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FROM HPV INFECTION TO CURE

INTEGRATING SCIENCE, CLINICAL CARE AND ARTIFICIAL INTELLIGENCE IN HPV-RELATED CANCER CONTROL

Congress Presidents

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ABSTRACTS

MAIN CONGRESS PROGRAM

SS01 - HPV screening in transgender individuals - who, why, how, and what to do with the result

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#14388

Cervical Cancer Screening in the Trans and Non-Binary Community

10 - HPV screening

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Background/Objectives: There is a dearth of literature that addresses cervical cancer (CCS) screening among transgender and non-binary persons. Unfortunately, transgender persons often have a history of sexual and physical abuse leading to barriers in obtaining health care. Current guidelines address cis-gender patients and are not easily applied to the transgender/non-binary communities. Unfortunately, there is also little information on the long-term effects of gender-affirming hormone therapy on a person's cervical cancer risk. Objective of this talk will be to examine the role of hormonal treatment and cancer risk and best practices for cervical and anal cancer screening of transgender and non-binary communities.

Methods: ASCCP recommends following CCS guidelines for cis-patients starting at age 21 years and include cervical cytology 21-29 years of age at 3 year intervals and primary HPV screening starting at 30 years. Self-testing for HPV may be more acceptable, and some guidelines start HPV testing at 25 years of age since testosterone therapy can result in inconclusive cytology.

Results: Screening for HPV in neovaginas in transgender women is controversial but some advocate screening with HPV. Anal cancer screening (ACS) is recommended HIV+ transgender women (TW) starting at 35 years of age and HIV- TW at 45 years of age. ACS is also recommended for HIV+ transgender men (TM) starting at 35 yrs and for those engaging in regular anal intercourse some advocate starting at 45 years. Other risks include history of CIN 3, cervical, vaginal and vulvar cancer and solid organ transplant. Anal cytology, HPV testing and HPV-cytology co-testing are different strategies that show acceptable performances.

Conclusions: It will be critical to educate health professionals about best practices as well as educate transgender and non-binary communities about the importance of cervical and anal cancer screening.

References:

Milerad Hanna
Sweden

#14129

Screening for anal cancer and precancer in TGNBP living with HIV (trans-SANCA)

27 - Anal neoplasia

Milerad H[1], Borch-jensen P[2], Brännström J[3], Carrick D[1], Clifford G[4], Edvardsson H[1], Ekström A[3], Elfström M[1], Gisslen M[5], Kärrberg C[5], Lagheden C[1], Lei J[1], Sundström K[1], Wagner P[1], Wang J[1], Nygren J[2], Carlander C[1]

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Background/Objectives: Recent guidelines recommend anal cancer screening from age 35 in transgender women living with HIV, but implementation data are sparse. The trans-SANCA study aims to evaluate feasibility and acceptability of implementing international anal cancer screening guidelines in transgender and non-binary people (TGNBP) living with HIV in Sweden, and explore the clinical assessment of HPV-positive findings.

Methods: This multicentre cross-sectional study will start recruiting TGNBP from the age of 18 years living with HIV from three Swedish sites: Karolinska University Hospital, Stockholm South General Hospital and Sahlgrenska University Hospital. Approximately 150 TGNBP will included from all sites. Anal cancer screening of TGNBP will be nested into a larger anal cancer screening study of cis-women 45+ living with HIV (SANCA). All participants provide self-collected anal and vaginal HPV tests using Copan FLOQSwabs and complete acceptability questionnaires. HPV testing is performed using BD Onclarity with extended genotyping detecting 14 high-risk HPV (hrHPV) types. TGNBP with anal hrHPV positivity will undergo high-resolution flexible endoscopy of the anal canal (Stockholm) or high-resolution anoscopy (Gothenburg) with anal cytology sampling, repeat HPV testing, and DNA methylation sampling. Detected lesions are resected and analyzed for histopathology. TGNBP with vaginal or neovaginal hrHPV positivity will undergo a gynecologic assessment including colposcopy according to a clinical protocol designed for the study, and in relevant cases a neovaginal flexible endoscopic evaluation. Detected lesions will be treated.

Results: Recruitment will start during spring 2026. The study protocol will be presented at the transgender session at Eurogin.

Conclusions: Anal cancer screening of TGNBP adresses a critical evidence gap by focusing on a population with elevated anal cancer risk with very limited screening data. Findings from this pilot study will add to the base of knowledge for this field and inform the design of future larger studies including TGNBP with and without HIV.

References:

CS01 - Application of methylation tests in the management of women with CIN, vulvar or anal lesions

Dovnik Andraž
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#14266

Risk stratification of CIN by methylation analysis

17 - Methylation

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Background/Objectives: High-grade cervical intraepithelial neoplasia (CIN2/3) has historically been treated with excisional procedure which is highly effective in the prevention of cervical cancer but also associated with possible adverse pregnancy outcomes. CIN3 as an immediate precursor of cervical cancer is generally accepted as an indication for surgical treatment. On the other hand, the management of CIN2 is highly diverse and active surveillance can be proposed in some cases. Various prognostic biomarkers have been studied with the aim of differentiating between regressive and progressive high-grade lesions. Viral load and p16/Ki67 immunostaining as independent markers have not been shown to accurately predict the prognosis of CIN.

Methods: In recent years, DNA methylation analysis has emerged as a novel biomarker which could further help to identify patients in whom active surveillance is safe.

Results: So far, the role of methylation in predicting the outcome of conservative management of CIN2 was evaluated in three studies (1-3). A Finnish prospective cohort study on 149 patients with histologically confirmed CIN2 evaluated the prognostic role of the methylation panel S5 classifier (3). The sensitivity of methylation analysis in predicting the clinical outcome was higher for methylation analysis compared to cervical cytology (3).
A Dutch prospective study included 93 patients with CIN2 and CIN3 and evaluated the predictive value of the FAM19A4 and miR124-2 methylation marker (2). Negative methylation was associated with higher rates of disease regression. A wait-and-see policy was advocated for women with a negative methylation result provided they had low-grade cytology and were HPV16 negative since this combination was associated with 85% of clinical regressions (2). Negative methylation was associated with regression in women with low-grade cytology results but not in those with high-grade cytology, indicating that methylation strengthens the interpretation in minor cytologic changes (2).
Just recently, an Italian prospective study on 319 patients with CIN2 evaluated the predictive value of various biomarkers for the regression of CIN2, including methylation of FAM19A4 and miR124-2 (1). Similarly to our results, 67.9% of patients with negative methylation regressed (1). The analysis of odds of regression by biomarkers showed statistically significant associations with regression for negative p16/Ki67 (OR 2.49) and unmethylated status (OR 2.12). The patients who were p16/Ki67 and methylation negative were 6-8 times more likely to regress compared to patients with positive p16/Ki56 and positive methylation status (1).

Conclusions: These studies indicate that methylation analysis is a valuable addition to cervical cytology and HPV testing. According to current data, methylation analysis is particularly useful in cases with low-grade cytology and HPV16 negative result as it helps to identify a subgroup with very high levels of clinical regression.

References: Frayle H, Gori S, Pagan A, Soldà M, Romagnolo C, Insacco E, Laurino L, Matteucci M, Sordi G, Busato E, Zorzi M, Maggino T, Del Mistro A; CIN2 Study Working Group. Predictive biomarkers for regression in women undergoing active surveillance for cervical intraepithelial neoplasia grade 2: A prospective multicenter study in Italy. Int J Cancer. 2025 Aug 30. doi: 10.1002/ijc.70104. Epub ahead of print. PMID: 40884232.

2. Kremer WW, Dick S, Heideman DAM, Steenbergen RDM, Bleeker MCG, Verhoeve HR, van Baal WM, van Trommel N, Kenter GG, Meijer CJLM, Berkhof J. Clinical Regression of High-Grade Cervical Intraepithelial Neoplasia Is Associated With Absence of *FAM19A4/miR124-2* DNA Methylation (CONCERVE Study). J Clin Oncol. 2022 Sep 10;40(26):3037-3046. doi: 10.1200/JCO.21.02433. Epub 2022 May 5. PMID: 35512257; PMCID: PMC9462536.

3. Louvanto K, Aro K, Nedjai B, Bützow R, Jakobsson M, Kalliala I, Dillner J, Nieminen P, Lorincz A. Methylation in Predicting Progression of Untreated High-grade Cervical Intraepithelial Neoplasia. Clin Infect Dis. 2020 Jun 10;70(12):2582-2590. doi: 10.1093/cid/ciz677. PMID: 31344234; PMCID: PMC7286376.

SS02 -HPV point of care tests - harnessing the efforts of the wider molecular diagnostics community to effect real change

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#14348

The challenges and wins of developing a low-cost point-of-care screening test for high-risk human papillomavirus (HR-HPV)

11 - Screening for women difficult to reach

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Background/Objectives: Low-cost point-of-care tests for high-risk human papillomavirus (HR-HPV) are essential to expand screening in low-resource settings. The World Health Organisation (WHO) recommends DNA-based isothermal amplification (e.g., LAMP [1], RPA [2]) and guides development through a Target Product Profile [3]. In brief, tests should use self-collected vaginal swabs, require few simple steps with less than 1 h turnaround, deliver high sensitivity/specificity with a clear visual readout, operate with portable equipment across harsh conditions, and be affordable.

Methods: Tests must undergo three stages of development before they can be considered for implementation [4] (Fig. 1). During ‘assay design’, primers (and probes, if required) are tested, and the analytical limit of detection is determined using analytical samples; progression to the next stage depends on achieving an appropriate limit. During ‘early-stage validation’, selected assays are evaluated using >30 clinical samples and a low-cost point-of-care sample preparation method. During ‘mid-stage validation’, platforms are validated using >100 samples from low-resource populations with intended hardware. Each stage brings challenges and wins which, along with recommendations, will now be discussed.

Results: A challenge in ‘assay design’ is the absence of defined limit-of-detection targets; current WHO guidance emphasises comparative clinical performance [3]. We recommend that a consensus on the required limit of detection could be agreed upon, to aid decision-making.
A challenge in ‘early-stage validation’ is that only 13 of 6,320 studies addressing DNA-based HPV isothermal amplification progressed their assays into this phase [4]. We therefore recommend that focus should be on moving assays into this phase, either through increased access to clinical samples and/or by updating research goals. This is supported by the fact that HPV’s small genome limits gains from further assay redesign. Publication of negative results would also prevent redundant effort.
A further challenge is that, of studies that did progress into the ‘early-stage validation’ phase, only three used vaginal samples, and only one used fresh samples (as recommended in the TPP [3]). Most used cervical swabs that had been stored (and the protocols for storage were not always clear). We recommend that studies would gain impact by increased access to freshly-obtained vaginal swabs, the use of standardised cell-preserving buffers and methodologies, and estimates of cervical–vaginal viral load differences to enable extrapolation.
One win is that sample preparation for HR-HPV can be very simple: twelve studies used only a combination of lysis buffer and heat, and we have found from our own work that the heat step is not required.
The key challenge in mid-stage valuation is that only six studies found, perhaps due to the lack of tests in the early-stage validation phase with appropriate sensitivity. We suggest that this underscores the need focus on the early-stage validation phase.

Conclusions: Guidance on target limits of detection and on cervical–vaginal viral-load differences would accelerate development. Practitioners should adopt standardised buffers and methods, prioritise access to freshly collected vaginal swabs, and publish negative findings. The community should concentrate on supporting early-stage validation and advancing promising assays into mid-stage studies.

References: [1] [1] T. Notomi *et al.*, “Loop-mediated isothermal amplification of DNA,” *Nucleic Acids Res*, vol. 28, no. 12, pp. e63–e63, 2000, doi: 10.1093/nar/28.12.e63.
[2] [2] O. Piepenburg, C. H. Williams, D. L. Stemple, and N. A. Armes, “DNA detection using recombination proteins,” *PLoS Biol*, vol. 4, no. 7, p. e204, 2006, doi: 10.1371/journal.pbio.0040204.
[3] [3] World Health Organisation, “Target product profiles for human papillomavirus screening tests to detect cervical pre-cancer and cancer,” Geneva, 2024.
[4] [4] E. Boswell, B. Webster, J. M. Cooper, and J. Reboud, “Incorporating real-world scenarios in early-stage validation of point-of-care human papillomavirus (hpv) screening tests: a scoping review,” *submitted*, 2025.

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#14126

Development, evaluation, and translation of point-of-care high-risk HPV tests

10 - HPV screening

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Background/Objectives: Affordable point-of-care DNA testing is needed for cervical cancer screening in low- and middle-income countries, where most cervical cancer cases occur. HPV DNA testing typically requires complex lab infrastructure and trained personnel.

Methods: We are developing isothermal amplification assays targeting eight high risk HPV DNA types and a cellular control. This talk will describe efforts to develop and evaluate assays with extraction-free sample preparation, lyophilized reagents, and simple workflows that require minimal equipment and deliver results in less than one hour.

Results: Preliminary results from clinical samples collected in Houston, Texas (n = 38) and Maputo, Mozambique (n = 191) demonstrate that a test detecting three high-risk HPV DNA types achieved 100% and 93% concordance, respectively, with a reference assay widely used in low-resource settings.

Conclusions: This sensitive and specific point-of-care assay can potentially expand cervical cancer screening in resource-limited settings.

References:

Pelechano Vicent
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#14040

Rapid electronic quantification of pathogens using DNA nanoballs

09 - HPV testing

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Background/Objectives: Rapid and accurate detection of pathogens is vital for effective disease control. Existing diagnostic methods can be slow or require complex equipment. Our aim was to develop a straightforward, sensitive platform for pathogen quantification combining isothermal DNA amplification, microfluidics and electric detection.

Methods: We modified a common isothermal DNA amplification technique (LAMP, Loop-mediated DNA Amplification) to generate self-assembled DNA nanoballs (1 µm). These nanoballs are then detected and quantified electronically. This approach enables direct, amplification-free detection.

Results: Our platform demonstrated high sensitivity and specificity for pathogen RNA/DNA. While our initial focus was on detecting SARS-CoV-2 in clinical samples, we showed that the same method is easily applicable to other pathogens. Established LAMP diagnostic protocols can be adapted to produce self-assembled DNA nanoballs.

Conclusions: The DNA nanoball-based electronic quantification platform offers a potential solution for rapid, point-of-care pathogen detection. Its simplicity and robustness make it suitable for diverse settings, and it has the potential to improve diagnostic workflows for HPV and other infectious agents. Future work should focus on instrument deployability and further increasing specificity.

References: Muhammad Tayyab et al. Digital assay for rapid electronic quantification of clinical pathogens using DNA nanoballs.Sci. Adv.9,eadi4997(2023).DOI:10.1126/sciadv.adi4997

SS03 - Global HPV laboratory network: Strengthening HPV laboratory capacity for cervical cancer elimination

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#14217

Proficiency studies 2.0: Evaluation of novel HPV assays

09 - HPV testing

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Background/Objectives: In 2006, the WHO initiated international HPV proficiency studies, that have been organized by the International HPV Reference Center (IHRC) ever since. There is one proficiency panel evaluating HPV typing services (genotyping panel) and another panel assessing quality of HPV screening services (screening panel), both issued annually. IHRC has now organised an international collaborative study to determine the optimal analytical sensitivity thresholds that would result in optimal sensitivity and specificity of HPV screening assays. Establishment of such thresholds will enable simple, yet internationally standardized evaluation of the performance of novel HPV assays for screening.

Methods: The WHO-established international standards (IS) for twelve oncogenic HPV types are used to assess analytical assay sensitivity, using thresholds derived from the international collaborative study: 3 IU/µl for HPV16 and 18; 25 IU/µl for HPV31, 33, 45, 52 and 58; 25 GE/µl for HPV35 as well as 100 GE/µl for HPV39, 51, 56 and 59. The standards are anonymized and distributed blinded to laboratories wishing to evaluate their novel HPV testing method. The results from the blinded analysis will be reported to IHRC which will decode the results and report the IS-defined sensitivity and specificity for screening of the assay.

Results: The evaluation using IS of the established comparator HPV tests (BD Onclarity/Roche Cobas) found an Invasive Cervical Cancer (ICC)-weighted sensitivity of 92,7% (type-specific detection of HPV in CIN lesions, weighted according to the importance for cervical cancer of the different HPV types) and a specificity of 87,6% (1-proportion positives among healthy population-based matched controls).

Conclusions: We present a structured internationally standardized evaluation framework for novel HPV testing methods based on simple serial dilutions of IS.

References:

Soares Marcelo
Brazil

#14368

Updates from NRL countries: Brazil

10 - HPV screening

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Background/Objectives: In this presentation, we will discuss the updates to the major activities conducted by the Brazilian HPV Reference Laboratory, as part of the International HPV Reference Laboratory Network.

Methods: The Brazilian HPV NRL, since its entrance to the HPV LabNet in late 2024, has been involved in different activities related to the implementation of the HPV molecular test-based screening for cervical cancer in Brazil, including the international clinical validation of a locally-developed HPV partial genotyping assay and more recently the certification of the national laboratories that will perform the molecular assays countrywide.

Results: It has also joined the International Papillomavirus Society (IPVS) HPV Awareness campaigns, being one of only two centers in Brazil that are members of this initiative.

Conclusions: Finally, at the research level, the Brazilian HPV NRL is also joining research efforts by the International HPV LabNet and, at national level, conducting multi-omic molecular studies on HPV-related cancers such as cervical, anal and penile cancer. Those latter studies are targeted to unveil potential new biomarkers associated with progression from premalignant disease to cancer and with response to therapy and disease recurrence in those malignancies.

References:

SS07 -Developments and standardization of methylation tests in cervical, anal and urine samples

Van Keer Severien
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#13813

The position of urine samples for methylation-based screening of female gynaecological cancers

17 - Methylation

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Background/Objectives: HPV testing in urine using validated PCR-based HPV DNA assays has recently proven to be similarly sensitive and specific to identify high-grade cervical intraepithelial neoplasia (CIN2+), compared to HPV testing in cervical samples collected by a physician. The clinical performance is enhanced by the collection of the first part of the urine stream - first-void urine - to capture biomarker-containing (tumour) cell fragments from the female genital tract ending up in vaginal secretions via local shedding. Simultaneously, it captures transrenal excreted circulating tumour DNA. Still, due to the inherent low specificity of HPV testing, triage of high-risk (hr)HPV infections is needed to identify people with high-grade cervical disease in need of treatment. Cytology is being largely adopted as reflex test but requires a physician-collected cervical sample, delaying diagnostic procedures and increasing loss to follow up.

Methods: Recent developments in molecular diagnostics have supported the potential of methylation-based testing for triage of hrHPV infections, and their suitability on self-samples. Methylation of human genes has been shown to play a critical role in (cervical cancer) carcinogenesis. This is exceptionally valuable for risk stratification due to the ability to distinguish low-grade cervical neoplasia with productive hrHPV infections from transforming infections in high-grade lesions with a high short-term cancer progression risk, detecting virtually all carcinomas.

Results: Shadowing the established clinical value of DNA methylation in cervical samples, data on the usefulness of (first-void) urine to detect viral and human DNA methylation for cervical cancer screening accumulates.
The use of DNA methylation in this “golden liquid biopsy” however stretches beyond risk stratification of baseline hrHPV positive tests for cervical cancer screening. Certainly, based on the same rationale, it might present a suitable sample type for screening of other tumours of the female genital tract, not necessarily caused by an hrHPV infection (e.g., vaginal, vulvar, endometrium and ovarian cancer). Simultaneous screening for all female gynaecological tumours is appealing, and infrequent detection of endometrial and ovarian cancer cells via cervical cytology has been observed. Yet, the global shift from cytology- to HPV-based cervical cancer screening takes away this opportunity. The potential of DNA methylation as diagnostic marker for female gynaecological tumour detection in minimally invasive samples has been reported by few research groups, including recently on urine.

Conclusions: The anatomical proximity of female gynaecological organs and link between methylation and carcinogenesis let us conceive that DNA methylation signatures for all these tumours can be accurately measured in first-void urine. Yet, it requires further clinical evaluation.

References:

CS03 - Turning cervical diagnostic uncertainty into clinical decision

#14202

DNA methylation for risk stratification of women without fully visible transformation zone at colposcopy

17 - Methylation

Binderup K[1,2,3], Boers J[4,5], Gustafson L[1,6], Andersen B[1,3], Petersen L[1,7,8], Bor P[3,6], Gribnau J[4,5], Quint W[5], Van Den Munckhof H[5], Tranberg M[1,3,9], Hammer A[2,3,10]

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Background/Objectives: Colposcopy performance is impaired in older women as the transformation zone retracts into the cervical canal (TZ3), making adequate sampling challenging and increasing diagnostic uncertainty. To reduce risk of overtreatment while avoiding underdiagnosis, reliable biomarkers are needed to identify women at increased risk of cervical precancer who require treatment. We evaluated the performance of DNA methylation markers for the detection of cervical intraepithelial neoplasia among screen-positive older women with a TZ3.

Methods: We conducted a cross-sectional study in colposcopy clinics in the Central Denmark Region (2019–2021). Eligible women were ≥45 years, referred for colposcopy due to an abnormal screening result, and with a TZ3. At colposcopy, women underwent cervical cytology sampling, biopsies, and had a large loop excision of the transformation zone (LLETZ) performed. Cervical samples were analysed for three methylation marker panels: *FAM19A4/miR124-2* (Qiasure), *ARID3C/ARL5C* and *METloc001/METloc002* (MeD-Scan). LLETZ histology served as the reference standard. We calculated sensitivity and specificity for detection of cervical intraepithelial neoplasia grade 2 or worse (CIN2+) and cervical intraepithelial neoplasia grade 3 or worse (CIN3+).

Results: A total of 89 women were included (median age: 67.9 years). CIN2+ was detected in 31 (34.8%) and CIN3+ in 16 (18.0%) women. Sensitivity for CIN2+ was similar across markers: 77.4% for *FAM19A4/miR124-2*, 74.2% for *ARID3C/ARL5C*, and 74.2% for *METloc001/METloc002*. Specificity varied substantially, being lowest for *FAM19A4/miR124-2* (39.7%), higher for *ARID3C/ARL5C* (65.5%), and highest for *METloc001/METloc002* (82.8%). For CIN3+, sensitivity was 75.0%, 87.5%, and 93.8% for *FAM19A4/miR124-2*, *ARID3C/ARL5C*, and *METloc001/METloc002*, respectively, with CIN3+ specificity of 35.6%, 60.3%, and 75.3%.

Conclusions: Colposcopic assessment of the cervix is unreliable in women with TZ3. In this group, *METloc001/METloc002* (MeD-Scan) demonstrated high sensitivity and specificity for CIN2+. These findings support its potential to reduce diagnostic uncertainty and enhance clinical decision-making in screen-positive women without a fully visible transformation zone.

References:

WS02 - Anal diseases workshop: Vulvar and Anal intraepithelial neoplasia: Time to expand HPV-related screening

Vieira-baptista Pedro
Portugal

#14230

Vulvar screening at the time of cervical cancer screening

26 - Vulvar diseases and neoplasia

Vieira-baptista P[1,2,3]

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Background/Objectives: This lectures' objective is to highlight the clinical and public health rationale for integrating systematic vulvar inspection into routine cervical cancer screening, and to summarize practical recommendations aimed at improving early detection of vulvar preinvasive and invasive disease.

Methods: We based this lecture on a critical narrative review of the literature and on the recently published multidisciplinary consensus statements developed by ESGO, ISSVD, ECSVD, and EFC. Evidence on epidemiology, risk factors, diagnostic delay, and clinical presentation of vulvar cancer and its precursors was synthesized, with particular focus on opportunities arising during organized cervical cancer screening. Key elements of vulvar inspection, symptom assessment, risk stratification, and referral pathways were reviewed and integrated into a pragmatic clinical framework.

