The science behind the changes to cervical screening in New Zealand

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Disclosures and acknowledgements

- I am co-PI of an investigator-initiated trial of cytology and primary HPV screening (‘Compass’) (NCT02328872), which is conducted and funded by the Victorian Cytology Service (VCS), a government-funded health promotion charity. The VCS have received equipment and a funding contribution for the Compass trial from Roche Molecular Systems and Ventana Inc USA.

- I am also a PI on Compass in New Zealand, (‘Compass NZ’) (ACTRN12614000714684) which is conducted and funded by Diagnostic Medlab, now Auckland District Health Board. DML received an equipment and a funding contribution for the Compass trial from Roche Molecular Systems.

- The Australian Renewal and guidelines evaluations were funded by the Medical Services Advisory Committee, Department of Health Australia and The Screening Section, Department of Health Australia

- The New Zealand evaluation was funded by the NCSP, NZ Ministry of Health

- Transitional Australian modelling work was commissioned by the Victorian Cytology Service

- The model platform used was developed with grants from the National Health and Medical Research Council (NHMRC) Australia and funding from a number of other non-commercial agencies including Cancer Council NSW, Australia.

- I receive salary support (Career Development Fellowship) from NHMRC
Today’s talk

• HPV natural history, immunisation and cervical screening
• Achieving a balance of benefits and harms in screening
• Impact of the NZ NCSP: Evaluating the benefits to date
• The emergent evidence on primary HPV screening
• Evaluation of the impact and cost-effectiveness of primary HPV screening in Australia.
• Evaluation of the impact and cost-effectiveness of primary HPV screening in NZ

HPV natural history, immunisation and cervical screening
Human papillomavirus (HPV)

HPV is a common sexually transmitted virus, which can cause:

- Cervical cancer
- Vulvar cancer
- Vaginal cancer
- Anal cancer
- Penile cancer
- Oropharyngeal cancers
- Anogenital warts

There are over 100 types:
- 15 anogenital types are ‘oncogenic’
- Virtually all cervical cancers caused by HPV, ~70-80% by HPV types 16/18
- HPV6/11 implicated in ~90% anogenital warts

Cervical screening tests

- Pap smear
  - (1st gen) Conventional cytology
  - (2nd gen) Manually-read liquid-based cytology (LBC)
  - (‘3rd gen’) Image-read LBC

- HPV DNA/mRNA testing
  - (1st gen) For pooled oncogenic types
  - (2nd gen) With partial genotyping for HPV16/18 (+/-45) vs. other on
HPV to cervical cancer

Secondary prevention via screening with cytology

Secondary prevention via HPV screening

Primary prevention via HPV vaccination

High grade squamous epithelial abnormality (HSIL or CIN2/3)

Persistence & Progression

Invasion in small proportion of women

Cervical cancer

Treated via cervical excisional procedure

Persistence & Progression

Regression

HPV vaccines

• Prophylactic HPV vaccination is highly effective for HPV-naïve females and males prior to exposure

• Protects younger cohorts against persistent HPV 16,18 infection and associated disease:
  • Cervarix (GSK) bivalent vaccine: HPV 16,18
  • Gardasil (Merck/CSL) quadrivalent vaccine: +HPV 6,11 – warts
  • Gardasil9 second generation nonavalent vaccine is now available

• HPV vaccination of pre-adolescent females effective and cost-effective and has been implemented in most developed countries

Adapted from Schiffman and Castle, NEJM 2005

1 Canfell, Chesson, Kulasingham, Berkhof, Diaz and Kim, Vaccine 2012
The NZ National HPV Immunization Programme

- Commenced in 2009
- Targets females born after 1990 (women now aged <27 years)
- School-based immunisation for 12-13 year old girls commenced in most regions in 2009.¹
- 3-dose coverage in cohorts born in 1991-2000: ~48-54%.¹
- Coverage for 2000 birth cohort: 60% Maori; 69% Pacific; 54% overall.¹

The policy question

A woman’s lifetime risk of cervical cancer now depends on vaccination...

Population screening: Achieving a balance of benefits to harms

Population Screening

- Investment in cancer screening is appropriate for those screening applications that satisfy a set of key principles first formulated by the World Health Organisation in 1968. These classic criteria include:
  - The requirement to adequately understand the underlying disease process - which, for screening to be effective, must have a precancerous or early symptomatic stage.
  - The availability and acceptability of a suitable screening test
  - The capacity to perform effective treatment for the identified condition
  - The cost-effectiveness of the process.

- Over time, these criteria have been revised and extended to include a number of additional concepts:
  - Equity of access
  - Integrated quality assurance and program evaluation processes
  - The requirement that the benefits outweigh the potential harms.
    - Harms can include the potential for false-positive results as well as over-diagnosis and over-treatment of cancers that would not have otherwise progressed

- All screening programs thus involve the balancing of benefits, potential harms and cost-effectiveness considerations.
Cervical Screening

• **Benefits:**
  - Early detection and treatment of cervical abnormalities
  - A reduction in the incidence of invasive cervical cancer and associated mortality.

• **Potential harms:**
  - Psychosocial impact of receiving a positive screening result
  - Being referred for subsequent colposcopy and treatment:
    - Treatment of the cervix may be unnecessary for some lesions that would have regressed
    - There is some evidence to suggest that treatment may adversely impact obstetric outcomes in a small proportion of women.

• **Cost-effectiveness:**
  - Considers life years saved in relation to the total costs involved in screening, management of detected abnormalities, and treatment for invasive cervical cancer.
  - Is this the best value for money compared to other health care interventions?

Impact of the NZ NCSP: Evaluating the benefits to date
**Background**

- The New Zealand (NZ) National Cervical Screening Programme (NCSP) was est. 1990
- Recommends 3-yearly routine screening with liquid-based cytology (LBC) for 20-69 year-old women
- Two consecutive annual screens at first visit and/or after 5 years non-attendance, before returning to 3-yearly screening
- In 2009, Liquid-based cytology (LBC) with HPV triage testing for low-grade cytology (ASCUS/LSIL) in women 30+ years was introduced.

**Impact of the NZ NCSP**

- Five-year average cervical cancer incidence, by age (age-standardised, per 100,000)

% change in cervical cancer incidence in 2009-2013 compared to pre-NCSP (1985-1989)

- 25-49 yrs: ↓ 49%
- 50-69 yrs: ↓ 66%
- 70+ yrs: ↓ 58%
- 20-24 yrs: Increase

Average for five-year period prior to NCSP (1985-1989)

Draft results

Impact of the NZ NCSP by ethnicity

• Five-year average cervical cancer incidence, by age (age-standardised, per 100,000)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Māori</th>
<th>Non-Māori</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-24</td>
<td>↑</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td>25-49</td>
<td>↓50%</td>
<td>↓52%</td>
<td>↓49%</td>
</tr>
<tr>
<td>50-69</td>
<td>↓65%</td>
<td>↓69%</td>
<td>↓66%</td>
</tr>
<tr>
<td>70+</td>
<td>NS</td>
<td>↓59%</td>
<td>↓58%</td>
</tr>
</tbody>
</table>


Implications: overall

• At the population level, the NZ NCSP has been very effective in women aged 25-69 years, halving cervical cancer incidence in 20 years.

• There is a “carry over” beneficial effect to older women, of a similar magnitude.

• Although there remains an important equity gap in terms of absolute rates, the relative reductions in cervical cancer incidence in women aged 25-69 years appear to have been similar in Māori and non-Māori women.

• These overall relative reductions in cervical cancer rates in these same age groups are consistent with organised cervical screening programs in other countries.1-3

Impact of the NZ NCSP in women <25 years

- Incidence appeared to increase after around 1996 in women aged 20-24 years.
- The increasing trend was significant for women aged 20-24 overall and for non-Māori women (P<0.01 in both cases), but not for Māori women (P=0.3).
- However, rates still remain >3x lower than those in older women.

**Implications: Women <25**

- Unfortunately, no impact of NCSP on cancer rates in <25 years has been observed in 20 years
- Consistent with international evidence on the low effectiveness of cervical screening in this age group
- Screening women in this age group is associated with greater harms than at older ages:
  - More women have ‘productive’, temporary, HPV infections which manifest as cytological abnormalities, regress naturally in ~12 months
- These factors need to be considered in terms of the overall balance of benefits to harms

Emergent Data on Primary HPV Screening

Primary HPV screening:
Longitudinal results for screen-negative women

Primary HPV screening:
Longitudinal results for screen-positive women

![Graph showing cumulative incidence rate over time for different HPV types.]

*Cumulative CIN3+ in 20,514 women (median age 34 years)*


Primary HPV screening:
Cross-sectional PPV and longitudinal results by type

![Graphs showing cumulative incidence rate over time for CIN2+ and CIN3+ categories for different HPV types.]

*ATHENA (USA) trial: 42,209 women aged 25-49 years*

Wright et al., *Gynecol Oncol* 2015
Primary HPV screening:
Pooled data on invasive cervical cancer outcomes from four European trials - 176,000 women

“[At longer intervals] HPV-based screening provides 60—70% greater protection against invasive cervical carcinomas compared with cytology”

Ronco et al, Lancet 2014

Effectiveness modelling and economic evaluation of primary HPV screening for cervical cancer prevention in Australia
Vaccine impact in Australia
Females, early twenties

**Vaccine-included HPV types**
77%↓
Tabrizi S/Brotherton J et al JID 2012

**Confirmed CIN2/3**
21%↓

### Renewal of the National Cervical Screening Program

- Announced November 2011
- **Aim:** “To ensure that all Australian women, HPV vaccinated and unvaccinated, have access to a cervical screening program that is acceptable, effective, efficient and based on current evidence.”
- The government’s Medical Services Advisory Committee (MSAC) commissioned a systematic review of the international evidence & modelled evaluation of health outcomes and costs
  - i.e. a linked evidence approach to guide decision making
- Process guided by an expert reference group, the Renewal Steering Committee
- Evidence report released April 28th 2014

http://www.cancerscreening.gov.au
Renewal of the National Cervical Screening Program

<table>
<thead>
<tr>
<th>Primary screening test</th>
<th>Age range</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>CURRENT PRACTICE: Conventional cytology</td>
<td>18-20 to 69 years</td>
<td>2</td>
</tr>
<tr>
<td>1 Conventional cytology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Manually-read LBC +/- HPV triage of LSIL</td>
<td>25-65 years</td>
<td>IARC intervals</td>
</tr>
<tr>
<td>3 Image-read LBC +/- HPV triage of LSIL</td>
<td></td>
<td>(3-yearly&lt;50; 5-yearly&gt;50 years)</td>
</tr>
<tr>
<td>4 HPV with LBC triage of pooled oncogenic types</td>
<td></td>
<td>5-yearly</td>
</tr>
<tr>
<td>5 HPV with partial genotyping for HPV 16/18 &amp; direct referral to colposcopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Co-testing with both HPV and LBC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LBC=Liquid-based cytology; LSIL=low grade cytology

- Modelled evaluation in both unvaccinated and cohorts offered vaccination
- Total of 132 detailed screening algorithms in main evaluation
- Supplementary analysis: screening end age 65 or 70 years

Algorithm for HPV screening with partial genotyping

HPV screening

- Negative
  - Routine screening in 5 years
- Other oncogenic HPV
  - Cytology negative or low grade
  - 12 month HPV FU
    - Refer to colposcopy if any HPV +ve
    - Otherwise return to routine screening
- HPV16/18
  - Cytology high grade
  - Colposcopy (diagnostic referral)

