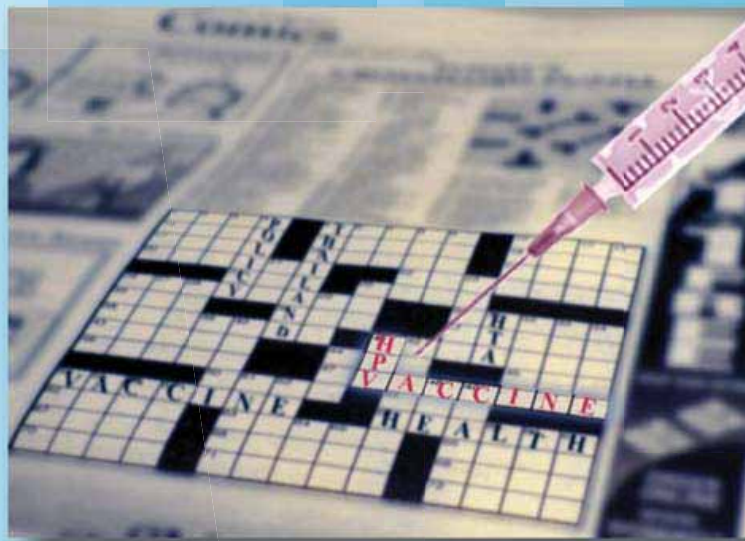


The role of health technology assessment evidence in decision making : the case of human papillomavirus vaccination policy in Thailand

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6 th Floor, 6 th Building Department of Health,

Ministry of Public Health Tiwanon Rd.,

Muang, Nonthaburi 11000, Thailand

Tel : 66-2590-4549, 66-2590-4374-5

Fax : 66-2590-4369

E-mail : hitap@hitap.net

Website : www.hitap.net



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E-mail : graphico__sys@yahoo.com

บทคัดย่อ

บทนำ : มะเร็งปากมดลูกเป็นสาเหตุการตายอันดับต้นของสตรีในประเทศที่มีรายได้ระดับปานกลางและระดับต่ำ การติดเชื้อ Human Papillomavirus (HPV) เป็นปัจจัยสำคัญของการเกิดมะเร็งดังกล่าว อย่างไรก็ตาม โรคนี้สามารถป้องกันได้ด้วยการตรวจคัดกรองหาความผิดปกติของเซลล์ในระยะเริ่มแรกและบำบัดรักษาก่อนที่จะพัฒนาไปเป็นเนื้อร้าย ในปัจจุบันการตรวจคัดกรองทำได้หลายวิธี เช่น แป็บสเมียร์ (Pap smear) การใช้กรดน้ำส้มเจือจางป้ายที่ปากมดลูก (Visual inspection with acetic acid, VIA) และการตรวจหาดีเอ็นเอของเชื้อ HPV (HPV DNA test) ในปี 2549 วัคซีนป้องกันการติดเชื้อ HPV ได้รับอนุญาตให้จำหน่ายในสหรัฐอเมริกาเป็นประเทศแรก แต่ด้วยราคาที่สูงมากทำให้หลายประเทศโดยเฉพาะประเทศกำลังพัฒนาไม่สามารถซื้อมาให้บริการแก่ประชาชน จนถึงเดือนกรกฎาคม 2552 รัฐบาลไทยยังไม่นำวัคซีนนี้เข้าสู่โครงการเสริมสร้างภูมิคุ้มกันโรค (Expanded Program on Immunization, EPI) และโครงการหลักประกันสุขภาพถ้วนหน้า การศึกษานี้มีวัตถุประสงค์เพื่อวิเคราะห์กระบวนการในการพัฒนานโยบายวัคซีนป้องกันการติดเชื้อ HPV ในประเทศไทย โดยเน้นการศึกษาบทบาทของหลักฐานทางวิทยาศาสตร์โดยเฉพาะข้อมูลการประเมินเทคโนโลยีในกระบวนการตัดสินใจ

วิธีการศึกษา : การวิจัยเชิงคุณภาพโดยทบทวนเอกสาร การสัมภาษณ์เชิงลึก การสนทนากลุ่ม การเข้าไปมีส่วนร่วมโดยตรงกับเหตุการณ์ที่เกี่ยวข้องกับนโยบาย และการจัดการประชุมเชิงปฏิบัติการเพื่อระดมสมองระหว่างผู้มีส่วนได้ส่วนเสียในนโยบายดังกล่าว โดยศึกษาพัฒนาการของนโยบายวัคซีนป้องกันการติดเชื้อ HPV ในประเทศไทยตั้งแต่เดือนมกราคม 2549 ถึงเดือนกรกฎาคม 2552

ผลการศึกษา : องค์กรที่มีหน้าที่รับผิดชอบการกำหนดนโยบายวัคซีนของประเทศไทย ได้แก่ คณะกรรมการวัคซีนแห่งชาติ (National Vaccine Committee, NVC) ซึ่งได้รับการสนับสนุนข้อมูลด้านวิชาการจากคณะอนุกรรมการสร้างเสริมภูมิคุ้มกันโรค (Advisory Committee on Immunization Practices, ACIP) ร่วมกับหน่วยงานอื่นๆ เช่น กรมควบคุมโรค กระทรวงสาธารณสุข สำนักงานหลักประกันสุขภาพแห่งชาติ ตลอดจนสำนักงานงบประมาณ คณะรัฐมนตรีและรัฐสภา โดยข้อมูลที่ใช้ประกอบการพิจารณา ได้แก่ ขนาดของปัญหาหรือโรคที่สามารถป้องกันได้ด้วยวัคซีน ความปลอดภัยและประสิทธิผลของวัคซีน ต้นทุนการผลิตและต้นทุนประสิทธิผลของวัคซีนเมื่อเปรียบเทียบกับมาตรการอื่น ผลกระทบด้านงบประมาณ การให้บริการวัคซีน และการยอมรับวัคซีนในกลุ่มประชาชน ซึ่งจนถึงเดือนกรกฎาคม 2552 ACIP และ NVC ยังไม่เคยนำเรื่องการนำวัคซีนป้องกันการติดเชื้อ HPV เข้าสู่ EPI มาจัดเข้าในวาระการประชุม ในขณะเดียวกันกระทรวงสาธารณสุขประกาศว่าไม่สามารถให้วัคซีนป้องกันการติดเชื้อ HPV ในระบบบริการสุขภาพภาครัฐได้เนื่องจากราคาที่สูงมากจนไม่สามารถรับภาระด้านงบประมาณได้

การศึกษานี้พบว่าผู้เชี่ยวชาญในประเทศไทยโดยเฉพาะอย่างยิ่งกลุ่มแพทย์แสดงจุดยืนที่แตกต่างกันต่อการให้วัคซีนป้องกันการติดเชื้อ HPV ภายใต้โครงการหลักประกันสุขภาพถ้วนหน้า โดยแสดงความคิดเห็นผ่านการประชุมวิชาการรวมทั้งกิจกรรมให้ความรู้แก่สาธารณะ อีกกลุ่มที่สำคัญคือนักวิจัยด้านนโยบายในหน่วยงานวิจัยกึ่งอิสระในกระทรวงสาธารณสุข ซึ่งเป็นผู้มีส่วนร่วมในนโยบายวัคซีนป้องกันการติดเชื้อ HPV โดยในช่วงปลายปี 2550 ได้นำเสนอผลการศึกษาที่พบว่าการตรวจคัดกรองมะเร็งปากมดลูกในประเทศไทยยังมี

ผลสัมฤทธิ์ต่ำทั้งที่เป็นมาตรการที่มีความคุ้มค่าที่สุดเมื่อเปรียบเทียบกับการรักษา ในขณะที่การฉีดวัคซีนป้องกันการติดเชื้อ HPV ไม่คุ้มค่าเนื่องจากมีราคาแพง การศึกษานี้ไม่มีผลต่อการเปลี่ยนแปลงนโยบาย หากแต่สนับสนุนการตัดสินใจของรัฐบาลที่ไม่นำวัคซีนนี้มาให้บริการในภาครัฐ นอกจากนี้ งานวิจัยดังกล่าวยังสนับสนุนให้ปรับปรุงโครงการให้บริการตรวจคัดกรองเพื่อป้องกันมะเร็งปากมดลูกแทน

บริษัทผู้ผลิตและจำหน่ายวัคซีนเป็นแหล่งสำคัญในการให้ข้อมูลแก่หน่วยงานภาครัฐ ประกอบด้วยข้อมูลประสิทธิภาพและความปลอดภัยของวัคซีน ขนาดการใช้ ข้อควรระวัง ค่าเตือน รวมถึงค่าใช้จ่าย โดยนำเสนอผ่านการประชุมวิชาการและกิจกรรมสาธารณะ ถึงแม้จะมีการเผยแพร่ข้อมูลเกี่ยวกับวัคซีนผ่านสื่อมวลชนมาก่อนที่วัคซีนจะได้รับอนุมัติจากสำนักงานคณะกรรมการอาหารและยา แต่ก็ไม่ได้ส่งผลต่อการขับเคลื่อนทางสังคมในเรื่องที่เกี่ยวข้องกับนโยบายของรัฐแต่อย่างใด ในปี 2552 บริษัทผู้ผลิตและจำหน่ายวัคซีนประกาศลดราคาวัคซีนลงอย่างมาก แต่ไม่สามารถทำให้เกิดการเปลี่ยนแปลงนโยบายไปสู่การให้บริการวัคซีนในภาครัฐ นอกจากนี้ ยังคงไม่มีความชัดเจนเกี่ยวกับราคาวัคซีนที่ภาครัฐจะยอมรับได้

สรุปผลการศึกษา: ปัจจัยที่มีอิทธิพลอย่างมากต่อนโยบายวัคซีนป้องกันการติดเชื้อ HPV ในประเทศไทยได้แก่ การที่วัคซีนมีราคาแพง ซึ่งจะมีผลกระทบอย่างมากต่อรายจ่ายด้านสุขภาพ ถึงแม้จะมีข้อมูลการประเมินเทคโนโลยีชนิดนี้ได้แก่ ข้อมูลการประเมินทางเศรษฐศาสตร์ ในประเทศไทย ข้อมูลดังกล่าวกลับมีบทบาทน้อยมากในการกำหนดนโยบาย อย่างไรก็ตาม ราคาของวัคซีนและการศึกษาต้นทุนประสิทธิภาพของวัคซีนเปรียบเทียบกับ การตรวจคัดกรองมะเร็งปากมดลูกทำให้ผู้กำหนดนโยบายและบุคลากรสุขภาพหันกลับมาให้ความสนใจต่อการป้องกันมะเร็งดังกล่าว ซึ่งได้ส่งผลให้เกิดความพยายามในการปรับปรุงการให้บริการตรวจคัดกรองที่มีอยู่

คำสำคัญ: วัคซีนป้องกันการติดเชื้อ HPV, การประเมินเทคโนโลยีด้านสุขภาพ, การตัดสินใจเชิงนโยบาย, การวิเคราะห์นโยบาย, ประเทศไทย

Abstract

Introduction: Cervical cancer is a major cause of deaths in female in low- and middle-income countries. The disease is preventable by introducing screening tests such as Pap smears, visual inspection with acetic acid (VIA) and HPV DNA testing. Recently, the first vaccine against human papillomavirus (HPV) was introduced to the health care market though the high cost of the vaccine makes it unaffordable especially in resource-poor settings. As of July 2009, the Thai government had not provided universal access to HPV vaccination. This study aims to shed light on the processes by which national HPV vaccination policy in Thailand has developed, with the focus on the role of scientific evidence, including health technology assessment information, in policy decisions.

Methods: Qualitative approaches including documentary review, in-depth interviews, personal communication, direct participation in the policy-related events by the researchers, and brainstorming workshops among key stakeholders were deployed in this study. This research focuses on the development of HPV vaccination policy at the national level in Thailand during the period January 2006 to July 2009.

Results: In Thailand, the responsible relevant bodies regarding this policy process are the National Vaccine Committee (NVC), with technical support from its Advisory Committee on Immunization Practice (ACIP), the expanded program on immunization (EPI), the Department of Disease Control, the Ministry of Public Health (MoPH), the National Health Security Office, the Bureau of Budget, the cabinet and the Thai parliament. The issues under consideration include: the magnitude of the disease prevented by the vaccine, vaccine safety and efficacy, cost-benefit and cost-effectiveness compared to other interventions, budget implications, vaccine delivery, and acceptance of the vaccine among the public. As of July 2009 the ACIP and the NVC had never included the issue of HPV vaccination in the EPI on its meeting agenda. At the same time, the MoPH publicly maintained that universal HPV vaccination could not be provided, owing to the unaffordable vaccine costs.

It was also found that Thai experts including clinicians possessed different positions towards a nationwide introduction of the HPV vaccination and expressed their opinions in academic conferences and public education events. Another important group, policy researchers at two semi-autonomous research institutes in the MoPH, were key participants in the Thai HPV vaccination policy. From late 2007, they presented their study findings addressing the inadequate performance of cervical cancer screening services in Thailand, and the value for money of different policy options for the prevention and control of cervical cancer. They indicated that screening services were cost-saving in comparison to treatment, and that HPV vaccination is cost-ineffective owing to the very high price of the vaccine. This study reaffirmed the government's position not to fund the immunization program, and was used to encourage the improvement of the screening programs.

The vaccine industry was among several sources of information concerning HPV vaccinations obtained by government officials, experts and professionals. The information includes the vaccine's effectiveness, safety, doses and administration, precautions, warnings and costs were disseminated through academic conferences and public events. This new intervention had been publicized through the mass media before being licensed in Thailand. However, the campaigns did not lead to any social mobilization that supported public immunization program. Furthermore, despite reductions of vaccine prices offered by the industry in early 2009, an unclear position on a preferable price from policy makers remains.

Conclusions: HPV vaccination policy in Thailand has been largely driven by the unaffordable prices of vaccine products and associated implications for health expenditure. Although domestic HTA information including health economic data of this newly-emerging intervention had been available, such evidence played a limited role in the making of HPV vaccination policy. However, the high prices and existing cost-effectiveness studies of the vaccine drew significant attention from policymakers and health officials to the issues of cervical cancer prevention and resulted in the efforts to improve the existing screening services.

