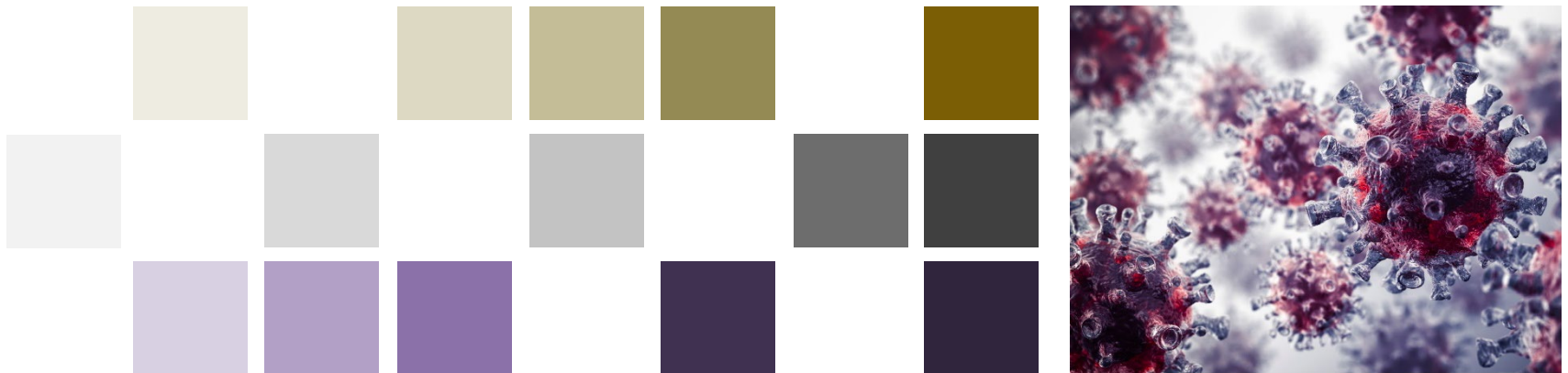


Economic Burden of HPV-related Cancers

Final report

17 July 2024



In a nutshell

- Each year, around 600 New Zealanders are diagnosed with a cancer that can be caused by HPV infection.
- **The cost of cancers associated with HPV are high and avoidable: >\$105 million in 2019–2022.**
 - This measure is very conservative—it includes hospital and cancer pharmaceutical costs incurred *after* a diagnosis and registration of cancer. Future costs may include very significant pharmaceutical costs.
 - Further costs of pre-cancer detection and treatment could also be avoided. For instance, colposcopy and colposcopy directed treatments of **\$49 million** were incurred during 2019-2022.
- Some of these cancers have been increasing—the incidence of oropharyngeal cancer in New Zealand increased by around 5% per year over 15 years.
- HPV vaccination is recognised internationally as being cost-effective at preventing HPV-related cancers (especially for females) but New Zealand has poor vaccination rates and unacceptable inequities.
 - The World Health Organization goal to eliminate cervical cancer is that by 2030, 90% of girls worldwide will be fully vaccinated by age 15.
 - New Zealand’s own national targets are low by international standards, yet the country has continually failed to meet these lower targets. Vaccination rates dropped even further during and post-Covid.
 - In comparison, other countries are achieving herd immunity with HPV vaccination programmes and are able to wind down cervical screening programmes and avoid other health costs.
- Low HPV vaccination rates represent a missed opportunity to reduce health system costs, as well as costs and burden of disease for individuals and whānau.

Context

Research focus: The Head and Neck Cancer Foundation Aotearoa asked Sapere to quantify the economic burden of HPV-related cancers in Aotearoa New Zealand. Here, economic burden refers to the direct costs associated with HPV-related cancers

This slide-deck provides background information about HPV-related cancer incidence and prevention programmes in New Zealand, evidence on the cost-effectiveness of HPV-vaccination programmes and the findings from our cost-of-illness estimation showing the economic burden of HPV-related cancer to the health system in Aotearoa New Zealand.

HPV-related cancers covered in this report include the following six cancers, which were identified in discussion with the steering group:

- Oropharynx
- Anus and anal canal
- Cervix uteri
- Vulva
- Vagina
- Penis

A note on language

In this report we use the terms female and male referring to sex, which is required to be reported to the NZ Cancer Registry. A person's gender may or may not align with their sex assigned at birth.

<https://www.publicservice.govt.nz/guidance/glossary/diversity-and-inclusion>

Chapter 1: Burden of illness and prevention



- HPV-related cancer incidence
- Prevention: screening and vaccination
- Cost-effectiveness of HPV vaccine

Chapter 2: Calculating the cost of HPV illness



- Methodology
- Cost of HPV-related cancer
- Discussion

Chapter 1: Burden of illness and prevention

HPV-related cancer incidence

Previously published data for comparison purposes



Age-standardised* incidence rates per 100,000 population in 2021		
	New Zealand	High-Income Countries
Cervical Cancer		
Male	.	.
Female	7.1	8.4
Anal Cancer		
Male	1.14	0.74
Female	1.84	1.24
Vulva Cancer		
Male	.	.
Female	2.65	1.56
Vaginal Cancer		
Male	.	.
Female	0.73	0.33
Penile Cancer		
Male	0.89	0.66
Female	.	.
Oropharyngeal Cancer		
Male	3.08	3.28
Female	0.77	0.8

Note: Age-standardised rates have been estimated using the WHO-approach. Using the World population as the reference; Source:

<https://hpvcentre.net/statistics/reports/NZL.pdf?t=1712784858751>

<https://hpvcentre.net/statistics/reports/XWX.pdf?t=1712784907478>

Data are derived from the systematic review and meta-analysis of published literature and official reports by the WHO, United Nations, The World Bank, IARC's *Globocan* and *Cancer Incidence in Five Continents*

- Compared to high-income countries, **NZ has higher incidence rates for anal, vulva, vaginal and penile cancer**; rates are lower for cervical cancer.
- The greatest burden of HPV-related cancer in NZ is cervical cancer, causing around 50 deaths annually. Cervical cancer is the 4th most frequent cancer in women 15-44 years of age.
- Two preventative public health strategies exist in New Zealand that could reduce the burden of HPV related cancer: cervical screening and HPV vaccination.

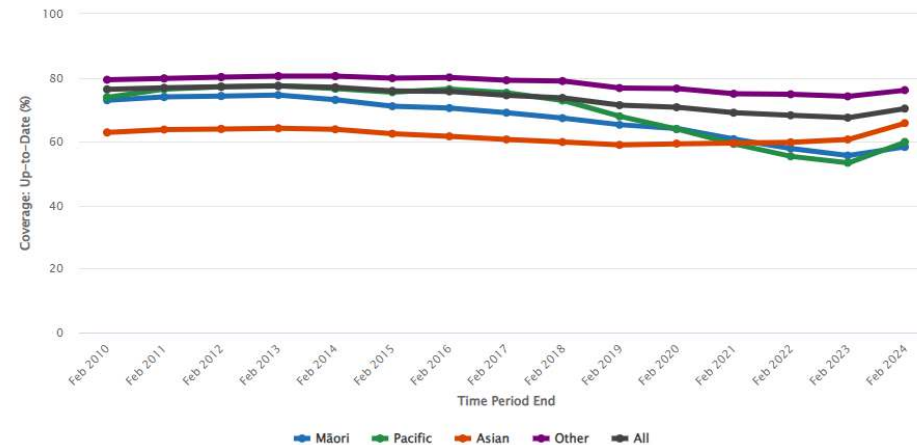
Prevention: cervical cancer screening

- The National Cervical Screening Programme (NCSP) has been in place since 1990 and aims to detect and treat cervical pre-cancerous changes before they develop into cervical cancer.
- Cervical screening tests are currently offered every three years to individuals aged 25–69 years who have a cervix (including trans and non-binary people) and have ever been sexually active.
- The programme is not fully publicly funded so user charges apply, but since September 2023 is free for those over 30 who have never had a screening test, have not had a test for more than five years, are Māori or Pacific, or have a Community Services Card.
- Since the NCSP began, the incidence of cervical cancer has **decreased by about 50%** and **mortality from cervical cancer by about 60%**. The reductions are larger for Māori, although inequities in incidence and mortality persist (Ministry of Health 2020). These reductions are also a reflection of other trends over this time, such as reduced smoking and improved cervical cancer treatment.
- The coverage target is to have 80% of eligible people screened within the previous three years. This target has not been achieved and coverage has been slowly declining since 2012.

Source: <https://www.nsu.govt.nz/health-professionals/national-cervical-screening-programme-hpv-primary-screening>



Up-to-date cervical cancer screening in females 25-65 years from 2010-2024 in New Zealand, by ethnicity



Source: https://tewhatuora.shinyapps.io/nsu-ncsp-coverage/_w_d0f5cd6b/#shiny-tab-introduction

- The graph shows the percentage of women screened in the last three years.
- Screening rates had been **declining among Māori and Pacific**, a trend that started prior to the advent of COVID-19 and continued afterwards.
- In late 2023, a new national cervical screening test was introduced, that should be more accessible and provide more accurate results. There has been an uptick in screening coverage as at February 2024.

