

# The association between preterm birth, vaginal microbiome, immune defence and HPV among women with cervical precancer

<b>Submission date</b> 15/09/2015	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 22/03/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 04/01/2023	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Human papilloma virus (HPV) are common viruses that affect the skin and moist membranes lining parts of the body, for example, the mouth, cervix and vagina. Most people will be infected with HPV at some point in their lives. It rarely causes any problems and goes away on its own. Some HPVs can cause changes to the cells of the cervix. These changed cells are then more likely to become cancerous. HPV infection is a necessary, but not sufficient cause for the development of cervical cancer and its precursors (that is, pre-cancerous changes). Our knowledge about human microbiome (the microorganisms – such as bacteria and viruses - on and in our body) has increased vastly after the development of novel sequencing methods and only recently HPV clearance rate (i.e how long it takes for the infection to go away) was shown to be dependent on vaginal microbiome type. Since development of cervical cancer requires HPV infection, studying the interplay between vaginal microbiome, mucosal immune system (the part of the immune system that protects mucous membranes), HPV status (state of infection, if any), and the clinical presentation of the disease simultaneously is crucial for understanding why only a fraction of women infected with HPV develop cervical cancer. The aim of this study is to investigate whether the removal of abnormal (mucus secreting) cells during LEEP (loop electrosurgical excision procedure) treatment affects the immune defence system of the cervix, leading to an imbalance in the normal vaginal microbiome (dysbiosis) and possibly increasing the likelihood of inflammation and prolonged HPV infection.

### Who can participate?

Women aged between 18-45, not pregnant and have been referred to colposcopy (a procedure to check for abnormal cells in a woman's cervix or vagina) due to an abnormal Pap smear result.

### What does the study involve?

Participants are placed into one of three groups. Those in group 1 are referred to colposcopy and LEEP treatment. Those in group 2 are referred to colposcopy, but do not have lesions (pre-cancerous changes) requiring LEEP treatment. Those in group 3 (the control group) have been recruited during routine Pap smear screening. Samples are taken from all participants before colposcopy and then six months later.

What are the possible benefits and risks of participating?  
Not provided at time of registration

Where is the study run from?  
Helsinki University Central Hospital (HUCH) Womens Hospital

When is the study starting and how long is it expected to run for?  
September 2015 to December 2023

Who is funding the study?  
Helsinki University Central Hospital

Who is the main contact?  
Dr Pekka Nieminen

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Dr Pekka Nieminen

**Contact details**  
Kätilöopiston Sairaala  
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## Additional identifiers

**Protocol serial number**  
N/A

## Study information

**Scientific Title**  
The association between preterm birth, vaginal microbiome, immune defence and HPV among women with cervical precancer: an observational single-center study

**Acronym**  
MI-HPV

**Study objectives**  
Our hypothesis is that the removal of mucus secreting cells in LEEP treatment compromises cervical immune defense and thus predisposes to ascending infection or inflammatory response against normal flora altering microbiota in the vagina and the microbiota might be dysbiotic in the first place to allow prolonged HPV-infection.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

University of Helsinki Institutional Review Board, 30/01/2014, ref: 21/13/03/2014

**Study design**

Observational single-center study

**Primary study design**

Observational

**Study type(s)**

Diagnostic

**Health condition(s) or problem(s) studied**

HPV infection

**Interventions**

We will recruit women referred to colposcopy due to an abnormal Pap smear result, age 18 to 45, who are not pregnant and have no previous cervical operation. There are then allocated to one of three groups.

1. Main study group: Women referred to colposcopy and LEEP treatment
2. Control group 1: Women referred to colposcopy, but do not have lesions requiring LEEP treatment.
3. Control group 2: Women recruited during routine Pap smear screening at HUSLab

Samples are taken before colposcopy and after six months follow-up, during the first control visit.

**Intervention Type**

Procedure/Surgery

**Primary outcome(s)**

1. Presence of immunomarkers, using multiplex ELISA
2. HPV-status, using PCR
3. Analysis of microbiota, by measuring hypervariable 16S

Results are compared between patients receiving treatment for HPV lesions with those that do not require treatment for lesions. Measurements are taken at baseline and 6 months later.

**Key secondary outcome(s)**

1. Presence of immunomarkers
2. HPV-status
3. Analysis of microbiota

Results are compared between patients with HPV at a colposcopy clinic to "healthy" controls undergoing Pap screening. Measurements are taken at baseline and 6 months later.

**Completion date**

31/12/2023

## Eligibility

### Key inclusion criteria

Healthy volunteers and colposcopy patients.

### Participant type(s)

Mixed

### Healthy volunteers allowed

No

### Age group

Adult

### Sex

Female

### Key exclusion criteria

1. Pregnancy
2. Vaginal bleeding
3. Previous cervical surgery

### Date of first enrolment

17/09/2015

### Date of final enrolment

31/12/2019

## Locations

### Countries of recruitment

Finland

### Study participating centre

Helsinki University Central Hospital (HUCH) Womens Hospital

Helsinki

Finland

00610

## Sponsor information

### Organisation

Helsinki University Central Hospital

ROR

<https://ror.org/02e8hzhf44>

## Funder(s)

### Funder type

Not defined

### Funder Name

Helsingin ja Uudenmaan Sairaanhoidopiiri

### Alternative Name(s)

Helsinki University Central Hospital, HUS

### Funding Body Type

Government organisation

### Funding Body Subtype

Local government

### Location

Finland

### Funder Name

Helsingin Yliopisto

### Alternative Name(s)

University of Helsinki, Helsingfors Universitet, Universitas Helsingiensis, HY, UH

### Funding Body Type

Government organisation

### Funding Body Subtype

Universities (academic only)

### Location

Finland

## Results and Publications

### Individual participant data (IPD) sharing plan

Not provided at time of registration

## **IPD sharing plan summary**

Not provided at time of registration