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HPV FOCAL study: human papillomavirus testing for cervical cancer screening

Submission date 20/04/2007	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/04/2007	**Overall study status** Completed	
Last Edited 11/10/2021	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Cervical cancer is a type of cancer that develops in a woman's cervix (the entrance to the womb from the vagina). Almost all cases of cervical cancer are caused by the human papilloma virus (HPV). The aim of this study is to evaluate primary HPV testing for cervical cancer screening in an organized program setting in Canada.

Who can participate?
Women aged 25 to 65 attending a collaborating BC healthcare provider for regular cervical cancer screening (pap tests)

What does the study involve?
Participants have a cervical sample obtained from their usual health care provider. Upon receipt at the lab, the cervical sample (liquid based collection device) is randomly allocated to either HPV testing or cytology testing (Pap test, to detect abnormal cells that may develop into cancer if left untreated). Participants with negative results are recalled at either 2 years or 4 years after their first sample. Participants with positive results are managed according to a specific study protocol. The incidence of cervical cancer is measured after four years.

What are the possible benefits and risks of participating?
Participants have access to close monitoring and enhanced screening. Some participants may be recommended for colposcopies they would not have received outside of the study setting.

Where is the study run from?
BC Cancer (Canada)

When is the study starting and how long is it expected to run for?
August 2007 to December 2014

Who is funding the study?
Canadian Institutes of Health Research (Canada)

Who is the main contact?
1. Dr Andrew J Coldman (scientific)
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Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00461760

Protocol serial number
MCT-82072

Study information

Scientific Title

A multicentre randomised controlled parallel group evaluation of Human PapillomaVirus testing for cervical cancer screening

Acronym
HPV FOCAL

Study objectives
1. Establish efficacy of human papillomavirus (HPV) testing as stand alone screening test with cytology triage of HPV positive women
2. Establish an appropriate screening interval for HPV negative women
3. Determine cost-effectiveness of HPV testing as a primary screening test

Ethics approval required
Old ethics approval format

Ethics approval(s)
Research Ethics Board of the University of British Columbia-British Columbia Cancer Agency, 03 /04/2007, ref: H06-04032

Study design
Multicentre three-arm randomised parallel-trial on diagnostic strategy with data analyst blinding

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Human papillomavirus (HPV), cervical cancer

Interventions
1. HPV testing two-year safety check arm - liquid based cytology (LBC) sample tested only for HPV:
Those who are HPV negative will be screened again in two years for their exit screen, only with cytology so the results correlate with women in the control arm. Those who are HPV positive on the initial screening test will be managed the same way as HPV positive women in the four-year intervention arm.

2. HPV testing four-year intervention arm - 24. a.2.d. experimental intervention dose, duration, etc - LBC sample will only be tested for HPV:
HPV negatives will have their exit screen at four years (or earlier if deemed by Data Safety and Monitoring Committee) when they will be screened with HPV and cytology testing and those positive on either test referred for Colposcopy. HPV positive on their initial screen will have the residual of that specimen analysed with cytology.

Initial information at time of registration:
a. If cytology negative they will be recalled at six month intervals for HPV/cytology testing and referred for colposcopy if greater than or equal to abnormal squamous cells of undetermined significance (ASCUS-US) at any recall or persistently HPV positive after three recalls

Amended as of 12/03/2018:
2. a: If cytology negative they will be recalled at twelve month intervals for HPV/cytology testing and referred for colposcopy if greater than or equal to abnormal squamous cells of undetermined significance (ASCUS-US) at any recall or persistently HPV positive

b. If cytology is greater than or equal to ASCUS-US they will be immediately referred for colposcopy and managed according to those results.

Initial information at time of registration:
3. Control arm - Conventional cytology with liquid based cytology - 24. b.1.cd. control intervention dose, duration, etc:
Liquid based cytology sample processed for cytology and followed according to existing provincial guidelines. Recalled again at two years for their second routine screen and at four years for their exit screen where they will be screened with cytology and HPV testing.

Amended as of 19/03/2009:
3. Control arm - Conventional cytology with liquid based cytology -
On the basis of this result women will be managed as follows:
Within normal limits (negative results): Recalled for their next routine screen at 2 years, where the sample will undergo cytology testing. If negative again at the 2 year screen, recalled, for the exit screen at 4 years. At the 4 year exit screen, the sample obtained will undergo both HPV and cytology testing with those positive on either test being referred for colposcopy and then treated based on the colposcopy results.
ASC-H or greater than LSIL (12/03/2018: changed to greater than or equal to LSIL): (at recruitment visit or at the 2 year screen) will receive immediate colposcopy and treated based on the colposcopy results.
ASC-US: (at recruitment visit or at the 2 year screen) the residual of the specimen collected will undergo HPV testing. Follow-up based on the result of the HPV test:
a. HPV-positive: referred for immediate colposcopy and treated based on the colposcopy results
b. HPV-negative: recalled for repeat cytology testing in 12 months. If greater than or equal to ASC-US, referred for colposcopy and treated based on the colposcopy results. If cytology negative they will be returned to the routine screening pool for this arm.

Added 10/01/2011:
Recruitment to the safety arm will terminate 31/12/2010 and from that point forward, women will be randomized 1:1 into the cytology or intervention arms only. A total of ~28,000 women (11,000 each in the Control and Intervention arms respectively, and ~6,000 in the Safety arm) will be enrolled in the FOCAL trial.

Added 12/03/2018:
(Ethics board approved amendment 2011): After review and modifications to safety analysis plan, the overall sample size calculation was revised. Revising this calculation and using an 80% power threshold for the comparisons originally included, indicates that a sample size of ~9,140 subjects in the cytology and intervention arms is appropriate.

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)

Current primary outcome measures as of 12/03/2018:
1. CIN grade 3 or greater (CIN3+) detected over the four years post recruitment in the control and intervention arms evaluated and compared as a surrogate marker for estimating reductions in incidence of cervical cancer, measured at four years

Previous primary outcome measures:
1. Histologically confirmed cervical intraepithelial neoplasia (CIN) greater than or equal to grade two detected at two years in both the control and safety-check arms
2. CIN grade three (CIN3) or greater detected over the four years post recruitment in the control and intervention arms evaluated and compared as a surrogate marker for estimating reductions in incidence of cervical cancer, measured at four years
3. Detection of histologically confirmed greater than or equal to CIN3 in the participants allocated to six month re-testing, measured at two years
4. Total estimated cost per woman screened and total estimated cost per quality-adjusted life-year gained for each technology, measured at four years

Key secondary outcome(s))
Current secondary outcome measures:
1. Histologically confirmed cervical intraepithelial neoplasia grade 2 or greater (CIN2+) two detected at two years in both the control and safety-check arms
2. CIN2+ detected in the control and intervention arms over the four years post recruitment
3. Clearance of HPV infection in women who are HPV positive at recruitment, measured at two and four years
4. Detection of histologically confirmed greater than or equal to CIN3 in the participants allocated to 12 month re-testing, measured at two years
5. Evaluation of the impact of primary HPV testing on colposcopy services through evaluation of colposcopy referral rates in each arm through the trial follow-up period
6. Total estimated cost per woman screened and total estimated cost per quality-adjusted life-year gained for each technology, measured at four years

Previous secondary outcome measures:
Clearance of HPV infection in women who are HPV positive at recruitment, measured at two and four years

Completion date
31/12/2014

Eligibility

Key inclusion criteria
Current information as of 04/11/2008:
1. Women aged 25 to 65 years
2. Registered with MSP
3. Attending a collaborating BC healthcare provider for regular cervical cancer screening (pap tests)

Initial information at time of registration:
1. Women aged 25 to 65 years
2. British Columbia residents
3. Eligible for routine cervical screening

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
Current information as of 01/12/2009 (effective 25/11/2009):
1. Pap smear less than one year ago
2. Pregnant (at time of initial sample)
3. History of moderate to severe cervical intraepithelial neoplasia (greater than CIN2) requiring treatment less than 5 years ago
4. History of invasive cervical cancer at any time
5. Complete hysterectomy with cervix removal
6. Human immunodeficiency virus (HIV) positive or receiving immunosuppressive treatments
7. Unable or unwilling to sign the Information and Consent form

Information as of 04/11/2008:
1. Pap smear less than one year ago
2. Pregnant
3. History of moderate to severe cervical intraepithelial neoplasia (greater than CIN2) requiring treatment less than 5 years ago
4. History of cervical cancer at any time
5. Complete hysterectomy with cervix removal
6. Human immunodeficiency virus (HIV) positive or receiving immunosuppressive treatments
7. Received HPV vaccination
8. Unable or unwilling to sign the Information and Consent form

Initial information at time of registration:
1. Pregnant
2. History of cervical cancer
3. Hysterectomy
4. Human immunodeficiency virus (HIV) positive
5. Unable to give informed consent

Date of first enrolment
01/01/2008

Date of final enrolment
30/05/2012

Locations

Countries of recruitment

Canada

Study participating centre
BC Cancer
750 West Broadway
Vancouver
Canada
V5Z 4G8

Study participating centre
Cervical Cancer Screening Laboratory
686 West Broadway
Vancouver
Canada
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Study participating centre
BC Centre for Disease Control Public Health Laboratory
655 West 12th Ave
Vancouver
Canada
V5Z 4R4

Study participating centre
BC Cancer Pathology Laboratory
600 West 10th Avenue
Vancouver
Canada
-

Study participating centre
Royal Jubilee Pathology Laboratory
1952 Bay St.
Victoria
Canada
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Sponsor information

Organisation
Provincial Health Services Authority (Canada)

ROR
https://ror.org/01jvd8304

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (ref: MCT-82072)

Alternative Name(s)
Instituts de Recherche en Santé du Canada, The Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	preliminary results	24/03/2010		Yes	No
Results article	results	16/12/2015		Yes	No
Results article	results	03/07/2018		Yes	No

Results article		07/10/2021	11/10/2021	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes