

HPV Vaccination Program in Indonesia: Effectiveness, Dose, Scale-Up Costs, Future Prospects, and Policy Recommendations

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Abstract

Background: Among females, Cervical cancer affects more frequently than any other type of cancer in Indonesia. Cervical cancer and illnesses linked to HPV infection are potentially preventable through vaccination. The aim of his study was to describe the characteristics of the available vaccines, the policy, and the implementation of HPV vaccination in Indonesia. **Methods:** A scoping review was performed by collecting information from previous studies, including general information about vaccines, vaccine efficacy, effectiveness, and safety. **Results:** Approved HPV vaccine products in Indonesia have proven efficacy, effectiveness, and safety. Procuring vaccines through GAVI/ UNICEF and the government has both advantages and disadvantages. Alongside the limited supply, numerous research studies show that dosage reduction to a single dose provides equal protection compared to 2-3 doses. The benchmark implementation of the single dose has been done in many countries, ranging from high-income to low-middle-income countries. Therefore, considering other countries and Indonesia's high population and vaccination burden, proposed updates for vaccination programs are recommended to achieve the cancer elimination target by 2030. **Conclusion:** Improvement of vaccination programs using single-dose HPV vaccine to prevent cervical cancer requires a coherent framework, sufficient funds, effective management of stakeholder interests, and sensitivity to contextual factors.

Keywords: Cervical cancer- cost- HPV Vaccine- policy- single dose

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Introduction

Among females, cervical cancer affects more than any other type of cancer in the world. The incidence of cervical cancer was 604,127 (6.5%) and it becomes the fourth highest among new cancer cases in 2020 [1] and half of it occurred in Asia with 351,720 (7.8%) cases [2]. In Indonesia, there were 36,633 (17.2%) of cervical cases and it becomes top two of cancer cases among females [3]. The burden of the disease increased beginning at age of 25 and peaked at age 95 or beyond for women who have cervical cancer [4].

Factors hypothesized to enhance the risk of cervical cancer are smoking, prolonged oral contraceptive usage, high numbers of parity, and persistent infection with oncogenic human papilloma virus (HPV) types. There are 13 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) and 5 moderately high-risk HPV types (53, 66, 70, 73 MM9, and 82 MM4) [5]. HPV types 16 and 18, which are mostly associated with carcinogenesis, are the most prevalent types on a global scale [5]. They have been linked to almost 70% of cervical cancer

incidences worldwide [6]. Nonetheless, apart from the high prevalence of cervical cancer cases caused by HPV, the disease is actually preventable.

Cervical cancer and other illnesses linked to HPV infection are preventable [7]. There are three HPV vaccines approved by the Indonesian Food and Drug Administration (Badan Pengawasan Obat dan Makanan / BPOM): the bivalent vaccine (2vHPV), the quadrivalent vaccine (4vHPV), and the nine-valent vaccine (9vHPV). In terms of HPV infection, the 4vHPV vaccine provides protection against infection from HPV types 6 and 11, which are thought to be responsible for 90% of genital warts and recurrent respiratory papillomatosis. The 4vHPV and 2vHPV vaccines also provide protection against types 16 and 18, which are thought to be responsible for approximately 66% of cervical cancers [8]. On the other hand, the 9vHPV vaccine protects against types 6, 11, 16, 18, 31, 33, 45, 52, and 58; hence preventing approximately 81% of cervical cancers [9].

HPV Vaccine has been introduced as national immunization programs by 60% of World Health Organization (WHO) member states. However, only

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13% of female adolescents on the global scale received HPV vaccination. In addition, as of 2019, only 19% of low- to middle-income nations had implemented HPV vaccination, compared to 77% of countries in Europe and 85% of countries in the Americas [10]. One of the reasons for this gap is that many LMIC either do not have national HPV vaccination programs or, if they do, they have significant obstacles, such as huge amounts of the required budget. Therefore, in response to this case, financial planning and implementation of an effective and efficient HPV immunization program are crucial.

In 2022, the WHO has revised its recommendations for the human papillomavirus (HPV) vaccine in a new position paper. Particularly, the paper claims that a single-dose schedule can offer protection that is just as effective and long-lasting as a two-dose regimen. The position paper occurs at a correct moment considering the critically alarming global decrease in HPV vaccination rates. The coverage of the first HPV vaccine dose decreased from 15% to 25% between 2019 and 2021. As a result, 3.5 million more girls in 2021 than in 2019 did not receive complete dose of HPV vaccination [11]. Alongside the benchmark implementation of a single-dose in many countries, whereas yet to be implemented in Indonesia, therefore the study of product, schedule, and options of procurement in Indonesia related to a single-dose HPV need to be observed. This paper studied the existing evidence on product, schedule, and procurement options for HPV vaccination strategy for HPV; scale-up costs with options of each HPV type/product and procurement methods; and a proposed update to HPV technical guidelines and/or HPV national roadmap plan according to the current recommendation on single dose.

Materials and Methods

To provide comprehensive information on the effectiveness of currently available vaccine in the Indonesian market, a scoping review was performed by collecting information from previous studies including general information on the vaccines, vaccine efficacy, effectiveness, and safety. The latest recommendation on HPV vaccination was collected from WHO and SAGE publications. Formal information from the Ministry of Health (MoH), the department of health and also

primary health care in Indonesia, including the vaccine procurement process and policy, vaccine local price, and target population for HPV vaccination policy were collected through interview and Focus Group Discussion (FGD). The current implementation of the nationwide HPV vaccination policy was obtained from the technical guideline from MoH and the official report on its application in 2023. The benchmark implementations of single dose policy in other countries were also collected from the respective official websites. This study also included calculations regarding the scale-up cost for 1 dose and 2 doses of the Nationwide HPV Vaccination Program.

Results

General Information among Currently Available HPV Vaccines in Indonesia

There are three different HPV vaccine which are available in Indonesia. All of the HPV vaccine products have been approved by the Indonesian Food & Drug Administration of (BPOM) (Table 1).

HPV Vaccine Efficacy and Effectiveness

According to the Center for Disease Control and Prevention (2021), clinical trials limited to people without signs of infection with the vaccine types at the time of vaccination revealed that all HPV vaccines had high efficacy (nearly 100%) for preventing HPV vaccine type-related persistent infection, cervical intraepithelial neoplasia (CIN) 2/3, and adenocarcinoma in situ (AIS) [15]. Furthermore, females who receive the vaccine prior to HPV exposure in nations with high vaccine uptake, the effect of HPV immunization in real life circumstances is clear. Maximum reductions have been reported to be approximately 90% for HPV 6/11/16/18 infections, 90% for genital warts, 45% for low-grade cytological cervical abnormalities, and 85% for high-grade histologically confirmed cervical abnormalities [12].

In Indonesia, according to its country specific HPV infection incidence, the weighted efficacy ranged from 83% to 96.1% (Table 2). The quadrivalent HPV vaccines are considerably effective since it has 95% efficacy against HPV 16 and 18 infections [16]. Meanwhile, for the bivalent vaccine was 100% effective against CIN 2+ linked with HPV-16/18 and 100% effective against

Table 1. Product Details of HPV Vaccines

Vaccine Characteristics	Product Types			Source
	Cervarix (2vHPV)	Gardasil (4vHPV)	Gardasil 9 (9vHPV)	
Target of HPV strains	HPV-16 and HPV-18	HPV-6, 11, 16, and 18	HPV-6, 11, 16, 18, 31, 33, 45, 52, and 58	[12]
Disease Protection	HPV-Related Cancers	HPV-Related Cancers and Genital Warts	HPV-Related Cancers and Genital Warts	[12]
Adjuvant	A composed of monophosphoryl-lipid A, adsorbed to aluminium hydroxide (AS04)	amorphous aluminium hydroxyphosphate sulfate	amorphous aluminium hydroxyphosphate sulfate	[13,14]
Administration Method	Intramuscular injection	Intramuscular injection	Intramuscular injection	[12]
Manufacturer	Glaxo-Smith Kline Biologicals (GSK)	Merck Sharp and Dohme (MSD)	Merck Sharp and Dohme (MSD)	[12, 14]

