

Efficacy of addition of hrHPV testing by Hybrid Capture II to conventional cytological screening for cervical cancer.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26473

Source

NTR

Brief title

VUSABOB

Health condition

Cervical intraepithelial neoplasia and cervical cancer.

Due to the low prevalence of invasive cervical cancer in the Netherlands, and the aim of cervical screening to prevent the occurrence of and death caused by to cervical cancer, we evaluate the prevalence of a surrogate marker for cervical cancer incidence, namely the immediate precursor lesion of cervical cancer cervical intra-epithelial neoplasia grade 3.

Sponsors and support

Primary sponsor: - Department of Pathology, VU University Medical Center, Amsterdam
- SALTRO Artsenlaboratorium & Trombosedienst, Utrecht

Source(s) of monetary or material Support: - Department of Pathology, VU University Medical Center
- SALTRO Artsenlaboratorium & Trombosedienst, Utrecht

Intervention

Outcome measures

Primary outcome

The primary outcome measure of VUSABOB is the occurrence of histologically confirmed cervical intra-epithelial neoplasia grade 3 (CIN3) lesions or (micro-) invasive carcinoma of the cervix found during the follow-up of currently diagnosed abnormalities, i.e., within 2 years. For women whose cytology results either regress to normal (in the unblinded trial of women with mild cytological abnormalities) or who clear an infection with hrHPV without cytological abnormalities (in the blinded trial of women with normal cytology diagnoses), we assume that no precursor lesions of cervical cancer are present.

They will not be referred for colposcopically-directed biopsies and therefore will not have a histological endpoint. This policy complies with regular cervical screening in The Netherlands.

Secondary outcome

As a secondary outcome measure, histologically confirmed cervical intra-epithelial neoplasia grade 2 will also be investigated, since current guidelines recommend ablative treatment for these lesions as well.

Other secondary parameters obtained include progression and regression of cytology diagnoses, clearance and acquisition of hrHPV infections and the number of referrals for colposcopically-directed biopsies.

Study description

Background summary

Cervical cancer almost exclusively develops in the presence of high-risk types of the human papillomavirus (hrHPV). A prolonged and persistent infection of the cervix with hrHPV is necessary for the development of premalignant (cervical intra-epithelial neoplasia, CIN) and finally malignant lesions. Prolonged presence of hrHPV types will lead to cytomorphological aberrations that can be detected in a cervical smear.

Research has shown that borderline and mild dyskaryotic (BMD) lesions tested positive for hrHPV significantly increase the risk for lesions \geq CIN3, and that progression to lesions \geq CIN3 will not occur in the absence of hrHPV. Secondly, women with normal smears (Pap 1) positive for hrHPV have a significantly increased risk for the development of lesions \geq CIN3.

Thus, we will investigate the efficacy of additional testing for hrHPV in the cervical cancer screening program both for women with normal smears (Pap 1) and for women with BMD smears (Pap 2-3a1).

In this study, hrHPV testing will be performed by the Hybrid Capture II test (HCII). The HCII is a commercially available and FDA-approved test for hrHPV.

This study has been designed as a population-based cohort study with a follow-up period of 2 years, in which 25,000 women invited for program-based screening in a geographically defined region in the Netherlands will participate.

All participants will undergo at least the routine strategy for repeat smears and referrals as is the standard level of care in the program-based screening in the Netherlands. Most participants (> 80%) will not even undergo a different treatment, as they will be diagnosed with hrHPV negative normal cytology (Pap 1).

The extra care in this study will involve

1. Women with hrHPV positive BMD (Pap 2-3a1) who will be referred to the gynaecologist for colposcopy immediately, as the presence of lesions \geq CIN3 will be expected solely in this group, and not in the group of women with hrHPV negative BMD;
2. All women with hrHPV positive normal cytology and 12.5% of the women with hrHPV negative cytology who will undergo extra cytologic control to evaluate the role of hrHPV in the development of cytologic and histologic lesion. For these women, the hrHPV results will be blinded for the duration of the study. In order to evaluate the hrHPV-based referral strategies with the regular repeat and referral recommendations, we compare the results of the study cohort with an historical cohort of women screened in the previous calendar year at the study laboratory.

The research questions that will be answered in the study include the following:

1. Can women with BMD and a positive HCII hrHPV test be referred to the gynaecologist immediately, whereas women with a negative hrHPV test will be referred back to the regular screening program, without an increase in risk of missing lesions \geq CIN3?
2. Is the risk of lesions \geq CIN3 for women with hrHPV negative BMD not increased compared to women with normal cytology (Pap 1) and an unknown result of the HCII hrHPV test (i.e. women who are at present given an advice to repeat the smear after 5 years in the Netherlands)?
3. To what extent will lesions \geq CIN3 and/or cytologic progression to \geq moderate dyskaryosis develop in women with HCII hrHPV positive normal cytology (Pap 1) compared to women diagnosed with HCII hrHPV negative normal cytology (Pap 1)?
4. Will the repeat and referral strategy based on classical cytology and HCII hrHPV testing not result in less women diagnosed with lesions \geq CIN3 for the women with BMD, than in a historical cohort of women diagnosed with BMD in the preceding year in the program-based cervical cancer screening?

Study objective

In this study, we expect to decrease the number of referrals and repeat smears by immediately referring those women who are positive for hrHPV with mildly abnormal smears for colposcopically-directed biopsies. Thus, for the remaining women with BMD who have tested hrHPV negative, repeat smears will not be necessary.

Secondly, we expect to be able to narrowly define a risk group of women within the group with normal cytology, that has an increased risk for the development of high-grade lesions based on the presence of hrHPV in the smear.

The hrHPV negative women with normal smears will be at a decreased risk for the development of high-grade lesions, and for them, the interval between screening smears could be increased (from an interval of 5 years, to an interval of 8-10 years).

Study design

N/A

Intervention

In the VUSABOB, the addition of a high-risk human papillomavirus (hrHPV) test, using the commercially available and FDA approved Hybrid Capture II test, to the regular cervical screening programme in order to improve detection of precursor lesions of cervical cancer is evaluated using a cohort study of women whose smears were consecutively screened at a single laboratory in The Netherlands. Within this cohort study, we nested an unblinded trial of women with mildly abnormal screening smears and repeat and referral recommendations were based on the presence or absence of high-risk human papillomavirus.

Secondly, we nested a randomized trial of women with normal cytology whose hrHPV test results were triple blinded to participants, treating clinicians and study personnel, and advised all women with blinded test results to repeat cervical screening at earlier intervals than current screening guidelines in the Netherlands recommend in order to evaluate screening strategies for women with normal cytology and a positive hrHPV test.

Contacts

Public

SALTRO,
P.O. Box 9300
M. Herreilers
Mississippidreef 83
Utrecht 3565 CE
The Netherlands
+31 (0)30 2361136

Scientific

SALTRO,
P.O. Box 9300
M. Herreilers

Mississippidreef 83
Utrecht 3565 CE
The Netherlands
+31 (0)30 2361136

Eligibility criteria

Inclusion criteria

1. Women invited for the cervical cancer screening program (ages 30-60 years);
2. General practitioner affiliated with SALTRO laboratory.

Exclusion criteria

1. Not called for screening, i.e., ages under 30 years, or over 60 years;
2. Follow-up of previous non-normal cytology within the current screening round of the program, i.e., abnormal cytology or lesion iŸCIN3 less than 2 years before inclusion;
3. Current pregnancy;
4. Status after extirpation of the uterus or amputation of the portio.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2003
Enrollment:	25000
Type:	Actual

Ethics review

Positive opinion	
Date:	05-09-2005
Application type:	First submission

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
NTR-new	NL178
NTR-old	NTR215
Other	: 2002/02WBO
ISRCTN	ISRCTN64621295

Study results

Summary results

N/A