Key words

Human papillomavirus vaccine, health technology assessment, decision making, policy analysis, Thailand

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Abbreviations

ACIP	Advisory Committee on Immunization Practice
ART	Antiretroviral therapy
CEA	Cost-effectiveness analysis
DALY	Disability-adjusted life year
DDC	Department of Disease Control
DMS	Department of Medical Services
DOH	Department of Health
EPI	Expanded Program on Immunization
FDA	Food and drug administration
FHI	Family Health International
GAVCS	Global Advisory Committee on Vaccine Safety
GAVI Alliance	Global Alliance for Vaccines and Immunization
GPO	Government Pharmaceutical Organization
GSK	GlaxoSmithKline
HITAP	Health Intervention and Technology Assessment Program
HPSR	Health policy and systems research
HPV	Human papillomavirus
HTA	Health technology assessment
ICER	Incremental cost effectiveness ratio
IHPP	International Health Policy Program
IVI	International Vaccine Institute
MoPH	Ministry of Public Health
NCI	National Cancer Institute
NEDL	National essential drug list
NGOs	Nongovernmental organizations
NHSO	National Health Security Office
NVC	National Vaccine Committee
NVCO	National Vaccination Committee Office
PBAC	Pharmaceutical Benefits Advisory Committee
QALY	Quality-adjusted life year
RTCOCG	Royal Thai College of Obstetricians and Gynecologists
SAGE	Strategy Advisory Group of Experts
TGCS	Thai Gynecologic Cancer Society
VIA	Visual inspection with acetic acid
UC	Universal Health Coverage
UNICEF	United Nations Children's Fund
US	United States of America
USD	United States Dollar
WHA	World Health Assembly
WHO	World Health Organization

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Conflict of interest

The authors of this report are researchers employed by the Health Intervention and Technology Assessment Program (HITAP), Thailand. We were involved in conducting a study comprising the performance assessment of the national cervical cancer screening program and economic evaluation of HPV vaccine in comparison to Pap smear and VIA in 2007-2008. In addition, we carried out the research dissemination activities including giving presentations to policymakers, health professionals and academics. The HITAP also convened a public forum to support rational interventions for cervical cancer prevention in Thailand.

1. Introduction

Cervical cancer is the second most common cancer in women worldwide (WHO 2007a). In particular, it is a major cause of deaths in the female population in low- and middle-income countries. The development of this cancer is associated with the infection of some strains of the human papillomavirus (HPV). This disease is preventable by introducing screening tests such as Pap smears, Visual inspection with acetic acid (VIA) and HPV DNA test. While such preventive approaches are notably effective in reducing morbidity and mortality associated with cervical cancer in industrialized countries, the disease remains a serious public health problem in the developing world, owing to the poor coverage and quality of screening programs (Parry 2006). In 2006, the first vaccine against HPV was approved by the United States Food and Drug Administration (US FDA). Currently, there are two prophylactic HPV vaccine products on the global market. These are a quadrivalent vaccine, developed by MSD under the trade name Gardasil®, and GlaxoSmithKline (GSK)'s bivalent vaccine: Cervarix®; both were approved by the US FDA in 2007.

Considering that HPV vaccination is an effective tool for reducing the burden of illness, including deaths associated with cervical cancer, the World Health Organization (WHO) has developed policy and program guidance notes on introducing this intervention in developing countries (Aguado 2008). Nevertheless, in resource-poor settings, the high cost of these products makes their availability and accessibility very limited. Meanwhile, governments of many industrialized nations have adopted a policy of providing HPV vaccination through publicly-funded benefit or insurance schemes (Haas et al. 2009; Van Damme, Pecorelli, and Joura 2008). The literature suggests, however, that the public provision and subsidization of the vaccines for schoolgirls and adolescents is contentious. Debates both for and against these immunization programs involve a wide range of arguments, not only regarding the health benefits, budget impact and cost-effectiveness, but also religious and moral concerns including equity, child rights, potential promiscuity and other unsafe sex practices (Lancet 2006; Priest 2006). Given that these assertions and the involvement of vaccine advocates are context-specific, the role of health technology assessment (HTA)¹ information in decision-making inevitably varies across different health systems.

HPV vaccination policy in Thailand has been selected as a case study because cervical cancer, the target disease of the vaccine, is life-threatening and afflicts a large number of the female population. Unlike most developing countries, the capacity concerning health policy and system research including HTA in the Thai setting has, to a certain extent, been strengthened (Teerawattananon et al. 2009). In part, this made up-to-date evidence concerning national cervical cancer control programs in the country available. Funded by the World Bank, a research project was conducted in 2007-8 to evaluate the performance of screening initiatives which provided Pap smear tests, VIA, and their combination (IHPP and HITAP 2008). In this study, economic appraisals of HPV vaccinations and the said screening interventions were also carried out. In addition, other facets such as the financial resources and workforces required for scaling up the

¹ The term 'HTA' has been defined differently by different organizations. According to the International Network of Agencies for Health Technology Assessment, HTA is '*the systematic evaluation of properties, effects, and/or impacts of health care technology. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care. HTA is conducted by interdisciplinary groups using explicit analytical frameworks drawing from a variety of methods.*' (Available at http://www.inahta.org/upload/HTA_resources/Edu_INAHTA_glossary_July_2006_final.pdf, accessed July 20, 2009)

existing screening programs as well as the opinions of key stakeholders towards different policy options were assessed. It appears, however, that the World Bank-supported study was not the sole source of evidence concerning the measures to prevent and mitigate the impact of cervical cancer. Information based on the individual judgment of leading health professionals regarding the clinical benefits and cost-effectiveness of HPV vaccinations drawn on vaccine trials along with economic studies in different settings have also been disseminated in Thailand by many interested stakeholders, including the vaccine industry and certain groups of health professionals.

This research aims to enhance the understanding on how policy decisions concerning HPV vaccination adoption in Thailand have been made at the national level. The focus of this study is on the extent to which scientific evidence, including HTA information, has a role in policy development.

2. Literature review

2.1 Cervical cancer screening in developing countries

Although cervical cancer is preventable by introducing secondary prevention approaches for early detection of abnormal cells and precancerous lesions in the cervix, and providing effective treatment, access to these services in poor settings is limited. Pap smear testing is a technique that gathers cells from the outer part of the cervix to be examined under a microscope. These cells are checked for abnormalities. This cytology-based testing is resource intensive as it requires a well-established infrastructure, including laboratories and well-trained health workers to interpret the results (Parry 2006). In many developing countries, the lack of cytopathologists, cytoscreeners and cytotechnicians is a critical factor limiting service provision (Anorlu 2008). In addition, there are often no facilities or necessary equipment for cervical cancer screening or treatment.

In contrast, VIA is a naked-eye screening tool for the detection of precancerous tissues after the application of dilute acetic acid to the uterus cervix. Since 2005, VIA followed by immediate cryotherapy, the exposure of tissues to extreme cold to eliminate abnormal cells, has been encouraged by international health organizations including nongovernmental organizations (NGOs) as a viable alternative screening test of cervical cancer (Parry 2006). The effectiveness of this intervention as a population-based initiative has been studied in many projects, not only in resource-limited areas but also in higher-income countries (Denny, Kitchener, and Pollack 2000; Jeronimo et al. 2005; Sankaranarayanan, Wesley, and Somanathan 1998).

Apart from the financial and technical constraints on the supply side, multiple visits for Pap smear testing, results and subsequent treatment are critical hurdles to effective screening, especially among people in remote areas (WHO 2002). An analysis of population-based surveys indicates a low coverage of cervical cancer screening in developing countries, 19%, compared to 63% in developed nations (Gakidou, Nordhagen, and Obermeyer 2008). The inequalities are wealth-related and can be observed within and across countries: women in older age groups and the poor are least likely to have access to screening services, even though they are at the highest risk (Arrossi et al. 2008). In some areas, incorrect beliefs and a lack of knowledge concerning the disease among target populations are key factors impeding cervical cancer screening coverage (Garland et al. 2008).

2.2 HPV vaccination: evidence, information and introduction

The success in the development of HPV vaccine as the primary prevention of HPV infection, cervical cancer and other HPV-related diseases has been acknowledged as a breakthrough in

public health, as this technology is expected to be the most effective tool for saving the lives of millions of women. From the research and development phase until present, several studies of the vaccine have been carried out in many parts of the world. These studies have concerned with different aspects of the vaccination such as the efficacy, effectiveness, safety, cost-effectiveness, delivery capacity and public acceptance. This results in a diverse range of information, some of which is drawn on research findings, and is disseminated in the global health community by various interests and with different purposes. In some aspects, the information is contentious, and to a certain extent, the debatable issues make policy decisions regarding the introduction of HPV vaccination in particular settings highly complex.

2.2.1 Safety and effectiveness

It is a standard procedure in most countries that a new health intervention needs to meet a set of requirements concerning the effectiveness, safety and quality before gaining approval. Pre-marketing evaluation of the clinical benefits and the adverse effects of pharmaceuticals and vaccines are conducted in clinical trials phases I, II and III. As studies before product approval are limited in terms of the number and diversity of subjects, as well as the short time span, monitoring and assessment of clinical outcomes and undesirable reactions of medicines and other health-related products are required in the post-marketing phase where these interventions are administered in larger numbers of people with more diverse characteristics than in the research and development period.

As prophylactic vaccines are indicated in healthy populations, the safety profile is of a major concern. The literature suggests that there is a common agreement that HPV vaccination is safe in up to 5-year follow-up study (Bayas, Costas, and Munoz 2008). The most common side effects are mild, and include pain, redness, or swelling at the injection-site and/or systemic symptoms such as headaches and fatigue. Meanwhile, some argue that HPV vaccination's safety is unclear, as these products were monitored during short time-span field trials and have been available on the market for a limited period. This raises the question: *'What are the odds of serious harm from the vaccine itself. ... , and several hundred thousand girls must be vaccinated and followed for many years before any rare or even uncommon serious adverse reactions can be documented.'* (Napoli 2007).

A systematic review of clinical trials published between 2004 and 2007 to examine HPV vaccine efficacy, carried out by Rambout et al (2007), indicated that the vaccine significantly reduced the frequency of high-grade cervical lesions caused by vaccine-type HPV strains (16/18) compared with the control groups. The vaccine was also highly efficacious, but not of 100 per cent, in preventing persistent HPV infection, low-grade lesions and genital warts. It is noteworthy that there is no evidence of vaccine efficacy in the long-run because the longest follow-up of a vaccinated population is less than six years (Harper and Paavonen 2008). Therefore, there is still a concern with regard to the need for booster doses. Furthermore, some have argued that the efficacy of the vaccines against cervical cancer due to HPV serotypes other than HPV 16 and 18 is unknown (Okonofua 2007). This means that each country should determine the effectiveness of particular HPV vaccination products and assess whether or not the vaccination is useful in preventing HPV infection with the most prevalent sub-types in its territory.

The appropriate age of HPV vaccination is another controversial issue and it can vary widely across settings. Because of the fact that the vaccine is for prophylaxis, and not for therapeutic purposes, it should be administered to girls prior to their HPV exposure. It has been agreed that the suitable age of vaccination largely depends on the age at first intercourse or exposure to the virus, epidemiology, and existing vaccination programs in each country (Wright et al. 2006). For example, in countries where school-based vaccination is established, it is possible that the vaccine

can cover a large group of young adolescents throughout the country. In contrast, in countries where a school-based program does not exist, the feasibility of reaching the targeted populations is problematic.

Following Haug (2008), existing trials of HPV vaccines show promising results in the prevention of precancerous lesions. She maintains, however, that there are reasons for caution when policymakers consider introducing HPV vaccination: if the vaccine will prevent not only the lesions but also cervical cancer; the length of protection of the vaccine; how vaccination will affect natural immunity against HPV and what, if any, the implications are. As the author further puts it, more long-term studies of the overall effectiveness and undesirable reactions of the vaccine are required before large-scale vaccination programs could be recommended.

2.2.2 Value for money

Economic evaluation, including cost-effectiveness analysis (CEA), has been increasingly demanded by decision makers, owing mainly to resource constraints and the growing needs for health services, as well as calls for evidence-based policy decisions in the health sector. Model-based economic evaluation is particularly useful in the case of HPV vaccine because its benefits can only be observed in the long-term i.e. 20-30 years after vaccination. In addition, there are uncertainties surrounding important factors in the assessment of this intervention, for example, the duration of vaccine protection and the appropriate age for vaccination. Economic modeling allows researchers to explore the effects of these uncertainties in the evaluation. However, to set up such an analysis of a preventive intervention that might have an effect on the incidence of cervical cancer in the next decades is extremely complex, as the assessment has to model the natural development of HPV infection in 12 years-old girls over their lifetime, the long-term effectiveness of the vaccine, the activity of the vaccine against other HPV strains, the sexual behavior of the girls and women and their partners, and cervical-cancer screening practices among these women (Haug 2008).

Out of the 8 articles regarding economic evaluation of HPV vaccine reviewed by the researchers, four are drawn on studies in the US (Goldie et al. 2004; Kulasingam and Myers 2003; Sanders and Taira 2003), and three papers are on studies in the Netherlands, Canada, the United Kingdom (UK), the US and Taiwan (Boot et al. 2007; Brisson et al. 2007; Rogoza et al. 2008). Among other studies, an economic assessment of HPV vaccine in resource-limited settings, namely 72 GAVI-eligible countries, was recently published (Goldie et al. 2008b). The conclusions of all the papers support the introduction of HPV vaccination, citing that the vaccine offers good value for money. They did, however, apply different ceiling thresholds. Following Kulasingam and Myers (2003), for instance, HPV vaccination in girls 12 years of age combined with biennial screening starting at 24 years in the US was cost-effective with an incremental cost effectiveness ratio (ICER) of 44,889 USD per life-year saved, provided that the threshold of 50,000 USD was introduced. Meanwhile, Goldie et al (2004) suggests that HPV vaccination in 12-years-old girls combined with triennial screening starting at 25 years in the US is cost-effective with an ICER of 58,500 USD per Quality-Adjusted Life Year (QALY) gained, as 60,000 USD was applied as threshold.

Using population based and epidemiological data of GAVI-eligible countries, Goldie et al (2004) estimated that at a vaccine price of 10 international dollars per three doses, HPV vaccination was cost-effective given a threshold of 1 GDP per capita per QALY gained. The cost per Disability-Adjusted Life Year (DALY) averted was less than 100 international dollars for 49 out of 72 countries, especially those in African, American and the Western Pacific region. However, the authors provided no justification regarding the use of 10 international dollars as the vaccine cost. It should be noted that most papers report economic consequences of the vaccine when the

government's viewpoint is applied. This means that only direct medical costs are taken into account. It also indicates that the duration of HPV vaccination protection and the costs of the vaccine are amongst the most significant factors affecting the ICER.

Another problem of using HPV vaccination cost-effectiveness information in policy decisions is that the vaccine cost applied in the studies may be significantly different from the real purchasing cost. As maintained by Gakidou et al (2008), if a total cost of HPV vaccination of 25 USD per course was applied as found in the study by Goldies et al (2007), then the vaccination and three screening visits would be very cost-effective; however, the current prices of the vaccine in 2008 varied between 300-400 USD per course. Also, the costs of introducing HPV vaccination into some settings will be substantial if essential infrastructure such as cold chains are not already in place. Importantly, one should be aware that the discrepancies in the cost-effectiveness of HPV vaccination in different studies are associated with the variation in economic models and assumptions introduced. There are also a number of other uncertainties including epidemiological profiles of HPV infection due to particular subtypes of the virus, the long-term effectiveness and the safety of the vaccine and changes in sexual behavior amongst vaccinated people (Ferko et al. 2008).

2.2.3 Vaccine costs and affordability

Health policy scholars argue that many cost-effective interventions are neglected by policymakers because the governments cannot afford the budget implications. The high prices of HPV vaccine are among the major impediments in introducing this preventive intervention in poor countries, where the morbidity and mortality of cervical cancer are high. As asserted by Gauden Galea (quoted in Parry 2006), the Regional Adviser on Noncommunicable Diseases at WHO's Regional Office for the Western Pacific '*Vaccination holds much promise for primary prevention of cervical cancer in the future. It will be well-accepted, but for that to happen the evidence of efficacy has to be firmly established and the cost has to be affordable to developing countries.*'

To accelerate access to HPV vaccination in the developing world, different financing mechanisms for the vaccine purchasing and immunization programs have been recommended (WHO 2007c). These include, for instance, advanced market commitment and differential pricing, both of which require collaboration from the vaccine industry. In addition, it is possible that international organizations and donors negotiate vaccine prices through bulk purchasing initiatives (Gakidou, Nordhagen, and Obermeyer 2008). However, despite such collaborative efforts, the unaffordable costs of vaccine delivery remain unresolved in those settings where infrastructure and other health service resources are inadequate. This holds true even for the treatment and control of common infectious diseases (Sarin 2008). There are also concerns over the potential diversion of resources from existing health programs, such as those for HIV/AIDS, tuberculosis and malaria. Moreover, Gakidou and colleagues (2008) emphasize that even when HPV vaccination is introduced, the costs of providing cervical cancer screening are not obviated.

2.2.4 Attitudes, knowledge and acceptability towards the vaccine

Social construction of public policies plays a crucial role in different stages of policy processes (Rochefort and Cobb 1994). Policymakers usually take into account social acceptability and stakeholders' attitudes towards new health interventions, since public support or rejection of the programs can affect not only the success in the implementation phase, but also the popularity towards the policymakers themselves (Kingdon 1984). With regard to HPV vaccination, there are a number of studies examining the attitudes, knowledge and acceptability among target populations including adolescents, parents and health care providers. These surveys were conducted prior to the introduction of HPV vaccination in a number of settings to explore the

factors affecting the willingness to accept the vaccine as well as the potential change in risk behaviour patterns among those vaccinated.

A systematic review by Klug et al (2008) of the studies carried out in rich countries such as the UK and the US suggests that knowledge about HPV infection varied widely within the respondent groups. The relationship between HPV and cervical cancer was known among 8-68% of respondents and varied across age groups and genders: women knew more than men, and older women knew more than the younger ones. Most studies indicate that knowledge regarding HPV infection was inadequate; thus, providing reliable evidence to the public is greatly needed. However, knowledge of HPV vaccine alone is not enough to persuade people to seek vaccination. A population-based survey in the US suggests that although the target population might be aware of HPV infection and HPV vaccine availability, they were not well-informed of the protective impact against cervical cancer of the vaccine. This would be necessary in making correct decisions about the vaccination (Ragin et al. 2009). The authors point out the need for education campaigns targeting particular groups with inadequate knowledge.

In similar vein, another study in the US during the period October 2006 to May 2007 suggests that despite knowledge about the potential health benefits of HPV vaccination, only a small portion of young women had been vaccinated (Kahn et al. 2008). Importantly, the vaccine uptake rates among poor women were relatively lower, compared with the higher-income group. This will result in an increase in the existing disparities in cervical cancer incidence and mortality. As argued by the authors, different vaccine uptakes were likely to be a consequence of a delay in vaccine provision to low-income women. This may be due to a number of factors including the complex process of adding a vaccine to the formularies of the health facilities that serve these women, and a lack of commercial incentive to provide vaccines. There may also be barriers to vaccination, either real or perceived, in this population.

It is noteworthy that the majority of these studies were conducted in female parents. This may be because mothers usually played an important part in making decisions concerning whether their daughters should be vaccinated. A number of parents, however, maintained that it should be a collective decision between the two parties (Brabin et al. 2006). The findings suggest that the parents were generally in favour of the vaccine (Davis et al. 2004; Dinh et al. 2007; Marlow, Waller, and Wardle 2007; Woodhall et al. 2007) despite differences in study methods used and social issues concerned. However, research gaps concerning this issue are substantial, as most existing studies were conducted in developed countries, while only a few address the problems in poor settings.

It is widely recognised that health professionals' attitudes and practices are important factors in implementing health programs including immunization. Three studies examine the perceptions towards HPV vaccination amongst American health providers such as nurse practitioners, obstetricians and gynecologists, family physicians and pediatricians. It has been found that most respondents are willing to recommend the vaccine to their clients (Kahn et al. 2005; Raley et al. 2004). Meanwhile, a review conducted by Zimet et al (2006) indicates that providers are willing to accept the vaccine if it is formally approved by professional organizations. In addition, the professionals prefer to recommend the vaccine to older youths rather than younger ones because they felt that it would be difficult to provide sex education to the relatively younger populations. Nevertheless, some scholars argue that clinicians may be reluctant to persuade girls and women to get immunized against sexually-transmitted diseases like HPV infection since it can stigmatize them (Parry 2006). Some low- and middle-income countries including India, Peru, Uganda and Vietnam had experience of HPV vaccination delivery as part of research studies supported by an international NGO, PATH (PATH 2009). It was suggested that the vaccination programs required

education for vaccinees and parents, as well as community education, sensitization and mobilization.

2.3 Adoption of new vaccines in developing countries

In the developing world, infectious diseases remain crucial public health problems. This is partly because immunization against these infections cannot be introduced, even though effective vaccines have long been available for people in richer countries. The delay in the adoption of new and underutilized vaccines which results in slow expansion of immunization initiatives in poorly resourced settings is influenced by several factors. Clemens and Jodar (2005) highlight the importance of evidence, scientific, epidemiological, clinical and economic factors in new vaccine licensure and introduction. Owing to inadequate resources, policymakers tend to demand evidence as a prerequisite for financing new vaccination initiatives. Moreover, evidence is necessary for vaccine advocacy to convince policymakers to expand the immunization programs. However, studies to indicate the burden of diseases, types of microorganisms, and the effectiveness, safety and value for money of particular vaccines in developing countries are limited. This results in policymakers showing a reluctance to allocate public resources to the new interventions. Meanwhile, Levine and Levine (1997) emphasize the roles played by different actors such as policymakers, scientists, health professionals, the vaccine industry and the public in generating and using information and evidence to advocate vaccine introduction. They also assert that public pressures associated with the perceptions towards the magnitude and health consequences of a disease, the cost of vaccines, and the health system capacity to integrate the vaccine into existing immunization programs are the key elements that need to be considered by policymakers in vaccine adoption.

A comprehensive study to examine the factors facilitating and constraining the adoption of new and underutilized vaccines in developing countries suggests the influences of contextual factors, data, information, and actors (Brooks et al. 1999). Important political, economic and international contextual elements include: the expansion of immunization coverage at the global level and the efforts of international agencies, especially the WHO and the United Nation Children's Fund (UNICEF); a conducive funding system for immunization programs including tier pricing of vaccines; decentralization of health delivery; and an economic environment which affects the willingness and ability of governments to invest in national vaccination programs. This study also illustrates the role of data and the way data was used. The absence or inaccessibility of information including that derived from cost-effective evaluation might hamper vaccine introduction. While vaccine prices and 'perceived' affordability had a crucial role in national policy making, the efficacy and effectiveness of vaccines were influential in policy decisions at international level. Concerning the roles of actors, the study argues that several international agencies and public-private partnerships were active in advocating new vaccine adoption. These included, for instance, the World Bank, the Rockefeller Foundation, PATH, and the Bill & Melinda Gates Foundation. It was emphasized, however, that developing countries had no space to express their views even though vaccine introduction should have been their priority concern.

2.4 Policy decisions regarding HPV vaccination introduction: Experiences in other countries

The launch of HPV vaccines has generated significant policy debates, and even opposition in some societies (Priest 2006; The Lancet 2006). Among others, the very high prices of the vaccine products, competition from other health interventions, resource constraints and insufficient health system capacity are potential impediments in introducing such a new technology in poor countries (Everett 2006). Moreover, as HPV vaccine is indicated in adolescent and young adults,

not in infants under the expanded program on immunization (EPI) schedule, how to efficiently deliver the vaccine to the target populations is a challenge for policy makers and program managers. Like many other health interventions, the adoption of HPV vaccination in a particular country comes about from debates amongst policymakers and stakeholders on different issues.

According to Agosti and Goldie (2007), the considerations include the burden of cervical cancer and other HPV-related diseases, the health systems' infrastructure including its capacity to deliver vaccines to the adolescent population, the affordability and cost-effectiveness of vaccination in comparison to other interventions competing for government budgets, public acceptance and support, and political will, while the greatest barrier to an HPV immunization service is the price of the vaccine. At the same time, socio-cultural factors play a key role in some settings, where the vaccination and related policies are perceived and interpreted in particular ways. For instance, an article by Haber and colleagues (2007) discusses whether getting girls vaccinated against HPV infection implies tacit consent in engaging in sexual activity, and confers a false sense of being protected from sexually-transmitted diseases that will in turn lead to a release of sexual inhibitions. Other illustrations can be drawn on the US and some European countries where conservative Christian groups rejected the vaccination program because it would promote sexual promiscuity among children (Parry 2006).

An article shows that there are three key conditions necessary for the introduction of HPV vaccination in national immunization programs in industrialized countries. These include (1) licensure by a national authority that confirms the safety and efficacy of the vaccine, (2) development of recommendations for use by experts on immunization, and (3) full financial support from the government (Wright et al. 2006). It is inevitable that many individuals and institutions are involved in the policy process. In the US, for example, the FDA approved the vaccine to be sold on the market; the Centers for Disease Control and Prevention provided national recommendations for vaccine use including vaccination schedules and the appropriate age for vaccination, while the Advisory Committee on Immunization Practice (ACIP) in conjunction with the American Academy of Pediatrics formulated the immunization guidelines. Furthermore, the federal government, state and local governments ensured the financial feasibility for the vaccination programs. Private health care providers, state and local public health providers are responsible for vaccine delivery. Subsequent to the implementation, many institutes take part in monitoring the program performance, vaccine safety and effectiveness, and the enforcement of regulations related to vaccine injury compensation and liability.

In some settings such as European countries, HPV vaccination has been expanded rapidly. According to Van Damme, Pecorelli and Joura (2008), it was not only the promise of the vaccine to prevent HPV infection and its potential consequences, life-threatening cancer, but also the concrete evidence generated by research studies that convinced policymakers and other stakeholders to support the policy adoption. The authors argue that vaccine approval, risk assessment and management, and HTA context in the European Union was supportive and led to rapid vaccine adoption in most countries. In addition, a wide range of interest organizations including scientific societies and academic institutions put in concerted efforts in this respect, by shedding light on the burden of HPV infection and the need for primary prevention of cervical cancer including using HPV vaccination. Such development took place while cancer prevention was high on the policy agenda of countries in the region, and recommendations from respective health agencies, to some extent, resulted in the swift adoption of the vaccine.

In a few countries such as Finland, the introduction of HPV vaccination was deferred because policymakers considered that the existing cervical cancer screening programs needed to be enhanced (Nohynek 2008 quoted in Van Damme, Pecorelli, Joura 2008). This was in contrast with the idea of introducing the vaccine as a complement approach to the screening service in the

countries where high coverage of the screening tests had been achieved. Before recommending HPV vaccination in March 2008, the Netherlands had delayed reimbursement for this intervention. Such a reluctant decision was guided by an economic evaluation indicating the cost-ineffectiveness of the vaccine (Van Damme, Pecorelli, and Joura 2008). In the same vein, cost-effectiveness information hindered HPV vaccination introduction in Austria.

A policy analysis conducted regarding funding for HPV vaccination in Australia sheds light on the complex policy processes including the involvement of key stakeholders and public media (Roughhead, Gilbert, and Vitry 2008). At first, on 3rd November 2006 the Pharmaceutical Benefits Advisory Committee (PBAC) – an independent legislative body responsible for considering comparative efficacy, effectiveness and cost-effectiveness of a product and making recommendations if the product should be covered by the publicly-funded plan – advised the reject of the quadrivalent HPV vaccination. The decision was made due to the fact that there was a lack of information concerning the long-term effectiveness and on how to determine the appropriate target group to be monitored for follow-up. The Committee also argued that the vaccine was not cost-effective, and so should not be included in the national immunization program. This policy decision prompted negative reactions from a diverse range of interests including politicians in opposition parties, women senators, consumer groups, physicians, the Cancer Council and cancer advocacy NGOs. Over 300 newspaper articles reported the concerns of these policy actors and stated that the delays in the introduction of this effective vaccine meant missing an opportunity to save lives and reduce treatment costs. In contrast, the PBAC's recommendations were supported by only a small number of health professionals. As revealed in the study, the vaccine company was asked to resubmit its file with minor changes. Subsequently, on 22nd November 2006 the PBAC recommended funding HPV vaccination.