Results: Vulvar squamous cell cancer incidence is increasing, particularly among women under 60 years, while diagnosis remains frequently delayed. Cervical cancer screening programs cover an age range that overlaps with the peak incidence of HPV-related vulvar high-grade squamous intraepithelial lesions and the onset of inflammatory dermatoses associated with HPV-independent vulvar cancer. Routine vulvar inspection adds minimal time or discomfort to screening visits but allows identification of suspicious lesions, inflammatory fields at risk, and early invasive disease. Consensus recommendations emphasize systematic inspection prior to speculum insertion, brief assessment of vulvar symptoms, standardized lesion description, low threshold for biopsy or referral, and patient education on vulvar self-examination. Particular vigilance is warranted in women with positive HPV tests, prior anogenital neoplasia, immunosuppression, or chronic vulvar symptoms.

Conclusions: Integrating standardized vulvar inspection into cervical cancer screening represents a low-cost, high-impact strategy to reduce diagnostic delay and morbidity associated with vulvar cancer. Training of all healthcare professionals involved in screening and increased patient awareness are essential to translate this opportunity into meaningful prevention and earlier diagnosis.

References: Preti M, Lewis F, Carcopino X, Bevilacqua F, Ellis LB, Halonen P, Hemida R, Jach R, Kesic V, Kyrgiou M, Maggino T, Pedro A, Querleu D, Stockdale C, Taumberger N, Temiz BE, Vieira-Baptista P, Gultekin M. Vulvar inspection at the time of cervical cancer screening: European Society of Gynaecological Oncology (ESGO), International Society for the Study of Vulvovaginal Disease (ISSVD), European College for the Study of Vulval Disease (ECSVD), and European Federation for Colposcopy (EFC) consensus statements. Int J Gynecol Cancer. 2025 Jan;35(1):100007. doi: 10.1016/j.ijgc.2024.100007. Epub 2024 Dec 18. PMID: 39878267.

CS04 - Real-life evidence of screening in post-menopausal women

Gilham Clare
United Kingdom

#14050

Using at-home urine sampling to screen women aged 60-79 in the UK: Catch-Up Screen

10 - HPV screening

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Background/Objectives: Since 2019, the NHS Cervical Screening Programme (CSP) has offered primary HPV testing to women aged 25-64 years. Women who have a negative HPV test before they stop screening are at much lower risk of developing cervical cancer than those screened by and negative for cytology. There are around 400 cervical cancer deaths every year in the UK among those aged ≥65, most of whom have never been offered an HPV test because they were already above the upper age of screening when primary HPV testing was introduced. Offering a catch-up HPV test has the potential to prevent future cervical cancer in these older birth cohorts.

Methods: “Catch-Up Screen” offers a catch-up HPV test to women aged 60-79 who have not had a primary HPV test. Recruitment began in January 2024. About 18,000 women will be invited with the aim of screening 10,000 women by June 2027.

A Colli-pee urine collection device (DNA Genotek) is being posted to women living in the north of England (Manchester and Hull) and consenting participants return their sample by freepost to the laboratory. The Colli-pee device is easy to use, less invasive than other devices and avoids the embarrassment of a speculum examination which older women often find uncomfortable. It is hoped that this will encourage women who were not screened regularly to take part.

The BD Onclarity HPV testing assay is used to test the urine samples. HPV positive women will be invited to repeat their urine test after 6 months, and persistently positive women will be referred to colposcopy. Vaginal oestrogen will be prescribed prior to colposcopy to increase the visibility of the transformation zone.

The project is funded by Yorkshire Cancer Research.

Results: The study is ongoing with around 5,000 women screened to date. The screening invite has been well received so far with around 55% of those invited returning a urine sample. The HPV prevalence is estimated to be around 5% in Hull and 6% in Manchester with a quarter of them positive for HPV16. Three quarters remained positive after retesting after 6 months and are undergoing colposcopy. Colposcopy outcomes will be presented. Almost all of those who were screened found the sample easy to collect with the Colli-pee device and over 85% gave preference for future screening with at-home urine sampling.

Conclusions: At-home urine-based screening is acceptable to older women in the north of England. We hope to demonstrate that a national HPV catch-up programme is feasible and an effective way to reduce cancer in this older age group.

References:

SS08 - HPV vaccination: Evidence for utility of one dose

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#14206

Programmatic cost implications of a single-dose HPV vaccine regimen

07 - HPV therapeutic vaccines

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Background/Objectives: In 2022, the World Health Organization endorsed a single-dose human papillomavirus (HPV) vaccination regimen based on high-quality evidence of its comparable efficacy and duration of protection as multiple doses. As external funding for public health programs becomes more constrained, the single-dose regimen creates opportunities for immunization programs to lower vaccine procurement and programmatic delivery costs. However, real-world evidence is lacking on the magnitude of cost savings that could be achieved with the switch to a single-dose regimen. Our study aimed to estimate the programmatic delivery costs, describe the operational context of delivering a single-dose HPV vaccine regimen, and compare delivery cost estimates with those for a two-dose regimen.

Methods: A retrospective microcosting and operations research study was conducted in Ethiopia, where we collected primary data from 82 health facilities, from affiliated subnational program offices in four regions, and at the national level. Data were collected after the country conducted an HPV vaccination campaign in late 2024, during which a multi-age cohort (MAC) of 9-to-14-year-old girls was vaccinated. We estimated the financial costs (direct monetary outlays), opportunity costs (use of existing resources), and economic costs (combined financial and opportunity costs) of the campaign and described the program context. Costing was done from the health system perspective, and costs were reported in 2024 United States dollars (US$). Cost estimates were compared with those generated using similar research methods, when the country administered a two-dose regimen to a single-age cohort between 2019 and 2021.

Results: School-based delivery was the primary setting for HPV vaccination sessions during the MAC campaign; staff from 90% of health facilities in our sample conducted sessions in schools. Non-school-based settings were also used to augment delivery in schools, as 73% of health facilities in our sample conducted outreach. On average, each health facility in our sample administered 910 doses during the MAC campaign. Our data show that opportunity costs of using existing resources, primarily health worker and non–health worker time, accounted for the larger share of delivery costs (79%) at health facilities. At administrative levels, financial costs represented the larger share of costs. We estimated that the delivery costs per dose or per fully vaccinated girl, aggregated across all levels of the health system, were US$0.66 for financial costs, US$1.01 for opportunity costs, and US$1.67 for economic costs. When comparing the costs of delivering a two-dose regimen to a single-age cohort versus a single-dose regimen to a single-age cohort, we modeled that delivery costs could decline by 31% for financial costs, 49% for opportunity costs, and 43% for economic costs.

Conclusions: A switch to a single-dose regimen can reduce delivery costs and enhance program sustainability, while also reducing vaccine procurement costs.

References:

CS05 - VAIN: The forgotten territory

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#14193

Anti-HPV Vaginal Preparations - Breakthrough or Hype?

18 - Microbiome

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Background/Objectives: Topical anti-HPV vaginal gels and sprays are promoted as potential options in the armamentarium for the treatment and prevention of low-grade cervical lesions or persistent high-risk HPV (hr-HPV) infection. However, the evidence is limited. We aim to weigh the evidence of these non-invasive interventions considering the limited body of evidence.

Methods: A narrative review was conducted of preclinical and clinical studies evaluating: (1) Carrageenan-based gels for primary prevention of genital HPV infection; (2) Adsorptive/antioxidant vaginal gels such as DeflaGyn in women with hr-HPV and CIN1–2; and (3) Mucosal repair products such as Papilocare in HPV-positive women with low-grade cytologic and colposcopic abnormalities. Key outcomes included incident HPV infection, hr-HPV clearance, cytologic/colposcopic regression, CIN1–2 regression, safety, and integration with current standards of care.

Results: Carrageenan gels reduced incident genital HPV infection by about 36–37% in sexually active women in a phase IIb randomized, double-blind, placebo-controlled trial, with no increase in adverse events. Adsorptive and antioxidant vaginal gels (e.g., DeflaGyn) achieved CIN1–2 regression in approximately 70% versus 25% under observation, alongside substantial hr-HPV clearance, in prospective randomized and prospective cohort studies, with good tolerability. Cervico-vaginal repair gels such as Papilocare improved epithelialization, normalized microbiota, and yielded higher rates of cytologic normalization with concordant colposcopy (≈80–90% vs ≈55–60% “watch and wait”) in HPV-positive women with ASC-US/LSIL, while also increasing hr-HPV clearance in multicenter randomized trials.

Conclusions: Anti-HPV vaginal gels and sprays constitute an heterogeneous but interesting class of topical interventions that can reduce incident HPV infection, facilitate clearance of established hr-HPV, and support regression of low-grade cervical lesions, with an excellent safety profile across studies. However, variability in study design, endpoints, and follow-up, as well as the absence of robust CIN3+ and cancer outcomes, currently limits their integration into evidence-based guidelines, underscoring the need for large, high-quality randomized trials that position these agents as adjuvants to vaccination and conservative colposcopic management rather than as stand-alone alternatives to treatment.

References: Laurie C, et al. Efficacy and safety of a self-applied carrageenan-based gel to prevent human papillomavirus infection in sexually active young women (CATCH study): an exploratory phase IIB randomised, placebo-controlled trial. EClinicalMedicine. 2023 Jun 8;60:102038.Buck CB, et al. Carrageenan Is a Potent Inhibitor of Papillomavirus Infection. PLOS Pathogens. 2006, 2(7): e69.Major AL, et al. An Adsorptive and Antioxidant Vaginal Gel Clears High-Risk HPV- and p16/Ki-67-Associated Abnormal Cytological Cervical Findings: A *post-hoc* Subgroup Analysis of a Prospective Randomized Controlled Trial on CIN2 and p16 Positive CIN1. Front Med (Lausanne). 2021 May 25;8:645559.Ozmen F, et al. Vaginal Adsorbent Gel as a Therapeutic Agent: Is a New Era Beginning for HPV? *Journal of Clinical Medicine*. 2025; 14(14):4826.Huber J, et al. Human papillomavirus persistence or clearance after infection in reproductive age. What is the status? Review of the literature and new data of a vaginal gel containing silicate dioxide, citric acid, and selenite. Womens Health (Lond). 2021 Jan-Dec;17:17455065211020702PMC8785287.Cortés Bordoy J, et al. Effect of a Multi-Ingredient *Coriolus-versicolor*-Based Vaginal Gel in Women with HPV–Dependent Cervical Lesions: The Papilobs Real-Life Prospective Study. *Cancers*. 2023; 15(15):3863.

AI02 - Smart screening to precision care: Opportunities for artificial intelligence in HPV related & other head & neck cancers

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#14138

Web-based Systems for Toxicity Prediction in Head and Neck Cancer

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: In the precision medicine paradigm, oncological treatment leverages complex ensemble datasets of similar patients to estimate the outcomes for a current patient.

Methods: A key challenge is developing and deploying easy-to-understand AI predictive models for the toxicity outcomes of a specific patient, based on patient data from one or several institutions.

Results: We describe the design and the lessons learned from the development and deployment of several web-based systems for toxicity prediction in head and neck cancer.

Conclusions: These systems leverage data from the MD Anderson Cancer Center and other major treatment centers, combine AI solutions with interactive interfaces, and aim to serve a large client base.

References: Wentzel, A., Attia, S., Zhang, X., Canahuate, G., Fuller, C.D. and Marai, G.E., 2024. DITTO: A visual digital twin for interventions and temporal treatment outcomes in head and neck cancer. *IEEE transactions on visualization and computer graphics*.
Humbert-Vidan, L., Kamel, S., Wentzel, A., Kaffey, Z., Abdelaal, M., Spier, K.B., West, N.A., Marai, G.E., Canahuate, G., Zhang, X. and Chen, M.M., 2025. Externally validated digital decision support tool for time-to-osteoradionecrosis risk-stratification using right-censored multi-institutional observational cohorts. *Radiotherapy and oncology*, *207*, p.110890.
van Dijk, L.V., Mohamed, A.S., Ahmed, S., Nipu, N., Marai, G.E., Wahid, K., Sijtsema, N.M., Gunn, B., Garden, A.S., Moreno, A. and Hope, A.J., 2023. Head and neck cancer predictive risk estimator to determine control and therapeutic outcomes of radiotherapy (HNC-PREDICTOR): development, international multi-institutional validation, and web implementation of clinic-ready model-based risk stratification for head and neck cancer. *European Journal of Cancer*, *178*, pp.150-161.

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#14010

Privacy and security considerations in multi-institutional collaboration for AI model development and deployment

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Artificial intelligence (AI) can substantially improve both the efficiency and effectiveness of cancer care. In head and neck (H&N) oncology, efficiency gains come from imaging-based tools that automate and standardize tasks such as diagnosis and tumor/organ-at-risk contouring for radiotherapy planning. Effectiveness gains arise from predictive models that inform therapy indication, supporting personalized care. However, realizing these benefits requires large, diverse datasets that are difficult to centralize due to privacy regulations, institutional policies, data sovereignty, and cybersecurity risk. Federated learning (FL) offers a privacy-preserving alternative by enabling multi-site model training without transferring patient-level data.

Methods: We outline a privacy-by-design FL framework for multi-institutional AI development that integrates: (1) secure orchestration of distributed training/evaluation; (2) security ; (3) privacy safeguards; (4) governance and compliance and (5) rigorous validation. We situate these within current AI trends—machine learning, deep learning, and foundation models.

Results: Across collaborating centers, FL enables development of imaging models for diagnosis and treatment planning and outcome-prediction models to guide treatment selection and anticipate toxicities. Compared with single-site training, FL expands data diversity, reduces overfitting, and improves external validity while maintaining data locality.

Conclusions: Federated learning operationalizes privacy-preserving, secure, and scalable AI development across institutions—an essential capability for H&N cancer where data are heterogeneous and sensitive.

References:

HN02 - Epidemiology and prevention of HPV+ oropharyngeal cancer

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#12558

Age and tumour presentations differ between HPV type 16 positive and other high-risk HPV type-positive oropharyngeal squamous cell carcinomas in a Swedish cohort of 2000-2022

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: The incidence of human papillomavirus positive oropharyngeal squamous cell carcinoma (HPV+ OPSCC) has increased the past decades. Initial reports disclosed that HPV type 16 (HPV16) was predominant and that patients with HPV+ OPSCC were generally younger and had a better prognosis than those with HPV negative (HPV-) OPSCC. However, recent reports suggest that age differences between patients with HPV+ and HPV-OPSCC are less pronounced and that other high-risk HPV types (HR-HPV) are becoming more common. Here, we therefore investigated whether there were age differences between patients with HPV16-positive and other HR-HPV type positive OPSCC.

Methods: During 2000-2022, in the Stockholm-Gotland-Region, Sweden, 1681 patients with OPSCC tested for the presence of common mucosal HPV types were included. The clinical characteristics of the patients, their ages and tumor stages were correlated to their HPV type.

Results: Among these, 1180 cases had a HR-HPV type infection, with 1032 identified as HPV16 and 148 as other HR-HPV types; one with a low-risk HPV type infection; and 500 classified as HPV-. Patients with HPV+ OPSCC were significantly younger than those with HPV- OPSCC (mean 63 vs. 66.5, $p < .001$). Among patients with HPV+ OPSCC, those diagnosed with HPV16 were significantly younger than those with other HR-HPV types (mean 61.1 vs. 64.5, $p < 0.001$). These age differences were present irrespective of sex, but patients with HPV16-positive OPSCC were significantly more likely to present with smaller tumours upon diagnosis ($p = 0.002$). Moreover, notably, statistically significant age differences between HPV16 and other HR-HPV types were mainly observed in the more recent years (2010-2022).

Conclusions: To conclude, patients with HPV16 positive OPSCC were generally younger than those diagnosed with other HR-HPV type positive OPSCC. Moreover, patients with HPV16 positive OPSCC more often also presented smaller tumors than those with other HR-HPV type positive OPSCC. The increasing influence of HR-HPV types other than HPV16 in OPSCC warrants further investigation.

References: Näsman A, Birgersson M, Näsman T, Jörtsö E, Zupancic M, Bark R, Marklund L, Dalianis T. Age and tumour presentations differ between HPV type 16 positive and other high-risk HPV type-positive oropharyngeal squamous cell carcinomas in a Swedish cohort of 2000-2022. Int J Cancer. 2025 Nov 15;157(10):2019-2024. doi: 10.1002/ijc.70087. Epub 2025 Aug 15. PMID: 40879311; PMCID: PMC12439091.

SS15 - HPV screening in LMIC

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#13985

HPV Screening in Ethiopia and the International Cancer Screening Network (ICSN)

10 - HPV screening

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Background/Objectives: Background:
Cervical cancer continues to impose a disproportionate burden on low- and middle-income countries (LMICs), which account for 90% of the 342,000 cervical cancer deaths in 2020. Although WHO aims for 70% screening coverage using high-performance tests, HPV-based screening remains limited in LMICs, with lifetime coverage of only 9–11%. Weak screening registries and challenges in program monitoring further hinder progress. Ethiopia has adopted the WHO elimination targets and updated its national guidelines to prioritize HPV testing, yet implementation remains inconsistent and mostly limited to women living with HIV. With support from global partners, including the International HPV Laboratory Network, the Swedish National Cervical Screening Registry, and ICSN collaborators,this initiative aims to (1) assess barriers and facilitators to establishing laboratory quality assurance systems and screening registries; (2) promote equitable and affordable access to HPV testing; and (3) evaluate pathways of care and triage options for HPV-positive women.

Methods: Methods:
An ICSN Working Group on Implementation of HPV-Based Screening in LMICs has been established to support WHO-aligned strategies for expanding HPV screening. The group focuses on strengthening screening capacity, improving national and regional laboratory quality assurance systems (including proficiency testing), and enhancing screening registries for robust monitoring and evaluation. Initial activities include a comprehensive assessment of implementation barriers and facilitators, followed by coordinated approaches for cross-country learning, capacity-building, and tool-sharing.

Results: Results:
Self-sampling for HPV testing shows high acceptability across many LMICs; however, substantial gaps remain in scaling HPV-based screening. Early assessments highlight the need for detailed landscape analyses covering laboratory infrastructure, human resources, equipment, supply chains, and feasibility of context-appropriate solutions. Aligning national efforts with global initiatives—such as the WHO Cervical Cancer Elimination Strategy and the HPV LabNet Target Product Profile, is essential to ensure synergy and minimize duplication. At the ICSN 2025 meeting in Aarhus, the Working Group emphasized improving collaboration among LMIC partners, particularly on proficiency testing and laboratory quality improvement, and mobilizing global stakeholders to support pilot implementations and accelerate adoption of high-performance HPV screening.

Conclusions: Conclusion:
Preliminary findings underscore the urgent need to expand HPV-based screening in Ethiopia and other LMICs. Scaling up requires parallel investments in laboratory quality assurance, improved access and affordability of HPV tests, and strengthened regional capacity for proficiency testing. Enhanced coordination among global and regional stakeholders is essential to optimize limited resources and avoid duplication. Strengthening domestic financing mechanisms will also be critical to address funding gaps,especially for procuring HPV tests and reagents—and to support sustainable HPV-based screening programs.

References:

SS12 - Expanding HPV vaccine use beyond girls and young women: Who should receive the HPV vaccine next?

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#13993

HPV Vaccination of Older Infants and Toddlers

06 - HPV prophylactic vaccines

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Background/Objectives: Global uptake of HPV vaccine remains challenging with estimates of global coverage of at least a single dose among girls at 31%.[1] Although the burden of cervical cancer is higher in LMIC, the coverage is lower posing serious challenges to achieving WHO goals for cervical cancer elimination. Challenges to high HPV vaccine coverage continue to be cost and complexity of implementation of vaccination programs targeting 9-14yo girls through school and community-based delivery. The costs to deliver vaccine to reach school aged girls are higher than for routine EPI. In some settings there is negative social stigma when vaccinating pre-sexual debut girls against a sexually transmitted infection. And unfortunately, too many girls do not attend school.
Yet even in countries challenged with high HPV vaccine coverage, EPI program coverage at 9 and 15mo is high (>85%). Delivery of HPV vaccines could be much less resource intensive, achieve higher coverage with greater equity, and be less stigmatizing if delivered to older infants or toddlers (both genders) as part of the routine immunization schedule. The longevity of the immune response to HPV vaccines suggests that even a single dose can provide durable protection for multiple decades.[2]
In this trial we will evaluate the Safety, Immunogenicity (including durability) and Acceptability of Single Dose HPV vaccine in 9 mo and 15 mo children.

Methods: The evaluation of HPV vaccination in older infants and toddlers will be in two stages. Stage 1 will be proof-of-concept trial (N=115) conducted in Ghana to demonstrate safety and tolerability of a bivalent HPV vaccine administered to 9 mo and 15 mo toddlers with concomitant MR vaccine to demonstrate if short-term immune responses (1 month post dose 1) are reasonably comparable to older populations where efficacy has been shown (15-20yo). In parallel, a pilot acceptability study will be conducted in the same population exploring the acceptability of this approach among parents/caregivers and healthcare providers.
If the results of Stage 1 are favorable, Stage 2 is designed as a multi-country, statistically robust comparison (N=900) of safety and immune non-inferiority of a nonavalent HPV vaccine among 9 mo and 15 mo toddlers with concomitant MR vaccine as compared to an older populations where efficacy has been shown (15-20yo). A larger multi-country qualitative acceptability study would be conducted concurrently. Safety and immunogenicity follow-up would extend for two years.

Results: Stage 1 results will be available in early 2027.

Conclusions: Achieving the WHO goals for cervical cancer elimination may require exploring new approaches to achieving high vaccination coverage. This trial will provide important information on the feasibility of a strategy to leverage the success of Expanded Program of Immunization (EPI).

References: [1] https://www.who.int/news-room/fact-sheets/detail/immunization-coverage
[2] Aimée R Kreimer, Deborah Watson-Jones, Jane J Kim, Peter Dull, Single-dose human papillomavirus vaccination: an update, *JNCI Monographs*, Volume 2024, Issue 67, October-November 2024, Pages 313–316, https://doi.org/10.1093/jncimonographs/lgae030

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#14070

Determining context-specific economically feasible age ranges of female HPV catch-up vaccination in LMICs: a model-based health economic assessment

35 - Economics and modelling

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Background/Objectives: As global supply constraints are easing, catch-up HPV vaccination will be pivotal in achieving WHO's cervical cancer (CC) elimination goals for several low- and middle-income countries (LMICs). In this study, we assessed the health-economic impact of catch-up HPV vaccination for females in LMICs.

Methods: We adapted the IARC's METHIS modelling platform with data from 132 LMICs. Beyond primary target age (9-14 years), HPV catch-up vaccination was simulated varying the maximum catch-up age up to 30 years. The budget impact was reported for each LMIC as a fraction of national 5-year immunization budgets and current health expenditure. Cervical cancer treatment costs were informed from selected high-quality data countries, allowing assessment of cost-effectiveness. The 30% GDP-per-capita was used as cost-effectiveness threshold.

Results: In LMICs, catch-up HPV vaccination up to age 30 was estimated to avert 9.2 million cervical cancers over the lifetime of females aged 9–30 years. Across countries, the budget impact of catch-up vaccination targeting females up to age 30 ranged from 0.007% to 2.24% of 5-year current health expenditure; and from 0.0016% to 236.65% of 5-year immunization budgets. Vaccine procurement accounted for about 70% of total costs. Gavi support was estimated to reduce the budget by 69.5% in eligible countries for catch-up vaccination up to age 18. HPV catch-up vaccination up to age 30 years was cost-effective in all countries except Nigeria (cost-effective up to age 21).

Conclusions: In LMICs, once adequate coverage among the primary target age group (9–14 years) is achieved, expanding HPV catch-up vaccination programs was impactful and cost-effective. Sustainable financing, Gavi support, and efforts to minimize vaccination costs remain critical to the success of catch-up programs and progress toward cervical cancer elimination.

References:

SS10 - Urine-based biomarkers: A promising avenue for gynecological cancer prevention

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#15000

IMPRESS for cervical cancer screening - improved methylation profiling using restriction enzymes and smMIP sequencing

13 - Self-sampling

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Background/Objectives: Research efforts to enhance cervical cancer screening are currently centered on self-sampling approaches as well as molecular diagnostics. In this setting, DNA methylation has evolved as a biomarker of interest due to its early occurrence in carcinogenesis and applicability to first-void urine (FVU). Sampling the first fraction of the urine stream (first void) improves accuracy by capturing biomarker-rich material deposited on the external female genital tract. Although recent studies report promising results, technical hurdles include a limited number of methylation markers for simultaneous analysis and the need for bisulfite conversion. As a result of this harsh chemical treatment, DNA becomes fragmented with consequences for clinical accuracy. Certainly, in low-concentrated urine samples, the effects become more pronounced.

Methods: With these challenges in mind, a novel technique called IMPRESS (Improved Methylation Profiling using Restriction Enzymes and smMIP Sequencing) has been developed by our research group to circumvent bisulfite conversion and enable large-scale multiplexing. IMPRESS cuts unmethylated DNA using methylation-sensitive restriction enzymes (MSREs) and captures remaining intact DNA with single-molecule molecular inversion probes (smMIPs). Here, we apply IMPRESS for cervical screening using cervical cancer-specific methylation markers that we previously identified. In total, 1536 smMIPs were developed for methylation detection in cervical (pre)cancer. To test the markers, 111 FVU samples were analysed from patients referred to colposcopy after aberrant cervical results (NCT02714127, NCT03064087, and NCT03542513). 85 patients had no or low-grade cervical intraepithelial lesions (<HSIL) and 26 high-grade lesions (HSIL). The optimal set of smMIPs was selected to achieve the highest Area Under the Receiver Operator Characteristic (ROC) Curve (AUC) to correctly distinguish HSIL vs. <HSIL. Histology served as a reference, and if a biopsy was not performed, colposcopy results were used instead.

Results: Based on the sequencing results, the highest (5-fold cross-validated) AUC of 0.79 was achieved with the combination of the top 156 methylation markers, giving a sensitivity of 69% and specificity of 84%. Total normalized and corrected smMIP sequencing counts were significantly higher for HSIL vs. <HSIL ($p < 0.001$). When aiming for a lower number of smMIPs, and thus lower data complexity, an AUC of 0.78 is reached using the top 28 smMIPs, with a sensitivity of 77% and specificity of 74%. The differences in total normalized and corrected smMIP counts were also significant between the groups ($p < 0.001$).

Conclusions: These results show the feasibility of using IMPRESS for the discrimination of HSIL vs. <HSIL in a referral setting using FVU samples. Further marker selection, model training and refinement, and cut-off optimization could improve this proof-of-concept analysis. As such, these results could aid in introducing a full molecular cervical cancer screening approach applicable on FVU, warranting validation in a larger cohort.

References:

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#14085

Mutation sequencing for endometrial cancer detection in urine

13 - Self-sampling

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Background/Objectives: Endometrial cancer is the second most common gynecologic cancer, and it is among the tumor types with the sharpest rise in incidence over the past 10 years. Endometrial cancer usually presents with postmenopausal bleeding, and the likelihood of endometrial cancer being the cause of postmenopausal bleeding increases with age. The usual method for diagnosing endometrial cancer involves pelvic ultrasound and endometrial biopsy when endometrial thickness is increased. However, the lack of ultrasound specificity exposes a high proportion of healthy women to invasive tests. In addition, endometrial biopsies are not informative or impractical in a large proportion of women, and further investigations under general anesthesia are required. Thus, there is an urgent need to develop non-invasive methods to detect this cancer. In a previous pilot study, we identified mutations in 100% of the cases and 5% of the controls by evaluating DNA mutations in urine samples from 19 endometrial cancer cases and 20 controls [1]. The aim of the present study is to validate the detection of somatic mutations in urine to accurately distinguish endometrial cancer patients from healthy controls in a multicenter study.

Methods: Urine samples were collected from cases and controls at 6 hospitals in Spain and Amsterdam. Urine samples were evaluated using next-generation sequencing (NGS) with molecular identifiers targeting a custom panel of 47 genes. NGS was performed at high depth (median coverage before deduplication =24,339X, interquartile range -IQR-=18,892X-32,128X; and after deduplication = 1,507X, IQR= 1,068–2,130) on Illumina Novaseq (Illumina) using an SP flow cell and 150 bp paired-end sequencing protocol. Survival analyses according to the molecular group using urine samples were performed using Kaplan-Meier curves with log-rank tests and Cox proportional hazards models adjusted for age.

Results: To date, we have analyzed 343 urine supernatant samples from 207 cases and 136 controls. Overall, we identified mutations in DNA from urine supernatant samples in 78.3% (162/207) of endometrial cancers, with a specificity of 75.0% (102/136). Excluding variants with a variant allele frequency (VAF)<2% increased specificity to 94.9% (129/136) but reduced sensitivity to 65.2% (135/207). Results were consistent across centers, though analyses are still ongoing. Sensitivity among bleeding cases was 79.1% (125/158), and specificity 76.8% (76/99). Sensitivity was lowest in non-endometrioid cancers (33/48, 68.8%), while it was highest in MMRd cases (42/49, 85.7%). Cases with *POLE* mutations detected in urine exhibited an excellent prognosis, while the presence of *TP53* mutations was associated with poor clinical outcomes.

Conclusions: Analysis of somatic mutations in urine samples represents a practical method for the detection and molecular classification endometrial cancer. Although efforts are ongoing to complete enrollment and further optimize diagnostic accuracy and classification, these noninvasive, self-collected samples hold promise for detecting endometrial cancer and predicting patient clinical outcomes.

References: 1 Costas L, Onieva I, Pelegrina B, *et al.* Evaluation of Somatic Mutations in Urine Samples as a Noninvasive Method for the Detection and Molecular Classification of Endometrial Cancer. *Clin Cancer Res.* 2023;29:3681–90. doi: 10.1158/1078-0432.CCR-23-0367

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#14128

Feasibility of first-void urinary high-risk human papillomavirus testing among women living with HIV in Guinea-Bissau - A multicenter cross-sectional study

09 - HPV testing

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Background/Objectives: Cervical cancer screening is not implemented in Guinea-Bissau, and data on high-risk human papillomavirus (hrHPV) prevalence among women living with HIV (WLWH) in sub-Saharan Africa remain limited and heterogeneous. This study was the first to assess the acceptability of first-void urine (FVU) and vaginal self-sampling for hrHPV testing, as well as hrHPV prevalence and genotype concordance, among WLWH in Guinea-Bissau.

Methods: In this multicentre cross-sectional study, 498 WLWH aged 18–64 years were recruited from nine HIV clinics in Guinea-Bissau. Participants self-collected paired FVU samples using the 20 mL Colli-Pee device and vaginal samples using the Evalyn Brush at the clinic. HPV DNA testing was performed using the Allplex HPV-HR extended genotyping assay. Acceptability and sampling preferences were assessed using a questionnaire, and hrHPV genotype concordance between sample types was evaluated using Cohen's kappa (κ).

Results: Overall, 78% (389/498) of the participants tested positive for hrHPV in FVU and/or vaginal samples. The overall hrHPV prevalence in FVU was significantly higher as compared to vaginal samples (75% vs 64%, $p<0.001$) Good genotype concordance was observed between sampling methods (κ range 0·64–0·78). The most prevalent genotypes were HPV52 and HPV58 (21% each), followed by HPV66 and HPV16 (18% each). Both self-sampling approaches were well accepted in terms of comfort and ease of use, with FVU sampling preferred by most participants.

Conclusions: Clinic-based FVU and vaginal self-sampling for hrHPV testing were feasible and highly acceptable among WLWH in West Africa, with urine sampling emerging as the preferred modality. The very high hrHPV prevalence highlights the urgent need to integrate HPV-based cervical cancer screening and treatment into HIV care programmes in sub-Saharan Africa.

References:

HN04 - Liquid biopsy for HPV+ oropharyngeal cancer: Transforming diagnosis and surveillance

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#14261

Economic Considerations for Circulating Tumor DNA in HPV-Associated Oropharyngeal Cancer

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Circulating tumor DNA (ctDNA) is increasingly recognized as a clinically informative biomarker in HPV-associated oropharyngeal squamous cell carcinoma (HPV+ OPSCC), with potential applications spanning diagnosis, treatment selection, and long-term surveillance. In a disease characterized by high cure rates and extended survivorship, understanding the economic implications of ctDNA integration is critical to its sustainable adoption.

Methods: This presentation reviews the economic implications of ctDNA use across the care continuum, from diagnosis through treatment and surveillance.

Results: At the time of diagnosis, ctDNA offers a noninvasive approach that may improve diagnostic efficiency while reducing reliance on invasive procedures and repeat biopsies. Earlier and more accurate diagnosis has the potential to shorten diagnostic pathways, lower procedural costs, and streamline downstream care delivery.
During treatment, ctDNA provides a biologically informed framework for risk-adapted de-escalation. In non-surgical patients, ctDNA-guided strategies may support reductions in radiation intensity, while in surgically treated patients, postoperative ctDNA assessment may help identify those who can safely avoid adjuvant therapy. By minimizing overtreatment, ctDNA-guided approaches have the potential to reduce treatment-related toxicity and associated healthcare costs without compromising oncologic outcomes.
In survivorship, ctDNA-based surveillance may further enhance value by enabling earlier detection of recurrence, allowing for intervention at lower disease burden and potentially reducing the intensity of salvage therapy. At the same time, ctDNA may decrease dependence on routine imaging and frequent in-person visits, facilitating remote surveillance models that reduce cumulative costs and improve convenience for long-term survivors.

Conclusions: Together, these considerations position ctDNA as a tool not only for clinical innovation but also for advancing value-based care across the continuum of HPV-associated oropharyngeal cancer management. Future clinical trials and implementation strategies should incorporate economic endpoints to ensure that the promise of ctDNA translates into durable, system-level benefit.

References:

SS13 - How to improve accuracy in cervical cancer screening in settings with limited infrastructure

#14264

DHIS2 as an electronic data collection system for completeness of screening rounds

38 - Low resource settings

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Background/Objectives: The PAVE study (Automated Visual Evaluation for HPV) is a large-scale, multinational initiative aimed at assessing an innovative strategy for cervical cancer prevention in resource-constrained settings. Specifically, the study evaluated a comprehensive approach that combines HPV testing with self-sampling, deep learning-based Automated Visual Evaluation (AVE), and targeted therapies [1]. To evaluate the strategy, it was crucial to implement a system capable of standardizing data collection across all participating centers in nine countries, while addressing key challenges such as limited connectivity, staff unfamiliar with electronic records, and the potential use of mobile teams. The system was designed with two primary objectives: ensuring patient follow-up for appropriate clinical management and providing reliable, consistent data for periodic evaluation of the strategy. A secondary goal was to enable long-term sustainability of the system beyond the project's duration. This presentation will describe the methodology used to design the system and summarize the outcomes achieved in data collection.

Methods: The design and implementation of the project's information system were structured into the following stages:
Identifying the variables to be collected in collaboration with the consortium's lead research team.
Validating additional context-specific variables with the research teams in each participating country.
Designing the data collection system using open-source software tools.
Deploying the system in each country and assessing the quality of the collected data.

Results: The information system developed for the project consisted of three core components, while allowing each country to incorporate ad

- **Three DHIS2-based programs** (dhis2.org): one for recording visit data, another for storing colposcopy images, and a third for HPV te
- **A custom Android application**, built on the DHIS2 Android Skeleton App, which connects to the colposcope to capture and upload im
- **An image-sharing platform for histopathology**, implemented using Nextcloud (nextcloud.com).

A unique Participant ID linked participant information across different data sources. HPV test results were associated through the swab code,
The system collected data from December 2022 to December 2025. Among 50,450 women screened, 49,074 (97.27%) had valid HPV results.
triage data, including expert pathology.
The main challenges in data collection included staff turnover in some countries, connectivity issues, and ensuring system compatibility as equ

Conclusions: The information system developed for the PAVE project enabled the collection and standardization of reliable data across diverse contexts and languages. Leveraging a platform such as DHIS2 allowed customization of data entry forms to meet local needs and provided user-friendly tools for healthcare personnel. Because these tools are based on open-source software, country teams have the option to continue using them beyond the scope of this research.

References: [1] B. Befano *et al.*, «Initial evaluation of a new cervical screening strategy combining human papillomavirus genotyping and automated visual evaluation: the Human Papillomavirus–Automated Visual Evaluation Consortium», *JNCI J. Natl. Cancer Inst.*, vol. 117, n.o 10, pp. 2124-2129, oct. 2025, doi: 10.1093/jnci/djaf054.

AI05 - Submitted papers

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#12595

Artificial intelligence for individualized cancer risk prediction in cervical screening

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Risk-based screening can be used to tailor screening programs to the need of each participant, improving sensitivity, with more intense screening for high-risk subjects, and specificity, by less intense screening of low-risk subjects. We explored the predictive value of artificial intelligence (AI) using screening histories to assess individual cervical cancer risk.

Methods: We trained Light Gradient Boost Machine (LightGBM) models to predict cervical cancer risk after bayesian optimization for hyperparameter tunning, using data from the Swedish National Cervical Screening Registry (NKCx). An unsupervised score based on isolation forests was incorporated as an additional feature and evaluated. The dataset was split into 80% for training using stratified 10-fold cross-validation and 20% for testing.

Results: The best performing models were without using the unsupervised score feature and achieved an AUC of 90.60% on the test set. Using the top 10% scores as threshold, sensitivity was 81.97%, weighted accuracy 41.21%, precision 0.44%, F1-score 0.88%, and NPV 99.99%. The most informative features were the number of years since latest Human Papillomavirus (HPV) test, year of birth, latest HPV result, and year of censoring, in agreement with clinical knowledge.

Conclusions: AI using screening histories holds promise for tailoring screening efforts focusing on women with high risk of cervical cancer.

References:

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#12696

Deep learning-assisted versus manual reading in routine cervical cytopathology: a multicentre randomised crossover trial

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Deep learning (DL) systems could improve diagnostic accuracy and efficiency in detecting cervical atypia, but their effectiveness in routine cytopathology remains insufficiently explored. Therefore, we conducted a multicentre, randomised, crossover trial following the CONSORT-AI guidelines to assess whether a DL system could improve the diagnostic accuracy and efficiency of nonexpert cytopathologists.

Methods: This multicentre, randomised crossover trial was done at four centres in China. We recruited consecutive women aged 18 or older undergoing liquid-based cytology for cervical screening. Their slides were digitized and randomly assigned to groups A or B (1:1) using a computer-generated random numerical series. Four nonexpert cytopathologists assessed group A using DL assistance and group B through manual reading under a microscope. After a four-week washout period, the groups switched roles. Each slide was evaluated twice, once with DL and once without, but in a different randomly shuffled order. The cytopathologists were not blinded to the randomization status. The primary outcome was the sensitivity and specificity of DL-assisted versus manual reading for detecting abnormal cervical cells. Secondary outcomes included reading efficiency. This study is registered under ChiCTR2300078722.

Results: Between April 7 and Sep 27, 2023, 1920 women with satisfactory slides were included and randomly assigned to groups A (n=960) and B (n=960). DL assistance significantly improved the nonexpert cytopathologists' sensitivity (0.713 [95%CI 0.658–0.763] to 0.857 [0.811–0.893], $p<0.0001$), with the lower 95% CI limit for the difference (0.143 [0.076–0.211]) exceeding the superiority margin of 0.05. Specificity showed no significant difference between DL-assisted and manual reading (0.851 [0.833–0.867] vs 0.865 [0.847–0.880], $p=0.238$), with the difference (0.014 [-0.010–0.038]), confirming non-inferiority as the lower 95% CI limit was above -0.05. Reading time was significantly reduced with DL (mean: 175 seconds vs 31 seconds, $p<0.0001$).

Conclusions: This multicentre randomised crossover trial demonstrated the benefits of DL-assisted reading over manual reading in detecting abnormal cervical cells. The results show that the DL system can enhance the sensitivity of nonexpert cytopathologists without compromising specificity, while reducing reading time. Future efforts to optimize the integration of DL systems into practice are crucial for improving diagnostic accuracy and efficiency.

References:

#13317

Reduction in cytological triage after a positive HPV self-test: performance of CIN3+ prediction based on HPV viral load, age, and screening history

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: The implementation of primary HPV testing on self-collected samples in the Netherlands has increased cervical cancer screening uptake, but triage of women with a positive self-test still relies on cytological assessment of clinician-collected smears. Accurate prediction of (pre)cancerous lesions (CIN3+) without cytological triage is desirable to reduce demand on cytology labs and loss to follow-up of HPV-positive women with a self-test.

Methods: We developed and validated CIN3+ prediction models for women with a HPV-positive self-test using information available from screening registries besides cytology results. We included 13,673 women with a HPV-positive self-test (BD Onclarity HPV test, Copan collection swab) who attended the Dutch HPV-based screening program between July-December 2023 (histological follow-up until July 2025). Logistic regression and four machine learners (XGBoost, Random Forest, BART, and Naïve Bayes) were used with variables that were on file at the screening registry: age, HPV genotype, Ct-value (viral load marker), and screening history. HPV genotypes 16/18/31/45/51/52 were included individually and P1 (33/58), P2 (56/59/66) and P3 (35/39/68) were included as pooled genotypes. Ct-value was included for each detected genotype (or genotype group) as a continuous variable. Previous round HPV screening history had three categories: (1) HPV-positive, (2) HPV-negative, (3) unknown/no history. Interaction effects of HPV16 and other high-risk HPV types were included in the logistic regression model.
We defined a region (“*grey zone”)* of predicted CIN3+ risks where the risk is too low for immediate referral to the gynaecologist, but too high for repeat testing after 1 year. The PPV for immediate referral and the NPV for repeat testing after one year were set equal to those observed in the national programme, Our triage strategy was as follows: (1) if the CIN3+ risk was above the grey zone region, colposcopy referral was advised, (2) inside the grey zone, cytological triage in combination with HPV16/18 genotyping was advised as per the Dutch triage protocol, and (3) below the grey zone repeat testing after 12 months was advised. Models were compared based on AUC (Area Under the Curve) values and triage strategies were compared to the current Dutch screening program based on the percentage receiving cytology, gynaecologist referral rate, PPV and NPV for CIN3+.

Results: Logistic regression (AUC=0.805) performed similar to machine learners for CIN3+ prediction (AUCs between 0.778-0.803) and was selected for defining the grey zone. The current Dutch triage strategy has a PPV of 33.1% (95%CI: 29.0-37.4), NPV of 98.4 (95%CI: 97.7-98.6), and referral rate of 14.1% (95%CI: 12.9-15.3). Similar performance can be achieved with our approach, yielding an overall PPV of 33.0% (95%CI: 28.9-37.5), NPV of 97.9% (95%CI: 97.4-98.4), and referral rate of 13.2% (95%CI: 12.2-14.5). However, with our CIN3+ prediction model, the number of women requiring a cytological test decreased from 100% to 44% of HPV-positive women.

Conclusions: Selective cytological assessment of HPV-positive women can maintain high predictive performance for CIN3+ while reducing the workload of cytology labs by nearly 60%, supporting a more streamlined and efficient referral pathway.

References:

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#12885

Improving workforce efficiency using AI-assisted digital cytology: A model-based evaluation for the NHS Cervical Screening Programmes

20 - New technologies

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Background/Objectives: Cervical screening requires a skilled workforce in laboratories to review and report cytology slides. In the UK, vacancies amongst screening staff are putting services under strain and impacting on the timely reporting of results for patients. New AI-assisted digital cytology technology, such as the Genius™Digital Diagnostics System, could support laboratories in developing more resilient and productive services.

Methods: This study aims to evaluate the impact of introducing the AI-assisted cytology Genius™Digital Diagnostics System (Genius™) on the laboratory workforce involved in cytology triage after primary HPV screening compared to current standard of care (manual microscopy) in UK, using the NHS Cervical Screening Programme (NHSCSP) workflow in England as an example. A decision tree model of the flow of slides through the cervical screening programme in the UK was developed following NHSCSP guidelines. Model parameter inputs were obtained from published sources and several NHS Trust laboratories, including a service evaluation. Consultants from five laboratories participated in workshops to validate model structure, key inputs and assumptions. Model outcomes were annual staff time (hours) required for screening and reporting. Most inputs were varied in an uncertainty analysis to assess their impact on outcomes and explore key assumptions, including an alternative workflow for Scotland.

Results: Screening and reporting 479,125 cytology slides annually would require 31,842 staff hours with Genius™, versus 103,151 hours using manual methods. The average time to review and report per slide (including negative and abnormal) was 4.0 minutes (Genius™) and 12.9 minutes (manually). This represents a potential 69% increase in overall staff productivity, with gains of 76% in primary screening and 64% in consultant review. Results for a Scottish workflow were similar with a 67% increase in staff productivity. Scenario results indicated that the time to screen and report slides using both methods were key inputs driving results.

Conclusions: Implementing Genius™ could significantly reduce the time required for staff to screen and report slides, thereby improving workforce productivity and alleviating chronic staffing shortages. This is the first study to compare Genius™ with manual cytology screening workflows in the UK. Studies from the US and Germany have similarly shown that Genius™ reduces the average time needed to screen a cytology slide by approximately 50% [1,2]. These results can inform policymakers as they consider measures to improve resilience of cervical screening programmes in the UK and other countries.

References: [1] Ikenberg H, Lieder S, Ahr A, Wilhelm M, Schön C, Xhaja A. Comparison of the Hologic Genius Digital Diagnostics System with the ThinPrep Imaging System—A retrospective assessment. Cancer Cytopathol. 2023;131(7):424–32.

[2] Cantley RL, Jing X, Smola B, Hao W, Harrington S, Pantanowitz L. Validation of AI-assisted ThinPrep® Pap test screening using the GeniusTM Digital Diagnostics System. J Pathol Inform. 2024 Dec 1;15:100391.

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#12687

Towards Comprehensive AI-Assisted Colposcopy: Automatic Differentiation of Cervical, Vaginal, and Vulvar HSIL and LSIL Lesions

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: While HPV is a well-established driver of cervical cancer, its role also extends to vaginal and vulvar cancers. Colposcopy, though capable of examining the entire lower genital tract, suffers from limited diagnostic accuracy. This study aimed to develop and validate artificial intelligence (AI) models capable of differentiating low-grade (LSIL) from high-grade (HSIL) squamous intraepithelial lesions in cervical, vaginal, and vulvar regions.

Methods: Three independent convolutional neural network (CNN) models were trained on colposcopy image datasets: 22,693 cervical frames (from 70 procedures), 57,250 vaginal frames (from 71 procedures), and 9,857 vulvar frames (from 28 procedures). Each model was evaluated using sensitivity and positive predictive value (PPV).

Results: The cervical CNN achieved 99.7% sensitivity and 97.8% PPV. The vaginal model reached 98.7% sensitivity and 98.9% PPV. The vulvar model achieved 99.7% sensitivity and 99.1% PPV.

Conclusions: This study presents the first dedicated CNN models for lesion classification across the cervix, vagina, and vulva, demonstrating high performance. They represent the initial step towards a comprehensive, AI-powered colposcopic assessment encompassing the entire female genital tract.

References:

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#13443

AI in Colposcopy: A Promising Alternative to VIA for Cervical Cancer Screening in Cambodia

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Visual Inspection with Acetic Acid (VIA) is widely used for cervical cancer screening in Low- and Middle-Income Countries (LMIC), but its subjectivity and low specificity often lead to unnecessary biopsies and overtreatment. The Ettics Initiative's screening study in Cambodia highlighted this limitation, showing that many VIA-positive women were found to have benign findings such as metaplasia on biopsy. Artificial Intelligence (AI) integration in colposcopy may provide more consistent and objective assessments. The objective of this study was to evaluate whether an AI algorithm for colposcopy could serve as a more specific alternative to VIA in such settings.

Methods: A convolutional neural network–based AI model was trained on colposcopic images provided by the MVZ im Fürstenberg-Karree Berlin and the IZD Hannover, designed to detect cervical High-Grade Squamous Intraepithelial Lesions (HSIL). In the preliminary study by the Ettics Intiative in Cambodia, all VIA- or colposcopy-positive women underwent a biopsy. The biopsies were examined by expert pathologists in Cambodia and Germany. We retrospectively applied our model to the Cambodian colposcopy images with biopsy confirmation (n=139) and compared its sensitivity and specificity against VIA.

Results: From 2844 screened patients, 139 were tested positive by VIA or colposcopy and underwent biopsy. Biopsy confirmed 18 HSIL cases. Our AI model correctly identified all HSIL cases, achieving a sensitivity of 100% and a specificity of 79%. In comparison, VIA showed a high sensitivity of 89% but a poor specificity of only 12%.

Conclusions: Our findings suggest that AI-assisted colposcopy systems can approach high sensitivity while substantially lowering the false-positive rate. AI-assisted colposcopy could reduce overtreatment, representing a promising alternative to VIA in LMIC cervical cancer screening programs.

References:

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#13376

Artificial Intelligence as a potential tool to manage increased gynaecological inquiries faced by a patient advocacy organisation in the United Kingdom

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Following the closure of a major cervical cancer trust in 2024, another leading UK patient advocacy organisation covering all five gynaecological cancers experienced a substantial increase (approximately 1141%) in monthly contacts.i This surge placed considerable strain on the charity's Ask Eve service, a nurse-led information service, which is staffed by one full-time nurse and one part-time consultant. The service was able to keep within normal response times, but this was only managed by increasing time from the service staff and was not a sustainable model going forward. To address the significant increase in gynaecological inquiries, the patient advocacy organisation initiated a service development project to evaluate the feasibility and potential impact of an artificial intelligence (AI) chatbot, Ask Eve Assist. The goal of this tool is to increase scalability of the service as well as increase the capacity for complex cases requiring nurse time and expertise.

Methods: A comprehensive risk management strategy was developed in alignment with the Care Act 2014. The AI vendor selection process included a detailed market scan, assessing ethical, clinical, and technical criteria, as well as safeguarding capabilities. The chatbot was designed as a retrieval-only AI system (sourcing information from pre-existing data only), using PIF TICK-accredited content and adhering to GDPR standards.i It was designed to maintain the empathetic but expert tone of the patient advocacy organisation's information and the Ask Eve service. Training data comprised 3,400 anonymised queries submitted to the charity between August 2023 and March 2024.i User acceptance testing involved anonymised real-world scenarios and a total of 42 participants took part, representing diverse user groups including lay reviewers and nurses.ii Both quantitative metrics, such as user satisfaction, and qualitative metrics, such as tone consistency, are in place to evaluate performance.

Results: Analysis of the 3,400 training data queries indicated that the chatbot could autonomously respond to 61% of cases, equating to approximately 259 out of 425 monthly queries.i These included logistical questions, HPV screening inquiries, requests for general emotional reassurance, and frequently asked questions. Initial user testing findings were overall positive, with responses frequently described as intuitive, comprehensive and easy to use and with testers valuing rapid safety response and human options. The Ask Eve Assist's tone was widely regarded as warm, reassuring, and non-judgemental, consistent with Ask Eve's ethos, although some testers felt that generic phrases created over-personification. Other minor issues included occasional glitches, unnecessary safety responses and a need for a short onboarding message about the AI.

Conclusions: Phase one and initial user testing findings suggest that Ask Eve Assist has strong potential to reduce the workload burden on clinical staff, enabling nurses to focus on complex cases. Planned next steps include pilot deployment, multilingual proof-of-concept testing, development of a CRM integration roadmap, and establishment of user feedback and analytics mechanisms. Pre-pilot refinements will focus on tuning safety triggers and enabling safe resumption after escalation. Ongoing work will ensure compliance with UK/EU data standards and WCAG 2.1 AA accessibility requirements, while safeguarding the compassionate Ask Eve voice.

References: i. The Eve Appeal. (2025). *Ask Eve Assist Phase One Report* [Data on file].
ii. The Eve Appeal. (2025). *Ask Eve Assist: User Acceptance Testing Pack v1.0* [Data on file].

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#13613

Empowering Cervical Cancer Screening in Africa: The Role of Artificial Intelligence and Medical Students When Expert Access Is Limited

38 - Low resource settings

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Background/Objectives: In Africa, cervical cancer is the second most common cancer among women, with an incidence three times higher than in developed countries due to limited vaccination and screening programs. The WHO aims to achieve 70% screening coverage among women by 2030. In low-resource settings, access to HPV testing, cervical pathology, and colposcopy experts is limited, making visual inspection essential. The Elikia project aims to implement a sustainable and reproducible cervical cancer screening system in Kinshasa using local resources. This study seeks: (1) to assess interobserver agreement in visual inspection with acetic acid and Lugol (VIA/VILI) among trained medical students, an untrained AI model (Perplexity Pro), and a gynecologist specialized in cervical pathology; and (2) to determine the diagnostic validity of each observer compared to cytology, the gold standard.

Methods: A diagnostic accuracy study was conducted during a cervical cancer screening campaign in July 2023 at Monkole Hospital, Kinshasa (DRC), as part of the Elikia project. Trained medical students screened 548 women using cytology and visual inspection with acetic acid (VIA) and Lugol (VILI), taking two cervical photos per patient. Images were later analyzed by a gynecologist and an untrained AI model (Perplexity Pro). Results were classified as positive, negative, not assessable, or no data. Agreement was measured with Cohen's and Fleiss's Kappa; sensitivity, specificity, PPV, and NPV were calculated using cytology as the gold standard. Perplexity's validity was also compared to students and the expert, and AUC/ROC analyses excluded non-assessable images.

Results: A total of 465 patients were analyzed. Interobserver agreement showed moderate concordance between Perplexity Pro and the expert (κ=0.43), very low between Perplexity Pro and students (κ=0.16), and low–moderate between expert and students (κ=0.27). Overall group agreement (Fleiss κ=0.29) was low–moderate. Using cytology as the gold standard, sensitivity/specificity were: students 0.30/0.83, Perplexity Pro 0.49/0.46, expert 0.38/0.63. NPV was high in all ($\geq$0.88). When students were the reference, Perplexity Pro showed sensitivity 0.82 and specificity 0.52; the expert 0.81 and 0.72. With the expert as reference, Perplexity Pro reached 0.85 sensitivity and 0.64 specificity. ROC analysis (n=441) showed low AUC vs cytology (Perplexity 0.47; expert 0.50; students 0.56), but improved when comparing visual inspection methods (up to 0.76 for expert vs students, 0.74 for Perplexity vs expert).

Conclusions: All observers (students, Perplexity Pro, and the expert) showed low agreement levels, which improved to moderate in "deferred" analyses between Perplexity Pro and the expert, indicating differences between in situ and deferred visual inspections. Overall, visual inspection showed low discriminatory capacity versus cytology, but performance (sensitivity, specificity, PPV, NPV) improved in deferred evaluations, supporting its usefulness in low-resource settings. The high NPV across observers confirms that negative visual results reliably indicate absence of lesions.

References:

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#13911

Bridging the Communication Gap: Family Physician-Specialist Referral Challenges and AI-Enabled Solutions in Canadian Healthcare

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Effective physician-to-physician communication is essential for coordinated patient care, yet Canada's referral process remains fragmented and reliant on outdated methods. Limited research has systematically examined both family physician and specialist perspectives on these communication barriers. We conducted a two-part study across Canada to identify referral communication challenges, assess their impacts, and explore technology-based solutions.
Objective: identify communication challenges between family physicians and specialists during referrals, assess their impacts on patient care and physician workflow, and evaluate how AI-enabled technology can address these challenges.

Methods: This Canada-wide qualitative study employed structured surveys with closed and open-ended questions to capture physician experiences and perspectives on referral communication. Coordinated from Ottawa, the two-part study included 50 physicians from multiple provinces across urban, suburban, and rural settings. Part one engaged 25 family physicians completing a five-question survey on referral communication experiences, while part two involved 25 specialists from 19 specialties (including cardiology, orthopedics, psychiatry, and dermatology) responding to a 10-question survey on receiving and managing referrals.

Results: Despite role-specific differences, family physicians and specialists reported consistent fundamental challenges in referral communication. Key barriers included outdated technology (persistent fax reliance), limited secure messaging, lack of standardized forms, incomplete patient information and investigations, and unclear referral status and specialist availability. Physicians identified these barriers as sources of care delays, duplicated investigations, medical errors, and burnout. AI-enabled solutions addressing these challenges - through intelligent form completion, automated routing, real-time tracking, secure messaging, and decision support - can reduce administrative burden, improve information transfer, and enhance patient outcomes.

Conclusions: Outdated communication tools and fragmented information systems between family physicians and specialists are reducing healthcare system efficiency and diminishing care quality. Convergent perspectives from both physician groups underscore the urgency of addressing these barriers. AI-enabled technology solutions that streamline workflows, standardize information exchange, and enhance care coordination offer significant opportunity to improve the healthcare experience for physicians and patients.

References:

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#13577

Artificial intelligence-assisted decision-making to improve vulnerable women\'s participation in cervical cancer screening in France - design and early implementation of a cluster randomized trial

11 - Screening for women difficult to reach

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Background/Objectives: Despite organized cervical cancer screening in France, participation remains suboptimal, particularly among women in disadvantaged areas. Self-sampling for HPV testing has shown promise, yet uptake remains below 20% when kits are mailed home. Following successful user-centered development, the AppDate-You chatbot provides women with instant access to evidence-based information addressing their cervical cancer screening concerns.

Methods: This cluster-randomized controlled trial was conducted in 60 disadvantaged areas (IRIS) of Occitanie region, randomized into intervention (n=30) and control (n=30) arms. Women aged 30-65 years who had not participated after initial screening invitation received either an HPV self-sampling kit with chatbot access (intervention) or kit only (control). Primary outcome: completion of full screening pathway (HPV test + triage cytology if positive). Secondary outcomes: time to screening completion, test quality, chatbot engagement metrics, and cost-effectiveness.

Results: Study recruitment started in September 2025 and is planned to be completed by November 2025, with a target of 5,141 women across both arms. Six-month follow-up data on screening participation and chatbot engagement will be available for presentation at the conference.

Conclusions: This study aims to estimate the effect of an AI-based conversational tool on cervical cancer screening participation among women in disadvantaged areas. Preliminary findings will describe implementation challenges, chatbot engagement metrics, and early screening uptake. Final analyses will provide effect estimates for screening completion rates, time to completion, and cost-effectiveness to inform decision-making regarding integration of digital tools into organized screening programs.

References: Sancho-Garnier H, Tamalet C, Halfon P, Leandri F, Le Retraite L, Djoufelkit K, et al. HPV self-sampling or the Pap-smear: a randomized study among cervical screening nonattenders from lower socioeconomic groups in France. Int J Cancer 2013 Dec 01;133(11):2681-2687
Haguenoer K, Sengchanh S, Gaudy-Graffin C, Boyard J, Fontenay R, Marret H, et al. Vaginal self-sampling is a cost-effective way to increase participation in a cervical cancer screening programme: a randomised trial. Br J Cancer 2014 Nov 25;111(11):2187-2196
Le Bonniec A, Sauvaget C, Lucas E, Nassiri A, Selmouni F. Design and Validation of a Chatbot-Based Cervical Cancer Screening Decision Aid for Women Experiencing Socioeconomic Disadvantage: User-Centered Approach Study. JMIR Cancer. 2025 Jul 24;11:e70251.
Selmouni F, Guy M, Muwonge R, Nassiri A, Lucas E, Basu P, Sauvaget C. Effectiveness of Artificial Intelligence-Assisted Decision-making to Improve Vulnerable Women's Participation in Cervical Cancer Screening in France: Protocol for a Cluster Randomized Controlled Trial (AppDate-You). JMIR Res Protoc. 2022 Aug 2;11(8):e39288.
Webster, P., Healey, N. Eleven clinical trials that will shape medicine in 2025. Nat Med 30, 3384–3388 (2024). https://doi.org/10.1038/s41591-024-03383-y

SS16 - Microbiome, inflammation and progression to cervical cancer

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#14384

Microbiome, Metabolome and Cytokine association with the development of HPV16 associated CIN 2 in a longitudinal cohort

18 - Microbiome

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Background/Objectives: Evidence continues to grow showing that the vaginal microbiome (VM) is important in CIN development. However, most studies are cross-sectional making causality difficult. Aims of our study were to examine microbiome, metabolome and cytokine profiles in women who developed HPV 16-CIN 2 and to compare these to sample obtained from the same women 1-2 years prior and to women with HPV 16 who never developed CIN2.

Methods: Cervical lavage samples from a 25-year cohort study of women aged 13-21 years at entry were characterized for microbiome, metabolome and cytokine. Two samples from 12 HPV 16 CIN 2+ women were tested: HPV 16+ and ~1-year pre CIN 2+ and at CIN 2+. In comparison, a sample from each of 15 women who were HPV 16+ but never developed CIN 2+ were analyzed. Comparison was made for bacterial species, metabolites and cytokines between the 3 samples.

Results: Microbiome; pre-CIN 2 was more similar to never CIN 2 when examining alpha and beta diversity. However, bacterial species analysis showed L. *crispatus* to be more abundant in those never-CIN 2 than pre-CIN 2. Given that the microbiome dysbiosis was not there prior to CIN 2, this suggest that HPV 16 persistence drove a change in the microbiome resulting in CIN 2+. On the other hand, it continues to support the important of L. *crispatus* in maintaining “health” in that it was more abundant in never-CIN 2 than pre-CIN 2.

Conclusions: Metabolites from the samples that were never destined to develop CIN 2+ appeared to more abundant than the other 2 groups. Many of the metabolites are important in immune functions including essential aa and lactic acid known to be critical in vaginal health, The abundance of essential aa and lactic acid likely reflected the greater abundance of L. *crispatus* in the never-CIN. Of note, 5-aminovaleric acid was also elevated in the pre-CIN 2+ compared to never CIN 2+ possibly reflecting a biomarker of those destined to progress to CIN 2+.

Cytokines: Both pre-CIN 2 and CIN 2 reflected an inflammatory environment in comparison to never CIN 2. This study suggest that this inflammatory environment helped HPV 16 progress to CIN 2. The pre-CIN2 was predominantly TH1 proinflammatory, which then switched to a much more mixed picture of TH1 and Th2 at CIN2. This suggests that HPV may dampen appropriate immune response by developing anti-inflammatory responses resulting in an overall failure to clear HPV. Examining HPV 16 infections with a strong inflammatory environment may lead to biomarkers to predict progression as well as inform treatments that would result in less inflammation.

References:

HN05 - Submitted papers II

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#13027

Episomal HPV16-A1 in oropharyngeal squamous cell carcinoma (OPSCC) is associated with good response to treatment.

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Human papillomavirus (HPV)-positive OPSCC represents a distinct clinical entity with better prognosis than HPV-negative tumours. However, a significant proportion of HPV-positive patients experience disease recurrence or progression despite standard treatment. Biomarkers for individual risk assessment are needed. A deeper characterization of HPV genomic status, including genotype, sublineage, integration, and structural rearrangements, could improve patient stratification. The objective of this study is to comprehensively characterize HPV genomic profiles in OPSCC and to evaluate the association between viral molecular status and disease progression after treatment.

Methods: Biopsies at diagnosis from IMMUNEBOOST-HPV trial (NCT03838263) and from OROPAP cohort (Georges Pompidou European Hospital, Paris, monocentric) were used for this work. All tumours were positive for p16 immunohistochemistry and HPV DNA by PCR. HPV whole genome sequencing was performed using HPV-Capture followed by Illumina sequencing (Holmes et al, 2016). Data were analysed with our bash and R-based pipeline, ViroCapt2, a improved version of ViroCapt (Wack et al., 2022), with enhanced sensitivity for HPV genotype determination, variant calling, detection of viral integration within the human genome and structural variants detection (virus-virus fusion with viral genome deletion or amplification). HPV-molecular signatures were classified into two types: i) episomal (or wild-type) HPV when only complete genomes that do not integrate into the human genome and do not present structural variants were found within the sample; ii) HPV with altered genomes when integration into the human genome, presence of viral structural-variant, or a combination of the two were detected. Using a Kaplan-Meier methods we analysed the association between these two molecular signatures and clinical outcome (disease specific survival).

Results: Of the 121 samples, 115 (95%) were positive for HPV16 and 6 (5%) for HPV33. HPV16_A1 was the predominant sublineage (n = 98, 80% of HPV16 cases). Within the HPV16_A1 subgroup, a recurrent mutation (n=4) at position 7316 (A>C) was associated with poorer progression-free survival ($p < 0.001$). Episomal HPV was detected in 21% of samples, and HPV with viral genome alterations was detected in 79% of samples (integration: 21%, structural variant: 18%, integration and structural variant: 40%). Within the HPV16_A1 subgroup, patients with episomal HPV genomes showed no disease progression, while those with integration and/or structural variants had significantly shorter PFS ($p = 0.03$).

Conclusions: HPV whole genome sequencing using HPV-Capture method and sequence analysis using ViroCapt2 tool showed that 79% of HPV-positive OPSCCs exhibited integration and/or structural variants while 21% were considered as episomal (or wild-type) HPV. The description of these structural variants has mostly been neglected in previous studies, leading to an overestimation of episomal HPV. Here, using samples from 2 different cohorts, we showed that within the HPV16_A1 population, episomal HPV status was associated with favorable outcome and absence of relapse after treatment. These findings suggest that this relatively simple molecular classification of HPV could be relevant to identify patients to whom therapeutic de-escalation could be proposed.

References: Holmes, Allyson, Sonia Lameiras, Emmanuelle Jeannot, et al. « Mechanistic Signatures of HPV Insertions in Cervical Carcinomas ». *Npj Genomic Medicine* 1, no 1 (2016): 1. https://doi.org/10.1038/npjgenmed.2016.4. Wack, Maxime, David Veyer, Camille Peneau, et al. « viroCapt: A Bioinformatics Pipeline for Identifying Viral Insertion in Human Host Genome ». In *Challenges of Trustable AI and Added-Value on Health*. IOS Press, 2022. https://doi.org/10.3233/SHTI220602.

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#12396

Immunological profiling of HPV-associated oropharyngeal cancers: development of a personalized prognostic score

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: The incidence of human papillomavirus (HPV)-associated oropharyngeal cancer (OPC) has increased significantly over the past decades 1-6. While most patients achieve favorable outcomes, approximately 20–25% relapse within 3 years 7, limiting treatment de-escalation strategies 8-14. Reliable prognostic biomarkers are therefore needed. This study aimed to characterize the tumor microenvironment (TME) of HPV+ OPC and develop prognostic scores to identify candidates for therapeutic de-escalation trials.

Methods: A retrospective monocentric cohort of 124 OPC patients (96 HPV+, 28 HPV-) treated between 2019–2024 was analyzed. The HPV+ cohort was randomly divided into training (n=48) and validation (n=48) sets. Immunoscore® (IS) was assessed on 4 µm FFPE sections by $CD3^+/CD8^+$ immunohistochemistry in the tumor core and invasive margins. Cut-offs for “High” and “Low” infiltration were defined by ROC analysis based on relapse status in the training cohort and subsequently validated in the validation cohort. Hyperplex spatial proteomics using a 26-plex panel immunofluorescent staining enabled phenotypic and spatial analyses. Based on the most discriminant markers, we developed a novel prognostic score (**ImmunORO**) to predict relapse in HPV+ OPC. RNA-seq on 20-µm FFPE sections analyzed cell composition via Cell Type Enrichment Analysis xCell 2.0 15

Results: The cohort (n=124) had mean age 68.5±10 years, predominantly male (77.4%), with 75.8% smokers, 43.5% T1–2 stage, and 69.4% N0–1 stage. Treatments included surgery only (8.1%), RT ± CT (36.3%), and surgery + RT ± CT (55.6%). Relapsed patients (n=29) differed from non-relapsed (n=95) only by a higher proportion of advanced T3-4 stage (p=0.028).
In the HPV+ training cohort, relapse occurred in **8.1% of IS-High** vs **63.6% of IS-Low** (**p<0.001**), and in the validation set, **4.2%** vs **37.5%** (**p=0.0002**). In the whole HPV+ cohort (n=96), IS showed strong prognostic accuracy (**AUC=0.775; sensitivity 80%; specificity 75%**) and remained independently associated with worse Disease-Free Survival (**DFS**) after **T stage adjustment** (**HR=5.58; p<0.001**).
No effect was seen in HPV- cases (p = 0.538).
Spatial proteomics revealed higher densities of CD3+, CD4+, CD8+, CD20+, PD1+ cells in HPV+ compared to HPV- tumors (p<0.05). HPV+ non-relapsers had significantly higher **MUM1+, CD20+, CD4+, CD3+,** CD8+, GZMB+, Ki67+ cell densities, with closer cytotoxic T cell–proliferating tumor cell proximity than HPV+ relapsers (p<0.05).
The **ImmunORO** score, integrating **MUM1+, CD20+, CD4+, CD3+,** stratified relapse risk: in the training cohort, relapse occurred in **5.9% of ImmunORO-High** vs **57.1% of ImmunORO-Low** patients; in the validation cohort, **6.3%** vs **50.0%** (**p<0.001**). In all HPV+ cases, ImmunORO achieved **AUC=0.801, sensitivity 80%, specificity 80.3%**, and was an independent predictor of poor DFS (**HR=5.28; p<0.001**). RNA-seq confirmed stronger T- and B-cell signatures in HPV+ non-relapsers, consistent with spatial proteomics findings.

Conclusions: The Immunoscore® and ImmunORO are strong independent prognostic biomarkers for HPV-positive OPC. Their performance was validated internally and supported by transcriptomic data. Patients with IS-High or ImmunORO-High profiles may be ideal candidates for therapeutic de-escalation trials. Multicenter validation and prospective studies are recommended before clinical implementation.

References: 1. Bray, F. et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin **74**, 229–263 (2024).
2. Nibu, K.-I. et al. Human papillomavirus-driven head and neck cancers in Japan during 2008-2009 and 2018-2019: The BROADEN study. Cancer Sci (2024) doi:10.1111/cas.16230.
3. Zamani, M. et al. The current epidemic of HPV-associated oropharyngeal cancer: An 18-year Danish population-based study with 2,169 patients. Eur J Cancer **134**, 52–59 (2020).
4. Tota, J. E. et al. Evolution of the Oropharynx Cancer Epidemic in the United States: Moderation of Increasing Incidence in Younger Individuals and Shift in the Burden to Older Individuals. J Clin Oncol **37**, 1538–1546 (2019).
5. Jéhannin-Ligier, K. et al. Incidence trends for potentially human papillomavirus-related and -unrelated head and neck cancers in France using population-based cancer registries data: 1980-2012. Int J Cancer 140, 2032–2039 (2017).
6. Mirghani, H. et al. HPV-driven oropharyngeal cancer burden in Paris and its region (ILE DE FRANCE) from 1981 TO 2021. Cancer Epidemiol 91, 102603 (2024).
7. Ang, K. K. et al. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med 363, 24–35 (2010).
8. Swisher-McClure, S. et al. A Phase 2 Trial of Alternative Volumes of Oropharyngeal Irradiation for De-intensification (AVOID): Omission of the Resected Primary Tumor Bed After Transoral Robotic Surgery for Human Papilloma Virus-Related Squamous Cell Carcinoma of the Oropharynx. Int J Radiat Oncol Biol Phys 106, 725–732 (2020).
9. Kang, J. J. et al. Consensuses, controversies, and future directions in treatment deintensification for human papillomavirus-associated oropharyngeal cancer. CA Cancer J Clin 73, 164–197 (2023).
10. Chera, B. S. et al. Phase II Trial of De-Intensified Chemoradiotherapy for Human Papillomavirus-Associated Oropharyngeal Squamous Cell Carcinoma. J Clin Oncol 37, 2661–2669 (2019).
11. Ferris, R. L. et al. Phase II Randomized Trial of Transoral Surgery and Low-Dose Intensity Modulated Radiation Therapy in Resectable p16+ Locally Advanced Oropharynx Cancer: An ECOG-ACRIN Cancer Research Group Trial (E3311). J Clin Oncol 40, 138–149 (2022).
12. Yom, S. S. et al. Reduced-Dose Radiation Therapy for HPV-Associated Oropharyngeal Carcinoma (NRG Oncology HN002). J Clin Oncol 39, 956–965 (2021).
13. Chen, A. M. et al. Reduced-dose radiotherapy for human papillomavirus-associated squamous-cell carcinoma of the oropharynx: a single-arm, phase 2 study. Lancet Oncol 18, 803–811 (2017).
14. Mirghani, H. et al. Treatment de-escalation in HPV-positive oropharyngeal carcinoma: ongoing trials, critical issues and perspectives. Int J Cancer 136, 1494–1503 (2015).
15. Aran, D., Hu, Z. & Butte, A.J. xCell: digitally portraying the tissue cellular heterogeneity landscape. Genome Biol 18, 220 (2017). https://doi.org/10.1186/s13059-017-1349-1

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#12771

Broadening a multiplex HPV early antigen biomarker beyond HPV16 for diagnosis of HPV-driven oropharyngeal cancer: pooled analysis from 10 studies

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: The prevalence of HPV-driven oropharyngeal cancer (HPV-OPC) continues to rise globally, with HPV16 being responsible for 89% of HPV-OPC. A commonly used serological multiplex biomarker definition in research for classifying HPV status of OPC uses HPV16 early antigens. Multiplex serology detects antibodies to multiple high-risk HPV genotypes, and limiting assays to HPV16 may miss OPC driven by other high-risk types. We evaluated whether including additional high-risk HPV genotypes could improve diagnostic performance.

