaches in health-economic analysis is important, especially for vaccination programs yielding health effects far into the future. Our study underlines the relevance of ongoing discussions on how and at what rates to discount.

Keywords: discounting, health gains, HPV vaccination, QALY.

Copyright © 2012, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

Introduction

In economic evaluations of health interventions, typically a comparison between competing programs is made [1–3]. By comparing two or more programs, differences in costs and health outcomes can be estimated. The latter are often expressed in quality-adjusted life-years (QALYs) gained. This comparison can be summarized in the incremental cost-effectiveness ratio (ICER), expressed as incremental costs per QALY gained. This ICER is calculated by dividing the estimated difference in costs by the estimated difference in health outcomes. By relating the ICER to a relevant threshold, health care decisionmakers can subsequently judge the desirability of funding a certain health intervention.

To secure the quality and comparability of health-economic evaluations, many countries have established national guidelines for such analyses. These guidelines, for example, specify the appropriate study perspective and indicate how specific costs and health effects should be measured and valued. Furthermore, these

guidelines often specify how future costs and health benefits need to be weighed relative to current costs and benefits (i.e., how to discount and at which discount rate). While all country-specific guidelines known to us advise the use of the same stationary (or constant) discount model, the recommended discount rates for costs and health outcomes differ from one country to the next. Table 1 gives an overview of the discount rates applied for costs and health outcomes for a number of Western countries [4]. Broad consensus exists on the discounting of monetized costs and benefits. By contrast, which methods to use to discount nonmonetized health outcomes relative to money has been a topic of considerable controversy for decades.

Vaccination programs against infectious diseases, but also other preventive programs, often involve dominant intervention costs occurring years before the health effects emerge. Although, to a certain degree, this is intervention specific and disease specific, generally the discounting method and rate do determine the weight that future health outcomes of vaccination programs re-

* Address correspondence to: Tjalke A. Westra, Department of Medical Microbiology, Molecular Virology Section, University Medical Center Groningen, University of Groningen, HPC EB88, PO Box 30.001, Groningen 9700 RB, The Netherlands.

E-mail: t.a.westra@umcg.nl.

1098-3015/\$36.00 – see front matter Copyright © 2012, International Society for Pharmacoeconomics and Outcomes Research (ISPOR).

Published by Elsevier Inc.

doi:10.1016/j.jval.2012.01.005

Table 1 – Country-specific discount rates for costs and health outcomes.

Country	Discount rate (%)	
	Costs	Health
Austria	5	5
Belgium	3	1.5
Canada	5	5
England and Wales	3.5	3.5
France	0, 3, 5	0, 3, 5
Germany	3	3
Switzerland	2.5, 5, 10	2.5, 5, 10
Sweden	3	3
The Netherlands	4	1.5
United States	3	3

ceive in an evaluation [5,6]. With costs being borne in the present and health effects often far in the future, discounting has a large impact on the final cost-effectiveness ratio of such programs, increasing the ratio compared with the undiscounted ratio. One of the most extreme examples relates to vaccination against human papillomavirus (HPV), for which the major health gains of interest start to occur approximately 30 years after the initial vaccination through the prevention of cervical cancer and associated morbidity and mortality. For instance, Brisson et al. [7] determined the age-specific undiscounted and discounted net present value of HPV vaccination. Specifically, these authors showed that especially in the older age groups health gains of preventing cervical cancer are strongly affected by discounting. Consequently, the cost-effectiveness of HPV vaccination, which has recently gained considerable attention in many countries particularly with regard to the issue of whether or not to fund (large-scale) vaccination programs, is highly sensitive to discounting [5].

The ICERs of preventive interventions such as vaccination are so heavily influenced by discounting [8] that the uncertainty related to methodological disagreement between economists on this issue can lead to opposite conclusions and decisions. Therefore, some researchers have argued that specific discounting rules should be applied for preventive interventions or for exploring the decision uncertainty related to discounting [9]. Recently, Beutels et al. [10] suggested that alternative discounting approaches using rates decreasing over time, such as hyperbolic or stepwise discounting, should be applied in sensitivity analyses, which was previously suggested by Bleichrodt and Brouwer [11]. This should then provide an insight into whether and to which extent the choice of the discounting procedure (over which economists disagree) would influence the policy decision based on the economic evaluation. Naturally, it is more likely for preventive interventions (with long-term health impacts) than for curative interventions (with short-term health impacts) that the choice of one specific discounting method could be decisive in judging the interventions to be cost-ineffective or cost-effective.

In this article, we aimed to provide an overview of alternative discounting approaches proposed in the literature. Furthermore, we investigated the impact of adopting these different discounting approaches in the context of the economic evaluation of a particular preventive program (i.e., prophylactic HPV vaccination in the Netherlands [5]). Given that the health outcomes of HPV vaccination for the prevention of cervical cancer occur several decades after the initial vaccination (see Figure 1), this preventive intervention provides an excellent example—possibly one of the most extreme ones—to demonstrate the influence of different discounting approaches.

Methods

To investigate the influence of different discount rates and approaches, we used a previously published in-house Markov model for HPV infection [5]. This model simulates the transmission of HPV infection through cervical intraepithelial neoplasia stages to cervical cancer. By simulating a cohort twice, once as an unvaccinated cohort and once as a vaccinated cohort, the age-specific health gains of HPV vaccination can be estimated by considering the differences between both simulations.

We investigated five discounting approaches and focused on changing discount rates and approaches for health effects. We did not vary the discount rate for costs in the current study (which will be set at a constant level of 4% according to Dutch guidelines), and thus emphasize the differences in the net present value of health effects depending on different discounting approaches and rates. Below we summarize the different approaches used for discounting of health effects that were considered in this study.

Constant discounting approach

The constant (or stationary) discounting approach (Equation 1) is well founded in economic theory and reflects the most generally used and accepted discounting approach for future costs and health outcomes in health-economic evaluations [12]. In the constant discounting approach, future costs and health outcomes are devalued at a constant rate. So, both future costs and health outcomes are exponentially devalued to the moment the intervention (e.g., the vaccination) took place. The magnitude of the discount rate for costs is commonly informed by the rate of return on risk-free government bonds, in line with the societal perspective that is often used. Furthermore, the discount rate for costs is usually determined by this interest rate after correcting for the deflator (i.e., the real interest rate is used instead of the nominal rate). A discount rate of 3% to 5% for costs is most often used internationally (Table 1). In the Netherlands, this discount rate is 4%. Most countries prescribe the same discount rate for health effects (i.e., uniform discounting; e.g., 4% for costs and 4% for health effects). The reason for this is especially that it has been argued that inconsistencies might occur if discounting is done nonuniformly or differentially [13]. Yet, others have rejected the idea that differential discounting would be impossible based on grounds of consistency [8,9]. Indeed, it has been argued that health outcomes could well be discounted with a lower discount rate than costs, without risking inconsistency [14–20]. The justification of a lower (but still con-

Cervical cancer is the second most common cancer worldwide. Infection with the Human PapillomaVirus (HPV) is a prerequisite for cervical cancer, and the persistence of the infection is especially important. In particular, infection with one of the oncogenic types of HPV may develop into cervical intraepithelial neoplasia (CIN) of grades I – III and ultimately into invasive cancer. Major oncogenic serotypes are 16, 18, 31, 33, 45, and 52. Of these serotypes, HPV 16 and 18 have shown to be responsible for approximately 70% of cervical cancer cases worldwide.

In the Netherlands, HPV infection peaks are found in women aged 20 – 25 years. Although most women are able to clear the infection within one year, some of them will develop persistent infection. Women can develop CIN I – III and cervical cancer after some years of persistent infection. In the Netherlands the average age of cervical cancer is estimated between 40 – 45 years.

Currently, highly effective prophylactic HPV vaccines are available. HPV vaccines are most effective if administered to women who are HPV negative. Therefore, women should be vaccinated before they become sexually active. Most developed countries decided to implement HPV vaccination of girls aged 12-years in National immunization programmes.

Health benefits following HPV-vaccination comprise of prevention of cervical intraepithelial neoplasia or development of cervical cancer. These health benefits are expected to occur approximately 20 and 30 years after the initial immunization, respectively.

Fig. 1 – Pathogenesis of cervical cancer.

stant in time) discount rate for health outcomes lies in the growth of the value of health effects over time, which is not otherwise accounted for in economic evaluations. The difference between the discount rate for costs and effects would be the expected growth rate in the value of health. In the Netherlands, this growth rate has been estimated to be 2.6% [21]. With a discount rate of 4% for costs, this would imply an appropriate discount rate of $4.0 - 2.5 = 1.5\%$ for effects. In the Netherlands, a discount rate of 1.5% for health effects is indeed currently used in differential discounting. In the present study, to illustrate the impact of the discount rate for health outcomes, we applied different discount rates for health, specifically 0%, 1.5%, 3%, and 4%, while the discount rate for costs was set at 4%.

$$a(t) = \frac{1}{(1+r)^t} \quad (1)$$

where $a(t)$ is the weight attached to time t and r is the discount rate.

Empirical discounting approaches

In contrast to the constant discounting approach, empirical studies have shown that the individuals' time preference may decline over time, both from an individual and a societal perspective [22-25]. This was recently confirmed for health effects in a meta-regression analysis by Asenso-Boadi et al. [25]. In particular, the time preference for a short-term delay (i.e., a 5-year delay) was approximately 25%, which decreased to approximately 3.5% for a long-term delay (i.e., a 100-year delay). Alternative discounting approaches have been proposed to better reflect such observed time preferences. Two prominent examples are hyperbolic (Equation 2) and proportional (Equation 3) discounting [26-28]. Applying these discounting approaches obviously still implies that future health effects are weighed less than current ones, although at a decreasing incremental rate. This could more appropriately capture the exact nature of time preference as conceived by the public in the real world.

$$a(t) = \frac{1}{(1+gt)^{hg}} \quad (2)$$

$$a(t) = \left(\frac{b}{b+t} \right)^\gamma \quad (3)$$

Hyperbolic discounting (Equation 2) has been proposed by Loewenstein and Prelec [28]. In Equation 2, h reflects the individual's preference for the future or timing in general. An individual does not have any time preference (i.e., a discount rate of 0) if $h = 0$; by increasing h , the preference for the present increases. Parameter g determines how much the function differs from the constant discounting model [29], with $g = 1$ actually representing the constant discount model. Proportional discounting (Equation 3) has been proposed by Harvey [27]. In Equation 3, b reflects the magnitude of the time preference and γ determines the shape of the curve. Initially, Harvey suggested that γ should be 1, but others have introduced different values for γ . For example, Cairns and van der Pol [24] estimated that the proportional discounting model would fit empirical data best if γ would be set at 1.5.

Here, the proportional and hyperbolic discounting approaches were fitted to time preference rates as reported by Asenso-Boadi et al. [25] by varying the values of the variables to minimize the sum of squares and maximize the explanatory power (reflected in r^2) [25]. In particular, for the hyperbolic discounting approach, the values of h and g were estimated at 0.32 and 0.29, respectively. For

the proportional discounting approach, the values of b and γ were estimated at 3.4 and 1.1, respectively.

Stepwise approaches

In the stepwise discounting approach, a constant discount rate is used during a specified period, but this is lowered in subsequent consecutive time periods. (It thus resembles a discontinuous hyperbolic discounting function.) Stepwise discounting was previously recommended by the UK treasury (in 1996), and it has also been mentioned as one of the options for discounting in economic evaluations in at least two recent articles [10,19,30]. For the United Kingdom, the time intervals after which the discount rate decreases at 0.5% were based on empirical data [31], and a normative framework was the starting point of the analysis. We applied the rates recommended by the UK treasury (i.e., 3.5% for years 0-30, 3% for years 31-75, 2.5% for years 76-125, 2% for years 126-200, 1.5% for years 201-300, and 1% thereafter). Note, in the static HPV model that we used, the time horizon of our analyses was set at 100 years, and so the minimum discount rate applied was 2.5%.

Time-shifted approach

Specifically for vaccines, in an attempt to appropriately value the outcomes of evaluations of preventive interventions, it has been proposed that the health outcomes might be discounted from the moment of risk reduction (i.e., averted infections) instead of from the moment that health is actually gained [32,33]. Bos and colleagues argued that in the case of a vaccination program health gains of preventing infections are undervalued because of discounting, in particular for some infectious diseases with a long-term delay between the initial infection and disease development. To account for this, they recommended the time-shifted discounting approach, by which health outcomes are discounted from the moment the infection is prevented rather than from the moment each individual life year or QALY is gained. Although this method has been used by others as a pragmatic discounting approach, an exact underpinned normative rationale for it has not been given. Furthermore, this method can easily be criticized because the individuals' time preference in the period after an infection is prevented is ignored. Still, we used this method with two discount rates (4% and 1.5%) in the period in which discounting is required according to the method. Specifically, QALY losses due to cervical cancer were discounted only in the period between vaccination and the moment of HPV infection in the time-shifted approach (i.e., all QALY losses were implicitly assumed to have been prevented at the same time as the causal factor, an HPV infection, was prevented).

