EFC X EUROPEAN CONGRESS

Cervical cancer prevention and colposcopy

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Abstracts

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All abstracts have been published without modification or editing as submitted to the EFC.

Does active surveillance for CIN2 reduce the risk of preterm birth? A Danish registry-based cohort study

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Background:

Management of CIN2 amongst fertile women has transitioned from LLETZ to active surveillance due to the high spontaneous regression rates of CIN2 and the association of LLETZ and preterm birth. Yet, cervical dysplasia itself is also associated with preterm birth.

Aims:

We aimed to investigate if active surveillance of CIN2 is associated with a lower risk of preterm birth than LLETZ.

Methods:

We included all Danish women of fertile age with CIN2 and a subsequent singleton birth, 1998-2018. The women were categorized into active surveillance (cervical biopsy and/or cytology) or immediate LLETZ, depending on the first sample after CIN2 diagnosis. Also, we identified women in the active surveillance group, who underwent delayed LLETZ within the active surveillance period of 2 years. We calculated adjusted relative risks (aRR) of preterm birth (<37+0) using modified Poisson regression including
adjustment for confounders.

Results:

We identified 10,537 women CIN2 and a singleton birth of which 869 births (8.2%) were preterm. The preterm birth risk was comparable between active surveillance and immediate LLETZ (aRR 1.03 (95% CI 0.90-1.18)). However, for women treated with delayed LLETZ after initial active surveillance, the risk was higher than for women treated with immediate LLETZ (aRR 1.29 (95% CI 1.08-1.55)).

Conclusions:

Overall, the preterm birth risk is comparable between active surveillance and immediate LLETZ for CIN2, but women treated with delayed LLETZ after active surveillance have a higher risk. This highlights the importance of early identification of women at CIN2 diagnosis, who possess an increased risk of delayed LLETZ.

Distribution of intraepithelial lymphocytes and macrophages in the cervical microenvironment during the progression of cervical intraepithelial neoplasia

By author Ketevan Manjgaladze & co-authors G. Tevdorashvili, T. Muzashvili, M. Gachechiladze, G. Burkadze

Background/Objectives:

Microenvironment plays central role in the development of cervical precancerous and cancerous lesions. Cervical intraepithelial neoplasia (CIN) represents a group of precancerous lesions, divided into three degrees. The aim of our study was to investigate the distribution of CD68+ macrophages and CD103 intraepithelial lymphocytes during the progression of CIN and cervical carcinoma in situ. We investigated the distribution of intraepithelial lymphocytes and macrophages in different grades of CIN.

Methods:

Archival formalin-fixed and paraffin-embedded (FFPE) tissue samples, diagnosed as CIN or in situ CA, between 2015-2018 years, were obtained from the department of pathological anatomy, N. Kipshidze central university clinic, Tbilisi, Georgia. Study cohort included 20 cases with normal cervical tissue, 31 cases of CIN1, 24 cases of CIN2, 26 cases of CIN3 and 42 cases of in situ carcinoma (CA), and 35 cases of invasive cervical carcinoma (CA), altogether 178 cases. Standard Hematoxylin and Eosin (H&E) stained sections were revised by two independent pathologists (T.M. and G.B.). From 31 CIN1 cases, 8 cases were further progressed in CIN2 and from original 24 CIN2 cases, 12 cases were progressed into CIN3 or in situ CA. The age of patients varied from 30 to 50 years. We analyzed lymphocyte marker CD103, macrophage marker CD68 and proliferation marker Ki67 using standard immunohistochemistry. Tumor infiltrating lymphocytes (TILs), were analyzed on standard H&E stained sections, in three areas of the tumor, including tumor bead, invasive tumor margin and tumor associated stroma by semiquantitative approach. TILs were classified as following, no infiltration (0), low infiltration (1), moderate infiltration (2) and high infiltration (3). Comparisons between different groups has been performed by the use of Kruskall-Wallis test and non-parametric correlations have been estimated by Spearman's rank test. In all tests, p values < 0.05 considered as significant. Statistical analysis of data has been performed using SPSS 19 statistical program.

Results:

The results of our study indicated that grade I CIN which subsequently progressed into grade II CIN was characterized with low lymphocytic infiltration, low lympho-epithelial index and low lymphocyte proliferation index. Similar results were seen in cases of CIN2 which were later progressed into CIN3 or in carcinoma. Therefore, we would like to recommend the analysis of microenvironment alterations in CIN lesions, in order to assess their progression potential.

Conclusions:

Immune infiltrates as well as lympho-epithelial index is significantly increased in higher grades of CIN and in situ and invasive CA. Evaluation of lympho-epithelial index is superior compared to the evaluation of the raw immune infiltrates in the assessment of the risk of the CIN progression, and it might be used for the assessment of the risk of CIN progression. In addition, the complex analysis together with lymphocyte proliferation index might represent more functional analytical approach to evaluate the efficiency of anti-tumor immune response and therefore to estimate the risk of progression of CIN lesions

References:

[1] K. G. et al. A. Gamkrelidze, M. Kereselidze, M. Tsintsadze, “Health statistics in Georgia,” Minist. Labour, Heal. Soc. Aff., 2015. [2] R. J. Kurman, M. L. Carcangiu, C. S. Herrington, and R. H. Young, WHO Classification of Tumours of Female Reproductive Organs. Fourth Edition. 2014.

Women's reasoning and experience in the cervical cancer screening program when offered a self-sampling HPV test: a qualitative content analysis.

By author Caroline Hellsten & co-authors Lina Magnusson, Christer Borgfeldt

Background:
The HPV vaginal self-sampling test was implemented in the southern part of Sweden in September 2021 to increase the attendance in the cervical cancer screening program.

Aim:
The objective was to explore women's reasoning and experience when offered a self-sampling HPV-test.

Methods:
A qualitative study design and content analysis with an inductive approach was applied to the data. Questionnaires with nine open-ended questions were used to collect narratives from the invited women. Women were eligible if they had been offered a self-sampling device since the implementation in September 2021 and resident in the southern part of Sweden. Results: An invitation letter for participation was sent to 1915 women, and 174 women answered the questionnaire. Amongst these, 102 women had participated in the last screening round, 37 women had been absent and 35 women had a history of cervical dysplasia. The content analysis resulted in seven categories: (1) unpleasant experience with a vaginal examination, (2) acceptability of self-sampling and gratefulness, (3) varied perception on own capacity to perform the self-sampling, (4) preference to cervical sampling by health care professionals, (5) anxiety and fear concerning a potential and detected HPV infection, (6) different risk assessments for acquiring an HPV infection, and (7) considerable negative impact on mental well-being and sex life due to cervical dysplasia.

Conclusions:
The HPV self-test simplifies attendance by reducing practical and emotional barries, but the detection of an HPV infection and cervical dysplasia leads to anxiety.

HPV E4/p16^{INK4a} immunohistochemistry for the prediction of CIN2 regression - a historical cohort study

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Introduction:

CIN2 is a heterogenous diagnosis with a high likelihood of regression, suggesting that some women with CIN2 may benefit from undergoing active surveillance instead of an immediate excision. Here, we aimed to examine the performance of p16INK4a and HPV E4 immunohistochemistry for predicting CIN2 regression.

Methods:

We conducted a historical cohort study including women aged 23-40 undergoing active surveillance for CIN2 at Aarhus University Hospital, Denmark, from 2000 to 2010. Archived tissue samples were sectioned for H&E, HPV genotyping, and p16INK4a and HPV E4 immunohistochemestry We calculated absolute and adjusted relative risks (aRR) of regression by p16INK4a status, stratified by HPV E4, HPV type, cytology, and age.

Results:

Of 455 included women, most (73.8%) were aged £30 and half had a high-grade index cytology (48.8%). A total of 47.6% regressed to CIN1 or normal during the 2-year surveillance period. CIN2 regression rates were lower in p16INK4a-positive compared to p16INK4a-negative women (40.5% vs 63.3%, aRR: 0.77 ; 95%CI 0.64-0.94). In p16INK4apositive women, risk of regression was significantly lower in HPV E4-negative compared to HPV E4-positive women (37.7% vs 53.8%, aRR 0.73; 95%CI 0.54-0.98) and in HPV16-positive compared to HPV16-negative women (27.9% vs 49.7%, aRR 0.54; 95%CI 0.40- 0.75). Risks did not differ by cytology (≤Low-grade vs high-grade: 40.6% vs 43.0%, aRR 0.78 ; 95%CI 0.60-1.02) or age at diagnosis (≤30 vs >30: 41.8% vs 36.7%; aRR 0.85; 95%CI 0.62-1.17).

