

# Preventing overtreatment of CIN using methylation markers

No registrations found.

<b>Ethical review</b>	Positive opinion
<b>Status</b>	Pending
<b>Health condition type</b>	-
<b>Study type</b>	Observational non invasive

## Summary

### ID

NL-OMON29301

### Source

NTR

### Brief title

CONCERVE

### Health condition

Cervical intraepithelial neoplasia  
Overtreatment  
Methylation markers  
Regression

Cervicale intraepitheliale neoplasie  
Overbehandeling  
Methylerings markers  
Regressie

## Sponsors and support

**Primary sponsor:** VU medical center

**Source(s) of monetary or material Support:** ZonMw

## Intervention

## Outcome measures

### Primary outcome

The primary study endpoint is (non-) regression at the end of the study based on histology of the cervical exit biopsy. All cervical biopsies will be examined by a gynaeco-pathologist and classified as no CIN, CIN1, CIN2, CIN3 or cervical carcinoma. Regression is defined as CIN1 or less on the exit biopsy based on morphology. Non-regression is defined as CIN2+ on the exit biopsy based on morphology.

### Secondary outcome

It has been shown that HPV-clearance precedes regression of cervical lesions by an average of 3 months. Therefore, the secondary study endpoint is defined as HPV clearance (double negative hrHPV test at two consecutive time points). HPV DNA detection will be done with the clinically validated HPV-Risk assay, a multiplex real-time PCR-based assay designed for the clinical detection of high-risk HPV DNA of 15 (probably) high-risk HPV types (i.e. HPV16, -18, -31, -33, -35, -39, -45, -51, -52, -56, -58, -59, -66, -67, and -68). This assay detects HPV 16 and 18 in separate channels, and the other HPV types as a pool.

## Study description

### Background summary

Current cytology-based cervical screening programmes serve to detect and treat high-grade precursor lesions (CIN2/3) to prevent cervical cancer. However, the diagnostic-treatment trajectory is associated with considerable overtreatment since CIN2/3 lesions, particularly in young women, have a high spontaneous regression rate. Pathologists are unable to differentiate between CIN2/3 lesions with a low short-term progression risk to cervical cancer (productive lesions), not in need of immediate treatment, and those with a high short-term progression risk (transforming lesions) that need immediate treatment. Individual cancer risk prediction of CIN2/3 is therefore essential to reduce overtreatment. Recently, it has been shown that DNA methylation markers can differentiate between productive and transforming CIN2/3. Here, we aim to validate prospectively that testing for the methylation status of a CIN2/3 predicts (non-) regression leading to prevention of overtreatment.

### Study objective

Analysis of methylation status can predict which CIN2/3 lesions will regress and which not, determining the need of immediate treatment versus active surveillance.

### Study design

Baseline, 6, 12, 18, 24 months

## **Intervention**

Standard therapy for CIN2/3 lesions consists of excision of the lesion by either LLETZ or cold knife conisation. In this study, treatment consists of a watchful waiting policy. Participants will be monitored by an intense follow-up schedule consisting of 6-monthly visits to the colposcopy clinic for 2 years. During these visits, cervical cytology, hrHPV testing, methylation marker analysis and colposcopic evaluation of the cervix will be performed.

Control:

Women not included in the study population and who will receive standard excisional therapy for

their CIN2/3 lesion will be asked to participate in a reference group. This standard therapy consists of

a LLETZ or cold knife conisation and will be performed according to national guidelines. By including a

reference population in our study, we aim to assess the clinical 'cutoff' for lesion size that gynaecologists use in their decision to treat patients and not to include them in the study protocol. One

hundred subjects will be included in this group.

Women participating in the reference group will be asked to use the Evalyn brush to self-collect a

cervico-vaginal specimen. Furthermore, a cervical scrape will be collected by the gynaecologist.

Sample collection will be done prior to treatment, so that no extra visits or gynaecological examinations will be needed.

## **Contacts**

### **Public**

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## Eligibility criteria

### Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- CIN2 or CIN3 on a cervical punch biopsy
- CIN covering 50% or less of the visible cervix
- Female aged 18-55 years

### Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

- History of cervical pathology
- Transformation zone is not visible at colposcopy
- Prenatal diethylstilboestrol exposure
- Concomitant cancer
- Insufficient Dutch or English language skills

## Study design

### Design

Study type: Observational non invasive

Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

## Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	01-12-2016
Enrollment:	200
Type:	Anticipated

## IPD sharing statement

**Plan to share IPD:** Undecided

## Ethics review

Positive opinion	
Date:	31-08-2016
Application type:	First submission

## Study registrations

### Followed up by the following (possibly more current) registration

ID: 45770  
Bron: ToetsingOnline  
Titel:

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

No registrations found.

### In other registers

**Register**

NTR-new

NTR-old

CCMO

OMON

**ID**

NL5794

NTR6069

NL56187.029.16

NL-OMON45770

**Study results**