ISRCTN41319771 https://doi.org/10.1186/ISRCTN41319771

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	[_] Prospectively registered [_] Protocol
Registration date 25/03/2010	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 25/03/2010	**Condition category** Cancer	[_] Individual participant data [_] 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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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 event 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

Secondary study design
Randomised controlled trial

Study setting(s)

Other

Study type(s)
Screening

Participant information sheet
Not available in web format, please use contact details below to request a patient information sheet

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 measure
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 colpscopy
6. Positive Predictive value of colposcopy
7. Detection rate of histologically confirmed high-grade lesions (CIN2+ and CIN3+)

Secondary outcome measures

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

Overall study start date
22/03/2010

Completion date
31/12/2012

Eligibility

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

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
130,000

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
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Sponsor information

Organisation
CPO Piemonte (Italy)

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Sponsor type
Research organisation

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration