HPV Vaccination of Boys

Is expanding HPV vaccination to include boys cost-effective?

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. With the current programme, there is direct benefit to females and indirect benefit to males through herd immunity (sexual contact with vaccinated females). Vaccinating boys directly will deliver extra health benefits, but it is unclear how *much* more benefit and for how much extra cost. This pamphlet assesses the cost-effectiveness of adding school-aged boys to the current girls-only HPV vaccination programme in NZ (the published paper is full-free text online).

We evaluated four HPV vaccination programmes

These were:

- *Current Girls-Only*: what we do in NZ currently, where the vaccine is offered through schools or primary care. The observed coverage was only 47% (in the 2011 base year).
- *Intensified Girls-Only*: where the vaccine is offered only through schools. The estimated coverage is 73%.
- *Current Girls-Only + Boys*: extension of the current girls-only programme to include boys. The estimated coverage is 47% for girls and 47% for boys.
- *Intensified Girls-Only + Boys*: extension of the intensified girls-only programme to include boys. The estimated coverage is 73% for girls and 73% for boys.

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

The model estimates the effect of each programme (directly and via herd immunity, for both males and females) on cervical cancer and pre-cancer, genital warts, anal cancer, oropharyngeal cancer, and vulval cancer. These health benefits are quantified using quality-adjusted life-years or QALYs. The model also estimates the cost to the health system. QALYs and costs are then combined into a single Incremental Cost-Effectiveness Ratio or ICER.

Which is the most cost-effective?

Here we assume that government or society is willing to pay NZ$ 45,000 to gain one extra QALY (or one year of life in full health). By this threshold, adding boys to the current girls-only programme would not be cost-effective (ICER of NZ$ 117,500 per QALY gained). It would be more cost-effective to intensify the current girls-only programme instead (ICER of NZ$ 33,500 per QALY). Adding the vaccination of boys to an intensified programme for girls was not cost-effective either (ICER of NZ$ 247,000 per QALY).

Our bottom line

Adding boys to the current girls-only HPV vaccination programme in NZ is highly unlikely to be cost-effective. Policy-makers in NZ should probably focus more on improving HPV vaccination in girls than adding HPV vaccination for boys. However, if very low vaccine and programme administration costs are achieved in the future, vaccination of school boys may become cost-effective.

For more detail please refer to Pearson AL, et al. Is expanding HPV vaccination programs to include school-aged boys likely to be value-for-money? A cost-utility analysis in a country with an existing school-girl program *BMC Infectious Diseases* (2014), http://www.biomedcentral.com/1471-2334/14/351

IN MORE DETAIL

HPV Vaccination in NZ

Human papillomaviruses (HPV) are common sexually transmitted viruses. They can cause several types of cancer (e.g. cancers of the cervix, vulva, anus, oropharynx, etc.) as well as illnesses like genital warts, in both sexes. An HPV vaccine is available (Gardasil) which provides direct protection against HPV infection for vaccinated individuals, and also unvaccinated individuals through 'herd immunity' (sexual contact with vaccinated individuals). 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 (albeit rising to over 55% in more recent years).

Vaccinating boys directly will deliver extra health benefits, but it is unclear how *much* more benefit and for how much extra cost. The extent of the benefit will critically depend on coverage in females. It was therefore unclear if it was more cost-effective to add boys or to intensify girls-only vaccination (e.g. by delivering vaccination exclusively in schools, which has been shown to improve coverage), or some combination of both. HPV vaccination of boys has been publicly funded in Australia since 2013. In this pamphlet we assess the cost-effectiveness of adding school-aged boys to a girls-only vaccination programme in NZ.

Four HPV Vaccination Programmes

The four programmes we evaluated were:

	Programme	Population Vaccinated	Setting/Avenue	Estimated Coverage
1	*Current Girls-Only*	School-age girls	School or Primary Care	45-56%
2	*Intensified Girls-Only*	School-age girls	School only	73% (as in Australia)
3	*Current Girls-Only + Boys*	School-age girls and boys	School or Primary Care	45-56% for girls 45-56% for boys
4	*Intensified Girls-Only + Boys*	School-age girls and boys	School only	73% for girls 73% for boys

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 age 110 years. We modelled this population as they moved through the health states we expected HPV vaccination to prevent: genital warts, pre-cancer (CIN I to III), cervical cancer, and three other HPV-related cancers (oropharyngeal, anal, and vulval 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.