Table 2 summarizes the five approaches introduced above.

Results

All five discounting approaches were applied to the health outcomes of a Dutch HPV model. This model predicts the incidence of cervical intraepithelial neoplasia and cervical cancer incidence with and without HPV vaccination, reflecting the current Dutch situation. The implementation of HPV vaccination for the full cohort of 12-year-old Dutch girls (i.e., cohort size was set at 100,000) resulted in an undiscounted lifetime gain of 2907 life-years or 3462 QALYs. The total undiscounted costs of implementing HPV vaccination to the Dutch National Immunization program ("Rijksvaccinatieprogramma") were €31.5 million (€30.9 million discounted) and resulted in €11.5 million undiscounted cost offsets (€2.8 million discounted).

The application of the different discounting approaches for health gains resulted in different numbers of discounted QALYs

Table 2 – Overview of different discounting approaches.

Approach	Name	Description
1	Constant	Discount rate is constant over time (Equation 1), can be uniform or differential
2	Stepwise	Discount rate declines stepwise after specific time intervals (Table 2)
3	Hyperbolic	Discount rate declines gradually over time (Equation 2)
4	Proportional	Discount rate declines gradually over time (Equation 3)
5	Time-shifted	Time period between vaccination and the prevention of infection is discounted rather than full period up to actual quality-adjusted life-year gains

gained by HPV vaccination. Figure 2 illustrates the time-specific discount rates of the different discount approaches applied. Clearly, when applying the proportional or hyperbolic discounting approach, the short-term gains are highly devalued; however, the long-term benefits are discounted with a relatively lower discount rate compared with a constant discount rate at 4%. Figure 3 illustrates the age-specific net present value of the health gains of HPV vaccination when applying the different discounting approaches. The time-shifted discounting approach resulted in the highest present value of QALYs while the proportional or hyperbolic discounting approach resulted in the lowest estimates (Table 3). Obviously, these results are driven by the relatively high initial discount rates in these latter two methods (i.e., much higher than 4%). If one would use lower rates in a hyperbolic discount function (e.g., Meerding et al. [34] recently reported empirically observed hyperbolic discounting with relatively low discount rates), this would yield much higher net present health benefits. For instance, applying these two approaches, but now starting at a 4% discount rate, we find a net present value of 1613 and 1607 QALYs for the proportional and hyperbolic discounting approach, respectively. Notably, in the time-shifted discounting approach [32], health outcomes of HPV vaccination were discounted at a constant rate only for the period between vaccination and infection, and in the period after infection a zero discount rate was applied.

When the stepwise discounting approach was applied, the total number of discounted QALYs were comparable to those obtained at a constant rate of 3%. Note that the total number of discounted QALYs is sensitive to the time interval and decline in discount rate.

When the conventional constant discounting approach was applied, the present value of QALYs gained was highly sensitive to the chosen discount rate. Lower discount rates for health outcomes resulted in substantial increases in the total number of discounted QALYs gained with HPV vaccination (Table 3).

To give an indication of the impact of these different approaches on the final ICER, we also combined these results with the discounted costs (4%). It should be noted that we do this mainly for illustrative purposes and that it might not always be logical to combine our results on health gains with a cost-estimate based on constant discounting using a 4% discount rate. In particular, if one prefers an empirically based approach such as hyperbolic discounting for health effects, it is likely that one also wishes to discount costs on a similar basis, that is, using a hyperbolic discount function. Table 3 shows the results for the ICERs. According to Dutch guidelines (constant discount rates of 4% for money and 1.5% for health; i.e., differential discounting), we found an ICER of €18,400 per QALY gained for HPV vaccination. Furthermore, varying the discount rate for health effects from 0% to 4% resulted in estimated ICERs of €7,600 to €59,100 per QALY, still

using constant discounting. When we applied the proportional discounting approach to health effects, we found an ICER that was nine times higher than the benchmark of €18,400 per QALY gained. Ergo, extremely large and relevant differences in the ICER were found between the various approaches investigated, moving from extremely cost-effective up to extremely cost-ineffective (when compared with commonly cited thresholds).

Discussion

Discounting of health outcomes is controversial and has been the subject of extensive debate since it was introduced and recommended for economic evaluations. These discussions often evolve around uniform or differential discounting of health outcomes and money, the exact rate of discounting, and whether or not to use decreasing discount rates. Different discounting approaches have been suggested. For example, it has been proposed to take the individual's time preference more explicitly into account or to apply lower discount rates in later periods. The aim of using such alternative methods in applied economic evaluations would be to explore the decision uncertainty associated with the different prevailing opinions on this matter [10]. It has been suggested to include alternative discount approaches in national guidelines [10,11]. In particular, it was proposed to apply alternative discount approaches in sensitivity analyses. In the current study, we evaluated the influence of using different discounting approaches for health outcomes. We illustrated what the impact is of alternative discounting approaches on future health outcomes and the cost-effectiveness of HPV vaccination. Because the health outcomes related to HPV vaccination are expected to occur several decades after the initial vaccination, the number of QALYs gained by HPV vaccination is highly sensitive to the discounting method that is applied [5]. Here, we compared the standard constant discounting to alternative approaches.

Indeed, our results show that alternative discounting approaches devalue the long-term health outcomes of HPV vaccination very differently compared with the constant discounting approach. For these alternative discounting approaches, the valuation of future health out-

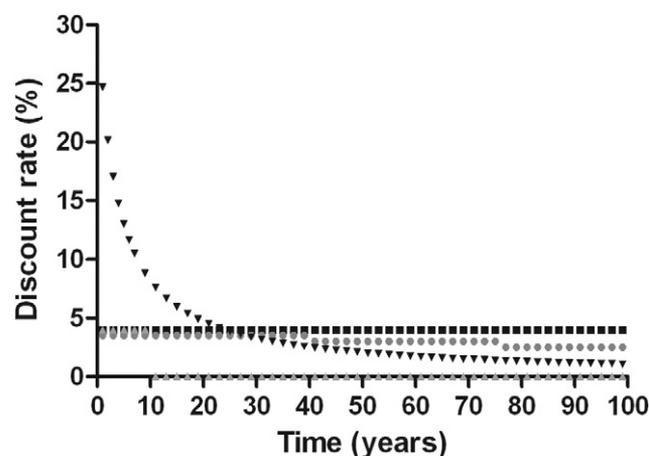


Fig. 2 – Time-specific discount rates of the different discount approaches applied. Black squares denote the constant discounting approach (4%), dark gray dots the stepwise discounting approach, light gray triangle the time-shifted discounting approach (4%), and black triangles the hyperbolic discounting approach. Note that for the time-shifted approach, here we assumed that the infection was prevented 10 years after the intervention. The proportional and hyperbolic discounting approach followed similar patterns.

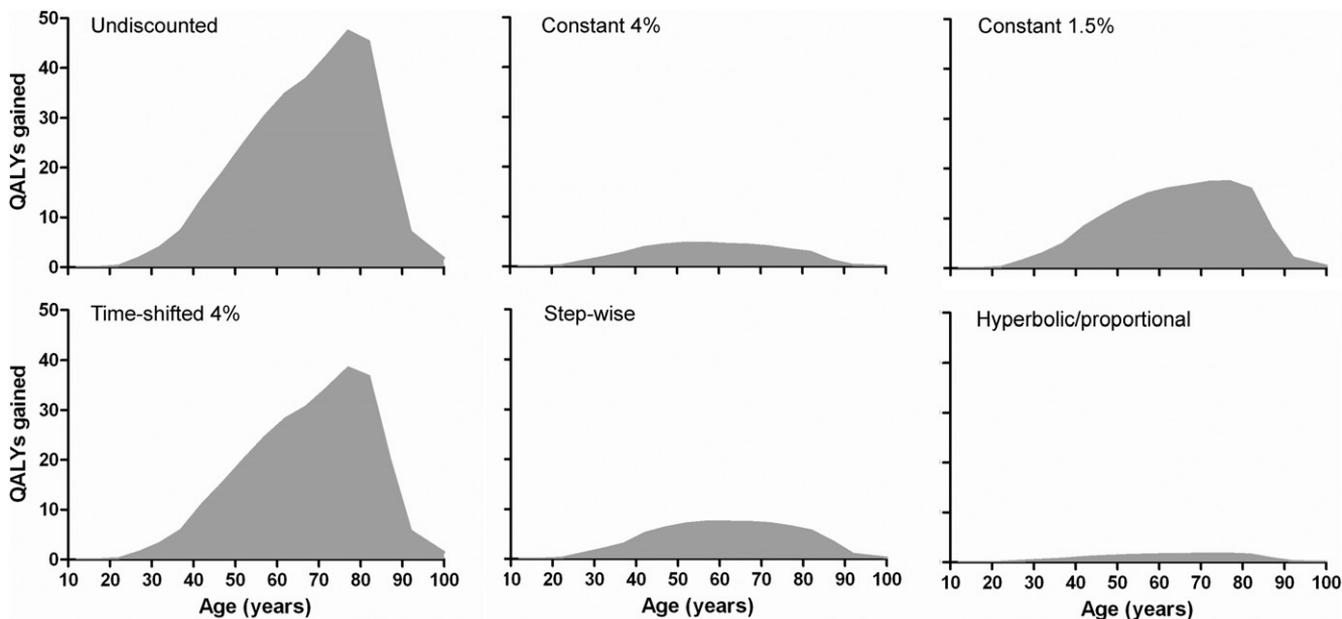


Fig. 3 – Age-specific health gains of HPV vaccination in the Dutch simulation model using different approaches. For the time-shifted discounting approach, a 4% discount rate for the period between intervention and prevented infection was used. HPV = human papillomavirus.

comes was dependent on both the parameter values used in the discounting approaches and the nature of the approaches themselves. Obviously, the variation identified in the net present value of QALYs gained had a large impact on the actual ICERs (Table 2).

Our current model represents a static model that does not explicitly simulate the spread of HPV in the population. Models that do simulate this spread explicitly are labeled dynamic transmission models [9,35]. As argued, for interventions that impact on the transmission dynamics of infectious diseases, it is preferable to use a dynamic transmission model for the simulation of infectious diseases [10,35]. In the current article, we illustrate the effect of different discounting approaches in the static approach. Nevertheless, how to apply constant discounting or alternative approaches in a dynamic transmission model framework is of high interest. Because herd immunity induced by HPV vaccination is highly associated with age (young people tend to have sex with partners of similar age), one can speculate that the qualitative impacts of the various discounting techniques are roughly similar between dynamic and static models when the same vaccination and screening strategies are compared (i.e., vaccinating a single cohort every year). Once vaccination starts, in addition to a static model, a dynamic model projects the prevention of infections in unvaccinated people. The consequences (warts, precancerous lesions, cancer cases, and deaths prevented) of these additional preventions, however, are likely to follow a pattern over time that is similar for vaccinated (directly protected) girls and for unvaccinated (indirectly protected) girls and boys, mainly because they are all of similar age. This contrasts with some childhood vaccinations for which the herd effects reach across generations. Nevertheless, the herd immunity benefit in the population induced by HPV vaccination depends on the proportion of vaccinated individuals in the population. As a consequence, the health gain and the cost-effectiveness of HPV vaccination might vary between vaccinated cohorts until a new steady state has been reached. In addition, it has been shown that for multicohort models the cost-effectiveness ratio will change for vaccinated cohorts from year to year if differential discounting is applied [36-38]. In particular, HPV vaccination becomes more favorable if additional cohorts are vaccinated.

In general, it seems important for decision-making and guideline-prescribing bodies in different jurisdictions to have transparent, defensible, and plausible discount rules. Constant uniform discounting is well founded in economic theory, and it is the generally accepted and recommended discounting approach. It purposely does not reflect commonly observed declining time preference of individuals, because this enhances stability by avoiding time inconsistency and paradoxes in policy making. It has been argued, however, that it can be adjusted to account for the growing value of health over time [19,39]. Therefore, constant differential discounting has been proposed, which allows for a lower discount rate for health effects relative to costs to adjust for the growing value of health over time [9,19]. Differential discounting, which has been adopted in some current (e.g., The Netherlands and Belgium) and previous (e.g., United Kingdom) Health Technology Assessment guidelines, often significantly lowers the ICERs of interventions. In particular, the ICER of interventions with health gains in the (far) future is more favorable when differential discounting is applied. Again, given the impact that discounting has on final outcomes, the

Table 3 – Discounted health outcomes of HPV vaccination using the different discounting approaches.		
Discounting approach	QALYs gained	ICER (€/QALY)
Undiscounted	3462	7,600
Constant 1.5%	1423	18,400
Constant 3%	715	37,000
Constant 4%	438	59,100
Proportional	164	165,400
Hyperbolic	160	164,500
Stepwise*	718	36,800
Shifted 4%	2117	13,200
Shifted 1.5%	2811	9,400

HPV = human papillomavirus; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year.
 * As proposed by the UK treasury.

exact underpinning of the discount rules adopted in studies and prescribed in guidelines needs to be fully transparent. Although the topic which discounting approaches to consider as most appropriate is beyond the scope of this article, it must be noted that some approaches appear to have a better normative and/or empirical underpinning than do others. Nevertheless, because discounting strongly affects the present value of costs and outcomes especially of interventions with long-term outcomes, alternative discount approaches should be applied in sensitivity analysis. For example, differential discounting or stepwise discounting should be investigated. Recently, the United Kingdom already recommended lowering the discount rate of outcomes from 3.5% to 1.5% when health outcomes extend beyond 30 years in sensitivity analysis [40].

Proportional and hyperbolic discounting approaches are important because they reflect individual and societal time preferences for health outcomes [24]. Caution, however, is required in their use because these models introduce risk time of time-inconsistent behavior. Furthermore, empirical studies show high variance in time preference, and the high observed discount rates may result in policies that unfairly harm future generations. Still, it is useful to use them more frequently in economic evaluations, for instance, in sensitivity analyses [11,39]. This is also interesting, because the approach of differential discounting, as prescribed in the Netherlands, and the proportional and hyperbolic discounting functions more or less represent extremes in terms of outcomes. Thus, using them in sensitivity analysis also would make sense and be informative for decisionmakers.

Our results highlight the importance of discounting and ongoing discussions in the literature on this topic. Furthermore, our study underlines the importance of discount rates as well as discount approaches. It illustrates that the recommendation to carefully identify appropriate discount methods and rates, and to investigate the sensitivity of results to the application of alternative discounting approaches, holds even stronger if vaccination programs are considered with health effects far into the future. HPV vaccination can be considered as one of the most extreme examples of such a program. We hope that this article will contribute to the debate in this area and to a fair discounting practice, such that all interventions for cure and prevention can be compared at the same level playing field.

Source of financial support: This work benefited from the Dutch ZonMw grant 152002008. Furthermore, T.A.W. and M.P. are recipients of unrestricted education grants from GlaxoSmithKline. The authors' work was independent of the funders, who had no role in the study design, analysis of data, writing of the manuscript, or decision to submit for publication.

REFERENCES

- [1] Simoens S. Health economic assessment: a methodological primer. *Int J Environ Res Public Health* 2009;6:2950–66.
- [2] Drummond MF, Sculpher MJ, Torrance GW, et al. *Methods for the Economic Evaluation of Health Care Programmes* (3rd ed.). Oxford: Oxford University Press, 2005.
- [3] Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-effectiveness in Health and Medicine*. Oxford: Oxford University Press, 1996.
- [4] ISPOR Pharmacoeconomics guidelines. Available from: <http://www.ispor.org/peguidelines/index.asp>. [Accessed April 1, 2011].
- [5] Rogoza RM, Westra TA, Ferko N, et al. Cost-effectiveness of prophylactic vaccination against human papillomavirus 16/18 for the prevention of cervical cancer: adaptation of an existing cohort model to the situation in the Netherlands. *Vaccine* 2009;27:4776–83.
- [6] Mangen MJ, van Duynhoven YT, Vennema H, et al. Is it cost-effective to introduce rotavirus vaccination in the Dutch national immunization program? *Vaccine* 2010;28:2624–35.
- [7] Brisson M, Van de Velde N, De Wals P, Boily MC. The potential cost-effectiveness of prophylactic human papillomavirus vaccines in Canada. *Vaccine* 2007;25:5399–408.
- [8] Tasset A, Nguyen VH, Wood S, Amazian K. Discounting: technical issues in economic evaluations of vaccination. *Vaccine* 1999;17(Suppl. 3):S75–80.
- [9] Beutels P, Edmunds WJ, Antonanzas F, et al. Economic evaluation of vaccination programmes: a consensus statement focusing on viral hepatitis. *Pharmacoeconomics* 2002;20:1–7.
- [10] Beutels P, Scuffham PA, MacIntyre GR. Funding of drugs: do vaccines warrant a different approach? *Lancet Infect Dis* 2008;8:727–33.
- [11] Bleichrodt H, Brouwer W. Discounting. In: Rutten-vanMölkken MPMH, Busschbach van JJ, Rutten FFH, et al. *Van Kosten tot Effecten. Een handleiding voor evaluatiestudies in de gezondheidszorg*. Maarssen: Elsevier, 2000.
- [12] Keeler EB, Cretin S. Discounting of life-saving and other non-monetary effects. *Manage Sci* 1983;29:300–6.
- [13] Claxton K, Sculpher M, Culyer A, et al. Discounting and cost-effectiveness in NICE—stepping back to sort out a confusion. *Health Econ* 2006;15:1–4.
- [14] Olsen JA. Time preferences for health gains: an empirical investigation. *Health Econ* 1993;2:257–65.
- [15] Lazaro A. Theoretical arguments for the discounting of health consequences: where do we go from here? *Pharmacoeconomics* 2002;20:943–61.
- [16] Cohen BJ. Discounting in cost-utility analysis of healthcare interventions: reassessing current practice. *Pharmacoeconomics* 2003;21:75–87.
- [17] van Hout BA. Discounting costs and effects: a reconsideration. *Health Econ* 1998;7:581–94.
- [18] Brouwer W, van Hout B, Rutten F. A fair approach to discounting future effects: taking a societal perspective. *J Health Serv Res Policy* 2000;5:114–8.
- [19] Brouwer WB, Niessen LW, Postma MJ, Rutten FF. Need for differential discounting of costs and health effects in cost effectiveness analyses. *BMJ* 2005;331:446–8.
- [20] Brouwer WB, van Exel NJ. Discounting in decision making: the consistency argument revisited empirically. *Health Pol* 2004;67:187–94.
- [21] Klok RM, Brouwer WBF, Annemans LJP, et al. Towards a healthier discount procedure. *Expert Rev Pharmacoecon Outcomes Res* 2005;5(1):59–63.
- [22] Van Der Pol MM, Cairns JA. Negative and zero time preference for health. *Health Econ* 2000;9:171–5.
- [23] van der Pol M, Cairns J. Estimating time preferences for health using discrete choice experiments. *Soc Sci Med* 2001;52:1459–70.
- [24] Cairns JA, van der Pol MM. Saving future lives: a comparison of three discounting models. *Health Econ* 1997;6:341–50.
- [25] Asenso-Boadi F, Peters TJ, Coast J. Exploring differences in empirical time preference rates for health: an application of meta-regression. *Health Econ* 2008;17:235–48.
- [26] Cairns J, van der Pol M. Constant and decreasing timing aversion for saving lives. *Soc Sci Med* 1997;45:1653–9.
- [27] Harvey C. Proportional discounting of future health gains: an empirical investigation. *Health Econ* 1995;20:18.
- [28] Loewenstein GF, Prelec D. Anomalies in intertemporal choice: evidence and an interpretation. *Q J Econ* 1992;107:573–97.
- [29] van der Pol M, Cairns J. Descriptive validity of alternative intertemporal models for health outcomes: an axiomatic test. *Health Econ* 2011;20:770–82.
- [30] Bazelon B. Discounting in the long term. *Loyola Los Angeles Law Rev* 2002;35:277.
- [31] Oxera. A social time preference rate for use in long-term discounting. Available from: <http://www.oxera.com>. [Accessed January 1, 2011].
- [32] Bos JM, Beutels P, Annemans L, Postma MJ. Valuing prevention through economic evaluation: some considerations regarding the choice of discount model for health effects with focus on infectious diseases. *Pharmacoeconomics* 2004;22:1171–9.
- [33] Drummond M, Chevat C, Lothgren M. Do we fully understand the economic value of vaccines? *Vaccine* 2007;25:5945–57.
- [34] Meerding WJ, Bonsel GJ, Brouwer WB, et al. Social time preference for health and money elicited with a choice experiment. *Value Health* 2010;13:368–74.
- [35] Jit M, Brisson M. Modelling the epidemiology of infectious diseases for decision analysis: a primer. *Pharmacoeconomics* 2011;29:371–86.
- [36] O'Mahony JF, de Kok IM, van Rosmalen J, et al. Practical implication of differential discounting in cost-effectiveness analysis with varying numbers of cohorts. *Value Health* 2011;14(4):438–42.
- [37] Westra TA, Parouty MB, Wilschut JC, et al. Practical implication of differential discounting of costs and health effects in cost-effectiveness analysis. *Value Health* 2011;14(8):1173–4.
- [38] O'Mahony JF, de Kok IM, van Rosmalen J, et al. Practical implication of differential discounting of costs and health effects in cost-effectiveness analysis. *Value Health* 2011;14(8):1174–5.
- [39] Bobinac A, Brouwer W, van Exel J. Discounting future health gains: an empirical enquiry into the influence of growing life expectancy. *Health Econ* 2011;20:111–9.
- [40] National Institute of Clinical Excellence. Available from: <http://www.nice.org.uk>. [Accessed January 1, 2012].