HPV testing and the long term risk at cervical disease

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The primary objectives of our study are: - Determining the long-term predictive value of a positive HPV test for (pre)malignant cervical disease.- Determining the long-term protective value of a negative HPV test. - Determining the long-term...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON32541

Source
ToetsingOnline

Brief title
HPV test and long term follow-up

Condition

- Reproductive neoplasms male malignant and unspecified
- Cervix disorders (excl infections and inflammations)

Synonym
(pre) malignant cervical disease, Cervical Intraepithelial Neoplasia), CIN

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cervical Intraepithelial Neoplasia (CIN), cervix, Human papillomavirus (HPV), long term follow-up

Outcome measures

Primary outcome

The main study parameter is the cumulative number of histological confirmed cases of Cervical Intraepithelial Neoplasia (CIN) 2 or 3 or adenocarcinoma in situ (AIS), diagnosed after a follow up period of up to 18 years after an abnormal cervical smear.

Secondary outcome

The secondary study parameters include:

- the results of cervical cytology
- the presence of hrHPV
- type of hrHPV
- serum E6/E7 antibody level
- the results of the questionnaire (including sexual behavior, smoking and previous vaccination)
- histology results of all endocervix samples and biopsies taken

Study description

Background summary

In the Netherlands each year approximately 8000 women are treated for a high-grade pre-malignant cervical lesion. The majority of these lesions are detected in the population based cervical cancer screening program, in which exfoliated cells of the cervix are microscopically examined.
A disadvantage of the current (cytological) test is the poor sensitivity

(around 60%), leading to false-negative results. Since a persistent infection with human papillomavirus (HPV) is the key causative agent in the development of cervical lesions, women at risk can be identified by a HPV test (GP5+/6+ primer-mediated PCR with enzyme immuno assay read-out). This test has a sensitivity of approximately 90% and a negative predictive value of almost 100% for high-grade pre-malignant lesions measured over a short period of time (up to 2 years). In order to give a well-founded advice how to adjust the screening test for cervical cancer to the HPV test, the predictive value on the long term development of cervical abnormalities has to be known.

Study objective

The primary objectives of our study are:
- Determining the long-term predictive value of a positive HPV test for (pre)malignant cervical disease.
- Determining the long-term protective value of a negative HPV test.
- Determining the long-term protective value of a negative cervical smear test.

The secondary objectives of our study are:
- Determining the cumulative incidence of cervical disease in the investigated group.
- Comparison of the long term predictive value of the HPV test to cytology.
- Determining acquisition of HPV infection in women with a previous cytological abnormality.
- Evaluation of the presence of E6/E7 antibodies in women with an abnormal smear history.
- Comparison of the cost-effectiveness of the HPV test to the current situation of cytology.

Study design

The study is designed as an open prospective longitudinal clinical cohort study. A flow chart of the study is presented at page 17 of the protocol.

In this study we will follow up the cohort described in the study conducted by Nobbenhuis et al. *Relation of Human papillomavirus status to cervical lesions and consequences for cervical cancer screening: A prospective study*.
We will contact all subjects by phone to check the current addresses and to give a brief overview of the study.

During the visit at the outpatients clinic, which takes approximately 30 minutes all together, the following acts are scheduled:
- Check if patient information form has been read and understood.
- Check inclusion and exclusion criteria.
- Obtain written informed consent. All enrolled subjects must sign an original informed consent form in duplicate prior to

any study procedures.
- Assign a study number for all study procedures.
- Collect gynecological history.
- Complete questionnaire.
- Collect a cervical (vaginal) sample for HPV testing as well as for cytological evaluation.
- Collect a blood sample
- Verify if the subject agrees to inform the general practitioner about the results of the tests.
- Make an appointment to discuss the results, in case the result of the cervical smear is *abnormal* (classified CISOE-A * S2, E3 or O3) or if the subject is tested hrHPV positive a follow-up visit will be scheduled in order to perform a colposcopy by an experienced colposcopist.

In case the subject participates by self-sampling, a colposcopic axamination will be planned in case a high-risk HPV type is present.

Study burden and risks

The possible benefit for the participating subject may be the earlier detection of a cervical lesion in comparison to those subjects who only participate in the population based screening program.

Risks and burden are linked to protocol procedures, such as blood withdrawal, cervical sampling and, if applicable colposcopy. Although these are routine procedures, carried out by medical qualified personnel, they may cause side effects or discomfort to the subject. However, it is expected that these procedures will generally be well tolerated.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Previous participation in study mentioned in study by M. Nobbenhuis; Relation of human papillomavirus status to cervical lesions and the consequences for cervical cancer screening; a prospective study
Written informed consent
Sufficient knowledge of Dutch/ English language
Intention to comply with protocol requirements

Exclusion criteria

Pregnancy

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-01-2009
Enrollment:	353
Type:	Actual

Ethics review

Approved WMO

Date:	31-10-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL24874.029.08