The iPap trial: HPV self-sampling for underscreened women

Dorota Gertig
Medical Director, VCCR
Urine-based HPV test ‘feasible alternative for cervical cancer screening’

A new study published in The BMJ claims that a simple urine test for human papillomavirus (HPV), the main cause of cervical cancer, could increase screening uptake among women by offering them a non-invasive option.

The most common screening method for human papillomavirus (HPV) is a Pap smear test, also known as a smear test. This involves a doctor or nurse taking samples from the opening of a woman’s cervix, before sending them to a laboratory to be analyzed for abnormalities.

The American Cancer Society claims that between 1955 and 1990, death rates from cervical cancer fell by almost 90% due to increased Pap testing. But despite this success, screening uptake in recent years has been low.

Current screening recommendations from the US Preventive Services Task Force (USPSTF) state that women between the ages of 21 and 65 should have a Pap test every 3 years. However, figures show the percentage of women following these recommendations stands at 37%—well below the target of 92%. In the UK, cervical screening rates have fallen below 83%.

Remained was a non-invasive HPV test could offer an effective, non-invasive screening option for cancer.

A new home-based HPV test is launched in SA

New HPV home test provides solution to growing cancer statistics

A new cervical cancer screening test called test in vivo is transforming the way in which women are tested for the disease. The test has recently released a new self-collection test for HPV, the virus which causes cervical cancer, which has received widespread acceptance from the medical industry, and is claimed to provide greater accuracy from conventional tests. It also provides the added appeal of enabling women to test themselves at home.

According to the latest health organization, approximately 600,000 South African women are diagnosed with cervical cancer each year, with approximately 11,000 women dying from the disease in the same period. In the last 10 years cervical cancer is on the rise, with 20% of South African women have ever been below the age of 35. "There is no doubt that the HPV test is a more effective in detecting possible cervical cancer cases than a pap smear or a gold standard," says Prof. O. Greer, Principal investigator, Pretoria Academic Hospital and Adjunct Professor, Oral Oncology and Gynecology, Head of Gynecologic Oncology Unit, University of Pretoria.
Outline

• Role and acceptability of self-sampling
• Validity of self-sampling
• iPap trial
• Focus group findings
• Preliminary results
Pap smear vs. HPV testing

- Cervical cytology – conventional Pap smear or liquid-based+/-image read
  - Resource intensive
  - Maintenance of skills
  - Quality assurance requirements
  - Relatively low sensitivity but high specificity

- HPV testing – pooled/partial genotyping;
  - More sensitive than a Pap
  - Better negative predictive value
  - Has an opportunity for self-sampling
Table 9: Screening history of Victorian women diagnosed with cervical cancer for the period 1 January 2008 to 31 December 2008.

<table>
<thead>
<tr>
<th>Screening History</th>
<th>Invasive Squamous cell carcinoma Number (%)</th>
<th>Other invasive cervical cancer Number (%)</th>
<th>Invasive Sub-Total</th>
<th>Micro-invasive Sub-Total</th>
<th>Invasive &amp; Micro-invasive Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Never screened</td>
<td>46 61%</td>
<td>36 56%</td>
<td>82 59%</td>
<td>13 32%</td>
<td>95 52%</td>
</tr>
<tr>
<td>B. Lapsed screeners (last screen greater than 2.5 years)</td>
<td>17 22%</td>
<td>14 22%</td>
<td>31 22%</td>
<td>9 22%</td>
<td>40 22%</td>
</tr>
<tr>
<td>C. Adequately screened (last screen within 2.5 years)</td>
<td>5 7%</td>
<td>12 19%</td>
<td>17 12%</td>
<td>11 27%</td>
<td>28 15%</td>
</tr>
<tr>
<td>D. Delayed diagnosis</td>
<td>3 4%</td>
<td>1 2%</td>
<td>4 3%</td>
<td>7 17%</td>
<td>11 6%</td>
</tr>
<tr>
<td>E. Not eligible</td>
<td>5 7%</td>
<td>1 2%</td>
<td>6 4%</td>
<td>1 2%</td>
<td>7 4%</td>
</tr>
<tr>
<td>Total</td>
<td>76 100%</td>
<td>64 100%</td>
<td>140 100%</td>
<td>41 100%</td>
<td>181 100%</td>
</tr>
</tbody>
</table>

1 Women over 70 years and with a negative screening history are outside the eligible range for the screening program. Refer to the National Cervical Screening Program at www.cancerscreening.gov.au

HPV Vaginal Self-sampling

May overcome barriers to screening

Lack of access to health care

Barriers to Pap test include embarassment, discomfort, cultural issues

Self-sampling at home may therefore increase participation in screening

Alternative option for underscreened women
What is HPV self-sampling?

Self-sampling (SS)

Physician sampling (PS)

Arbyn, M (2007). Cytopathology
HPV self-sampling improves participation

### Table 1: Review of trials comparing participation in HPV self-sampling (SS) and reminder letter to attend for a Pap test

<table>
<thead>
<tr>
<th>Study</th>
<th>Area</th>
<th>Eligibility</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Device</th>
<th>Test, HPV+</th>
<th>Participation</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sancho-Gamier</td>
<td>France</td>
<td>35-69 yrs; no Pap smear for ≥2 years; did not respond to first invitation</td>
<td>HPV SS kit*</td>
<td>Standard invitation</td>
<td>Dacron swab</td>
<td>Abbott real Time, 17.6%</td>
<td>18.3%</td>
<td>41%</td>
</tr>
<tr>
<td>Szarewski</td>
<td>UK</td>
<td>25-65 yrs; ≥6 years overdue</td>
<td>HPV SS kit</td>
<td>Standard invitation</td>
<td>Cotton swab</td>
<td>HClI, 8.3%</td>
<td>10.2%</td>
<td>87.5%</td>
</tr>
<tr>
<td>Wikstrom</td>
<td>Sweden</td>
<td>39-60 yrs; ≥6 years overdue</td>
<td>HPV SS kit* + 2nd reminder</td>
<td>Standard invitation</td>
<td>Qvintip</td>
<td>HClI, 6%</td>
<td>39%</td>
<td>98%</td>
</tr>
<tr>
<td>Rossi</td>
<td>Italy</td>
<td>35-65 yrs; 3–5 months overdue</td>
<td>HPV SS kit</td>
<td>2 control arms</td>
<td>Pantarhei device</td>
<td>HClI, 1 = 21.8%, 4 = 6.5%</td>
<td>1 = 19.6%, 3 = 13.9%, 2 = 8.7%, 4 = 14.9%</td>
<td>1 = 91%</td>
</tr>
<tr>
<td>Virtanen</td>
<td>Finland</td>
<td>30-60 yrs; did not respond to primary invitation</td>
<td>HPV SS kit</td>
<td>Reminder letter</td>
<td>Delphi Screener</td>
<td>HClI, 12.3%</td>
<td>32%</td>
<td>86.6%</td>
</tr>
<tr>
<td>Virtanen</td>
<td>Finland</td>
<td>30-60 yrs; did not respond to primary invitation</td>
<td>HPV SS kit*</td>
<td>Reminder letter</td>
<td>Delphi Screener</td>
<td>HClI, 12.3%</td>
<td>32%</td>
<td>86.6%</td>
</tr>
<tr>
<td>Gok</td>
<td>Netherlands</td>
<td>30-60 yrs; did not respond to invitation or 6 month reminder</td>
<td>HPV SS kit*</td>
<td>Second reminder letter*</td>
<td>Delphi screener</td>
<td>HClI, 10.3%</td>
<td>26.6%</td>
<td>90.4%</td>
</tr>
<tr>
<td>Bais</td>
<td></td>
<td>30-50 yrs; did not respond to invitation or 6 month reminder</td>
<td>HPV SS kit</td>
<td>Second reminder letter</td>
<td>Viba-brush + collection tube</td>
<td>GP 5+/6+ PCR, 8%</td>
<td>34.2%</td>
<td>86%</td>
</tr>
</tbody>
</table>

*Pre-invitation letter informing of the arrival of the kit or reminder, and in Finland trial, this letter included “opt out” option.
Self-collected vs Physician-collected

• Five reviews comparing SC samples with PC samples
  – 2005 by Ogilvie et al: 12 studies; kappa: ranging 0.45-1
  – 2007 by Petignat et al: 18 studies, kappa: 0.66
  – 2007 by Stewart et al: 19 studies, kappa: >half studies 0.60
  – 2011 by Schmeink et al: 21 studies, kappa: 0.73

• All studies concluded that SC samples were comparable to PC samples and an alternative for women who circumvent gynaecological examination
  – 2014 by Arbyn et al: 36 studies, sensitivity and specificity
    – Sen CIN2+, SC vs PC (76% vs 91%)
    – Sen CIN3+, SC vs PC (84% vs 95%)

• SC showed similar sensitivity to PC with PCR based test irrespective of the type of device used
The difference in HPV prevalence between the self-and-clinician collected sampling was not significantly different from zero, whatever sampling devices and diagnostic methods were used.

Petigant, P (2007). Gynaecologic Oncology

Fig. 2. Forest plot of prevalence differences for the 18 studies evaluating self-sampling versus physician-sampling for all HPV types.
# Sensitivity

<table>
<thead>
<tr>
<th>Device</th>
<th>Test*</th>
<th>Relative sensitivity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Screening</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girianelli et al, 2006&lt;sup&gt;39&lt;/sup&gt;</td>
<td>Brush</td>
<td>HC2</td>
</tr>
<tr>
<td>Holanda et al, 2006&lt;sup&gt;40&lt;/sup&gt;</td>
<td>Brush</td>
<td>HC2</td>
</tr>
<tr>
<td>Qiao et al, 2008&lt;sup&gt;43&lt;/sup&gt;</td>
<td>Brush</td>
<td>cHPV[.5]</td>
</tr>
<tr>
<td>Belinson et al, 2012&lt;sup&gt;51&lt;/sup&gt;</td>
<td>Brush</td>
<td>M-TOF</td>
</tr>
<tr>
<td>Zhao et al, 2012a&lt;sup&gt;55&lt;/sup&gt;</td>
<td>Brush</td>
<td>HC2</td>
</tr>
<tr>
<td>Zhao et al, 2012b&lt;sup&gt;55&lt;/sup&gt;</td>
<td>Brush</td>
<td>HC2</td>
</tr>
<tr>
<td>Zhao et al, 2012c&lt;sup&gt;55&lt;/sup&gt;</td>
<td>Brush</td>
<td>HC2</td>
</tr>
<tr>
<td>Guan et al, 2013&lt;sup&gt;58&lt;/sup&gt;</td>
<td>Brush</td>
<td>LA</td>
</tr>
<tr>
<td>Nieves et al, 2013&lt;sup&gt;61&lt;/sup&gt;</td>
<td>Brush</td>
<td>HC2</td>
</tr>
<tr>
<td>Wright et al, 2000&lt;sup&gt;33&lt;/sup&gt;</td>
<td>Swab</td>
<td>HC2</td>
</tr>
<tr>
<td>Belinson et al, 2001&lt;sup&gt;34&lt;/sup&gt;</td>
<td>Swab</td>
<td>HC2</td>
</tr>
<tr>
<td>Salmeron et al, 2003&lt;sup&gt;36&lt;/sup&gt;</td>
<td>Swab</td>
<td>HC2</td>
</tr>
<tr>
<td>Szarewski et al, 2007&lt;sup&gt;42&lt;/sup&gt;</td>
<td>Swab</td>
<td>HC2</td>
</tr>
<tr>
<td>Longatto-F et al, 2012&lt;sup&gt;53&lt;/sup&gt;</td>
<td>Tampon</td>
<td>HC2</td>
</tr>
<tr>
<td><strong>Subtotal</strong> (I&lt;sup&gt;2&lt;/sup&gt;=74.7%; p&lt;0.001)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Arbyn et.al Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis *Lancet Oncology* 2014
### Specificity

