

LETTER to the EDITOR

Regarding 'HPV Vaccination for Cervical Cancer Prevention is not Cost-effective in Japan'*Asian Pac J Cancer Prev*, 16 (6), 2583-2584**Dear Editor**

The authors of this letter read the article of Isshiki et al. (2014) on the cost-benefit analysis of HPV vaccination for cervical cancer prevention, and they found it interesting and unique. The article concluded that HPV vaccination at the price of US\$500 is not cost-effective, but becomes cost-effective at half that price. This conclusion misevaluates prophylactic cervical cancer programmes by both vaccination and screening in Japan, as the authors found a number of issues in the scenario analysis that Isshiki conducted. Therefore, this article is not suitable for forming political decisions. The authors would like to identify critical issues by discussing Model A, Model B, and the methodology of economic evaluation. The aim of our comment is to help make Isshiki's analysis more accurate and clear and to provide comprehensive information to support political decision-making by Japanese central and regional authorities.

Regarding Model A, it was assumed that screening with cytology was conducted every year from the age of 30 using base-case analysis. Based on current guidance of policy by the Japan regulatory authority, however, women should be screened with cytology every two years (Hamashima et al., 2010). Hence, given that frequency of screening was a factor in the scenario analysis, our concern is that screening costs in 'Model A' are overestimated. The article should also have taken into consideration the prophylactic effectiveness of screening for precancerous conditions (it was assumed that women are screened 11 times). Moreover, the authors could not find an appropriate reason why loss of earnings was calculated for only five years in this article, relating to the use of 13.163 of the Leibniz coefficient (at the age of 45, the feasible estimate of working years is 22).

With regard to Model B, the authors suggest that the article should incorporate cost of screening weighted by 23.7% (OECD, 2011) because the uptake rate of screening is based on screening not only with but also without vaccinations. It is also unclear why the article did not consider direct costs for mass-screening, treatment, and palliative care (home care may also be relevant), even though it stated that a woman was diagnosed with cervical cancer of stage IIIB at age of 40 and treated with hysterectomy, irradiation, and anticancer drugs in Model B. According to 'Methods for economic evaluation of health care' (Drummond et al., 2005), all the important and relevant costs identified and related to prevention

and treatment of a disease should fundamentally be valued and involved in any analysis. The authors argue that specifying such costs is essential. It is, for example, unclear why the article does not consider rate of evasion of death from cervical cancer due to vaccination and/or screening in Model B, even though the article stated that a woman received neither HPV vaccination nor screening. As for value of a statistical life (VSL) and value of life year (VLY) (Boardman et al., 2011), the authors would like to point out some issues and provide recommendations:

A) The article used the value of \$188,460 for stage IV cancer citing a report of Uchida et al. (2011). Alternatively, the authors recommend that the value of \$140,550 for stage IIIB cancer be used in the analysis.

B) The article stated that the equation of VSL for five years was:

$$VSL(5) = VLY \times \sum_{t=0}^{T(4)} (1-r)^t$$

However, the following equation should be used:

$$VSL(5) = VLY \times \sum_{t=0}^{T(4)} \frac{1}{(1+r)^t}$$

Therefore, VSL for five years is correctly \$1,010,610, where VLY is assumed to be US\$188,460 for stage IV cancer.

$$VSL(5) = \$188,460 \times \sum_{t=0}^{T(4)} \frac{1}{(1+r)^t} = \$1,010,610$$

C) VSL refers to the utility gained by vaccinated women as compared to unvaccinated women. Therefore, vaccinated women can gain an incremental outcome with prevention. VSL should be incorporated into Model A.

The authors would like to point out a few methodological issues regarding the cost-effectiveness analysis. Given that a longitudinal observation was carried out for the cost-effectiveness of vaccination, the article should consider an annual 3.5% discount of almost all costs, including psychosocial cost. The time horizon was unclear due to the differentiation of time horizons between Model A and Model B. The authors suggest that the time horizon should be the same in both models. According to the guideline for authors and peer reviewers of economic submissions to the BMJ (Drummond et al., 1996), time horizon and discount rate should be stated.