For more detail please refer to Pearson AL, et al. Is expanding HPV vaccination programs to include school-aged boys likely to be value-for-money? A cost-utility analysis in a country with an existing school-girl program *BMC Infectious Diseases* (2014), http://www.biomedcentral.com/1471-2334/14/351

Assumptions in the Model

Our model contains multiple assumptions. Some of these assumptions apply across all BODE[3] evaluations, and are described in a range of protocols at the BODE[3] 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 impacts on economic productivity from reducing deaths in working-age adults. We included unrelated health system costs (average expected costs to the health system).
- We allowed for expected or background disease and limited the maximum amount of QALYs that could be gained with increasing age.
- We applied a 3% discount rate to costs and QALYs gained.
- Our model included genital warts, pre-cancer (CIN I to III), cervical cancer, and three other HPV-related cancers (oropharyngeal, anal, and vulval cancers). Vaginal and penile cancers were excluded due to their small contribution to HPV burden.
- The vaccine cost-per-dose was NZ$ 113 based on the annual vaccine cost paid by the Ministry of Health in 2011. The administration costs were NZ$ 141 per dose if the vaccine was delivered through school and primary care, or NZ$ 126 if delivered only through school.
- We use a cost-effectiveness threshold of NZ$ 45,000 per QALY (around the GDP-per-capita of NZ) as per World Health Organization guidance. If the ICER for a programme is less than NZ$ 45,000 per QALY, we deem it cost-effective.

Health gain (QALYs), Costs & Cost-Effectiveness

As a starting point, the *Current Girls-Only* programme delivers 267 QALYs over the lifetime of the modelled cohort at a net cost of NZ$ 10.3 million, compared to no vaccination programme and is thus cost-effective at an ICER of NZ$ 18,800 per QALY. Adding boys to this current programme (*Current Girls-Only + Boys*) delivers an extra 83 QALYs but at a cost of NZ$ 10.8 million and is thus not cost-effective compared to the *Current Girls-Only* programme (ICER of NZ$ 118,000, ranging from $57,100 to $215,000). On the other hand, intensifying the *Current Girls-Only* programme (*Intensified Girls-Only*) delivers an extra 83 QALYs but at a much lower cost of NZ$ 4.6 million, making it cost-effective (ICER of NZ$ 33,500, ranging from $-10,700 to $88,600). Adding boys to the *Intensified Girls-Only* programme (*Intensified Girls-Only + Boys*) delivers an extra 63 QALYs but at large extra cost (NZ$ 15.7 million) and is also not a cost-effective move (ICER of NZ$ 247,000, ranging from $119,000 to $474,000). The table below shows total population costs, QALYs, and ICERs for all four programmes compared to no vaccination and to each other.

	Each programme compared to no vaccination				Each programme compared to the other			
	Current Girls-Only	*Intensified Girls-Only*	*Current Girls-Only + Boys*	*Intensified Girls-Only + Boys*	*Intensified Girls-Only* versus *Current Girls-Only*	*Current Girls-Only + Boys* versus *Current Girls-Only*	*Intensified Girls-Only + Boys* versus *Current Girls-Only + Boys*	*Intensified Girls-Only + Boys* versus *Intensified Girls-Only*
Direct cost of intervention (NZ$; 1,000s)	$10,332 ($8,537 - $12,383)	$14,995 ($11,877 - $18,491)	$21,157 ($17,482 - $25,360)	$30,632 ($24,325 - $37,873)	$4,624 ($829 - $8,656)	$10,826 ($8,945 - $12,977)	$8,252 ($544 - $16,561)	$15,676 ($12,449 - $19,382)
Net cost to the health system (NZ$; 1,000s)	$4,644 ($2,269 - $7,045)	$7,326 ($3,873 - $11,126)	$13,610 ($9,223 - $18,370)	$21,474 ($14,932 - $28,858	$2,683 ($-784 - $6,409)	$8,966 ($6,643 - $11,406)	$7,864 ($296 - $15,921)	$14,147 ($10,588 - $17,975)
QALYs gained	267 (162 - 413)	350 (218-530)	350 (222–529)	413 (266–608)	83 (48–127)	83 (47–134)	63 (19–115)	63 (33–104)
ICER (NZ$ per QALY)	$18,800 ($6,500 - $36,700)	$22,300 ($9,500 - $41,100)	$41,100 ($20,700 - $70,000)	$54,600 ($29,900 - $90,400)	$33,500 ($-10,700 - $88,600)	$118,000 ($57,100 - $215,000)	$148,000 ($1,300 - $438,000)	$247,000 ($119,000 - $474,000)

*ICERs rounded to nearest $100 or nearest $1,000 if > $100,000. Discount rate 3%.

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

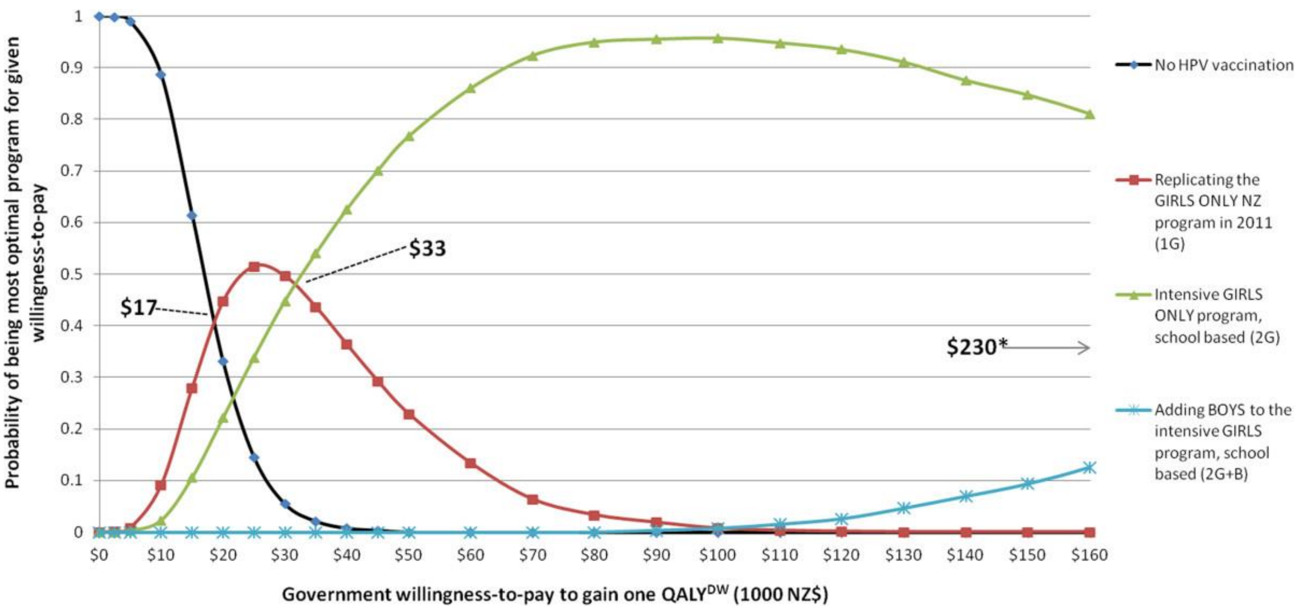
There is no consensus on a cost-effectiveness threshold in NZ. Our statements on cost-effectiveness stem from World Health Organization guidance, which is based on Gross Domestic Product (GDP) per capita. In NZ, GDP per capita is approximately NZ$ 45,000. If the ICER for an intervention is less than NZ$ 45,000 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 (e.g., equity impact, up-front costs etc), 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 on economic grounds.

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 one extra 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 four.



The graph shows that if government is willing to pay:

- Up to NZ$ 17,000 per QALY gained: no vaccination is the optimal choice.
- Up to NZ$ 33,000 per QALY gained: *Current Girls-Only* vaccination is the optimal choice.
- Between NZ$ 33,000 and NZ $230,000 per QALY gained: *Intensified Girls-Only* vaccination is the optimal choice.

Only if government is willing to pay above NZ$ 230,000 per QALY would vaccination of boys be optimal.

For more detail please refer to Pearson AL, et al. Is expanding HPV vaccination programs to include school-aged boys likely to be value-for-money? A cost-utility analysis in a country with an existing school-girl program *BMC Infectious Diseases* (2014), http://www.biomedcentral.com/1471-2334/14/351

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 was around the extra HPV reduction from vaccinating boys in addition to girls. However, even assuming the greatest extra benefit, vaccinating boys was still not cost-effective.

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 across all programmes, but vaccinating boys in addition to girls remains cost-ineffective.
What if administration costs were much lower?	Cost-effectiveness improves across all programmes, but vaccinating boys in addition to girls remains cost-ineffective.
What if we had very low vaccine prices *and* low administration costs?	Vaccinating boys in addition to girls would only become cost-effective if the combined administration and vaccine costs were $125 per dose or less. It is plausible that these lower costs might be achieved at some point in the next decade for NZ. This issue is discussed further on the Public Health Expert blog (July 2014).

Our Bottom Line

1. Adding boys to the girls-only HPV vaccination programme in NZ is highly unlikely to be cost-effective.
2. Policy-makers in NZ should probably focus more on improving HPV vaccination for girls (e.g., reaching levels achieved in Australia) than adding HPV vaccination for boys.
3. If very low vaccine and programme administration costs are achieved in the future, vaccination of school boys in NZ may become cost-effective.

For more detail please refer to Pearson AL, et al. Is expanding HPV vaccination programs to include school-aged boys likely to be value-for-money? A cost-utility analysis in a country with an existing school-girl program *BMC Infectious Diseases* (2014), http://www.biomedcentral.com/1471-2334/14/351