Welcome to our review of the 27th International Papillomavirus Conference and Clinical Workshop, which was held in Berlin, Germany, 17–22 September, 2011. The meeting was designed to meet two challenges i) the definition of future directions of papillomavirus research and ii) a transition of responsibility to young researchers – the next generation.

The Conference programme featured information on all essential topics and important aspects of papillomavirus research, presented by international experts and promising younger colleagues in the field. All presentations were peer reviewed to ensure the highest quality in content and relevance.

This Review has been created to allow those unable to attend, but with a keen professional interest in HPV-associated diseases, to access a summary of the most recent papillomavirus research and up-to-date background knowledge that are likely to increase your knowledge on clinical aspects or on public health-related issues in your ongoing or future practice. Selection and review of the research has been carried out independently by Dr Min Lo, MBCChB FACHSHM (RACP), Specialist Sexual Health Physician. We hope you find these abstracts interesting and helpful in your daily clinical practice.

Kind regards,
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Quadrivalent HPV vaccination and genital warts in Australia 2004–2010

**Presenter:** Grulich AE

**Summary:** Outcomes are reported from a national surveillance network set up to measure trends in clinical presentations in genital warts in Australia between 2004–2010, to assess the impact of a universal free vaccination program introduced in 2007 for all females aged between 12 and 26 years. Eight sexual health services provided nationwide data on 134,939 new patients between 2004–2010; 11,194 new cases of genital warts were identified. Before the vaccination program there was no change in the proportion of women or heterosexual men diagnosed with genital warts. To the end of 2010, there was a 73% decline in the proportion of young resident women diagnosed with genital warts (p-trend <0.0001) that is ongoing. In contrast, the 25% decline in young non-resident women only approached significance (p-trend=0.06), and there was no significant decline in genital warts among older women, or men who have sex with men. The proportion of resident heterosexual men diagnosed with genital warts declined by 35% (p-trend <0.0001); the decline was greater (44%) among younger men.

**Comment:** See below.

**Session 04. Prevention. Abstract O-04.01**


Impact of vaccination on colposcopy referral and treatment rates

**Presenters:** Rodriguez AC, Schiffman M

**Summary:** The impact of adult vaccination on colposcopy referral and treatment is reported for 7,466 women aged 18–25 years vaccinated in 2004–5 in the Costa Rica Vaccine Trial with Cervarix or Hepatitis A. Women were followed for four years and those with cytological evidence of high-grade disease (HSIL+ or ASC-H or persistent low-grade disease (LSIL and HPV+ ASC-US) were referred to colposcopy and treatment, as needed. After excluding women with evidence of high-grade disease at entry, the overall referral and LEEP treatment rates were 22.1% in the Cervarix arm and 3.5% in the Hepatitis A arm. Colposcopy referral was 11.5% lower and the treatment rate 27.4% lower among Cervarix recipients than in controls.

**Comment:** Since vaccination has begun, there have been several key publications demonstrating the decrease in occurrence of external genital warts, referral rates to colposcopy services and cervical disease. Australia was a key player in the development of the HPV vaccination and was the first country in the world to fund HPV vaccination. The article by AE Grulich outlined here shows early success for the vaccine with a decrease in the occurrence of genital wart diagnoses, and flow-on protection for heterosexual males. It is also clear that acceptance of vaccine is highly dependent on doctor/nurse encouragement and this is a key obstacle for many.

**Session 05. Cost effectiveness and awareness. Abstract O-05.01**

Alternate Dosing Schedules for HPV Vaccination

Two dose vaccine trial of Q-HPV: Results at 36 months

Presenters: Dobson S et al
Summary: 36-month follow-up immunogenicity data were detailed from this post-licensure trial that assessed three vaccine groups and two dosing regimens: Group 1, 9–13 years old—2 doses at 0, 6 months (n=194); Group 2, 9–13 years old—3 doses at 0, 2, and 6 months (n=183); Group 3, 16–26 year olds—3 doses at 0, 2, and 6 months (n=203). At 36 months, HPV-16 and 11 antibody responses following the 2-dose regimen were non-inferior to the 3-dose regimen, but not for HPV-genotypes 6 and 18, for which the lower bounds of the 95% CI were below 0.5.

Comment: The possibility of alternate dosing schedules for HPV vaccine is a cause for major excitement as this will have huge implications for resource-poor areas in terms of better coverage, reduced costs and better implementation. Could the vaccine be given at a much younger age? Can the vaccine be given in 2 doses and can the 3-dose schedule be varied? Currently, British Columbia has changed to a 2-dose (0.6) schedule and Mexico and Quebec have started a 0.6 60 schedule. Recent data from British Columbia on the 2-dose vaccine schedule shows that the immune response in younger girls is good and follow-up has occurred for up to 36 months. The data would indicate that older girls and women still require 3 doses. Further study is needed to monitor ongoing antibody response and efficacy against HPV disease. However, it would seem that alternative dosing schedules are entirely possible in young girls (12–15 years).