<table>
<thead>
<tr>
<th>Device</th>
<th>Test</th>
<th>Relative specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Screening</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girianelli et al, 2006</td>
<td>Brush</td>
<td>0.97 (0.95–0.99)</td>
</tr>
<tr>
<td>Holanda et al, 2006</td>
<td>Brush</td>
<td>0.92 (0.87–0.98)</td>
</tr>
<tr>
<td>Qiao et al, 2008</td>
<td>Brush</td>
<td>0.98 (0.95–1.00)</td>
</tr>
<tr>
<td>Belinon et al, 2012</td>
<td>Brush</td>
<td>0.98 (0.97–0.99)</td>
</tr>
<tr>
<td>Zhao et al, 2012a</td>
<td>Brush</td>
<td>0.97 (0.94–1.01)</td>
</tr>
<tr>
<td>Zhao et al, 2012b</td>
<td>Brush</td>
<td>0.99 (0.95–1.02)</td>
</tr>
<tr>
<td>Zhao et al, 2012c</td>
<td>Brush</td>
<td>0.98 (0.96–1.01)</td>
</tr>
<tr>
<td>Guan et al, 2013</td>
<td>Brush</td>
<td>1.00 (0.89–1.12)</td>
</tr>
<tr>
<td>Nieves et al, 2013</td>
<td>Brush</td>
<td>0.98 (0.96–1.00)</td>
</tr>
<tr>
<td>Wright et al, 2000</td>
<td>Swab</td>
<td>0.99 (0.95–1.02)</td>
</tr>
<tr>
<td>Belinon et al, 2001</td>
<td>Swab</td>
<td>1.01 (0.98–1.03)</td>
</tr>
<tr>
<td>Salmeron et al, 2003</td>
<td>Swab</td>
<td>0.98 (0.97–0.99)</td>
</tr>
<tr>
<td>Szarewski et al, 2007</td>
<td>Swab</td>
<td>0.97 (0.93–1.01)</td>
</tr>
<tr>
<td>Longatto-F et al, 2012</td>
<td>Tampon</td>
<td>1.01 (1.00–1.02)</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td>0.98 (0.97–0.99)</td>
</tr>
</tbody>
</table>

Advantages of dry sample

• Cheap
• Safe in home environment
• Easy to process
• Feasible for large-scale implementation of self-sampling
• Low resource settings
• Acceptable
Comparison of dry vs wet swabs

Aim:
• To evaluate if a cervical sample taken with a flocked swab and placed in a dry tube (dry sample) is suitable for HPV DNA testing using a PCR based (Roche Cobas® 4800 HPV Test) test compared to the standard practice of a cervical sample taken with a cyto-broom and directly into liquid media PreservCyt® Solution (Hologic Corp.) (wet sample)

Objectives:
• To compare HR HPV detection in dry and wet samples
• To determine agreement in HR HPV detection between dry and wet samples
• To estimate the sensitivity (95% CI) of dry sample considering wet samples as the reference standard
Informed consent from women coming to dysplasia clinic prior to appointment

Physician collected 2 cervical samples, one wet and one dry, order randomised (50:50)

Colposcopy plus usual medical care +/- biopsy not influenced by HPV result

Picked by courier as per routine

“Dry sample” (swab), kept at ambient room temperature for 1 week then placed in 2ml PreservCyt media and tested as per usual practice

“Wet sample” (brush), kept at ambient room temp for 1 week and tested as per usual practice