Methods: Multiplex serology was performed on 4,702 OPC patients across 10 studies with available tumour HPV status. Of these, 633 had type-specific tumour HPV data (training dataset), and 4,069 had only tumour p16 data (p16 validation dataset). Optimal cut-offs for using HPV16-E6, and -E7 to detect HPV16-OPC in the training dataset were determined using ROC curves and Youden's index. In total, 28 biomarker definitions were evaluated in the training dataset, calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (PNV) and correctly classified value. Subsequently, analyses were repeated and validated in the p16 dataset.

Results: Optimal cut-offs for HPV16-E6 and -E7 antibodies were determined at 251 and 466 MFI, respectively, with HPV16-E6 showing the strongest discriminating performance. The currently used HPV16-based definition achieved the highest specificity (sensitivity 87.3%, specificity 90.8%). Adding HPV33, 35, and 18 could increase sensitivity, but lowered specificity. Similar patterns were observed in the p16 validation dataset. Across all definitions, HPV16-E6 was the most informative single antibody, whereas E7 antibodies were less informative.

Conclusions: The currently used HPV16-based biomarker achieved the highest specificity, confirming its robustness for HPV-OPC diagnosis. HPV16-E6 remains the most informative single antibody, while broader panels including HPV33, 35, and 18 modestly increase sensitivity but reduce specificity, representing a trade-off that must be considered in clinical use.

References:

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#12721

Analytical Validation Demonstrates High Performing Lab-Developed Droplet Digital PCR Test for HPV ctDNA

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Human Papillomavirus (HPV) is the causal oncogenic factor for most oropharyngeal squamous cell carcinomas (OPSCC). The incidence of HPV-positive (HPV+) OPSCC and other HPV+ cancers continues to rise, despite the development of effective multivalent vaccines, confirming the need for accurate liquid biomarkers for diagnosis, precision treatment, and surveillance. Here we characterize the performance of a droplet digital PCR (ddPCR) lab developed test (LDT) to detect HPV circulating tumor DNA (ctDNA). The MyHPVscore test detects HPV16, 18, 31, 33, 35, and 39 in plasma from patients with HPV+ cancer.

Methods: The MyHPVscore test was validated in our CLIA-certified laboratory, and testing included accuracy, precision, reportable range (limit of quantification (LOQ)/ linear range), sensitivity (limit of detection (LOD)), specificity/cross reactivity, carry-over, and analyte stability. Plasma and tumor samples from HPV+ OPSCC patients, plasma and tissue from non-cancer controls, and synthetic analytical controls were used.

Results: The test for accuracy showed that all plasma samples from patients with HPV+ tumors (verified by sequencing) were also positive by the MyHPVscore test, and all plasma samples from patients with HPV-negative tumors were also negative by the MyHPVscore test. Precision testing showed concordant results of the same sample evaluated multiple times across several days and different instruments. For the HPV16 assay, the limit of blank (LOB) was 2.7 positive droplets/well, the LOD was 15.3 positive droplets/well, and the LOQ was 21.9 positive droplets/well. For combined high-risk HPV types HPV18, 31, 33, 35 and 39 (referred to here as other hrHPV), the LOB was 2.6 positive droplets/well, the LOD was 20.9 positive droplets/well, and the LOQ was 78 positive droplets/well. Regression of the expected copy number versus quantitative test value had excellent correlation in the linear range of the assays ($R2 > 0.99$ for both HPV16 and other hrHPV). For HPV16, the assay had a linear range from 15.2 to 62,500 targets/mL plasma. For the other hrHPV types, the assay had a linear range from 12 to 100,000 targets/mL plasma. Above the linear range for both HPV16 and other hrHPV, the analytes were detected but recovery was $<90\%$. Cross-reactivity was tested using each set of primers and probes (individually and multiplexed) to evaluate synthetic HPV16, 18, 31, 33, 35, and 39 (alone and in combination), as well as common low-risk variants HPV6 and 11. This test demonstrated there was no substantial cross-reactivity between the assays or HPV types, confirming the high specificity of each assay for its particular HPV type. Testing of no template control wells following known positive samples did not find substantial carryover. Stability testing of plasma and ctDNA frozen at -20°C for 96 hours showed appropriate stability of both primary and processed analytes. Primary samples showed consistent qualitative results after being frozen at -20°C for 400 days.

Conclusions: The MyHPVscore LDT demonstrates excellent analytical performance, and early trials show strong clinical performance consistent with other published ctDNA assays [1 and in review].While HPV ctDNA LDTs are currently used to complement patient care, robust clinical utility trials comparing multiple assays are still needed. The addition of the MyHPVscore assay to the clinical landscape for HPV+ cancers allows us to leverage liquid biopsy technology to improve oncologic outcomes.

References: Regan, S.N., et al., *Prospective Phase II Trial of Definitive Chemoradiation and Concurrent Nivolumab in Locally Advanced p16+ Oropharynx Cancer.* Advances in Radiation Oncology, 2025. **10**(10).

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#13520

Analysis of oxidative stress and metabolic reprogramming in HPV positive head and neck squamous cell carcinoma

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Head and neck squamous cell carcinoma (HNSCC) associated with human papillomavirus (HPV) infection display altered energy metabolic pathways due to numerous oncogenic events activated by viral oncoproteins (E6 and E7) and their splice variants. A subgroup of HPV+ (HPV positive) HNSCC presents with high expression levels of E6*I, the major splice variant of E6, and correlates with oxidative and metabolic stress pathway signatures indicative for unfavorable prognosis. Here, we aimed to understand the effects of E6*I overexpression on oxidative stress (OS) defense and metabolic pathways.

Methods: HEK 293 cells overexpressing HPV16-E6*I-GFP and -E6-GFP were established and subjected to in vitro characterization by mimicking the atmospheric O2 conditions of the healthy and tumor tissue (5% O2 normoxia and 2% O2 hypoxia). The effects of E6 and E6*I on OS defense pathway components and metabolic reprogramming were studied by monitoring the expression and subcellular localization of viral proteins, immunofluorescence, live-cell imaging, ddPCR and protein expression analysis of key energy metabolic enzymes as well as cell metabolic assays.

Results: Studying cells treated at different O2 concentrations, ROS and metabolic markers showed highly divergent expression in control and E6 compared to E6*I overexpressing cells. This highlights a distinct role of E6*I and the dependence of viral oncogene expression on oxygenation and ROS production in HPV+ tissue. Particularly, under hypoxic conditions, overexpression of E6*I was associated with increased proliferation, increased expression of OS defense components, and altered glycolysis and OXPHOS activity.

Conclusions: In summary, in vitro analysis of E6*I overexpression revealed signatures of OS defense and metabolic reprogramming, which were also observed in a subset of HNSCC patients presenting with E6*I overexpression, viral host genome integration, and unfavorable prognosis. Testing for E6*I expression in patient samples could be of interest in the future to determine prognostically and therapeutically relevant subgroups.

References:

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#13544

Methylation Biomarkers in Liquid Biopsies of Patients with HPV-Related Oropharyngeal Squamous Cell Carcinomas

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Methylation biomarkers offer a promising diagnostic and prognostic tool in the management HPV-associated cancers. In particular, in HPV-associated oropharyngeal squamous cell carcinomas (OPSCC), there is a clinical need for non-invasive biomarker detection, as current laboratory diagnosis often relies on the use of invasive tissue biopsies. A recent report on oral rinse and gargles for methylation analysis in OPSCC did not show promising results [1]. This preliminary study aimed to evaluate the detection of methylation markers *FAM19A4* and *hsa-miR124-2* in liquid biopsies in HPV-related OPSCC patients.

Methods: As part of an ongoing longitudinal study, blood (Cell-Free DNA BCT® tubes, Streck) and saliva samples (FLOQSwab resuspended in 1mL eNAT, Copan) were obtained from patients with locally advanced and histologically confirmed HPV-related OPSCC at the time of diagnosis. Nucleic acids were extracted using NucliSENS easyMAG (bioMérieux) starting from 1 ml of plasma and 0.5 ml of saliva sample. HPV DNA was detected and quantified using OncoPredict HPV quantitative typing (QT) assay (Hiantis Srl, Italy). The PrecursorM+ assay (distributed by Fujirebio Europe) was used for methylation analysis. The assay targets the promoter regions of *FAM19A4* and *hsa-miR124-2*, genes whose hypermethylation is associated with carcinogenesis. Bisulfite conversion was carried out using the Zymo EZ DNA Methylation kit, following the overnight protocol. Methylation levels were calculated using the ΔΔCt ratio, which starts at zero for unmethylated samples and increases proportionally to the number of methylated cells present. To minimise data dispersion, values were square root–transformed.

Results: HPV DNA was detected in 19/20 (95%) of plasma with a viral load ranging from 59 to 6.96E+05 viral copies/ml. HPV DNA positivity in saliva swab samples was 90% (18/20). HPV16 was the most common genotype identified among both sample types. Hypermethylation of one or both target genes was observed in 10/20 (50%) plasma samples and 16/20 (80%) saliva samples. 6/20 (30%) patients showed hypermethylation of both *FAM19A4* and *hsa-miR124-2* in plasma and 10/20 (50%) in saliva, respectively (Fig 1a and 1b). An increasing percentage of methylation based on disease stage (AJCC classification) was observed from the analysis of both sample types (positivity rates in plasma: stage I =42.8%, II =50%, III =57.1%; saliva: stage I =71.4%, II =75%, III =85.7%). Interestingly, the patient with the highest methylation values for *FAM19A4* and *hsa-miR124-2* in saliva also showed the highest HPV16 viral load.

Conclusions: These preliminary results demonstrate the potential use of HPV viral load and methylation markers detection in non-invasive plasma and saliva liquid biopsies as novel diagnostic and prognostic biomarkers, for the early detection and risk stratification of HPV-driven OPSCCs. Further investigations on larger cohorts are needed to confirm these findings and explore the clinical utility of these biomarkers in the management of HPV-related OPSCC.

References: Donà MG, Giuliani E, Laquintana V, et al. FAM19A4 and miR124-2 methylation status in human papillomavirus-driven and human papillomavirus-negative oropharyngeal squamous cell carcinomas. Infect Agent Cancer. 2025;20(1):71. Published 2025 Oct 15. doi:10.1186/s13027-025-00697-5

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#13565

Mapping the spatial heterogeneity of the immune microenvironment in recurrent respiratory papillomatosis

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Low-risk human papillomavirus (HPV) types are associated with recurrent respiratory papillomatosis (RRP), a challenging condition where the immune system fails to clear infections. Our previous studies [1] revealed enhanced neutrophil-associated transcripts in laryngeal papilloma (LP) compared to the adjacent healthy larynx. In the present study, we aimed to investigate the spatial distribution of immune-related transcripts, neutrophil localization, and the presence of a selection of microbial species within RRP tissue.

Methods: Formalin-fixed paraffin-embedded (FFPE) biopsies from 15 RRP patients were mounted into tissue microarrays and analyzed using Nanostring GeoMx spatial transcriptomics. Samples were stained with antibodies against CD45, PanCK, and neutrophil elastase (ELANE/ELA2) to identify immune cells and to guide transcript collection. HPV typing and microbial PCR assays were performed for four different bacterial species. Patients were stratified into 'Acute LP' (remission after ≤5 surgeries, N=7) and 'Chronic LP' (>30 surgeries, N=8) subgroups. Spatial profiling identified immune cell transcripts within RRP tissues.

Results: Neutrophils comprised the predominant immune population infiltrating the hyperplastic stratified squamous epithelium layers of LP in 46% of samples. Samples from Acute LP exhibited higher levels of transcripts associated with inflammatory response pathways, antigen presentation, immune cell trafficking, and T cell-mediated cytotoxicity within papilloma cores compared to chronic LP. Samples from Chronic LP displayed higher expression levels of transcripts associated with fibroblast activation, extracellular matrix remodelling, hypoxic signalling, and neutrophils, as well as increased neutrophil infiltration. Concerning bacterial species, *Hemophilus influenzae*, *Staphylococcus aureus*, *Streptococcus dysgalactiae subspecies equisimilis* (SDSE), and group B Streptococcus (GBS) were detected in 60% (9/15), 20% (3/15), 6.2% (0/15), and 0% (0/15) of first visit appointment samples (FFPE-samples), respectively. Although we detected a relatively high prevalence of *Hemophilus influenzae*, its proportions were not robust enough to predict clinical outcomes accurately (Acute LP: 42% (3/7) vs. Chronic LP: 75% (6/8), p-value = 0.3147).

Conclusions: This study highlights characteristics of the RRP microenvironment and indicates distinct transcriptomic profiles linked to clinical outcomes. The predominance of neutrophils and potential bacterial involvement in Chronic LP warrant further investigation to better understand their roles in disease progression.

References: Sobti, A., C. Sakellariou, M. Nilsson, S. Schwartz, K. Olofsson, R. Rydell, M. Lindstedt, and O. Forslund. Immune delineation of laryngeal papilloma reveals enhanced neutrophil associated gene profile. Eur J Immunol, 2021. 51(10): p. 2535-2539.

SS14 - Anal cancer screening: Moving beyond the high-risk groups

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#12741

Prevalence and determinants of anal HPV infection in adults aged 50-74 years: findings from a population-based pilot study in Costa Rica (PREVENIR study)

03 - Epidemiology and natural history

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Background/Objectives: Persistent anal high-risk (HR) HPV infection, particularly HPV16, is a key risk factor for anal cancer) which is rare worldwide (0.54 per 100,000) but has recently increased. Studies have focused on high-risk groups, whereas data in the general population, especially older adults, who account for most cases, remain limited. Understanding anal HPV epidemiology in this age group is important to assess the need for preventive interventions. We estimated anal HPV prevalence and its sociodemographic, clinical, and behavioral determinants in adults aged 50–74 years in Costa Rica (CR).

Methods: A population-based, cross-sectional study was conducted in 12 CR districts representing national socioeconomic distribution (urban/rural residence and poverty indicators). Between June and October 2025, 629 eligible adults aged 50–74 years (340 women, 289 men) were recruited through house-to-house visits. After consent, participants completed questionnaires on sociodemographic, behavioral, and health characteristics. All participants self-collected anal samples, and women also collected cervicovaginal samples for HR HPV testing. Anal samples were processed with the ScreenFire HPV RS Kit (Zebra Biodome), detecting 13 HR types grouped as HPV16, HPV18/45, HPV31/33/35/52/58, and HPV39/51/56/59/68. Of 629 samples, 582 were valid (93%). Anal HPV prevalence (95%CI) was estimated by sex, age, and genotype, weighted to the CR population by sex, age, area, and socioeconomic status. Associations with determinants were analyzed using logistic regression adjusted for age, sex, and confounders.

Results: Participation rate was 57.4% and most subjects accepted the self-collected anal specimen. Prevalence of anal HR-HPV was 24% (95%CI: 20–30) in women and 16% (95%CI: 12–21) in men ($p<0.01$). HPV16 prevalence was similar in both sexes (7%, 95%CI: 4–10 and 5–12, respectively), whereas HPV18/45 was more frequent in women (5%, 95%CI: 3–9) than in men (1%, 95%CI: 0–2). Other HR types were more common in women. No significant age trend was observed ($p=0.52$). Among men, anal HPV was associated with receptive anal sex ($p<0.01$): 63% (5/8) of those reporting this practice were infected, but only 5 of 38 infected men (11% weighted) reported anal sex. In women, anal HPV was not associated with anal sex but was significantly associated with number of lifetime vaginal partners (p-trend<0.01) after age adjustment. Higher prevalence among those reporting receptive oral–anal sex was observed in both men (OR=1.6 [95%CI: 0.7–3.7]) and women (OR=2.0 [95%CI: 1.0–4.1]), though not statistically significant. When sexes were combined, receptive oral–anal sex was significantly associated with HPV prevalence (OR=2.0 [95%CI: 1.2–3.3]) (Table).

Conclusions: Anal HR-HPV infection is common among adults aged 50–74 years in CR, with prevalence about two to threefold higher than reported in this age group in previous studies. Prevalence was higher in women than in men, differing from estimates in similar age groups elsewhere. History of receptive oral–anal sex (in both sexes), receptive anal sex in men, and lifetime vaginal partners in women were associated with anal HPV prevalence. Anal HPV positive subjects will undergo high-resolution anoscopy to assess the prevalence of lesions to explore the need for large-scale studies and guide targeted prevention strategies for older adults in the general population.

References: 1. de Martel C, Plummer M, Vignat J, Franceschi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. International journal of cancer. 2017;141(4):664-70. doi: 10.1002/ijc.30716.
2. International Agency for Research on Cancer WHO. [Available from: https://gco.iarc.fr/today/en/dataviz/tables?mode=population&cancers=10
3. Islami F, Ferlay J, Lortet-Tieulent J, Bray F, Jemal A. International trends in anal cancer incidence rates. Int J Epidemiol. 2017;46(3):924-38. doi: 10.1093/ije/dyw276. PubMed PMID: 27789668.
4. Wei F, Xia N, Ocampo R, Goodman MT, Hessol NA, Grinsztejn B, et al. Age-Specific Prevalence of Anal and Cervical Human Papillomavirus Infection and High-Grade Lesions in 11 177 Women by Human Immunodeficiency Virus Status: A Collaborative Pooled Analysis of 26 Studies. The Journal of Infectious Diseases. 2023;227(4):488-97.

#14210

Concordance between cervical and anal HPV infection in a population-based study of women aged 50-74 years in Costa Rica, PREVENIR study

03 - Epidemiology and natural history

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Background/Objectives: Persistent infection with a high-risk HPV (HR-HPV), the cause of cervical cancer, is also implicated in anal cancer, mainly with HPV16. Although anal HPV infection is well documented in immunocompromised populations, its epidemiology among healthy older women, and its relationship to cervical infection, remains poorly understood. Understanding the epidemiology of HPV infection in this population is important given increasing incidence of anal cancer after age 65. While receptive anal intercourse is a recognized route of transmission, autoinoculation or spread from the genital tract may also play a role. We evaluated the concordance between cervical and anal HPV infection in women aged 50-74 in Costa Rica.

Methods: A population-based, cross-sectional study is being conducted in 12 Costa Rican districts representing national socioeconomic distribution. Between June and October 2025, 629 eligible adults aged 50–74 years (340 women, 289 men) were recruited house-to-house. After consent, participants completed questionnaires on sociodemographic, behavioral and health characteristics. For HR-HPV detection, anal and cervical self-samples were collected from all participating women. Cervicovaginal samples were tested using Cobas 5800® HPV-GT PCR assay detecting 14 HPV types grouped as: HPV16, HPV18, and HPV 31/33/35/39/45/51/52/56/58/59/66/68. Anal samples were processed with the ScreenFire HPV RS Kit (Zebra Biodome), detecting 13 HR types grouped as HPV16, HPV18/45, HPV31/33/35/52/58, and HPV39/51/56/59/68. To date, 340 anal and 340 cervical samples from women have been processed. Of the total number of women, 326 had results for both anal and cervical samples. Overall concordance was defined as infection with at least one anal and one cervical HPV type. HPV16 concordance was defined as HPV16 at both anatomical sites. Determinants of overall concordance will be analyzed using bivariate analysis and chi-square.

Results: Among the 326 women, 25.5% had anal HPV (any type) and 14.4% had cervical HPV (any type). Overall, 10% of women had concurrent anal and cervical HPV infection. Cervical HPV was detected in 39% of women with anal HPV, compared with 6% among those without anal HPV, and 68% of women with cervical infection had anal infection (table 1). Anal and cervical HPV16 were detected in 6.4% and 4.6% of women, respectively. Concurrent anal and cervical HPV16 infection was identified in eight of the 326 women (2.5%). Of those women positive for anal HPV16, 38% also had cervical HPV16, compared with 2% among those negative for anal HPV16, and among those with cervical HPV16, 53% had anal HPV16 (table 2).

Conclusions: Anal HPV infection is common in the healthy general population of Costa Rican women aged 50 years or older, and was more common than cervical HPV infection. Co-occurrence of infection at both anatomical sites was common in this group. Cervical HPV was more frequently detected among women with anal HPV than in those without anal infection.The observed co-occurrence supports the evaluation of concordant type-specific HPV infection patterns in future epidemiological research.

References:

SS17 - HPV self-sampling in routine screening programs

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#14216

The Dutch experience in switching towards self-sampling in the national cervical screening program

13 - Self-sampling

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Background/Objectives: In 2017, the Netherlands were amongst the first countries to introduce primary high-risk HPV (hrHPV) testing in the national cervical screening program using the PCR-based cobas 4800 platform. Parallel to the introduction of primary hrHPV testing, efforts were made to broaden participation through offering, upon request, the self-sampling kit (SSK) containing the Evalyn Brush. An initial analysis of screening test results with histological follow-up until August 2019 demonstrated that hrHPV testing on a self-collected sample led to a higher cycle threshold (Ct) value in the PCR-based assay (1). As a consequence, self-sampling had slightly increased specificity as compared to hrHPV testing on a clinician-collected sample, but a slightly reduced sensitivity for CIN3+ detection. Nevertheless, consensus guidelines for the diagnostic accuracy of HPV DNA testing in regular screening were still met, prompting broader deployment of self-sampling in the screening program. The performance of the SSK has recently been re-evaluated.

Methods: Since July 2023, the SSK has taken a more prominent position in the Netherlands: it is now mentioned explicitly in the invitation letter to screening, and kits are sent directly to first-time invitees at the age of 30 as well as to individuals of any age who do not respond within 12 weeks of the initial invitation. Alongside the wider use of the SSK, the Dutch program has also switched to using the FLOQ swab and the BD Onclarity assay for hrHPV testing, and the number of screening laboratories has been reduced. The evaluation of self-sampling performance after this switch was based on 226,655 screening participants in the second half of 2023, including Ct values and genotype subgroups according to the BD Onclarity HPV assay, with linked histological follow-up through June 2025.

Results: The prominent position of the SSK in the national cervical screening program has led to widespread acceptance of self-sampling in the Netherlands. Currently, nearly two-thirds of Dutch cervical screening participants make use of self-sampling, which clearly confirms the preference of the general population. The re-evaluation of self-sampling performance yielded strikingly divergent results as compared to the findings after initial introduction of the SSK in the Dutch program. Now, it was found that hrHPV testing on a self-collected sample has similar sensitivity for detection of CIN3+ but a lower specificity relative to clinician-collected sampling, resulting in 4% more false positives in women who participate via the SSK. Ct-based ROC analyses indicated that this difference is due to HPV16-negative self-samples and that it cannot be corrected by adjustment of hrHPV positivity thresholds within the assay.

Conclusions: Participation via self-sampling is safe and effective, suggesting that protection against cervical cancer in the general population has improved through broad deployment of the SSK in the Netherlands. However, the slightly reduced specificity of hrHPV testing on self-collected samples may require programmatic adjustments to manage the need for cytological triage against the backdrop of reduced capacity.

References: (1) F Inturrisi et al. Clinical performance of high-risk HPV testing on self-samples versus clinician samples in routine primary HPV screening in the Netherlands: An observational study. Lancet Reg Health Eur 2021; 11:100235.

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#14127

Experiences of HPV self-sampling in routine screening in the Indo-Pacific region (Nauru, PNG, Fiji, Malaysia & Timor Leste)

10 - HPV screening

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Background/Objectives: Background/objectives
Cervical cancer remains a major public health challenge in the Indo-Pacific region, where screening coverage is often limited by geographic, cultural, and health system barriers. HPV self-sampling offers a promising strategy to overcome these barriers by providing a more acceptable and accessible screening option. This screening must, however, be delivered within a continuum of care that ensures that screen-positive women are navigated to appropriate management.
This presentation shares experiences of implementing HPV self-sampling in routine screening programmes across Nauru, Papua New Guinea (PNG), Fiji, Malaysia, and Timor-Leste, highlighting feasibility, acceptability, and lessons learned for scale-up.

Methods: Methods
Under the Elimination Partnership in the Indo-Pacific for Cervical Cancer (EPICC), HPV self-sampling was introduced as part of national and sub-national screening initiatives in a variety of delivery models. In each case, the delivery model was developed in partnership with in-country teams, resulting in variations in how screening was implemented, but in all cases using evidence-based approaches, underpinned by WHO cervical screening guidelines[MS1] . Activities included stakeholder engagement, training of healthcare providers, adaptation of protocols, laboratory support, and integration of digital registries (canSCREEN®) for data management.

Results: Results
Across the five countries, HPV self-sampling was critical to the feasibility of scale up of screening, particularly in rural and remote settings. Country case studies will be presented illustrating a range of implementation approaches and highlighting successes and challenges.
Key enablers have included culturally tailored community and clinical education, strong local partnerships, laboratory support and digital tools, that are fit for purpose in a range of settings. While the challenges varied by setting, they commonly included supply chain constraints and sustaining workforce capacity.

Conclusions: Conclusion
HPV self-sampling is a feasible and broadly acceptable approach to enhance cervical cancer screening coverage in the Indo-Pacific region. Indeed, it will be essential if the WHO screening coverage target is to be met by 20230.
Self-sampling, however, must be delivered within a “whole-of-screening-pathway” approach that links screen-positive women to appropriate clinical care. Experiences from Nauru, PNG, Fiji, Malaysia, and Timor-Leste underscore the importance of co-design with local stakeholders underpinned appropriate technical support.
Lessons learnt from these experiences can inform roadmaps for scaling up self-sampling within national programmes, contributing to WHO’s global strategy to eliminate cervical cancer.

References: WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. content

SS19 - HPV primary screening in women over 50

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#14130

Clinical implications of the updated understanding of HPV natural history

03 - Epidemiology and natural history

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Background/Objectives: Recent work by the International Papillomavirus Society (IPVS) working group on cervical human papillomavirus (HPV) latency has led to an updated and more nuanced understanding of HPV natural history. Traditional models interpreted HPV detection primarily as a marker of new acquisition or reinfection, and loss of detection as viral clearance. However, emerging evidence indicates that HPV detection may also reflect autoinoculation, transient deposition following recent sexual activity, or redetection of a previously acquired infection. Conversely, loss of HPV detection may represent immune-mediated suppression rather than complete viral eradication.
As the underlying biological mechanisms driving HPV (re)detection and nondetection cannot be reliably distinguished at the individual level, it is suggested to use the terminology *HPV detected* and *HPV not detected* in both clinical and research settings. This updated understanding is further contextualized within cervical cancer prevention, discussing implications for patient counseling, interpretation of HPV-based screening results, screening recommendations, and HPV vaccination strategies.

Methods: *

Results: *

Conclusions: *

References:

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#14078

Cervical screening attitudes, intentions and interventions in women over 50

39 - Public health

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Background/Objectives: With increasing numbers of younger women vaccinated against HPV, uptake of screening in older women has become and important focus, particularly as screening participation in declining across all age-groups in many countries. Older women face different barriers to uptake, including low perceived risk due to relationship status, and post-menopausal increases in discomfort associated with the speculum examination. It is important to understand age-specific barriers and identify potential interventions to facilitate participation in this age-group.

Methods: This talk will review recent literature including my own work that has used theory-based approaches to develop information targeting barriers to screening experienced by women over 50 [1]. An online experimental study with women aged 50-64 (n=998) evaluated the impact on screening intention of an age-tailored infographic incorporating elements of social norms, acknowledgement of discomfort and the long timeline from HPV infection to cervical cancer.

Results: In line with other studies evaluating print-based materials, the infographic had only a marginal impact on intention, although it did increase knowledge and shift attitudes in a positive direction.

Conclusions: Our studies and other literature suggest print-based materials have limited capacity to change screening uptake behaviour. Other approaches including HPV self-sample and non-speculum HPV testing, or interventions improve the negative screening experiences of many women may be more fruitful avenues for future research, although it continues to be important that women have adequate information to make informed choices about screening.

References: [1] Waite F, Marlow LAV, Nemec M, Waller J. The impact of age-relevant and generic infographics on knowledge, attitudes and intention to attend cervical screening: A randomized controlled trial. Br J Health Psychol. 2024 Feb;29(1):204-220. doi: 10.1111/bjhp.12695. Epub 2023 Sep 28.

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#14049

HPV screening in women aged over 50 years: 20-year follow-up of the ARTISTIC trial cohort

10 - HPV screening

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Background/Objectives: There is limited evidence to justify the UK policy of stopping cervical screening at age 65. Since 2019, when primary HPV screening was introduced in the UK, the age at last screen has not been reconsidered. The ARTISTIC cohort provides longitudinal HPV screening data over more than 20 years for almost 25,000 women, including 10,858 who underwent HPV testing while aged 50-59.

Methods: The ARTISTIC trial cohort recruited in 2001-03 and has been followed up via national registration for cancer incidence and mortality for over 20 years. Routine cervical samples were tested for HPV using HC2 followed by PCR genotyping between 2001-09 as part of the trial and by Roche Cobas between 2016-22 after ARTISTIC women attended for primary HPV testing as part of the NHS cervical screening programme. The first HPV test done aged 50-59 (after the age of 50 and up to age 60) was taken as the start of follow-up. Kaplan-Meier methods were used to estimate the cumulative incidence of CIN3 and cancer, and newly detected HPV infections.

Results: Results are reported for the 10,858 women who underwent HPV testing while aged 50-59 with median subsequent follow-up of 15.7 years.

Among the 4,172 women who tested HPV negative at age 50-59 and had at least one subsequent HPV test recorded, the annual average incidence of newly detected HPV infections was 0.95% (95%CI: 0.83-1.11), with 5.49% (95%CI: 4.57-6.58) testing positive for a new HPV infection by 5 years.

A total of 19 CIN3s and 9 invasive cervical cancers were diagnosed via national registrations during follow-up after the initial HPV test at age 50-59. Among 10,116 women testing HPV negative at age 50-59, 3 CIN3s and 6 cervical cancers were diagnosed giving a cumulative risk of 0.04% (95%CI: 0.01-0.13) for CIN3 and 0.10% (95%CI: 0.05-0.24) for invasive cervical cancer. Among 742 women testing HPV positive at age 50-59, 16 CIN3s and 3 cervical cancers were diagnosed giving a cumulative risk of 2.46% (95%CI:1.49-4.05) for CIN3 and 0.55% (95%CI: 0.17-1.76) for invasive cervical cancer.

Conclusions: Six of the nine invasive cervical cancers in this cohort were diagnosed in women who had tested HPV negative in their 50s. Further research is required to determine whether a more sensitive HPV test will detect these cancers earlier in this population. It is not known what proportion of newly detected HPV infections among women in their 50s and 60s are newly acquired rather than recurrences of old infections. Continuing screening past age 65 is likely to be beneficial, primarily through early detection rather than prevention of invasive cervical cancer.

References:

CS06 - Navigating HPV disclosure and partner management: Clinical and psychosocial perspectives

Vieira-baptista Pedro
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#14231

The patient experience: understanding the emotional response to a positive HPV diagnosis

36 - Advocacy, acceptability and psychology

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Background/Objectives: The objective of this lecture is explore the emotional, psychological, and sexual impact of a detection of human papillomavirus (HPV) , and to identify communication strategies that may mitigate distress and improve patient-centered care within HPV-based cervical cancer screening programs.

Methods: We based this lecture on a narrative synthesis of quantitative and qualitative studies evaluating the psychosocial consequences of HPV positivity, including anxiety, cancer-related fear, stigma, and sexual dysfunction. Evidence from cross-sectional and longitudinal observational studies, patient-reported outcome measures, and qualitative research was integrated with clinical experience in HPV-based screening and colposcopy settings. Particular attention was given to the impact of HPV genotyping, screening context, and timing of follow-up on patient emotional responses. Adding to that, we also refer to our clinical experience and daily interaction with women who have tested positive for HPV.

Results: A positive HPV test is consistently associated with increased anxiety, fear of cancer, guilt, and concerns related to sexual relationships and partner transmission. Compared with cytology-based screening, HPV-based screening appears to generate higher initial distress, particularly among women testing positive for HPV16/18. Psychological impact may persist even after normal colposcopy findings and reassurance regarding low cancer risk. Several studies demonstrate transient but clinically relevant impairments in sexual function, partly independent of anxiety or depression. Emotional responses evolve over time, with greatest distress occurring in the first months following diagnosis, highlighting the importance of timely follow-up and effective communication. Misconceptions regarding infectivity, infertility, partner management, and disease chronicity frequently exacerbate distress and may lead to avoidance of intimacy, relationship strain, or pursuit of ineffective medical interventions.

Conclusions: The emotional response to a positive HPV diagnosis represents a significant and often underestimated consequence of HPV-based screening. Clear, empathetic, and tailored communication by well-informed clinicians, along with prompt access to triage and colposcopy, can substantially reduce psychological harm. Strategies such as patient education prior to testing, contextualized risk communication, avoidance of overscreening, and destigmatization of HPV are essential to optimize the patient experience while preserving the benefits of HPV-based cervical cancer prevention.

References:

- Chadwick V, Bennett KF, McCaffery KJ, Brotherton JML, Dodd RH.
  Psychosocial impact of testing human papillomavirus positive in Australia's human papillomavirus-based cervical screening program: A cross-sectional survey.
  Psychooncology. 2022;31(7):1110–1119. doi:10.1002/pon.5897
- Hsu YY, Wang WM, Fetzer SJ, Cheng YM, Hsu KF.
  Longitudinal psychosocial adjustment of women to human papillomavirus infection.
  J Adv Nurs. 2018;74(11):2523–2532. doi:10.1111/jan.13725
- McCaffery K, Waller J, Nazroo J, Wardle J.
  Social and psychological impact of HPV testing in cervical screening: A qualitative study.
  Sex Transm Infect. 2006;82(2):169–174. doi:10.1136/sti.2005.016436
- Mercan R, Mercan S, Durmaz B, et al.
  Sexual dysfunction in women with human papillomavirus infection.
  J Obstet Gynaecol. 2019;39(5):659–663. doi:10.1080/01443615.2018.1547694
- Aker ŞŞ, Ağar E, Tinelli A, Hatirnaz S, Ortaç F.
  The impact of HPV diagnosis and abnormal cervical cytology results on sexual dysfunction and anxiety.
  Int J Environ Res Public Health. 2023;20(4):3630. doi:10.3390/ijerph20043630
- Wang H, Nie K, Liu Z, et al.
  Effects of cervical HPV infection on female sexual function and anxiety: A multicenter study.
  Front Oncol. 2024;14:1468160. doi:10.3389/fonc.2024.1468160
- Nahidi M, Nahidi Y, Kardan G, et al.
  Evaluation of sexual life and marital satisfaction in patients with anogenital warts.
  Actas Dermosifiliogr. 2019;110(6):521–525. doi:10.1016/j.ad.2018.11.012
- Santos BD, Moreira CS, Vilhena E, Carvalho E, Pereira MG.
  Validation of the HPV Impact Profile in Portuguese women with human papillomavirus.
  Curr Med Res Opin. 2019;35(7):1275–1282. doi:10.1080/03007995.2019.1580770
- Sanchez Antelo V, Szwarc L, Paolino M, et al.
  A counseling mobile app to reduce the psychosocial impact of HPV testing: Formative research using a user-centered design approach.
  JMIR Form Res. 2022;6(1):e32610. doi:10.2196/32610

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#13766

The overlooked partner: Health and psychosexual consequences

32 - HPV transmission

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Background/Objectives: Human papillomavirus (HPV) is the most prevalent sexually transmitted infection, with a lifetime acquisition risk of 91% in men. Despite its high burden, HPV-related disease in males remains underrecognized

Methods: We reviewed epidemiological data, clinical studies, and psychosocial research on HPV infection in men, focusing on genital warts, penile intraepithelial neoplasia (PeIN), and associated cancers.

Results: HPV infection in men is often persistent. High-risk types (16, 18) contribute to penile, anal, and oropharyngeal cancers, while low-risk types (6, 11) cause >90% of anogenital warts. PeIN lesions are HPV-positive in up to 100% of cases. HPV also affects fertility through sperm DNA fragmentation and impaired embryo development. Psychosocial impacts include anxiety, stigma, and relationship strain. Partners of HPV-positive individuals face increased cancer risks, highlighting the need for couple-centered prevention. Vaccination programs significantly reduce genital warts and HPV-related cancers.

Conclusions: HPV in men is a critical public health issue with physical and emotional dimensions. Comprehensive care should integrate medical treatment, vaccination, education, and psychosocial support. Gender-neutral HPV vaccination is essential to reduce disease burden and improve quality of life.

References: Nielson CM, Harris RB, Dunne EF, Abrahamsen M, Papenfuss MR, Flores R, Markowitz LE, Giuliano AR. Risk factors for anogenital human papillomavirus infection in men. J Infect Dis. 2007 Oct 15;196(8):1137-45. .\Dis. 2014 Nov;41(11):660-4/Giuliano AR, Nyitray AG, Kreimer AR, Pierce Campbell CM, Goodman MT, Sudenga SL, Monsonego J, Franceschi S. EUROGIN 2014 roadmap: differences in human papillomavirus infection natural history, transmission and human papillomavirus-related cancer incidence by gender and anatomic site of infection. Int J Cancer. 2015 Jun 15;136(12):2752-60/1 Bean, SM, Chhieng, DC, Anal-Rectal Cytology: A Review. Diagnostic Cytopathology 2009; Vol 38 No 7, 538-546

Palefsky, J. Screening for Anal and Cervical Dysplasia in HIV-Infected Patients. The PRN Notebook. Volume 6, No. 3, Sept. 2001. 24-31.

Darragh, TM. Anal Cytology for Anal Cancer Screening: Is it Time Yet? Diagnostic Cytopathology, 2004; Vol 30, No 6, 371-374

American Cancer Society, Cancer Facts and Figures, 2010/Milano G, Guarducci G, Nante N, Montomoli E, Manini I. Human Papillomavirus Epidemiology and Prevention: Is There Still a Gender Gap? Vaccines (Basel). 2023 Jun 4;11(6):1060./Straub Hogan MM, Spieker AJ, Orejudos M, Gheit T, Herfs M, Tommasino M, Sanchez DF, Fernandez-Nestosa MJ, Pena MDCR, Gordetsky JB, Epstein JI, Canete-Portillo S, Gellert LL, Prieto Granada CN, Magi-Galluzzi C, Cubilla AL, Giannico GA. Pathological characterization and clinical outcome of penile intraepithelial neoplasia variants: a North American series. Mod Pathol. 2022 Aug;35(8):1101-1109. / Weinberg M, Sar-Shalom Nahshon C, Feferkorn I, Bornstein J. Evaluation of human papilloma virus in semen as a risk factor for low sperm quality and poor in vitro fertilization outcomes: a systematic review and meta-analysis. Fertil Steril. 2020;113(5):955-969.e4. Jansen KU, Shaw AR. *Annu* Rev Med. 2004;55:319–331. 2. Koutsky L. Am J Med. 1997;102:3–8. 3. Franco EL, Villa LL, Richardson H, Rohan TE, Ferenczy A. In: Franco EL, Monsonego J, eds. Oxford, UK: Blackwell Science; 1997:14–22. 4. Tortolero-Luna G. Hematol Oncol Clin North Am. 1999;13:245–257, x

Drolet et al. "The Impact of Anogenital Warts on Health-Related

Quality of Life: A 6-Month Prospective Study" Sexually Transmitted Diseases Volume 38, Number 10, October 2011 Lee TS, Kothari-Talwar S, Singhal PK, Yee K, Kulkarni A, Lara N, Roset M, Giuliano AR, Garland SM, Ju W. Cross-sectional study estimating the psychosocial impact of genital warts and other anogenital diseases in South Korea. BMJ Open. 2019 Mar 20;9(3

SS21 - Vaginal microbiome as a biomarker to predict response to treatment of cervical cancer precursors

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#14262

Microbiome diagnostics - potential for wider application in cervical cancer prevention

18 - Microbiome

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Background/Objectives: Over the past decade, driven by advances in sequencing technologies, the cervicovaginal microbiome has emerged as a key determinant of cervicovaginal health, influencing susceptibility to human papillomavirus (HPV) infection, viral persistence, and progression to cervical intraepithelial neoplasia (CIN), with growing evidence linking dysbiosis to an increased risk of HPV persistence and disease progression.

Methods: This lecture will explore the potential of microbiome diagnostics as a complementary tool to HPV testing within cervical cancer prevention strategies, including their possible role in predicting responses to therapeutic interventions for cervical precancerous lesions. The lecture will address cutting-edge technologies for microbiome diagnostics and discuss key implementation challenges. Considerations for cost-effective implementation across diverse healthcare settings, including low- and middle-income countries, will also be examined. Finally, potential interventional strategies aimed at maintaining or restoring a beneficial microbiome will be outlined as future directions for personalized prevention.

Results: Incorporating microbiome profiling into cervical cancer screening and management pathways has the potential to possibly refine risk stratification, guide post-treatment follow-up, and identify women most likely to benefit from targeted interventions.

Conclusions: Microbiome diagnostics therefore represent a promising frontier for next-generation cervical cancer prevention strategies grounded in personalized medicine.

References:

SS18 - Policies for accelerated cervical cancer elimination and cervical cancer screening among vaccinated women/birth cohorts

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#14069

Cervical cancer screening in vaccinated cohorts: using public health decision modelling to support recommendations

39 - Public health

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Background/Objectives: Despite declining cervical cancer rates in HPV-vaccinated women, the optimal balance between screening benefits, harms, and resource use remains uncertain. Using public health decision modelling, we estimated future screening impacts to inform the European Commission initiative on Cervical Cancer (EC-CvC) in developing the first screening recommendations for HPV-vaccinated cohorts.

Methods: We used the IARC METHIS platform to project the impact of screening in European HPV-vaccinated cohorts. Analyses considered variations in HPV prevalence, vaccination coverage (50%–100%), target (girls only or gender-neutral), and vaccine type (bivalent/quadrivalent or nonavalent). Assuming full adherence, several HPV-based screening strategies were evaluated, differing by starting age (25, 30, 35 years), stopping age (40, 50, 65 years), and interval (5 vs 10 years). Strategies were considered relevant if consistently efficient and with an incremental cost-effectiveness ratio (ICER) less than €100,000 per life-year gained. Outcomes were compared with a reference strategy (5-yearly screening from ages 25 to 65) and reported per 100,000 women.

Results: Without screening, lifetime cervical cancer cases in a European vaccinated cohort ranged from 90 to 1520, depending on HPV prevalence and vaccination assumptions. HPV-based screening every 5 years was not cost-effective (ICER > €100,000 per life-year gained). Efficient 10-year strategies included: screening at ages 25–45, which missed 0.9 cancers but avoided 14 preterm births (<37 weeks) and 1,129 colposcopies compared with the reference strategy; and screening only at ages 30 and 40, which minimized resources and harms (−2,438 colposcopies; −87 preterm births) but left 18.3 cancers unprevented. Extending screening to age 65 increased colposcopies with negligible gains in cancer or preterm birth reduction.

Conclusions: Extending HPV-based screening intervals in vaccinated cohorts offers clear benefits, while a 5-year interval is unlikely to be optimal. These findings played a key role in shaping the first EC-CvC recommendations for cervical cancer screening in HPV-vaccinated populations.

References:

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#14353

Evaluating the impact of ECDC vaccination and screening policies for newly arrived migrants: A pathway to reducing infection-related (including cervical) cancers in Europe

39 - Public health

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Background/Objectives: In 2023, over five million people immigrated to countries in the European Union (EU). These newly arrived migrants have been identified by the ECDC as a priority population for entry health assessments [1], which represent a key opportunity to prevent infection-related cancers. However, implementation is inconsistent in practice. Information on cancer risk among migrants remains fragmented but indicates that migrants generally have a higher risk of infection-related cancers than their host populations. Infection-related cancers are well suited to prevention through screening and vaccination, and 90% worldwide are caused by four pathogens: hepatitis B, hepatitis C, human papillomavirus, and *H. pylori.*

Methods: Using data on migration flows, cancer incidence, the proportion of cancer attributable to each infectious agent, and the effectiveness of preventive interventions, we estimated the burden of hepatocellular carcinoma (HCC), cervical cancer (CvC), and gastric cancer (GC) over the next 60 years among migrants who arrived in the EU in 2023. We then estimated the proportion of cases preventable through vaccination and screening, first as defined in ECDC recommendations (focusing on viral hepatitis) and then including expanded services for CvC and GC prevention.

Results: An estimated 5.8 million people immigrated to EU countries in 2023, 45% of whom came from other European countries. With respect to cancer risk, 46% of migrants originated from countries with age-standardised CvC incidence rates above the global median, compared with 66% for GC and 18% for HCC. Among all migrants, we project 140,000 cancer cases over the next 60 years (33,000 HCC, 34,000 CvC, and 73,000 GC). Over half (52%) of these cases are expected to occur among men, driven by the high projected burden of GC in this group (49,000 cases).
Hepatitis screening and vaccination as currently recommended by the ECDC could prevent 16% of HCC cases among migrants. Adding CvC and GC prevention could prevent 56% and 49% of cases, respectively. Expanding ECDC-defined eligibility for HCC prevention to include all migrants from countries with above-global-median HCC incidence would prevent 29% of HCC cases, compared with 16% under current criteria.

Conclusions: A large proportion of infection-related cancer burden among migrants entering to countries in the EU could be prevented through effective screening and vaccination soon after arrival. These findings support including CvC and GC prevention alongside expanded HCC prevention in regional and country-specific migrant health guidance. Providing these interventions at entry could overcome healthcare access barriers by delivering simple and effective care. Ensuring continuity of care as migrants integrate into host-country health systems remains essential and could further increase impact.

References: [1] Public health guidance on screening and vaccination for infectious diseases in newly arrived migrants in the EU/EEA. Stockholm: European Centre for Disease Prevention and Control; 2018.

LW02 - II Zervix - HPV Infektion und Dysplasie

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#14502

Critical steps in HPV-associated cervical pathogenesis

25 - Cervical neoplasia

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Background/Objectives: Approximately 5% of all human cancers are caused by human papillomavirus (HPV) infection. Although HPV oncoproteins and their transforming capacity are well characterized, the mechanisms underlying malignant progression in vivo remain incompletely understood.

Methods: This presentation reviews our previously published work identifying critical steps in HPV-associated cervical pathogenesis.

Results: We focus on the role of the specific cellular compartment infected within the cervical epithelium, and the contribution of the microenvironment and chronic inflammation to carcinogenesis. In particular, we present evidence that stromal inflammation is clinically and mechanistically linked to cervical stem cell expansion and cancer progression.

Conclusions: Our findings identify novel targets for therapeutic intervention.

References:

WS04 - Vulvar diseases workshop

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#14232

Microbiome in vulvar disease: Is it relevant?

18 - Microbiome

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Background/Objectives: To critically assess the evidence supporting a role for the microbiome in vulvar diseases, with particular focus on vulvodynia, lichen sclerosus, and vulvar cancer, and to distinguish biologically plausible associations from clinically actionable knowledge, while clearly differentiating vulvar from vaginal microbial ecosystems.

