HPV Vaccination of School-Age Girls

comparing the cost-effectiveness of 3 delivery programmes

SUMMARY

Human papillomaviruses (HPV) are common sexually transmitted viruses. They can cause several types of cancer (such as cancers of the cervix, anus, and oropharynx) and illnesses like genital warts. New Zealand has a national HPV vaccination programme aimed at preventing these diseases. Three doses of HPV vaccine (Gardasil) are currently offered to 12-year-old girls, in school or through their primary care provider. This pamphlet compares the cost-effectiveness of the existing HPV vaccination programme to two other alternative vaccine delivery programmes with higher estimated coverage. All three programmes vaccinate only school-age girls, but we include benefits to both males and females (via herd immunity) in our evaluation.

We evaluated three HPV vaccine delivery programmes

These were:

- Status Quo: what we do currently, where the vaccine is offered through schools or primary care. The observed coverage is only 47%.
- School-Based Only: where the vaccine is offered only through schools. The estimated coverage is 73%.
- School-Based Only + Opt-Out: where the vaccine is offered only through schools and a new law requires parents to actively opt-out if they do not want their daughter vaccinated. The estimated coverage is 93%.

We used a simulation model to estimate cost-effectiveness using NZ data

For each programme, the model estimates how much health benefit is gained (in quality-adjusted life-years or QALYs), and how much it costs the health system. These are combined into a single Incremental Cost-Effectiveness Ratio or ICER.

Most health gain is through prevention of genital warts

The greatest health gain was from the prevention of genital warts, with smaller gains from reduced rates of cervical, oropharyngeal, and anal cancer. Moving from no vaccination to Status Quo gives 266 QALYs gained, at a net cost of NZ$ 4.65 million per year. Moving from Status Quo to School-Based Only adds 82 QALYs, at an extra net cost of NZ$ 2.77 million per year. Moving from there to School-Based Only + Opt-Out adds another 35 QALYs, but for an additional net cost of $3.78 million per year (mainly from the cost of passing the law).

Which is the most cost-effective?

Each programme can be compared to no programme at all, or to each other. Status Quo appears cost-effective compared to no vaccination (ICER of NZ$ 18,800 per QALY). Going from Status Quo to School-Based Only is probably cost-effective (ICER of NZ$ 34,700 per QALY). Going from there to School-Based Only + Opt-Out is probably not cost-effective (ICER of NZ$ 122,500 per QALY).

Our bottom line

If the Government is willing to pay between NZ $17,000 to NZ$ 30,000 per QALY gained, then Status Quo is the most optimal programme. If the Government is willing to pay NZ$ 30,000 to NZ$ 115,000 per QALY, then School-Based Only is the most optimal programme. Only above NZ$ 115,000 per QALY gained would School-Based Only + Opt-Out be preferred.

For more detail please refer to Blakely T, et al. Cost-effectiveness and equity impacts of three HPV vaccination programmes for school-aged girls in New Zealand. Vaccine (2014), http://dx.doi.org/10.1016/j.vaccine.2014.02.071

IN MORE DETAIL

Basics of HPV

Human papillomaviruses (HPV) are common sexually transmitted viruses. They can cause several types of cancer (e.g. cancers of the cervix, vulva, anus, larynx, oropharynx, etc.) as well as illnesses like genital warts. Diseases from HPV infection pose a significant health burden and also contribute to health inequalities. For example, Māori women have twice the rates of cervical cancer of non-Māori women.

HPV Vaccination in NZ

An HPV vaccine is available (Gardasil) which protects against HPV infection for vaccinated females, and also unvaccinated males and females through 'herd immunity'. New Zealand has had a national HPV vaccination programme since 2008. As of 2013, three doses of the Gardasil vaccine are offered to 12-year-old girls, in school or through their primary care provider. However, HPV vaccination coverage for the third dose was only 47% in 2011. We need to consider how to improve coverage in a cost-effective manner. In this pamphlet we compare the cost-effectiveness of three different vaccine delivery programmes. We include the status quo as well as two other alternatives with higher estimated coverage.

Three Options for HPV Vaccine Delivery

The three programmes we evaluated were:

	Programme	Population Vaccinated	Similar to	Setting/Avenue	Estimated Coverage
1	Status Quo	School-age girls	What we do in NZ now	School or Primary Care	47%
2	School-Based Only	School-age girls	Australia	School Only	73%
3	School-Based Only + Opt Out	School-age girls	Some US states	School Only but with a law for vaccination that means parents have to actively opt-out	93%

Model

We began with a population of healthy 12-year-old girls and boys in 2011 and used a Markov macro-simulation model to follow this population through to death or 110 years. We modelled this population as they moved through the health states we expected HPV vaccination to prevent: cervical cancer, pre-cancer (CIN I to III), genital warts, and three other HPV-related cancers (oropharyngeal, anal, and vulvar cancers).

For each of the three programmes, we estimated:

- Health gain in quality-adjusted life-years or QALYs (including spill-over benefits to unvaccinated males and females through herd immunity)
- Health system costs in NZ$ (including additional health costs from extra life)
- Cost-effectiveness of each programme in Incremental Cost-Effectiveness Ratios or ICERs (with each programme compared to no vaccination or to each other).