Prevention: HPV vaccination

- HPV vaccination protects people from HPV infection and the risk of developing cervical cancer and a range of other HPV-related cancers and other diseases later in life; it is most effective in young people.
- The World Health Organization goal to eliminate cervical cancer is that by 2030, **90% of girls worldwide will be fully vaccinated by age 15**. The vaccination of boys adds to herd immunity from HPV.
- HPV vaccination began in New Zealand in 2008 and was initially only funded for females. Full dose vaccination rates achieved in the eligible population were 55-60% in the period up to 2018.
- From January 2017, HPV vaccination became free for all young people aged nine through 26, including non-residents under the age of 18. It is available through participating schools, family doctors, local health centres and some Family Planning clinics and pharmacies.
- Prior to COVID, around two-thirds of the programme population were fully vaccinated but final dose coverage dropped post-COVID.



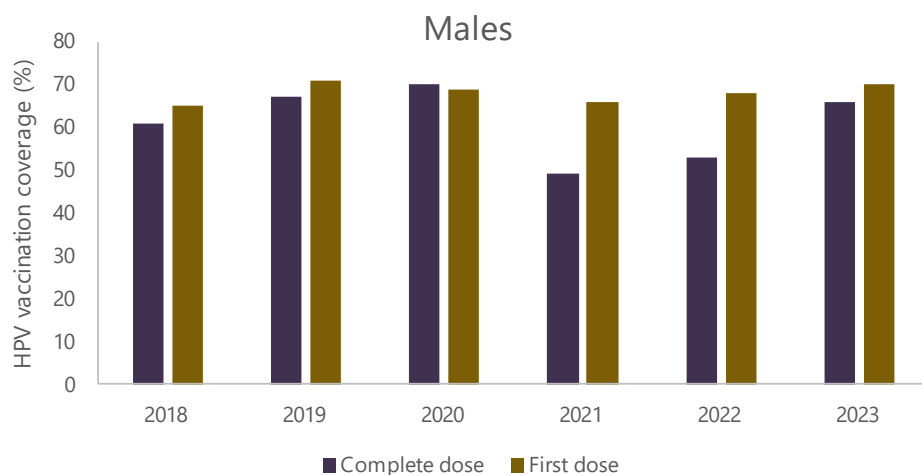
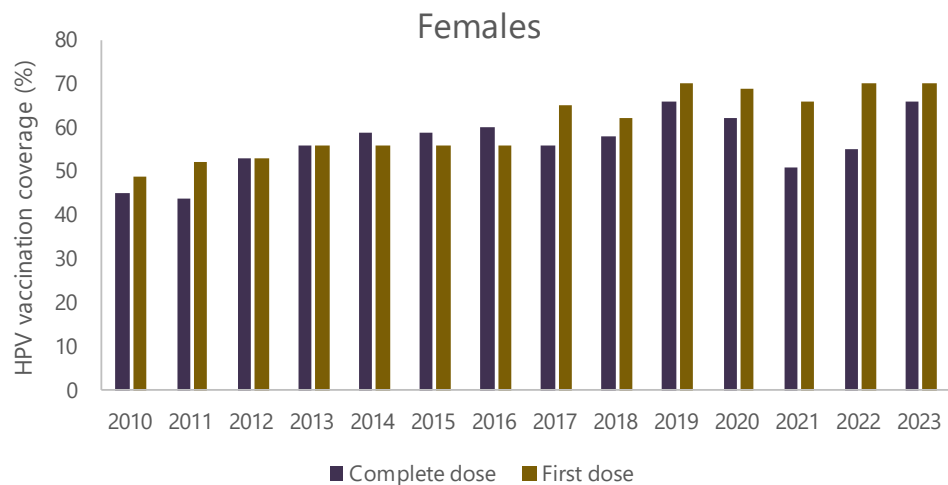
In a UK study of **the impact of HPV vaccination rates** for females since 2008, the **prevalence of HPV 16/18** in sexually active 16 to 24-year-old females had **reduced from 15%** prior to the vaccination programme **to under 1%** by 2020. The UK had achieved full course vaccination rates per year averaging 83% (range 76-87%) in its first 10 years (Checchi et al., 2023).

The New Zealand vaccination target was to achieve 75% of all 12-year-old females by December 2017—**significantly lower than the WHO target** of 90% of girls fully vaccinated by age 15.

The New Zealand target has still not been met, and coverage declined in the years post-COVID.

Source: <https://www.health.govt.nz/system/files/documents/publications/hpv-revitalisation-oct15.pdf>

Prevention: WHO estimated HPV vaccination coverage for the New Zealand target population



- In 2023, female **vaccination NZ programme coverage** was estimated to be **66% for the complete dose, and 70% for one dose.**



