ASCCP2019 Annual Scientific Meeting on Anogenital and HPV-Related Diseases

April 4 – 7, 2019
Atlanta, GA

Late-Breaking Abstracts
HPV Screening and Management

Primary cervical screening with high-risk human papillomavirus testing: Evaluation of the English screening pilot

John Tidy1, Matejka Rebolj2, Karin Denton3, Henry Kitchener1, 1Gynecological Oncology, 2School of Cancer and Pharmaceutical Sciences, 3Department of Pathology

Objective: To report prevalence and incidence rounds of a large pilot of routine primary hrHPV testing, in comparison with primary liquid-based cytology (LBC) screening at six screening laboratories within the English Screening Programme.

Methods: Screening with hrHPV testing and LBC triage including two early recalls for hrHPV positive/cytology negative women following the national screening age and interval recommendations. Assessment of referral to colposcopy; adherence to early recall; detection of high-grade cervical intraepithelial neoplasia (CIN2+) of HR-HPV testing compared with LBC in two consecutive screening rounds.

Results: 578,547 women underwent cervical screening in primary care between May 2013 and December 2014, with follow-up until May 2017; 183,970 (32%) were screened with HR-HPV testing. Baseline HR-HPV testing and early recall required approximately 80% more colposcopies over two years, ORadj: 1.77 (1.73 to 1.82), but detected substantially more CIN than LBC: ORadj for CIN2+ 1.49 (95% CI: 1.43 to 1.55), for CIN3+ 1.44 (95% CI: 1.36 to 1.51) and for cervical cancer 1.27 (95% CI: 0.99 to 1.63). Attendance at early recall and colposcopy referral was 80% and 95%, respectively. Early recall contributed 25% of CIN2+ detected in the prevalent round. At the incidence screen, 33,506 women screened with HR-HPV testing had substantially less CIN3+ than 77,017 women screened with LBC: ORadj 0.14 (95% CI: 0.09 to 0.23).

Conclusions: In England, primary HR-HPV screening increased the detection of CIN3+ and cervical cancer by approximately 40 and 30%, respectively, compared to LBC. The changes to screening were practicable and acceptable to women. The very low incidence of CIN3+ after three years supports an extension of the screening interval.

Comparison of HPV positivity and viral load in self-collected vaginal samples and urine using four collection devices

Jack Cuzick1, Louise Cadman2, Caroline Reuter2, Michelle Kleeman2, Mark Jitlal2, Lesley Ashdown-Barr2, Janet Austin2, Anna Parberry3, Tony Hollingworth2, Attila Lorincz2, 1Centre for Cancer Prevention, Wolfson Institute of Preventive Medicine, 2Queen Mary University of London, 3Royal London Hospital

Objective: Comparison of hrHPV positivity rates and viral loads (VL) of self-collected vaginal samples collected by 4 devices and a urine sample.

Methods: Self-collected samples using 4 different collection devices (dry Copan Flocswab™ (DF), Wet Digene Female Collection Swab in STM medium (WD), dry Herswab™ (HS) and dry Qvintip® (QT)), and a first void urine sample (Colli-Pee™ device) in 600 women who had been referred to colposcopy for abnormal cytology were assayed for hrHPV by the Onclarity HPV test. Women took two vaginal samples with different devices in random order and 500 also provided a urine sample. HPV positivity rates and viral loads overall and in CIN2+ and CIN3+ were compared between the different devices and urine for 14 hrHPV types combined and individual types or pools of types in our labs in paired and unpaired analyses via Wilcoxon tests and Spearman rank correlations.

Results: No differences between the first and second sample were seen. Similar positivity rates and viral load were seen for DF, WD and Urine, but lower positivity was seen for QT and HS (Table). 43% of women were CIN2+ and similar differences were seen for this group and for CIN3+. A high correlation was seen between the viral loads between DF and WD (ρ = 0.81), but were lower for other comparisons (typically 0.6-0.7).

Conclusions: DF, WD and urine are good methods for HPV self-sampling, but QT and especially HS have lower detection rates.

Development and Application of an internet-facilitated cervical cancer screening model

Xinfeng Qu1, Yutao Du2, Zhang Lin2, Ruirfang Wu3, Hui Du3, Jerome Belinson1, Guozheng Hu2, Hongbao Du3. 1Preventive Oncology International, 2BGI-Shenzhen Co., Ltd, 3Peking University Shenzhen Hospital
Objective: Develop an internet-facilitated community-based participatory model for cervical cancer screening and evaluate the application of the model in a population-based screening event.

Methods: The internet system was developed to include a project-specific app to facilitate registration of thousands of women through mobile devices simultaneously and a general website linked with the app. The app first collected the registration data from the participants who desired to be screened, and then the website functioned to link the participants with an ID number and their self-collected samples. All women tested negative could search their results from the app via mobile devices. The website also facilitated test reports and data collection for managing those participants who tested positive. Multiple screening events were programed with each conducted by a team consisting of 3 community workers and 2 local doctors who were available to assist and answer questions in regard to the self-sampling. 3 distinct models: centralized screening, mobile community screening, and distributive screening were adopted. These refer to self-sampling at fixed hospital sites, self-sampling in communities organized by mobile teams, and home self-sampling with samplers distributed by community leaders.

Results: In total, 11 teams including 33 community workers and 22 local doctors screened 187,970 women in 29 days in downtown and rural Xinxiang, China, with only 0.05% uncorrectable errors. The largest number screened in one day was 14,890.

Conclusions: A well-designed internet system facilitates registration, data collection, ID-sample linking, and results reporting, which enables program planning, faster screening, and supports strategizing resource management.

Feasibility of a community based Cervical Cancer Screening strategy with Self-Collected HPV Testing in rural Africa

Joel Fokom Domgue1, Beatrice Futuh2, Calvin Ngalla2, Peter Kakute2, Florence Manjuh2, Simon Manga3, Kathleen Nulah2, Edith Welty2, Kathleen Schmeler1, Thomas Welty2.
1The University of Texas MD Anderson, 2Cameroon Baptist Convention Health Services, PO Box 1, Bamenda, North West Region, Cameroon, 3University of Massachusetts Boston

Objective: We examined the feasibility of a community based Cervical Cancer Screening strategy with Self-Collected HPV Testing and Follow-up Visual Inspection to Determine Treatment Modality in rural and remote villages in Cameroon.

Methods: In 2016, nurses of the Cameroon Baptist Convention Health Services (CBCHS) educated women in villages on cervical cancer prevention. At a follow-up visit, they explained to eligible women aged 30-65 how to self-collect vaginal specimens for HPV testing with the CareHPV assay in their local dialect. The cytobrush specimens were transported in coolers to a CBCHS laboratory for HPV testing. The nurses returned to villages to inform women of their results, examined HPV positive women in the primary health center using visual inspection with acetic acid and Lugol’s iodine (VIA/VILI) to guide treatment. Thermal coagulation was offered to all HPV positive patients, except those with LEEP-eligible lesions or with lesions suspicious for cancer, who were referred for appropriate treatment.

Results: Of the 1,270 eligible women screened by careHPV, 196 (15.4%) were HPV-positive. Only 60 (4.7%) had previously been screened for cervical cancer. Up to 185 HPV-positive women (94.4%) were examined, and 17 (9.2%) were VIA/VILI positive. Treatment consisted of thermo-coagulation in 161 women, LEEP in one woman, and hysterectomy in one woman for ICC (88.1% treatment rate). The cytobrushes broke off in the vagina of two women (removed in the village) and in the bladder of another (surgically removed).

Conclusions: Community based screening for cervical cancer with self-collected HPV tests is feasible in rural areas of Cameroon. Education on the proper sampling procedure and follow-up of women who are HPV positive is essential.

Innovative Technology

Introduction and Evaluation of A Simplest and Fastest Cervical Cancer Screening Technology for Resources Limited Area

Youxiang Wang1, Xin Chen1, Zhijie Yang1, Rong Wang1, Yu Zhao1. 1Atila BioSystems, Inc.

Objective: AmpFire HPV screening technology (isothermal amplification and real time fluorescent detection 15 high risk HPV and simultaneously genotypes HPV 16 and 18 in single tube reaction) is different from all others available on the market as it can detect HPV directly from raw samples without needing to extract DNA, which dramatically simplifies the detection process. Not only do you save time but also additional costs. It is simple and easily performed in a clinic setting, and is therefore well suited for Low Middle Income Countries to be a point-of-care HPV test. Objective: to evaluate the agreement of HPV detection between AmpFire HPV test and HC2 and their performance for HPV screening.

Methods: A total of 80 patients samples were studied (collected by Lehay Clinic). The AmpFire assay detects HPV virus by centrifuging 1ml ThinPrep sample solution, discharging the supernatant and then, the cell pellets were heat treated in a Atila lyse buffer for 10 minutes without
DNA extraction. 2ul lysed simple was mixed with reaction solution for real time fluorescent detection in an hour. HC2 detection was done by Lehay Clinic following manufacturer’s instruction.

**Results:** Comparing HPV results of Ampfire HPV to HC2, amount the 80 samples, 78 samples are agreed with each other (56 positive samples and 22 negative samples). The %OA is 97.5%. %PA was 98.2. %NA 95.5%.

**Conclusions:** The Ampfire HPV assay performed equally well as HC2. Ampfire HPV assay did not require DNA extraction with very simple sample process and yielded results rapidly within an hour.

**Underserved Populations (Transgender, Homeless, Native American, etc.)**

Exploring Cervical Cancer Screening Understanding and Adherence Among Masculine of Center Females

Shareene Lindquist1, Minh Ly Nguyen2, Dominique Jodry2, Lisa Haddad2, Laurie Gaydos3, Jason Schneider2, Lisa Flowers2, 1Santa Clara Valley Medical Center, 2Emory University School of Medicine, 3Emory University

**Objective:** Within the community of women of who have sex with women (WSW), masculine of center (MoC) females, broadly referring to lesbian/queer women and gender nonconforming/trans people who identify towards the masculine side of the spectrum, may have lower rates of engagement with sexual health services. Little is known, however, regarding their risk of developing cervical cancer. We sought to characterize cervical cancer risk factors, knowledge, and screening practices among MoC females.

**Methods:** An electronic version of a validated HPV Knowledge, Attitudes, and Practices (KAP) survey was distributed via social media by grassroots organizations that provide resources to MoC females. Inclusion criteria were age over 18, born with female genitalia and self-identification as MoC (n = 483).

**Results:** Respondents were predominantly young (84% between ages 21-39), highly educated (95%), and insured with access to a healthcare provider (92%). 97% had heard of HPV, but 30% did not know that HPV caused cervical cancer. Notably, nearly half (49.65%) reported intercourse with a male partner, but 56.09% did not perceive themselves to be at risk for cervical cancer. 63.45% reported current or past tobacco use. 20% of survey respondents did not have up-to-date cervical cancer screening (CCS).

**Conclusions:** Despite high educational levels and high levels of interaction with the healthcare system, knowledge about the role of HPV in CCS was surprisingly low, and CCS coverage was suboptimal in our survey population. More nuanced efforts are needed to educate MoC females about HPV and CCS recommendations.

**ASCCP2019 E-POSTERS**

**Cervical Cancer**

Cultured cervical cancer cell lines are susceptible to Zika virus-mediated lysis

Harini Krishnapura1, Kenneth Alexander2, Rajarajeshwari Venkataraman2, 1University of Central Florida, 2Nemours Children’s Hospital

**Objective:** Cervical cancer is the fourth most frequent cancer in women with an estimated 570,000 new cases in 2018 alone, which represents 6.6% of all female cancers. Treatment of advanced cervical cancer is often unsuccessful leading to high cancer-related mortality rates, especially in under-resourced countries. The aim of this study is to determine the permissiveness of cervical cancer cells to Zika virus infection and its association with cell surface glycoprotein CD24.

**Methods:** We assessed cytopathic effect (CPE) induced by Zika virus in cervical cancer cell lines (HeLa, SiHa and CaSki) by light microscopy and CellTox™ Green cytotoxicity assay. Expression of non-structural protein 1 (NS1) was used to measure viral replication. Since CD24 expression was found to be important for Zika virus infection in other cells, CD24 expression was assessed in cervical cancer cells.

**Results:** Cervical cancer cells were susceptible to Zika virus-induced lysis. Upon infection, the morphology of cervical cancer cells changed exhibiting Zika virus-induced cytopathic effect. Expression of Non-structural protein 1 (NS1) in cervical cancer cells post-infection revealed viral growth. Cervical cancer cells showed a low but measurable expression of CD24. The necessity of CD24 expression is now being assessed.

**Conclusions:** Cervical cancer cells are susceptible to Zika virus-mediated lysis and this opens the possibility for the use of Zika virus as a potential oncolytic therapy for cervical cancer.

Dissecting the recent decline in cervical cancer incidence among young women in the U.S.: vaccine, screening, or both?