At VCS laboratory

PCR-based cobas test

N=209 pairs

Invalid

HPV16/18

Other HPV+ (not 16/18)*

HRHPV-

*(31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68)

Any HRHPV+
# Results – HR HPV detection

<table>
<thead>
<tr>
<th>HPV types</th>
<th>Dry sample (n=209)</th>
<th>Wet sample (n=209)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>HPV16/18</td>
<td>22</td>
<td>10.5 (6.7-15.5)</td>
</tr>
<tr>
<td>Other HPV types (not 16/18)</td>
<td>60</td>
<td>28.7 (22.7-35.4)</td>
</tr>
<tr>
<td>Any HR HPV</td>
<td>82</td>
<td>39.2 (32.6-46.2)</td>
</tr>
</tbody>
</table>

• None of the women were concurrently positive for HPV16 (n=19) and HPV18 (n=3)
Results – Sensitivity of dry & wet samples when combined positive in either sample type (ref standard)

<table>
<thead>
<tr>
<th>HPV types</th>
<th>Sensitivity</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dry</td>
<td>Wet</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n/Total</td>
<td>% (95% CI*)</td>
<td>n/Total</td>
</tr>
<tr>
<td>HPV16/18</td>
<td>22/23</td>
<td>95.7 (86.9-100)</td>
<td>22/23</td>
</tr>
<tr>
<td>Other HPV types (not 16/18)</td>
<td>60/69</td>
<td>86.9 (78.3-94.2)</td>
<td>65/69</td>
</tr>
<tr>
<td>Any HR HPV</td>
<td>82/92</td>
<td>89.1 (81.5-95.7)</td>
<td>87/92</td>
</tr>
</tbody>
</table>

• Wet samples also missed one case of HPV18

*CI derived by bootstrapping using 1000 repetitions
Validation study summary

• HPV detection was similar in dry and wet samples
• Dry samples (flocked swab) showed almost perfect agreement with wet samples (cyto-broom) (kappa=0.94 for HPV16/18)
• Sensitivity of dry samples was high when wet samples were the reference standard (Sen=95.5% for HPV 16/18)
• Sensitivity of dry and wet samples were exactly the same when HPV positive in either sample type was the reference standard (Sen=95.7% for HPV 16/18)
• 209/210 dry samples had a valid HPV result

• Dry samples kept at ambient room temperature for one week perform as well as wet samples using PCR based test
iPAP trial

- Randomised trial comparing mailing of an vaginal HPV self-sample kit to a cervical screening reminder letter among 16,000 Victorian underscreened and never screened women
- Funded by NHMRC 2013.
iPAP trial aims

1. Whether offering home-based HPV SS increases participation compared to reminder letters for a Pap test

2. Estimate proportion of women who have a +HPV test who undergo further investigation

3. Document women’s experience with home-based HPV SS using flocked swabs, and their willingness to participate in self-sampling screening in future

4. Explore women’s reasons for not returning a completed HPV SS kit
Design overview

*Design*: RCT stratified by never-and-underscreened (7:1 ratio)

- **Intervention**: HPV SS kit (n=14,280)
- **Comparison**: Reminder letter for Pap (current policy) (n=2,040)

*Participants*: Victorian women, 30-69 years

- **Never screened**: no record of a Pap test in the Registry (*VCCR will be linked with the Victorian Electoral Roll*)
- **Underscreened**: last recorded Pap test is ≥5 years (*VCCR*)

*Primary outcome*: Uptake of offer

- **Return** of completed SS kit in the HPV SS
- **Notification** of Pap test to the Registry

*Secondary outcome*: +ve HPV women undergo further testing
Focus groups: HPV SS enablers

Motivating factors are
• Cost (free)
• Convenience (home based)
• Anticipated less pain or discomfort

Valued for
• Personal relevance
• Establishing personal susceptibility

“It’s not embarrassing you just do it yourself. (30-49, Never)

“I pretty much decided when I read the first line of the letter......test at home” (30-49, never-screened)