QALY or Quality-Adjusted Life-Year:

The remaining life expectancy, adjusted for quality of life. Think of one QALY as one year of life in perfect health.

ICER or Incremental Cost-Effectiveness Ratio:

The difference in costs between one intervention and its comparator, divided by the difference in health gain. An ICER tells you how much more cost-effective an intervention is compared to something else.

Assumptions in the Model

Our model contains multiple assumptions. Some of these assumptions apply across all BODE3 evaluations, and are described in a range of protocols at the BODE3 website here. Some assumptions are specific to this topic: please email tony.blakely@otago.ac.nz for more information.

Some of our key assumptions include:

- We used a health system perspective and so did not include costs and consequences beyond the health system (such as productivity costs).
- We allowed for expected or background disease and limited the maximum amount of QALYs that could be gained with increasing age.
- Our model was such that individuals could only have one disease condition at a time.
- We applied a 3% discount rate to costs and QALYs gained.
- We included unrelated health system costs (average expected costs to the health system).
- The vaccine cost-per-dose was NZ$ 113 based on the annual cost paid by the Ministry of Health. The delivery and administration costs were NZ$ 141 if the vaccine was delivered through school and primary care (Status Quo) and NZ$ 126 if delivered only through schools (School-Based Only and School-Based Only + Opt-Out).
- With the School-Based Only + Opt-Out programme, we also included the cost of enacting a new immunisation law based on the average cost of a new act in NZ.

QALYs, Costs & Cost-Effectiveness

The results table below shows the direct programme cost, net cost to the health system, QALYs, and ICERs for all three programmes. In the left half, all programmes are compared to no vaccination. In the right half, the programmes are compared to each other.

	Each programme compared to no vaccination			Each programme compared to the other	
	Status Quo	School-Based Only	School-Based Only + Opt-Out	School-Based Only versus Status Quo	School-Based Only + Opt-Out versus School-Based Only
Direct cost of intervention (NZ$, 1000s)	$10,333 ($8,275 -$12,587)	$14,885 ($11,706 - $18,532)	$19,392 ($15,763 - $23,340)	$4,552 ($557 - $870)	$4,507 ($2221 - $6970)
Net cost to health system (NZ$, 1000s)	$4,650 ($2,443 - $6,973)	$7,423 ($4,114 - $10,943)	$11,207 ($7,227 - $15,179)	$2,773 (cost-saving- $6,626)	$3,784 ($1,980 - $5,814)
QALYs gained	266 (164 - 413)	348 (224 - 527)	382 (246 - 573)	82 (47 - 128)	35 (12 - 71)
ICER (NZ$ per QALY)	$18,800 ($7,300 - $35,400)	$22,600 ($9,800 - $40,200)	$31,000 ($15,400- $52,000)	$34,700 (cost-saving - $88,100)	$122,500 ($58,800 - $230,600)

Figures in brackets are 95% uncertainty intervals. ICERs rounded to nearest 100. Discount rate 3%.

Key points to note from the table:

- Moving from no vaccination to Status Quo gives 266 QALYs, mainly from reduction of genital warts with some smaller gains from reduced cervical, oropharyngeal, and anal cancer. Going from Status Quo to School-Based Only adds another 82 QALYs (31% increase) and from there to School-Based Only + Opt-Out adds another 35 QALYs (10% increase).
- Status Quo has an estimated net cost of NZ$4.65 million compared to no vaccination. The net cost is less than the actual direct cost of the programme as future health system costs are averted by preventing HPV-related disease. Moving from Status Quo to School-Based Only costs an additional net NZ$ 2.77 million (60% increase). Moving from there to School-Based Only + Opt-Out costs an additional net NZ$ 3.78 million (51% increase, mainly from the cost of passing the law).
- Each programme can be compared to no programme at all, or to each other. Status Quo appears cost-effective compared to no vaccination (ICER of NZ$ 18,800 per QALY). Going from Status Quo to School-Based Only is probably cost-effective (ICER of NZ$ 34,700 per QALY). Going from there to School-Based Only + Opt-Out is probably not cost-effective (ICER of NZ$ 122,500 per QALY).

A Note on Cost-Effectiveness Thresholds and Willingness-To-Pay

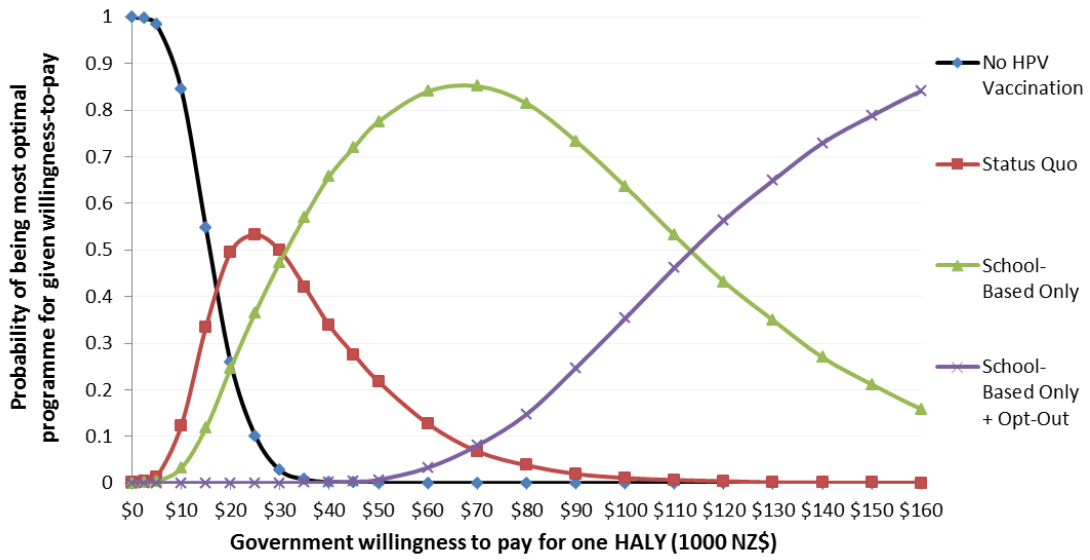
There is no consensus on a cost-effectiveness threshold in NZ. Our statements on cost-effectiveness stem from World Health Organization guidance, which is based on Gross Domestic Product (GDP) per capita. In NZ, GDP per capita is approximately NZ$ 40,000. If the ICER for an intervention is less than NZ$ 40,000 per QALY, we deem it cost-effective. However, our evaluations also make allowance for other thresholds, as shown below. It should also be noted that policy decisions are made on multiple considerations, and cost-effectiveness is only one of these.

Cost-effectiveness Threshold or Willingness-To-Pay:

Society's willingness to pay for an extra unit of health gain e.g. a QALY. If the ICER for an intervention is less than the threshold, the government can view it as cost-effective and may fund it. If ICER is greater than the threshold, it is not deemed to be cost-effective and the government may not fund it.

Which HPV Vaccination Programme is Optimal?

There is always uncertainty around the estimates of cost-effectiveness. There is also variation in how much the government is willing to pay to gain 1 QALY. The graph below is a cost-effectiveness acceptability curve which takes both these factors into account. At different levels of willingness-to-pay, it shows the probability of each programme being the most optimal of the three.



The graph shows that if government is willing to pay:

- Up to NZ$ 17,000 per QALY gained: no vaccination is the optimal choice.
- Between NZ $17,000 and NZ$ 30,000 per QALY gained: Status Quo is the optimal choice
- Between NZ$ 30,000 and NZ $115,000 per QALY gained: School-Based Only is the optimal choice.

Only if government is willing to pay above NZ$ 115,000 per QALY would School-Based Only + Opt-Out be the optimal choice*

*The falling costs of the HPV vaccine or including vaccination for boys would alter these conclusions.

Costs, QALYs & Cost-Effectiveness in Different Populations

In our best estimate model, we found that all three programmes are pro-equity compared to no vaccination, as long as coverage is as high or higher for Māori and for deprived groups.

Ethnicity	More health gain for Māori (as Māori have higher burden for HPV-related disease), so more cost-effective for Māori then non- Māori.
Deprivation	More health gain for the most deprived groups, so more cost-effective for the most deprived than the least deprived.

Equity Analysis

Māori have higher background disease and death compared to non-Māori. Māori are thus automatically disadvantaged in economic evaluations because they have a limited envelope of QALYs that can be gained. We conducted an 'equity analysis' to adjust for this, applying non-Māori rates of background disease and death to Māori instead of using Māori rates. Health gains increased for all three programmes by about 20%, and cost-effectiveness for Māori improved further still.

Uncertainty in our Results

There is unavoidable uncertainty present in the values we put into our models, and thus uncertainty in estimates of costs, health gains, and cost-effectiveness. These are reflected as uncertainty intervals in brackets in the table above. The most uncertainty came from the cost of the vaccine, the incidence of genital warts and its associated morbidity, and the incidence of cervical cancer.

Changing Some Assumptions

The results of the evaluation are sensitive to different assumptions. For example:

What if we halved the vaccine price?	This is plausible in the near future. Cost-effectiveness improves dramatically across all programmes with most ICERs dropping to less than NZ$ 19,000 per QALY gained (except for School-Based Only + Opt-Out compared to School-Based Only).
What if we ignore background disease as people age?	Health gains and cost-effectiveness improve by about 20%.
What if we discounted at different rates?	At a discount rate of 0%, all programmes are cost-saving. At a discount rate of 6%, cost-effectiveness worsens with all ICERs increasing to at least NZ$ 50,000 per QALY gained.

Our Bottom Line

1. Intensifying NZ's current vaccination programme for school-age girls to a school-based only programme is probably cost-effective.
2. Moving to a mandatory law is not cost-effective given current vaccine prices.
3. Māori are expected to have greater health gain than non- Māori in absolute terms across all three HPV vaccination programmes.