Methods: This lecture is based on a narrative review of observational, translational, and clinical studies evaluating the vulvar and lower genital tract microbiome in inflammatory, pain-related, and neoplastic vulvar conditions. Evidence from the author’s previously published work and international consensus documents was integrated, with emphasis on study design, sampling methodology, confounders, and relevance to clinical decision-making.

Results: While the vaginal microbiome is a relatively well-defined ecosystem, usually characterized by lactobacilli dominance during the fertile age, the vulvar microbiome resembles a modified skin microbiome, marked by high interpersonal and anatomical variability. Vulvar microbial communities are influenced by age, hormonal status, hygiene practices, inflammation, and proximity to adjacent skin and gastrointestinal reservoirs.
In vulvodynia, several studies report reduced microbial diversity and relative overrepresentation of specific taxa, alongside evidence of epithelial barrier dysfunction and altered local immune responses. However, findings are inconsistent across cohorts, and no reproducible vulvar microbiome signature has been identified, limiting causal inference.
In lichen sclerosus, small observational studies describe shifts toward dysbiosis and reduced commensal diversity in affected skin, but these changes appear more likely to be secondary to chronic inflammation and architectural disruption rather than primary drivers of disease.
In vulvar squamous cell cancer and its precursors, emerging data suggest microbiome alterations associated with chronic inflammation, HPV-related pathways, and immune modulation. Nevertheless, evidence remains preliminary, and no microbiome-based biomarkers or therapeutic interventions have demonstrated clinical utility.

Conclusions: Objective data support an association between microbiome alterations and several vulvar diseases, including vulvodynia, lichen sclerosus, and vulvar cancer; however, current evidence is largely associative and insufficient to guide routine clinical interventions. The vulvar microbiome must be conceptualized separately from the vaginal microbiome. Future research should prioritize mechanistic studies and clinically relevant outcomes over descriptive profiling to avoid perpetuating microbiome-related hype in vulvar care.

References:

- Sacinti KG, Razeghian H, Awad-Igbaria Y, Lima-Silva J, Palzur E, Vieira-Baptista P, Verstraelen H, Bornstein J. Is Vulvodynia Associated With an Altered Vaginal Microbiota?: A Systematic Review. J Low Genit Tract Dis. 2
- De Seta F, Lonnee-Hoffmann R, Campisciano G, Comar M, Verstraelen H, Vieira-Baptista P, Ventolini G, Lev-Sagie A. The Vaginal Microbiome: III. The Vaginal Microbiome in Various Urogenital Disorders. J Low Genit T
- Ventolini G, Vieira-Baptista P, De Seta F, Verstraelen H, Lonnee-Hoffmann R, Lev-Sagie A. The Vaginal Microbiome: IV. The Role of Vaginal Microbiome in Reproduction and in Gynecologic Cancers. J Low Genit Tract Di

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#13844

Anal disease: it\'s not a male phenomenon, what should the vulvologist know?

26 - Vulvar diseases and neoplasia

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Background/Objectives: Like cervical cancer, anal cancer and its precursor lesions (anal intraepithelial neoplasia, AIN) are highly prevalent in certain high-risk populations. While most HPV-infections in the general population are eliminated by the immune system within a short period of time, HPV-infection tends to persist in immunosuppressed individuals. In HIV-infected men who have sex with men (MSM), anal HPV-infection is almost always present and infections with multiple HPV types are common. HPV-associated anogenital malignancies occur with high frequency in these patients. However, other high-risk groups exist, including women with HIV, women with a history of vulvar dysplasia or cancer, as well as solid organ transplant recipients, especially women. Anal cancer screening has recently been recommended by the "International anal neoplasia society" in such at-risk populations. Individuals with abnormal cytology should undergo high resolution anoscopy to appropriately identify and treat dysplastic lesions. A large multicenter trial (ANCHOR) demonstrated that treatment of high-grade AIN can effectively prevent anal cancer development. Therapeutic strategies for AIN might be distinguished in topical (e.g. trichloroacetic acid, podophyllotoxin, imiquimod, photodynamic therapy) and ablative (e.g. surgical excision, laser ablation, infrared coagulation, electrocautery) interventions. This presentation is a short overview on the current status of AIN diagnostics and treatment.

Methods: .

Results: .

Conclusions: .

References: .

CS08 - HPV in early childhood: Transmission, immunity, and implications for vaccination

Kalliomaa Nelli
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#13811

Vertical transmission and HPV prevalence in newborns

32 - HPV transmission

Kalliomaa N[1,2]

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Background/Objectives: Vertical transmission from mother to newborn is the most significant route of perinatal HPV infection. Transmission is thought to take place during childbirth or pregnancy, as HPV DNA has also been detected in amniotic fluid and the placenta. The father's role in perinatal HPV transmission remains unknown. Most perinatal HPV infections are asymptomatic and clear spontaneously during the first months of life.

Methods: The Finnish Family HPV (FFHPV) Study is a longitudinal cohort study conducted at the Department of Gynaecology and Obstetrics, Turku University Hospital, and the Department of Oral Pathology, University of Turku. Originally a total of 329 families with 329 mothers, 132 fathers and their 331 newborns were recruited between 1998 and 2002. Parents' genital and oral brush samples and semen samples were collected for HPV testing at baseline (36 weeks of pregnancy). After delivery, oral, genital, and umbilical samples from the newborn, and placenta samples, were collected for HPV testing. Mothers, fathers and children were followed up for six years to elucidate the natural history of HPV infection between family members.

Results: Among newborns, *oral* HPV prevalence was 23.0% (n=74) and *genital* HPV prevalence 10.0% (n=32). HPV16 and HPV6 were found in 15.9% (n=51) and 4.7% (n=15) of the newborns' samples, respectively. The rate of vertical transmission was 35.1% (33/94 from mothers' *genital site* to newborns' *any anatomic site*. Statistically significant HPV concordances were observed with HPV6, HPV16, HPV18, HPV31, and HPV56; ORs ranged from HPV16 OR of 3.41 (95% CI 1.80–6.48) to HPV31 OR of 634 (95% CI 28.5–14087). Interestingly, among father-newborn pairs, statistically significant HPV concordances were observed with HPV6 (OR 4.89, 95% CI, 1.09–21.9) and HPV31 (OR 65.0, 95% CI 2.92–1448).

Conclusions: The presence of HPV DNA in newborn oral and genital samples is common. The mother appears to be the most likely source of transmission to the newborn. However, the exact routes of vertical transmission, as well as the father's role in perinatal infection, require further investigation.

References:

#13535

Human papillomavirus dynamics in early childhood

03 - Epidemiology and natural history

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Background/Objectives: Although Human papillomavirus-related complications in childhood are rare, persistence of certain genotypes can lead to conditions ranging from benign to severe (e.g., common warts, recurrent respiratory papillomatosis). Both host-related and viral factors may contribute to infection risk. However, HPV transmission dynamics and health outcomes in children remain poorly documented. Understanding the natural history of HPV infection in early childhood is therefore important.

Methods: Data were obtained from the HERITAGE cohort (2010–2016), which aims to evaluate the association between maternal HPV infection, adverse pregnancy outcomes, and HPV infection dynamics in children. Descriptive analyses were performed to estimate perinatal transmission rates, prevalence, incidence, recurrence, and persistence of HPV in children, with a focus on specific HPV genotypes and anatomical sites sampled (conjunctival, genital, pharyngeal, and oral). HPV clearance time was estimated using Kaplan–Meier survival analysis.

Results: Across the follow-up period, 91 HPV detections all sites combined were identified among 51 children out of 373 children. The most prevalent genotype being HR-HPV66 (3.2%, 95% CI: 1.8–5.5%). Vertical transmission of HPV was estimated at 7.3% (95% CI: 5.0–10.4%), with a high genotype concordance (85.2%) between mothers and children. Two recurrent (4.5%) and one persistent (2.1%) genotype-specific infections were observed, although all paediatric infections resolved within approximately 3.9 months (95% CI: 3.6–4.2).

Conclusions: Vertical and horizontal HPV transmission in children are possible. However, the risk of persistence or recurrence is overall very low, typically clearing within a few months without observed complications.

References:

HN09 - Living well after HPV associated head and neck cancer: The importance of survivorship

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#14169

Early survivorship interventions to optimize function and quality of life

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Head and neck cancer (HNC) survivors face unique challenges, including dysphagia, xerostomia, musculoskeletal changes, pain, fatigue, and psychosocial distress that profoundly affect daily function and quality of life. The rising incidence of HPV-associated oropharyngeal cancer has created a younger survivor population living decades with treatment sequelae. While guidelines traditionally recommend survivorship care after treatment completion, emerging evidence supports early intervention strategies.

Methods: This presentation reviews current evidence on early survivorship interventions for HNC, including prehabilitation programs and survivorship programs such as multidisciplinary clinic models.

Results: Early identification and management of treatment-related symptoms and toxicities can mitigate functional decline and improve outcomes. Swallowing interventions delivered during radiotherapy, whether initiated proactively or reactively when symptoms develop, demonstrate effectiveness in preserving function. A recent systematic review and meta-analysis found that prehabilitation programs combining exercise and nutrition demonstrated significant improvements in dysphagia reduction, weight retention, length of stay, and complications. Multidisciplinary survivorship clinics integrating speech-language pathology, nutrition, physical therapy, and psychosocial support demonstrate improved functional outcomes. Proactive screening enables the timely identification of dysphagia and facilitates appropriate interventions.

Conclusions: Early survivorship interventions show promise for optimizing functional outcomes and quality of life in HNC survivors, particularly for the growing HPV+ population facing decades of survivorship.

References: Obuekwe, F., Li, J., Sereika, S. M., Mazul, A. L., Maxwell, J. H., Contrera, K. J., Spector, M. E., Zandberg, D. P., Mowery, Y. M., Johnson, J. T., & Nilsen, M. L. (2025). Pre-radiotherapy multidisciplinary survivorship care and patient-reported outcomes in head and neck cancer survivors. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*, *33*(8), 734. https://doi.org/10.1007/s00520-025-09797-9Vester, S., Muhr, A., Meier, J., Süß, C., Kummer, P., & Künzel, J. (2023). Prehabilitation of dysphagia in the therapy of head and neck cancer- a systematic review of the literature and evidence evaluation. *Frontiers in oncology*, *13*, 1273430. https://doi.org/10.3389/fonc.2023.1273430Seth, I., Bulloch, G., Qin, K. R., Xie, Y., Sebastian, B., Liew, H., Rozen, W. M., & Lee, C. H. A. (2024). Pre-rehabilitation interventions for patients with head and neck cancers: A systematic review and meta-analysis. *Head & neck*, *46*(1), 86–117. https://doi.org/10.1002/hed.27561

SS22 - Next-generation sequencing and bioinformatics: HPV biomarkers in the genomic era

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#14167

Methylation of host genes: From research to clinical application

22 - Diagnostic procedures / management

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Background/Objectives: Primary high-risk HPV screening is being implemented worldwide, yet most HPV-positive women do not harbor clinically relevant lesions and will not progress to cervical cancer. The current triage tool, cytology, is subjective, infrastructure-dependent, and not applicable to self-samples, contributing to loss to follow-up. Host-cell DNA methylation (DNAme) alterations are early, objective markers of carcinogenic transformation. We developed a simple, automatable PCR DNAme triage test (WID-qCIN) designed for high throughput and, in principle, use on self-collected samples, with the added goal of predicting future risk rather than only detecting prevalent disease.

Methods: Epigenome-wide discovery (~850.000 CpGs) in HPV+ controls and CIN3+ cases identified candidate regions, followed by MethyLight assay development and feature selection. The final WID-qCIN test measures DNA methylation at three loci (*DPP6*, *RALYL*, and *GSX1*) and classifies a sample as positive if ≥1 gene shows evidence of fully methylated alleles (Percentage of fully Methylated Reference, PMR > 0). Diagnostic performance was first validated in Swedish liquid-based cytology samples and in a nested predictive design with 1–4-year follow-up. The optimized assay was then evaluated in a real-world Swedish screening cohort (i.e. all women attending screening in Greater Stockholm between 1 January and 31 March 2017) with six year follow-up and in a prospective multicentre Nigerian study including histology for all participants.

Results: After development of the assay in a total of 492 samples, an initial validation (n=761) was performed: The WID-qCIN detected invasive cancer with 100% sensitivity and CIN3 in women with ≥30 years 83% sensitivity at ~90% specificity. Importantly, among HPV+/cytology-negative women, WID-qCIN was positive in 52% of those ≥30 years who developed CIN3 within 1 - 4 years, outperforming cytology for risk prediction.
In a real-world Swedish screening cohort of 28,017 women, WID-qCIN plus HPV16/18 genotyping detected 93.4% of prevalent CIN3 and 100% of prevalent cancers. Over 6 years, it predicted 69.4% of incident CIN2+ and 80% of incident cancers, compared with 18.2% and 20%, respectively, predicted by cytology. This was achieved with fewer colposcopies per CIN2+ detected than required as a consequence of using cytology (2.4 vs 4.1).
In Nigeria (n=182; enriched for disease), WID-qCIN triage among hrHPV+ women showed high sensitivity for CIN3+ (89.3%), rising to 92.9% with HPV16/18 co-triage and outperformed colposcopic assessment and cytology, supporting transferability to sub-Saharan Africa and settings with self-sampling pathways.

Conclusions: WID-qCIN is an objective, scalable DNAme triage test for HPV-positive women. Across discovery, clinical validation, real-world implementation, and African prospective evaluation, it shows strong diagnostic accuracy and uniquely predicts future CIN risk. The DNA-only and readily automatable nature of the assay makes it suitable for high-throughput screening and, subject to additional research, for integration into single-visit self-sampling approaches, thereby tackling critical barriers to cervical cancer elimination.

References: Herzog et al., *Clin Epigenetics* 2022 (WID-qCIN development/validation).
Schreiberhuber et al., *Nat Med* 2024 (real-world Swedish cohort).
Illah et al., *in preparation* 2025 (sub-Saharan Africa evaluation).

Stosic Milan
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#14265

Variant Calling: Accuracy, Filtering, and Interpretation

15 - Molecular markers

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Background/Objectives: Accurate variant calling is essential for interpreting viral genome data, but becomes most challenging at low allele frequencies where technical noise can resemble true biological variation. This talk will highlight how the distinction between consensus-level variants and intrahost low-frequency variants should guide both filtering strategies and biological interpretation.

Methods: I will introduce practical definitions (SNV as any single-base change; SNP as a population-level variant often discussed at the consensus/lineage level; iSNV as a within-host minor allele below the consensus threshold) and outline a general variant-calling workflow. This includes read QC, alignment and primer/amplicon considerations, base- and mapping-quality filters, depth requirements, strand and positional bias checks, and frequency- and context-aware thresholds designed for low-frequency variant detection.

Results: Across viral sequencing applications, iSNV calling is consistently more error-prone than consensus SNV/SNP calling. Minor allele signals are enriched for PCR and sequencing errors, mapping ambiguity, homopolymer-related artefacts, and batch/instrument effects, and are strongly influenced by viral load and coverage heterogeneity. Common “rule-of-thumb” cutoffs (minimum depth, base quality, strand balance, and fixed VAF thresholds) can substantially shift sensitivity and specificity, leading to unstable results across datasets if not tuned to the experimental setup.

Conclusions: Correct interpretation requires separating true HPV diversity from artefacts. I will outline practical guidelines and validation strategies grounded in known error modes and expected mutational processes.

References:

CS09 - New European guidelines for cervical cancer prevention

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#14215

Prediction of treatment failure after excisional treatment of cervical precancer

09 - HPV testing

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Background/Objectives: Cervical cancer is the fourth most common cancer in women globally and the most frequent cancer of the female reproductive system. Invasive cervical cancer is preceded by precursor lesions called cervical intraepithelial neoplasia (CIN). Early detection and treatment of premalignant cervical lesions is a highly effective intervention to prevent cervical cancer. After treatment, women remain at an increased risk of developing invasive cervical cancer compared with the general population, and *treatment failure*, defined as residual or recurrent high-grade CIN, occurs in an average 7% of treated patients within 2 years, varying between 8% and 14% among studies. Several post-treatment tests are used in clinical practice to predict recurrence, including margin status, cytology, and high-risk human papillomavirus (hrHPV) testing, alone or in combination. However, their relative accuracy and clinical utility for guiding risk-based follow-up remain uncertain.

Methods: We conducted a systematic review and meta-analysis of studies evaluating post-treatment tests to predict residual or recurrent CIN2+ after excisional treatment. Electronic databases were searched for studies published between 1975 and August 2024. Eligible studies included women treated for histologically confirmed CIN2+ with at least 18 months of follow-up and assessed margin status, cytology, hrHPV testing, or combinations thereof. Diagnostic accuracy measures were pooled using random-effects models, and post-test risks were estimated to assess clinical utility using predefined risk thresholds for management decisions.

Results: Forty-six studies including 20,385 women were analysed. The pooled rate of treatment failure was 6.6%. Stand-alone hrHPV testing showed the best overall performance, with a pooled sensitivity of 86.8% and specificity of 80.5%. Cytology and margin status were substantially less sensitive (70.8% and 48.9%, respectively), despite similar or slightly higher specificity. Co-testing with cytology or margin status increased sensitivity (up to 95–97%) but resulted in markedly lower specificity. Risk-based analyses demonstrated that a negative hrHPV test reduced the post-treatment risk of CIN2+ to below 1%, supporting a return to routine screening. In contrast, negative margins or normal cytology alone did not reduce risk sufficiently. Positive hrHPV results, particularly when combined with abnormal cytology or involved margins, were associated with post-treatment risks exceeding 20%, indicating a need for intensified surveillance or colposcopy.

Conclusions: High-risk HPV testing alone is the most accurate and clinically informative tool for follow-up after excisional treatment of cervical precancer. Cytology and margin status, either alone or in combination with hrHPV testing, do not provide meaningful additional benefit and may increase false-positive results. Risk-based follow-up strategies centred on hrHPV testing can safely guide post-treatment management while minimising unnecessary interventions.

References: Bomans, L., Ramirez, A. T., Hillemanns, P., Gultekin, M., & Arbyn, M. (2025). Prediction of Treatment Failure After Excisional Treatment of Cervical Precancer: A Systematic Review and Meta-analysis. Obstetrics and Gynecology. https://doi.org/10.1097/AOG.0000000000005997

CEE02 - Tackling cervical cancer in Eastern and Central Europe: Current status, lessons learned and the way forward - Part II

#14315

History of HPV vaccine implementation in The Republic of North Macedonia: ups and downs

06 - HPV prophylactic vaccines

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Background/Objectives: Human papillomavirus (HPV) infection is the principal cause of cervical cancer and a significant contributor to other anogenital and oropharyngeal malignancies. The Republic of North Macedonia was among the first countries in Southeast Europe to introduce HPV vaccination into its National Immunization Program. However, implementation over time has been characterized by both achievements and setbacks.

Methods: To review the history of HPV vaccine implementation in the Republic of North Macedonia, highlighting key milestones, challenges, and recent strategic developments.
Methods:
This review summarizes national immunization policies, publicly available reports from health authorities and international organizations, and published data on HPV vaccination coverage.

Results: HPV vaccination was officially introduced in October 2009, initially targeting 12-year-old girls with the quadrivalent vaccine, free of charge. Early adoption positioned North Macedonia as a regional leader in HPV prevention. Despite this, vaccine uptake remained suboptimal over subsequent years, with coverage fluctuating and below levels required for effective population protection. Factors contributing to limited uptake included vaccine hesitancy, misinformation regarding safety and fertility, cultural sensitivities related to sexually transmitted infections, and regional disparities in access to preventive health services. The COVID-19 pandemic further disrupted routine immunization activities, exacerbating existing challenges. The initial coverage rates after its introduction into the school calendar in 2009 reached over 60% coverage among 12-year-old girls, while the two negative effects followed afterwards due to the lingering impact of the 2008/2009 financial crisis in the Eurozone, when the government temporarily suspended vaccination, and the second factor — the emergence of several anti-vaccination groups (some of which included medical personnel). In response, national authorities strengthened public education campaigns and collaborated with medical professional organizations and international partners to restore confidence in immunization programs. A major positive development occurred with the transition to the nine-valent HPV vaccine (April 2024) and the expansion of the program to include boys aged 12–19 years, marking a shift toward gender-neutral vaccination and alignment with World Health Organization recommendations. The "door-to-door" immunization campaign in North Macedonia (2025) focused on delivering human papillomavirus (HPV) vaccines directly to households. Over the course of the 5-week campaign, health-care teams were mobilized across 15 towns and 174 villages in 19 municipalities, reaching a wide range of communities – from densely populated neighbor-hoods to more isolated rural areas, all with vaccination coverage below the national average.

Conclusions: The history of HPV vaccine implementation in the Republic of North Macedonia illustrates a dynamic process marked by early innovation, subsequent implementation difficulties, and renewed strategic momentum. While the country demonstrated strong initial commitment, sustained success has been hindered by sociocultural barriers and inconsistent coverage. Continued efforts focusing on public trust, health professional engagement, and equitable service delivery are essential to fully realize the long-term benefits of HPV vaccination and reduce the burden of HPV-related cancers.

References: World Health Organization. Human papillomavirus vaccination included in national immunization programme – Republic of North Macedonia. WHO SAGE presentation, November 2012.
Maver PJ, Seme K, Korać T, Dimitrov G, Döbrőssy L, Engele L, Iljazović E, Kesić V, Kostova P, Laušević D, Maurina A, Nicula FA, Panayotova Y, Primic Žakelj M, Repše Fokter A, Romejko-Wolniewicz E, Smailytė G, Şuteu O, Świderska-Kiec J, Tachezy R, Valerianova Z, Veerus P, Vīberga I, Znaor A, Zubor P, Poljak M. Cervical cancer screening practices in central and eastern Europe in 2012. Acta Dermatovenerol Alp Pannonica Adriat. 2013;22(1):7-19. PMID: 23674180
Dimitrievska S, Stojanovska L, Grozdanova B. Knowledge gaps and knowledge acquisition of HPV infection and HPV vaccines among medical students in North Macedonia. *J Pediatr Adolesc Gynecol.* 2023;36(2):259. DOI:10.1016/j.jpag.2023.01.212.
Meri Stojanovska, Zorica Naumovska, Aleksandra Kapedanovska, Aleksandra Kapedanovska, Aleksandra Grozdanova, Maja Simonoska Crcarevska Knowledge, opinions and attitudes of the general population in the Republic of N. Macedonia about vaccines and vaccination Macedonian Pharmaceutical Bulletin 68(03):453-454 DOI: 10.33320/maced.pharm.bull.2022.68.03.218
Republic of North Macedonia Ministry of Health. HPV vaccine in Republic of North Macedonia: national immunization schedule and policy. Skopje; 2024.
World Health Organization. Bringing health to every home – door-to-door immunization campaign in North Macedonia. WHO Europe; 2025.

Ludwikowska Kamila
Poland

#13958

Overcoming challenges in HPV vaccination: A case study from Wroclaw, Poland

39 - Public health

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Background/Objectives: Achieving and sustaining high Human Papillomavirus (HPV) vaccine coverage remains challenging worldwide despite strong evidence of effectiveness. While some countries have reached coverage above 80%, others continue to struggle. Poland belongs to the group of low-coverage countries; however, Wrocław represents a notable exception. This study evaluates a decade-long local HPV vaccination programme in Wrocław, the impact of its transition to a national programme, and the implementation of new tailored strategies in response to recent declines.

Methods: Vaccination coverage, participation rates, and characteristics of interventions implemented between 2013–2023 within the municipal programme were analysed, including education cascades and free vaccination in primary care. Coverage trends following replacement of the local programme by the national HPV programme were also assessed. Intervention components were mapped to changes in vaccine uptake.