“Brilliant, very good, better than nothing, good, easier, convenient, private, able to be comfortable, fantastic, I think it’s great, thought it was a terrific idea, like the bowel kit. (50-69, Under)”
Focus groups: HPV SS barriers

• Concern about accuracy / lack of confidence it was equivalent to as a physician performed screening test

• Researchers noted a lack understanding between the difference of HPV and Pap tests

• More information required about the organisation providing the test

“When it’s done by the doctor you know you feel it’s being done correctly” (50-69, Under)

“The convenience of it is definitely ideal and very Inviting but I think it’s the accuracy that blocks it off.” (30-49, Under)
Focus groups - conclusion

• Positive response to iPap as it overcame barriers
• Groups identified which information was important to emphasise
• The pre-invitation letters are crucial
• More information about who was providing the test

“brilliant”
“convenient”
“easier”
“private”
Methods: Procedure in self-sampling arm

1. **Mail out #1**
   - 3 weeks
   - Pre-invitation letter

2. **Mail out #2**
   - Up to 12 weeks
   - HPV SS kit
     - Invitation letter
     - Pathology information form
     - Instruction sheet
     - Information brochure
     - Post-paid envelope
     - Dry flocked swab

3. **Mail out #3**
   - Questionnaire
     - Experience SS
     - Reasons not returning kit
     - Willingness to participate in SS

**Pathology info form:**
1. Country of birth
2. Indigenous
3. Hysterectomy
4. Pregnancy
5. Previous Pap
6. GP contact

1. **OPT-OUT**
2. Update record
Intervention Arm: Both Never and Under Screened Women: Flow Chart: Clinical management

16,000 women 30-69 years with no record of a Pap test in the Pap test Registry (matched from VEC), or lost Pap test ≥5 years (from VCCR records). Randomised 7:1 to receive mailout either:

- Home-based HPV self-sampling (Invitation letter + RR) N=14,000
  - Kits not returned to VCS (Non-responders)
  - Kits returned to VCS (Responders)
  - New kits mailed for re-testing
  - VCCR Usual Practice
  - HPV testing and typing
  - Unsatisfactory HPV
    - HPV 16/18 (≥45)
    - Other oncogenic HPV+
    - Negative oncogenic HPV
      - High-grade
      - Low-grade
      - Negative
      - Unsatisfactory
        - Non-compliant
        - Specialist
        - GP
        - Follow-up
        - Colposcopy
        - Pap smear
        - Reminder for 2 yearly Pap test as per national guidelines and monitoring through VCCR
        - Managed as per the National Policy.

- Current practice (Reminder letter for Pap test) N=2,000
  - No record of Pap test (Non-responders)
  - Pap test (Responders)
  - VCCR Usual Practice
  - Pap smear

*As women will be >80 years and no prior Pap in 8 years they will be referred for colposcopy as per Guidelines
iPAP Timeline

• Ethics approval April 2013
• Focus groups July 2013
• IT changes, finalise resources, selection of HPV test November 2013
• Matching with VEC electoral roll
• Recruitment April-July 2014
• 6 month participation completed
• Followup of women testing positive
• Data analysis 2015
## Randomisation & interim participation

<table>
<thead>
<tr>
<th>Stage</th>
<th>Pap reminder arm</th>
<th>Self-sampling intervention arm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>apparently never-screened</td>
<td>apparently under-screened</td>
</tr>
<tr>
<td>Randomised</td>
<td>1,020</td>
<td>1,020</td>
</tr>
<tr>
<td>Received invitation letter</td>
<td>1,014</td>
<td>1,011</td>
</tr>
<tr>
<td>Refused iPap</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Exclusions *</td>
<td>111</td>
<td>213</td>
</tr>
<tr>
<td>Returned self-sample swab</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Had a pap test **</td>
<td>51</td>
<td>58</td>
</tr>
<tr>
<td>Participation @ 5 months since last mailout</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pap participation % of eligible</td>
<td>5.6%</td>
<td>7.2%</td>
</tr>
<tr>
<td>Pap participation % intention to treat</td>
<td>5.0%</td>
<td>5.7%</td>
</tr>
<tr>
<td>HPVSS participation % of eligible</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HPVSS participation % intention to treat</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total Participation (Pap or HPVSS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– % of eligible</td>
<td>5.6%</td>
<td>7.2%</td>
</tr>
<tr>
<td>– % intention to treat</td>
<td>5.0%</td>
<td>5.7%</td>
</tr>
</tbody>
</table>

* Includes RTS and those ineligible as self reporting recently screened, pregnant, left Victoria, cancer, deceased and other
** may include recent screeners
HPV self-sampling interim results

<table>
<thead>
<tr>
<th>HPV Self-sampling result</th>
<th>apparently never-screened</th>
<th>under-screened</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no.</td>
<td>%</td>
</tr>
<tr>
<td>Negative</td>
<td>1046</td>
<td>90.1%</td>
</tr>
<tr>
<td>Positive 16 or 18 HPV (high risk)</td>
<td>32</td>
<td>2.8%</td>
</tr>
<tr>
<td>Positive other HPV (intermediate risk)</td>
<td>73</td>
<td>6.3%</td>
</tr>
<tr>
<td>Unsatisfactory *</td>
<td>10</td>
<td>0.9%</td>
</tr>
<tr>
<td>Grand Total</td>
<td>1161</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

*38 samples were tested and had an unsatisfactory result. As per the protocol the laboratory tested all samples that they believed to be opened or used. Only “true” unsatisfactory results are counted in the table, where a woman appeared to return a valid test and wasn’t ineligible due to hysterectomy etc. Two women had repeat unsatisfactory HPVSS results and have had subsequent cervical screening (their unsatisfactory result is only counted once). Unsatisfactory results which were retested and provided a valid result are not included in this figure.

Preliminary findings, not for citation or circulation
Data prepared 18.02.15
Subsequent Pap Test Result for HPV positive women (n=115) ongoing followup

To date 80% of women have had some GP/Specialist followup

<table>
<thead>
<tr>
<th>Subsequent Pap Test Result</th>
<th>Positive HPV 1618</th>
<th>Positive HPV Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no.</td>
<td>%</td>
</tr>
<tr>
<td>Possible Invasion</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>High Grade result</td>
<td>7</td>
<td>20.6%</td>
</tr>
<tr>
<td>possible high grade result</td>
<td>1</td>
<td>2.9%</td>
</tr>
<tr>
<td>low grade result</td>
<td>6</td>
<td>17.6%</td>
</tr>
<tr>
<td>Negative</td>
<td>18</td>
<td>52.9%</td>
</tr>
<tr>
<td>In processing</td>
<td>2</td>
<td>5.9%</td>
</tr>
<tr>
<td>Grand Total</td>
<td>34</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Preliminary findings, not for citation or circulation
Data prepared 18.02.15
Summary

• HPV self-sampling is an acceptable alternative for underscreened women
• At least as accurate as cytology, slightly less sensitive to physician collected sample (unless PCR)
• SS improved participation cf reminder for Pap and has potential to reach never and underscreened women
• Ensuring follow up is critical
• Australian renewal proposes self-sampling in health care settings; however, home-based SS may have a role in targeted campaigns
Cervical screening renewal: self-sampling

- PIP payments adjusted to relate to use of HPV self-sampling testing in a health care setting and also adjusted to reflect the longer recommended intervals in the program.
- MBS item for HPV testing is adjusted to reflect the possibility of self-sampled collection in a health care setting for underscreened women.
- Limited to use in healthcare settings that can provide:
  - a) patient counselling and clinical interpretation of results
  - b) patient follow-up and confirmatory testing for positive results when required
  - c) testing in a safe environment with infection control procedures
- Questions about implementation to be addressed
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