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

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26473

Bron
NTR

Verkorte titel
VUSABOB

Aandoening

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.

Ondersteuning

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

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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 abnormalties, 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.

Toelichting onderzoek

Achtergrond van het onderzoek

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 ¡Ý CIN3, and that progression to lesions ¡Ý 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 ¡Ý 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 ¡Ý 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 ¡Ý CIN3?

2. Is the risk of lesions ¡Ý 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 ¡Ý CIN3 and/or cytologic progression to ¡Ý 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 ¡Ý 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?

Doel van het onderzoek

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).

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

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.

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Women invited for the cervical cancer screening program (ages 30-60 years);

2. General practitioner affiliated with SALTRO laboratory.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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 ¡ÝCIN3 less than 2 years before inclusion;

3. Current pregnancy;

4. Status after extirpation of the uterus or amputation of the portio.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-10-2003
Aantal proefpersonen:	25000
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	05-09-2005
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL178
NTR-old	NTR215
Ander register	: 2002/02WBO
ISRCTN	ISRCTN64621295

Resultaten

Samenvatting resultaten
N/A