



Meeting
Barriers in HPV vaccination & cervical screening programmes.
27-28 June 2016, Antwerp, Belgium

BACKGROUND DOCUMENT

Alex Vorsters & Ina Lodewyckx
HPV Prevention & Control Board

Executive Secretariat, Vaccine and Invetious disease Institute, University of Antwerp, Campus Drie Eiken,
Universiteitsplein 1, 2610 Antwerpen, Belgium, +32 (0)3 265 26 64; alex.vorst@uantwerpen.be

Content

Introduction	4
Purpose of the background document	4
Part 1: Presentation related references by session	5
<i>Session 2 Interpretation of safety data</i>	<i>6</i>
<i>Session 3 Vaccine confidence</i>	<i>14</i>
<i>Session 4 HPV vaccination programs: country experiences and lessons learnt.</i>	<i>17</i>
<i>Session 5 Barriers and opportunities in HPV screening programs.....</i>	<i>30</i>
<i>Session 6 HPV-faster: Broadening the scope for prevention of HPV-related cancer.</i>	<i>35</i>
Part 2: References based on a Pubmed search, by session	38
<i>Session 2 Interpretation of safety data</i>	<i>39</i>
<i>Session 3 Vaccine confidence</i>	<i>48</i>
<i>Session 4 HPV vaccination programs: country experiences and lessons learnt.</i>	<i>83</i>
<i>African Region.....</i>	<i>83</i>
<i>Eastern Mediterranean Region</i>	<i>88</i>
<i>European Region</i>	<i>90</i>
<i>Region of the Americas</i>	<i>100</i>
<i>South-East Asia Region</i>	<i>111</i>
<i>Western Pacific Region</i>	<i>115</i>
<i>Low- and middle-income countries</i>	<i>122</i>
<i>Not region specific.....</i>	<i>124</i>
<i>Session 5 Barriers and opportunities in HPV screening programs.....</i>	<i>126</i>
<i>Session 6 HPV-faster: Broadening the scope for prevention of HPV-related cancer.</i>	<i>154</i>
Part 3: Bibliography of Speakers	155
Patriciu Achimas, The Oncology Institute "Prof. Dr. Ion Chiricuta" (Romania)	156
Marc Arbyn, Scientific Institute of Public Health (Belgium)	157
Iacopo Baussano, International Agency for Research on Cancer (France)	163
Xavier F. Bosch, Catalanian Institute of Oology (Spain)	165
Monica Chaturvedi, Monica Chaturvedi, Public Health Foundation (India)	169
Silvia de Sanjose, Catalanian Institute of Oology (Spain).....	170
Kate Gallagher, London school of Hygiene and Tropical Medicine (UK)	173
Sharon Hanley, Hokkaido University Graduate School of Medicine (Japan)	175
Emilie Karafillakis, London School of Hygiene and Tropical Medicine (UK).....	179
Heidi Larson,.....	181
Pier Luigi Lopalco, University of Pisa (Italy)	183
Lauri Markowitz, Centre for Disease Control & Prevention (CDC) (US).....	185

Laura Marlow, Department of Epidemiology and Public Health, UCL (UK)	189
Kåre Mølbak, Statens Serum Institute (Denmark)	194
Hannah Nohynek, National Institute for Health and Welfare (Finland)	197
Robert Pless, Public Health Agency of Canada	201
Kevin Pollock, Health Protection (Scotland)	202
Geert Top, Agentschap Zorg en Gezondheid (Belgium)	207
Pamela Wakewich, Lakehead University (Canada)	208
Scott Wittet, PATH (US)	210
Joanne Yarwood, National Infection Service, Public Health England	211

Introduction

Since being licensed in 2006, over 200 million doses of HPV vaccines have been distributed globally and since 2013, HPV vaccination has been part of the national programs in 66 countries. However some countries experience major obstacles when introducing the vaccination leading to low vaccination coverage or even abortion of the vaccination program. Similar for successful implementation of cervical screening programmes many countries do not have an organized cervical screening programme and coverage of this live saving intervention is sometimes very limited. Increasing and maintaining high participation rates are equally essential to have impact on HPV-induced morbidity and mortality.

The purpose of this meeting is to strengthen the prevention of HPV-related cancers by better defining the barriers, learn from certain country situations, and proposing evidence based solutions to overcome identified challenges.

Specific objective of the meeting are:

1. To review cultural, infrastructural and financial barriers that impact implementation of vaccination and screening programmes;
2. To review the adverse events profile following HPV vaccination.
3. To update the points of view regarding safety issues and describe new developments.
4. To discuss the impact of safety issues and crises in an international perspective.
5. To review factors impacting adherence to cervical screening programmes.
6. To learn from country initiatives in HPV vaccine safety monitoring and HPV screening adherence.
7. To propose strategies to counter vaccination and screening hesitancy and to build public confidence in the HPV prevention programs
8. To discuss a new approach to implement HPV prevention and control: HPV-Faster.

Target audience:

- Projects and organisation representatives involved in HPV control and prevention
- Representatives of health organisations involved in the prevention and control of HPV and/or other health issues
- HPV prevention and control Board advisors

Purpose of the background document

This background document provides an overview of articles related to the meeting and a concise bibliography of speakers. The main purpose of the document is to frame the topics of the meeting on 'Barriers in HPV vaccination & cervical screening programmes'.

The document should not be considered as an an exhaustive report of scientific articles related to the themes of the meeting.

Inclusion of references in this document does not indicate that the Executive Secretariat agrees with the content or correctness of the content. The first objective of this list is to give an overview of what has been published on this topic.

Part 1: Presentation related references by session

List obtained via speaker forms or (if speaker form was not available) via a Pubmed search on Name of the speaker. Maximum ten articles are shown.

Session 2 *Interpretation of safety data*

HPV vaccine safety; past, current and future actions undertaken by the GACVS.
Robert Pless, Public Health Agency of Canada

Asturias EJ , Wharton M, Pless R, MacDonald NE, Chen RT, Andrews N, Salisbury D, Dodoo AN, Hartigan-Go K, Zuber PL.. **Contributions and challenges for worldwide vaccine safety: The Global Advisory Committee on Vaccine Safety at 15 years.** *Vaccine.* 2016; 34: 3342–3349.

In 1999, the Global Advisory Committee on Vaccine Safety (GACVS) was established by the World Health Organization (WHO) to provide independent scientific advice on issues relating to the safety of vaccines and immunization. Fifteen years onward, we conducted a multi-faceted review to evaluate the impact, reach and challenges facing GACVS, including the role GACVS plays in informing global, regional and WHO member state vaccine policy. The methods included measures of organizational structure, citation impact, themes approached, and a discussion by previous and current members to evaluate past, present and future challenges. Given the increasing range of data sources and the deployment of many new vaccines, the Committee is facing the complex task of identifying the best available evidence for recommendations on vaccine safety. To help meet the increased demand for public transparency in decision making, GACVS-structured methodology for evidence-based decisions is evolving. GACVS also promotes best practices and capacity building for timely and accurate risk assessment; risk communications; outreach to help countries maintain and, if needed, rebuild public trust in vaccines; and advocacy for bridging the major gaps in vaccine safety capacity globally.

Global Advisory Committee on Vaccine Safety (GACVS); WHO secretariat. **Global safety of vaccines: strengthening systems for monitoring, management and the role of GACVS.** *Expert Rev Vaccines.* 2009; 8(6):705-16.