Jacqueline Mix1, Elizabeth Van Dyne1, Mona Saraiya1, Jane Henley1, Cheryll Thomas1, Vicki Benard1, 1CDC

**Objective:** Human papillomavirus (HPV) vaccination and screening are effective methods to prevent cervical cancer.
In the U.S., routine HPV vaccination began in 2006, screening guidelines were revised during 2009-2012 to include later initiation and longer screening intervals, and screening rates declined among women aged 21-29 from 2005-2016. Cervical cancer incidence among women aged 15–39 years was examined to help determine the impact of these factors.

Methods: Data from U.S. Cancer Statistics covering 98% of the population during 1999–2015 were used to calculate incidence rates of invasive cervical squamous cell carcinoma (SCC) and adenocarcinoma (AC) among women aged 15–39 years, standardized to the 2000 U.S. population per 100,000 persons. Joinpoint regression was used to calculate the average annual percent change (AAPC) over the time interval by age group and histology.

Results: During 1999–2015, 36,553 SCC and 14,883 AC cases were reported. SCC incidence rates decreased significantly from 1999 to 2015 among all age groups: 15-20 (AAPC= -12.3%), 21-24 (AAPC= -4.1%), 25-29 (AAPC= -2.8%), 30-34 (AAPC= -2.4%), and 35-39 (AAPC= -1.8%). AC decreased significantly in women 21-24 years of age (AAPC= -3.6%), and increased significantly among women 35-39 (AAPC= 2.2%).

Conclusions: SCC incidence declined among all age groups, suggesting later screening initiation did not increase incidence rates in women aged ≤40. Increasing trends of AC in women aged 35-39 may reflect increased detection from HPV co-testing. The largest declines of SCC and AC were observed in women aged 15-20. Whether this indicates HPV vaccine impact requires further study.

National Program of Cancer Registries (NPCR) Surveillance of Cervical Cancer Precursors in Four U.S. Cancer Registries

Paran Pordell1, Virginia Senkomago1, Jean Shapiro1, 2CDC

Objective: Objective: To examine the feasibility of collecting population-based data on advanced cervical cancer precursor lesions through the National Program of Cancer Registries (NPCR).

Methods: Methods: Funded by the Centers for Disease Control and Prevention, cancer registries in Kentucky, Louisiana, Michigan, and Puerto Rico are collecting cervical precancer data, and as of January 1, 2019, these registries will implement a new case definition for high-grade cervical precancers, which aligns with the Lower Anogenital Squamous Terminology (LAST) classifications. Registries will collect data on high grade lesions using the two-tiered LAST classification of low and high-grade squamous intraepithelial lesion (LSIL, HSIL) in addition to collecting data on lesions classified as cervical intraepithelial neoplasia III (CIN III), adenocarcinoma in situ (AIS), carcinoma in situ (CIS), and severe dysplasia.

Results: Results: The addition of terms such as HSIL, combined with CIN III, will influence the number of cases detected via submission of pathology reports to central cancer registries. Louisiana completed an audit in 2018 comparing data collection using the CIN III terminology with the addition of HSIL terminology and found that the LAST terminology picked up an additional 42% of reportable, advanced cervical cancer precursor cases.

Conclusions: Conclusions: In order to capture all advanced pre-invasive cervical cancer cases, data on HSIL could be collected in addition to data on CIN III. Population-based surveillance of cervical cancer precursors may provide critical information about the cervical cancer disease burden and extent of HPV vaccine uptake across the US.

Colposcopy

Assessing patient experience and sense of reassurance after having colposcopy with the DYSIS digital colposcope

Emmanouil Papagiannakis2, Audrey Arona1, Peter Khamvongsa3, 1Preferred Womens Healthcare, 2DYSIS Medical, 3The Miami Institute of Urogynecology and Robotic Surgery

Objective: Technology could help make colposcopy, sometimes intimidating procedure, more patient-friendly. This survey assessed the experience of women undergoing colposcopy with a digital colposcope (DYSIS, DYSIS Medical, Edinburgh, UK) that provides a color-coded map of cervical acetowhiteness and digital tools to educate patients through a dedicated video monitor.

Methods: Two questionnaires were used at six private community-based clinics in the US; one for patients with, and one for patients without, prior colposcopy experience. Responses were between 1-10, grading anxiety before/during/after colposcopy, perception of duration, feedback on device and map, and whether it would be a colposcope-of-choice. Results are reported as median scores (MS).

Results: Patients having their first colposcopy (n=305), thought that colposcopy with DYSIS didn’t last much longer than their pap-test (median score 5); patients with prior colposcopy (n=210) felt that their DYSIS examination didn’t take longer than their previous one (MS=1). The self-reported level of anxiety, for all patients, dropped considerably after the examination. All patients reported that they understood the color-coded map (MS=8&9) and found that seeing it was reassuring (MS=9&9). Patients with prior colposcopy, declared they preferred having it with DYSIS (MS=10). All patients reported that they preferred DYSIS for future colposcopies (MS=10&10) and

Page 4 of 12
would recommend it to family/friends requiring colposcopy (MS=10&10). Results were consistent across clinics.

**Conclusions:** Patients received their colposcopy with DYSIS well. Our data suggest that their overall experience improved, and that digital imaging and mapping helped them understand their condition better. This could help reduce non-attendance rates at colposcopy clinics.

Detection of cervical intraepithelial neoplasia (CIN) by electrical impedance spectroscopy (EIS) in hrHPV positive women

**John Tidy**¹, **Brian Brown**². ¹Gynecological Oncology, ²Sheffield Teaching Hospitals

**Objective:** To establish the performance of colposcopy with EIS (ZedScan) to detect CIN2+ in women with hrHPV +ve/cytology -ve referrals to colposcopy.

**Methods:** A prospective cohort study of women undergoing both colposcopic and ZedScan examination for investigation of a persistent high-risk HPV infection with negative cervical cytology result at a single colposcopy clinic. Partial HPV genotyping was performed using Roche Cobas 4800 on the screening sample prior to referral to colposcopy. ZedScan detects changes in tissue electrical impedance which are independent of aceto-white change.

**Results:** 315 women were referred with positive hrHPV but cytology negative screening results. 117 (37.1%) had HPV16 either alone, with HPV18 or other hrHPV(O) genotypes, 43 (13.7%) had HPV18 alone or with HPV0. 155 (49.2%) had HPVO. 132 women underwent biopsy with 130 having a single biopsy. 38 women (12.1%) were found to have HGCIN. Compared to colposcopic impression (CI>CIN1) alone, the use of EIS increased detection of HGCIN by 81%. 34 cases of high-grade disease (CIN2+) were detected only by a positive ZedScan result compared to 17 detected by CI alone. The PPV (CIN2+) for biopsies with CI>CIN1 and positive ZedScan was 47.2%. The PPV of biopsies with ZedScan alone was 28.5%. The NPV for colposcopy with ZedScan was 97.9%.