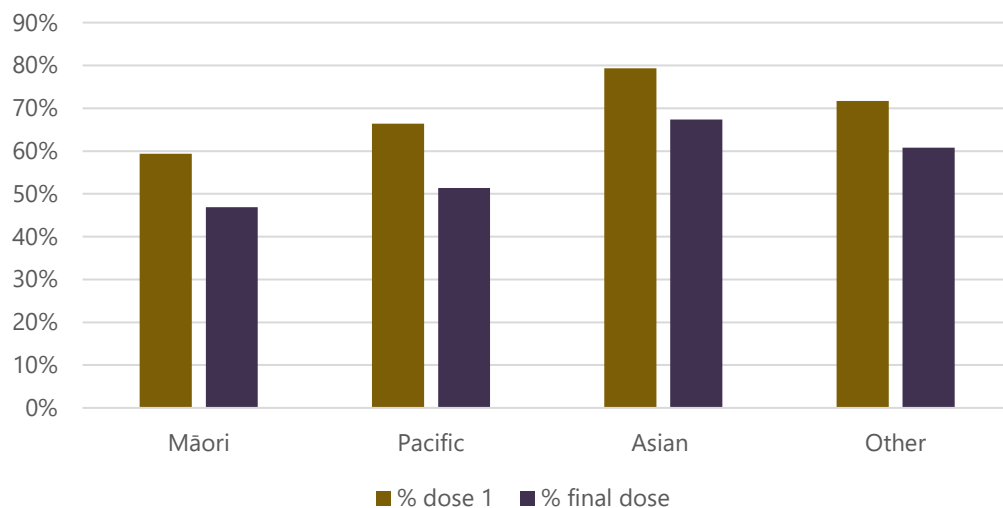
- In 2023, male **vaccination NZ programme coverage** was estimated to be **66% for the complete dose, and 70% for one dose.**

Note the WHO estimates for complete dose are higher than locally reported coverage for birth cohorts in NZ

Prevention: Locally reported HPV vaccination coverage in New Zealand by ethnicity



Vaccination coverage of 2010 birth-cohort to 31 December 2023



Source: own calculations based on data from: <https://www.tewhatauora.govt.nz/for-the-health-sector/vaccine-information/hpv-immunisation-programme/>

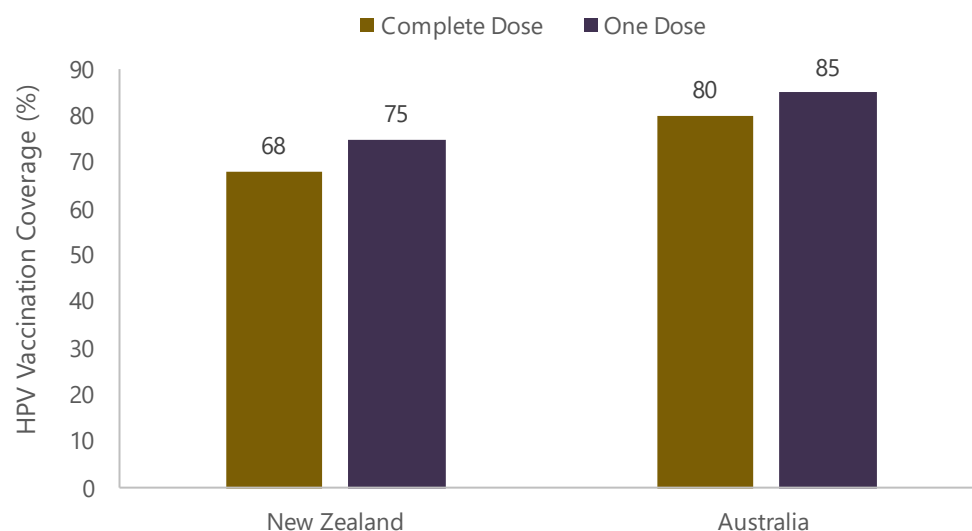
Note: 'Other' includes all ethnicities except for Māori, Pacific and Asian ethnic groups

- Taking a snapshot from recent data on vaccination coverage, it is evident that:
 - (1) **observed under-vaccination is persistent two years post COVID-19**
 - (2) **there are stark inequities between ethnic groups, demonstrated by final dose vaccination rates of only 47% and 51% for Māori and Pacific, compared with 67% and 61% for Asian and Other groups.**
- **Vaccination coverage is lowest for Māori and Pacific, which links to observed lowest screening uptake in these population groups.**

Prevention: WHO estimated female HPV vaccination coverage by age 15 – New Zealand vs Australia, 2022



WHO target by 15 years = 90%



Source: WHO immunisation data coverage estimates from:

[https://immunizationdata.who.int/global/wiise-detail-page/human-papillomavirus-\(hpv\)-vaccination-coverage](https://immunizationdata.who.int/global/wiise-detail-page/human-papillomavirus-(hpv)-vaccination-coverage)

- New Zealand is falling behind on HPV vaccination in comparison Australia
- We can see this by comparing rates among females by age 15, between New Zealand and Australia
- New Zealand's **one dose rate of 75% was lower than Australia (85%)**
- New Zealand's **complete dose rate of 68% was lower than Australia (80%)**
- Comparing reported full **female target population numbers** for the **final HPV dose**, the **gap is even wider**, with 80.27% in Australia compared to 55.16% in New Zealand.

