

Pilot project on the use of HPV DNA testing as primary screening test for cervical cancer precursors

Submission date 01/03/2010	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 25/03/2010	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
Last Edited 25/03/2010	Condition category Cancer	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Pilot project on the use of HPV DNA testing as primary screening test for cervical cancer precursors: A multicentre randomised controlled trial

Acronym

PROPH

Study objectives

Available scientific data show that testing for the DNA of high-risk types of human papilloma virus (HPV) is more sensitive than cytology in detecting high-grade cervical intraepithelial lesions. Four randomised controlled trials (RCTs) conducted in industrialised countries showed that HPV based screening allows earlier detection than cytology of persistent high-grade intraepithelial lesions. One of them also showed increased effectiveness, compared to cytology, in preventing invasive cervical cancer. A RCT conducted in rural India showed increased effectiveness of HPV testing vs. cytology in preventing the incidence of advanced (stage 2+) cervical cancers and death from cervical cancer. RCT results suggest the same protection, independent of having used HPV testing alone or in combination with cytology as primary screening test. In addition protection seems to be the same if all HPV positive women are referred to colposcopy or if cytological triage (as described below) is applied. On the other hand the positive predictive value of referral to cytology is similar to or even better than that of cytology if stand alone HPV is used as primary screening test. Instead it decreases if HPV testing is used in combination with cytology as primary screening test and if all HPV positive women are referred to colposcopy. One RCT suggests relevant over-diagnosis of regressive CIN by HPV testing in women below age 35 years. Therefore stand-alone HPV testing for primary screening with cytological triage women aged 35 years or more seems an effective and safe screening strategy.

In this situation it is needed to evaluate the applicability and sustainability of this approach in routine practice and its impact on costs, participation to screening. The objective is also to define the best organisation, define the best methods of communication with women, methods for quality control and indicators for process monitoring.

Ethics approval required

Old ethics approval format

Ethics approval(s)

The ethics committee of University Hospital University Hospital San Giovanni Battista (Comitato Etico Interaziendale) approved on the 1st of February 2010 (ref: CEI/585)

Study design

Interventional pragmatic open label multicentre cluster randomised controlled study.

Primary study design

Interventional

Study type(s)

Screening

Health condition(s) or problem(s) studied

Cervical cancer screening

Interventions

Intervention arm. Women will have two cervical samples taken, first one for a conventional cytological smear (by Ayres spatula and cytobrush) and one for HPV testing (by brush). Initially only the HPV test will be performed. The Hybrid Capture 2 (HC2) test, that is designed to detect the DNA of 13 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68) will

be applied. The cut-off of 1 RLU will be used as recommended by the manufacturer. Women negative to HC2 will be referred to a new screening round at standard interval. The cytological smears of women who test positive to HC2 will be stained and interpreted. Cytology will be interpreted according to the Bethesda 2001 system. If cytology is found to be Atypical Squamous Cells of Undetermined Significance (ASCUS) or more severe, women will be referred directly to colposcopy. The remaining HPV positive women will be re-invited after one year to repeat the HP test. At such repeat, women will be referred to colposcopy if the HPV test is positive, otherwise referred to the new screening round at standard interval. The standard interval for this group will be initially 3 years but could be changed to 5 years according to national guidelines.

Colposcopies will be conducted according to standard protocols, as will treatments and repeats needed according to colposcopy and related histology and cytology results. Above this, women will be re-invited for new cytology and HPV test at yearly intervals until the HPV test will be negative for two consecutive tests. They will be referred to colposcopy if cytology is ASCUS or more severe.

Control arm. Women will be tested by conventional cytology and managed according to the standard protocols of participating centres.

Intervention Type

Other

Phase

Not Specified

Primary outcome(s)

1. Compliance to invitation to screening
2. Proportion screened of women who test positive to HPV and cytology
3. Proportion of screened women referred to new tests
4. Referral rate to colposcopy
5. Compliance to referral to new tests and to colposcopy
6. Positive Predictive value of colposcopy
7. Detection rate of histologically confirmed high-grade lesions (CIN2+ and CIN3+)

Key secondary outcome(s)

1. Cost of each screening approach
2. Time needed to provide test results
3. Anxiety caused a positive test result

Completion date

31/12/2012

Eligibility

Key inclusion criteria

Women aged 35 to 64 years resident in the relevant areas.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

Female

Key exclusion criteria

1. Women previously enrolled in the NTCC trial (ISRCTN81678807)
2. Women unable to provide informed consent

Date of first enrolment

22/03/2010

Date of final enrolment

31/12/2012

Locations**Countries of recruitment**

Italy

Study participating centre

Via San Francesco da Paola 31

Torino

Italy

10123

Sponsor information**Organisation**

CPO Piemonte (Italy)

ROR

<https://ror.org/05v0e5774>

Funder(s)**Funder type**

Government

Funder Name

Italian Ministry of Health (Italy) - Costs of each screening methods will be partly covered by the funds locally allocated for routine screening.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration