Colposcopy vs. HR-HPV testing to identify persistent/recurrent cervical high-grade lesions post-treatment: final results of the CoHIPP trial

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Disclosures

• I was a site PI for the Merck nonavalent vaccine trial
Acknowledgments

<table>
<thead>
<tr>
<th>Study team</th>
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<tr>
<td>H Trottier, F Coutlée, M Abrahamowicz, AC Guédon, V Brunetti, C Danieli, N Zanré, J Lacaille</td>
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<thead>
<tr>
<th>Colposcopy unit (City)</th>
<th>Site PI</th>
<th>Colposcopy unit (City)</th>
<th>Site PI</th>
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<tr>
<td>Juravinski Cancer Center (Hamilton)</td>
<td>L Elit</td>
<td>CHUM. Hôpital Notre-Dame (Montreal)</td>
<td>P Sauthier</td>
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<td>Vancouver General Hospital (Vancouver)</td>
<td>T Ehlen</td>
<td>CHUS (Sherbrooke)</td>
<td>P Bessette</td>
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<td>CHUM. Hôpital St-Luc (Montreal)</td>
<td>MH Mayrand</td>
<td>Regina General Hospital (Regina)</td>
<td>L Brydon</td>
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<td>Jewish General Hospital(Montreal)</td>
<td>S Lau</td>
<td>Foothills Medical Center (Calgary)</td>
<td>B. Hauck</td>
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<td>QEII Health Sciences Centre (Halifax)</td>
<td>J Bentley</td>
<td>CHUQ (Quebec city)</td>
<td>M Plante</td>
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<td>Princess Margaret Hospital (Toronto)</td>
<td>J. Murphy</td>
<td>CSSS de Chicoutimi (Chicoutimi)</td>
<td>P Fisch</td>
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<td>Eastern Health (St. John’s)</td>
<td>P. Power</td>
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Background

• In Canada, waiting times for diagnostic colposcopy can be problematic

• The introduction of HPV triage for ASC-US cytology has decreased the number of women referred to colposcopy clinics for borderline smears

• Concurrently, the proportion of women followed up for surveillance after treatment of HSIL/AIS has increased
Importance of post-treatment follow-up

• Treatment success rate: 75-99%
• Most failures occur within 2 years, but risk remains higher for up to 6 years
• Rates of cervical cancer of 37/100,000 (compared to baseline risk of 6/100,000)
• Standardized mortality ratio of 2.35

Melnikow JNCI 2009; Strander BMJ 2014
Sensitivity of strategies to identify persistent/recurrent HSIL/AIS

- Colposcopy: ?
- Pap smear: 70-72% versus HR-HPV testing: 94-95%
  - Several small studies
  - No RCT
- Algorithms based on risk factors such as age, smoking, size of lesion, margins, not clinically helpful

Thompson, ANZJOG 2013; Smart, ANZJOG 2010 Cuschieri, JCV2016; Costa, ecancermedicalscience 2015
Objective

• To determine if a strategy based on HPV testing is more sensitive than routine follow-up to identify HSIL/AIS treatment failures in Canada
Design and population

• Design: open label randomized controlled trial

• Inclusion criteria:
  • Age for consent, treated for biopsy proven CIN 2, 3 or AIS, planned excisional treatment

• Exclusion criteria:
  • Has been treated for cervical cancer or pre-cancer in the past; known immunosuppression or immunodeficiency; planned hysterectomy
Study visits and procedures

- **Visit 1:** Treatment
- **Visit 2:** Randomization if HSIL/AIS on LEEP/cone
  - Standard follow-up: colposcopy and/or Pap and/or Biopsy and/or endocervical curettage, excluding HR-HPV testing
  - Intervention group: HR-HPV testing, using Hybrid Capture 2, colposcopy only if HR-HPV positive
- **Visit 3 and 4:**
  - Colposcopy, biopsy and ECC, both groups
Statistical analysis

• Intention to treat analysis
• Test performance assessed by GEE, taking into account within center correlation.
• Different outcomes were analysed separately
• 95% confidence intervals for the difference between groups were estimated using bootstrap sampling
Results
Test performance, by study group (2)

<table>
<thead>
<tr>
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<th>Routine follow-up “low threshold”</th>
<th>HR-HPV testing</th>
<th>Difference</th>
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<tbody>
<tr>
<td><strong>CONFIRMED PERSISTENT/RECURRENT HSIL/AIS</strong></td>
<td></td>
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<tr>
<td>Sensitivity, %</td>
<td>90.6</td>
<td>95.1</td>
<td>4.5 (-6.0; 15.2)</td>
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<tr>
<td>“Specificity”, %</td>
<td>72.8</td>
<td>82.2</td>
<td>9.5 (2.6; 11.8)</td>
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<tr>
<td><strong>PROBABLE PERSISTENT/RECURRENT HSIL/AIS</strong></td>
<td></td>
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<tr>
<td>Sensitivity, %</td>
<td>84.0</td>
<td>77.7</td>
<td>-6.3 (-20.4; 9.5)</td>
</tr>
<tr>
<td>“Specificity”, %</td>
<td>73.6</td>
<td>83.0</td>
<td>9.4 (3.2; 12.6)</td>
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Comparison to the literature

• Risk of recurrence: 4.0%-11.9% at 18-24 months years
• Proportion HPV+ at 6 months: 21%
• Sensitivity of HPV testing: 92-93%; Specificity of HPV testing: 76-81%
• Sensitivity of colposcopy: 47%, no added value, frequently unsatisfactory

(Kocken, Gynecol Oncol 2012; Hoffman SR IJC2017; Thompson ANZJOG 2013; Cuschieri, J clin virol 2016; Souter Gynecol Oncol 2006)
Conclusion

• Routine follow-up in a colposcopy clinic does not improve detection of HSIL/AIS treatment failure

• HR-HPV testing identifies women at risk, who can then be referred to colposcopy

• A strategy based on HR-HPV testing uses resources more efficiently, limits uncomfortable and invasive procedures, and prevents complications associated with repeated cervical treatment
Questions/Comments?