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CHAPTER 7

Assessment of the broader economic consequences of HPV prevention from a government-perspective: A fiscal analytic approach

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Assessment of the broader economic consequences of HPV prevention from a government-perspective: A fiscal analytic approach

Abstract

Background: Cervical cancer poses a substantial burden in terms of morbidity, mortality, and economic losses, especially in low/middle-income countries. HPV vaccination and/or cervical cancer screening among females may reduce the burden of HPV-related diseases, including cervical cancer. However, limited funds may impede the implementation of population-based programmes. Governmental investments in the prevention of infectious disease may have broader economic and fiscal benefits, which are not accounted in conventional economic analyses. This study estimates the broader economic and fiscal impacts of implementing HPV vaccination and/or cervical cancer screening in Indonesia from the perspective of the government.

Methods: A government-perspective quantitative analytic framework was applied to assess the Net Present Value (NPV) of investment on cervical cancer prevention strategies including HPV vaccination, cervical screening and its combination in Indonesia. All monetary values were presented in International Dollars (I$)

Results: Based on a cohort of 10,000,000 Indonesian 12-year-old females, it was estimated that HPV vaccination and/or cervical cancer screening result in a positive NPV for the Indonesian government. The combination of cervical screening and HPV vaccination generated a substantial reduction of cervical cancer incidence and HPV-related mortality of 87,862 and 19,359, respectively. It was estimated that HPV vaccination in combination with cervical screening is the most favorable option for cervical cancer prevention (NPV I$2.031.786.000), followed by HPV vaccination alone (NPV I$1.860.783.000) and cervical screening alone (NPV I$375.244.000).

Conclusion: In addition to clinical benefits, investing in HPV vaccination and cervical screening may yield considerable fiscal benefits for the Indonesian governments due to lifelong benefits resulting from reduction of cervical cancer-related morbidity and mortality.

Keywords

HPV, HPV vaccination, cervical cancer, cervical cancer screening, broader economic analysis

Introduction

High-risk human papillomaviruses (hrHPV), in particular HPV16 and HPV18, are responsible for cervical cancer and premalignant cervical disease among woman (1–5). Although cervical cancer is considered as a preventable disease when detected and managed in the early stages, it still poses a serious health and economic burden, especially in developing countries (6–8). The WHO recommends primary prevention through vaccination against HPV and secondary prevention through cervical screening for pre-cancerous lesions (9). Numerous studies have shown that cervical screening is beneficial in terms of lowering the incidence of pre-cancerous lesions and cervical cancer (8,10,11). Moreover, the two approved
prophylactic vaccines against HPV have also demonstrated considerable benefits in terms of reduction of HPV infection and Cervical Intraepithelial Neoplasia (CIN) (9,12–15).

Several health-economic analyses have shown that HPV vaccination combined with cervical cancer screening results in an efficient use of healthcare resources (16–19). Such analyses typically assess the cost-effectiveness of adding HPV vaccination to screening. Hence, most economic analyses focus on evaluating the technical efficiency of the healthcare budget (20). Implementation of vaccination and cervical cancer screening programmes is dependent on affordability and local infrastructure especially in low/middle-income countries, which have limited infrastructure, human resources, and funds. In low/middle-income countries, implementation of population-based HPV vaccination and screening programmes, such as VIA screening which is suitable for low/middle-income countries, may require funds additional to the healthcare budget. Hence, economic analyses should be capable of providing decision-makers with measures for the broader economic impact and cross-sectorial consequences of resource allocation decisions.

HPV infection and cervical cancer disease pose a substantial morbidity and mortality burden. In 2012, there were over 20,000 new cases of cervical cancer and 9,000 cervical-cancer related deaths (7). The implementation of a population-based HPV vaccination and/or VIA screening programme requires a substantial investment, but it potentially reduces the burden of cervical cancer. Additional benefits including more women who are able to work, more women gain income (21–23), and on the government perspective, there will be more workers who pay the taxes and health/social security premium. Notably, health-economic and broader economic benefits including fiscal benefits for the Indonesian government could be achieved. In this study, we assess the broader economic consequences of introducing HPV vaccination in Indonesia with emphasis on the potential positive and negative fiscal effects of the latest policy of the Indonesian National Social Security System (SJSN) for HPV prevention.

Methods & Data

The natural history of cervical cancer for Indonesian women was modeled based on a previously published population-based Markov model (24). The cervical cancer prevention strategies, including HPV vaccination (3 doses of vaccination and 76.6% coverage) and/ or VIA screening (every three years for 30-60 years old and 21.2% yearly coverage), were also adopted from the same study. An additional strategy, HPV vaccination alone, was also added in the analysis. This population-based Markov model was chosen given the scarce availability of data, hampering the development of a more complex modeling approach. Several validation steps were taken, including face validity checks for both the conceptual model and the input parameters, extreme value testing and testing of traces.

The fiscal analysis described here simulates the natural history and costs of cervical cancer patients in Indonesia. Susceptible, cervical cancer and death states were modeled and a
Assessment of the broader economic consequences of HPV prevention from a government-perspective: A fiscal analytic approach

A simulation was run for a cohort of 10,000,000 Indonesian 12-year-old girls over their lifetime (25,26). Cervical cancer prevention strategies, that were assessed, included (i) cervical screening, (ii) HPV vaccination and (iii) HPV vaccination plus cervical cancer screening. The reduction of HPV-related morbidity and mortality resulting from each of the assessed strategies was quantified and translated into changes in age-specific gross tax revenue and government transfer costs over the lifetime of the cohort. Specifically, based on previously published methods for assessing of the broader economic consequences of health-care interventions (27–29), morbidity and mortality reductions were translated into discounted, lifetime fiscal benefits for the Indonesian government. Hence, prevention of HPV-related mortality and morbidity benefits were converted into discounted lifetime (i) additional gross, direct and indirect tax revenues, (ii) health-care cost savings and (iii) social insurance cost-savings. Fiscal expenses, i.e. the cost of vaccination and the additional governmental transfers (i.e. pensions) resulting from the additional survival produced by HPV prevention in Indonesia, were discounted and deducted from the fiscal benefits of HPV prevention to produce the Net Present Value (NPV) of each HPV prevention strategy.

In order to estimate the lifetime earnings and, thus, the lifetime tax revenues to be gained from the average Indonesian female, earnings distribution was categorized into three levels (20% high-income earners, 40% middle-income earners, and 40% low-income earners) and the average of each earnings level, based on the Indonesian Gross Domestic Product (GDP) using Gini index of 0.41 (30,31), was estimated. Furthermore, annual earnings were adjusted for future productivity based on the labor productivity index from The Organization for Economic Cooperation and Development (OECD) (32). Earnings were also adjusted to reflect the proportion of female workforce participation (25,33). Moreover, the average age of entering the workforce and the average retirement age of Indonesian civil servants were considered in the model (34,35). Direct tax was estimated based on the Indonesian earnings tax law (36,37) and applied for each level of income. Thus, the model assumed that tax revenue stems from middle- and high-income earnings only, since the average earnings of the low-income population lies below the taxable earnings threshold. Indirect tax was estimated based on the Value Added Tax (VAT) policy (38,39) and household consumption expenditure per capita (40). Furthermore, we assumed that VAT adherence and collectability rate was 50% (41) (Table 1).
### Table 1. Model input Parameters

