

Title:

Drugs, Sex, Money and Power: An HPV vaccine case study

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1 **Abstract**

2 In this paper we compare experiences of seven industrialized countries in considering
3 approval and introduction of the world's first cervical cancer-preventing vaccine.
4 Based on case studies, articles from public agencies, professional journals and
5 newspapers we analyse the public debate about the vaccine, examine positions of
6 stakeholder groups and their influence on the course and outcome of this policy
7 process. The analysis shows that the countries considered here approved the vaccine
8 and established related immunization programs exceptionally quickly even though
9 there still exist many uncertainties as to the vaccine's long term effectiveness, cost-
10 effectiveness and safety. Some countries even bypassed established decision-making
11 processes. The voice of special interest groups has been prominent in all countries,
12 drawing on societal values and fears of the public. Even though positions differed
13 among countries, all seven decided to publicly fund the vaccine, illustrating a
14 widespread convergence of interests. It is important that decision-makers adhere to
15 transparent and robust guidelines in making funding decisions in the future to avoid
16 capture by vested interests and potentially negative effects on access and equity.

17

18 *Keywords (3-6):* Vaccination; Human Papillomavirus; Decision Making; Public
19 Health; Pharmaceutical Policy; Public Policy

20

21 **1. Introduction**

22 “It took 15 years for Gardasil to make a national hero of its creator, Ian Frazer. But it
23 took just three days for the world's first cancer-preventing vaccine to make a national
24 dill of federal Health Minister Tony Abbott. [...] John Howard, alert as ever to the
25 public mood, delivered sparkling prime ministerial endorsement to Gardasil along

26 with a clear direction to Minister Abbott that the immunisation program should
27 proceed. And pronto.” [1]
28
29 “[T]he public, as well as policy makers, must be provided with sound and
30 comprehensive multidisciplinary evidence for vaccination as well as unbiased data
31 about the potential benefits and harms expected from widespread immunization with
32 the HPV vaccine, and all this information must come **before** governments allocate
33 huge sums of already limited health care dollars to such programs. Individual girls
34 and women, as well as policy makers, can only make truly informed decisions about
35 vaccinations when they have all the evidence. At this point in time, there are more
36 questions than answers.” [2, p.16]
37
38 In this paper, we analyze and compare the experiences of seven countries (Australia,
39 Canada, Denmark, Germany, New Zealand, Switzerland and the U.S.) in considering
40 the world’s first cervical cancer-preventing vaccine and making a decision about its
41 introduction and/or funding. The above quotations nicely illustrate two characteristics
42 of this process. First, on the whole, the countries considered here approved the HPV
43 vaccine and related programs with marked haste, some circumventing established
44 channels and procedures in the process. Second, public debates ensued in many
45 countries, fuelled by uncertainties about the duration of the vaccine’s efficacy and the
46 precise nature of the link between HPV and cervical cancer. Because vaccine
47 programs are still new, the rate of the HPV vaccine’s uptake—and its impact on
48 routine Pap test utilization—remains largely to be determined. With respect to the
49 establishment of such programs, however, our analysis suggests that countries with
50 different decision-making processes can arrive at a similar decision about the value of

a health policy or program, a pattern that reflects the influence of a particularly strong and ubiquitous set of political pressures at work.

2. Materials and methods

The International Network Health Policy and Reform¹ convenes experts from 20 countries to report on and compare health policy processes from around the industrialized world. In 2007, several countries in the Network reported on the introduction of a human papillomavirus (HPV) vaccine for the prevention of cervical cancer. The almost simultaneous consideration and adoption of this particular policy issue in several countries provides a unique opportunity to compare in detail the relevant policy processes and outcomes. Here we use Network member case studies [3-8] from six of the seven countries mentioned above as well as publications by public agencies, in journals and newspapers to examine the debate about the vaccine and the actors who influenced the debate and its outcome. For Denmark we only employed the latter resources [9-14].

3. Human Papillomavirus and the development of a vaccine

Worldwide, cervical cancer is the second or third most common cancer among women; nearly half a million women are diagnosed with and more than 270,000 die of the disease each year [15, 16]. Cervical cancer is a rare outcome of a fairly common infection with HPV. Of the more than 100 HPV strains that infect humans, only a few

¹ Since 2002 the International Network Health Policy and Reform has brought together health policy experts from around the world to report on current health reform issues and health policy developments in their countries. In two survey rounds per year, Network members report up to five health policy issues using a questionnaire aimed at describing and analysing the dynamics or the processes of the policy or policy proposal under review. Although members are experts in policy research, their reports are based on expert assessment, not the results of structured research. All reports are available on the Network's website www.healthpolicymonitor.org

are linked to cervical cancer; most low- and high-risk HPV infections spontaneously regress [17, 18].

Nonetheless, the establishment of a viral cause of cervical cancer paved the way for the development of a vaccine with the potential to prevent this cancer [19, 20]. In 1991, investigators at the University of Queensland found a way to form non-infectious virus-like particles (VLPs) that strongly activated the immune system. In 1993, a laboratory at the U.S. National Cancer Institute generated the VLPs that formed the basis for the HPV16 component of the first cervical cancer vaccine, Gardasil, which was jointly developed by Sanofi-Pasteur and Merck. Later, GlaxoSmithKline developed its own cervical cancer vaccine, Cervarix.

Both Gardasil and Cervarix target HPV types 16 and 18, which together cause more than 70% of all cervical cancers [21]. (Neither vaccine prevents 100% of cervical cancers.) Gardasil also targets HPV types 6 and 11, which cause genital warts. Three doses of the vaccine are required (at 0, 1 and 6 months), and the duration of protection appears to be at least five years. As HPV is easily transmitted and most infections occur soon after a woman first becomes sexually active, the vaccines are most effective if administered prior to the commencement of sexual activity. Widespread use of the vaccines is expected to reduce the incidence of cervical cancer; however, women who receive the vaccine will continue to need regular Pap screening because neither vaccine protects against all oncogenic HPV types and because the duration of protection remains uncertain [22]. The European Commission also recommends that authorities carry out population-wide, quality assured cervical screening by pap smear

(according to the EU guidelines) before introducing HPV vaccination into the population [3].

4. Comparing and contrasting the approval process

In all seven countries considered here, the vaccine was approved for use in 2006 and made available to women as a three-dose schedule for between 292 PPP-\$ and 527 PPP-\$² (see also table 1). Although there was debate in the scientific community about issues of safety and efficacy in connection with the approval process, the public debate, which is the subject of this paper, occurred during and after policy processes concerned with developing or implementing subsidized vaccination programs were commenced.

In Canada, Gardasil was approved for use in the summer of 2006. Following advice from Canada's National Advisory Committee on Immunisation that the vaccine's high cost was preventing its adoption, the Canadian government approved CAN\$300m (248m PPP-\$) in new funding to the provinces to provide free vaccination to girls aged 9 to 13 [8]. By June 2008, five provinces had adopted a free vaccination program, and all ten provinces have now approved voluntary school-based programs. Implementation of the vaccination program has been accompanied by media and professional articles questioning the wisdom of the free vaccination program in light of ongoing concerns about the vaccine's necessity [23]. It has also been reported that this is the most expensive vaccination program ever introduced in Canada [24].

² In this paper, all costs were converted using 2007 OECD purchasing power parities (see <http://www.oecd.org/dataoecd/61/56/39653523.xls>).

119 In October 2007, Denmark's National Board of Health recommended HPV
120 vaccination for girls at the age of 12 as a component of the general-tax financed child
121 vaccination program [13]. In addition, a two-year catch-up program was
122 recommended for girls aged 13 to 15 years; both recommendations were based on an
123 evaluation by the Danish Centre for Health Technology Assessment [12]. The
124 government obtained broad acceptance for the introduction of the program towards
125 the end of 2007, but financing of the program was debated, and a parliamentary
126 election delayed the final decision until early 2008. The program, set to start in 2009,
127 is being financed through a reduction in public support for other pharmaceuticals, a
128 fact that cost the program the support of the Social Democratic and Socialist parties.
129 The program's funded product is Gardasil, which was selected because it also protects
130 against genital warts.

131
132 In New Zealand, most pharmaceuticals are subjected to a systematic review process
133 by an independent government entity, Pharmac, for the purposes of public funding.
134 Vaccination programs, however, fall outside of this review process; decisions are
135 instead made by the Ministry of Health. In November 2006, the Ministry ignored the
136 advice of its Therapeutic Advisory Group when it decided not to fund the vaccine,
137 citing insufficient information about its long-term efficacy, impact on health
138 inequalities and cost-effectiveness [25]. However, the decision was reversed in May
139 2008, when the Minister of Health announced that an "interim" program would
140 provide free Gardasil vaccinations for teenagers up to age 18 who are not at school,
141 beginning in September 2008, followed by a national program for girls aged 12 to 13
142 years starting in 2009 [6].