3. Conceptual framework

3.1 Related public policy models

In order to understand why and how a policy is developed in a particular way, the three main elements to be addressed comprise of the actors, the processes involved and the context (Walt and Gilson 1994). The actors, as individuals groups or organizations, can be classified by their positions towards a policy: supporters, opponents or neutral. The positions and roles of actors in each policy stage, i.e. policy agenda setting, adoption, formulation and implementation, are determined by their interests and power (Brugha and Varvasovszky 2000). While actors engage in particular policies to pursue benefits for themselves and/or for other persons or groups to which they support, those with relatively high levels of power can have a leading role in the policy decisions and processes. In many instances, policy actors create networks with others who have common objectives and interests in order to share and exchange their resources. Furthermore, contextual factors, both inside and outside health systems, are important in determining not only the involvement of policy actors, but also policy choices.

The adoption of particular public policies is implicated by several elements including the socio-political concerns of policymakers. Policy advocacy campaigns carried out by policy supporters and opponents are crucial in many cases. When a problematic issue catches the attention of the government, responsible policymakers, including politicians and public officials, seek different policy options from within their organizations and elsewhere (Rose 1991). After assessing each option against certain criteria, the most appropriate ones will be adopted. Most of the time political desirability is the major determinant of policy decisions (Kingdon 1984). In addition, policymakers normally take into account the social acceptability, affordability and feasibility of the programs or interventions to be adopted. On some occasions, scientific evidence and research

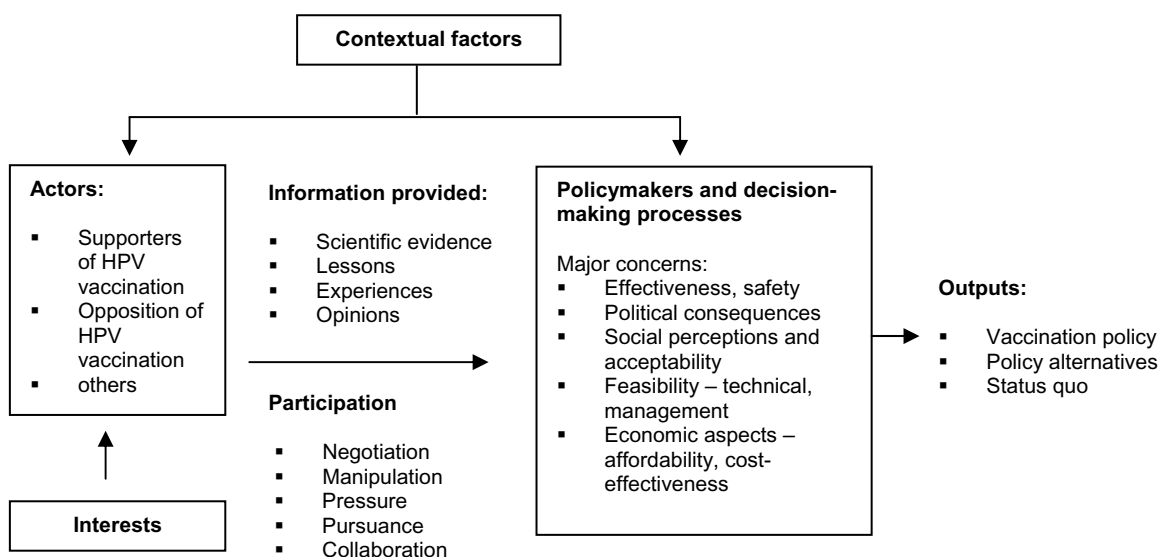
findings can have a role in guiding public policies. However, owing to several impediments, some research studies are neglected and not influential in policy processes (Mills 2004; Reichenbach 2002).

3.2 Analytical framework analyzing HPV vaccination policy in Thailand

HPV vaccine is mainly indicated as a prophylactic intervention for cervical cancer. Given that screening tests including Pap smears and VIA services have been introduced in Thailand as cervical cancer control approaches, the adoption of the policy to provide universal access to HPV vaccination can be regarded as a radical policy shift. Public policy theories indicate that substantial changes in a policy domain are rare, and innovations take place only in conducive circumstances, and require new actors with new ideas to dominate policy communities (Baumgartner and Jones 1991). This argument has been elaborated by Kingdon (1984) in his agenda setting model: a window of opportunity for policy innovation opens when three independent streams of problem, solution and politics meet, i.e. a social phenomenon is recognised as a problematic issue, an appropriate solution to tackle such a problem is available, and there is political development in a way that allows the involvement of new sets of policymakers including changes in administration or decision-making agencies.

This study seeks to understand the policy processes by which the policy concerning publicly-funded HPV vaccination is developed, by exploring the involvement of different actors, both inside and outside the Ministry of Public Health (MoPH), as well as the influence of contextual factors in determining problem recognition, policy identification, and political mobilization (figure 1). Key stakeholders, either supporters or opponents of HPV vaccination might participate in the policy making processes, by negotiating and seeking collaborations with each other. Some might put pressure on and manipulate other interests. In so doing, it is likely that the policy participants provide responsible politicians and health officials in the MoPH and national health benefit plans with information, drawn on research findings, related lessons in other settings and past experiences in the Thai health systems and elsewhere. Such information might encourage policymakers to be aware of not only cervical cancer problems but also screening services and HPV vaccine. Similar information might be exchanged amongst policy network members and across institutes. The position, for or against universal HPV vaccination, is guided by the anticipation of the gain or loss of benefits from the policy, amongst certain stakeholders. The policy authorities assess the information provided by different parties as well as that from other sources, and thereafter decide to adopt HPV vaccination policy and/or other alternatives. As Kingdon (1984) also argues, among many available options, the ones likely to be adopted by policymakers are those with certain characteristics. In the Thai case study, critical elements of concern might include the effectiveness and safety of HPV vaccine, and the affordability, feasibility and economic dimension. However, policymakers might emphasize only some of these factors when they consider and make their choices. It is also possible that some contextual elements such as economic status and political situation play a crucial role in shaping the stakeholders' participation and policy decisions.

Figure 1: Framework for analyzing HPV vaccination policy in Thailand



4. Objectives

4.1 General objective

This study aims to shed light on the processes by which national HPV vaccination policy in Thailand has developed, with the focus on the role of scientific evidence including HTA information in policy decisions.

4.2 Specific objectives

- (1) to review the current development of cervical cancer control policy including the introduction of universal coverage for HPV vaccination in Thailand;
- (2) to analyze the processes by which the national policy on HPV vaccination has been considered and discussed;
- (3) to identify key stakeholders involved in the policy processes, such as politicians, academics, clinicians, vaccine industry and civil society organizations;
- (4) to explore the positions and involvement of key stakeholders in the policy development processes and decisions;
- (5) to assess the influences of international and national policy context on the adoption of HPV vaccination policy; and
- (6) to examine the roles of evidence drawn on HTA and other types of research in the policy decisions.

5. Research methods

Qualitative approaches including documentary review, in-depth interviews, personal communication and direct participation in policy-related events by the researchers were deployed in this study. Documents reviewed comprised memoranda, meeting minutes, information sheets, research reports, letters and other types of papers including web-based documents produced by

government institutes, private companies, NGOs and public media. The information obtained from these documents comprised the features of the cervical cancer control programs including the performance and obstacles, the positions and roles of different organizations related to the use of HPV vaccination in Thailand and other developing countries, and key contextual factors such as socioeconomic status, political situation and health system characteristics in Thailand.

In-depth interviews were performed with key stakeholders identified through document reviews and the use of the snowball technique. The interviewees included senior officials in the MoPH who were responsible for cervical cancer and general disease control programs, senior administrators in the National Cancer Institute (NCI) and the National Vaccination Committee Office (NVCO), senior managers of the national health benefit schemes, researchers in the Health Intervention and Technology Assessment Program (HITAP) who were involved in conducting and disseminating a study on cervical cancer prevention, a representative of an international NGOs and managers in two vaccine companies. An interview guide was developed according to the responsibility and potential role of each interviewee in cervical cancer control and vaccine introduction. The information sought in the interviews comprised the major drivers of the rejection of publicly-funded HPV vaccination program and the scale-up of screening services for cervical cancer, characteristics of the policy formulation and implementation including the interactions between key interests took part in different stages of the policy as well as the use of HTA data and findings in decision making. The information collected was verified and triangulated across existing sources in order to assure the quality of the study. The content analysis approach was conducted against the conceptual framework including the newly-emerging themes. Furthermore, a brainstorming workshop was organized among experts and key stakeholders of the policy to fine tune the preliminary results of the study.

All researchers in this study were involved in the policy under investigation. They conducted a series of studies concerning preventive measures for cervical cancer in many aspects including economic consequences, program performance, preferences and perceptions towards particular policy options of key stakeholders, and the effects of marketing strategies to encourage immunization against HPV in Thailand. Some of them participated in research dissemination and policy consultations concerning the issue of cervical cancer control. Such experiences allowed the researchers to get insight into the policy development processes. At the same time, however, the close participation in the policy might challenge the researchers' impartiality to a certain extent.

This research focuses on the development of HPV vaccination policy at the national level in Thailand from January 2006 to July 2009.

6. Results

6.1 Development of cervical cancer prevention policy in Thailand

Like many other developing countries, cervical cancer is an important public health problem in Thailand. The number of Thai female population aged 15 years and older who are at risk of the cancer stands at 25 million. Every year 6,000 women are diagnosed with cervical cancer and 2,600 cases reportedly die of the disease (The Thai Working Group on Burden of Disease and Injuries 2002). HPV type 16 or 18 is found as attributing agents in 70% of patients with invasive cervical cancer (Sukvirach et al. 2003). The effort to control this cancer in the country can be traced back to the 1960s when Pap smear testing was introduced as a clinical examination for individuals who attended hospital services such as family planning, ante- and post-natal clinics, and sexually-transmitted infection treatment (Table 1) (Sriamporn, Khuhaprema, and Parkin 2006). It was not until 2002, however, that the MoPH's Department of Medical Services (DMS)

established a cytology-based screening program, for the early detection of abnormal cells and pre-cancerous lesions, to cover the entire female population 35 to 60 years of age. In 2000 delivery of VIA for screening purposes and immediate cryotherapy in positive cases began as a demonstration project in a small number of provinces with support from an American NGO, the JHPIEGO Corporation, the Royal Thai College of Obstetricians and Gynecologists (RTCOCG) and the MoPH's Department of Health (DOH) (Sherris et al. 2005). This single-visit approach is now available in 16 out of 76 provinces, with a history of slow expansion. From 2004 the two screening approaches have been financed by the National Health Security Office (NHSO) – the manager of the Universal Health Coverage (UC) plan.

Table 1: Chronological events related to cervical cancer prevention policy in Thailand

Date	Important event
1960s	Introduction of Pap smear as clinical examination in women who attended particular services in hospitals
2000	Instigation of VIA program as a pilot project for screening purposes
2002	Pap smear offered, as screening test, to entire female population between 35 and 60 years old
2004	Cervical cancer screening tests covered by national Universal Coverage scheme
2006	<ul style="list-style-type: none"> ▪ Launch of first HPV vaccine in the US ▪ Distribution of first WHO policy and technical document concerning HPV vaccination to policymakers and health workers
2007	<ul style="list-style-type: none"> ▪ Two HPV vaccine products licensed for use in Thailand ▪ Consultations on cervical cancer control and HPV vaccination among WHO Member States in 6 regions including the South-east Asia and Western Pacific regional meeting in Thailand in April ▪ A study to identify an optimal strategy for cervical cancer prevention in Thailand was conducted by 2 research institutes under the MoPH, namely IHPP and HITAP. The preliminary results were disseminated in December
2008	<ul style="list-style-type: none"> ▪ The GAVI Alliance announced it would consider future support of new and underused vaccines to fight deadly disease in developing countries which included cervical cancer ▪ A Declaration made at the World Cancer Congress in Geneva in August called for action to ensure that HPV vaccines and other effective strategies to prevent cancer-causing infection were made widely available ▪ Changes in Thailand's Prime Minister in January, September and December and many cabinet reshuffles ▪ IHPP-HITAP study report launched in August ▪ From August to December, the MoPH introduced a campaign to extend the coverage of its cervical cancer screening service: the '116-Day initiative'
2009	<ul style="list-style-type: none"> ▪ Price for the two HPV vaccine products were reduced by the vaccine companies in February and April

Note: GAVI Alliance stands for Global Alliance for Vaccines and Immunization; IHPP for International Health Policy Program; and HITAP for Health Intervention and Technology Assessment Program.

Despite the long-time introduction of cervical cancer screening tests in Thailand, the services have not contributed to a significant health impact. A study suggests the coverage of Pap smear and VIA of as low as 11% and 8% of the defined target population, respectively in 2005 (IHPP

and HITAP 2008). With regard to Pap smear provision, poor quality service such as mismatch between slides and names of clients, delays in delivering test results and loss of follow-up was evident. The lack of public awareness and knowledge of cervical cancer has also been identified as a problem on the demand side. Prospective clients of the screening tests are usually afraid and uncomfortable as the interventions involve the genital organs (Angkasuwapala quoted in Putchong 2008). Impediments in the supply side also play an important role, as the demand for screening is beyond the capacity of the available facilities and health providers (Chumworathayi et al. 2006). The problems related to the workforce include the inadequacy in numbers and poor distribution. According to an expert in Chulalongkorn University's Department of Obstetrics and Gynaecology, *'We have a shortage of cytopathologists and not enough coverage. Pap smears are done in urban areas and not in the rural areas where most of the high-risk women live,'* (Limpapayom quoted in Parry 2006).

In addition to the above-mentioned obstacles on the demand and supply side, the introduction of a cervical cancer screening program in Thailand is hampered by the lack of clear policy direction concerning the introduction of Pap smears and VIA and inadequate collaboration between the two responsible departments (IHPP and HITAP 2008). Furthermore, reliable and regularly updated databases and information systems related to cervical cancer screening and treatment are not in place. Following respective health administrators, an effective information system is necessary for strategy development, program management and planning. Finally, a poor attitude towards VIA among medical doctors has resulted in resistance to the use of this approach. VIA is perceived as a 'low-grade' approach, suitable for only least-developed countries, while some argue that this intervention is not an appropriate alternative to Pap smears, since evidence from randomised control studies indicate that the test is inaccurate and not of high quality (Tomyabatra 2007). It is noteworthy that there were past efforts to solve some of these difficulties. For instance, in 2004 the DMS and the DOH jointly organized a meeting to discuss the optimal strategy in introducing screening services for cervical cancer and reached an agreement that Pap smears should be provided in well-resourced areas, and that VIA and cryotherapy should be considered in areas with inadequate resources where Pap testing could not be effectively carried out (Chumworathayi et al. 2006). However, the conflict concerning such issues remains.

The discovery of the association between HPV infection and cancer of the uterus cervix in the 1980s (Durst et al. 1983) led to the development of a prophylactic vaccine which was expected to be a major breakthrough in reducing the morbidity and mortality of cervical cancer and other HPV-related diseases. In 2006, the first vaccine against this virus was approved by the US FDA (US FDA 2006). One year later, two HPV vaccine products were licensed in Thailand. However, the MoPH adopted a strong position not to provide HPV vaccine in the national vaccination program, but recommended that the target population regularly seek cervical cancer screening tests for prevention of the disease. The Director General of the Department of Disease Control (DDC) (quoted in Sarnsamak 2007), revealed that the Ministry would not consider putting HPV vaccination into its program even though it could prevent up to 70% of infections. The justification of this policy was the unaffordable vaccine price of 14,000-21,000 baht (400-600 USD) per 3-dose course which could not be covered by the government budget, and that the conventional method for cervical cancer prevention was effective. As of July 2009 the vaccine had neither been included in the national EPI nor covered by public health benefit plans, but was available in the private sector for those who pay out of pocket.

Although the MoPH considered screening tests to be the most appropriate and practical strategy for cervical cancer control, it was not until 15th August 2008 that the authority declared a policy to strengthen its screening services. The Health Minister revealed at a press conference that the Ministry would scale up its Pap smear and VIA tests to reach one million women between 35 and 60 years of age, irrespective of their health benefit or insurance plans (The MoPH Information

and Public Relations Office 2008). This campaign was carried out during the 116-day period from 12th August to 5th December 2008, Mother's Day and Father's Day, respectively. However, an evaluation suggests that only 80,000 women throughout the country were screened under this initiative. Interviews with responsible officials indicate that the rapid scaling-up of cervical cancer screening did not meet the target because of many reasons, especially the lack of time for planning and preparation. As a consequence, neither an operation plan nor monitoring and evaluation mechanisms of the service extension were devised. Also, there was no participation from stakeholders such as clinical experts and health providers in the policy formulation and implementation. Furthermore, importantly, there was no effort to solve the existing impediments in the service provision.

Another policy shift in the area of cervical cancer control taking place in 2008 was the decision to implement a pilot program to provide 5-yearly VIA or Pap smear tests to women in certain age groups, i.e. VIA for those 30 to 45 years of age, and Pap smear for those between 46 and 60 years old (Department of Health 2008). With the DoH taking responsibility, the main objective of this initiative was to strengthen the screening services in 2 provinces: Chiangmai and Nakon Si Thammarat, by introducing comprehensive information and public relation campaigns regarding cervical cancer and prevention approaches in public hospitals, workplaces and communities, in order to persuade the targeted population to obtain screening tests. Data collection and analysis would be conducted to assess the program coverage, the prevalence of precancerous cells and cervical cancer at different stages, and the cost-effectiveness of combining the screening tests in particular areas. Furthermore, the project, which would be implemented in 2009 and 2010, aimed at the research and development of an effective package of cervical cancer control activities comprising public relations, screening provisions and referral mechanisms. The findings and lessons learned from introducing this project would provide a platform for improving the performance of cervical cancer screening and treatment in the future.

In summary, a cervical cancer control program has long been established in Thailand with significant development. However, the screening services face several difficulties that result in inadequate coverage and quality. Moreover, it is suggested that despite the availability of HPV vaccine, this newly-emerging technology was not adopted by the government owing to the very high prices. Instead, national health authorities chose to strengthen the screening test provision. The following sections of this report seek to explain why and how the policies were shaped in such a way.

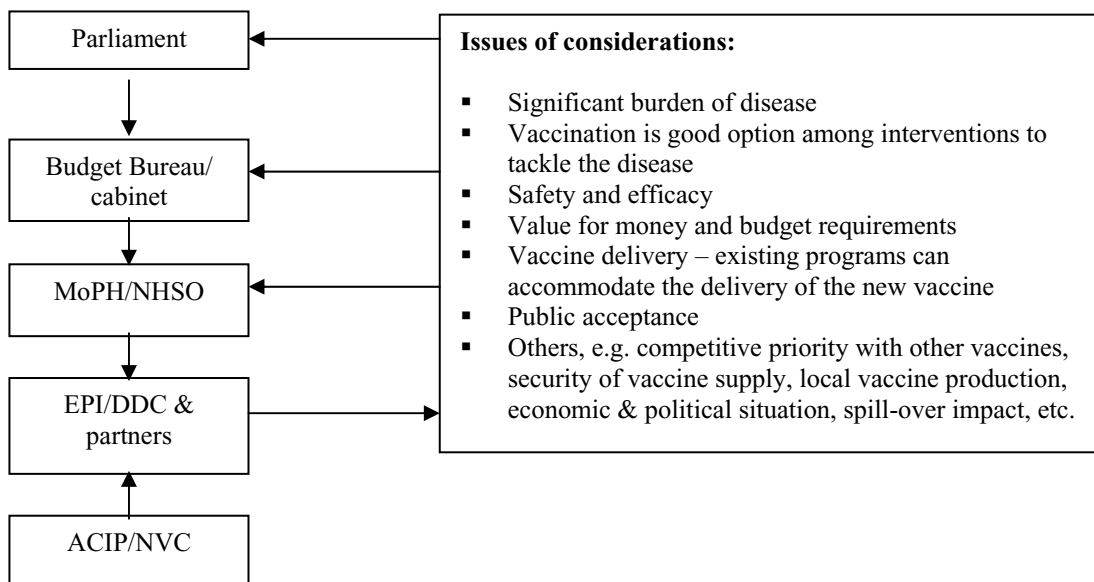
6.2 Official processes concerning government immunization plans and the case of HPV vaccination

In Thailand, the policies concerning vaccines that include research, development, production, quality assurance, as well as immunization are recommended by the National Vaccine Committee (NVC), with technical support from its ACIP (National Vaccine Committee Office 2009). Chaired by the Minister of Public Health, the NVC comprises representatives from different departments in the MoPH including the Government Pharmaceutical Organization, the National Economics and Social Development Board Office, the National Science and Technology Development Administration, the Thai Red Cross Society, the Thailand Development Research Institute Foundation, the Royal College of Pediatricians, the Federation of Thai Industries, and various medical schools. Meanwhile, the ACIP, headed by the Director General of the DDC, consists of experts in immunization, representatives from the MoPH and other respective government agencies, academic institutes including Royal Colleges, medical associations and the Medical Council. The DDC's senior officials in preventive medicine and immunization and EPI managers serve as the Committee's Secretariat. The ACIP is responsible for both the

development of immunization guidelines and schedules, including vaccine management approaches, and also the proposal of optimal immunization policy options to the NVC.

According to a DDC expert in immunization, Chunsuttiwat (2009), it is not only the NVC and ACIP that make decisions concerning what vaccines are adopted and provided under the EPI, but also many other government agencies also play important roles. Furthermore, several issues are taken into account by these authorities (figure 2). The NVC and ACIP are responsible for providing evidence and necessary information on different facets of the vaccines under consideration to the MoPH and the NHSO, as the major public health provider and purchaser, respectively. However, the final decision involves the Bureau of Budget, the cabinet and the Thai Parliament. The issues of considerations by these organizations include the magnitude of the disease prevented by the vaccine, vaccine safety and efficacy, cost-benefit and cost-effectiveness compared to other interventions, budget implications, vaccine delivery, and acceptance of the vaccine among the public. From the viewpoint of different agencies, however, some of these elements may be more important than others. As Chunsuttiwat further argues, the MoPH and the NHSO usually emphasize the public health benefits and value for money when the vaccines are introduced at the national level; whereas, the major concerns of the government, the cabinet, and the Bureau of Budget are the impact on the budget and affordability. On some occasions, other elements are influential in policy making. For instance, influenza vaccination has been introduced since 2008, because Thailand invests in local vaccine manufacture as part of the national strategy for avian influenza pandemic preparedness. As a consequence, there is a need to generate regular demands for seasonal influenza vaccines in the country in order to maintain a minimal scale of vaccine production in the same plant.

Figure 2: Overview of decision process for introduction of new vaccines in national immunization program in Thailand



Source: Chunsuttiwat (2009)

As of July 2009 the ACIP had never included the issue of HPV vaccination under the EPI on its meeting agenda. As argued by a senior health official in interview in August 2009, the decision to insert a particular item to the ACIP agenda was made by the Secretariat team including the Head of the NVCO, EPI managers and officials in the DDC's Bureau of General Communicable Diseases. With regard to HPV vaccination, the Secretariat considered it would not be rational to

push this issue forward to the ACIP owing to the lack of ability to purchase the vaccine and the fact that it would take a long time to introduce this intervention in Thailand. This was the case even though this vaccine had been shown to be effective in preventing cervical cancer. The interview also indicates that the issue of vaccine prices was the most critical parameter: HPV vaccination costing 3,000 baht (86 USD) per dose was too high, especially when compared with the total budget of 300 million baht (8.59 million USD) a year which covered 10 vaccines provided in the EPI. In view of this informant, apart from the unaffordable cost of HPV vaccine, there was no point to opposing the provision of this immunization nationwide, since it could be integrated into school-based vaccine delivery. Concerning Pap smears and VIA as alternatives of HPV vaccination in cervical cancer prophylaxis, the official pointed out that both screening tests were secondary prevention tools which needed to be maintained even when the vaccination program had already been in place.

During 2006 to 2008 the concern of this technical body focused on the dissemination of inaccurate information on the vaccine to the public by some interests. In a meeting in December 2006 the ACIP considered a report on HPV vaccination in other countries, as well as the vaccines' indications and effectiveness in preventing HPV infection and HPV-related diseases (Thailand ACIP 2006). Although at that time the first HPV vaccine product, manufactured by MSD, was in the registration process at the Thai FDA, the ACIP recommended that the DDC provide reliable information about HPV vaccination to the public. This was to counter the widely introduced advertisements and marketing campaigns run by the vaccine companies and private hospitals to promote vaccination (Putchong et al. 2009). It was not until a meeting in July 2008 that the ACIP assigned an expert to revise the vaccine information statements proposed by the Secretariat (Thailand ACIP 2008). The main content of the statements was drawn on those jointly issued by the RTCOG and the Thai Gynecologic Cancer Society (TGCS). Later such information was distributed through the DDC's Bureau of General Communicable Diseases website, along with the statements on some twenty child's vaccines.

6.3 International context

6.3.1 Recent global policy development relating to cervical cancer prevention

At the 58th World Health Assembly (WHA) in 2005, WHO Member States discussed the issues concerning cancer prevention and control and agreed to adopt a resolution, WHA 58.22 (WHO 2005). During the discussion, representatives of some developing nations including Bulgaria, Costa Rica, India, Kenya, Malawi, Mauritius, South Africa and the Caribbean states reported the progress made in providing screening services and prevention of cervical cancer in their countries. These delegations and civil society organizations such as the International Union against Cancer and the International Agency for Research on Cancer argued for the urgent need to tackle the high prevalence of the disease in resource-constraint settings. Although the WHA resolution addresses the prevention and control of all types of cancer, cervical cancer is emphasized as it causes a significant portion of all cancer deaths among women in low-resource societies (World Health Assembly 2005). Scientific studies are encouraged to increase knowledge about tumors including cervical cancer are amenable to cost-effective interventions (Box 1). At the same time, the WHO is requested to promote research on development of an effective vaccine against cervical cancer. In addition, the annex of this resolution recommends national health authorities to consider outcome-oriented objectives for their cancer control initiatives. With regard to cervical cancer, given that the disease is amenable to early detection and treatment, the programs should aim to *'reduce late presentation and ensure appropriate treatment, in order to increase survival, reduce mortality and improve quality of life'*.

Box 1: Cervical cancer-related clauses in the resolution WHA 58.22

Recognizing that among all cancer sites cervical cancer, causing 11% of all cancer deaths in women in developing countries, has one of the greatest potentials for early detection and cure, that cost effective interventions for early detection are available and not yet widely used, and that the control of cervical cancer will contribute to the attainment of international development goals and targets related to reproductive health; ...

1. Urges Member States: ...

(6) to encourage the scientific research necessary to increase knowledge about the burden and causes of human cancer, giving priority to tumors, such as cervical and oral cancer, that have a high incidence in low-resource settings and are amenable to cost-effective interventions; ...

2. REQUESTS the Director-General: ...

(9) to promote research on development of an effective vaccine against cervical cancer; ...

Source: World Health Assembly 2005

The WHO's recommendations on cervical cancer control emphasize comprehensive approaches, including prevention, early detection and screening, treatment and palliative care. As argued by Andreas Ullrich (quoted in Parry 2006), WHO's Medical Officer at the Department of Chronic Diseases and Health Promotion, *'Immunization if available will have to be added (in the area of prevention) to the other components of cervical cancer control. There is no question that early detection will continue to be a key element even once a vaccine is available.'* An action plan was developed by the WHO for new and under-utilized vaccines including HPV vaccine during the period 2007-2010 (box 2). Many activities were carried out by the WHO Headquarters and its Regional Offices. These included the distribution of policy and technical information to policymakers and health professionals, through a set of documents: (a) Preparing for the introduction of HPV vaccines: Policy and program guidance for countries (WHO 2006); (b) Human papillomavirus and HPV vaccines: Technical information for policy makers and health professionals (WHO 2007b); and (c) Cervical cancer, HPV and HPV vaccines. Key points for policy makers and health professionals (WHO 2007a). Moreover, in 2008 a global WHO HPV Laboratory Network was established with the aim to *'contribute to improving the quality of laboratory services for effective surveillance and monitoring of HPV vaccination impact through enhanced, state-of-the-art laboratory support.'* (Ferguson, Wilkinson, and Zhou 2009).

Box 2: Proposed milestones according to WHO plan of action for new and under-utilized vaccines implementation: 2007-2010

By end of 2008

- Detailed safety review at the Global Advisory Committee on Vaccine Safety (GAVCS).
- Regional meetings on cervical cancer control and HPV vaccines in all 6 regions.
- Initial country, regional and global information to guide country-level decision making about HPV vaccine introduction on the WHO website.
- Establishment of a WHO Laboratory Network for HPV as a platform for sentinel surveillance in all regions to monitor vaccine impact.

By end of 2010

- Selected countries in at least three WHO regions have developed integrated plans for cervical cancer prevention.

