The National Cervical Screening Program Renewal: An Overview

Dr Caroline Harvey
28 November 2017
## Current NCSP

- Pap smear
- 2 yearly
- Start 18-20 years
- End 69 years
- State based registries
- Reminders

## 1 Dec 2017

- Cervical Screening Test (oncogenic HPV test)
- 5 yearly
- Start 25 years
- End 70-74 years
- National Registry
- Invitations/Reminders
- Self-collection
Overview

• Rationale for Change: The Renewal
• The test, the age range and the interval
• Understanding HPV
• National Cervical Screening Policies
  – NCSP policy
  – Self-Collection policy
  – Transitioning women to new program policy
  – Specific populations
• The National Cancer Screening Register
Cervical screening in Australia

- 1991 NCSP Policy:
  - 2-yearly (Pap test)
  - 18 to 69 years\(^1\)
  - Registry reminder

- Participation:\(^2\)
  - 2-yearly 58%
  - 5-yearly 83%\(^2\)

- 50% reduction in incidence & deaths

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Figure 1. Incidence of carcinoma of the cervix (squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma and other carcinoma) in women aged 20–69, by year, 1982 to 2008

Number of new cases per 100,000 women

- Squamous cell carcinoma
- Adenocarcinoma
- Adenosquamous carcinoma
- Other carcinoma

Source: AIHW 2014[7]
## Cervical Cancer in Australia

### Incidence and mortality rates of cervical cancer: selected countries-2012

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence per 100,000 women</th>
<th>Mortality per 100,000 women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>7.4</td>
<td>1.9</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>7.1</td>
<td>1.8</td>
</tr>
<tr>
<td>USA</td>
<td>6.6</td>
<td>2.7</td>
</tr>
<tr>
<td>Canada</td>
<td>6.3</td>
<td>1.7</td>
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<tr>
<td><strong>Australia</strong></td>
<td><strong>5.5</strong></td>
<td><strong>1.6</strong></td>
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<tr>
<td>New Zealand</td>
<td>5.3</td>
<td>1.4</td>
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<tr>
<td>Finland</td>
<td>4.3</td>
<td>1.0</td>
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*Source: GLOBOCAN 2012*
Why

- New knowledge on the development of cervical cancer.
- New evidence for cervical cancer prevention and screening
- New technologies
  - liquid-based technology
  - computer assisted image analysis
  - HPV tests
- 2007 - National HPV Vaccination Program (girls)
- 2013 - National HPV Vaccination Program (girls + boys)

- Current NCSP is intensive compared to other countries
Renewal of the NCSP

What is the aim of the Renewal

• Ensure the success of the program continues

• All women, HPV vaccinated and unvaccinated…….

• Access to a cervical screening program based on current evidence and best practice.
George Papanicolaou

1928- Pap test developed
1943- Diagnosis of uterine cancer by the vaginal smear
1948- American Cancer Society “Pap smear is a valuable test”
Harald zur Hausen

1982
Demonstrated that HPV was the cause of cervical cancer

2008
Nobel Prize in Medicine
Ian Frazer AC
1991-2005 Developed the first vaccine for HPV
2007/2013 National HPV Vaccination Program – girls/boys
# Options for Screening Approaches

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

- Evaluated
- Safety
- Effectiveness
- Cost effectiveness
- in both unvaccinated and cohorts offered HPV vaccination
- 132 screening algorithms
- Supplementary analysis: screening end age 65 or 70 years
• New - screening test: Oncogenic HPV
• New - screening interval: 5 years
• New - starting age: 25 years
• New - finishing age: 74 years
• New - self-collection
• New - National Cancer Screening Register
HPV–Nucleic Acid Testing

• More sensitive than cytology
• Earlier detection of high grade lesions
• Prevents more cervical cancer
• + Potential to reduce invasive adenocarcinoma
• Allows for individual risk based assessment
  – Partial genotyping improves risk stratification
• A negative oncogenic HPV test is protective for at least 5 years
HPV
• Cervical cancer is the first solid tumour to be shown to be virally induced in essentially every case
• High risk HPV causes ~5% of all cancers worldwide