Results: Between 2013–2023, participation of 41,160 adolescents and 35,225 parents in educational meetings was recorded, and at least one HPV vaccine dose was received by 26,851 adolescents. During the early phase of the programme, coverage exceeding 80% was achieved, followed by a decline to 61% in the 2017/2018 edition. In response, tailored interventions were introduced, including:

- adaptation of educational content based on identified reasons for refusal (concerns regarding safety and effectiveness),
- use of local safety data to support communication,
- dissemination of information on access to 24/7 specialist consultation in case of adverse events,
- implementation of motivational training for nurses with a focus on vaccine confidence and communication skills, and
- provision of annually updated online resources including a frequently-asked-questions section.

Following implementation of these interventions, partial restoration of vaccine coverage to 72% was achieved, with a median coverage of 72.33% across the entire 10-year period. After replacement of the tailored municipal programme with the national HPV programme, a renewed decline in coverage was observed. Nevertheless, higher uptake has continued to be achieved in Wrocław compared with most other large Polish cities.

Conclusions: High HPV vaccine coverage can be achieved in low-uptake countries when locally adapted, tailored strategies are implemented. Replacement of effective local interventions with uniform national solutions may result in reduced vaccine uptake. In response, a new generation of tailored interventions based on structured microlearning online courses for healthcare professionals and families has been developed and is scheduled for implementation in 2025/2026. Continuous adaptation and targeted communication are required for sustained public health impact.

References: Nowakowski A, Prusaczyk A, Szenborn L, Ludwikowska K, Paradowska-Stankiewicz I, Machalek DA, Baay M, Burdier FR, Waheed DE, Vorsters A. The HPV prevention and control program in Poland: progress and the way forward. Acta Dermatovenerol Alp Pannonica Adriat. 2024 Dec;33(4):189-197. PMID: 39707894.Ludwikowska KM, Biela M, Szenborn L. HPV vaccine acceptance and hesitancy - lessons learned during 8 years of regional HPV prophylaxis program in Wroclaw, Poland. Eur J Cancer Prev. 2020 Jul;29(4):346-349. doi: 10.1097/CEJ.0000000000000556. PMID: 31770346.

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#13878

Implementation of HPV based Cervical Cancer Screening Programme in Lithuania

10 - HPV screening

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Background/Objectives: Cervical cancer incidence and mortality in Lithuania remain among the highest in the EU (18.3 and 11.0 per 100,000 women in 2022, versus EU averages of 11.7 and 5.3). The national screening program, implemented since 2004, shifted from primary screening with cytology for women aged 30 – 60 to primary screening with cytology for women 25-34 and High-Risk Human Papillomavirus (HR HPV) -based screening for women 35 – 60 in 2022. This study aims to present the overview of the implementation status of national organized cervical cancer screening programme, based on HR HPV primary testing in Lithuania.

Methods: We reviewed relevant ongoing national processes, documents and available national data to assess the implementation status and early preliminary results of national HR HPV based cervical cancer screening program in Lithuania. The organizational and methodological updates were revealed through the analysis of national legislative documents, the overview of other cancer screening programme elements were revealed from National cervical cancer screening methodology guidance group and the quantitative data was analyzed using specific cervical cancer screening subsystem in National Data Agency platform.

Results: The national cervical cancer screening program in Lithuania has been implemented since July 2004. First cytology-based screening was offered to women aged 30–60 years every 3 years. During these years the programme was updated several times, and recently the country has implemented HR HPV based screening for women 35-60 years old, leaving conventional cytology (CT) based screening for women aged 25–34 years. The HR HPV based screening includes primary testing with HR HPV, triage test – liquid based cytology, follow-up HR HPV test in 12 months for HR HPV positives and cytology negatives and direct referral for colposcopy for women with HR HPV positive results and cytology ≥ASCUS. National updates of the programme included preparation and legislation of national quality assurance guidelines, fully organized programme coordination and management as well as renewal of E-health system with electronic data forms for screening. The assessment of key performance indicators for 2024 revealed that the test coverage rate was 54.27% among women aged 25–34 years tested with CT and 96.56% among women aged 35–59 years tested with HR HPV. The response-to-invitation rate was 36.32% among women aged 25–34 years tested with CT and 41.73% among women aged 35–59 years tested with HR HPV.

Conclusions: Lithuania has implemented evidence-based changes in national cervical cancer screening programme. HR HPV based screening strategy preliminary demonstrates high coverage rates, but further analysis is needed to clarify whether such results are related to screening method (HR HPV) or to better response from older age group of the programme population.

References:

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#14352

Implementation of HPV self-sampling for Cervical Cancer Screening in Albania, 2019-2024

13 - Self-sampling

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Background/Objectives: To support the transition from opportunistic cytology-based screening to an organized, population-based cervical cancer screening program, Albania introduced HPV self-sampling in 2019. We describe the implementation model and early programmatic outcomes.

Methods: The screening program combined home-based HPV self-sampling, health-center–based self-sampling, and clinician-collected samples. Invitations were coordinated by family doctors and delivered via telephone or face-to-face contact. A structured follow-up pathway ensured referral of all HPV-positive women for colposcopy.

Results: Between January 2019 and December 2024, 62,310 eligible women were invited to participate in HPV self-sampling. Participation following invitation was high, with an invitation attendance rate of 95.5%. Overall HPV positivity was 7%, and all HPV-positive women were referred for colposcopy evaluation. Population screening coverage over the five-year period reached 42.1%, with annual coverage ranging from 28.1% to 47%. Population coverage should be distinguished from invitation attendance, which reflects participation among invited women and was likely enhanced by the simplicity, privacy, and acceptability of self-sampling. The organized approach enabled timely follow-up and continuity of care.

Conclusions: Within an opportunistic screening context and a relatively short follow-up period, HPV self-sampling demonstrated high acceptability, feasibility, and effective linkage to diagnostic services. These findings support HPV self-sampling as an effective primary screening strategy and provide key evidence to inform scale-up within an organized, population-based cervical cancer screening program in Albania.

References: 1. Serrano B, Ibáñez R, Robles C, Peremiquel-Trillas P, de Sanjosé S, Bruni L. Worldwide use of HPV self-sampling for cervical cancer screening. Prev Med. (2022) 154:106900. doi: 10.1016/j.ypmed.2021.106900
2. European Union. Council Recommendation of 9 December 2022 on strengthening prevention through early detection: A new EU approach on cancer screening replacing Council Recommendation 2003/878/EC 2022/C 473/01 [Internet]. (2022). Available online at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=oj:JOC_202 2_473_R_0001.
3. European Commission. Europe's Beating Cancer Plan. Communication from the commission to the European Parliament and the Council. [Internet] (2021). Available online at: https://health.ec.europa.eu/system/files/2022-02/eu_cancer-plan_en_0.pdf
4. Nishimura H, Yeh PT, Oguntade H, Kennedy CE, Narasimhan M. HPV selfsampling for cervical cancer screening: a systematic review of values and preferences. BMJ Glob Health. (2021) 6:e003743. doi: 10.1136/bmjgh-2020-003743
5. Daponte N, Valasoulis G, Michail G, Magaliou I, Daponte AI, Garas A, et al. HPVbased self-sampling in cervical cancer screening: an updated review of the current evidence in the literature. Cancers. (2023) 15:1669. doi: 10.3390/cancers15061669

#14450

Implementation status of national organized HPV-based cervical cancer screening in Montenegro

10 - HPV screening

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Background/Objectives: In Montenegro, cervical cancer, for many years, had been diagnosed predominantly at advanced stages, mainly based on the presence of symptoms, resulting in poorer prognosis and a greater burden on the health care system. In order to improve early detection and reduce mortality, a pilot project of an organized cervical cancer screening program was launched on July 18, 2016, at the Primary Health Care Center in Podgorica. Based on the positive results of the pilot phase, the program was expanded to the national level on February 1, 2018, and is currently implemented in all primary health care centers across Montenegro.The defined screening interval is five years, and the target population includes women aged 30 to 54 years, with a planned extension up to 64 years in accordance with the 2022 recommendations of the Council of the European Union. A significant enhancement of the program was introduced in January 2025 through the implementation of a screening model based on individual risk assessment, enabling a personalized approach to cervical cancer prevention.

Methods: A descriptive analysis of data from the national organized cervical cancer screening program in Montenegro was conducted for the period 2016–2025, with particular focus on the last three-year period following the program's reactivation after the COVID-19 pandemic.Data were collected from the screening information system, which integrates data from all primary health care centers, the Institute of Public Health of Montenegro, the Clinical Center of Montenegro, and general hospitals. Indicators analyzed included target population coverage, response rates among invited women, results of HPV testing, triage and diagnostic procedures, and histopathological biopsy findings.

Results: From the initiation of the national organized cervical cancer screening program until the end of 2025, at least 50,724 women were tested for HPV infection at least once. This figure indicates a continuous expansion of access to preventive testing, while also highlighting the need for further increases in target population coverage.
In the most recent three-year period, 94,623 women met the criteria for invitation to screening. Of these, 42,879 women (45%) were invited, and 33,646 (78%) responded. A total of 30,285 cervical samples were collected for HPV testing. Screening coverage of the target population during this period was 32.01%, while participation among respondents reached 89.98%.

Conclusions: The national organized cervical cancer screening program in Montenegro enables early detection of premalignant lesions and cervical cancer at early stages, when treatment is most effective and least burdensome for patients. The introduction of an individual risk assessment model represents a significant step toward personalized prevention and further improves program efficiency.Despite the achieved results, coverage of the target population remains suboptimal, indicating the need to strengthen active invitation systems, continue education of women, and enhance the role of primary health care professionals. The integration of organized screening and HPV vaccination remains a key strategy in the long-term fight against cervical cancer.

References:

SS23 - Prevention of HPV-related cancers among people living with HIV in the Americas

Madeleine Margaret
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#14188

Cervical cancer screening in WLWH in the Dominican Republic

10 - HPV screening

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Background/Objectives: More evidence is required to support HPV testing for primary cervical cancer screening among women living with HIV (WLWH). We compared usual care cytology to HPV testing among WLWH in the Dominican Republic (DR).

Methods: This cross-sectional analysis includes 575 WLWH enrolled in ULACNet Trial 302: Estudio Oportunidad. Participants contributed provider- and self-collected samples for cytology and HPV hierarchical testing (ScreenFire, Atila BioSystems). Women with positive results on cytology or either HPV sample were referred for colposcopy and biopsy, and screening test characteristics were evaluated. HPV test results were further compared between positivity for 13 versus 8 high-risk HPV (hrHPV) genotypes. Local histology results were used for participant management and CIN2+ endpoints were adjudicated by a central expert pathologist.

Results: Women with positive results on any screening test had higher HIV viral loads, lower CD4 counts, and were younger than women with screen negative results. Sensitivity to detect cervical intraepithelial neoplasia grade 3 or worse (CIN3+) by cytology (66.7%, 95% CI 49.2-80.5) was lower than sensitivity of provider-collected results with 13 hrHPV results (93.9, 95% CI 78.7-98.5) or 8 hrHPV results (84.8%, 95% CI 68.3-98.6) and self-collected samples with either 13 hrHPV or 8 hrHPV results (97.0%, 95% CI 81.3-99.6). Cytology missed 11 CIN3+, 13 hrHPV testing of provider-collected samples missed 2 CIN3+, and 8 hrHPV testing of self-collected samples missed 1 CIN3+.

Conclusions: These data provide evidence to support HPV testing among WLWH in the Dominican Republic, by provider- or self-collected sampling methods. Additionally, testing with either 13 or 8 hrHPV results detected more CIN3+ than cytology. The change to primary HPV testing in the DR will lead to more accurate detection of cervical precancer among WLWH.

References:

Duerr Ann
United States

#14195

HPV Antibody Responses To Three, Two and One Dose(s) of 9-valent HPV Vaccine in Children With HIV

06 - HPV prophylactic vaccines

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Background/Objectives: HPV vaccination dramatically reduces the increased HPV disease risk for people living with HIV. We investigated responses to one-, two- and three-dose regimens of Gardasil®9 HPV vaccine (G9) in 9-to-13-year-old children with perinatally-acquired HIV (CWH) in Peru, Brazil, and Haiti. We compared responses to a single dose in CWH to responses in a control group of HIV-negative children from the same communities who also received one dose.

Methods: CWH were vaccinated with 1, 2 or 3 doses of G9 as follows: 1 dose - at month 0 (Arm 3), 2 doses - at months 0,6 (Arm 2), or 3 doses - at months 0,2,6 (Arm 1). HIV-uninfected children received 1 dose at month 0 (Arm 4). All participants (total N=93) received an anamnestic vaccine dose (boost) 24 months after the last dose of their study vaccine regimen (i.e. after 1, 2, or 3 doses). Plasma was collected at day 0, at 1, 18 and 24 months after the last dose of each vaccine regimen, and one-month post-boost. Luminex bead-based immunoassay was used to measure HPV-type-specific IgG (IU/mL) responses against the G9 HPV types (Pinto Lab). HPV16 and HPV18 neutralizing antibody (NAb) IC50s were measured in pseudovirus-based neutralization assays (Galloway Lab). Data is presented for 25 participants in Peru, where follow-up is complete.

Results: All participants but one seroconverted for all G9-related HPV types one month after their vaccine regimens; binding antibody (Ab) titers differed significantly by arm (lower in Arms 3 & 4) (Figure 1). Twenty-four months later, at the boost time point, seronegativity (titers below the seropositivity cut-off) was more common in the one-dose arms, especially for HPV45 and 52. Ab concentrations in Arms 3 & 4 were significantly lower than in Arm 1 for all HPV types except HPV6 (p values ≤ 0.02). One-month post-boost all children were seropositive for all G9 HPV types. Binding Ab concentrations were not significantly different in CWH in 1-, 2- or 3-dose arms or in CWH vs HIV-uninfected children in 1-dose arms (N=7 each arm) (p=NS for all comparisons but one; data not shown). HPV16 and HPV18 NAb responses were robust one month after the two- or three-dose regimens; IC50s then fell by ~1 log and plateaued, rebounding one month after boosting. In CWH, the response after one dose was >2 logs lower than after two or three doses, declining little over time. Interestingly, the response post-boost was approximately 2 logs greater than at one month and equivalent to responses in CWH who had received more doses. Responses after one dose in HIV-uninfected children were similar (although IC50s were slightly higher).

Conclusions: In Peru, CWH seroconverted for all G9 HPV types after receiving 1, 2 or 3 doses. Subsequent seronegativity was greater in the one-dose arms. The implications are unclear as rates were similar in CWH vs. uninfected children (who are expected to be protected by a single dose). CWH showed strong NAb response after 2 or 3 doses of G9; NAb responses to a single dose were similar in CWH vs. without HIV. The high NAb response in Peruvian children after boosting suggests effective priming, even by a single vaccine dose.

References:

SS28 - Challenges in the laboratory methods for the screening, diagnosis and management of HPV-associated oropharyngeal cancer

Connor Linzi
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#14198

Optimal molecular annotation of oropharyngeal cancer

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Molecular annotation of solid oropharyngeal squamous cell carcinoma (OPSCC) for HPV status supports staging and prognostication of this disease. Understanding type specific prevalence of HPV in OPSCC also provides insight into the vaccine preventable component. The Scottish HPV Reference Laboratory (SHPVRL) has provided a national molecular HPV typing service for solid OPSCC biopsies diagnosed in Scotland and undertakes companion research to support enhanced risk stratification of individuals at high risk of OPSCC including through detection of HPV DNA in blood (liquid biopsy).
Here we aim to provide “lessons learned” relating to the detection of HPV in OPSCC patients when delivered as part of national service. Perspectives on service and research developments will also be covered.

Methods: SHPVRL has received oropharyngeal biopsies from Scottish territorial health boards for HPV typing since 2014; we present a recent audit relating concordance of HPV and p16 immunohistochemistry status where drivers of observed discordance are evaluated. Additionally, as part of a research work stream, inheritance of a droplet digital PCR (ddPCR) system for HPV cell-free DNA (cfDNA) detection in blood necessitated internal validation and optimisation of the extraction procedure to improve workflow and cost efficiencies. A new method, QIAamp MinElute ccfDNA Mini Kit (“Mini Kit”, QIAGEN), was evaluated against the previous method QIAamp MinElute Virus Spin kit (“Spin Kit”, QIAGEN). cfDNA yield and proportion, and total and mean droplet count from ddPCR were compared. Qualitative (Pos/Neg) and quantitative (copies/ml) were also assessed for agreement between methods.

Results: Between May 2022-May 2024, SHPVRL received 665 oropharyngeal biopsies for HPV typing with an accompanying p16 result. Using Anyplex II HPV28 or Allplex HPV28 (Seegene), HPV was detected in 67.4% (448/665) biopsies and HPV/p16 agreement was high (>90%). Discordance was more often observed as HPV-/p16+ compared to HPV+/p16- (4.8%, 32/665 vs 1.5%, 10/665, respectively) (**Table 1**). In univariate analysis, no particular variable appeared to drive discordance – health board ($p = 0.146$), age ($p = 0.142$), sex ($p = 0.920$), assay ($p = 0.582$).
With respect to optimisation of cfDNA extraction, cfDNA yield and proportion were comparable between the Spin Kit and Mini Kit (12.1ng and 77.2% vs 11.7ng 79.6%, respectively). In ddPCR, total and mean droplet counts were higher in Mini Kit extracts compared to Spin Kit (100604 and 12575 vs 108700 and 13588 droplets, respectively). Qualitative agreement was 87.5% (95% CI: 46.7 – 99.3) for the detection of HPV16 using ddPCR – the single discordant specimen was weakly positive for HPV16 by the Spin Kit (1.17 copies/ml, i.e. 1 positive droplet).

Conclusions: Centralised, national testing of OPSCC through a reference lab provides data of relevance both at the individual patient level and population level and contributes to a representative biobank of samples that can support further, relevant research. While agreement between HPV and p16 status in OPSCC was high, irrespective of HPV assay, the implications of discordance on prognosis and treatment options requires further research. Optimising the liquid biopsy workflows to increase cost and practical efficiencies while not compromising performance is crucial as evidence accumulates to indicate the clinical utility of this technology.

References:

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#14201

HPV DNA in liquid biopsies as a diagnostic marker for the early detection and management of HPV-associated cancers

15 - Molecular markers

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Background/Objectives: The incidence of HPV-related oropharyngeal squamous cell carcinoma (HPV-OPSCC) has markedly increased over recent decades, making it an emerging public health priority. Distinguishing HPV-related from HPV-unrelated OPSCC is crucial, as HPV-OPSCCs are associated with a significantly better prognosis; however, patients with HPV-OPSCC also show a higher propensity to develop distant metastases (1). In recent years, several clinical needs have been identified to address challenges related to HPV-OPSCC, including the development of more accurate and less invasive diagnostic approaches, improved tools for treatment monitoring, and the identification of specific biomarkers capable of detecting disease recurrence. Recent studies indicate that the detection of circulating HPV DNA in liquid biopsy represents a promising predictive and prognostic biomarker for HPV-associated oropharyngeal cancers (2). The aim of this work is to provide a comprehensive overview of the use of HPV-related biomarkers in liquid biopsies for the early detection and clinical management of HPV-associated OPSCC.

Methods: Current research on HPV-associated OPSCC focuses on several molecular biomarkers, including HPV DNA genotyping, viral load quantification, oncogenic transcript expression, and viral or host gene methylation. Blood and saliva are the most commonly analysed liquid biopsy samples. The detection and characterization of these biomarkers rely primarily on quantitative PCR (qPCR), digital PCR (dPCR), and next-generation sequencing (NGS) (3).

Results: Different studies report that most of patients with HPV-associated OPSCC have detectable HPV DNA in plasma at diagnosis, and higher circulating levels correlate with advanced tumour stage and increased distant metastases. Studies evaluating HPV DNA and RNA biomarkers in saliva have produced mixed results. While blood and saliva represent useful matrices for detecting oncogenic HPV DNA, pre-analytical and analytical procedures still require stronger standardization. Additionally, several highly specific differentially methylated regions (DMRs) have been identified in HPV-related OPSCC, offering promising applications for molecular-based detection and improved disease management (4,5).

Conclusions: Liquid biopsy has emerged as a non-invasive approach for cancer diagnosis and monitoring. It provides a cost-effective alternative to traditional tissue biopsies and enables the detection of tumour-derived components in blood and saliva. Beyond facilitating early diagnosis, this technique also supports the identification of tumour recurrence or metastasis after treatment, thus contributing to more personalised and dynamic patient management.

References: (1) Wittekindt C et al. HPV - A different view on Head and Neck Cancer. Laryngorhinootologie. 2018 Mar;97(S 01):S48-S113. doi: 10.1055/s-0043-121596. (2) Veyer D et al. HPV circulating tumoral DNA quantification by droplet-based digital PCR: A promising predictive and prognostic biomarker for HPV-associated oropharyngeal cancers. Int J Cancer. 2020 Aug 15;147(4):1222-1227. doi: 10.1002/ijc.32804. (3) Jahraus T et al. Circulating Human Papillomavirus DNA-Liquid Biopsy in Head and Neck Cancers. J Med Virol. 2025 Dec;97(12):e70705. doi: 10.1002/jmv.70705. (4) Smith DH et al. Current salivary biomarkers for detection of human papilloma virus-induced oropharyngeal squamous cell carcinoma. Head Neck. 2021 Nov;43(11):3618-3630. doi: 10.1002/hed.26830. (5) Ren S et al. Discovery and development of differentially methylated regions in human papillomavirus-related oropharyngeal squamous cell carcinoma. Int J Cancer. 2018 Nov 15;143(10):2425-2436. doi: 10.1002/ijc.31778.

SS29 - Comparing experiences and protocols: Screening protocols with genotyping and p16 as a triage test

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#14150

Primary human papillomavirus-based cervical screening in Denmark: Comparison of extended genotyping, CinTec Plus or HPV16/18/other HR as triage of screening positive samples

12 - Triage of HPV positive women

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Background/Objectives: As cervical cancer screening programs target entire populations with "one-size-fits-all screening" as entry point, the choice of triage becomes pivotal in securing an optimal balance between sensitivity of detection and specificity. Therefore, and as part of the health policy trial, the triage question was addressed by introducing three distinct triage options for HPV positive screening samples; liquid based cytology in combination with either p16/ki67 dual staining, partial genotyping for HPV 16, HPV 18 or "other 12 high risk HPV genotypes" in bulk, or extended genotyping with subdifferentiation between HPV genotypes HPV16,18,31,33,52 and HPV35,39,45,51,56,59,66,and 68.
The objective of this paper was to report the performance of the three algorithms in terms of their ability to identify high grade cervical lesions and reducing unnecessary referrals for re-test or colposcopy.

Methods: Women 30-59 years were allocated to either HPV-based screening or cytology-based screening in this Danish health care policy trial. The optimal triage of HPV positive women could be a combination of cytology triage with HPV genotyping or p16/Ki67 staining. We report number of screen positives, colposcopies and cervical lesions of three different triage algorithms (p16/Ki67, HPV16/18 or HPV16/18/31/33/52) in HPV positive women with low grade cytological abnormalities.

Results: We included 178,317 women with a sample in 2021 of which 91,517 were screened with HPV and 86,800 with cytology. All women were followed for 18 months. Almost three times as many women screened positive with HPV-based screening compared to cytology-based screening (RR 2.99, 95% 2.93-3.05) and colposcopies derived from the screening program were also more common (RR 1.68 95% 1.63-1.73). P16/Ki67 triage resulted in more colposcopies (RR 1.86 95% 1.76-1.95) than HPV16/18 (RR 1.54 95% 1.44-1.65) and HPV 16/18/31/33/52 (RR 1.63 95% 1.55-1.71). The excess in colposcopy referrals was reduced when non-screening derived colposcopies were included (intention-to-treat). Nevertheless, more women with CIN2 or worse were detected in the HPV group than in the cytology group per screened woman; in the p16/Ki67 triage group (RR 1.65 95% 1.54-1.77), in the HPV16/18 group (RR 1.36 95% 1.23-1.50), and in the HPV16/18/31/33/52 group (RR 1.48 95% 1.37-1.59). HPV-based screening, as compared with cytology screening, resulted in more screen positives, but all three triage algorithms substantially reduced the excess number of referrals to colposcopy.

Conclusions: The three triage algorithms resulted in similar outcomes, but we found slightly more severe and moderate cervical lesions with p16/Ki67 compared to partial and extended genotyping.

References: