EUROGIN

INTERNATIONAL MULTIDISCIPLINARY HPV CONGRESS

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ALFÂNDEGA CONGRESS CENTER • PORTO, PORTUGAL

ADVANCING SCIENTIFIC EFFORTS TO CONTROL HPV-RELATED CANCERS

CONGRESS PRESIDENTS
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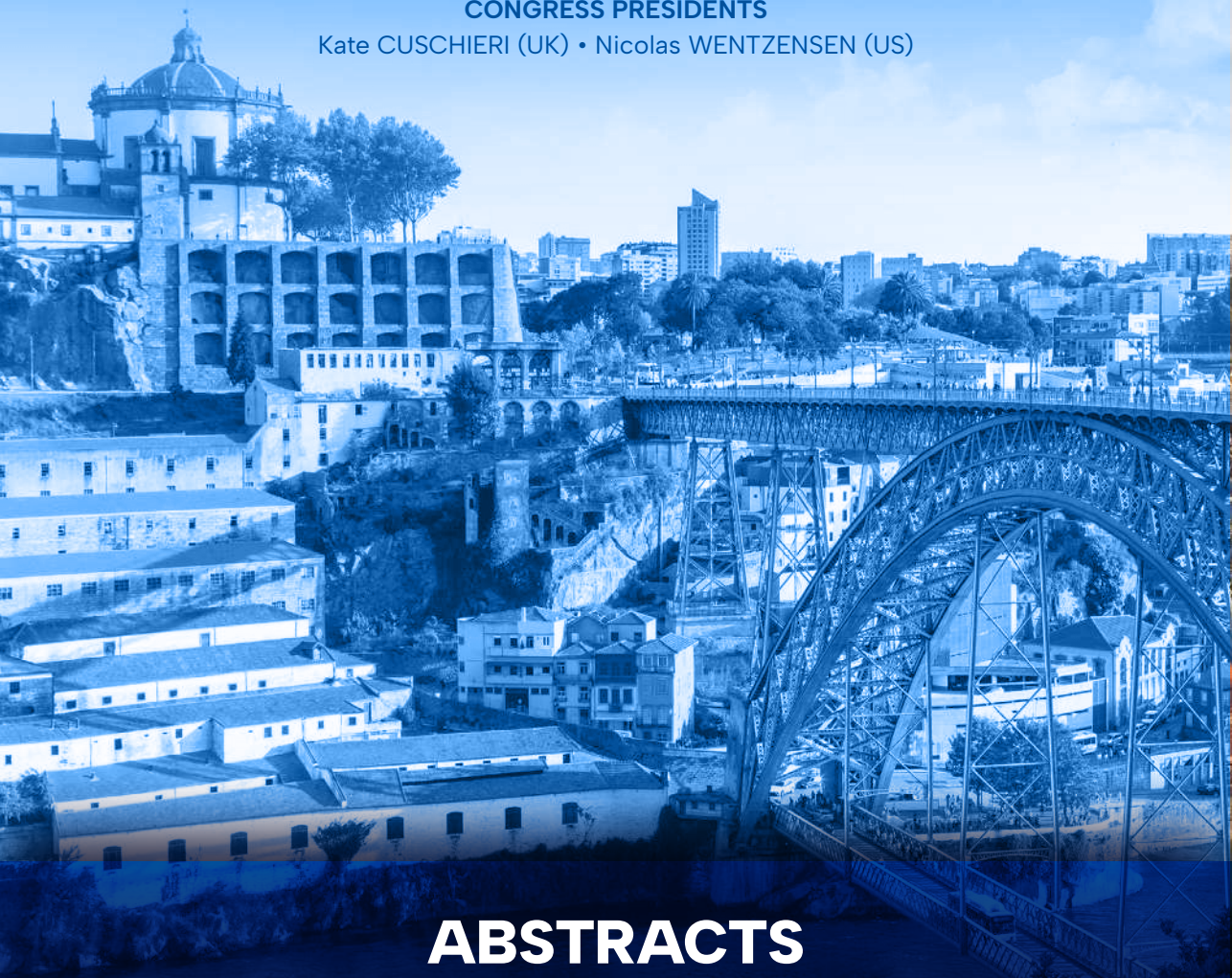

ABSTRACTS

MAIN CONGRESS PROGRAM

SS05 - Update on anogenital carcinogenesis

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#9584

The role of reserve cells in cervical squamous cell carcinogenesis

04 - Pathogenesis

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Background/Objectives: The up to now most widely accepted concept of cervical squamous cell carcinogenesis is based on research on stratified squamous epithelium. It is commonly believed that only differentiating squamous epithelial cells are permissive for HPV since other cells lack the factors required for HPV gene expression and replication of the viral genome.The clinical pattern of high-grade squamous intraepithelial lesions (HSIL) and squamous cell cervical cancer (SCC), however, strongly suggests that immature metaplastic squamous epithelium of the transformation zone including endocervical columnar epithelium with reserve cells (RC) is the area of risk and site of origin of most SCC.RC are believed to be pluripotential cells with stem cell (-like) properties native to the endocervical mucosa. In healthy women they bring about the day-to-day regeneration of columnar cells and initiate the squamous metaplastic process. Two types of RC cells exist: p63/CK17 co-expressing RC of Urogenital Sinus origin. The second type is of Müllerian origin and expresses CK7. During early squamous metaplasia RC multiply and give rise to a distinct morphologic entity called immature metaplasia. If immature metaplasia co-exists with HPV exposure minor lacerations of the epithelium may permit HPV to meet RC. It is reasonable to assume that HPV infected RC have carried HPV for a long time in a silenced form and serve as a reservoir of HPV. In individual RC for so far unknown reasons HPV E6/7 expression may start and permit a transforming mode of viral gene expression characterized by high-level expression of E6 and E7 genes resulting in de novo development of HSIL. Residual RC after HSIL treatment are capable of forming new squamous epithelium, recurrent HSIL and subsequent SCC.

Methods: xx

Results: xx

Conclusions: xx

References: xx

SS01 - Structural and social factors that impact HPV driven cancers

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#9603

Cervical Cancer Screening Among Women by HIV-Status in Eswatini

10 - HPV screening

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Background/Objectives: Eswatini (formerly Swaziland) has the highest HIV prevalence worldwide, with women ≥15-years having a prevalence of 30.4%. The country also has the highest incidence of cervical cancer (CC) globally, at 84.5 per 100,000 women, along with a CC mortality rate of 55.7 per 100,000 women. It is therefore important to evaluate CC screening outcomes by HIV status in Eswatini.

Methods: The study used data from the Eswatini National Cancer Registry (ENCR), Client Management Information System (CMIS) and hospital administrative records for facilities not implementing CMIS. Data was collected across the country's regional and national facilities from 2020-2023. Probabilistic Record Linkage (PRL) techniques were used to match data on invasive CC with corresponding CC screening records. Descriptive statistical methods were utilized to describe characteristics and outcomes of screened women by HIV status.

Results: From the total of 99,698 women (≥15 years) screened, 68.9% were HIV-positive, 4% were HIV-negative and 27.1% had unknown HIV-status. The mean age of 36.7(SD±10.04) years. Majority of patients (89.6%) used visual inspection with acetic acid (VIA), 10.2% had Pap smears and 0.2% had HPV DNA testing. Average screen interval was 14 and 19 months for HIV-positive and HIV-negative women, respectively. Using PRL, we identified 684 (42.6% of all women with CC) who had been previously screened. These confirmed cases were predominantly among HIV-positive women (68.2%), 4.9% were HIV-negative and 26.7% cases had unknown HIV status. Furthermore, 17.5% were screen-negative, 11.7% screen-positive, 13.6% had pending-screening results and 9.5% had suspicious result at last screen.

Conclusions: The CC screening programme in Eswatini has several gaps which include a significant bias towards HIV-positive women and leaving HIV-negative women largely unscreened. The results suggest that VIA is a low performance test in a HIV high prevalence setting with a significant proportion of HIV-positive women getting CC within a year of a negative VIA screen. There is urgent need for transition to a high-performance test and implementation strategies that include more HIV-negative women.

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#9588

Disparities in Cervical Cancer Survival by Province in Rwanda: Insights from Record Linkage (2007-2023)

03 - Epidemiology and natural history

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Background/Objectives: Cervical cancer is the leading cause of cancer-related mortality among women in Rwanda, despite preventive measures such as HPV vaccination and screening programs. However, survival disparities remain a challenge, influenced by factors such as geography, age, stage at diagnosis, and access to treatment.The study aimed to evaluate survival disparities among cervical cancer patients across Rwanda's five provinces (Kigali, South, North, East, West), focusing on determinants such as age, cancer stage, and treatment initiation.

Methods: Data from the Rwanda National Cancer Registry (2007-2022) and civil registration mortality records (2020-2023) were linked using probabilistic record linkage method. Descriptive statistics were used to summarize patient demographics and clinical characteristics. Survival analyses were performed using Kaplan-Meier estimates to calculate survival probabilities, and Cox proportional hazards models were applied to identify risk factors for mortality

Results: A total of 5,162 cervical cancer patients were included in the analysis. Survival disparities across provinces were evident, with Kigali City having the highest survival rate (83.4%) and the lowest mortality rate 154 (16.6%). In contrast, the Southern Province exhibited the highest mortality rate at 424 (32.1%), followed by the Northern Province 215 (30.8%), Western Province 252 (30.4%) and Eastern Province 363 (28.7%). Patients diagnosed at stage IV had the lowest survival probability, with a mortality rate of 41.7%. Interestingly, patients who did not initiate treatment had a mortality rate of 16.8%, compared to 35.9% among those who initiated treatment. Cox regression analysis indicated advanced stage at diagnosis (stage IV: HR = 2.63, 95% CI: 1.93-3.58), older age (≥65 years: HR = 1.81, 95% CI: 1.35-2.44), and residing in the Southern Province (HR = 1.76, 95% CI: 1.46-2.11) as major risk factors for higher mortality.

Conclusions: The findings highlight significant survival disparities in cervical cancer patients across Rwanda's provinces. These disparities highlight the urgent need to strengthen early detection programs, ensure timely access to treatment, and address disparities in healthcare access across regions. Strengthening cancer data systems through improved linkage is essential for guiding effective cervical cancer control strategies in Rwanda

SS04 - Global HPV laboratory network

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#9609

International collaborative study on sensitivity and specificity for CIN2+ of viral amounts and types of HPV

09 - HPV testing

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Background/Objectives: Different HPV tests vary greatly regarding which HPV types they detect and what the detection limit is. When designing campaigns for cervical cancer elimination using HPV screening it would be an advantage to know the optimal type of composition and analytical detection limit of the tests.

Methods: A study consisting of 101 cases and 202 controls was conducted.The cases were a consecutive series of histopathology-verified CIN2+ lesions identified among women resident in the capital region of Sweden who had had a cervical liquid-based cytology sample taken at most three months before the histopathology diagnosis. Controls were identified among women resident in the capital region of Sweden who were participating in the population-based cervical screening program. Only primary screening samples were eligible (not reflex samples or samples from non-organized screening). Two controls matched by years of age were selected per case. The HPV status of all samples was extracted from the laboratory database of the screening program, but not used for selection of cases or amounts using QuantStudioTM 3 Real-Time PCR System (Thermo Fisher Scientific) for HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59. National reference laboratories (NRL) in the HPV LabNet were invited to participate and aliquots from all samples were sent to 9 laboratories from 9 different countries for analysis.

Results: NRL Sweden found that 99 cases (98%) and 34 controls (17%) were positive for HPV. The most important type was HPV16, >0 virus amount found in 34.7% of cases (35/101) and 4.4 % of controls (9/202). The 7 oncogenic types HPV16/18/45/33/58/31/52 (ranked according to IARC's ranking of oncogenicity) were jointly found in 80.2 % of cases and 12,4% of controls.

Conclusions: The 7 most oncogenic HPV types were the most important for CIN2+ detection. We expect the data to be useful on determining which HPV types should be detected with what analytical sensitivity by HPV screening tests and the amounts of virus found in cases and controls using consensus from all participating laboratories.

SS02 - 3rd edition of the European guidelines for quality assurance in cervical cancer screening

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#9606

EU Initiative on Cervical Cancer - key healthcare questions to be addressed

10 - HPV screening

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Background/Objectives: The development of clinical guidelines prioritizes research questions and outcomes to ensure they are relevant for clinicians, patients, and policymakers. This process involves selecting populations, interventions, comparators, and outcomes for each healthcare question. The European Commission Initiative on Cervical Cancer (EC-CvC) aims to update guidelines for the primary and secondary prevention of cervical cancer. The main objectives are to map healthcare questions and outcomes addressed in previous guidelines, identify gaps in available recommendations, and avoid duplication of efforts.

Methods: We adapted the European Commission's Joint Research Centre methodology for mapping existing guidelines and prioritisation of key questions. First we conducted a systematic review to summarize existing guidelines on cervical cancer prevention published between 2013 and 2023 and assessed their quality using the AGREE Global Rating Scale. We extracted and categorized recommendations and their PICO (Population, Intervention, Comparator, Outcome) components and stage in the screening pathway. This mapping of existing recommendations was presented to the working group through structured surveys, allowing them to review the evidence and identify important gaps that should be addressed in the update of the EC-CvC guidelines.

Results: We included 32 guidelines, of which 24 (75%) were recently published or updated within the last 5 years. Five guidelines covered multiple global regions. Most guidelines focused on population-based screening (97%). Approximately half of the guidelines used the GRADE approach (50%). Moreover, 21 guidelines (65%) reported conflict of interest management, 17 (53%) indicated an external review process, and 13 (40%) disclosed funding sources. The results from the mapping survey were reviewed by the IARC steering group and WG chairs, who considered the suggestions from the working group and updated the PICO elements into those that would require further focused group discussions. In February 2024, the EC-CvC WG generated the first detailed PICO questions on screening start and stop ages, screening tests, and screening algorithms.

Conclusions: The preparatory phase of the EC-CvC project successfully mapped existing guidelines and identified important gaps in recommendations. The WG has generated the first detailed PICO questions which set the foundation for the development of recommendations aimed to updated guidelines and ultimately improve cervical cancer prevention strategies.

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#9612

Integrated guidelines and quality assurance for cervical cancer prevention in Europe

39 - Public health

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Background/Objectives: Europe's cervical cancer incidence rate exceeds the global elimination target (10.7 vs. 4 cases per 100,000 persons), with wide disparities across countries (3.4-26.2 per 100,000 persons). The European Commission (EC) calls for 90% screening coverage and a coordinated, patient-centred approach to prevention. The EC Initiative on Cervical Cancer (EC-CvC) integrates evidence-based guidelines with a quality assurance (QA) scheme via an accessible and interactive web-based platform.

Methods: The EC-CvC links the development of evidence-based recommendations with quality indicators which are incorporated into the QA scheme. The EC-CvC working group (WG) identifies priority PICO questions and evaluates evidence using the GRADE approach. In parallel, quality indicators relevant to each recommendation are systematically reviewed, selected and integrated into the QA scheme. All recommendations and supporting information, including EtD tables with expert comments, are published on the Commission's web-hub with both technical and lay language.

Results: The initiative is guided by a multidisciplinary working group (WG) of 20 experts and patient representatives from 13 European countries. They identify priority PICO questions through surveys and focussed discussions and critical points in the patient journey, essential to quality assurance. The PICO questions guide independent systematic reviews, summarised on evidence-to-decision tables and evaluated by the working group to inform guideline recommendations linked with implementation indicators. The QA scheme emphasizes quality at critical points in the patient journey, essential or currently lacking, with evaluation tools for compliance. Accreditation under Regulation No 765/2008 ensures consistent standards across Europe. Public access to final products on the web-hub, improve accessibility, facilitate timely updates, and enhance transparency.

Conclusions: The EC-CvC offers a novel evidence-based patient centred framework for integrating guidelines and quality assurance which addresses inequities and implementation challenges.

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#9574

European guidelines for quality assurance in cervical cancer screening: Developing a quality assurance scheme

39 - Public health

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Background/Objectives: The European Commission Initiative on Cervical Cancer (EC-CvC) project is part of the European Commission Initiatives on Cancer (https://cancer-screening-and-care.jrc.ec.europa.eu/en) which aim to develop evidence-based guidelines and quality assurance (QA) schemes for cancer prevention and care services. The objective of the EC-CvC QA scheme is to contribute to improvement of outcomes for persons and patients by defining a set of quality requirements for the cervical cancer prevention and care services across Europe, to be implemented through the established procedures of an accredited certification framework of the European cooperation for accreditation (https://european-accreditation.org/).

Methods: The EC-CvC QA scheme covers services related to primary, secondary and tertiary prevention of cervical cancer and assesses compliance for the following quality domains: clinical effectiveness, facilities, resources and workforce, personal empowerment and experience, and safety. The requirements included in the QA scheme have been developed by a panel of experts with relevant professional profiles, and patients, who follow a structured approach from reviewing the existing QA schemes, preparing patient pathways, identifying quality aspects and areas where there is a potential to improve quality (known as quality potentials), to formulating specific, measurable and actionable quality indicators.

Results: The EC-CvC QA scheme consists of several sections: Prevention (HPV vaccination), Screening, Diagnosis, Treatment, Rehabilitation, Follow-up and survivorship, and Palliative care. Patient pathways have been developed for specific processes included in each section. Quality aspects and quality potentials have been defined for the treatment section and will be gradually expanded to the remaining sections, during the project until the end of 2026. A database with about 2000 performance measures has been prepared as a result of systematic review on publications and websites of relevant organisations. This database is the main source for the experts to select measures for each requirement and to identify the gaps to be filled in with newly developed indicators. The requirements will be grouped into flexible certifiable modules to accommodate varying contexts and capacities of cervical cancer prevention and care services in different countries.

Conclusions: The EC-CvC QA scheme, which is under development as part of the European Commission Initiatives on Cancer, will allow for voluntary adoption, and will offer flexibility and modularity in its implementation towards improving cervical cancer prevention and care.

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Italy
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#9620

Session title: 3rd edition of the European guidelines for quality assurance in cervical cancer screening. Talk: The principles of risk-based screening

10 - HPV screening

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Background/Objectives: The European Council has recommended risk stratification in screening when feasible and appropriate (1). Some of the most recent cervical cancer screening guidelines have adopted the principle of "equal risk, equal management" to group women with similar risks of CIN3+ and determine the correct management (2-4). The European Commission Initiative on Cervical Cancer (EC-CvC) (5) Working Group is considering this approach to frame the PICO (population, intervention, comparator, outcomes) questions and develop the European screening recommendations. The intervention will present the rationale of the risk stratification in the EC-CvC guidelines, how it could be used to develop the recommendations and the critical issues anticipated by the working group.

Methods: Within the fforts of the EUCanScreen Joint Action, a scoping review has been conducted to identify the conceptual frameworks of risk stratification in cervical cancer screening and previous experiences of its application in guideline development. The working group is reviewing how other guidelines adopted risk stratification and how they framed PICO questions on the basis of risk stratification. An online survey is ongoing to guide the discussion regarding how many couples of risk stratum/management should be determined and the thresholds to define the upper and lower bound of each risk stratum.

Results: According to the conceptual frameworks identified in the literature, the main elements of risk-stratified screening are: 1) the information used to stratify the population according to the individual risk, 2) the definition of the risk strata, and 3) the coupling with risk-specific screening management. In cervical cancer screening, two main phases of risk stratification can be identified: one in the general population, before knowing any recent result of the HPV test, in which the risk stratification is based mostly on the vaccination status, the vaccination coverage in the birth cohort, and the screening history; the second after the HPV test results, in which the risk stratification is based on the information about HPV infection and the HPV genotype. and on the triage tests that can be performed. Some of the critical issues anticipated by the working group are related to the proxy used to measure the risk of cancer in previous guidelines, i.e. the risk of CIN3+. This proxy may have important limitations when measured in unvaccinated populations and applied in vaccinated populations because the mix of HPV genotypes underlying CIN3 in the two populations will be different, thus the underlying risk of cancer will be different given the different probability of progression inherent to different genotypes. For the same reason, using the risk of CIN3 as a proxy of the risk of cancer needs some corrections when applied to risk groups defined by genotyping.

Conclusions: Risk stratification is an evidence-based approach to determine the appropriate management of women in screening. The best way to measure the risk is still a matter of investigation and scientific debate. The working group will try to conjugate the application of a risk stratification principle with the GRADE methodology (6,7) to develop recommendations.

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SS07 - Real-world experience of the implementation of a screen-triage-treat strategy in LMICs

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#9618

Quality of HPV testing: considerations on training, tests and performance of HPV laboratories

10 - HPV screening

Background/Objectives: The PAVE study is a multi-country NCI-led initiative aimed at validating a cost-effective and accurate screen-triage-treat strategy for resource-limited settings. In nine low- and middle-income countries (LMICs), cervical screening of women aged 25 (for WLHIV) or 30 to 49 years is performed using self-collected dry vaginal samples (FLOQSwab) and HPV testing (ScreenFire RS HPV assay). ScreenFire HPV RS assay is an isothermal amplification extended genotyping test (HPV16, 18/45, 31/33/35/52/58, 39/51/56/59/68) that can assay up to 96 samples/controls in one hour plus preparation time. The assay has been independently evaluated in prior studies, demonstrating high clinical accuracy 1,2,3,4. Extended genotyping is proposed to stratify HPV-positive women according to their risk of developing cervical cancer and to guide clinical management. This presentation discusses key aspects of establishing HPV testing in LMIC settings, including quality laboratory aspects and the role of extended genotyping for management.

Methods: Dedicated HPV laboratories were established in each participating country (Brazil, El Salvador, Honduras, Dominican Republic, Cambodia, Nigeria, Tanzania, Malawi, Eswatini). Laboratories implemented standardized operating procedures (SOPs) addressing sample collection, transport, storage, processing and testing. Anti-contamination and pre-packed reagent solutions were introduced to reduce the chance of post-amplification contamination and the time needed for assay preparation 5. Continuous monitoring and technical support focused on maintaining a clean testing environment and evaluation of results. Laboratories utilized flexible workflows to accommodate local infrastructure and workforce capacity. Most sites used fixed laboratories and some conducted high-yield outreach screening campaigns in remote areas (e.g., Brazil, Honduras).

Results: As of December 2024, ~50,000 women have been screened using the ScreenFire HPV assay across the nine countries. Despite varying levels of infrastructure and laboratory experience, all participating sites achieved high quality and high throughput, reflecting the success of optimized workflows, training and monitoring. The introduction of the pre-packed HPV assay version significantly reduced the chances of post-amplification contamination and the time needed to run the assay, enabling single-day screening in remote areas. A preliminary analysis based on enrollment through July 2024 (N=28,038) showed a CIN2+ yield (absolute risk) of 8% for overall HPV positives and, by genotype channel, 20% for HPV16, else 8% for HPV18/45 combined with 31/33/35/52/58, else 3% for HPV39/51/56/59/68. CIN3+ yield strengthened the risk-based hierarchy of ScreenFire HPV type channels.

Conclusions: The PAVE study demonstrates that high-quality, high-throughput HPV testing is achievable in LMICs conditional on training, infrastructure adaptation, and quality assurance measures. Moreover, the observed disease yield by ScreenFire HPV type group highlights the importance of extended genotyping for risk-based management, especially in LMIC settings where follow-up and treatment resources are often limited.

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#9569

High-yield single-day strategy in vulnerable areas, Amazonas, Brazil

11 - Screening for women difficult to reach

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Background/Objectives: Brazil recently approved the inclusion of HPV testing in the Unified Health System (SUS) for cervical cancer screening. However, developing new screening guidelines poses significant challenges due to the country's vast geographic size and diverse socioeconomic contexts. The MARCO Project (Management of Risk of Cervical Cancer), part of the PAVE Consortium (HPV-Automated Visual Assessment), conducted a proof-of-principle study of a high-yield, risk-based, single-day approach in a remote and hard-to-reach area, São Gabriel da Cachoeira, located in the interior of the Amazonas region-targeting under-screened women.

Methods: Women aged 30 to 49 years old, residing within the São Gabriel da Cachoeira (SGC) municipality, were invited to participate in the study. Participants self-collected cervicovaginal samples (FLOQSwab, Copan), that were tested with ScreenFire Risk Stratification (RS) HPV assay (Atila BioSystems). HPV+ women underwent speculum insertion for cervical image collection after acetic acid application with a portable colposcope (Liger Medical, USA) and exfoliated cells collection for cytology (for later us as comparator). Additionally, ectocervical and/or endocervical biopsies were collected of any visible aceto-white lesion or if no lesion was visible an endocervical biopsy was collected using less invasive-disposable devices (SoftECC-SoftBiopsy, Histologics LLC). Eligible participants who required treatment were offered immediate thermal ablation or next-day excisional treatment.

Results: The 6-day proof-of-principle effort recruited 701 women, 94% of them self-declared as indigenous. A total of 177 (25.2%) tested HPV positive. Hierarchically, HPV16 was detected in 12.5% of the HPV+ participants, HPV18/45 in 21.0%, the HPV31/33/35/52/58 group in 39.2% and in 27.3% HPV39/51/56/59/68 was the only group detected. Regarding age groups, the highest HPV prevalence was observed in the 48% 30-34 years group, followed by 33% 40-44 years group, 32% 35-39 years group, and 21% 45-49 years group. A total of 175 HPV+ (98.9%) participants attended the same-day second visit. Most women underwent inmediate thermoablation 142 (81.1%) and 13 participants had an excisional procedure done the same or the following day. Local histology reported 158 < CIN2, 7 CIN2 and 10 CIN3 results. Among the CIN2 cases, 2 were found only in the ectocervical biopsies and another 2 only in the endocervical biopsies. Then by CIN3, 2 were identified just in the ectocervical biopsies and 1 just in the endocervical biopsies. Expert pathology review is underway.

Conclusions: The study aims to assess the acceptability of the strategy, including same-day treatment with thermoablation, a method to be introduced in Brazil. Successfully, 701 women were recruited and 98.9% of HPV-positive women were evaluated in the high-yield strategy on a single day. Samples and histology were used for research purposes and to and to assess the adequacy of the treatment. Participants who required and were not eligible for immediate treatment were referred to LEEP and and followed up until completion of treatment in SUS colposcopy centers or hospitals.

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#9628

Follow-up and treatment among women living with HIV in Dominican Republic

10 - HPV screening

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Background/Objectives: Timely and effective treatment is one of the three pillars of cervical cancer prevention. Women living with HIV (WLWH) are marginalized in many settings that can impact treatment follow up. The goal of our clinical trial team in Santo Domingo is to ensure high retention of WLWH enrolled in Estudio Oportunidad (ULACNet-302, ClinicalTrials.gov NCT05556772) and timely navigation to treatment.

Methods: Women are asked to attend three study visits at 0, 12, and 24 months. At each visit they have a clinical exam, provide demographic and health history information, and provide clinician- and self-collected samples. Women return in-person to receive their primary screening result if screen test positive, as positive results cannot be delivered by phone. Women set up a separate follow-up appointment for a colposcopy with biopsy and are recalled to discuss biopsy results and treatment options if needed. Treatment referrals are made for all CIN2+ diagnoses and require multiple visits.

Results: A total of 619 women were recruited and 600 completed sample collection at baseline. There are currently 551 participants actively being followed for M12 study visits, with a retention rate of 91.8% (551/600). Among them, 63.2% (348/551) were screen-positive and referred for colposcopy. A total of 46 have been referred for treatment of CIN2+ after M0 and M12 visits. Obstacles to treatment for women include logistics, such as arranging for childcare, lost wages, and transportation, fear of stigma or study procedures, immigration insecurity, and housing insecurity with frequent changes of address or phone number. To encourage retention, study personnel combine in-person results delivery with group education about study procedures. Navigators make visits to HIV clinics and women's home to reconnect women to the study. Clinicians opened an outpatient LEEP clinic with donated supplies at the National Oncology Hospital (INCART), so women referred to treatment have one rather than up to five consult visits before treatment. Average number of days to treatment decreased from 131 days at baseline to 39 days for M12.

Conclusions: A combination of the clinic counselors and navigators reaching out to women on the study, providing a welcoming environment at the clinic and education sessions, and the clinical team working closely with our oncology partners to accelerate time to treatment have led to high retention and improved time to treatment.

WS02 - Vulvar diseases workshop

Hampl Monika
Germany
Hampl Monika
Germany

#9552

New developments in nonsurgical treatment of vulvar HSIL (part of the vulvar disease workshop)

26 - Vulvar diseases and neoplasia

Background/Objectives: This Abstract is part of the vulvar disease workshon in Sunday March 16 Vulvar intraepithelial neoplasia (VIN) can be divided into human papillomavirus (HPV)-associated high-grade squamous intraepithelial lesion (HSIL) and HPV-independent VIN (d-VIN). HPV-associated HSIL is the most common precursor and usually affects patients between the ages of 40 and 50. HPV-independent VIN occurs mainly in older patients (>65 years) and is associated with vulvar inflammatory dermatoses such as lichen sclerosus (LS). Also young women with LS may develop d-VIN. The clinical course of d-VIN is more aggressive and the time to progression to invasive cancer often short.

Methods: Treatment options in VIN are surgical resection/laservaporisation or local medical treatment.

Results: Imiquimod 5% is used in an off label manner in u-VIN with good results. A new treatment option - tested in a Phase 1-2 study recently- is a demethylating substance applied locally. Results on both medial treatments are presented.

Conclusions: VIN can be treated surgically an medically/locally with similar results concerning recurrence and outcome

LW06 - Sessão Científica IV: A Investigação e o Mundo Lusófono

Maocha Izamara
Portugal

Maocha Izamara
Portugal

#9383

Targeted Therapy for HPV-Associated Lesions Using Imiquimod-Loaded Lipid Nanoparticles

08 - Immunotherapy - Immuno-oncology - New treatments

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Background/Objectives: Human papillomavirus (HPV)-associated cervical cancer remains the most prevalent cancer among women globally, with current treatments often leading to increased infertility. The silent nature of the HPV infection, which is asymptomatic in most cases, does not allow for early diagnosis and easily leads to cancer on the cervix. Imiquimod (IQ), an imidazoquinoline with proven antiviral effects against persistent HPV infections, activates immune cells via Toll-like receptors 7/8 when formulated in carriers like nanogels for topical application. Aptamer-based therapies have emerged as a promising field of medicine, offering innovative solutions for diverse applications, to overcome immune therapy's limitations. G-rich aptamers that form G-quadruplex (G4) structures are small oligonucleotide sequences that exhibit enhanced stability, improving cellular uptake andincreased nuclease resistance, with superior thermodynamic and chemical stability. This study explores lipidic nanoparticles loaded with IQ (Lipo IQ) and functionalized with a DNA aptamer, AT11 (Lipo IQ AT11), aimed at enhancing selectivity for cervical cancer cells, combined with the efficacy of essential oils.

Methods: The IQ-loaded lipid nanoparticle was produced using the ethanol injection method and then incorporated into a formulation developed using a universal placebo base enriched with Thymus vulgaris (TEO) or Origanum vulgare (OEO) essential oils. The formulation was characterized by evaluating its pH, buffering capacity, viscosity, osmolality, and bioadhesive properties, alongside assessing the permeation of imiquimod into vaginal tissue. To determine its biological effects, cell viability, and nanoparticle internalization were examined through the MTT assay and confocal microscopy, respectively. Additionally, the formulation's antimicrobial resistance profile was tested against various microorganisms.

Results: The formulations demonstrated favorable physicochemical and physiological properties for vaginal drug delivery and effectively penetrated cells, significantly reducing viability, particularly in cancer cell lines. The addition of essential oils significantly enhanced the cytotoxic effect of Lipo IQ, and the incorporation of AT11 further increased selectivity for cervical cancer cells Additionally, they demonstrated strong antibacterial and antifungal activity in microbial tests, indicating promising antimicrobial activity at higher concentrations, with MIC50 values starting from 0.625%. Permeation studies confirmed effective internalization by cancer cells.

Conclusions: Overall, these results suggest that essential oils can enhance the anticancer effectiveness of IQ-associated liposomes, while AT11 further increases their selectivity for targeting cancer cells offering a potent and selective treatment strategy for HPV-associated cervical lesions.

SS09 - The utility of urine for improved cervical cancer prevention

Gilham Clare
United Kingdom

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#9557

The use of first-void urine to screen women aged 65-79 in the UK: the Catch-Up Screen Project

13 - Self-sampling

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Background/Objectives: Almost half of all cervical cancer deaths in England are among women aged ≥65 years. Women currently being discharged from the NHS screening programme with a negative HPV test will be at extremely low risk of developing cervical cancer, but the lifelong risk will be substantially higher in women who were screened only with cytology (aged ≥65 in 2019 when primary HPV testing was introduced). Cervical cancer screening has been extended to older women in other countries such as in Australia where women are screened up to age 74, and in Denmark where a national catch-up test was offered to every woman born before 1948.

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 over 3 years. 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. The project is funded by Yorkshire Cancer Research.

Results: Uptake rates, HPV prevalence and HPV genotyping will be presented for the first ~5000 women who have been invited to take part. The screening invite has been well received so far with 57% of those invited returning a urine sample. The response rate was highest among those adequately screened when aged 60-64. The HPV prevalence is around 5.0%.

Conclusions: 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. We anticipate that at-home urine tests will address common barriers to screening particularly in under-screened women.

Ducancelle Alexandra
France

Ducancelle Alexandra
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#9192

Efficacy of self-sampling strategies for cervical cancer screening in France: CapU4 study

13 - Self-sampling

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Background/Objectives: Despite the implementation of organised cervical cancer screening since 2018, cervical cancer screening coverage remains moderate in France (60%). Human Papillomavirus (HPV) testing on clinician-collected sample is performed for women aged 30 to 65. Vaginal self-sampling (VSS) is currently recommended for women who are not regularly screened. The aim of the CapU4 study is to evaluate the effectiveness of two experimental invitation strategies (urinary self-sampling [USS] or VSS) in reaching under-screened populations, and to compare them with the conventional invitation strategy, in three French rural administrative departments (Mayenne, Sarthe and Vendée).

Methods: CapU4 is a randomised controlled trial with three arms (5000 women per arm): a control arm in which women receive a conventional invitation letter encouraging them to make an appointment with a healthcare professional for a cervical sample; and two experimental arms in which women receive a conventional invitation letter combined with a USS kit or a VSS kit, depending on the intervention arm. The trial invited 15,000 women aged 30-65 years, who had no screening test recorded since more than four years and who did not respond to an invitation letter within 12 months before. Two types of analysis are performed: per protocol analysis where only responses foreseen in the respective arm will be considered, whereas in the intention to treat analysis also women that are screened not according to the foreseen intervention will be considered as well (also those performed on samples taken by a clinician in the self-sampling arms).

Results: 13,061 women were included in the analysis of the study results. 12.9% of the women invited to the study were excluded: 3.6% for non-distribution of invitation letter, 8.4% for recent cervical sample, 0.8% for hysterectomy, 0.1% for death and less than 0.1% for refusal of consent. 60% of the women invited have previously screened for cervical cancer. The participation rate (per protocol) was 12.9% in the control arm and 11.1% and 12.6% respectively in USS and VSS arms. The participation rate (intention to treat) was 12.9% in the control arm and 23.6% and 23.4% respectively in USS and VSS arms.

Conclusions: Self-sampling at home appears to increase participation in cervical cancer screening by almost 10%. Participation by self-sampling is identical regardless of the strategy offered to women.

Bell Margo
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#9585

Understanding local HPV-related immunity using first-void urine

13 - Self-sampling

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Background/Objectives: Human papillomavirus (HPV) vaccination induces neutralizing antibodies that bind to HPV virions, preventing infection. First-void urine is a valuable sample type for detecting these antibodies, as it captures mucus and debris from exfoliated cells from the female genital organs, providing a local source of immunological information.

Methods: This presentation will provide an overview of the available evidence and future experiments planned to help understand the local HPV-related immunity using first-void urine.

Results: Over the past years, various studies utilizing first-void urine have helped increase our understanding of local HPV-related immunity. In this presentation, results on the detection and stability of HPV-specific antibodies in first-void urine will be shown. Moreover, findings on the sustained neutralizing ability of these local HPV-specific antibodies will be demonstrated. Additionally, progress on the development of (high throughput) assays to assess binding and neutralizing antibodies against all nonavalent HPV vaccine types will be presented. Furthermore, an update will be provided on ongoing studies to address variability in antibody levels caused by factors such as menstrual cycle fluctuations, contraceptive use and menopausal status, exploring biomarkers for normalization of intra- and inter-individual variability.

Conclusions: First-void urine is a powerful and non-invasive tool for assessing local HPV-related immunity. Our work highlights its utility for monitoring HPV vaccine-induced antibodies, understanding transmission dynamics, and evaluating immune responses at the site of infection. Ongoing and future studies using first-void urine will enhance our understanding of local HPV-related immunity, contributing to improved HPV vaccine monitoring and HPV prevention strategies globally.

Griffioen Mila
Netherlands

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#9450

The dynamics of HPV and methylation testing in urine

13 - Self-sampling

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Background/Objectives: Cervical cancer arises from a persistent infection with human papillomavirus (HPV) and typically develops following cervical intraepithelial neoplasia (CIN, graded 1-3). Existing screening programs utilize HPV testing on cervical scrapings and self-swabs. However, to address the challenge of low participation rates, there is a pressing need for novel, less invasive screening methods. Detection of DNA methylation markers, such as ASCL1 and LHX8, in urine has emerged as a promising approach for identifying CIN3+ lesions.

Methods: This study aims to investigate the dynamics of DNA methylation markers in cell-free DNA present in urine samples. A cohort consisting of 25 cervical cancer patients, 25 individuals with CIN2/3 and 25 healthy controls will be recruited to provide six urine samples over the course of three consecutive days, collected both in the morning and evening.

Results: First findings indicate that DNA methylation levels exhibit an increasing trend with disease severity. Notably, cervical cancer patients consistently show elevated DNA methylation levels, whereas healthy controls exhibit lower levels. In contrast, individuals with CIN2 and CIN3 exhibit varying DNA methylation levels across different collection time points, potentially impacting sensitivity. More preliminary data will be shown during presentation.

Conclusions: This investigation will enhance our understanding of the dynamics of DNA methylation markers in the urine of cervical (pre)cancer patients, improving novel screening strategies.

Tranberg Mette
Denmark

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#9653

Methylation of human tumour suppressor genes in first-void urine: the Danish experience

17 - Methylation

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Background/Objectives: First-void urine (FVU) collection for high-risk human papillomavirus (HPV) testing has the potential to improve cervical cancer prevention among under-screened women. In this cross-sectional study, we investigated the clinical performance of DNA methylation markers ASCL1and LHX8 in HPV-positive FVU samples and paired HPV-positive clinician-collected cervical samples (CS) to detect high-grade cervical intraepithelial neoplasia (CIN2+/CIN3+). Methylation-based triage of HPV-positive FVU was compared with HPV16/18 and extended HPV16/18/31/33/52 genotyping.

Methods: First-void urine (FVU) collection for high-risk human papillomavirus (HPV) testing has the potential to improve cervical cancer prevention among under-screened women. In this cross-sectional study, we investigated the clinical performance of DNA methylation markers ASCL1and LHX8 in HPV-positive FVU samples and paired HPV-positive clinician-collected cervical samples (CS) to detect high-grade cervical intraepithelial neoplasia (CIN2+/CIN3+). Methylation-based triage of HPV-positive FVU was compared with HPV16/18 and extended HPV16/18/31/33/52 genotyping.

Results: Data analyses are ongoing.

Conclusions: The final results and conclusions will be presented at the conference.

De Vries Dominique
Netherlands

De Vries Dominique C.
Netherlands

#9627

Methylation testing in vulvar scrapes and urine: the VULVA-screen pilot study

26 - Vulvar diseases and neoplasia

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Background/Objectives: Introduction: Women with vulvar intraepithelial neoplasia (VIN) and vulvar cancer (VC) often face intensive follow-up involving multiple burdensome biopsies to monitor potential disease progression and recurrence. Given the substantial burden of these invasive procedures there is a need for patient-friendly and minimally invasive sampling methods to monitor disease in patients with VIN and VC. Building on evidence from previous studies utilizing urine and scrapes for detecting other anogenital neoplasia, we aim to explore the feasibility of these non-invasive methods for patients with VIN and VC Aim: This proof-of-concept study aims to explore the feasibility and potential of patient-friendly sampling methods for patients with VIN and VC.

Methods: Methods: 20 patients with VC were included. Vulvar scrapes (from the cancer site, adjacent LS or VIN sites, and unaffected sites), as well as self-collected and catheter urine samples were collected pre-operatively. Paired vulvar tissue samples were post-operatively collected. Vaginal scrapes and urine samples from age-matched healthy individuals (control group) were collected as well. All samples were tested for methylation on two multiplex assays, each targeting three genes; ASCL1/LHX8/ZNF582 and GHSR/SST/ZIC1.

Results: Results: A total of 78 vulvar scrapes, collected from the cancer site (n=20) as well as adjacent sites that were affected by LS (n=6), VIN (n=17) or clinically not affected by LS or VIN (n=35) were analyzed as well as 107 vaginal scrapes and 34 urines from controls. Methylation levels were higher in scrapes from the cancer site and its precursor lesions (LS and VIN) compared to clinically unaffected vulvar sites and controls. It was also demonstrated that the methylation levels in vulvar scrapes were comparable with the methylation levels observed in the paired vulvar tissue samples. For the urine samples, higher methylation levels were observed in VC patients compared to controls. In VC patients, methylation levels were higher in self-collected urine than in catheter urine.

Conclusions: Conclusion: DNA methylation testing in vulvar scrapes and urine samples appears feasible as a non-invasive alternative to burdensome biopsies. Moreover, DNA methylation levels in scrapes and urine correlate with disease severity and were similar as found in paired tissue samples.

WS03 - Anal cancer: Screening guidelines

Abramowitz Laurent
France

Laurent Abramowitz
France

#9567

Published anal precancer screening SNFCP guidelines and FAQ, the French perspective (1)

27 - Anal neoplasia

Laurent A[1]

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Background/Objectives: About 2000 new cases of anal cancer are diagnosed annually in France. Squamous cell carcinoma is the most common histological type, mostly occurring secondary to persistent HPV16 infection. Invasive cancer is preceded by precancerous lesions whose treatment benefit has been demonstrated (2).

Methods: In addition to patients with a personal history of precancerous lesions and anal cancer, three groups are at very high risk of anal cancer: (i) men who have sex with men and are living with HIV, (ii) women with a history of high-grade squamous intraepithelial lesions (HSILs) or vulvar HPV cancer, and (iii) women who received a solid organ transplant more than 10 years ago (3). The purpose of screening is to detect HSILs so that they can be treated, thereby reducing the risk of progression to cancer. All patients with symptoms should undergo a proctological examination including standard anoscopy.

Results: For asymptomatic patients at risk, an initial HPV16 test makes it possible to target patients at risk of HSILs likely to progress to cancer. Anal cytology is a sensitive test for HSIL detection. Its sensitivity is greater than 80% and exceeds that of proctological examination with standard anoscopy. It is indicated in the event of a positive HPV16 test. In the presence of cytological abnormalities and/or lesions and a suspicion of dysplasia on clinical examination, high-resolution anoscopy is indicated. Performance is superior to that of proctological examination with standard anoscopy. However, this technique is not widely available, which limits its use.

Conclusions: If high-resolution anoscopy is not possible, screening by a standard proctological examination is an alternative. There is a need to develop high-resolution anoscopy and triage tests and to evaluate screening strategies.

References: (1) Spindler L, Société Nationale Française de Colo-Proctologie (SNFCP) et al. Screening for precancerous anal lesions linked to human papillomaviruses: French recommendations for clinical practice. Tech Coloproctol. 2024 Jan 10;28(1):23. (2) Palefsky JM, et al. Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer. N Engl J Med. 16 juin 2022;386(24):2273-82. (3) Clifford GM, et al. A meta-analysis of anal cancer incidence by risk group: Toward a unified anal cancer risk scale. Int J Cancer. 2021 Jan 1;148

Hillman Richard
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#9615

Cytology or HPV testing, or both?

27 - Anal neoplasia

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Background/Objectives: Anal High grade Squamous Intraepithelial Lesions (HSIL) are the precursors of Anal Squamous Cell Carcinomas (ASCCs). ASCC screening programs typically include an individualised patient risk assessment and Digital Anal Rectal Examination (DARE). A moistened anal swab is also routinely recommended, to triage high-risk patients into more detailed assessment with High Resolution Anoscopy (HRA). HRA is then used to assess the presence, extent and response to treatment of biopsy-proven HSIL. HRA is unpleasant for the patient, is expensive, requires considerable technical expertise and has severely limited access in most jurisdictions. Thus, the tests performed on the anal swab should be chosen to yield maximum sensitivity for the prediction of HSIL, but also keep the numbers of patients referred for HRA to an absolute minimum.

Methods: This presentation will discuss optimal ways of triaging, using various combinations of anal cytology, HPV (hrHPV) genotyping and other tests.

Results: A combination of anal swab cytology and hrHPV genotyping, if deployed in a specific manner, can result in markedly lower HRA referral rates, improved specificity, whilst maintaining high levels of high sensitivity.

Conclusions: Selective use of anal cytology can substantially improve the performance of hrHPV genotyping-based anal cancer screening, by reducing the HRA referral rate, without any substantial loss of sensitivity. However, the exact choice of screening technologies will depend on the local HSIL epidemiology, as well as both laboratory and clinical expertise.

Nyitray Alan
United States

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#9625

Invasive anal cancer detection through DARE and self-palpation

27 - Anal neoplasia

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Background/Objectives: Detection and treatment of anal high-grade squamous intraepithelial lesions can prevent anal cancer; however, healthcare infrastructure for detection of the lesions is poor and stigma related to anal cancer is high which will result in delayed diagnoses of early invasive disease. This talk will review measures that are likely to detect early invasive disease, including digital anal rectal examinations (DARE) and data on self- and companion palpation from the Prevent Anal Cancer Palpation Study.

Methods: A narrative review of the literature was used to collect data on the role of DARE in anal cancer screening and examples of disease detection. Concerning the Prevent Anal Cancer (PAC) Palpation study, 714 sexual and gender minorities who have sex with men in Chicago and Houston received a DARE after performing an anal self- or companion examination (ASE/ACE) to detect any anal abnormality. Agreement between the healthcare provider (HCP)-conducted DARE result and the participant's ASE/ACE result was assessed. Participants were then randomized to practice or not practice the ASE/ACE at home between visit 1 and visit 2 six-months later. Within a day of visit 2, participants performed an ASE/ACE at home and recorded the result. At visit 2, HCPs performed a DARE blinded to the lay result. Agreement and kappa between DARE and ASE/ACE results were assessed.

Results: There is evidence in the literature that DARE can detect small perianal and anal canal malignant masses including superficially invasive squamous cell carcinomas of the anus (SISCCA). Of 714 participants enrolled in the PAC Palpation Study, 564 (79%) returned for visit 2 (282 each in practice and non-practice arms). Visit 2 agreement between ASE/ACE and DARE was 95% (95%CI 94%-97%). Kappa was 0.87, 95%CI 0.82-0.92. Practice did not increase ASE/ACE accuracy, p=0.69. However, number of times performing the ASE/ACE between visits led to more agreement with the clinician's DARE: performing the ASE/ACE 0, 1, and 2 or more times between visits resulted in 89%, 93%, and 98% agreement with DARE, respectively, (p=0.001). The proportion of false negatives declined from 14% at visit 1 to 3% at visit 2 (p<0.001) and false positives declined from 13% to 1%, p<0.001.

Conclusions: Anal cancer screening guidelines recommend DARE given its ability to detect lesions and masses at the perianus and in the anal canal, including SISCCA. In the PAC Palpation Study, agreement was almost perfect between lay exams and an HCP's DARE at visit 2. HCPs who teach their patients how to do a lay anal examination may help patients discover anal abnormalities including cases of early invasive disease.

SS10 - Cervical cancer control in underserved populations

Alberts Catharina
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Alberts C.j.
Netherlands

#9650

Cancer RADAR - A study to assess the current cancer risk among individuals with a migration background across Europe

39 - Public health

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Background/Objectives: The WHO Action Plan for Refugee and Migrant Health highlights the need for strengthened migration health governance and data-driven policymaking. However, the absence of systematically collected and comparable health data among migrants remains a critical barrier. Approximately 12% of the European population (87 million people) has a migration background, and the risk of cancer, particularly cervical cancer, among migrants can differ significantly from both their country of birth and their host country. Cancer RADAR aims to address this knowledge gap by providing a Europe-wide quantification of infection-related and screening-detectable cancer risks, stratified by migration background. This study presents the feasibility of such systematic data collection.

Methods: In collaboration with European cancer registries, we are developing an infrastructure to collect data on infection-related cancers (liver, stomach, and cervical) and screening-detectable cancers (cervical, breast, colorectal, and lung), stratified by migration background. Migration background is defined as a person living in a country different from their country of birth, serving as a proxy for first-generation migration. Working with pilot cancer registries, we developed a protocol to systematically collect cancer data stratified by birth country. Next, we sent out a survey to cancer registries across Europe to assess the feasibility of such data collection.

Results: Cancer data stratified by birth country is (potentially) available from 44 cancer registries across 18 European countries. Barriers to data collection include time constraints, limited infrastructure, financial resources, and the need for ethical approvals for data linkage. Facilitators include the shared vision to reduce inequalities in cancer outcomes and enhance the visibility of registries.

Conclusions: We propose a framework for quantifying and monitoring cancer risks among migrants, providing actionable evidence to inform data-driven policymaking aimed at reducing health disparities.

Mosquera Isabel
France

Mosquera Isabel
France

#9572

CBIG-SCREEN: implementation research to increase participation to cervical cancer screening among vulnerable populations in Europe

11 - Screening for women difficult to reach

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Background/Objectives: In Europe annually 59,000 new cases of cervical cancer are diagnosed, and 27,000 women die of this disease, which is largely preventable. This can be partly explained by low cervical cancer (CC) screening rates among vulnerable women. Several strategies have been proposed to increase participation in CC screening, including offering HPV self-sampling. The CBIG-SCREEN multi-centric implementation research study aims to identify and evaluate context-specific strategies to increase participation of vulnerable women in CC screening in the European Union. Our objective is to report the process to identify the strategies to be piloted in the three intervention countries: Estonia, Portugal and Romania.

Methods: Using the Integrative Systems Praxis for Implementation Research (INSPIRE) approach, we sought to understand the context in the 3 countries. For this we: a) conducted a scoping review on CC screening participation barriers and facilitators among underserved groups, b) engaged with micro, meso and macro level stakeholders to understand their perspectives through collaborative user boards, c) assessed the capacity of CC screening related services, and carried out a SWOT analysis of the health-system building blocks, and d) evaluated the standard of care in the 3 countries. The information was triangulated and we applied the INTERVENER tool, which matches barriers to the cancer continuum organization with evidence-based interventions, to contribute to the identification of the potential interventions to be evaluated. The definition of implementation strategies was guided by the ERIC framework. Discussions were conducted with investigators from each country to draft operational plans to implement and evaluate, using screening based on HPV self-sampling as the main intervention. The discussions on the operational plans addressed each step of the screening pathway from invitation to screening, to follow-up and further assessment for those women who tested positive.

Results: A series of barriers and facilitators were identified. Barriers included knowledge gaps in CC screening, emotions (fear, stigma), challenges in navigating the healthcare system, lack of follow-up and management for screen-positive women, and insufficient human resources. Facilitators included patient reminders, multilingual education for women, and self-sampling options. Several strategies to improve all steps along the CC screening pathway were identified independently in three countries. These included refining of the invitation content, using SMS/emails, sending HPV self-sampling kits to women's homes with prepaid envelopes to send the swab to the laboratory, improving communication methods, and providing patient navigation, such as offering a helpline or support service for scheduling appointments and addressing concerns that may arise throughout the entire screening pathway.

Conclusions: The INSPIRE approach facilitated the planning of the CBIG-SCREEN project. Although the evaluation phase is yet to be completed, preliminary results highlight the value of implementation science in understanding CC screening barriers and selecting tailored strategies to address them. Implementing these strategies will contribute to making CC screening more equitable and responsive to the needs of vulnerable women in European countries.

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#9579

Cervical cancer screening in the trans and non-binary community

11 - Screening for women difficult to reach

Background/Objectives: Background: There is a dearth of literature that addresses cervical cancer 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. In addition, providers, often unaware, treat transgender and non-binary person in belittling ways leading to mistrust in the entire health professional field.

Methods: Objective of this talk will be to review barriers, role of hormonal treatment and cancer risk and best practices for care of transgender and non-binary communities.

Results: Data on the above will be discussed.

Conclusions: Conclusion: To combat these negative experiences, it will be critical to create guidelines for cancer screening based on relevant anatomy and high-risk behaviors, educate health professionals about best practices as well as educate transgender and non-binary communities about the importance of cervical cancer screening.

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Prevention of HPV-associated malignancies in disabled populations

39 - Public health

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Background/Objectives: Individuals with disabilities have a basic right to equal access to healthcare. However, significant multidimensional discrimination violates these rights. This inequitable experience of healthcare is particularly concerning within cancer prevention, particularly as many people with disabilities demonstrate higher vulnerability to cancer risk factors when compared to the general population. This vulnerability in addition to barriers to care have resulted in significant disparities in cancer screening for the disability community. With the goal of informing interventions to support guideline-concordant care for individuals with disabilities, the objective of the current study was to conduct a systematic scoping review of research examining screening for HPV-associated malignances across populations with disabilities.

Methods: Systematic scoping review protocols were followed. Four search approaches (peer-reviewed literature databases, grey literature, search engines, and targeted journal searches) were used to identify research examining HPV-associated screening among IWD.

Results: Eighty-four studies were identified. Over 95% of studies were quantitative and used national health surveys or disability records to demonstrate disparities in screening experienced by IWD, with few interventional studies or studies seeking to reduce gaps in care. The most common HPV-associated screening examined was cervical cancer. The most common types of disabilities studied were physical and intellectual disabilities. Limitations in the research mirrored those identified for disability research among other cancer types, including (1) overlooking key components of disability research, including clearly defining disability; (2) not recognizing the heterogeneity in types of disability and the unique healthcare needs and barriers experienced based on each disability; (3) reinforcing an ableist lens that situated screening disparities with the person with a disability despite evidence of significant influential barriers resulting from provider perspectives and education, as well as clinic accessibility; and (4) minimal consideration of intersectional identities.

Conclusions: Findings reinforce the prevalence of disparities in HPV-related cancer screening experienced by individuals with disabilities, particularly for cervical cancer screening. With disparities in screening established, future research should consider approaches for improving HPV-related cancer screening across disability populations. Furthermore, the literature would benefit from studies examining different types of HPV-related malignancies, and address ableist tendencies in healthcare delivery and cancer screening research.

AI02 - Artificial intelligence in HPV-related precancers and cancers | Part II - Free Communications

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#9310

Artificial intelligence as a potential tool to boost cervical cancer screening programs using individualised risk prediction

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: More than 80% of Swedish women consistently participate in cervical screening and typically receive normal results, resulting in a very low cervical cancer risk of less than 1/100,000 person-years. However, Sweden's current cervical cancer rate stands at over 11/100,000 women-years. We identified 6 different groups of women at high risk and launched a nationwide trial that once per year invites all these women to self-sampling for HPV screening (1). The present work aimed to better understand why cervical cancer rate is so high in presence of very high population attendance of screening by exploring the predictive values of machine learning techniques. The main objective is to train a model that assess individualized cervical cancer risk among women residing in Sweden using their previous screening records. Screening focus on high-risk women will reduce harms of unnecessary screening in women at low risk as well as provide an efficient usage of screening resources.

Methods: The present study used the Swedish national cervical screening registry (NKCx), which records all screening-related data at the individual level, including all HPV and histopathology tests with 100% national coverage of a total of 5.1 million women (2). The dataset comprises birth year, HPV screening results with genotyping data, and histology results. Women follow-up was censored individually using cervical cancer diagnosis, deregistration, or last database screening entry. Models were trained using a light gradient boost classifier to predict cervical cancer risk with 80% of the dataset and stratified 10-fold cross-validation, with similar class proportions, after Bayesian Optimization of hyperparameters. Performance evaluation was performed for cross-validation test sets and validation set of the ensemble model using area under the curve (AUC), weighted accuracy, precision, recall, and F1-score.

Results: Model preliminary results obtained an AUC of 0.95 and a weighted accuracy of 0.4. Precision was 0.013 while recall was 0.78 (F1-score of 0.025). By screening women with highest 10% scores (0.22-0.999), we will predict 69.5% of the total cancer cases. This would correspond to a decline of the current cervical cancer rate of 11.5/100,000 to 3.4/100,000 (below the elimination threshold). As the current one-size fits all program performs 750,000 HPV tests per year in Sweden, risk-based screening of only 300,000 women (10% of Swedish women currently in the program) should be possible to perform in a very short time. The most informative variables for the preliminary model were birth year, calendar year of the last HPV test performed, and last HPV result. Other important variables for risk prediction were number of unorganized screenings, histology HSIL, histology normal diagnosis, immigration, and number of HPV negative results. Further analysis will be focused on refining hyperparameter optimization, addition of features, and performance comparison of different classification algorithms.

Conclusions: Artificial intelligence is a potential suitable solution for identifying women at high risk for developing cervical cancer, but further improvements in the models need to be done to refine the risk scores. Once the model outperforms the current screening strategies, it could be integrated into the clinical settings.

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#8861

A prediction model for high-grade cervical lesions using machine learning in Swedish women

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Cervical cancer remains a major cause of cancer incidence and mortality among women globally. Previous research has used traditional and machine learning methods to predict high-grade cervical lesions (HCL) and cervical cancer, but limitations such as small sample sizes and insufficient validation were noted. This study aims to develop and validate machine-learning models to predict the 1-, 3-, and 5-year incidence probability of HCL or worse (HCL+) among Swedish women.

Methods: Data were retrieved from several Swedish registers. The source populations were 664,919 women who were invited for cervical cancer screening in 2016 and completed their index screening (cytology or human papillomavirus [HPV] test) within one recommended interval (inf50 years: 3 years; sup50 years: 5 years) after invitation. We considered HCL+ diagnoses at least more than 6 months after the index screening (T1). We excluded women who immigrated after T1, died, emigrated, were lost to follow-up, had total hysterectomies, or had HCL+ before T1 (N=46,547). Finally, 618,372 women were included in the study, with 80% randomly assigned to the training set and 20% to the validation set (Figure 1). The included features were: (1) Screening histories: Cytology and HPV test results at the index screening, along with previous screening histories; (2) HPV-related factors: HPV vaccination status and doses, human immunodeficiency virus infection, genital warts, HPV-related non-inflammatory diseases, pre-cancer, and cancer, and maternal history of cervical intraepithelial neoplasia grade 3 or worse; and (3) Demographics: Age at the index screening, women's country of birth, county of residence, education, income, high parity, smoking status during pregnancy, maternal country of birth, and parental education. All feature data were retrospectively retrieved prior to the index screening date. We fitted random forest prediction models to the training set with 10-fold cross-validation. External validation will be performed on the validation set. Model performance was assessed using the receiver operating characteristic (ROC) curve and area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the importance value of each predictor.

Results: Our preliminary results showed that, among the 618,372 women, the 1-, 3-, and 5-year incidence probability of HCL+ were 0.42% (2,587 cases), 1.05% (6,484 cases), and 1.62% (10,018 cases), respectively. In the training set, model performance declined as the prediction interval increased. For the 1-year HCL+ incidence probability, the AUC, sensitivity, specificity, PPV, and NPV were 0.962, 0.940, 0.926, 0.050, and 1.000. For the 3-year incidence probability, the corresponding values were 0.873, 0.755, 0.811, 0.041, and 0.997. For the 5-year incidence probability, these metrics were 0.836, 0.778, 0.726, 0.045, and 0.995. Across all models, the five most important predictors in the training set were cytology at the index screening, age at the index screening, county of residence, high-risk HPV history, and income.

Conclusions: The machine learning models for predicting HCL+ showed strong predictive performance in the training set. Further analyses will be conducted to optimize the models. Furthermore, external validation will be conducted using the 20% validation set, as well as data from another year's invitation (e.g., in women invited for cervical cancer screening in 2017).

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#9479

New Method for hrHPV Screening Using the DeepFM-RF Model: A Multi-Center, Multi-Ethnic Validation Study

16 - Screening methods

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Background/Objectives: To develop and validate a predictive model that integrates DeepFM and Random Forest (RF) algorithms for assessing the risk of hrHPV infection. The model aims to enhance the convenience and timeliness of cervical cancer screenings and improve risk assessments across diverse socio-economic and biological populations.

Methods: This study retrospectively collected epidemiological survey questionnaires from women who underwent cervical cancer screenings (HPV testing and cytology) from December 2016 to December 2017 at nine hospitals in Shanghai, chiefly at Renji Hospital affiliated with Shanghai Jiao Tong University School of Medicine. A hybrid model integrating DeepFM and RF algorithms is employed to assess the hrHPV risk. The model is trained and validated on a comprehensive dataset encompassing demographic, biological, and health-related features, collected from multiple centers and including populations of various ethnicities. To address the class imbalance and ensure representative training and testing splits, stratified k-fold cross-validation is utilized. Performance metrics such as accuracy, sensitivity, specificity, and the area under the receiver operating characteristic curve (AUC) are measured to evaluate the model's effectiveness.

Results: A total of 6,619 patients were included, with 632 in the hrHPV infection group and 5987 in the non-hrHPV infection group. There were 59 items in the survey questionnaire. The model was validated at the Renji Hospital and the Xinjiang Production and Construction Corps ninth division hospital, enrolling 104 and 61 patients respectively. The integrated DeepFM-RF model demonstrated excellent performance across various datasets, achieving an accuracy range between 93.91% to 96.75%, AUC ranging from 0.87 to 0.93, sensitivity between 74.16% to 85.27%, and specificity between 97.23% to 97.94%.

Conclusions: The study has successfully developed a DeepFM-based predictive model which provides a critical tool for early cervical cancer screening, significantly enhancing the accuracy and timeliness of hrHPV risk assessments. This AI-based approach, as a non-invasive model that emphasizes privacy and is easy to promote, significantly complements existing cervical cancer screening strategies. It is expected to improve the accuracy and coverage of screenings, thereby reducing HPV infection rates globally, especially in regions with limited resources and low health education levels.

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#9626

Deep learning and HPV pleomorphic multiorgan induced lesions: automated detection and differentiation of cervical and anal squamous cancers precursors - a multicentric study

25 - Cervical neoplasia

Background/Objectives: Human papillomavirus (HPV) infection carries significant neoplastic risks in both the cervix and anus. Colposcopy and anoscopy are now essential for assessing HPV-related lesions in these regions, but their complexity has led to a shortage of skilled physicians, especially for early detection. This study aimed to develop an AI-based algorithm to identify and differentiate HPV-related dysplastic lesions, specifically between low-grade (LSIL) and high-grade squamous intraepithelial lesions (HSIL), across cervical and anal exams.

Methods: A multicenter retrospective study using 295 colposcopy and anoscopy exams from high-volume centers across four countries (USA, Brazil, France, and Portugal), using three different device types. A total of 80,167 frames were labeled as LSIL or HSIL, based on pathology, to develop a Convolutional Neural Network (CNN). The dataset was divided into training (90%, n=71,890) and testing (10%, n=8,277) sets to evaluate model performance. Key metrics included sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), and the area under the receiver operating curve (AUC-ROC).

Results: In the test set, the CNN achieved 93.9% accuracy, with sensitivity and specificity of 91.5% and 96.1%, respectively, and PPV and NPV of 95.6% and 92.4%. The AUC-ROC was 0.96.

Conclusions: This study introduces the first worldwide AI model for detecting and differentiating HPV-related dysplastic lesions in cervical and anal regions. The high accuracy suggests potential improvements in diagnostic precision and cost-effectiveness, enhancing HPV-related dysplasia detection in clinical practice.

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#9215

Automated evaluation of p16/ki67 dual stain cytology as an artificial intelligence-based biomarker for detection of cervical intraepithelial neoplasia of grade 2 or worse in HPV-positive women in cervical cancer screening

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: HPV-based cervical screening has been implemented in several countries and has shown better performance than cytology-based screening, but relies on additional triage to limit unnecessary colposcopy referrals of HPV-positive women without precancer. p16/Ki67 dual immunostaining cytology test (DS) has shown superior performance for triage of HPV-positive women compared to cytology. The artificial intelligence-based CYTOREADER system with automated scanning and evaluation of DS slides (automated DS) has been developed and showed improved performance compared to manual DS. Here, we compared the clinical performance of DS triage testing versus cytology and automated DS versus manual DS evaluation for the detection of Cervical Intraepithelial Neoplasia, CIN, grade 2 or worse (CIN2+) in HPV-screen-positive women.

Methods: We are conducting a prospective follow-up study including paired cytology and DS slides from HPV-screen-positive women aged 30-59 years from January 2021- April 2023. DS was performed using the CINtec® PLUS assay (Roche Diagnostics, Switzerland). Cytotechnicians are interpreting the cytology and DS slides. A slide is scored manual DS positive if ≥ 1 cervical epithelial cell stain was positive for both p16 and Ki67. Automated DS evaluation is used to quantify the number of DS-positive cells above a likelihood threshold (a ≥ 2 DS cells threshold was used). Histology is grouped as <CIN2 (normal and CIN1) and CIN2+ (CIN2, CIN3, AIS, and cancer) giving a length of follow-up ranging from 20-48 months. The McNemar's $\chi 2$ test is used to compare differences in sensitivity and specificity between the triage tests.

Results: A total of 3000 HPV-positive women aged 30-59 years were included. Cytology and DS evaluations and analyses are currently underway.

Conclusions: The results and conclusions will be presented at the conference.

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#9052

The IMP Diagnostics Roadmap to Implement the GeniusTM Digital Diagnostics System in Real-Life Clinical Practice

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Digital Pathology (DP) systems offer a transformative opportunity to improve diagnostic accuracy and streamline workflows1. Despite these benefits, integrating such systems into clinical practice is complex, involving changes in processes, infrastructure, and training. We present a roadmap for the successful implementation of the GeniusTM Digital Diagnostics System (Hologic), an advanced AI platform for cervical cancer screening2-3, detailing strategic planning, execution, and adaptive measures taken to overcome real-life challenges and optimize diagnostic performance in a high-volume Pathology laboratory.

Methods: IMP Diagnostics implementation began in August 2023, following a preparatory phase to negotiate and assess logistical needs, with the installation of the digital equipment. A workflow redesign was initiated to shift from the analogic cytology process to the digital workflow. The training was conducted in two phases: an initial training session by Hologic (November 2023), involving hands-on experience, case reviews, and competency evaluation; followed by an internal training program in early 2024 to reinforce the new diagnostic protocols and ensure staff proficiency (n=1300 cases, 8 participants). Subsequently, a satisfaction enquiry was performed (1-5 rating scale). Routine roll-out started in May 2024. Continuous monitoring and iterative adjustments were made throughout the early adoption phase to address emerging challenges. Workload capacity was evaluated following the system's implementation. Descriptive statistical analysis was performed using Microsoft® Excel® 2019.

Results: Regarding workflow adaptations, the most significant changes were: batch case registration in the morning (instead of continuous daily registration); staining protocol modification; and the use of the system's dedicated workstations. The GeniusTM system identified 22 additional cases with ≥LSIL compared to the analogic screening, representing a 10% increase in detected lesions. Regarding challenges faced, there were initial delays in service distribution (due to unforeseen increase in overall exam volume; initial learning curve; limitation to three workstations and technical errors, which affected the targeted digitization timeframe). To mitigate these issues, new staff schedules were developed, an additional digital viewing station was acquired, and further expansion, including the potential addition of a second scanner, is under consideration. Staff satisfaction surveys revealed a positive response, with high scores for ease of navigation (4.8), diagnostic quality (3.9), and overall system evaluation (4.1), indicating growing confidence and acceptance of the system. The system enables the resident cytotechnicians to screen two to three times more cases per day.

Conclusions: The successful implementation of the GeniusTM system in a Pathology Laboratory setting requires meticulous planning, comprehensive training, and dynamic problem-solving to adapt to unforeseen challenges. We present a practical framework for other laboratories aiming to adopt similar DP systems, highlighting the critical role of continuous staff engagement, flexible resource management, and data-driven decision-making in achieving seamless integration. Our findings demonstrate that this system can significantly enhance diagnostic accuracy and operational efficiency, providing a replicable model for digital transformation in cytopathology practices.

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#9560

Effect of an artificial intelligence-guided colposcopy for detection of cervical precancer and cancer: a multicentre, randomized, crossover trial

21 - Artificial intelligence - Big data - Machine learning

Background/Objectives: Colposcopy remains as the standard procedure to guide both biopsy for identifying cervical precancer and cancer and treatment approaches. Our team has developed an artificial intelligence (AI)-guided colposcopy to improve cervical intraepithelial neoplasia (CIN) grade 2 or higher (CIN2+) detection. We aimed to evaluate the auxiliary effect of the AI-guided colposcopy in clinical practice.

Methods: We did a multicentre, randomized, crossover trial at four hospitals in China. Eligible patients, who were 18 years of age or older and tested positive on cervical screening, underwent colposcopy procedure. Ten colposcopists of varying levels of expertise were randomly assigned to independently evaluated cervical images with or without AI assistance. The AI produced a binary diagnosis and the patient-level probability of the presence of CIN2+. The main study outcome was histologically confirmed CIN2+ detected at cervical biopsies. Diagnostic performance of the colposcopists with or without AI assistance was compared.

Results: Between Jan 1, 2023 and Jan 1, 2024, A total of 815 patients were prospectively recruited for the crossover trial. For AI alone to detect CIN2+, diagnostic sensitivity was 85.3% with a specificity of 56.4%. The AI assistance demonstrated improved specificity compared with the colposcopy impressions of colposcopists (52.5% vs 35.3%, $p<0.001$), but no statistic difference in sensitivity (89.1% vs 89.5%, $p>0.999$).

Conclusions: In this randomized crossover trial of detecting CIN2+ with or without AI assistance, the AI-guided colposcopy demonstrated positive human-AI interaction, which suggested its potential to facilitate an assistive clinical diagnosis. Further utilization of this system could help colposcopists confirm where to perform a biopsy to diagnose high-grade lesions and reduce unnecessary biopsies

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#9217

Large language models in cervical cancer control education: Comparing ChatGPT and Baichuan4 to human-generated multiple choice questions

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: The shortage of experienced colposcopists hinders cervical cancer control, underscoring the importance of effective education. Test-enhanced learning, facilitated by well-crafted questions, improves student outcomes. However, creating medical exam questions is labor-intensive. Automated generation of high-quality multiple-choice questions (MCQ)using large language models (LLMs) could be beneficial. This study compares the quality of LLM-generated MCQ with those created by humans in colposcopy and treatment of cervical precancer.

Methods: This cross-section study comprised 2 phases: MCQs generation and evaluation. For the first phase, an experienced clinician panel, ChatGPT 4o (Open AI), and Baichuan4 (Baichuan AI) generated MCQs based on the textbook "Colposcopy and Treatment of Cervical Precancer" published by the IARC using optimized prompts. Each group was tasked with generating 40 MCQs across three thematic domains: general colposcopy, treatment of cervical precancer, and management of cervical precancer. The generated 120 MCQs were then evaluated from two perspectives: experts and general practitioners. Twelve experts subjectively assessed the quality of the MCQs across five dimensions: correctness, clarity and specificity, cognitive level, clinical relevance, and explainability. The difficulty and discriminatory power of the MCQs were objectively tested by practitioners. They were all asked to identify whether each MCQ was generated by clinicians or LLMs.

Results: A total of 312 practitioners from 28 provinces in China, specializing in colposcopy and cervical precancer treatment, were recruited to test the MCQs. MCQs generated by clinicians exhibit a higher overall cognitive level (4.00 ± 1.08) compared to those by ChatGPT 4o (3.68 ± 1.07, p = 0.024) and Baichuan 4 (3.71 ± 1.13, p=0.043). There were no differences between ChatGPT 4o and Baichuan 4 across these five dimensions. After stratifying by knowledge domains, clinicians surpassed LLMs' performance in cognitive level (4.10 ± 0.86 versus 3.18 ± 1.07, p < 0.001; 3.47 ± 1.11, p = 0.017) and clinical relevance (4.55 ± 0.63 versus 4.12 ± 1.05, p = 0.053; 4.07 ± 1.14, p = 0.049) for the treatment domain, while no significant differences were found in the general and management domains. After excluding 12 MCQs that failed the correctness criteria, 108 MCQs were evaluated by practitioners, including 38 from clinicians, 37 from ChatGPT 4o, and 33 from Baichuan4. No significant differences were observed in overall difficulty among clinicians (59.51 ± 24.50), ChatGPT 4o (61.89 ± 25.36), and Baichuan4 (59.79 ± 26.25). MCQs generated by clinicians demonstrated a slightly higher overall mean discriminatory power (0.38 ± 0.14) compared to ChatGPT 4o (0.30 ± 0.19, p = 0.052) and Baichuan4 (0.33 ± 0.15, p = 0.180). The recognition rates for clinician-generated questions are similar between experts and general practitioners, at 58.33% (49.51% - 67.15%) and 58.53% (56.76% - 60.31%), respectively. However, experts outperform general practitioners in identifying LLM-generated questions.

Conclusions: Our study demonstrated the feasibility of generating MCQs using LLMs with engineered prompts. The LLM-generated MCQs were largely comparable to those produced by clinicians, but clinicians maintained an edge in cognitive level and clinical relevance. While LLM-assisted MCQ generation has the potential to enhance efficiency, it must undergo a rigorous fact-checking and validation process to ensure the quality of medical education.

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#9156

Artificial intelligence based screening by colposcopy: an image catalogue to build machine learning algorithms for Female Genital Schistosomiasis and gynaecological disorders

38 - Low resource settings

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Background/Objectives: Schistosomiasis, a neglected tropical disease, is widely spread in Madagascar with prevalence of up to 61% in some regions. Cervical cancer, mainly associated with HPV infection, is the most frequent cancer among women in Madagascar. HPV prevalence of 43% is described among screened population in Madagascar. Opportunities to screen for cervical cancer or neoplasia as well as other gynaecological disorders are scarce, especially in remote areas. So far, no regular screening for HPV exists, neither is there an implemented HPV vaccination programme in the country.The diagnosis of female genital schistosomiasis (FGS), a chronic manifestation of S. haematobium infection, is also hampered by the limited diagnostic techniques adapted to endemic conditions. The symptoms' resemblance to sexually transmitted diseases complicates the diagnosis, likewise, does the existing general scarce knowledge of the disease among clinicians due to missing training and mention of the disease in medical textbooks. This results in misdiagnosis and mistreatment ranging from repeatedly prescribed antibiotics to radical surgical treatment due to suspected cervical cancer lesions. According to the WHO FGS Atlas, the following clinical findings should be screened for by visual inspection or colposcopy in cases of suspected FGS: grainy sandy patches, homogenous yellow sandy patches, abnormal blood vessels and rubbery papules. The use of Artificial Intelligence has been shown to be auspicious in supporting medical diagnosisin which visual investigations are involved. Multiple studies have shown promising results in the diagnosis of cervical neoplasia with the help of automated image analysis.

Methods: Colposcopy images of 500 women between 18 - 49 years living in the rural area of Boeny region of Madagascar were collected at three primary health care centres by trained midwives with handheld colposcopies. The images were reviewed by two independent double-blinded gynaecologists, both experts in FGS diagnostic. A catalogue of these images was produced in order to allocate images in three different groups: healthy, FGS, non-FGS lesions. An image annotation tool, called Label Studio, was used to label the clinical findings of FGS.

Results: 307 images were included in the analysis, 194 FGS positive images and 113 FGS negative images. All images with discordant diagnosis results between the two gynaecologists were excluded. An image catalogue was constructed to build a machine learning algorithm.

Conclusions: Our preliminary results show the importance of creating standardized assessment tools for the detection of diseases that is not as objective as a laboratory result. The establishment of artificial intelligence based technology for the detection of FGS would also create the opportunity to integrate colposcopy screening for the diagnosis of cervical neoplasia and/or cervical cancer as well as to integrate HPV screening especially for women difficult to reach living in remote areas.

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#9370

County-Level HPV Vaccination Rates: Analysis Of 10 Million Publicly-Insured US Adolescents

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Nearly 40% of US children and adolescents are covered by public-funded health insurance. We estimated state and county-specific HPV vaccination rates from a large nationwide dataset of publicly-insured US adolescents.

Methods: ublicly-insuredadolescents across 50 states were identified during 2016 to 2020 (latest-available years) from the dataset. Analyses were restricted to adolescents aged 13-15 years with no insurance gaps from their 11th birthday. Data from ten states with universal vaccine purchase policies were excluded. HPV vaccination rates (≥1 dose) were examined, at the national-, state-, and county-(stratified by urban and rural designation) levels, using the Current Procedural Terminology codes for HPV vaccines. Significance was tested at P<.05 (two-tailed).

Results: Of 10 million enrollees aged 11-15 years,2.8 million [2.4 million urban and 0.4 million rural] adolescents met the study criteria. Over one-half (54.3%) of the publicly-insured adolescents in 2020 had received an HPV vaccine dose. Nationally, rate was 8.8%-point higher in urban counties (P<.001). State averages exceeded 70% for Maryland, Delaware, Nebraska, and Tennessee, but were <30% in Mississippi, North Dakota, New Jersey, and Oklahoma. In most states, urban counties had higher HPV vaccination rates; the urban-rural difference exceeded 25%-points in Utah, Missouri, Nevada, Montana, and Illinois. Rates varied from 1.7% in Benson County (North Dakota state) to 90.9% in Brooks County (Texas state).

Conclusions: Substantial urban-rural HPV vaccination disparities among publicly-insured adolescents. Given that most of these children are from low-income families, interventions to mitigate geographic disparities in this vulnerable population are urgently needed.

HN04 - HPV and Head & Neck Forum - Screening for HPV+ oropharyngeal cancer

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#9646

Update on the Hamburg HPV-OPC Screening Study (PHORECAST)

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: An increasing proportion of oropharyngeal cancers (OPC) are caused by human papillomavirus (HPV-OPC). Serum antibodies against HPV16 early proteins as well as cell-free HPV DNA (cfHPV DNA) in liquid biopsies are emerging pre-diagnostic markers. We present an update of our prospective study on HPV serology-based screening and early detection of HPV-OPC.

Methods: HPV16 antibodies were measured in 4,424 sera of the Hamburg City Health Study (HCHS), a population-based cohort. The following participants were enrolled in a clinical follow-up study: 1) participants seropositive for HPV16 E6 and at least one additional early antigen (high-risk for HPV-OPC development); 2) participants positive for E6 alone. Participants underwent 6-monthly head and neck examinations and blood draws. Suspicious lesions were evaluated by MRI and panendoscopy with biopsy. cfHPV DNA detection in blood plasma was performed by dPCR.

Results: Ten of 12 participants considered to be at high-risk participated in regular follow-up examinations. After 5 years of active follow-up, 5/10 were diagnosed with stage I HPV-OPC. Of the 24 participants seropositive for HPV16 E6 only, 11 attended follow-up, among which a further stage I HPV-OPC was diagnosed. This case was seropositive for a second early antigen at the time of diagnosis. Three of the overall 6 cases presented with either no or a single lymph node metastasis. cfHPV DNA was detectable at diagnosis in 5 cases at varying levels, but not in the only patient without lymph node involvement. Three cases with available pre-diagnostic blood samples showed a steep increase in cfHPV DNA levels in the 6 months prior to diagnosis.

Conclusions: HPV16 serology-based screening is suited to prospectively identify HPV-OPC cases. In a future screening scenario, longitudinal assessment of additional biomarkers may dynamically refine the risk classification.

SS12 - Strategies for faster cervical cancer elimination

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#9565

Cervical cancer screening after elimination of incident HPV

16 - Screening methods

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Background/Objectives: As the era is approaching when vaccinations will have resulted in that HPV infection is no longer transmitted, design of effective campaign strategies to target screening efforts and identify women at-risk will become increasingly important. In 2019, Sweden launched a nationwide trial aimed at enhancing screening participation among women at elevated risk of cervical cancer. This initiative has persisted annually being optimized over time to improve efficiency and resource utilization to the needs of each woman.

Methods: In Sweden, where comprehensive screening records are maintained in the national quality register (NKCx), it is straightforward to calculate each woman's cervical cancer risk utilizing these records. Previous research has shown significant variability in cervical cancer risk based on screening history.1-4 Key high-risk profiles identified include: a) Women with atypical glandular cells (AGC); b) Women with abnormal screening findings above the age of 50, but without sufficient follow-up; c) Women with low-grade/high-grade squamous intraepithelial lesions (LSIL/HSIL), lacking follow-up; d) Women testing positive for HPV 16/18 with no cytology abnormality afterwards and; e) Women who have never attended screening in the past 10 years.1-4 In 2019, a risk-based pilot study was initiated targeting 920 women with AGC or abnormal findings over age 50 in the region of Skåne, Sweden. Women were invited via SMS and letters to perform HPV self-sampling. The pilot demonstrated feasibility, with 13% of women ordering the self-sampling test. Between 2019 and 2021, this approach expanded to include all five high-risk profiles. By 2021, we reached approximately 26,000 high-risk women and since 2022, risk-stratified screening has been implemented nationwide, covering up to 90,000 women annually.

Results: In the 2020 pilot, we invited 6,398 women with high risk profiles and 20.0% responded and ordered a self-sampling kit. In the 2021 pilot, we invited 23,318 women (mostly long-term non-attenders) and 9.51% responded. The full-scale campaign targeting 93,609 women all over Sweden was launched in September 2022. Among self-samples returned, 14.6% were HPV-positive and, for women testing positive for HPV 16/18/45, the positive predictive value (PPV) for high-grade lesions (HSIL+) was 22.8%, emphasizing the effectiveness of targeted follow-up. Additionally, the PPV for long-time non-attenders was 100%, indicating significant lesions are likely to be detected once these women engage with screening. Ongoing efforts focus on improving convenience for women (we are nowadays sending self-sampling kits directly to women´s home addresses when the 5-year cumulative risk is > 1% and see double participation), ensuring follow up for HPV positive women and refining risk stratification.

Conclusions: Effective campaigns to reaching populations at high risk of cervical cancer will be important for cervical screening after elimination of incident HPV infections. We find that a nationwide campaign using self-sampling and multiple contact strategies can be readily implemented in the whole country as a regular process. Further efforts are directed to improve the precision of the risk-stratification algorithm, to improve participant convenience, and to ensure that screen-positive women are followed-up.

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SS14 - Evidence on the comparability of self-sampling VS provider-sampling for HPV testing

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#9568

Comparison of the ScreenFire and Xpert HPV assays for the detection of human papillomavirus and cervical precancer among women living with HIV in Malawi

09 - HPV testing

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Background/Objectives: The World Health Organization (WHO) recommends human papillomavirus (HPV) testing for primary cervical cancer screening, including among women living with HIV (WLWH). Low-and-middle-income countries (LMICs) account for 85% of the cervical cancer burden globally, yet have limited access to HPV-based screening, largely due to cost. This study aims to compare the performance of a rapid, isothermal amplification HPV assay (ScreenFire) to that of the Xpert HPV assay for the detection of HPV and cervical precancer among WLWH in Malawi.

Methods: We utilized stored self- and provider-collected specimens from a prospective cohort study of WLWH in Malawi from July 2020 to February 2022. Specimens were tested with both Xpert and ScreenFire HPV assays. The overall and within-channel non-hierarchical agreement between ScreenFire and Xpert was determined for both self- and provider-collected specimens. Hierarchical ScreenFire HPV positivity by channel was compared to Xpert for each histological diagnosis - cervical intraepithelial neoplasia grade 2 or worse (CIN2+) compared to <CIN2.

Results: 315 matched self- and provider-collected specimens had valid results from both Xpert and ScreenFire testing and were included in analyses, of which 279 and 36 where HPV positive and HPV negative, respectively, on Xpert self-collection. Of the 315, 245 (78%) had normal pathology, 21 CIN1 (7%), 14 CIN2 (4%), and 35 CIN3 (11%). Of the 245 with normal pathology, 213 (87%) and 188 (77%) were HPV-positive on Xpert and ScreenFire self-collected specimens, respectively. Among provider-collected specimens, the assays had 80% agreement on overall HPV positivity (unweighted kappa 0.59, 95% 0.50-0.69). ScreenFire was HPV-positive in 90% of self-collected specimens that were HPV-positive on Xpert. Channel agreement between the assays was high for both self- and provider-collected specimens, but slightly lower for HPV18/45. In hierarchical analysis, ScreenFire demonstrated high concordance with Xpert testing for detecting CIN2+ cases in all channels, missing no HPV 16 or HPV 18/45 positive CIN2+ case that was positive on Xpert, in both self- and provider-collected specimens.

Conclusions: In this study of stored specimens,the ScreenFire HPV assay performed well in the detection of HPV and CIN2+ among WLWH compared to the Xpert HPV assay. If supported by larger validation studies, ScreenFire could be an affordable alternative point-of-care HPV assay for use in LMICs.

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#9630

Performance of ScreenFire HPV testing on provider-collected vs self-collected samples in the Oportunidad Study in the Dominican Republic

09 - HPV testing

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Background/Objectives: Cervical cancer incidence remains high (ASR 17.9 per 100,000) among women in the general population in the Dominican Republic, with even higher rates among women living with HIV (WLWH).Estudio Oportunidad (ULACNet-302, ClinicalTrials.gov NCT05556772) enrolled 619 WLWH in Santo Domingo in an ongoing longitudinal cervical cancer screening trial.

Methods: The goal of this analysis is to determine whether the diagnostic accuracy of high-risk HPV genotyping to detect CIN2+ among WLWH is comparable in provider vs self-collected samples using the Screen-Fire Assay (Atila BioSystems, Sunnyvale, CA) at baseline. The assay detects 13 high-risk HPV (hrHPV) types: HPV16, HPV18/45, HPV31/33/35/52/58, and HPV39/51/56/59/68. Data from 505 women with valid paired samples were available for this analysis, including 46 CIN2+.

Results: Overall, there was 77.2% agreement to detect hrHPV between provider and self-collected samples (kappa 0.54), with 37.6% and 48.9% hrHPV positive, respectively. There was identical sensitivity to detect CIN2+ (91.3%, 95% CI 79.0-96.7) for both approaches to sampling. Specificity was higher for provider-collected (67.8%, 95% CI 63.3-71.9) than self-collected samples (55.3%, 95% CI 50.7-59.8). When positive results were restricted to eight types (HPV16/18/45/31/33/35/52/58), sensitivity was higher for self-collected (89.1%, 95% CI 76.4-95.4) than provider-collected samples (80.4%, 95% CI 73.3-81.0). More women would be referred to colposcopy with self-collected HPV positive samples under either the unrestricted or restricted algorithm; however, restriction missed only one CIN2 (HPV group 39+) with self-collected samples compared to missing two CIN2s and three CIN3s with provider collected samples (HPV group 39+).

Conclusions: Overall, self-collected samples performed as well as provider-collected samples to detect CIN2+. Further, restriction to eight types and use of self-collected samples may be the best approach to primary HPV screening in this WLWH population.

CS02 - Recommendations for the management of partners of women infected with high-risk HPV

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#9573

Physical and Emotional Implications for the Partner of HPV-Positive Women

32 - HPV transmission

Background/Objectives: This presentation explores the multifaceted implications of human papillomavirue (HPV) on partners of carriers

Methods: It delves into the modes fo transmission, epidemiology , health risks associated with HPV, emphasizing both short-term and long-term effects

Results: Partners of HPV carriers may faced increase susceptibility to HPV related conditions, including genital warts and cancers such as penile, anal throat snd cervical cancers. Key fingings highlight the transmission dynamics whitin couples, revealing significant oral-genital and genital-genital concordance rates, along with risks of sequential infections. Psychological and emotional impacts are addressed. emphasizing the stress, stigma, and relationship challenges HPV carriers and their partners experience.

Conclusions: The presentation underscores the importance of vaccination and safe practices in reducing transmission and overall community prevalence. Recommendation include fostering open communication within relationships. promoting mutual emotional support. and adopting preventive measuers like regular screenings and vaccination campaing. The conclusion reiterates HPV's commonality and manageability, advocating fo education, proactive health measures, and stronger support systems to build healthier relationships

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SS11 - Cervical cancer accelerated elimination policies

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#9586

How public health decision modeling can inform cervical cancer accelerated elimination policies

39 - Public health

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Background/Objectives: HPV vaccination and cervical cancer screening are globally recommended public health policies. In several countries, vaccinated birth-cohorts are progressively reaching the screening age range, leading to the need of tailored risk-based recommendations for optimizing resource allocation and to minimize screening-related adverse effects among these women. The objective of this presentation is to illustrate how mathematical models can be informative tools to support screening context-specific decisions, integrating HPV vaccination and HPV risk-based screening.

Methods: To assess effectiveness, screening-related harms, and cost-effectiveness of integrating HPV vaccination and risk-based screening, we used a set of mathematical models of transmission of multiple oncogenic HPV types and disease progression from infection to cervical cancer. Models were informed with data describing demographic, behavioural, and epidemiological characteristics of several European populations as well as with figures descriptive of the performances of vaccination and screening program. Strategies integrating HPV vaccination and HPV-based screening were explored, estimating short-term reductions on the incidence of high-risk HPV infections. Risk-based screening algorithms were designed to explore less intensive screening intervals among vaccinated women. To virtually adapt risk-based screening to any setting in Europe, we structured risk-stratified policies accounting for determinants of woman's cervical cancer risk, such as age, screening history, HPV vaccination status, and population vaccination coverage.

Results: Demographic, behavioural, and epidemiological data useful to inform mathematical modes will be summarized during the presentation. Integrating HPV vaccination and screening was estimated to lead to an accelerated decline of high-risk HPV infections, whereas using risk profiles was found to be cost-effective, optimizing resource requirement and allocation in vaccinated populations.

Conclusions: Mathematical models have the potential to inform cervical cancer decisions, extrapolating available evidence to project impact and cost-effectiveness of cancer prevention in understudied populations. In vaccinated populations, moving towards risk-based screening can provide an efficient allocation of health resources, producing similar benefits than one-size-fits-all approaches. These findings, methodologies, and tools will provide a substantial contribution to elimination of cervical cancer, helping also to evaluate strategies maximizing protection for underserved population hard to reach within cervical cancer screening programmes.

SS16 - Cervical cancer in sub-Saharan Africa

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#9576

Harmonizing cervical cancer screening data and population-based cervical cancer data in sub-Saharan Africa - The IARC-GICR Centre of Expertise

37 - Health education

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Background/Objectives: Elimination of cervical cancer is a global health priority. While monitoring cervical cancer screening is a critical tool to achieve WHO's eliminating target, essential skills for monitoring and evaluating cervical cancer elimination are lacking in SSA. The National Cancer Registry of South Africa was inaugurated as the International Agency for Research on Cancer (IARC)-Global Initiative on Cancer Registry Development (GICR) Centre of Expertise in 2022 to provide skills for research and training in cervical and childhood cancers. Its primary focus is to provide skills for monitoring the elimination of cervical cancer using the population-based cancer registries in Sub-Saharan Africa. The aim of this abstract is to provide an introduction and summary of training activities conducted by the IARC-GICR Centre of Expertise in SSA.

Methods: The African Cancer Registry Network invited members from cancer registries and organizations involved in cervical cancer to participate in a training program on record linkage of cervical cancer screening and cancer registry data. Participants were selected based on merit, relevance, and role in cancer registration. The training program consisted of online and in-person sessions, with a blended learning approach combining live Zoom sessions and self-paced online content with mentorship support provided. Participants were trained in using the Stata statistical tool, data cleaning, and record linkage. The in-person training included additional training on stakeholder engagement and multisectoral research collaboration.

Results: Sixteen participants from eight SSA countries, with various roles such as Epidemiologists, Cancer registrars, Statisticians, Data managers and Data clerks were trained online on record linkage of cervical cancer screening registers and the Cancer registry database. 38% of participants were females, and 62% were males from SSA countries such as Zimbabwe, Namibia, Mauritius, South Africa, Rwanda, Eswatini, Tanzania and Nigeria. The training outcomes were the development of a research topic and abstract. Some of the research topics are as follows: Cervical cancer screening in women with and without HIV in Eswatini Cervical cancer survival in Mauritius Cervical cancer screening outcomes by HIV status in Bulawayo, Zimbabwe Cervical cancer screening outcomes by HIV status in Kilimanjaro, Tanzania Cervical cancer survival in Rwanda Evaluation of cervical cancer screening programmes in Ekurhuleni, South Africa

Conclusions: Training program on record linkage of cervical cancer screening and cancer registry data has successfully equipped participants from various SSA countries with essential skills for monitoring and evaluating cervical cancer elimination indicators. The blended learning approach, combining online and in-person sessions with mentorship, proved effective in transferring knowledge and enhancing participants' abilities in record linkage. This capacity-building initiative contributes to the global effort in eliminating cervical cancer and improving women's health outcomes in the SSA region.

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#9592

Cervical Cancer Survival in the Republic of Mauritius: A Retrospective Cohort Analysis

03 - Epidemiology and natural history

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Background/Objectives: Despite a decline in cervical cancer incidence in Mauritius, a Small Island Developing State (SIDS) off the east coast of Africa, it remains the fifth most common cancer and third leading cause of cancer mortality among women. The age-standardized incidence rate decreased from 24 to 11 per 100,000 between 1991-1995 and 2011-2015. This study evaluates population-based cervical cancer survival and excess mortality hazards by age, community, and histological group.

Methods: Data on 880 confirmed cervical cancer cases (2011-2020) from the Mauritius National Cancer Registry were linked to national mortality records. Observed survival rates at 1-, 3-, and 5-years were calculated by age category (<45, 45-54, 55-64, >65 years), community (Hindu, Muslim, General Population, Sino-Mauritian), and histological group using "sts" function in Stata 18.0. Excess hazards were analysed using multivariate Cox proportional hazards models.

Results: A total of 824 cases were included in the survival analysis, with 56 cases excluded due to missing or invalid dates of incidence or last contact. The mean (sd) age at diagnosis was 56.4 (15.3) years, with a median follow-up of 5.3 years. Overall survival rates were 93.1% (95% CI 91.1% - 94.7%), 88.6% (95% CI 86.1% - 90.7%) and 87.1% (95% CI 84.4% - 89.3%) at 1-, 3-, and 5-years, respectively. Patients >65 years had an 80% higher mortality risk (HR 1.8, 95% CI 1.1-2.9) compared to those <45 years. Excess hazard ratios were higher among the General Population (HR 1.6, 95% CI 1.0-2.3) and Sino-Mauritian (HR 3.1, 95% CI 1.3-7.5) communities compared to the Hindu community. There were no significant differences between histological groups.

Conclusions: Mauritius exhibits high cervical cancer survival rates compared to Sub-Saharan Africa. Key mortality predictors include advanced age and belonging to specific communities. Ongoing efforts aim to meet the WHO cervical cancer elimination target.

References: Koon Sun Pat, Marvin, et al. "Trends in Cancer Incidence in the Republic of Mauritius, 1991-2015'. Cancer Epidemiology, vol. 63, Dec. 2019, p. 101616. DOI.org (Crossref), https://doi.org/10.1016/j.canep.2019.101616. Ministry of Health and Wellness. Mauritius National Cancer Registry Report 2022.

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#9599

cervical cancer screening outcomes by hiv status in bulawayo, zimbabwe

25 - Cervical neoplasia

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Background/Objectives: Cervical cancer is a major public health concern in Zimbabwe particularly among women living with HIV. In Bulawayo, cervical cancer accounted for 36% of all cancer diagnosed among women for period 2012-2021. The Visual Inspection with Acetic acid and Cervicography(VIAC) clinic was opened at Mpilo Central Hospital to offer free service to women(30-49 years) and HIV positive women at any age in Bulawayo and southern region of Zimbabwe. Understanding the intersection of HIV status and cervical cancer screening outcomes is critical for improving cervical cancer elimination strategies .This study aims to evaluate cervical cancer screening outcomes stratified by HIV status.

Methods: Using STATA, we linked and matched records from Bulawayo Cancer Registry for women diagnosed with cervical cancer(n=2244 cases) and records(11401) of women who were screened for cervical cancer using VIAC method at Mpilo Central Hospital from 2012-2021.The cancer registry data included only women diagnosed with cervical cancer in Bulawayo Metropolitan province.Descriptive statistical methods were applied to describe the cervical cancer screening outcomes by HIV status.

Results: A total of 13645 records constituted this study. The probabilistic record linkage revealed that 254 women from Bulawayo with cervical cancer were screened for cervical cancer during 2012-2021.About 114 negative women screened 86(75.4%) tested VIAC negative, 7(6.1%) had VIAC positive results with 21(18.4%) VIAC suspicious results. Of the 135 HIV positive women screened 80(59%) tested VIAC negative results, 13(10%) tested VIAC positive with 42(31%) being VIAC suspicious. Only 5 women had unknown HIV status with 3(60%) VIAC negative and 2(40%) VIAC suspicious results. A total of 169(66.5%) women tested VIAC negative and yet diagnosed with cervical during this period.Only 20(7.9%) had VIAC positive results and cervical cancer diagnosis whilst 65(25.6%) women had VIAC suspicious results and cervical cancer diagnosis during the period of study.

Conclusions: This study indicates that HIV positive women have a significant higher proportion of abnormal VIAC results compared to HIV negative women . These screening results highlights the need for ongoing monitoring and follow-up for women with suspected abnormalities , especially those who are HIV positive. There is a greater need for targeted interventions to address the dual burden of cervical cancer and HIV among women in Bulawayo. Addressing this issue requires a multifaceted approach including improved screening, education on cervical cancer risks and the integration of healthcare service to reduce morbidity and mortality rates. The finding that a significant number of women diagnosed with cervical cancer in Bulawayo had previously tested VIAC negative highlights critical issues related to screening efficacy and the potential for false negatives.This situation calls for increased awareness about limitations of VIAC screening tests, improved education efforts regarding follow-up care and possibly the intergration of more sensitive diagnostic techniques to ensure timely detection and treatment of cervical cancer in Bulawayo and the country at large.

#9593

Cervical screening outcomes by HIV status in Kilimanjaro, Tanzania

03 - Epidemiology and natural history

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[9], ,

Background/Objectives: Cervical cancer is the most common cancer among women in Tanzania both incidence and mortality. Cervical cancer screening is critical to preventing the disease. Women with HIV have an increased risk of cervical cancer due to their impaired immune system. Our study intended to determine cervical cancer screening outcomes by HIV status in Kilimanjaro region of northern Tanzania.

Methods: We conducted a retrospective cohort study between 2010 and 2024, linking cervical cancer screening data from the Reproductive Health Centre (23,294 women) with cervical cancer incidence data from the Kilimanjaro Population-Based Cancer Registry (2,814 women). The analysis examined demographic, clinical, and screening variables to uncover patterns and risk factors linked with progression to cervical cancer after past screening.

Results: 213 women who were screened for cervical cancer had later developed the disease. Thirty-five percent (75) had abnormal pap smear results, while 64.79% (138) had normal results. Among the 159 HIV-negative women, 36.48% (58) had normal pap smears, while 63.52% (101 women) had abnormal results. Among the 54 HIV-positive women, 31.48% (17) had normal pap smears and 68.52% (37 women) had abnormal results. The majority of women 65.91% (29) with high-grade squamous intraepithelial lesions (HSIL) were negative for HIV while 34.09% (15) women were HIV-positive. Out of 58 women who had low-grade squamous intraepithelial lesions (LSIL) 70.69% (41) were negative for HIV while 29.31% (17) were positive for HIV. Among the 213 women involved in the study, 34.27% (73 women) got a negative VIA (Visual Inspection with Acetic Acid) test during cervical cancer screening but were later diagnosed with the disease.

Conclusions: HIV status has an impact on cervical cancer screening outcomes, with HIV-positive women having a higher prevalence of severe cervical abnormalities than HIV-negative women. Furthermore, a considerable proportion of women later diagnosed with cervical cancer had negative VIA results. This underlines the need for improved screening methods and follow-up protocols, particularly for high-risk groups such as HIV-positive women.

References: Gesink, M. P., Chamberlain, R. M., Mwaiselage, J., Kahesa, C., Jackson, K., Mueller, W., Meza, J. L., & Soliman, A. S. (2020). Quantifying the under-estimation of cervical Cancer in remote regions of Tanzania. BMC Cancer, 20(1), 1-8. https://doi.org/10.1186/s12885-020-07439-3 McHome, B., Swai, P., Wu, C., Katanga, J., Kahesa, C., Manongi, R., Mwaiselage, J. D., Kjaer, S., Rasch, V., & Linde, Di. S. (2020). Comprehensive Cervical Cancer Prevention in Tanzania (CONCEPT) study: Cohort profile. BMJ Open, 10(9), 1-13. https://doi.org/10.1136/bmjopen-2020-038531 Mwantake, M. R., Kajoka, H. D., Kimondo, F. C., Amour, C., & Mboya, I. B. (2022). Factors associated with cervical cancer screening among women living with HIV in the Kilimanjaro region, northern Tanzania: A cross-sectional study. Preventive Medicine Reports, 30(March), 101985. https://doi.org/10.1016/j.pmedr.2022.101985 World Health Organization. (2020). Costing the National Response to Cervical Cancer : United Republic of Tanzania , 2020 - 2024. Who, November, 2020-2024.

CS03 - HPV and reproductive health

Trottier Helen
Canada

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#9580

Session title: HPV and reproductive health (90 min) (invited speaker) / Title: HPV during pregnancy and risk of birth complications

03 - Epidemiology and natural history

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Background/Objectives: The impact of Human papillomavirus (HPV) on cancer is now well known, but the epidemiology of HPV in pregnant women and the impact of HPV on birth complications are less studied. The objective is to review the evidence regarding the epidemiology of HPV during pregnancy and birth complications associated with HPV.

Methods: A review of the evidence from the various studies that have been conducted to measure the association between HPV during pregnancy and pregnancy outcomes will be presented.

Results: The prevalence of HPV is usually high in pregnant women. Evidence suggest an association between HPV during pregnancy and preterm birth. A possible association for rupture of membranes (ROM), and low birth weight (LBW) is also possible. HPV may also be associated with spontaneous abortion, intrauterine growth restriction and fetal death, but findings are limited by suboptimal control of biases.

Conclusions: HPV infection is frequent among pregnant women. A significant association between HPV and preterm birth is usually found. Possible associations have been suggested for ROM and LBW. It is not clear for the other pregnancy outcomes.

Bénard Alice
Canada

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#9581

Session title: HPV and reproductive health (90 min) (invited speaker) / Title : Vertical transmission of HPV during perinatal period

03 - Epidemiology and natural history

Bénard A[1,2]

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[2]Centre de Recherche du Centre Hospitalier Universitaire Sainte-Justine, Université de Montréal, Montréal, Canada

Background/Objectives: The epidemiology of HPV is now relatively well known in adults but remains less well documented in children. The objective is to review the evidence regarding the epidemiology of HPV vertical transmission, with a particular emphasis on the risk of HPV transmission and persistence in children during the perinatal period.

Methods: Studies conducted on HPV vertical transmission will be reviewed.

Results: The probability of HPV vertical transmission reported from studies varied considerably ranging from 5% to 100% depending on the population studied and methodology. The meta-analyses on vertical HPV transmission reported a pooled transmission probabilities ranging from 1% to 46%. A large cohort in Finland showed a transmission probability of 22% with almost perfect genotype concordance between infected mothers and children. In another large Canadian cohort study conducted by our team, HPV transmission was observed in approximately 7% of children, with rare cases of persistence or recurrence during perinatal period. Although most studies found that HPV did not usually persist more than few weeks/months in children, one study has identified that HPV acquired during infancy can persist much longer.

Conclusions: The review of the evidence suggests that the risk of HPV vertical transmission is relatively high. However, the risk of HPV persistence during the perinatal period appears to be low, as most HPV infections detected at birth clear within a few weeks/months.

SS19 - Enhancing cervical cancer screening by improving attendance and self-sampling

Tranberg Mette
Denmark

Mette Tranberg
Denmark

#9652

Extended HPV genotyping in hrHPV-positive women using self-sampling

13 - Self-sampling

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[2]Dept. of Clinical Medicine, Aarhus, Denmark

Background/Objectives: High-risk human papillomavirus (HPV) testing on self-collected vaginal samples (self-samples) has emerged as an effective screening method to improve screening uptake among under-screened women. However, because HPV tests cannot discriminate between transient infections and persistent HPV infections associated with cervical intraepithelial neoplasia of grade 2 or worse (CIN2+), a treatable screening endpoint, additional triage for HPV-positive women is necessary to minimize colposcopy referrals. In many countries, women with an HPV-positive self-sample, regardless of HPV-genotype, are recommended to visit a clinician for additional cervical cytology triage before potential colposcopy referral. However, this two-step triage approach may be associated with loss to follow-up and diagnostic delay. To address this issue, HPV-genotype-specific referral strategies could be designed that takes the risk of underlying disease for each specific HPV-type into consideration. Implementing such strategies would require the availability of extended HPV genotype assays that perform equally well in clinician-collected cervical samples and self-samples. This presentation will summarize findings from our study comparing the two types of samples using the CLART HPV4S assay with respect to HPV detection and genotype agreement in a referral population. Furthermore, we will share initial experiences with extended genotyping in vaginal self-samples collected as part of the routine cervical cancer screening program in the Central Denmark Region.

Methods: NONE

Results: NONE

Conclusions: None

HN08 - HPV and Head & Neck Forum - Molecular insights into HPV+ OPC Oncogenesis

Fenton Tim
United Kingdom

Fenton Tim
United Kingdom

#9632

The APOBEC3 genes, their role in HPV+ OPC and variation across the global population

29 - HPV and oropharynx / Head and neck cancer

Fenton T[1]

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Background/Objectives: The development of HPV-associated oropharyngeal cancer (HPV+ OPC) involves both the disruption of host cell tumour suppressor mechanisms by the viral oncoproteins and somatic alterations to the host cell genome. A major source of these somatic alterations is the deamination of genomic cytosine bases by members of the apolipoprotein-B mRNA editing catalytic polypeptide (APOBEC) family of enzymes, that also form part of the innate immune response to HPV infection. Two APOBEC genes (APOBEC3A and APOBEC3B) have been implicated in both the host cell response to HPV and in generating somatic mutations in HPV+ OPC. These two closely related genes are arrayed in tandem within the APOBEC3 locus on chromosome 22, and in approximately 20% of the global population, a 30kb deletion has removed part of APOBEC3A and the entire coding sequence of APOBEC3B, generating a hybrid allele (APOBEC3A_B). The APOBEC3A_B allele displays striking stratification across the global population, varying from a frequency of 1% in Africa and 6% in Europe, to 40% and 58% in East Asians and Amerindians respectively, and near fixation in the Oceanic population. In this talk, I will give an update on recent developments in our understanding of how APOBEC-mediated mutagenesis may occur in HPV+ OPC, including the possible implications for treatment. I will also discuss recent research on the APOBEC3A_B polymorphism and its importance to understanding HPV+ OPC risk and pathogenesis in different populations.

Methods: x

Results: x

Conclusions: x

References: x

Schwartz Stefan
Sweden

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#9649

Expression of the HPV E6 and E7 oncogenes is controlled at the level of RNA splicing

02 - Viral and molecular biology

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Background/Objectives: A subset of the HPVs termed high-risk HPVs (HR-HPVs) are causative agents of anogenital cancers and head-and-neck cancers. Cancer is the result of persistent high-risk HPV infections that have not been cleared by the immune system of the host. These infections are characterized by dysregulated HPV gene expression, in particular constitutive high expression of the HPV E6 and E7 oncogenes and absence of the highly immunogenic viral L1 and L2 capsid proteins. HPV makes extensive use of alternative RNA splicing to control gene expression.

Methods: .Analysis of HPV RNA splicing may uncover movel targets for therpy.

Results: Alternative RNA splicing is extensively used by human papillomaviruses to express all their genes and HPV16 is no exception. This process must function to perfection since mis-splicing could perturb the HPV gene expression program by altering mRNA levels or by generating dysfunctional mRNAs. Cis-acting RNA elements on the viral mRNAs and their cognate cellular trans-acting factors control papillomavirus RNA splicing. The precise but delicate nature of the splicing process renders splicing sensitive to interference. As such, papillomavirus RNA splicing is a potential target for therapy. Here we summarize our current understanding of cis-acting HPV16 RNA elements that control HPV16 mRNA splicing via cellular proteins and discuss how they may be exploited as targets for therapy to papillomavirus infections and cancer.

Conclusions: RNA-binding proteins control expression of the HPV E6 and E7 oncogenes since by controlling splicing of the E6 and E7 mRNAs.. Since cellular RNA-binding proteins are essential for HPV gene expression they may be exploited as targets for therapy to HPV infections and HPV-driven cancers.

References: - Schwartz, S., Wu, C., Kajitani, N. 2024. RNA elements that control HPV mRNA splicing - targets for therapy? J. Med. Virol., 96:e29473. - Kajitani, N., Schwartz, S. 2022. The role of RNA-binding proteins in the processing of mRNAs produced by cancer-associated papillomaviruses. Seminars in Cancer Biology, 86:482-496.

Näsman Anders
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#9362

Time to recognize carcinoma in situ (CIS) as an entity in HPV-related tonsillar carcinoma (TSCC): CIS in tonsils is similar to HSIL in cervix and precedes invasive growth.

29 - HPV and oropharynx / Head and neck cancer

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[4]Department of Surgical Sciences, Section of Otolaryngology and Head and Neck Surgery, Uppsala University, Uppsala, Sweden

Background/Objectives: Human papillomavirus (HPV)-related tonsillar squamous cell carcinoma (TSCC) is suggested to arise in tonsillar crypts. They also constitute an exception in the literature of carcinoma development, as carcinoma in situ (CIS) is not a recognized entity and dysplastic stages are not evident. To investigate the evidence of this, we conducted a systematic review and meta-analysis to study tumor origin in TSCC. Moreover, we used spatial transcriptomics on HPV-related TSCC, cervical and HPV-negative oral cancer cases and compared TSCC CIS to high-grade intraepithelial lesion (HSIL) in cervix and dysplasia in oral cancer. We also studied sequential stages of TSCC progression.

Methods: MEDLINE was searched and a systematic review and meta-analysis, including all original studies reporting tumor origin in HPV-related oropharyngeal cancer, was performed. Spatial transcriptomics (10x Visium) was used to study histological epithelial cell gene expression across sample types (3 HPV-related TSCC, 3 cervical cancer and 2 oral cancer) and cellular states.

Results: 14% of all TSCC had a surface origin in the systematic review. In a pseudo-bulk approach, spatial transcriptomics revealed that dysplasia (CIS and HSIL) in TSCC and cervical cancer clustered with a high correlation. Moreover, ten epithelial cell clusters, that correlated to histology were identified when all epithelial cells were analyzed un-supervised. Two of these were dysplastic and occurred in all samples. A sequential progression from dysplasia into invasive disease was observed in both TSCC and cervical cancer in a trajectory analysis.

Conclusions: Cryptal origin is not obligate and there is a sequential progression towards invasive disease in HPV-related TSCC, similar to that of cervical cancer. The findings suggest that CIS in TSCC is an entity and that pure tonsillar dysplastic lesions should exist.

Morgan Ethan
United Kingdom

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United Kingdom

#9644

The deubiquitinase USP14 promotes NFkB activity and radiation-resistance in HNSCC

29 - HPV and oropharynx / Head and neck cancer

Morgan E[1]

[1]University of Sussex, Brighton, United kingdom

Background/Objectives: Despite recent advances in treatment options for Human Papillomavirus (HPV)- head and neck squamous cell carcinoma (HNSCC), the overall survival (OS) rate for HNSCC is low, demonstrating the need for novel therapies for these cancers. Targeting the ubiquitin-proteasome system (UPS) has emerged as a potential target for the development of novel anti-cancer therapies. Bortezomib, a first generation proteasome inhibitor clinically approved for the treatment of Multiple Myeloma, has previously been demonstrated to induce tumor regression in a subset of HNSCC patients through the inhibition of canonical NFκB activity; however, the failure of Bortezomib to inhibit other pro-survival pathways such as MAPK and STAT3 signalling resulted in heterologous responses. A recently developed alternative to proteasome inhibitors is the small molecule b-AP15, which inhibits the proteasomal deubiquitinases USP14 and UCHL5, thus allowing more specificity and less toxicity than proteasome inhibitors.

Methods: To investigate the potential of proteosomal deubiquitinases in HNSCC, we analysed the TCGA and GEO databases for expression of USP14 and UCHL5 in HNSCC. For mechanistic studies, we used the small molecule b-AP15, an inhibitor of both USP14 and UCHL5, and specific siRNA targeting each deubiquitinase in a range of well established HNSCC cell lines. We utilsed an NFkB reporter call line, western blot and immunofluorescence analysis to investigate the impacr of b-AP15 on NFkB activity. For proliferation studies, we performed colony formation assays and, in combination with radiation treatment, clonogenic survival assays. For the assessment of apoptosis and DNA damage, flow cytometry and immunofluorescence (DNA damage only) was used. Finally, we used two xenograft models to assess the impact of b-AP15 activity in vivo.

Results: Here, we demonstrate that the expression of proteasome-associated deubiquitinase USP14 is significantly increased in HNSCC and correlates with worse progression free survival in Human Papillomavirus (HPV)- HNSCC. Inhibition or depletion of USP14 inhibited the proliferation and survival of HNSCC cells. Further, USP14 inhibition reduced both basal and TNFa-inducible NFκB activity, NFκB-dependent gene expression and the nuclear translocation of the NFκB subunit RELA. Mechanistically, USP14 bound to both RELA and IκBa and reduced IκBa K48-ubiquitination leading to the degradation of IκBa, a critical inhibitor of the canonical NFκB pathway. Furthermore, we demonstrated that b-AP15, an inhibitor of USP14 and UCHL5, sensitized HNSCC cells to TNFa-mediated cell death, as well as radiation-induced cell death in vitro. Finally, b-AP15 delayed tumor growth and enhanced survival, both as a monotherapy and in combination with radiation, in HNSCC tumor xenograft models in vivo.

Conclusions: Together, we have identified that inhibition of proteasomal deubiquitinases inhibits the proliferation and survival of HNSCC cells and enhanced TNFa-induced cell death via the inhibition of NFκB activity. Our data suggest that combination therapies with b-AP15 could potentially offer a clinical benefit in HNSCC patients by promoting TNFa-induced cytotoxicity. Further studies will focus on the mechanism by which USP14 regulates NFκB signalling in HNSCC cells and the effect of b-AP15 activity in combination with radiation treatment in in vivo mouse xenograft models.

References: Morgan EL, Toni T, Viswanathan R, Robbins Y, Yang X, Cheng H, Gunti S, Huynh A, Sowers AL, Mitchell JB, Allen CT. Inhibition of USP14 promotes TNFa-induced cell death in head and neck squamous cell carcinoma (HNSCC). Cell Death & Differentiation. 2023 May;30(5):1382-96.

HN09 - HPV and Head & Neck Forum - New discoveries in molecular epidemiology

George Julie
Germany

George Julie
Germany

#9643

Genetic Changes in HPV-Driven OPSCC

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Head and neck squamous cell carcinomas (HNSCCs) account for the seventh most common cancer worldwide. A major distinction is based on the HPV infection status, which is associated with differences in clinical presentation and prognosis of patients with HNSCCs. While smoking-related HPV-negative HNSCC frequently harbor somatic changes of cell cycle genes, viral HPV proteins in HNSCC drive oncogenic transformation through inactivation of cell cycle proteins.

Methods: Genomic and transcriptomic profiling studies provide a comprehensive map of somatic alterations and molecular phenotypes that define HPV-driven HNSCC. Large-scale sequencing data available as part of the ICGC and the TCGA provide information for single tumors acquired at single-timepoints. Recent studies on tumors acquired throughout therapy provide insights on tumor progression in HNSCCs.

Results: Similar to HPV-negative HNSCC, HPV-driven tumors are frequently identified with alterations of PIK3CA. Computational tools to deconvolute the clonal composition from bulk genome sequencing allow for the analysis of genomic tumor heterogeneity. In comparison to other cancers, tumors from HNSCC patients reveal little levels of clonal diversity when referring to single nucleotide variants determined from single time point analyses in treatment-naïve primary tumors. HPV+ and HPV- subgroups show similar levels of intra-tumor heterogeneity. First studies on relapsing tumors from HPV+ HNSCC patients with dismal prognosis reveal a higher prevalence of somatic alterations in TP63, STK11, PI3K and RAS family members. Multi-regional analyses provide insight into patterns of tumor evolution.

Conclusions: Large-scale integrative studies provide insights on key molecular mechanisms that drive HNSCC. Tracking tumor evolution will potentially reveal dependencies of HPV-driven HNSCC.

SS24 - HPV self-sampling among transgender and gender diverse individuals

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United States

Nyitray Alan

#9617

Anal cancer screening beliefs, behaviors, and knowledge among cisgender, transgender, and gender-diverse people in the Prevent Anal Cancer Studies

27 - Anal neoplasia

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Background/Objectives: Transgender women with HIV in the ANCHOR study had a higher prevalence of anal high-grade squamous intraepithelial lesions than gay and bisexual cisgender men with HIV. As anal cancer screening programs are implemented, understanding barriers and facilitators for transgender and gender-diverse (TGD) people may help prevent disparities in anal cancer screening.

Methods: In the Prevent Anal Cancer (PAC) Self-Swab and Palpation studies, sexual and gender minorities who have sex with men in Milwaukee, Chicago, and Houston, USA were consented into studies of anal self-sampling and self-palpation for anal abnormalities. We assessed the studies' outcomes by gender and then assessed the studies' combined survey data from 1058 individuals including 72 who identified as non-binary (NB, n=28), transgender men (TM, n=16), transgender women (TW, n=24), another gender (n=4), or cisgender men (CM, n=986).

Results: At baseline in the PAC Self-Swab Study (n=240) a nonsignificantly lower proportion of TGD people (62%) engaged in screening compared to CM (83%), p=0.07. At baseline in the PAC Palpation Study (n=714), NB (89%), TM (78%), TW (83%) had nonsignificantly increased concordance with a clinician in detecting anal and perianal abnormalities when compared with CM (73%, p=0.15 for TGD group vs CM). In the survey data, the median ages of NB, TM, TW, and CM were 32, 39, 34, and 41 years, respectively. A majority of NB, TM and CM identified as non-Hispanic white, while 61% of TW identified as non-Hispanic Black. A total of 11%, 19%, 46%, and 35% of NB, TM, TW, and CM, respectively, reported living with HIV (p=0.01) while HPV vaccination was reported by 46%, 50%, 21%, and 26% of NB, TM, TW, and CM, respectively (p=0.04). A total of 82%, 63%, 48% and 76% of NB, TM, TW, and CM knew that HPV infection was a risk for anal cancer (p=0.01). Regardless of gender, 31%-39% of individuals did not believe anal sex was a risk factor for anal cancer. 14% of CM vs 4% of TGD people had a friend or family member with an anal cancer diagnosis (p=0.02). Similar proportions of CM (11%) and TW (12%) had a history of HRA while CM were more likely to report a digital anal rectal exam in the past compared to TW (47% vs 13%, respectively, p<0.001). Having a doctor recommend screening was the biggest motivator for getting screening with >50% of each TGD category listing it as a motivator. A total of 33%, 13%, 30% and 49% of NB, TM, TW, and CM said they prefer a doctor of their own gender to conduct anal cancer screening (p=0.01). When asked for reasons why some people may not get anal cancer screening, embarrassment was cited by at least 75% of individuals in each gender. A total of 43% and 68% of CM and TGD people, respectively, believed some people may not get screened out of concern for doctors being rude to transgender people, p<0.001.

Conclusions: Differences by gender may be obscured if gender-diverse individuals are not assessed separately by gender category. TGD people may be less likely to screen for anal cancer than CM. Regardless of gender, individuals have limited knowledge of risk factors for anal cancer and limited experience with anal cancer screening.

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#9543

HPV self-sampling for transgender and gender diverse people assigned female at birth: HPV prevalence and self-sampling experiences

10 - HPV screening

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Background/Objectives: The human papillomavirus (HPV) causes cervicovaginal, oral, and anogenital cancer, and cervical cancer screening options include HPV testing of a physician-collected sample. Transgender and gender diverse (TGD) people assigned female at birth (AFAB) face many barriers to preventive care, including cancer screening. Self-sampling options may increase access and participation in HPV testing and cancer screening.

Methods: We estimated the prevalence of HPV in self-collected cervicovaginal, oral, and anal samples from Midwestern TGD individuals AFAB. We recruited 137 TGD individuals AFAB for an observational study, mailing them materials to self-collect cervicovaginal, oral, and anal samples at home. We tested samples for high-risk (HR) and other HPV genotypes using a PCR mass array test. Individuals reported their perceptions of cervicovaginal and anal self-sampling.

Results: A total of 101 participants completed the sample collection and the self-collection survey. Among those with valid tests, 8.8% (HR: 6.6%; 16/18: 3.3%) were positive for oral HPV, 30.5% (HR 26.8%; 16/18: 9.7%) for cervicovaginal HPV, and 39.6% (HR 33.3%; 16/18: 8.3%) for anal HPV. A larger fraction of oral (71.4%) than anal infections (46.4%) were concordant with a cervicovaginal infection of the same type. Most participants reported that the cervicovaginal self-swab was not uncomfortable (68.3%) and not difficult to use (86.1%), and nearly all (96.0%) were willing to use the swab in the future.

Conclusions: It is essential that we reduce barriers to cancer screening for TGD populations, such as through the development of a clinically approved self-screening HPV test.

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#9594

HPV Self-Sampling among transmasculine and non-binary adults with a cervix

13 - Self-sampling

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Background/Objectives: Transmasculine and non-binary (TMNB) adults assigned female at birth with a cervix are just as likely as cisgender women to be exposed to HPV, but are less likely to have undergone cervical cancer screening. TMNB patients face many barriers to cervical screening including gender dysphoria (distress associated with the disconnect between identity and anatomy) and pain with speculum insertion due to testosterone-induced vaginal atrophy. Therefore, HPV self-sampling has been proposed to overcome many barriers to HPV-related cancer screening among TMNB individuals. Here we present the data for the first 25 participants enrolled in The Self-TI Study, a pilot study to compare the feasibility and acceptability of HPV self-sampling to clinician collected sampling.

Methods: The Self-TI Study seeks to enroll 50 TMNB participants with exposure to testosterone therapy undergoing cervical cancer screening via smear test at one of three sexual health clinics in England. In addition to a clinician-collected cervical sample via speculum exam, participants self-collect samples from four body sites, vaginal and anal swabs, oral rinse, and urine. Feasibility is measured with the proportion of samples completed and returned. Acceptability is measured by comparing questions about the physical and emotional comfort of each sampling method using a 7-point Likert scale ranging from 1 (very uncomfortable) to 7 (very uncomfortable). For description, we collapsed the scales into categories of uncomfortable (1 - 3), neutral (4), and comfortable (5-7).

Results: The average age of the 25 participants was 31.5 years (range: 25-47). Seventy-two percent of individuals identified as men and 28% identified as non-binary. Another 12% also identified as genderqueer, gender nonconforming, or transmasculine. Eighty-eight percent identified their race as White. All but one person completed the clinician-collected cervical sample and all self-sampling swabs for a compliance rate of 96%. Twenty-three of the 25 participants completed the acceptability survey. When asked about physical comfort, 87% indicated clinician swabbing was uncomfortable compared to 39% who indicated self-swabbing was uncomfortable. When asked about emotional comfort, 65% said clinician swabbing was uncomfortable compared to 30% who said self-swabbing was uncomfortable.

Conclusions: HPV self-sampling is highly feasible for the TMNB population. Vaginal self-sampling may be more acceptable than clinician-collected sampling due to an increase in physical and emotional comfort. We anticipate the results from the fully enrolled study will allow us to make statistical comparisons that could lead to recommendations for cervical cancer screening in this population.

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Feasibility and acceptability of HPV self-sampling among transfeminine and non-binary adults assigned male at birth

13 - Self-sampling

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Background/Objectives: In transfeminine and non-binary (TFNB) people assigned male at birth, infection with persistent high-risk human papillomavirus (hrHPV) may result in cancers of the oropharynx, anus, vulva, vagina or penis. Reported rates of hrHPV infection in TFNB vary widely by country and body site.(1-6) TFNB may be at increased risk of hrHPV in cases of HIV co-infection, which is more common in this community.(7) Because TFNB have been placed in the highest risk group for anal cancer screening,(8) triage would help avoid over-screening. Self-testing for hrHPV may help individuals understand their risk and improve symptom awareness. The Self-TI Study (Self-TI) is a pilot study codesigned with members of the transgender and nonbinary community, aiming to assess acceptability and feasibility of multi-body site hrHPV self-testing for transgender people. We report the results of the first 25 TFNB participants.

Methods: The TFNB arm of Self-TI will enrol 50 participants, aged 18 or over, across 3 UK sexual health services for the transgender people. TFNB participants self-collect oral rinse, first void urine, vaginal swab and anal swab in-clinic, with repeat self-collection of oral, vaginal (if applicable) and anal samples at home. Feasibility is measured by proportion of samples completed and returned. All participants complete an online survey to assess acceptability of self-sampling methods and settings (Likert scale ranging from 1 (very uncomfortable) to 7 (very uncomfortable).

Results: For the first 25 TFNB participants, average age was 36 years (range 21-77) with the majority (84%) of white ethnicity. In terms of gender identity, 14 identified as female, 4 as non-binary, 2 as non-binary feminine and 5 as another identity. Two participants had undergone vaginoplasty, both by penile inversion. Ten participants (40%) had received the HPV vaccine (all as adults via sexual health clinic) with five (20%) unsure. Seven (28%) were positive for HIV. For in-clinic samples, 100% of participants completed the anal swab and 96% completed urine and oral samples. Both participants with vaginas completed vaginal samples. Nineteen participants (76%) returned at-home samples and completed the acceptability questionnaire, including two participants with vaginas. In-clinic, both participants with vaginas rated the vaginal sampling procedure as 3/7 for both emotional and physical comfort. At home, physical comfort remained 3/7 but emotional comfort improved to 5/7. Median physical comfort scores in clinic were 3/7, 6/7 and 6/7 for anal, oral and urine sampling respectively. This improved at-home to 4/7 for anal samples. Median emotional comfort scores in-clinic 4/7 for anal samples, 6/7 for oral rinse and 4/7 for urine. For anal samples this improved with at-home sampling to 6/7. Most participants felt they would be more likely to access HPV testing if self-sampling was possible, with preference for at-home sampling.

Conclusions: Self-sampling for hrHPV by vaginal and anal swab, oral rinse and urine collection are all highly acceptable to TFNB and feasible. At-home sampling brings increased physical and emotional comfort though may result in lower feasibility. Full cohort results, alongside hrHPV prevalence, concordance of at-home and in-clinic samples, will help inform future self-testing strategies.

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CS05 - Colposcopy: Discussion on challenging cases

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#9647

Obesity in Colposcopy part of Colposcopy: discussion on challenging cases

24 - Colposcopy

Background/Objectives: Golbally Obesity is an increasing problem. Evidence suggests that obesity is associated with challenges in screening and hence higher rates of cancer. The obesity pandemic and how it affects screening and colposcopy will be discussed. Practical examples of how to perform colposcopy in this population will be discussed.

Methods: REview of relavant publications

Results: Obesity is a significant challenge

Conclusions: The colposcopist needs to be aware of different methods to manage colposcopy in this population

SS25 - Role of HLA in immune evasion of HPV-induced tumors

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#9564

HLA variants as risk factors in cervical cancer

25 - Cervical neoplasia

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Background/Objectives: Cervical cancer is the second leading cause of cancer-associated deaths in women worldwide in 2023. Infection with high-risk human papillomavirus (hrHPV) causes lesions and persisting lesions can increase the risk of developing high-grade cervical disease. Genome-wide association studies (GWASs) for cervical cancer and HPV seropositivity have identified multiple genomic variants at the human leukocyte antigen (HLA) locus (6p21.32-33) containing genes with an essential role in modulating host immune response against the virus. We aim to validate reported associations and investigate the functional relevance of variants by expression quantitative trait loci (eQTL) analysis in cervical tissues.

Methods: We genotyped multiple genomic variants at the HLA locus from recent cervical cancer GWASs in the German Cervigen cohort of about 1200 invasive cervical cancers, 1500 dysplasias, and 1700 healthy controls. We tested the replicating SNPs to be eQTLs for 36 gene transcripts at this locus in 317 cervical tissues. In a normal immortalized cervical epithelial cell culture model, we added the inflammatory cytokine interferon-γ and analysed MHC gene expression after 24, 48, and 72 hours.

Results: In overall and stratified association analysis, we replicated multiple independent risk loci at the HLA region in our case-control series. We analysed HPV-type specific signals and provide supportive evidence of replication for additional cervical cancer risk loci. We identified transcripts upregulated in HPV positive samples (HLA-B, NFKBIL1, DDX39B, and LTB), and specifically upregulated (MICA and HCP5), and downregulated (HLA-DPB2) in HPV16+ samples. We find strong eQTLs after correction for multiple testing and identify regulatory variants affecting HLA gene expression and correlation. We identified HLA genes that are up- or down-regulated in cervical epithelial cells after treatment with interferon-γ in a dose-dependent manner.

Conclusions: We corroborate recent GWAS signals at 6p21 in a hospital-based cohort. We identify genetic variants that modulate gene transcript levels together with HPV infection, indicating that highly controlled gene regulation underlies cervical cancer susceptibility at the HLA locus.

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#9601

HLA class I loss of function and Its Association with the Progression of Cervical Intraepithelial Neoplasia

05 - Immunology

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Background/Objectives: HLA class I loss of function has been implicated in cervical intraepithelial neoplasia (CIN) and cervical cancer, but its association with CIN progression remains insufficiently understood. Potential mechanisms underlying this loss include nucleotide substitution, insertions/deletions, loss of heterozygosity (LOH), and epigenetic silencing through DNA methylation. This study aimed to investigate the impact of HLA class I LOH on the antigen-presenting capacity and its association with the progression of CIN in individuals harboring human papillomavirus (HPV).

Methods: We analyzed HLA class I allelic status in tissue samples from individuals with varying stages of CIN. HPV genotypes, HLA types. In addition, the peptide-binding potential of individual HLA alleles were assessed. Statistical correlations were examined between peptide-binding, allelic loss, and disease progression. HPV E5 protein binding was specifically analyzed to evaluate its relationship with LOH in HLA-B alleles.

Results: Binding potential against viral peptides was found to vary based on HLA type rather than HPV genotype. A positive correlation was observed between HPV peptide-binding potential and the frequency of HLA class I LOH. The lost HLA-B alleles exhibited higher peptide-binding potential for HPV-derived antigens compared to the retained alleles. LOH frequency was significantly higher in advanced CIN (CIN2-3) compared to early CIN (CIN1) or cervical inflammation, with approximately 50% of CIN2-3 cases exhibiting LOH in at least one HLA class I allele. LOH in HLA-B alleles significantly impacted HPV E5 antigen binding.

Conclusions: These findings suggest that loss of antigen-presenting capacity mediated by HLA class I facilitates immune evasion by HPV, promoting persistent infection and progression to advanced CIN. Understanding these mechanisms may inform strategies to target immune evasion in HPV-associated diseases.

References: 1. Kawase et al., HLA 2024, 103(6):e15509, doi: 10.1111/tan.15509.

HN10 - HPV and Head & Neck Forum - Innovations in personalized therapy

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#9648

Neoadjuvant Chemoimmunotherapy with Response-Adaptive Therapy for HPV+ Oropharyngeal Cancer

08 - Immunotherapy - Immuno-oncology - New treatments

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Background/Objectives: HPV associated oropharyngeal cancer is associated with favorable survival, however standard multimodality treatment is associated with substantial treatment-related toxicities. As such there is unmet need to improve surival while reducing treatment-related toxicities. While the role of immunotherapy in curative HPV+ oropharyngeal cancer remains undefined, leveraging neoadjuvant immunotherapic approaches may lead to improved oncologic outcomes while facilitating reduced radiation for some patients.

Methods: A series of phase II clinical trials, the OPTIMA II clinical trial (NCT03107182) and more recently the TARGET-HPV clinical trial (NCT05108870) are testing neoadjuvant chemoimmunotherapeutic approaches followed by response-adaptive de-escalated treatment in non-metastastatic HPV+ oropharyngeal carcinoma. Patients receive neoadjuvant chemotherapy with either nivolumab (OPTIMA II) or HB200 (TARGET HPV) , followed by risk and response-adaptive treatment: Low-risk patients with deep response (>=50% shrinkage per RECIST v1.1) receive single modality treatment (transoral robotic surgery or radiotherapy to 50Gy), low-risk patients with suboptimal response 30-50% shrinkage or high-risk patients with deep response receive intermediate dose de-escalation (50Gy with concurrent cisplatin), while patients with stable or progressive disease or high-risk patients with suboptimal response receive standard chemoradiotherapy to 70Gy with concurrent cisplatin. The primary endpoint of both trials is deep response (proportion of patients achieving at least 50% tumor shrinkage.

Results: The OPTIMA II trial demonstrated a deep response rate of 70.8% (95% CI, 0.59-0.81). Two-year PFS and OS were 90.0% (95% CI, 0.80-0.95) and 91.4% (95% CI, 0.82-0.96), respectively. By response-adapted group, 2-year PFS and OS for single modality patients were 96.4% and 96.4%, and intermediate dose de-escalation, 88.0% and 91.0%, respectively. Lower enteral feeding rates and changes in weight, as well as improved swallowing, were observed among patients who received response-adapted locoregional treatment. Pathologic complete response rate among patients who underwent transoral robotic surgery was 67.0%. PD-L1 expression was nonsignificantly higher for deeper responses and improved PFS, and ctHPV-DNA clearance was significantly associated with improved PFS. The phase I part of the TARGET HPV trial demonstrated that neoadjuvant chemotherapy/HB200 is safe and tolerable to maximal doses, with deep responses following HB-200/chemotherapy observed in 81% of patients, with HPV16-specific T-cell responses observed alone with reductions in circulating tumor HPV-DNA levels.

Conclusions: Neoadjuvant chemoimmunotherapeutic approaches followed by response-adaptive de-escalation demonstrate early promising results and warrant further investigation.

SS23 - Next generation analysis and bioinformatics

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Quality assurance and NGS for HPV detection

09 - HPV testing

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Background/Objectives: DNA sequence homology is critical for classifying human papillomavirus (HPV) genotypes. HPV tests clinically validated for cervical cancer screening are based on European HPV prototype sequences, which may not represent global sequence diversity. Next-generation sequencing (NGS) begins with primer design and gene selection. While the L1 gene is conserved across HPV types and ideal for broad detection, E6/E7 oncogenes are relevant in high-grade lesions given their role in cellular transformation but insufficient for deeper classification, such as lineage. When feasible, whole-genome sequencing provides the most comprehensive data. Standardized guidelines for NGS analysis are lacking and pipeline differences (i.e., code-based vs user-friendly) can significantly impact binary HPV detection. This study aims to: 1) compare commercial HPV tests (Cobas and Anyplex) with NGS, 2) evaluate homology deviations in E6/E7 sequences relative to PaVE references, and 3) examine pipeline differences in positivity and concordance.

Methods: HPV data from 934 women in the ELEVATE study with matched commercial test results were selected for analysis. Participants were recruited in Belgium, Portugal, Brazil, and Ecuador between 2019 and 2022. Mocked self-collected cervicovaginal samples were tested using Cobas 4800 and Anyplex II HPV assays. Cobas detects HPV16/18 and a pool of 12 other high-risk types, while Anyplex detects 14 HPV types separately. NGS amplified the E6/E7 regions of 14 high-risk types using AmpliSeq and Ion Torrent. Quality thresholds included a depth >100 and mean base quality >20; >25% unknown bases in a given sequence were classified as HPV-negative samples. Cohen's kappa analysis assessed concordance between commercial tests and NGS. Lack of homology (%) was calculated by dividing single nucleotide polymorphisms (SNPs) by sequence length. Two pipelines were compared: a code-based vs user-friendly pipeline (Qiagen). Both pipelines applied similar filtering, mapping, and extraction steps.

Results: Among the 934 samples, kappa values for NGS-Cobas for any HPV, HPV16, HPV18, and pooled HPVs were 0.75, 0.87, 0.85, and 0.74, respectively. In comparison, the NGS-Anyplex values were 0.73, 0.84, 0.81, and 0.71. Lack of homology was higher in NGS-negative samples for HPV16 (0.46% vs 0.13%) and HPV18 (0.44% vs 0.37%), with similar findings for HPV33, 58, and 66. For HPV45, homology deviations were higher in NGS-positive samples (0.87% vs 0.43%). Pipeline comparison showed lower positivity for code-based analysis (54.7%) vs the user-friendly pipeline (58.6%), with concordance ranging from kappa=0.85 (HPV68) to kappa=0.97 (HPV45).

Conclusions: NGS demonstrated equal performance to commercial tests while offering insights into sequence variability and polymorphisms. Higher lack of homology in E6/E7 oncogenes can affect commercial test detection; more studies using L1 are needed to validate this finding, particularly in diverse and resource-limited settings. Pipeline differences emphasize the need for standardized NGS guidelines to improve test accuracy and reproducibility.

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#9589

HPV Variant Calling - Insights into Evolution and Cervical Cancer Development

02 - Viral and molecular biology

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Background/Objectives: Human papillomavirus (HPV) plays a major role in cervical cancer development. However, the diverse oncogenic potential across HPV types, as well as their lineages, sublineages, and specific genetic variations such as SNPs (single nucleotide polymorphisms) or SNVs (single nucleotide variants), makes precise risk assessment challenging. Emerging evidence suggests that certain HPV16 sublineages are more frequently associated with high-grade lesions and cervical cancer. In contrast, intrahost single nucleotide variants (iSNVs) seem to be linked to infection clearance rather than cancer progression. Sequencing technologies can detect these subtle variations in HPV, which is crucial for understanding the HPV evolution and its implications in cervical cancer development.

Methods: Amplicon-based HPV whole-genome sequencing methods, such as our TaME-seq2 approach, integrate multiplex PCR, Illumina sequencing, and customized bioinformatics pipelines. Quality control and careful filtering of errors ensure the reconstruction of sample consensus sequence and variant detection. This framework enables the identification of SNPs/SNVs, lineages, sublineages and iSNVs. However, determining appropriate cut-offs to distinguish true biological variants from technical artefacts remains challenging. These thresholds are often context-dependent, influenced by the specific experimental design, sequencing depth, and analytical tools.

Results: Amplicon-sequencing methods reliably identify high-risk HPV lineages/sublineages and SNP profiles. The results also suggest a unique set of HPV SNVs in every analyzed woman. Using TaME-seq, we have confirmed that increased iSNV counts can be found predominantly in low-grade or normal cervical samples, suggesting iSNVs are linked to infection clearance, offering insights into host-virus interactions.

Conclusions: Variant calling is an important approach to enhance our understanding of HPV diversity and its evolutionary and clinical significance. However, the accuracy and reproducibility of detected variants, depends on the methodology employed. Factors such as library preparation, sequencing platforms, bioinformatics tools, and the selection of cutoffs can significantly influence variant detection outcomes. Therefore, developing standardized protocols, improving error-correction techniques, and adjusting thresholds according to experimental design, is essential for improving the reliability of variant calling.

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#9610

The interplay between the constituents of the microbiome in cancer development

18 - Microbiome

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Background/Objectives: The human microbiome is a dynamic ecological system characterized by intricate interactions among viruses, bacteria, fungi, and their host. Disruptions in the balance within and between these microbiome constituents can initiate or facilitate cancer development. Understanding these interactions is essential in the context of HPV infections.

Methods: We utilized simulated microbiome datasets to evaluate the accuracy of existing bioinformatics tools. Additionally, we developed robust and user-friendly tools to address unmet needs, with a specific focus on the virome and mycobiome.

Results: Our findings reveal significant limitations in current bioinformatics tools for virome and mycobiome analysis. In response, we developed a robust framework for virome analysis. Furthermore, we identified substantial weaknesses in tools designed to characterize the mycobiome, highlighting an urgent need for improvement in this area.

Conclusions: To understand the human microbiome interplay more reliable and comprehensive bioinformatics tools are needed.

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#9655

A novel triaging tool in cervical cancer screening - perforamnce of a DNA methylation test in a population-based cohort

17 - Methylation

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Background/Objectives: The WHO has specified the need to eliminate cervical cancer, being the second most prevalent, deadly neoplasia in women. Strategies include broad HPV vaccination and improved cervical screening. Currently, HPV testing is often accompanied by cytology triaging. Yet, the low and operator-dependent sensitivity of cytology to detect cervical (pre-)cancers necessitates alternative triaging techniques. This study investigates the efficiency of the DNA methylation (DNAme)-based WID-qCIN test, HPV16/18 genotyping, and their combination compared to cytology in identifying cervical intraepithelial neoplasia grade two or worse (CIN2+) and cervical cancer (CC).

Methods: Between January 1 and March 31, 2017, 28,017 women aged ≥30 years participated in the Swedish cervical screening in Greater Stockholm. Following HPV-based primary screening, 2,377 women tested positive for HPV and were further triaged with cytology. Clinical data for all participants were documented. DNA from biobanked cervical smear samples of HPV-positive patients was analyzed using the WID-qCIN test. The performance of the WID-qCIN test, HPV16/18 genotyping, and their combination was compared to cytology for detecting CIN2+ and CC. Performances were assessed for prevalent and incident cases defined via histological outcomes after 0-12 months and 13-72 months post-baseline visit, respectively.

Results: Cytology showed a 98.4% (95% CI, 96.0 to 99.4) sensitivity for detecting CIN2+. WID-qCIN/HPV16/18 sensitivities were 93.4% to 100% for CIN3 and CC detection, respectively, similar to cytology. Only 18.2% of incident CIN2+ and 20% of incident CC arising 12 months post-baseline were detected by baseline cytology triaging, whereas 69.4% and 80.0%, respectively, were identified by WID-qCIN/HPV16/18 testing. WID-qCIN/HPV16/18 triaging would have resulted in only 2.4 colposcopies per CIN2+ detection compared to 4.1 colposcopies with cytology.

Conclusions: The DNAme-based WID-qCIN test combined with HPV16/18 genotyping detected CIN3+ in HPV-positive women with similar efficiency as cytology. The WID-qCIN/HPV16/18 strategy outperformed cytology in predicting incident CIN2+ and would have substantially reduced the number of required colposcopies.

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#9590

Simulations: Optimizing Laboratory and Bioinformatics Methods

02 - Viral and molecular biology

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Background/Objectives: Technical noise introduced during library preparation and sequencing often hinders the accurate detection of mutations. Simulation-based approaches offer a controlled environment to evaluate and optimize laboratory and bioinformatic strategies. We have developed GENOMICON-Seq, a simulation framework designed to replicate the complexity of amplicon and whole-exome sequencing (WES). By modeling biases, errors, and various experimental parameters, GENOMICON-Seq provides a "ground truth" benchmark that can guide the selection of optimal variant-calling thresholds and help interpret results more accurately, ultimately improving our understanding of underlying biological processes.

Methods: Most existing simulators focus on replicating the error models of sequencing instruments or generating reads from reference genomes, while only a few incorporate library preparation biases or PCR-induced errors. GENOMICON-Seq differs by offering functionalities beyond standard read simulation. It introduces complex mutation patterns in the input sequences, simulates PCR biases at every amplification cycle, and applies probe-capture enrichment steps. GENOMICON-Seq provides a comprehensive and realistic testing environment for low-frequency mutation detection methods by simulating entire workflows from DNA templates to post-sequencing data analysis.

Results: Using GENOMICON-Seq, we have demonstrated how different experimental conditions, such as varying input DNA amounts, PCR cycles, and sequencing depths, affect the detection of rare mutations. As a result, researchers can test how different variant calling strategies will be affected by different simulated conditions. In addition, the tool's ability to introduce custom mutation patterns enables the evaluation of mutation detection tools in contexts that closely resemble biologically relevant scenarios, such as APOBEC3-driven mutation signatures in viral populations or low variant allele frequencies in heterogeneous human samples.

Conclusions: Simulation tools provide a controllable and realistic framework that enables researchers to refine their laboratory protocols, validate bioinformatic pipelines, and improve strategies for detecting low-frequency mutations. Ultimately, simulations bridge the gap between theoretical method development and practical application, contributing to more reliable downstream biological interpretations and advancing genomic research.

CS06 - Management of early stage cervical cancer & AIS

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#9614

The role of conization prior to hysterectomy in early cervical cancer

25 - Cervical neoplasia

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Background/Objectives: Conization prior to hysterectomy in early cervical cancer is a critical approach in the management of patients diagnosed with stage IA2 and IB1 cervical cancer. This procedure achieves a histological diagnosis and assesses the extent of cancer before proceeding with more radical treatment. Conization allows for accurate staging and offers valuable information regarding the tumor's depth of invasion and lymphovascular space involvement, which are important prognostic factors in early-stage cervical cancer (1-2).

Methods: Bizzari et al assessed retrospectively the prognostic role and the perioperative outcomes of conization performed before radical hysterectomy in 332 patients with FIGO 2009 stage IB1 cervical carcinoma. Patients undergoing conization before radical hysterectomy received less adjuvant treatment ($p < 0.001$) and had a better 5-year disease-free survival (DFS) than patients who did not receive conization (89.8% vs. 80.0%, respectively; $p = 0.010$). No difference in 5-year overall survival (OS) (97.1% vs. 91.4%, respectively; $p = 0.114$) or recurrence pattern ($p = 0.115$) was reported between the two groups (3).

Results: Rameriz et al recently published the updated survival final analysis of the LACC trial comparing open versus minimally invasive radical hysterectomy for early-stage cervical cancer. For the subgroup analysis by previous conization, the effect of treatment differed between those who had a previous conization compared with those who did not (P-interaction 5.042) for DFS. There was no difference between treatment groups in those who had a previous conization (HR, 1.27 [95% CI, 0.39 to 4.17]; P 5 .69), while in those participants who had not had a previous conization, minimally invasive surgery was associated with higher recurrence rate (HR, 5.85 [95%CI, 2.47 to 13.9]; P < .0001). (5) Lastly, in the SUCCOR cone study investigators evaluated the DFS of cervical conization prior to radical hysterectomy in patients with stage IB1 cervical cancer (FIGO 2009). a cohort of 374 patients (187 with prior conization) were included in te final analysis and there was a 65% reduction in the risk of relapse for patients who had cervical conization prior to radical hysterectomy (p=0.007) and a 75% reduction in the risk of death for the same sample (p=0.033). In addition, patients who underwent minimally invasive surgery without prior conization had a 5.63 times higher chance of relapse compared with those who had an open approach and previous conization (p=0.006). Similar to the LACC trial results, patients who underwent minimally invasive surgery with prior conization and those who underwent open surgery without prior conization showed no differences in relapse rates compared with those who underwent open surgery with prior cone biopsy (HR 1.94, 95% CI 0.49 to 7.76, p=0.349 and HR 2.94, 95% CI 0.80 to 10.86, p=0.106 respectively).

Conclusions: Overall, conization prior to hysterectomy allows for accurate staging and offers valuable information regarding the tumor's depth of invasion and lymphovascular space involvement, which are important prognostic factors in early-stage cervical cancer and can help in tailoring surgical approach. Additionally, recent publications support this procedure role in improving survival and allowing the performance of MIS simple hysterectomy instead of open radical hysterectomy, therefore conization should be offered to all patients with early stage cervical cancer and are candidates for hysterectomy.

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#9621

Conservative Management of Adenocarcinoma in situ of the Cervix (AIS)

25 - Cervical neoplasia

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Background/Objectives: Adenocarcinoma in situ (AIS) is an HPV-associated precancerous lesion of the glandular cells of the endocervix and a precursor to endocervical adenocarcinoma. Its management should be individualized based on the patient's age, fertility desires, lesion characteristics, and ability to comply with follow-up protocols.

Methods: Conservative management is an option for appropriately selected patients, particularly young women desiring future fertility, provided there is no evidence of invasive disease (as confirmed by colposcopy, biopsy, and imaging) and excisional procedures achieve negative margins or there is high confidence in complete lesion removal.

Results: However, conservative management presents several challenges. AIS is often characterized by skip lesions or multifocal disease, making complete excision difficult. Positive resection margins are common, necessitating re-excision or close surveillance. Furthermore, AIS carries a long-term risk of recurrence or progression to invasive adenocarcinoma, emphasizing the critical importance of meticulous and sustained follow-up. Recent advances, such as the identification of specific HPV genotypes and molecular markers, can aid in risk stratification and guide personalized care.

Conclusions: The conservative management of AIS requires a careful, patient-centered approach aimed at preserving fertility and minimizing overtreatment while ensuring the complete excision of the lesion.

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#9561

HPV as a test of cure after conization of Early Stage Cervical cancer and AIS?

25 - Cervical neoplasia

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Background/Objectives: Test of cure or test of low risk for residual pathology are needed in early stage cervical cancer (ESCC) and adenocarcinoma in situ (AIS). We examined if negative High Risk Human papilloma virus (HT-HPV) short time ' mean 6 weeks after conization in women diagnosed with ESCC and AIS can be a prognostic sign of normal histology in the final pathology sample.

Methods: We present data of 138 women , 94 with ESCC and 44 with AIS.positive to HR-HPV. Short time after Large Loop Excision of Transformation Zone (LLETZ) . beetwen 3-12 weeks and before the final treatment a HR+HPV test was obtain from the cervix.We compared characteristics and outcome of negative and positive HR-HPV women.

Results: After LLETZ 65 women were negative 73 positive for HR-HPV. HR HPV negative after LLETZ included higher incidence of adenocarcinoma and AIS . In the negative HR-HPV post-LLETZ the final pathology was without cancer in 63 women (96.9%) and 2 (3.1%0 had residual cancer. In 34 women with cancer and 31women with AIS negative HR-HPV after LLETZ was corelated with absence of cancer in final pathology in 94.1% and 100% respectively. 17 HR-HPV negative women after LLETZ underwent radical hysterectomy/trachelectomy and 88.3% had no residual tumor. The negative predictive value for residual cancer in HR-HPV negative women was 96.9%

Conclusions: Clearence of HR-HPV short time after LLETZ has ahigh correlation with absence of residual cancer in the final pathology or during the follow up.HR-HPV test after LLETZ should serve as a new parameter for risk assesment in women with ESCC and AIS and may lead to less radical operations.

References: 1.

SS26 - Impact of interventions in the post-HPV vaccination world

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#9413

HPV types ecology sixteen years post randomized implementation of HPV vaccination

02 - Viral and molecular biology

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Background/Objectives: Comprehensive human papillomavirus (HPV) vaccine implementation will change the ecological conditions of the virus-host interaction. Total effects of HPV vaccination programs can comprehensively be best estimated with long-term follow-up of community-randomized implementation trials.

Methods: We performed a long-term follow-up of 33 communities 1:1:1 randomized to either gender-neutral HPV16/18 vaccination, girls-only HPV16/18 vaccination, and control communities without HPV vaccination. In the 1992-94 birth cohorts, 8,618/31,117 eligible boys and 15,615/30,139 eligible girls were vaccinated between 2007-2009 approximately at the age of fourteen. Post vaccination visits for cervico-vaginal sampling at the age of 22, 25 and 28 were attended by 5,602, 5,452 and 2,992 HPV16/18 vaccinated participants, respectively. Prevalence and ecological diversity of HPV types was assessed up to 16 years post vaccination.

Results: Previously reported significant decrease in the prevalence of vaccine targeted HPV types 16/18/31/45 eight years post vaccination (ie. niche vacation) was sustained up to sixteen years. The non-vaccine targeted HPV types: HPV33/35/52/58 and 56/66 continued to show changes(ie. niche occupation) in prevalence and diversity reported earlier following gender-neutral vaccination strategy (Pimenoff et al. 2023) among the vaccinees up to sixteen years post HPV vaccination.

Conclusions: Sixteen years follow-up post moderate coverage HPV vaccination confirmed the discovery of a vaccination strategy specific HPVs ecological response. Most prevalent HPV types occupying the ecological niche after the elimination of vaccine-targeted types likely have low oncogenic potential. The established, albeit evolving distribution of remaining HPV types will probably affect future cervical cancer screening programs

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#9604

Potential of interventions in differently evolving situations

10 - HPV screening

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Background/Objectives: Countries, and even the vaccinated birth cohorts within each country, differ in their HPV vaccination strategy (girls-only/girls&boys), coverage, and/or vaccine used. We study how these differences influence potential of cervical cancer screening.

Methods: Different screening scenarios are run with a mathematical multiple-type HPV transmission model, combined with a cervical cancer screening model, for vaccinated birth cohorts in different situations of HPV vaccination. The birth cohorts include both vaccinated and unvaccinated individuals. The model outcomes, including numbers of cervical cancers and treated precancerous lesions, are compared between different scenarios and situations.

Results: Cervical cancer risk and feasible screening scenarios depend on realized HPV vaccination, especially for the unvaccinated women of vaccinated birth cohorts. However, the difference between vaccinated and unvaccinated women diminish by the herd effects as vaccination gets stronger (girls&boys strategy, high coverage).

Conclusions: Besides less intensive screening of vaccinated women, screening of unvaccinated women in vaccinated birth cohorts require attention. High vaccination coverage in girls and boys is worth aiming for.

CS08 - Challenges and opportunities to implementation of secondary anal cancer prevention programs

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#9616

What standards are needed for HRA competence and how can we increase the number of HRA providers?

27 - Anal neoplasia

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Background/Objectives: High-Resolution Anoscopy (HRA) is the pivotal diagnostic procedure for the detection and management of anal High grade Squamous Intraepithelial Lesions (HSIL), as well as other conditions associated with Anal Squamous Cell Carcinoma (ASCC). Consistent, high quality, HRA is essential for both diagnostic accuracy and patient safety.

Methods: The relevance, importance and components of standardised HRA practice will be discussed, together with the key approaches which support excellence and consistency in HRA practice.

Results: Increasing realisation of the importance of HRA in the prevention and management of ASCC-related conditions has led to rising demand for HRA practitioners in all jurisdictions. Strategies to increase the number of HRA providers will be discussed, including components such as high-quality training programs, professional certification, integration with routine clinical practice, financial support and the roles of advocacy.

Conclusions: By establishing rigorous standards and creating incentives for training and practice, we can expand the number of competent HRA providers, ultimately improving access to high quality care and leading to significant reductions in the burden of ASCC.

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#9622

When do we stop screening for anal HSIL?

27 - Anal neoplasia

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Background/Objectives: To maximize benefits and reduce harms, a successful anal cancer screening program will screen those most likely to benefit and avoid screening those least likely to benefit. Recently published anal cancer screening guidelines have identified when to start screening populations at highest risk for anal cancer, but generally do not guide clinicians on when to stop screening to reduce harms. This talk, given from a public health perspective, will discuss relevant issues on the question of when to stop screening for anal HSIL and provide time for clinicians to discuss their current practice of anal cancer screening cessation.

Methods: A narrative review of Ovid MEDLINE and SCOPUS was conducted for relevant articles discussing concepts related to the cessation of anal cancer screening.

Results: Concepts for discussion include: 1) Cessation of cervical cancer screening; 2) Consideration of similarities and differences between the anal and cervical cancer screening models; and 3) Considerations for terminating anal cancer screening including HIV status, patient age, results of consecutive HPV/cytology tests, prior history of HSIL, resumption of screening after cessation, and the role of DARE and self-palpation.

Conclusions: In the absence of professional guidelines on stopping screening for anal HSIL, clinicians might look to cervical cancer screening recommendations and the current practice of other anal cancer screening clinicians to understand issues to consider for anal cancer screening.

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#9651

How do we follow people after HSIL treatment and when do we stop?

27 - Anal neoplasia

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Background/Objectives: High-risk Human Papillomavirus (HPV)-associated anal high-grade squamous intraepithelial lesions (HSIL) are the precursors to anal cancer. Treatment of anal HSIL reduces anal cancer incidence in high-risk individuals; it does not, however, prevent all cancers and post-treatment anal HSIL recurrence is common, raising the question of how to best conduct post-treatment surveillance and whether surveillance can ever be stopped.

Methods: A literature review was conducted with emphasis on rates of anal HSIL recurrence as well as incident anal cancer following HSIL treatment. Risk factors for either clinical outcome were assessed to determine most effective surveillance strategies.

Results: Most data exists on persons living with HIV whose anal HSIL was treated with thermocoagulation (mainly electrocautery). Anal HSIL recurrence rates ranged between 23.5% and 53% at 1 year and between 68% and 79% at 3 years. Risk factors for post-treatment recurrence and progression to cancer include smoking, low nadir and overall CD4 T-cell count, poorly controlled HIV infection as expressed by ongoing HIV-1 viremia, baseline and longitudinal HPV 16 infection and multiple as well as larger index HSIL lesions prior to treatment. Repeated anal HSIL treatment has been shown to gradually decrease number and size of recurrent lesions and to thereby significantly reduce (yet not entirely eliminate) the risk of anal cancer. Anal cancer diagnoses in the setting of ongoing surveillance are more likely to occur at an earlier stage, possibly translating into more favorable clinical outcomes.

Conclusions: Anal HSIL recurrence following treatment is common and cancer can develop despite treatment and surveillance with currently available therapeutic and diagnostic modalities. Long-term, close follow-up is key to reducing anal cancer risk. Particularly in patients with risk factors for recurrence and progression of anal HSIL, surveillance should likely never cease. More research is needed to effectively treat anal HSIL and to better risk stratify the oncogenic potential of individual lesions.

SS27 - Global evidence on HPV involvement in human malignancies at specified non-genital sites

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#9605

Genetic Susceptibility of HPV infection in Lung Cancer Study - GeSP Lung Study

09 - HPV testing

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Background/Objectives: Infectious diseases represent a major cause of cancer worldwide, ranking third, right after nutritional factors and tobacco smoking. Syrjanen et al. estimated that the average rate of HPV infection in lung cancer cases worldwide is approximately 26.5%, with rates of 17% and 15% indicated for Europe and the United States, respectively. According to the characteristics of HPV, it is hypothesised that HPV may be related to lung cancer given that the predominant cells in the lungs and bronchi are epithelial in nature. A recent meta-analysis was able to determine that regardless of the stage of lung cancer and its degree of differentiation, HPV infection was a risk factor for lung cancer. HPV infection is necessary but not sufficient on its own to cause cancer; the presence of other cofactors is required to play an important role in the disease. We seek to investigate if candidate biomarkers have a role in patients HPV+ and lung cancer development; evaluate the prevalence of HPV infection, determine if HPV infection can be eligible as prognostic biomarker. This is a bold area of investigation with scarce information published in this area.

Methods: GeSP Lung study is an interventional, retrospective and multicentric study. This study aims to determine genetic susceptibility of HPV infection in lung cancer. As such we collected medical data, bronchial aspirates or broncho-alveolar lavage and blood samples for posterior studying. Patients with lung cancer suspicion that have formal clinical indication to undergo a bronchoscopy had a bronchial aspirate or broncho-alveolar lavage done for posterior genotyping of HPV, cytological and cytochemical study (CINtec®) of HPV. Additionally, a blood sample was collected before or after the bronchoscopy procedure, for determination of biomarkers (for example: haptoglobin - Hp; acid phosphatse 1 - ACP1; glutathione - GSH; Methylenetetrahydrofolate reductase MTHFR; among others).

Results: GeSP Lung Study in ongoing and still recruiting in Lisbon, Portugal. Until December 2024 a total of 195 patients have been included (from a predicted total population of 300 patients). Of the 195 patients recruited in two centers, 145 are cancer patients and only 50 are controls. Until present 14 cases of HPV+ have been observed, with the majority being in the cancer population (13 cases in cancer patients vs 1 case in control group). The HPV genotypes observed were: 16, 18, 26, 31, 33, 35, 56 and 58. The determination of biomarkers in blood in ongoing in the laboratory.

Conclusions: This exciting new field of investigation is still ongoing, with preliminary data in Portugal with an incidence of HPV in lung cancer slightly lower than described in literature, although some caution should be taken since the study is ongoing and maturity of data is small.

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SS30 - Public advocacy and awareness campaigns to address barriers in HPV-associated cancer prevention

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#9600

Vaccine hesitancy and recovery in Ireland

36 - Advocacy, acceptability and psychology

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Background/Objectives: The HPV Vaccination Programme was introducted in Ireland in 2010 for females for free through the school immunisation programme. Uptake was high for the first 5 years of the programme. However, in 2016 there was a confidence crisis. It results in a substantial drop in uptake of the vaccination programme to 48%. The National Immunisation Office implemented dedicated stakeholder engagement to understand and address the cause of the concerns from parents and guardians about the vaccination. We also put in place support for health and care professionals who deliver the programme and other stakeholders who are often asked about vaccines. Through ongoing engagement and using the right communications channels the vaccination programme has stablised and confidence has been reinstated. Work continues to ensure the programme is stable.

Methods: Using focus groups with parents and guardians we aimed to understand concerns about the HPV vaccine and discussed their needs for information and their preferred channels for receiving information. We used stakeholder engagement through regular meetings with health and care professionals to understand the queries they receive from parents and guardians about the HPV vaccine. We also engaged with them to understand the channels they use to access information and the channels they use to share information.

Results: Through structured stakeholder engagement the HPV vaccination programme uptake has increased from a low uptake of 48% in 2016 to 78% in 2023. A catch up programme in 2023 resulted in an additional 11,000 people receiving the HPV vaccination. Many of those vaccinated were in the cohort who refused vaccination in 2016, this resulted in the uptake for the 2016 cohort to increase to 58% when data was last published in February 2024. Through regular engagement with identified stakeholders channels for sharing information are updated to ensure we are reaching our target audiences in a timely manner with factual information.

Conclusions: The HPV vaccination programme in Ireland delivered through the school immunisation programme has stabilised. However, work continues to increase vaccine uptake and to maintain high levels of vaccine uptake. The lessons we have learnt from reintstating confidence in the HPV vaccination programme are also used to maintain confidence in our other vaccination programmes in Ireland. We continue to monitor the programme channels to ensure we are reaching our audience. We continue to evaluate best practice from all over the world and adapt our programmes as required.

CS09 - Targeted therapies of HPV related cancers

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#9631

Therapeutic vaccination approaches to treat HPV-mediated (pre)cancers

07 - HPV therapeutic vaccines

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Background/Objectives: Therapeutic HPV vaccines are considered to be a promising approach to intercept the development of HPV-driven cancers in already HPV-infected people. As reflected in the recently published preferred product characteristics (PPCs) for therapeutic HPV vaccines by the WHO, two major areas of application are considered to be most effective: therapeutic vaccines that primarily clear oncogenic HPV infection, and therapeutic vaccines that cause regression of HPV-associated precancerous lesions. There is a large body of research addressing therapeutic HPV vaccines, ranging from preclinical studies in murine tumor models to approaches in clinical development. This review talk aims to give an overview of existing strategies.

Methods: An extensive literature search was conducted to gain an overview of the current state of the field.

Results: The talk will cover novel approaches to vaccine design, optimized preclinical HPV tumor models, data of therapeutic HPV vaccines using such models, and an overview of strategies that have reached the clinical phase. Of note, the use of therapeutic HPV vaccination in advanced disease is now typically considered in the scope of combination therapies.

Conclusions: Therapeutic HPV vaccines are currently in early clinical development, and there are several promising approaches in the preclinical stage. Unlike existing prophylactic HPV vaccines, which prevent new infections, therapeutic vaccines are designed to clear or treat existing HPV infections, HPV-associated precancers or invasive cervical cancer. They may thus complement therapeutic options for people that have not received the prophylactic vaccine. Due to their specificity for HPV-positive cells, they can be used with minimal side effects in people with persistent infections or precursor lesions, and thus contribute to cancer interception.

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#9660

Demethylating Treatment as a Novel Therapeutic Concept against HPV-Induced Precancerous Lesions: Update on the DelVIN Trial, a Clinical Phase I Study Evaluating The Safety And Preliminary Efficacy Of Local Decitabine Treatment Of Human Papillomavirus-Indu

08 - Immunotherapy - Immuno-oncology - New treatments

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Background/Objectives: To date, no causally effective medicinal products have been approved for human papillomavirus (HPV)-induced precancerous lesions in the anogenital area. The current treatment standard for these lesions comprises ablative and excisional approaches, which may cause considerable acute or chronic adverse effects in treated patients. Aberrant epigenetic patterns in the viral and host genome, specifically increased methylation, are functionally involved in HPV-induced carcinogenesis, e.g. by fostering the expression of the HPV E6/E7 oncoproteins. Interfering with these aberrant methylation patterns therefore opens the door for pharmacological treatment approaches against HPV-induced (pre)cancerous lesions. Such pharmacological interference may be feasible with the demethylating agent decitabine, a DNA methyltransferase (DNMT) 1 inhibitor, that has been approved for intravenous administration in certain hemato-oncological diseases. In the clinical study "The DelVIN Trial" (NCT05717621) we are investigating the safety and preliminary efficacy of a novel, topical dosage form of decitabine, VTD-101 ointment, in patients with vulvar intraepithelial neoplasia (VIN) grade 2/3.

Methods: The study has been designed as a prospective, single-arm, multicenter, open label, phase I study, including 29 patients with high-risk HPV DNA-positive, p16INK4a-positive VIN 2/3 occurring in a uni- or multi-focal pattern. The primary study objective is to determine the recommended phase 2 dose (RP2D) of the investigational medicinal product (IMP) VTD-101 ointment for the topical treatment of HPV-induced VIN grade 2/3. The RP2D is defined as the dose that is safe, tolerable, and effective. Corresponding endpoints are the rate of patients experiencing at least one dose limiting toxicity (DLT) and the rate of patients with clinical complete or partial response (cCR/cPR) according to adapted RECIST criteria. In addition, safety, efficacy, and quality of life (QoL) are further characterized by multiple secondary endpoints.

Results: An initial safety run-in phase conducted in the first three enrolled patients was successfully completed without the occurrence of any DLTs allowing enrollment of the remaining patients. A protocol-scheduled interim analysis conducted after the first ten enrolled patients had completed their treatment demonstrated an overall response rate (ORR) determined as best overall response (BOR) of 50% (four patients with cPR, one patient with cCR). None of the patients included in the interim analysis experienced any DLTs, serious adverse events (SAEs), serious adverse reactions (SARs) or suspected unexpected serious adverse reactions (SUSARs). The study was consequently continued per protocol. All 29 patients enrolled into the study have now completed their study treatment and the subsequent follow-up period (up to 12 months after the end of treatment).

Conclusions: Investigation of a new, topical treatment concept for patients with HPV-induced precancerous lesions using a demethylating agent has been successfully translated to the clinical setting. Interim data from the DelVIN phase I trial demonstrate first evidence for clinical efficacy and for a favorable safety profile of this treatment approach in patients with HPV-induced VIN 2/3. Analysis of the complete data set of the now concluded study will provide further insight into the effects of the novel IMP VTD-101 ointment.

SS29 - Quality assurance measures in countries that switched to HPV primary screening

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Experiences of HPV-based screening in low-resource countries (PAVE study)

10 - HPV screening

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Background/Objectives: The PAVE study is a multi-country NCI-led initiative aimed at validating a cost-effective and accurate screen-triage-treat strategy for resource-limited settings. In nine low- and middle-income countries (LMICs), cervical screening of women aged 25 (for WLHIV) or 30 to 49 years is performed using self-collected dry vaginal samples (FLOQSwab) and HPV testing (ScreenFire RS HPV assay). ScreenFire HPV RS assay is an isothermal amplification extended genotyping test (HPV16, 18/45, 31/33/35/52/58, 39/51/56/59/68) that can assay up to 96 samples/controls in one hour plus preparation time. The assay has been independently evaluated in prior studies, demonstrating high clinical accuracy [1,2,3,4]. Extended genotyping is proposed to stratify HPV-positive women according to their risk of developing cervical cancer and to guide clinical management. This presentation discusses key aspects of establishing HPV testing in LMIC settings, including quality laboratory aspects and the role of extended genotyping for management.

Methods: Dedicated HPV laboratories were established in each participating country (Brazil, El Salvador, Honduras, Dominican Republic, Cambodia, Nigeria, Tanzania, Malawi, Eswatini). Laboratories implemented standardized operating procedures (SOPs) addressing sample collection, transport, storage, processing and testing. Anti-contamination and pre-packed reagent solutions were introduced to reduce the chance of post-amplification contamination and the time needed for assay preparation [5]. Continuous monitoring and technical support focused on maintaining a clean testing environment and evaluation of results. Laboratories utilized flexible workflows to accommodate local infrastructure and workforce capacity. Most sites used fixed laboratories and some conducted high-yield outreach screening campaigns in remote areas (e.g., Brazil, Honduras).

Results: As of December 2024, ~50,000 women have been screened using the ScreenFire HPV assay across the nine countries. Despite varying levels of infrastructure and laboratory experience, all participating sites achieved high quality and high throughput, reflecting the success of optimized workflows, training and monitoring. The introduction of the pre-packed HPV assay version significantly reduced the chances of post-amplification contamination and the time needed to run the assay, enabling single-day screening in remote areas. A preliminary analysis based on enrollment through July 2024 (N=28,038) showed a CIN2+ yield (absolute risk) of 8% for overall HPV positives and, by genotype channel, 20% for HPV16, else 8% for HPV18/45 combined with 31/33/35/52/58, else 3% for HPV39/51/56/59/68. CIN3+ yield strengthened the risk-based hierarchy of ScreenFire HPV type channels.

Conclusions: The PAVE study demonstrates that high-quality, high-throughput HPV testing is achievable in LMICs conditional on training, infrastructure adaptation, and quality assurance measures. Moreover, the observed disease yield by ScreenFire HPV type group highlights the importance of extended genotyping for risk-based management, especially in LMIC settings where follow-up and treatment resources are often limited.

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Audits for quality assurance of HPV-based screening

10 - HPV screening

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Background/Objectives: Cervical cancer screening programs are transitioning to HPV testing as the primary screening method. Ensuring the accuracy and reliability of HPV testing requires rigorous quality assurance processes, including regular audits. Annual systematic reviews allow continuous evaluation of the clinical sensitivity of HPV tests in identifying women at risk for high-grade squamous intraepithelial lesions or worse (HSIL+). Since the implementation of HPV testing in Sweden as a screening method in 2012, we have adopted routine laboratory audits similar to those used in cytology-based screening.1 Key expectation is that specimens collected within the screening interval prior to a cancer diagnosis should test positive for HPV if laboratory quality is adequate. This approach ensures consistent monitoring of the HPV testing process and its sensitivity.

Methods: The Center for Cervical Cancer Elimination (CCCE) conducts HPV testing for the screening program in the capital region. CCCE identified cases of HSIL+ through histopathology and reviewed their corresponding prior screening samples (up to 3 years before the cancer diagnosis). Each year, 300 random liquid-based cytology (LBC) samples (corresponding to cases of HSIL+) are audited. Initially, HPV testing was conducted using Roche Cobas 4800 System, but starting in 2022, BD COR system was utilized. Samples lacking HPV results were re-analyzed using COBAS/BD COR and samples negative for HPV were re-analyzed with BD-core/Cobas/Luminex. If the re-analysis still showed negative results, re-review of the subsequent biopsies (PAD) was performed and PADs with confirmed HSIL+ (biopsies) were analyzed according to the same protocol as LBC samples. If still HPV-negative, both the LBCs and biopsies were whole-genome sequenced.

Results: From the beginning of HPV testing, Cobas 4800 and BD COR systems detected HPV in 2756/2842 (97.0%) of randomly selected LBC samples taken before HSIL. Re-testing HPV negative samples with Cobas/BD COR/Luminex detected HPV in further 51/86 samples. Sequencing was performed in 35 samples. Year Sample Size (n) Detected HPV (n) Detection Rate (%) 2012/2013 154 148 96.1% 2014/2015 299 291 97.3% 2016 300 293 97.7% 2017 299 288 96.3% 2018 291 286 98.3% 2019 299 290 97.0% 2020 300 289 96.3% 2021 300 289 96.3% 2022 300 293 97.7% 2023 300 289 96.3% Total 2842 2756 97,0%

Conclusions: Swedish laboratory audits of HPV testing within a real-life cervical screening program demonstrate a clinical sensitivity of 97.0% for detecting HSIL+. Comprehensive methodologies, including general PCR, broad HPV type detection, and whole-genome sequencing, ensured reliable evaluation of "HPV-negative" samples. Regular audits of samples collected before HSIL+ diagnoses can be seamlessly integrated into real-life screening programs. This provides robust assurance of program performance and the quality of HPV testing. The global HPV LabNet now recommends that audit of HSIL+ cases should be performed as part of routine quality assurance and that high quality laboratories should always have >95% HPV positives before HSIL+.2

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