| Type                          | Description                                      | value   | Comments                                      | Reference |
|-------------------------------|--------------------------------------------------|---------|-----------------------------------------------|-----------|
| **National economic parameters** |                                                  |         |                                               |           |
| Life expectancy               |                                                  | 70.10   |                                               | (42)      |
| Gross Domestic Products (I$) |                                                  | 7,463   | per capita                                     | (31)      |
| Average Earnings(I$)          | Low                                              | 3,183   | as percentage of national GDP                 | (30,31)  |
|                               | Middle                                           | 6,375   | as percentage of national GDP                 | (30,31)  |
|                               | High                                             | 18,198  | as percentage of national GDP                 | (30,31)  |
| Retirement age                |                                                  | 60      |                                               | (35)      |
| Annual inflation (%)          |                                                  | 6.42    | inflation rate                                | (43)      |
| Civil servant (%)             | Low                                              | 2.00    | as percentage of female population            | (33)      |
|                               | Middle                                           | 6.375   | as percentage of female population            | (33)      |
|                               | High                                             | 18,198  | as percentage of female population            | (33)      |
| Minimum age as a civil servant|                                                  | 18      |                                               | (34)      |
| Labor Productivity (%)        |                                                  | 3.60    | Yearly                                        | (32)      |
| Discount rate (%)             |                                                  | 3.00    |                                               |           |
| Direct tax (%)                | < I$6,390                                        | 0.00    | as percentage of income                       | (36,37)  |
|                               | I$6,390 - I$13,150                               | 5.00    | as percentage of income                       | (36,37)  |
|                               | I$13,150 - I$65,748                              | 15.00   | as percentage of income                       | (36,37)  |
| Indirect tax                  | VAT (%)                                          | 10.00   | value added tax                               | (38,39)  |
|                               | Earnings consumed (I$)                           | 1,960   | household consumption expenditure per capita  | (40)      |
| Tax adherence (%)             |                                                  | 50.00   | Assumption                                    | -         |
| **Revenue**                   |                                                  |         |                                               |           |
| Pension fund benefit (%)      | Employee                                        | 2.00    | as percentage of income                       | (44,45)  |
|                               | Employer                                        | 3.70    | as percentage of income                       | (44,45)  |
|                               | Net revenue                                     | 47.10   | after deducted by claim                       | (46)      |
| Work-related accident benefit | Employer                                        | 0.90    | as percentage of income                       | (44,45)  |
|                               | Net revenue                                     | 71.00   | after deducted by claim                       | (46)      |
| Death benefit (%)             | Employer                                        | 0.30    | as percentage of income                       | (44,45)  |
|                               | Net revenue                                     | 60.00   | after deducted by claim                       | (46)      |
| Membership of social security |                                                  | 75.00   |                                               | (47)      |
| Health security (%)           | Employee (civil servants)                       | 2.00    | as percentage of income                       | (44,45)  |
|                               | Employee (non-civil servants)                   | 2.00    | as percentage of income                       | (44,45)  |
|                               | Employer (non-civil servants)                   | 3.00    | as percentage of income                       | (44,45)  |
|                               | Membership of health security (%)                | 75.00   |                                               | (47)      |
| **Expenditure**               | Social security for civil servant (%)           | 6.00    |                                               |           |
|                               | Pension fund benefit                            | 3.70    | as percentage of income                       | (44,45)  |
|                               | Employer                                        |         |                                               |           |
Governmental transfers to citizens were estimated based on the national social and health security system. The benefits provided by the social security system are pension funds, and work-related accident and death benefits (44,45). Old-age pensions were estimated based on 60% of the earnings in the last employment year (48). Direct costs related to pre-cancerous lesions, cervical cancer and investment costs for prevention programs were included in the model based on the study by Setiawan, et al. (24). Costs were inflated to current prices using an inflation rate of 6.42% which reflects the average inflation in 2014 (43). Direct costs attributed to genital warts have not been included in this analysis as they are likely to have limited fiscal consequences in the context of treatment in Indonesia.

The discounted cash flow method was used to obtain the present value of cash inflows and outflows. The results were presented in terms of the Net Present Value (NPV) of the investment decision for each of the cervical cancer prevention strategies under study as follows:

\[
NPV = \sum_{t=0}^{T} \left( \frac{R_t - E_t}{(1 + r)^t} \right) - K_0
\]

NPVs were calculated by subtracting incremental expenses (E_t), including vaccine cost at t=0 (K_0) from incremental revenues (R_t) for each of strategy. Increments refer to the difference between the revenue and expenses with and without the HPV prevention strategy under consideration. All values were discounted (r) by 3% according to WHO recommendation and also consistent with previous cost-effectiveness studies on cervical cancer prevention programmes in Indonesia.

In order to examine the sensitivity of the model to its parameters, univariate sensitivity analyses were conducted for the NPV of each HPV prevention strategy. The ranges around input parameters including inflation rate, discount rate, Gross domestic products (GDP), tax compliance, membership of health and social security, percentage of earnings consumed and percentage of work-related accident premium. Inflation and discount rates were varied by the lowest and highest value of Indonesian inflation rate in 2014 (43) and acceptable discount rates from various countries (49), respectively. The lower and upper limits for GDP were defined by the lowest and highest GDP value of the previous 5 years (50), while the
Chapter 7

ranges for the proportion of earnings consumed were based on previous 3 years’ data (51). Tax compliance, health and social security membership were varied based on assumptions since the distributions for this parameters were not available.

Results

Based on a single cohort of 10,000,000 girls in Indonesia, our model showed that in the absence of any cervical cancer prevention strategy, 147,632 cases of cervical cancer will ultimately occur within the cohort. The implementation of cervical cancer prevention strategies, including screening alone, HPV vaccination alone, or cervical screening in combination with HPV vaccination was projected to prevent 15,641, 80,750 or 87,862 cases of cervical cancer, respectively. Furthermore, the combination of cervical screening and HPV vaccination generated the highest reduction of deaths caused by cervical cancer (19,359), followed by HPV vaccination alone (17,541) and screening alone (4,005) (Table 2).

Table 2. The impact of cervical cancer prevention strategies on incidence and mortality cases over a 58-years period

| Clinical Parameters       | No Intervention | Screening | Cervical Screening & HPV Vaccination | HPV Vaccination |
|---------------------------|-----------------|-----------|-------------------------------------|-----------------|
| Cumulative incidence      | 147,632         | 131,991   | 59,770                              | 66,882          |
| Incremental incidence     | -               | 15,641    | 87,862                              | 80,750          |
| Cumulative mortality      | 32,046          | 28,041    | 12,687                              | 14,505          |
| Incremental mortality     | -               | 4,005     | 19,359                              | 17,541          |

The lifetime NPV for the study cohort of Indonesian 12-year-old females is illustrated in Table 3 for the three prevention strategies. All three strategies resulted in a positive NPV. HPV vaccination in combination with cervical screening generates the highest NPV for the government (I$2,031,786,000), followed by HPV vaccination only (I$1,860,783,000) and cervical screening alone (I$375,244,000). Indirect tax produces the highest revenue for the government compared to direct tax, social- or health-security contributions. With respect to HPV-related governments’ expenses, the highest saving is generated by treatment cost savings. HPV vaccination in combination with cervical cancer screening results in the highest healthcare cost-savings. Similarly, the combined prevention strategy resulted in the highest savings in terms of social security costs. All prevention strategies resulted in increased governments’ expenses in terms of health security and pension costs.
Table 3. The impact of cervical cancer prevention strategies on future governments’ revenue and expenses (x IS$1,000; year 2014).

| Strategy                        | Direct Tax | Indirect Tax | Social Security | Health Security | Gross Tax Revenue per strategy | Transfers Social Security | Transfers Health Security | Transfers pension | Treatment Cost | Total Transfers | Total Value (NPV) |
|--------------------------------|------------|--------------|-----------------|-----------------|--------------------------------|--------------------------|--------------------------|-------------------|----------------|-----------------|------------------|
| No Intervention                | 273,405,393| 125,213,166  | 67,387,009      | 79,908,077      | 545,913,646                     | 7,468                    | 290,926                  | 363,881,820       | 4,040,308       | 368,220,522     | 177,693,124      |
| Cervical Screening             | 273,405,666| 125,213,470  | 67,387,071      | 79,908,151      | 545,914,348                     | 7,440                    | 290,926                  | 363,885,561       | 3,662,052        | 367,845,980     | 178,068,368      |
| Cervical screening and HPV vaccination | 273,406,098| 125,214,083  | 67,387,175      | 79,908,274      | 545,915,630                     | 7,344                    | 290,926                  | 363,893,627       | 1,998,824        | 366,190,721     | 179,724,910      |
| HPV Vaccination                | 273,405,980| 125,213,945  | 67,387,147      | 79,908,241      | 545,915,313                     | 7,356                    | 290,926                  | 363,891,933       | 2,171,191        | 366,361,406     | 179,553,907      |

| Incremental value              |            |              |                 |                 |                              |                          |                          |                   |                |                 |                  |
|--------------------------------|------------|--------------|-----------------|-----------------|--------------------------------|--------------------------|--------------------------|-------------------|----------------|-----------------|------------------|
| Cervical Screening             | 263        | 304          | 62              | 73              | 702                            | -28                      | 0                        | 3,741             | -378,256       | -374,542        | 375,244          |
| Cervical screening and HPV vaccination | 705        | 917          | 166             | 197              | 1,985                          | -124                     | 0                        | 11,807            | -2,041,484     | -2,029,801      | 2,031,786        |
| HPV Vaccination                | 588        | 779          | 138             | 163              | 1,667                          | -112                     | 0                        | 10,112            | -1,869,117     | -1,859,116      | 1,860,783        |
Fig 1 illustrates the results of the univariate sensitivity analyses evaluating the influence of several input parameters on the NPV. The analysis shows that inflation and discount rate are the most influential parameters in this study [data not shown]. The further analysis illustrates that NPV is also sensitive to GDP (as a measure of earnings) and tax compliance. Health and social security membership, the percentage of earnings consumed, and percentage of work-related accident premium are considered as non-influential parameters to the NPV.

**Discussion**

Implementation of population-based healthcare intervention unambiguously results in fiscal costs due to changes in morbidity and mortality that influence national accounts over the lifetime of the cohort. However, similar to other public investments, investment in healthcare interventions may also result in measurable, long-term fiscal benefits (i.e. tax revenue) attributed to changes in population health that may outweigh or considerably
offset the costs (52). In this study, we evaluated how different levels of investment in HPV prevention influence the Indonesian governments’ fiscal accounts. The study showed that investing in HPV vaccination in combination with cervical screening yields long-term fiscal benefits for the Indonesian government. These results are supplementary to a previously published study on the cost-effectiveness of cervical cancer prevention strategies in Indonesia (24). Both studies suggest that cervical cancer prevention strategies are not only beneficial for the health of Indonesian women, they also improve the efficiency of healthcare resource use and have a long-term fiscal benefit for the government by increasing the quality and quantity of the human capital and thus by increasing the tax base in the country compared to not investing in HPV prevention.

The main clinical benefit of cervical cancer prevention programmes is the reduction of morbidity and mortality (16,53–55). In traditional health-economic analyses the comparative clinical benefits and associated costs would be reflected in the incremental cost-effectiveness ratio (ICER) in terms of cost per quality-adjusted survival as a result of vaccination. The latter ratio responds to the question of which is the most efficient use of healthcare resources for a given healthcare budget. A cost-effectiveness analysis may also quantify productivity losses from premature mortality and/or absenteeism or presentism and thus reflect the benefits from a societal perspective which are distinct from benefits accrued to government. In the model described here, we apply the tax burden to reflect the proportion of lifetime earnings that are transferred to the government to reflect fiscal benefits.

The underlying assumption of taking a broader economic analytic perspective with emphasis on fiscal effects is that changes in health status or the prevention of infectious diseases have several external effects. The benefits of HPV prevention imply that more women who would be able to work thus, gain more earnings and pay more taxes and security premiums for the government. As a result of this, it is expected that the prevention of HPV infection and HPV-related diseases will yield increased governmental fiscal revenues from (direct and indirect) taxes and also (health and social) security insurance premium. Moreover, there are significant cost-savings resulting from reduced need for cervical cancer treatment which is captured in conventional cost-effectiveness analyses and also demonstrated by application of a "government-perspective" framework to assess different HPV investment strategies.

A key limitation of this type of study is that it is largely dependent on the mathematical modeling of long-term clinical, economic and fiscal parameters. Although the population-based model included high-quality clinical-trial data, including vaccine and VIA screening efficacy on incidence and mortality, further model validation using observed-country-specific data could still further assure the outcomes of the model. However, the Indonesia-specific observational information is not available. Such further validation and comparing our model with more sophisticated models from other countries with better data availability remains an option for future research.
Some of the key parameters dynamically change over time in the real life. Sensitivity analyses may address some of the uncertainty around these parameters. However, further observational data may be needed to assess the real-life fiscal effect of HPV prevention programmes. In addition, the current analysis does not take into account the effects of herd immunity, inequalities in access to health-care services due to socio-economic and regional differences, further distinctions in specific stages of both pre-cancer and cervical cancer, nor the benefits that HPV vaccination may have in terms of (i) protection of males and (ii) prevention of genital warts.

By conducting a broader economic analysis, evidence is produced to inform analyses regarding the cross-sectorial allocation of resources and perhaps the transfer of funds from other sectors of the public economy to universal population-based vaccination and screening programmes. The evidence generated in this study may address the affordability of implementing an HPV prevention program in Indonesia. Our study results suggest that investments in HPV prevention programmes may generate epidemiological benefits that translate into health-economic and fiscal benefits for the Indonesian government that may fully offset the investment costs and thus may have a positive impact on national accounts in the long-run.

Supplementary files
Data are available at doi:10.5061/dryad.9n34t

References
1. Clifford GM, Smith JS, Plummer M, Muñoz N, Franceschi S. Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis. Br J Cancer [Internet]. 2003 Jan 13 [cited 2014 Jul 14];88(1):63–73. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2376782&tool=pmcrender&rendertype=abstract
2. Woodman CBJ, Collins SI, Young LS. The natural history of cervical HPV infection: unresolved issues. Nat Rev Cancer [Internet]. 2007 Jan [cited 2014 Sep 16];7(1):11–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17186016
3. Domingo EJ, Noviani R, Noor MRM, Ngelangel C a, Limpaphayom KK, Thuan T Van, et al. Epidemiology and prevention of cervical cancer in Indonesia, Malaysia, the Philippines, Thailand and Vietnam. Vaccine [Internet]. 2008 Aug 19 [cited 2014 Aug 20];26 Suppl 1:M71–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18945416
4. zur Hausen H. Papillomaviruses in anogenital cancer as a model to understand the role of viruses in human cancers. Cancer Res. 1989;49(17):4677–81.
5. Burd E. Human papillomavirus and cervical cancer. Clin Microbiol Rev [Internet]. 2003;16(1):1–17. Available from: http://www.sciencedirect.com/science/article/pii/S0140673607614160
6. The World Bank. Country and Lending Groups [Internet]. 2014 [cited 2014 Aug 20].
Assessment of the broader economic consequences of HPV prevention from a
government-perspective: A fiscal analytic approach

Available from: http://data.worldbank.org/about/country-and-lending-groups#Lower_middle_income

7. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer. 2013 [cited 2014 Aug 17]. Available from: http://globocan.iarc.fr

8. Denny L, Prendiville W. Cancer of the cervix: Early detection and cost-effective solutions. Int J Gynecol Obstet [Internet]. Elsevier B.V.; 2015;131:528–32. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0020729215000880

9. World Health Organization. Comprehensive cervical cancer prevention and control: a healthier future for girls and women. Villars-sous-Yens, Switzerland; 2013.

10. Sankaranarayanan R, Esmy PO, Rajkumar R, Muwonge R, Swaminathan R, Shanthakumari S, et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. Lancet [Internet]. 2007 Aug 4;370(9585):398–406. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17679017

11. Deerasamee S, Srivatanakul P, Sriplung H, Nilvachararung S, Tansuwan U, Pitakpripawan P, et al. Monitoring and evaluation of a model demonstration project for the control of cervical cancer in Nakhon Phanom province, Thailand. Asian Pac J Cancer Prev [Internet]. 2007;8(4):547–56. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18260727

12. Dillner J, Kjaer SK, Wheeler CM, Sigurdsson K, Iversen O-E, Hernandez-Avila M, et al. Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. BMJ [Internet]. 2010 Jan [cited 2014 Sep 19];340:c3493. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2907480&tool=pmcentrez&rendertype=abstract

13. The FUTURE II Study Group. Quadrivalent Vaccine against Human Papillomavirus to Prevent High-Grade Cervical Lesions. N Engl J Med. 2007;356(19):1915–27.

14. Wheeler CM, Castellsagué X, Garland SM, Szarewski A, Paavonen J, Naud P, et al. Cross-protective efficacy of HPV-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by non-vaccine oncogenic HPV types: 4-year end-of-study analysis of the randomised, double-blind PATRICIA trial. Lancet Oncol. 2012;13(1):100–10.

15. Descamps D, Hardt K, Spiessens B, Izurieta P, Verstraeten T, Breuer T, et al. Safety of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine for cervical cancer prevention: a pooled analysis of 11 clinical trials. Hum Vaccin. 2009;5(5):332–40.

16. Coupé VMH, van Ginkel J, de Melker HE, Snijders PJF, Meijer CJLM, Berkhof J. HPV16/18 vaccination to prevent cervical cancer in The Netherlands: model-based cost-effectiveness. Int J Cancer [Internet]. 2009 Feb 15 [cited 2014 Oct 8];124(4):970–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19035448

17. Lee VJ, Tay SK, Teoh YL, Tok MY. Cost-effectiveness of different human
18. Jit M, Brisson M, Portnoy A, Hutubessy R. Cost-effectiveness of female human papillomavirus vaccination in 179 countries: a PRIME modelling study. Lancet Glob Heal [Internet]. World Health Organization; 2014 Jul [cited 2014 Sep 19];2(7):e406–14. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25103394

19. Setiawan D, Lutjehoer J, Westra TA, Wilschut JCJC, Suwantika AAA, Daemen T, et al. The cost–effectiveness of HPV vaccination in addition to screening: a Dutch perspective. Expert Rev Vaccines [Internet]. 2015;14(4):589–604. Available from: http://informahealthcare.com/doi/abs/10.1586/14760584.2014.990386

20. Palmer S, Torgerson DJ. Economic notes: definitions of efficiency. BMJ. 1999;318(7191):1136.

21. Kim JJ, Kobus KE, Diaz M, O’Shea M, Van Minh H, Goldie SJ. Exploring the cost-effectiveness of HPV vaccination in Vietnam: insights for evidence-based cervical cancer prevention policy. Vaccine [Internet]. 2008 Jul 29 [cited 2014 Sep 19];26(32):4015–24. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18602731

22. Mandelblatt JS, Lawrence WF, Gaffikin L, Limphayom KK, Lumbiganon P, Warakamin S, et al. Costs and benefits of different strategies to screen for cervical cancer in less-developed countries. J Natl Cancer Inst [Internet]. 2002 Oct 2;94(19):1469–83. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12359856

23. Diaz M, Kim JJ, Albero G, de Sanjosé S, Clifford G, Bosch FX, et al. Health and economic impact of HPV 16 and 18 vaccination and cervical cancer screening in India. Br J Cancer [Internet]. 2008 Jul 22 [cited 2014 Aug 20];99(2):230–8. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2480962&tool=pmcendeztrezrendertype=abstract

24. Setiawan D, Dolk FFC, Suwantika AAA, Westra TA, Wilschut JCJC, Postma MJMJ. Cost Utility Analysis of Human Papillomavirus Vaccination and cervical screening on cervical cancer patient in Indonesia. Value Heal Reg Issues. 2016;9:84–92.

25. Badan Pusat Statistik. Penduduk Berumur 15 Tahun Ke Atas Menurut Golongan Umur dan Jenis Kegiatan Selama Seminggu yang Lalu, 2000-2013 [Internet]. 2014 [cited 2014 Aug 29]. Available from: http://www.bps.go.id/linkTabelStatis/view/id/974

26. Badan Pusat Statistik. Penduduk Indonesia menurut Provinsi 1971, 1980, 1990, 1995, 2000 dan 2010 [Internet]. 2014 [cited 2014 Aug 29]. Available from: http://www.bps.go.id/tab_sub/view.php?kat=1&tabel=1&daftar=1&id_subyek=12&notab=1

27. Kotsopoulos N, Connolly MP, Postma MJ, Hutubessy RCW. Fiscal consequences of changes in morbidity and mortality attributed to rotavirus immunisation. Vaccine [Internet]. Elsevier Ltd; 2013;31(46):5430–4. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0264410X13012164
Assessment of the broader economic consequences of HPV prevention from a government-perspective: A fiscal analytic approach

28. Connolly MP, Topachevskyi O, Standaert B, Ortega O, Postma M. The impact of rotavirus vaccination on discounted net tax revenue in Egypt: A government perspective analysis. Pharmacoeconomics. 2012;30(8):681–95.

29. Kotsopoulos N, Connolly MP, Sobanski E, Postma MJ. The fiscal consequences of ADHD in Germany: A quantitative analysis based on differences in educational attainment and lifetime earnings. J Ment Health Policy Econ. 2013;16(1):27–33.

30. Lorenz MO. Methods of measuring the concentration of wealth [Internet]. Publications of the American Statistical Association. 1905. p. 209–19. Available from: http://www.jstor.org/stable/2276207

31. Badan Pusat Statistik. Produk Domestik Bruto Per Kapita, Produk Nasional Bruto Per Kapita dan Pendapatan Nasional Per Kapita, 2000-2013 (Rupiah) [Internet]. 2014 [cited 2014 Aug 20]. Available from: http://www.bps.go.id/linkTabelStatis/view/id/1241

32. The Organisation for Economic Co-operation and Development. Productivity and long term growth [Internet]. 2013 [cited 2014 Aug 21]. p. 167–70. Available from: http://www.oecd.org/eco/growth/Indonesia.pdf

33. Badan Pusat Statistik. Jumlah Pegawai Negeri Sipil Menurut Provinsi dan Jenis Kelamin,2007-2013 [Internet]. 2014 [cited 2014 Aug 20]. Available from: http://www.bps.go.id/linkTabelStatis/view/id/1163

34. Presiden Republik Indonesia. Pengadaan Pegawai Negeri Sipil. Indonesia; 2002 p. 8.

35. Presiden Republik Indonesia. Pemberhentian Pegawai Negeri Sipil yang Mencapai Batas Usia Pensiun bagi Pejabat Fungsional. Indonesia; 2014 p. 6.

36. Menteri Keuangan Republik Indonesia. Penyesuaian Besarnya Penghasilan Tidak Kena Pajak. Indonesia; 2012 p. 1–12.

37. Presiden Republik Indonesia. Pajak Penghasilan. 36 Indonesia; 2008.

38. KPMG. Asia Pacific Indirect Tax Country Guide. 2011.

39. Direktorat Jenderal Pajak. Pajak Pertambahan Nilai [Internet]. Jakarta Selatan: Kementrian Keuangan Republik Indonesia; 2013. 0-77 p. Available from: http://www.pajak.go.id/sites/default/files/Buku PPN ver 25102013 Upload.pdf

40. Badan Pusat Statistik. Rata- rata Pengeluaran per Kapita Sebulan di Daerah Perkotaan dan Perdesaan Menurut Provinsi dan Kelompok Barang (rupiah), 2011-2013 [Internet]. 2014 [cited 2014 Aug 20]. Available from: http://www.bps.go.id/linkTabelStatis/view/id/942

41. Manurung S. Kompleksitas Kepatuhan Pajak [Internet]. 2013 [cited 2014 Aug 23]. Available from: http://www.pajak.go.id/content/article/kompleksitas-kepatuhan-pajak

42. Badan Pusat Statistik. Angka Harapan Hidup Penduduk Beberapa Negara (tahun), 1995-2015 [Internet]. 2014 [cited 2014 Sep 27]. Available from: http://www.bps.go.id/index.php/linkTabelStatis/1517

43. Triami Media BV. Inflation Indonesia 2014 [Internet]. 2014 [cited 2014 Aug 31]. Available from: http://www.inflation.eu/inflation-rates/indonesia/historic-inflation/cpi-inflation-indonesia-2014.aspx
44. Presiden Republik Indonesia. Penyelenggaraan Program Jaminan Sosial Tenaga Kerja. Indonesia; 1993 p. 1–43.

45. Presiden Republik Indonesia. Sistem Jaminan Sosial Nasional. Jakarta, Indonesia; 2004.

46. BPJS Ketenagakerjaan. Laporan Tahunan 2013 [Internet]. Jakarta; 2014. Available from: http://www.bpjsketenagakerjaan.go.id/assets/uploads/tiny_mce/Annual Report/26032015_133805_ARA BPJS Ketenagakerjaan 2013.pdf

47. Dewan Jaminan Sosial Nasional. Jaminan sosial bidang ketenagakerjaan 2013 - 2019. Jakarta: Dewan Jaminan Sosial Nasional; 2014.

48. Presiden Republik Indonesia. Dana pensiun. Indonesia; 1992 p. 1–67.

49. Westra T a., Parouty M, Brouwer WB, Beutels PH, Rogoza RM, Rozenbaum MH, et al. On Discounting of Health Gains from Human Papillomavirus Vaccination: Effects of Different Approaches. Value Heal [Internet]. Elsevier Inc.; 2012;15(3):562–7. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1098301512000186

50. Badan Pusat SStatistik. National Income of Indonesia 2010-2014. Badan Pusat Statistik. Jakarta Selatan; 2014.

51. Badan Pusat Statistik. Rata-Rata Pengeluaran per Kapita Sebulan di Daerah Perkotaan dan Perdesaan Menurut Provinsi dan Kelompok Barang (rupiah), 2011-2014 [Internet]. 2014 [cited 2014 Aug 23]. Available from: http://www.bps.go.id/index.php/linkTabelStatistik/945

52. Jit M, Hutubessy R, Png ME, Sundaram N, Audimulam J, Salim S, et al. The broader economic impact of vaccination: reviewing and appraising the strength of evidence. BMC Med [Internet]. BMC Medicine; 2015;13(1):1–9. Available from: 10.1186/s12916-015-0446-9\n
53. Praditsitthikorn N, Teerawattananon Y, Tantivess S, Limwattananon S, Riewpaiboon A, Chichareon S, et al. Economic evaluation of policy options for prevention and control of cervical cancer in Thailand. Pharmacoeconomics [Internet]. 2011 Sep;29(9):781–806. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21838332

54. Rogoza RM, Ferko N, Bentley J, Meijer CJLM, Berkhof J, Wang K-L, et al. Optimization of primary and secondary cervical cancer prevention strategies in an era of cervical cancer vaccination: a multi-regional health economic analysis. Vaccine [Internet]. 2008 Sep 15 [cited 2014 Sep 19];26 Suppl 5:F46–58. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18992382

55. Marty R, Roze S, Bresse X, Largeron N, Smith-Palmer J. Estimating the clinical benefits of vaccinating boys and girls against HPV-related diseases in Europe. BMC Cancer [Internet]. 2013;13:10. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3561184&tool=pmcentrez&rendertype=abstract
Assessment of the broader economic consequences of HPV prevention from a government-perspective: A fiscal analytic approach