Conclusion:

Our findings support the use of p16INK4a immunohistochemistry in clinical practice, possibly in addition to HPV typing and E4 testing.

Cervical cancer screening in a health centre in Lisbon - a retrospective observational study

By author Cordeiro Inês & co-authors Gomes Catarina, Li Yifan, Duarte Diana

Background:

Cervical cancer is the second most common cancer among women aged 15-44 years in the European Union. In resource-rich countries, different screening methods have significantly decreased the incidence and mortality rates of cervical cancer.

Aims:

Evaluate the execution and describe the results of co-testing (simultaneous HPV and cytology) for cervical cancer screening at a primary healthcare centre in Lisbon (USF Tejo), in 2023.

Methods:

Data was collected using MIM@UF and SiiMA Screening platforms and analysed in Microsoft Office Excel®.

Results:

There were 1279 women eligible for co-testing screening, of which 343 were tested in USF Tejo. The women were 29-64 years old, with a mean age of 46,9. There were 36 (10,5%) positive results for high-risk HPV, 23 with a negative cytology and 13 with cytology abnormalities. The time between the execution and the result varied from 42 to 145 days (mean 77,9). The interval between the result and the referral to the hospital was 1-253 days (mean 57,9). The mean time between the referral and the gynaecology consultation was 128,5 days and ranged from 4 (HSIL) to 350 days (LSIL).

Conclusions:

This study demonstrates the relevance of co-testing. It is important to mention that there is no available information about women tested in private facilities. There are timings to improve, including the time taken to obtain the result and the time between the result and the gynaecology consultation. A universal platform and an automated referral process could enhance the efficiency and effectiveness of this screening program.

Clinical management of postmenopausal women attending colposcopy after an abnormal cervical cancer screening test – a survey across EFC member countries.

By authors Lotte K. Eriksen[1,2,3], Ane-Kerstin Skaarup Knudsen [1,2,3], Simon Leeson[4], Jane Zodzika[5], Anne-Marie van Haaften-de Jong[6], Laura Kotaniemi-Talonen[7,8], Jens Quaas[9] , Anne Hammer[1,2,3] on behalf of the EFC Quality and Standards Group

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Background:

Diagnostic work-up of postmenopausal women is often challenging as the transformation zone retracts into the cervical canal. This compromises the ability to identify potential lesions at colposcopy and collect adequate samples, resulting in an increased risk of missing high-grade disease. As there is currently no consensus across countries regarding clinical management of postmenopausal women in cervical screening, we want to gain knowledge on this matter for future purposes.

Aim:

Our goal is to explore how postmenopausal screening-positive women are managed across EFC member countries.

Methods:

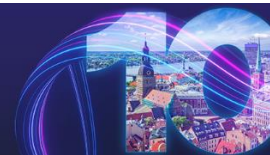
We conducted a survey across all EFC member countries from April – May 2024. Respondents were asked to complete a survey including questions on basic characteristics of the screening setting, the respondent, and local practices in clinical management of screen-positive postmenopausal women with a transformation zone type 3 (T3). Results will be reported descriptively using numbers and proportions. Comparison of results across countries will be made using chi2.

Results:

The data is being collected and will be presented at the conference.

Conclusion:

Results from this survey will reveal if different treatment strategies are used and disparities exist in clinical management of screen-positive postmenopausal women in cervical screening, potentially providing the foundation of a future consensus statement. Finally, results might uncover areas where further research is needed.



Gastric type endocervical adenocarcinoma with bilateral metastases to ovaries: a case report

By author Emeri Laas, a resident doctor in obstetrics and gynaecology

Background:

Gastric type endocervical adenocarcinoma (GEA) constitutes 10% of all cases of endocervical adenocarcinoma in the general population. It is a rare subtype of cervical cancer that is generally sporadic and not associated with HPV. Patients with GEA have a higher risk of ovarian metastasis compared to other subtypes of cervical cancer and are typically diagnosed at an advanced stage. GEA also has a worse prognosis than HPV-associated cervical cancer.

Clinical Case:

A 74-year-old female presented for a gynecological check-up with a 1.5-year history of lower abdominal pain. There was no history of gynecological examination in the past four years. A vaginal ultrasound revealed a tumor behind the uterus with associated ascites. A PAP test revealed HSIL. A CT scan demonstrated a bilateral ovarian tumor of unknown etiology. A midline laparotomy was performed along with a total hysterectomy with adnexectomy, omentectomy, and parailiacal lymphadenectomy. Cytology of the ascitic fluid was negative for malignancy. Histology revealed metastases in both ovaries and left fallopian tube with the primary tumor located in the cervix. The diagnosis was endocervical mucinous adenocarcinoma, gastric type (GEA); pT1B1 pN1A pM1(OTH) G2 LVI R0 IVB. Adjuvant radio chemotherapy was planned.

Conclusions:

The patient was not participating in the national screening program due to her age, but this case highlights the importance of the PAP test. Current trends favor HPV testing for cervical cancer screening, which will miss HPV-negative GEA.

Comparison of cytological and HPV-based screening within population-based screening program in Finland

By author Iiris Turunen & co-authors Ilkka Kalliala, Maiju Pankakoski, Veli-Matti Partanen

Background:

Cervical cancer screening in Finland started in the1960s, reducing both the incidence and mortality by approximately 80% since. HPV-based screening with cytology triage was introduced in Finland in organized screening 2012 onwards. HPV-based screening exceeded cytology-based tests in organized screening in 2019.

Aims:

We aimed to compare performance between primary HPV- and cytological screening and also between the first and second rounds of HPV-based screening within a routine screening program.

Methods:

We calculated the attendees, the proportions of positive primary screening tests, risk-group screening referrals, colposcopy referrals and CIN2+ findings for both HPV and cytological screening. The data covered all tests taken within the Finnish cervical cancer screening program between 2012 and 2022 from Finland's Mass Screening Registry. We included data only from full screening rounds.

Results:

were adjusted for age, region, socioeconomic status, and mother tongue. Results We identified 1,441,042 screening rounds, where 243,214 rounds were HPV-based and 1,197,828 cytology-based. In the preliminary analysis, the proportion of positive primary tests, risk group referrals, referrals for colposcopy and CIN2+-findings were more common in primary HPV screening. In the second HPV-screening round, the difference between groups was less pronounced. Complete data and final analysis adjusted for covariates are conducted within summer 2024 and results presented at the conference.

Conclusions:

In a well-established population-based screening program, in the first screening round, HPV-screening results in higher referral and CIN2+ detection rate, but in the second round, both the referral and CIN2+ detection rate seem to decline.

Reproducibility of colposcopy quality indicators - A survey among members of the European Federation for Colposcopy

By authors Tina Hovgaard Randrup[1], Simon Leeson[2], Andrea Ciavattini[3], Ahmed Eldib[4], Mihaela Grigore[5], Anne-Marie van Haaften-de Jong[6], Kristina Jariene[7], Vesna Kesic[8], Róbert Koiss[9], Laura Kotaniemi-Talonen[10], Jens Quaas[11], Terje Raud[12], Jana Zodzika[13], Anne Hammer[2,14]

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Background:

Colposcopy is essential in the diagnostic work-up of women with an abnormal cervical screening test as it guides the collection of biopsies. Although quality assurance has been used in evaluating screening programmes, not much is known on quality indicators (QIs) for diagnostics and treatment of screen-positive women. Therefore, the European Federation for Colposcopy (EFC) developed QIs aiming to support colposcopy practice across Europe.

Aim:

The aim of the survey was to determine if the developed QIs were understandable, relevant, and reproducible.

Methods:

We conducted a survey among all members of the EFC Quality and Standards Group from November 2022 to March 2023. Members were asked to collect information on a total of 17 QIs for 50 women who had been newly referred for colposcopy due to an abnormal screening test between January 1, 2020 to December 31, 2021. Results are reported descriptively.

Results:

We included data on 609 cases from 12 members across Europe. The majority of the QIs were either achieved or within reach of the agreed standard, often due to few countries with outlying data. One QI had very low performance, although stratified results indicated that two countries had different clinical management of the patient type thereby skewing the results. In addition, discrepancies between the number of cases included in each QI raised concerns regarding potential misunderstanding of the QI and its objective.

Conclusion:

QIs on colposcopy must be understandable to those collecting data, highlighting the importance of validating QIs before data collection.

Can implementing Swede score at conization increase the proportion of coni with negative resection margins? Preliminary data

By author Astrid Bakke Orvik & co-authors Tina Randrup, Maja Iversen, Sofie Lindman Juul, Anne Hammer. Dept. of Obstetrics and Gynecology, Goedstrup Hospital, Herning, Denmark

Background:

Every year, more than 5000 Danish women undergo conization due to cervical dysplasia. However, the proportion of coni with negative resection margins has declined in the past decades, currently at 54% nationally, with large regional variability. Positive margin is associated with an increased risk of recurrent dysplasia and cancer for up to 20 years. Different techniques exist to aid the clinician in securing negative margins. Iodine solution stains healthy epithelium mahogany brown, dysplastic or inflamed tissue stains yellow. In Denmark there is no tradition of using this test, which is, in addition to acetowhite staining, part of the standardized Swede score.

Aims and Method:

Quality assurance study in conjunction with implementation of Swede score at the Department of Obstetrics and Gynecology at Goedstrup Hospital, Denmark. Primary outcome was negative resection margins and cone size. Secondary outcome negative Test of Cure 6 months post conization. Cases with no dysplasia in cone was excluded.

Results:

To date we have included a total of 271 women: 171 controls, and 100 cases. CIN3 or AIS was found in 62% and 47% of coni, for controls and cases, respectively. Negative resection margin was found in 77% and 69%. TOC results are awaited.

Conclusion:

So far, we found no significant difference in the proportion of women with negative resection margins; however, the department performed better than the national and regional average, even before Swede score was introduced. A randomized study, including hospitals from different regions across Denmark, is welcomed.

Recognition of reserved cells and their proliferative pattern at clear margins of LEEP sample as possible marker of high risk of CIN2+ recurrences

By author Muryzina Iryna & co-authors Gargin V, Belodid O, Alekseeva V.

Background:

The excisional treatment (LEEP) of CIN2+ significantly reduced mortality from squamous cervical cancer (CC) but it still leaves gaps: still insufficient sensitivity of PAP-smear makes follow-up capable to miss the site of dormant HPV-infection (below test's sensitivity to recognize it) that might later cause recurrence of high-grade lesion. Reserved cells (RC) as progenitors of both squamous and columnar epithelium are considered as a HPV-habour and may experience transformation to AIS at the boundaries around excised squamous CIN2+ even with clear margins.

Aims:

Our study was to ascertain if recognition of RC with elevated markers of cellular proliferative activity in the clear margins might provide well-defined indications for the next LEEP necessary to reduce the risk of underdiagnosed cervical glandular intraepithelial neoplasia (CGIN) considering that SCJ is no longer available for colposcopy after prior LEEP.

Methods:

The study had accrued 83 patients with recognized CIN2+ selected for LEEP. Their LEEP samples were scrutinized using hematoxylin-eosin staining, immunohistochemistry to reveal RC (expression of cytokeratin CK7, CK19) and check their proliferative status (p63, Ki68), their pattern was then analyzed by approach of measurement uncertainty (coverage factor for the probability of 0.95 is assumed to be 2).

Results:

It turned out that 16% patients remained postoperative HPV-positive, 41% showed CK7 expression at clear margins, 18% CK7+ any of CK19, p63, Ki68 (CK7+); 21% were recognized with recurrent CIN2+ including all CK7+patients, in 8% recurrences it was CGIN (all CK7+).

Conclusions:

Recognition of RC and markers of RC-proliferation at clear margins might be viewed as high risk of CIN2+recurrence.

Probability and predictive factors of the absence of high-grade intraepithelial lesion on excision specimen following histological diagnosis of high-grade intraepithelial lesion

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Background:

Large loop excision, of the transformation zone is the reference treatment for high-grade intraepithelial lesion (HGIL). Such diagnosis should be achieved in at least 80% of cervical excision specimen.

Aim:

To identify the probability and predictive factors of the absence of HGIL on excision specimen from patients with previously proven HGIL.

Methods:

We conducted a multicenter retrospective study (2015-2021). All patients treated by loop excision following histological diagnosis of HGIL on cervical biopsy and/or endocervical curettage were included. Data were extracted from medical charts. Primary endpoint was the absence of HGIL on excision specimen, defined by the identification of a low-grade intraepithelial lesion only or no lesion at all.

Results:

A total of 2037 patients were included, with no HGIL in 191 (9.4%) cases. Three predictive factors of the absence of HGIL on excision specimen were identified: a small abnormal transformation zone (TZ) defined by the cervical involvement of only one quadrant (aOR: 2.01; 95% CI: 1.47-2.75; p<0.001), a colposcopic impression of minor changes or normal cervix (aOR: 1.73; 95% CI: 1.24-2.42; p=0.001), and negative, low-grade or ASCUS referral cytology (aOR: 1.37; 95% CI: 1.00-1.87; p=0.049). The proportion of patients with no HGIL on excision specimen ranged from 4.6% to 18.1% depending on how many forementioned factors were present.

Conclusion:

In patients with proven HGIL, absence of HGIL on excision specimen was observed in 9.4%. Predictive factors were a small abnormal TZ, a colposcopic impression of minor changes or normal cervix, and negative, low-grade or ASCUS cytology.

Parity as a predictive factor of cervical length regeneration after large loop excision of the transformation zone

By author Dr. Laura Lūse[1,3,4] & co-authors , Prof. Jana Žodžika[1,2], Prof. Natālija Vedmedovska[1,3], Maksims Zolovs[1]

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Introduction:

Large loop excision of transformation (LLETZ) increases preterm delivery risk, probably due to mechanical cervical defect or an alteration of the cervical barrier. There is insufficient data on the impact of cervical length regeneration after LLETZ.

Aim:

The present study aims to compare the cervical length regeneration three and six months after the LLETZ procedure between parous and nulliparous women.

Methods:

A prospective cohort study was performed in Riga East University Hospital 2022-2024. Women who were scheduled for LLETZ and agreed to participate in the study were included. CL measurements were carried out with a predefined ultrasound measurement technique. Cervical length regeneration (%) was calculated as cone specimen length minus the cervical deficit at 3 and 6 months divided by cone length and multiplied by 100. Cervical length regeneration between parous and nulliparous women was compared with a mixed ANOVA test. Ethical committee permission was obtained.

Results:

These are the preliminary results of ongoing study. We included 17 women. Cervical regeneration amount after 3 months was 48.0% for nulliparas and 56.1 % for multiparas, and after 6 months 62% and 118% for nulliparous and multiparous women respectively. Comparing cervical length regeneration of nullipara (CI 95% 29-69%) and multiparous (CI 95% 15-158%) regeneration, multiparas had 32% higher regeneration rate (p tuckey=0.032).

Conclusions:

Cervical length regeneration differs between parous and nulliparous women. Parous women have more pronounced cervical regeneration 6 months after LLETZ, indicating regeneration is more effective in parous women. Further studies are needed to draw further conclusions.

Risk of gestational diabetes mellitus following management for cervical intraepithelial neoplasia grade 2

By author Kirstine K. Katholm[1,2,3] & co-authors Ninna Lund Larsen[1,4], Kathrine D. Lycke[1,2,4], Lotte K. Eriksen[1,2,4], Tina H. Randrup[1,2], Anne Hammer[1,2,4]

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Introduction:

Active surveillance for cervical intraepithelial neoplasia grade 2 (CIN2) has been adopted as an option in women of reproductive age in many countries due to high regression rates and because a loop electrosurgical excision procedure (LEEP) is associated with reproductive harm. However, a recent study reported that active surveillance does not reduce the risk of preterm birth compared to LEEP, and other studies suggest HPV and dysplasia may pose obstetric risks.

Aim:

The aim is to investigate risk of gestational diabetes mellitus (GDM) in women undergoing active surveillance compared to LEEP.

Methods:

We conducted a historical cohort study using data from Danish national registers. We included women aged 18-40 with CIN2 and a subsequent singleton birth during 1998-2018. Using logistic regression we calculated odds ratios (OR) of GDM with the LEEP group as reference. We adjusted for year of CIN2 diagnosis, age, and cytology (aOR).

Results:

We included 10,537 women with CIN2 and a subsequent singleton birth; 4,430 women (42%) underwent active surveillance, and 6,107 women (58%) had a LEEP. The absolute risk of GDM was 3.0% (n=315). No significant difference was found between the active surveillance and the LEEP group (aOR 0.90 [95% CI: 0.71;1.14]). When stratifying by age, BMI, index cytology, and parity, results were similar.

Conclusion:

The prevalence of GDM was low with no major difference between active surveillance and LEEP, however, the prevalence was lower than in the general population. This suggests a need to investigate risk of GDM between women with and without CIN.

Evaluating the efficacy of Coriolus versicolor-based vaginal gel in conservative management of CIN2 lesions: an observational study

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Background:

Cervical intraepithelial neoplasia grade 2 (CIN2) has a 50% spontaneous regression rate under conservative management, posing a clinical challenge in treatment decisions.

Objective:

To assess the therapeutic impact of a Coriolus versicolor-based vaginal gel (Papilocare®) on the conservative management of CIN2 lesions.

Methods:

This single-center observational study combined retrospective and prospective analyses. The study included women aged ≥18 years diagnosed with CIN2, adhering to the AEPCC guidelines. Eligibility criteria included a visible transition zone on colposcopy, lesions affecting less than two quadrants, an uninvolved endocervix, and agreement to follow-up cytology/colposcopy after 6 months. The retrospective cohort (2010-2017) analyzed natural regression, persistence, and progression rates of CIN2 managed conservatively. The prospective cohort was treated with Papilocare®, administered as one cannula per day for the first month, followed by one cannula every other day for five months. Both cohorts had baseline and 6- month follow-up biopsies.

Results:

The study included 117 women in the retrospective cohort (mean age: 35.91 years) and 44 in the prospective cohort (mean age: 36.09 years). At 6 months, the treatment cohort showed a regression rate of 68.2%, persistence at 11.4%, and progression to CIN3 at 18.2%. In contrast, the retrospective cohort exhibited a 55% regression rate, with 13% persisting and 32% progressing.

Conclusion:

Preliminary findings suggest that treatment with Papilocare® may enhance lesion regression Further studies are needed to validate these results and potentially recommend this treatment as a preferable clinical option within the "wait and see" strategy for eligible patients with CIN2 lesions.

Efficacy of intensive regimen of a multi-ingredient Coriolus versicolor-based vaginal gel (Papilocare®) in HR-HPV clearance: preliminary pooled results from the PALOMA 1 and PALOMA 2 clinical trials

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Background:

PALOMA 1 clinical trial (CT) demonstrated the efficacy of Papilocare® in repairing HPV-related low-grade cervical lesions.

Aim:

The PALOMA 2 CT aimed to assess the efficacy of Papilocare® in promoting HR-HPV clearance.

Methods:

Randomized, multicenter, prospective, open-label, parallel-group, watchful waiting approach-controlled CTs. Unvaccinated HR-HPV positive women aged between 30-65 with ASCUS/LSIL cytology and concordant colposcopy were randomized into 3 groups: Standard Papilocare® regimen (A): 1 cannula/day (1 month)+1 cannula/alternate days (5 months); Intensive Papilocare® regimen (B): 1 cannula/day (3 months)+1 cannula/alternate days (3 months); Control group (C): watchful waiting approach. Pooled preliminary results on HR-HPV clearance (secondary endpoint) at six months for B versus C are presented. HPV clearance was considered as total (negative HPV test/disappearance of all species detected at baseline) or partial (disappearance of ≥1 HPV genotype present at baseline, together with normal cytology and concordant colposcopy observations). All patients signed informed consent. Studies were approved by centralized IRBs.

Results:

101 patients have been evaluated, 48 from regime B (22 from PALOMA 1; 26 from PALOMA 2) and 53 patients from control group (25 from PALOMA 1; 28 from PALOMA 2). Significant increase of HR-HPV clearance was shown in B vs C (85.4% vs 43.4.%, p< 0.0011). Patients with genotype 16 and/or 18 and/or 31 at baseline showed similar results: 82.6% vs 37.0.% (p< 0.0011) for B and C, respectively.

Conclusion:

These preliminary findings suggest that the intensive regimen of Papilocare® significantly enhances HR-HPV clearance, affirming its potential as a valuable clinical tool for managing HR-HPV infection compared to watchful waiting approach.

Efficacy of a multi-ingredient Coriolus versicolor-based vaginal gel on high-risk HPV clearance: preliminary results from the PALOMA 2 clinical trial

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Introduction:

High-risk (HR)-HPV infection is a critical precursor to cervical cancer.

Aim:

The PALOMA 2 clinical trial assessed the efficacy of a Coriolus versicolor-based vaginal gel (Papilocare®) in facilitating HR-HPV clearance as a secondary endpoint.

Methods:

Randomized, multi-centre, prospective, open-label, parallel-group, watchful waiting approach-controlled clinical trial. Unvaccinated HR-HPV positive women between 30-65 years old, with ASCUS/LSIL cytology and concordant colposcopy were randomized into 4 groups: A) Standard Papilocare® regimen: 1 cannula/day (1 month)+1 cannula/alternate days (5 months); B) Intensive Papilocare® regimen: 1 cannula/day (3 months)+1 cannula/alternate days (3 months); C) Very Intensive Papilocare® regimen: 1 cannula/day (6 months) D) Control group: watchful waiting approach. Preliminary results of arm A, B and A+B vs D on HR-HPV clearance after a 6 month-treatment are presented. HR-HPV clearance was categorized as complete (negative HR-HPV test or no detectable baseline genotypes) or partial (disappearance of ≥1 genotype with normal cytology and concordant colposcopy). Ethical approval was obtained. All participants gave informed consent.

Results:

116 patients with a mean age of 40.5 years were randomized. The 48.5% were smokers without differences between groups. From the 80 patients (A= 26; B= 26; D= 28) who completed the 6-month treatment, 57.7% (A), 88.5% (B), 73.1% (A+B) vs 46.4% (D) obtained HR-HPV clearance (pAvsD=0.4078, pBvsD=0.0011 and pA+BvsD=0.0180).

Conclusion:

Preliminary findings indicate that Papilocare®, particularly the intensive regimen, significantly enhances HR-HPV clearance compared to watchful waiting approach. These results support the potential of Papilocare® as a proactive management option for women with HPV-dependent low-grade cervical lesions. Final analysis will further clarify these impacts.

Efficacy of intensive regimen of a multi-ingredient Coriolus versicolor-based vaginal gel in increasing HPV clearance: results from the PALOMA clinical trial

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Background:

Cervical cancer is intimately linked to HPV persistency. Viral genotype increases persistency risk.

Aim:

A secondary endpoint in the PALOMA clinical trial was assessing the efficacy of a Coriolus versicolor-based vaginal gel (Papilocare®) increasing viral clearance.

Methods:

Randomized, multi-center, open-label, parallel-group, watchful waiting approach controlled clinical trial. Unvaccinated HPV-positive women aged between 30-65 with ASCUS/LSIL cytology and concordant colposcopy were randomized into 3 groups: A) Standard Papilocare® regimen: 1 cannula/day for 1 month+1 cannula/alternate days for 5 months; B) Intensive Papilocare® regimen: 1 cannula/day for 3 months+1 cannula/alternate days for 3 months; C) Control group: watchful waiting approach. Results of arm B vs C on HPV clearance are presented. HPV clearance was considered as total (negative HPV test or disappearance of all species detected at baseline) or partial (disappearance of ≥1 HPV genotype present at baseline visit, together with normal cytology and concordant colposcopy observations).

Results:

91 HPV-positive women with a mean age of 40.5 years were included in the study. At baseline, from the 31 HPV-positive women in the B arm, 24 were high-risk (HR)-HPV positive, whereas 26/31 women were HR-HPV positive in the control group. The intensive regimen showed significant increase of HPV clearance compared with the control group, both in total HPV (75.9% vs. 41.9%, p=0.007) and HR-HPV positive (81.8% vs. 40.0%, p=0.0036) population.

Conclusions:

intensive Papilocare® regimen significantly increased HPV clearance in HR-HPV patients compared to conventional watchful waiting approach. These findings underscore the potential of Papilocare® as an effective intervention in promoting HPV clearance and reducing cervical cancer risk.

Effect of a multi-ingredient Coriolus versicolor-based vaginal gel on HPV 16/18 clearance: preliminary results from the PAPILOCAN clinical trial

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Introduction:

HPV 16/18 persistent infections increase cervical cancer risk.

Aim:

The PAPILOCAN clinical trial investigates the efficacy of a Coriolus versicolor-based vaginal gel (Papilocare®) in high-risk (HR)-HPV clearance in persistently infected individuals, as a secondary objecөve.

Methods:

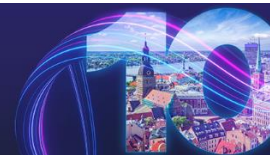
Randomized, prospective, double-blind, parallel-group, lactic acid-controlled clinical trial. Vaccinated or unvaccinated persistent HR-HPV positive women aged between 30-65 with ASCUS/LSIL cytology and concordant colposcopy were included in a single Spanish hospital. Patients were randomized (1:1) into four groups: two treatment groups receiving the Standard Papilocare® regimen (A): 1 cannula/day (1st month)+1 cannula/alternate days (5 months), and Intensive Papilocare® regimen (B): 1 cannula/day (3 months)+1 cannula/alternate days (3 months); and two corresponding control groups (CA and CB). HPV 16/18 clearance assessed by Cobas 4800, comparing A, B, and A+B against respective active controls after a 6-month treatment period are presented. All patients signed informed consent. The study was approved by the hospital's IRB.