Table 2. The Comparison of HPV Vaccine Efficacy for Indonesian Population

HPV types	Prevalence of Infection (%) (a)	Vaccine efficacy (%) (b)			Source
		Bivalent	Quadrivalent	Nonavalent	
16	47	95	95	95	[17,18]
18	20	95	95	95	[17, 18, 19]
31	0	79	0	95	[17, 18, 19]
33	30	56	0	95	[17, 18, 19]
45	6	76	0	95	[17, 18, 19]
52	6	0	0	95	[18]
58	0	0	0	95	[18]
Vaccine efficacy (axb)		0.79	0.64	0.94	[20]

Table 3. The Cost Component of HPV Vaccination

Cost Component	GAVI/UNICEF* (USD)	Government contract price* (USD)	Source
Vaccine price	4.5	11.62	[27]
Shipping price	0.16	0	[27]
Handling fee	0.41		[27]
Insurance	0.23		[27]

*Vaccine price using Gardasil price for the budget impact analysis

12-month persistent infection (95% CI = 81.8-100). It was 93.3% effective against the incidence of HPV-16/18 infection (95% CI = 87.4-98.7). The effectiveness against lesions that were unrelated to the type of HPV DNA was 71.9% (95% CI = 20.6-91.9). The study also discovered that the concentration of anti-HPV-16 and anti-HPV-18 antibodies remained 12-fold or higher than that attained after natural infection [14].

Alongside the two types of vaccine above, according to epidemiology studies, Gardasil 9 is expected to provide protection against the HPV types that are thought to be responsible for approximately 90% of cervical cancers, more than 95% of adenocarcinoma in situ (AIS), 75-85% of high-grade cervical intraepithelial neoplasia (CIN 2/3), and 85-90% of HPV-related vulvar cancers [16].

Regarding cross-protection of HPV vaccines. A study in Japan exploring the cross protection of bivalent vaccine among Japanese women between 20 and 22 years old. Out of 1814 among 2197 women who were tested were also included in the analysis. A total of 1355 (74.6%) of them received the vaccination, and 1295 (95.5%) finished the three-dose course. The pooled Vaccine Effectiveness (VEs) on HPV 16 and 18 was 95.5% (P=0.01) and on HPV 31, 45, and 52 was 71.9% (P = 0.01). After adjusting for the number of sexual partners and birth year, the pooled VEs for HPV 16 and 18 was 93.9% (P = 0.01) and for HPV 31, 45, and 52 was 67.7% (P = 0.01). Against HPV16 and 18, the bivalent HPV vaccine has excellent protection. Significant cross-protection against HPV31, 45, and 52

was additionally shown and maintained up to 6 years following vaccination [21]. Alongside the effectiveness of vaccination in general, particularly for women, the effectiveness of HPV vaccination was also studied for catch-ups, boosters, and males.

Effectiveness of Catch-Up Vaccination

Catch-up vaccination describes the action of vaccinating individuals who do not have or have not received the required number of doses of a vaccine at the recommended age. If a person was not vaccinated against HPV when they were young, they could still get the benefit if they are vaccinated until the age of 26 (Table 3) [12]. Although the HPV vaccine has been approved for use in adults up to the age of 45, catch-up vaccination is better administered at 13-26 years old and not commonly advised for anyone older than 26 because the vaccine's benefits begin to decrease following HPV exposure [12].

There are, however, numerous studies on the effectiveness of vaccines in adult women. The effectiveness of the bivalent HPV vaccine against preventing persistent HPV 16/18 infection in adults >26 years old and previously uninfected women was 83% (95% CI = 71% to 90%) and 43% (95% CI = 31% to 53%), respectively. In naive infection, the vaccine's effectiveness against CIN2+ linked to HPV 16/18 was 70% (95% CI = 19% to 89%) [12]. The effectiveness of the cross-protective vaccine against HPV 31 infection was 79.1% (97.7% CI = 27.6% to 95.9%) and against HPV 45 infection was 76.9% (95%

Table 4. The Cost of New Vaccine Introduction (NVI) for HPV Vaccine in Indonesia

Year	Total Budget of Vaccine Provision (IDR)	Total Budget of HPV Vaccine Provision (IDR)	Percentage of HPV Vaccine
2022	2,597,669,856,000.00	151,101,665,000.00	5.90%
2023	2,414,641,213,000.00	547,723,068,750.00	23%

Source: personal discussion with Indonesian Ministry of Health

CI = 18.5% to 95.6%). The quadrivalent vaccine had an efficacy of 88.7% (95% CI = 78.1% to 94.8%) against CIN and external genital lesions related to HPV 6/11/16/18 in naive HPV infection at baseline compared to an efficacy of 30.9% (95% CI = 11.1% to 46.5%) in the placebo group against CIN2+ associated with HPV 6/11/16/18/23 [12].

In England, a catch-up bivalent human papillomavirus vaccination on cervical screening outcomes was also studied. As part of the English HPV screening pilot between 2013 and 2018, 108,138 women between the ages of 24 and 25 (offered vaccination) and 26 and 29 (not offered vaccination) were screened [22]. With an estimated vaccine effectiveness of 87% (95% CI: 82-91%), it demonstrates that at 24–25 years of age, the detection of high-grade cervical intraepithelial neoplasia (CIN2+) associated with HPV16/18 dropped from 3 to 1% ($p < 0.001$). With an estimated vaccination efficiency of 72% (95% CI: 66-77%), the detection of any CIN2+ decreased from 6 to 3% ($p < 0.001$) [22]. These results demonstrate the excellent efficacy of the bivalent HPV vaccination given in England via a population-based catch-up effort.

Effectiveness of Booster Vaccination

Booster vaccination refers to an additional dosage or doses of a vaccination administered where protection from initial shot(s) has started to decline over time. Research on the effectiveness of booster dose was previously conducted to evaluate the safety and immunogenicity of the booster dose of Gardasil (qHPV) or Cervarix (bHPV) given to 12–13-year-old females who received 2 doses of qHPV (0–6 months) at the age of 9–10 years old. HPV booster vaccinations were given to 366 out of 416 eligible females. Approximately 99–100% of the females showed detectable antibodies to 4 HPV genotypes included in the qHPV three years after receiving their first vaccination [23]. A total of 88–98% of individuals showed a 4-fold rise in antibody titers to the genotypes covered by the vaccination after receiving a booster dose of qHPV [23]. A 4-fold increase in antibody titers to HPV16 and HPV18 was observed in 93-99% of individuals following a booster of bHPV. Both vaccines safety profiles were satisfactory. When administered as a booster to females who have already received two doses of the qHPV vaccine, both qHPV and bHPV raise antibody titers [23].

Initially, the HPV vaccine was authorized for girls aged 9 to 26. However, according to the CDC [15], immunogenicity examinations showed that two HPV vaccination doses given to 9–14-year-olds at least six months apart from one another offered an equal amount of protection to three doses given to older adolescents or young adults. This may indicate the effective age for booster vaccination.

Effectiveness of HPV Vaccination in Males

In the US, the Advisory Committee on Immunization Practices (ACIP) upgraded its recommendation in October 2011 by advising routine HPV vaccination for boys aged 11 to 12 and catch-up immunization for males aged 13 to 21 [24]. Male vaccination is particularly encouraged because the HPV types 16 and 18 are responsible for 92% of cases of anal cancer, 63% of cases of penile cancer,

and 89% of cases of oral or oropharyngeal cancer [25].

The vaccine efficacy against the incidence of HPV 16 and HPV 18 infection was 28.0–45.1% and 33.9–49.5%, respectively [26]. According to reports, vaccines were successful against anal condyloma between 57.2 and 67.2% [26]. Infection with HPV-6, 11, 16, and 18 as well as the emergence of associated external genital lesions are prevented in males between the ages of 16 and 26 by the quadrivalent HPV vaccine26. Vaccination is moderately successful for individuals against genital HPV infection and high-grade anal intraepithelial lesions in people, regardless of their HPV status [12].