Evidence: Cost-effectiveness of HPV vaccine



Summary of studies on the cost-effectiveness of HPV vaccinations

Study	Country	Population vaccinated	Cost-effectiveness in ICERs (USD)
Females-only			
Sanders and Taira (2003)	United States	12-year-olds	\$14,583 per QALY
Elbasha et al. (2007)	United States	12-year-olds	\$2,964 per QALY
Marra et al. (2009)	Multiple	Not stated	\$23,000 to \$31,000 per QALY
Seto et al. (2012)	Multiple	Not stated	Cost effective compared to cervical cancer screening
Blakely et al. (2014)	New Zealand	12-year-olds	\$9,700 per QALY
Male and female			
Taira et al. (2003)	United States	12-year-olds	\$442,039 per QALY
Elbasha et al. (2007)	United States	12-year-olds	\$31,308 per QALY
Seto et al. (2012)	Multiple	Not stated	Generally exceeds \$50,000 per QALY
Unknown/both			
Wilson et al. (2020)	United States	Not stated	\$79,022 per LYS
Rosettie et al. (2021)	New Zealand	Female-only and male and	\$11,100 per DALY
	195 countries	female	\$4,217 per DALY

Units are given in quality adjusted life years (QALY) gained, life years saved (LYS) or disability adjusted life years (DALY) averted.

- The incremental cost ratios (ICERs) for female-only vaccination programmes are stated relative to either current screening programmes or no vaccination.
- The ICERs of male and female programmes are reported relative to female-only programmes (i.e. the marginal cost per measure).
- Caution is required when comparing the cost-effectiveness figures as the results vary with methodology, health system costs, assumptions about vaccine characteristics, and data credibility. They have also not been adjusted for price changes over time.
- More detail is provided in the Appendix.

Summary

There are six cancers that can be caused by HPV. Oropharyngeal cancer has the highest number and cervical cancer has the highest burden of HPV-related cancers.

These cancers are also some of the most preventable, with two prevention measures used in New Zealand.

The data shows a long history of missed vaccination targets in New Zealand with inequitable coverage, and drops in vaccination and screening post-COVID, particularly exposing Māori and Pacific to greater risk.

Studies demonstrate that vaccination of females is cost-effective; we anticipate greater costs if coverage of prevention does not improve.

Improving HPV vaccination coverage is thus crucial to keep costs to a minimum and to address equity issues.

We therefore need a cost estimation to identify possible cost if the current situation does not improve. The next chapter will address this.

Chapter 2: Calculating the cost of HPV illness

Methodology: Prevalence cost-of-illness approach

Prevalence

Estimates the total cost of a disease per year.

Available data lends itself to this approach (limited time-frame of data available).

Incidence

Estimates the lifetime costs of a disease for a patient.

Would require more data than available to undertake fully empirically – would likely need to take a modelling approach that combines utilisation data, existing literature and clinical opinion.

Incidence of HPV-related cancer in the last five years

HPV-associated cancer cohort

- All patients with an HPV-related cancer registered between July 2017 and June 2022. Data from the Cancer Registry.
- Cohort is only counted if they have received treatment in a year.

Comparator cohort

- Total population estimate excluding the HPV-associated cancer cohort.

Aligning cohorts

Grouped and matched cohort with comparator group by combination of demographics:

- Sex
- Prioritised level 1 ethnicity (Māori, Pacific, Asian, Other)
- NZDep18
- 5-year age-band (10-14 – 85+).

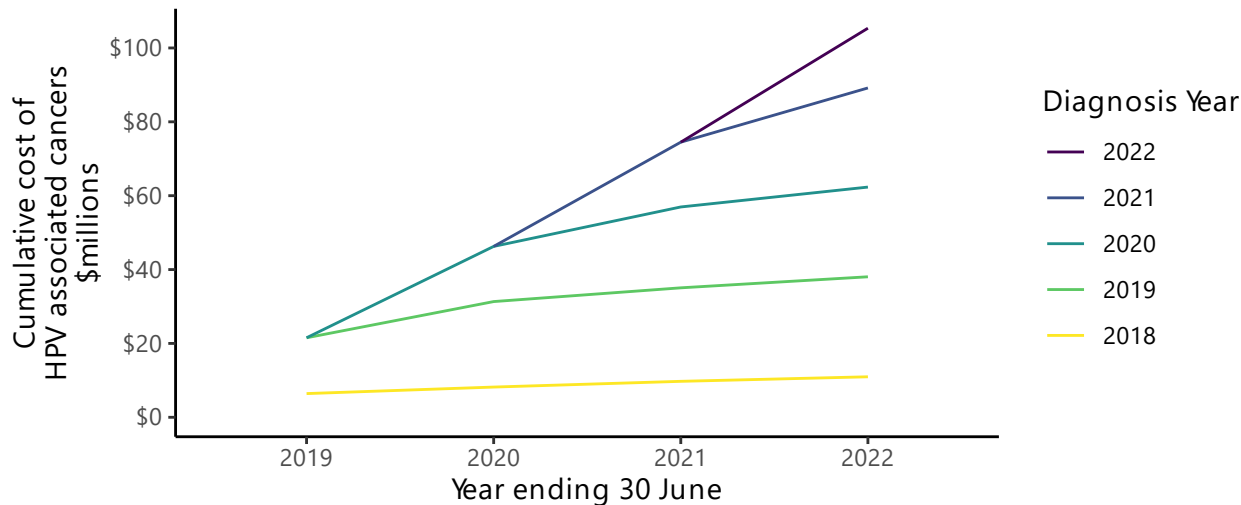
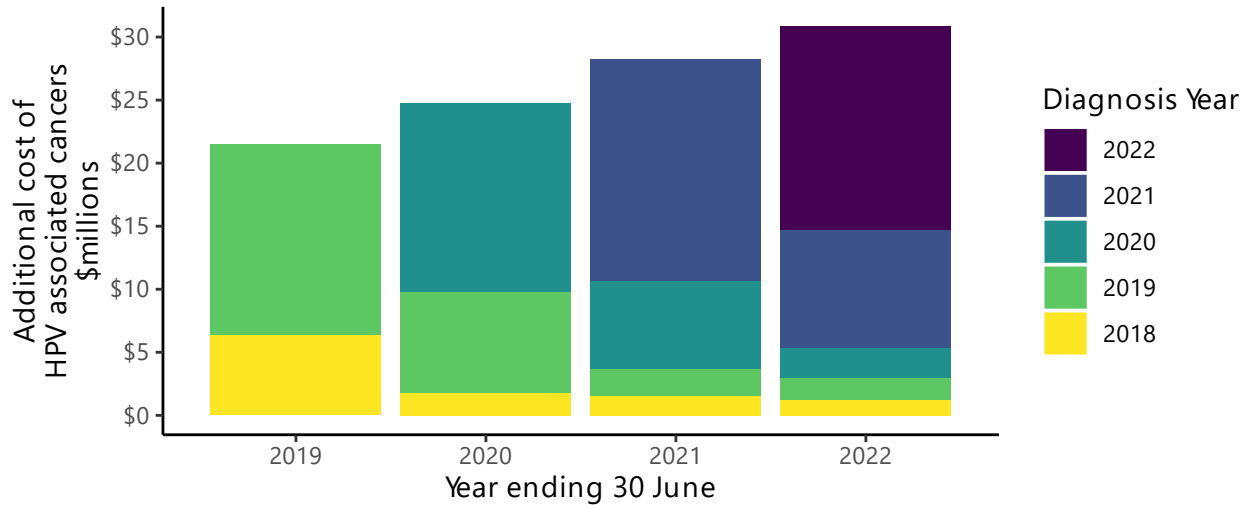
	ICD coding
Cervix	C53
Vulva	C51
Vagina	C52
Anus	C21
Penis	C60
Oropharynx	C01.9, C02.4, C02.8, C05.1, C05.2, C05.9, C09.0, C09.1, C09.8, C09.9, C10.0, C10.2, C10.8, C10.9, C14.0, C14.2, and C14.8
Excluding	9590–9729, 9827 (lymphoma), 8800–8991 (sarcoma), and 8720–8790 (melanoma)

Incidence	Year ending 30 June					Total
	2018	2019	2020	2021	2022	
Anus and anal canal	65	89	80	104	78	416
Cervix uteri	165	184	183	185	152	869
Oropharynx*	234	248	224	255	247	1,208
Penis	21	20	22	24	25	112
Vagina	13	20	19	9	14	75
Vulva	61	49	59	45	67	281
Total	559	610	587	622	583	2,961

Source <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4838063/>

*Head and neck multidisciplinary meeting teams in NZ report a higher number of oropharyngeal cancers than those identified in the NZ Cancer Registry using the ICD code definition published in literature.

Cost of HPV-related cancer



Data sourced from National Collections:

- Outpatient, sourced from the National Non-Admitted Patient Collection (NNPAC).
- Inpatient, sourced from the National Minimum Dataset (NMDS).
- Hospital-delivered pharmaceutical cancer treatments (PCTs), sourced from the Pharmaceutical Collection.

Key takeaways:

- Majority of cost occurs in the year of diagnosis (some additional cost in the following year, likely due to diagnosis late in the year).
- Costs, relative to diagnosis year are stable over time.

Cost of HPV-related cancer: by ethnicity and deprivation level (\$ millions)

Ethnicity	Female	Male	Total
Māori	\$8.3	\$6.0	\$14.2
Pacific	\$0.8	\$0.6	\$1.4
Asian	\$0.4	\$0.2	\$0.6
Other	\$46.1	\$43.1	\$89.1
Total	\$55.5	\$49.9	\$105.3

NZ Dep 18	Female	Male	Total
1	\$3.5	\$4.8	\$8.3
2	\$5.8	\$5.3	\$11.1
3	\$4.7	\$6.5	\$11.3
4	\$5.1	\$5.1	\$10.2
5	\$5.0	\$4.1	\$9.1
6	\$4.9	\$3.9	\$8.8
7	\$5.4	\$5.3	\$10.7
8	\$8.0	\$5.8	\$13.8
9	\$6.8	\$5.1	\$11.9
10	\$6.3	\$3.9	\$10.3
Total	\$55.5	\$49.9	\$105.3



Key takeaways:

- Higher additional costs for females (in aggregate).
- However, female:male cost ratio is lower than prevalence ratio.
- Cost by ethnicity is roughly aligned with prevalence.
- Relative to population, much higher prevalence for “Other” ethnicities.
- Significantly lower rates for Pacific and Asian ethnicities.
- Slightly higher costs with higher deprivation.
- Cost relative to prevalence generally increases slightly with deprivation.

Sensitivity analyses



	Service cost year ending 30 June \$millions				
	2019	2020	2021	2022	Total
HPV-associated cancers (base estimate)	\$21.5	\$24.7	\$28.2	\$30.8	\$105.3
HPV-attributable portion	\$16.7	\$19.3	\$22.1	\$23.9	\$82.1
Comparator cohort: health service users	\$19.0	\$21.1	\$23.2	\$24.2	\$87.5

Cancer site	Sex	Attributable proportion
Cervix uteri	Female	91%
Vagina	Female	75%
Vulva	Female	69%
Penis	Male	63%
Anus and anal canal	Female	93%
	Male	89%
Oropharynx	Female	63%
	Male	72%

Source: <https://www.cdc.gov/cancer/hpv/statistics/cases.htm>

Attributable % is based on US data and may differ in NZ.

- e.g. NZ head and neck MDMs report a higher HPV positive rate among oropharyngeal cancers.

Limitations

Estimates are likely to be understated:

- Missing cohort of people with entries on cancer registry prior to 1 July 2017 (but incur costs in 2019+).
- Costs not included – primary/non-hospital care, private/out of pocket costs.
- The number of oropharyngeal cancers identified using ICD codes published in literature is lower than NZ MDMs report.

Additional HPV-related costs

In addition to our very conservative estimate, there are further HPV-associated costs that could be (at least partially) avoided with higher vaccination rates.

- Pre-cancer treatment costs avoided:
 - For instance, colposcopy and colposcopy directed treatments of **\$49M** from 2019-2022 (excludes costs already included in HPV cancer cohort).
- Screening costs may be decreased if herd immunity achieved.
- Immunotherapy treatments – although many of these aren't currently funded, if funding does become more available, this would then increase the cost-effectiveness of vaccination (due to the avoidance of these very significant treatment costs).
- Out-of-pocket/privately funded treatments e.g. aforementioned PCTs.

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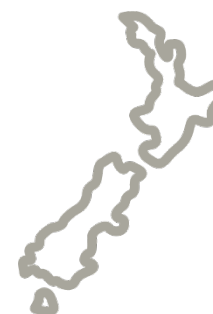
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Appendix: Evidence for cost-effectiveness of HPV vaccine in New Zealand

One study assessed the cost-effectiveness and equity impacts of three HPV vaccination programmes for school-aged girls in New Zealand (Blakely et al. 2014). The study implemented a Markov macro-simulation model for a population of 12-year-olds in 2011. The results were expressed as the cost per quality adjusted life year (QALY) gained relative to a scenario of no vaccination.

The three HPV vaccination programmes and their associated cost effectiveness are as follows:

1. New Zealand 2008 'as implemented' HPV vaccination programme of **females only**. Intervention 1 resulted in a cost effectiveness of USD \$9,700 per QALY gained.
2. Enhanced with a modification to be a **school only** programme (similar to Australia). Intervention 2 resulted in a cost effectiveness of USD \$11,661 per QALY gained, with an ICER of USD \$17,904 per additional QALY.
3. **Mandated vaccination** with opting out permitted (similar to the United States). Intervention 3 resulted in a cost effectiveness of USD \$15,995 per QALY gained, with an ICER of USD \$63,205 per additional QALY.



A more recent study by Rosettie et al. (2021) conducts a meta-regression analysis of the cost-effectiveness of HPV vaccination in 195 countries. New Zealand is included in this analysis.