144 In Germany, the Standing Vaccination Committee (STIKO) recommended in March
145 2007 that all girls aged 12 to 17 be immunized. Some sickness funds swiftly included
146 the HPV vaccine in their benefit baskets and heavily marketed it to compete for
147 members. Only a few months earlier, however, the funds criticized the part of the
148 2007 health reform bill—enacted in April 2007—that would oblige them to
149 automatically cover vaccinations recommended by STIKO (including standard safe
150 childhood vaccinations), fearing additional immunization-related costs of up to €1.6
151 billion (1.8 billion PPP-\$). Since the 2007 reform that placed new emphasis on
152 effective prevention, some states have launched programs to vaccinate girls at school,
153 and some funds cover the immunization for women up to age 26. The decisions to
154 recommend and fund the vaccine were initially welcomed in Germany; however,
155 some criticism regarding vaccine safety and the efficiency of its inclusion in the
156 benefit basket has been reported in the media [3].

157
158 In Switzerland, Swissmedic, the Swiss Agency for Therapeutic Products, approved
159 Gardasil in November 2006. In June 2007, the Federal Commission for Vaccination
160 recommended that girls aged 11 to 14 (and girls aged 15 to 19 in a five year
161 “transition program”) be vaccinated within the scope of the country’s mandatory
162 health insurance [26]. However, responsibility for formal reimbursement decisions
163 with respect to the benefit basket rests with the Federal Department of Home Affairs,
164 which politically endorses the final recommendation by the federal benefit basket
165 commission; the decision on Gardasil took several months. In summer 2007, three
166 cantonal departments of public health—Geneva, Valais and Basel Land—decided to
167 finance the HPV vaccination out of fiscal funds and started a pilot vaccination project
168 in their schools. Their action placed strong political pressure on the federal benefit

basket commission [4], which granted formal reimbursement approval in November 2007. Since January 2008, mandatory health insurance has covered HPV vaccination, as long as it is carried out within a formal vaccination program designed at cantonal level [27].

In the U.S., Gardasil was reviewed and endorsed by the federal Advisory Committee on Immunization Practices (ACIP) in 2006. The Committee recommended that girls aged 11 to 12 be vaccinated and that girls and young women aged 13 to 26 be vaccinated using a “catch-up” approach. The committee also determined that the vaccine should be made available through Vaccines for Children, a federal program that makes immunizations available to children from low-income families. State legislatures, which determine school vaccination requirements, typically rely on ACIP’s findings when considering whether to require a vaccine for school enrolment. In 2006 and 2007, more than two dozen states considered legislation to make HPV vaccination a requirement for girls’ school entry. However, most bills met with strong resistance, and only in Virginia was a school mandate approved and signed into law. In several states, such as California, school mandates were ultimately removed from HPV-related legislation. In nearly every state where mandate bills were introduced, vaccine-related legislative activity has been dogged by questions about the safety and long-term effects of the vaccine as well as controversy over the manufacturer’s role in the political process [5].

In Australia, the vaccine was approved for use by the Therapeutic Goods Administration (TGA) in June 2006. However, in early November 2006, the Pharmaceutical Benefits Advisory Committee (PBAC) rejected an application by the

manufacturer of the vaccine to list it on the Pharmaceutical Benefits Schedule (PBS) on the grounds that it was not cost-effective. Typically, a revised application would be submitted to a subsequent meeting of the PBAC, but the committee was not scheduled to meet until March 2007. The Australian government supported the inclusion of the vaccine on the PBS and encouraged discussions between the Department of Health and Ageing and the manufacturer to reduce the price of the vaccine. At the end of November 2006, the PBAC convened a special meeting, at which it approved the vaccine for listing on the PBS. In 2007, a program of school vaccination was introduced for girls aged 13, together with a catch-up program for girls aged 14 to 17. The two-year catch-up program is also available to women aged 18 to 26, who can receive the vaccination free from their general practitioner [7].

