P10.06 PROGNOSTIC IMPORTANCE OF DNA REPAIR GENE POLYMORPHISMS IN CERVICAL CANCER PATIENTS FROM INDIA

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Background The cell's ability to repair DNA damage is important. Genetic variation in DNA repair genes can modulate DNA repair capacity and may be related to cancer risk. Human papillomavirus (HPV) is considered to be a necessary but not sufficient cause for cervical cancer and, therefore, other factors contribute to the carcinogenic process.
Objectives To evaluate polymorphisms in the DNA repair genes: XRCC1 (Arg194Trp, Arg280His, and Arg399Gln), ERCC1 (Asp118Asp), ERCC2 (Lys751Gln) and ERCC4 (Arg415Gln) with the risk of cervical cancer progression and to analyse their expression profile.
Material and methods A case control study consisting of 178 samples [65 cervical cancer (CaCx), 45 squamous intraepithelial lesion (SIL) and 68 controls] was carried out. Genotypes were determined by PCR-RFLP and DNA sequencing. Expression analysis was done by RT-PCR and Western blotting.
Results Positive association was seen between the polymorphisms of XRCC1 genes i.e., in codons 194 (OR = 20.1, 95% CI = 5.9–68.8), 280 (OR = 5.4, 95% CI = 2.3–12.6) and 399 (OR = 4.2, 95% CI = 1.5–12.1) and cervical cancer. SIL patients also showed a significant association with codon 194 (OR = 7.56, 95% CI = 3.42–16.70). Positive correlation was also found in ERCC4 Gln415Gln in both CaCx and SILs (OR = 21.3 95% CI = 7.1–64.0 and OR = 7.8, 95% CI = 2.9–20.9, respectively). For ERCC2 Gln751Gln the association was significant for both CaCx (OR = 10.1, 95% CI = 2.6–37.9) and SILs (OR = 8.9, 95% CI = 2.8–28.3). However the risk for CaCx and SILs did not appear to differ significantly amongst individuals featuring the ERCC1 Asp118Asp genotype. The invasive cancer and SIL subjects also demonstrated lower relative expression of the above DNA repair genes at both mRNA and protein level ($p < 0.001$).
Conclusions This study indicates that variant types of DNA repair genes play an important role in modifying individual susceptibility to cervical cancer. Since cervical cancer is a multi-factorial disease, the contribution of DNA repair enzymes to the development of cervical cancer, if it exists may be concealed by HPV infection.
Disclosure of interests The authors declare that they have no competing interests.

P10.07 MAPPING THE INTEGRATION SITES E1-E2 OF HPV-16 ANDHPV-18 AS A TOOL TO EVALUATE DIFFERENT STAGES OF CERVICAL DISEASE PROGRESSION

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Introduction Different methodologies have been developed to analyse integration. Most of them are expensive and laborious. Since the most frequent disrupting happen in E1 or E2 genes we believe that amplify fragments covering theses genes could be associated to virus integration status.
Methods Hence, in order to evaluate the physical state (episomal or integrated) of HPV 16 and 18 genomes, a PCR combining 10 primers pairs for HPV16 and 11 primers pairs for HPV18 were used, covering the E1-E2 region, adapted as described by Vernon *et al*. (1997)[1] and Collins Constandinou-Williams *et al*. (2009).[2] CASKI and HeLa lineage were used as control.
Results Our preliminary results involved 93 samples cervical samples from patients infected by HPV16 and 37 by HPV18, harbouring cervical lesions in different stages of progression, except HPV18, exclusively associated with cancer lesions. Among HPV16, 26 (28%) were presented episomal, 30 (32%) mixed and 37 (40%) integrated forms. The upper region E1a were the most frequently absent (disrupted) (n = 30, 32%), followed by the downstream E2c region, (n = 21, 22,6%). Among HPV 18 cervical cancers, 5 (13,5%) were presented as episomal forms, 8 (21,5%) mixed and 24 (65%) were integrated. The downstream region E2P3 was the most frequently disrupted, (n = 30, 81%).
Conclusion It is interesting to observe that literature points out a predominance of disruption in E2 region but our results suggested a highly prevalent E1 inactivation. The approach here described is a very specific methodology that can successfully map the HPV 16 and 18 genome fragile areas. Data are being analysed in order to search for statistical correlation between integration and severity of the lesion but it has been observed that E1-E2 absences were suggestively frequent in HSIL and cancer. In a few cases, episomal forms were observed in cancer samples, suggesting additional biomarkers as responsible for carcinogenesis.
Disclosure of interest statement PCR, Genomic integration, episomal, HPV16.

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P10.08 PREVALENCE OF LOW- AND HIGH-GRADE CERVICAL INTRAEPITHELIAL LESIONS AMONG FEMALE PARTICIPANTS IN PRIVATE HEALTH PLANS IN THE UNITED STATES, 2007–2013: ECOLOGIC EVIDENCE OF POPULATION EFFECTIVENESS OF HUMAN PAPILLOMAVIRUS VACCINATION

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Introduction Human papillomavirus (HPV) vaccine, which provides protection against oncogenic HPV types 16 and 18, was licensed in the United States (US) in late 2006. HPV 16 and 18 are associated with approximately 25% of low-grade and 50% of high-grade cervical intraepithelial lesions worldwide. HPV vaccination is recommended for US girls aged 11–12 years, with catch-up vaccination through age 26; in 2013 coverage among girls aged 13–17 was 57% for 1 dose and 38% for 3 doses.
Methods Using health care claims data from 9.7 million privately insured females aged 10–39 years, we estimated the annual

prevalence of cytologically-detected cervical low-grade and high-grade squamous intraepithelial lesions (LSIL and HSIL, respectively), and of histologically-detected cervical intraepithelial neoplasia grades 2 and 3 (high-grade lesions, collectively termed CIN2+), during 2007–2013. To account for changes in cervical cancer screening over time, analyses were restricted to females who were screened during the same calendar year. Age-stratified trend tests were conducted using binomial regression.

Results Prevalence of LSIL, HSIL and CIN2+ decreased significantly during 2007–2013 for females aged 10–14 and 15–19. For those aged 15–19, prevalence of LSIL decreased by 50% (53.2 to 26.8 per 1000 person-years, $P < 0.001$) and HSIL decreased by 72% (5.9 to 1.6, $P < 0.001$); CIN2+ prevalence in this age group decreased by 83% (13.4 to 2.3, $P < 0.001$). Prevalence of HSIL and CIN2+ also decreased significantly for women aged 20–24. No decreases were seen in older women.

Conclusion This is the first US study to find decreased prevalence of cervical lesions in the age groups most likely to be impacted by HPV vaccination, while accounting for changes in cervical cancer screening. Decreases in low-grade and high-grade lesions reflected their relative associations with HPV types 16 and 18. These results provide ecologic evidence of population effectiveness of HPV vaccination among young, privately-insured US women.

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P10.09 VIEW ON HUMAN PAPILLOMAVIRUS VACCINATION AMONG AT-RISK MEN IN WUXI, CHINA: A CROSS-SECTIONAL STUDY

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Introduction Human papillomavirus (HPV) infection is common among sexually active men who have sex with men (MSM) and men who have sex with women (MSW). The quadrivalent HPV vaccine is effective in preventing HPV infection and HPV related morbidities in both MSM and MSW. View on HPV vaccination among MSM and MSW in China has not been studied.

Methods We enrolled MSM from the community and MSW from a sexual health clinic in Wuxi, China. A questionnaire about participants' socio-demographic characteristics and view on HPV vaccination was collected.

Results A number of 186 MSM and 182 MSW were recruited. The proportions of having ever heard of HPV among these two groups were 18.4% and 23.1%, respectively. The proportions of having ever heard of HPV vaccine were 10.2% and 15.4%, respectively. MSW (70.9%) were significantly more willing to take HPV vaccine than MSM (34.9%) ($p < 0.001$). Only 26.2% of MSM and 20.2% of MSW were willing to take free HPV vaccine before the age of 20 when they commenced their sexual behaviours. MSM preferred receptive anal sex (OR: 3.8, 95% CI: 1.7–13.5), never using condom in anal sex in the past 6 months (OR: 3.4, 95% CI: 1.4–20.1), ever diagnosed with STIs (OR: 3.3, 95% CI: 1.2–8.3) and ever receiving HIV/AIDS related service (OR: 1.6, 95% CI: 1.1–4.3) and MSW having female commercial sex (OR: 1.7, 95% CI: 1.2–8.5), never using condom in commercial sex (OR: 1.9, 95% CI: 1.3–8.5) and diagnosis of an STI (OR: 2.0, 95% CI: 1.6–7.2) were more likely to accept free HPV vaccine.

Conclusion Sexually active MSM and MSW in China lacked knowledge of HPV. The majority of homosexual men would not benefit from HPV vaccination as their sexual debut proceeds vaccine uptake. Aggressive education aimed at increasing knowledge of HPV and HPV vaccination among these men is warranted.

Disclosure of interest statement All authors declare no competing interests.

P10.10 T-CELLS IN THE ANAL MUCOSA OF MEN WITH HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS

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Introduction The host cellular immune response plays an integral role in controlling human papilloma virus (HPV)-induced precancerous lesions. Anal mucosal cellular immune responses have not been previously studied.

Methods The Study of the Prevention of Anal Cancer (SPANC) is a longitudinal natural history study of anal HPV infection in men ≥35 years who have sex with men. 26 participants with anal, high-grade (grade 2 or 3) squamous intraepithelial lesions (HSIL) at study entry had 44 anal biopsies. Lymphoid aggregates in these biopsies were detected by inspection of haematoxylin and eosin-stained sections. Additional sections were immunofluorescently stained to enumerate submucosal and intra-epithelial $CD4^+$ and $CD8^+$ T-cell counts. Whole slide imaging to reveal full tissue architecture at high resolution (x600) was used. Student's t-test of $\log_{10}$-transformed T-cell density was used to compare means; a generalised, linear model was used to determine factors associated with total T-cell density (biopsy-based analysis with intra-subject adjustment).

Results Of 26 men with mean age 53 years [standard deviation (SD) 10.5], 7 (27%) were HIV-infected and 17 (68%) had concurrent anal HPV16 in anal swabs. Of 44 biopsies, 26 (59%) revealed HSIL and 24 (55%) had lymphoid aggregates localised in the submucosa adjacent to the epithelium. Presence of lymphoid aggregates was associated with higher $CD4^+$ T-cell density (mean 192 vs. 69 cells/mm^2, $P < 0.001$), but not higher $CD8^+$ T-cell density (106 vs. 62 cells/mm^2, $P = 0.077$). A biopsy diagnosed with HSIL was significantly associated with higher total T-cell density [odds ratio (OR) 11.80, 95% confidence interval (CI) 1.51 – 92.08, $P = 0.02$], as was having anal HPV16 detected (OR 14.08, 95% CI 1.15 – 172.71, $P = 0.04$). Presence of low-risk HPV genotype (s) was not associated (OR 1.37, 95% CI 0.12 – 15.14, $P = 0.80$).

Conclusion $CD4^+$ T-cell enriched lymphoid aggregates in the anal mucosa were associated with anal HSIL and HPV 16.

Disclosure of interest statement Winnie Tong and Jennifer Roberts declare no conflicts of interest.

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