Use the same strategy, whether or not a woman has been offered vaccination against HPV 16,18
Exploits our knowledge about HPV natural history

Cumulative CIN3+ in 20,514 women (median age 34 years)

Khan MJ, Castle PE, et al. JNCI 2005

Predicted cancer outcomes, unvaccinated
Relative impact of different screening strategies in unvaccinated women over the long term

<table>
<thead>
<tr>
<th>Example strategy</th>
<th>% change ASR mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional cytology at IARC intervals</td>
<td>7%</td>
</tr>
<tr>
<td>Manually-read LBC at IARC intervals</td>
<td>-15%</td>
</tr>
<tr>
<td>Image-read LBC at IARC intervals</td>
<td>-17%</td>
</tr>
<tr>
<td>5-yrly HPV with LBC triage</td>
<td>-21%</td>
</tr>
<tr>
<td>5-yrly HPV with partial genotyping</td>
<td>-23%</td>
</tr>
<tr>
<td>5-yrly co-testing with immediate referral of HPV+/any cyto abnormality</td>
<td>-22%</td>
</tr>
</tbody>
</table>
Predicted cancer outcomes, vaccinated
Relative impact of different screening strategies in vaccinated women over the long term

Policy recommendation, 2014

This work led to the following renewed national policy:

1. Australian women should start having HPV tests at 25 years.
2. HPV tests should be undertaken every 5 years.
3. Women 70 to 74 years of age, with a negative HPV test result may exit the cervical screening program.
4. Women 74 years of age and older who have never had, or who request a HPV test at least 5 years after their last cervical screening test, should be screened.
5. HPV and cytology co-testing is not recommended.
Implementation in Australia

• The transition from evidence to practice is being guided by the Steering Committee for the Renewal Implementation Project (SCRIP)

• A Quality and Safety Monitoring Committee (QSMC) has been configured

• Telstra Health appointed to develop and operate a new National Cancer Screening Register which will support the renewed NCSP and the expansion of the National Bowel Cancer Screening Program.

• The National Pathology Accreditation Advisory Council Standards (NPAAC) Cervical Screening Drafting Committee is currently drafting performance measures and standards for HPV testing and cytology.

• Implementation date: **1st May 2017**.

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Clinical management guidelines for the HPV-based screening program

National Cervical Screening Program:
Guidelines for the Management of Screen Detected Abnormalities, Screening in Specific Populations and Investigation of Abnormal Vaginal Bleeding.

Draft released for public consultation March 2016:
**Updated (2016) predictions of cancer outcomes**
Updated estimates of long term impact, taking account of new guidelines

<table>
<thead>
<tr>
<th></th>
<th>Current cytology-based program</th>
<th>Renewed HPV-based program</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>If HPV vaccination had not been introduced</td>
<td>For cohorts offered vaccination as 12 year olds</td>
</tr>
<tr>
<td>Cervical cancer cases</td>
<td>850</td>
<td>353</td>
</tr>
<tr>
<td>Cervical cancer deaths</td>
<td>227</td>
<td>94</td>
</tr>
</tbody>
</table>

Predicted annual numbers of cervical cancer cases and deaths for the pre-renewal NCSP and the renewed NCSP (showing differences in case numbers and relative percentage differences)

*Using the female Australian population as predicted for 2017.

**Transitional screening volume predictions**
Under alternate assumptions about transitional strategy

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*Smith M et al. BMC Health Services 2016*
Transitional test volume predictions
Reflex cytology and colposcopy

- Damped fluctuation carrying through to secondary tests/procedures
  - Fluctuations of +25%/-31% in first five-year period; decreasing to +8%/−10% by third round.
- By 2030, test volumes will be relatively stable

Effectiveness modelling and economic evaluation of primary HPV screening for cervical cancer prevention in New Zealand

Smith M et al. BMC Health Services 2016
Objectives

1. In consultation with the NZ NCSP Advisory Group, to determine a set of possible strategies (i.e. clinical management pathways) suitable to the NZ context using HPV as the primary screening test.