HPV Vaccine Safety

Safety in the use of vaccines is crucial and carefully considered. A study showed that overall adverse effects at the injection site of bivalent and quadrivalent vaccines result in 1.18 relative risk and 1.16 to 1.20 95% CI [12]. Recent studies have looked specifically at outcomes such as complex regional pain syndrome (CRPS), Bell's palsy, postural orthostatic tachycardia syndrome (POTS), premature ovarian insufficiency, primary ovarian failure, and venous thromboembolism, but they have not found any new evidence linking the HPV vaccine to those conditions. Although there is no evidence linking the HPV vaccine to worse pregnancy outcomes, it is still not advised during pregnancy [12].

Procurement Options

There are two current options for procuring HPV vaccines in Indonesia. First, vaccines can be purchased by the government from MSD and the products are repackaged by Biofarma. For the second option, the vaccines can be bought through UNICEF with the price standardized by GAVI. Through GAVI, bivalent, quadrivalent, and nonavalent vaccine costs were US\$4.6, US\$4.5, and US\$6.9, respectively (Table 3). In addition, Indonesia currently has a contract price of US\$11.79 for the quadrivalent vaccine if the government purchases it from the pharmaceutical industry [27].

The Scale-Up Cost of the Nationwide HPV Vaccination Policy in Indonesia

Based on the Indonesia Cervical Cancer Profile [11], the total population of Indonesian females in 2019 was 134,400,000, with a total female mortality of cervical cancer deaths (2019) of 19,300 and a cancer mortality-to-incidence ratio (2020) of 0.57 [34]. In response to these statistics and WHO recommendations related to HPV vaccination programs, Indonesia has been initiating HPV vaccination programs for female children aged 11-12 years old since 2016, starting with coverage of 75,124 female students in Jakarta. The latest implementation was conducting HPV vaccination in 9 provinces, including Jakarta, Central Java, Yogyakarta, East Java, Bali, North Sulawesi, South Sulawesi, Southeast Sulawesi, and Gorontalo, with total coverage of 5th grade and 6th grade female students of 740,767 and 208,129, respectively (Table 5). With the plan of nationwide vaccination programs in 34 provinces (Table 5), the government strategy for scaling up costs related to HPV products and

Table 5. HPV Vaccination Coverage in BIAS 2020-2022 and Population Data of Female Children of Health Development Program Targets 2021-2025

No.	Province	HPV Vaccination Coverage through BIAS						Targeted Female Children for HPV Vaccination					
		2020		2021		2022		2023		2024		2025	
		Gr.5/11 y.o	Gr.6/y.o	Gr.5/11 y.o	Gr.6/12 y.o	Gr.5/11 y.o	Gr.6/12 y.o	Gr.5/11 y.o	Gr.6/12 y.o	Gr.5/11 y.o	Gr.6/12 y.o	Gr.5/11 y.o	Gr.6/12 y.o
1	Aceh	0	0	0	0	0	0	49,924	49,827	50,006	49,919	49,928	49,848
2	North Sumatra	0	0	0	0	0	0	135,234	135,350	135,070	135,273	134,467	134,697
3	West Sumatra	0	0	0	0	0	0	51,150	50,854	51,480	51,227	51,797	51,634
4	Riau	0	0	0	0	0	0	69,213	69,910	68,182	68,904	66,056	66,663
5	Jambi	0	0	0	0	0	0	29,587	29,518	29,588	29,510	29,550	29,461
6	South Sumatra	0	0	0	0	0	0	74,796	74,058	75,152	74,330	75,756	74,984
7	Bengkulu	0	0	0	0	0	0	16,287	16,234	16,314	16,246	16,305	16,222
8	Lampung	0	0	0	0	0	0	70,543	70,632	70,358	70,472	69,978	70,091
9	Kep. Bangka Belitung	0	0	0	0	0	0	12,119	12,069	12,203	12,161	12,279	12,250
10	Kepulauan Riau	0	0	0	0	0	0	19,479	19,160	19,606	19,184	19,927	19,462
11	DKI Jakarta	75,124	0	0	0	73,266	68,694	73,089	71,836	74,595	73,247	75,562	74,069
12	West Java	0	0	0	0	0	0	394,608	397,125	392,407	394,585	389,623	391,163
13	Central Java	0	0	0	0	277,325	12,977	258,088	261,167	255,150	258,161	251,405	254,122
14	D.I. Yogyakarta	0	0	0	0	25,889	25,536	25,258	25,016	25,626	25,318	26,091	25,734
15	East Java	0	0	0	0	271,059	35,227	264,178	263,336	262,359	260,482	263,897	261,869
16	Banten	0	0	0	0	0	0	108,686	108,564	108,807	108,671	108,597	108,397
17	Bali	0	0	0	0	34,107	24,350	31,613	31,966	30,913	31,100	30,281	30,288
18	West Nusa Tenggara	0	0	0	0	0	0	46,401	45,852	46,784	46,252	47,217	46,733
19	East Nusa Tenggara	0	0	0	0	0	0	52,750	52,036	53,426	52,664	53,955	53,139
20	West Kalimantan	0	0	0	0	0	0	43,202	43,143	43,133	43,040	43,004	42,873
21	Central Kalimantan	0	0	0	0	0	0	22,076	22,022	22,094	22,028	22,059	21,978
22	South Kalimantan	0	0	0	0	0	0	37,602	37,305	38,020	37,872	38,269	38,276
23	East Kalimantan	0	0	0	0	0	0	28,984	28,878	29,016	28,895	29,009	28,866
24	North Kalimantan	0	0	0	0	0	0	6,208	6,206	6,253	6,260	6,271	6,283
25	North Sulawesi	0	0	0	0	16,706	3,292	19,038	18,956	19,128	19,071	19,252	19,242
26	Central Sulawesi	0	0	0	0	0	0	27,073	26,870	27,339	27,165	27,524	27,380
27	South Sulawesi	0	0	0	0	11,736	11,302	71,751	71,886	71,625	71,822	71,332	71,595
28	Southeast Sulawesi	0	0	0	0	23,601	26,751	24,845	24,762	24,866	24,719	24,976	24,778
29	Gorontalo	0	0	0	0	7,078	0	9,732	9,751	9,710	9,736	9,651	9,679

Table 5. Continued

No.	Province	HPV Vaccination Coverage through BIAS						Targeted Female Children for HPV Vaccination					
		2020		2021		2022		2023		2024		2025	
		Gr.5/11 y.o	Gr.6/y.o	Gr.5/11 y.o	Gr.6/12 y.o	Gr.5/11 y.o	Gr.6/12 y.o	Gr.5/11 y.o	Gr.6/12 y.o	Gr.5/11 y.o	Gr.6/12 y.o	Gr.5/11 y.o	Gr.6/12 y.o
30	West Sulawesi	0	0	0	0	0	0	12,793	12,728	12,833	12,775	12,843	12,785
31	Maluku	0	0	0	0	0	0	16,389	16,378	16,373	16,358	16,304	16,273
32	North Maluku	0	0	0	0	0	0	11,498	11,499	11,506	11,510	11,460	11,463
33	West Papua	0	0	0	0	0	0	9,024	9,002	9,073	9,050	9,116	9,078
34	Papua	0	0	0	0	0	0	30,253	30,083	30,371	30,212	30,447	30,299
	Indonesia	75,124	0	0	0	740,767	208,129	2,153,471	2,153,979	2,149,366	2,148,219	2,144,188	2,141,674

procurement methods is critical.

The annual cost scheme of 2-dose HPV vaccines for grade 5 and 6 female students or those aged 11-12 years old in 34 provinces is shown in Table 6. It costs IDR 522,777,527,226.00; 776,259,885,795.00; and 774,142,395,474.00 for the respective years of 2023, 2024, and 2025. A comparison to the annual cost scheme of the 1-dose HPV vaccine for grade 5 or 11 years old is presented in Table 7. This vaccination in 2023-2025 costs IDR 388,975,006,317.00; 388,233,532,482.00; and 387,298,245,876.00. This will result in 29% lower cost of New Vaccine Introduction (NVI) compared to total budget of HPV vaccine provision, which is 547,723,068,750.00, in 2023 by Indonesian Ministry of Health (Table 4). These calculations are based on the price of Gardasil, as there is no other brand and prices available on the Indonesian government website. To conclude, 1-dose HPV vaccination costs half as much than 2-doses. This surely can result in wider coverage with less budget.

