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Congress Presidents | **Hans Berkhof (Netherlands) • Miriam Elfström (Sweden)**

ABSTRACTS

POSTERS

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#6739

P01-01 | Impact of the COVID-19 Pandemic on HPV Vaccinations in Switzerland and Greece: Road to Recovery

01 - HPV disease and COVID-19

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Background/Objectives: Switzerland and Greece faced significant declines in HPV vaccinations during the COVID-19 pandemic period. Our previous analysis highlighted that at the start of the HPV catch-up period (e.g., 03/2022 and 09/2022 for Switzerland and Greece, respectively), the HPV vaccination deficit was up to 2.9 and 2.6 months of vaccination of 2019 in Switzerland and Greece, respectively (Gountas et al. Vaccines 2023). This study aims to update the HPV vaccination deficit estimation and assess the progress of the current HPV vaccination catch-up in each country.

Methods: A previously published calculator (Gountas et al. Vaccines 2023) was seeded with the latest local HPV vaccine sales data. The dose deficit was estimated by subtracting the monthly doses distributed during and after COVID-19 (i.e., from 03/2020 to 06/2022) from the distributed doses in the corresponding month of 2019 (i.e., last pre-pandemic year). Country-specific numbers of monthly HPV vaccine doses were sourced from the IQVIA vaccine sales database (Switzerland) and monthly vaccine sales data (Greece). In Greece, during the pandemic, only girls were eligible for HPV vaccination, thus the dose deficit was only attributed to them. On the contrary in Switzerland, the dose deficit was comprised of both adolescent boys and girls.

Results: In December 2022, the HPV vaccination deficit in Switzerland and Greece was 3.2 months (14.3% increase compared to the start of the catch-up) and 5.9 months (126.9% increase compared to the start of the catch-up), respectively. Similarly, in September 2023, our tool estimated that the HPV vaccination deficit in Switzerland was 3.2 months, showing no increase compared to December 2022. In Greece, the vaccination deficit was estimated at 6.2 months, indicating a 5.1% increase compared to December 2022. To clear the deficit by the end of 2025, the monthly vaccination rates in 2024 and 2025 should be increased by 10.5% and 97.8% in Switzerland and Greece, respectively, compared to the total annual doses administered during 2023. The corresponding increase to clear the deficit by the end of 2026 in Switzerland and Greece is 6.7% and 75.0%, respectively.

Conclusions: Monitoring the effectiveness of an ongoing catch-up is a vital procedure. Although, at the start of the catch-up period, the difference in the HPV vaccination deficit between the two examined countries was low, in September 2023, the gap between them highly increased. In contrast to Switzerland, the observed performance of the HPV catch-up in Greece was low. A sustained increase in vaccination rates over the upcoming years, especially for Greece, is required to eliminate the deficit and prevent long-term public health and economic consequences.

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P03-01 | Human development index and burden of cervical cancer: an ecological study

03 - Epidemiology and natural history

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Background/Objectives: The study aims to understand the cervical cancer burden in different socioeconomic patterns by evaluating the association of the Human Development Index (HDI) with the age at incidence and death of cervical cancer, as well as with the incidence and mortality rate.

Methods: Data on cervical cancer (ICD-10, C53) was obtained from the GLOBOCAN 2020 database. HDI in 2020 was extracted from the Human Development Reports. 174 countries/territories with accessible records on both metrics were included. The mean age, standardized (WHO standard and Segi's standard) mean age, and the age group with the highest rate (peak age group) at incidence and death were calculated for world (174 countries/territories), each HDI category (very high, high, medium, and low), and each country/territory. Formulas utilized for the mean age and the standardized mean age were "Σfx/Σf' and "Σfwx/Σfw' respectively, where f and x represented the number of cases in each age group and the mid value of each group interval. The mid value of the 85+ group was assumed to be 87.5 years. W represented the weight of each age group in the standard population, and the WHO standard and Segi's standard were both applied. The crude rate (CR) and age-standardized rate (Segi's standard) (ASR-S) of incidence and mortality for each country/territory were obtained directly from the online database, while the age-standardized rate (WHO standard) (ASR-W) were calculated using the number of cases in each age group and the weight in WHO standard population. The correlations between the age (mean age, standardized [WHO and Segi's standard] age, and peak age group) and the HDI, as well as between the rate (CR, ASR-S, and ASR-W) and the HDI, were analyzed using the Spearman rank correlation coefficient. The statistical significance of the correlation coefficient was evaluated by a t-test with a significance level of $p<0.05$.

Results: In 2020, the mean age at incidence of cervical cancer worldwide was 53.49 years, with 53.25, 52.97, 55.09, and 51.52 years in very high, high, medium, and low HDI countries respectively. The mean age at death of cervical cancer worldwide was 58.73 years, with respective mean ages of 62.42, 59.02, 58.68, and 55.07 years in the 4 HDI categories (Table 1). The peak age group at incidence was negatively correlated with the HDI (rho=-0.348, $p<0.001$). The mean age, standardized (WHO standard) mean age, standardized (Segi's standard) mean age, and peak age group at death were positively correlated with the HDI (rho=0.654, 0.498, 0.473, and 0.441 respectively; all $p<0.001$). Incidence and mortality rates were both negatively correlated with the HDI (rho=-0.219, -0.580, and -0.582 for CR, ASR-W, and ASR-S of incidence respectively; rho=-0.450, -0.753, -0.757 for CR, ASR-W, and ASR-S of mortality respectively; all $p<0.05$).

Conclusions: The associations of HDI with the epidemiological patterns and the burden of cervical cancer may be attributed to the discrepancies in the distribution of risk and protective factors among different areas, including citizens' health literacy and behaviors, HIV/AIDS burden, implementation of HPV vaccination, accessibility to cervical cancer screening that promotes early diagnosis and prevents advanced cases in the elderly population, and capability of standard treatment that improves the prognosis. Effective strategies should be developed and adopted in the future to reduce health inequities and alleviate the burden of cervical cancer.

Table 1. Age at incidence and death of cervical cancer by HDI category, 2020

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P03-02 | HPV genotypes distribution in urethral samples in French men

03 - Epidemiology and natural history

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Background/Objectives: We analysed all the results for which a HPV-LIPA hybridization assay was performed between 21/12/2017 and 23/05/2022. These were obtained from samples that arrived at the laboratory in refrigerated various transport media, mainly M4RT, Lingen, Preservcyt. Samples DNA was then extracted using EasyMag extractor (Biomerieux) assay until 2018, and then Chemagic C360 (Perkin Elmer). After that, HPV genotyping using PCR and reverse hybridization INNO-LIPA HPV Genotyping Extra II Amp assay (Fujirebio) was performed. This technique allows the detection of 32 different high- and low-risk oncogenic HPV genotypes (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 66, 67, 68, 70, 73, 81, 82, 83, 89). We used a generalized linear model to investigate factors that could explain differences in HPV prevalence in urethral samples. We also used descriptive statistics to compare proportions of HPV genotypes and a type II ANOVA for HPV genotypes prevalence. Patients under 18 were not included in the statistical analyses.

Methods: We analysed all the results for which a HPV-LIPA hybridization assay was performed between 21/12/2017 and 23/05/2022. These were obtained from samples that arrived at the laboratory in refrigerated various transport media, mainly M4RT, Lingen, Preservcyt. Samples DNA was then extracted using EasyMag extractor (Biomerieux) assay until 2018, and then Chemagic C360 (Perkin Elmer). After that, HPV genotyping using PCR and reverse hybridization INNO-LIPA HPV Genotyping Extra II Amp assay (Fujirebio) was performed. This technique allows the detection of 32 different high- and low-risk oncogenic HPV genotypes (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 66, 67, 68, 70, 73, 81, 82, 83, 89). We used a generalized linear model to investigate factors that could explain differences in HPV prevalence in urethral samples. We also used descriptive statistics to compare proportions of HPV genotypes and a type II ANOVA for HPV genotypes prevalence. Patients under 18 were not included in the statistical analyses.

Results: In this analysis, we obtained 1,665 results, in men and women, in oral, anal, biopsies, respiratory, mucous membranes, skin, and urethral samples. By keeping only urethral samples, we obtained 1019 male urethral samples of which 484 (47%) were positive for at least one HPV genotype. The median age was 40 years (IC 95% = [24-71 years]) (see figure 1). According to the type II ANOVA, HPV prevalence decreased over time, especially between 2018 and 2020 (see figure 2). We found no clear difference with age but there were HPV variations accross French departments (data not shown). The genotypes most frequently found were HPV6 (19% of the positive samples), HPV53 (14%), 51 (13%), 66 (13%), 52 (11%), 16 (11%) (see figure 3). Interestingly, HPV 53 was almost as frequent as HPV6 in co-infection (23 and 24% of the coinfections respectively) in these urethral samples of French men.

Conclusions: Studies describing circulating HPV genotypes in men are scarce. This study confirms earlier studies by finding that the low risk genotype HPV6 is the most frequent genotype detected in urethral samples. Co-infected samples exhibit similar genotype relative frequency, with the noticeable exception of HPV53, which was more frequent. At the population level, we detected a decrease in HPV prevalence in these samples over the last years. Further studies, particularly prospective ones, are needed to assess the exact circulation of HPV strains in men in the general population.

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#6836

P03-03 | The burden of HPV-related cancer, precancerous lesions, and anogenital warts in Denmark during 2010-2021

03 - Epidemiology and natural history

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Background/Objectives: Since the human papillomavirus (HPV) vaccine was approved in Denmark in 2006, research has shown a decrease in the incidence of cervical cancer and precancer. It is relevant to evaluate the effect of HPV vaccination on the burden of all HPV-related cancers, precancerous lesions, and anogenital warts in Denmark. The objective of this study is to analyze trends in the incidence and burden of HPV-related cancers, precancerous lesions, and anogenital warts in Denmark during 2010-2021, both overall and by specific site.

Methods: We used the Danish Cancer Register and the Danish Pathology Register to identify all HPV-related cancers and precancerous lesions, this including cervical, vulvar, vaginal, anal, oropharyngeal (only cancer), and penile cancer and precancerous lesions. Information on anogenital warts was obtained from the Danish National Patient Registry and the Danish National Prescription Registry. Age-standardized incidence rates of HPV-related cancers, precancerous lesions, and anogenital warts will be calculated according to gender, year of diagnosis, and birth cohort, and according to gender, age, and site during 2010-2021. Furthermore, we want to assess the current burden by calculating the average annual number of HPV-related cancers, precancerous lesions, and anogenital warts in Denmark during 2019-2021.

Results: During 2010-2021, we identified 4 288 HPV-related cancers in men and 8 171 HPV-related cancers in women in Denmark. The most frequent HPV-related cancer in men was oropharyngeal cancer (n = 3 017), followed by penile (n = 771) and anal cancer (n = 500). For women, cervical cancer was the most frequent cancer (n = 4 261), followed by vulvar (n = 1 435) and anal cancer (n = 1177). Penile high-grade squamous intraepithelial lesion (HSIL) was the most prevalent precancerous lesion in men (n = 464), followed by anal HSIL (n = 336). For women, cervical intraepithelial neoplasia (CIN2/3), was the most frequent precancerous lesion in women (n = 67 012), followed by vulvar HSIL (n = 3 560). Lastly, we identified 88 150 cases of anogenital warts in men and 51 386 in women.

Conclusions: Data analyses for the study are ongoing. Results of the analyses described in the methods will be presented.

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#6737

P03-04 | Prevalences of HPV and other sexually transmitted diseases among women living in remote areas along the Amazon rivers - Brazil

03 - Epidemiology and natural history

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Background/Objectives: Sexually transmitted infections (STIs) cause morbidity worldwide and, depending on the specific pathogen, may cause serious complications in the female reproductive tract such as infertility, miscarriage, premature labour and severe chronic diseases. The human papilloma virus (HPV) is a sexually transmitted pathogen, whose high-risk subtypes are involved in the development of cervical cancer (CC). The CC incidence rate is high in Brazil, particularly in the Amazon and Roraima states, where numerous Riverside population communities live in remote areas with no or limited access to health care services, including cancer screening and treatment. Furthermore, inequalities in social and economic indicators are present which contribute to the vulnerability of these populations. Here we retrospectively characterised prevalences of HPV infections and other STIs among women living along the Amazon rivers.

Methods: Cervical smear samples from 123 women (age range 14-78 years, mean 33.7 years) living in communities along the Negro and Madeira rivers in the Amazonas region, Brazil, were collected and submitted to cytological examination. The prevalences of thirty genital HPV subtypes and eleven other STIs (Chlamydia trachomatis, Neisseria gonorrhoeae, Herpes simplex virus 1 and 2, Haemophilus ducreyi, Mycoplasma genitalium and hominis, Treponema pallidum, Trichomonas vaginalis, Ureaplasma parvum and urealyticum) were determined by molecular typing using EUROArray HPV and EUROArray STI (EUROIMMUN), respectively. The study was approved by the ethics committee of Santo Amaro University São Paulo (Brazil Platform - CAAE: 61414216.4.0000.0081).

Results: The prevalence of cytological abnormalities (ASC-US, LSIL, HSIL) was 9.9% (12/121, two unsatisfactory samples were excluded). LSIL and HSIL were observed in five (4.1%) and five (4.1%) women, respectively. The overall prevalence of HPV was 25.4% (31 of 122 women, one sample with insufficient volume was excluded). Among the infected women, 6 (19.4%) had a low-risk subtype, 19 (61.3%) had a high-risk subtype and 6 (19.4%) had both subtypes. Eleven women (35.5%) were infected with two or more subtypes. HPV-16 (19.4%, 6/31), HPV-31, HPV-45 and HPV-53 (12.9%, 4 of 31 women each) were the most detected types. The overall prevalence of other STIs was 72.4 % (89/123 women). Up to four different pathogens were found among infected women. The most frequent pathogens were Ureaplasma parvum (53.7%), Mycoplasma hominis (32.5%) and Ureaplasma urealyticum (10.6%).

Conclusions: In this study we have demonstrated that there is a high prevalence of STIs and infections with oncogenic high-risk HPV types among women living in communities along the Negro and Madeira rivers in the Amazonas region, Brazil. Such data is pivotal for policy making and for formulating a best practice approach regarding how to screen, how to prevent onward transmission, and how to provide appropriate care for these vulnerable women.

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P03-05 | Other HPV as important as HPV16 and 18 in developing High-Grade CIN?

03 - Epidemiology and natural history

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Background/Objectives: High-risk (HR) HPV infection is the major cause of cervical cancer, which is still one of the most common cancers among women. Based on some not and published results, it seems that some of the other HR HPVs might be as important as HPV 16, and 18 in developing high-grade CIN. This study was designed to investigate the possible relationship between Other HPV and high-grade CIN.

Methods: In this prospective study from 2019 to 2022 (approved by the ethics committee), all women with positive HR-HPV based on the COBAS method were invited to participate in the study (N=646). The liquid-based samples of women with Other HPV positives were reanalyzed by HPV typing, and for all colposcopy was done.

Results: All the patients who were infected with HPV18 were involved in CIN1 among who 50% of patients were involved in CIN2. Fifty percent of patients with HPV45 had CIN2 in colposcopy biopsy of the cervix. There is also a significant relationship between HPV31 and CIN3.

Conclusions: Based on our study, there was a significant relationship between CIN3 and HPV31; and CIN2 with HPV45. Therefore, some other type of HR HPV might be as important as HPV 16 and 18 as a risk of developping high grade CIN. And that just reporting Other HPV in some method of HPV DNA typing ,like COBAS, is not enough and it might be necessary to analyze the other HPV with HPV typing to know who need the colposcopy. Further studies are needed to confirm our findings.

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P05-01 | Normalization of HPV-specific antibody detection in first-void urine: lessons learned from a pilot study

05 - Immunology

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Background/Objectives: Total and HPV-specific antibody (Ab) levels within cervicovaginal secretions (CVS) exhibit fluctuations tied to, among other factors, the menstrual cycle. As first-void urine (FVU) captures CVS and debris of exfoliated cells from the female genital organs, we expect similar fluctuations in FVU and hence, the need for normalization of specific Ab levels. In a forthcoming study, our research group will investigate the inter- and intra-individual variability in urinary Ab levels and identify appropriate biomarkers to normalize variation between FVU samples. To anticipate potential insights and difficulties associated with this study, an observational pilot study was conducted.

Methods: A total of ten HPV-vaccinated women (aged 18-30), that were either using the contraceptive pill (n=3), hormonal IUD (n=3), or had a natural cycle (n=4), were included. Over a period of 36 days, women were each asked to collect one FVU sample every four days (n=10), using a 20 mL Colli-Pee prefilled with urine conservation medium. HPV16-specific Abs were measured using dissociation enhanced lanthanide fluoroimmunoassay (DELFIA). Moreover, for normalization purposes, total IgG (bead-based multiplex immunoassay), total protein (BCA), and total glyceraldehyde-3-phosphate dehydrogenase (GAPDH) concentrations (qPCR) were quantified. HPV16-specific Ab concentrations were evaluated at the different timepoints, and both before and after normalization for the different biomarkers.

Results: All participants demonstrated detectable titers of HPV16-specific IgGs in their FVU samples. Throughout the menstrual and contraceptive cycle, fluctuations in both total and HPV16-specific IgG levels were observed in all women, with no discernible pattern. Among the seven menstruating women, five exhibited a notable increase in both total and HPV16-specific IgG levels during their menstruation, the latter being more pronounced. Remarkably, in contrast to what is suggested in literature, no significant decrease in total or HPV16-specific IgG was observed during ovulation. Normalization of the HPV16-specific Ab levels using total IgG concentrations was found to diminish variations between consecutive samples to some extent. Moreover, additional normalization for total GAPDH and protein levels was tested to further investigate the optimal combination of normalization biomarkers.

Conclusions: Although this observational pilot study featured a relatively low sample size, its findings offer valuable insights for future studies. The absence of a discernible pattern in total and HPV16-specific IgG levels throughout the menstrual or contraceptive cycle, highlights the importance of augmenting sample size, enhancing sampling frequency, and closely monitoring female hormone levels. These improvements are essential for establishing significant connections between cycle phases and specific fluctuation patterns, and corresponding normalization. Besides, the inconsistent reduction in variation after normalizing with total human IgG, DNA, and protein levels, emphasizes the imperative of identifying the most suitable (combination of) biomarkers for accurately quantifying CVS within a sample, accounting for variations throughout the menstrual and contraceptive cycle. Hence, our upcoming study will be instrumental in addressing these prevailing gaps, that must be filled to establish FVU as a suitable sample for monitoring HPV immunization in the female genital tract.

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P06-01 | Introduction of HPV Vaccine in a Country with Low Routine Immunization Coverage

06 - HPV prophylactic vaccines

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Background/Objectives: World Health Organization (WHO) estimates for the year 2020 place Montenegro at the top in Europe for age-standardized (World) incidence rate (26.2/100,000 women) and age-standardized (World) mortality rate (10.5/100,000 women) of cervical cancer. These alarming statistics were a primary motivator for Montenegro to introduce vaccination against the Human Papillomavirus (HPV) into its national immunization program. Routine vaccine coverage has been consistently low in recent years. Official coverage in Montenegro for the year 2022 in the target cohort for the first dose of measles, mumps, and rubella vaccine was 32.86%; coverage for three doses of hepatitis B vaccine in the target cohort was 44.73%; coverage for three doses of diphtheria, tetanus, and pertussis (DTP3), polio (Polio3), Haemophilus influenzae type b (Hib3) vaccines in the reported cohort was 80.25%, and BCG vaccine coverage was 85.55%. These vaccines are mandatory according to the immunization schedule. In these circumstances and following the exhaustive COVID-19 pandemic, HPV immunization in Montenegro commenced on September 26, 2022, targeting 9-year-old girls (birth cohort 2013). HPV vaccination has been introduced as recommended but not mandatory. Catch-up vaccination among girls aged 10-14 started on February 15, 2023. Vaccination is exclusively carried out in primary healthcare institutions (Primary Health Care Centers). Montenegro implements a one-dose vaccine schedule in all cohorts that have been the target group (ages 9-14).

Methods: This study aims to present the introduction and implementation of recommended HPV vaccination in Montenegro, as well as the results during the first year after the start of vaccination. The data analysis utilized a method of monitoring coverage at the national level, with particular attention given to tracking the achieved results in the cohort of girls born in 2013, which initiated the vaccination and was set as the primary target group in the 2022/2023 academic year. A cross-sectional coverage analysis in the primary cohort of girls born in 2013 was conducted one year after the start of vaccination, while a cross-sectional study for ages 10-14 was performed seven months after the birth of the catch-up vaccination. Monitoring coverage is facilitated through a unique national electronic immunization registry, allowing tracking by cohorts, municipalities, and the dynamics of vaccination over time.

Results: One year after the start of vaccination in Montenegro, coverage in the cohort of girls born in 2013 was 31.13%. Catch-up vaccination for girls aged 10-14 began on February 15, 2023, resulting in overall coverage of 20.25% across six cohorts (2008, 2009, 2010, 2011, 2012, and 2013) after eight months of vaccination implementation in all these groups.

Conclusions: Despite the relatively modest coverage achieved in the primary cohort (2013) and catch-up vaccination in the remaining five cohorts over eight months, considering the range of vaccines that are formally mandatory, it is encouraging. The results demonstrate significant potential for further improvement in the HPV vaccination program, especially given the performance of neighboring countries, some of which are just starting vaccination or had significantly weaker results in the first year.

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#7064

P06-02 | Acceptance of Human papillomavirus vaccination and parents' willingness to vaccinate their adolescents in Ethiopia: a systematic review and meta-analysis

06 - HPV prophylactic vaccines

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Background/Objectives: Despite the global vaccination campaign to prevent HPV-related morbidity, HPV vaccination uptake remains unacceptably low in the developing world, like Ethiopia. For strong interventional measures, compiled data in the field is required, which is otherwise missed in the Ethiopian context. Therefore, this systematic review aimed to provide an estimate of the HPV vaccination uptake, mothers" willingness to vaccinate their adolescent girls, and associated factors in Ethiopia.

Methods: Articles were systematically searched using comprehensive search strings from PubMed/Medline, SCOPUS, and gray literature from Google Scholar. Two reviewers assessed study eligibility, extracted data, and assessed the risk of bias independently. A meta-analysis was performed using STATA v 14 to pool the vaccination uptake and mothers" willingness toward HPV vaccination in Ethiopia.

Results: We included 10 articles published between 2019 and 2022 covering reports of 3,388 adolescent girls and 2,741 parents. All the included articles had good methodological quality. The pooled estimate of the proportion of girls with good knowledge about HPV vaccination and their agreement to get the vaccine was 60% (95%CI: 59-62) and 65% (95%CI: 64-67), respectively. The pooled estimate of vaccination uptake of at least one dose of HPV vaccine among girls was 55% (95%CI: 53-57). Positive attitudes to the vaccine, higher maternal education, and having knowledge about HPV and its vaccine were reported as statistically significant predictors. On the contrary, not having adequate information about the vaccine and concerns about possible side effects were reported as reasons to reject the vaccine. Likewise, the pooled estimate of mothers who were knowledgeable about HPV vaccination, who had a positive attitude, and who were willing to vaccinate their children was 38% (95%CI: 36-40) 58% (95%CI: 56-60), and 74% (95%CI: 72-75), respectively.

Conclusions: Knowledge about the HPV vaccine among girls and their vaccination uptake is suboptimal and falls short of the 2030 WHO targets. Therefore, stakeholders need major efforts to roll out vaccination programs and monitor their uptake. Social mobilization towards the primary prevention of HPV infection should focus on adolescents. The existing strategies need to address the predictors of uptake by educating girls and parents.

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P06-03 | Effect of HPV vaccination on virus disappearance in a cervical swab in a cohort of HPV-positive Polish patients

06 - HPV prophylactic vaccines

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Background/Objectives: Cervical cancer (CC) is theoretically preventable but still the fourth most common malignancy in women worldwide, with an estimated 604 000 new cases and 342 000 deaths in 2020. The introduction of human papillomavirus vaccines revolutionized cervical cancer prevention. However, there is more and more talk about vaccination of the adult population after sexual initiation and, thus, after contact with the HPV virus. Thanks to the increasing social awareness and education, many women underwent a course of vaccinations primarily - as prevention or after sexual initiation but before the CIN lesion's development. No data are available describing the disappearance of HPV infection in the cervical swab after an entire course of 9 - valent vaccination. This study aims to investigate the possible implications of receiving adjuvant HPV vaccination in HPV - a positive population, evaluating the clinical effectiveness of the human papillomavirus 9-valent vaccine in vanishing some HPV genotypes in cervical swabs.

Methods: We provide a prospective, ongoing 24-month, non - randomized study in HPV - positive patients. We enrolled 60 patients with positive HPV swab from cervix (51 vaccinated with the 9-valent vaccine against HPV and 9 unvaccinated). Using an enzyme-linked immunosorbent assay, we determined IgG class antibodies to HPV in patients' serum.

Results: Positive swab from the cervix for HPV performed after vaccination was significantly less frequent in the group vaccinated with 9-valent (23.5%) compared to a control group (88.9%; $p < 0.001$). Antibody level after vaccination was significantly higher in the vaccinated group compared to the control group. The reactive antibody level was seen in the case of all patients in the vaccinated group and one-third of the unvaccinated group (33.3%, $n = 3$).

Conclusions: In conclusion, adjuvant vaccination of HPV-positive patients increases the chances of HPV remission. It is a prophylactic element worth attention for each patient and a post- treatment effect. The observed high level of antibodies was found in a group of patients who were HPV positive within 6-12 months after vaccination, indicating a response to active viral replication.

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#6768

P06-04 | Investigation of mtDod multimerization platform on the immunogenicity of minor capsid protein l2-based prophylactic HPV vaccine antigens

06 - HPV prophylactic vaccines

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Background/Objectives: The N- terminus region of the L2 minor capsid protein of Human papillomavirus (HPV) spanning amino acids 17-38 represents a cross-neutralization epitope highly conserved among different papillomavirus types. Our group has pre-clinically demonstrated that OVX313 heptamerization domain affords increased immunogenicity to the amino acid region 20-38 of the L2 protein of eight HPV types (16, 18, 31, 33, 35, 6, 51 and 59), fused to the thioredoxin scafold protein from hyperthermophilic Pyrococcus furiosus (PfTrx-L2). In the presented study, we exploited the Mycobacterium tuberculosis dodecin protein (mtDod), which has the ability to form spherical homododecameric structures displaying 12 to 24 peptides with the aid of exposed N- and C- termini, as a multimerization platform.

Methods: We designed two mtDod contructs with gene level fusion of mtDod either to the N- or C- terminal of Trx-L2-8mer. MtDod proteins were expressed in E.coli BL21(DE) and purified by cation exchange chromatography. Multimerization status was confirmed by using size exclusion chromatography (SEC) and dynamic light scattering (DLS). We compared the humoral immune response induced by the nanoparticle Trx-L2-8mer-mtDod antigens to their counterpart Trx-L2-8mer-OVX313 in BALB/c mice by using Pseudovirion-based neutralization assays (PBNA).

Results: Trx-8mer-mtDod antigen could be produced at a required concentration and purity. It was shown that Trx-8mer-mtDod forms multimers which expose the L2 epitopes to induce neutralizing antibodies. However, for all tested HPV types, we found the highest neutralizing antibody titers being induced by the Trx-L2-8mer-OVX313 antigen among all antigen groups, whereas the immunogenicity of Trx-L2-8mer-mtDod was significantly higher than the that of mtDod-Trx-L2-8mer.

Conclusions: We concluded from the preliminary data that mtDod platform did not outperform to OVX313 platform in the induction of humoral responses and we are currently investigating the reason behind this result.

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#6847

P09-01 | Coilocytosis in urine samples

09 - HPV testing

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Background/Objectives: The Human Papillomavirus (HPV) can be present in various bodily fluids, secretions, and tissues. The objective of this study is to demonstrate the sensitivity in detecting genital tract lesions caused by HPV, which are shed in urine samples.

Methods: A total of 8514 urine samples from the urology service were collected between March 2018 and September 2023. Presence of coilocytes and/or cells compatible with low-grade dysplasia was detected in 25 samples. HPV testing was performed on 21 of these samples. The samples belonged to 18 patients, including 12 women and 6 men. Among the HPV tests conducted on 11 samples, both high and low-risk testing was performed, with genome detection and typing using real-time multiplex PCR with the commercial AllplexTM II HPV28 Detection CE-IVD kit (Seegene) on the CFX96 platform (Biorad). This analysis can identify up to 28 strains, including 19 high-risk strains (66, 45, 58, 51, 59, 16, 33, 39, 52, 35, 18, 56, 68, 31, 26, 69, 73, 82, 53) and 9 low-risk strains (42, 43, 54, 70, 61, 6, 44, 40, 11). High-risk HPV testing was also conducted on 5 samples using the Cobas 4800 HPV test (Roche Diagnostics, Mannheim, Germany), which can detect genotypes 16, 18, and 12 other high-risk genotypes (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) in a single pool. Both HPV tests were performed on 5 samples, while 4 samples did not undergo HPV testing.

Results: Out of all urine samples collected during the study period, 0.29% exhibited coilocytosis and/or low-grade dysplasia. The average age of the patients in the study was 52 years. Out of the 21 samples tested, 15 (71.43%) tested positive, and 6 (28.57%) tested negative. Of the positive samples, 6 (40%) were positive for both high and low risk, 8 (53.33%) were positive for high risk, and there was a single sample (6.66%) positive for low risk and negative for high risk. The low-risk genotype with the highest incidence was 42, followed by 43 and 70. Genotypes 54, 44, and 6 also demonstrated positivity to a lesser extent. As for high-risk genotypes with higher incidence, no specific observations could be made because the high-risk test in Cobas is a pool of 12 genotypes, which does not allow for individual results. Cytology was conducted on 6 out of the 12 women who tested positive, resulting in 5 (83.33%) cases of L-SIL and 1 (16.67%) case of negative cytology. In the latter case, the HPV result was negative for high risk and positive for low risk (6, 42, 43).

Conclusions: Urine has proven to be a sensitive fluid for HPV testing, detecting both high and low-risk genotypes. The cytopathic effect of HPV (coilocytosis and dysplastic cells) allows the detection of gynecological lesions in patients from the urology service. Referring patients to the gynecology service for the management of potential cervical lesions is beneficial for the patients.

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#6732

P09-02 | Comparison of AnyplexTM HPV HR and AllplexTM HPV HR Detection assays

09 - HPV testing

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Background/Objectives: AnyplexTM HPV HR Detection and AllplexTM HPV HR Detection are two novel Seegene's HPV genotyping assays for separate detection of 14 high-risk HPV genotypes. The main difference between these two assays is how they present the results of the HPV genotype's viral load. Anyplex HPV HR assay provides only a semiquantitative viral load measurement as high (+++), moderate (++) and low (+), whereas Allplex HPV HR assay generates results with individual cycle threshold value for all detected HPV genotypes. Here, our objective was to compare the performance of AnyplexTM HPV HR and AllplexTM HPV HR assays in the detection of 14 high-risk HPV genotypes.

Methods: The study was performed on 330 cervical samples from women who were referred to triage with HPV testing and cytology in accordance with Slovenian guidelines. All 330 samples were tested with both AnyplexTM HPV HR Detection and AllplexTM HPV HR Detection assay (Seegene Inc, Seoul, Korea). The agreement for overall positivity and genotype-specific agreement between assays were evaluated by Cohen's kappa (κ) statistics. κ values ≤ 0 were considered as no agreement, 0.01-0.20 as none to slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81-1.00 as almost perfect agreement.

Results: The overall positivity agreement for AnyplexTM HPV HR and AllplexTM HPV HR was almost perfect (κ = 0.94; 95 % CI, 0.8938-0.9836). Both assays were positive in 97.9 % and negative in 21.2 % of the tested samples, while discrepancies were observed in 2.1 % of the samples. The genotype-specific agreement was also almost perfect for all high-risk HPV genotypes. The highest agreement between AnyplexTM HPV HR and AllplexTM HPV HR was observed for HPV45 (κ = 0.98; 95 % CI 0.93 - 1.00) and the lowest for HPV33 (κ = 0.86; 95 % CI, 0.75 - 0.98) (Table 1).

Conclusions: Our results showed that AllplexTM HPV HR has comparable performance in detecting 14 high-risk HPV genotypes to the already validated AnyplexTM HPV HR assay. The agreement between both assays was almost prefect in both overall positivity and in HPV genotype-specific detection. Considering the comparable performance and shorter turnaround time, the use of AllplexTM HPV HR instead of AnyplexTM HPV HR assay could increase the laboratory's efficiency in reporting results.

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#6734

P09-03 | The impact of HPV triage on CIN2+ cumulative incidence in Slovenian National Cervical Cancer Screening Program ZORA

09 - HPV testing

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Background/Objectives: Hybrid Capture 2 High-Risk HPV DNA assay (HC2 test) has been a part of the Slovenian National Cervical Cancer Screening Program ZORA (ZORA program) since 2012. According to the ZORA program Guidelines, the HC2 test serves as an additional triage method alongside conventional cytology for women with low-grade cytology abnormalities or atypical glandular cells, as well as a test of cure after CIN treatment. Our objective was to determine the impact of HC2 test-based triage on the CIN2+ cumulative incidence for all referral indications separately.

Methods: The study group consisted of 47,225 women from the ZORA program who were referred for their first HPV triage test based on a cervical smear collected between 2011 and 2017. Data for the HPV triage indication, HC2 test results, colposcopy and histology results, and follow-up were collected for all participants from the ZORA registry. CIN2+ cumulative incidences for each individual referral indication, as well as for HPV-positive and HPV-negative women were calculated for the first, third, and fifth year after triage with HPV. CIN2+ cumulative incidences were evaluated according to 2 % and 20 % risk thresholds. Women with a one-year CIN2+ cumulative incidence higher than 20 % need an immediate referral for a colposcopy, women with a three-year CIN2+ cumulative incidence lower than 2 % can return to regular screening in three years.

Results: The highest one-year CIN2+ cumulative incidence was achieved by women with LSIL ≥ 35 years (14.9 %), and the lowest by women after CIN treatment (1.3%) (Figure 1). Women with ASC-US, AGUS and CIN 1 had comparable one-year CIN2+ cumulative incidences (7.3 %, 7.2 % and 7.6 %). A similar trend was observed for three- and five-year CIN2+ cumulative incidences. When HC2 test results were incorporated into the analysis, all HPV-positive women (with the exception of those after CIN treatment) exceeded the risk threshold for undergoing immediate colposcopy after one year (Figure 2). Furthermore, the CIN2+ cumulative incidence of all HPV-negative women except LSIL ≥ 35 years stayed below the risk threshold for a follow-up visit for at least five years (Figure 2).

Conclusions: Our results showed that the addition of HPV testing as a triage method improves the management of women with low-grade cytology abnormalities, atypical glandular cells, and after CIN treatment. HC2 test results separated these women into two distinct groups with a significantly different risk for CIN2+. All HPV-positive women exceeded the immediate colposcopy risk threshold after one year, and all HPV-negative women stayed below the risk threshold for a follow-up visit even after a period of five years. The exception were HPV-positive women after CIN treatment with a five-year CIN2+ cumulative incidence below the risk threshold for colposcopy, and HPV-negative women with LSIL ≥ 35 that exceeded the risk threshold for a follow-up already within one year after HPV triage. The low CIN2+ cumulative incidence of HPV-positive women after CIN treatment can be attributed to modern and high-quality treatment. The higher CIN2+ cumulative incidence of HPV-negative women with LSIL ≥ 35 suggests a need for an early follow-up before the routine three years screening interval. This is in line with Slovenian guidelines according to which results from cytology triage determine the final management of HPV-negative women.

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#6776

P09-04 | High risk HPV-specific testing in oropharyngeal carcinoma by RNA ISH has clinical value beyond p16 IHC

09 - HPV testing

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Background/Objectives: Transcriptionally active human papillomavirus has been identified to frequently cause oropharyngeal squamous cell carcinoma (OPSCC). In 2016, nearly 66,000 cases of OPSCC were diagnosed in Europe. Approximately 70% of these cases are associated with High Risk (HR-HPV), of which HPV-16 is the most common HR-HPV subtype (1). HR-HPV status in OPSCC has been associated with favorable outcomes and has become a part of the diagnostic work-up, within the broader clinical context of the patient (1). Current practice guidelines recommend immunohistochemistry (IHC) testing for p16INK4a protein as a surrogate marker for HR-HPV status. While p16 IHC is a widely available, low-cost test, overexpression of p16 may occur in the absence of HR-HPV, compromising the specificity of p16 IHC as a true measure of HR-HPV status. Reports show that up to 20% of tumors testing positive for p16 IHC may lack a transcriptionally active HPV infection (2). HPV-specific testing together with p16 IHC has been recommended. College of American Pathologists (CAP) also recommends HPV-specific testing in combination with p16 IHC in metastatic cases of unknown primary identified in cervical upper or mid jugular chain lymph nodes. OPSCC lesions frequently metastasize to these locations, so an HR-HPV result can guide the clinical team in searching for the primary tumor. Herein we assess the feasibility and performance of an RNA-ISH based assay as an alternative to current HR-HPV testing.

Methods: RNAscope High Risk HPV probe (HR18) detecting the following high-risk HPV sub-types (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, and 82) along with control probes (DapB= negative control) and (UBC= positive control) were qualified for probe specificity using a DNA plasmid slide-based identity test (assay) followed by functional staining of the RNAscope ISH Probe HR HPV using FFPE slides containing 5 cell lines (HPV 5 Core). Furthermore, FFPE tissue specimens of OPSCC (n=47) were procured, de-identified and evaluated with the RNAscope ISH Probe High Risk HPV for testing performance and feasibility. The RNAscope results were then compared to p16 IHC. All experiments were performed on the Leica Bond III clinical platform.

Results: DNA plasmid slide-based identity test demonstrated that HPV HR18 RNAscope ISH probes were able to specifically identify all HPV high-risk subtypes that were spotted on the plasmid slide with no cross-reactivity shown to the low risk subtypes. Functional staining of the RNAscope HR ISH probe showed staining as expected in the HPV 5-core cell pellets. In the FFPE OPSCC cases, RNAscope ISH Probe High Risk HPV identified 24/47 (51%) of the samples as positive. IHC with p16 identified 27/47 (57%) of the samples as positive resulting in a positive agreement of 89% and a negative agreement of 100% between the two methods.

Conclusions: RNAscope ISH Probe High Risk HPV is a sensitive and specific method with robust performance and easy interpretation, suitable for the traditional anatomic pathology workflow. The agreement observed between RNAscope ISH Probe High Risk HPV and p16 IHC is consistent with the expectation for some p16 positive cases to be negative by ISH. The three discrepant cases may be the result of p16 activation through a non-HPV related mechanism. Studies have shown that patients with discordant p16 IHC and RNA ISH results have less favorable prognosis. RNA ISH is an HPV-specific method to assess for HR-HPV in OPSCC that adds clinical value beyond p16 IHC.

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#6684

P09-05 | Assessment of HPV characteristics in cervical cancer screening samples from elderly women - a new stratification tool?

09 - HPV testing

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Background/Objectives: In Denmark, cervical cancer screening of women ≥60 years old is based on an HPV test followed by a cytology-based stratification in cases with an HPV-positive test result. However, due to anatomical changes of the cervix throughout a woman's life, it is difficult to obtain adequate cytological samples and biopsies from these women. This may result in prolonged diagnostic work-up including the collection of several inadequate cytological samples and biopsies. Therefore, to avoid the collection of inadequate samples and the unnecessary procedures performed on these HPV-screen-positive elderly women, there is a need for a better stratification tool. Thus, this study aims to provide additional information on specific characteristics of HPV infections in women ≥60 years old, such as HPV genotype and sublineage, HPV integration status, and infection with single versus multiple HPV genotypes. By comparing this extra information with the severity of the women's cervical dysplasia, we hope to be able to assess the usefulness of specific HPV characteristics in future cervical cancer screening risk stratification.

Methods: A targeted next-generation sequencing (NGS) panel will be designed for sequencing of 27 different HPV genotypes, including all HPV genotypes classified as carcinogenic or probably/possibly carcinogenic to humans. The panel will cover >97% of the HPV genome for each of the included HPV genotypes. The NGS analyses will be performed on excess liquid-based cytology screening material from HPV screen-positive women aged ≥60 years old and compared to the women's subsequent cytological and histological diagnoses.

Results: The NGS panel has been designed and is currently being validated on formalin-fixed, paraffin-embedded (FFPE) samples, liquid-based cytology samples, and FFPE HeLa and SiHa cell lines for its usefulness in assessing the above-mentioned HPV characteristics.

Conclusions: Specific HPV characteristics may show an association with the severity of cervical dysplasia and may thus prove useful in the improvement of risk stratification in HPV screen-positive women.

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#6612

P09-06 | Clinical validation of Allplex HPV hr detection assay on SurePath collected cervical samples: comparison with Clart® HPV4S genotyping test in a French laboratory

09 - HPV testing

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Background/Objectives: In 2020, high-risk human papillomavirus (hrHPV) testing was introduced in France in primary cervical cancer screening for improved detection or follow-up of cervical precancerous and cancerous lesions in women between 30 and 65 years old according to the French national guidelines (HAS) [1]. Molecular hrHPV testing is more sensitive than cytology (Pap test) for cancer cervical screening [2]. Its specificity is improved by subsequent cytology triage of hrHPV positive samples. Today about 250 HPV assays are commercially available. Clinical validation based on 2009 Meijer international guidelines remains pivotal to ensure screening-relevant assay performance [3]. We present the results of the first European comparative clinical evaluation of AllplexTM HPV HR Detection assay relative to Clart® HPV4S genotyping test validated in 2020 [4].

Methods: The recently developed AllplexTM HPV HR Detection assay (Seegene, Seoul, Korea) is a new multiplex real time PCR test designed to individually detect, in a single tube, 12 hrHPV types (HPV 16 18 31 33 35 39 45 51 52 56 58 59), one probably oncogenic type (68) and one potentially oncogenic type (66), according to the IARC [5]. This assay also allows quantification of the viral load providing the cycle threshold (Ct) value of each genotype [6]. We compared the clinical performance of this assay with the Clart® HPV4S genotyping test (Genomica, Madrid, Spain) on 280 liquid-based cervical samples of women followed up for a recent lesion treated or not and known for less than two years.

Results: Overall agreement between the two assays was 95% with k value of 0.90. Clinical sensitivity for high grade squamous intra epithelial lesion (≥ CIN2) was similar for AllplexTM HPV HR Detection assay and Clart® HPV4S genotyping test. Specificity was determined by comparison with cytology in all 280 cases and with histology or follow up in 80 cases.

Conclusions: Our study demonstrates that AllplexTM HPV HR Detection assay (Seegene, Seoul, Korea) has comparable performance to the robust Clart® HPV4S genotyping test (Genomica, Madrid, Spain) and can be useful for HPV based cervical cancer screening test.

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#6722

P09-07 | Completing the international validation status of the AmpFire® HPV screening 16/18/hr assay

09 - HPV testing

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Background/Objectives: To meet the screening goal of WHO's 90-70-90 strategy aimed at eliminating cervical cancer by 2030, clinical validation of human papillomavirus (HPV) assays is essential to provide accurate and valid results through fulfilling three criteria of the international validation guidelines. Previously, the clinical accuracy of the AmpFire® HPV Screening 16/18/HR assay (AmpFire assay) was reported but reproducibility data are lacking. Here, we aim to evaluate the intra- and inter-laboratory reproducibility of the AmpFire assay.

Methods: The reproducibility of the isothermal AmpFire assay was assessed using 556 cervical cell samples collected from women attending cervical cancer screening and biobanked in a Belgian HPV national reference center. This assay detects HPV16, HPV18 and 12 other high-risk HPV (hrHPV) types (31/33/35/39/45/51/52/56/58/59/66/68) in aggregate. Lower 95% confidence interval bound around the assay's reproducibility should exceed 87%, with $\kappa \geq 0.50$. Additionally, a literature review of the AmpFire assay's clinical performance was performed.

Results: The AmpFire assay showed an excellent intra-laboratory (96.4%, 95% CI: 94.5 - 97.8%, $\kappa = 0.920$) and inter-laboratory (95.3%, 95% CI: 93.2 - 96.9%, $\kappa = 0.897$) reproducibility. One study demonstrated non-inferior sensitivity of a prototype AmpFire assay targeting 15 hrHPV types (including HPV53) to detect CIN2+. However, non-inferior specificity was observed after removing HPV53 from analyses.

Conclusions: The AmpFire® HPV Screening 16/18/HR assay fulfills the third criterion of the international validation guidelines. Our study completed the validation status of a new isothermal HPV assay that presents interestingly low-cost and easy-to-use applicability.

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#6798

P09-08 | The detection of multiple human papillomavirus (HPV) types through the development of an isothermal DNA amplification assay

09 - HPV testing

Background/Objectives: Human Papillomaviruses (HPV) are categorised into different groups based on their carcinogenic potential with Group 1 being mostly associated with cervical cancer. HPV infections are common, and most individuals will be infected with HPV during their lifetime. These infections often go unnoticed as they are typically asymptomatic and tend to resolve naturally, with the body clearing the infection. However, persistent HPV infection is the most prevalent causative agent of cervical cancer. Due to the strong correlation between high-risk HPV infection and cervical cancer development, routine HPV testing has become a standard practice in cervical screening programmes. Current HPV detection methods are limited due to their inability to discriminate between all high-risk HPV types. HPV genotypes are frequently reported as a pooled result despite the prevalence of co-infection with multiple HPV types. It is advantageous for both monitoring and potential treatment strategies to detect and identify specific HPV types. This project's primary aim is to develop an isothermal HPV DNA amplification assay capable of detecting and discriminating between several LR-HPV and HR-HPV types.

Methods: HPV DNA reference sequences were obtained from PaVE: Papillomavirus Episteme. The reference sequences were aligned and compared using Clustal Omega sequence alignment software. Oligonucleotide primers were designed to universally bind to conserved regions across all the HPV types. Oligonucleotide probes were designed to bind to regions of low homology across all the HPV types in order to facilitate discrimination of each HPV type. The capability of universal HPV primers to amplify DNA from selected HPV types was evaluated by conventional PCR. The efficacy of the probes was determined using RT-PCR.

Results: To date, the efficacy of the universal oligonucleotide primers has been determined via conventional and real time PCR. The primers amplify all HPV types with the same efficiency. The detection of and the discrimination between several LR-HPV and HR-HPV types has been achieved by real-time PCR. Successful amplification of HPV DNA has been achieved via isothermal amplification and the target sequence verified by DNA sequencing.

Conclusions: HPV DNA has been successfully amplified isothermally, and work is ongoing to discriminate between all of the types under study.

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#7849

P10-01 | Does the oncogenic potential and genotypic prevalence of HPV change every year?

10 - HPV screening

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Background/Objectives: The distribution of oncogenicity of HPV types changes due to virus mutations, population exposure to a specific virus type, or changes in our immune response to the same virus. Over 118 types of HPV have been detected in the anogenital region. Clinical experiences have shown that they have different oncogenic potentials, categorized as follows: high-risk types 16, 18, 31, 33, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82; probably high-risk types 26, 53, 66; and low-risk types 6, 11, 40, 42, 43, 44, 54, 61, 70 (1).

Methods: From the high-risk group, types 16 and 18 stand out in terms of oncogenicity, as the risk for progression to cancer for these two types is twice as high compared to all other types in this group (2). The presence of HPV type 16 in women older than 30 years should be considered risky, similar to a cytological ASCUS smear. However, HPV type 16 has its subtypes that differ in the DNA sequence, altering the oncogenic potential of HPV 16 and categorizing it into subtypes such as European, Asian, African, etc. (3). The oncogenic potential of HPV also depends on the geographical region, race, religion, etc. The initial studies on the oncogenic potential and geographical tropism in Southeast Serbia were conducted in 2017. At that time, types 56 and 58 were identified as having a specific tropism for this region. Further studies in the following years until 2020 showed changes in the distribution of oncogenicity compared to the year of the initial study.

Results: Every year, a new type tends to emerge and enter the top 10, only to be absent in the following years. In our region, these types include 56, 54, 59, and 39. If these types are excluded, a pattern in the distribution of oncogenic potential becomes noticeable. The order of the top 17 HPV types by oncogenicity would then appear as follows: 16, 31, 58, 33, 18, 45, and 51. Understanding the distribution of oncogenic potential is important for several reasons: Assessment of oncogenic risk and the need for a personalized, more aggressive diagnostic-therapeutic approach: Knowledge of which types of HPV predominate in a specific population enables a more accurate assessment of the risk of oncogenesis. A personalized diagnostic-therapeutic approach can be implemented based on the specificity of the present HPV types, tailoring treatment according to their oncogenic potential. Triaging HPV-positive tests and cytologically negative HPV+ tests: Awareness of dominant HPV types assists in a more precise triage of positive tests. Different types may pose varying risks of cancer development, allowing triage to be directed towards the most relevant interventions.

Conclusions: Assessment and selection of the most effective HPV vaccine in a specific geographic area: Various vaccines cover different HPV types. Understanding the distribution of oncogenic potential helps identify the most common and high-risk types in a given region, leading to a better choice of vaccine for preventing HPV infections and related diseases.

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#7014

P10-03 | An economic evaluation of two cervical screening algorithms in Belgium: HPV primary compared to HPV and liquid-based cytology (LBC) co-testing

10 - HPV screening

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Background/Objectives: To compare the benefits and costs of high-risk human papillomavirus (HPV) primary screening versus HPV and liquid-based cytology (LBC) co-testing for cervical cancer screening in Belgium.

Methods: A decision tree was parameterised using observed test result data using LBC and HPV-testing from the peer-reviewed HORIZON study data (1, 2) and from current Belgium cost (3) and population data (4, 5). The theoretical model represents two screening algorithms for a cohort of 577,846 women aged 25 - 64 attending cervical screening in Belgium annually. The clinical follow-up algorithm for HPV primary was adopted from the Dutch cervical cancer screening programme, and from German screening practice for the co-testing arm. Cost of an HPV test (€67.90) was the current HPV reimbursement in Belgium. It was assumed that the annual test cost for co-testing with a 5-year interval was the same as the annual cost of LBC with a 3-year interval.

Results: Compared to HPV primary, co-testing identified 2,351 more CIN2+ cases annually (27% more than HPV primary) and 1,602 additional CIN3+ cases (24% more). Co-testing resulted in 13,173 additional colposcopies, 67,731 additional HPV tests and 477,020 additional LBC tests. The cost per woman screened was €113.50 for HPV primary screening and €101.70 for co-testing. The average cost per CIN2+ case detected was €5,381 with co-testing vs €7,650 with HPV primary; the average cost per CIN3+ case detected was €7,169 with co-testing vs €9,942 with HPV primary.

Conclusions: Co-testing could increase cervical precancer detection rates compared to HPV primary. Co-testing could cost less than HPV primary if the cost of HPV and LBC in the co-testing arm were cost-neutral compared to the current cost of LBC screening but would cost more if the HPV and LBC test costs were the same in both co-testing and HPV primary strategies. These findings support a co-testing algorithm in Belgium if the aim is to maximise the number of women with abnormalities found and minimise the risk of missing cases. Statements: Aquarius Population Health received funding from Hologic for this study. Content of this abstract was accepted by the European Journal for Cancer Prevention for publication.

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#6922

P10-04 | hrHPV infection prevalence in women with NILM cytology

10 - HPV screening

Background/Objectives: Background/Objectives HPV can persist in the cervix, even in women with normal cytology results. Some women can have a persistent HPV infection for an extended period without developing precancerous or cancerous changes. The duration of HPV persistence can vary widely among individuals and may be influenced by factors such as the specific HPV type, the person's immune system, and other variables. The aim of this study is to estimate the prevalence of hrHPV infection in women who had a repeated HPV test one year after a positive test with negative (NILM) cytology and to analyse the factors that might be associated with persistent infections.

Methods: Methods We conducted a cross-sectional, observational study on women who had primary HPV testing between March 2019 and December 2022 and had a positive HPV test for other high-risk HPV types other than 16/18, with a NILM reflex cytology. According to our screening program, these women were asked to repeat the test after one year. We collected demographic information such as age, educational level, parity, type of contraception used, HPV vaccination status and smoking habits. Data were obtained from the Siima-Rastreios clinical files and recorded anonymously. Categorical variables are presented through absolute frequencies and percentages. In univariate analyses, the Chi-Square test was employed. In multivariate analysis, both univariate and multivariate logistic regression were used to examine the impact of each parameter on persistence. The significance level was set at 0,05. All data were analyzed using IBM-SPSS software version 28.0.

Results: Results In a population of women with NILM cytology (n=6686) two populations were compared, one with no HPV persistence and the other with HPV persistence in two or more observations, to investigate factors contributing to HPV persistence. Out of the women studied, 759 maintained HPV persistence (11.4%). HPV persistence was more prevalent in the 30-39 age group (n=210). The risk of HPV persistence increases with age with statistically significant differences (p inf0,05). The risk of persistence was associated with hormonal oral contraception, secondary or higher education, smoking, and primiparity (but without statistically significant association).

Conclusions: Conclusion Risk factors associated with HPV persistence in the literature can vary depending on the studies and populations investigated. Our study is in line with what we can find in the literature that age is one of the most important risk factors. It's important to discuss any concerns or risk factors with a healthcare professional for proper monitoring and preventive measures.

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#6728

P10-05 | Comparison of clinical efficacy of human papillomavirus (HPV) testing with partial genotyping to liquid-based cytology as primary test in cervical screening for women between 25 and 29 years old in Singapore

10 - HPV screening

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Background/Objectives: The Singapore national cervical screening launched in 2003 was cytology-based (LBC), targeting women between 25 years and 65 years old. In 2019, primary hrHPV-DNA testing was recommended in place of cytology for women aged 30 years and above. LBC continues for women below 30 years old on the argument that the predictive value of HPV test was lower than cytology for high-grade lesions owing to a high prevalence of HPV infection and a high regression rate of low-grade lesions in these women. The arguments lack convincing supportive evidence. This study was therefore conducted to compare the clinical efficacy of primary HPV testing and LBC in cervical cancer screening for women below 30 years old in Singapore.

Methods: This retrospective cohort study included women attending cervical cancer screening using co-testing with LBC and hrHPV testing with partial genotyping for HPV16 and HPV18 performed on cobas® 4800 System. Women with history of CIN or attendance for management of abnormal screening were excluded. The criteria for referral to colposcopy were LBC showing ASCUS with positive hrHPV, LSIL, HSIL or ASC-H, or positive for HPV16 or HPV18 regardless of cytology results. The primary outcomes of analysis included rate of discharge to routine screening, colposcopy referral rate, and number of colposcopies performed to detect one case of CIN2+. Data was compared for women below 30 years old and the test performance was further compared to women at older 5-year-groupings up to 44 years old.

Results: Of 6,398 women studied, 503 women (7.9%) were positive for hrHPV-DNA at initial testing. The rate of hrHPV positivity and abnormal cytology showed a declining trend from 25 to 69 years old. The rate of hrHPV positivity was higher (pinf0.001) in women aged 25 to 29 years old (12.6%) compared to women aged 30 and above collectively (7.3%) but was not statistically significant compared to age-groupings of 30-34,35-39 and 40-44 years old (p=0.764). For women between 25 and 29 years old, the rate of discharge to routine screening was 92.2% for LBC and 92.5% for hrHPV testing (p=0.621). The colposcopy referral rate was 3.7% for LBC and 4.6% for hrHPV testing (p=0.232). The colposcopy referral rate from both LBC and hrHPV testing was higher (pinf0.001) compared to women between 30 and 44 years old. Overall, 27 cases of CIN2+ were detected on LBC screening and 30 cases on HPV screening. More high-grade lesions were detected among younger women aged 25-29 and 30-44 years old compared to women ≥ 44 years old. A total of 163 colposcopies were performed in women screened by LBC and 210 by primary HPV screening. Among women aged 25-29 years old, the number of colposcopies per case of CIN2+ was 5 for LBC screening and 7 for HPV-based screening (p=0.5582). This trend was similarly observed for women aged 30-44 years old. In comparison, the number of colposcopies needed for detection of a case of CIN2+ was more than 2-fold higher for women above 45 years old, owing to a higher detection rate of CIN2+ among the younger women.

Conclusions: The findings of this study confirmed that clinical efficacy of primary HPV testing was comparable to cytology in cervical cancer screening in women between 25 and 29 years old. More importantly, the efficacy was comparable to older women between 30 and 44 years old who are recommended primary HPV-based screening. These data give strong support for incorporating women aged 25 to 29 years old into HPV-base primary screening program in Singapore.

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#6738

P10-06 | Cervical cancer incidence and screening in Sweden 2017-2022

10 - HPV screening

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Background/Objectives: The Swedish National Cervical Screening Registry (nkcx.se) collects all data on cervical screening in Sweden (e.g. individual invitations, test results and cervical histopathologies). The data is evaluated annually to inform the program of whether changes are needed in order to improve the benefits (reduce the incidence and mortality of cervical cancer) and reduce the harms of screening. We wished to summarize the trends discovered and observations made during the last five years, including effects of the pandemic on the screening program.

Methods: Nationwide data on number of invitations, screening tests, number of cervical histopathologies and number of CIN2+ cases and their follow-up, as well as the number of self-sampling tests performed, were collected from the registry and compiled per year for the period 2017-2022.

Results: The test coverage among women 23-70 years old remained high and stable with an average of >80% coverage during the last four years, with the highest coverage among the youngest women. The number of CIN2+ cases that were followed-up with colposcopy and histology within 3 months after diagnosis (according to recommendations) were only 60% but increased to 95% or more 1 year after diagnosis. The use of self-sampling increased dramatically during the period and by the end of the period accounted for almost half of all screening samples taken in 8/21 counties, including all three major metropolitan regions.

Conclusions: The number of screening tests performed during the period has remained high despite of an on-going pandemic. During the pandemic, a temporary government regulation allowed primary self-sampling instead of an invitation to clinician sampling. This allowed for a continuous high screening coverage during the pandemic and explains the huge increase in the use of self-samples. The follow-up of CIN2+ positive women remains high, albeit with longer follow-up times than recommended. Despite this, there was a proportion of Swedish women with invasive cervical cancer who had had abnormal screening results but had not been followed up. As the program has high coverage and today uses convenient and up-to-date tests (self-samples for HPV), an improvement with large potential gains appears to be ensuring follow-up of screen-positives.

References: Annual reports from 2018-2023 available at nkcx.se

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#6749

P10-07 | HPV prevalence and genotype profile in primary HPV screening of Norwegian women aged 25-33 years

10 - HPV screening

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Background/Objectives: National implementation of primary HPV screening started in Norway in 2019 for women aged 34-69 with a five-year screening interval. Following implementation, all cytology and HPV testing in the South-Eastern Norway Regional Health Authority were centralised from ten to three laboratories. In addition, a new platform for HPV DNA detection with extended genotyping and a new laboratory data system, Lab Vantage Medical Suite (LVMS), which is linked to the Cancer Registry of Norway's national databases for HPV, cytology and histology, were implemented. From January 2023 HPV primary screening was implemented also for women aged 30-33 years and from June 14th 2023 HPV primary screening covered the entire screening population aged 25-69 years living in the South-East Health Region. In 2022 the first cohort of women vaccinated against HPV as part of the Childhood Immunisation Programme were invited to cervical cancer screening. In 2021 the vaccination coverage in the Norwegian Childhood Immunisation Programme was 92%, and 59% in the catch-up programme for women born between 1991-1996.

Methods: Cervical samples were collected in BD SurePath medium, and allocated to appropriate testing (either HPV or both cytology and HPV, according to the women's previous screening history and the current algorithms) using a function available within LVMS. The screening history from local and national databases for the last ten years was automatically acquired by LVMS. HPV-analyses were performed using the BD OnclarityTM HPV assay on a fully automated, real-time PCR DNA assay, targeting the E6/E7 region of the HPV genome. BD Onclarity detects six HPV genotypes individually (16, 18, 31, 45, 51 and 52) and eight genotypes collectively in three groups (33/58, 56/59/66 and 35/39/68). Data for women 30-33 years old was collected from January 1st 2023, and for women 25-29 years old from June 14th 2023.

Results: The HPV prevalence among the 24,750 women eligible for HPV primary screening test was 25% and 17% among the 25-29 years old and 30-33 years old women, respectively. For women aged 25-29 years triage cytology of the HPV positive samples revealed unsatisfactory cytology in 1%, normal cytology in 40%, low-grade cytology in 44 % and high-grade cytology in 15 % of the cases. For women aged 30-33 years, the triage cytology showed unsatisfactory cytology in 1%, normal cytology in 45%, low-grade cytology in 36 % and high-grade cytology in 18 % of the cases. In women with normal or low-grade cytology the most prevalent genotypes were HPV 56/59/66 and HPV 35/39/68, while HPV 16 and HPV 31 were most prevalent in high-grade lesions for both age groups.

Conclusions: Among the youngest age group (25-29 years) the HPV prevalence was 25% and the majority of genotypes detected were those not covered by the HPV vaccines. Histological data is currently under review and will be presented.

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#6783

P10-08 | High risk HPV genotypes prevalence in Mexico

10 - HPV screening

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Background/Objectives: The greatest risk factor for the development of cervical cancer is infection by human papillomavirus (HPV). To date, more than 200 genotypes have been described, 14 of them considered by the WHO as high risk genotypes (HR) due to their high oncogenic capacity, with special attention given to genotypes 16 and 18. In Mexico, cervical cancer is the third cause of cancer-associated death in women, therefore, the timely detection of HR genotypes in women becomes an imperative issue for the reduction of the burden of this disease. The detection of high-risk HPV genotypes through the PCR molecular test is part of primary cervical cancer screening, however, this practice is not common in Mexico. In this study, we analyzed the results of HPV genotyping studies in women who attended cervical cancer screening studies at Salud Digna clinics throughout the country with the objective of determining the prevalence and distribution of high-risk genotypes HPV in Mexico.

Methods: Retrospective analysis of the results obtained for the detection of human papillomavirus in cervical samples from patients who attended the Salud Digna clinics in the period from june to august 2023. The samples were processed by a molecular test (RT-PCR) indicated for HPV screening (ROCHE COBAS PRIME-Cobas 6800). The kit used was the COBAS HPV kit which detects the 14 high-risk genotypes and generates 4 types of results: negative, positive for HPV16, positive for HPV18 and positive for POOL (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68). For the analysis, Mexico was divided into 7 regions which share sociocultural factors (Northwest, North, West, Center, Gulf, South, Southeast).

Results: The study population was 95,934 patients with a mean age of 41 years. At the national level, 18.93% (18,159) of patients are positive for HPV POOL, 3.54% (3,399) for HPV 16 and 1.78% (1709) for HPV 18. The regions with the highest percentage of positive patients are the southeast region for HPV POOL (22.32%), and the south region for HPV 16 (3.77%) and HPV 18 (2.44%) while the region with the lowest percentage is the Northwest region (HPV POOL 17.86%, HPV16 3.39%, HPV18 1.57%). The age range with the highest percentage of positive patients is 14-29 years for HPV POOL, 30-39 years for HPV 16, and 30-39 years for HPV 18.

Conclusions: We found that Mexican patients are becoming infected at an early age with the genotypes that are part of the pool, however, we observe a marked trend towards a decrease in cases as the age of the population advances. The regions of the country with a higher percentage of HPV positive patients are the south and the southeast, regions that also concentrate most of the extreme poverty in Mexico. These numbers should be taken with caution given that in absolute values these are also are the regions of the country where the least people go for a cervical cancer screening study, emphasizing the need to promote these studies in these regions. In the case of genotypes with a greater oncogenic capacity, both HPV16 and HPV18 show a greater prevalence in economically productive age ranges. Retrospective studies like provide information that allow governments to generate public policies focused on the most affected regions, taking into account the sociocultural factors of such a large and diverse country.

Graphs

Haba Moya Julia
Spain
Haba Moya Julia
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#6679

P10-09 | Evaluation of a new self-sampling device for HPV detection in cervical cancer screening

10 - HPV screening

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Background/Objectives: Self-sampling has been recommended by the WHO as an additional approach to sampling for cervical cancer screening in order to reach the established goals on cervical cancer screening and treatment. Vitro S.A (Granada, Spain) has developed a very convenient and easy to use self-sampling kit, which allows to detect effectively high oncogenic risk HPV present in the cervix samples. The aim of this study is to evaluate the performance of the self-collection device (VITROVEIL; VITRO SA) for the detection of high-risk HPV (hr-HPV) by real-time PCR, compared with traditional physician-collected liquid-base cytology (LBC).

Methods: A cross-sectional study involving 345 women aged 25-72 years was conducted from September to December 2022. Patients collected the cervical sample using the Vitroveil device and then the conventional sample was taken. In addition, they completed a socio-demographic and satisfaction questionnaire. Self-samplings were processed with the RNA/DNA extraction kit and the Vitro HPV Screening Real Time PCR kit. At the same time, liquid-base cytologies were processed with Cobas 4800 ® System. Paired samples giving discordant results were retested using the opposite assay. To study the effect of the different co-variables measured, a one-way analysis of variance was used. Differences were significant if pinf0.05.

Results: Out of 345 samples, 21 were non-valuable samples since they arrived unidentified, spilled, or contaminated and 5 samples were eliminated for giving an invalid result after processing. Finally, 321 paired samples were included in the study. Cytological evaluation was normal in 90%, 1.5% ASCUS, 4.38% L-SIL and 3% H-SIL. Hr-HPV positivity was higher (28.5 %) in self-sampling than in standard samples (23.8 %) but this difference was statistically no significant. The agreement for hr-HPV between samples collected by a health professional and self-sampling was 93.7% with a Cohen's kappa coefficient of 0.842. Out of 11 samples with H-SIL, 10 were hr-HPV positive in both samples. Of the 14 samples with L-SIL, 10 were hr-HPV positive by self-sampling and 9 by LBC sampling. Of the 5 samples with ASCUS, 3 were hr-HPV positive with both methods. Of the 21 discordant samples, 18 of the self-tests repeated the same results obtained with VITRO when tested with the cobas®4800 system. Regarding the results of the questionnaire, the satisfaction score for self-testing is on average 2.36 times higher than for cytology, Pinf0.0001.

Conclusions: It was concluded that HPV self-testing is a convenient and safe option with detection rates comparable to conventional screening. This new device has the advantage of being less invasive and more reliable than rush/swab self-samplings for the patient, promoting the participation in screening programs.

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Bulgaria

Milanova Valentina

#7318

P10-10 | Efficacy and Acceptability of Self-Collected Medical Grade Tampon as a Novel Vaginal Sample Collection Tool for the Detection of HPV and STIs

10 - HPV screening

Background/Objectives: Objective: Cervical cancer remains a significant health concern, particularly in low-income and middle-income countries (LMICs). This study aims to compare the efficacy and suitability of a self-collected tampon for the detection of human papillomavirus (HPV) and sexually transmitted infections (STIs) using qualitative TMA-based assays (Transcription Mediated Amplification; APTIMA® HPV, APTIMA® Combo 2 (CT/NG; AC2 from now on) and APTIMA®Bacterial Vaginosis (BV from now on). Additionally, we assess the acceptability of tampons as a self-collection tool.

Methods: Methods: A cohort of 75 female participants aged 18-54 years was recruited through female-focused social networks. Participants provided informed consent and underwent both Health Care Workers (HCW-collected) and self-collected sample collection using the Daye Diagnostic Tampon. Samples were stored in ThinPrep Vials (TP Vial) or Aptima® Multitest Swab Collection Kit (APTIMA®) solutions. HPV and STI testing were performed using TMA-based assay on the fully automated Panther® Platform. Acceptability was assessed through a questionnaire with Likert-scale responses.

Results: Results: The study involved 60 participants who completed the study (80% of recruited participants). The self-collected tampons showed sensitivity and specificity of 66.67% and 90.74% (when rinsed in TP Vial) and 83.33% and 85.42% (when rinsed in APTIMA®) for HPV detection, respectively. For bacterial vaginosis (BV) detection, the tampons exhibited sensitivity and specificity of 100.0% and 96.43% (TP Vial) and 88.89% and 98.04% (APTIMA), respectively. For detection of chlamydia and gonorrhoea (AC2), the sensitivity and specificity were 100.00% and 100.0% (TP Vial) and 100.00% and 98.31% (APTIMA), respectively. Participants expressed a preference for tampon self-collection over HCW-collected swabs (90%).

Conclusions: Conclusion: Self-collected tampons demonstrated promising diagnostic accuracy to HCW-collected swabs for HPV and STI detection. The tampon self-collection method was well-accepted and preferred by participants, suggesting its potential as an alternative screening tool, particularly in low-resource settings. Further research with larger and more diverse populations is recommended to validate these findings and inform tampon-based self-collection programs for cervical cancer screening. Randomised controlled trials and comparisons with gold standard methods would enhance validation.

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#7076

P10-11 | Prevalence of the human papillomavirus (HPV) types among cervical dysplasia women attending a gynaecological clinic in Sweden

10 - HPV screening

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Background/Objectives: Cervical cancer is one of the most common cancers and a leading cause of cancer death in women. HPV infection is found in 99.7% of cervical cancer cases worldwide. Studies have shown an HPV-prevalence up to 91.6% in cervical intraepithelial neoplasia grade 3 among women in the Nordic countries. HPV-testing has been endorsed as a primary screening method for cervical cancer in Europe. Vaccination has lead to a reduction in the prevalence of severe dysplasia. Surveillance of HPV-types that continuously appear in dysplasia cases is of great importance. Here's, we identify the current prevalence of 27 HPV-types among 168 women with histologically verified low-and high-grade squamous intraepithelial lesion (LSIL and HSIL). In addition, we compared the HPV-prevalence in both dysplasia grades with special consideration to age and vaccination status.

Methods: Women with histological cervical dysplasia were recruited at the gynaecological clinic of Uppsala University Hospital, Sweden. Cervical swabs for HPV-testing were collected during gynaecological examinations between mid-2017 and late-2019. Vaccination status was obtained through questionnaires. HPV-genotyping was performed using a multiplex bead-based immunoassay on 27 different HPV-types: 15 oncogenic types; six probably oncogenic types; and six non-oncogenic types. R packages were used to perform data and statistical analysis.

Results: The prevalence of the oncogenic HPV-types increases as with increased severity of dysplasia(1). 45.0% of the women with LSIL were infected by oncogenic- (oHPV) types and 10.0% by non oncogenic- (non oHPV) types, and 43.8% were HPV-negative. The group of women with HSIL showed the highest prevalence of the oHPV-types with 75.0%, the absence of non oHPV-types and 22.7% of HPV-negative cases. Significantly more cases of oHPV in the HSIL than in LSIL group were observed ($p < 0.01$). Oncogenic HPV-types are the most prevalent across all ages in women regardless stage of dysplasia(2,3). HPV16 was the most prevalent among all the HPV-types followed by another two oHPV-types HPV52 and 33. The highest prevalence of oHPV-types (66.6%) was found in the youngest group (ages 21-25). It bottomed in individuals aged 36-40 (40.9%) with at least one oHPV-type. Then it peaked with 63.6% of oHPV-types among women aged 50-70 years old. Oncogenic HPV-types among vaccinated women with dysplasia was different compared to the unvaccinated women(4,5). Less women were infected with HPV-types covered in the vaccine among the vaccinated (v_) women (n=1) compared to the non-vaccinated (nv_) women (n=22). Most of the v_women were positive for the oHPV-types not covered in the vaccines administered. When considering multiple-HPV-type infections per woman, HPV58 was the most common oHPV-type in v_women, while HPV16, 52, 18, and 39 were the most prevalent oHPV-types in nv_women. Among nv_women, significantly ($p < 0.01$) higher number of individuals infected with oHPV-vaccine-types 16 and 18 were found in the HSIL group in contrast to the LSIL group. Among women with HSIL, 51.3% of nv_women were infected by one or both of the oHPV-types covered in the vaccines and 25.6% by one or more of the oHPV-types not covered.

Conclusions: Oncogenic-HPV-types are highly prevalent among women with HSIL. The distribution of oncogenic HPV types among vaccinated women with dysplasia differed from that of unvaccinated women. The current vaccines present effectiveness for reducing the covered HPV-types among dysplasia patients.

hpv_all.png

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#7087

P11-01 | Enhancing cervical cancer screening for Dutch women over 60: evaluating the need for regular screening at age 65

11 - Screening for women difficult to reach

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Background/Objectives: Background Screening and early treatment will prevent most cervical cancer cases and deaths. Although overall incidence and mortality has significantly decreased over the decades, cervical cancer is still the 4th most common cause of cancer in women. Recent studies show that incidence has slightly increased in women above the age of 60 and they are at risk of being diagnosed with late-stage cancer with a high mortality rate. In the Netherlands, women are offered regular screening until the age of 60, with recent changes in 2017, as women at age 65 are also invited if they tested positive for HPV at 60 and were not referred for cytology. In addition, the overall incidence of the disease has increased slightly in recent years. This study will evaluate which women would benefit from regular screening at the age of 65 to reduce the incidence and mortality of the disease. In order to do this, we will first evaluate risk of disease in older women with a special focus on the last screening history around 60, as this is the last opportunity to screen these women in the current program. Aim We aim to determine the association between last screening and subsequent diagnosis of cervical (pre) cancer in women above age 60 years. In addition, we will examine the influence of sociodemographic, lifestyle, and sexually-reproductive factors on this association.

Methods: We will conduct a case-control study nested in Lifelines, a large cohort in the Northern Netherlands, linked with data from the Nationwide Pathology Databank (PALGA). Cases will include all women diagnosed with cervical (pre) cancer after the age 60, while controls will consist of women without any cancer matched by age and inclusion date to Lifelines. We had requested for data access for both and we intend to complete the analysis by January 2023. Analysis The data analysis for this study will be conducted using SPSS 28.0. First, Missing data will be imputed using multiple imputations by chained equations (MICE). Descriptive statistics will be used to summarize the characteristics of both cases and controls, including demographic variables, lifestyle factors, and screening history. The proportion of participants who underwent cervical cancer screening in the last screening round of the study cohort will also be reported. In the initial phase of the analysis, a univariate analysis will be performed to assess the association between individual variables and cervical (pre) cancer diagnosis. Following this, multivariable logistic regression models will be used to estimate the odds ratio (OR) and the associated 95% confidence interval. The models will be adjusted for potential covariates such as smoking status, contraceptive use, and socioeconomic status, educational level, which contribute as risk factors for the development and progression of cervical cancer, will be adjusted for in the analysis

Results: Still penidng as application for data is taking time, we will have the data by November and will complete the analysis by january 2024.

Conclusions: Still penidng as application for data is taking time, we will have the data by November and will complete the analysis by january 2024.

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#7116

P11-02 | Identifying barriers and facilitators to implementing a community health worker (CHW)-engaged cervical cancer screening program in Shenzhen, China using the consolidated framework for implementation research (CFIR)

11 - Screening for women difficult to reach

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Background/Objectives: The barriers and facilitators to implementing CHW-engaged cancer screening programs remain unclear in China. A CHW-engaged cervical cancer screening program was piloted in Shenzhen, China in 2022 to address the poor screening rate and colposcopy adherence among underserved women. This program was led by hospital screening centers, with CHWs conducting initial screenings and collaborating with hospital health workers (HHWs) on referrals and provider-patient communications. This study aimed to identify barriers and facilitators to implementing the program.

Methods: From July 2022 to August 2023, semi-structured interviews were conducted with six comprehensive hospitals and eighteen community-based health centers. Thirty-five participants included six program directors, eleven HHWs (including seven gynecologists) and eightneen CHWs. All transcripts were audio-recorded, transcribed verbatim, and analyzed using deductive thematic analysis guided by CFIR. A 13-item scale was developed assessing intervention, outer settings, inner settings, individual and process. The informed consent was obtained from all participants.

Results: Five barriers and four facilitators were identified. CHWs highlighted the complexities and time-consuming nature of referrals and provider-patient communications. They offered practical recommendations for improving these processes through the implementation of chatbots and automated notification systems. Unclear division of responsibilities and overlapping patient status between CHWs and HHWs caused redundancy. Inadequate engagement of important stakeholders such as community health promoters and gynecologists, alongside the absence of individual incentives like bonuses and overtime pay, were identified as significant barriers. However, it is essential to note that CHWs' proficiency in cancer prevention and chronic disease management positively contributed to the quality of health promotion and provider-patient communications in the program. Additionally, facilitators included the willingness of patients to engage in health promotion activities, their unmet demands for screening services, the program's adaptability to diverse communities, and the flat organizational structures of community-based health centers that facilitated efficient coordination.

Conclusions: While the CHW-engaged screening program has the potential to improve screening coverage and follow-up communications for underserved women, significant barriers to its implementation exist. Improving workflows for referral and notification, engaging multi-level stakeholders, and providing personal incentives will be critical for effective implementation.

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#6911

P11-03 | Barriers to follow-up care after a positive HPV test among Hispanic women in the united states

11 - Screening for women difficult to reach

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Background/Objectives: Of all cervical cancers, 91% are caused by the human papillomavirus or HPV. Therefore, HPV testing plays an important role in cervical cancer screening in addition to traditional Pap tests. A positive HPV test result determines the type of follow-up testing and procedures women need to prevent the infection from progressing to cervical cancer. Hispanic women in the United States (U.S.) have lower cervical cancer screening rates and higher cervical cancer incidence than non-Hispanic White Women. In addition, they are less likely to adhere to the recommended follow-up care after a positive HPV test, increasing their risk of developing cervical cancer. Using the Intervention Mapping Framework (IMF), the objective of this research is to increase understanding of barriers and facilitators that influence adherence to recommended follow-up care after positive HPV test results among Hispanic women.

Methods: The study population is self-identified Hispanic women aged 30-65 years who received a positive HPV test in the last three years. Using an observational, cross-sectional design, we conducted individual in-depth interviews and a demographic questionnaire. We performed thematic analysis of the interview transcripts.

Results: To date, 13 individual interviews have been conducted in Spanish; data collection and analysis are ongoing. All participants were born outside the US, with a mean age of 38.2. Over two-thirds (69.2%) of participants had no health insurance, and more than three-quarters (76.9%) reported having a gynecologist. More than half (61.5%) had less than a high school degree, over three quarters (84.6%) had a monthly income of less than $3,000, and only 7.7% were employed full-time. A common barrier was the lack of knowledge about HPV and HPV testing. Most women knew that HPV is sexually transmitted, but they did not know there was a test to detect HPV infection. Another barrier was patriarchal cultural gender roles. Many women did not want to tell their partners they tested positive for HPV because they feared their partners would accuse them of being unfaithful. Additional barriers to follow-up care included lack of transportation, low literacy levels, limited English proficiency, undocumented immigration status, and lack of health insurance. Facilitators included access to safety net community clinics, financial assistance from safety net clinics, and transportation vouchers issued by safety net clinics.

Conclusions: Hispanic women face several barriers to adhering to follow-up care after a positive HPV test, including traditional healthcare access barriers, cultural gender roles, and stigma around sexually transmitted infections. The assistance provided by safety net clinics in the U.S. is crucial to help low-income, uninsured Hispanic women overcome healthcare access barriers. Culturally and linguistically tailored, low-literacy educational materials about HPV and HPV testing should be created in English and Spanish for Hispanic women and their romantic partners to address the cultural stigma about sexually transmitted infections in this population.

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#7932

P12-01 | High-risk human papillomavirus testing is superior to visual inspection with acetic acid in cervical cancer screening of Kenyan and Ugandan women living with HIV

12 - Triage of HPV positive women

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Background/Objectives: Invasive cervical cancer (ICC) continues to be one of the most common cancers among women globally despite the availability of screening and HPV vaccines. This is especially true in Sub-Saharan Africa where HIV infection further increases the risk of ICC. Many low- and middle-income countries (LMICs) utilize visual inspection by acetic acid (VIA) as the primary screening method. Testing for high-risk HR-HPV DNA is sensitive for detection of cervical precancers but may lack specificity. In this study, we directly compared HR-HPV DNA testing and VIA for detection of precancerous lesions of the cervix and examined the utility of VIA as a triage method for women living with HIV (WLWH) who were positive for HR-HPV DNA.

Methods: Eligibility criteria included WLWH, aged 21-60 years seen at facilities in Eldoret, Kenya and Mulago, Uganda. All women had self-collected cervicovaginal samples for HR-HPV DNA testing using the cobas® HPV test, then underwent VIA. Two cervical biopsies were obtained from all participants. VIA and HR-HPV DNA testing were compared for detection of precancers. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for HR-HPV DNA testing and VIA using cervical biopsy results as the gold standard.

Results: From November 2021 to March 2022, 122 WLWH were enrolled; two women refused biopsy and were excluded, leaving 120 women in the analytical sample. All participants were receiving antiretroviral therapy and most (107/120, 89.2%) had an undetectable HIV viral load. There were no significant differences in CD4 count, detectable HIV viral load or median lifetime sex partners between women in the two countries. The Kenyan participants were older than the Ugandan participants, 40.2 vs. 34.9 years ($p<.001$), respectively. Forty-nine of 120 (40.8%) women were positive for HR-HPV DNA. Overall, 17 of 120 women (14.2%) had an abnormal VIA. Cervical biopsy showed 8 cases of CIN2 and 6 cases of CIN3. Of the women with CIN2, none were positive for HPV 16, one was positive for HPV 18, and five were positive for the Non16/18HR-HPV types included in the cobas® HPV test. Of the six women with CIN3, one was positive for HPV 16, three were positive for HPV 18, and all were positive for the Non16/18HR-HPV types. For detection of CIN2/3, HR-HPV DNA testing had a sensitivity of 78.6% (95% CI: 57.1-100) and specificity of 64.2% (95%CI: 55.0-73.3); VIA had a sensitivity of 57.1% (95%CI: 31.2%-83.1) and specificity of 91.5% (95%CI: 86.2-96.8). For detection of CIN3 amongst all participants, HR-HPV DNA testing had a sensitivity of 100% (95%CI 100.0-100.0) and specificity of 62.3% (95%CI: 53.4-71.2); VIA had sensitivity of 50% (95%CI 10.0-90.0) and a specificity of 87.7% (95%CI: 81.7-93.7). All six cases of CIN3 occurred among the 49 women who were positive for HR-HPV DNA. However, only three of the six women had an abnormal VIA examination. Among the 49 women with a positive HR-HPV DNA test, the sensitivity of VIA for detection of CIN3 was 50% (95%CI 10.0-90.0) and the specificity was 81.4% (95%CI: 69.8-93.0).

Conclusions: In this prospective study of WLWH, HR-HPV DNA testing demonstrated greater sensitivity than VIA in the detection of CIN2/3 or CIN3. The specificity of HR-HPV DNA testing was lower when compared to VIA. Our findings do not support the use of VIA as a triage for WLWH who are positive for HR-HPV DNA.

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#6997

P13-01 | Clinical performance of hr-HPV testing on self-taken vaginal samples for the detection of CIN2+ and CIN3+ over three screening rounds

13 - Self-sampling

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Background/Objectives: Vaginal self-sampling provides a rapid, accessible modality for the engagement of women in cervical screening. There are few data on longitudinal performance of Hr-HPV testing on vaginal self-samples. We previously reported clinical performance Hr-HPV testing on self-samples for detection of CIN2+ over two screening rounds.1 Here is preliminary outcome of the same over three screening round with up-to 9 years of follow up.

Methods: Women attending for routine screening provided a self-taken vaginal sample in addition to a clinician-taken liquid-based cytology (LBC) sample. All women from the original cohort were invited to participate in further screening cycles of LBC screening, and after March of 2020 primary HPV screening. The sensitivity, specificity, positive predictive value (PPV), and complement of the negative predictive value (cNPV) of the self-sample Hr-HPV test for detection of CIN2+ and CIN3+ for up to 9 years after testing were determined. Additionally, clinical performance of Hr-HPV testing in vaginal vs clinician-collected LBC samples was assessed.

Results: A total of 224 of CIN2+ and 127 of CIN3+ lesions were diagnosed over three screening rounds. The risk of CIN2+ and CIN3+ in self-sampled Hr-HPV negative (Hr-HPV-) women was 1.5% and 0.8%, respectively for up-to 9 years after primary testing. The risk of CIN2+ and CIN3+ in cervical Hr-HPV- women was 1% and 0.4% respectively. Women with LBC negative results at first screening round had the risk of CIN2+ and CIN3+ at of 1.6% and 0.8% at the following screening round 3-5 years later. This increased furthet to 3.1% and 1.6% for CIN2+ and CIN3+ respectively at the time of third round of screening.

Conclusions: Our follow up results in women with Hr-HPV negative self-sample suggests, that the three-year recall for women younger than 50 may be beneficial. Further follow up study of self-sampling Hr-HPV screening are needed to identify safety of screening intervals.

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P13-02 | HPV self-sampling pilot and program implementation strategies used to engage under screened communities in cervical cancer screening: a scoping review

13 - Self-sampling

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Background/Objectives: Human papillomavirus (HPV) testing as a method of cervical cancer screening can be performed by healthcare providers or by patients through self-sampling directly in the community. HPV testing via self-sampling may increase cervical cancer screening rates by addressing key Papanicolaou test barriers (e.g., access to a provider, transportation, etc,) experienced by historically under screened populations such as Indigenous, newcomer and remote communities. As provinces across Canada prepare to pilot or implement HPV self-sampling in their screening programs, the objective of this scoping review was to determine which HPV self-sampling implementation and engagement strategies have been used to recruit or engage Indigenous, newcomer and remote populations in cervical cancer screening.

Methods: We conducted a scoping review searching MEDLINE, CINAHL, EMBASE, Cochrane Library, and SocINDEX from inception to August 2023. The inclusion criteria were: 1) Indigenous, newcomer (refugee or immigrant to a country for inf10 years) and remote communities; 2) countries identified as members of the Organisation for Economic Co-operation and Development; and 3) intervention included HPV self-sampling. Systematic reviews, meta-analysis, scoping reviews, and literature reviews were not included. Two reviewers screened the abstracts and subsequently full text to determine relevance. Relevant studies that met the inclusion criteria were described using a best-evidence summary.

Results: A total of 26 studies out of 2741 studies met our inclusion criteria. Seven studies specifically addressed Indigenous engagement while nine and ten addressed newcomer and remote communities, respectively. In-person engagement with trusted community leaders was the most widely used and accepted recruitment and engagement strategy across all three populations. Six out of seven studies with Indigenous communities distributed HPV self-sampling kits to eligible participants in person in a clinical setting for collection on site or at home. Similarly, nine of the identified studies that engaged newcomers recruited participants in person through the community, where eligible participants were either given a kit (n=7) or received one in the mail (n=2). Lastly, of the ten identified studies engaging remote participants in HPV self-sampling, six recruited eligible participants in person at various community locations and 4 used electronic medical records or registries to identify and mail kits to participants.

Conclusions: A variety of evidence exists to support engaging Indigenous, newcomer and remote communities in HPV self-sampling to promote cervical cancer screening. We found preliminary evidence to support the use of in person distribution and mail out of HPV self-sampling kits for these under screened populations.

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#6853

P13-03 | Cost-effectiveness of HPV self-sampling recruitment strategies for cervical cancer screening compared to clinician-sampling in Singapore

13 - Self-sampling

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Background/Objectives: Using self-sampling kits, individuals can take their own vaginal samples for a human papillomavirus (HPV) test. Self-sampling can increase cervical cancer screening (CCS) uptake compared to clinician-collected samples. CCS uptake differs by how screening participants are recruited for self-sampling. This study aimed to evaluate the cost-effectiveness of self-sampling recruitment strategies for the Singapore national CCS program.

Methods: Using a decision tree model, five strategies with different CCS uptake rates were compared with routine care of invitation mail (INV) and clinician-collected HPV sample: 1) mail-to-all (MTA); 2) opt-in (OPT); 3) primary care recruitment (PRI); 4) community pharmacy recruitment (PHA); 5) community outreach event (COM). A combination of recruitment strategies was also considered in this study: INV, MTA and OPT were complemented with either PRI, PHA, or COM, resulting in nine different combinations. Singapore-specific data were prioritized and supplemented with published literature and expert opinion from Singapore clinicians. Individuals unscreened in the past five years were modelled over one year from the healthcare payer's perspective. The self-sampling recruitment strategies were compared to INV according to three criteria: 1) incremental cost; 2) CCS uptake; 3) incremental cost-effectiveness ratio (ICER). The ICER represents the additional cost per additional cervical intraepithelial neoplasia or worse (CIN2+) diagnosed. One-way uncertainty analyses were conducted.

Results: Individually, PHA or COM had the lowest incremental cost while MTA had the highest CCS uptake. In terms of cost-effectiveness, PRI was cost-saving (ICER:-S$3,058/CIN2+), while OPT or MTA (ICER:S$33,983-S$36,190/CIN2+) were more cost-effective than PHA or COM (ICER:S$41,069-S$42,422/CIN2+). Among combination strategies, INV with either COM or PHA had the lowest incremental cost of S$1.1 million to S$2.2 million compared to INV alone. INV with PRI was the most cost-effective (ICER:S$30,786/CIN2+) combination strategy, while MTA with PRI resulted in the highest screening uptake of 3.7 times compared to INV alone. Overall, the model results were sensitive to the screening uptake of INV, screening uptake of PRI, and the proportion of screening participants offered self-sampling at the primary care setting.

Conclusions: Depending on prioritization criteria, self-sampling with PHA or COM may be considered based on lowest incremental costs; MTA based on highest screening uptake; PRI alone, or in combination with INV, based on cost-saving or cost-effectiveness.

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#6858

P13-04 | A nationwide trial of risk-stratified cervical screening for faster cervical cancer elimination

13 - Self-sampling

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Background/Objectives: As the era is approaching when vaccinations will have resulted in that new HPV infections are no longer occurring, design of effective campaign strategies for screening to find infected women at risk will become increasingly important.

Methods: Results of previous HPV screening by genotype provides a strong marker for risk. Also non-attendance, previous cytologies and previous treatments (or non-treatments) are strong risk predictors. We use the Swedish national cervical screening registry to once per year calculate the cervical cancer risk of each woman in the country. Women with an invasive cervical cancer risk of >100/100.000 women/year are sent a self-sampling kit to the registered home address. Women with an invasive cervical cancer risk of 30-100/100.000 women/years are sent both online letters and physical letters with a website link to order a self-sampling kit. Women with HPV positive results are referred to a regional gynecologist for follow-up.

Results: The project started with small scale piloting in 2009 and has gradually been extended to since 2022 encompass all 93,000 women with cervical cancer risk above 30/100,000 woman years. Until 2021, 10% (2,853/28,689) of contacted women ordered a self-sampling kit and returned a sample for testing. There was low participation among never-attending women, but up to 22.5% attended in other high-risk groups. The highest risk HPV types (16/18) were detected in 8.3% of samples (238/2,853) and 158 of them had a cervical biopsy. HSIL or worse in histopathology was detected in 36/158 women (22.8%). Repeat invitations gave modest additional participation. Direct send results in approximately twice as high participation rate compared to invitation to order a kit.

Conclusions: Effective campaigns to reach populations at high risk of cervical cancer will be important for faster cervical cancer elimination. 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.

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#7145

P14-01 | Prevalence and genotype distribution of human papillomavirus (HPV) in penile cancer in Brazil: systematic literature review and meta-analysis

14 - Genotyping

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Background/Objectives: Penile cancer (PC) is a rare neoplasia, and most of the cases occurs in developing countries. In Brazil, a high prevalence of penile cancer is observed, with 1,933 new cases estimated in 2022, and 539 deaths due to the disease registered in 2020. Among the risk factors, human Papillomavirus (HPV) infection accounts to 50% of the cases. Although the prevalence of HPV in penile cancer is high, prevention measures capable of reducing disease rates and affecting patients' quality of life are still scarce. Estimating the prevalence and genotypic distribution of HPV in penile cancer in Brazil is relevant to identify regional differences in the distribution of viral genotypes, to guide current HPV vaccination programs in the country, and to plan global initiatives to prevent the disease. The aim of this study was to investigate, through a systematic literature review of the literature and meta-analysis, the prevalence and genotypic distribution of HPV in penile cancer in Brazil.