HPV Facts

• There are >100 types of HPV

• 4 groups important in humans:
  1. Skin warts – HPV 1 & 2
  2. Epidermodysplasia verruciformis (EV) and cutaneous SCC – HPV 5 & 8
  3. Anogenital warts – HPV 6 & 11
  4. Anogenital cancer – HPV 16 & 18

De Villiers et al. Virology. 2004
• Low risk HPV types: 6 and 11 (42, 43, 44)
  Types 6 & 11:
  - 90% genital warts
  - 100% Recurrent respiratory papillomatosis (4 per 100,000)

• High risk/Oncogenic HPV types: 16 and 18
  (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68)
  Cancer predominantly caused by HPV 16 & 18

  This group of viruses will be detected with the new screening test
  i.e. ‘HPV detected’ = ‘Oncogenic HPV detected’
Anogenital HPV

- > 40 anogenital HPV types
- Transmitted by skin/skin or mucosa/mucosa contact
- Mean duration of infection is 8-10 months
- Most infections cleared by the immune system within 1-2 years
- Age is important - < 25 y.o. more likely to clear infection

Stanley M. Vaccine. 2006
HPV

“THE COMMON COLD OF SEXUAL ACTIVITY”

Professor Ian Hammond

• Everyday occurrence
(30% within 1 yr of start of sexual activity, 48% within 3 yrs, 80-90% at some point¹)

• Understanding of viral response (rhinovirus vs HPV)

Natural history of HPV

• <10% of HPV infections will persist (low risk and high risk)
• Progression to HSIL takes 5-10 years
• Invasive cancer arises rarely from pre-cancer and typically takes many years to occur

Schiffman M. Lancet. 2007
Natural history of HPV infection:

- 5% of CIN2
- Up to 30% of CIN3

HPV INFECTION (low grade abnormality)

PRE-CANCER (high grade abnormality, CIN2/3 or AIS)

CERVICAL CANCER

SECONDARY PREVENTION VIA SCREENING WITH CYTOLOGY

SECONDARY PREVENTION VIA HPV SCREENING

Acknowledgment: Adapted from Schiffman M, 2005.
HPV Vaccination

- Gardasil® (HPV 6,11,16,18)
  - 70 - 80% cervical cancer
  - TGA approval for females 9 – 45y.o., males 9 – 26y.o.

- Cervarix® (HPV 16,18)
  - TGA approval for females 10 – 45y.o.

- Gardasil 9® (HPV 6,11,16,18,31,33,45,52,58)
  - 90% cervical cancer
  - TGA approval for females 9 – 45y.o., males 9 – 26y.o.
Australia – World Leaders

National Immunisation Program (NIP) - Gardasil®:

- Catch-up program 2007 – 2009
  Females < 27 yrs old

- Since 2009
  Girls – 1st year of high school

- Since 2013
  Boys – 1st year of high school
  (2 year catch-up of Grade 10 boys)

- Since July 1 2017
  Ongoing catch-up, individuals aged 10-19

- 2018 – 2 dose Gardasil 9 schedule
Why has the recommended age for commencing screening been raised to 25 years?

Is it safe?
Three-year average cervical cancer incidence (with 95% CIs), by all ages and histological type, 1982-2010

Three-year average cervical cancer incidence (with 95% CIs), by age and histological type, 1982-2010

M. Smith, K. Canfell: Med J Aust
2016; 205(8): 359-64
Three-year average cervical cancer incidence (with 95% CIs), by age and histological type, 1982-201

Safety of not screening women < 25 years

- **25 years of screening women under 25 years of age**
  - no impact on incidence of cervical cancer in this age group

- **Systematic literature review**
  - No evidence for screening effectiveness in other countries

- **Very low incidence of cervical cancer in these women**
  - Expected to decline further due to HPV vaccination

- **IARC recommendation**
  - Do not screen women under age 25 years
Why has the screening interval been extended from two years to five years?

Is it safe?
Principles of screening

• Definition

Screening involves examining and/or testing a population of well individuals to identify risk factors or to detect disease at an early stage.

By detecting risks or disease early, the intervention aims to improve the outcome for the individual and influence population prevalence/severity.
Screening

Suitable cut off

Well

Highly sensitive
High false positive

Disease

Highly specific
High false negative
The Pap smear (cytology) has high specificity but is only moderately sensitive (false negatives ~ 15+%).

- Regular screening has prevented adverse outcome from false negative results.

HPV testing – much greater sensitivity

- Higher negative predictive value -> extension of screening intervals
- More reliable clinical performance
- Greater sensitivity for detection of glandular abnormalities
Primary HPV screening
Longitudinal results for screen-negative women

Dillner, J. et al. Joint European Cohort Analysis. BMJ
2008;337:a1754
After 1 December 2017?
What does it mean for women?

- Will still need a speculum vaginal examination

- Will be **invited** to have a screening test every 5 years

- A sample will be taken from her cervix and sent to lab
  - If cytology needed – no additional visit to GP/provider

- Women will receive results from their GP/provider

- Test results: kept by National Cancer Screening Registry
What does it mean for providers?

• Pap *******→ Cervical Screening Test (CST)
• Different test, same collection procedure
• Collect as cytology sample BUT no slide prepared
• “Direct to vial” (not “split sample”)
• “CST” or “Co test” requested but both collected in same way
Talking to women about the changes

“more accurate, less often”
“looking for the causal agent”
“assessing risk for a future cancer”

Health literacy considerations

Cervical Screening: the lab report?

- An overall cervical screening risk assessment
  - Low risk
  - Higher risk
  - Intermediate risk

- A statement of test(s) performed and the results
  HPV test result including any LBC result

- A recommendation for follow-up/action
  Taking account of screening history and clinical notes
Cervical Screening Test
Women’s Risk Based Assessment

**Low risk**
HPV not detected
ACTION: REPEAT CST in 5 YEARS

**Higher risk**
HPV (16/18) detected
(with any LBC result)
OR
HPV (not 16/18) detected
(with LBC: pHSIL, HSIL or any glandular abnormality)
ACTION: REFER for COLPOSCOPY

Source: Prof Ian Hammond
Intermediate risk
(risk is determined by combined HPV and LBC result)

HPV (not 16/18) detected
(with LBC negative or pLSIL/LSIL)

ACTION: Follow-up HPV test in 12 months

Source: Prof Ian Hammond
Follow up of Intermediate risk women after initial cervical screening test result

**Women at Intermediate risk**

**Follow-up HPV test in 12 months**

**At follow-up 12 month test**
- HPV not detected
- **ACTION:** REPEAT CST in 5 YEARS

**At follow-up 12 month test**
- HPV detected (any type) with any LBC result
  - (= persistent HPV infection)
  - **ACTION:** REFER for COLPOSCOPY

Source: Prof Ian Hammond
Emerging issues in quality collection

Liquid Based Cytology

- Lubricants – carbomers/ carbopol copolymers

- Endocervical cells - collection
  - transferring
80% cervical cancer occurs in women never screened or under-screened

(VCCR 2012)
Self collection of vaginal sample for HPV test

- Under screened and never screened women only
- Facilitated by nurse or medical practitioner
  - Carried out at the practice *not* at home

- Or on behalf of a medical practitioner
- Who also offers routine cervical screening
Self-collection of cervical screening test

- Opportunity for increased participation rate for never and under-screened
- Not as effective as health professional collected sample
- More effective than the current Pap test
- Less cost effective than routine pathway

- If HPV +ve will need separate visit for LBC sample

- Only available to under or never screeners.
• **Women already participating in program**
  
  – >23yr and <70yr at last test
    • Will be invited to screen when due for next test
  
  – <23yrs at last negative test
    • Will be advised test not needed until age 25
    • Will be invited at that time
  
  – Overdue by < 2 years and >25yr age
    • Advised overdue and reminded to screen
  
  – Overdue by ≥ 2 years and >30 yr age
    • Invited to screen and advised re self-collection option
  
