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Cervical cancer screening in younger women

Submission date 02/08/2019	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 12/12/2019	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 24/10/2023	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
HPV-based screening for cervical cancer is more effective than cytology-based screening but at younger ages, it entails strongly increased referral to colposcopy and plausibly increased over-diagnosis/treatment and is therefore not recommended below 30 years of age. We hypothesize that at such age using HPV testing as a filter to select the women who do not need screening until age 30 entails lower referral to colposcopy and less over-diagnosis/treatment than cytology-based screening while maintaining protection.

Who can participate?
Some 20,000 women aged 25 years and coming for screening within the organised screening programmes in Piemonte and Toscana.

What does the study involve?
Participants will be randomly assigned either to such protocol or to cytology-based screening and compared as for detection of high-grade CIN at baseline and at 30 yrs of age, cumulative CIN detection and cumulative referral to colposcopy from 25 to30 yrs. Routine screening will automatically provide followup after enrolment.

What are the possible benefits and risks of participating?
The study would allow relevant reductions of the undesired effects of screening (over diagnosis and over treatments) and of its costs for the national health service and would strongly simplify the management of organized screening programs.

Given the very low incidence of invasive cancer between 25 and 29 years and the very low risk of invasive cancer observed in HPV negative women within 5.5 years, the recall after 5 years of negative HPV women, as already occurs in older women, does not imply a reduction of protection compared to the cytological screening currently in use.

Where is the study run from?
The study is being run from SSD Epidemiology and Screening – CPO Piemonte (AOU Città della Salute e della Scienza di Torino) and takes place in the Piedmont region.

When is the study starting and how long is it expected to run for?
November 2018 to December 2020.

Who is funding the study?
The study is funded by the Italian Ministry of Health.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Management of women younger than 30 years in cervical cancer screening: CIN2+ detection rate and referral rate to colposcopy with a screening strategy using HPV testing compared to current practice

Acronym
HPV25

Study objectives

The incidence of invasive cervical cancers within 5.5 years after a negative HPV test is much lower than the incidence of invasive cancers within 3.5 years (see preliminary data). Thus, recalling HPV negative women after 5 years is safe. Overdiagnosis with HPV mainly depends on lesions detected by HPV testing but negative for cytology. Therefore, using the HPV test just to select those women aged 25 years who need screening up to age 30 should not cause overdiagnosis. Moreover, this approach should reduce the number of women who are screened by cytology at 25 and 28 years. Thus, we expect that it will reduce the number of colposcopies and could reduce the over-diagnosis compared with the conventional approach.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/05/2016, Comitato Etico Interaziendale A.O.U. Città della Salute e della Scienza di Torino - A.O. Ordine Mauriziano – ASL TO1 (Corso Bramante 88/90, 10126 Turin; comitatoetico@cittadellasalute.to.it; +39 0116336547), ref: CS/923.

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Cervical cancer screening

Interventions
Women aged 25 years who come for the first screening round for cervical cancer after invitation within the organised screening programmes in the Piedmont Region will be eligible. No exclusion is planned. Women
will receive an information sheet with the letter of invitation. When they come for screening, they will be asked an informed consent to enter the study. Those who accept will be randomly assigned to the experimental or conventional arm. Randomisation will be centralised and done by a computer.

Experimental Arm
Women will have a sample of cervical cells taken and put in a transport medium for liquid-based cytology (LBC). All women will be tested for HPV by Hybrid Capture 2. Only HC2 positive women will have cytology prepared and interpreted. These women will be managed only on the basis of cytology, like women in the conventional arm. No HPV test repeat for HPV positive, cytology negative women (like at older ages) will be performed. Women with HPV positive test but normal cytology will be invited for a new cytology at age 28 years. On such occasion, they will be referred to colposcopy if cytology is ASC-US or more.

If the analysis conducted after the first year of enrolment will not show a significant reduction of the detection rate of CIN2 or more severe (CIN2+) histology in the experimental vs. conventional arm then HPV negative women will be referred to a new screening round after 5 years.

At the age of 30 years, all women from both arms will be invited to screening with HPV according to Italian recommendations for women aged 30-64 years (i.e. HPV positive but cytology-negative women will be re-invited for new HPV test after 1 year).

Conventional Arm
Women will be invited for screening at 25 and 28 years of age and managed according to the current cytological protocol, i.e.:
1. A cytological slide will be prepared
2. Women with cytology ASC-US or more severe will be referred for colposcopy.
3. Women with cytology <ASC-US will be invited for a new cytology at 28 years of age. On such occasion, they will be referred to colposcopy if cytology is ASC-US or more severe.

Intervention Type
Other

Primary outcome(s)
The reduced disadvantages of the screening strategy are determined using:
1. Cumulative referral to colposcopy in participants aged 25 to 30 years (including screening at 28 if done).
2. Cumulative detection of CIN2+ in participants aged 25 to 30 years.

Key secondary outcome(s))
The ability of the screening strategy using HPV testing to select only those under the age of 30 years who need screening up to 30 years is determined using the detection rate of histologically determined CIN2+ at baseline.

Completion date
31/12/2020

Eligibility

Key inclusion criteria
1. Female
2. Aged 25-28 years
3. Attend the first or second screening round for cervical cancer after invitation within the organised screening programmes in the Piedmont Region

Participant type(s)
Other

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
25 years

Upper age limit

28 years

Sex
Female

Total final enrolment
5623

Key exclusion criteria
Second round of screening:
1. Previous positive cytological test or previous histologically confirmed CIN2+.

Date of first enrolment
12/11/2018

Date of final enrolment
30/11/2019

Locations

Countries of recruitment
Italy

Study participating centre
SSD Epidemiology and Screening – CPO Piemonte
Via Cavour 31
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Sponsor information

Organisation
AOU Città della Salute e della Scienza di Torino

ROR
https://ror.org/001f7a930

Funder(s)

Funder type
Government

Funder Name
Ministero della Salute

Alternative Name(s)
Italian Ministry of Health, Italy Ministry of Health, Ministry of Health of Italy, Ministry of Health - Italy, Ministry of Health, Italy

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Italy

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?
Other files	version Interim basic results	24/10/2023	24/10/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	English		13/09/2022	No	No
Protocol file	Italian		13/09/2022	No	No