Methods: The systematic review and meta-analysis included all articles that investigated the prevalence and genotypic distribution of HPV in penile cancer in different regions of the country, from 2000 to 2021. The review was registered in the International Prospective Register of Systematic Reviews (PROSPERO), conducted according to the Preferred Reporting of Systematic Reviews and Meta-Analysis Statement (PRISMA), and the quality of the studies was assessed by the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data. All the included studies presented with histopathological confirmed diagnostic of penile cancer and used molecular assays for HPV detection and genotyping.

Results: Fifteen studies that met the inclusion criteria were included, comprising 1,250 cases of penile cancer diagnosed in Brazil, of which 615 were positive for HPV DNA. The combined prevalence of HPV in penile cancer was 52.0% (95% CI: 40.0-63.0%; I^2= 92.0%) and the highest combined prevalence was observed in the Northeast region (79%) (95% CI: 64.0 -89.0%; I^2= 84%), followed by the North region (54%) (95% CI: 43.0 -65.0%; I^2= 68%), Southeast (44%) (95% CI: 32.0 -56.0%; I^2= 92%), and Midwest (31%) (95% CI: 24.0 -38.0%; I^2 not applied). HPV16 was the most prevalent genotype, followed by HPV6, HPV11, HPV18, HPV51, HPV59, HPV74, HPV31, HPV35 and HPV68.

Conclusions: Our results present a robust estimate of the prevalence and genotypic distribution of HPV in penile cancer in Brazil, confirming the association of HPV with more than half of the cases, and highlights the association of these tumors predominantly with HPV16, but also emphasizing the presence of other viral genotypes not included by the prophylactic tetravalent vaccine, currently distributed by the public health system in Brazil.

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#7130

P14-02 | Prevalence of HPV and Assessing Type-Specific HPV Testing in Cervical High-Grade Squamous Intraepithelial Lesions in Poland

14 - Genotyping

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Background/Objectives: Human papillomavirus (HPV) plays a proven and undisputed role in cancer development among humans—cervical, anogenital, head and neck, and other locations. All over the world clinicians and researchers began to consider the most effective methods of population screening and looked forward to the vaccine, known as one of the most effective public health interventions. Until now, more than 200 types of HPV have been fully sequenced. Viruses typing allows HPV-based cervical cancer screening tests with some degree of genotyping, treatment of HPV infection, and application of HPV vaccines. The prevalence and distribution of oncogenic HPV genotypes in women who underwent screening for cervical cancer in the Wielkopolska region, Poland, were assessed, and the correlation of genotypes with the histological results was evaluated.

Methods: Cervical samples were collected from 2969 women for cervical cancer screening. Participants were screened by liquid-based cytology and HPV genotyping (n = 1654) and referred to colposcopy and punch biopsy (n = 616) if recommended. We collected liquid-based cytology and molecular assessment samples with an endocervical Cyto-Brush preserved in PreservCyt ® (Roche). Then, the probes were passed to an independent, standardized laboratory. PCR was performed, followed by a DNA enzyme immunoassay and genotyping with a reverse hybridization line probe assay for HPV detection. The lab technicians performed sequence analysis to characterize HPV-positive samples. The molecular test detected the DNA of 37 HPV genotypes (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, IS39, and CP6108).

Results: HPV genotypes 16, 31, 52, 66, 53, and 51 are the most frequent types in the studied population. Genotypes 16 and 31 account for nearly one-fifth of the infections of diagnosed HPV infections. HPV 16, 31, and 52 are found in nearly 80% of premalignant HSIL lesions (CIN 2 and CIN 3). There was a statistically significant dependency between age and HPV type 16, 31, and 51. HPV 16 was observed more often among subjects aged between 25 and 34 ($p < 0.001$). HPV type 31 was more common among the youngest and oldest groups ($p < 0.001$). HPV 51 was observed among 9% of the youngest group, 4% of subjects aged 25-44, 2% of subjects aged 45-54; ($p = 0.031$). These three HPV genotypes were also related to biopsy results. Among subjects from the HSIL group, there were a greater proportion of patients with those types of HPV than among patients from the remaining groups.

Conclusions: Modern knowledge and the rapid development of molecular testing techniques make it necessary to modify the current programs of both primary and secondary prevention.The impact of the implementation of HPV vaccination programs can already be seen in Australia and New Zealand, where the highest decrease in the incidence of HPV-related diseases has been recorded. HPV infection is one of the most common sexually transmitted infections in the study group; it was close to 47%. HPV genotypes 16, 31, 52, 66, 53, and 51 are the most common types. Genotypes 16 and 31 account for nearly one-fifth of the infections of diagnosed HPV infections. HPV 16, 31, and 52 are found in nearly 80% of premalignant HSIL lesions (CIN 2 and CIN 3). Vaccination programs should cover as many types of HPV as possible. The above study confirms the need to vaccinate the Polish population with a 9-valent vaccine.

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#6761

P14-03 | Analytical comparison of Allplex HPV hr and Anyplex HPV hr in population-based cervical cancer screening setting

14 - Genotyping

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Background/Objectives: The Allplex HPV HR Detection (Allplex; Seegene, Seoul, South Korea) assay, launched in late 2022, is a fully automated real-time PCR-based assay that surpasses its predecessor Anyplex II HPV HR Detection Test (Anyplex; Seegene) by utilizing multiple detection temperature technology (MuDT), combined with TOCE system that enables detection of multiple targets generating individual cycle threshold (Ct) values in a single channel. Allplex detects and concurrently individually distinct 14 hrHPV genotypes (HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, HPV59, HPV66 and HPV68). The present study aimed to assess the analytical performance of Allplex compared to that of Anyplex.

Methods: Validation panel consisted of 973 residual ThinPrep samples obtained from women aged 30-64 years (median age of 40) attending national organized population-based cytology-based cervical cancer screening in Slovenia between January 2016 and May 2017. Allplex and Anyplex testing was performed between November 2022 and January 2023 using Microlab STARlet IVD instrument for DNA extraction and PCR set-up and CFX96 real-time thermocycler for PCR amplification and detection. For genotype concordant analyses of Allplex versus Anyplex, Cohen's kappa statistic was used as well as McNemar exact $\chi 2$ test.

Results: The overall genotype agreement between two assays was high (96.3%; 95% CI; 94.9-97.3%) with kappa value of 0.88; however McNemar test indicated statistically significant difference in overall genotype detection (pinf0.0001). Same apply for detection of three genotypes: HPV31, HPV51, and HPV68 (p values 0.002, 0.02, and 0.008, respectively). Observed agreement across all individual genotypes was consistently high (all above 98.5%), with kappa values indicating substantial agreement for HPV56, HPV59, HPV66, and HPV68 (range 0.66-0.75) and almost perfect agreement for the remaining HPV genotypes: HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, and HPV58) (range 0.88-1.00).

Conclusions: Analytical head-to-head comparison of Allplex and its predecessor Anyplex revealed some differences in detection capability of individual HPV genotypes. Although high overall analytical agreement between two assays was observed (96.3% with kappa value of 0.88), statistically significant differences were observed in assays' performance in particular for HPV31, HPV51, HPV68, and overall. Although reproducibility of detection of the individual targeted HPV genotypes is neither required in the validation guidelines nor usually reported it might become crucial if HPV genotype information beyond HPV16 and HPV18 will be incorporated in clinical practice to better guide further clinical management.

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#6600

P14-04 | Evaluating the performance of two ScreenFire HPV genotyping assays on various PCR platforms

14 - Genotyping

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Background/Objectives: High-risk human papillomavirus infection stands as a significant risk factor for the development of cervical cancer. Easy-to-use and scalable point-of-care HPV tests urgently needed, especially in the Low-and middle-income countries (LMICs) where cervical cancer is a major public health threat. ATILA BioSystems (ATILA) recently re-designed its existing HPV assay kit AmpFire HPV assay (GHPVF-100), which has been widely used in many LMICs, into SceenFire HPV RS assay, which detects 13 high-risk HPV strains. The ScreenFire HPV RS assay is available in two distinct formats. The first format (M5FHPV-100) requires manual preparation of the master mix. The second format (M5FHPV-96) is presented in a simplified pre-packed biodome configuration, which is high-throughput, easy-to-use and contamination free, thus more suitable for risk stratification at large population level and more feasible for the implementation purpose in LMICs. The objective of this study is to examine the two distinct ScreenFire assay formats across various PCR platforms with clinical samples to compare the performance of the assay formats.

Methods: Two hundred and forty (n=240) DNA samples retrieved from ongoing cervical cancer studies in West Africa were assessed using two formats of ScreenFire HPV RS assays on four different real-time PCR machines (ATILA iAMP-PS96, ATILA Powergene9600 Plus, Thermo Fisher QuantStudio 7 and Biorad CFX-96). AmpFire HPV assay was used as a reference method to evaluate sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) of two assay formats in detecting HPV infections.

Results: Based on the AmpFire HPV assay, both assay formats demonstrated robust performance, with the highest level of accuracy rate (97.50%) achieved by M5FHPV-100 assay on ATILA iAMP-PS96. In contrast, pre-packed M5FHPV-96 assay consistently produced an accuracy rate of 94.16% across three instruments: iAMP-PS96, Powergene9600 Plus and QuantStudio 7. Furthermore, when employing Biorad CFX-96, both M5FHPV-100 and M5FHPV-96 assays exhibited similar levels of accuracy at 95.83%. In terms of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), all assays demonstrated favourable performance. The M5FHPV-100 testing kit, when used with the ATILA iAMP-PS96, excelled by achieving a sensitivity of 96.55%, specificity of 98.95%, PPV of 99.29%, and NPV of 94.95%. Following closely in performance were in the order of Thermo Fisher QuantStudio 7, ATILA Powergene9600 Plus and Biorad CFX-96.

Conclusions: All four PCR machines consistently produced remarkable accuracy when employed with either assay format (M5FHPV-100 and M5FHPV-96), with the ATILA iAMP-PS96 instrument generated the highest performance. This collective evidence demonstrates the reliability and suitability of the tests as robust screening tools for HPV infection and genotyping. The implementation of the tests holds substantial promise for enhancing cancer prevention and management strategies.

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#7149

P14-05 | Risk stratification for cervical neoplasia by HPV genotypes and cytology results in pilot HPV-based screening "hippo" project

14 - Genotyping

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Background/Objectives: Risk stratification of CIN3+ by screening test results is important for selection of optimal triage in HPV-based cervical cancer (CC) screening. We estimated risks of CIN3+ for various screening results in the pilot HPV-based screening project in Poland.

Methods: The HIPPO (HPV Testing In Polish POpulation-based Cervical Cancer Screening Program) is a pilot study comparing performance of the current standard (cytology) to HR HPV-based screening protocol. Over 33,000 women aged 30-59 were recruited and randomized in a 1:1 ratio to either HR-HPV testing or cytology, with age stratification (three strata: 30-39, 40-49, and 50-59 years) between 2019 and 2023 around Poland. Women with a positive HR HPV test result (HPV-16, 18 or other 12 HR genotypes) and one of the following: (1) abnormal reflex-LBC result, (2) normal reflex-LBC result and abnormal LBC after 6 months result, (3) twice normal LBC and a positive results of either CINtec® PLUS Cytology test and QIASURE methylation test, were referred for colposcopy in the HPV arm. We calculated risk of CIN3+ on the sample analyzed in an interim analysis of women recruited in the HIPPO study up to July 2022.

Results: A total of 13,656 women were assigned to the HPV arm, of which 993 (7.3%) tested positive for HR HPV. We calculated risk of CIN3+ risk by HR HPV genotypes (single and multiple infections) and cytology results. The results are presented in tables (Table 1 and 2).

Conclusions: The highest risk of CIN3+ was observed for women with HPV 16 and 18 (single and multiple infections) and cytology ≥ASC-H. However, HPV 18 was very rare. Women with HPV-other than 16 and 18 (both single and mixed infections) and NILM cytology presented the lowest risk of CIN3+. Our results in the Polish cohort are concordant with previous data form other countries and implicate intensive triage of women with an HPV-16 positive screening result.

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#7042

P15-01 | CTLA4 polymorphisms (rs5742909, rs231775, rs3087243) influence on HPV vulnerability, intraepithelial lesions, and cervical cancer susceptibility

15 - Molecular markers

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Background/Objectives: Human papillomavirus (HPV) can cause different degrees of squamous intraepithelial lesions, influenced by factors such as the individual's immune response. In this context CTLA-4 is a receptor expressed on the surface of regulatory T cells (Tregs), CD4+ T cells, and CD8+ T cells, with particularly high expression in Tregs. When active, it negatively regulates T cell proliferation and activation, potentially reducing immunity against HPV and tumors. Polymorphisms in CTLA4 can lead to altered receptor activity, affecting T lymphocyte regulation, and this alteration may be associated to cancer development. Therefore, the aim of this study was to investigate the association of the rs5742909 C>T, rs231775 A>G, and rs3087243 G>A polymorphisms in CTLA4 with HPV infection and the development of squamous intraepithelial lesions and cervical cancer.

Methods: This case-control study which was approved by the Ethics Committee for Research Involving Human Beings of the State University of Londrina (CAAE 38937520.2.0000.5231). Peripheral blood and cervical secretion samples were collected from women (n=445) assisted by the Public Unified Health System in the southern region of Brazil (Parana State)for the extraction of genomic DNA, which were used for genotyping and HPV molecular diagnosis, respectively. The CTLA4 polymorphisms rs5742909, rs231775, rs3087243 were assessed by predesigned TaqMan SNV Genotyping assays. Statistical analyses were performed using the SPSS Statistics 22.0 software, adopting a significance level of $p<0.05$.

Results: Women were initially grouped into two groups based on the presence (n=181) or absence of HPV infection (n=264). The HPV positive group was further subdivided according to the presented intraepithelial lesions, which included No Lesion (n=84), Low Grade Squamous Intraepithelial Lesion (LSIL) (n=19), High Grade Squamous Intraepithelial Lesion (HSIL) (n=56) and cervical cancer (n=105). Analyzing the polymorphisms association with HPV infection, it was observed that only the SNV rs5742909 C>T was associated to HPV infection ($p<0.001$) and the allele T carriers presented an odds ratio of 1.980 for infection (IC95 = 1.225-3.104) when compared to CC individuals. When considering only HPV positive women to assess the SNVs influence on lesions and cancer development, only the SNV rs5742909 C>T was associated. Allele T carriers had 2.633 more chances (IC95=1.39-4.955, $p=0.003$) of developing HSIL and 2.962 more chances (IC95=1.784-4.918, $p<0.001$) of developing cervical cancer when compared to individuals carrying the CC genotype.

Conclusions: This is the first study to investigate the association of the CTLA-4 rs5742909, rs231775, rs3087243 polymorphisms with HPV infection and the development of squamous intraepithelial lesions and cervical cancer in the Brazilian women, a highly mixed population, from the southern region. Although further studies evaluating the CTLA-4 haplotypes are currently underway, our study demonstrated a significant association of the allele T of rs5742909 with HPV infection, HSIL and cervical cancer development, suggesting it as a potential molecular biomarker for HPV infection and its progression to HSIL and cervical cancer.

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P15-02 | Genetic (CHRNA5, SCL6A4) and epigenetic (BDNF, NTRK2) contributions to cervical carcinoma or precursor lesions

15 - Molecular markers

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Background/Objectives: Cervical carcinoma is considered one of the most common cancers in women worldwide. It is associated with sexually transmitted HPV infection, and its presence is necessary, but not sufficient for the development of the disease. Due to its high incidence, it is important to understand which mechanisms are involved and to identify the genetic factors for its development and progression. The effects of the Autonomic Nervous System on cancer biology are well recognized, namely by the link between stress and cancer progression. CHRNA5 gene encodes for a subunit of the nicotinic acetylcholine receptor, SLC6A4 gene encodes a serotonin transporter, BDNF gene encodes a Brain Derived Neurotrophic Factor, and NTRK2 encodes for Neurotrophic Receptor Tyrosine Kinase 2. In this project we studied the association between rs16969968 (CHRNA5) and a 5-HTTLPR (SLC6A4) and cervical carcinoma or precursor lesions. We also investigated the DNA methylation status of BDNF and NTRK2 in HPV infected women with cervical carcinoma or precursor lesions.

Methods: Endpoint-genotyping was used to genotype and MCA-Meth to check for DNA methylation patterns. Statistic analysis was performed with SPSS.

Results: RegardingCHRNA5, we found an association of the GG genotype (p=0.025; OR = 2.336; CI (95%) = [1.103; 4.950]) and the G allele (p=0.035; OR = 1.740, CI (95%) = [1.037 - 2.922]) with the disease. We also found that having the GG - (12/10) epistatic interaction involving CHRNA5 and SLC6A4 respectively, is a risk factor for the disease (p=0.039; OR = 6.4, CI (95%) = [1.198 - 34.203]). Changes in the DNA methylation status of HPV infected women was observed only in BDNF gene.

Conclusions: These results reinforce the involvement of the Autonomic Nervous System in the developmentof HPV cervical lesions.

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P15-03 | Identifying molecular biomarkers of cervical disease progression

15 - Molecular markers

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Background/Objectives: Background/Objectives. Current testing strategies for HPV infection in the cervical epithelium are effective at identifying virus presence, however they do not provide evidence of viral activity, nor can they aid risk stratification of disease. This study aimed to identify novel biomarkers to identify progression of HPV-induced cervical disease in clinical samples.

Methods: Methods. Liquid based cytology (LBC) samples were obtained from the Scottish HPV Archive, a biobank for HPV-associated research which comes under the auspice of NHS Lothian Bioresource- REC 20/ES/0061. It includes residual cervical samples from women attending routine cervical screening and colposcopy clinics and samples from HPV-associated research consented for storage. Optiplex HPV genotyping PCR assay (Diamex, Heidelberg, Germany) was used according to the manufacturer's specification. This study adhered to the ethical standards of the Declaration of Helsinki. Gene ontology analysis was used to identify genes whose expression was altered by HPV infection using WebGestalt (www.webgestalt.org). RTq-PCR was used to measure the expression of innate immune regulatory genes selected as potential biomarkers for cervical disease.

Results: Results. The most significantly altered genes due to HPV infection were involved in innate immune responses and cellular antiviral defence, suggesting that antiviral immune regulators may be useful as cervical disease biomarkers1. The expression of inflammatory mediators IL-1b and NLRP3 was reduced following HPV16 infection, whereas expression of antiviral defence genes IRF-1 and IFN-k was upregulated. The expression of T-cell suppressor VTCN-1 was highly upregulated following HPV16 infection. For these reasons, the expression of these immune regulators was measured in clinical samples representing different stages of cervical disease ranging from no detectable disease to cervical cancer. There was little variation in expression recorded at each disease level for any immune regulators except for IL-1b, which was reduced significantly in cervical cancer samples only.

Conclusions: Conclusions. Although HPV16 infection was predicted to alter expression of genes involved in antiviral defence and host immune responses, in clinical samples, there was a wide variation in expression values of the immune regulators. These may not be suitable biomarkers for HPV associated disease, but IL-1b may be a useful marker of cervical cancer.

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P15-04 | Programmed Death-Ligand 1 Expression in Uterine Cervical Carcinoma in Indian Population

15 - Molecular markers

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Background/Objectives: Programmed death-ligand 1(PD-L1) binds to its receptor PD-1 on T-cells and inhibits immune response of T-lymphocytes. Cancer cells evade immune surveillance by upregulating PD-L1 expression, leading to tumor progression (1). FDA has approved PD-1/PD-L1 axis immunotherapy for cervical cancer which are PD-L1 -positive on immunohistochemistry (2). In India, cervical cancer accounts for approximately 17% of all cancer deaths among women between 30 and 70 years (3). More than three-fourths of patients are diagnosed at advanced stage. This study, evaluated the expression of PD-L1 in Indian women with cervical carcinoma.

Methods: A hospital-based cross-sectional prospective study was conducted over a period of five years. 119 histologically diagnosed cases of cervical carcinoma meeting the inclusion criterion of being treatment naïve and at least one tumor tissue section with 40% viable tumor with stroma. Sections were stained with PD-L1 antibody clone SP263 as recommended on Ventana Benchmark XT. Criteria for positivity of tumor cells was ≥25% cytoplasmic staining with PD-L1 and for immune cells cytoplasmic or membrane PD-L1 positivity ≥1% as per protocol.

Results: Of 119 cases, squamous cell carcinoma accounted for 89.1% cases and adenocarcinoma 5.9%. The mean age was 54.4 years, with majority of patients in 51-60-year group. Most common histological grade was moderately differentiated (78%). 41% women had advanced FIGO stage. 35% cases showed PD-L1 expression. Patients over 45 years (75.6%) had higher PD-L1 positivity than those under 45 (24.4%). 31% of squamous cell carcinoma were PD-L1 positive as compared to adenocarcinoma (29%). PD-L1 expression was most frequent in poorly differentiated carcinoma (37.5%).

Conclusions: A significant proportion of cervical cancer expressed PD-L1. Increased PD-L1 expression was seen with increasing age and poorly differentiated histological grade. Anti-PD-L1 immunotherapy can be an option in PD-L1 positive cervical cancer.

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P15-05 | Plasma cell-free DNA concentration and fragmentomes predict neoadjuvant chemotherapy response in cervical cancer patients

15 - Molecular markers

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Background/Objectives: Since neoadjuvant chemotherapy (NACT) is a promising treatment for advanced cervical cancer, biomarkers for predicting patients who are unlikely to respond to NACT are an unmet need. This study aims to explore the characteristics of plasma cell-free DNA (cfDNA), including concentration and fragmentomes during the treatment of cervical cancer, and to find suitable markers from cfDNA to assess the effect of treatment.

Methods: This study collected 285 plasma samples from 84 patients diagnosed with confirmed cervical cancer through pathological examination. We analyzed the concentration and fragmentomic characteristics of cfDNA in cervical patients across the NACT treatment to investigate cfDNA characteristics' utility in predicting NACT response.

Results: This study first identified critical factors affecting cfDNA concentration including surgical trauma, chemotherapy, infection, and bone marrow depression. Besides, patients with poor NACT response exhibited a significantly greater escalation in cfDNA levels following the initial cycle of treatment, in comparison to patients with a favorable response. Distinctive end motif profiles and promoter coverages of cfDNA in initial plasma were observed between patients with differing NACT responses, achieving high AUCs of 0.81 and 0.96, respectively, for non-responder prediction. Finally, our investigation further unveiled the pivotal role of DNASE1L3 in shaping cfDNA characteristics in non-responders and its involvement in chemotherapy resistance and unfavorable prognosis.

Conclusions: In summary, cfDNA fold-change values are associated with NACT response. Our study supports the potential of cfDNA fragmentomes as predictive biomarkers for NACT response in cervical cancer. Our advancements in predictive biomarkers may optimize treatment selection, minimize unnecessary treatment, and assist in establishing personalized treatment strategies for cervical cancer patients.

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#6729

P16-01 | The 2023 global HPV screening proficiency study

16 - Screening methods

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Background/Objectives: The International HPV Reference Center supports quality and order in HPV research and diagnostics. Notably, the center assigns HPV type numbers to novel HPV types, maintains a reference clone repository, and issues international proficiency panels for HPV genotyping and screening. In 2023, we issued two different proficiency panels: The HPV DNA screening panel assesses the sensitivity and specificity of the various HPV screening assays, as used in different laboratories. Valid HPV screening is an important part of the elimination of cervical cancer.

Methods: Participating laboratories were asked to perform HPV screening-tests using one or more of their usual assays on coded samples composed of purified whole genomic plasmids of thirteen HPV types (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68a and 68b) in a background of human cellular DNA. Proficient screening requires detection of 10 International Units of HPV 16 and HPV 18 DNA/ ul, with no false positive results. HPV 31, 33, 45, 52 and 58 are include as single infections where detection of 1000 copies /ul, are required for proficiency, whereas HPV types rarely found in cancers are included only as pools optional to detect.

Results: The 2023 screening proficiency study was subscribed to by 114 different laboratories worldwide. The screening study had 126 panels distributed during October, particularly to laboratories from Latin America, Europe, Africa and Asia. Public health laboratories, research laboratories and diagnostic test manufacturers are participating. National Reference Laboratories are offered to organise national HPV screening programs using the panels, this is done by NRL in Argentina, Norway and Germany.

Conclusions: A continuing global proficiency program will promote reliable laboratory services for HPV-based cervical screening.

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#7815

P17-01 | WID-qCIN - optimization and recalibration of a DNA-methylation based test to triage HPV-positive women

17 - Methylation

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Background/Objectives: With cervical cancer being the second most prevalent type of neoplasia leading to death in women worldwide, the WHO has recently specified the necessity to eliminate this disease. Key strategies cover HPV vaccination and improved cervical screening. At present, HPV testing is frequently accompanied with cytology triaging. Yet, a concerningly low and operator-dependent sensitivity of cytology to detect cervical (pre-)cancers requires the establishment of alternative triaging techniques.

Methods: Here, we optimized, analytically verified and recalibrated the recently published DNA methylation (DNAme) based WID-qCIN test, making it applicable for high-throughput sample analyses. Based on three distinct targets (DPP6, GSX1, RALYL) and one reference region (COL2A1), we generated a duplex version of the assay. Furthermore, we defined technical parameters including assay linearity, analytical specificity, limit of detection and limit of blank. Test recalibration was conducted on a set of age-matched cervical smear samples from women diagnosed with cervical intraepithelial neoplasia grade 2 or worse (CIN2+) and healthy individuals.

Results: -

Conclusions: Our observations suggest that the optimized WID-qCIN assay is high-throughput applicable, robust and extremely efficient to correctly identify women at risk of progressive (pre-)invasive cervical cancer.

References: Herzog C, Sundstrom K, Jones A, et al. DNA methylation-based detection and prediction of cervical intraepithelial neoplasia grade 3 and invasive cervical cancer with the WID-qCIN test. Clin Epigenetics 2022;14(1):150. DOI: 10.1186/s13148-022-01353-0.

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P17-02 | Screening and functional study of methylation modification of genes associated with cervical cancer

17 - Methylation

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Background/Objectives: Cervical cancer is the fourth most common cancer in women worldwide, and the main cause of cervical cancer is the persistent infection of High-risk human papillomavirus (HPV). While increasing HPV vaccine use and screening coverage has led to a significant reduction in the average incidence of cervical cancer, there are still many people who would not benefit from the use of the vaccine who urgently need high-quality screening and accurate diagnosis. It is of great significance to search for new tumor molecular markers to improve the sensitivity and specificity of the diagnosis of cervical cancer and precancerous lesions. This study first collected different types of cervical tissue from the clinic. Including cervical tissue without cervical lesions and HPV-positive cervical tissue, Low-Grade Squamous Intraepithelial Lesion, LSIL), High-Grade Squamous Intraepithelial Lesion (HSIL), cervical cancer, and adjacent cervical cancer tissue, by comparing the differences in gene methylation modification in different types of cervical tissue, The sites with differential methylation modification between different groups were selected and further studies were carried out to find molecular markers that may participate in and regulate the occurrence and growth of cervical cancer.

Methods: Clinical tissue samples were obtained and divided into five groups according to pathological diagnosis: HPV-positive group without lesions, low-grade squamous epithelial lesion group, high-grade squamous epithelial lesion group, cervical cancer group, and cervical cancer para cancer group. Gene methylation capture sequencing chips were used to analyze the methylation levels of each gene/location in each group of samples. Methylation modification genes EGFR and CAPZB, which may be related to the degree of cervical intraepithelial neoplasia, were selected and verified by bisulfite modification sequencing (BSP). The specific methylation modification sites were obtained by further analysis. Using the traditional RNAi interference method to knock down EGFR as an analogy reference, dCas9-Tet1-CD mediated methylation site-specific editing was used to eliminate the methylation modification level of EGFR gene locus, and the role of this site methylation in cervical cancer growth was evaluated in vitro and in vivo cervical cancer cell models. At the same time, the signal pathway that methylation of this site may affect was preliminarily revealed.

Results: At the intersection of 5 groups of differentially modified genes, CAPZB and EGFR genes related to the degree of cervical intraepithelial neoplasia were obtained. The methylation level of the CpG1 site in the A segment of the EGFR gene may be related to the incidence of cervical cancer, and the CpG1 site in the B segment (genomic segment) may be related to the degree of cervical lesions. The methylation modification of the CpG2 site in the CAPZB gene may also be related to the pathogenesis of cervical cancer. Elimination of CpG1 methylation modification in the B segment of the EGFR gene has similar effects on the function of cervical cancer cells as down-regulation of EGFR expression by interference method. Signaling pathway studies indicate that methylation of this site may be an apparent modification that promotes virus infection of cells.

Conclusions: The CpG1 methylation modification of the EGFR gene may be a candidate marker for cervical cancer diagnosis, treatment, and follow-up, and a target for regulating cervical cancer growth.

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P17-03 | Feasibility of FAM19A4/mir124-2 DNA methylation test for cervical and endometrial glandular lesions in formalin-fixed paraffin-embedded histology - a pilot study

17 - Methylation

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Background/Objectives: The vast majority of cervical cancers could be prevented by screening and HPV (human papillomavirus) vaccination, however, cervical screening is less effective for endocervical adenocarcinoma due to its different pathogenesis, and sometimes more aggressive biological behavior, the lower sensitivity of PAP smear in glandular lesions compared to squamous ones, and usually different anatomic localization associated with the worse visualization of the lesion and difficult evaluation of the lesion by colposcopy. A positive methylation test in cervical cytology corresponds to the presence of a biologically significant cervical lesion and persistent HR-HPV infection. It is also associated with a lower rate of lesion regression. For cervical cancer screening, commercial methylation tests have been developed that are standardized to perform from cervical smears in liquid-based cytology (LBC) samples in a routine clinical laboratory. LBCs represent a minority of cervical samples in the routine screening population in the Czech Republic, as most women are screened via conventional cytology. However, formalin-fixed paraffin-embedded (FFPE) histological material is often available for further analysis. Therefore, the aim of our study was to assess the feasibility of a FAM19A4/mir124-2 DNA methylation test validated for cervical cytology in FFPE histology in women with available LBC samples containing cervical or endometrial glandular lesions.

Methods: LBC from 26 women with glandular atypia/lesion in cytology and their FFPE histological correlates were retrieved. After bisulfite conversion, a methylation test QIAsure (Qiagen) was performed from DNA isolated from LBC and lesional histological tissue. Overall status of methylation positivity and negativity were established and results of each methylation marker in LBC were compared with those from FFPE histology.

Results: Out of 23 analyzable histological samples, the methylation status of LBC matched that of the biopsy in 19 women (82,6 %). 4 samples negative in LBC were positive in FFPE histology, but either the positivity was borderline or the interval since the biopsy was more than 6 months. Complete concordance in methylation markers was in 11 biopsies, and partial in 5. In three biopsies, a different marker was methylated than in LBC. 3 histological samples were excluded from the analyses because of deficient quality of DNA.

Conclusions: FAM19A4/mir124-2 DNA methylation test is highly effective for the detection of the presence of cervical precancer and cancer in LBC samples including those of glandular origin. In our pilot study, we proved a solid concordance between the results of the methylation test in LBC samples and those performed from DNA retrieved from FFPE histological material in the same patients. However, further studies are needed to evaluate the effectiveness of the methylation test in FFPE material.

References: Study was supported by grant:FNPl 00669806/Ministry of Health of the Czech Republic and Charles University, Cooperatio program, research area Maternity and Childhood care.

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#6712

P19-01 | Serosurveillance to support the HPV vaccination programme in England: durability of antibody responses against vaccine and non-vaccine types 3-4, 8-9 and 13-14 years after each programmatic change

19 - Serology

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Background/Objectives: The UK national school-based HPV vaccination programme was introduced routinely for 12-13-year-old girls in September 2008, with an initial catch-up programme for 13-18-year-olds, following a recommendation by the Joint Committee on Vaccination and Immunisation (JCVI). Three doses of the bivalent (Cervarix®) vaccine were offered initially, replaced by three doses of the quadrivalent (Gardasil®) vaccine from 2012 which was reduced to a two-dose schedule from 2014. From 2019 the programme became gender neutral with 12-13-year-old boys included in the routine schedule. Two doses of the nonavalent (Gardasil®9) vaccine were introduced from 2021/22 which has been reduced to a 1 dose regimen from 2023. Vaccine uptake in the UK exceeds 80% in most years but was reduced significantly during the COVID-19 pandemic. Programmatic changes in the vaccine regimen offered and the impact of COVID-19 on coverage present unique challenges for monitoring the HPV vaccination programme and the study of outcomes that may inform future vaccination strategies.

Methods: We designed a serosurveillance study designed to assess serostatus and antibody levels to vaccine-relevant types by sampling specific birth cohorts at 3-4 (15-16 years old), 8-9 (20-21 years old) and 13-14 (25-26 years old) years following the introduction of each programmatic change. Sample size estimates suggested that 50-100 individuals per cohort timepoint were required to detect a 20% difference in serostatus or a 2-fold or greater difference in the geometric mean concentration of antibody levels between any two groups. Serum samples were retrieved from the Seroepidemiology Unit depository of anonymised residual sera from routine diagnostic testing at participating laboratories. Age, sex, year of collection was known for individual samples: immunisation status was not. Testing was performed using a Luminex®-based 9-valent virus-like particle ligand binding assay with the testing laboratory blinded to the sample metadata until testing was complete.

Results: Samples representing all regions in England, albeit with some regional biases, were retrieved from the serum archive. Bivalent vaccine responses are available through 13-14 years, while quadrivalent three-dose data are available to 8-9 years and two-dose data to 3-4 years following their introductions. Both vaccines demonstrate high seropositivity rates against vaccine (HPV16/18 or HPV6/11/16/18) and some non-vaccine (HPV31/45) types over the length of follow-up.

Conclusions: Initial data from the serosurveillance show durability of high vaccine-induced antibody levels in vaccinated girls into adulthood (starting eligibility for cervical screening). In time, as additional age-specific cohorts are included, this surveillance will be able to compare antibody levels between the girls' and boys' programmes, the bivalent, quadrivalent and nonavalent vaccines and different dosing regimens. This serosurveillance will aim to identify any reductions in vaccine-induced antibodies that could foretell of a potential weakening in HPV control.

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#6803

P20-01 | Potential of AI technology and digital cytology in cervical cancer screening: an evaluation of the Hologic GeniusTM digital cytology system

20 - New technologies

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Background/Objectives: The application of digital pathology and AI in clinical pathology diagnostics is rapidly advancing in developed countries. It is understood to improve accuracy and quality of diagnostics, while optimizing workflow and workforce in laboratories. With a global shortage of pathologists, increasing demand and costs of healthcare, the use of technological advances in pathology is critical in overcoming these challenges. The era of primary HPV testing in cervical screening programmes is associated with geographically dispersed, centralized laboratories. This significantly exacerbates the difficulties of staff training, retention, and recruitment in cervical laboratories, risking sustainability of cervical screening services. The Hologic GeniusTM Digital Cytology System is a ThinPrep Imaging device that combines AI technology with digital scanning to assist in cervical cancer screening of ThinPrep Pap Test slides for the presence of pre-cancerous lesions and cervical cancer.The system is designed to increase workflow efficiencies and improve working across geographically dispersed areas. In England, digital cytopathology is not approved for use in the NHS cervical screening programme. There is little published literature on the potential use of the Hologic GeniusTM Digital Cytology System in cervical screening laboratories in England. In this context, this study explores the potential role of this new technology in innovatively supporting delivery of cervical screening in a centralized laboratory in England.

Methods: This is a prospective, randomized, single-blinded, controlled, single site study. The current primary objective of this study is to determine the non-inferiority performance and workflow efficiencies when assessing cases reviewed on the Digital Cytology System as compared with same cases manually reviewed. 1000 cases have been selected for this study. 500 cases were made from the residual sample after the case had been stained with conventional Papanicoloaou stain and reviewed manually. An additional slide was made using the ThinPrep 5000 Processor and stained using the Hologic Imager stain. The other 500 cases were selected from routine work that had been made using the ThinPrep 5000 Processor, stained using Hologic Imager stain and reviewed using Hologic ThinPrep Imaging System. All 1000 slides were imaged using the Hologic Digital Cytology System. All slides were anonymized, and randomized by a study coordinator. Two screeners and a Consultant indepentently reviewed each case. For the workflow analysis the individual screeners recorded the time taken to assess each case in both the Genius Digital arm and the Manual screening arm using a stopwatch. The times were collated, and the mean screening time collated for the 2 arms for all cases as a direct comparison for speed and accuracy at the end of the study.

Results: Results will be presented at EUROGIN 2024.

Conclusions: Conclusion will be presented at EUROGIN 2024. The findings of this study can inform future strategies and decision making, on the use of digital imaging and AI in cervical screening programmes that balance workforce challenges with sustainable delivery of cervical cytology to eliminate cervical cancer.

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#6782

P20-02 | Metabolomic profiling of cervical mucus for diagnosis and pathway analysis in cervical neoplasia

20 - New technologies

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Background/Objectives: Recent advancements in technology have made metabolomics more accessible in clinical settings. We conducted a comprehensive analysis to determine whether the metabolites in cervical mucus change with the progression of lesions in patients with cervical neoplasia. We explored whether the results could be utilized as diagnostic markers. Furthermore, we investigated activated metabolic pathways.

Methods: Cervical mucus was collected from 298 patients who visited outpatient clinic in our institution. Patients were classified into normal (n = 48), cervical intraepithelial neoplasia (CIN1; n = 19), CIN2 (n = 80), CIN3 (n = 82), and squamous cell carcinoma (SCC; n = 69). Specimen were analyzed by a triple quadrupole mass spectrometer of the liquid chromatographic mass spectrometry (LCMS-8060 system: Shimadzu Corporation, Kyoto, Japan). Statistical analysis was conducted using ROC curve analysis with SPSS ver. 29 (IBM Co.) to validate its utility as a diagnostic biomarker. Pathway analysis was performed using the online analysis software MetaboAnalyst 5.0 (https://www.metaboanalyst.ca/).

Results: It was possible to analyze as 84 primary metabolites. Malic acid exhibited an AUC > 0.81 for CIN1, CIN2, CIN3, and SCC when compared to normal (derived from HPV-negative infertile patients). In the comparison between normal and SCC, oxidative glutathione, malic acid and kynurenine had an AUC of 0.924 (0.877-0.971), 0.914 (0.859-0.968), and 0.884 (0.823-0.945), respectively. When comparing CIN3 to SCC, that of oxidative glutathione was 0.904 (0.858-0.950). The TCA cycle showed significant metabolic changes in cervical neoplasia (FDR p inf 0.01, Impact > 0.20). The cysteine and methionine metabolism pathway exhibited significant changes in the normal vs. SCC and CIN3 vs. SCC comparisons (FDR p inf 0.01, Impact > 0.30). Nicotinic acid and nicotinamide metabolism showed significant metabolic changes in the normal vs. SCC (FDR inf 0.05, Impact: 0.43).

Conclusions: Metabolites that increase with the progression of lesions in cervical neoplasia were extracted, and metabolic pathways associated with cervical neoplasia were identified. These results not only shed light on novel biological features of cervical neoplasia but also suggest the potential for their utility in the development of new diagnostic markers.

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#7101

P21-01 | Artificial intelligence in cervical colposcopy: a review

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Detection and treatment of cervical precancerous lesions and early stages of cancer are the most important ways of secondary prevention of cervical cancer which remains the fourth most common malignancy among women globally. Colposcopy plays a major role in the diagnosis especially in low- and middle-income countries (LMIC) where the availability of additional screening and triage methods such as HPV testing or cytology is often limited due to insufficient resources. At the same time the highest rates of cervical cancer are found in these countries. The lack of resource-intensive screening methods can be mitigated by utilizing diagnostic AI methods that can easily operate on digital colposcopes or even smartphone devices. In recent years, artificial intelligence (AI) has achieved significant progress in image pattern recognition, including the domain of medical images. AI techniques have showcased their ability to improve diagnostic accuracy based on medical image from a variety of imaging modalities and in different disease contexts. As a result, AI in medical image analysis has emerged as a rapidly growing research area within the medical field. In this review we elaborate the current status of research in the field of AI-based digital image analysis approaches for the detection of (pre-) cancerous lesions in cervical colposcopy.

Methods: A search in MEDLINE via PubMed was conducted. The keywords used were "artificial intelligence", "ai", "deep learning", "machine learning" or "neural network" combined with "colposcopy" and results in English language were screened to identify publications relevant to this subject.

Results:

Conclusions: Even though more research on this topic is needed and the field of AI-based image analysis is still evolving at a rapid pace, application of deep-learning based image analysis methods in cervical colposcopy is a promising approach to improve cervical cancer screening. This is especially true for LMIC where colposcopy often remain the only resource for clinical decision making and the relative lack of trained colposcopists is a significant hurdle in the implementation of public screening programs with broad outreach.

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P21-02 | A.I. Strategies for Predicting Regression Potential in H&E images of Cervical Precancerous Lesions

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: In Finland, over 2000 women undergo Cervical intraepithelial neoplasia (CIN) treatment annually [1]. The median age of women at treatment of a CIN-lesion is approximately 30, a common age for first delivery in Finland. The treatment of a CIN-lesion has been associated with 2-3 times increased risk of preterm birth [2]. Given the unpredictable nature of substantial number of CIN2 cases spontaneously regressing to normal, many women undergo an unnecessary CIN-treatment [3]. The treatment decision of CIN patients heavily relies on the precise analysis of cell and tissue structures within histopathological images, however, the traditional diagnostic methods of manual interpretation are prone to subjectivity and human error, leading to uncertainty in treatment decisions [5]. In recent years, digital pathology has emerged as a powerful tool for cancer diagnosis and prognosis [6]. While digital pathology has shown immense promise, its full potential is yet to be realized. Deep learning (DL) based computer vision methods have already demonstrated their potential in image analysis, and when applied to digital pathology, they offer the opportunity to unlock a level of precision that surpasses human capabilities [7]. We have developed advanced DL models for cell and tissue segmentation in digitized whole slide images (WSI), the cornerstone of digital pathology. Coupled with our novel spatial analysis techniques, we can extract histologically meaningful and human-readable features for pathologists. Our aim is to use these tools to quantify different spatially compartmentalized histomorphological features within cervical tissue to predict the regression potential of CIN2 lesions.

Methods: We have developed a novel DL based panoptic segmentation method, along with sophisticated spatial analysis methods that enable the localization and extraction of clinically relevant features from H&E stained WSI. These complementary methodologies allow the accurate quantification of different types of cell characteristics and cell-cell interactions at different tissue compartments. In the context of immune cell mediated CIN2 regression potential, we can quantify tumor infiltrating lymphocytes (TILs) inside the lesion and at the lesion-stroma interface, and identify immune hotspots of the stroma and their vicinity to lesion. Moreover, we can quantify the shape irregularities of the neoplastic cells alongside other morphological and spatial trends of cells within any tissue compartment. These spatially compartmentalized features will be mapped into clinical variables, enabling us to predict the regression potential of CIN lesions.

Results: We have segmented the tissue compartments and nuclei of over 300 H&E-stained whole slide images (WSI), collected as routine diagnostic biopsies, at the Helsinki University Hospital, from over 200 CIN2 diagnosed women that have not undergone CIN treatment. In the conference, we will present whether the TILs, immune hotspots, and morphological features of the neoplastic cellshold predictive power for regression of CIN2 lesions.

Conclusions: In summary, our research seamlessly integrates AI with clinical practice, offering potential new diagnostic tools for clinical practice of CIN treatment. Furthermore, the nature of the developed methods allow the integration of otherdata modalities to further complement the information landscape of CIN2 lesions, enabling even more accurate prediction of the natural history of cervical precancerous lesions in future studies.

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#6988

P21-03 | Development and validation of artificial intelligence-based analysis software to support screening system of cervical intraepithelial neoplasia

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Cervical cancer, the fourth most common cancer among women worldwide, often proves fatal and stems from precursor lesions caused by high-risk human papillomavirus (HR-HPV) infection. Accurate and early diagnosis is crucial for effective treatment. Current screening methods, such as the Pap test, liquid-based cytology (LBC), visual inspection with acetic acid (VIA), and HPV DNA testing, have limitations, requiring confirmation through colposcopy. This study introduces CerviCARE® AI, an artificial intelligence (AI) analysis software, to address colposcopy challenges.

Methods: This study is multicenter, blinded, single-arm, retrospective pivotal clinical trial. Women aged 19 years or older with cervical histologic or cytologic findings were eligible. All patients underwent Tele-cervicography and had a Tele-cervicography image, and an images with a favorable response to acetic acid application were selected. By analyzing and evaluating the sensitivity and specificity of CerviCARE® AI against the reference standard, we determined that the target sensitivity and specificity for clinical significance in high-risk groups (P2, P3, HSIL or higher, CIN2 or higher) were set at 90% or higher, respectively. In addition, the lower limits of the cutoff sensitivity and specificity were determined to be clinically significant at 80% or above, respectively.

Results: In a multicenter retrospective study, CerviCARE® AI achieved a remarkable sensitivity of 98% for high-risk groups (P2, P3, HSIL or higher, CIN2 or higher) and a specificity of 95.5%. Analyzing a total of 400 slides with CerviCARE® AI, the sensitivity against high-risk groups (P2, P3, HSIL or higher, CIN2 or higher) is 0.98 with a Wald 95% confidence interval of 0.9526 to 1.0000. The sensitivity was 98% and the lower limit of the target sensitivity was 95.26%, which is considered clinically significant. These findings underscore CerviCARE® AI's potential as a valuable diagnostic tool for highly accurate identification of cervical precancerous lesions.

Conclusions: Its integration into clinical practice could enhance early detection and reduce screening disparities, especially in regions with limited access to skilled colposcopists. While further prospective research is needed to validate its clinical utility, this AI system holds promise for improving cervical cancer screening and lessening the burden of this deadly disease.

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P22-01 | Clinical factors influencing the occurrence of discordant results between cytology, colposcopy and histopathology in the diagnosis of cervical lesions

21 - Artificial intelligence - Big data - Machine learning

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Background/Objectives: Management according to the 2019 ASCCP guideline is no longer based on an outcome, but on a clinical situation based on which the risk for CIN3+ is calculated, considering equal management for equal risks. The objectifs are to identify and analyse the factors influencing the occurrence of discordant results between cytology/colposcopic impression/initial histology and final histopathological result after an excisional procedure.

Methods: Differents clinical scenarious characterized by discordant results between cytology, colposcopy and histopathology were analyzed on a group of 103 patients investigated by colposcopy between 2019-june 2023 with cytological abnormalities and positive HR-HPV tests. Management was particularly influenced in young patients seeking pregnancy with ASC-US/LSIL cytology, infection with HR-HPV by p16/ki67 immunocytochemistry results.

Results: The concordance between colposcopic impression and final histopathological examination was 67,9%, with a colposcopy sensitivity in identifying CIN3+ lesions of 76,.9%. Concordance between colposcopic impression and histopathological examination was higher in the case of HPV 16/18 infections; for other HR-HPV, more frequently the colposcopic impression was underdiagnosed. Factors associated with colposcopic under-staging were: the absence of vaginal births, TZ type 3, HPV genotype, age ≥ 50 years, menopausal status.

Conclusions: Colposcopic impression, transformation zone type, initial histology, cytological changes, age, HPV genotype, molecular markers should be taken into account when diagnosing and determining the management of cervical lesions. The use of molecular markers or increasing the number of colposcopic guided biopsies has been useful in identifying patients with HSIL lesions but LSIL/ASCUS cytology. Age ≥ 50 years and the presence of TZ type 3 are frequently associated with underdiagnosis of HSIL lesions. For the association of HSIL cytology and HPV 16/18 infection, this study recommend surgical treatment not preceded by colposcopic guided biopsy (CGB). Cytological changes, a TZ type 3 and an infection with HR-HPV, if the initial biopsy gives us a less severe result than that suggested by the colposcopic examination, surgical excision is preferable. Thus, the colposcopy examination has a great importance in the management of TZ type 3 cases.

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P24-01 | Can pre-treatment with vaginal estrogen improve the colposcopy performance in postmenopausal women? - a randomized controlled trial

24 - Colposcopy

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Background/Objectives: Colposcopy is the most important diagnostic tool to detect cervical precancerous lesions and thereby prevention of cervical cancer. Though, colposcopy is challenging in postmenopausal women, as the majority will have a nonvisible transformation zone, due to age dependent changes of the cervix. The risk is lengthy follow-up with repeated colposcopies and increased risk of missing disease. This study will be among the first to investigate, if treatment with vaginal estrogen prior to colposcopy, will improve the colposcopy performance in postmenopausal women.

Methods: A randomized controlled multicenter trial. Enrollment will be performed at gynecology departments in the Central- and Southern Regions in Denmark. A total of 150 postmenopausal womenaged ≥ 50 years referred for colposcopy due toabnormal cervical screening results will be included. Eligible women will be randomized 1:1 to pretreatment with either vaginal application of Vagifem 30 µg or placebo once a day for 14 days prior to colposcopy.

Results: The trial has just started inclusion. The primary outcome will be to compare the two groups regarding the percentage of women with a visible transformation zone at colposcopy, and biopsies representative of the transformation zone. Secondary outcomes will be to compare the percentage of detected CIN2+ in the cervical biopsies; the percentage of diagnostics cone biopsies; the patients' report on possible side effects and compliance to the pretreatment.

Conclusions: The study results are clinically relevant and may contribute with new evidence on how to improve diagnostic work-up of postmenopausal women. This study has the potential to ensure accurate and timely diagnosis of precancerous cervical lesions among postmenopausal women, which is necessary to further reduce the number of women with late-stage cervical cancers and poor prognosis.

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P24-02 | Complete visualization of transformation zone in colposcopy using estradiol or misoprostol: a clinical trial

24 - Colposcopy

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Background/Objectives: Both estradiol and misoprostol have been used for complete visualization of the transformation zone (TZ) in colposcopy. However, no consensus has been reached on the priority of one medication over the other. This study aimed to compare the efficacy of estradiol and misoprostol for complete visualization of TZ in colposcopy of premenopausal and postmenopausal women.

Methods: In this clinical trial, 78 patients with unsatisfactory colposcopy were randomly divided into three groups using a block randomization software package. Group 1 (n=25) received 25 µg of vaginal estradiol for 14 days prior to colposcopy. Group 2 (n=27) received 400 µg of misoprostol 12 h prior to colposcopy. Group 3 (n=26) served as the control group and did not receive any medication. TZ visibility, age, BMI, history of vaginal delivery or sexually transmitted diseases or human papillomavirus (HPV), and drug-related side effects were compared among the three groups and also between premenopausal and postmenopausal women. Data were analyzed using analysis of variance, and Kruskal-Wallis tests.

Results: The percentage of complete TZ visualization was 72%, 55.6%, and 26.9% in the estradiol, misoprostol, and control groups, respectively (P=0.005). These values were 70%, 33.3%, and 0%, respectively, in postmenopausal women (P=0.043) and 60%, 72.7%, and 33.3%, respectively, in premenopausal women (P=0.152). With regard to drug-related side effects, there was no statistically significant difference between the three groups (P=0.374).

Conclusions: Estradiol was significantly superior to misoprostol for complete visualization of TZ, particularly in postmenopausal women, with no difference in side effects.

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P25-01 | p16/ki67 dual stain cytology in cervical smears: is it still useful?

25 - Cervical neoplasia

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Background/Objectives: Cervical cancer screening has substantially evolved with the advent of innovative diagnostic tools like p16/Ki67 dual stain cytology, offering a more nuanced approach to identifying high-grade cervical intraepithelial neoplasia (CIN). We explored the applications, advantages, and challenges of p16/Ki67 dual stain cytology in cervical smears, highlighting its potential impact on enhancing early detection and precision in cervical cancer screening. P16/Ki67 dual stain cytology, based on detecting p16 and Ki-67 biomarkers, serves as a promising adjunct to traditional Pap smears. It focuses on identifying molecular and protein markers associated with precancerous changes, aiding in the accurate classification of abnormal cells. This abstract discusses our experience with p16/Ki67 dual stain cytology, its efficacy in distinguishing high-grade lesions from benign abnormalities and its potential in reducing false-positive results, thereby refining patient management strategies.

Methods: We studied the effectiveness of p16/Ki67 dual stain cytology when integrated into routine cervical cancer screening programs for women between 25 and 64 years old included in the national screening program. The drawback of our study is the fact that p16/Ki67 dual stain cytology were not available for all patients.

Results: The study encompassed a total of 276 cases, for which both Pap smear and p16/Ki67 dual stain cytology was performed, and comprised 119 (43,11%) cases of Negative for Intraepithelial Lesion or Malignancy (NILM), 52 (18,84%) cases of Atypical Squamous Cells of Undetermined Significance (ASC-US), 26 (9,42%) cases of Atypical Squamous Cells cannot exclude High Grade Squamous Lesion (ASC-H), 36 (13,04%) cases of Low-Grade Squamous Intraepithelial Lesion (LSIL), 39 (14,13%) cases of High-Grade Squamous Intraepithelial Lesion (HSIL), and 4 (1,44%) cases of Squamous Cell Carcinoma (SCC). Of these cases, 53 had cervical biopsies available for analysis. Out of the total cases, 146 (52,89%) were tested positive for high risk HPV-DNA. p16/Ki67 dual stain cytology, showed positivity in 122 cases. This included 11 of 119 (9,24%) NILM cases, 24 out of 52 (46,15%) ASC-US cases, 25 out of 26 (96,15%) ASC-H cases, 19 out of 36 (52,77%) LSIL cases, all HSIL cases, and all SCC cases. Its capacity to stratify women into distinct risk categories for cervical cancer progression underscores its potential as a supplementary tool for more precise risk assessment.

Conclusions: The integration of biomarker-based testing methods like p16/Ki67 dual stain cytology holds the potential to reduce unnecessary colposcopies and overtreatment while improving the identification of women at high risk for cervical cancer. p16/Ki67 dual stain cytology presents a progressive shift in cervical cancer screening paradigms, offering a more refined and precise approach to detecting high-grade cervical abnormalities. There is still need for continued research to establish standardized protocols, address cost implications, and facilitate the integration of p16/Ki67 dual stain cytology into routine cervical cancer screening programs, ensuring its optimal utilization and realization of its potential benefits.

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#6846

P25-02 | Postoperative prognosis of patients harboring human papillomavirus who underwent minimally invasive radical trachelectomy for early-stage cervical cancer

25 - Cervical neoplasia

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Background/Objectives: The safety of minimally invasive surgery (MIS) for cervical cancer has been questioned. It can be a big challenge to radical trachelectomy because those patients are child-bearing age with stage IA2 or IB1 cervical cancer, whereas they are usually infected with high risk human papillomavirus (HPV) which is related to the recurrence. This study aimed to analyze the clinical outcomes of patients with cervical cancer who underwent MIS radical trachelectomy including the association between the recurrence and HPV status.

Methods: A retrospective chart review was conducted at the obstetrics and gynecological department of a tertiary hospital in Seoul, South Korea. It involved 154 women at child-bearing age with a strong fertility desire, and who underwent MIS radical trachelectomy for a histologically confirmed diagnosis of invasive cervical cancer. Baseline demographic, clinical, and pathology data, as well as management data were collected. Outcome data included recurrence, death, last follow-up status, as well as pregnancy.

Results: The median follow-up time of 57.50 months. The majority of participants underwent laparoscopy (90.9%) or robot-assisted intervention (5.2%) as the surgical approach for MIS radical trachelectomy. Almost patients showed HPV infection when they were diagnosed with cervical cancer and the most common subtype was HPV 16. Outcomes showed that 9.7% of patients experienced recurrence, occurring 1 year after surgery on average. The mean recurrence-free survival (RFS) was 158.13 (95%CI: 148.59 - 167.67) months. Women who did not specify their marital status and those who were overweight or obese had shorter mean survival compared to their counterparts. Poorly differentiated tumors had a higher incidence of recurrence. Parametrial involvement, positive lymphovascular invasion (LVSI), and more than half of the depth of cervix invasion were associated with lower mean survival times. HPV subtype was not associated to the recurrence, however, there was a tendency for recurrence to increase if the viral loads are sustained or increase after surgery. Cox-regression analysis identified FIGO stage IB2 or above as the independent factor associated with RFS. Seventeen (11%) patients experience pregnancy post MIS radical trachelectomy, of whom 6 had premature rupture of membranes, one abortion and one pregnancy termination.

Conclusions: MIS radical trachelectomy is an adequate surgical approach in patients with early-stage cervical cancer, representing a valuable chance for women who have a strong desire for fertility. Further research is warranted to analyze the risk profiles in patients with early-stage cervix cancer, especially the HPV status or HPV vaccinated status, and provide therapeutic recommendations and fertility counseling based on evidence-based risk stratification.

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#6697

P25-03 | Clinical, economic, and humanistic burden of high grade cervical intraepithelial neoplasia in Europe: systematic literature review

25 - Cervical neoplasia

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Background/Objectives: Persistent human papilloma virus (HPV) infection is a significant risk factor for the development of cervical intraepithelial neoplasia (CIN). CIN grade 2 and 3 are high-grade squamous intraepithelial lesions (HSIL) that can progress into invasive cervical cancer, if left untreated. Three systematic literature reviews (SLRs) were undertaken in order to assess clinical, economic, and humanistic burden associated with CIN grade 2 and 3 among the adult female population in Europe.

Methods: The systematic literature reviews were conducted in line with the guidelines from the Cochrane Group and PRISMA. Databases searched included Medline®, Embase®, and Cochrane databases and conference proceedings published from January 2012 to August 2022. The outcomes of interest were clinical (i.e., incidence, prevalence, HPV genotype), economic (i.e., costs, indirect costs, resource use), and humanistic (quality of life) burdens.

Results: The three systematic literature reviews identified data from 41 clinical burden, 11 economic burden, and 8 humanistic burden studies. In Europe, the incidence of CIN2 and CIN3 was 38-118/100,000 and 31-186/100,000 women-years in a screened population, respectively. The prevalence of CIN2 and CIN3 was 0.1-1.4% and 0.2-2.2%, respectively. The incidence and prevalence of CIN2/3 peaked in women aged 25-39 years. The proportion of HPV 16 in CIN2+ ranged between 47-52%, followed by HPV 31/33/45 (38%), and HPV 18 (4-15%). Patients with CIN3 showed higher costs and resource utilization (medical and treatment procedures) compared to patients with CIN2. Diagnosis of CIN2/3 had a considerable negative impact on psychosocial wellbeing and physical functioning.

Conclusions: The published evidence showed substantial clinical, economic, and humanistic burden associated with CIN2 and CIN3 diagnoses in Europe in the past 10 years. More urgent measures should be taken to prevent HPV infection and subsequent HPV-related diseases across the European region.

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#6659

P25-04 | Circulating cell-free tumor human papillomavirus DNA is a promising biomarker in cervical cancer

25 - Cervical neoplasia

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Background/Objectives: Tumor cells release fragments of their DNA into the circulation, so called cell-free tumor DNA (ctDNA) or liquid biopsy. Here, we analyze if cell-free human papillomavirus DNA (ctHPV DNA) is detectable before, during and after treatment, in patients with cervical cancer or pre-malignant lesions that may develop into cervical cancer, and whether ctHPV DNA levels were correlated to patient or tumor characteristics and outcome. Furthermore, total cell-free DNA load is studied using cfAlbumin DNA as a surrogate marker.

Methods: 18 patients with locally advanced CC (LACC), 15 patients with early stage CC (ESCC) and 21 patients with pre-malignant lesions, all with verified HPV16, 18 or 45-positive lesions, were included. Pre- during- and post-treatment plasma were tested for HPV16, 18 & 45 and total cfDNA load using droplet digital PCR.

Results: ctHPV DNA was found in 94.4% and 26.7% of pre-treatment plasma of patients with LACC and ESCC respectively, while all samples from patients with pre-malignant lesions were negative. Higher levels of ctHPV DNA were correlated to higher FIGO2018 stage. Patients with LACC and persistent ctHPV DNA at end-of-treatment had significantly worse progression-free survival (PFS) than patients who had cleared the ctHPV DNA ($p = 0.007$). Patients with total ctDNA-levels above median in pre-treatment plasma had a worse PFS ($p = 0.026$), compared to patients with total ctDNA-levels below median.

Conclusions: ctHPV DNA is a promising prognostic biomarker in locally advanced cervical cancer that should be studied further for clinical use.

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#6998

P25-05 | One carbon metabolism and CIN

25 - Cervical neoplasia

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Background/Objectives: The incidence of CIN lesion requiring surgical treatment peaks around the age of thirty, so the effects of treatment on future reproductive function are of particular importance. It is necesseary to treat only lesions that have a real potential for progression. The goal is to increase the individualisation of the patient's approach and treatment. There are limited nonsurgical options for eradicating established HPV infection in cervical tissue. Identification of any reversible cofactors, such as parameters od one-carbon metabolism (vitamn B9, vitamine B12 and homocysteine) that may modulate HPV expression are worthy of stydy.

Methods: This was prospective observational cohort study that included 183 patients with abnormal cytological smear and/or suspicious colposcopic images.Determination of one-carbon metabolic parameters was performed from blood samples. Based on the pathohistological findings, the subjects were divided into a control group without CIN lesion (61 subjects) and test group with CIN lesion (122 subjects).

Results: The level of homocysteine corresponds to the greatest extent with CIN lesions ($p<0.01$). Higher values correspond to highly suspicious PH changes, while low values most likely indicate the absence of lesions. The ANOVA test showed that there are significant differences in the level of homocysteine, in relation to the presence of the HPV virus: $F(1,177)=8.03$, $p<0.01$, $\eta^2=.043$. There is a 2x more chance of HPV16 or 18 positive result, if the homocysteine value is 9.35 and above.The lowest level of vitamin B9 was recorded in the group with the most severe, CIN3 lesions ($p<0.05$). Based on the ROC analysis (Figure 1), the cut-off values of vitamin B9≤19.5nmol/L and homocysteine≥9.35μmol/l ($p<0.01$, AUC:0.635 95%IP:0.554-0.716) together show an almost 4x higher risk for CIN2+ lesions (OR:3.90 95%CI:1.95-7.77). The level of vitamin B12 did not prove to be a relevant parameter for distinguishing pathohistological changes, because the values did not correlate with the severity of CIN lesion. The highest values of this vitamin were recorded in the control group, which may indicate its protective effect.

Conclusions: Homocysteine values positively correlated with degree of CIN lesions. Calculated values of vitamin B9≤19.5nmol/L and homocysteine≥9.35μmol/l can serve as parameters for deciding on folate and vitB12 supplementation in clinical practice as conservative treatment of HPV infection especially in young patients with CIN lesions.

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Figure 1

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#6769

P25-06 | Genomic Risk Variants and HPV Infection Modulate Gene Expression at the Human Leukocyte Antigen Locus in Cervical Cancer

25 - Cervical neoplasia

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Background/Objectives: Cervical cancer is the fourth most common gynecological malignancy in women. Human papillomavirus (HPV) infection influences disease progression, and hereditary risk factors from genome-wide association studies (GWASs) 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. We aim to validate these associations and investigate the functional relevance of variants by expression quantitative trait loci (eQTL) analysis in cervical tissues.

Methods: We genotyped four variants at the HLA locus from recent cervical cancer GWASs (rs17190106, rs535777, rs2763979, and rs3117027) in the German Cervigen cohort of 1099 invasive cervical cancers, 1345 dysplasias, and 1196 healthy controls. We tested these and four known GWAS variants (rs9272117, rs2844511, rs2856437, and rs2299059) to be eQTLs for 36 gene transcripts at this locus in 235 cervical tissues.

Results: In addition to previous findings from our cohort, rs17190106 associated with overall cervical disease (p=0.03, OR=0.82, 95%CI=0.68-0.98) and invasive cancer (p=0.001, OR=0.69, 95%CI=0.55-0.86), whereas rs535777 associated with adenocarcinomas (p=0.004, OR=1.63, 95%CI=1.17-2.27). 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 rs9272117 as a master regulatory variant for coordinated HLA gene expression.

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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#7073

P26-01 | Association of human papillomavirus infection with other microbial pathogens in cervical samples with normal and abnormal cytopathological findings

26 - Vulvar diseases and neoplasia

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Background/Objectives: Cervical intraepithelial neoplasia (CIN) is a common neoplastic change-affecting women in reproductive age. Low grade CIN, can resolve without treatment or develop into higher intraepithelial lesions or cervical cancer the second most common cancer among 20-39years women world-wide. Other microbial agents that also can infect the cervicovaginal epithelium could act as co-factor and increase the risk for cervical cancer in the presence of high-risk HPV infection. Objective: The aim of this study was to investigate the correlation between infection with HPV other microbial pathogens (Trichomonas vaginalis, Mycoplasma hominis, Mycoplasma genitalis, Chlamydia trachomatis, Neisseria gonorrhea, Ureaplasma urealiticum, Ureaplasma hominis) and to investigate the association between abnormal cytopathological findings and STD`s infections.

Methods: Material and Methods: We investigate 520 cervical exfoliated cell specimens from women with negative and positive cytopathological findings. We used assay based on the reverse hybridization principle for the identification of 28 different genotypes of HPV by detection of specific sequences in theL1 region of the HPV genome. The assay uses SPF10 primer set for amplification of HPV genotypes and a set of primers for the amplification of the human HLA-DPB1gene to multiplex real-time PCR assay with TOCE technology which makes it possible to detect multi-pathogens in a single fluorescence channel on real-time PCR instruments. This technology is designed not to be affected by sequence variations

Results: Results: Among all patients 387 patient (74,4%) were negative, ASCUS was detected at 15 patients (2,9%), LSIL (low grade squamous intraepithelial lesion) at 75 patients (14,4%), HSIL (high grade squamous intraepithelial lesion) at 34 patients (6,5%) and cervical invasive cancer at 9 patients(1,7%). HPV negative samples were more frequent among patients with normal cytological findings (22%) and LSIL (50%). HPV positive samples were most frequent among patients with HSIL (82%) and invasive carcinoma (99%). The most frequent HPV type was 16. Ureaplasma urealiticum was the most frequent among all groups of patients and Neisseria gonorrhea was the rarest. There was not significant correlation between HPV and infection with other STD. Although other STD infections were not significantly associated with positive cytological findings, they were more common among the HPV positive women with normal cytological finding (7,2%) and patients with ASCUS(12,7%). In these group there was the weak correlation (0,3) between HPV and Chlamydia trachomatis or Ureaplasma urealyticum.

Conclusions: Conclusion: Our results have shown no association between infection with HPV and infection with other STD infections and strong correlation between HPV and HSIL and cervical invasive carcinoma. There was not significant association between abnormal cytopathological findings and other STD infections. Only in the ASCUS group, there was the significant association between HPV and Chlamydia trachomatis or Ureaplasam urealiticum. These data suggest that in these patients it may be important to screen for the simultaneous presence of different microorganisms in cervical epithelium which may have synergic pathological effect.

References: //

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#6636

P27-01 | Long-term outcomes of high-risk human papillomavirus in anal infection support HPV men vaccination

27 - Anal neoplasia

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Background/Objectives: The clinical laboratory in a local hospital has an important role in population surveillance. The clinical laboratory performs analyses on patients admitted to the hospital as inpatients or critical patients and it is also a reference point for people's health check-ups and health surveillance. Infectious diseases normally have severe symptoms. To ensure benefits from therapeutic treatment, a timely diagnosis is necessary. The human papillomavirus (HPV) virus is among the most diagnosed sexually transmitted infections worldwide, and the male gender is not exempt from it. In fact, 1 out of 3 male individuals is infected with HPV and 1 out of 5 male individuals is infected with a high-risk strain (1). In Italy, vaccination is underway for women only. Vaccine prevention extended to male individuals could lead to a halving of HPV cases.

Methods: From 2018 to 2022, we performed 7362 HPV tests using DNA extraction technique (QiaSimphony) and real-time Multiplex PCR (SeeGene 28 strains).

Results: 3762 out of 7362 HPV tests performed were positive for one (2059 patients) or more (1969 patients) HPV strains. Women, who are more aware of prevention, are more represented in our sample of subjects. The tests performed on women are 6499 and half (3331) are positive for at least one strain of HPV. Regarding men, 863 tests were performed. About half (431 patients) were positive for at least one HPV strain. Noteworthy, out of 175 anal HPV tests, 48% were positive and 1 patient had squamous cell carcinoma. Furthermore, in our male patients tested 2 - 12% had low or medium-risk injuries. In total, out of 7529 tests carried out from 2018 to 2022, over than 50% were found to be high-risk viral strains (5231). Of these, however, approximately half (2781) are now preventable with the monovalent HPV vaccine (strains covered: 6, 11, 16, 18, 31, 33, 45, 52, 58).

Conclusions: The Ospedale Isola Tiberina - Gemelli Isola is an Institution in the center of Rome, Italy. It is also a reference center for birthrates and women's prevention. Therefore, our Institution is very efficient in raising awareness of the prevention of HPV-related cancer. Current data indicate that male cases are not negligible, being positive in almost 50% of anal tests, and associated with an increased risk of the related cancers. These data can have an important impact on the Italian population, both in terms of the spread of HPV and healthcare burden and in terms of high healthcare costs.

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#7243

P29-01 | Evaluating Diagnostic Workflows for HPV-Positive Oropharyngeal Squamous Cell Carcinoma Detection Using Simulated Specimens Mounted on Slides

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Oropharyngeal Squamous Cell Carcinoma (OPSCC) is a subcategory of Head and Neck Cancer that is largely associated with human papillomavirus (HPV) infections. Individuals with HPV-positive OPSCC have significantly better prognosis and survival rates than those with HPV-negative cases; therefore, it is critical to establish a standardized diagnostic workflow to differentiate types and promote therapeutic success. To date, p16 immunohistochemistry (IHC) followed by high-risk HPV Polymerase Chain Reaction (PCR) or in situ Hybridization reflex testing are methodologies used in practice; however, the lack of available reference materials makes it challenging to standardize the recommended workflows. To ensure accurate and reliable testing, contrived samples must be used in quality control, calibration, assay validation, sensitivity and specificity assessment, troubleshooting, and inter-laboratory standardization. Currently, shared patient specimens are used to fulfill this requirement; however, these samples are inconsistent, require lengthy IRB approvals for use, and are present in limited quantities. Ultimately, these drawbacks prevent large-scale inter-laboratory standardization; thereby emphasizing the need for reliable quality control materials.

Methods: Microbix Biosystems Inc. developed prototype HPV-positive and HPV-negative OPSCC simulated specimens in paraffin blocks that were cut in 5 micrometer sections and mounted on slides. The positive and negative samples were derived from chemically fixed human cells that were either transfected with HPV type 16 or were not infected with high-risk HPV, respectively. Samples were H&E stained for homogeneity assessment, and further evaluated by p16 IHC (Roche CINtec Histology Kit) and reflex nucleic acid amplification testing (Purigen FFPE Extraction Protocol; QuanDx MeltPro High-Risk HPV Genotyping Laboratory Developed Test), as specified in CAP guidelines.

Results: The HPV PCR assay showed high concordance with p16 IHC results. The contrived HPV-positive OPSCC samples tested positive for HPV16 (DNA concentration 0.71ng/l) and p16 IHC, and the contrived HPV-negative OPSCC samples tested negative for all high-risk HPV genotypes tested (DNA concentration 4.4 ng/l) and p16 IHC.

Conclusions: To our knowledge, Microbix is the first to develop simulated and standardized OPSCC slides for use as prospective quality controls for existing histology and PCR workflows that detect HPV-positive OPSCC tumors. The prototype HPV-positive and HPV-negative OPSCC contrived specimen slides are reproducible quality control materials that could be used to standardize inter-laboratory methodologies and monitor the accuracy of diagnostic workflows. Additionally, they can be used in the context of External Quality Assessment (EQA) to evaluate inter-disciplinary diagnostic workflows, bringing a valuable one-step solution for evaluating the proficiency of laboratories conducting HPV-positive OPSCC reflex testing.

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#7083

P29-03 | Evaluation of a prognostic HPV biomarker assay for risk stratification of HPV16+ oropharyngeal squamous cell carcinoma patients

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: The increasing incidence of HPV-positive oropharyngeal squamous cell carcinoma (OPSCC) is driven primarily by HPV16. In Denmark, more than 70% of newly diagnosed patients with OPSCC are HPV-positive. Standard treatment of chemo-and radiotherapy has high survival and response rates, but a subset of patients does not respond to this treatment. The aim of this project was to evaluate a prognostic biomarker gene assay developed by the MD Anderson Cancer Center, USA, in a Danish patient cohort.

Methods: We collected FFPE tissue from 189 Danish HPV16+/p16+ OPSCC patients with no prior cancers, who had been treated with a combination of chemo-and radiotherapy between July 2012 and December 2017 and had a minimum of two years of follow-up. The samples were tested with an HPV Biomarker NanoString assay consisting of 38 genes related to HPV function.

Results: We were able to divide the patients into two groups based on gene expression of the 38 genes in the HPV Biomarker. There was no significant difference in overall survival or progression-free survival between the groups, also when stratifying for T-stage or UICC 8th Stage.

Conclusions: In Denmark, all OPSCC patients are treated according to national guidelines regardless of socioeconomic status, resulting in an extremely heterogenous patient population. In the US, patients rely heavily on privately funded health insurances, thus comprising a more homogenous population. Thus, we were unable to confirm the prognostic validity of the HPV Biomarker in the Danish patient cohort.

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#7118

P29-04 | Incidence and prevalence of human papillomavirus in tonsillar and base of tongue cancer during 2000-2022 in the Stockholm region and Sweden

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Tonsillar and base of tongue squamous cell carcinoma (TSCC/BOTSCC) has increased in Stockholm and Sweden until 2016. The proportion of human papillomavirus (HPV)-positive cases and the incidence of TSCC rose between 1970 and 2006, then stabilized. HPV-prevalence and TSCC/BOTSCC incidence 2000-2016 has already been followed. Now we have collected the data on HPV prevalence and incidence of TSCC/BOTSCC from 2016-2022. HPV is a risk factor for oropharyngeal squamous cell carcinoma (OSCC), where TSCC and BOTSCC account for most of the HPV positive cases.

Methods: Incidence both for Stockholm and for Sweden 2000-2022 were retrieved from the Swedish Cancer Registry. TSCC/BOTSCC biopsies 2017-2022 from Stockholm were examined for HPV DNA and p16, or data was obtained from medical reports. For cases 2000-2016 data were available from previous studies.

Results: The incidence of TSCC/BOTSCC has continued to rise in both Stockholm and Sweden 2000-2022, especially after 2008 and more in men than in women. HPV DNA and p16 analysis was determined for approximately 1000 Stockholm cases from 2000-2022, with XX % being HPV DNA and p16 postive. (Right now we are complementing HPV analysis and/or p16 for some patients that were missing data, therefore we cannot present exact numbers in this abstract.) The most frequent HPV types were 16 and 33, and 33 has become more common 2017-2022 than previously.

Conclusions: During 2000-2022, and especially after 2008, the incidence of TSCC/BOTSCC has continued to increase in Stockholm and Sweden, with an HPV-prevalence of approximately XX % in Stockholm. Some changes have been observed in the HPV type in the cases.

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#7126

P29-05 | HPV related OrophaRyngeAL CancerS in CANada: HPV ORAL SCAN

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Oral HPV infection is a known risk factor for HPV-related oropharyngeal cancer (OPC). The incidence rates have been increasing steadily since the mid-1990s and oropharyngeal cancer in males is the leading HPV-related cancer in Canada. Routine testing for all OPC for HPV status has been implemented across all major Canadian cancer centers since 2015. The study objective is to determine the proportion of recent OPC cases in Canada attributable to HPV.

Methods: This was a retrospective chart review at 4 Canadian hospital sites to identify all squamous cell OPC cases in adult patients > 18 years of age diagnosed from 2016 to 2020 and capturing patient demographics and HPV status. HPV status was defined using p16 protein immunohistochemistry.

Results: A total of 1154 patient charts were reviewed. Most patients (85.4%) were male and 40.6% were past smokers while 23.4% were current smokers and 23.4% never smoked. The overall proportion of P16 positive OPC was 80.6%. Nearly all P16 positive OPC were located at the base of the tongue(47.6%) or in the tonsil (47.1%). P16 positivity was associated with younger age (mean age P16(+)= 61.6 vs. 66.5 P16(-), $p<0.0001$), male gender (males 83.9% P16(+) vs females 60.9% P16(+), $p<0.0001$), lower tumor stage (Stage 1 P16(+)= 88.1% vs Stage 4 P16(+)=69.4%, $p<0.001$), and never smoking (never smoker = 92.3% vs past smoker =82.8% vs current smoker = 65.0%, $p<0.001$). Alcohol use was not associated with P16 positivity.

Conclusions: This study confirmed that the majority of OPC cases occur in men and are HPV-related. These data extend the previously documented trend of increasing OPC from 47.3% in 2000 to 73.7% in 2012 to 80.6% within the period between 2016 to 2020. These findings highlight the HPV-related disease burden in men and support HPV vaccination in males to prevent head and neck cancer.

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#6882

P29-06 | Circulating and salivary DNA-based biomarkers for early diagnosis and recurrence monitoring of OPSCC

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Oropharyngeal squamous cell carcinoma (OPSCC) incidence has significantly increased over the last decades. OPSCCs are etiologically divided into two distinct groups: human papillomavirus (HPV) related OPSCCs and non-HPV OPSCCs. The overall number of annually diagnosed OPCs has more than tripled during the last 30 years in the Czech Republic. Almost 800 OPC cases were newly diagnosed in 20211, making OPSCCs more prevalent than etiologically related cervical cancers. As well as in cervical cancer, risk stratification, early diagnosis, and eventually locoregional recurrence monitoring methods are needed. Liquid biopsies, including blood and saliva, represent a promising approach for OPSCC management. This study aims to validate the applicability of liquid biopsies and DNA-based biomarkers for early OPC diagnosis and its recurrence in clinical practice.

Methods: In this study, newly diagnosed OPSCC patients (prospective group) and patients in remission (retrospective group) were enrolled. HPV tumour status was determined by combined high-risk HPV detection and p16 immunohistochemistry. Pre & post-treatment HPV testing in gargle lavage (GL), oropharyngeal swabs (OPS), and plasma samples were performed, followed by regular testing according to the standard follow-up protocol.

Results: In total, 85 OPSCC patients have been enrolled. HPV-related OPSCC was diagnosed in 87% (65/75) of cases, while the HPV16 genotype was detected in 100 % of cases. GL and OPS's sensitivity (SE) and specificity (SP) for newly diagnosed HPV-related OPSCCs were 80 %, 90.5 %, and 100 %, 100 %, respectively. Detection of circulating tumour HPV DNA showed 92% SE and 100% SP. Post-treatment/follow-up HPV infection remained persistent in 8 OPSCC patients.

Conclusions: In conclusion, these preliminary data show a predominant incidence of HPV-related OPSCCs compared to non-HPV OPSCCs. At diagnosis, combined HPV testing in saliva and plasma showed excellent sensitivity. This work was supported by the project National Institute of Virology and Bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) - Funded by the European Union - Next Generation EU, the Internal Grant Agency of Palacký University (IGA LF UP 2023_006).

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#6920

P29-07 | Studies on the effects of curcumin targeting CDC27 alone or combined with other inhibitors on HPV positive and negative head and neck cancer cell lines

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Human papillomavirus positive (HPV+) tonsillar and base of tongue cancer (TSCC/BOTSCC) accounting for 40% of all head neck cancer (HNSCC) in Sweden are still rising in incidence, and are despite their better outcome compared to HPV-negative (HPV-) HNSCC (80% vs. 50% resp. 5-year survival) treated like HNSCC with chemoradiotherapy (ChRT). ChRT has severe side effects reducing the quality of life without improving the previously obtained efficacy of 80% 5-year survival with only radiotherapy (RT) given before, so new therapeutic options are urgently needed. Previous studies by others and us have focused on identifying prognostic or targetable markers for HPV+ TSCC/BOTSCC. Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA) and Fibroblast Growth Factor Receptor (FGFR3) mutations have been found fairly frequently in HPV+ TSCC/BOTSCC and in vitro targeted therapy combining phosphoinositide 3-kinase (PI3K) and FGFR inhibitors have shown synergistic effects. More recently, upon whole exome sequencing (WES) we identified a deletion variant of CDC27 in patients with a poor prognosis. Here we therefore wanted to investigate the effects of Curcumin a drug that potentially targets CDC27, either using it alone or combination with other inhibitors on TSCC/BOTSCC cell lines grown in vitro as monolayers (2D) or spheroids (3D).

Methods: The effects of Curcumin as single inhibitor or combined with other inhibitors e.g. BYL719 (a PI3K inhibitor) on TSCC/BOTSCC cell lines such as e.g. HPV+ CU-OP-2, and -20 and others grown as monolayers (2D) and spheroids (3D) are now being assessed. Effects of the various drug treatments will be analysed by viability (WST-1 assay), proliferation (IncuCyte S3 Live-cell Analysis System), and FACS assays on various TSCC/BOTSCC.

Results: Preliminary data using Curcumin as a single agent presented dose dependent responses with decreased viability and proliferation. Combination experiments are now ongoing.

Conclusions: To summarize, our preliminary data disclose that using Curcumin as a single agent reveals promising effects on HPV+/HPV- TSCC/BOTSCC cell lines.

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#6660

P29-07 | Combining specific PI3K, PARP, and WEE1 inhibitors or corresponding single inhibitors with radiotherapy in HPV positive and negative tonsillar SCC cell lines reveals synergistic effects, while the effects with APR-246 are limi

29 - HPV and oropharynx / Head and neck cancer

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Background/Objectives: Human papillomavirus positive (HPV+) tonsillar and base of tongue cancer (TSCC/BOTSCC) is rising in incidence, but chemoradiotherapy is not curative for all and moreover it comes with serious acute and chronic side effects, so novel therapeutic options could be of use. Since, we have recently disclosed that HPV+ TSCC/BOTSCC frequently display PI3K and FGFR3 mutations, we wanted to investigate whether targeted therapies could be of potential use for our patients. To explore and disclose novel therapeutic options, the effects of targeted therapy with PI3K (BYL719), PARP (BMN-673), and WEE1 (MK-1775) inhibitors alone or combined was investigated either with or without 10 Gy in TSCC/BOTSCC cell lines grown as monolayers. In addition, APR-246 was assessed on several TSCC/BOTSCC cell lines.

Methods: More specifically, the effects of the above single inhibitor, inhibitor/inhibitor combinations or inhibitor/10 Gy combinations were analyzed by viability, proliferation, and cytotoxicity assays on various TSCC/BOTSCC cell lines such as e.g. HPV+ UPCI-SCC-154, CU-OP-2, 3 and 20 and HPV-negative (HPV-) UT-SCC-60A and CU-OP17 all grown in vitro as monolayers.

Results: Single inhibitors all induced dose dependent effects. Furthermore, combining BYL719, BMN-673, and MK-1775 treatments with 10 Gy synergistic responses in HPV+ UPCI-SCC-154 and HPV- UT-SCC-60A. Moreover BYL719/BMN-673, BYL719/MK-1775, or BMN-673/MK-1775 combinations on HPV+ UPCI-SCC-154 and HPV- UT-SCC-60A also induced synergy compared to single drug administrations, but adding 10 Gy to these synergistic drug combinations had no further major effects. However, low APR-246 concentrations had limited usefulness on a number of TSCC/BOTSCC cell lines.

Conclusions: To conclude, synergistic effects were disclosed when complementing single BYL719 BMN-673 and MK-1775 administrations with 10 Gy or when combining the inhibitors, while adding 10 Gy to combinations of the various inhibitors did not further enhance their already additive/synergistic effects. APR-246 was suboptimal in the present context.

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P30-01 | Oncological treatment to men with penile cancer, survival in correlation to treatment and HPV-status

30 - HPV and associated skin diseases

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Background/Objectives: Penile cancer is a rare malignancy with poor prognosis when presented with lymph node metastases. Two different pathways are considered in penile carcinogenesis, one related to HPV-infection and the other to chronic inflammatory disease. In other HPV-related malignancies, such as cancer of the head and neck and in cervical cancer the finding of high risk HPV is found to be both a positive prognostic marker and a predictive marker for benefit from oncological treatments. There are few studies evaluating the prognostic and predictive use of HPV-status in patients diagnosed with penile cancer. The aim of this study was to investigate the correlation between HPV-status, given oncological treatment and survival in penile cancer.

Methods: The study cohort is composed of 52 consecutive penile cancer patients diagnosed and treated between 2009 and 2018, at Örebro University Hospital, Sweden. Tumor tissue from each tumor was analyzed for the presence of HPV DNA. Information concerning oncological treatments was collected from medical records. All patients were in a curative situation and had indication for perioperative oncological treatment according to Swedish guidelines. Penile cancer specific survival (peCSS) was calculated using Kaplan-Meier estimates.

Results: Perioperative oncological treatment, predominately neoadjuvant chemotherapy and adjuvant radiotherapy to the groins, was given to 33 of the 52 men. Of the 52 primary tumors, 27 were HPV negative and 24 were HPV positive. One was not analyzed due to limited tumor tissue. A higher survival probability was found for men who received perioperative oncological treatment, compared to men who did not receive any treatment regardless of HPV-status. When adding HPV-status to the statistical analyses we found a higher survival probability for men with HPV positive tumors compared to men with HPV negative tumors. In the group of men who had received oncological perioperative treatment according to guidelines, peCSS was higher in men with HPV positive tumors than in men with HPV negative tumors (p=0,026). For example at three years, peCSS was just over 40% for men with HPV negative tumors while it was slightly over 80% for men with HPV positive tumors.

Conclusions: HPV-status is an important factor in understanding penile cancer and in finding better treatments in the future. Our study shows a potential value of HPV-status both as a prognostic marker as well as a predictive marker for the effect of oncological treatment.

Kaplan-meier curve for penile cancer specific survival

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#6689

P32-01 | Regression of HPV-derived VaIN using an adjuvant treatment with a coriolus versicolor-based vaginal gel

32 - HPV transmission

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Background/Objectives: Vaginal intraepithelial neoplasia (VaIN) is considered the precursor lesion of vaginal cancer. Due to its low prevalence (its diagnosis accounts for 0.4% of all premalignant lesions of the lower genital tract) there are few studies in the literature that provide an in-depth understanding of its aetiopathogenesis and natural history. Therefore, it makes clinical management of VaIN a real challenge. Human papillomavirus (HPV) infection has been identified as the causative agent in up to 90% of VaIN cases, with HPV 16 being the most frequent genotype. With these four case reports, we aimed to evaluate the effect of a Coriolus versicolor-based vaginal gel in the management of VaIN lesions.

Methods: In this study, four patients between 44 and 64 years old diagnosed with VaIN through cytology, vaginoscopy and/or biopsy were included. Two of the patients were immunocompromised due to previous history of cancer and multiple sclerosis. The patient diagnosed with low-grade VaIN followed a conservative management with the Coriolus versicolor-based vaginal gel alone. The other three patients with high-grade VaIN, were subject to either an excisional treatment or a CO2/Laser vaporization, in combination with the Coriolus versicolor-based vaginal gel for 6 months as an adjuvant treatment. Follow-up cytology, vaginoscopy, biopsy, and HPV tests were performed over time for monitoring patients.

Results: After 6 months of adjuvant treatment with the Coriolus versicolor-based vaginal gel, all patients showed regression (1 patient) or complete normalization (3 patients) of their cytology, vaginoscopy, and/or biopsy results. Additionally, patients showed negative results for HPV tests.

Conclusions: The application of a Coriolus versicolor-based vaginal gel could be useful both, in conservative treatment (patients with LSIL VaIN) and in post-intervention treatment to prevent lesion's recurrence and aid in HPV clearance, representing a possible clinical advantage approach in this patient population.

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P34-01 | Remission of HPV-related diseases during antiviral treatment of herpesvirus: a case series

34 - Conventional therapies

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Background/Objectives: Papillomavirus (HPV) and Herpesvirus (HHV) infections are often associated in genital infections and share the same risk factors as sexually transmitted infections. This report covers the case history of seven women affected by multiple genital pathologies related to HPV and HHV-2. Patients visited the gynaecology outpatient clinic for gynaecology and colposcopy examination.

Methods: Patients underwent cervical cancer screening which included Pap-Test, HPV-DNA test and genotyping, biopsy and histology exam if necessary. Patients received conventional oral and topical treatment with acyclovir (ACV) or oral treatment with valacyclovir (VCV). All the patients received also a topical antifungal treatment based on econazole, and intimate sanitizing mousse and protective cream for restoring local microbial flora. Patients received gynaecology follow-up visits every 2 weeks with colposcopy examination.

Results: Patients presented clinical sign of HHV-2 infections in the cervix and vulva. Cervical lesions, characteristic of HPV infection, were detected, such as: ASCUS (HPV16-66); L-SIL (HPV16-42), L-SIL (HPV-negative) and H-SIL-CIN2 (HPV16). Vulvar and perineal condylomatosis was detected. Genital candidiasis was also observed in some patients. They received conventional antiviral therapies. Patients showed different HHV-2 remission times, and a complete resolution of vulvar and cervical HPV lesions during the antiviral treatment with a restitutio ad integrum of the tissues. No recurrence of HPV infections was observed at follow-up visits in the years after treatments.

Conclusions: The observed remission of HPV-related pathologies during ACV and VCV treatments may suggest that antivirals are also effective in the treatment of HPV lesions. ACV and its prodrug VCV must be phosphorylated within infected cells by HHV-encoded tyrosine kinase before to act as HHV-DNA polymerase inhibitors. However, in HPV-infected cells the DNA metabolism enzymes, (e.g. TK-1, 1 and DNA Pol-a, 2) are strongly induced, therefore ACV may be phosphorylated by the host-kinases before to inhibit host DNA-Pol. Our observation (3) and those of others (4-8), could pave the way for future studies concerning the clinical efficacy of ACV and VCV in the treatment of HPV-pathologies.

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P35-01 | Health economic impact model of a digital health solution

35 - Economics and modelling

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Background/Objectives: Cervical cancer is a significant global health concern, with substantial social and economic costs. The WHO's Cervical Cancer Elimination Initiative aims to eradicate the disease, promoting digital solutions for improved access, efficiency, and adherence to guidelines. (1) Healthcare provider (HCP) adherence to guidelines can improve patient outcomes and reduce the economic burden on healthcare systems. (2) The economic burden is estimated at $682 billion from 2020-2050. (3) A health economic impact model assesses the benefits of a digital health solution, navify Cervical Screening. This digital health solution is designed to guide HCPs on local and standardized screening guidelines, offering a customized and centralized view of all patients under care, categorizes patients by next recommended action, and flags actions to prioritize tasks.

Methods: The health and economic impact model focuses on HCP adherence to cervical cancer screening and treatment guidelines and the benefits of implementing navify Cervical Screening. The model considers variables like screening participation, excessive testing and interventions, as economic costs. The model is based on the Catalonia region of Spain but could be adaptable to other healthcare systems. The model provides outputs for three scenarios based on HCP adoption rates and adherence improvements: top-case (best-case), mid-case (average), and low-case (low-level adoption).

Results: The model assesses the impact of implementing the navify Cervical Screening digital health solution in cervical cancer screening for women aged 25-65 in Catalonia. Considering local guidelines and incorporating medical and economic factors, the model calculates an annual cost of 12.641.219 EUR in cervical cancer. Cancer screening constitutes the largest portion of these costs. The health economic impact model projects potential annual savings of 5-20% under various adoption scenarios of navify Cervical Screening, amounting to 1.652.136 EUR in the mid-case scenario. These savings are attributed to reduced cancer treatment costs, decrease of under- and over-screening, and fewer unnecessary colposcopies. The model highlights the potential cost-effective advantages of the digital health solution in cervical cancer screening programs.

Conclusions: Adherence to cervical cancer screening guidelines is vital for a successful program. Improved adherence reduces cancer cases, unnecessary testing, and colposcopies. (1) The health and economic model quantifies potential savings, emphasizing the alignment of strategies with guidelines. HCPs face challenges like guideline awareness, data collection, and patient follow-up. (4) The model shows that patient navigation with a digital health solution leads to financial savings and improved patient outcomes.

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P35-02 | Financial Difficulty in Acquiring Menstrual Hygiene Products in Lithuania

35 - Economics and modelling

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Background/Objectives: According to World Bank data, approximately 500 million women around the world encounter difficulties in acquiring menstrual hygiene (MH) products on an annual basis. It is often assumed that MH is only inaccessible in developing countries. However, there has been increasing emphasis that the issue is relevant in developed countries as well, especially among students, low-income individuals and homeless women. In Lithuania, the minimum montly wage (net) is 633 euros, while the state-set average net wage is 1684 euros. A set of 10 disposable pads costs around 3 euros, and on average, a menstral cycle lasting 5 days requires 1 or 2 sets. Therefore, the aim of this study was to evaluate the financial difficulties encountered by lithuanian women from various social groups in acquiring MH products, as well as monthly expenses.

Methods: An original questionnaire comprising 38 questions was developed, with its validity assessed through an online pilot survey (n=30), and subsequently refined based on expert feedback. The questionnaire was distributed via social media platforms, with the study period ranging from January 1st to January 31st, 2023. Statistical data analysis was performed using IBM SPSS Statistics 29.0. Descriptive statistical analysis, Student's t and chi-square ($\chi 2$) tests were used. Differences were considered statistically significant when pinf0.05.

Results: There were 642 women included in the study and all filled-out questionnaires were suitable for analysis. On average, respondents spent 10.2 Euros on MH products per month (1.6% of minimal wage and 0.6% of the average net wage). Respondents most commonly rated the difficulty of acquiring MH products at two out of ten (0 - no difficulty, 10 - great difficulty), with a significant majority of women noting that price influences their choice of MH products (n=374; 57.9%; p=0.001). Women who earned more than 1000 Euros, were older than 25 years, were married or cohabiting, and had a higher education degree were more likely to experience financial difficulties when purchasing MH products. Price most commonly influenced the choice of MH products for women who had children (n=129, 67.9%; p=0.027) and those earning more than 1000 Euros (n=157; 72%; p=0.042). Women who earned more than 1000 Euros and with the higher education spent 11,3 Euros montly for MH products. Moreover, working women (n=378; 60.1%; p=0.001), single or divorced women (n=177; 28.1%; p=0.027), and women with children (n=179; 28.5%; p=0.009) spent more money on acquiring MH products (respectively 10,4 Euros, 10,1 Euros and 10,7 Euros).

Conclusions: Respondents did not face major financial difficulties when obtaining MH supplies. However, comparing various social groups, the financial difficulties in acquiring MH products were influenced by age, social status, monthly income and education. Women who earned more than 1000 Euros and with the higher education spent more money for MH products per month.

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P35-03 | Health impact and cost-effectiveness analysis of nonavalent versus bivalent human papillomavirus national immunization strategies in Thailand

35 - Economics and modelling

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Background/Objectives: The current Thailand national immunization program (NIP) for human papillomavirus (HPV) includes a bivalent vaccine (2vHPV) for girls 11 years of age. Nonavalent HPV vaccine (9vHPV) may provide greater benefits through direct protection against seven additional HPV types. This study assessed the health impact and cost-effectiveness of switching from 2vHPV to 9vHPV in Thailand.

Methods: A previously validated dynamic transmission model simulating the natural history of HPV infections and estimating the cost associated with HPV-related diseases was adapted to Thailand setting. The analysis compared NIP strategies with 2vHPV or 9vHPV for girls 11-12 years old. The model assumed a 90% vaccination coverage rate in girls 11 years of age with a 2-dose schedule. HPV-associated health outcomes included cervical lesions (CIN-1/2/3), cervical, head and neck (H&N), and anal cancers as well as genital warts (GWs). Number of diseases cases prevented, costs, quality-adjusted life-years (QALY), and incremental cost-effectiveness ratio (ICER) were estimated. The model assumed lifelong duration of vaccine protection, herd immunity, a discount rate of 3% for costs and QALYs.

Results: Compared to 2vHPV strategy, 9vHPV strategy would prevent additional cases of HPV-related diseases and cancers (119,150 cervical cancer, 5,912,997 CIN-1/2/3, 17,972 H&N cancer, 668 anal cancer, and 5,300,409 GWs) and death (53,896 cervical cancer, 8,425 H&N cancer, and 238 anal cancer). 9vHPV strategy resulted in a 14% reduction in disease management cost as compared to 2vHPV strategy. The ICER of 9vHPV strategy vs. 2vHPV strategy was THB 75,676/QALY.

Conclusions: A 9vHPV strategy for 11-year old girls is projected to provide additional public health benefits with reductions in both HPV-related disease incidence and costs. 9vHPV strategy is considered highly cost-effective as compared to the current 2vHPV strategy, relative to the Thailand recommended threshold of THB 160,000/QALY.

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#7142

P35-04 | Community-driven software development for HPV modeling: reflections and lessons learned

35 - Economics and modelling

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Background/Objectives: In late 2022 we launched HPVsim, an open-source software tool for simulating HPV transmission and progression within populations. HPVsim belongs to a group of similar models collectively known as Starsim, which are designed to make modeling simpler and more accessible for people with diverse backgrounds and skill sets, with particular emphasis on building capacity for modeling work in lower and middle income countries. In the year since HPVsim launched, we have run training workshops in Uganda, Kenya, and India. Here, we reflect upon the challenges and successes that we encountered, and how we are working with collaborators to strengthen the software for ongoing work.

Methods: We ran Starsim modeling workshops at Makerere University, Kampala (July 2023), Strathmore University, Nairobi (July 2023), and the National Disease Modeling Consortium at IIT Bombay, Mumbai (September 2023). Each workshop included background sessions on disease modeling, as well as hands-on sessions working with the software to create models and analyze policy questions. We present a case study developed with the National Disease Modeling Consortium of India, which illustrates the typical workflows for conducting an analysis with the HPVsim software, and shows how we were able to adapt the software to specific user needs.

Results: Over 12 months, we trained ~80 people in running HPV epidemic simulations using the Starsim software. Overall, we found that the HPVsim software was both simple enough that most users were able to run their models, and flexible enough to model all requested policy scenarios. However, model calibration and validation remained time-consuming and computationally intensive tasks. We achieved significant speed-ups by implementing array-based computation, parallelization, and pre-allocation of outcomes, which reduced the time taken to customize a model to a given epidemic setting.

Conclusions: Community-driven software development is gaining traction in a number of different fields. By shifting emphasis from "models as finished products" to the development process itself, there is potential to create more value for the community that will benefit from it. We reflect on a number of lessons for other modelers and software developers, including the importance of documentation, transparency around inputs, and open communication. By improving access to modeling tools, targets can be more easily updated as technologies and guidelines change, paving the way for faster elimination of cervical cancer worldwide.

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P37-01 | Factors affecting young women's participation in cervical cancer testing - a population-based survey study

37 - Health education

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Background/Objectives: Organized cervical cancer (CC) screening in Finland has significantly reduced CC incidence and mortality. Although organized screening has proved more effective in reducing cancer incidence and mortality than non-organized testing, non-organized testing is still routine in Finland, particularly among young women. Frequent testing, especially in those under 25 years, can lead to overdiagnosis and unnecessary treatment. This study aimed to identify factors influencing women's participation in organized and non-organized CC screening to improve adherence, reduce healthcare costs, and minimize harm.

Methods: We invited a randomly selected sample of 5000 Finnish women aged 15-35 from September 2020 to May 2021 to participate a survey about their knowledge and attitudes toward CC testing. The survey, comprising 28 questions, was conducted online. We matched the survey data with the participants' sociodemographic information, organized screening participation data, and non-organized CC test data. We assessed the participants' knowledge of human papillomavirus (HPV), cervical cytology, and HPV testing, along with factors influencing their willingness to participate in organized screening. Using binary logistic regression, we evaluated the impact of sociodemographic and survey-related factors on young women's participation in both organized and non-organized CC testing.

Results: Of the 5000 invited, 1411 (28.2%) responded to the survey.In non-organized testing, significant predictors of participation included HPV vaccination status, medical contraception use, and frequent gynecologist visits. Those with a positive HPV vaccination status had an OR to participate in non-organized screening of 0.3 (95% CI 0.2-0.5) compared to those with a negative HPV vaccination status. Medical contraception users had an OR of 4.9 (95% CI 3.1-8.0) compared to non-users. Regular gynecologist visitors had an OR 1.7 (1.2 -2.4) compared to non-regular visitors. Survey results showed high HPV awareness among participants but gaps in knowledge about the virus' properties and cervical cytology testing.

Conclusions: Negative HPV vaccination status and medical contraception usage increased non-organized testing participation, possibly due to heightened CC risk perception. While most knew about HPV, knowledge gaps existed, particularly regarding cervical cytology testing misconceptions. Organized CC screening in Finland mostly aligns with young women's preferences but concerns about male sample takers persist.

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#6927

P37-02 | It's time: a campaign to increase HPV vaccination awareness and cervical cancer screening among Hispanic/Latina and Korean women

37 - Health education

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Background/Objectives: In Los Angeles County, U.S. Latina and Korean women have the highest incidence of cervical cancer (14.3 and 9.3 respectively) per 100,000. Cervical cancer mortality rates among Hispanic/Latinas are significantly higher (3.4 deaths per 100,000) compared to non-Hispanic White women (2.5 deaths per 100,000). Though vaccines are effective in preventing cervical cancer, in L.A. County only 47% and 36% respectively of Latinas and Asian women have received all three doses of the HPV vaccine. We created It's Time, a campaign to raise HPV awareness, vaccinations and cervical cancer screening among Latinas, and tested the campaign among Korean audiences. The campaign uses the annual bloom of the stunningly beautiful purple jacaranda tree as a natural reminder for women to vaccinate their children or ask if it "its time" to get screened for cervical cancer. We evaluated the effectiveness of the campaign and conducted focus groups to identify strategies for cultural adaptation among Korean women.

Methods: Survey data were on HPV knowledge were collected via community intercept surveys among 431 women. Twelve focus groups were conducted (nine with Latinas, three with Koreans) to determine cultural and linguistic appropriateness. Participating clinics reviewed clinic records pre and post campaign and documented cervical cancer screening. Mailers were sent home to a subset of 359 women tied to the clinics, with screening reminders. Outdoor posters, banners, street signs, billboards, were utilized as reminders carrying messages of "It's Time, It's Easy, It's Important". A phone line for women's referrals was provided.

Results: Of the women surveyed, seventy-four percent had not had the HPV vaccine. Sixty-eight percent did not know what causes most cervical cancer. Thirty-three percent had not heard about the HPV vaccine. Focus groups findings showed 25% of Latinas and 12.5% of Korean participants had not ever received a Pap test. 50% of Latinas and 37.5% of Koreans respectively where out of compliance with screening guidelines (not had a Pap test in more than three years). Images of the purple jacaranda tree were accepted by both communities. For cultural adaptation, educational materials such as postcards, posters, and outdoor media needed to reflect images of Korean women and families. Most participants felt clinics needed to extend hours and reduce wait times to accommodate working women. Incentives were seen as necessary to draw women to clinics. Community health workers (promotores de salud) were an effective mechanism to inform Latinas. Korean women preferred to receive information directly from female doctors. Seventy-six percent requested more information on HPV vaccines and cervical cancer early detection. 46% in the intervention clinic became compliant vs 33% in the control clinic (13% difference, p inf.001). Sixty-five percent of women who received educational materials on Es Tiempo at home came in and got a pap test vs 34% in control clinic (p inf.001).

Conclusions: The It's Time campaign proved to be effective among Latinas. It can be applied to Korean women with cultural adaptation. Campaign elements need reflect Korean women and their families using multigenerational images. Overall materials used in the Hispanic/Latino population would be well received among Koreans, including images of the purple jacaranda tree and health education messages.

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#6641

P37-03 | HPV decide: the development of a comprehensive tool for facilitating informed HPV vaccination choices among adults aged 27 to 45

37 - Health education

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Background/Objectives: The shared clinical decision-making recommendation for mid-adult HPV vaccination in the United States (i.e., CDC 2019) may be successfully facilitated using patient-facing decision aids. The purpose of this study was to design, develop, and field test the HPV Decide decision tool among the target patient population (unvaccinated adults aged 27 to 45) and healthcare providers who provide care to this patient population in the United States.

Methods: The online tool (HPV Decide) was developed over a 6-step process that included engagement of a Community Advisory Board (CAB) and a Provider Advisory Board (PAB), usability testing with end users (N = 10), field testing with end users (N = 10), and interviews with healthcare providers (N = 18). Qualitative data were collected and analyzed using inductive and deductive approaches.

Results: The development process began with the creation of a logic model rooted in the Ottawa Decision Support Framework and informed by a systematic literature review (step 1). The main decisional outcomes targeted were objective knowledge and subjective decisional conflict. Following this, our team collaborated with a systems designer to produce storyboards for the HPV Decide decision tool (Step 2). Alpha testing was subsequently conducted, involving feedback from both advisory boards, which led to pivotal modifications in the tool's design and content (Step 3). Usability testing produced varied responses to the tool, necessitating comprehensive revisions (Step 4). In total, 10 participants completed field testing interviews (Step 5). Eight parent codes were generated based on the semi-structured interview guide. From these 8 parent codes, 25 child codes were inductively generated (inter-coder agreement was 78.3%; coding differences were discussed and resolved). Participants found the HPV Decide tool informative and user-friendly, appreciating its straightforward design and lack of medical jargon. Many expressed a desire to access the tool before doctor appointments for preparation, emphasizing its value in a healthcare context and in partnership with informed providers. Lastly, insights were gleaned from healthcare providers (Step 6) focusing on the tool's information quality, structure, acceptability, and future implementation.

Conclusions: The HPV Decide decision tool, refined based on structured feedback from diverse stakeholders, demonstrates promise in supporting informed decisions about HPV vaccination among mid-adults. While users recognized its information quality and user-centric design, full evaluation focused on changes in informed decision making and clinic-based implementation are needed.

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#6611

P37-04 | A descriptive study of first female south African HPV vaccine recipients eleven years later: sociodemographics, sexual behaviour and knowledge

37 - Health education

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Background/Objectives: Infection with the human papillomavirus (HPV) is a necessary cause of cervical cancer and is one of the most prevalent sexually transmitted infections worldwide. The primary prevention of cervical cancer aims to reduce the risk of HPV acquisition. This may include vaccination against HPV, reduction of exposure to HPV (delayed sexual debut or barrier contraception), or health education focused on sexual behaviour and tobacco use. The present study aimed at reporting the typical female vaccine recipients' socio-demographic characteristics, sexual practices and knowledge of cervical cancer and the HPV vaccine, to understand risks and protection.

Methods: The ImmunoVACCS (Immunity, knowledge, behaviour and HPV infection rates after pre-adolescent HPV vaccination during the VACCS 1 and 2 trials) study was a descriptive cross-sectional, multi-centric study conducted from 2020 to 2022 in Gauteng and the Western Cape provinces of South Africa and included vaccinated girls from VACCS 1 and VACCS 2, performed in 2012. The protocol was reviewed and approved by the institutional research ethics committees of the universities of Pretoria (330/2018) and Stellenbosch (N19/02/023 Reciprocal UP 330/2018). Potential participants were contacted telephonically by a trained nurse investigator or research assistant. Young women aged 16 to 22 were recruited from three sites in South Africa. Data was collected through a self-administered structured questionnaire.

Results: One hundred and eleven young women with a median age of 20 years were included in this analysis. The majority of young women who have ever been sexually active, 96.2% (75/78), stated their first time of sexual engagement was in their secondary school-years and 77.2% (61/79), used some form of contraception the last time they were sexually active. Although only 4 respondents (3.6%) knew that it was caused by a virus, a high number of respondents (70.3%, 78/111) said that they have heard of a vaccine/injection to prevent cervical cancer. Less than half of the respondents knew that one must have a regular Pap smear (49.5%, 55/111), that vaccination can protect one (44.1%, 49/111), and that condom use can act as protection (20.7%, 23/111) against HPV and cervical cancer.

Conclusions: The current study demonstrates that young women lack complete information on cervical cancer and its risk factors. Educating young girls about HPV vaccination which offers protection against the primary cause of cervical cancer, can increase acceptance by providing accurate information about the vaccine, its safety, and effectiveness, young girls and their parents can make informed decisions about getting vaccinated. Increasing awareness can also help address any misconceptions or concerns that may exist around cervical cancer and the HPV vaccination.

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#6318

P37-05 | Identifying educational needs for anal cancer prevention among patients taking pre-exposure prophylaxis (PREP)

37 - Health education

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Background/Objectives: Anal cancer (AC) disproportionately affects gay/ bisexual men (GBM) and transgender women (TGW) because of prevalent oncogenic anal human papillomavirus (HPV) infections. Limited diffusion of targeted anal cancer prevention information hinders prevention efforts and perpetuates disparities. The purpose of this study was to understand preferences for anal cancer education among GBM/TGW engaged in HIV preventive care (i.e., pre-exposure prophylaxis [PrEP]).

Methods: Participants identified as sexual/gender minority (SGM), were between the ages of 18-45, and had at least one PrEP-related healthcare visit in the past two years at a federally qualified health center in Philadelphia, PA. The Information-Motivation-Behavioral Skills Model informed survey items. Analyses include descriptive statistics regarding educational needs.

Results: The sample (N=88) was primarily cisgender gay-identified men, ethnoracially diverse, and participants had a variety of health insurance types. Most participants (80.7%) felt comfortable discussing AC with a doctor; however, 51.1% were uncomfortable discussing their sexual behaviors. Before deciding on the HPV vaccine, 50.0% of participants wanted more information about the vaccine and their risk for AC. When considering the vaccine, the majority (51.1%) wanted to know its effectiveness, while fewer (29.6%) were interested in non-HPV vaccination methods for preventing AC. Regarding information sources, most participants (73.9%) preferred accessing websites at their convenience, while fewer indicated they would seek information from doctors (e.g., pamphlets, questions answered by a healthcare provider over text messaging). The majority (72.7%) perceived themselves as more likely to visit a website with AC information if it also contained more general information about having anal sex (e.g., anorectal douching). Most participants (53.4%) would follow a doctor on social media who provided this type of content.

Conclusions: GBM/TGW lack basic information about AC prevention. PrEP providers can help meet this need by providing targeted, culturally relevant messages about AC prevention to their patient populations. Our findings suggest that social media is a viable medium to disseminate targeted AC information to at-risk populations.

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#7135

P37-06 | A Pilot Evaluation of a Sexual Health High-School Educational Intervention on HPV knowledge, beliefs and behaviours

37 - Health education

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Background/Objectives: The majority of interventions focused on increasing HPV vaccination have focused on parents of young children and adolescents. Young people are eager to be informed and involved in their own health decision-making and in many jurisdictions have the right to do so. Positive sexual health education outcomes are most likely to happen when the sexual health education integrates understanding (knowledge), motivation, and skill-building opportunities. HPV Global Action, a Canadian registered charity, has been delivering a Healthy Relationships_101, a1.5 hour in-person presentation to high school students for over 20 years. The presentation offers a comprehensive overview of sexual health and relationships and provides actionable behaviours to sexual and reproductive health resources including HPV vaccination. The present pilot evaluation study aimed to assess the effectiveness of the education program on increasing knowledge and improving perceptions and attitudes of students' toward sexual health and healthy relationships, including HPV vaccine as a prevention tool to reduce this sexually transmitted infection. By helping young people to understand the importance of HPV in the context of their health as a personal responsibility, we expect to see an increase in actual HPV vaccine acceptance.

Methods: Canadian high school students (n = 10 females, 9 males) completed two short evaluations of knowledge, attitudes and behaviours about sexual health topics before and 1 month after the presentation. The questionnaire contained items about students' perceptions, behaviours, attitudes and knowledge on sexual health including 5 knowledge items about HPV, 4 attitudinal items about HPV vaccine, their own vaccination status and if they had plans to talk to someone about the HPV vaccine.

Results: Most participants knew nothing at all about or very little about HPV at baseline prior to the presentation, and most often selected "I don't know' to knowledge items. HPV Knowledge significantly increased from a mean of 2.3 (SD =1.74) at pre-evaluation to 3.73 (SD =1.75) , pinf0.05. Attitudes towards HPV vaccination were more favourable post presentation. 20% were motivated by the intervention and received the HPV vaccine by 1 month post presentation.

Conclusions: This educational presentation effectively increases students' knowledge and improves their attitudes and perceptions about various sexual health topics. For some, the intervention also translated into a behaviour modification, which is key to link knowledge with action. We are currently evaluating the presentation with a larger sample of Canadian high school students. We will be able to present subsequent data and evaluate the impact of this educational tool as a way to modify health practices among adolescents. This study is the first of its kind to understand adolescents' perspectives on sexual health without requiring parental perspectives and consent, an innovative approach to studying HPV vaccine knowledge and practices.

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#7081

P39-01 | Surveillance of Adverse Events Following National HPV Vaccine Immunization in Taiwan

39 - Public health

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Background/Objectives: Taiwan national HPV vaccination program (bivalent) policy funding, administered by HPA, was officially launched in December 2018[1, 2]. This program is specifically directed towards seventh-grade girls aged 12-13. To assess the occurrence of adverse events following the nationwide implementation of publicly funded HPV vaccination for middle school girls, this study utilizes data from the national HPV vaccine database and the national health insurance database spanning 2018 to 2020.

Methods: Data source Taiwan's National Health Insurance Database, covering nearly 99.9% of the population, records personal and clinical data. It includes inpatient/outpatient records, disease diagnoses (ICD-9-CM/ICD-10-CM), and drug prescriptions. The National HPV vaccine database obtained its information from the National Immunization Information System (NIIS), which stores data on vaccine type, vaccination date, dosing, recipient's age, and place of residence. Two databases are linked by de-identified IDs. AE selection A total of 19 diseases related to adverse events were included for studies in the project, including 7 major diseases (Autoimmune disease, Rheumatoid arthritis, Juvenile rheumatoid arthritis, Systemic lupus erythematosus, Multiple sclerosis, Crohn's disease, Ulcerative colitis) listed in the Registry for Catastrophic Illness Patients of the National Health Insurance and 12 non-major diseases (Guillain-Barre Syndrome, Immune thrombocytopenia purpura, Autoimmune thyroiditis, Primary ovarian failure, Type 1 diabetes mellitus, Acute disseminated encephalomyelitis, Myelitis, Neuromyelitis optica, Demyelinating diseases of the central nervous system, Complex Regional Pain Syndrome, Chronic Fatigue Syndrome, Fibromyalgia). The diseases and their corresponding ICD codes were not shown. Statistical analysis The calculation of the Standardized Incidence Ratio (SIR) was based on the incidence rate of severe adverse events within the vaccinated cohort compared to that of adolescent girls in the corresponding age group across the entire country. 95% confidence interval (95% CI) was also provided. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Ethical issue The study protocol was approved by the Institutional Review Board of Fu Jen Catholic University on 31 December 2021 (IRB NO. C110060).

Results: The total number of female students aged 12-15 receiving the HPV vaccine from 2018 to 2020 was 199,049. Among females who received the vaccine, the most common newly developed conditions post-vaccination, in descending order, were Chronic Fatigue Syndrome (CFS), Autoimmune disease (AID), Type 1 diabetes mellitus, and Autoimmune thyroiditis, with 34, 29, 27, and 21 cases, respectively. Juvenile Rheumatoid Arthritis (JRA), Systemic lupus erythematosus (SLE), and Fibromyalgia each had 10 new cases. The incidence rate of the above-mentioned seven diseases ranged from 14.47 to 4.25 per one hundred thousand, and in comparison to the non-vaccinated group, the Standardized Incidence Ratio (SIR) did not reach statistical significance. The number of cases for the other 12 diseases was all fewer than 5 individuals, and the Standardized Incidence Ratio (SIR) did not reach statistical significance.

Conclusions: This study relies on national health databases, and its findings indicate that the occurrences of different adverse events in the vaccinated group are not significantly elevated compared to those in the female population of the same age.

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#7099

P39-02 | Epidemiological Characteristic of p16 Among Oropharyngeal Squamous Cell Carcinoma in a Oral Cancer Endemic Area

39 - Public health

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Background/Objectives: Human papillomavirus (HPV) infection in oropharyngeal squamous cell carcinoma (OPSCC) is well established, but incidence and proportion of HPV attributable OPSCC in Taiwan was not known due to lack of screening for HPV. By some local studies, the HPV positive rate was around 25-30%. However, those data were from single-center studies, and a comprehensive, population data is still lacking. p16 overexpression is considered as a diagnostic tool and has been directly associated with infection by high-risk genotypes of HPV. this study aims to explore the HPV attributable OPSCC incidence and survival characteristic

Methods: Between 2018 and 2020, the newly diagnosis primary OPSCC cases were extracted from the Taiwan Cancer Registry database (TCR). Clinical and p16 data were collected from the TCR long from records. Crude rates and age-standardized rates (ASRs) of incidence were calculated by the direct method using the 2000 world standard population and expressed as cases per 100,000 populations. Cox proportional hazards regression models to calculate hazard ratios (HRs) and their 95% CIs.All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA). The study protocol was approved by the Institutional Review Board of Fu Jen Catholic University (C112033).

Results: A total of 4,955 patients were enrolled in this retrospective study, comprising 4,515 men and 440 women, with a mean age (± years).The histopathological confirmation rate for these cases was exceptionally high, reaching 98.95%. The age-standardized incidence rate of p16+ OPSCC stood at 21.8% for men and 22.8% for women per 100,000 individuals, respectively. Notably, nearly half of the p16- OPSCC patients reported concurrent exposure to alcohol, betel quid, and cigarettes. Furthermore, 65% of OPSCC patients with p16+ were exposed to at least one form of high-risk behavior. A majority of p16+ OPSCC tumors were found in the tonsils (65%), while p16- OPSCC patients also had a higher proportion of tonsil tumors, though at a lower incidence rate (approximately one-third).In the present study, it was observed that 70% of p16+ OPSCC patients were diagnosed at early stages (Stage I and Stage II) during their initial diagnosis, while over 50% of p16- OPSCC patients were already at Stage IV. Notably, OPSCC patients with p16+ demonstrated more favorable relative and observed survival rates, particularly in early stages. In the 3-year overall survival rates, p16+ OPSCC patients had a 73.4% survival rate, while those with p16- had a lower rate of 49.3%.

Conclusions: p16 is a useful surrogate marker for HPV infection in OPSCC and a good prognostic indicator for treatment outcome of OPSCC.

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#7030

P39-03 | Cervical Cancer Prevention in Rural Kenyan Communities: The Mother-Daughter Project

39 - Public health

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Background/Objectives: Cervical cancer is caused by "high-risk" human papillomavirus (HR-HPV) and is the main cause of cancer-related deaths among rural Kenyan women. Cervical cancer is preventable through screening of women and vaccination of children against HPV infection. However, only 5% of Kenyan women are regularly screened (using Visual Inspection with Acetic Acid, or VIA), and very few (<5%) Kenyan children have been vaccinated. We developed a community-based prevention program in Kenya known as the Mother-Daughter Project (MDP). The aims of the MDP are to 1) screen rural Kenyan women for cervical cancer using HR-HPV testing of self-collected vaginal swabs, 2) vaccinate daughters/granddaughters against HPV. As an exploratory aim, vaccinated girls will be tested to determine the effects of aflatoxin exposure on the immune response to vaccination.

Methods: A community entry strategy was utilized to introduce the MDP and invite participants in the Webuye region of Kenya. At community meetings, women ages 18 to 60 (later changed to ages 30 to 55) were educated about cervical cancer. Women then provided self-collected vaginal swabs for HR-HPV testing (Roche Cobas Assay). All women travelled to the local clinic for VIA. Cervical biopsy was performed on women with abnormal VIA according to the local standard of care; HR-HPV testing was not used in clinical management. Women were instructed in the efficacy, safety, and potential adverse effects of HPV vaccination. Gardasil 9 (Merck) was then offered to daughters/granddaughters (ages 9 through 15) at the community meetings. Blood samples were collected from a subset of girls, 6 months after receiving the 2nd vaccine dose, for HPV antibody and aflatoxin testing. Questionnaires were administered to mothers and daughters regarding 1) knowledge and beliefs about HPV and cervical cancer, and 2) opinions about self-collected swabs, travel to community meetings and the clinic, and acceptability of HPV vaccination.

Results: To date, 500 women have enrolled in the MDP, with a mean age of 36.0 years; 83 (16.6%) are HIV-infected and receiving anti-retroviral therapy. Vaginal swabs were performed by all women; all were adequate for HPV testing.HR-HPV was detected in 144 (28.8%) women. HR-HPV, HPV 18, and non-16/18 HR-HPV were detected significantly more often in HIV-infected women compared to HIV-uninfected women.VIA was performed in 491 women and was abnormal in 20 (4.0%); VIA abnormality was not significantly different between HIV-infected and HIV-uninfected women. Cervical biopsy was performed on 19 of 20 women with abnormal VIA; CIN2/3+ detected in 6 of 19 women. HPV vaccination was provided to900 girls (ages 9 to 15 years), no vaccine-related serious adverse events occurred. Results of HPV antibody and aflatoxin testing will be presented.

Conclusions: The MDP has built trust in the community. Rural Kenyan women are willing to attend community meetings, learn about cervical cancer, provide swabs for HR-HPV testing. Cervical cancer screening using HR-HPV testing of self-collected vaginal swabs was highly acceptable among rural Kenyan women; this method can be utilized as an alternative to clinic-based screening using VIA. Vaccination against HPV was highly acceptable among Kenyan women and girls. As a result of this pilot study, our community-based strategy of cervical cancer prevention will be continued and expanded in western Kenya.

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#6843

P39-04 | Informatics platform for a cervical cancer elimination campaign using HPV vaccination and HPV screening

39 - Public health

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Background/Objectives: In the era of cervical cancer elimination, a robust and easy open-source solution for managing and documenting HPV vaccination and HPV testing is essential. We developed an integrated informatics platform which is open-source, generic, easily deployable and can be accessed from any ordinary mobile or PC.

Methods: The cervical cancer elimination software platform has three main components: HPV vaccination, to manage participant's vaccinations; HPV screening,to manage self-sampling orders and register samples and analyses, and manage results; and Monitoring, to graphically present statistics. The HPV vaccination system has a user-friendly interface where the participants can (on their own mobile phone) register, provide informed consent, and answer the health declaration questions. Participant registration can either be authenticated via the traditional username/password method or using electronic ID. The vaccinator can read the patient's information, assess the health declaration, document everything needed for vaccination (date, time, vaccinator ID, patient ID, batch number, vaccine, dose, and the vaccination site ID) as well as provide information on whether a self-sampling kit was provided. The Sampling system manages participants' kit orders, registers their HPV self-sampling kits (the subject authenticates using a QR code and their mobile phone) and provides personal access to their HPV test results. All results and metadata associated with the HPV self-sampling kits are also weekly exported to the regional health data systems, where physicians can access the patient´s HPV results together with other clinical history. The Monitoring system is a web service where stakeholders and policymakers can get an overview of the screening program, focused on the vaccination statistics. The web service provides a graphical interface with the main statistics to evaluate the screening process.

Results: The platform was tested as a pilot in 2021 at a single site in Södertälje, Sweden. Since October 2022, it has been expanding to the whole country, where it serves both i) a national campaign aiming at vaccinating and HPV screening all women born between 1994 and 1999. Currently about 500 vaccination sites and more than 1600 vaccinators use the platform. As the system was developed when the project was already running, not all about 85,000 enrolled women are registered, but 77820 of them are. The HPV screening in the campaign can either use clinician-taken samples or self-samples. So far, there were more than 46000 self-sampling orders and about 44000 results from HPV tests. ii) a national campaign targeting non-attending women and other women with cancer risks above 30/100,000 woman years (about 90,000 in Sweden). These were contacted to participate using self-sampling. Between 2022 and 2023, more than 9500 self-sampling kit orders have been placed up to October 2023, and 5467 results have been provided to these women.

Conclusions: The software platform developed by the Center for Cervical Cancer Elimination (CCCE) is being validated by the elimination program in Sweden. The open-source platform can be easily deployed in other countries with minor modifications. It can facilitate the workflows from recruitment, sampling, vaccination, testing and results, and integration with the healthcare system. The platform can contribute to the quality assurance in HPV testing and vaccination programs, which are essential for the ongoing HPV elimination worldwide.

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#6910

P39-05 | Children's perceptions about being offered the HPV vaccination: a focus group study

39 - Public health

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Background/Objectives: According to the UN Convention on the Rights of the Child, children have the right to be heard and participate in decisions regarding their own health. In Sweden, all children regardless of gender are offered HPV vaccinations through the school-based vaccination program in fifth grade (10-12 years of age). Timely vaccinations are crucial for effective HPV-related cancer prevention1. In order to improve HPV vaccination rates in areas with low vaccination coverage, children's perspectives and research participation are important. However, studies with children who are offered HPV vaccination are limited. Therefore, the aim was to explore children's perceptions about being offered the HPV vaccination.

Methods: Six focus group interviews were conducted with children (n=49) 10-12 years of age, who had been offered HPV vaccination through the School health services in mid-north Sweden. Data was collected between November 2022 and March 2023. Data was analyzed using content analysis2.

Results: Four main themes were formed:1) I want someone I trust to tell me so that I can feel safe, 2) I was mostly afraid it would hurt, 3) The grown-ups decide but they must listen to me, 4) It has to be fair, it's for the common good. How children experienced their participation in the vaccination offer largely varied. Experiences ranged from having been well-informed and included in the decision-making to not having received any information or opportunity to voice concerns and questions, either in school or at home. While children foremost trusted the competence of the school nurse and their caregivers to make a good decision for them it was crucial to feel safe both before and during vaccination. Means to feel safe was to prepare by being informed, supported, and included according to the child's individual preferences. That the injection would be painful was a main concern among participants. Views of long-term consequences, for one's own health and for the society as a whole, also influenced their attitudes towards vaccination. That everyone, despite age or gender or having declined a vaccination offer, were able to get vaccinated was recognized as important for the common good and a question of fairness. Furthermore, a lack of knowledge and insufficient information about why boys are vaccinated were expressed. This was described as unfair to boys and a barrier to their motivation to be vaccinated.

Conclusions: There is a need for improved HPV vaccination information for children, especially for boys. Children's right to participate on their own terms is not fulfilled today. Children are aware and can reflect on their own limitations to participate. The responsibility of vaccine education and promotion, both to children and parents, should be actively managed by the school nurse.

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#6758

P39-06 | Using Immunization Registry Data to explore disparities in early HPV vaccine initiation in a rural, midwestern state, US

39 - Public health

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Background/Objectives: Initiating the HPV vaccine series at ages 9/10 compared to 11+, results in on-time completion. This evidence is strong enough that several organizations in the United States, including the American Cancer Society and the American Academy of Peditrics, have updated their recommendation language to indicate conversations about HPV vaccination should begin at earlier ages. However, since little is known about factors associated with early initiation, our goal was to explore sociodemographic factors associated with early initiation using immunization registry data.

Methods: Immunization registries are state-wide databases that are able to work bidirectionally with electronic medical record systems to keep immunization history up-to-date. Iowa, a rural, midwestern state, has a robust registry that captures nearly 100% of the immunizations that occur in the state. We used data from the Iowa Immunization Registry for children born between 2004 and 2013 to explore sociodemographic factors (e.g., gender, race/ethnicity, rurality, and insurance type) associated with early initiation. We then used logistic regression to model the factors associated with likelihood of early HPV vaccine initiation.

Results: Of the 255,833 children who initiated the series in our data set, 3.2% (n=8,355) initiated at ages 9 or 10, 173,831 (67.9%) initiated at ages 11 or 12, and the remaining 73,647 (28.8%) initiated after 12. We observed significant differences between the children who initiated at ages 9/10 compared to later across all sociodemographic categories. Males were less likely to initiate early (OR: 0.77, 0.74;0.81) compared to females. Compared to white children, racial and ethnic minority children were more likely to initiate the series early; for example, black children had an odds ratio of 1.99 (CI: 1.87, 2.13) and Hispanic or Latino children had an odds ratio of 1.67 (CI: 1.57, 1.79). Those living in the most rural areas (OR: 0.76, CI: 0.72, 0.81) and those with either no insurance (OR: 0.84, CI: 0.80, 0.89) or public insurance (OR: 0.53, CI: 0.50, 0.56) were less likely to initiate early.

Conclusions: Given the recent focus on early initiation for the series, our results contribute to a growing understanding of who is initiating the series earlier and where disparities are occurring. In some ways, these results echo patterns previously seen in analyses of initiation; males, racial/ethnic minorities, and adolescents living in rural areas are less likely to initiate the series in general compared to females, non-Hispanic white, and urban-dwelling adolescents. Whereas, national data has shown that adolescents with public insurance have higher initiation and completion rates, we found that public insurance was associated with a lower likelihood of early initiation. Immunization registry data are highly valuable in providing these nuanced, population-level details about immunization uptake and we can now use this data to inform development of tailored interventions to better promote early-initiation of HPV vaccination. Our future steps will include geospatial analysis so that we can not only develop tailored messaging based on these identified sociodemographic characteristics but also based on geographic areas where early initiation is lagging.

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#6668

P39-07 | The Opinion of Women Aged 16-55 on Free or Partially Subsidized Menstrual Hygiene Products in Lithuania and Its Influential Factors

39 - Public health

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Background/Objectives: WHO and UNICEF Joint Monitoring Programme for drinking water, sanitation, and hygiene define menstrual hygiene management (MHM) as "Women and adolescent girls are using a clean menstrual management material to absorb or collect menstrual blood, that can be changed in privacy as often as necessary for the duration of a menstrual period, using soap and water for washing the body as required, and having access to safe and convenient facilities to dispose of used menstrual management materials. They understand the basic facts linked to the menstrual cycle and how to manage it with dignity and without discomfort or fear". New research suggests that the experience of "period poverty" or the lack of previously mentioned practices, may be a common concern for not only women and girls in low- and middle-income countries but also for vulnerable populations in high-income countries. Our objective was to assess the opinion of women aged 16-55 regarding free or partially subsidized MHM products in Lithuania, along with its influencing factors.

Methods: An original questionnaire comprising 38 questions was developed, with its validity assessed through an online pilot survey (n=30), and subsequently refined based on expert feedback. The questionnaire was distributed via social media platforms, with the study period ranging from January 1st to January 31st , 2023. Statistical data analysis was performed using IBM SPSS Statistics 29.0. Descriptive statistical analysis, Student's t and chi-square ($\chi 2$) tests were used. Differences were considered statistically significant when inf0.05.

Results: In total, 629 women completed the survey. The mean age of respondents was 28.2 years (SD=7,4). N=588 (93.5%) of the respondents would have agreed with free or partially subsidized MHM products in Lithuania. Particular groups of women statistically significantly more often agreed with the MHM products initiative: respondents under the age of 25 (298/309 (96.4%) vs >25 years old 290/320 (90.6%); p=0.003); women who did not have children (429/450 (95.3%) vs women with children 159/179 (88.8%); p=0.002); those who earned ≤ 1000 Eur per month (inf500 Eur 165/172 (95.9%) vs 500-1000 Eur 228/239 (95.4%) vs >1000 Eur 195/218 (89.4%); p=0.008); women who used disposable MHM products (455/468 (97.2%) vs re-usable products users 133/161 (82.6%); p=0.004); respondents who have heard about the access to free period products in other countries (476/490 (97.1%) vs 112/139 (80.6%); p=0.027).

Conclusions: Nine out of ten surveyed women would support free or partially subsidized MHM products in Lithuania. Women's opinions were influenced by age, number of children, monthly income, the type of MHM products used and previous knowledge about the initiative.

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#6647

P39-08 | Impact of the pandemic on cervical cancer screening in the state of Rio de Janeiro - Brazil

39 - Public health

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Background/Objectives: To analyze the influence that the covid-19 pandemic had on cervical cancer screening in the state of Rio de Janeiro - Brazil.

Methods: This is a Cross sectional study, carried out using the public dissemination platform of the Unified Health System (DATASUS-Brazil), in the "Cancer Information System" (SISCAN). The total number of cytopathological exams that were collected in the state of Rio de Janeiro-Brazil, in the period between 2018 and 2022, was analyzed. The percentages of altered cytopathological exams within the total number of exams collected were evaluated. The period surveyed was intended to compare two years before and after the start of the Covid-19 pandemic. Due to the use of public domain data, this study is exempt from analysis by the Research Ethics Committee.

Results: It was found that in the state of Rio de Janeiro-Brazil, between 2018 and 2022, 593,376 cervical cytopathology exams were carried out for screening. In the two-year pre-pandemic period 2018-2019, 205,868 (34.7%) were collected. In the year of the Covid-19 pandemic (2020), 85,107 were carried out (14.3%). In the period after the 2021-2022 pandemic, 302,401 were carried out (50.9%). In 2020, there was a significant reduction in the number of cytopathological tests collected, when compared to the tests collected in 2019 (109,855), with a reduction of 22.5%. The number of low-grade squamous intraepithelial lesion(LSIL) registered between 2018 and 2019 was 2,455. In 2020, there were 1,351 exams, and 3,051 between 2021 and 2022. Between 2018 and 2019, the number of high-grade squamous intraepithelial lesion (HSIL) and Squamous cell carcinoma, was 457 and, between 2021 and 2022, the number of these changes was 1,202.

Conclusions: With the declaring of the Covid-19 pandemic in March 2020 throughout the Brazilian national territory, there was a reduction in cervical cancer prevention actions and, consequently, in opportunities to track precursor lesions or those related to cervical cancer. Despite a drop in the number of exams in 2020, there was a recovery in the following year, when an increase in the diagnosis of all precursor lesions was observed in the short period analyzed. This study may contribute to the understanding of possible challenges that we will face in the post-pandemic period.

Table: exam results per year

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#6807

P39-09 | Knowledge Regarding Menstrual Cycle and Menstrual Hygiene of Lithuanian Women Aged 16-55 years

39 - Public health

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Background/Objectives: Knowledge about menstrual health (MH) and menstrual cycle (MC) are pivotal elements contributing to the overall well-being and empowerment of women and adolescent girls. "Health, sexuality education and family planning programme" was confirmed by Ministry of Education and Science of the Republic of Lithuania in 2016. However, it had only few statements about sexuality education, contraception as all the emphasis was on abstention from sex and lacked information about MC and MH. Renewed program caused many discussions between students' parents, teachers and other members of our society. Therefore, in order to assess the need for MH education and evaluate the knowledge gap, we investigated and compared the knowledge regarding the MC and MH among different age groups of Lithuanian women.

Methods: An original questionnaire comprising 38 questions was developed, with its validity assessed through an online pilot survey (n=30), and subsequently refined based on expert feedback. The questionnaire was distributed via social media platforms, with the study period ranging from January 1st to January 31st, 2023. For comparison, women were divided into two groups according to their age: Group I - women younger than 25 years old (n=320, 49.8%) and Group II - women older than 25 years old (n=322, 50.2%). Descriptive statistical analysis, Student's t and chi-square ($\chi 2$) tests were used. Differences were considered statistically significant when pinf0.05.

Results: There were 642 women included in the study. The average age of the surveyed women was 28.2 years (SD=7.4). Women's knowledge about the MC was assessed on a scale from 0 to 4. The average knowledge score for women was 2.5, and no statistically significant difference was found between the age groups. A total of 473 respondents (74.8%) correctly assessed the regularity of their MC. Women whose MC lasted between 21 and 35 days were statistically more likely to incorrectly believe that their MC were irregular (p=0.006). Moreover, women in group I more often thought their MC were irregular (p=0.028). The primary sources of information about MC and MH for women were from their mothers (n=489; 76.2%), specialized school lessons about MC and MH (n=402; 62.6%), and the internet (n=395; 61.5%). Respondents of Group I sought information on the internet statistically more frequently (p=0.013), while women in group II - from their mothers (p=0.026). Respondents were asked to agree/disagree with various definitions of MH. Most of the women defined MH as clean MH materials for absorbing menstrual blood (n=621; 96.7%) and agreed with the fact that the accessibility of MH products is an important aspect of MH (n=625; 97.4%). Fewer respondents agreed that privacy in changing MH products (n=529; 82.4%) and women's and girls' knowledge about menstruation (n=528; 82.2%) are included in the definition of MH. Less than half the respondents (n=274; 42.9%) disagreed with the statement "MH does not define women's and girls' right to manage menstruation with dignity and without discomfort or fear".

Conclusions: The average women's knowledge about MC was evaluated 2.5 points out of 4, with younger women more often having a false believe about their MC regularity. Younger women more often chose the internet as their primary information source about MC and MH, while older - their relatives. Nearly all of the respondents possessed the correct knowledge about the definition of MH.

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#7124

P40-01 | HPV and recurrent pregnancy loss

40 - Fertility and HPV

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Background/Objectives: HPV infection is the most common sexually transmitted infection worldwide. The virus has a strong affinity for the squamous epithelium of the uterine cervix, and although most cases resolve spontaneously within 1-2 years, persistent HPV infection can lead to cervical cancer. Pregnant women are more susceptible to HPV infection, and as gestational age increases, so does the prevalence of HPV during pregnancy, with higher rates seen in the second and third trimesters compared to the first trimester

Methods: Review of the papers published in pubmed between Jan 1st 2015 and September 30th 2023 was performed to try and draw some conclusions about HPV relation with RPL.

Results: It is believed that HPV infection can result in the death of placental trophoblasts and cause miscarriages or preterm birth. In clinical cases of placental villi positive for HPV DNA reported by other authors, contamination is suspected in the act of crossing the cervical The presence of HPV in sperm has also been reported to increase the risk of pregnancy loss.The prevalence of HPV sperm infection was found significantly higher in couples affected by RPL than in their fertile counterparts. The semen sample was infected by HPV in approximately 1 out of 5 patients. As far as HPV vaccination in pregnancy is concerned, there has been no evidence of an increased risk of SA and other adverse pregnancy outcomes in young women vaccinated around gestation.

Conclusions: Lately, it has been suggested that the presence of HPV alone is not sufficient to cause a miscarriage, but a high viral load in early pregnancy may increase the risk of negative outcomes. The possibility for women who are pregnant or trying to become pregnant to be advised to postpone vaccination until completion of pregnancy is discussed.

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P40-02 | Cervical adenocarcinoma in nulliparous woman - is it possible for a patient to become a mother?

40 - Fertility and HPV

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Background/Objectives: Cervical cancer is one of the most common cancers in the world. It is the fourth most often diagnosed cancers in women. The main types of cervical pathologies are squamous-cell carcinoma and adenocarcinoma. The 5-year survival rate is above 90% in case of detection cancer in early stages.

Methods: In 2020 a patient presented for a routine gynecological visit. After abnormal cytology ASC-H and positive HPV test a biopsy was performed. No pathology was confirmed. She was qualified for LEEP-conization. The results were correct. Parallel, the patient was vaccinated against HPV. The subsequent LBC came in with result LSIL. She referred to clinic to perform another colposcopy, biopsy and endocervical curretage. Histopathology report described adenocarcinoma in situ. The patient was admitted to hospital to undergo surgical conization of cervix. The histopathological report confirmed, that the tumor was removed radically with clean margins. Supervision was recommended. In December 2020 a schedule visit was planned. The patient referred with positive pregnancy test. Analyzing the patient's history, she was in the risk group of developing cervical insufficiency. During this visit the cervical length was 30mm. As prevention of miscarriage and premature birth resulting from earlier treatment, progestagen supplementation was joined. Next follow ups showed no pathology till 18 week of pregnancy. Cervix shortened to 20mm. The patient was admitted to hospital. Myco- and Ureaplasma infection was ruled out. During the stay, the cervix didn't shorten, so the physicians did not decide for cervical cerclage. Patient was discharged from hospital in good condition. At 38 weeks of pregnancy, the patient was admitted to hospital for elective caesarean section. The male newborn with a weight of 3200 g was given 10 points in Apgar score. The puerperium was uncomplicated. Because of the diagnose of adenocarcinoma, the patient had gynecological check-ups every 3 months. All LBC were described as NILM.In June 2022 the patient took a positive pregnancy test. Progestagen supplementation was joined. During first and second trimester, cervical length was normal. In the beginning of third trimester the cervix shortened to 30 mm, resting at home was recommended.

Results: In this pregnancy, the patient reffered to hospital only once - to gave birth. At 37 weeks of pregnancy, a male newborn was delivered through caesarean section. The birthweight was 3220g and the boy was given 9/10 points in Apgar score. After puerperium, in August 2023, the patient had a check-up during which many test were performed - LBC, HPV molecular test and immunohistochemical detection of p16 and Ki67. All of them came out negative. The patient underwent oncological consultation - no complementary treatment was recommended.

Conclusions: The presented situation shows, that even with disadvantageous biopsy test results, for many patients the dream of motherhood can become possible. Early detection and treatment of pre-cancerous lesions and cancer in lower stages is significant.

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P40-03 | Associations between loop electrosurgical excision (LEEP) for cervical precancer after primary human papillomavirus (HPV) screening and adverse birth outcomes

40 - Fertility and HPV

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Background/Objectives: Previous studies have suggested that Loop Electrosurgical Excision (LEEP) is a potential risk factor of preterm birth (PTB) and low birth weight (LBW). With a transition from cytology to primary HPV screening, there will be an initial increase in precancer detections and referrals to treatment given that HPV primary screening identifies cervical precancer earlier and better than cytology, causing concerns regarding the impact in women of childbearing age. This study examined the risk of PTB and LBW among those who received LEEP within the context of primary HPV screening.

Methods: The HPV for Cervical Cancer Screening (HPV FOCAL) study in British Columbia (BC), Canada was a randomized controlled trial to evaluate the effectiveness of primary HPV screening compared to cytology. In HPV FOCAL, women who were HPV positive were referred for reflex cytology to determine if a LEEP was required. After trial completion, women were followed for 10 years through the BC cervix screening program, where cytology is used for cervix screening. HPV FOCAL was further linked to the BC perinatal data registry to assess pregnancy outcomes during and after trial completion. In this study, women who had singleton live births after trial baseline HPV testing were included. Women were considered to have had an HPV screening-related LEEP if they received a LEEP anytime between baseline HPV testing and two years after they completed the trial. Adjusted odds ratios (ORs) were calculated to compare the risk of PTB (gestational week < 37) and LBW (birthweight< 2500g) between women treated with LEEP and women untreated with LEEP prior to the first birth after HPV testing (index birth). Among women treated with LEEP, ORs were also calculated to examine whether the time interval from LEEP to pregnancy was associated with PTB or LBW.

Results: A total of 1765 women had a singleton live birth after HPV testing in HPV FOCAL; 160 (9.0%) women had PTB and 85 (4.8%) had LBW in the index birth. 71/1765 (4.0%) women received a LEEP after a positive HPV test result (total HPV positive N=331, 18.8%). Women's median age at index birth was 34 (IQR, 32-37). Among women treated with LEEP, the median time interval from HPV test to LEEP was 5 months (IQR, 3-15) and the median time interval from LEEP to the index pregnancy was 26 months (IQR, 15-49). There were more nulliparous women at the index birth among women treated with LEEP (55/71, 77.5%) compared to women untreated with LEEP (1018/1694, 60.1%, p=0.005). There was no significant difference found in age at delivery, history of PTB, history of LBW, history of preeclampsia, BMI, and smoking during pregnancy between women with treated LEEP and women untreated with LEEP. The increased risks in women treated with LEEP were not significant (PTB: adjusted OR=1.4, 95% CI, 0.7-3.1; LBW: adjusted OR=1.5, 95% CI, 0.5-3.9). Among women treated with LEEP, there was no significant association between time interval from LEEP to pregnancy and PTB (adjusted OR=1.0, 95% CI, 0.96-1.03) or LBW (adjusted OR=0.96, 95% CI, 0.9-1.0).

Conclusions: When HPV testing was used as part of routine primary screening, we did not find a significant association between LEEP and PTB or LBW in the subsequent birth. Further research is needed to compare the impact of LEEP between those undergoing primary cytology and HPV screening.

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#6901

P18-01 | The role of the vaginal microbiome and the immune system in the process of cervical carcinogenesis

18 - Microbiome

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Background/Objectives: Cervical cancer is the fourth most common cause of death in women among malignancies worldwide. It is preceded by the cervical intraepithelial changes, the development of which is closely related to human papillomavirus infection. The goal of this research is to clarify the association between the local imune system, vaginal microbiome and the development of precancerous changes of the cervix.

Methods: In a prospective study, 38 patients with confirmed squamous intraepithelial lesions, and 10 samples from healthy women were examined. In 29 cases, a biopsy was performed under colposcopic control. After processing pathogenic strains of bacteria, and also species from the Lactobacillus genus were detected by the real-time PCR method. To examine the gene profile, the extracted RNA was transcribed into complementary DNA, and after real-time PCR, the presence of the investigated genes was examined. In the statistical processing of the results, the presence of bacterial strains and their association with HPV status, cytological and biopsy results were evaluated with the determination of statistical significance. Changes in the expression of selected genes of the local immune profile were also determined, including the definition of their upregulation or downregulation.

Results: We demonstrated the presence of 28 of the 42 examined pathogenic species of bacteria. The association of Lactobacillus iners with high-grade lesions was statistically significant (p 0.05). The Ureaplasma species (p 0.076) and Parvimonas micra (p 0.077), were also associated with high-grade lesions. Furthermore, Parvimonas micra was associated with HPV 16, 18 positivity (p 0.072). Our work also shows the relationship of Lactobacillus gasseri with HPV 16 and HPV 18 positivity (p 0.045). Changes in the expression of CXCL-10, GZMB, IFNG, IL-6, IL-12A, RIPK3, TGF-ß1 and TMEM173 genes were similarly observed in the examined samples.

Conclusions: Our research indicates a relationship between the presence of selected bacteria in the vaginal microbiome and the development of intraepithelial neoplasia, as well as a change in the expression of selected genes in the immune response to human papillomavirus infection and developing cervical lesions.

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#6913

P18-02 | Cervicovaginal bacterial infections and HPV-DNA positivity in females of reproductive age harbouring cervical dysplasias

18 - Microbiome

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Background/Objectives: To investigate HPV-DNA positivity and possible co-infection with other sexually transmitted bacterial pathogens (Chlamydia-Mycoplasma-Ureaplasma) in the lower genital tract in women with cervical precancer (CIN) referred for colposcopic evaluation and their correlation with histological grade.

Methods: All women were evaluated cytologically (liquid-based cytology sample-LBC) and additionally with HPV DNA genotyping as well as common STIs (Ct-Mg-Mh-Up-Uu) using NAATs. All women underwent colposcopically-guided cervical biopsies; full demographic and sexual history data were also recorded.

Results: A total of 158 women have been so far included in the study with the average age of 33.2 years; only 37% had received the anti-HPV vaccine. Seventy-nine percent harboured HR-HPV while 7% of the population tested positive for LR-HPV. All individuals with cytological HSIL tested positive for HR-HPV. Of note was that 62,7% of the study population tested positive for STIs. Ninety-six individuals (60,8%%) tested positive for Ureaplasma spp (Up & Uu), while other pathogens (Chlamydia trachomatis, Mycoplasma hominis & HSV-1) were present in only 13 women. From the total population, in 105 women (66.5%) histology documented a low-grade lesion (CIN1) and in 40 individuals (25.3%) a high-grade lesion (CIN2+).

Conclusions: Sexually transmitted infections are an important public health problem, although these infections can be prevented or effectively treated with anti-HPV vaccination and antibiotics. Co-testing for STIs as part of cervical cancer screening is a technically feasible strategy for young individuals, with the potential to reduce the risk of long-term complications such as infertility and adverse obstetric outcomes. The results and cost-effectiveness of this pilot study merit further investigation.

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P03-06 | 10-year trend of vaccine- and non-vaccine-type high risk HPV among women in Western Austria

03 - Epidemiology and natural history

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Background/Objectives: In autumn of 2014, Austria introduced a government sponsored/ free-of-charge HPV vaccination campaign for youth of 9-12 years of age in a bid to reduce the incidence of cervix carcinoma in the Austrian population in accordance with WHO recommendations. According to modelling estimates of the Austrian Ministry of Health, vaccination rate was less than 5% before the implementation of the campaign and has since risen to approximately 53% in 14-year olds in 2022. Since HPV vaccines are considered to be highly effective in preventing infection with HPV vaccine types, we aimed to investigate real world data on its effect on HPV infection and genotype distribution dynamic in a retrospective analysis over a period of 10 years.

Methods: Lab-data from all genital HPV samples taken of women between the ages of 18-25 and received for testing between 2013 and 2023 were analyzed in the study. All testing throughout the study period was done using the same testing kit (AmpliQuality HPV-TYPE EXPRESS, AB Analitica®, Padova, Italy), an assay able to identify 40 HR- and LR- HPV genotypes. Descriptive statistics, chi square tests and linear regression analysis were used to characterize the trend of positivity across time.

Results: The analysis included 1398 samples with a median age of participants of 22 years. Using simple linear regression model, a statistically significant downward trend could be shown for HPV vaccine types (Gardasil 9) when grouped together (regression coefficient (ß) = -2.361, p=0.001 for trend). Each vaccine type showed a downward trend when analyzed independently with clear statistical significance for the trend seen for HPV 6 (ß= -0.706, p= 0.020), HPV 16 (ß=-1.349, p=0.004), HPV 18 (ß=-0.598, p=0.003), HPV 31 (ß= -0.653, p=0.016), and HPV 33 (ß= -0.686, p=0.002). No statistically significant trends could be found for non-vaccine high-risk HPV types.

Conclusions: Lab data indicate that vaccine type HPVs decrease successively in the post-vaccine era in western Austria, substantiating the effectiveness of the ongoing immunization efforts in the region. Since the dynamic in non-vaccine types was observed to be modest and statistically insignificant, the further inclusion of these HPV genotypes in the vaccine cannot be argued based on our research at this time.

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P17-04 | Clinical validation of methylation triage assays: the VALMETH concept

17 - Methylation

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Background/Objectives: In the fast-changing HPV screening landscape, increasing emphasis is placed on molecular triage markers, allowing for immediate reflex testing on a wide variety of primary samples (e.g. selfcollected samples, urine, anal, etc.). In order to discriminate persistent HPV infections displaying oncogenic aspects from transient infections, characteristic host-methylation signatures have been identified and proposed as useful triage markers. Every methylation assay typically exploits a discrete set of markers, not only rendering it challenging to assess head-to-head comparison, but also confronting diagnostic companies with clinical validation requirements. To this end, guidelines for clinical validation of methylation assays should be developed, in line with previous HPV-DNA PCR assay validation efforts, i.e. the VALMETH framework. Ideally, a prospective study should follow up women at risk of developing cancer over a long time period while developing disease, which is not only ethically arguable but due to extremely low rate of disease prevalence, even impossible in reallife practice. To overcome these limitations, bio-banked cervical DNA samples were investigated to test validity, positive predictive value, and accuracy aspects of selected methylation assays.

Methods: DNA extracts referent to clinician-collected cervical samples from women attending national program since 2007, retrieved from the AML - Sonic Healthcare Benelux biorepository (Antwerp, Belgium) underwent DNA quality control. Serial HPV positive samples from the same patient were selected based on pre-defined conditions: (1) cytology negative baseline collection point, (2) multiple sampling longitudinal HPV positive collection points spanning full natural history of disease progression, 3) available confirmed histological endpoint (CIN 1/2/3 or cancer), and (4) an age-matched healthy control.

Results: The in-silico querying of the biorepository rendered a high number of longitudinal series of cervical DNA extracts fulfilling selection criteria, covering a full range of histological endpoints including CIN1, CIN2, CIN3 and invasive cancer. A pilot study was performed to assess the sample integrity of stored DNA and demonstrated successfully performed bisulphite conversion with both Qiagen EpiTect Fast Bisulfite Kit as well as Zymo EZ DNA Methylation-Lightning Kit. Five different methylation assays i.e.: Methica CC kit (CC Diagnostics), GynTect assay (Oncgnostics), Precursor-M+ test (Self-screen), CONFIDENCE Marker (Neumann), and DNA Methylation Detection Kit for Human PAX1, SOX1 and HAS1 Gene (YanengBio), are used to confirm compatibility with bio-banked DNA extracts as proof-ofprinciple. The validity rate, sensitivity, and specificity of all assays was topic of investigation in a headto-head setting.

Conclusions: Methylation assays display highly promising triage capacity, but clinical validation of these assays is often logistically challenging rendering the need for the VALMETH-framework. Here, a proof-ofconcept is provided towards the use of long-term bio-banked DNA extracts to support assay validation needs. A VALMETH expert working group should be established to define and formulate these criteria (e.g. clinical sensitivity, clinical specificity, reproducibility) and eventually likewise evaluate the prognostic value of these assays in the natural history of disease (i.e. early versus late methylation markers).