Vaccines have contributed enormously in reducing the impact of many infectious diseases, and the expanded use of new and existing vaccines provides unprecedented potential for further reducing the global burden of infectious diseases. Yet, as with the deployment of other technologies, their use may also sometimes be associated with undesirable effects that need to be identified rapidly, understood and minimized. In this article, we review the models and systems that have been developed to monitor and respond to concerns regarding vaccine safety and we give illustrative examples of real or perceived vaccine safety issues. The Global Advisory Committee on Vaccine Safety (GACVS) was set up 10 years ago and charged to provide the WHO with independent advice on vaccine safety issues. The role of the GACVS is both to analyze and to interpret reports of the adverse effects of vaccines that impact on global vaccination programs and strategies, and to foster the development of improved surveillance systems to detect any adverse effects of vaccines, particularly in low- and middle-income countries. It also monitors the development of new vaccines during clinical testing and advises on the safe use of vaccines in immunization programs. As success is achieved with reducing the burden of vaccine-preventable diseases, there will be increasing attention focused on potential adverse effects, on the development of effective surveillance systems to detect adverse effects, and on improved methods to manage and control any harmful consequences of vaccination.

Review of Safety data of initials clinical trials
Pier Luigi Lopalco, University of Pisa (Italy)

Stillo M, Carrillo Santistevé P, Lopalco PL. **Safety of human papillomavirus vaccines: a review.** Expert Opin Drug Saf. 2015; 1-16.

INTRODUCTION: Between 2006 and 2009, two different human papillomavirus virus (HPV) vaccines were licensed for use: a quadrivalent (qHPVv) and a bivalent (bHPVv) vaccine. Since 2008, HPV vaccination programmes have been implemented in the majority of the industrialized countries. Since 2013, HPV vaccination has been part of the national programs of 66 countries including almost all countries in North America and Western Europe. Despite all the efforts made by individual countries, coverage rates are lower than expected. Vaccine safety represents one of the main concerns associated with the lack of acceptance of HPV vaccination both in the European Union/European Economic Area and elsewhere. **AREAS COVERED:** Safety data published on bivalent and quadrivalent HPV vaccines, both in pre-licensure and post-licensure phase, are reviewed. **EXPERT OPINION:** Based on the latest scientific evidence, both HPV vaccines seem to be safe. Nevertheless, public concern and rumors about adverse events (AE) represent an important barrier to overcome in order to increase vaccine coverage. Passive surveillance of AEs is an important tool for detecting safety signals, but it should be complemented by activities aimed at assessing the real cause of all suspect AEs. Improved vaccine safety surveillance is the first step for effective communication based on scientific evidence.

Van Damme P et al. **Immunogenicity and safety of a 9-valent HPV vaccine.** Pediatrics. 2015; 136(1):e28–e39.

OBJECTIVES: Prophylactic vaccination of youngwomen aged 16 to 26 years with the 9-valent (6/11/16/18/31/33/45/52/58) human papillomavirus (HPV) virus-like particle (9vHPV) vaccine prevents infection and disease. We conducted a noninferiority immunogenicity study to bridge the findings in young women to girls and boys aged 9 to 15 years. **METHODS:** Subjects (N = 3066) received a 3-dose regimen of 9vHPV vaccine administered at day 1, month 2, and month 6. Anti-HPV serologic assays were performed at day 1 and month 7. Noninferiority required that the lower bound of 2-sided 95% confidence intervals of geometric mean titer ratios (boys:young women or girls:young women) be >0.67 for each HPV type. Systemic and injection-site adverse experiences (AEs) and serious AEs were monitored. **RESULTS:** At 4 weeks after dose 3, >99% of girls, boys, and young women seroconverted for each vaccine HPV type. Increases in geometric mean titers to HPV types 6/11/16/18/31/33/45/52/58 were elicited in all vaccine groups. Responses in girls and boys were noninferior to those of young women. Persistence of anti-HPV responses was demonstrated through 2.5 years after dose 3. Administration of the 9vHPV vaccine was generally well tolerated. A lower proportion of girls (81.9%) and boys (72.8%) than young women (85.4%) reported injection-site AEs, most of which were mild to moderate in intensity. **CONCLUSIONS:** These data support bridging the efficacy findings with 9vHPV vaccine in young women 16 to 26 years of age to girls and boys 9 to 15 years of age and implementing gender-neutral HPV vaccination programs in preadolescents and adolescents.

Vesikari T et al. **A Randomized, Double-Blind, Phase III Study of the Immunogenicity and Safety of a 9-Valent Human Papillomavirus L1 Virus-Like Particle Vaccine (V503) Versus GARDASIL® in 9-15-Year-Old Girls.** Pediatr Infect Dis J. 2015; 34:992–998.

BACKGROUND: A 9-valent human papillomavirus (9vHPV) vaccine has been developed to prevent infections and diseases related to HPV 6/11/16/18 [as per the licensed quadrivalent HPV (qHPV) vaccine],

as well as 5 additional oncogenic HPV types (HPV 31/33/45/52/58). Compared with the qHPV vaccine, the 9vHPV vaccine potentially increases the coverage of protection from 70% to 90% of cervical cancers. We compared the immunogenicity and safety of the 9vHPV vaccine versus the qHPV vaccine in 9-15-year-old girls. METHODS: Participants (n = 600) were randomized to receive 9vHPV or qHPV vaccines on day 1, month 2 and month 6. Serology testing was performed on day 1 and month 7. HPV type-specific antibody titers (anti-HPV 6/11/16/18/31/33/45/52/58) were determined by competitive Luminex immunoassay and expressed as geometric mean titers and seroconversion rates. Vaccine safety was also assessed. RESULTS: The HPV 6/11/16/18 immune responses elicited by the 9vHPV vaccine were comparable with those elicited by the qHPV vaccine. All participants (except 1 for HPV 45) receiving the 9vHPV vaccine seroconverted for HPV 31/33/45/52/58. The 9vHPV and qHPV vaccines showed comparable safety profiles, although the incidence of injection-site swelling was higher in the 9vHPV vaccine group. CONCLUSIONS: In addition to immune responses to HPV 31/33/45/52/58, a 3-dose regimen of the 9vHPV vaccine elicited a similar immune response to HPV 6/11/16/18 when compared with the qHPV vaccine in girls aged 9-15 years. The safety profile was also similar for the 2 vaccines.

Castellsague, X et al. **Immunogenicity and safety of the 9-valent HPV vaccine in men.** *Vaccine.* 2015; 33(48), 6892-6901.

OBJECTIVES: This study was designed to evaluate the immunogenicity and tolerability of a prophylactic 9-valent HPV (types 6/11/16/18/31/33/45/52/58) VLP (9vHPV) vaccine in young men 16-26 years of age in comparison to young women 16-26 years of age (the population that was used to establish 9vHPV vaccine efficacy). Safety and immunogenicity data from this study will be used to bridge 9vHPV vaccine efficacy findings in 16-26 year old women to 16-26 year old men. METHODS: This study enrolled 1106 heterosexual men (HM) and 1101 women who had not yet received HPV vaccination. In addition, 313 men having sex with men (MSM) were enrolled and were evaluated separately for immunogenicity because previous results showed that antibody responses to quadrivalent HPV (types 6/11/16/18) VLP (qHPV) vaccine were lower in MSM than in HM. All subjects were administered a 3-dose regimen (Day 1, Month 2, Month 6) of 9vHPV vaccine. Serum samples were collected for anti-HPV assays. Safety information was collected for ~ 12 months. RESULTS: The geometric mean titers (GMTs) for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 for HM were non-inferior to those of women at Month 7. For all vaccine HPV types, Month 7 GMTs were numerically lower in MSM than in HM. Over 99.5% of subjects were seropositive at Month 7 for each vaccine HPV type. Administration of 9vHPV vaccine to both 16-26 year old men and women was generally well tolerated. CONCLUSIONS: These results support bridging the efficacy findings with 9vHPV vaccine in young women 16-26 years of age to men 16-26 years of age.

Garland S et al. **Safety and immunogenicity of a 9-valent HPV vaccine in females 12–26 years of age who previously received the quadrivalent HPV vaccine.** *Vaccine.* 2015; 33(48), 6855-6864.

OBJECTIVES: To assess the safety and immunogenicity of the investigational 9-valent (6/11/16/18/31/33/45/52/58) HPV (9vHPV) vaccine in prior recipients of a 3-dose regimen of quadrivalent (6/11/16/18) HPV (qHPV) vaccine. METHODS: V503-006 was a randomized, double-blinded, safety/tolerability and immunogenicity study of the 9vHPV vaccine in females 12-26 years of age who were previously vaccinated with qHPV vaccine. Subjects were randomized in a 2:1 ratio to receive 3 doses of 9vHPV vaccine (n=618) or saline placebo (n=306) at day 1, month 2, and month 6. Systemic, injection-site and serious adverse experiences (AEs) were monitored. Serum samples were collected at day 1, month 2, and month 7. Anti-HPV 6/11/16/18/31/33/45/52/58 titers were measured using the 9-valent HPV competitive Luminex Immunoassay (cLIA). RESULTS: The frequency of injection-site AEs (days 1-5

following any vaccination) was higher in the 9vHPV vaccine group than in the placebo group (91.1% and 43.9%, respectively). The frequencies of vaccine-related systemic AEs (days 1-15 following any vaccination) were generally comparable between the 2 groups (30.6% in the 9vHPV vaccine group, and 25.9% in the placebo group). One vaccine-related serious AE was reported in each of the 9vHPV vaccine and placebo groups. Few subjects (9vHPV=0.5%; placebo=0%) discontinued due to an AE. At 4 weeks post-dose 3, over 98% of subjects in the 9vHPV vaccine group were seropositive for HPV types 31/33/45/52/58, with marked elevations in cLIA geometric mean titers (GMTs) to these HPV types. Anti-HPV 31/33/45/52/58 GMTs were lower than in subjects administered 9vHPV vaccine who had not previously received qHPV vaccine (based on cross-study analyses); the clinical significance of this difference is unknown. CONCLUSIONS: Administration of a 3-dose regimen of 9vHPV vaccine to adolescent girls and young women 12-26 years of age who are prior qHPV vaccine recipients is highly immunogenic with respect to HPV types 31/33/45/52/58 and generally well tolerated.

Exploring incidence rates of Guillain Barré (GBS), Chronic Fatigue (CFS) and Postural Orthostatic Tachycardia Syndrome (POTS) prior to HPV vaccine introduction among adolescent girls in Finland.

Hannah Nohynek, National Institute for Health and Welfare (Finland).

Donegan K, Beau-Lejdstrom R, King B, Seabroke S, Thomson A, Bryan P. **Bivalent human papillomavirus vaccine and the risk of fatigue syndromes in girls in the UK.** *Vaccine.* 2013; 31: 4961-7.

INTRODUCTION: Over 70% of cervical cancers are related to human papillomavirus types 16 and 18. In 2008, the vaccine Cervarix, protecting against these two strains, was introduced into the routine UK immunisation programme for girls aged 12-13 years, with a catch-up in girls aged up to 18 years. As part of the risk management planning for this new campaign, the Medicines and Healthcare products Regulatory Agency (MHRA) anticipated a range of conditions, including chronic fatigue syndrome, which might be reported as adverse events in temporal association with the vaccine. METHODS: Near-real time 'observed vs. expected' analyses were conducted comparing the number of reports of fatigue syndromes submitted via the MHRA's Yellow Card passive surveillance scheme to the expected number, using background rates calculated from the Clinical Practice Research Datalink (CPRD) and estimates of vaccination coverage. Subsequently, an ecological analysis and a self-controlled case series (SCCS), both using CPRD, compared the incidence rate of fatigue syndromes in girls before and after the start of the vaccination campaign and the risk in the year post-vaccination compared to other periods. RESULTS: The number of spontaneous reports of chronic fatigue following Cervarix vaccination was consistent with estimated background rates even assuming low reporting. Ecological analyses suggested that there had been no change in the incidence of fatigue syndromes in girls aged 12-20 years after the introduction of the vaccination despite high uptake (IRR: 0.94, 95% CI: 0.78-1.14). The SCCS, including 187 girls, also showed no evidence of an increased risk of fatigue syndromes in the year post first vaccination (IRR: 1.07, 95% CI: 0.57-2.00, p=0.84). DISCUSSION: The successful implementation of an enhanced pharmacovigilance plan provided immediate reassuring evidence that there was no association between vaccination with Cervarix and an increased risk of chronic fatigue syndromes. This has now also been further demonstrated in more comprehensive epidemiological studies.

Arnheim-Dahlstrom L, Pasternak B, Svanstrom H et al. **Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study.** *BMJ.* 2013; 347:f5906.

OBJECTIVE: To assess the risk of serious adverse events after vaccination of adolescent girls with quadrivalent human papillomavirus (qHPV) vaccine. **DESIGN:** Register based cohort study. **SETTING:** Denmark and Sweden, October 2006 to December 2010. **PARTICIPANTS:** 997,585 girls aged 10-17, among whom 296,826 received a total of 696,420 qHPV vaccine doses. **MAIN OUTCOME MEASURES:** Incident hospital diagnosed autoimmune, neurological, and venous thromboembolic events (53 different outcomes) up to 180 days after each qHPV vaccine dose. Only events with at least five vaccine exposed cases were considered for further assessment. Rate ratios adjusted for age, country, calendar year, and parental country of birth, education, and socioeconomic status were estimated, comparing vaccinated and unvaccinated person time. For outcomes where the rate ratio was significantly increased, we regarded three criteria as signal strengthening: analysis based on 20 or more vaccine exposed cases (reliability), rate ratio 3.0 or more (strength), and significantly increased rate ratio in country specific analyses (consistency). We additionally assessed clustering of events in time and estimated rate ratios for a risk period that started on day 181. **RESULTS:** Among the 53 outcomes, at least five vaccine exposed cases occurred in 29 and these were analysed further. Whereas the rate ratios for 20 of 23 autoimmune events were not significantly increased, exposure to qHPV vaccine was significantly associated with Behcet's syndrome, Raynaud's disease, and type 1 diabetes. Each of these three outcomes fulfilled only one of three predefined signal strengthening criteria. Furthermore, the pattern of distribution in time after vaccination was random for all three and the rate ratios for these outcomes in the period from day 181 after vaccination were similar to the rate ratios in the primary risk period. The rate ratios for five neurological events were not significantly increased and there were inverse associations with epilepsy (rate ratio 0.66, 95% confidence interval 0.54 to 0.80) and paralysis (0.56, 0.35 to 0.90). There was no association between exposure to qHPV vaccine and venous thromboembolism (0.86, 0.55 to 1.36). **CONCLUSIONS:** This large cohort study found no evidence supporting associations between exposure to qHPV vaccine and autoimmune, neurological, and venous thromboembolic adverse events. Although associations for three autoimmune events were initially observed, on further assessment these were weak and not temporally related to vaccine exposure. Furthermore, the findings need to be interpreted considering the multiple outcomes assessed.

Brinth LS, Pors K, Theibel AC, Mehlsen J. **Orthostatic intolerance and postural tachycardia syndrome as suspected adverse effects of vaccination against human papillomavirus.** Vaccine. 2015; 33:2602-5.

BACKGROUND: Infections with human papilloma virus (HPV) can result in cervical, oropharyngeal, anal, and penile cancer and vaccination programs have been launched in many countries as a preventive measure. We report the characteristics of a number of patients with a syndrome of orthostatic intolerance, headache, fatigue, cognitive dysfunction, and neuropathic pain starting in close relation to HPV vaccination. **METHODS:** Patients were referred for orthostatic intolerance following HPV vaccination. Symptoms of autonomic dysfunction were quantified by standardised questionnaire. The diagnosis of postural orthostatic tachycardia syndrome (POTS) rested on finding a sustained heart rate increment of $>30 \text{ min}^{-1}$ ($>40 \text{ min}^{-1}$ in adolescents) or to levels $>120 \text{ min}^{-1}$ during orthostatic challenge. **RESULTS:** 35 women aged 23.3 ± 7.1 years participated. Twenty-five had a high level of physical activity before vaccination and irregular periods were reported by all patients not on treatment with oral contraception. Serum bilirubin was below the lower detection limit in 17 patients. Twenty-one of the referred patients fulfilled the criteria for a diagnosis of POTS (60%, 95%CI 43-77%). All patients had orthostatic intolerance, 94% nausea, 82% chronic headache, 82% fatigue, 77% cognitive dysfunction, 72% segmental dystonia, 68% neuropathic pain. **CONCLUSIONS:** In a population referred for symptoms of orthostatic intolerance and other symptoms consistent with autonomic dysfunction that began in close temporal association with a quadrivalent HPV vaccination, we identified a 60% prevalence of POTS. Further work is urgently needed

to elucidate the potential for a causal link between the vaccine and circulatory abnormalities and to establish targeted treatment options for the affected patients.

Brinth L, Theibel AC, Pors K, & Mehlsen J. **Suspected side effects to the quadrivalent human papilloma vaccine.** Dan Med J. 2015; 62:4.

INTRODUCTION: The quadrivalent vaccine that protects against human papilloma virus types 6, 11, 16 and 18 (Q-HPV vaccine, Gardasil) was included into the Danish childhood vaccination programme in 2009. During the past years, a collection of symptoms primarily consistent with sympathetic nervous system dysfunction have been described as suspected side effects to the Q-HPV vaccine. **METHODS:**We present a description of suspected side effects to the Q-HPV vaccine in 53 patients referred to our Syncope Unit for tilt table test and evaluation of autonomic nervous system function. **RESULTS:** All patients had symptoms consistent with pronounced autonomic dysfunction including different degrees of orthostatic intolerance, severe non-migraine-like headache, excessive fatigue, cognitive dysfunction, gastrointestinal discomfort and widespread pain of a neuropathic character. **CONCLUSION:** We found consistency in the reported symptoms as well as between our findings and those described by others. Our findings neither confirm nor dismiss a causal link to the Q-HPV vaccine, but they suggest that further research is urgently warranted to clarify the pathophysiology behind the symptoms experienced in these patients and to evaluate the possibility and the nature of any causal link and hopefully establish targeted treatment options.

EMA public communication. **HPV vaccines: EMA confirms evidence does not support that they cause CRPS or POTS.** EMA/788882/2015. Published on www.ema.europa.eu 12. January 2016

Vaccine safety - Mortality after HPV vaccination observed in RCTs
Marc Arbyn, Scientific Institute of Public Health (Belgium)

Arbyn M. **Effects of quadrivalent human papillomavirus vaccination.** Lancet. 2007; 370: 1031-2.

No abstract available.

Arbyn M, Simoens C, Van Damme P, Scharpantgen A, Meijer CJLM, Beutels P. **Introduction of HPV vaccination in Belgium, Luxembourg and the Netherlands.** Gynecol Obstet Invest. 2010; 70: 152-60.

AIMS: To document progress with human papillomavirus (HPV) vaccine introduction in three closely related European countries, one with organized (the Netherlands) and two with opportunistic cervical cancer screening (Belgium and Luxembourg). METHODS: Experts involved in cervical cancer screening and national immunization programs from the three countries were contacted to provide information on the decision-making process concerning the introduction of HPV vaccine. Sales statistics were obtained from Intercontinental Marketing Services. RESULTS: Advisory boards in all three countries advised organized HPV vaccination of girls of 12 years with variable catch-up policies. In Belgium, the national health authority partially reimburses the HPV vaccine for girls of 12-15 years (recently extended until 18 years). In Luxembourg, 12-year-old girls are invited for free vaccination, but the HPV vaccine is also free of charge for female adolescents of 13-17 years. The number of vaccines reimbursed in Belgium in December 2007 to May 2008 corresponds with the amount required to fully vaccinate 29% of the female population aged 12-15 years. In Luxembourg, between March and November 2008, the immunization program delivered a quantity of HPV vaccines which theoretically covered 29% of females aged 12-17 years. In the Netherlands, nationwide HPV vaccination of girls of 12 years will start in September 2009. The sales of HPV vaccines (all ages combined) were by far the lowest in the Netherlands. CONCLUSION: Up to the end of 2008, HPV vaccination efforts reached less than a third of the target population in Belgium and Luxembourg. If the latest trend continues, the current policy is expected to reach to most half of the target population. Well-planned introduction of vaccination combined with an organized screening program and active surveillance are crucial for the program to achieve and monitor its desired aims. Such surveillance should include linkage between vaccination, screening and cancer registries.

Arbyn M, Martin-Hirsch PL, Xu L, Simoens C, Markowitz L. **Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors (Protocol).** Cochrane Database Syst Rev. 2015; 12: submitted.

No abstract available.

Arbyn M, Vanden Broeck D, Benoy I, Bogers J, Depuydt C, Praet M, De Sutter P, Hoorens A, Hauben E et al. **Surveillance of effects of HPV vaccination in Belgium.** Cancer Epidemiol. 2016; 41: 152-8.

BACKGROUND: Early effects of HPV (human papillomavirus) vaccination are reflected by changes observable in young women attending cervical cancer screening. SUBJECT AND METHODS: The SEHIB study included HPV geno-typing of ~6000 continuous and 650 pathological cervical cell specimen as well as biopsies, collected from women in Belgium in 2010-2014. Data were linked to vaccination status. RESULTS: HPV vaccination offered protection among women aged <30years against infection with HPV16

(vaccine effectiveness [VE]=67%, 95% CI: 48-79%), HPV18 (VE=93%, 95% CI: 52-99%), and high-risk HPV (VE=16%, 95% CI: 2-29%). Vaccination protected also against cytological lesions. Vaccination protected against histologically confirmed lesions: significantly lower absolute risks of CIN1+ (risk difference [RD]=-1.6%, 95% CI: -2.6% to -0.7%) and CIN3+ associated with HPV16/18 (RD=-0.3%, 95% CI -0.6% to -0.1%). Vaccine effectiveness decreased with age. Protection against HPV16 and 18 infection was significant in all age groups, however no protection was observed against cytological lesions associated with these types in age-group 25-29. CONCLUSION: The SEHIB study demonstrates the effectiveness of HPV vaccination in Belgian young women in particular in age group 18-19. Declining effectiveness with increasing age may be explained by higher tendency of women already exposed to infection to get the vaccine.

Session 3 Vaccine confidence

The state of vaccine confidence in the world & factors influencing vaccine acceptance (incl. the global spread of HPV rumours)

Heidi Larson and Emilie Karafillakis, London School of Hygiene and Tropical Medicine (UK)

Strategies to measure and address vaccine hesitancy

Heidi Larson and Emilie Karafillakis

Larson HJ, Jarrett C, Eckersberger E, Smith D, Paterson P. Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: A systematic review of published literature, 2007–2012. *Vaccine*. 2014; 32: 2150-2159.

