Active, not recruiting

Effectiveness of Cervical Screening in HPV Vaccinated Women (HPV-004)

ClinicalTrials.gov ID NCT02149030

Sponsor Tampere University

Information provided by Matti Lehtinen, Tampere University (Responsible Party)

Last Update Posted 2025-01-20

Study Details Tab

Study Overview

Brief Summary

The main objective of the study is to identify whether or not being informed infrequently results about screening is: 1) At least as safe and accurate as frequently obtaining all information from the present combination of opportunistic/organized cervical screening by comparing regimen results of three screening visits at the ages of 22, 25 and 30 years (Arm A1) vs. results of one screening visit at the age of 30 years (Arm A2) in Human papillomavirus (HPV) vaccinated young women.

Detailed Description

Altogether 16.500 1992-1995 born women vaccinated with the bi-valent human papillomavirus type 16 and 18 (HPV16/18) vaccine as adolescents either at the age of 12 to 15 or at the age of 18 will be invited to an effectiveness trial at the age of 22 years, and randomized into Arms A1 and A2, and A3, respectively.

Cervical samples and cervico-vaginal self-samples rinsed in first-void urine will be analysed for HPV and C. trachomatis DNA with MGP primer system followed by MALDITOF mass spectrometry on the SEQUENOM platform (HPV) and the Abbott™ PCR (Chlamydia trachomatis), respectively.

With assumed >50% participation the trial has 80% power to show non-inferiority of the infrequent vs. the frequent screening information.

A one-way (participant) blinded interim analysis among the 1992-born study participants in A1 and A3 arms, who have attended the 2nd study visit at the age of 25 years, will be performed in 2017 for assuring no statistically significant differences in the cervical intraepithelial neoplasia grade 2/3 (CIN2/CIN3) incidences of the two arms.

At the study end testing the null hypotheses of no difference in the incidence of the CIN2/3 end-points between the A1 and A2 intervention arms will be done using the Mantel-Haenszel one degree of freedom chi-square statistics.

Official Title

Effectiveness of Cervical Screening in HPV Vaccinated Women - a Randomized Trial

Conditions

Cervical Intraepithelial Neoplasia Grade 2/3

Intervention / Treatment

- Other: Cytological screening in A1 and A3

Other Study ID Numbers

- HPV-004

Study Start

2014-03

Primary Completion (Estimated)

2025-01

Study Completion (Estimated)

2025-01

Enrollment (Actual)

6958

Study Type

Interventional

Phase

Not Applicable

Resource links provided by the National Library of Medicine

FDA Drug and Device Resources (https://clinicaltrials.gov/fda-links)

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the Contacts and Locations section in How to Read a Study Record (https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations).

This study has 31 locations

Finland

Äänekoski, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Hämeenlinna, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Helsinki, Finland
HUS

Hyvinkää, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Iisalmi, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Jämsä, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Joensuu, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Jyväskylä, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Kajaani, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Kemi, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Kokkola, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Kotka, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Kouvola, Finland

Nuorisotutkimusasema: Tampereen yliopisto

Kuopio, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Lahti, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Lappeenranta, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Lohja, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Mikkeli, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Oulu, Finland
THL

Pori, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Porvoo, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Rauma, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Rovaniemi, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Salo, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Savonlinna, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Seinäjoki, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Tampere, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Turku, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Vaasa, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Vammala, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Varkaus, Finland
Nuorisotutkimusasema: Tampereen yliopisto

Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read Learn About Studies (https://clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Inclusion Criteria:

- HPV 16/18 vaccinated. Born 1992-1995.

Exclusion Criteria:

- Immunocompromising disease. HPV 6/11/16/18 vaccination.

Ages Eligible for Study

22 Years to 22 Years (Adult)

Sexes Eligible for Study

Female

Accepts Healthy Volunteers

Yes

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose : Screening
Allocation : Randomized
Interventional Model : Parallel Assignment
Masking : Single (Participant)

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Active Comparator: A1 A1) Cytological screening in A1 and A3. Frequent information of screening results for cytology and/or HPV DNA at the ages of 22 (cytology only), 25 and 30.	Other: Cytological screening in A1 and A3 • Cytological screening.
No Intervention: A2 A2) infrequent information of screening results, only at the age 30 years.	
Other: A3 A3) Cytological screening in A1 and A3. With at least 1000 participants is enrolled for interim safety analysis when the 1992 birth cohort is 25 years of age and cytology results are being revealed.	Other: Cytological screening in A1 and A3 • Cytological screening.

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Occurrence of intraepithelial neoplasia grade 2/3 (CIN2/3).	1a) No marked difference in the incidence of CIN2/3 between arms A1 (participants frequently informed of the cytological results) and A3 (participants not informed of the cytological findings at the age of 22) (interim analysis). 1b) No difference in the incidence of CIN2/3 between arms A1 (participants frequently informed of the cytological results) and A2 (participants infrequently informed of the cytological results). The participants will be followed for 9 years starting from the year they turn 22. For 1992 born the follow-up will start in 2014 and end in 2023. For 1995 born the follow-up will start in 2017 and end in 2026. The interim analysis will include only 1992 cohort. The final analysis will include all cohorts (1992, 1993, 1994, 1995).	2017-2020, i.e. four years (interim), 2021-2025, i.e. five years (final analysis). Participants will be followed for the duration of the study until 2026, an expected average of 9 years.

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame

Type-replacement	Whether the post-vaccination distributions of vaccine-covered and/or non-vaccine covered HPV types develop differentially in the different vaccination arms by vaccination arm over time up to 15 years post vaccination.	2021-2025, i.e. four years

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Tampere University

Collaborators

- European Union
- Academy of Finland
- Cancer Society of Finland

Investigators

- Principal Investigator: Matti Lehtinen, MD, PhD, Tampere University

Publications

General

These publications are provided voluntarily by the person who enters information about the study and may be about anything related to the study.

- Vanska S, Luostarinen T, Baussano I, Apter D, Eriksson T, Natunen K, Nieminen P, Paavonen J, Pimenoff VN, Pukkala E, Soderlund-Strand A, Dubin G, Garnett G, Dillner J, Lehtinen M. Vaccination With Moderate Coverage Eradicates Oncogenic Human Papillomaviruses If a Gender-Neutral Strategy Is Applied. J Infect Dis. 2020 Aug 17;222(6):948-956. doi: 10.1093/infdis/jiaa099. (https://pubmed.ncbi.nlm.nih.gov/32161969)

- Louvanto K, Eriksson T, Gray P, Apter D, Baussano I, Bly A, Harjula K, Heikkila K, Hokkanen M, Huhtinen L, Ikonen M, Karttunen H, Nummela M, Soderlund-Strand A, Veivo U, Dillner J, Elfstom M, Nieminen P, Lehtinen M. Baseline findings and safety of infrequent vs. frequent

screening of human papillomavirus vaccinated women. Int J Cancer. 2020 Jul 15;147(2):440-447. doi: 10.1002/ijc.32802. Epub 2019 Dec 16. (https://pubmed.ncbi.nlm.nih.gov/31749143)

- Gray P, Kann H, Pimenoff VN, Eriksson T, Luostarinen T, Vanska S, Surcel HM, Faust H, Dillner J, Lehtinen M. Human papillomavirus seroprevalence in pregnant women following gender-neutral and girls-only vaccination programs in Finland: A cross-sectional cohort analysis following a cluster randomized trial. PLoS Med. 2021 Jun 7;18(6):e1003588. doi: 10.1371/journal.pmed.1003588. eCollection 2021 Jun. (https://pubmed.ncbi.nlm.nih.gov/34097688)

- Kalliala I, Eriksson T, Aro K, Hokkanen M, Lehtinen M, Gissler M, Nieminen P. Preterm birth rate after bivalent HPV vaccination: Registry-based follow-up of a randomized clinical trial. Prev Med. 2021 May;146:106473. doi: 10.1016/j.ypmed.2021.106473. Epub 2021 Feb 24. (https://pubmed.ncbi.nlm.nih.gov/33639181)

- Lehtinen M, Gray P, Louvanto K, Vanska S. In 30 years, gender-neutral vaccination eradicates oncogenic human papillomavirus (HPV) types while screening eliminates HPV-associated cancers. Expert Rev Vaccines. 2022 Jun;21(6):735-738. doi: 10.1080/14760584.2022.2064279. Epub 2022 Apr 15. No abstract available. (https://pubmed.ncbi.nlm.nih.gov/35404177)

- Lehtinen M, Pimenoff VN, Nedjai B, Louvanto K, Verhoef L, Heideman DAM, El-Zein M, Widschwendter M, Dillner J. Assessing the risk of cervical neoplasia in the post-HPV vaccination era. Int J Cancer. 2023 Mar 15;152(6):1060-1068. doi: 10.1002/ijc.34286. Epub 2022 Oct 10. (https://pubmed.ncbi.nlm.nih.gov/36093582)

- Pimenoff VN, Gray P, Louvanto K, Eriksson T, Lagheden C, Soderlund-Strand A, Dillner J, Lehtinen M. Ecological diversity profiles of non-vaccine-targeted HPVs after gender-based community vaccination efforts. Cell Host Microbe. 2023 Nov 8;31(11):1921-1929.e3. doi: 10.1016/j.chom.2023.10.001. (https://pubmed.ncbi.nlm.nih.gov/37944494)

- Lehtinen M, Bruni L, Elfstrom M, Gray P, Logel M, Mariz FC, Baussano I, Vanska S, Franco EL, Dillner J. Scientific approaches toward improving cervical cancer elimination strategies. Int J Cancer. 2024 May 1;154(9):1537-1548. doi: 10.1002/ijc.34839. Epub 2024 Jan 9. (https://pubmed.ncbi.nlm.nih.gov/38196123)

- Lehtinen M, Elfstrom M, Vanska S, Dillner J. Elimination of cervical cancer by refined vaccination and screening. Int J Cancer. 2025 Feb 15;156(4):886-888. doi: 10.1002/ijc.35228. Epub 2024 Oct 25. No abstract available. (https://pubmed.ncbi.nlm.nih.gov/39450703)

- Louvanto K, Verhoef L, Pimenoff V, Eriksson T, Leppala S, Lagheden C, Gray P, Scibior-Bentkowska D, Sumiec E, Nieminen P, Dillner J, Berkhof J, Meijer CJLM, Lehtinen M, Nedjai B, Heideman DAM. Low methylation marker levels among human papillomavirus-vaccinated women with cervical high-grade squamous intraepithelial lesions. Int J Cancer. 2024 Nov 1;155(9):1549-1557. doi: 10.1002/ijc.35044. Epub 2024 May 27. (https://pubmed.ncbi.nlm.nih.gov/38801336)

- Taavela K, Eriksson T, Huhtala H, Bly A, Harjula K, Heikkila K, Hokkanen M, Nummela M, Kotaniemi-Talonen L, Lehtinen M, Louvanto K. The quality of life of frequently vs. infrequently

screened HPV vaccinated women. Qual Life Res. 2024 Apr;33(4):941-949. doi: 10.1007/s11136-023-03575-y. Epub 2024 Jan 18. (https://pubmed.ncbi.nlm.nih.gov/38238599)

- Lehtinen M, Apter D, Baussano I, Eriksson T, Natunen K, Paavonen J, Vanska S, Bi D, David MP, Datta S, Struyf F, Jenkins D, Pukkala E, Garnett G, Dubin G. Characteristics of a cluster-randomized phase IV human papillomavirus vaccination effectiveness trial. Vaccine. 2015 Mar 3;33(10):1284-90. doi: 10.1016/j.vaccine.2014.12.019. Epub 2015 Jan 12. (https://pubmed.ncbi.nlm.nih.gov/25593103)

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted
2014-05-19

First Submitted that Met QC Criteria
2014-05-28

First Posted (Estimated)
2014-05-29

Study Record Updates

Last Update Submitted that Met QC Criteria
2025-01-15

Last Update Posted
2025-01-20

Last Verified
2025-01

More Information