Single Dose HPV Vaccine in Indonesia: Future Perspective The Current evidence on the Efficacy and Effectiveness of single-dose HPV vaccination

According to the WHO’s Strategic Advisory Group of Experts on Immunization (SAGE), a single dose of HPV vaccination offers equal protection against human papillomavirus (HPV) infections for types 16 and 18, which are responsible for 70% of instances of cervical cancer, as two or three doses with several supporting evidence. As demonstrated in the Costa Rica Vaccine Trial (CVT) and Indian International Agency for Research on Cancer (IARC) studies, a single dose of bivalent or quadrivalent vaccine can last up to 10 to 11 years with stable antibody levels, and is as effective as three doses combined. The Kenya single-dose HPV vaccine efficacy (KEN SHE) also evaluated the efficacy of the 9-valent HPV vaccine in young African women after a single dose of HPV vaccination. It appears that adolescent girls and young women were effectively protected from HPV infection over the first 18 months following vaccination; vaccine efficacy (VE) for the HPV 16/18 vaccine was greater than 97%, consistent with licensure trial results for 3 doses; and VE against the 7 HR HPV types in the 9-valent group was 95% in the preplanned efficacy and sensitivity analyses, excluding participants with HPV DNA at 6 months. Moreover, in the immunobridging of Dose Reduction Immunobridging and Safety Study (DoRIS) from Tanzania with the KEN SHE trials study, the one-dose immune response observed in DoRIS was not inferior to KEN SHE at month 18, demonstrating noninferiority to KEN SHE. In the 9-valent group, efficacy was measured 6 months after the first dose and demonstrated a VE of 95% against HPV 16/18 and 95% against the seven high-risk HPV types [15]. Finally, the number of females who can receive this vital, life-saving vaccine might possibly double if nations decide to follow this new suggestion [28].

The Current WHO Recommendation on Cervical Cancer Elimination Strategy

The WHO conveyed the agenda of WHO Cervical

Table 6. Annual Cost Scheme for 2 Doses of HPV Vaccination Program

No.	Province	Targeted Female Children					
		2023		2024		2025	
		Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1
1	Aceh	0	49,924	49,919	50,006	49,848	49,928
2	North Sumatera	0	135,234	135,273	135,070	134,697	134,467
3	West Sumatera	0	51,150	51,227	51,480	51,634	51,797
4	Riau	0	69,213	68,904	68,182	66,663	66,056
5	Jambi	0	29,587	29,510	29,588	29,461	29,550
6	South Sumatera	0	74,796	74,330	75,152	74,984	75,756
7	Bengkulu	0	16,287	16,246	16,314	16,222	16,305
8	Lampung	0	70,543	70,472	70,358	70,091	69,978
9	Kep. Bangka Belitung	0	12,119	12,161	12,203	12,250	12,279
10	Kepulauan Riau	0	19,479	19,184	19,606	19,462	19,927
11	DKI Jakarta	73,266	73,089	73,247	74,595	74,069	75,562
12	West Java	0	394,608	394,585	392,407	391,163	389,623
13	Central Java	277,325	258,088	258,161	255,150	254,122	251,405
14	D.I. Yogyakarta	25,889	25,258	25,318	25,626	25,734	26,091
15	East Java	271,059	264,178	260,482	262,359	261,869	263,897
16	Banten	0	108,686	108,671	108,807	108,397	108,597
17	Bali	34,107	31,613	31,100	30,913	30,288	30,281
18	West Nusa Tenggara	0	46,401	46,252	46,784	46,733	47,217
19	East Nusa Tenggara	0	52,750	52,664	53,426	53,139	53,955
20	West Kalimantan	0	43,202	43,040	43,133	42,873	43,004
21	Central Kalimantan	0	22,076	22,028	22,094	21,978	22,059
22	South Kalimantan	0	37,602	37,872	38,020	38,276	38,269
23	East Kalimantan	0	28,984	28,895	29,016	28,866	29,009
24	North Kalimantan	0	6,208	6,260	6,253	6,283	6,271
25	North Sulawesi	16,706	19,038	19,071	19,128	19,242	19,252
26	Central Sulawesi	0	27,073	27,165	27,339	27,380	27,524
27	South Sulawesi	11,736	71,751	71,822	71,625	71,595	71,332
28	Southeast Sulawesi	23,601	24,845	24,719	24,866	24,778	24,976
29	Gorontalo	7,078	9,732	9,736	9,710	9,679	9,651
30	West Sulawesi	0	12,793	12,775	12,833	12,785	12,843
31	Maluku	0	16,389	16,358	16,373	16,273	16,304
32	North Maluku	0	11,498	11,510	11,506	11,463	11,460
33	West Papua	0	9,024	9,050	9,073	9,078	9,116
34	Papua	0	30,253	30,212	30,371	30,299	30,447
	Indonesia	740,767	2,153,471	2,148,219	2,149,366	2,141,674	2,144,188
	Gardasil purchasing cost through government (Rp)	522,777,527,226		776,259,885,795		774,142,395,474	
	GAVI/UNICEF Bivalent (Rp)	234,433,278,000.00		348,104,385,000.00		347,154,822,000.00	
	GAVI/UNICEF Quadrivalent (Rp)	230,091,921,000.00		341,658,007,500.00		340,726,029,000.00	
	GAVI/UNICEF Nonavalent (Rp)	334,284,489,000.00		496,371,067,500.00		495,017,061,000.00	

Cancer Elimination Strategy Targets for 2030 in order to achieve up the elimination of cervical cancer as a public health issue and prevent more deaths [11]. The WHO Cervical Cancer Elimination Strategy Targets for 2030 are as follows:

a. Ninety percent (90%) of girls are fully vaccinated with the HPV vaccine by the age of 15.

b. Seventy percent (70%) of women are screened with a high-performance test by 35 years of age and again by 45 years of age.

c. Ninety percent (90%) of women identified with cervical disease receive treatment.

HPV schedule optimization is expected to broaden access to the vaccine, giving nations the chance to

Table 7. Annual Cost Scheme for 1 Dose of HPV Vaccination Program

No.	Province	Targeted Female Children (Grade 5 and 11 years old)		
		2023	2024	2025
		Dose 1	Dose 1	Dose 1
1	Aceh	49,924	50,006	49,928
2	North Sumatera	135,234	135,070	134,467
3	West Sumatera	51,150	51,480	51,797
4	Riau	69,213	68,182	66,056
5	Jambi	29,587	29,588	29,550
6	South Sumatera	74,796	75,152	75,756
7	Bengkulu	16,287	16,314	16,305
8	Lampung	70,543	70,358	69,978
9	Kep. Bangka Belitung	12,119	12,203	12,279
10	Kepulauan Riau	19,479	19,606	19,927
11	DKI Jakarta	73,089	74,595	75,562
12	West Java	394,608	392,407	389,623
13	Central Java	258,088	255,150	251,405
14	D.I. Yogyakarta	25,258	25,626	26,091
15	East Java	264,178	262,359	263,897
16	Banten	108,686	108,807	108,597
17	Bali	31,613	30,913	30,281
18	West Nusa Tenggara	46,401	46,784	47,217
19	East Nusa Tenggara	52,750	53,426	53,955
20	West Kalimantan	43,202	43,133	43,004
21	Central Kalimantan	22,076	22,094	22,059
22	South Kalimantan	37,602	38,020	38,269
23	East Kalimantan	28,984	29,016	29,009
24	North Kalimantan	6,208	6,253	6,271
25	North Sulawesi	19,038	19,128	19,252
26	Central Sulawesi	27,073	27,339	27,524
27	South Sulawesi	71,751	71,625	71,332
28	Southeast Sulawesi	24,845	24,866	24,976
29	Gorontalo	9,732	9,710	9,651
30	West Sulawesi	12,793	12,833	12,843
31	Maluku	16,389	16,373	16,304
32	North Maluku	11,498	11,506	11,460
33	West Papua	9,024	9,073	9,116
34	Papua	30,253	30,371	30,447
	Indonesia	2,153,471	2,149,366	2,144,188
	Gardasil purchasing cost through government (Rp)	388,975,006,317.00	388,233,532,482.00	387,298,245,876.00
	GAVI/UNICEF Bivalent (Rp)	174,431,151,000.00	174,098,646,000.00	173,679,228,000.00
	GAVI/UNICEF Quadrivalent (Rp)	171,200,944,500.00	170,874,597,000.00	170,462,946,000.00
	GAVI/UNICEF Nonavalent (Rp)	248,725,900,500.00	248,251,773,000.00	247,653,714,000.00

increase the number of girls who can receive the vaccine and reduce the burden of vaccination follow-up costs. A very important step in reducing avoidable disease and death is to increase access to vaccines that can prevent cervical cancer with an effective schedule and dose, as recommended by the WHO [11].

Schedule

Girls between the ages of 9 and 14 are the main target

of immunization, prior to sexual activity. Vaccination of secondary targets, such as boys and older females, is advised where possible and affordable.

Dose

a. A one- or two-dose schedule for girls aged 9 to 14 years old.

b. A one- or two-dose schedule for girls and women aged 15 to 20 years old.

c. Two doses with a 6-month interval for women older than 21 years old.

Regarding this agenda, several countries, namely, the United Kingdom, Australia, and Ireland, have been trying to create and implement their updated guidelines for HPV vaccination programs. This is also supported by various updated studies from research stakeholders, such as the Strategic Advisory Group of Experts on Immunization (SAGE) and the UK's Joint Committee on Vaccination and Immunisation (JCVI), particularly those associated with a single-dose HPV vaccine.

Benchmark Implementation of single dose HPV Vaccination in Some Countries of Several Regions

Europe

United Kingdom

As published in August 2022, JCVI - an independent committee of experts that advises the UK government on issues involving immunization and vaccination-recommended single dose of HPV vaccination [29]. According to the evidence on single-dose vaccine effectiveness and the cost-effectiveness, JCVI's recommendations aim to maximize the health benefits from immunization. The JCVI advises a single-dose schedule for all teenagers (boys and girls) in year 8 (usually aged 12 and 13) and men who have sex with men (MSM) before the 25th birthday; a 2-dose schedule from the age of 25 in the MSM programme; and a 3-dose schedule for individuals who are immunosuppressed and those known to be HIV-positive. Even though the universal adolescent HPV program will be implemented in schools, eligible students who are homeschooled or educated in other settings should also be provided with the vaccine [29].

Prior to the announcement, JCVI reviewed a modeling study by Daniels et al. [30] funded by the MSD manufacturer. The modeling showed that at the standard WTP threshold, the probability of single-dose HPV vaccine being cost-effective compared to 2 doses was less than 50% across its sensitivity analysis. In comparison to the 2-doses program, the adoption of a single-dose 9vHPV vaccination program increased the cases of vaccine-preventable HPV-related cancer and disease in both men and women, implied significant uncertainty in the health and economic outcomes, and had a low likelihood of being cost-effective. Moreover, they calculated that the percentage of females obtaining a follow-up screening due to abnormal cytology is 70.52%. This results in higher costs of screening and monitoring costs of adopting a single-dose vaccination to ensure HPV infection, and related health aspects will not increase due to the lower effectiveness of single-dose vaccination [30].

However, Burger et al. [31] sent a letter to the editor of the mentioned publication stating that a recent economic evaluation of 1-dose HPV vaccination by Daniels et al. [30] used unsupported assumptions. The highlights of the letter included the underestimated vaccine efficacy by Daniels et al. [30] vaccine protection waning is unrealistic, and characterization of uncertainty is not evidence-based [31]. In addition, JCVI also assessed Professor Marc Brisson's modeling study using the HPV ADVISE model,

which showed that switching to a one-dose regular HPV vaccination is not expected to significantly raise cervical cancer rates if the lifetime of protection is more than 20 years. Brisson's modeling did not consider the future impacts of scale-up or current cervical cancer screening programmes as they may result in health losses due to postponed HPV vaccine implementation, particularly in countries with a high burden [32]. Given this, JCVI remarked that the modeling gave reassurance to those who were worried about potential future decline. Nonetheless, JCVI will look at new evidence from the clinical trials and surveillance of the UK program [33].

The coverage of cervical screening also probably strengthens the decision to implement this single-dose vaccination program. As of 2022, the total eligible populations for cervical screening were 10,472,750 (for women aged 25 to 49), and 5,360,285 (for women aged 50 to 64) in England. A total of 67.1% of women aged 25 to 49 had an adequate screening test recorded in the previous 3.5 years. In addition, 74.8% of women aged 50 to 64 had an adequate screening test recorded in the previous 5.5 years. This is a large number, as they targeted 80% coverage of cervical screening [34].

For the vaccination program, Gardasil 9 vaccines would replace Gardasil as the vaccine offered for adolescent HPV and HPV-MSM in 2022. The timeframe depends on when the UK Health Security Agency's (UKHSA) stock of Gardasil runs out. Both vaccines may be locally accessible in various locations for a while after UKHSA begins to supply Gardasil 9 because teams use their local Gardasil stockpiles at various rates [29].

Ireland

The Ireland National Immunization Advisory Committee (NIAC) has modified its recommendations regarding how many doses of the HPV vaccine are necessary for young people. A single-dose of the HPV vaccine is now sufficient for those with healthy immune systems. This adjustment was made because current research did not demonstrate a significant variation in the efficacy of the HPV vaccine in individuals with healthy immune systems, aged 9 to 24, who received one, two, or three doses of the HPV vaccine [34].

The decision to implement single-dose HPV vaccination is also supported by a successful screening program. Based on the report from the National Screening Service, 78.7% programme coverage (standard is 80% and was reached in 2012/2017) was obtained in 2017-2020 through a national cervical screening programme called CervicalCheck. This resulted from almost 3.2 million cervical screening tests provided from September 2008 to March 2020 [35].

Albania

There are 1.20 million women in Albania who are 15 years of age or older and at risk of having cervical cancer. According to current statistics, 133 women are given a cervical cancer diagnosis each year, and 74 of them pass away from the condition [36]. In response, Albania introduced HPV vaccination in 2022 and introduced 1-dose vaccination for 13-year-old girls in 2023.

Western Pacific Region Australia

Australia reduced the number of doses of the Gardasil9 administered to children as part of the National Immunization Program from two to one (NIP), as stated on February 6th, 2023, by the Australian Department of Health and Aged Care. This change is supported by the most recent worldwide scientific and clinical research, which demonstrates that in healthy young people, a single dose provides equivalent protection against HPV infection. It is also supported by the World Health Organization immunization expert group, the Australian Technical Advisory Group on Immunization (ATAGI), and the United Kingdom immunization expert [37].

Children between the ages of 12 and 13 can receive the HPV vaccine for free through school immunization programs. An immunization clinic at a school, a general practitioner, a local pharmacy, or other primary care providers can administer a catch-up vaccination. Since the implementation of a national school-based vaccination program in 2007, Australia the first nation to provide free HPV vaccinations for 12- and 13-year-old girls and catch-up programs for girls and women under 26 has witnessed a significant decrease in HPV infections. The percentage of 18- to 24-year-old women in the nation who have HPV has decreased from 22.7-1.5% in just ten years [37].

Altogether with the fast action on vaccination, there has been a considerable decline in cervical cancer cases since the National Cervical Screening Program in 1991. Every five years, women and people with cervixes between the ages of 25 and 74 are encouraged by the healthcare provider to undergo a cervical screening test. Women who had received the HPV vaccine participated in cervical screening at a higher rate than women who had not. Participation in 2013-2014 by HPV vaccination status revealed that for women aged 20–24, participation was 46% for HPV–vaccinated women and 33% for unvaccinated women; for women aged 25–29, participation was 57% for HPV–vaccinated women and 44% for unvaccinated women; and for both age groups 20–24 and 25-29, participation in cervical screening increased with an increasing number of vaccine doses received [38]. The National Cervical Screening Program has proven to lower cervical cancer-related disease and fatalities [39].

Tonga

Since 2022, Tonga has started vaccinating children against cervical cancer to girls between 9-14 years of

age. The policy in Tonga has recently been changed to introduce a 1-dose HPV vaccine in girls [40].

America

United States

The U.S. Preventive Services Task Force (USPSTF) -a voluntary, independent group of specialists in evidence-based medicine and disease prevention-recommends screening for cervical cancer in women aged 21 to 29 years with cytology (pap smear) every 3 years, and for women aged 30 to 65, a screening with cytology alone every 3 years, a high-risk human papillomavirus (hrHPV) test every 5 years, or cytology in combination with hrHPV every 5 years [41].

In addition to screening, HPV vaccination has been introduced since 2006. Instead of the original guideline of three doses, the federal Advisory Committee on Immunization Practices (ACIP) now advises 9–14-year-old adolescents to take the HPV vaccine in two doses over the course of six–12 months. Young adults who begin vaccination at ages 15 to 26 should receive three doses spaced out over a six-month period. As a result, 70% of boys and 73% of adolescent girls received at least one dose of the HPV vaccine in 2019 [42].

Latin America

Several countries in the Latin American region with HPV vaccination included in national routine programs have decided to switch to a single-dose schedule, as stated in Table 8 below.

Asia

Japan

The HPV vaccine was briefly withheld from June 2013 onward in Japan. However, in November 2021, specialists concluded that the HPV vaccine should be actively recommended. Presently, girls in the sixth grade of elementary school through the first year of high school are frequently given the HPV vaccine, which prevents HPV infection. Women born between April 2, 1997, and April 1, 2006, or between April 2, 1997, and April 1, 2007, should have their regular HPV vaccination when they reach the recommended age [43].

Japan also provides catch-up for individuals who have not previously received it. From April 2023, women born in 2006 (born between April 2, 2006 and April 1, 2007) will also be eligible for catch-up immunization. The same vaccine is administered in a total of two or three doses at regular intervals. Depending on the age and the

Table 8. Countries in Latin America Switching to the 1-Dose Schedule

No.	Country	Year Intro	Policy Change
1	Bolivia	2017	Switch to 1-dose in routine program
2	Guatemala	2018	Switch to 1-dose in routine program
3	Guyana	2011	Switch to 1-dose in routine program
4	Jamaica	2017	Switch to 1-dose in routine program
5	Mexico	2008	Switch to 1-dose in routine program
6	Peru	2015	Switch to 1-dose in routine program

Source from personal talk/discussion with an expert

vaccine being administered, many vaccination schedules are provided by the government [43].

Bangladesh

Bangladesh adopted the human papillomavirus (HPV) vaccine in 2016 as part of a two-year demonstration study⁴⁵. The bivalent HPV vaccine (Cervarix), administered by the Ministry of Health and Family Welfare of Bangladesh with financial assistance from the Global Alliance for Vaccines and Immunization (GAVI, the Vaccine Alliance). It has been given to girls in fifth grade as well as girls who are not enrolled in school who are between the ages of 10 and 12 living in five chosen areas of Gazipur District, close to the capital city Dhaka. As one of the countries with the highest burden, UNICEF and GAVI, the Vaccine Alliance, are supporting this program. NITAGs have also recommended switching to a 1-dose schedule in Bangladesh in 2023/2024 [44].

India

Although the HPV vaccine was first made available in India in 2008, the National Immunization Program has not yet incorporated it, and there is little information available regarding the country's overall HPV vaccination coverage. The launch of CERVAVAC, India's first locally developed cervical cancer vaccine, was announced by the Indian government in collaboration with the Serum Institute of India on September 1, 2022, promising not only accessibility but also affordability. Similar to Gardasil, it provides defense against four different HPV virus types. However, unfortunately, awareness of the importance of vaccination among women in India is alarmingly low. With the support of NITAG and GAVI, India will be assisted with this vaccination program and have received recommendations to switch to a single-dose schedule starting from this year or the next year [45].

Africa

Cabo Verde

Cabo Verde had introduced a vaccine to prevent cervical cancer associated with the human papillomavirus (HPV) for children and adolescents in 2021 [46]. The vaccine program is fully funded by the Cabo Verdean government through the State Budget and involves partnerships with UNICEF and other organizations [47]. Recently, Cabo Verde decided to switch to single-dose HPV vaccination in 14-year-old girls.

Nigeria

Several African nations, notably Nigeria, are now running immunization experimental programs. In Nigeria, GAVI continues to support vaccination efforts using a variety of vaccines. However, as HPV vaccines are not on the list of vaccines that are offered without charge under the National Immunization Program (NIP) in Nigeria, people currently have to pay for them out of their individual money [48]. In effort to increase coverage and follow the WHO direction, UNICEF and GAVI will procure HPV vaccines in this country and recommend switching to a 1-dose schedule in the upcoming two years [49].

Current Indonesian Technical Guidelines for HPV National Plan on Target and Schedule

The agenda for the elimination of cervical cancer has been attempted by Indonesia step by step. HPV was included in the national vaccination program in 2020, initially started in 2018. Current HPV vaccination technical guidelines available by the Indonesian Ministry of Health highlight the target and schedule for HPV vaccination [50]. This implies that:

Target

a. HPV immunization is part of the “Bulan Imunisasi Anak Nasional” (BIAS) or National Month of Immunization for Children aimed for girls or female adolescents in the 5th and 6th grades of elementary school.

b. The program should reach out not only to those who study at formal schools but also to informal schools.

c. Those who do not study at school can receive HPV immunization through the closest public healthcare facilities.

d. Immunization can also be conducted at any places other than healthcare facilities where those usually gather, e.g., orphanages, informal schools, rumah singgah anak jalanan, and many more.

Schedule

a. The first dose is given to female adolescents in 5th grade or age 11.

b. The second dose is given in 6th grade or age 12 with a 12-month interval (min. 6 months) through BIAS.

However, achieving the WHO cervical cancer elimination targets for 2030 is difficult with the current relatively low coverage. HPV vaccination program coverage among girls in Indonesia in 2020 is 8% for the first dose and 7% for the final dose of the target population (among ages 9-14). Fewer than 1 in 10 girls in the primary target cohort in 2020 received their final HPV vaccination dose¹¹. Therefore, to achieve the targets, several revisions to technical guidelines for the HPV vaccination program in Indonesia are urgently needed.

Discussion

Proposed Update to HPV Technical Guideline and/or HPV National Roadmap Plan

The changes in technical guidelines need to highlight the schedule and dose of HPV vaccination based on its effectiveness both clinically and economically. The recommendations for Indonesian technical guidelines for the national HPV vaccination programme include the following:

Schedule

HPV vaccination is aimed at the primarily targeted group of 5th-grade female adolescents or those aged 11.

Dosage

The HPV vaccine is primarily given 1 dose once in a lifetime through BIAS.

Evaluation of Whether Boosters Are Necessary

The evaluation of whether HPV vaccine boosters are

required if the immunogenicity of vaccines given to the population decreases over time.

Eligible Age for Immunization – case per case basis

The age limitation of 11-15 years old eligible for HPV immunization at school, if there is any case where the 5th grade students are older than 11 years old e.g., students in Papua and students of special needs school (Sekolah Luar Biasa).

Considering the number of 7 to 15-year-old female adolescents of 19.387.318 and 16 to 64-year-old productive females of 96.336.779 in 2025 (data from the Indonesian Ministry of Health), modeling in a high burden setting is relevant to Indonesia. The adoption of HPV-ADVISE modeling by Marc Brisson of implementing a single-dose vaccine is proven to be a better move than postponing it to prevent more health losses. Considering the low number of cervical cancer-related screenings, the modeling is even better, as Brisson does not consider the scale-up and ongoing screening programme; however, it is able to provide better health impacts [32].

The one-dose schedule of HPV vaccination will be effective in reducing the required budget; hence, increasing the coverage of vaccination by reaching out to more females, particularly adolescents both in schools and outside schools. By considering the cost-offsets from future cancers avoided, routine one-dose HPV vaccination of 9-year-old girls was less expensive than not vaccinating them. One-dose HPV vaccination with equal coverage (70%) prevented 15-16% of cervical cancer cases forty years after routine vaccination began, compared to 21% with two-dose vaccination [51]. In conclusion, a one-dose HPV vaccination could be more affordable than two doses if protection is long-lasting and better coverage can be attained than with a two-dose vaccination.

Considering the beneficial coverage, a single dose of HPV vaccination is also a better choice for efficient vaccination programs. This is because no follow-up vaccination is in a later year. Therefore, the possibilities of technical issues caused by students who move to other schools, and change home addresses can be prevented. These may seem simple but important because such issues will probably affect the accuracy of the database and also become obstacles for final reporting.

This is also to prevent worsening social issues such as black campaigns. Under normal circumstances, some parents choose not to vaccinate their children for various considerations and reasons, most likely fear of substances and black campaign issues. Most parents get bombarded with stories about the harm of vaccines; parents who claimed their children were fine, but no more fine ones once after getting vaccinated [52]. This happened for most of the sake of society in Indonesia once the vaccination program was publicized. Therefore, one dose of HPV vaccine shots could reduce the trust issues resulting from the black campaign, as there will be no follow-up for second vaccine shots.

In conclusions, numerous studies have demonstrated that the single-dose HPV vaccine offers comparable protection to 2 doses. Many nations, ranging from high-income to low- and middle-income countries, have

implemented single-dose vaccination programs. To meet the goal of eliminating cancer by 2030, proposed improvements to vaccination programs are advised in light of other nations' experiences and Indonesia's large population by implementing single-dose HPV vaccine in the near future.

Future Directions

Following the recent confirmation of single-dose HPV vaccine efficacy and effectiveness, further research is needed to determine whether catch-up and booster vaccinations are required.

Author Contribution Statement

Conceptualization: DS, PR, L, GFG. Formal analysis: DS, PR. Investigation: DS, PR, L, GFG. Methodology: DS, PR, L, GFG. Resources: DS, PR. Manuscript writing and revision: DS, PR.

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Conflict of Interest

Clinton Health Access Initiative (CHAI) does not interfere the professional judgment or action regarding the study processes and outcomes.

References

1. Globocan international agency for research on cancer. Int agency res cancer. Published online 2020.
2. Globocan asia. Asia : Globocan 2020 summary statistic. Int agency res cancer. 2021;136:2. Available from: <https://gco.iarc.fr/today/data/factsheets/populations/935-asia-fact-sheets.Pdf>.
3. Globocan. Cancer in indonesia. Int agency res cancer. Published online; 2020. <https://doi:10.1001/jama.247.22.3087>.
4. Wahidin M, Febrianti R, Susanty F. Burden of cervical cancer in indonesia: Findings from the global burden of disease study 1990–2017. 2020.
5. Park E, Kim JY, Choi S, Kim DS, Oh YL. Carcinogenic risk of human papillomavirus (hpv) genotypes and potential effects of hpv vaccines in korea. *Sci Rep*. 2019;9(1):12556. <https://doi.org/10.1038/s41598-019-49060-w>.
6. Garland SM, Brotherton JML, Moscicki AB, Kaufmann AM, Stanley M, Bhatla N, et al. Hpv vaccination of immunocompromised hosts. *Papillomavirus Res*. 2017;4:35-8. <https://doi.org/10.1016/j.pvr.2017.06.002>.
7. Small W, Jr., Bacon MA, Bajaj A, Chuang LT, Fisher BJ, Harkenrider MM, et al. Cervical cancer: A global health crisis. *Cancer*. 2017;123(13):2404-12. <https://doi.org/10.1002/cncr.30667>.
8. Smulian EA, Mitchell KR, Stokley S. Interventions to increase hpv vaccination coverage: A systematic review. *Hum Vaccin Immunother*. 2016;12(6):1566-88. <https://doi.org/10.1080/2>

- 1645515.2015.1125055.
9. Saraiya M, Unger ER, Thompson TD, Lynch CF, Hernandez BY, Lyu CW, et al. Us assessment of hpv types in cancers: Implications for current and 9-valent hpv vaccines. *J Natl Cancer Inst.* 2015;107(6):djv086. <https://doi.org/10.1093/jnci/djv086>.
 10. Kreimer AR, Cernuschi T, Rees H, Brotherton JML, Porras C, Schiller J. Public health opportunities resulting from sufficient hpv vaccine supply and a single-dose vaccination schedule. *J Natl Cancer Inst.* 2023;115(3):246-9. <https://doi.org/10.1093/jnci/djac189>.
 11. World health organization. Who. Published 2022. Available from: <https://www.who.int/news/item/20-12-2022-who-updates-recommendations-on-hpv-vaccination-schedule#:~:Text=who now recommends%3a,women older than 21 years>.
 12. Kamolratanakul S, Pitisuttithum P. Human papillomavirus vaccine efficacy and effectiveness against cancer. *Vaccines (Basel)*. 2021;9(12):1-21. <https://doi.org/10.3390/vaccines9121413>.
 13. Julius JM, Ramondeta L, Tipton KA, Lal LS, Schneider K, Smith JA. Clinical perspectives on the role of the human papillomavirus vaccine in the prevention of cancer. *Pharmacotherapy*. 2011;31(3):280-97. <https://doi.org/10.1592/phco.31.3.280>.
 14. Kash N, Lee MA, Kollipara R, Downing C, Guidry J, Tying SK. Safety and efficacy data on vaccines and immunization to human papillomavirus. *J Clin Med.* 2015;4(4):614-33. <https://doi.org/10.3390/jcm4040614>.
 15. Cdc. Center for disease control and prevention. Published online; 2021. Available from: <https://www.Cdc.Gov/vaccines/vpd/hpv/public/index.html>.
 16. Soliman M, Oredein O, Dass CR. Update on safety and efficacy of hpv vaccines: Focus on gardasil. *Int J Mol Cell Med.* 2021;10(2):101-13. <https://doi.org/10.22088/ijmcm.Bums.10.2.101>.
 17. Paavonen J, Naud P, Salmerón J, Wheeler CM, Chow SN, Apter D, et al. Efficacy of human papillomavirus (hpv)-16/18 as04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic hpv types (patricia): Final analysis of a double-blind, randomised study in young women. *Lancet.* 2009;374(9686):301-14. [https://doi.org/10.1016/s0140-6736\(09\)61248-4](https://doi.org/10.1016/s0140-6736(09)61248-4).
 18. David MP, Van Herck K, Hardt K, Tibaldi F, Dubin G, Descamps D, et al. Long-term persistence of anti-hpv-16 and -18 antibodies induced by vaccination with the as04-adjuvanted cervical cancer vaccine: Modeling of sustained antibody responses. *Gynecol Oncol.* 2009;115(3 Suppl):S1-6. <https://doi.org/10.1016/j.ygyno.2009.01.011>.
 19. Esposito S, Birlutiu V, Jarcuska P, Perino A, Man SC, Vladareanu R, et al. Immunogenicity and safety of human papillomavirus-16/18 as04-adjuvanted vaccine administered according to an alternative dosing schedule compared with the standard dosing schedule in healthy women aged 15 to 25 years: Results from a randomized study. *Pediatr Infect Dis J.* 2011;30(3):e49-55. <https://doi.org/10.1097/INF.0b013e318206c26e>.
 20. Lee VJ, Tay SK, Teoh YL, Tok MY. Cost-effectiveness of different human papillomavirus vaccines in singapore. *BMC Public Health.* 2011;11:203. <https://doi.org/10.1186/1471-2458-11-203>.
 21. Kudo R, Yamaguchi M, Sekine M, Adachi S, Ueda Y, Miyagi E, et al. Bivalent human papillomavirus vaccine effectiveness in a japanese population: High vaccine-type-specific effectiveness and evidence of cross-protection. *J Infect Dis.* 2019;219(3):382-90. <https://doi.org/10.1093/infdis/jiy516>.
 22. Rebolj M, Pesola F, Mathews C, Meshner D, Soldan K, Kitchener H. The impact of catch-up bivalent human papillomavirus vaccination on cervical screening outcomes: An observational study from the english hpv primary screening pilot. *Br J Cancer.* 2022;127(2):278-87. <https://doi.org/10.1038/s41416-022-01791-w>.
 23. Gilca V, Sauvageau C, Boulianne N, De Serres G, Crajden M, Ouakki M, et al. The effect of a booster dose of quadrivalent or bivalent hpv vaccine when administered to girls previously vaccinated with two doses of quadrivalent hpv vaccine. *Hum Vaccin Immunother.* 2015;11(3):732-8. <https://doi.org/10.1080/21645515.2015.1011570>.
 24. Reiter PL, Gilkey MB, Brewer NT. Hpv vaccination among adolescent males: Results from the national immunization survey-teen. *Vaccine.* 2013;31(26):2816-21. <https://doi.org/10.1016/j.vaccine.2013.04.010>.
 25. Steinau M, Unger ER, Hernandez BY, Goodman MT, Copeland G, Hopenhayn C, et al. Human papillomavirus prevalence in invasive anal cancers in the united states before vaccine introduction. *J Low Genit Tract Dis.* 2013;17(4):397-403. <https://doi.org/10.1097/LGT.0b013e31827ed372>.
 26. Amarencu p, bogousslavsky j, callahan 3rd a, goldstein lb, hennerici m, rudolph ae, sillesen h, simunovic l, szarek m, welch km. Justin a zivin sp by ar in cl (sparcl) i. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N engl j med.* 2011;365:687-96.
 27. Setiawan D, Andrijono, Hadinegoro SR, Meyta H, Sitohang RV, Tandy G, et al. Cervical cancer prevention in indonesia: An updated clinical impact, cost-effectiveness and budget impact analysis. *PLoS One.* 2020;15(3):e0230359. <https://doi.org/10.1371/journal.pone.0230359>.
 28. World health organization. One-dose human papillomavirus (hpv) vaccine offers solid protection against cervical cancer. Geneva: World health organization. 2022 apr 30.
 29. Jcvi. Jcvi statement on a one-dose schedule for hpv for the routine hpv immunization programme. Available from: <https://www.Gov.Uk/government/publications/single-dose-of-hpv-vaccine-jcvi-concluding-advice/jcvi-statement-on-a-one-dose-schedule-for-the-routine-hpv-immunisation-programme>.
 30. Daniels V, Saxena K, Patterson-Lomba O, Gomez-Lievano A, Saah A, Luxembourg A, et al. Modeling the health and economic implications of adopting a 1-dose 9-valent human papillomavirus vaccination regimen in a high-income country setting: An analysis in the united kingdom. *Vaccine.* 2022;40(14):2173-83. <https://doi.org/10.1016/j.vaccine.2022.02.067>.
 31. Burger E, Baussano I, Kim JJ, Laprise JF, Berkhof J, Schiller JT, et al. Recent economic evaluation of 1-dose hpv vaccination uses unsupported assumptions. *Vaccine.* 2023;41(16):2648-9. <https://doi.org/10.1016/j.vaccine.2022.07.022>.
 32. Burger EA, Laprise JF, Sy S, Regan MC, Prem K, Jit M, et al. Now or later: Health impacts of delaying single-dose hpv vaccine implementation in a high-burden setting. *Int J Cancer.* 2022;151(10):1804-9. <https://doi.org/10.1002/ijc.34054>.
 33. Cervical screening program in the uk. The first invitation is sent,who has not been invited. Available from: <https://www.Gov.Uk/guidance/cervical-screening-programme-overview#:~:Text>.
 34. Human papillomavirus (hpv) vaccine. Hpv vaccination program in schools in ireland. Available from: <https://www.Hse.Ie/eng/health/immunisation/pubinfo/schoolprog/hpv/hpv-vaccination-programme/hpv-vaccination-programme.html>.
 35. Cervical check program in ireland; september 2017-march 2020. Available from: <https://assets.Hse.Ie/media/>

- documents/cervicalcheck_programme_report_2017-2020.Pdf.
36. Albania human papillomavirus and related cancers. Available from: https://hvpcentre.Net/statistics/reports/alb_fs.Pdf.
 37. Australia change to single dose hpv vaccine. Published 2023. Available from: <https://www.Health.Gov.Au/ministers/the-hon-mark-butler-mp/media/change-to-single-dose-hpv-vaccine>.
 38. Australia g of. National screening program in australia; 2019. Available from: <https://www.Aihw.Gov.Au/reports/cancer-screening/analysis-of-cervical-cancer-and-abnormality/summary>.
 39. Cancer institute nsw. About the national cervical screening program. Available from: <https://www.Cancer.Nsw.Gov.Au/prevention-and-screening/screening-and-early-detection/cervical-screening/about-the-national-cervical-screening-program>.
 40. Unicef pacific islands health. Available from: <https://www.Unicef.Org/pacificislands/media/3741/file/health-programme-brief.Pdf>.
 41. Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, et al. Screening for cervical cancer: Us preventive services task force recommendation statement. *Jama*. 2018;320(7):674-86. <https://doi.org/10.1001/jama.2018.10897>.
 42. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years — united states; 2019. Published 2019. Available from: <https://www.Cdc.Gov/mmwr/volumes/69/wr/mm6933a1.Htm>.
 43. Human papilloma virus infection and hpv vaccine in japan. Available from: <https://www.Mhlw.Go.Jp/bunya/kenkou/kekaku-kansenshou28/index.Html>.
 44. Hpv vaccine introduced in bangladesh. Available from: <https://www.Who.Int/bangladesh/news/detail/18-05-2016-hpv-vaccine-introduced-in-bangladesh>.
 45. Hpv vaccination and the quest to solve india's cervical cancer problem. Available from: <https://www.Thinkglobalhealth.Org/article/hpv-vaccination-and-quest-solve-indias-cervical-cancer-problem>.
 46. Ico. Human papillomavirus and related diseases report. 2016;(october). Available from: Www.Hpvcentre.Com.
 47. Girls today, women tomorrow: An hpv vaccine sets a new course for women and girls in cabo verde. Available from: [https://unsdg.Un.Org/latest/stories/girls-today-women-tomorrow-hpv-vaccine-sets-new-course-women-and-girls-cabo-verde#:~:Text=cabo verde has recently introduced,vaccinated during this first phase](https://unsdg.Un.Org/latest/stories/girls-today-women-tomorrow-hpv-vaccine-sets-new-course-women-and-girls-cabo-verde#:~:Text=cabo%20verde%20has%20recently%20introduced,vaccinated%20during%20this%20first%20phase).
 48. Akinsolu ft, abodunrin o, adewole ie, olagunju m, gambari ao, raji do, et al. Willingness to pay for hpv vaccine among women living with hiv in nigeria. *Vaccines*. 2023;11(5):928.
 49. Unicef. Closing the gap: Unicef bolsters country efforts to increase hpv vaccination [internet]; 2023. Available from: <https://www.Unicef.Org/supply/stories/closing-gap-unicef-bolsters-country-efforts-increase-hpv-vaccination>.
 50. Kesehatan k. Hindal teknis perakanasi bulan imunisasi anak sekolah (bias). Published online 2018.
 51. Burger EA, Campos NG, Sy S, Regan C, Kim JJ. Health and economic benefits of single-dose hpv vaccination in a gavi-eligible country. *Vaccine*. 2018;36(32 Pt A):4823-9. <https://doi.org/10.1016/j.vaccine.2018.04.061>.
 52. Nurlaela n, karlinah s, setianti y, susilawati s. Parent trust on the immunization program: Media coverage over counterfeite vaccine in indonesia. In3rd international conference on transformation in communications 2017 (icotic 2017) 2017 nov (pp. 49-61). Atlantis press.



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