2. To evaluate the lifetime effects (cervical cancer incidence, mortality), resource utilisation (colposcopy referrals) and cost-effectiveness of each primary HPV strategy:
   - In relation to current practice for cervical screening;
   - In both unvaccinated women and cohorts offered vaccination;
   - Considering the levels of vaccine coverage achieved in NZ.

3. To thereby identify the optimal cervical screening strategy, in the context of HPV vaccination, for NZ.
Policy1-Cervix

- Dynamic model of HPV transmission and cervical screening, extensively validated across multiple country settings and data sources
- For this evaluation, incorporated national NZ data on vaccine coverage in females
- Test characteristics consistent with systematic review but validated against NCSP data
- The platform was used to evaluate 4 main strategies for primary HPV screening, considering in each case 4 strategy variants (i.e. 16 strategies in total).

- Canfell et al. Br J Cancer 2004
- Smith et al. Int J Cancer 2008
- Creighton et al. BMC Pm 2010
- Canfell et al. Vaccine 2010
- Smith et al. Vaccine 2011
- Shi et al. BMC Cancer 2011
- Lew et al., BMC HSR, 2012
- Legood et al., BMJ 2012
- Hitchener et al., HTA UK 2014
- Smith and Canfell, BMC RN 2014
- Lew and Simms et al., Renewal Report Australia 2014
- Smith and Canfell, PLoSOne 2014
- Smith et al BMJ HSR 2016
- Lew et al PLoSOne 2016

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Strategy S1: HPV testing with cytology triage for all HPV positive women

- **HPV screening**
  - Negative: Routine screening in 5 years
  - HPV positive:
    - Reflex LBC
    - LBC negative/ASCUS/LSIL: 12 month HPV & cytology FU
    - LBC ASH-H/HSIL: Refer to colposcopy if any HPV +ve; otherwise return to routine screening in 5 years
  - Colposcopy
**Strategy S2: HPV testing with partial genotyping and cytology triage for other oncogenic HPV (OHR)**

- **HPV screening**
  - **Negative**
    - Routine screening in 5 years
  - **Other onc HPV positive**
    - Reflex LBC
    - 12 month HPV FU
      - Refer to colposcopy if any HPV +ve; otherwise return to 5-yearly routine screening
  - **HPV16/18 positive**
    - Colposcopy

**This is same as the pathway for the renewed Australian program**

**Strategy S3: HPV and cytology co-testing**

- **HPV & cytology screening**
  - **LBC negative, HPV negative**
    - Routine screening in 5 years
  - **HPV pos & LBC neg/ASCUS/LSIL**
    - or
  - **HPV neg & LBC ASCUS/LSIL**
  - 12 month HPV & cytology FU
    - Refer to colposcopy if any HPV +ve
    - Otherwise return to routine screening in 5 years
  - **LBC ASC-H/HSIL, any HPV result**
    - Colposcopy
Strategy S4: HPV with partial genotyping and cytology co-testing

Methods: Sub-strategies

Four sub-strategies were considered for each primary strategy

<table>
<thead>
<tr>
<th>Sub-strategy</th>
<th>Screening age range</th>
<th>Primary screening approach</th>
<th>Management of HPV+, triage ASCUS/LSIL group</th>
</tr>
</thead>
<tbody>
<tr>
<td>A “HPV screening”</td>
<td>25-69 years</td>
<td>Primary HPV screening in women 25-69 years</td>
<td>Follow-up in 12 months *</td>
</tr>
<tr>
<td>B “HPV screening with aggressive management of intermediate risk”</td>
<td>25-69 years</td>
<td>Primary HPV screening in women 25-69 years</td>
<td>Refer to colposcopy</td>
</tr>
</tbody>
</table>
| C “Switchover screening” | 20-69 years | • Cytology screening for 20-29 years*  
• Primary HPV screening for 30-69 years | Follow-up in 12 months * |
| D “Switchover screening with aggressive management of intermediate risk” | 20-60 years | • Cytology screening for 20-29 years  
• Primary HPV screening for 30-69 years | Refer to colposcopy |

* Strategies 1 and 3 (no partial genotyping): follow-up with co-testing; Strategies 2 and 4 (partial genotyping): follow-up with HPV testing alone.
* As per current practice: two initial annual screens followed by 3-yearly screening with LBC; no HPV triage in women <30 years; ASCUS/LSIL have 12 month follow-up.
Results: Change in cervical cancer incidence
Compared to rates in the current program

<table>
<thead>
<tr>
<th>% change age-standardised rate (ASR) compared to current practice</th>
<th>Unvaccinated</th>
<th>Offered vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>All primary HPV strategies</td>
<td>-19.5% to 3.3%</td>
<td>-17.8% to 3.5%</td>
</tr>
<tr>
<td>S1: HPV testing + LBC triage strategies</td>
<td>-11.1% to 3.3%</td>
<td>-10.9% to 3.5%</td>
</tr>
<tr>
<td>S2: HPV testing with 16/18 genotyping + LBC triage strategies</td>
<td>-17.3% to -2.1%</td>
<td>-15.7% to -0.3%</td>
</tr>
<tr>
<td>S3: Co-testing strategies</td>
<td>-12.6% to 2.0%</td>
<td>-12.5% to 2.1%</td>
</tr>
<tr>
<td>S4: Co-testing with 16/18 genotyping strategies</td>
<td>-19.5% to -4.6%</td>
<td>-17.8% to -2.7%</td>
</tr>
<tr>
<td>S2a: NZ/Australian recommended pathway</td>
<td>-15%</td>
<td>-12%</td>
</tr>
</tbody>
</table>

* Range includes all four variants in the strategy group

Results: Change in cervical cancer mortality
Compared to rates in the current program

<table>
<thead>
<tr>
<th>% change age-standardised rate (ASR) compared to current practice</th>
<th>Unvaccinated</th>
<th>Offered vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>All primary HPV strategies</td>
<td>-19.9% to 5%</td>
<td>-18.2% to 5.3%</td>
</tr>
<tr>
<td>S1: HPV testing + LBC triage strategies</td>
<td>-11.9% to 5%</td>
<td>-11.8% to 5.3%</td>
</tr>
<tr>
<td>S2: HPV testing with 16/18 genotyping + LBC triage strategies</td>
<td>-18% to -2.1%</td>
<td>-16.5% to 0.3%</td>
</tr>
<tr>
<td>S3: Co-testing strategies</td>
<td>-12.6% to 3.9%</td>
<td>-12.6% to 4.1%</td>
</tr>
<tr>
<td>S4: Co-testing with 16/18 genotyping strategies</td>
<td>-19.9% to -4.6%</td>
<td>-18.2% to -2%</td>
</tr>
<tr>
<td>S2a: NZ/Australian recommended pathway</td>
<td>-16%</td>
<td>-12%</td>
</tr>
</tbody>
</table>

* Range includes all four variants in the strategy group
Results: Long term change in colposcopy referrals
Compared to estimated referral numbers in the current program

Unvaccinated

Cohorts offered vaccination

Estimated colposcopies in 2017

<table>
<thead>
<tr>
<th>Strategy</th>
<th>No vaccination</th>
<th>% change</th>
<th>Vaccination</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current practice</td>
<td>28,800</td>
<td>--</td>
<td>21,000</td>
<td>--</td>
</tr>
<tr>
<td>S1: HPV testing + LBCA</td>
<td>27,200 - 33,300</td>
<td>-5% to 16%</td>
<td>19,200 - 24,300</td>
<td>-9% to 16%</td>
</tr>
<tr>
<td>S2: HPV testing with 16/18 genotyping + LBCA</td>
<td>29,200 - 37,000</td>
<td>1% to 29%</td>
<td>19,600 - 25,600</td>
<td>-7% to 22%</td>
</tr>
<tr>
<td>S3: Co-testing</td>
<td>28,900 - 35,700</td>
<td>0% to 24%</td>
<td>20,800 - 26,500</td>
<td>-1% to 26%</td>
</tr>
<tr>
<td>S4: Co-testing with 16/18 genotyping</td>
<td>31,400 - 39,800</td>
<td>9% to 38%</td>
<td>21,400 - 27,900</td>
<td>2% to 32%</td>
</tr>
<tr>
<td>S2a: NZ/Australian rec. pathway</td>
<td>33,200</td>
<td>15%</td>
<td>21,300</td>
<td>1%</td>
</tr>
</tbody>
</table>

* Range includes all four variants in the strategy group

Results: Cost-effectiveness

- Several options for primary HPV screening were both more effective and less costly than current practice in both unvaccinated women and cohorts offered vaccination.
- The dominating strategies employed partial genotyping.
- Among the dominating strategies, the “preferred pathway” was the most cost-effective strategy.
  - This would save NZ$1.3-3.2M annually compared to the current program (4-13% decrease in program costs).
- When considering primary HPV screening with partial genotyping, incorporating more aggressive management for HPV OHR-ASCUS/LSIL (direct colposcopy referral) was not cost-effective compared to referring this group for 12 month follow-up:
  - ICER >NZ$160,000 for both unvacc/vacc [NZ WTP $20,000-50,000]
- Co-testing options were generally more effective than current practice but not cost-effective:
  - The only co-testing strategy that was not dominated was co-testing with genotyping and aggressive management of intermediate risk
  - ICER >NZ$700,000 for both unvacc/vacc [NZ WTP $20,000-50,000].

Conclusions from the modelling

• 5-yearly primary HPV screening will be both more effective and also potentially cost-saving compared to the current 3-yearly cytology screening program in NZ.

• Managing women based on HPV partial genotyping was found to be a highly effective, and the most cost-effective, option.

• Co-testing with HPV & cytology is not cost-effective in NZ (this is highly cost-ineffective compared to primary HPV screening)

• The optimal strategy is 5-yearly HPV screening in women aged 25-69 years, with partial genotyping for HPV 16/18 and direct referral to colposcopy.
  ➢ In NZ, this strategy is predicted to further reduce cervical cancer incidence and mortality by 12-16% and to reduce annual program costs by 4-12%
  ➢ This is the same strategy as the Australian renewed program
  ➢ Also the same strategy as in the Compass trial, which is thus acting as a sentinel experience of primary HPV screening in NZ as well as Australia.

We have a way forward for cervical screening in NZ

Primary HPV screening allows a consistent approach to population-based risk assessment for all women, vaccinated or not AND Will improve outcomes for both unvaccinated and vaccinated women.
Primary HPV screening
Risk stratify based on test result...
...whether vaccinated or unvaccinated

Cumulative CIN3+ in 20,514 women (median age 34 years)

Khan MJ, Castle PE, et al. JNCI 2005

Acknowledgements

Cervix/HPV/Breast Group
- Megan Smith
- Jie-Bin Lew
- Kate Simms
- Michaela Hall
- Michael Caruana
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- Hazel Lewis
- And the NZ NCSP AG

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- Jeff Tan
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- Annabelle Farnsworth
- Other Investigators and SAC members

The NZ modelling report can be found as:

The Renewal evaluation report can be found at:


Compass details:
Website www.compasstrial.org.au
Pilot Study Registration ACTRN12613001207707
Main Trial Registration: Clinicaltrials.gov NCT02328872