**Conclusions:** EIS identifies more high grade CIN than colposcopy alone. The performance of colposcopy for detection of CIN (PPV) in cytology negative referrals is reduced because of the low prevalence of disease. ZedScan identified 89.5% of HGCIN cases compared with 44.7% for colposcopy.

Investigation and analysis of HPV infection status in patients with colposcopy from 2013 to 2017

**Fei Chen**¹, **Huiying Hu**¹. ¹Peking Union Medical College Hospital

**Objective:** To investigate HPV infection and test status of patients with colposcopy at Peking Union Medical College Hospital (PUMCH).

**Methods:** To collect the general information and HPV test data of patients with colposcopy at PUMCH from January 2013 to May 2017, follow up colposcopy pathology results. The date were analyzed in SPSS 19.0 and Excel 2007.

**Results:** A total of 5,831 colposcopy clinic patients were included in this study, ranging in age from 18 to 88 years with a mean age of (40.9 ± 10.5) years. There were 4,532 HPV positive tests and the HPV positive rate was 94.3%. From 2013 to 2017, the proportion of HPV testing in patients with colposcopy was 69.6%, 94.5%, 94.6%, 97.4% and 82.7%, respectively. The proportion of HPV subtype detection in HPV testing was 24.7%, 35.8%, 50.7%, 73.7% and 88.2%, respectively. Among the patients with colposcopy pathology, the positive rates of HPV 16 were 34.9% in pathological negative group, 32.0% in CIN1 group, 48.5% in CIN2 group, 65.7% in CIN3 group and 64.6% in invasive cervical cancer group.

**Conclusions:** HPV detection rate in colposcopy clinics is on the rise in recent years, and the proportion of subtype detection methods also increases year by year. HPV infection in patients with colposcopy clinics was significantly higher than the general population and gynecological clinic patients. High-risk HPV type 16 infection is the most common type of infection in all cervical disorders, and its infection rate increases with the degree of cervical lesions.

**HPV Diseases**

A Phase II Study of Immunotherapy with Gene-Engineered E7 T cells for Vulvar High-Grade Squamous Intraepithelial Lesions

**Scott Norberg**¹, **Nisha Nagarsheth**¹, **Nikolaos Gkitsas**², **Steven Highfill**², **Christian Hinrichs**¹. ¹National Cancer Institute, ²NIH Clinical Center

**Objective:** Adoptive T cell therapy with gene-engineered T cells is an emerging cancer treatment strategy. Clinical trials using gene-engineered T cells targeting HPV16 E7 have resulted in regression of HPV-associated epithelial cancers. A phase II clinical trial using gene-engineered autologous T cells targeting HPV16 E7 (E7 T cells) to treat patients with HPV-associated vulvar high-grade intraepithelial lesions (HSIL) will test whether this therapy can cause regression of a premalignant condition driven by chronic HPV infection.

**Methods:** This is a single center, phase II clinical trial of gene-engineered E7 T cells. Treatment consists of a one-time infusion of 1 x 10ⁱ¹ autologous T cells gene-engineered to express an HLA-A*02:01-restricted T-cell receptor that
targets HPV-16 E7. Eligible patients have recurrent HPV16-associated vulvar HSIL in which further surgery would result in disfigurement or functional impairment.

**Results:** We have recently completed a phase I clinical trial of gene-engineered E7 T cells for patients with metastatic HPV16-associated cancers. Twelve patients were treated. Six patients experienced objective responses. The maximum tested dose was tolerated and will be used in this phase II trial. E7 T cell cross-reactivity against healthy tissue was not identified. Cytokine-release syndrome was not observed. These findings support the study of E7 T cells for other HPV-associated conditions.

**Conclusions:** Tumor regression can occur following treatment of an HPV-associated cancer with gene-engineered T cells. A new clinical trial will test this therapy in HPV-associated vulvar HSIL.

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**HPV Screening and Management**

Correlation between integration of hr-hpv, detected by molecular combing, and the severity/outcome of cervical lesions.

Florence Mahé¹, Stéphanie Bouchilloux¹, Frederic Fer¹, Vladimir Dvorak², Simona Kubickova³, Pavel Venturba³, Ruth Tachezy⁴, Market Trmkova⁵, Aaron Bensimon¹.
¹Genomic Vision, ²Center of gynecology and primary care, ³Gynecological and Obstetrics clinic, ⁴NRL for Papillomaviruses and polyomaviruses, IHBT, ⁵Aeskulab Pathology

**Objective:** The aim of the EXPL-HPV-002 study is to evaluate the integration of 14 high-risk HPV as a biomarker of the severity and the progression of cervical lesions. Such a «triage biomarker» would help to reduce the number of unnecessary coloscopies, to avoid over-treatment of lesions that spontaneously regress and to better target the lesions requiring treatment.

**Methods:** EXPL-HPV-002 is a prospective study conducted in 2 clinical sites in Czech Republic. 688 patients aged 25-65, referred to colposcopy after an abnormal Pap-smear, were enrolled in the study. Among them 60% were found HPV high-risk. The study is divided in 2 phases: 1) a cross-sectional phase using data collected at first visit (colposcopy images +/- histology, pap-smear for HPV genotyping and molecular combing) to study the association between HPV integration status versus colposcopy and histology grades. 2) a longitudinal phase using data collected in follow-up visits: cytology at 6, 18 and 30 months and colposcopy +/- histology at 12, 24 and 36 months. A pap-smear collected at 12, 24 and 36 months allows to perform genotyping and molecular combing. HPV integration status is analyzed in comparison with the evolution of lesions, viral clearance and HPV genotype.

**Results:** HPV integration level measurement by molecular combing can differentiate normal subjects from women with a risk to exhibit precancerous cervical lesions or cancer. Preliminary results of the longitudinal phase are very encouraging.

**Conclusions:** HPV integration monitored by Genomic Vision’s technology is a reliable diagnostic biomarker. Prognostic value validation is also in progress.

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**Does Equal Management for Equal Risks Apply to Low-Income Women served by CDC’s Program 2009-2017**

Mona Saraiya¹, Li Cheung², Ashwini Soman¹, Jacqueline Mix³, Kristy Kenney⁴, Nicolas Wentzensen², Mark Schiffman¹, Jaqueline Miller¹, ¹CDC, ²NCI

**Objective:** The American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines use the principle of equal management for equal risk to determine management after an abnormal screening result. However, the data source to assess risk comes from a large integrated health care delivery system that may not apply to low-income women.

**Methods:** Using data from a cohort of approximately 360,000 low-income women ages 30-64 from CDC’s National Breast and Early Detection Program from 2009 to 2017, we estimated the prevalent risks of CIN3+ (cervical intraepithelial neoplasia grade 3 or higher) among women who had abnormal HPV and Pap test results. We stratified these risks by screening history in past 5 years (yes/no) and compared these risks to that of women ages 30-65 from an integrated healthcare data. We focused our results on women who had a combination of tests that required immediate colposcopy such as ASC-US/HPV+ and LSIL/HPV+.

**Results:** Among women with an ASC-US/HPV+, the prevalent CIN3+ risk was 6.6% if not screened in past 5 years or 4.6% if screened within the past 5 years (vs. 3.8% for integrated health system). Among women who were HPV+/LSIL, the prevalent risk for CIN3+ was 5.3% if not screened in past 5 years and 4.1% if they were screened in the past 5 years (vs. 3.7% for integrated health system).

**Conclusions:** While the risks of CIN3+ in managed care populations may be similar to that of screened women in low-income, women without up-to-date screening may have greater prevalent risks of CIN3+.

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**Effect of a Coriolus Versicolor-Based Vaginal Gel in a High-Risk HPV Infected Patients. Results of Different Studies.**

Gilles Seydoux², Javier Cortes¹, Damián Dexeus³, Santiago Palacios⁴, Luis Serrano⁵, Elena Marin⁶, Clara Gajino⁷,
Objective: A new multi-ingredient non-hormonal Coriolus versicolor-based vaginal gel has been recently commercialized in Europe to prevent and treat the HPV-dependent low-grade cervical lesions. Evaluate the consistency of the effect of this gel in patients infected with high-risk HPV.

Methods: Results from 3 independent observational non-comparative studies carried out in 3 different centers of Spain and preliminary results of 1 clinical trial were evaluated. One of them was prospective (Vigo study) and the other two were retrospective (Coruña and Hospitalet studies). Vigo study: HPV clearance at 6 months of 25 patients infected by HPV 16 and/or 18 older than 24 years was evaluated as a secondary endpoint. Coruña study: A total of 57 medical records of patients with high-risk HPV (mean age 38.4 years) were analyzed. HPV clearance at 6 months was evaluated as primary endpoint. Hospitalet study: Data of 91 high-risk HP patients between 20 and 65 years. Primary endpoint: composite efficacy variable consists of percentage of patients with normal cytology and/or HPV clearance at 6 months Patients were treated at recommended dose of vaginal gel: 1 cannula/day for 1 month + 1 cannula/alternate days for 5 months (except menstrual days).

Results: After the 6 month-period of treatment, 48% of HPV 16-18 infected patients have cleared (Vigo study), reduction of 58% was observed in number of high-risk positive HPV patients (Coruña study) and 72.5% of patients negativized cytology and/or cleared HPV (Hospitalet study) vs baseline (p<0.0001 for all results, Chi-square). These results are consistent among them and with 3 months preliminary results of a phase II B RCT, randomized, open, parallel comparing the Coriolus-based vaginal gel vs wait and see approach. (Figure 1)

Conclusions: Use of Coriolus-versicolor vaginal gel in clinical practice shows a significant and consistent benefit in high-risk HPV clearance. Data of further observational studies and clinical trials should confirm these exciting results.

The effect of lubricant on the adequacy of cervical cytology specimens

Megan Lander1, Kristina Feldman1, Barry Perlman1, Debra Heller1, Adanna Ukuazu1, Bernadette Cracchiolo1, Mark Einstein1, Jenna Marcus1. 1Rutgers/New Jersey Medical School

Objective: The effects of lubricant on adequacy of cervical cytology has been previously evaluated with inconclusive results. Here, we evaluate the effect of prospectively changing surgical lubricant on cervical cytology adequacy rates and elucidate risk factors associated with an unsatisfactory cytology result.

Methods: We evaluated the effect of change to non-carbomer containing lubricant in a prospectively followed cohort of consecutive women who had cervical cytology. From January to December 2017, a retrospective chart review was performed examining patient cervical cytology results from all OB/GYN patients at a large public hospital system. Rate ratios were calculated as proportions and univariate analysis was performed with chi-square analysis.

Results: Data was collected from 957 patients, 670 underwent cervical cytology prior to lubricant change and 287 after lubricant change. After change in lubricant there
was a significant decline in rates of unsatisfactory pap from 9.6% to 4.5%, p=0.008. There were no differences in age (41.5 vs. 41.0), BMI (30.2 vs. 29.6), HPV status (negative 8.2% vs. 11.5%; positive 6.7% vs. 6.6%) or specimen type (cervical 96.0% vs. 98.6%; vaginal 4.0% vs. 1.4%) between the two groups.

**Conclusions:** Change in use from a carborber containing to non-carborber containing lubricant was associated with a statistically significant decline in the rates of unsatisfactory cervical cytology. Although prior data has had mixed results as to the etiology of unsatisfactory cytology, we feel that this directly contributed to the high rates observed at our institution and should be considered as a quality issue as cytology laboratories review unsatisfactory Pap rates.

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**Thermo-ablation vs. Cryo for the treatment of cervical pre-cancers**

Lyufang Duan1, Hui Du1, Zhihong Liu1, Ai MIN Xiao1, Shuangyan Liu1, Liwei Zhao1, Chun Wang1, Xinfeng Qu2, Jerome Belinson2, Ruifang Wu1. 1Peking University Shenzhen Hospital, 2Preventive Oncology International

**Objective:** Evaluate the effectiveness of thermo-ablation for the treatment of high grade CIN.

**Methods:** Patients were recruited with CIN2/3, May 2017 to May 2018. They were randomized into 2 treatment groups (T or C) using either Liger UH-100 (1-4 applications) or cryotherapy with MedGyn (max. 2 applications). Follow-up was conducted with cytology and Cobas4800 HPV at 4 and 8 months after treatment. At follow-up, Colpo/biopsy was conducted on patients HPV positive and/or cytology ≥ASCUS.

**Results:** patients randomized. 4 from the cryo arm, were referred for thermo-ablation due to large lesions uncoverable with the 19mm cryo-probe; therefore 74 (55 CIN2s & 19 CIN3s) were randomized to be treated with thermo-ablation and 71 (60 CIN2s & 11 CIN3s) with cryo-therapy. The 4/8-month follow-ups showed no difference between therapies (T vs. C) in rates of HPV clearance and negative pathology (4 mos. T/C - 72.5%/86.2% vs. 68.6%/80.6% and 8 mos.- T/C 97.1%/98.5%vs. 94.3%/92.3%, P>0.05). The cytology normal rate of thermo-group was the same as the cryo-group at 4-month follow-up (79.7% vs. 78.9%, P>0.05) but higher than cryo-group (100% vs. 88.7%, P<0.05) at 8-month follow-up. The four referral patients who were thermo-ablated were negative at follow-up. Compared with cryotherapy, thermo-ablation had shorter duration and smaller volume of post-therapy discharge but scaled higher pain during application and more bleeding reported after treatment.

**Conclusions:** Thermo-ablation with Liger UH-100 is as effective and safe as cryotherapy. We found it easier to use and it avoids the need for treatment gases such as nitrous or CO2.

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**Adherence to Guidelines for Management of Cytology Negative Human Papilloma Virus Positive Screening Pap Tests**

Hany Eraqi1, Elie Mulhem1, Badrea Elder1. 1Beaumont Medical Center

**Objective:** To evaluate adherence to the American Society for Colposcopy and Cervical Pathology guidelines when managing cytology negative, Human Papilloma Virus (HPV) positive screening Pap tests (Paps) in women 30-65 years of age.

**Methods:** We performed a retrospective review of Pap tests performed in 2016 on women 30-65 years of age. Paps were excluded if the patient had previous abnormal Paps or colposcopies. For the HPV-other group, we defined adherence as a follow-up Pap within 12-24 months after the index Pap. For the HPV 16 or 18 group, we defined adherence as a colposcopy before Pap within 12 months of the index Pap.

**Results:** After excluding diagnostic Paps, 1626 were included, 1269 with positive HPV-other and 357 with positive HPV 16 or 18. In the HPV-other group, 779 (61.4%) had documented follow up; of those 635 (81.5%) were adherent to guidelines, and 144 (18.5%) were non-adherent because they had a repeat Pap (12.5%) or colposcopy (6%) at ≤ 11 months follow up. In the positive HPV 16 or 18 group, 267 (74.8%) had documented follow up; of those, 175 (70.4%) were adherent, and 79 (29.6%) had Paps for follow up and were considered non-adherent.

**Conclusions:** Adherence to guidelines in the positive HPV-other group was high in our institution with over 81% of providers having used a Pap test for follow up. We found less adherence in the HPV 16 or 18 group where almost 30% of cases were followed with a Pap test instead of a colposcopy.

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**HPV Vaccination**

**Human Papillomavirus Vaccinations in Singapore: Have we improved?**

Ida Ismail-Pratt1, Judith Ong1, Li Min Lim1. 1National University Hospital, Singapore

**Objective:** Human papillomavirus (HPV) vaccination plays a crucial role in cervical cancer prevention. Singapore does not have an HPV school vaccination programme. However, vaccination provision has been available in our institution since 2013.

**Methods:** This is a retrospective comparative study of women who underwent HPV vaccination in the
gynaecology department in a tertiary institution in Singapore over 2 time periods; years 2013-2015 and years 2016-2017. Data of participants including age, sexual activity at start of vaccination, history of abnormal cervical smear and vaccination completion have been attained.

Results: Between the years 2013-2015 and 2016-2017, the number of women between 9 to 26 years of age eligible for the HPV vaccine attending for various other gynaecological reasons was 7835 and 5252 respectively. Out of these, 362 (4.2%) and 231 (4.3%) received HPV vaccinations over these time periods. 62.9% of those vaccinated were aged 26 years and below over years 2013-2015, which improved to 65.8% in the years 2016-2017. Previously, 42.5% of the vaccinated population was virgo intacta, this has increased to 50% between 2016-2017. 92% of the population completed the entire vaccination schedule in 2016-2017, compared to 44% in 2013-2015. 32% of women had abnormal cervical smears prior to the start of the vaccination schedule, in contrast to 8% previously.

Conclusions: In recent years, the percentage of vaccinations for those 26 years of age and below or virgo intacta have improved in our centre. The higher percentage of women with abnormal cervical smears receiving the vaccine likely reflects the active counselling for post treatment HPV vaccination. Vaccination completion rate has increased tremendously. As HPV vaccination is purely opportunistic, only 4% of women aged 9-26 years from our institution have been vaccinated. A school based HPV vaccination programme remains pertinent for optimal protection against cervical cancer in Singapore.

Variations in knowledge and beliefs about HPV vaccine’s effectiveness for cervical cancer prevention among US women

Joel Fokom Domgue1, Onyema Chido-Amajuoyi1, Robert Yu2, Sanjay Shete3, 1Department of Epidemiology, The University of Texas MD Anderson Cancer Center, Houston, Texas, 2Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, Texas, 3Departments of Epidemiology and Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, Texas

Objective: We assessed socio-demographic, health-related and behavioral variations in knowledge and beliefs about the successfullness of HPV vaccine in preventing cervical cancer (CC), among US adult women.

Methods: Data from the Health Information National Trends Survey 5 Cycle 1 (January – May 2017) were analyzed for 1,851 female respondents aged 18 years and older, using weighted multinomial logistic regression. The study outcome was assessed with the question: “In your opinion, how successful is HPV vaccine at preventing cervical cancer?”, which was recoded into 3 categories (successful/don’t know/not successful).

Results: Overall, 29.8% of eligible respondents believed that HPV vaccine is successful at preventing CC. Nearly two thirds (63.6%) had no knowledge on the successfullness of HPV vaccine in preventing CC, while 6.6% believed it is not successful. Non-Hispanic Blacks (NHBs) (aOR: 1.72; 95% CI: 1.06 – 2.78), women aged between 35 and 49 years (2.17 (1.19 – 3.96)) and those unaware of a family history of cancer (5.07 (1.49 – 17.27)), were more likely to not know whether HPV vaccine prevents CC. Women with a College/Postgraduate degree (0.48 (0.27 – 0.86)), and those advised by a healthcare provider to get HPV shot (0.56 (0.32 – 0.97)) were less likely to not know that HPV vaccine prevents CC. Women aged ≥ 65 years (0.10 (0.02 – 0.44)), those who were divorced, separated or widowed (0.33 (0.14 – 0.77)), and those with a household income ≥ $75,000 (0.37 (0.14 – 0.97)) were less likely to believe that HPV vaccine is not successful at preventing CC.

Conclusions: Findings from our study demonstrate significant knowledge gaps on the role of HPV vaccine in preventing CC. To foster improvements in HPV vaccine uptake and reduce disparities in cervical cancer burden in the US, future interventions should incorporate educational programs, particularly targeting NHBs, under-educated and lower income women.

Innovative Teaching

Comparison of 3 colposcopy training simulator for effective training in cervical cancer prevention

Ida Ismail-Pratt1, Jieying Mandi Lee1, Wai Tung Eason Chow1, Sai Ming Raymond Hon2, Joseph Ng1, Jeffrey Low1, Ilancheran Arunachalam1, 1National University Hospital, 2National University Singapore

Objective: Cervical cancer is preventable by successfully treating the preinvasive stage. Training should focus on acquiring procedural skills and ensuring good clinical outcome i.e. complete removal of disease with minimal risk to women. Current available colposcopy simulators focus mainly on acquiring skills. We designed a colposcopy simulator that can meet these 2 desired goals.

Methods: This is a randomized control clinical trial designed to study outcomes of LLETZ training using three simulators. Main outcomes measured were skill acquisition (OSATS) and ability to produce an optimal LLETZ specimen. The study participants are Year 5 medical students who have completed their obstetrics & gynaecology attachment and experienced practitioners who have completed at least 2 LLETZ on a patient. Study participants were allocated equally to the three models; Plastic cup model; Toilet roll model and NUH/NUS model.
Each session was identical except for the order of interventions. Statistical analysis were done using SPSS. An outcome was considered statistically significance if $P < 0.05$.

**Results:** There was no significant difference in skill acquisition for novice group between the three simulators (OSATS scores, $P > 0.05$). In terms of acquiring free margin for specimen, there are significant difference between experienced practitioners and novice ($P<0.01$), and between the models ($P<0.01$) for both groups. Novices have a significantly shallower cut with all models and fail to remove the entire lesion to meet the standard of at least 0.7 mm depth. With the new colposcopy simulator however, novices produces significantly better specimen comparable to specimen produced by the experienced participants.

**Conclusions:** The NUH/NUS simulator shows the ability to provide training in skill acquisition and optimal LLETZ specimen compared to other published model.

## Innovative Technology

### Acceptability of intravaginal curcumin: a qualitative study

Brittany Manobianco$^1$, Dominique Jodry$^1$, Ashley Urrutia$^1$, Paula Frew$^2$, Damaris Henderson$^3$, Rachel Farrah-Abraham$^1$, Lisa Flowers$^1$, 1Emory University School of Medicine, 2University of Nevada-Las Vegas, 3SisterLove Inc.

**Objective:** This study sought to gain a deeper understanding of patients’ attitudes towards an intravaginal treatment for cervical intraepithelial neoplasia. This study also examined clinical trial participation and protocol adherence in a population comprised largely of women of color and of lower socioeconomic status, a population historically underrepresented in clinical trial research.

**Methods:** Data for this qualitative study were collected through a focus group. Participants were recruited to participate in the group after their completion of a 12-week protocol utilizing intravaginal administration of the study drug. Prior to the focus group, participants filled out a study diary/medication log, and completed a brief questionnaire on their use of the study drug.

**Results:** Six women participated in the focus group, and seven filled out the acceptability questionnaire. Themes from the focus group highlighted the importance of tangible motivators in protocol adherence, including positive feedback in the form of visual and/or verbal affirmation that the study protocol was resulting in improvement. In-spite of a rigorous dosing protocol and difficulties with physical characteristics of the treatment, participants were motivated by active engagement in the treatment process. A third theme was overall satisfaction with clinical trial participation, despite some difficulties with protocol adherence.

**Conclusions:** Findings from this study allude to important characteristics of research protocol design as well as clinician-patient dynamic that may improve medication adherence, especially among demanding medication protocols among populations historically underrepresented in clinical research. Overall protocol satisfaction and adherence were high in this study, suggesting a future market potential for the treatment should it prove efficacious.

### Automated cervicography using a machine learning classifier

Jonah Mink$^1$, Sung Rim Kim$^2$, Sung Wook Song$^3$, So Young Kwon$^4$, Jung Yeon Kim$^5$, Ronen Nissim$^1$, David Levitz$^6$, Kim Jiyoun$^6$, 1MobileODT, 2Dr. Kim ob/gyn clinic, 3Roen ob/gyn clinic, 4Riz ob/gyn clinic, 5Jin ob/gyn clinic, 6Y-QUEEN WOMAN CLINIC

**Objective:** To evaluate the programmatic and clinical feasibility of automated cervicography review by a machine learning (ML) system as an augmentation to standard of care cervicography.

**Methods:** An ML classifier was developed from an existing image set from 1473 colposcopy patients (80% training, 20% validation). The built classifier assigns a quality score to each image. Annotations by two colposcopy experts were used as ground truth. The classifier was then integrated into a web service feature called from the image portal storing patient images and test results. The feature evaluates all images from the selected procedure, and provides both an automated impression and targeted feedback. This feature was piloted in a network of seven clinics in Korea, where combined cervicography and cytology are the screening standard of care. The results of the classifier were used to counsel patients on risk in order to improve loss to follow-up for high risk cases.

**Results:** The ML classifier developed had an area under the (ROC) curve (AUC) of 0.93. The quality score and classifier output were almost completely uncorrelated ($r=0.019$), meaning that the classifier analyzed entirely different features. The Korea pilot is the first ML algorithm on cervical images tested in a clinical setting. To date, 343 patients were enrolled, with provider utilization at 100%. Enrollment is ongoing for another nine weeks. Biopsy results for further analysis are pending.

**Conclusions:** Preliminary results show widespread acceptance of AI at the point of care, and highlight potential to improve care and reduce costs related to cervical cancer screening.
Human Uterine Cervix-On-A-Chip: The First In Vitro Model to Study HPV Infection and Mechanism of Action

Gilles Seydoux¹, DANIAL KHORSANDI¹, Santiago Palacios², Yann Gaslain¹, Josep Combalia¹, Carine Emsellem¹. ¹Procare Health, ²Instituto Palacios de Salud y Medicina de la Mujer

**Objective:** The objective of this study was to develop a microfluidic ‘uterine cervix-on-a-chip’ platform that lets the cultured cells to take characteristic positions similar to those observed in native human uterine cervix. This platform would be able to be used as an in vitro model to study the transformation zone of cervix during Human Papilloma virus (HPV) infection and cervical cancer developing.