  – ≥ 70yr and <75yr invited to have exit screening test
TRANSITION TO THE RENEWED NATIONAL CERVICAL SCREENING PROGRAM

Women with Existing Abnormalities* (cytology or histopathology)

Prior December 2017

Pap test result pLSIL/LSIL

Treated for histologically confirmed HSIL (CIN2 or CIN3)

Treated for histologically confirmed AIS

After December 2017

HPV test at next scheduled appointment

Start or continue with Test of Cure**

Annual co-test (HPV & LBC) indefinitely#

HPV not detected

HPV detected (any type)

Reflex LBC

Refer for colposcopic assessment

Routine 5-yearly screening with HPV test

* Prior to December 2017
** A woman who has been treated for HSIL (CIN2/3) should have a co-test (HPV and LBC) performed at 12 months after treatment, and annually thereafter, until both tests are negative on two consecutive occasions, when she can return to routine 5-yearly screening
# Until sufficient data become available that may support a policy decision that cessation of testing is appropriate


NATIONAL CERVICAL SCREENING PROGRAM
A joint Australian States and Territories Screening Program

Australian Government
Department of Health

Cancer Council Australia
Specific populations

- ATSI women
- Pregnant women
- Post Hysterectomy
- Early sexual activity including CSA
- DES exposed
- Immune Deficient
- Symptomatic women
Aboriginal and Torres Strait Islander women

- Encourage participation
- Specific efforts re delivery of invitations
- Accessible and culturally appropriate services
- Self collection as appropriate
- Identifiers to improve data
- Screening and management recommendations the same
- Follow up and referral systems and approaches
Pregnant women

- Offer screening if due or overdue

- Women can be safely screened at any time during pregnancy

- Use correct implements (do not insert a cytobrush or combi-brush into the cervical canal as they can cause bleeding & associated distress)

- Self-collection: not recommended in pregnancy

- Management: follows new guidelines for low, intermediate and higher risk outcomes

- Referral for colposcopy/gynae oncology review should not be deferred
Post Hysterectomy

VAGINAL SCREENING AFTER TOTAL HYSTERECTOMY

Total hysterectomy

- Normal prior screening history
- Treated HSIL (CIN2/3) with completed Test of Cure**
- Previously treated AIS by excision
- Abnormal screening with histologically confirmed HSIL (CIN2/3)
- Previous treatment for HSIL (CIN2/3) (prior to Test of Cure**) on routine surveillance with normal tests
- No known screening history

Benign gynaecological disease (prolapse, fibroids, menstrual problem)

- No cervical pathology
- Unexpected positive cervical pathology LSIL or HSIL
- No cervical pathology
- Unexpected positive cervical pathology LSIL or HSIL

AIS negative margins
- No cervical pathology

No follow-up
- Test of Cure**
- No follow-up
- Test of Cure**
- Annual co-testing indefinitely

Benign gynaecological disease (prolapse, fibroids, menstrual problem)

- No cervical pathology
- Unexpected positive cervical pathology LSIL or HSIL
- No cervical pathology
- Unexpected positive cervical pathology LSIL or HSIL

Regardless of findings
- No cervical pathology
- Unexpected positive cervical pathology LSIL or HSIL
- No cervical pathology
- Unexpected positive cervical pathology LSIL or HSIL

- Test of Cure**
- Test of Cure**
- Test of Cure**
- HPV test
- Test of Cure**

* HPV test to be taken from the vaginal vault 12 months after treatment & annually thereafter until the woman has tested negative on 2 consecutive occasions, after which she does not need further testing

** Until sufficient data become available that may support a policy decision that cessation of testing is appropriate

Immune Deficient

MANAGEMENT OF SCREEN DETECTED ABNORMALITIES IN IMMUNE-DEFICIENT WOMEN

**Immune-deficient**

Screening HPV test 3 yearly

HPV detected (any type)

Colposcopy
Reflex LBC result

Assess entire lower anogenital tract

Histologically confirmed abnormalities managed according to these guidelines

- HSIL (CIN 2/3)
  - Excisional treatment recommended
  - Test of Cure** completed
  - Return to routine HPV testing every 3 years

- AIS
  - Type 3 excisional TZ
  - Annual co-test (HPV/LBC)*

No confirmed histological abnormality

Follow up based on HPV/LBC/colposcopy in accordance with these guidelines

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**Co-test (HPV and LBC) test 12 months after treatment & annually thereafter until the woman has had negative co-test on 2 consecutive occasions, after which she returns to routine 3-yearly screening

# Until sufficient data become available to support return to 3-yearly screening

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Women with early sexual activity and victims of child sexual abuse

- Women with first sexual activity < 14 years prior to vaccination plus victims of child sexual abuse: consider a single HPV test between 20 and 24 years of age on an individual basis
- Routine screening at 25 still safe in event of non-disclosure (a cohort study of young women would be useful to determine risk in this group)
- Women at any age with symptoms suggestive of cervical cancer: perform a co-test (HPV and LBC) and refer for appropriate investigation
Symptomatic women

ABNORMAL BLEEDING

• CO TEST recommended

• CO TEST = HPV plus cytology (clinician decision/request)
INVESTIGATION OF WOMEN WITH ABNORMAL VAGINAL BLEEDING

Women with abnormal vaginal bleeding

- Consider sexual health history & perform appropriate tests
- Postcoital bleeding (PCB)
  - Co-test (HPV & LBC)
    - HPV not detected & negative LBC
      - Single episode PCB (Pre-menopausal women)
      - Clinically normal cervix
        - No colposcopy required (advise to see healthcare professional if symptoms persist)
      - Recurrent or persistent PCB (any age)*
        - Refer for gynaecological assessment*
    - HPV detected (any type) &/or abnormal LBC result
      - Refer for gynaecological assessment (regardless of test result)*
- Unexplained intermenstrual bleeding
  - Co-test (HPV & LBC)
- Post-menopausal bleeding
  - Co-test (HPV & LBC)

* May include colposcopy
# If significant delay (3–6 months from the previous test) following original HPV/LBC test, a repeat LBC could be considered

National Cancer Screening Register

- Linked to HPV register
- Used to issue invitations/reminders
- Full history from vaccination-diagnosis
- Colposcopy and pathology data

Monitoring and service improvement

- One woman = One record
Quality and Safety

• QSMC
  – Quality and Safety Monitoring Committee
  – Chair: Professor David Roder

• Protocols for monitoring the NCSP

• Quality Framework
  – Principles of quality control
  – Program standards
  – Colposcopy standards
Further information:

NCSP 2016 Guidelines
www.msac.gov.au
www.cancerscreening.gov.au

Email: Cervicalrenewal@health.gov.au
National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding

**Important note:** These guidelines have been made available to educate health professionals and enable them to prepare for the transition to the renewed National Cervical Screening Program in December 2017. They are for reference purposes only until the renewed program is implemented.

**Foreword**

**Introduction**

**Summary of recommendations**

1. Cervical cancer in Australia

2. The rationale for primary HPV screening

3. Terminology
   - HPV testing terminology
   - Cytology and AMBS 2004 terminology for reporting cervical cytology
NATIONAL CERVICAL SCREENING PROGRAM:

Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.
Further information

National Prescribing Service
• On line education modules
• Practical training modules
(For all CST providers)

Cancer Council Australia
• On line education clinical scenarios
• (For GPs, O&G specialists, Nurses and others)

Department of Health Australia
• Cancer screening website, Publications for all

Iris Education
• Recorded presentations and powerpoints
Primary HPV screening program will lead to

Up to 30%

Fewer cases of cervical cancer

Fewer deaths from cervical cancer
• 80 – 90% of people will be exposed to infection at some point
• Most likely outcome of infection is spontaneous resolution

However:
• Most significant infectious cause of cancer in Australia
  (1706 cases in 2010¹)
• Unprecedented opportunity for primary and secondary prevention

¹. Antonsson et al. ANZ J Public Health. 2015