The authors attempted an alternative analysis by revising the following variables: *i*) Incorporating mass-screening cost into Model B; *ii*) Incorporating the same curative treatment cost in Model A into Model B; *iii*) The curative cost for stage IIIB cancer was derived from the article of Konno et al. (2010), set at ¥332,000, and

Table 1. Alternative Cost-Benefit Analyses of Prophylactic HPV Vaccines Based on Given Scenarios

| Cost variables | Model A | Model B |
|---------------------------|------------------|------------------|
| Vaccine | \$291,500,000.00 | \$0.00 |
| Screening | \$75,994,050.00 | \$75,994,050.00 |
| Curative | \$2,346,510.00 | \$29,285,900.00 |
| Palliative | \$0.00 | \$3,959,812.50 |
| Indirect | \$4,481,015.55 | \$137,257,820.00 |
| Non-Medication | \$368,074.65 | \$1,057,714.00 |
| Subtotal | \$374,689,650.20 | \$247,555,296.50 |
| Psychosocial (Δ) | \$129,359,783.19 | \$0.00 |
| Net Present Value | \$2,225,429.49 | - |

incorporated into Model B; iv) The curative cost for stage 0 cancer was derived from the article of Konno et al. (2010), set at ¥89,000, and incorporated into Model A; v) VSL was recalculated by using a VLY of \$140,550 and incorporated into Model A

In conclusion, it is likely that introduction of a HPV vaccination programme for cervical cancer prevention would result in net present value of approximately \$2 million and is thus more cost-effective than not introducing a vaccination programme (see Table above). Our alternative analysis should be carefully considered. The authors emphasize that Isshiki's scenario analysis with varying variables is less robust than dynamic and Markov models.

The authors warn that his analysis may be inconsistent with contemporary economic scholarship based on international policies. Finally, his article would be more objective if potential fallacies in assumptions and conclusions were clearly communicated.

Acknowledgement

Regarding conflicts of interest, this manuscript has received no support, per se. However, Ichiro Arakawa was an employee of GlaxoSmithKline K.K. (Japan) and has gained funding support from the GlaxoSmithKline group of companies and Qiagen. Hideki Murasawa declared to be an employee of the Japanese government and receives support from the National Personnel Authority of Japan. Ryo Konno received funding support and lecture honoraria from Merck Sharp & Dohme (MDS), the GlaxoSmithKline group of companies, and Qiagen.

References

- Boardman AE, Greenberg DH, Vining AR, et al (2011). Cost-Benefit Analysis Concept and Practice 4th Edition Upper Saddle River. NJ, 408-13.
- Drummond M, Sculpher MJ, Torrance GW, et al. (2005). Methods for Economic Evaluation of Health Care 3rd Edition Oxford Press, NY, 31-34.
- Drummond M, Jefferson TO (1996). Guideline for the authors and peer reviewers of economic submissions to the BMJ. *BMJ*, **313**, 275-83.
- Hamashima C, Aoki D, Miyagi E, et al (2010). The Japanese guidance for cervical cancer screening. *Jpn J Clin Oncol*, **40**, 485-502.

Isshiki T (2014). HPV vaccination for cervical cancer prevention is not cost-effective in Japan. *Asian Pac J Can Prev*, **15**, 6177-80.

Konno R, Sasagawa T, Fukuda T, et al (2010). Cost-effectiveness analysis of prophylactic cervical cancer vaccination in Japanese women. *Int J Gynecol Can*, **20**, 385-92.

OECD (2011). OECD health data.

Uchida A, Tango M, Hosokawa K, et al (2010). Cost-Benefit Analysis: Cervical Cancer Vaccination. [online] <http://www.pp.u-tokyo.ac.jp/courses/2010/documents/>

Ichiro Arakawa^{1*}, Hideki Murasawa^{1,2}, Ryo Konno³

¹Unit of Health Economics, Faculty of Pharmaceutical Science, Teikyo Heisei University, ²Department of Health Care Policy and Management, Graduate School of Comprehensive Human Sciences, University of Tsukuba, ³Department of Obstetrics and Gynecology, Saitama Medical Center, Jichi Medical University, Japan *For correspondence: i.arakawa@thu.ac.jp