Session 18: Prophylactic vaccination: clinical studies. Abstract O-18.03

Colposcopy

HPV negative at baseline: Risk of subsequent abnormal smears

Presenters: Petry KU et al
Summary: 3,389 women (30–65 years) who were negative for HR-HPV (HCV) and had normal Pap smears at baseline were followed for 5 years with annual Pap smears within the German cervical cancer prevention program and had ≥1 follow-up smear. The risk of atypical Pap smear findings ranged from 2.2% to 3.03% per screening round. The accumulated risk of receiving ≥1 atypical Pap smear was 12.8% in women who underwent 5 subsequent annual screening visits. No CIN+ cases were reported in the complete double negative group or among 96 randomly selected women undergoing colposcopy at study entry and another 296 participants at study end.

Comment: HPV testing has very good negative predictive value so it is pointless doing cytology on a woman who is negative for HPV at baseline.

Session 17. Cervical screening. Abstract P-17.36
The incremental benefit of taking multiple biopsies for detecting HGCIN

Presenters: Wentzensen N et al

Summary: Of 568 previously untreated women referred to the University of Oklahoma colposcopy clinic for abnormal screening results, worst diagnoses from biopsies were CIN3 (n=61), CIN2 (n=169), CIN1 (n=208) and no dysplasia (n=130). 116/383 women (30.3%) with a low-grade or benign colposcopic impression had CIN2 in one of multiple biopsies. Conversely, 71/185 (38.4%) with a high-grade colposcopic impression had <CIN2 in their worst biopsy result. In 61.7% of women with CIN2+, the worst lesion was detected in the first biopsy, in 26.1% it was found at the second biopsy and in 12.2% it was detected in the third or fourth biopsies. Similarly, 68.9% of CIN3 were detected with the first biopsy, 21.3% with the second biopsy, and 9.8% with the third and fourth biopsies. Only one CIN3 was detected with a random biopsy (1.6%).

Comment: Colposcopy and single-targeted biopsy will pick up 70% of high-grade lesions but only 30% of prevalent high-grade [ALTs study]. The general consensus is that two biopsies significantly increases sensitivity of colposcopy. One targeted biopsy is not enough. 3+ biopsies do not improve results any further. Performing the second biopsy adjacent to the ‘worst’ area will increase the pick-up rate by another 20%. There is no need for endocervical curettage. CIN3+ is rarely found in ‘true random’ biopsies, therefore the utility of doing ‘random’ biopsies is still being debated.

Session 15. Screening and patient management. Abstract O-15.02
http://tinyurl.com/biopsy-pick-up-rate

HPV test of cure: Effective protection for 5 years

Presenters: Cruickshank M et al

Summary: Extended follow-up data are reported from a study (Kitchener et al, BJOG 2008;115:1001-7) in which women treated for CIN 65% CIN3; 32% CIN2; 217 CIN1 and 9 CGIN underwent test of cure at 6 and 12 months post-treatment with HC2 and LBC and were followed-up annually with cytology only. 70% of screen positives by 36%. Triage strategies incorporating HPV-16 and/or HPV-18 detection alone or in combination with ASC-US cytology yielded equal or superior performance for identifying HPV-positive women with CIN3 compared to triage strategies based solely on non-cytologic

Comment: HPV DNA testing is more sensitive, more objective and better at detecting high-grade abnormality than cytology. HPV DNA testing is much more sensitive (99–100%) for CIN3 than cytology-based (50–75%), but is less specific. There is almost no doubt that HPV testing will in the future take over cervical cytology as primary screening for cervical cancer. Mexico is one of the first countries to adopt HPV testing in favour of cytology. The value of the HPV test is in its negative result. It is meaningless to perform cytology on a HPV-negative woman. One HPV test is also approximately equal to two pap tests; you are protected against CIN3 for twice as long. There is still some work to be done though. Important decisions are required as to how to triage positive HPV results, as HPV positivity is common and will often reflect non-persistent and transient infection.

Oral poster presentations 201-236. Abstract OP-228

HPV testing protects against CIN3+ in subsequent screening round

Presenters: Meijer C et al

Summary: Outcomes are reported for 40,105 women aged 30–60 years who participated between January 1999 and September 2002 in the regular cervical screening programme in The Netherlands and were assigned to a control (conventional cytology) or intervention (HPV DNA/cytology co-testing) group. During the subsequent screening round after 5 years, HPV DNA/cytology co-testing was performed on both groups. Over two screening rounds, detection rates of CIN2+ were similar in the intervention and control groups. However, compared to the control group, more CIN2+ lesions were observed in the intervention group at baseline (RR 1.29; p=0.01), and fewer cervical cancer cases and CIN3+ at the subsequent round (RR 0.29; p=0.031 and RR 0.72; p=0.023, respectively).

Comment: See below.

Session 17. Cervical screening. Abstract O-17.01

COBAS HPV test performance including HPV16/18 in cervical cancer screening

Presenters: Stoler M et al

Summary: Of 41,955 US-based women aged ≥25 years, whose cervical specimens were collected for liquid-based cytology (LBC) and HPV DNA testing by the cobas HPV Test, 10.4% tested positive for HPV and 6.4% had non-normal cytology. HPV testing was more sensitive for detection of ≥CIN3 than LBC (92.0% vs 53.3%; p<0.0001); this sensitivity remained after adjusting for verification bias (75.1% vs 43.2%). Co-testing increased diagnostic yield for ≥CIN3 by 5% and increased the number of screen positives by 36%. Triage strategies incorporating HPV-16 and/or HPV-18 detection alone or in combination with ASC-US cytology yielded equal or superior performance for identifying HPV-positive women with ≥CIN3 compared to triage strategies based solely on non-cytologic.

Comment: HPD DNA testing is more sensitive, more objective and better at detecting high-grade abnormality than cytology. HPV DNA testing is much more sensitive (90–100%) for CIN3 than cytology-based (50–75%), but is less specific. There is almost no doubt that HPV testing will in the future take over cervical cytology as primary screening for cervical cancer. Mexico is one of the first countries to adopt HPV testing in favour of cytology. The value of the HPV test is in its negative result. It is meaningless to perform cytology on a HPV-negative woman. One HPV test is also approximately equal to two pap tests; you are protected against CIN3 for twice as long. There is still some work to be done though. Important decisions are required as to how to triage positive HPV results, as HPV positivity is common and will often reflect non-persistent and transient infection.

Session 8. Natural history. Abstract O-08.02

HPV infection incidence and duration in previously unexposed women

Presenters: Ramanakumar AV et al

Summary: A cohort of 553 women aged 15–25 years enrolled in the placebo arm of a randomised trial of the HPV-16/18 AS04 adjuvant vaccine were followed for up to 6.3 years. Infections with HR-HPV types were more common and lasted longer on average than those with low-risk types. Cumulative risks were greater with cervicovaginal than with cervical sampling. HPV detection exclusively in cervical samples persisted longer than that based on cervicovaginal samples. Incidence rates were higher among women aged 15–20 versus those aged 21–25 and women with multiple sex partners had generally higher infection rates than those with a single partner.

Comment: How long does infection last? This study confirms previous epidemiological data showing that high-risk HPV has a longer duration of infection than low-risk types; of about one year. 1.1

Session 8. Natural history. Abstract O-08.05

HPV persistence and CIN2+ risk in the ARTISTIC trial

Presenters: Gilham C et al

Summary: The role of persistent (>26 months) HPV infection in predicting the risk of CIN2+ was assessed, using liquid-based cytology and HPV genotyping data from 17,294 women in the ARTISTIC trial. Women with persistent infection had nearly 3 times the CIN2+ risk (OR 2.8) versus newly infected women: 21% of persistent infections developed into CIN2+ within 30 months of the second HPV test compared to 8% of new HR-HPV infections; 32% of persistent HPV-16 infections developed into CIN2+ compared to 11% of newly acquired HPV-16 infections. The CIN2+ rate among new infections was similar in women who were HC2-negative at entry (7.5%) and in women who had other genotypes which cleared (7.7%).

Comment: The vast majority of high-risk infection is transient and becomes undetectable by HPV DNA testing. Those that remain detectable for more than two years are termed persistent and have a significant risk of progression.

Session 8. Natural history. Abstract O-08.05
HPV infection and progression to CIN in young women

**Presenters:** Castellsague X, Jaisamrann U

**Summary:** This analysis of 4-year follow-up data from 9,247 women aged 15–25 years enrolled in the control arm of an HPV-16/18 AS04-adjuvanted vaccine trial demonstrates a high rate of progression to CIN (CIN2 in 8%, CIN3 in 3%) among those with prior confirmed 6-month persistent cervical HPV infection, compared to those with no such confirmation.

**Comment:** 15–25-year-olds who are HPV-positive have a high rate of abnormal cytology. They will also have a high rate of progression. Screening this population results in over-detection of infection that has minimal risk of progression to cancer.

**Session 8. Natural history. Abstract P-08.17**

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Prevalent detection of vaccine HPV types in men

**Presenters:** Palefsky J et al

**Summary:** The burden of HPV 6/11/16/18 infection was examined in 4,065 males aged 15–27 years enrolled in a trial evaluating cHPV efficacy. Among all men on Day 1, HPV-16 (5.4%) was the most common type detected in anogenital swabs, followed by HPV-6 (5.0%), HPV-18 (3.0%) and HPV-11 (1.5%); corresponding prevalence rates were higher for the 602 men who had sex with men (MSM): 13.8%, 13.4%, 8.1% and 6.8%, respectively. Seropositivity at baseline for any vaccine HPV type was 5.4% in heterosexual males and 40.6% in MSM.

**Comment:** See below.

**Session 6. Non-cervical sites. Abstract P-06.14**

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Duration of HPV 6/11/16/18 infection in males

**Presenters:** Giuliano A et al

**Summary:** The median duration of HPV 6/11/16/18 infection was assessed in 2,033 men aged 15–27 (1732 heterosexual men and 301 men who have sex with men) in the placebo arm of a qHPV vaccine clinical trial. Overall, the duration of prevalently 2,033 men aged 15–27 (1732 heterosexual men and 301 men who have sex with men) in the placebo arm of a qHPV vaccine clinical trial. Overall, the duration of prevalently 2,033 men aged 15–27 (1732 heterosexual men and 301 men who have sex with men) in the placebo arm of a qHPV vaccine clinical trial. Overall, the duration of prevalently 2,033 men aged 15–27 (1732 heterosexual men and 301 men who have sex with men) in the placebo arm of a qHPV vaccine clinical trial. Overall, the duration of prevalently

**Comment:** Current data shows that the HPV vaccine is effective in the prevention of HGAIN in both females and males. In New Zealand, Gardasil is approved (but not funded) for use in males 9–26 years. The U.S. Centers for Disease Control and Prevention’s (CDC’s) Advisory Committee on Immunization Practices (ACIP) recommends that boys 11 to 12 years old be vaccinated routinely.

**Oral poster presentations 101-136. Abstract OP-134**

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HPV genotype distribution in anal cancer worldwide

**Presenters:** Saunier M et al

**Summary:** In a worldwide series of 45 intraepithelial neoplasia (AIN) 2/3 cases and 445 invasive squamous cell carcinoma cases, HPV DNA was identified in 97% of AIN2/3 and 86% of invasive cancer cases. In invasive anal cancer cases, the HPV prevalence was 80% in men and 88% in women (p<0.05). The most frequently detected types (as in single infections) were HPV-16 (75%) and HPV-18 (4%). Multiple infections were detected in 7.4% of HPV-positive cases.

**Comment:** Current data shows that the HPV vaccine is effective in the prevention of HGAIN in both females and males. In New Zealand, Gardasil is approved (but not funded) for use in males 9–26 years. The U.S. Centers for Disease Control and Prevention’s (CDC’s) Advisory Committee on Immunization Practices (ACIP) recommends that boys 11 to 12 years old be vaccinated routinely.

**Oral poster presentations 101-136. Abstract OP-134**

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HPV genotype attribution in vulvar intraepithelial and invasive lesions worldwide

**Presenters:** de Sanjosé S et al

**Summary:** HPV genotype distribution is described for a worldwide series of 1,571 histologically-confirmed vulvar high-grade intraepithelial lesions (VIN2/3) and 524 invasive (IVC) lesions, of which 28.6% and 87% were HPV/DNA-positive, respectively. Among invasive cases, squamous cell carcinomas (SCC) with warty-basaloid features were more likely to be HPV-positive (61.8%) than pure SCC (10.6%; p<0.001). Cases aged <55 years were more likely to be positive, irrespective of histology. The most common types were HPV-16 and HPV-33 in all regions with the exception of Central South America, where HPV-16 and HPV-18 were the two most common types. Agreement between p16INK4a and HPV attribution was 84% in SCC.

**Comment:** Current data shows that the HPV vaccine is effective in the prevention of HGAIN in both females and males. In New Zealand, Gardasil is approved (but not funded) for use in males 9–26 years. The U.S. Centers for Disease Control and Prevention’s (CDC’s) Advisory Committee on Immunization Practices (ACIP) recommends that boys 11 to 12 years old be vaccinated routinely.

**Oral poster presentations 201-236. Abstract OP-232**

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