Table 1 “Year of introduction or public funding for HPV vaccine and target groups” approximately here

5. Influencing the policy debate

5.1 Role of the manufacturers

In countries with a pharmaceutical industry, manufacturers adopt practices designed to enhance the chances of their product being recommended, approved or subsidized. Such practices include employing lobbyists, engaging the media, and identifying potentially supportive groups within the community. In this case, the presence of the manufacturer was more obvious in some countries than in others, and its public profile varied. In Canada, Germany and the U.S., public perception that Merck, Sharp and Dohme was “leading” the push for a subsidized program, as well as the perceived influence of the company on politicians and community groups, may have played a

role in the growth of substantial opposition to the vaccine. In the U.S., for instance, the local media reported on the Texas governor's ties to a Merck lobbyist and on a California lawmaker's ownership of Merck stock. In Germany, a perceived lack of independence and transparency by STIKO and the connection between STIKO and the pharmaceutical industry were implied by the opposition Green party in parliament and also featured in the public debate [28, 29].

The pharmaceutical companies' public profiles were markedly different in Denmark and Australia during the course of the policy process. In Denmark, one pharmaceutical company, Sanofi Pasteur MSD, employed the media to generate political debate about inequities in access to the vaccine, while the other, GlaxoSmithKline, resisted the decision to fund only a vaccine that also protected against genital warts. In Australia, meanwhile, the manufacturer's role was much less obvious; the widespread media coverage prior to and following the PBAC's initial decision portrayed the vaccine in a generally favourable light and it received strong political support from both government and opposition parties [30]. Media interest in the vaccine was particularly enhanced by the central role played by University of Queensland researchers in its development. One of the leaders of this research, Professor Ian Frazer, was named Australian of the Year in 2006 and was featured in the media personally administering the first publicly available injection of the vaccine in Australia. The presence of such a credible opinion leader is likely to have had a powerful influence on the debate in Australia.

5.1.1 Marketing the HPV vaccine

Direct-to-consumer advertising (DTCA) of drugs is permitted only in two of the case countries, New Zealand and the U.S. (in fact, New Zealand and the U.S. are the only industrialized countries worldwide that allow DTCA for prescription drugs). In New Zealand, Gardasil was not prominently advertised by the manufacturer following its approval. And while the New Zealand government may have liked to have advertised the launch of the vaccination program, its recently-passed Electoral Finance Act constrained its ability to do so during the lead-up to the election [31].

In the U.S., Gardasil has been marketed directly to consumers, particularly teenage girls and their mothers. Marketing efforts have focused heavily on the vaccine's potential to prevent cancer. Prior to Gardasil's approval, Merck sponsored a national campaign to promote awareness of the link between HPV and cervical cancer. A second campaign, launched after Gardasil's approval, urged adolescent girls to be "one less" victim of cervical cancer.

5.2 Special interest groups

Special interest groups, such as medical associations and consumer advocacy groups, play an important role in the public debate about policy proposals. In Canada, New Zealand, Australia and the U.S., most medical and public health agencies and societies supported a voluntary subsidized program, although several U.S. organisations stopped short of supporting a mandatory scheme. In the North American countries and in Denmark, some medical researchers questioned the need for such a program and were concerned about the long-term safety of the vaccine [11], while others, such as the Danish Cancer Society and the American College of Obstetricians and Gynecologists, argued for expanding the vaccine's availability [9].

268

269 In Canada, the Women's Health Network opposed the program [2]. Similarly, in New
270 Zealand, Women's Health Action expressed a number of concerns about the proposed
271 program, including its hurried introduction, and the lack of data on the long-term
272 efficacy of the vaccine and its effects on 11 and 12 year old girls [32]. In contrast, in
273 Australia, a petition sponsored by women supporting an immunization program was
274 presented to Parliament, asking that the PBAC review its initial decision. Concerns
275 about necessity and long-term safety were conspicuously absent from the debate.

276

277 In the U.S. and Canada, opposition was also voiced by social conservatives, including
278 some church groups, and parent groups; in Australia, again, such opposition was
279 muted. In New Zealand, medical practitioners responded to the initial decision not to
280 fund the vaccine with an outcry [33], while the general public expressed little
281 reaction. The precise reasons for this are obscure, but the absence of a pharmaceutical
282 industry in New Zealand may be relevant.

