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

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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 37/100,00 (compared to baseline risk of 6/100,00)
- 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

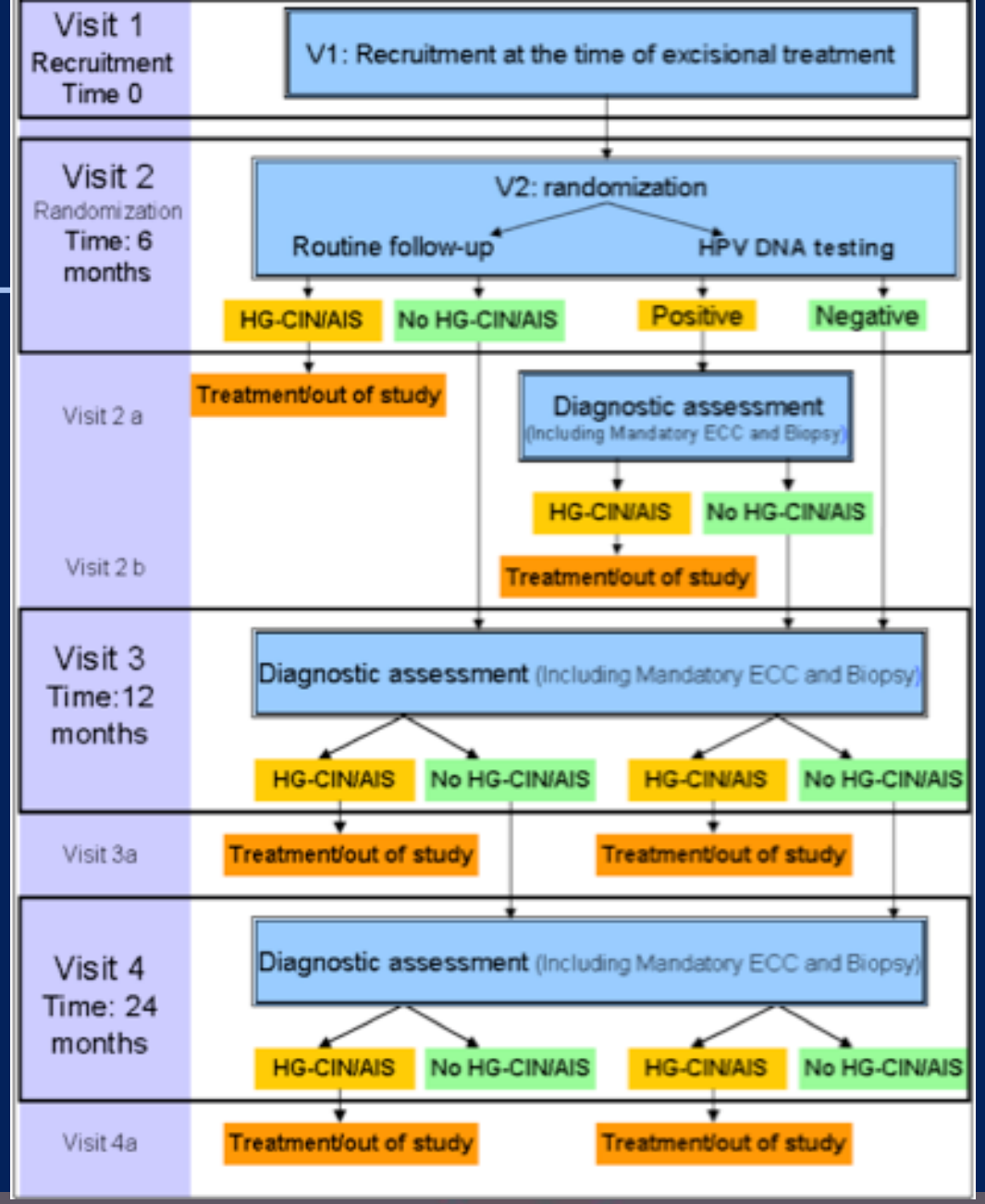
- To determine if a strategy based on HPV testing is more sensitive than routine follow-up to identify HSIL/AIS treatment failures in Canada

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)

	Routine follow-up "low threshold"	HR-HPV testing	Difference
CONFIRMED PERSISTENT/RECURRENT HSIL/AIS			
Sensitivity, %	90.6	95.1	4.5 (-6.0; 15.2)
"Specificity", %	72.8	82.2	9.5 (2.6; 11.8)
PROBABLE PERSISTENT/RECURRENT HSIL/AIS			
Sensitivity, %	84.0	77.7	-6.3 (-20.4; 9.5)
"Specificity", %	73.6	83.0	9.4 (3.2; 12.6)

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; Soutter 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?