EUROGIN 2021 ABSTRACTS

POSTERS

#2211

2 - Epidemiology and natural history

Incidence of HPV and HPV related dysplasia in elderly women in Sweden

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Background/Objectives: About one-third of the cervical cancer cases in Sweden occur in women over the age of 60. There are controversies concerning when to stop screening and the significance of a negative exit test. The primary aim of this study was to analyze the incidence of HPV, and HPV related dysplasia, in older women who had an HPV negative test at the age of 60 years or older.

Methods: From October 2004 to June 2019, 1784 women aged 60-90 years were sampled for an HPV test when attending an outpatient gynecology clinic. Of these women, 827 HPV-negative women had two or more HPV tests at intervals of three months to eleven years (mean 3.2 years). The women with positive results had a repeat HPV test and cytology after 2.5 months on average. Those with a positive repeat HPV test were examined by colposcopy and biopsy.

Results: The overall prevalence of HPV was 5.4%, (95%CI 4.4-6.6, 96/1784). The incidence of HPV in the 827 women, who were HPV negative in their first test, was 2.4 % (95%CI 1.5-3.8, n=20). At the repeat test 1.2% remained positive (95%CI 0.6-2.3, n=10). HPV-related dysplasia diagnosed by histology was found in 1.2 % (95%CI 0.6-2.3, n=10) of the 827 women. CIN2+ was found in 0.5% (95%CI 0.2-1.3, n=4). In the repeat HPV test 52.6% 10/19) were HPV positive. The time between an HPV negative test and an HPV positive test and CIN2+ was on average 45.5 months (range 10-85 months). The positive predictive value (PPV) for CIN2+ was 20.0% in the first positive HPV test and 40.0% in the repeat HPV test. The women with CIN 2+ had normal cytology. No cancer or glandular dysplasia was detected. HPV 16 was the most common HPV type. One woman had multiple infection.

Conclusions: In this study older HPV-negative women were at risk of becoming HPV positive. Among the women who were HPV positive in a repeat test, there was a high risk of dysplasia. We were unable to determine whether these newly detected infections resulted from a new sexually acquired HPV infection or a reactivated latent infection acquired many years earlier. Additional research is needed to determine whether elderly women with an HPV negative exit test result are sufficiently protected against cervical cancer.

#1401

6 - HPV therapeutic vaccines

PRELIMINARY RESULTS OF A PHASE 2 STUDY OF VGX-3100 FOR THE TREATMENT OF HPV16 AND/OR HPV18 (HPV16/18) RELATED ANAL HSIL

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Background/Objectives: The management of anal HSIL remains challenging. Treatment often involves lesion ablation, but this has a high recurrence rate of up to 50% [1]. This presentation will be the first report of the efficacy of VGX-3100, a DNA-based HPV16/18-specific immunotherapy, in a population with anal HSIL. We will be reporting initial data from this Phase 2 proof-of-concept study.

Methods: VGX-3100 is composed of DNA plasmids encoding the E6 and E7 proteins of HPV types 16 and 18, and was administered IM followed by electroporation. 22 participants with HPV16/18 positive anal HSIL, but otherwise healthy, received at least 3 doses of VGX-3100. 6 months after VGX-3100 treatment, subjects underwent biopsy of the qualifying lesions and the histology-based endpoints were determined by at least two independent pathologists. Clinical efficacy was assessed based upon resolution of HSIL, undetectable HPV16/18, or a reduction in anal lesion number without increase in lesion size.

Results: At this time, all 22 currently enrolled participants have received 3 doses and completed follow-up through 36 weeks. The proportion achieving both undetectable virus and regression of HSIL at the primary endpoint evaluation is shown in Table 1. Of these 22 subjects, 77% (17/22) showed a decrease in the number of HPV16/18 HSIL lesions, 50% (11/22) showed no HPV16/18 associated HSIL, and 48% (10/21) had a decrease in the total number of HSIL lesions. Overall safety data can be seen in Table 2. There has been 1 discontinuation due to an unrelated AE, and there have been no related SAEs. No cases of carcinoma have been observed on the trial.

Conclusions: Data from this ongoing study indicate that VGX-3100 has a therapeutic effect upon HPV16/18-associated anal HSIL. Given the high medical need and limitations of surgery, an immunotherapeutic approach would represent a significant advancement in the management of anal HSIL. Complete trial data will be based upon all enrolled subjects with follow up through 18 months after the third treatment dose (i.e. week 88).

References: Long KC, et al. Clin Colon Rectal Surg. 2016;29(1):57â€'64.

Abstract #1401 Supplementary Material

#1396

7 - Immunotherapy - Immuno-oncology - New treatments

EFFICACY OF A CORIOLUS VERSICOLOR-BASED MULTI-INGREDIENT VAGINAL GEL IN HPV+ WOMEN OLDER THAN 40 YEARS: SUB-ANALYSIS OF PALOMA CLINICAL TRIAL

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Background/Objectives: HPV clearance and resolution of cervical HPV-dependent lesions become difficult in peri and postmenopausal women. The objective of this sub-analysis was to evaluate the effect of the Papilocare®, a multi-ingredient Coriolus versicolor-based vaginal gel, on the normalization of cervical HPV-dependent atypia (ASCUS and LSIL) and associated colposcopic alterations in women older than 40 years.

Methods: Paloma clinical trial (ClinicalTrials.gov NCT04002154) was a multicenter, randomized, open-label, parallel-group, usual practice-controlled clinical trial. Unvaccinated HPV positive women aged between 30-65 with cytology of ASCUS or LSIL and concordant colposcopic image were randomized into 3 groups: A) Papilocare® 1 cannula/day for 1 month + 1 cannula/alternate days for 5 months; B) Papilocare® 1 cannula/day for 3 months + 1 cannula/alternate days for 3 months; C) Control group: no treatment (usual clinical practice). Primary endpoint: % of patients with normal cytology and concordant colposcopy after 6 months of treatment in the total population, high-risk HPV (16,18,31,33,35,39,45,51,52,56,58,59,68) and very high-risk HPV (patients infected by any combination of 16, 18 and 31) subpopulations. Pap smear evaluations were blind and centrally conducted by an independent researcher at the IECM laboratory (Lugo, Spain). Papilocare® arms (A+B) were combined as treatment group.

Results: A total of 41 out of 84 evaluated patients included in Paloma trial were older than 40y [mean (SD) age: 47.71 (5.56)], of which 30 and 13 were high-risk HPV and 16-18-31 HPV patients, respectively. At 6 months, normal cytology and concordant colposcopic image was observed in 92%, 90% and 75% of patients treated with Papilocare® vs 50%, 33% and 40% of patients in control group, in the total population, and high-risk and 16-18-31 subpopulations (p=0.0066; p=0.0031; p=0.2929, Fisher test) respectively.

Conclusions: Papilocare® showed a robust efficacy in normalizing cervical HPV lesions in women older than 40 years old, with a statistically significant difference vs control group in the total and high-risk populations.

#2290

8 - HPV testing

MSWABTM MEDIUM, A NON-ALCOHOL-BASED MEDIA FOR ELUTING DRY SELF-COLLECTED VAGINAL SWABS FOR HPV DETECTION WITH COMMERCIAL ASSAYS.

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Background/Objectives: HPV screening have been performed from residual cervical samples in 20 or 10mL alcohol-based-media. Vaginal self-collection has been used to improve women's participation to HPV screening. Dry self-collected vaginal swabs (SCVS) are eluted in 20mL, 10mL or 5mL alcohol-based-media, which are costly and problematic to transport. A medium to elute self-collected swab that support HPV stability at different temperatures is necessary. Copan MSwabTM is a non-alcohol based medium, PCR master-mix compatible, preserves intact cells, and has been tested for DNA and RNA virus's stability at different times and storage temperatures. The objectives were to: 1) compare the performance of HPV testing on professional collected cervical swabs (PCCS) to two dry SCVS eluted in 5mL of PreservCytTM (PC) and in 5mL of MSwabTM respectively; 2) Validate HPV stability from SCVS eluted in MSwabTM stored at 22°C and at 37°C for 1, 2, 3, 4 weeks (wks) and 1 year at -20°C.

Methods: PCCS and two SCVS were obtained from 10 women referred to colposcopy. Two SCVS were obtained first, using FLOQSwabs® (code 552.80), followed by PCCS collection, using L-Shape FLOQSwabs® (Copan). PCCS were placed in 20mL PC (Hologic) while SCVS were delivered dry to the Laboratory. One SCVS was eluted in 5mL of PC and the other in 5mL of MSwabTM. FLOQSwabs® were placed in each media, vortexed at high-speed for 30', left the swab inside for 60' and vortex again for 30'. An aliquot was used for zero-time, and other separate aliquots of MSwab sample were stored at -20°C for 1 year and at 22°C at 37°C and tested weekly for 4wks and after 1 year at -20°C. At each time point nucleic acids were extracted on the Nimbus and analyzed for HPV with the AnyplexIITM HPV28 assay (Seegene).

Results: HPV data obtained after 4wks from dry SCVS swabs, eluted in 5mL of PC or 5 ml of MSwabTM, revealed a good concordance for high-risk HPV (hrHPV) and low-risk HPV (lrHPV) detection compared to PCCS. In only one case, SCVS eluted in both type of media resulted HPV positive as compared to a negative result of PCCS. hrHPV genotypes detected 16, 18, 31, 33, 51, 59, and 68. Excellent stability in sample preservation and concordant hrHPV detection was observed in SCVS eluted in 5mL MSwabTM at both 22°C and 37°C for 4wks and after 1 year at -20°C.

Conclusions: Results obtained in this study demonstrated a high degree of concordance in hrHPV detection between PCCS and SCVS eluted in PreservCytTM and MSwabTM. Excellent stability was observed at both 22°C and 37°C after 4wks and up 1 year at -20°C. MSwabTM can be an optimal alternative to alcohol-based media, for the elution FLOQSwabs® SCVS for the detection of HPV.

#2369

8 - HPV testing

Cross-Platform High-Risk (hr) Low Occurrence HPV NAAT Positive Samples for Use in Nucleic Acid Detection Testing as Prospective External Quality Assessment Samples and User Defined Quality Controls

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Background/Objectives: HPV genotyping nucleic acid amplification testing (NAAT) is becoming a cornerstone triage method for stratifying the risk related to cancer development in the infected patients. Moreover, monitoring of the general population for the high-risk HPV (hrHPV)/low occurrence types is becoming routine to determine vaccination efficiency and to evaluate oncogenicity of HPV types. The monitoring of low occurrence hrHPV types is done using full genotyping NAAT diagnostic systems. However, there is a lack of adequate QC material for full genotype testing, which affects the transition from traditional HPV testing to full genotype HPV testing. Currently, the main categories of positive samples used by clinical laboratories are either plasmid-based or cell line-based preparations. Both types have the major disadvantage of not complying with FDA recommendations for QC material to monitor the entire workflow for NAAT: nucleic acid extraction, amplification, and detection. The composition of current controls (especially plasmids) limits their use on certain NAAT platforms. In addition, they only share some characteristics of a patient sample specimen. Most of these controls do not contain enough exogenous matrix material to make the detection of HPV challenging, and do not cover the full scope of patient sample testing options such as; DNA, RNA, and protein (antigen) detection methods. The main objective of our study was to illustrate a cross-platform compatibility of novel high risk HPV (hrHPV)/low occurrence materials and their potential use in a clinical quality management system as QC samples. The positive samples for hrHPV types 31, 33, 39, and HPV 67 (hr Negative Sample) contain all the components normally found in an infected patient specimen, such as: integrated and episomal viral DNA, RNA, and proteins, as well as host epithelial cells. These features make these materials fully compatible with multiple NAAT diagnostic systems.

Methods: The hrHPV panel performance was evaluated in the Original Equipment Manufacturer (OEM) labs, External Quality Assessment program by Labquality Oy and internally in Microbix by using either a full genotyping tests (EUROIMMUN AG, BD Lifesciences, Greiner Bio-One) (Table 2.), or by a genotyping tests that report low occurrence hrHPV by pooling results (Roche Molecular, Cepheid) (Table 1.).

Results: Based on the studies, HPV Positive Samples for hrHPV types 31, 33, 39, and HPV 67 hr Negative Sample (hrHPV panel) contain all the diagnostic targets normally found in an infected patient specimen (integrated and episomal presence of viral DNA as well as host epithelial cells).

Conclusions: The HPV Positive Samples formulated in a widely accepted sample transport medium, showed excellent compatibility with several hrHPV genotyping platforms. Overall, the performance of the hrHPV/ low occurrence panel in multiple NAAT methods targeting either sequences in the E6/E7, L1 and E1 regions demonstrates the successful development of cross-platform compatible samples for low occurrence hrHPV detection.

#1829

8 - HPV testing

CLINICAL SIGNIFICANCE OF HC2 TEST BORDERLINE RESULTS IN SLOVENIAN CERVICAL CANCER SCREENING PROGRAM ZORA

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Background/Objectives: The Slovenian national cervical cancer screening program ZORA uses Hybrid Capture 2 High-Risk HPV DNA assay (HC2, Qiagen, Hilden, Germany) as a triage method for women with borderline and low-grade cytology abnormalities and as a test of cure after CIN2+ (cervical intraepithelial neoplasia grade 2 or worse) treatment. To improve reported limited reproducibility of HC2 results near the cut-off, the manufacturer recommends that specimens collected in Standard Transport Medium (Qiagen) whose results fall near but bellow 1.0 relative unit/cut-off (RLU/CO) should be repeated or retested with an alternate testing method. Although several authors have confirmed the poor HC2 reproducibility of borderline samples, no study has determined their clinical significance. The aim of this study was to determine the cumulative incidenceof CIN2+ for women with borderline HC2 results.

Methods: Total of 47,225 women (aged from 20 to 65 years, mean 39.4) were referred to their first triage HC2 test between 2011 and 2017. We collected their HPV test results and subsequent histology diagnoses of CIN2+ from the national cervical cancer screening registry. Median follow-up time was at least 4.8 years for all HPV test indications. Only the first recorded CIN2+ was included into analysis. Using the Kaplan-Meier estimator we calculated 5-year CIN2+ cumulative incidence for each referral indication according to the HPV test result. We evaluated borderline samples with RLU/CO values within a grey zone interval which ranged from 0.4 to 4.0 RLU/CO. Based on grey zone interval we divided women into HC2 clearly negative, borderline negative, borderline positive and clearly positive (Figure 1).

Results: The 5-year cumulative CIN2+ incidence for HC2 clearly negative, borderline negative, borderline positive and clearly positive for all referral indications are presented in Table 1. Table 1: The 5-year cumulative CIN2+ incidence for clearly negative, borderline negative, borderline positive and clearly positive for all referral indications. ASCUS: atypical squamous cells of undetermined significance, LSIL≥35: low-grade squamous intraepithelial lesion in women older than 35 years, AGC: atypical glandular cells, CIN1: cervical intraepithelial neoplasia grade 1, CI: confidence interval. HC2 RLU/CO interval 5-year cumulative CIN2+ incidence (95% CI) by HPV triage test referral indication Clearly negative ASCUS: 1.0 (0.8-1.2%) LSIL≥35: 2.9% (2.0-3.7%) AGC: 1.9% (1.4-2.3%) CIN1: 1.5% (0.9-2.1%) test of cure: 0.6% (0.5-0.8%) Borderline negative ASCUS: 7.0 (5.1-8.8%) LSIL≥35: 6.6% (3.3-9.9%) AGC: 2.9% (1.6-4.2%) CIN1: 2.7% (0.3-5.0%) test of cure: 1.8% (0.7-2.8%) Borderline positive ASCUS: 17.3 (14.7-19.8%) LSIL≥35: 18.7% (13.1-23.9%) AGC: 15.0% (10.8-19.1%) CIN1: 22.7% (15.5-29.3%) test of cure: 7.0% (4.6-9.3%) Clearly positive ASCUS: 35.9% (34.7-37.1%) LSIL≥35: 41.2% (38.8-43.4%) AGC: 36.4% (33.9-38.7%) CIN1: 38.4% (34.7-41.8%) test of cure: 23.8% (21.3-26.3%)

Conclusions: Women with borderline negative HC2 test result have an intermediate 5-year CIN2+ risk between 2-7%. The risk for women with borderline positive result is 7% for test of cure indication and 15% or more for other indications, exceeding 20% only for CIN1 referral indication.

#1823

8 - HPV testing

FIVE-YEAR CUMULATIVE INCIDENCE OF CIN2+ FOR WOMEN WITH HPV TRIAGE TEST IN SLOVENIAN ORGANIZED CERVICAL CANCER SCREENING PROGRAM ZORA

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Background/Objectives: The Slovenian organized cervical cancer screening program ZORA, which was introduced in 2003, has led to steady decline in the incidence of cervical cancer. The lowest number of cervical cancers was reached in 2017 with an age-standardised incidence (world) rate of 4.9 per 100.000. Since the beginning of the program conventional cytology has been a primary screening tool and in 2011 HPV triage with Hybrid Capture 2 (HC2, Qiagen, Hilden, Germany) was implemented. According to the national guidelines the indications for HPV triage are: ASCUS, LSIL in women older than 35 years (LSIL≥35), AGC, CIN1 and test of cure (follow-up after CIN2+ treatment). The aim was to determine the 5-year cumulative incidence of CIN2+ for HPV positive and HPV negative women for each referral indication.

Methods: In total 47,225 women (aged from 20 to 65 years, mean 39.4) were referred to their first triage HC2 test between 2011 and 2017. We collected their HPV test results and subsequent histology diagnoses of CIN2+ from the national cervical cancer screening registry ZORA. Median follow-up time was at least 4.8 years for all HPV test indications. Only the first recorded CIN2+ was included into analysis. Using the Kaplan-Meier estimator we calculated 5-year cumulative incidence of CIN2+ for each referral indication and also according to the HC2 test result.

Results: The 5-year cumulative incidence of CIN2+ for women with HC2 triage test in Slovenian organized cervical cancer screening program ZORA are presented in Table 1.

Conclusions: 5-year cumulative incidence of CIN2+ for HPV positive women was between 38.8% and 18.9% for all referral indications. However, HPV negative women with ASCUS, CIN1 and CIN2+ after treatment referral indication had a risk below 2.0% and can safely return to regular screening program.

#2327

9 - HPV screening

COLPOSCOPY, CERVICAL AND CONE BIOPSY: THE CASUISTIC AFTER IMPLEMENTATION OF A POPULATION SCREENING PROGRAM

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Background/Objectives: Cervical cancer screening has allowed a reduction in mortality and morbidity rates. Programs based on high-risk Human Papillomavirus (HR-HPV) testing increase sensibility and contribute to a growth in referrals to colposcopy units, being crucial to promote high quality colposcopy technique and to evaluate the correlation of clinical and pathology aspects. Our screening is based on testing high-risk Human Papillomavirus (HPV) with genotyping for 16 and 18/45 and on performing reflex cytology test in case of HPV others. The primary aim of this study was to correlate histology of the cone biopsy and colposcopy impression, cervical punch biopsy, HPV test and cytology results. The secondary aim was to review all the cone biopsy with low grade squamous intraepithelial lesion (LSIL) or negative for intra-epithelial lesion or malignancy (NILM).

Methods: A retrospective cohort study of all the women submitted to cone biopsy referred to our center from the national organized screening program (May18-Nov20), was reviewed.

Results: In 1166 women, 352 cone biopsies were performed (women aged 28-66 years old; mean 41,3 years old). Most cases were HPV 16 positive (n = 159; 45.2%). If positive for HR-HPV others (n = 141; 40.1%), the most common cytological alterations were ASC-H (n = 36/141; 25.5%) and LSIL (n =37/141; 26.2%). High grade was the most frequent colposcopy impression (n = 210/352; 60.5%). Previous cervical punch biopsies revealed: 311 High-grade Squamous Intraepithelial Lesion (HSIL) cases, 11 LSIL, 6 adenocarcinomas in situ (AIS), 5 NILM, and 1 Squamous Cellular Carcinoma (SCC). HSIL was the main diagnosis of cone biopsy (n = 262; 74.4%). Remaining cases were: 70 ≤ LSIL (67 LSIL; 3 NLIM), 7 AIS, 2 microinvasive adenocarcinomas, 2 invasive adenocarcinomas and 9 SCC. In 20.1% of HSIL and 28.4% of LSIL occurred in women aged < 35 years old, with no significative differences in the result of cone biopsy with age inferior or superior to 35 or 40 years old (p=0.395; p=0.791). When cone biopsy ≥ HSIL, HPV 16 and/or 18/45 was found in 61.3%(n=173/382) and HR-HPV others in 38.7% (n=109/282) (p=0.280). If ≤ LSIL in the cone biopsy (n = 70/352; 19.9%), 59 (84.3%) had HSIL in cervical punch biopsy. The remainder corresponded to 1 AIS, 4 LSIL, 1 non-graded SIL, 2 NLIM, and in 3 cases punch biopsy had not been performed. In those HSIL, more than a half (n=31/59) had low grade, metaplasia, or a normal colposcopy impression (p=0.211). Regarding cases with cytology, 27.7% of ≤ LSIL had a low-grade cone biopsy, vs. 17.7% if cytology > LSIL (p=0.152). In women with HR-HPV others plus a cytology exam with ≤ LSIL and a colposcopy impression ≤ low grade (n = 41) we have found in cervical punch biopsy 40 HSIL and 1 non-graded SIL and in cone biopsy 29 HSIL, 11 LSIL and 1 SCC.

Conclusions: We observed that in 20% of cone biopsies the result was ≤ LSIL. Almost 90% of these cases had HSIL in a previous punch biopsy and may correspond to small cervical lesions or to an overvaluation of the cervical punch biopsy. Further studies are important to understand clinical and pathology diagnostic criteria that can lead to a more conservative management, avoiding cone biopsy.

#2408

9 - HPV screening

OPPORTUNISTIC DIAGNOSIS OF CERVICAL HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESION IN A WOMAN WITH PERIANAL WARTS

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Background/Objectives: Most international guidelines recommend cervical cancer screening, for every women aged between 25 and 65 years old, with a primary HPV test, with a reflex cervical cytology, if HPV test is positive. HPV testing, as the primary method of screening for cervical cancer, allows greater protection for invasive carcinoma, 60-70% higher than cervical cytology isolated. Despite this, the coverage of screening plans (based on the HPV test) in several countries, namely in Portugal, is not 100%, which can delay the diagnosis of low and high-grade cervical lesions (LSIL and HSIL) and cervical cancer.

Methods: Case report using information contained in clinical informatic records.

Results: We present a case of 40-year-old woman, referred to a gynaecology consultation after a diagnose of perianal warts. She had an updated and negative cervical cancer screening, performed outside the national health care system, based only on cervical cytology. Due to its much lower sensitivity and the fact that low-risk HPV infection coexists, responsible for perianal warts, a co-test was performed, and the result was LSIL and high-risk HPV positive. Concomitantly a colposcopy was performed, which revealed findings suggestive of a high-grade lesion at the level of the anterior lip of the cervix, which was biopsied. The result was inconsistent with the result of co-test, revealing HSIL, treated with excision of the transformation zone. Perianal warts presented a good response with trichloroacteic acid treatment.

Conclusions: Currently, it is known that the HPV test, as a primary screening method, is superior to cervical cytology. With isolated cervical cytology, a large number of cervical lesions will escape, some of which indicated for treatment. This case brings us back to the value of the HPV test as a primary test screening, due to its potential impact in reducing the incidence of cervical cancer.

References: - Practice Bulletin No. 168: Cervical Cancer Screening and Prevention. Obstet Gynecol. 2016 Oct;128(4):e111-e130
- Louise T Thomsen, et al. Clinical Performance of Human Papillomavirus (HPV) Testing versus Cytology for Cervical Cancer Screening: Results of a Large Danish Implementation Study. Clinical Epidemiology 2020:12 203-213

#1853

9 - HPV screening

PREVALENCES OF STI AND HPV IN A WOMEN'S PRISON IN THE STATE CAPITAL OF SÃO PAULO

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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 e.g. infertility, miscarriage, premature labor or severe chronic diseases. In Brazil, data from the São Paulo State Department of Health indicate that female inmates between 18 and 69 years of age are more susceptible to contracting STIs than the general female population. Here we retrospectively characterized the disease burden among female inmates in Brazil by investigating the prevalences of human papilloma virus (HPV) infections and other STIs.

Methods: Cervical smear samples from 299 women (age range: 18-64 years, mean 31.8 years) living in a women's prison in the state capital São Paulo, Brazil, were collected and submitted for cytological examination. The prevalences of thirty 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.

Results: The overall prevalence of cytological abnormalities was 5.8% (16 of 277 women, 22 invalid samples were excluded). Low-grade and high-grade squamous intraepithelial lesions were observed in five and five women, respectively. The overall prevalence of HPV was 62.2% (186 of 299 women). Among the infected women, 24 had a low-risk subtype, 92 had a high-risk subtype and 70 had both subtypes. Hundred women were infected with two or more subtypes. Among all HPV subtypes, high-risk subtypes were most prevalent: HPV-16 (38.7%, 72 of 186 women), HPV-33 and HPV-52 (16.7%, 31 of 186 women each). The overall prevalence of other STIs was 72.8% (217 of 298 women). Up to four different pathogens were found among infected women. The most frequent pathogens were Ureaplasma parvum (45.3%), Mycoplasma hominis (36.3%) and Trichomonas vaginalis (24.8%).

Conclusions: Compared to the prevalence of HPV among Brazilian women being in the range of 7% to 45%, the prevalence of 62.2% detected in the prison cohort is relatively elevated.Taken together with the occurrence of STIs and cytological evidence, we conclude that care for specific health issues and needs of female prisoners requires improvement, for example by establishing a timely detection of STIs and limiting disease transmission.

#2228

13 - Screening for women difficult to reach

PREFERENCE AND ACCEPTANCE OF HPV SELF-SAMPLING: GAINING INSIGHTS ON URINE AS A SAMPLE TYPE

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Background/Objectives: Although cervical cancer screening has successfully reduced incidence and mortality, a high proportion of women do not attend regular cervical cancer screening programs. Common reasons for non-attendance are physical discomfort of a cervical examination, lack of time and transportation, as well as inconvenient clinic hours. Self-sampling, including first-void urine sampling which accurately detects HPV, might overcome some of these barriers. The aim of this study was to perform a literature review on acceptance and preference of urine sampling as a potential strategy to increase screening uptake.

Methods: In November 2020, Pubmed was systematically searched for studies reporting on ("HPV" AND "Cervical cancer" AND "screening" AND "(preference OR acceptance OR non-attendance OR non-attenders)" AND "urine") over the last 10 years (2010-2020). This provided 15 results. Four studies were selected where one of the objectives was to compare sample preferences. Two studies were added based on participation in studies where Colli-Pee was used. Colli-Pee is a urine collector for user-friendly, standardized and volumetric collection of the initial stream (first-void) of urine (Novosanis, Belgium). One study was added based on an internal literature database.

Results: Studies were performed in Canada, Spain, Belgium, the UK, South Korea, Federated States of Micronesia and the US. The number of inclusions ranged from 91 to 732 women. All women were referred to colposcopy or attended a visit to obtain a Pap smear. Acceptance was evaluated on a 5- or 4-point ordinal scale, where it ranged from 86% to 98% for urine samples, and from 76% to 87% for clinician-taken samples. Acceptance was also evaluated as "feeling comfortable' or "positive feelings about a sample type' which resulted in higher acceptance of urine compared to clinician-taken samples as well. Almost all studies reported preference of urine over vaginal self-samples and clinician-taken samples. Only one study in Federated States of Micronesia reported a higher percentage of women who preferred a clinician-taken sample (44%) over a urine self-sample (38%). The authors reported that these women preferred to have skilled and knowledgeable screeners. However, this research also indicated that future screenings need to be more accessible which offers opportunities for home-based self-collection of samples for HPV detection.

Conclusions: Based on this literature review, urine is identified as the most accepted and preferred sample type for HPV-based cervical cancer screening. It should be noted that this evaluation is based on self-reported data from women who are visiting a clinician for screening purposes. Therefore, additional data should be collected and evaluated on actual preference reflected by participation rates in individual cohorts of women offered different sampling methods in the primary screening population. Moreover, the cost-effectiveness of these strategies should also be evaluated and compared.

#2195

10 - Self-sampling

ANALYTICAL VALIDATION OF THE BD ONCLARITY HPV ASSAY FOR SELF-COLLECTED SPECIMENS

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Background/Objectives: The World Health Organization has issued a global strategic objective to screen 70% of women under 35 for cervical cancer using a high-performance test by the year 2030 [1]. Recently, BD received CE mark approval for Self-Collection using the BD Onclarity HPV Assay on the BD Viper LT system. The Onclarity Self-Collection Assay can be used as a first-line primary cervical cancer screening test to qualitatively detect multiple high-risk genotypes and help reach underserved women. The assay detects 14 high-risk genotypes and provides genotype information on HPV 16, 18, 31, 45, 51, 52 and three groups of pooled types: HPV (33/58), (56/59/66), and (35/39/68). It is a Real-time PCR assay targeting HPV type specific E6/E7 DNA sequences which has been fully automated on the BD Viper LT System and is currently being migrated to the high-throughput BD COR System.

Methods: N/A

Results: The studies completed for CE Mark on the BD Viper LT instrument included analytical sensitivity, precision, cross-contamination rate, and the impact of interfering substances. In addition, a head-to-head comparison was performed between three devices, the Copan FLOQSwab, Rovers Evalyn brush, and Rovers Viba brush, to determine any difference in specimen collection and assay performance. All devices showed similar analytical sensitivity and thus had no impact on the collection of vaginal specimen. A study to determine equivalency between the BD Viper LT and the BD COR systems using prospectively collected samples from a general screening population was also completed. The study showed excellent agreement between the two platforms. Overall performance of the BD Onclarity Assay with Self-Collection specimens irrespective of collection device met or exceeded current analytical standards.

Conclusions: Self-Collection using the BD Onclarity HPV Assay is an important addition to current PCR based cervical cancer screening tools and can help address the World Health Organization stated goal of eliminating cervical cancer as a public health issue.

References: 1. "World Health Assembly Adopts Global Strategy to Accelerate Cervical Cancer Elimination." World Health Organization, World Health Organization, 19 Aug. 2020, www.who.int/news/item/19-08-2020-world-health-assembly-adopts-global-strategy-to-accelerate-cervical-cancer-elimination.

#2226

10 - Self-sampling

POST-COLLECTION STABILITY OF HUMAN PAPILLOMAVIRUS DNA IN FIRST-VOID URINE

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Background/Objectives: Women have shown to accept and prefer urine self-sampling for HPV-based cervical cancer screening. Colli-Pee allows for user-friendly, standardized and volumetric collection of first-void urine. The collector tube is prefilled with UCM, a proprietary preservative. Devices can be shipped via postal mail to the laboratory which overcomes the most common reasons for non-attendance of screening visits. The aim of the study was to assess the effect of environmental conditions on the degradation of urinary analytes such as HPV DNA.

Methods: Five urine samples were collected with Colli-Pee to evaluate the stability of HPV DNA in UCM-preserved urine samples. UCM was spiked with HPV16 DNA to obtain a concentration of 100 DNA copies/µL in the final aliquot. Afterwards, urine was added in a 2:1 (urine:UCM) ratio to mimic real-life use of Colli-Pee prefilled with UCM. In addition to the reference samples analyzed at day 0, aliquots were stored for 3, 7 and 14 days at room temperature (RT) and 4°C. Samples were also exposed to three freeze-thaw cycles (F/T), with each cycle consisting of freezing at -20°C for >3 hours, followed by ca. 3 hours at 50°C. Storage at RT was used as the reference condition since UCM allows for storage at RT for 7 days. DNA extraction was performed using the NucliSENS EasyMAG, and PCR was based on TaqMan technology using the Roche LightCycler 480 Real-Time PCR System.

Results: A total of 45 aliquots (i.e. 9 for each of 5 subjects) were analyzed, of which 44 were positive for HPV16. One sample was negative for HPV16 after 14 days of storage at RT. The sample of the same subject showed an outlying result after 7 days of storage at RT. In order to analyze the results, Ct values with a negative result for HPV16 were defined as the cut-off values i.e. a cycle threshold of 40. After 3, 7 and 14 days of storage respectively, average Ct-values were 32.76±0.31, 33.53±1.92 and 34.16±3.27 at RT, and 32.75±0.36, 32.70±0.18, and 33.00±0.32 at 4°C. The average Ct-value was 32.60±0.22 after undergoing F/T cycles.

Conclusions: Spiked HPV16 DNA stability in UCM-preserved urine samples was shown in post-collection conditions i.e. F/T cycles, and storage at 4°C and RT. Samples of one subject showed outlying results after storage at room temperature after 7 and 14 days. This indicates the added value of an internal control to provide feedback on sample quality from collection to analysis. Our results show that home-based collection and postal shipment of first-void urine samples for HPV-based cervical cancer screening is feasible when UCM is used as a preservative.

#2229

10 - Self-sampling

FEEDBACK FROM A COLPOSCOPY REFERRAL POPULATION ON THE USE OF COLLI-PEE FOR HPV-BASED CERVICAL CANCER SCREENING (CASUS)

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Background/Objectives: The CASUS project (NCT04530201) aims to develop the first fully molecular cervical cancer screen and triage approach, based on first-void urine as an easily accessible and non-invasive source of biomarkers. Colli-Pee Small Volumes (Novosanis, Belgium) is used for the collection of urine, which is a user-friendly device that allows for standardized and volumetric collection of the initial urine stream (i.e. first-void). In addition, Colli-Pee allows for immediate mixing with a preservative for HPV DNA. As part of this project, a clinical validation study is in progress, where the goal is to recruit 300 women who are referred to colposcopy. This population also provides user feedback on Colli-Pee Small Volumes and participation in cervical cancer screening programs. The aim of this study is to provide insights on usability of Colli-Pee Small Volumes.

Methods: Women collected two first-void urine samples on the day before colposcopy and completed an online usability questionnaire. A paper questionnaire was completed during the colposcopy visit if the woman indicated that she did not complete the online questionnaire. The Systems Usability Scale (SUS) is a questionnaire that provides a standardized score to evaluate systems. The SUS consists of 10 questions which are adapted to provide a usability score for Colli-Pee. All questions are rated on a 5-point scale where 5 means "strongly agree', and 1 represents "strongly disagree'. The score is calculated by subtracting 1 from odd numbered questions, and the value of even numbered questions is subtracted from 5. The sum is multiplied by 2.5 to obtain the SUS score which is considered good when it is greater than 68. Women also indicated whether urine was spilled during collection, the time needed to collect the urine sample from reading of the manual, whether they had read the manual and which sample type was preferred for cervical cancer screening. A random entry was selected if a participant completed the questionnaire multiple times online.

Results: Up to December 2020, 152 women provided informed consent to participate in the clinical study of which 104 completed the questionnaire. A total of 102 valid SUS scores were calculated. Two scores could not be calculated since the SUS tool was not completed. An average SUS score of 70.96±12.91 was observed. The SUS score changed when the self-reported time needed for collection increased i.e. the SUS decreased with an average of 10.02 points if the time from reading the manual to closing the tube was longer than five minutes compared to shorter than two minutes. Women who reported to prefer urine self-sampling over clinician-taken cervical samples for screening showed a trend towards higher SUS score by an average of 5.5 points.

Conclusions: Colli-Pee Small Volumes shows good usability results which are impacted by sample preference and the time needed for sampling. This research allows to further improve usability of Colli-Pee Small Volumes for the collection of first-void urine. We suggest to increase the use of standardized scores to study sample preference and usability.

#2373

10 - Self-sampling

VALIDATION OF FLOQSWABS® FOR CERVICAL AND VAGINAL PHYSICIAN SPECIMEN COLLECTION AND PATIENT'S VAGINAL SELF-COLLECTED SPECIMENS ANALYZED WITH THE FEMOFLOR® SCREEN AND HPV QUANT QUANTITATIVE REAL-TIME PCR ASSAYS.

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Background/Objectives: The diagnostic of biocenosis disorders, sexually transmitted infections and Human papillomavirus can be simplified by vaginal self-collecting. Timely diagnosis of these infections can reduce the risk of their progression. The objective of this study was to validate the quality of vagina self-collected (VSC) samples compared to physician collected cervical (PCC) and vaginal (PVC) using the Copan FLOQSwabs® (FS) and tested by microscopy and by FEMOFLOR® SCREEN and HPV QUANT Quantitative Real-Time PCR Kit.

Methods: In this study were included 40 women of reproductive age (18-45 years old): 27 with abnormal vaginal discharge and 13 healthy women. The PCC were collected using the L-shape endocervical FS, while both PVC and VSC were collected with a vaginal self-collection FLOQSwabs®. A self-collection acceptability questionnaire was completed by each patient. The PCC was stored in a 2 ml tube of Copan eNATTM medium. PVC and VSC swabs were placed in their own plastic tube and delivered to the laboratory than transferred to a 2 ml tube of eNATTM medium. All eNATTM samples were processed for nucleic acid extraction and analyzed with the FEMOFLOR® SCREEN and HPV QUANT Quantitative Real-Time PCR assays.

Results: All patients found vaginal self-collection easy to perform and comfortable, only 50% preferred self-collection. The HPV QUANT results of the 40 PCC, PVC and VSC samples had 25 HPV concordant negative,11 HPV concordant positive, 4 discordant HPV results, 4 VSC and 1 PVC had an invalid sample intake control (SIC). The FEMOFLOR® SCREEN results of the PCC, PVC and VSC had 40/40 positive total bacterial mass; 38 positive, 1 negative and 1 PCC negative PVC/VSC positive Lactobacillus spp.; 27 positive, 10 negative, 2 PVC positive PVC/VSC negative and 1 VSC positive PCC/PVC negative Gardnerella vaginalis+Prevotella+ bivia+Porphyromonas spp.; 12 positive, 26 negative, 1 PCC positive PVC/VSC negative and 1PCC negative PVC/VSC positive Ureaplasma spp.; 5 positive, 28 negative, 2 PCC negative PVC/VSC positive, 3 VSC positive PCC/PVC negative, 2 PCC positive PVC/VSC Negative, 2 PVC positive PPC/VSC Candida spp.; 4 VSC and 1 PVC had an invalid SIC. A high Pearson's correlation coefficient of the quantitative indicators of FEMOFLOR® SCREEN in different biotopes and methods of biomaterial collection was detected. No statistical significance was found between different methods of biomaterial collection in Ureaplasma. Candida spp. and HPV.

Conclusions: VSC, PCC PVC collected with FLOQSwabs® and eluted in eNATTM medium are fully compatible with the Femoflor®Screen and HPV Quant-21 testing assays for the detection of STI and HPV.

#1681

11 - Genotyping

EXPLORING CERVICAL HR-HPV GENOTYPES AMONG ASYMPTOMATIC WOMEN IN GRENADA, WEST INDIES

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Background/Objectives: Cervical, anogenital and head-and-neck cancers are linked to persistent infections with high-risk Human Papillomavirus (HR-HPV) genotypes, of which HPV16/18 contribute the highest proportion of cervical cancer cases worldwide.1 Previously unreported, this study explores the HR-HPV genotypes in cervical samples of asymptomatic Grenadian women seeking care at the island's medical university or government-run clinics. This study also resulted in the creation of a database of HPV-positive and cytologically abnormal samples, aiding practitioners with novel record-keeping and laying the groundwork for future studies in identifying circulating neoplastic genotypes.

Methods: Data was compiled from 3 datasets representing comprehensive HPV genotyping data available for Grenada. The datasets are the result of cervical cancer screening studies of asymptomatic Grenadian women. Dependent on the similarity in study population, exclusion criteria and quality of HPV genotyping methods, all datasets were used to explore the heterogeneity of HR-HPV distribution in Grenadian women. For the Self-Screening Pap data (n=101), the average age (years) was 38, the median age was 35 and the standard deviation was 12. For the Cervical Screening and HPV Genotyping combined dataset (n=117), the average age was 35, median age was 33, and the standard deviation was 12. Study participants included professionals, non-professionals, university employees, and university students. No meaningful difference between age, occupation and location of residence was found. All HPV genotyping methods were DNA-based, two-tiered and robust. The Self-Screening Pap dataset identified HPV genotypes by fragmentation patterns as well as confirmative Sanger sequencing. The Cervical Screening and HPV Genotyping combined dataset utilized PCR to detect type-specific HPV E6/E7 DNA with confirmation testing by gene hybridization using microsphere-based genotyping and conventional Nested PCR.

Results: The most prevalent HR-genotypes in the Cervical Screening and HPV Genotyping combined dataset were HPV 52 (23%, 29/60) and HPV 29 (23%, 29/60). For the Self-Screening Pap dataset, the most prevalent HR-genotypes were HPV 61 (31%, 14/45) and HPV 53 (14%, 7/45). When all datasets are combined, the most prevalent HR-genotypes were HPV 52 (16%, 17/105), HPV 59 (16%, 17/105) and HPV 39 (13%, 14/105). 218 cervical samples were sequenced; 105 samples (48%) were HPV positive, 98 (45 %) were HPV negative and 15 (7%) had unsatisfactory or missing results. 26 distinct genotypes were identified, and 176 genotypes were expressed in 105 women. Multiple HR-HPV genotypes were identified in some samples.

Conclusions: This study explored heterogeneity in the distribution of HR-HPV cervical infections showing a prevalence of non-16/18 genotypes, HPVs 52, 59 and 39. These findings are consistent with neighboring islands, Jamaica and Tobago. Further investigation into the oncogenicity of HPV 52, 59 and 39 specifically in Grenada is indicated.

References: 1.Thomsen, L. T., Frederiksen, K., Munk, C., Junge, J., Castle, P. E., Iftner, T., & Kjaer, S. K. (2014). High-risk and low-risk human papillomavirus and the absolute risk of cervical intraepithelial neoplasia or cancer. Obstetrics and gynecology, 123(1), 57-64. https://doi.org/10.1097/AOG.0000000000000056

#2251

11 - Genotyping

Human Papillomavirus genotype attribution in Wielkopolska region (Poland) - retrospective study.

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Background/Objectives: Human papillomavirus infection is one of the most common sexually transmitted infections. Long - term exposure to the HPV leads to high grade squamous intraepithelial lesions affecting cervical cancer. Knowledge about the distribution of HPV genotypes is crucial to guide the introduction of prophylactic vaccines. We aimed the genotype distribution in patients reporting due to abnormal Pap - smear test.

Methods: We obtained material from 674 women who registered to Specialist Medical Practice in years 2008 - 2020. The probe for molecular test was collected with a combi brush and passed to the independent, standardized laboratory. HPV detection was done by use of PCR followed by DNA enzyme immunoassay and genotyping with a reverse hybridization line probe assay. Sequence analyze was performed to characterize HPV - positive samples with unknown HPV genotypes. Molecular test detected DNA of 41 HPV genotypes.

Results: We found that 53% of patients received HPV - positive test result. The proportion of HPV- positive patients decreased with increasing age. We detected that following HPV types are the most common: HPV - 16 (24.5%), HPV - 53 (13.1%), HPV - 31 (10.3%), HPV - 51 (9.7%), HPV - 56 (9.5%). In the group up to the age of 25, the most frequently detected types of HPV included: HPV 51 (24.3%), HPV 66 (18.9%), HPV 54 (18.9%)- low oncogenic type, HPV 31 (16.2%), HPV 59 (16.2%), HPV 53 (16.2%). In the group from 25 to 30 years, the most frequently detected HPV types included: HPV 16 (26.3%), HPV 56 (14.1%), HPV53 (13.1%), HPV 59 (12.1%). In the group from 30 to 35 years, the most frequently detected HPV types included: HPV 16 (26.5%), HPV 54 (12.7%)- low oncogenic type, HPV 18 (10.8%), HPV 56 (10.8%), HPV 53 (10.8%). In the group from 35 to 40 years, the most frequently detected HPV types included: HPV 16 (19.4%), HPV 53 (16.1%), HPV 45 (11.3%), HPV 66 (11.3%). In the group from 40 to 45 and group over 40 years of age, the most frequently detected HPV is HPV 16 - 32.4% and 28% respectively.

Conclusions: To our knowledge, this study is the largest assessment of HPV genotypes in Poland. Our results suggest that type - specific high - risk HPV DNA - based screening should focus on HPV types 16, 31, 51, 56.

References: 1.Genotyping of oncogenic human papilloma viruses in women with HG SIL diagnosis. Kedzia W, Pruski D, Józefiak A, Rokita W, SpaczyÅ„ski M. Ginekol Pol. 2010 . 2.Human papilloma virus genotyping in women with CIN 1. Kedzia W, Józefiak A, Pruski D, Rokita W, Marek S. Ginekol Pol. 2010. 3. Genotyping of human papillomavirus (HPV) in a healthy patient population and in patients with suspected cervical intraephitelial neoplasia.Dominik Pruski, Marcin Przybylski, Sonja Millert-KaliÅ„ska, RadosÅ‚aw MÄ...dry, MaÅ‚gorzata Åagiedo - Å»elazowska, Jan Sikora. Abstract Book: Eurogin 2019.

#2410

11 - Genotyping

HPV16 SUBLINEAGES RELATED WITH PREINVASIVE LESIONS AND INVASIVE CERVICAL CANCER IN VENEZUELAN WOMEN

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Background/Objectives: Cancer of the uterine cervix still remains the most common cancer affecting incidence and mortality rates in Venezuelan women. Specific human papillomavirus (HPV) types have been associated with premalignant lesions and invasive carcinoma. There have been many efforts to study the risk factors associated with this disease but as far as we know, no studies have addressed the HPV16 viral lineages related to preinvasive and invasive lesions within the country. To determine the HPV16 lineages and sublineages in benign and malignant cervical lesions, we initiated a prospective collection of tissue.

Methods: DNA was used for overlapping amplicon sequencing of the full HPV16 genome, with phylogenetic analysis to determine viral sublineage.

Results: There is an average of 3 children born per woman and 69,2% of the cases used oral contraception. The A1, D2 and D3 sublineages of HPV16 were found. The average age of the patients is 44, with 39.6 the average age for A1, 40.3 for D2 and 53 for D3.

Conclusions: This is the first attempt to study the HPV16 lineages and sublineages related with cervical cancer al least in the Central Western region of Venezuela. A1, D2 and D3 were the most commonly lineages and sublineages found. Like in other Latin American countries D3 tend to be present in older and post-menopausal patients. Further studies will be required to evaluate risk factors, relationships between sublineages of HPV16 and the cervical cancer histology and diverse clinical manifestation of the disease.

References: 1.Mirabello,L, Yeager, M,Cullen,M, et al. HPV16 sublineage associations with histology-specific cancer risk using HPV whole-genome sequences in 3200 women. JNCI J Natl Cancer Inst. 2016;108(9):djw100. 2. Clifford,G, Tenet, V, Georges, D, et al. Human papillomavirus 16 sub-lineage dispersal and cervical cancer risk worldwide: Whole viral genome sequences from 7116 HPV16-positive women. Papillomavirus Res. 2019. Jun; 7:67-74.

#2413

11 - Genotyping

HUMAN PAPILLOMAVIRUS GENOTYPE DISTRIBUTION IN A PRIMARY SCREENING POPULATION IN SPAIN

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Background/Objectives: Human Papillomavirus (HPV) is the most common sexually transmitted infection in the world. It is spread by direct contact. It usually affects the skin and cervical mucosa, vulva, penis, anus, oral cavity and larynx. If the infection persists malignant lesions will develop. The HPV-16 and HPV-18 are considered high risk genotypes because they cause malignant injuries more frequently. The cancer of cervix caused by HPV is the fourth most frequent malignant lesion affecting women. Our aim was to know the proportion of endocervical samples in which HPV is detected and describing the genotypes affected in the south of Spain.

Methods: Three-thousand-five endocervical tests performed between 2015 and 2019 received in our hospital have been examined. Nucleic acid extraction was done with STARMag kit (Seegene). The extracts were analyzed through real-time PCR technique AnyplexTM II HPV28 (Seegene), which can detect HPV positive and 28 genotype (high and low risk). A descriptive study was done where frequency and percentage were qualitative variables and arithmetic mean and standard deviation were quantitative variables.

Results: One-hundred-sixteen (53.8%) of the samples were tested HPV positive. Genotypes 16, 31, 53 and 42 were found more frequently. Genotype 16 was the most common (23.8%) throughout all the study years for all age ranges, except for women older than 65 years of age and women younger than 24 years of age. The age, with an average of 39.95+/-10.739, was a significant variable. One single genotype was detected in 44.0% of all samples, while a combination of genotypes was found in 55.9%. The most common combination of genotypes was 53 and 42 (3.03%). The genotypes most associated with 16 were 18(1,48%), 53(2,35%) and 42(2,66%).

Conclusions: The proportion of samples in which HPV was detected was larger than the samples in which it was not detected. The most frequent genotype was HPV-16, even for all the years of the study and for every age range. Detection of multiple genotypes was more common than a single one and the most frequent combination was genotype 53 and 42.

#2000

12 - Molecular markers

CURRENT SCREENING TESTS FOR CERVICAL CANCER DETECTION: REVIEW, EVIDENCE AND FURTHER RECOMMENDATIONS

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Background/Objectives: The persistent infection with high-risk human papillomavirus (hr-HPV) is a direct cause of Cervical Intraepithelial Neoplasia (CIN) and Cervical Cancer. Based on historical evidence, HPV testing is more sensitive for detecting CIN-1, 2, and 3, or worse lesions (CIN-2+ and CIN-3+), than liquid-based cytology (LBC). Moreover, besides its higher sensitivity and negative predictive value (NPV), women with negative HPV test have lower risk of developing cervical cancer throughout the years. Currently, an optimal and efficient cervical cancer detection methodology is the hr-HPV testing coupled with a triage, based on one of these strategies: LBC, a p16/Ki-67 dual staining, a combined test (LBC + HPV test), or co-testing with a p16/Ki-67 dual staining. With these tests, accuracy rate for classification of positive hr-HPV women on the detection of the high-grade squamous intraepithelial lesion (HSIL) is reported to be greater than 90%. In this work, a review about cervical cancer screening tests was performed, based on the international available literature, evaluating the scientific and medical evidence, as well as the statistical performance for each one of them, alone or in combination.

Methods: Literature review based on more than 30 specialized references was performedon the screening tests for cervical cancer, its triage, and supporting evidence.

Results: For each screening test, sensitivity and specificity were evaluated, and the results for the specificity of HPV-16/18 test, LBC, and the LBC with p16/Ki-67 dual staining for CIN-2+ detection for hr-HPV positive women were 70.5%, 89.1% and 76.7%, respectively. The positive dual staining in HPV-16/18-negative women holds a risk of 1.7% after the CIN-2+ test but drops to 0.6% if it is negative. Moreover, there is a correlation between dual-positive staining and positive-LBC ($p < 0.001$). For the negative HPV-16/18 tests, before the dual staining, the probability after the CIN-2+ test is higher than 20%, but with a negative result, it decreases to 2%.

Conclusions: There is extensive evidence demonstrating that current hr-HPV screening tests are effective, showing better sensitivity and specificity at lower costs. Cervical cancer triage with dual p16/Ki-67 staining improves the stratification of precursor lesions, reducing colposcopy if they are negative. On the other hand, dual staining alone or combined with the HPV tests, if positive, means a sensitive and efficient approach for immediate referral to further colposcopy, suggesting a high risk of progression and need for close Background: The persistent infection with high-risk human papillomavirus (hr-HPV) is a direct cause of Cervical Intraepithelial Neoplasia (CIN) and Cervical Cancer. Based on historical evidence, HPV testing is more sensitive for detecting CIN-1, 2, and 3, or worse lesions (CIN-2+ and CIN-3+), than liquid-based cytology (LBC). Moreover, besides its higher sensitivity and negative predictive value (NPV), women with negative HPV test have lower risk of developing cervical cancer throughout the years. Currently, an optimal and efficient cervical cancer detection methodology is the hr-HPV testing coupled with a triage, based on one of these strategies: LBC, a p16/Ki-67 dual staining, a combined test (LBC + HPV test), or co-testing with a p16/Ki-67 dual staining. With these tests, accuracy rate for classification of positive hr-HPV women on the detection of the high-grade squamous intraepithelial lesion (HSIL) is reported to be greater than 90%.

#1920

12 - Molecular markers

Differential expression of microRNAs and their target genes in cervical intraepithelial neoplasias of varying severity

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Background/Objectives: Currently, little is known about the specific microRNAs involved in the development of cervical intraepithelial neoplasia (CIN1, 2, 3) and the transition to cancer in situ (CIS). Our meta-analysis allowed us to isolate 8 microRNAs (hsa-miR-1246, hsa-miR- 145-5p, hsa-miR-196b-5p, hsa-miR-34a-5p, hsa-miR-20a-5p, hsa-miR-21-5p, hsa-miR-375-5p, hsa-miR-96-5p) with potential significance in the progression of precancerous diseases to cervical cancer. Objective: to analyze the expression features of hsa-miR-1246, hsa-miR-145-5p, hsa-miR-196b-5p, hsa-miR-34a-5p, hsa-miR-20a-5p, hsa-miR-21-5p, hsa-miR-375-5p, hsa-miR-96-5p and their target genes, as well as genes associated with them in common signaling pathways in the tissues of the cervix in patients with CIN1-3 and CIS.

Methods: To assess the expression level of microRNA and matrixRNA, the quantitative polymerase chain reaction in real time method was used. Data analysis was carried out in the Python programming language using the SciPy library. Search for target genes was performed using the TarPmiR algorithm and the overrepresentation of microRNAs in signaling pathways (Over-Representation Analysis) was analyzed. To identify genes associated with target genes in common signaling pathways, GIANT (Genome-scale Integrated Analysis of gene Networks in Tissues) and network integration with several associations algorithms were used

Results: For microRNAs miR-145, miR-196b, miR-34a, miR-20a, miR-21, miR-375 and miR-96 a decrease in expression was found in the subgroup of patients with CIS, while for 4 microRNAs (miR-145, miR-34a, miR-20a and miR-375), an increase in the expression level was found for CIN1, 2. The detected features of microRNA expression in subgroups of patients with CIN1-3 and CIS also affected the expression of their target genes (CDKN2A, MKI67, TOP2A and CD82), as well as the genes associated with them in common signaling pathways (PGK1, THBS4 (TSP4) and ECM1).

Conclusions: Thus, the study revealed that each degree of CIN is characterized by its own specific molecular profile - the differential expression of microRNAs, their target genes and the genes associated with them in the general signaling pathways.

References: Dimitriadi T. A., Burtsev D. V., Dzhenkova E. A., Kutilin D. S. Differential expression of microRNAs and their target genes in cervical intraepithelial neoplasias of varying severity. Uspekhi molekulyarnoy onkologii = Advances in Molecular Oncology 2020;7(2):47-61. (In Russ.).

#2372

18 - Microbiome

Vaginal microbiota and human papillomavirus (HPV) infection among young Swedish women

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Background/Objectives: Human papillomavirus (HPV) infection is one of the most common sexually transmitted diseases. Although the HPV vaccine has contributed to reduce the prevalence of HPV infections and HPV related cancers, not all HPV subtypes are covered. Changes in vaginal microbiota, with the absence of Lactobacilli and increased microbial diversity, have been shown to facilitate sexually transmitted diseases in some countries.

Methods: To define the HPV associated microbial community in a Nordic country with a high vaccination coverage, we carried out the largest cross-sectional study with 345 young healthy Swedish women (youth clinic: n=206, age 14-22 years; cervical screening: n=139, 23-29 years). The microbial composition and its association with HPV infection status including 27 HPV subtypes were analyzed.

Results: Presence of the different HPV types in the cervix between 2008-2018 among vaccinated and non-vaccinated youth at the youth clinic will be presented very briefly. In essence, the prevalence of the tetravalent Gardasil types decreased considerably, in mainly HPV vaccinated but also non-vaccinated youth (due to herd immunity), but some high risk HPV types remained. Moreover, most of the remaining high-risk types are not present in Gardasil-9. Data on microbiota will also be presented. Microbial alpha-diversity was significantly higher in the HPV infected group compared to the HPV negative group, especially when infected with high-risk (HR) HPV types and multi-types. The vaginal microbiota among HPV infected women were characterized by a higher number of bacterial vaginosis-associated bacteria (BVAB), Sneathia, Prevotella and Megasphaera, which could be used as potential biomarkers and treatment targets. In addition, the correlation analysis demonstrated that there are as many as twice women with non-lactobacilli dominant vaginal microbiota presented with HR HPV types compared to L. crispatus dominated vaginal microbiota (odds ratio 2.0, 95% confidence intervals 1.0-3.9), after adjustment for age, population and vaccination status.

Conclusions: This suggests that HPV infection, especially HR HPV types, are strongly associated with certain vaginal microbiota regardless of age and vaccination status.

References: Ährlund-Richter A, Cheng L, Hu YOO, Svensson M, Pennhag AAL, Ursu RG, Haeggblom L, Grün N, Ramqvist T, Engstrand L, Dalianis T, Du J. Changes in Cervical Human Papillomavirus (HPV) Prevalence at a Youth Clinic in Stockholm, Sweden, a Decade After the Introduction of the HPV Vaccine. Front Cell Infect Microbiol. 2019 Mar 20;9:59. doi: 10.3389/fcimb.2019.00059. PMID: 30949454; PMCID: PMC6435486. Cheng L, Norenhag J, Hu YOO, Brusselaers N, Fransson E, Ährlund-Richter A, Guðnadóttir U, Angelidou P, Zha Y, Hamsten M, Schuppe-Koistinen I, Olovsson M, Engstrand L, Du J. Vaginal microbiota and human papillomavirus infection among young Swedish women. NPJ Biofilms Microbiomes. 2020 Oct 12;6(1):39. doi: 10.1038/s41522-020-00146-8. PMID: 33046723; PMCID: PMC7552401. Du J, Ährlund-Richter A, Näsman A, Dalianis T. Human papilloma virus (HPV) prevalence upon HPV vaccination in Swedish youth: a review based on our findings 2008-2018, and perspectives on cancer prevention. Arch Gynecol Obstet. 2021 Feb;303(2):329-335. doi: 10.1007/s00404-020-05879-7. Epub 2020 Nov 27. PMID: 33247317; PMCID: PMC7858554.

#2257

22 - Diagnostic procedures / management

Evaluation of managing CIN 3+-diagnosed pregnant women by methylation assessment using the QIASURE methylation test

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Background/Objectives: Pregnant women with Pap IVa and suspicion of CIN3+ are currently managed by colposcopy/biopsy to exclude invasive disease which allows a conservative monitoring approach instead of ablative therapy that increases the risk for late spontaneous abortion, premature labour and unnecessary perinatal morbidity and mortality. However, non-invasive biomarkers for triage of these women are lacking. Methylation assessment using the QIAsure Methylation Test specifically detects cancer and advanced CIN2/3 lesions with a high short-term progression risk for cancer. Methylation-negative results indicate no short-term risk of disease progression. In this study we evaluated methylation status analysis as molecular triage test to improve the management of pregnant women with CIN3+.

Methods: The German Study Group Colposcopy (SGK) collected residual FFPE samples of 6 different groups of CIN3+ diagnosed pregnant women from several participating institutes all over Germany. The groups were pregnant women with 1) cervical cancer (n=17); 2) CIN3 progressing to cancer during pregnancy (n=6); 3) CIN3 regressing to ≤CIN1 within 6 months after delivery (n=38); 4) CIN3 with lesions in 3-4 quadrants (n=12); 5) CIN3 not further specified (n=40); 6) HPV+ without CIN (controls, n=14). All samples underwent extensive expert pathology review before study inclusion. All samples were tested for methylation using the QIAsure Methylation Test in a blinded manner at Self-screen B.V..

Results: Pregnant women with cancer or with CIN3 progressing to cancer (group 1 and 2) scored 100% methylation-positive (17/17 and 6/6, respectively). Methylation-positivity for women with regressing CIN3 (group 3) was 50% (19/38) and for women with CIN3 in group 4 and 5 this was 83% (10/12) and 78% (31/40), respectively. The difference in methylation-positivity between pregnant women with progressing and regressing CIN3 (group 2 and 3) was significant (Ci-square, P=0.02).

Conclusions: Methylation-negative women did not have or showed no risk of progression to invasive disease during pregnancy and could be managed without intensified colposcopy follow-up and without excisional treatment. Methylation-positive cases require frequent colposcopy follow-up during pregnancy to select women in need of excisional treatment during pregnancy or shortly after delivery.

#2393

23 - Colposcopy

REVIEW OF PREDICTING FACTORS FOR AN HEMMORHAGIC LLETZ PROCEDURE IN A REPRESENTATIVE SAMPLE

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Background/Objectives: With the LLETZ surgery being the modality of choice for the treatment of cervical precancer worldwide, this procedure is being performed in a diversity of settings and varying levels of operator expertise. Despite usually related with minimal bleeding, this procedure can be extremely hemorrhagic. Prediction of excess hemorrhage during LLETZ is helpful to avert inconvenience, delays or cancelations in surgery lists and inpatient admittance.

Methods: We sought to identify predictors of excess bleeding during outpatient LLETZ. Available data of 243 patientstreated in a single Greek institution (Patras University Colposcopy Clinic) during the previous five years have been reviewed. Excess bleeding was arbitrarily determined as coagulative efforts that exceeded five minutes. For non-menopausal patients, all LLETZ procedures have been undertaken in the first phase of the menstrual cycle.

Results: Thirty-one procedures in total (12.7%) were related with excess bleeding; four patients have been admitted to be discharged the next day and no hysterectomies were needed. Gravidity and parity represented the most determining factors. Multiparas with enlarged cervixes and abundant metaplasia commonly illustrated excess bleeding, as was also observed in the puerperium. Excess metaplasia with abundant Nabothian cysts was independantly associated with increased blood loss and in a lesser extent vaginitis/cervicitis. Anticoagulant treatments (when the patient failed to report this medication) and hypertension contributed to painstaking hemostasis. Menopausal status almost universally predicted scarce bleeding; despite some Type 3 excisions in menopausal patients (which should anyway ideally be performed under general anesthesia) were often hemorrhagic.

Conclusions: Several factors contribute in rendering this simple outpatient procedure to a complicated task. Simple measures that can be advocated when excess bleeding is anticipated is input from senior and more experienced personnel and performing the procedure in an inpatient basis (in theatre under general anesthesia). Stitching of the descending branches of uterine arteries can be also considered. Review of medication is also advocated; in case of anticoagulant treatment the proceure should be postponed.

References: Prendiville W et al. BJOG 1989; 96:1054-1060 Bogliato F. J Low Genit Tract Dis 2016; 20:e20-e23. Dunn TS et al. J Reprod Med 2004; 49(2):76-78. Hilal Z et al. J Low Genit Tract Dis 2016; 20:169-173.

#1836

24 - Cervical neoplasia

CIN2+ DIAGNOSES BETWEEN 2013 AND 2018 IN WOMEN 18 TO 45 YEARS OLD - AN ANALYSIS OF GERMAN STATUTORY HEALTH INSURANCE CLAIMS DATA

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Background/Objectives: Cervical intraepithelial neoplasia (CIN) can result from persistent infection with human papillomavirus (HPV). If left untreated, CIN2+ (CIN2/CIN3) might progress to cervical cancer. CIN are mostly diagnosed through cervical screening and can present a considerable burden to patients through surgical procedures (e.g. cervical conization) and psychosocial consequences. The objective of this study was to estimate the annual proportion of women aged 18-45 years with CIN2+ diagnoses in Germany from 2013-2018.

Methods: We conducted a retrospective cross-sectional claims data analysis using the Institute for Applied Health Research Berlin (InGef) Research Database, which covers approximately 4 million lives and is representative for the German population regarding age and gender. The annual proportion of women aged 18-45 years old with CIN2+ diagnoses in the period from 2013-2018 was determined as the number of women observable throughout the respective calendar year (except for women who deceased) with at least one inpatient (main/secondary diagnosis) or outpatient (verified diagnosis) record for CIN 2 (N87.1) or CIN 3 (N87.2, D06.-) divided by the total number of eligible women in the respective calendar year in the database.

Results: The overall annual proportion of women aged 18-45 years with CIN2+ diagnoses was 7.9/1,000, 8.2/1,000, 7.7/1,000, 7.2/1,000, 7.0/1,000, and 6.7/1,000 in 2013, 2014, 2015, 2016, 2017, and 2018, respectively. In 2017 and 2018, women aged 31-35 and 36-40 presented the highest proportion of CIN2+ among all age groups. The share of women aged 31-45 years in all CIN2+ diagnoses increased from 61.3% in 2013 to 70.3% in 2018. Women between 31-35 years accounted for 23.2% (2013) and 28.3% (2018) of CIN2+ diagnoses. The proportion of CIN2+ diagnoses in women aged 20-26 was 6.3/1,000 in 2013 and 3.4/1,000 in 2018. Separate analyses of CIN2 and CIN3 diagnoses showed a higher between-year variability in proportions of CIN3 than in proportions of CIN2 diagnoses, especially in women below the age of 31 years.

Conclusions: Observed changes in the number of CIN2+ diagnoses from 2013-2018 particularly in younger women might be influenced by changes in HPV vaccination, changes in behavior, and/or screening patterns (including fewer screenings among younger women). The most substantial burden of CIN2+ diagnoses remains in women aged 31-45 years. Interventions to prevent CIN2+ in this population continue to be highly relevant.

References: Conflicts of interest: This study was funded by MSD Sharp & Dohme GmbH. AJS, MR, and RW are full time employees of MSD Sharp & Dohme GmbH. VP and KS are full-time employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. KMS, AS, and CJ are full-time employees of Xcenda GmbH, acting as contractors of MSD Sharp & Dohme GmbH for the execution of this study. WG declares no conflict of interest. MH received honoraria as speaker and member of medical advisory boards from MSD Sharp & Dohme GmbH.

#2155

24 - Cervical neoplasia

THE NEW CLASSIFICATION OF CERVICAL ADENOCARCINOMA - CORRELATION WITH HISTOLOGICAL FEATURES AND MOLECULAR MARKERS

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Background/Objectives: Despite the existence of screening, cervical cancer has still a high morbidity and mortality rate. Squamous lesions are more frequently detected by cytology and colposcopy, while it has a poorer sensitivity in detecting adenocarcinoma. The new WHO classification (2020) emphasizes the importance of human papillomavirus (HPV) infection in the development of endocervical adenocarcinomas, thus reflecting on patient management. Our review studies the correlation between clinical data, HPV status, histological features and molecular markers in cervical adenocarcinoma.

Methods: We selected cases diagnosed with endocervical adenocarcinoma and recorded clinicopathologic variables, as well as immunohistochemical test results. All slides were reviewed and classified according to the new WHO classification.

Results: Of a total of 27 cases, usual-type endocervical adenocarcinomas represented the majority of cases, while the non-HPV-associated ones showed distinctive morphology that suggested their nature even before the p16 staining. Although colposcopic features in cervical cancer have a high influence on treatment, findings in cervical adenocarcinoma are very variable, sometimes inconspicuous.

Conclusions: Cervical adenocarcinoma represents a heterogenous group of tumours, some with adverse outcome and although their recognition can be difficult, refinement of diagnosis and prognostication based on a systematic evidence review has great value in a better personalized treatment for these patients.

#2197

38 - Public health

REAL-WORLD IMPACT AND EFFECTIVENESS OF THE QUADRIVALENT HPV VACCINE: AN UPDATED SYSTEMATIC LITERATURE REVIEW

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Background/Objectives: Determining benefit of HPV vaccination in real world settings is challenging due to setting heterogeneity and need for long-term follow-up to assess impact on cancer, a key outcome. The impact and effectiveness of the quadrivalent HPV (4vHPV) vaccine ten years post licensing (2006-2015) was previously summarized in a systematic literature review (SLR) of 61 studies from 9 countries1, which demonstrated notable decreases in vaccine-type HPV infection and related diseases. Since then, continued vaccine implementation has led to availability of data with longer follow-up and program expansion has increased focus on disease endpoints beyond cervical cancer. Therefore, an updated summary is timely to guide vaccination initiatives worldwide.

Methods: A 4vHPV vaccine real world impact SLR (03/2016 to 03/2020) was performed to assess vaccine benefit using previously assessed endpoints (vaccine-type HPV genital infections, anogenital warts and cervical abnormalities) as well as new endpoints (recurrent respiratory papillomatosis, vaccine-type HPV oral/anal infections and oral/anal lesions). Studies were identified from peer-reviewed literature according to pre-defined search terms and selection criteria, with rigorous SLR protocols in place.

Results: Although covering half the time as the prior SLR1, the current SLR identified twice as many studies (N=122) and a 156% increase in countries reporting HPV vaccine impact across all endpoints (N=23). The current SLR identified substantial and statistically significant decreases in prevalence of HPV-type infection (up to 92%) and anogenital warts (up to 82%) among females of vaccine-targeted age groups. The level of decrease varied by cohort age, coverage rate, whether vaccine program included catchup and time since vaccination. There was also evidence of herd protection and cross-protection in men and women, and indication of vaccine benefit among males with gender-neutral vaccination. Vaccine effectiveness in preventing late-stage cervical lesions was well demonstrated, with up to 73% reduction in cervical intraepithelial neoplasia 3+ in vaccine-targeted females, with effectiveness varying according to doses received and age at vaccination. Fewer studies (16) reported on new endpoints; however, statistically significant decreased disease outcomes were shown for oral and anal infection, anal high-grade intraepithelial neoplasia, and juvenile onset RRP.

Conclusions: These data support elimination of cervical cancer and other HPV-related diseases as an achievable goal, especially in countries with high, sustained vaccine coverage and highlight the importance of 4vHPV vaccine as a key component in realizing that goal.

References: [1Garland SM, Kjaer SK, Munoz N, et al. Impact and Effectiveness of the Quadrivalent Human Papillomavirus Vaccine: A Systematic Review of 10 Years of Real-world Experience. Clin Infect Dis 2016; 63(4): 519-27.]

#2513

28 - Oral HPV infection

Lack of CD44 overexpression and application of concurrent chemoradiotherapy with cisplatin independently indicate excellent prognosis in patients with HPV-positive oropharyngeal cancer

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Background/Objectives: HPV-16 positivity in patients with squamous cell carcinoma of oropharynx (OPSCC) is associated with better prognosis. However, in more than 40% of HPV infected patients progression of cancer disease is observed,which indicates the presence of cancer cells resistant to therapy. Some studies suggest that there may be a subpopulation of cancer stem cells (CSCs), which simultaneously exhibit unlimited ability to self-renew and differentiate towards neoplastic cells. The relation between HPV16 infection and biomarkers of CSCs is unclear. The aim of the study was to compare the expression of CD44, CD98, ALDH1/2 and P16 in oropharyngeal cancer patients with or without HPV16 infection, as well as to analyze the prognostic potential of selected CSCs biomarkers in these two subgroups.

Methods: The study was performed in a group of 63 patients. HPV16 infection status was analyzed by quantitative polymerase chain reaction, while CD44, CD98, ALDH1/2 and P16 expression by immunohistochemistry. In survival analysis, two endpoints were applied: overall survival (OS) and disease-free survival (DFS).

Results: Among 63 cancers, HPV16 infection was found in 25 tumors (39.7%), overexpression of CD44, CD98, ALDH1/2 and P16 in 43 (68.2%), 30 (47.6%), 33 (52.4%) and 27 (42.9%) cancers, respectively. In the HPV16-positive subgroup, DFS rate of 100% was observed in patients with tumors characterized by lack of CD44 overexpression and those treated with concurrent chemoradiotherapy with cisplatin (CisPt-CRT). In the HPV16-negative subgroup 100% of DFS was noticed for patients (n = 6) with P16 immunopositive tumors. In this subgroup none of the CSCs biomarkers evaluated in the study had any impact on OS or DFS.

Conclusions: In patients with HPV16-positive oropharyngeal cancer, lack of CD44 overexpression and application of CisPt-CRT were found to be positive prognostic factors.

#2378

29 - HPV and oropharynx / Head and neck cancer

Studies of the presence of HPV in adenoid cystic carcinoma of the head and neck region

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Background/Objectives: Background: Adenoid cystic carcinomas (ACC) are rare cancers mainly arising within secretory glands, especially the major and minor salivary glands. They often have an indolent course, but can also take a very malignant course, and it is difficult to predict which carcinomas will do so. Here, we investigated whether human papillomaviruses (HPV) could be present in some of these tumors and whether the presence of HPV could be predictive in any way. Objectives: To investigate if HPV plays a causal or predictive role in ACC.

Methods: From 76 patients, DNA was extracted from 73 formalin-fixed-paraffin-embedded primary ACCs, 6 local relapses and 4 metastases and tested for 27 different HPV types by a multiplex bead-based assay. HPV DNA positive tumors were stained for p16INK4a overexpression.

Results: Three of the 73 primary ACC tumors and one metastasis were HPV-positive (HPV+). One sample from a sinonasal ACC primary tumor metastasis and was HPV33E6 positive. Two samples, both from a primary ACC in the tonsil were both HPV33E6 positive. The fourth sample case was from an HPV16 positive ACC, also in the tonsil. The three HPV-positive cases are analyzed in more detail from a molecular biological point of view and the data will be presented.

Conclusions: In conclusion, HPV DNA analysis in a large number of ACC indicates that HPV does not play a major role in the development of these tumors, however, the locations of the HPV+ ACCs do present differential diagnostic challenges.

#2387

29 - HPV and oropharynx / Head and neck cancer

Antitumor effects in vitro of FGFR and PI3K inhibitors on HPV positive and HPV negative tonsillar and base of tongue cancer cell lines

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Background/Objectives: Human papillomavirus positive (HPV+) tonsillar and base of tongue squamous cell carcinoma (TSCC/BOTSCC) have better outcome than corresponding HPV-negative (HPV-) cancers. Recently, we demonstrated that FGFR3 and PIK3CA are often mutated in HPV+ cancer. To investigate whether targeted therapy is an option for TSCC/BOTSCC, two HPV+ and one HPV- TSCC/BOTSCC cell lines were tested for their sensitivity towards FGFR and PI3K inhibitors. In addition, some attempts to combine chemotherapeutic drugs and FGFR and PI3K inhibitors were also performed.

Methods: HPV+ UPCI-SCC-154, and HPV- UT-SCC-60A were tested by competitive allele-specific TaqMan-PCR (CAST-PCR) for presence/absence of frequently occurring FGFR3 and PIK3CA mutations. All cells were then treated with FGFR inhibitor, JNJ-42756493 and PI3K inhibitors, BYL719, alone or combined. In addition, in separate experiments FGFR and PI3K inhibitors were also combined with cisplatin and docetaxel. Viability was analyzed by a WST-1 assay, cytotoxicity, apoptosis and proliferation tested by IncuCyte S3 Liveâ€"Cell Analysis System.

Results: HPV+ UPCI-SCC-154, and HPV- UT-SCC-60A, did not exhibit any common FGFR3 or PIK3CA mutations, but were all sensitive to FGFR inhibitor, JNJ-42756493, and PI3K inhibitors, BYL719. Notably, HPV+ UPCI-SCC-154 was generally slightly more sensitive than the other two cell lines. Furthermore, when the drugs were combined in HPV+ UPCI-SCC-154 and HPV- UT-SCC-60A, potentiated combination effects were observed. The cell lines were also sensitive to cisplatin and docetaxel, in a dose dependent way, but the sensitivity of the FGFR and PI3K inhibitors were not improved when combined with cisplatin or docetaxel.

Conclusions: HPV+ UPCI-SCC-154, and HPV- UT-SCC-60A had no common FGFR3 or PIK3CA mutations, but were sensitive to FGFR and PI3K inhibitors. Furthermore, the latter two cell lines were, especially sensitive to combinations of JNJ-42756493 and BYL719, but not to combinations of the FGFR and PI3K inhibitors, with cisplatin or docetaxel.

#2267

31 - Genital warts

REAL WORLD EVIDENCE ANSWERING QUESTIONS ABOUT HUMAN PAPILLOMAVIRUS VACCINES EFFECTIVENESS TO PREVENT GENITAL WARTS AND ITS RELATIONSHIP WITH THE IMMUNOLOGICAL STATUS IN WOMEN 14-23 Y/O.

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Background/Objectives: In the Valencian Region of Spain, the quadrivalent Human papillomavirus vaccine (HPV4) was administered between 2008 and 2010 in girls born in 1994 and 1995. Thereafter, the bivalent vaccine (HPV2) was used. The host immune system is principally important in the development and progression of HPV infection. Unlike the immunocompetent host, where Infection with anogenital HPV is usually asymptomatic and resolves spontaneously without consequences, infection in immunocompromised (IC) frequently results in severe, persistent, and extensive manifestations of HPV disease. Genital warts (GW) are a frequent sexually-transmitted disease, 90% of which are related to HPV6/11. There is a lack of studies based on GW in IC population. The objectives are to estimate the HPV vaccines effectiveness (VE) to prevent GW and to assess the risk of GW in IC women respect to IC-free.

Methods: A population-based, retrospective cohort study using real-world data from the Valencian Region's health databases including sociodemographic, hospital, outpatient information and immunization status at patient level. Study population: women aged between 14 and 23 years old residing in the Valencia Region from 2009-2017. Incident cases of GW and IC condition were ICD-coded identified. Exposure: bivalent (HPV2) and quadrivalent (HPV4) vaccination status (non-vaccinated, one-dose vaccinated, two-dose vaccinated and fully vaccinated). Statistical analysis: Adjusted VE for HPV2 and HPV4 and the risk of GW in IC women respect to IC-free were estimated by a negative binomial Bayesian model. Sociodemographic, spatial, and temporal variables were considered for the adjustment.

Results: The study included 563,240 women, of which 36,214 (6%) were IC. There were 2,615 cases of GW, 216 in IC. Risk of GW was 73% (95% CrI: 48-99) higher in IC woman as compared to IC-free. The 68% of women born in 1994 and 1995 were fully vaccinated with HPV4 and the 76% of women born in 1996-2003 with HPV2. In total, 194,123 women (17,930 IC) were vaccinated with some vaccine against HPV. HPV VE is shown in Table 1.

Conclusions: HPV4 vaccine was 75% effective against genital warts. Immunosuppression is a clear risk factor for suffering GW.

References: This study has been funded by MSD.

#2262

31 - Genital warts

HPV VACCINATION AND DECLINE OF HPV 6 AND GENITAL WARTS IN POPULATION OF YOUNG WOMEN IN GERMANY

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Background/Objectives: The vaccination of HPV naive women against HPV 6/11 protects sufficiently from genital warts and may even lead to protection of non-vaccinated men and women in the same population (herd protection). However, the level of vaccination coverage required to achieve herd protection is unknown.

Methods: WOLVES (Wolfsburg HPV epidemiological study) invited all women born 1983/84, 1988/89 and 1993/94 with first residency in Wolfsburg to participate. HC2-HPV testing and genotyping with SPF-10 PCR of all HPV positive and 10% of HC2 negative samples was performed annually for all participants. Women born in 1983/84, 1988/89, and 1993/94 participated in four cohorts between 2009/10 and 2014/15. Quadrivalent vaccination coverage and prevalence of HPV 6/11 infection and genital warts are presented for participants aged between 19–22 and 24–27 years at the time of sample collection. Statistical analyses were performed to compare participants of same age using 2 x 2 contingency tables (Röhmel-Mansmann unconditional exact test; two-side alpha of 0.05).

Results: A total of 2,456 women were recruited. During the period 10/2009-12/2010, full vaccine coverage rates were 40/659 (6.1%) in participants aged 24–27 years (cohort 1) and 142/600 (23.67%) in those aged 19–22 years (cohort 2). Five years later (11/2014-1/2016), vaccine coverage rates were increased to 135/733 (18.42%) and 177/368 (48.09%) in participants aged 24–27 years (cohort 3) and 19–22 years (cohort 4), respectively. Between 2010 and 2015, there was a statistically significant decrease in the prevalence of HPV 6 infection among women aged between 24–27 years (2.12% versus 0.00%; P<0.0001) and 19–22 years (2.0% versus 0.00%; P=0.0056). There was no significant decline in HPV 11 infection. In total, 52 of 2341 participants were diagnosed with genital warts. There was a statistically significant drop in the life-time risk of developing genital warts in women aged 24–27 years during 2010 and 2015 (4.7% versus 1.68%, respectively; P< 0.0018). The overall life-time risk of developing genital warts in women aged between 19–27 years decreased from 3.1% in 2010 to 1.2% in 2015 (P=0.0022). The observed decline in the prevalence of HPV 11 infection was not significant.

Conclusions: An increase in vaccination coverage was associated with a decreased prevalence of genital warts in young women. Quadrivalent vaccine had a protective effect on genital HPV 6 infection and an almost complete protective effect on the development of genital warts in the youngest population. We observed the unexpected decline of genital warts and almost complete disappearance of HPV 6 in a population with low HPV vaccine coverage

#2181

34 - Economics and modelling

Healthcare Related Costs During 24 Months Follow-up of Patients Undergoing Cervical Conization - A Retrospective Study of German Statutory Health Insurance Claims Data

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Background/Objectives: Cervical conization is a common surgical procedure for diagnosis and treatment of high-grade cervical intraepithelial neoplasia (CIN) caused by human papillomavirus (HPV). The objective of this study was to assess healthcare-related costs during 24 months follow-up in women 18-45 years-old who underwent a conization in Germany.

Methods: We conducted a retrospective longitudinal claims data analysis using the "Institute for Applied Health Research Berlin" (InGef) Research Database, which covers approximately 4 million individuals. All women aged 18-45 who underwent cervical conization (OPS code 5-671.0*) in the InGef Research Database between July 1st, 2013 and December 31st, 2016 were identified. Inclusion criterion was no former conization procedure record 6 months prior to conization (index conization), and minimum follow-up post-index conization of 24 months, beginning with the date of the index conization. Mean all-cause healthcare costs (excluding costs pre-conization) were reported by inpatient, outpatient, pharmaceutical, aids and remedies, sick leave costs and as sum, as well as mean conization-specific inpatient and outpatient costs during 24 months follow-up after index conization (including costs of the index conization). Missing data on sick leave costs were imputed using mean.

Results: Overall, 4,415 women who underwent a conization and were continuously observable for at least 24 months after the conization were identified. After 24 months follow-up, total mean all-cause healthcare costs were €5,089 (SD: €14,083). All-cause costs were driven by inpatient care (€2,018 (SD: €3,882)) followed by outpatient care (€1,690 (SD: €1,454)). The conization specific mean inpatient and outpatient costs were €907 (SD: €2,082) and €524 (SD: €535), respectively. The total of conization specific inpatient and outpatient costs (mean: €1,431; SD: €2,262) accounted for 28.1% of the all-cause healthcare costs during follow-up.

Conclusions: Cervical conization causes a considerable health economic burden in 18-45-year-old women in Germany. Further analyses to assess the health economic burden of women with CIN undergoing a conization compared to women without CIN are planned. Attempts should be made to reduce the burden of CIN as a main cause for subsequent conization.

#2252

34 - Economics and modelling

DISEASE BURDEN OF CERVICAL AND HEAD AND NECK CANCERS IN TAIWAN: A POPULATION-BASED DATABASE ANALYSIS

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Background/Objectives: HPV is considered a carcinogenic risk factor to both men and women. Previous research of HPV-associated disease burden mainly focused on cervical cancer in women.1 Increasing evidence attributes HPV as a risk factor for head and neck cancers.2 However, there is limited understanding of the clinical and economic burden of head and neck cancers. This study aims to estimate the clinical and economic burden of cervical and head and neck cancers in men and women in Taiwan.

Methods: Data from Taiwan Cancer Registry (TCR) and National Healthcare Insurance Reimbursement Database (NHIRD) between 2013 to 2016 were utilized to estimate the incidence and direct medical cost of cervical and head and neck cancers. All population without pre-existing cancers were eligible for the study. Confirmed cancer cases between 2014-15 without a cancer diagnosis 12 months prior were identified in TCR and linked to NHIRD for cost, incidence, and case fatality rate estimate. All claims in the 12 months following index cancer diagnosis were included in cost analysis. To determine direct medical costs associated with cancer management, a 1:1 matched control was identified for each cancer patient based on Charlson Comorbidity Score and top 10 conditions of healthcare expenditure in 2019 to adjust for costs not related to cancer management.

Results: Overall incidence of invasive cervical cancer in 2014-2015 was 10.14/100,000 person with highest incidence of 21.79/100,000 person in 80-84 year-old cohort. The average mortality rate was 4.45/ 100,000 person. Overall incidence of head and neck cancer is 49.26/100,000, predominately in males, and case fatality rate was 28.33 per 100,000 person. The highest incidence of 104.90/100,000 person occurs in 55-59 year-old men. The incidence of oropharyngeal cancer was 1.63/100,000 person. The average total annual medical cost due to cervical cancer was 15.29 times and 36 times of the average cost of the matched cohort for all stages and for stage IV cancer, respectively. Similar results were observed in head and neck cancer; the average total annual medical cost due to head and neck cancer was 18.4 times of the average cost of the matched cohort and disparity increases as the disease stage advances. Individual HPV status could not be ascertained through both databases and is a study limitation.

Conclusions: Both cervical and head and neck cancers result in substantial clinical and economic burden in adults in Taiwan; the disease burden increases with advancing age. To ameliorate the disease burden in the future, an effective HPV prevention approach such as vaccination could be considered.

References: 1. Hung, M. C., Liu, M. T., Cheng, Y. M., & Wang, J. D. (2014). Estimation of savings of life-years and cost from early detection of cervical cancer: a follow-up study using nationwide databases for the period 2002-2009. BMC Cancer, 14, 505. doi:10.1186/1471-2407-14-505 2. Hwang, T. Z., Hsiao, J. R., Tsai, C. R., & Chang, J. S. (2015). Incidence trends of human papillomavirus-related head and neck cancer in Taiwan, 1995-2009. Int J Cancer, 137(2), 395-408. doi:10.1002/ijc.29330

#2297

34 - Economics and modelling

Modelling the impact of using a DNA vs mRNA HPV assay as part of the cervical screening programmes in Sweden and Denmark

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Background/Objectives: Both Denmark and Sweden are currently assessing their cervical cancer screening programmes, including implementing primary HPV screening for certain populations. Evidence is required about how to implement screening, including how the choice of assay could impact on safety, patient follow-up, and resource use. Both DNA and mRNA assays are approved for use in screening programmes, and while both have demonstrated similar sensitivity in large longitudinal studies, mRNA assays have been shown to have higher specificity resulting in fewer false-positive results.

Methods: A decision tree model was developed to represent the current cervical screening algorithms in Sweden and in Denmark: primary HPV screening for older women and primary cytology screening for younger women. The model estimated the total costs and the number of colposcopies, HPV tests and cytology tests in a cohort screened and followed through recall, using either a DNA or mRNA assay, in either Sweden or Denmark. Published data from Sweden and Denmark were used for the inputs including the probabilities through the model (taken from the HORIZON study), costs, demographic and screening data. Sensitivity and scenario analyses were conducted to explore uncertainty.

Results: For Sweden, in a population of 546,615 women screened annually, the model estimated a cost savings of 39 million kr annually if an mRNA test vs a DNA test was used, with 12,621 unnecessary colposcopies averted. In Denmark, for 224,680 women screened there would be approximately 7.55 million kr saved and 5,427 colposcopies averted annually if mRNA tests were used. For both countries, there were also reductions in the annual number of HPV and cytology tests required.

Conclusions: For both Sweden and Denmark, choosing an mRNA over a DNA assay is estimated to yield cost savings and reduce the number of unnecessary colposcopies, HPV, and cytology tests. This can generate benefits for women and health services and the information can be used to inform the implementation of screening programmes.

#2296

34 - Economics and modelling

Evaluating the choice of HPV assay for a proposed French cervical screening programme using a health economic model

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Background/Objectives: Guidance on the use of high-risk human papillomavirus (HR-HPV) assays for primary and reflex testing in the proposed population-based national cervical screening programme in France was issued in 2020. To make the most efficient use of resources, the type of HR-HPV assay used in cervical screening should be considered. This study compares the use of a more specific mRNA HR-HPV assay to a DNA HR-HPV assay for a cohort of women aged 25 to 65 years in the new French cervical screening programme.

Methods: A decision tree model was developed reproducing the proposed French cervical screening algorithms for younger and older populations (cytology and HPV primary variations). Model parameters were sourced from published French cost and population data, and the HORIZON (Denmark) and FOCAL (Canadian) studies. Total costs, and number of colposcopies, HPV tests and cytology tests were estimated for the cohort. Parameter uncertainty was explored with one-way and probabilistic sensitivity analyses.

Results: For a cohort of 2,168,806 million women aged 25 to 65 years in the hypothetical French national screening programme, €6.5 million could be saved annually (95% CI €-0.8 - €13.8 million), with an accompanying reduction of 47,795 unnecessary colposcopies (95% CI 47,287 - 48,314), 38,666 unnecessary HPV tests and 121,670 unnecessary cytology tests for an mRNA assay compared a DNA assay. Results from the sensitivity analysis showed that the results were robust across a range of inputs.

Conclusions: When considering implementing HPV testing in the cervical screening programme in France, using an mRNA vs DNA HR-HPV assay is estimated to reduce unnecessary resource use whilst saving costs. This has knock-on benefits for women being screened and the healthcare system.

#2298

34 - Economics and modelling

Evaluating the benefits and costs of using an mRNA versus DNA hrHPV assay in the National Cervical Screening Programme in the Netherlands

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Background/Objectives: The National Cervical Screening Programme (NCSP) introduced high-risk human papillomavirus (hrHPV) primary screening in the Netherlands in 2017, and data are available for the first years of implementation using a DNA assay. However, the choice of hrHPV test (DNA vs mRNA) used in screening programmes can make a difference to resource use and costs, particularly follow-up testing and referral for colposcopy. Both mRNA and DNA tests have similar sensitivity, however, the specificity of mRNA is higher, resulting in fewer false-positive results and referral for follow-up. This is important to consider in any population-based cervical screening programme.

Methods: A health economic model was developed to evaluate the impact to costs, number of colposcopies, hrHPV and cytology tests of using an mRNA assay compared to a DNA assay for a cohort of women aged 30 to 65 years in the NCSP in the Netherlands. A decision tree model reflected the current cervical screening flowchart in the Netherlands. Demographic and screening data published by the NCSP and local costs were used to parameterise the model. Probabilities were sourced from the HORIZON study from Copenhagen. The outcomes were total costs, and the number of colposcopies, HPV tests and cytology tests. Scenario analyses were conducted using probabilities from the HORIZON and DUSC studies and the NCSP to explore uncertainty in the probability values and provide a range of possible outcomes from more to less conservative.

Results: Adopting an mRNA versus DNA test as part of the NCSP in the Netherlands is estimated to save €1.8 million annually and prevent 855 unnecessary colposcopies and 33,096 cytology tests for a cohort of women aged 30 to 65 years. Cost savings of 0.3% to 5.2% were found using mRNA testing in the scenario analyses.

Conclusions: Like results seen in the UK, Sweden, Denmark, Canada and France, choosing an mRNA hrHPV assay instead of a DNA assay could reduce the costs of delivering screening and prevent unnecessary tests, with no impact on the safety of the programme, and should be considered when making decisions about how to implement screening at the national level in the Netherlands.

#2299

34 - Economics and modelling

Estimating the costs and benefits of HR-HPV assay choice in a theoretical HPV primary cervical screening algorithm in Ontario, Canada

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Background/Objectives: Several provinces in Canada are moving towards implementing primary high-risk human papillomavirus (HR-HPV) screening as part of their cervical screening programs. Provinces will need to consider the choice of screening algorithm and how screening is organized and implemented, including the choice of HR-HPV assay, as this may impact on the safety of screening and the resource use.

Methods: This study explored the theoretical impact of choosing either a DNA or mRNA HR-HPV assay as part of a primary HPV screening algorithm in Ontario, Canada for a population of women aged 30-65 years. The estimated outcomes were the total program costs and the number of colposcopies, HPV tests and cytology tests. Final outcomes were estimated for one cohort undergoing screening over three years. A decision tree model was created based on a previously published model from England (Weston et al, 2019). Published local data from Ontario and Canada were used for the model inputs including the probabilities through the model, cost, demographic and screening data. The uncertainty in results was explored using sensitivity and scenario analyses.

Results: If an mRNA assay was used rather than a DNA assay, an estimated cost savings of CAD $4.01 million annually (95% credibility interval [CI]: -7,866,251 - 8,035) could be realized, with 10,639 unnecessary colposcopies averted (95% CI: 10,170 - 11,092) among 2.3 million women screened. The results were robust to changes in the inputs and various scenarios including screening younger women.

Conclusions: Findings show that the choice of HPV assay is an important consideration when developing a primary HPV cervical screening program in Ontario, Canada. Avoiding unnecessary tests and reducing health care costs has an additional positive impact on women and health care services.

#1714

35 - Advocacy, acceptability and psychology

PARENTAL KNOWLEDGE OF HPV AND VACCINE ACCEPTABILITY IN SPAIN: RESULTS FROM KAPPAS SURVEY

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Background/Objectives: In Spain, HPV vaccine was introduced in the vaccination calendar in 2007. It targets 12-y.o. girls with VCR of 79.4%, and with important differences between regions. No studies to assess HPV knowledge and vaccine acceptability have been previously performed in our country. Our objective is to describe HPV knowledge and acceptability within parents of 9-14 y.o. children in Spain.

Methods: Cross-sectional survey study administered to parents of 9-14 y.o. children in 24 public and private clinics across Spain. Sample was stratified according to gender, age (9-11, 12-14); and VCR. To create the questionnaire, a systematic literature review was previously performed. Patients were randomly selected by strata from the database to avoid sampling bias. The primary endpoints on HPV knowledge and vaccine acceptance were based on the % patients that respond correctly to specific items included in the survey. In addition, composite variables based on the responses were created.

Results: 3,110 surveys were distributed. Of them, 1405 were included in the final analysis. Most of the respondents were 40-49 y.o. mothers. Only 27.8% of the children were vaccinated; and of them, 88% were girls. Most participants (90.7%) had heard about HPV and the most common source of information was the pediatrician (44.8%). HPV knowledge level was modest-high: 28.9 (SD=4.5); max score to be obtained was 40 and the min score was 0. 73.7% knew that HPV is related with cervical cancer, but this percentage is lower for other diseases: 55.44% for genital warts; 36.09% for penile cancer, or 23.77% for oral cavity cancer. 87.2% considered that HPV vaccine could prevent HPV infection and diseases. 92.1% had heard about HPV vaccine, with pediatricians being the most frequent source of information. 57.4% answered that HPV vaccine is included only for girls and 25.1% did not know if the HPV vaccine was included in the vaccination calendar. 71% considered that cervical cancer can be prevented with HPV vaccine and 17.7% were not sure about what diseases can be prevented with the vaccine. The overall degree of acceptance of HPV vaccine is high: 3.4 (SD=1.4) (min score to be obtained 0, max score 5), although is lower for boys vaccination. Main reasons to vaccinate was to protect against cancer and genital warts (77.4%). Main reasons to not to vaccinate were lack of information (27.9%), afraid of possible adverse events (20.9%) and other unspecified reasons (29.3%)

Conclusions: After 13 years of the introduction of HPV vaccine in Spain, vaccine acceptance is high, although parents still have lack of information that should be addressed, especially in terms of HPV consequences and vaccination in males.

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A PROSPECTIVE COHORT STUDY OF CERVICAL DYSPLASIA AND TIME-TO-PREGNANCY.

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Background/Objectives: BACKGROUND: About 15% of couples experience infertility and few risk factors are known. Genital infections with human papillomavirus (HPV) can lead to cervical dysplasia. The prevalence of HPV infection is 25% in Danish women <30 years.

Methods: METHODS: We investigated the association between cervical dysplasia and fecundability, defined as the probability of conceiving per menstrual cycle, in two Danish preconception cohorts. Participants completed a baseline questionnaire on sociodemographic, anthropometric and lifestyle factors, and reproductive and medical history. Bimonthly follow-up questionnaires obtained data on pregnancy status and date of last menstrual period. Data on cervical cytologies and biopsies were retrieved from The National Pathology Registry, which holds records of all cervical specimens examined in Denmark. Women were categorized based on their most severe diagnosis of cervical dysplasia within ten years before study entry. We included 9,523 women: 68.9% with normal cytology, 10.8% with mild dysplasia, 2.1% with moderate dysplasia, 5.4% with severe dysplasia, and 12.7% with other non-malignant cervical diagnoses. We computed fecundability ratios (FR) and 95% confidence intervals (CI) using a proportional probabilities regression model. Women contributed cycles from study entry until pregnancy, initiation of fertility treatment, loss to follow-up or end of follow-up (12 cycles) whichever came first. We adjusted for age at diagnosis, age at study entry, partner age, body mass index, smoking status, timing of intercourse, parity, vocational training, number of sexual partners and household income.

Results: RESULTS: Compared with normal cells, FRs for dysplasia were mild, 1.05 (95% CI 0.97-1.14); moderate, 0.97 (95% CI 0.81-1.17); and severe, 0.96 (95% CI 0.86-1.08). When stratifying by time since diagnosis the FRs for diagnosis <2 years before study entry were 0.72 (95% CI 0.51-1.01) for moderate dysplasia and 0.87 (95% CI 0.72-1.05) for severe dysplasia compared with normal cells.

Conclusions: CONCLUSION: Preliminary results indicate little overall association between severity of cervical dysplasia and fecundability, whereas there may be a slight reduction in fecundability for recent diagnosis of moderate dysplasia.