**Methods:** A microfluidic device prepared by demolding cured polydimethylsiloxane (PDMS). On the chip, we carried out cell culture and co-culture of ectocervical epithelial cells (Ect1/E6E7) and endocervical epithelial cells (End1/E6E7) cell lines. Endocervix epithelial cell has been marked by AAV-GFP control viruses to provide a convenient way to measure transduction efficiency into endocervix cells via fluorescence and to differentiate them from ectocervix epithelial cells. Numbers of experiments have been designed to check the functionality of the chip, such as live/dead assay, prestoBlue cell viability, 2D migration of cells (scratch tests) and 3D migration of cells using 3D printers.

**Results:** We found that both cell lines can grow from both sides of the chip to reach each other in order to make the transformation zone and prepare the squamo-columnar junction. This multilayer-cell junction contains both types of epithelial cells and can mimic the transformation zone of cervix practically.

**Conclusions:** Uterine cervix-on-a-chip may provide a powerful alternative in vitro model for studies on uterine physiology, real-time, high-resolution imaging, and analysis of biological responses in the cervix, as well as drug development. This established uterine cervix-on-a-chip is simple, effective, and easy to operate. It is expected to have important applications in personalized treatment of HPV infection lesions and cervical cancer and to play a potential role in other clinical treatments and tissue engineering.

**Near-histologic resolution images of cervical dysplasia obtained with Gabor domain optical coherence microscopy**

Rachel O'Connell¹, Tamera Paczos¹, Adrienne Bonham¹, Cristina Canavesi², Jannick Rolland¹. ¹University of Rochester, ²LighTopTech Corp

**Objective:** To determine the activity and safety of integrated treatment with antimicrobials and holistic oral turmeric extract in women with cervical Low Grade Squamous Intraepithelial Lesions (LSIL) in Papanicolaou smears and colposcopy.

**Methods:** This pilot study is conducted in women from the routine cervical cancer screening program after informed consent and the inclusion/exclusion criteria. Participants are given an antibiotic kit for associated genital infections. Then they are given standardised oral extract of turmeric (Haldone®600 mg BD) for 10 weeks. End points are Pap smears and colposcopy at 4-6, and 10-12 weeks. Safety is assessed by history, examination, blood chemistry, organ function tests, bleeding and clotting time, urine examination, and post-therapy monthly follow up for 2 years. Manual micrometry was carried out in 25 worst cells from 5 fields in Pap smears from 17 cases.

**Results:** Out of 21 cases enrolled till 2018 end, 4 discontinued due to local genital symptoms, and 2 for unrelated reasons. Seventeen cases took treatment for 4-10 weeks 16 showed regression in Pap smear whilst 1 case had persistent LSIL. Five cases showed Grade 1 abnormality (Cervical Intraepithelial Neoplasia or CIN1) in colposcopy initially with improvement in 4 cases. None had any other significant clinical or biochemical side effect. Manual micrometry showed significant reduction in mean nuclear diameters (p<0.03) & N/C ratios (p<0.01) after treatment; paired t test.

**Conclusions:** This conservative non-invasive integrated therapy for 10 weeks appears to be promising and deserves further evaluation in countries with paucity of trained health personnel.

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**Integrated treatment with antimicrobials and oral turmeric extract for women with cervical LSIL in Pap smears**

Jayashree Joshi¹, Sujata Jagtap², Neerja Rastogi¹, Priya Walwatkar¹, Nutan Nabar¹, Lal Hingorani¹, Ashok Vaidya¹. ¹Kasturba Health Society's MRC, ²Ayurvediya Prasarak Mandal’s Ayurved Mahavidyalaya College, ³Pharmanza Herbals Pvt.Ltd.
for biopsy-proven cervical dysplasia. Freshly excised LEEP specimens were imaged with the GDOCM device at several regions of interest. After imaging, the samples underwent routine histopathology evaluation.

**Results:** Thirty-four images were obtained from five patients. Standard histopathologic features of cervical dysplasia could be observed in GDOCM images. The cervical epithelium, cervical stroma, and basement membrane could be clearly identified on images. Blood vessels, endocervical glands, and HPV effects such as vacuolization could also be identified.

**Conclusions:** This foundational feasibility study demonstrates that GDOCM can be used to obtain near-histologic resolution images of the cervix. While histopathology remains the gold standard, GDOCM offers the potential to noninvasively evaluate the cervical epithelium at the cellular level in real time. This work has established a foundation for a future, larger diagnostic accuracy study that could lead to *in vivo* GDOCM-guided colposcopy.

**Underserved Populations (Transgender, Homeless, Native American, etc.)**

**Trends in referral and management of abnormal pap smears in minority women at an academic colposcopy clinic**

Sarah Feldman¹, Stephanie Alimena¹, Beryl Manning-Geist¹, Allison Vitonis¹. ¹Brigham and Women's Hospital

**Objective:** To examine trends in management and referral of abnormal pap smears in minority women.

**Methods:** A prospective registry of patients referred for an abnormal pap smear or human papilloma virus (HPV) testing to an academic colposcopy clinic was queried from 2008 to 2018. Chi square, Poisson regression, and multivariate logistic regressions were performed to evaluate differences in colposcopy and loop electrosurgical excision procedure (LEEP) by race, adjusting for confounders and referral pap cytology.

**Results:** A total of 4,936 women were included (58.0% white, 42.0% non-white). Referral rates of high-grade cytology were higher among white (18.9%) compared to non-white (15.8%) women (p=0.005) and did not change significantly over time. Positive HPV testing on referral pap was more likely among white (16.2%) compared to non-white (10.9%) women (p<0.0001). Colposcopies decreased for all women over time (83.5% of women seen in 2008 versus 48.6% in 2018, p<0.0001), but decreased more for white compared to non-white women (43.2% versus 61.3% respectively in 2018, p<0.0001). Number of colposcopies per patient was relatively higher among black (ORadj 1.12, 95% CI 1.04-1.20, p=0.003) and Hispanic women (ORadj 1.20, 95% CI 1.13-1.29, p<0.0001) compared to white women (Table 1). Hispanic women were significantly more likely to undergo LEEP (ORadj 1.37, 95% CI 1.09-1.72, p=0.008). No other racial differences in LEEPs were noted.

**Conclusions:** Despite an overall reduction in the rate of colposcopy for abnormal pap smears over time, minority women undergo an increased number of interventions compared to white women after controlling for referral pap smear.