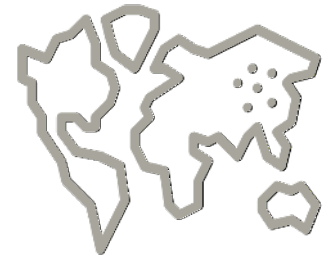
The study predicts that New Zealand has an ICER of \$11,010 per DALY averted. New Zealand's ICER is lower than the population-weighted mean ICER for high-income countries of \$14,667 per DALY averted. This is largely skewed by the USA (\$27,700 per DALY averted), with the large majority of high-income countries falling between \$8,850 and \$12,300 per DALY avoided.

Appendix: evidence for cost-effectiveness of HPV vaccine in the international context



The female-only HPV vaccine is cost-effective

- *Marra et al. (2009)*: examined 22 studies from between 2003 and 2008, 13 of these included a CEA. The incremental cost per QALY ranged from **USD \$23,000 to USD \$31,000** when compared to current screening programmes.
- *Seto et al. (2012)*: a further 29 studies examined, 27 of which evaluated the cost-effectiveness of female-only HPV vaccination. Noted that female-only HPV vaccination programmes are **cost effective compared with cervical cancer screening**.
- *Wilson et al. (2020)*: assessed the cost effectiveness of adult vaccination programmes, including HPV, in the United States. The cost effectiveness of the HPV vaccine was reported as **USD \$79,022 per LYS**.



There is a consensus that female-only HPV vaccination programmes are cost-effective, with studies showing lower ICER values in comparison to screening and male vaccination programmes.

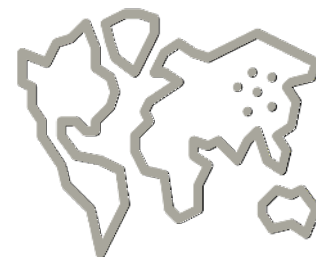
Appendix: evidence for cost-effectiveness of HPV vaccine in the international context



The male and female HPV vaccine is generally not cost-effective

- *Elbasha et al., (2007)*: reports an ICER for 12-year-old male and female vaccination of **USD \$31,308** per QALY compared to an equivalent female-only programme. This figure **increases to USD \$42,611** when 24-year-olds are included
- *Chesson et al., (2008)*: The cost-effectiveness of male HPV vaccination has been linked to the extent of the female-only vaccine's coverage. With female coverage of 20% at 12 years, male vaccination has an ICER of USD \$23,600. However, when female coverage increases to 75%, male vaccination's ICER increases to USD \$184,300. **Male vaccination can therefore be cost-effective in low female coverage scenarios.**

A high rate of female vaccination provides protection benefits to males. This lowers the incremental cost-effectiveness of vaccinating the male population.



As of December 2022, the WHO recommends the HPV vaccine for adolescent girls only (World Health Organization, 2023). In New Zealand, the HPV vaccine is provided for all eligible young people.

Appendix: evidence for cost-effectiveness of HPV vaccine in the international context

Cost-effectiveness of different vaccine doses

- WHO recommends one or two doses of the HPV vaccine for adolescents; generally feasible for high-income countries, however, financial and logistical barriers for low-income countries can mean delivering two doses is impractical (Prem et al., 2023).
- *Prem et al. (2023)*: examines cost-effectiveness of one dose versus two doses of the HPV vaccine across 188 countries. States that **“across all assumptions, the one-dose schedule provides large population benefits on cervical cancer cases averted, while the difference in population benefits of the one-dose versus two-dose vaccination schedule is small** if one dose confers ≥ 30 years of protection or lifelong protection but at 80% vaccine efficacy”.



Cost-effectiveness of different vaccine strategies

- Literature examines strategies and their cost effectiveness; strategies weigh up the cost per child in terms of vaccine costs and delivery costs. **Ineffective strategies and associated high costs can result in the vaccine becoming cost prohibitive.**
- *Akumbom et al. (2022)*: conducts a systematic review of the cost and effectiveness of HPV vaccination strategies. Found that strategies aim to increase access through two pathways:
 - **by increasing the availability of the vaccine**
 - **by increasing the uptake of the vaccine.**
- HPV vaccine delivery and programme costs found to be negligible for high income countries (Akumbom et al., 2022; Fesenfeld et al., 2013).



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Wellington	Auckland	Sydney	Melbourne	Canberra	Perth
Level 9 1 Willeston Street PO Box 587 Wellington 6140	Level 20 151 Queen Street PO Box 2475 Shortland Street Auckland 1140	Level 18 135 King Street Sydney NSW 2000	Level 5 171 Collins Street Melbourne VIC 3000	GPO Box 252 Canberra City ACT 2601	PO Box 1210 Booragoon WA 6954
P +64 4 915 7590	P +64 9 909 5810	P +61 2 9234 0200	P +61 3 9005 1454	P +61 2 6100 6363	P+61 8 6186 1410

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