Results:

40 participants (A=14, CA=11, B=5, CB=10) with a median age of 40.7 years were analysed. After the 6-month treatment, HPV 16/18 clearance rates were 50% (A) vs 45.4% (CA), 60% (B) vs 20% (CB), and 52.6% (A+B) vs 33.3% (CA+CB). During follow-up, 5 patients withdrew: 1 from Papilocare® arm due to known adverse event, and 4 from control group, 3 of whom had an excisional treatment due to lesion's progression.

Conclusion:

Although these results are preliminary, they suggest that intensive Papilocare® regimen may be effective in clearing persistent HPV 16/18 infections. This positions Papilocare® as a potentially valuable intervention in the management of HR-HPV infections.



Risk of anogenital precancer and cancer in women undergoing active surveillance for CIN2 – a population-based cohort study

By authors Dina O Eriksen[1,2,3], Kathrine D Lycke[1,2,3], Pernille T Jensen[2,4], Nicolas Wentzensen[5], Megan A Clarke[5], Anne Hammer[1,2] et al

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Presenter: Anne Hammer

Background:

Active surveillance for CIN2 has recently been implemented as an option for younger women with CIN2 in many countries due to high regression rates. However, a previous study reported an up to four-fold higher risk of cervical cancer in women undergoing active surveillance compared to those treated with loop electrosurgical excision procedure (LEEP).

Aim:

We aimed to investigate risk of vulvar, vaginal, and anal cancer and precancer in women undergoing active surveillance compared to LEEP.

Methods:

We conducted a nationwide population-based cohort study including all Danish women, aged 18-40 years, diagnosed with incident CIN2 during 1998-2020. Women were grouped into active surveillance (i.e., a subsequent record of a biopsy/cytology) or LEEP (i.e., a subsequent record of a LEEP). We calculated weighted hazard ratios (wHRs) of vulvar, vaginal, and anal cancer and cancer using Cox proportional hazards regression and inverse probability treatment weighting. Age, region of residence, calendar year, and index cytology were considered confounders.

Results:

We identified 27,505 women with CIN2, 12,507 (45.5%) of whom underwent active surveillance, and 14,998 (54.5%) underwent a LEEP. A total of 162 (0.6%) women had a subsequent diagnosis of vulva, vaginal, or anal cancer or precancer. No difference was found in the risk of disease between women undergoing active surveillance and LEEP (wHR=0.89 (95% CI 0.61-1.30)). Similar findings were observed when stratifying by age, site of lesion, and calendar time.

Conclusions:

Active surveillance for CIN2 is not associated with an increased risk of vulvar, vaginal, or anal cancer and precancer compared to LEEP.

Can Swedescore improve the diagnostic accuracy of cervical cancer and precancer? A Danish multicentre intervention study

By authors Knudsen, Ane-Kersti (presenter)[1,2], Randrup, Tina[2], Gustafson, Line[3,4], Booth, Berit[5,6], Kesmodel, Ulrik[1,7], Hammer, Anne[1,2] et al

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Background:

Women with abnormal cervical screening tests are referred for diagnostic work-up with colposcopy and cervical biopsies, which are the gold standard for detecting cervical cancer and precancer. Studies have shown considerable intra- and interobserver variability in colposcopy, even among experienced colposcopists. There is no formal colposcopy training or practice of using a colposcopic scoring tool in Denmark. A standardized colposcopic scoring tool, Swedescore, has been developed to find or exclude high-grade lesions as cervical intraepithelial neoplasia grade 2 or higher (CIN2+).

Aims:

To explore whether implementation of Swedescore can improve diagnostic accuracy of cervical cancer and precancer.

Methods:

Prospective multicenter, non-randomized intervention study with five public colposcopy clinics and two private colposcopy clinics in Denmark. Enrollment began in May 2023 and is expected to end in July 2025. Colposcopies with Swedescore (intervention clinics) are compared with colposcopies without Swedescore (reference clinics) in detecting CIN2+. Cervical biopsies at all inclusion sites are sent in two separate vials for target and random biopsies. Characteristics of the women are collected from medical records. From the Danish Pathology Databank, we collect data on previous screening history, cervical biopsies, and/or cervical excisions. The sensitivity, specificity, the negative and positive predictive value of the Swedescore for CIN2+ detection will be estimated and compared with reference clinics. ROC curves will be made.

Results:

Data collection is ongoing. Preliminary results will be presented.

Conclusion:

The study will provide important knowledge of using Swedescore for colposcopic examination in Denmark, potentially improving the detection of cervical cancer and precancer.

Internal audit of the Center of Expert Colposcopy: Is it possible to meet the ECF criteria?

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Abstract:

Centres of expert colposcopy help to reduce the incidence of invasive cervical cancer, and with accurate diagnosis and early treatment of high-grade precancerous lesions and microinvasive stages. Centers of colposcopic expertise play an important role in the prevention of overtreatment in the form of unnecessary conizations.

According to the recommendations of the EFC - 2017: Update of the EFC performance standards for the practice of colposcopy - the main criteria that should be met to achieve ideal results are set, these criteria are very difficult to achieve even for the best colposcopy centres in Europe. We assume that an internal audit is missing in most colposcopy centres, national audit is missing in almost all European countries. Without an audit, the work of colposcopists cannot be reliably evaluated and the full potential of available health care is not exploited. Centre of Outpatient Gynaecology Clinic and Primary care, Brno, Czech Republic is a centre of colposcopic expertise with more than 100 referring doctors from Czech Republic and other foreign countries. In 2022, we performed 800 conizations, all procedures were performed by only two gynaecologists. Every year we conduct a comprehensive internal audit, therefore we have collected unique numerical data due to the detailed nature of the analysis. The results are comparable to the best centres in Europe and the world.

An internal audit should be an important matter for every centre of colposcopic expertise and it is essential for quality assessment. But is it possible to meet the strict EFC criteria?

Adequacy of excisional treatment for cervical precancer in Denmark

By authors Knudsen, Ane-Kersti (presenter)[1,2], Randrup, Tina Hovgaard[2], Gustafson, Line[3,4], Booth, Berit[5,6], Kesmodel, Ulrik Schiøler[1,7], Hammer, Anne[1,2] et al.

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Background:

An effective cervical cancer screening program relies on a high-quality screening test and high participation rates. However, it is of utmost importance that women with cervical precancer receive adequate treatment to avoid progression to cancer. Adequacy can be evaluated by assessing margin status and test of cure (TOC)

Aims:

To describe the temporal trends in women with negative resection margins and a negative TOC among Danish women who had a large loop excision of the transformation zone (LLETZ).

Methods:

We conducted a nationwide cross-sectional study using The Danish Pathology Databank. We included women of all ages who had a LLETZ from 1995-2020. The primary outcome is a negative resection margin, and the secondary outcome is a negative TOC. We will report the proportion of women with the outcomes overall and stratified by histopathological diagnosis, age, residence region, and calendar time of LLETZ. Evaluation of time trends will be made using the Joint-Point regression analysis.

Results:

Preliminary results show that the proportion of women with negative margins decreased over time, from 66% in 1995-2012 to 54% in 2017-2021, and decreased with increasing severity, from 71% in CIN1 to 50% in CIN3. Women aged 23-30 were more likely to have negative margins than those aged 41-50 (57% vs. 46%). Women with negative margins varied from 42% in the Capital Region to 67% in the Central Denmark Region. Data on TOC will be presented at the conference.

Conclusion:

An increasing number of women receive inadequate treatment for cervical precancer in Denmark.

HPV vaccination and recurrence of cervical intraepithelial neoplasia: insights from a retrospective analysis

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Background:

Cervical cancer (CC) is primarily caused by persistent infection with oncogenic human papillomavirus (HPV). Nonavalent vaccine can prevent almost 90% of CC cases. Secondary prevention includes screening and treatment of premalignant lesions, but up to 8%mayrecur. Recent studies suggest that the vaccine may reduce recurrence rates in women undergoing conization.

Aims:

To evaluate the efficacy of vaccination in reducing cervical lesion recurrence and HPV infection.

Methods:

This observational and retrospective study evaluated the clinical records of patients who underwent conization for cervical intraepithelial neoplasia and subsequent cotest evaluation at the Santo Espírito Hospital, Ilha Terceira, from 2016 to 2023. Statistical analysis was conducted using SPSS Statistics 27.

Results:

The study included 80 women with an average age of 43 years. The vaccination rate was 55% (44 women). The post conization recurrence rate was 10% (8 patients) for low- and high- grade lesions, with 3 patients having high-grade lesions. In the cytology control, 41vaccinated women had negative intraepithelial malignancies compared to 29 unvaccinated women. Recurrence was found in 3 vaccinated patients versus 7 unvaccinated patients (p=0.1042, Fisher's exact test). Regarding posttreatment HPV status, 9 vaccinated patients were HPV positive, while 12 unvaccinated patients were HPV positive. HPV negativity was detected in 35 vaccinated and 24 unvaccinated patients (p =0.2123, Fisher's exact test).

Conclusions:

The results suggest a potential benefit of vaccination in reducing post conization intraepithelial lesions and HPV persistence. However, statistical significance was not achieved. Additional studies with larger sample sizes are necessary to confirm these trends.

Routine program audit of cervical cancer to identify remaining risks and guide elimination efforts

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Background:

Recurrent audits of the screening process are recommended in the European Guidelines for Quality Assurance in Cervical Cancer Prevention in order to systematically monitor and evaluate cervical cancer screening.

Aim:

The aim of this study was to present a model for routine annual audits that has been adopted and implemented nationally.

Method:

All cancer cases between 2018-2022 were collected from the Swedish Quality Register of Gynecological Cancer (SQRGC) where date of diagnosis, age, FIGO stage, histopathology, and mode of treatment were registered. Data on screening invitations and screening history and status were collected from the National Cervical Screening Registry (NKCx). Process related causes related to organization and sampling, lab procedures or management of positive tests were interpreted from register data. Incidence of cervical cancer was estimated by risk group to demonstrate where improvements in the screening program chain are needed.

Results:

Advanced cancer cases were dominating, especially among older women, who have left the screening program without a negative HPV-test. Cancers cases in younger women were mostly screen detected in early stages. Dominating cause of cancer was failure in screening participation. Twenty six percent of cases were explained by deficiencies in detection of abnormalities in samples.

Conclusion:

Annual national register based audits with local review of clinical charts are an important part of screening program quality assurance and can be used to identify patterns of increased risk. Annual national audits like the Swedish model should be performed to routinely identify patterns of increased risk and guide program optimization.

The role of colposcopy in identifying precancerous changes in the cervix

By author Nargiz Gurbatova, Department of Gynecology, Turan Hospital, Baku

Introduction:

Cervical cancer is a health problem in many countries. Azerbaijan is a country in the Transcaucasian region, located on the border of Europe and Asia. In Azerbaijan, every woman can undergo free cytological and colposcopic examination under the state insurance program.

The purpose of this study was to evaluate colposcopy in the detection of severe intraepithelial lesions of the cervix and the ratio of these results with the results of a biopsy at the Turan Private hospital in Baku, Azerbaijan.

Method:

This is a retrospective study of 241 colposcopies and 161 biopsies performed under the control of colposcopy. The 2011 IFCPC Nomenclature of Colposcopy was used.

Results:

The average age of the participants was 44 years, mostly multiparous (80%). The main indications were contact bleeding, suspicious cervical cancer, positive HPV, abnormal cytological examination. In 25% of cases, colposcopy was normal.

Abnormal pattern of the 2 degree (58/241) -24%
Invasion (5/241) -2 %
Abnormal colposcopik findigs of the 1 degree (118/241)-49%
Norm (60/241)- 25 %
Of the 118, 98 were taken for biopsy, the rest were under observation.
After histological analysis of biopsies, after a biopsy performed under the supervision of colposcopy,
we found:
41 HSIL - (49/161) 25 %
3 canser (3/161) - 1,8 %
64 LSİL (64/161) - 39,7 %
52 norm (52/161) 32,2%

The coincidence with the colposcopy was:
41/58 -71 % (HSİL)
64/98 -65% (LSİL)
3/5 60 % (Cr)

Conclusion:

colposcopy retains all its importance in the diagnosis of precancerous lesions of the cervix.

Outcomes of CIN 2, with special reference to 'conservatively' managed CIN 2

By authors Deirdre Lyons, Stacey Bryan - Dept of Colposcopy, Imperial College Healthcare NHS Trust (ICHT)

Introduction:

CIN 2 management has changed with more 'conservative' management for younger women. However the outcomes of conservative management does need to be regularly audited. Review of previous CIN 2 management at ICHT in 2013, (N=290) - 2 year follow-up period showed 19.67% patients improved or 'cleared' the CIN 2. 80% patients were treated, with most of them showing CIN 2+, Of those treated for CIN 2 –19% had a final outcome of ≤ CIN 1.

Methods:

This is a re-audit - Assessment of patients diagnosed with CIN 2 on biopsy over period 01/01/2021 - 31/12/2021 and review of outcomes in terms of longitudinal outcomes over a 2 year period. Review of outcomes of CIN 2, looking at time taken to improve, or progress and outcomes of final excision.

Results:

213 patients were diagnosed with CIN 2 in the time period 01/01/2021 – 31/12/2021. Total treated -157, 'Conservatively' managed CIN 2 – 56 (26%). Of those initially conservatively managed, 10 (17.6%), subsequently had an excisional treatment. Referrals for patients who were treated, showed significantly more HG referrals that those conservatively managed (P=0.000017) All conservatively managed patients exhibited a high grade abnormality in 2 quadrants only. MDT discussion occurred in 48 (14%) of conservatively managed CIN 2.

Conclusion:

80% Conservatively managed CIN 2 –regressed (54%) or improved (27%) over 2 years All conservatively managed CIN 2, deemed 1-2 quadrants of disease MDT discussion is mandatory for all conservatively managed CIN 2. Regular long term audit of outcomes is essential for safe management.

Evaluation of C-ARG and Equalis' national External Quality Assurance (EQA) scheme of colposcopy examinations 2024

Hanna Milerad (presenter)[1], Josefin Ågren[2], Karin Dahlin Robertsson[2], Henrik Edvardsson[3], Kristina Elfgren[1,3]

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Background:

The Swedish task force for cervical cancer prevention and colposcopy (C-ARG) and Equalis annually conduct quality assurance in colposcopy inviting all Swedish gynaecologists. External quality assurance ensure quality and accurate, comparable examination results. Equalis is a nonprofit provider of different quality assurance schemes including diagnostic imaging, The results of the latest round (2024) are presented as an example.

Aims:

To investigate the assessments of a colposcopy examination and to evaluate how/if an EQA scheme could be integrated in clinical praxis.

Methods:

The round consists of 5 patient cases including colposcopic images and anamnesis. The cases, selected by 6 expert colposcopists, are assessed regarding transformation zone, colposcopic assessability, Swedescore, and a combined colposcopic assessment. The clinics may register 5 individual and 1 consensus response.

Results:

Participants increased compared to previously, 42/35 clinics reported 107 individual and 25 consensus responses. The results were reviewed against a response assigned by experienced colposcopists based on the biopsies Location of the lesion, type of TZ and colposcopic assessability had a high concordance (85-99%) while Swedescore had a variation with 44-94% agreement to the expected response. The lowest agreement was for one cases with AIS and HSIL and a case with a small lesion of HSIL close to TZ3. These cases also seemed to be the hardest to assess for the combined colposcopic assessment with 69%-85% agreement and more than 30% assessing it LSIL or normal.

Conclusions:

External quality assurance is a promising tool for quality assurance of colposcopy as well as for further education of the colposcopists in Sweden.

Screening behaviour after HSIL/AIS and the risk of invasive cervical and vaginal cancer: A nationwide cohort study 1999-2018

By authors Hanna Milerad[1], Pär Sparen[2], Anna LV Johansson[3], Kristina Elfgren[4], Bengt Andrae[5], Alexander Ploner[6], Miriam Elfström[7]. Joint last authorship.

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Background:

Women previously treated for high grade intraepithelial lesions (HSIL) and adenocarcinoma in situ (AIS) have an increased risk of developing recurrent HSIL/AIS and invasive cervical or vaginal cancer compared to the general population. Follow-up after treatment is recommended, but the role of the first test after HSIL/AIS treatment (test of cure) with regard to subsequent follow-up is unknown.

Methods:

Women resident in Sweden 1999-2018 diagnosed with HSIL/AIS were identified through the National Cancer Register and their outcome of interest (cervical and vaginal cancer) was also assessed, and further linked to the National Cervical Screening Registry for information on cervical screening history. Adherence to follow-up was defined by National guidelines. Risk of cancer was modelled as Cox proportional hazard regression.