Source: WHO (2007c)

Global and regional campaigns to strengthen cervical cancer prevention through the introduction of screening tests and HPV vaccination have been carried out by international agencies and NGOs since 2006. For instance, a global initiative to contain the cervical cancer epidemic was launched in London in 2006, which called on national governments to prioritize the diseases in their development and health plans (Cervical Cancer Action 2007). At this meeting, a concerted advocacy strategy was recommended with an aim to accomplish 3 critical goals: scaling up HPV vaccine production capacity and securing financing; increasing awareness of, demand for and stakeholders buy-in for HPV vaccination; and establishing effective programs to provide HPV vaccines in communities in a conducive environment (Fisher and Bass 2006). Recently, the World Cancer Declaration made during the 2008 World Cancer Congress in Geneva advocated affordable screening programs and a call for the action to ensure that vaccines and other effective strategies to prevent cancer causing infection were made more widely available (International Union Against Cancer 2008). It is expected that these initiatives are necessary to generate awareness of cervical cancer in the developing world and the benefits of primary and secondary prevention interventions to reduce the disease incidence.

Provided that the high cost of HPV vaccine would be a serious impediment to introducing the vaccination programs in resource-constrained countries, the Global Alliance for Vaccines and Immunization (GAVI Alliance), an alliance of global health agencies, governments and private partners, is expected to work closely with other international organizations such as UNICEF and public-private-partnership initiatives to play a key role in providing financial support to encourage access to such an intervention among needy populations (Sarin 2008). On 25th June 2008 the Alliance announced that it had approved a plan that would consider future support of new and underused vaccines to fight deadly disease in the developing world, namely cervical cancer, cholera, typhoid, meningitis A, rabies, Japanese encephalitis and rubella (GAVI Alliance 2008). Despite the fact that the Alliance could bring the cost of vaccination down to a fraction of the current price through its large-scale purchasing power, in scaling up access to all these vaccines through 2015, there was a funding gap of approximately 4 billion USD.

The WHO Strategic Advisory Group of Experts (SAGE) concluded in April 2007 that HPV vaccination was likely to be beneficial to people around the world, and so it requested that the HPV vaccine Advisory Committee and WHO's experts review evidence concerning the safety, efficacy and delivery of the vaccine in order to support a WHO HPV vaccine position paper (WHO 2009a). A review of these outstanding issues was submitted to SAGE in September 2008, and it was decided at a SAGE meeting in November that HPV vaccines should be introduced as an element of well-coordinated strategies for cervical cancer control, along with other measures such as education, screening, diagnosis and treatment of precancerous lesions and cancer. However, as SAGE maintained, '*... vaccination should not be deferred in countries because one or more of these interventions cannot be implemented at the time when vaccination could be introduced.*' It was also suggested that in the introduction of HPV vaccination programs, systems for monitoring, surveillance and evaluation should be established by individual governments. Furthermore, SAGE requested that WHO swiftly draft an HPV vaccine position paper based on the evidence in the review report.

The SAGE recommendation was addressed by the GAVI Alliance. On 4th February 2009 its Chief Executive Officer revealed that the statements made by the WHO's Advisory Group was so encouraging that his organization would move ahead with plans to bring HPV vaccine to resource-poor settings (GAVI Alliance 2009). He maintained that the global health community must stop the inequality in access to this cervical cancer preventive intervention between women

in richer countries and those in the developing world. He also pointed out that with SAGE's guidance, the GAVI Alliance would be in demand to provide support to HPV vaccination: *'With SAGE's approval, developing countries will begin to ask for this vaccine. We must be ready to answer their call.'* As the officer put it, by obtaining sufficient finance from donors, the Alliance aims to make the vaccine available in the world's poorest countries in the next couple of years – the initiative would save 700,000 lives from premature death. Nevertheless, owing to the current global financial crisis and its potential effects for donor countries and institutes, filling the financing gap seems to be a great challenge (WHO 2009a).

In April 2009 WHO issued its first position paper on HPV vaccination, based on a review of information and data available in September 2008 (WHO 2009b). According to this document, it is recommended that in countries where prevention of cervical cancer and other HPV-related diseases is a public health priority, HPV vaccination should be included in national immunization programs, if the following conditions can be met: (1) vaccine introduction is programmatically feasible; (2) sustainable financing is assured; and (3) the cost-effectiveness of vaccination strategies in the country or region is considered (box 3). In addition, HPV vaccines should be integrated as part of a comprehensive strategy for cervical cancer prevention that includes education to reduce risk behavior, cervical cancer screening, and diagnosis and treatment of precancerous lesions and cancer, and that the vaccination should not undermine or divert resources from effective screening services. It is noteworthy that the WHO recommends that girls prior to the onset of sexual activity, i.e. those in the age range of 9 or 10 through 13 years, be the primary target population of HPV vaccination program.

Box 3: WHO position on HPV vaccines

'WHO recognizes the importance of cervical cancer and other HPV-related diseases as global public health problems and recommends that routine HPV vaccination should be included in national immunization programmes, provided that: prevention of cervical cancer or other HPV-related diseases, or both, constitutes a public health priority; vaccine introduction is programmatically feasible; sustainable financing can be secured; and the cost effectiveness of vaccination strategies in the country or region is considered.'

Source: WHO (2009b)

6.3.2 Policy transfer at regional and country level

During the past couple of years there have been technical and policy conferences and meetings in relation to cervical cancer control and HPV vaccination convened in different regions. For example, the Princess Nikky Foundation, a Nigerian NGO organized a conference in Abuja in 2007, involving a large number of participants from all African countries, where information on cervical-cancer interventions including HPV vaccines was distributed (Okonofua 2007). Another illustration can be drawn on the First Symposium on Human Papillomavirus Vaccination in the Asia-Pacific and Middle East Regions convened by the International Vaccine Institute (IVI) in June 2009. In this meeting, the participants called for action regarding the implementation of a cervical cancer prevention program which comprised the introduction of HPV vaccine and new screening tools. While government leaders, international institutions including philanthropic organizations were encouraged to make financing available to ensure access to HPV vaccine, the vaccine industry was asked to consider *'affordability in the pricing of HPV vaccine for developing countries.'* (IVI 2009).

Under the auspices of the WHO, meetings were convened in all regions to explore HPV vaccine introduction. In April 2007 a consultation of WHO Member States in the Western Pacific and South-East Asian regions was convened to discuss the current status of cervical cancer control programs in countries, means to strengthen these services, whether and how the HPV vaccine can be introduced, and the potential roles of WHO and other health and development partners (WHO-SEARO 2007). The main feedback from country participants was that their focus should be on strengthening screening programs, since HPV vaccination was not affordable due to its very high cost. Also, it would take some time to meet other challenges of social acceptance of this primary prevention approach and inadequate infrastructure for vaccine delivery. The participants from the two regions realized the need to '*do the best that they can afford to do*' by strengthening the efforts for cervical cancer screening through: identifying gaps in their program; developing advocates and supporters; strengthening cervical cancer prevention policies and guidelines; creating or supporting a data-gathering system for cervical cancer; pilot-testing resource-appropriate screening and treatment approaches; and, lastly, building the capacity to improve access to cervical cancer prevention services.

In the Latin America and the Caribbean, the meeting focused on comprehensive cervical cancer prevention and control, whereby a Regional Strategy was devised, and then adopted by the Pan American Health Organization Directing Council in October 2008 (Luciani and Andrus 2008). The Strategy was translated into a plan of action with the main priority to strengthen existing services and consider the introduction of innovative interventions to improve program performance including the coverage and effectiveness. This action plan includes 7 elements: conduct a situation analysis, intensify information, education and counseling, fortify screening and pre-cancer treatment programs, establish or strengthen information systems and cancer registries, improve access to and quality of cancer treatment and of palliative care, generate evidence to facilitate decision-making regarding HPV vaccine introduction, and advocate for equitable access and affordable HPV vaccines. As of January 2009, progress had been made in the inclusion of HPV vaccination as a component of comprehensive programs for cervical cancer prevention in this region (WHO 2009a). However, it was recognized that the implementation of an action plan in each country required the strengthening of screening services and achieving an affordable price for the vaccine.

As of July 2008, quadrivalent and bivalent HPV vaccines had been licensed in 105 and 71 countries, respectively (Irwin 2008). Despite a lack of data concerning effectiveness, the vaccines were approved for males in some countries. Nevertheless, HPV vaccines might not be available on these markets, owing to regulatory requirements on importation and distribution and price negotiations. HPV vaccination has been rapidly adopted in European countries at a faster rate than it had been with most previous vaccines (Van Damme, Pecorelli, and Joura 2008). In early 2008, Australia, Canada, the US and 12 European countries recommended vaccines for national immunization programs. Meanwhile, other countries including Bulgaria, Denmark, the Netherlands, New Zealand, Norway, Slovenia and Sweden were at the stage of finalizing decisions on vaccine delivery. The vaccination programs in all of these countries recommended HPV vaccination for older girls, young adolescent females, and/or young women. The primary target population was females 9 to 17 years of age, while 12 countries included those below 12, and 6 countries included those over 14 years old. Austria was the sole country formally including boys in the target population for wart prevention. Although these high-income countries provide HPV vaccination in their national initiatives, they continue to recommend screening tests for cervical cancer in both vaccinated and non-vaccinated women (Irwin 2008).

In summary, this section suggests that there was significant movement at both international and regional levels that support HPV vaccination in resource-poor settings. In particular, international agencies including WHO, the GAVI Alliance and the IVI carried out several activities to support

the use of the newly-launched technology as primary prophylactic tools for cervical cancer. Such actions were backed up by a consensus among WHO Member States at the 58th WHA in 2005. However, in the developing world, the transfer of this policy from the global to regional and country level was hampered by the unaffordable cost of the vaccine. At the same time, the deliberations about cervical cancer and HPV vaccination reminded the global health community, policymakers and other stakeholders of the existing prevention approaches for the disease, namely Pap smears, and VIA and other screening tests, which are much cheaper.

6.4 Roles of epistemic communities

In public policy, networks of knowledge-based experts, including researchers with expertise in particular areas – the so-called epistemic communities, are influential, as they can provide explanations about complex problems and help to identify suitable solutions by shedding light on the benefits and disadvantages of available alternatives (Haas 1992). Concerning cervical cancer control strategies, Thai experts possessed different positions towards a nationwide introduction of HPV vaccination. Some clinicians argued that the vaccine, when introduced along with Pap smear testing, would be the most effective means to prevent cervical cancer and other HPV-related diseases. For instance, a pediatrician at Chulalongkorn University's School of Medicine suggested that HPV vaccine was as important as screening tests. As this expert (quoted in Sarnsamak 2007) said in a press conference held by MSD (Thailand) in September 2007, *'The Public Health Ministry should remember that prevention of cervical cancer is a priority.'* Occasionally, these experts expressed their opinions to support the vaccination in conferences and public education events convened by NGOs and the vaccine companies (Putchong et al. 2009). At the same time, some groups of obstetricians and gynecologists emphasized the need for enhancing screening test provisions, since the cost of HPV vaccination was unaffordable (Chumworathayi et al. 2006). They argued that it was not time to think about using HPV vaccines, as 5 most common types of high-risk HPV (16, 18, 31, 33, or 45) accounted for 80% and types 16 or 18 infections accounted for only half of all high-risk HPV infections. They also pointed out that *'it would take more than ten years for the development, low cost commercialization and recommendation by the national immunization plan committee of a new vaccine.'*, and *'The authors cannot wait that long to decrease cervical cancer in Thailand.'*

In July 2008 the RTCOG and the TGCS issued a joint statement titled 'HPV vaccines and cervical cancer prevention' (box 4) (RTCOG and TGCS 2008). In the introduction section of this paper, the two organizations asserted that after HPV vaccines were licensed by the Thai FDA, several advertisements and public relation campaigns concerning the vaccines had been introduced through health professionals and public media, and some of the information disseminated in these campaigns was confusing and/or inaccurate. The joint statement aimed to provide the public with guidance for encouraging rational use of HPV vaccines.

Box 4: Key messages in the Joint Statement on HPV vaccines and cervical cancer prevention, issued by the RTCOG and the TGCS

- HPV vaccination is rational in girls and women 9 to 26 years of age (prior to first sexual activity). In cases over 26 years old or those with sexual experience, the vaccination should be considered on a case by case basis.
- A complete course of HPV vaccination consists of three doses: the second and third dose is scheduled 1-2 months and 6 months, respectively, after the first one.

- HPV vaccination is not recommended in pregnant women, in those with the intention to get pregnant within 6 months, and in males.
- The diagnosis of HPV infection prior to HPV vaccination is not recommended.
- Pregnant women who have incomplete vaccinations should get the remaining doses after child delivery.
- There is no information indicating the undesirable effects of HPV vaccines on reproductivity, pregnancy or infants.
- Studies to monitor antibodies against HPV (vaccine strains) 6 years after vaccination indicate adequately high titer, thus no booster doses are needed.

Source: RCTOG and the TCGS (2009)

In addition to clinical and public health experts, policy researchers have been key participants in the Thai HPV vaccination policy from 2006 to 2009. Health policy and systems research including HTA in the country has significantly developed during the past decades (Pitayarangsarit and Tangcharoensathien 2009; Teerawattananon et al. 2009). This serves as a platform for evidence-based policy decisions in the health sector. Furthermore, the increasing demands for research in this area, especially in fields of health financing, economic evaluation, and program performance assessment, provide opportunities to researchers to be involved in national policy making.

The International Health Policy Program (IHPP) is a semi-autonomous research arm of the MoPH. During the 10 years of its establishment this organization has played a crucial role in generating evidence to inform policy, especially those decisions concerning resource allocation to medical interventions and public health programs. Studies conducted by the IHPP and associated recommendations rejected the introduction of HPV vaccination in the national immunization plan. Viroj Tangcharoensathien, the IHPP Director, strongly opposed HPV immunization in the public sector, but rather supported the extension of Pap smears and VIA services. Based on his 20-year experience with health care financing, his major concern was the high cost of HPV vaccines and the budget impact of introducing the immunization as a benefit in the UC plan. In a consultation meeting between Thailand's MoPH and WHO on the introduction of new vaccines in March 2009, he asserted that although the vaccine prices had decreased 2-3 times during the first 2 years on the Thai market, it would take around 10 years for Thailand to adopt nationwide HPV vaccination. As he also pointed out, at that time the performance of the cervical cancer screening services should have been adequately improved. In addition, Tangcharoensathien expected that vaccine prices decrease to the lowest possible price, and that there would be better understanding concerning the long-term safety and effectiveness of the vaccine.

The opposition to publicly-financed HPV vaccination was reflected in many activities including discussion, presentations and policy recommendations made by IHPP researchers. In a consultation about strategy to prevent cervical cancer convened among WHO Member States in Southeast-Asia and Western Pacific regions in April 2007, a researcher from IHPP, who participated as a temporary advisor, gave a presentation on the cost-effectiveness issues of cervical cancer screenings and HPV vaccines. Based on a review of studies in many countries, it was suggested that the two vaccine products on the market were not cost-effective, in comparison to screening services (de Kok, van Ballegooijen, and Habbema 2009; Goldie et al. 2008a; Sinanovic et al. 2009). Recommendations drawn by this researcher included the production of country-specific evidence on the policy options and financial implications to control cervical cancer, taking into account health system contexts, existing screening programs and fiscal space.

Moreover, owing to the high cost of HPV vaccination, priority and support should be given to improving screening capacities until the country has more evidence and the vaccine becomes more affordable.

In 2007 and 2008 IHPP and HITAP, a newly-established HTA institute under the MoPH's Bureau of Policy and Strategy, carried out a project titled 'Research for the development of an optimal policy strategy for the prevention and control of cervical cancer in Thailand', with financial support from the World Bank's Population and Reproductive Health Capacity Building Program. Following Tangcharoensathien (quoted in IHPP and HITAP 2008: II), '*it is opportune time to conduct this study, as we observed aggressive market promotion of HPV vaccines in Thailand and elsewhere. Some of these marketing plans provide mis-leading information...*' and '*... in the current context, there is an urgent need to revisit the performance of cervical cancer programs.*' Furthermore, he argued that this study indicates that the adoption of new vaccines in a national program should be guided by country evidence, not market promotion and information from vaccine industry (Tangcharoensathien quoted in IHPP and HITAP 2008: III).

The World Bank-supported research project consists of 4 sections, addressing the inadequate performance of cervical cancer screening services in Thailand and the optimal strategy to control the disease in the midst of HPV vaccine promotion (IHPP and HITAP 2008). The findings of section 1 suggest substantial room for improvement in terms of coverage and quality of a national cervical cancer prevention and control program. The loss of the follow-up of screening results is a major problem found in the cytologic-based approach. Concerning the VIA and cryoscopy provision, the program has been scaled up at a slow rate – as of 2006, this service had been available in only 17 out of 76 provinces. Section 2 sheds light on the value for money of different policy options for prevention and control of cervical cancer. It has been found that the screening service is cost-saving, in comparison to treatment of cervical cancer, and that the most cost-effective option to prevent the disease is the combination of VIA and sequential Pap smears, by providing VIA every 5 years to women 30 to 45 years of age, and then followed by Pap smears every 5 years to those between 46 and 60 years old. Meanwhile, HPV vaccination is cost-ineffective owing to the very high price of the vaccines. Section 3 is drawn on the consultation with policymakers and key stakeholders, arguing for strengthening existing screening programs instead of introducing HPV vaccination. This requires strong political commitments and collaborations between the DOH and the DMS, as well as respective Royal Colleges and medical associations. In particular, the training of health workers to provide VIA and immediate treatment of detected abnormal cervical tissue would be needed, as the recommendation to introduce VIA-Pap smear sequential combination was agreed upon amongst the attendants of the meeting. The study in section 4 estimates resources available and requirements in scaling up cervical cancer screening programs in different regions of the country. These resources include cytology laboratories, colposcope and necessary personnel, i.e. VIA providers, cytologists, cytotechnicians, and colposcopists.

6.5 Influence of the IHPP-HITAP study on HPV vaccination policy?

Since the launch of a preliminary report in late 2007, the IHPP-HITAP study was widely disseminated to a range of key stakeholders in cervical cancer control policy, not only in Thailand but also in the international health community. These included, for instance, academic institutes, MoPH departments including the DOH, the DMS and the NCI, the NHSO, public health experts, professional associations, NGOs, the pharmaceutical industry, vaccine companies and international health and HTA organizations. Moreover, HITAP researchers gave presentations on their research findings at several academic conferences and policy fora such as at the meetings of the NHSO's Subcommittee on Development of Health Benefits and Services as well as at a

meeting of DOH administrators. This means that policymakers who were responsible for resource allocation in the health sector became exposed to the information regarding the performance of the existing cervical cancer prevention plan and also the economic aspects of screening tests in comparison to the new technology, HPV vaccines. In addition, in August 2008 a public discussion was organized by HITAP and its allies to enhance better understanding concerning cervical cancer and its prevention strategies including rational use of HPV vaccines.

It has been found that the IHPP-HITAP study did not make any significant change in the government's HPV vaccination policy, as its major findings opposed vaccine adoption, i.e. indicating that the introduction of free access to the vaccine in Thailand was cost-ineffective and unaffordable. Given that it was the only local research which provided explicit evidence derived from economic assessment, the study reaffirmed the government's position not to fund the immunization program. In an interview in May 2009, a senior health official argued that the study findings were not surprising, but only confirmed their belief that HPV vaccination was yet suitable for the Thai setting. He further stated that it would only become viable when the vaccine price was significantly reduced. It is noteworthy that the NVC Secretariat considered inviting HITAP researchers to present the results of the economic evaluation section to the committee. Nevertheless, this action was not actually pursued because the Secretariat thought it was untimely to discuss the inclusion of HPV vaccines in the EPI owing to the anticipated unaffordable costs. At the same time, given that Pap smears and VIA were introduced as HPV vaccination's comparators in the cost-effectiveness analysis and that the screening service assessment illustrated the inadequate coverage and quality, this research was used by some health officials to encourage the improvement of the existing screening programs. As a consequence, there were two policy shifts: the MoPH's campaign to scale up cervical cancer screening during three months, from August to December 2008, and the DOH's pilot program to provide a combination of VIA and Pap smear, every five years, to women in younger and older age groups, respectively.

Interview respondents assert that the dissemination of IHPP-HITAP research prompted them to become actively involved in the development of the screening services. As a high ranking official in the MoPH pointed out, *'If you ask whether my participation in the seminar (in August 2008-the authors) prompted me to raise this issue to the Health Minister, I can say that it played a part. It was because of the IHPP-HITAP study that drew my attention to the issues of HPV vaccination and cervical cancer screening.'* A similar argument was made by the Director General of the DOH: he recognized the results of the economic evaluation part of this research and felt the need to convey the information to the Health Minister, as he was among the few people who could lead the improvement in the fragmented screening program. As these officials put it, they made the proposal to this politician policymaker because they were aware that the cabinet was keen to introduce any programs to favour people, and that strengthening the national cervical cancer screening services would meet the political demand.

6.6 Involvement of the vaccine companies in the policy processes

In health policies, the pharmaceutical industry is a key player, as it makes medicines including biological products available to benefit people, and at the same time, appropriate regulations are needed to ensure that these products are effective, safe, of good quality and accessible for the needy population (Abraham 2002). Pricing and intellectual property protection are among the impediments to access to essential medicines in resource-poor countries (Commission on Intellectual Property Rights Innovation and Public Health 2006). Meanwhile, pharmaceutical companies are important informants as they generate and provide information to national medicine authorities, health professionals, the media and consumers (Collier and Iheanacho 2002; Hessel 2008). However, it appears that significant fractions of the industry's activities aim for

commercial purpose, i.e. to enhance the profits made on the sale of their products. In so doing, several strategies such as communication and making connections with politician policymakers, officials in health agencies and insurance organizations, medical societies, academic institutes and individual experts are introduced. Moreover, medicine companies substantially invest in marketing including advertising campaigns, many of which directly target patients, their caregivers and healthy people. In some cases, education and information programs implemented by the industry play an important part in encouraging NGOs, professional associations and patient networks to advocate particular prevention and treatment policies.

Interviews and personal communication with policymakers and senior administrators in the Health Ministry and the NHSO indicated that the vaccine industry were among several sources of information on HPV vaccines obtained by these government officials. It has been suggested that the two companies kept informing them about the progress concerning vaccine research and development as well as the findings of related epidemiological, clinical and economic studies. Mainly, the information provided concerned the vaccine's effectiveness, safety, doses and administration, precautions, warnings and costs. Issues of focus involved the cost-effectiveness of HPV vaccination and preliminary findings of a demonstration project on vaccine delivery were conducted in 4 developing countries by PATH, an international NGO. The vaccine industry also convened conferences and academic fora, occasionally in collaboration with NGOs such as the Family Health International (FHI) and universities in Thailand, to discuss the feasibility of and potential impediments to HPV vaccination (Family Health International 2006; Family Health International 2008).

In addition to the efforts of the vaccine industry in communicating with senior officials with the aim to convince respective authorities to include HPV vaccines in public health schemes, a media analysis suggests that the information concerning this preventive intervention has been publicized through mass media including newspapers and magazines before these products were licensed in Thailand in 2007 (Putchong et al. 2009). As direct-to-consumer advertisements of prescription-only medicines including vaccines are prohibited according to the Drugs Act B.E. 2510, such information campaigns were carried out in form of academic and business news and health education articles, in which some medical experts, professional associations and private hospitals were involved as presenters, event conveners and authors. It appears that the information contained in some study articles was incomplete and inaccurate. Meanwhile, the vaccine companies maintained that it was not their policy to deliver HPV vaccine information, including press releases, to the public. As the two companies further argued, HPV vaccine-related information provided to health professionals was comprehensive and based on rigorous evidence. This media review also illustrates the influence of the public information coverage on audiences' knowledge of cervical cancer and HPV vaccines. Nevertheless, the media could not affect the decision to seek vaccination of the study population, since the very high prices of the vaccine were influential. In addition, in contrast to policy processes in other countries such as Australia (Roughhead, Gilbert, and Vitry 2008), the media campaigns in Thailand did not have any social mobilization effect nor stimulated public debates on government-funded HPV vaccination programs.

6.7 How the vaccine price reductions affected HPV vaccination policy

Provided that the cost of HPV vaccine was the most critical factors hampering a nationwide immunization program, an appropriate pricing strategy might be effective in facilitating a policy change. This was because the lowered prices would result not only in a decreased financial burden on the administration but also in a more attractive cost-effectiveness ratio. Senior civil servants in the MoPH asserted in interviews in mid 2009 that they occasionally discussed vaccine

prices with company representatives, but that there was no formal negotiation between government agencies and industry. These health officials anticipated that cheaper vaccines would be available when the demand for vaccination increased and the production could be performed at its full capacity. Although domestic economic assessment of HPV vaccine was available with a recommendation concerning the cost-utility threshold, no acceptable vaccine price was formally declared by the authorities. The researchers of this study observed different maximum prices of the vaccine, ranging from 10 baht to 160 baht (0.29–4.58 USD) per dose, estimated by health officials if a nationwide vaccination policy were to be adopted. In this regard, we argue that the quoted price of as low as 10 baht (0.29 USD) per dose reflected that respective officials might hesitate to negotiate with the vaccine companies, as the two vaccine products were originally very expensive and it would be difficult to bring the prices down to an acceptable level.

This unclear policy stance regarding a preferable vaccine price was maintained even after price reductions were offered by the vaccine industry. In early 2009, when it became clear that a major concern of the government was related to the unaffordable costs of the vaccine, both companies proposed significantly lowered prices of their products. According to MSD (Thailand), the company reduced its HPV vaccine price by 40% in order to improve access to the vaccine amongst the needy population (Kijisripornchai quoted in Bovonratanachote 2009). Meanwhile, GSK staff maintained that the price reduction did not aim for facilitating vaccine adoption in the government sector, but it was attributed to the policy to provide cheaper medicines to people in the developing world – an action pledged by GSK's new chief executive who took office in February 2009. In view of some informants in the Health Ministry, the price reductions were inevitable as the two HPV vaccine products had to compete with each other, either to be included on the EPI vaccine list or to enhance the sale volumes in private hospitals and clinics. As revealed by staff of a vaccine company in an interview in August 2009, the number of vaccinees increased by 3 times after the price reduction.

While the price reductions were effective in improving access to HPV vaccines in the private sector, the pricing strategy had no role in the national policy development. The two vaccine companies circulated letters to inform health officials in respective authorities including the Health Ministry's departments and the NHSO as well as IHPP and HITAP administrators about the decrease in vaccine prices. However, there was no response from the decision makers and researchers. As recently mentioned, some senior civil servants informally quoted much lower prices than those offered by the industry. Although the vaccine companies asked HITAP researchers to revisit the economic evaluation models by inserting the new prices, the health economists did not do the reassessment, because they considered that there was no policy demand. However, given that the models did exist, introducing variations of prices and other parameters was not difficult or time-consuming.

In the view of the vaccine industry, HPV vaccination should be provided in EPI, with UC finance. To support this argument, a cost-saving concept, which in part is related to the vaccine prices, was mentioned in interview. Provided that cervical cancer afflicts a large number of Thai women, introducing national-scale HPV vaccination will contain the total health expenditure, as the cost of this prophylactic intervention is lower than the cost of treatment. Lives saved and disease avoided owing to the use of this vaccine will avert a loss in productivity which is beneficial to the country's economy. This assertion was in line with part of the findings of the IHPP-HITAP study, and also agreed upon by a health official in the MoPH. However, this official argued that the containment of treatment costs for cervical cancer and other benefits would occur in 20 to 30 years after vaccination, while providing universal coverage for HPV vaccination in the mean time was unaffordable. During an interview, representatives of a vaccine company pointed out that to address the problem of inadequate finance, there were several alternatives for financing free vaccination, for example providing the vaccine to girls and

adolescents in particular age groups or introducing co-payment by the vaccinees. Nevertheless, all these assertions were made in response to interview questions in this study, and could not be found in public policy deliberations.

7. Discussion and conclusions

HTA has been introduced as a tool to support evidence-based policy making. Although this field of research has been instigated in Thailand for more than three decades, there is substantial room for improvement (IHPP and HITAP 2008). It has not been until the past couple of years when the number of HTA publications, in particular those derived from economic evaluation of health interventions in the Thai setting, have increased significantly (Teerawattananon et al. 2009). At the same time, there has been a rising trend in the demand for HTA information in national health authorities including the MoPH and public health benefit plans. The establishment of HITAP as a semi-autonomous institute under the Health Ministry indicates the need not only for capacity building of HTA researchers and users of evidence, but also for the integration of research results in the policy development process. In order to ensure policy relevance and utilization of its studies, HITAP involves policymakers throughout its HTA processes of topic selection, defining research questions, conducting research and dissemination of research findings (Tantivess, Teerawattananon, and Mills 2009). Despite the fact that recommendations drawn on HTA studies were adopted by respective institutes such as the NHSO and the Subcommittee for Development of National Essential Drug List, the influence of those evidences in policy making has never been systematically analyzed.

Our case study of Thailand's HPV vaccination policy illustrates the processes of policy development, molding by interactions between context and actors, and among actors with different interests. Generally, HTA information may play a role in guiding policy decisions, while other elements are also important. The influence of ideologies, social values and related constructions of particular policy choices as well as a range of politico-economic factors concerning policy decisions has been discussed elsewhere (Buse, Mays, and Walt 2005; Walt 1994). With regard to the Thai HPV vaccination policy, we maintain, however, that the huge budget impact of publicly-subsidized HPV vaccination program was the most critical hindrance. This was similar to other developing countries where the adoption and accessibility of essential medicines and vaccines is mainly determined by national economic status and available health budgets (Brooks et al. 1999; Frost and Reich 2009). Because the price of vaccines at first launch, in mid-2007, was relatively very high the MoPH rejected the proposal to provide universal coverage for vaccination (Sarnsamak 2007), despite the fact that no thorough assessment of all policy options in the Thai setting existed. In the same vein, it was the vaccine prices and associated financial implications that made the ACIP Secretariat hesitate to include the issue of HPV vaccination on the committee's agenda. These indicate that merely basic estimations of the financial burden based on the potential number of target population and the vaccine cost per head seemed to be adequate in policy decision making.

Policy utility of HTA findings and related recommendations increased in later phases, as the IHPP-HITAP study shed light on different facets of different cervical cancer control programs, not only HPV vaccines. In particular, the study was among many factors, attracting the attention of policymakers and administrators in the Health Ministry to the existing screening services which had been inadequately performed and neglected for a long time. Due to the unaffordable costs of government-funded HPV vaccination, policymakers needed to look for other policy choices, and found that screening tests for cervical cancer were optimal alternatives to address the wide-spread disease in Thai women. In this connection, it is unclear if such a decision was underpinned by cost-effectiveness data or the much lower unit cost of providing cervical cancer

screening than HPV vaccination. It can be argued, however, that the high cost of an immunization program could raise the awareness of global stakeholders, not only those in Thailand, towards the issues of cervical cancer and its prevention strategies. In the Thai political context, the dissemination of the IHPP-HITAP study to senior officials in the MoPH resulted in substantial policy shifts: the expansion of Pap smears and VIA provisions during August to December 2008, and a pilot initiative to strengthen the national screening services in 2009 and 2010. Although the former effort could not achieve the target and it is too early to assess the performance and outcomes of the latter, lessons learned from the two initiatives will be beneficial in informing policy formulation and implementation in the future.

Focusing on HPV vaccination, HTA evidence derived from the IHPP-HITAP study indicates that this new intervention is not cost-effective if introduced into Thai society. This finding differs from economic evaluations conducted in other countries for several reasons as discussed earlier. Despite the discrepancies, no comment has been made, by the immunization proponents, to the public on the quality and reliability of the domestic evaluation. On the other hand, the vaccine companies often cited the results of the cost-effectiveness section in this study and raised questions to policymakers and researchers asking if the prices of their products decreased to a level lower than the cost-utility threshold of one time GDP per capita per QALY gained, would HPV vaccines be included in the benefit package of the national health benefit schemes or not. However, policymakers in the MoPH, National Vaccine Committee and public health benefit plans never stated clearly what price would be acceptable for universal HPV vaccination. This is not surprising since other factors such as program feasibility, social preferences and political desirability are also crucial in the adoption of new public interventions (Kingdon 1984), and all these elements had yet been explored in the Thai setting.

The analysis of HPV vaccination policy in this study illustrates the failure in agenda-setting and therefore, no policy shift has been implemented. Although the high burden of cervical cancer in Thailand and vaccine emergence caught the attention of policymakers, and subsequently succeeded in raising the issue of cervical cancer screening tests onto the government agenda, the situation was not conducive for the mass introduction of HPV vaccination. Following Kingdon (1984), the meeting of three independent streams of problem recognition, the availability of possible solutions and desirable political factors are necessary for policy innovation. As found in the study, the problem was recognized, in the absence of the other two elements, i.e. the vaccine cost was not affordable and strong, well-organized advocacy for publicly-subsidized immunization was lacking. Employing the framework proposed by Shiffman and Smith (2007), we assert that it was difficult for the HPV vaccination program to obtain priority from national health authorities in Thailand since the policy proponents were not powerful, and also unable to frame and portray policy-promoting messages in a way that could mobilize significant support from key stakeholders such as politicians, academics, health professionals, NGOs and the public. Our arguments are in line with Frost and Reich (2009): introducing new technologies in particular settings *'depends on effective product advocacy by a product champion to construct and manage the architecture of access.'* In addition to the capacity of policy advocators, it seemed that Thai politics at the time was not beneficial to the vaccine adoption, despite supportive movements existing at the international level.

The inability to mobilize support from a wide range of stakeholders may come as a result of four factors. First, the argument made by policymakers that nationwide HPV vaccination was not affordable could not be challenged, owing to resource constraints in the public sector. Second, HPV vaccination was firstly promoted by the vaccine industry through the introduction of marketing campaigns which employed celebrities as presenters. This strategy made for the intervention being perceived as a luxury, targeting the wealthy population. As a consequence, advocacy for the vaccination program seemed to be impossible and not legitimate in the views of

health and women's right NGOs and some health professionals. Third, given that HPV infection is a sexually transmitted disease, some civil society organizations might be reluctant to promote immunization against such infection because they were afraid that the public would falsely perceive that they supported early sexual activities in girls and adolescents. Fourth, it was well recognized by NGOs that cervical cancer screenings were freely available throughout the country, but yet received little attention from the target population. They considered it was not sensible to request that the government provide the more expensive intervention unless the uptake of the screening programs increased to the maximum level and the burden of cervical cancer remained.

Although Thailand has done well in providing EPI vaccines at high coverage rates (WHO-SEARO 2008), mass introduction of adult vaccines like vaccines against Japanese encephalitis, influenza, and HPV requires different delivery strategies including complementary information and educational plans. Especially, the effectiveness of HPV vaccine in preventing cervical cancer relies on vaccinees' compliance to a three-dose vaccination schedule. Nevertheless, a suitable strategy for HPV vaccination delivery in the Thai setting has never been examined. Furthermore, the knowledge about the implications of the vaccination for the uptake of cervical cancer screening services and the attitudes of the public and target population towards this new intervention is limited. Taking into consideration the studies on these issues in other countries, HTA evidence concerning HPV vaccination in Thailand should be extended to address a broader range of questions than those of value for money and budget impact. In addition, as Haug (2008) has pointed out, *'How can policymakers make rational choices about the introduction of medical interventions that might do good in the future, but for which evidence is insufficient, especially since we will not know for many years whether the intervention will work or — in the worst case — do harm?'* In a similar vein, although cost-effectiveness data of HPV vaccines in the Thai setting has been available, it is noteworthy that such information is based on the evidence currently existing, and that the said evidence remains uncertain. Researchers in related fields need to closely monitor the long-term epidemiological and clinical effects of the vaccine when it is introduced over a longer time span and in larger populations, since reassessment of vaccine implications may be required if there are significant changes in certain parameters.

In many developed nations, assessment of efficacy, safety, quality and cost effectiveness of health products is well established and usually employed in resource allocation including the development of formulary and reimbursement lists or benefit packages. Nevertheless, the case of HPV vaccination in some settings has illustrated the influence of political pressure on policy decisions. Following the literature, the debates over HPV vaccination are underpinned by many elements: apart from the question regarding value for money, this intervention has been available on the global market for a short period with limited information about long-term effectiveness and safety, and it is a prophylactic intervention for sexually-transmitted infections – a sensitive moral issue in many cultures. The vaccine is, however, expected to prevent a large number of deaths among women throughout the world. Evidence for this argument can be drawn on a review by Marquez-Calderon et al (2009) which suggests that medical societies' recommendations for HPV vaccination in different countries vary widely, and there are also discrepancies between experts' recommendations and government policies in some countries. This indicates that despite the same set of HTA data and information, different policies were developed. Moreover, Haas et al (2009) emphasizes the importance of policy advocacy including lobbying as well as the use of assertions based on social values to convince other stakeholders to either support or oppose publicly-subsidized immunization against HPV. As observed in cases in Australia and New Zealand, political movements were able to overturn first, rational policy decisions not to fund the vaccination programs (Haas et al. 2009; Roughead, Gilbert, and Vitry 2008). In contrast, there has been no public campaign to pursue publicly-funded HPV vaccination in the Thai setting.

We anticipate that in the future when prices of HPV vaccines decrease to certain levels, the introduction of this vaccination in public schemes will become highly politic. The Thai experience regarding antiretroviral therapy (ART) indicates that the significant reduction in drug costs was influential in setting public agenda and mobilizing advocacy by civil society organizations and resulted in a policy shift towards universal coverage for treatment in 2001 (Tantivess and Walt 2006). With regard to the policy on immunization against HPV, the government should be well-prepared so that it can provide the public and different interests with scientific information necessary for supporting evidence-based decision making. Drawing lessons from developed societies, we maintain, however, that the sole existence of evidence is inadequate. As illustrated in the reimbursement policy for HPV vaccination in Australia, robust HTA evidence is meaningless, if policy stakeholders including the public have limited understanding or misperceptions of the systems and principles by which the evidence is generated and utilized in resource allocation (Roughead, Gilbert, and Vitry 2008). Even in the US, although policy-making bodies like the ACIP acknowledge the important role of cost-effectiveness information in their deliberations, these decision makers have different levels of expertise in analyzing and interpreting such economic assessment results (Dempsey et al. 2008). This means that in parallel to conducting HTA studies and other research, responsible agencies, including academic institutes in Thailand, need to strengthen the country's HTA capacity at individual, organizational and contextual levels.

Concerning the role of HTA evidence in decision making, this study suggests different stakeholders were involved in providing, receiving and using such information. The information about HPV vaccines has been distributed in the Thai society before this new technology was first licensed in the US in 2006. The very first groups of Thai audiences were likely to be biomedical experts and scientists in the area of infectious diseases, reproductive health and cancer who got the information about the efficacy and safety derived from vaccine trials presented in academic conferences and published in international journals. Thereafter, HTA evidences concerning this vaccine were transferred between different groups of stakeholders. The vaccine industry was an important disseminator of the information on HPV vaccination. The information provided by the vaccine companies emphasized vaccine characteristics, benefits, risks, as well as the cost and public health consequences of vaccination programs, mainly drawn on international publications. The evidence on the efficacy, effectiveness, safety and quality were officially required by the Thai FDA when the vaccine products applied for medicine registration. Throughout the vaccine approval process, such information played a critical role. Meanwhile, the distribution of HPV vaccine information to promote the vaccine use could not be carried out to the public, as direct-to-consumer advertising is prohibited by Thai law.

Domestic academics including biomedical scientists and policy researchers are supposed to be knowledge-based information generators who provide Thai society with country-relevant evidence. It is suggested, however, that only a few of them conducted HTA studies on local introduction of HPV vaccine. As a consequence, the information disseminated by these policy actors was mostly based on research in other countries. At the same time, a number of experts were involved in business events convened by for-profit organizations such as private hospitals, while such vaccination-promotion activities were reported by the public media (Putchong et al. 2009). Health professionals, especially clinicians, were another group of informants who disseminated the information on HPV vaccination to stakeholders, in particular individual clients and the public. Most professionals relied on the effectiveness and safety evidence received from the vaccine industry, while some also spent their time retrieving such information from peer-review journals and other sources by themselves. It was possible that part of the information on the vaccine disseminated by physicians was shaped by their opinions and clinical experiences.

While policymakers including politicians and civil servants mainly obtained several types of evidence concerning HPV vaccines from the vaccine industry and experts in different fields, they also estimated the budget implications, if a government-subsidised vaccination program was introduced. However, the policymakers did not pay attention to the reduction of treatment costs as a result from HPV vaccination and cervical cancer averted in the future. The information regarding financial consequence was employed by policymakers to justify the decision not to include this new intervention in the EPI. At the same time, they made use of the IHPP-HITAP study in the decisions to improve the existing screening services for cervical cancer. On the other hand, the policy authorities apparently took no account of the vaccine price reduction offered by the vaccine industry. It is noteworthy that in Thailand there was no explicit framework, related criteria or thresholds for addressing the evidence derived from health economic assessment. Therefore, although some government agencies took the prices, budget impact and cost-effectiveness of HPV vaccination into consideration, it is unclear how such information was assessed.

Findings from this study depict the absence of a clear framework for vaccine adoption including who are the responsible bodies producing evidence for decision making? What types of evidence are required? And what criteria and threshold are introduced? This situation leads to a lack of transparency and inconsistency in policy decisions. We recommend that national authorities i.e. ACIP/NVC, EPI/DDC, MoPH/NHSO, Bureau of Budget/cabinet, and parliament develop explicit frameworks and mechanisms that allow stakeholders to be involved in the decision making process. This includes the submission of information, and participating in assessment, appraisals and appeals. This recommendation is highly relevant as there are a number of new vaccines in the pipeline, such as dengue, malaria, and HIV vaccines, all of which are likely to be costly and require serious consideration regarding ethical and moral dimensions.

In conclusion, HPV vaccination policy in Thailand has been largely driven by the unaffordable costs of vaccine products. In other words, the estimated implications for health expenditure was a crucial factor hampering the introduction of HPV vaccination in public schemes. Although domestic HTA information including health economic data of this newly-emerging intervention had been available, such evidence played a limited role in the making of HPV vaccination policy. At the same time, however, the high prices and existing cost-effectiveness studies of the vaccine drew significant attention from policymakers and health officials around the globe to the issues of cervical cancer and screening services, especially in resource-poor countries. In the Thai setting, the findings of and recommendations derived from local economic evaluation of HPV vaccination and performance assessment of Pap smears and VIA programs were influential in informing the national cervical cancer prevention policy.

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Health Intervention and Technology Assessment Program

6 th Floor, 6 th Building Department of Health

Ministry of Public Health Tiwanon Rd.,

Muang, Nonthaburi 11000, Thailand

Tel : 66-2590-4549, 66-2590-4374-5 Fax : 66-2590-4369

E-mail : hitap@hitap.net

www.hitap.net