283

284 In the U.S., some advocates for disadvantaged groups, such as the poor or minorities,
285 opposed the introduction of a mandatory scheme on the grounds that it would unfairly
286 target members of their constituency with an unproven vaccine; others, meanwhile,
287 argued that the cost of the vaccine would be prohibitive for many lower-income
288 women. In New Zealand, the Ministry of Health expressed concerns that a vaccination
289 program might increase inequalities if deprived populations did not achieve
290 vaccination coverage as high as more advantaged groups [25].

291

It is not surprising that a vaccine targeting a sexually transmitted disease raises moral issues, particularly as the vaccine has been shown to be most effective in girls prior to their becoming sexually active. Among the most common arguments presented in opposition to the vaccine was the argument that vaccination would encourage girls and young women to become sexually active at an earlier age, be promiscuous, or engage in sexual activity outside of marriage, because the vaccine would lead them to believe that sexual activity posed no risks. These arguments were most prominent in the U.S. and Canada, where they were raised largely by politically conservative and religious groups. They were also raised in Australia and New Zealand, but never gained prominent media coverage. In the U.S., young women themselves countered and at times echoed these arguments in a vibrant debate on the vaccine which took place in online forums.

In Switzerland, a fierce public debate erupted as the cantonal vaccination programs began in the summer of 2008. Anti-vaccination lobbyists strongly opposed the programs, and a forum of paediatricians argued that the programs would violate patient privacy, because cantonal authorities proposed collecting data on HPV infected women and vaccination uptake. A consumer association warned of the risk of mass vaccination without sufficient information and suggested that girls and parents boycott the cantonal programs until a more informed decision could be made [34, 35]. Cantons, health insurers and the manufacturer negotiated a lump-sum reimbursement of 291 PPP-\$ (the starting price was 429 PPP-\$) for the three injections, including the physician's fee (30 PPP-\$). Vaccination should mainly occur in schools, but families are free to choose to access the program through a paediatrician, gynaecologist or GP. The involvement of private doctors is crucial for the catch-up program, but the Swiss

Society of General Medicine claimed that a payment of 10 PPP-\$ per vaccination is not sufficient and recommended to its members that they boycott the cantonal vaccination programs.

5.3 Political influences

In New Zealand and Australia, the final decisions about implementing an HPV vaccination program were made in the context of upcoming national elections. Australia held parliamentary elections in late 2007 and New Zealand in late 2008. In New Zealand, it is not uncommon for new national health programs to be introduced just prior to a general election, an event that occurred with both the national cervical cancer and breast cancer screening programs [32].

5.4 Cost-effectiveness

The relevant decision-making authorities in Australia, Denmark and Switzerland considered modelled evaluations of the cost effectiveness of the vaccine, but as with all models, the results rest on assumptions which may not turn out to be representative of reality [36]. For example, two important variables are likely to be the cost of the vaccine and the rate of uptake. In Switzerland, an uptake rate of 80% and a price of 143 PPP-\$ per dose produced a cost per QALY gained of 15,757 PPP-\$ [37]. In Denmark, the cost-effectiveness ratios of various scenarios were estimated. A base scenario with an uptake of 70%, a time horizon of 62 years, and a price of 366 PPP-\$ produced a cost-effectiveness ratio of 9,993 PPP-\$ per life year gained. At the other extreme, vaccinating boys³ as well as girls with a catch-up program for young people

³ There have been calls for vaccination of boys, because boys infected with HPV can pass it on to girls. Moreover, bisexual and gay men are at risk too. Interestingly, such a call has been made by the nobel laureate who worked

up to age 19 and with an uptake of 85% resulted in a cost-effectiveness ratio of 41,194 PPP-\$ [12]. In Australia, the cost-effectiveness ratios on which decisions are based are not published; the committee indicated that it recommended funding on the basis of a “high, but acceptable cost-effectiveness ratio resulting from a price reduction” [38].

6. Implementation and outcomes of the policy

In all countries except the U.S., HPV vaccination programs, whether delivered as a school-based program or via a health insurance package, are being offered on a voluntary basis. In the U.S., making vaccines mandatory for school enrolment is commonly accepted as a nearly foolproof means of achieving universal vaccination, but HPV vaccine mandates proved to be a failure in state legislatures across the country. More than a dozen states, however, approved related legislation, allotting funding to vaccinate school-age or low-income girls, requiring public and/or private insurers to cover the vaccine, or providing support for public education about HPV and its role in cervical cancer.

Thus far, there are few data available about the rate of HPV vaccination uptake in any of the case countries. Where data are available, results are mixed. In Ontario, Canada, less than 50% of eligible girls have been vaccinated, compared to a usual acceptance rate for school-based vaccinations of 80 to 90% [39]. In Australia, a group of researchers in New South Wales (NSW) have used early coverage data to estimate that coverage in 2007/2008 will likely reach 86% (with a feasible range of 67-90%)

on HPV(www.xtra.ca/public/National/Nobel_laureate_calls_for_HPV_vaccine_for_boys-5754.aspx). However, the policy debate – and therefore this paper – focuses on vaccinating girls.

363 for girls aged 12 to 13, with lower rates in older females [40]. A family planning
364 organization in NSW found that of 213 women who had visited a GP in the previous 6
365 months, 59 (53.6%) of these had visited a GP specifically to have the HPV vaccine
366 [41]. In Geneva, Switzerland, a pilot project targeting 2,000 girls, which began in fall
367 2007, reported vaccination of 1200 girls i.e. a final uptake rate of 60% [42, 43].
368 Usually uptake rates for vaccination in Switzerland (in particular in the latin cantons)
369 are higher than 80%. In a survey of 409 young women by researchers in Cincinnati,
370 Ohio, in the U.S., 66% said they intended to get vaccinated, but just 42% said they
371 thought they could afford the vaccine [44].
372
373 There is likewise only limited information available about the vaccine's side effects,
374 due to the recent implementation of programs. In Australia, by the end of June 2008,
375 more than 3.7 million doses of Gardasil had been distributed and just over 1,000
376 suspected adverse events had been reported (27/100,000 doses). Seventy-eight percent
377 were mild or common problems, such as injection site reaction, headache, dizziness,
378 nausea and vomiting; there have also been 12 reports of anaphylaxis and 91 reports of
379 hives [45]. In the U.S., the Centers for Disease Control and Prevention reported in
380 August 2008 that of more than 10,000 reported adverse events linked to Gardasil, 6%
381 were considered serious, and included blood clots and Guillain Barré syndrome; 27
382 deaths of women who received the vaccine were attributed to non-vaccine-related
383 causes [46]. The Canadian Public Health Agency has reported that among more than
384 500,000 doses of Gardasil distributed so far, there have been no confirmed cases of
385 anaphylaxis and 220 less severe adverse events (44/100,000 doses) [39]. These rates
386 are comparable to those reported, for instance, for childhood immunization in
387 Australia for 2004, which ranged from a reporting rate of 6.3/100,000 doses for

bivalent *Haemophilus influenzae* type b-hepatitis B vaccine to 47.7/100,000 doses for
Diphtheria-tetanus-pertussis immunisation [47]

6. Discussion

Although the scientific issues associated with the HPV vaccine are not unique, the
case illustrates important issues associated with the interpretation of scientific
knowledge for policy-making purposes. The overall objectives of a vaccination
program are to reduce the morbidity and mortality associated with cervical cancer.
However, the relationship between many HPV strains and morbidity and mortality is
very complex and not well understood. Thus, there is, as yet, no direct scientific proof
of the effect of the vaccine on morbidity and mortality, and it will take significant
time and resources to obtain such evidence.

There is also, thus far, no evidence of the effect vaccination programs will have on
cervical cancer screening rates. Ongoing research is needed to build the evidence base
for the effectiveness of the HPV vaccine; it will also be important to monitor the rate
of uptake of both the vaccination and Pap tests. Delivering a “double-barrelled” public
health message (for example, obtain this vaccination AND *continue to* receive regular
Pap tests) may be less effective than the previous, simple public health message about
having regular Pap tests. In Switzerland the health insurer association accepted the
financing of the most expensive vaccination in Swiss history, but in exchange asked
the federal benefit basket commission to increase the time between two reimbursed
Pap tests (presently mandatory health insurance covers one Pap test every three
years).

413 Although Gardasil is more expensive than most other vaccines, the question of cost-
414 effectiveness has not been a central feature of the public debate. Perhaps the focus on
415 'saving lives' lost to cervical cancer overshadowed questions about cost and cost-
416 effectiveness. Whatever the reason, given the many competing demands on health
417 funds, open discussion about the relative cost-effectiveness of the vaccine compared
418 with other health interventions has been conspicuous for its absence from this debate.

419

420 The level of uncertainty about effectiveness and uptake, in addition to questions about
421 duration of immunity and cost-effectiveness, created the space for "struggle" between
422 interested parties. In some countries, such as Australia and New Zealand, the level of
423 scientific uncertainty was initially used by decision-makers as a reason for *not*
424 funding the vaccine. On the other hand, once a decision to approve or fund the
425 vaccine was made, scientific uncertainty often became a central focus of objections by
426 interest groups opposed to vaccination proposals.

427

428 The comparative analysis undertaken here shows that countries with different
429 decision-making processes can make similar decisions about the value of subsidizing
430 a program, even when the influence of supporters and opponents seems disparate.
431 This could be the result of the specific socio-political environments in each country.
432 In other words, since the science seems to be reasonably solid on the potential
433 efficacy of an HPV vaccine, and in spite of the debate about the vaccine's real-world
434 effectiveness, uptake and the merits of public subsidy, countries could come to similar
435 conclusions because those in policy decision-making roles are responding to specific,
436 and similar, political pressures.

437

Another interesting—and possibly unique—feature of the HPV vaccine case is that it prompted a number of countries in this study to divert from their usual decision-making processes. Few subjected the vaccine to a systematic process of review, and there seemed to be a degree of urgency among decision makers to approve the vaccine and fund organised programs. In at least two countries, Australia and New Zealand, initial decisions *not* to fund the vaccine were later overturned, even though no new scientific evidence had become available. One reason for this apparent urgency is clearly political; in a number of countries, decisions to fund the vaccine were made in the context of upcoming or current elections, raising questions about the extent to which political influence can override bureaucratic processes. Another reason may be that some countries are willing to be guided in their decisions by others who are perceived as leaders in pharmaceutical decision making processes. Countries with well-established decision-making processes, such as Australia, are widely perceived as credible and their lead often followed by others. There is a chance, however, that if “follower” countries are not aware of particular political or other circumstances at play in “leader” countries, their decisions may be based on factors irrelevant to their situation.

7. Conclusion

The speedy introduction of a subsidized vaccination program across a number of developed countries represents a convergence of interests, whether motivated by profit or public health. Lessons about how to influence the public debate and maintain pressure on bureaucrats and politicians will not have been lost on advocates and lobbyists. Supporters of vaccination programs used the values of caring (for your daughter) and prevention (of cancer) to effectively argue for the vaccine’s subsidy.

463 Both supporters and opponents drew on fear, of cancer and promiscuity, respectively,
464 to influence decision making. The media, not surprisingly, was deployed as an
465 important conveyor of messages, disparate as these messages were from one country
466 to another.

467

468 Interested parties will always try to influence decisions; attempts by individuals and
469 organisations to promote a particular agenda through the media and by directly
470 lobbying politicians and their advisors are a well-accepted aspect of the democratic
471 process. Increasing pressure to cover new drugs while maintaining coverage of the
472 existing basket of products and services requires policy-makers to use transparent and
473 robust guidelines in making funding decisions. Those guidelines should remain at
474 arms-length from political processes. It is up to decision makers, both bureaucratic
475 and political, to remain as firm as possible in their adherence to the agreed-upon
476 decision-making procedures.

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Table 1: Year of introduction or public funding for HPV vaccine and target groups

Country	Approval of vaccine and starting price (in PPP-\$)	Year vaccine publicly funded	Target group (all girls)
Australia	June 2006 315 \$ (Gardasil)	2007	Aged 13 + catch-up for those aged 14-17yrs
Canada	July 2006 335 \$ (Gardasil)	2006-2008	Aged 9-13
Denmark	October 2006 359 \$ (Gardasil)	2009	Aged 12 years + catch-up for those aged 13-14 years
Germany	September 2006 527 \$ (Gardasil), September 2007 (Cervarix);	2007	Aged 12-17, some sickness funds offer vaccine for women aged up to 26 years
New Zealand	July 2006 292 \$ (Gardasil)	2008	School aged 12–13 years + catch-up for those aged up to 18 years not at school.
Switzerland	November 2006	2008	Aged 11-14 + catch-up for those

	429 \$ (Gardasil) Since 2008: 291 \$		aged 15-19 years
USA	June 2006 \$360 (Gardasil)	2006	Aged 11-12 + catch-up for those aged 13-26 years