Results:

At baseline, 78,844 women with HSIL/AIS were identified, Out of these, 67,693 were still at risk one year after HSIL/AIS and assessed for a test of cure, and 213 were identified as having a subsequent cervical or vaginal cancer. Testing was divided into four different states defined by test of cure vs no test of cure stratified by follow-up testing. For each state there was an excess risk of invasive cervical or vaginal cancer for women without a test of cure: no followup (HR 13.9, CI 1.6-121.1), irregular follow-up (HR 2.3, CI 1.1-4.7), regular follow-up (HR 1.4, CI 0.8-2.2), the time period after being eligible for the test of cure and before initiating follow-up (HR 4.8, CI 1.8-13.1).

Conclusion:

The risk for cervical or vaginal cancer was elevated in women without a test of cure and subsequent irregular or no follow-up, with a statistically significant substantial extra risk for the time period after being eligible for the test of cure and before initiating follow-up. Efforts to increase participation in follow-up during the first three years after treatment of HSIL/AIS should be prioritized.

DNA methylation for risk-stratification of screen-positive women with a TZ3

By authors Binderup, K.O*[1,2,3], Boers, J.*[4,5], Gustafson, L.W.[1,6], Gribnau J.[4], Tranberg, M.[1,3,7], Hammer, A[2,3] et al

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Introduction:

The performance of colposcopy is often impaired in older women because the transformation zone retracts into the cervical canal. This challenges the identification of potential lesions and makes sampling difficult, resulting in an increased risk of underdiagnosis. Thus, there is a need to explore potential biomarkers that can identify women at increased risk of cervical cancer and its precursors to ensure timely treatment.

Aim:

To evaluate the clinical utility of DNA-methylation markers for CIN2+ detection among older women with a transformation zone type 3 (TZ3).

Methods:

We conducted a cross-sectional study in Denmark during 2019-2021. Eligible women were ≥45 years, referred for colposcopy due to an abnormal screening result, and had a TZ3. Each woman had a cervical cytology sample and biopsies collected followed by a loop electrosurgical excision procedure (LEEP). Cervical samples were subsequently analysed for 3 pairs of methylation markers; FAM19A4/miR124-2, ARID3C/ ARL5C, and METloc001/ METloc002 (two intergenic-regions). We calculated the sensitivity and specificity of the methylation markers for CIN2+ detection using the LEEP result as reference.

Results:

We included 89 women with a median age of 67.9 years. A total of 31 (34.8%) women had CIN2+ detected. The sensitivity of FAM19A4/miR124-2, ARID3C/ ARL5C, and METloc001/ METloc002 for CIN2+ detection was quite similar at 77.4%, 74.2% and 74.2%, respectively. In contrast, the specificity was lower for FAM19A4/miR124-2 (39.7%) compared to ARID3C/ ARL5C (65.5%) and METloc001/ METloc002 (82.8%).

Conclusion:

DNA methylation may be useful for risk-based management of older screen-positive women.

Analysis of screening history of cervical cancer cases in Latvia

By author Elvita Penka[1] & co-authors Renāte Putniņa[2] Jana Lepiksone[3], Jana Žodžika[4]

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Background:

Latvia has one of the highest cervical cancer rates in Europe. An organized population-based screening program was implemented in 2009, and in 2022, primary HPV screening was introduced.

Aims:

This study aims to analyze the screening history of women diagnosed with cervical cancer in 2022.

Methods:

Data from the Register of Patients Suffering from Certain Diseases was used in an observational study of women diagnosed with cervical cancer in 2022. The analysis included screening test history and HPV vaccination status from 2014 to 2022 from the National Health Service system for publicly funded outpatient services.

Results:

In 2022, 150 women with a diagnosis of cervical cancer were registered. The average age was 61.5 years. In the period, between 2014 and 2022, none had received the HPV vaccine. 117(78%) women were invited for screening at least once. 56(47.9%) women underwent at least one screening test and only 15(12.8%) women did all screening tests. 70%(n=14) of women with stage I cervical cancer, 46.7%(n=7) with stage II, 63.6%(n=21) with stage III, and 23.5%(n=4) of women with stage IV cervical cancer underwent screening. Between 2014 and 2022, 2 screening cytological tests were unsatisfactory, 37 had no intraepithelial lesion found, 5 had ASC-US, 3 had LSIL, 15 had HSIL, 2 had AGUS, and 10 showed signs of malignancy in cytology. 18(32%) of women underwent a colposcopy.

Conclusions:

There could be several reasons for the high incidence of cervical cancer in Latvia. Possible factors include low participation in screening, insufficient quality of screening tests, and non-adherence to existing guidelines.

Prevention of cervical cancer in Latvia

By author Gunta Lazdane & co-authors Anda Kivite-Urtane, Jana Zozika

Background:

Cervical cancer is a unique cancer having well developed primary and secondary prevention possibilities. Organized population based cervical cancer screening was introduced in Latvia in 2009 and Latvia was one of the first countries in the WHO European Region to include HPV vaccine in the vaccination calendar for girls in 2010.

Aims:

The aim is to analyze the dynamics of HPV vaccination and cervical cancer screening in Latvia and the impact of primary and secondary prevention of cervical cancer morbidity and mortality.

Methods:

Data from the National Health Statistics Database on HPV vaccination and cervical cancer screening and survey data from 2011 and 2023 have been analyzed.

Results:

The coverage of cervical cancer screening in Latvia has increased from 15.3% in 2010 to 55.2% in 2023. Recent survey data confirm that only 74% of women who have received the invitation to screening have performed it. According to the official statistics HPV vaccination rate for 12 years old girls one dose has increased from 49.2% in 2010 to 71.4% in 2022; complete HPV vaccination course rate has no progress as it was 56.5% in 2019 and 51.1% in 2022. Refusal from HPV vaccination has increased from 13% in 2011 to 20% in 2019. New cases of cervical cancer in Latvia have decreased from 22.1 per 100 000 population in 2010 to 16.7 in 2021.

Conclusions In Latvia the incidence of the cervical cancer is slowly decreasing as a result of improvement of primary and secondary prevention, but it is still behind the global goals on elimination of cervical cancer.

The effect of the COVID-19 pandemic on colposcopy services and practice: a systematic review and meta-analysis

By author Giovanni Delli Carpini & co-authors Zahid Mammadov, Simon Leeson, Andrea Ciavattini

Aim:

To evaluate the effect of the COVID-19 pandemic and its required pause in global colposcopy services on the detection of precancerous lesions and cervical cancer.

Methods:

Studies reporting comparative data on colposcopy services between the COVID-19 prepandemic and pandemic periods were included. MEDLINE and Embase were searched for studies published from March 2020. The number of colposcopies, CIN2+, cervical treatments, and cervical cancer diagnoses per month were compared between the prepandemic (before March 2020) and pandemic period (after March 2020). The effect measure was the standardized mean difference (SMD), reported as the difference in standard deviations (SDs) with 95% confidence intervals (CI). Heterogeneity was evaluated with the chi-squared test and quantified with the I^2 method. This review was registered on PROSPERO (CRD42023447188).

Results:

Sixteen studies were included. During the pandemic, the number of colposcopies per month decreased by -1.67 SD (95% CI -3.37 to -0.08, p = 0.04) (4 studies, I^2 = 85.57%, p < 0.0001). The number of CIN2+ diagnoses per month decreased by -2.06 SD (95% CI -4.01 to -0.12, p = 0.04) (4 studies, I^2 = 89.17%, p < 0.0001). The number of cervical treatments per month decreased by -2.80 SD (95% CI -4.61 to -0.99, p = 0.0024) (5 studies, I^2 = 87.54%, p < 0.0001). The number of invasive cancer diagnoses per month decreased by -1.86 SD (95% CI -2.89 to -0.83, p = 0.0004) (10 studies: I^2 = 84.60%, p < 0.0001).

Conclusions:

During the COVID-19 pandemic, there was a reduction in CIN2+, cervical treatments, and invasive cancer diagnoses, leading to a risk of missed or late diagnoses and potentially worse prognoses for affected patients.

The Risk Factors of Cervical Squamous Intraepithelial Lesions Among Women Attending Colposcopy Clinic

By authors Natalija Berza[1], Jana Zodzika[1,5], Anda Kivite-Urtane[1,6], Nicholas Baltzer[2], Alise Curkste[1], Ilva Pole[5], Mari Nygard[2], Kersti Parna[3], Mindaugas Stakunas[4], Anna Tisler[3], Anneli Uuskula[3]

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Background:

Cervical squamous intraepithelial lesions (SIL) is a long-lasting, pre-invasive disease that plays an essential role in the natural history of cervical cancer. The age-standardized incidence of cervical cancer in Latvia was relatively high and accounted for 18.4 cases per 100,000 (the 6th highest in Europe) in 2020. Early detection and treatment of cervical precancerous lesions reduces the incidence of cervical cancer. Different factors may affect SIL progression and cervical cancer development. The study aimed to identify risk factors for cervical SIL in a country with high cervical cancer incidence.

Materials and methods:

A cross-sectional study was conducted from February 2021 to April 2022 in Latvia among women of screening age (25-70 years). Women from two different populations were invited to participate in the study – the low-risk population visiting a general practitioner and the high-risk population referred to a colposcopy clinic due to abnormal screening tests or follow-up of previously diagnosed SIL. The study group consisted of a high-risk population having CIN on biopsies, and a control group consisted of women with negative HR-HPV from the low-risk population. Univariate and multivariate binary logistic regression was used to identify factors associated with cervical LSIL and HSIL in colposcopy biopsy. Results were considered statistically significant at $p<0.05$. The Riga Stradiņš University Ethics Committee approved the study (number of approval 6-1/07/ 33).

Results:

A total of 743 women from the high-risk population and 537 women from the low-risk population were included in the data analysis. During colposcopy examination in taken biopsies, histology revealed that 34.1% had LSIL, and HSIL was detected in 60.7%. Multivariate logistic regression adjustment showed that LSIL histological positivity was connected with another vs. Latvian ethnicity (OR 2.7, p=0.005), sexual and reproductive health behavior like 6 or more lifetime sex partners (vs. 1-2 partners, OR 3.1, p=0.025), and also with the last visit to gynecologist 1-5 years ago (vs. <=1 year ago, OR 0.156, p=0.003). For the HSIL group, statistical significance remained for those who gave up smoking (vs. never smoked) (OR 2.6, p=0.04) and also had the last visit to a gynecologist 1-5 years ago (vs. <=1 year ago) (OR 0.159; p=0.004).

Conclusion:

We documented that a higher cervical LSIL burden is associated with non-Latvian ethnicity. LSIL was significantly related to sexual and healthcare-seeking factors, and HSIL positivity was associated with health behavior and healthcare-seeking factors.

Comparative analysis of Pap-test and histological examination in various degrees of cervical intraepithelial neoplasia (CIN)

By author Dissyukeyva Ylena (Ph D ob-gyn of the Gynecology Unit of the Clinical Academic Department of Women's Health of the University Medical Center Corporate Fund) & co-author Gabdilashimova Zarema (professor ob Gyn Medical University Astana)

The study compared 80 paired abnormal cytological findings and histological reports of HPV-positive female patients with abnormal colposcopic patterns: ASCUS (n=207); LSIL (n=207); HSIL (n=57); ASC-H (n=57). The age of the patients was 30-70 years (mean age 30±11 years).

Inclusion criteria: fertile age, HPV carriage, cytological finding (ASCUS, LSIL, HSIL, ASC-H), abnormal colposcopic pattern indicating biopsy.

Exclusion criteria: pregnant women, normal cytological findings, cases with over 8-10 months interval from cytological examination to biopsy, and cervical biopsies without prior cytological examination.

Cytological and histological concordance was achieved in 23 (28.75%) patients. Minor mismatch occurred in 41 (51.25%) cases. Significant mismatch between cytological and histological findings was in 16 (20%) cases, with 9 (11.25%) patients with ASCUS cytology having a histological diagnosis consistent with HSIL (high-grade intraepithelial changes suspicious of ingrowth into subjacent tissues), and 3 (3.75%) patients with HSIL cytology having ASC-H on histological examination.

Cervical screening reduces CC risk via cytological examinations, but histological examinations are crucial for accurate diagnosis and therapeutic decisions. Comparative analysis showed underestimation and overdiagnosis in all groups, with significant treatment-impacting differences in 6.9% of cases.

Pelvic vessel embolization: life saving procedure for vaginal bleeding in advanced cervical cancer

By author Lubova Lapidus & co-authors Zane Grabe, Ella Ņesterenko, Aina Kratovska

Introduction:

Cervical cancer remains one of the most common cancers in women worldwide. 77% of patients have an advanced stage. About 6% of patients have uncontrolled massive bleeding from the genital tract and this is also the cause of death. Emergency ligation of the internal iliac arteries as life-saving operation was first used by Howard Kelly to stop bleeding due to cervical cancer in 1894. Today, alternative non-surgical treatment is more used pelvic artery embolization, which achieves good hemostasis.

Clinical case:

A 29-year-old patient is presented with cervical cancer. In 2018 patient's cervical cytology was A1 - normal. In 2019 patient had spontaneous labor. In October 2020, she had a hormonal intrauterine device inserted. After that, she complained of pathological vaginal bleeding and bleeding after sexual intercourse for last six months. In 2021, patient was diagnosed with advanced-stage cervical cancer IIB and was treated by radiotherapy and chemotherapy. During two years disease was progressing and patient had uncontrollable vaginal bleeding. In February 2023, patient underwent palliative uterine artery embolization. Despite this, after two weeks patient continued to bleed heavily and died of stage IIB cervical cancer in March 2023.

Conclusion:

Massive vaginal bleeding is a serious complication in advance cervical cancer with high risk of death. Today, endovascular treatment is the first choice for massive bleeding and more often used. Surgical blood vessels ligation is also optional method, which is imported and used, when embolisation is impossible.

Understanding Women's Values in Managing Human Papillomavirus (HPV)

By authors A.E. McGee[1], S. Bhattacharya[1], S.J.B. Hanley[1], M.E. Cruickshank[1]

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Background:

In March 2020, the Scottish Cervical Screening programme changed from cervical cytology testing to high-risk human papillomavirus (HR-HPV) testing. The anxiety of having HR-HPV has prompted some women to seek 'treatments' outside the screening programme recommendations. Our systematic review identified available treatments, including vaccinations, oral and topical medications, and non-surgical device treatments. We wanted to understand what women value in treatment.

Aims:

The aims of this study are to:

- Identify the most important factors in women's decisions about their care and potential treatment choices for persistent HR-HPV to inform a discrete choice experiment (DCE)
- Design a pilot DCE based on qualitative analysis

Methods:

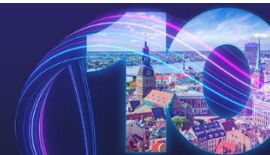
Qualitative interviews were conducted on Microsoft Teams. Women were recruited by a research nurse as they followed their normal care pathway. All interviews were recorded and transcribed manually by the researcher. Thematic analysis was undertaken to identify themes and key care factors. Ethical approval was obtained before conducting interviews.

Results:

From the nine interviews, four main themes were identified, including awareness, treatment preferences, willingness to pay, and the impact of diagnosis. Some women indicated satisfaction with current management, whereas others preferred treatment sooner. Some women indicated a high willingness to pay (WTP) for earlier treatment if approved and available. Further details and participant quotes will be presented at EFC 2024.

Conclusions:

There was a wide range of views on key topics regarding treatment options, willingness to pay, and awareness and education around HPV. The results of this study will be used to inform a health economics study (DCE).



Mapping the spread: spatial analysis of HPV infection and contributing factors

By author Rita Sousa & co-authors José .A. Fonseca Moutinho; Fábio Gomes; Fernanda Loureiro; Ana Rita Goes; Patrícia Soares

Background:
The cervical cancer screening(CCS) program switched to primary human papillomavirus(HPV) testing in March 2019. Identifying high-risk HPV(hrHPV) infections and related factors can help target preventive measures for cervical cancer.

Aims:
This study aimed to identify regions in Central Portugal with high rates of hrHPV and understand factors contributing to this at a municipality level.

Methods:
An ecological study in 78 municipalities in the Central Region of Portugal from March 2019 to December 2022. We used data from the CCS program database, including screening test results after transitioning to primary HPV testing. Demographic, socio-economic, and healthcare availability variables were sourced from official statistics. Spatial analysis with SaTScanTM software v10.1.1 identified clusters of high hrHPV prevalence at municipality level. Logistic generalised linear models identified contextual factors associated with high hrHPV prevalence rates.

Results:
Out of 191,887 samples collected between March 2019 and December 2022, 183,805 screening test results were included in the analysis after removing duplicates and cases outside the municipalities. hrHPV infection prevalence was 9.9%. with 2,2% positive for HPV 16/18. Three significant clusters were found in municipalities near major urban centres. Municipalities with higher population density, more younger women, higher income per inhabitant, more individuals with graduate degrees, and more healthcare units were more likely to have high rates of hrHPV infection.

Conclusions:
This study offers updated information on hrHPV prevalence and infection patterns at municipality level. Understanding of the relationship between clusters and contextual factors can improve prevention strategies by targeting areas with high infection rates.