Vaccine "hesitancy" is an emerging term in the literature and discourse on vaccine decision-making and determinants of vaccine acceptance. It recognizes a continuum between the domains of vaccine acceptance and vaccine refusal and de-polarizes previous characterization of individuals and groups as either anti-vaccine or pro-vaccine. The primary aims of this systematic review are to: 1) identify research on vaccine hesitancy; 2) identify determinants of vaccine hesitancy in different settings including its context-specific causes, its expression and its impact; and 3) inform the development of a model for assessing determinants of vaccine hesitancy in different settings as proposed by the Strategic Advisory Group of Experts Working Group (SAGE WG) for dealing with vaccine hesitancy. A broad search strategy, built to capture multiple dimensions of public trust, confidence and hesitancy around vaccines, was applied across multiple databases. Peer-reviewed studies were selected for inclusion if they focused on childhood vaccines [≤ 7 years of age], used multivariate analyses, and were published between January 2007 and November 2012. Our results show a variety of factors as being associated with vaccine hesitancy but they do not allow for a complete classification and confirmation of their independent and relative strength of influence. Determinants of vaccine hesitancy are complex and context-specific - varying across time, place and vaccines.

Larson H, Schulz W, Tucker J, Smith D. Measuring Vaccine Confidence: Introducing a Global Vaccine Confidence Index. *PLoS Currents Outbreaks*. 2015; 25 Feb. Edition 1.

BACKGROUND: Public confidence in vaccination is vital to the success of immunisation programmes worldwide. Understanding the dynamics of vaccine confidence is therefore of great importance for global public health. Few published studies permit global comparisons of vaccination sentiments and behaviours against a common metric. This article presents the findings of a multi-country survey of confidence in vaccines and immunisation programmes in Georgia, India, Nigeria, Pakistan, and the United Kingdom (UK) - these being the first results of a larger project to map vaccine confidence globally. **METHODS:** Data were collected from a sample of the general population and from those with children under 5 years old against a core set of confidence questions. All surveys were conducted in the relevant local-language in Georgia, India, Nigeria, Pakistan, and the UK. We examine confidence in immunisation programmes as compared to confidence in other government health services, the relationships between confidence in the system and levels of vaccine hesitancy, reasons for vaccine hesitancy, ultimate vaccination decisions, and their variation based on country contexts and demographic factors. **RESULTS:** The numbers of respondents by country were: Georgia (n=1000); India (n=1259); Pakistan (n=2609); UK (n=2055); Nigerian households (n=12554); and Nigerian health providers (n=1272).

The UK respondents with children under five years of age were more likely to hesitate to vaccinate, compared to other countries. Confidence in immunisation programmes was more closely associated with confidence in the broader health system in the UK (Spearman's $\rho=0.5990$), compared to Nigeria ($\rho=0.5477$), Pakistan ($\rho=0.4491$), and India ($\rho=0.4240$), all of which ranked confidence in immunisation programmes higher than confidence in the broader health system. Georgia had the highest rate of vaccine refusals (6 %) among those who reported initial hesitation. In all other countries surveyed most respondents who reported hesitating to vaccinate went on to receive the vaccine except in Kano state, Nigeria, where the percentage of those who ultimately refused vaccination after initially hesitating was as high as 76%) Reported reasons for hesitancy in all countries were classified under the domains of "confidence," "convenience," or "complacency," and confidence issues were found to be the primary driver of hesitancy in all countries surveyed.

Larson, H., & Schulz, W. [The State of Vaccine Confidence](#). 2015. London: London School of Hygiene and Tropical Medicine.

Vaccine confidence is a global phenomenon with deep local roots. A key goal of the Vaccine Confidence Project is to build our understanding of the broader global picture, while also delving deep into local dynamics through case studies, using both qualitative and quantitative methods. Our latest report on The State of Vaccine Confidence summarises this work to date. The report analyses a number of vaccine confidence issues and the paths to their resolution over the past decade, including polio eradication and beyond. It also presents options for monitoring and measuring public confidence to detect waning confidence early and identify issues of concern, as well as reporting on strategies that have had positive impacts in engaging populations to build trust and confidence. This report also introduces the Vaccine Confidence Index (VCI) global mapping project, including results from the first five countries surveyed: Nigeria, Pakistan, India, Georgia, and the UK. As the VCI dataset expands, the latest findings from additional countries will be posted here on our website. Vaccine confidence is a global phenomenon with deep local roots. A key goal of the Vaccine Confidence Project is to build our understanding of the broader global picture, while also delving deep into local dynamics through case studies, using both qualitative and quantitative methods. Our latest report on The State of Vaccine Confidence summarises this work to date. The report analyses a number of vaccine confidence issues and the paths to their resolution over the past decade, including polio eradication and beyond. It also presents options for monitoring and measuring public confidence to detect waning confidence early and identify issues of concern, as well as reporting on strategies that have had positive impacts in engaging populations to build trust and confidence. This report also introduces the Vaccine Confidence Index (VCI) global mapping project, including results from the first five countries surveyed: Nigeria, Pakistan, India, Georgia, and the UK. As the VCI dataset expands, the latest findings from additional countries will be posted here on our website.

SAGE. [Report of the SAGE Working Group on Vaccine Hesitancy](#). October 2014.

No abstract available.

World Health Organization. **HPV Vaccine Communication: Considerations for a unique vaccine**. Geneva: WHO. 2013.

The report aims to offer guidance in two main areas: 1) to offer advice on basic communication planning and implementation for immunization; 2) to discuss specific considerations for HPV vaccine. The basic elements of a communication plan include building a cross-sectoral team; having clear programme

and communication objectives; understanding community knowledge, attitudes and practices; setting SMART objectives; defining target audiences with key messages for each; ensuring use of the right strategies, activities, channels and materials for each audience; having a risk communication plan for adverse events following immunization; and ensuring a monitoring and evaluation plan.

Session 4 *HPV vaccination programs: country experiences and lessons learnt.*

The Scottish HPV vaccine programme – why is it a success story?

Kevin Pollock, Health Protection (Scotland)

Cuschieri K, Kavanagh K, Moore C, Bhatia R, Love J, Pollock KG. **Impact of partial bivalent HPV vaccination on vaccine-type infection: a population-based analysis.** Br J Cancer. 2016; 114(11): 1261-4.

BACKGROUND: Data on the effectiveness of one dose of HPV vaccine are lacking, particularly in population-based settings. Data from a national HPV immunisation catch-up programme of 14-18-year-old girls were used to assess the effectiveness of <3 doses of the bivalent vaccine on vaccine-type and cross-reactive-type HPV infection. **METHODS:** Cervical samples from women attending for their first cervical smear, which had been genotyped for HPV as part of a longitudinal HPV surveillance programme were linked to immunisation records to establish the number of vaccine doses (0, 1, 2 and 3) administered. Vaccine effectiveness (VE) adjusted for deprivation and age at first dose, was assessed for prevalent HPV 16/18 and HPV 31/33/45 infection. **RESULTS:** VE for prevalent HPV 16/18 infection associated with 1, 2 and 3 doses was 48.2% (95% CI 16.8, 68.9), 54.8% (95% CI 30.7, 70.8) and 72.8% (95% CI 62.8, 80.3). Equivalent VE for prevalent HPV 31/33/45 infection was -1.62% (95% CI -85.1, 45.3), 48.3% (95% CI 7.6, 71.8) and 55.2% (95% CI 32.6, 70.2). **CONCLUSIONS:** Consistent with recent aggregated trial data, we demonstrate the potential effectiveness of even one dose of HPV vaccine on vaccine-type infection. Given that these women were immunised as part of a catch-up campaign, the VE observed in this study is likely to be an underestimate of what will occur in girls vaccinated at younger ages. Further population-based studies which look at the clinical efficacy of one-dose schedules are warranted.

Cameron RL, Ahmed S, Pollock KG. **Adverse event monitoring of the human papillomavirus vaccines in Scotland.** Intern Med J. 2016; 46(4): 452-7.

AIM: In Scotland, we utilised hospital admissions data to assess the impact of the HPV immunisation programme on the incidence of 60 diagnoses between 2004 and 2014 in both girls and boys; with boys acting as a comparator group. **METHODS:** Tabular and graphical outputs of the number of admissions, the incidence and the incidence ratio of 59 diagnoses were created to assess trends before and after the introduction of the HPV vaccine. Data linkage was utilised to investigate further the increase in Bell palsy diagnoses. **RESULTS:** Fifty-four diagnoses showed no change in incidence following the introduction of the national immunisation programme, and while small increases in incidence were observed for Bell palsy, coeliac disease, ovarian dysfunction, juvenile onset of type 1 diabetes, demyelinating disease and juvenile rheumatoid arthritis, none was statistically significant. **CONCLUSIONS:** Consistent with previous evidence, we present disaggregate data that reiterate the safety of both HPV vaccines.

Cameron RL, Kavanagh K, Pan J, Love J, Cuschieri K, Robertson C, Ahmed S, Palmer T, Pollock KG. **Human Papillomavirus Prevalence and Herd Immunity after Introduction of Vaccination Program, Scotland, 2009-2013.** Emerg Infect Dis. 2016; 22(1): 56-64.

In 2008, a national human papillomavirus (HPV) immunization program using a bivalent vaccine against HPV types 16 and 18 was implemented in Scotland along with a national surveillance program designed to determine the longitudinal effects of vaccination on HPV infection at the population level. Each year during 2009-2013, the surveillance program conducted HPV testing on a

proportion of liquid-based cytology samples from women undergoing their first cervical screening test for precancerous cervical disease. By linking vaccination, cervical screening, and HPV testing data, over the study period we found a decline in HPV types 16 and 18, significant decreases in HPV types 31, 33, and 45 (suggesting cross-protection), and a nonsignificant increase in HPV 51. In addition, among nonvaccinated women, HPV types 16 and 18 infections were significantly lower in 2013 than in 2009. Our results preliminarily indicate herd immunity and sustained effectiveness of the bivalent vaccine on virologic outcomes at the population level.

Pollock KG, Kavanagh K, Potts A, Love J, Cuschieri K, Cubie H, Robertson C, Cruickshank M, Palmer TJ, Nicoll S, Donaghy M.. **Reduction of low- and high-grade cervical abnormalities associated with high uptake of the HPV bivalent vaccine in Scotland.** Br J Cancer. 2014 ;111(9):1824-30.

BACKGROUND: In Scotland, a national HPV immunisation programme began in 2008 for 12- to 13-year olds, with a catch-up campaign from 2008 to 2011 for those under the age of 18. To monitor the impact of HPV immunisation on cervical disease at the population level, a programme of national surveillance was established. **METHODS:** We analysed colposcopy data from a cohort of women born between 1988 and 1992 who entered the Scottish Cervical Screening Programme (SCSP) and were aged 20-21 in 2008-2012. **RESULTS:** By linking datasets from the SCSP and colposcopy services, we observed a significant reduction in diagnoses of cervical intraepithelial neoplasia 1 (CIN 1; RR 0.71, 95% CI 0.58 to 0.87; P=0.0008), CIN 2 (RR 0.5, 95% CI 0.4 to 0.63; P<0.0001) and CIN 3 (RR 0.45, 95% CI 0.35 to 0.58; P<0.0001) for women who received three doses of vaccine compared with unvaccinated women. **CONCLUSIONS:** To our knowledge, this is one of the first studies to show a reduction of low- and high-grade CIN associated with high uptake of the HPV bivalent vaccine at the population level. These data are very encouraging for countries that have achieved high HPV vaccine uptake.

Kavanagh K, Pollock KG, Potts A, Love J, Cuschieri K, Cubie H, Robertson C, Donaghy M. **Introduction and sustained high coverage of the HPV bivalent vaccine leads to a reduction in prevalence of HPV 16/18 and closely related HPV types.** Br J Cancer. 2014 ;110(11):2804-11.

BACKGROUND: In 2008, a national human papillomavirus (HPV) immunisation programme began in Scotland for 12-13 year old females with a three-year catch-up campaign for those under the age of 18. Since 2008, three-dose uptake of bivalent vaccine in the routine cohort aged 12-13 has exceeded 90% annually, while in the catch-up cohort overall uptake is 66%. **METHODS:** To monitor the impact of HPV immunisation, a programme of national surveillance was established (pre and post introduction) which included yearly sampling and HPV genotyping of women attending for cervical screening at age 20. By linking individual vaccination, screening and HPV testing records, we aim to determine the impact of the immunisation programme on circulating type-specific HPV infection particularly for four outcomes: (i) the vaccine types HPV 16 or 18 (ii) types considered to be associated with cross-protection: HPV 31, 33 or 45; (iii) all other high-risk types and (iv) any HPV. **RESULTS:** From a total of 4679 samples tested, we demonstrate that three doses (n=1100) of bivalent vaccine are associated with a significant reduction in prevalence of HPV 16 and 18 from 29.8% (95% confidence interval 28.3, 31.3%) to 13.6% (95% confidence interval 11.7, 15.8%). The data also suggest cross-protection against HPV 31, 33 and 45. HPV 51 and 56 emerged as the most prevalent (10.5% and 9.6%, respectively) non-vaccine high-risk types in those vaccinated, but at lower rates than HPV 16 (25.9%) in those unvaccinated. **CONCLUSIONS:** This data demonstrate the positive impact of bivalent vaccination on the prevalence of HPV 16, 18, 31, 33 and 45 in the target population and is encouraging for countries which have achieved high-vaccine uptake.

Barriers in HPV vaccination in India.

Monica Chaturvedi, Monica Chaturvedi, Public Health Foundation (India)

Agoti, J. M., & Goldie, S. J. **Introducing HPV vaccine in developing countries-Key challenges and Issues.** N Engl J Med. 2007; 356(19): 1908-10.

No abstract available.

Das, B. C., Hussain, S., Nasare, V., & Bharadwaj, M. **Prospects and prejudices of human papillomavirus vaccines in India.** Vaccine. 2008; 26, 2669-2679.

Cervical cancer is the most common cancer and a leading cause of cancer deaths among women in developing countries. The disease is caused due to persistent infection of one or more of about 15 high-risk human papillomaviruses (HR-HPVs), most commonly by HPV types 16/18. In India, over 98% of cervical cancer cases harbor HPV infection and HPV 16 is the type exclusively (80-90%) prevalent. Unlike the West, HPV infection is most common in women in their third decade (26-35 years) of sexual activity and invasive cancer also arises much later with a peak at about 45-55 years of age. Recently, two successful prophylactic HPV vaccines, a quadrivalent (HPV16/18/6/11) 'Gardasil' by Merck and a bivalent (HPV16/18) 'Cervarix' by GSK have been developed. Several other approaches including plant-based edible, pentameric capsomere-based intranasal and DNA-based vaccines have also been employed to develop prophylactic vaccines. Also, several therapeutic vaccines either protein/peptide based or DNA based are in clinical trials but are yet to establish their efficacy. Though there are several issues regarding implementation of the already developed vaccines in resource limited countries, efforts are being made to develop cost-effective second-generation vaccines. If cost minimized, HPV related new technologies involved in screening tests and vaccines are expected to reduce incidence of cervical cancer and deaths it causes in women from developing countries.

Diaz, M., Kim, J., Albero, G., Sanjose, S., Clifford, G., Bosch, F., & Goldie, S. **Health and economic impact of HPV 16 and 18 vaccination and cervical cancer screening in India.** Br J Cancer. 2008; 99, 230-238.

Cervical cancer is a leading cause of cancer death among women in low-income countries, with approximately 25% of cases worldwide occurring in India. We estimated the potential health and economic impact of different cervical cancer prevention strategies. After empirically calibrating a cervical cancer model to country-specific epidemiologic data, we projected cancer incidence, life expectancy, and lifetime costs (I\$2005), and calculated incremental cost-effectiveness ratios (I\$/YLS) for the following strategies: pre-adolescent vaccination of girls before age 12, screening of women over age 30, and combined vaccination and screening. Screening differed by test (cytology, visual inspection, HPV DNA testing), number of clinical visits (1, 2 or 3), frequency (1 x, 2 x, 3 x per lifetime), and age range (35-45). Vaccine efficacy, coverage, and costs were varied in sensitivity analyses. Assuming 70% coverage, mean reduction in lifetime cancer risk was 44% (range, 28-57%) with HPV 16,18 vaccination alone, and 21-33% with screening three times per lifetime. Combining vaccination and screening three times per lifetime provided a mean reduction of 56% (vaccination plus 3-visit conventional cytology) to 63% (vaccination plus 2-visit HPV DNA testing). At a cost per vaccinated girl of I\$10 (per dose cost of \$2), pre-adolescent vaccination followed by screening three times per lifetime using either VIA or HPV DNA testing, would be considered cost-effective using the country's per capita gross domestic product (I\$3452) as a threshold. In India, if high coverage of pre-adolescent girls with a low-cost HPV vaccine that provides long-term protection is achievable, vaccination followed by screening three times per lifetime is expected to reduce cancer deaths by half, and be cost-effective.

SAGE. [Report of the SAGE Working Group on Vaccine Hesitancy](#). October 2014.

No abstract available.

Karthigeyan, K. **Cervical cancer in India and HPV vaccination**. Indian Journal of Medical and Paediatric Oncology.2012; 33(1): 7-12.

Cervical cancer, mainly caused by Human Papillomavirus infection, is the leading cancer in Indian women and the second most common cancer in women worldwide. Though there are several methods of prevention of cervical cancer, prevention by vaccination is emerging as the most effective option, with the availability of two vaccines. Several studies have been published examining the vaccine's efficacy, immunogenicity and safety. Questions and controversy remain regarding mandatory vaccination, need for booster doses and cost-effectiveness, particularly in the Indian context.

Larson, H., & Schulz, W. [The State of Vaccine Confidence](#). 2015. London: London School of Hygiene and Tropical Medicine.

Vaccine confidence is a global phenomenon with deep local roots. A key goal of the Vaccine Confidence Project is to build our understanding of the broader global picture, while also delving deep into local dynamics through case studies, using both qualitative and quantitative methods. Our latest report on The State of Vaccine Confidence summarises this work to date. The report analyses a number of vaccine confidence issues and the paths to their resolution over the past decade, including polio eradication and beyond. It also presents options for monitoring and measuring public confidence to detect waning confidence early and identify issues of concern, as well as reporting on strategies that have had positive impacts in engaging populations to build trust and confidence. This report also introduces the Vaccine Confidence Index (VCI) global mapping project, including results from the first five countries surveyed: Nigeria, Pakistan, India, Georgia, and the UK. As the VCI dataset expands, the latest findings from additional countries will be posted here on our website.

Madhivanan P., Krupp K., Yashodha M., Marlow L., Klausner J. D., & Reingold A. L. **Attitudes toward HPV vaccination among parents of adolescent girls in Mysore, India**. Vaccine. 2009; 27(38):5203-8.

This study investigates attitudes toward human papillomavirus (HPV) vaccination among parents of adolescent girls in Mysore, India. Seven focus group discussions were held among parents of adolescent girls stratified by sex, religion and region to explore attitudes about cervical cancer and HPV vaccination. The study found that while parents have limited knowledge about HPV or cervical cancer, most are still highly accepting an HPV vaccine. In addition, high acceptability levels appear to reflect positive attitudes toward the government universal immunization program in general, rather than to the HPV vaccine in particular. The results highlight the need for additional education and health promotion regarding HPV and cervical cancer prevention in India.

Matteij, I., Pollock, A., & Brhlikova, P. **Do cervical cancer data justify HPV vaccination in India? Epidemiological data source and comprehensiveness**. J R Soc Med. 2012; 105, 250-262.

The Indian government suspended research in April 2010 on the feasibility and safety of human papillomavirus (HPV) vaccine in two Indian states (Andhra Pradesh and Gujarat) amid public concerns about its safety. This paper describes cervical cancer and cancer surveillance in India and reviews the epidemiological claims made by the Programme for Appropriate Technology in Health (PATH) in support

of the vaccine in these two states. National cancer data published by the Indian National Cancer Registry Programme of state registry returns and the International Agency for Research on Cancer cover around seven percent of the population with underrepresentation of rural, northern, eastern and north-eastern areas. There is no cancer registry in the state of Andhra Pradesh and PATH does not cite data from the Gujarat cancer registries. Age-adjusted cervical cancer mortality and incidence rates vary widely across and within states. National trends in age standardized cervical cancer incidence fell from 42.3 to 22.3 per 100,000 between 1982/1983 and 2004/2005 respectively. Incidence studies report low incidence and mortality rates in Gujarat and Andhra Pradesh. Although HPV prevalence is higher in cancer patients (93.3%) than healthy patients (7.0%) and HPV types 16 and 18 are most prevalent in cancer patients, population prevalence data are poor and studies highly variable in their findings. Current data on HPV type and cervical cancer incidence do not support PATH's claim that India has a large burden of cervical cancer or its decision to roll out the vaccine programme. In the absence of comprehensive cancer surveillance, World Health Organization criteria with respect to monitoring effectiveness of the vaccine and knowledge of disease trends cannot be fulfilled.

MoHFW. (n.d.). [Universal Immunization Program.](#)

No abstract available.

Paul P, Tanner AE, Gravitt PE, Vijayaraghavan K, Shah, KV, & Zimet GD. **Acceptability of HPV vaccine implementation among parents in India.** Health Care Women International. 2014; 35(10): 1148-1161.

Due to high cervical cancer rates and limited research on human papillomavirus (HPV) vaccine acceptability in India, the research team examined parental attitudes toward HPV vaccines. Thirty-six interviews with parents were conducted to assess sexually transmitted infection (STI)-related knowledge and HPV-specific vaccine awareness and acceptability. Despite limited knowledge, parents had positive views toward HPV vaccines. Common barriers included concerns about side effects, vaccine cost, and missing work to receive the vaccine. Parents were strongly influenced by health care providers' recommendations. Our findings suggest that addressing parental concerns, health worker training and policies, and efforts to minimize cost will be central to successful HPV vaccine implementation.

Sankaranarayanan, R., et al. **HPV screening for cervical cancer in rural India.** New Engl J Med. 2009; 360(14).

BACKGROUND: In October 1999, we began to measure the effect of a single round of screening by testing for human papillomavirus (HPV), cytologic testing, or visual inspection of the cervix with acetic acid (VIA) on the incidence of cervical cancer and the associated rates of death in the Osmanabad district in India. **METHODS:** In this cluster-randomized trial, 52 clusters of villages, with a total of 131,746 healthy women between the ages of 30 and 59 years, were randomly assigned to four groups of 13 clusters each. The groups were randomly assigned to undergo screening by HPV testing (34,126 women), cytologic testing (32,058), or VIA (34,074) or to receive standard care (31,488, control group). Women who had positive results on screening underwent colposcopy and directed biopsies, and those with cervical precancerous lesions or cancer received appropriate treatment. **RESULTS:** In the HPV-testing group, cervical cancer was diagnosed in 127 subjects (of whom 39 had stage II or higher), as compared with 118 subjects (of whom 82 had advanced disease) in the control group (hazard ratio for the detection of advanced cancer in the HPV-testing group, 0.47; 95% confidence interval [CI], 0.32 to 0.69). There were 34 deaths from cancer in the HPV-testing group, as compared with 64 in the control group (hazard ratio, 0.52; 95% CI, 0.33 to 0.83). No significant reductions in the numbers of advanced cancers or deaths were observed in the cytologic-testing group or in the VIA group, as compared with the control group. Mild

adverse events were reported in 0.1% of screened women. **CONCLUSIONS:** In a low-resource setting, a single round of HPV testing was associated with a significant reduction in the numbers of advanced cervical cancers and deaths from cervical cancer.

The Japanese HPV vaccine tragedy and the take-home message
Sharon Hanley, Hokkaido University Graduate School of Medicine (Japan)

Hanley SJB, Fujita H, Yokoyama S, Kunisawa S, Tamakoshi A, Dong P, Kobayashi N, Watari H, Kudo M and Sakuragi N. **HPV self-sampling in Japanese women: A feasibility study in a population with limited experience of tampon use**, J Med Screen, 2016.

OBJECTIVES: Cervical cancer incidence and mortality is increasing in Japanese women under age 50. Screening uptake is low and proactive recommendations for human papillomavirus vaccination have been suspended. Other cervical cancer prevention initiatives are urgently needed. We assessed whether human papillomavirus self-sampling might be an acceptable alternative to physician-led screening, particularly in women with limited experience of tampon use. We also sought to identify any practical, logistical, or safety issues in women already attending for screening, before carrying out further large-scale studies in non-responders. **METHODS:** In total, 203 women aged 20-49 attending their annual workplace healthcheck in Sapporo, northern Japan, performed unsupervised human papillomavirus self-sampling before undergoing a physician-led cervical smear and human papillomavirus test, and completing a measure of acceptability for both tests. **RESULTS:** Ninety per cent of participants stated they would use self-sampling again. They found instructions easy to follow and reported no issues with the usability of the self-sampling device. Compared with physician-led testing, women found self-sampling significantly less painful, less embarrassing and could relax more ($p < 0.001$), regardless of history of tampon use, which was associated with negative experiences in physician sampling ($p = 0.034$). Women lacked confidence the test had been performed correctly, despite no unsatisfactory samples. No safety issues were reported. **CONCLUSIONS:** Self-sampling was highly acceptable in this population of women. They could perform the test safely unsupervised, but lacked confidence the test has been carried out correctly. Japanese women need to be educated about the accuracy of human papillomavirus self-sampling and further large-scale studies are necessary in non-responders.

Hanley SJB, Yoshioka E, Ito Y, Kishi R. **HPV vaccination crisis in Japan**, Lancet. 2015; 385 (9987): 2571.

No abstract available

Hanley SJB, Pollock KG, Cuschieri K. **Peripheral sympathetic nerve dysfunction in adolescent Japanese girls following immunization with the human papillomavirus vaccine**. Intern Med. 2015; 54(15): 1953.

No abstract available

Larson HJ, Wilson R, Hanley SJB, Parys A & Paterson P. **Tracking the global spread of vaccine sentiments: The global response to Japan's suspension of its HPV vaccine recommendation.** *Hum Vaccin Immunother.* 2014; 10(9): 2543-50.

BACKGROUND: In June 2013 the Japanese Ministry of Health, Labor, and Welfare (MHLW) suspended its HPV vaccination recommendation after a series of highly publicized alleged adverse events following immunization stoked public doubts about the vaccine's safety. This paper examines the global spread of the news of Japan's HPV vaccine suspension through online media, and takes a retrospective look at non-Japanese media sources that were used to support those claiming HPV vaccine injury in Japan. **METHODS:** Two searches were conducted. One searched relevant content in an archive of Google Alerts on vaccines and vaccine preventable diseases. The second search was conducted using Google Search on January 6th 2014 and on July 18th 2014, using the keywords, "HPV vaccine Japan" and "cervical cancer vaccine Japan." Both searches were used as Google Searches render more (and some different) results than Google Alerts. **RESULTS:** Online media collected and analyzed totalled 57. Sixty 3 percent were published in the USA, 23% in Japan, 5% in the UK, 2% in France, 2% in Switzerland, 2% in the Philippines, 2% in Kenya and 2% in Denmark. The majority took a negative view of the HPV vaccine, the primary concern being vaccine safety. **DISCUSSION:** The news of Japan's suspension of the HPV vaccine recommendation has traveled globally through online media and social media networks, being applauded by anti-vaccination groups but not by the global scientific community. The longer the uncertainty around the Japanese HPV vaccine recommendation persists, the further the public concerns are likely to travel.

Hanley SJB, Yoshioka E, Ito Y, Konno R, Sasaki Y, Kishi R, Sakuragi N. An exploratory study of Japanese fathers' knowledge of and attitudes towards HPV and HPV vaccination: does marital status matter?, *Asian Pac J Cancer Prev.* 2014; 15(4): 1837-43.

BACKGROUND: No studies on male attitudes towards HPV and HPV vaccination have been conducted in Japan, and little is known globally whether attitudes of single fathers differ to those living with a female partner. This exploratory study assessed whether Japanese fathers were likely to have their daughter vaccinated against HPV in a publically funded program and whether any differences existed regarding attitudes and knowledge about HPV according to marital status. **MATERIALS AND METHODS:** Subjects were 27 fathers (16 single; 11 married) who took part in a study on HPV vaccine acceptability aimed at primary caregivers of girls aged 11-14 yrs in three Japanese cities between July and December 2010. **RESULTS:** Knowledge about HPV was extremely poor (mean score out of 13 being 2.74 +/- 3.22) with only one (3.7%) participant believing he had been infected with HPV and most (81.4%) believing they had no or low future risk. No difference existed regarding knowledge or awareness of HPV according to marital status. Concerning perceived risk for daughters, single fathers were significantly more likely to believe their daughter was at risk for both HPV (87.5% versus 36.4%; $p=0.01$) and cervical cancer (75.0% versus 27.3%; $p=0.02$). Acceptability of free HPV vaccination was high at 92% with no difference according to marital status, however single fathers were significantly more likely ($p=0.01$) to pay when vaccination came at a cost. Concerns specific to single fathers included explaining the sexual nature of HPV and taking a daughter to a gynecologist to be vaccinated. **CONCLUSIONS:** Knowledge about HPV among Japanese fathers is poor, but HPV vaccine acceptability is high and does not differ by marital status. Providing sexual health education in schools that addresses lack of knowledge about HPV as well as information preferences expressed by single fathers, may not only increase HPV vaccine acceptance, but also actively involve men in cervical cancer prevention strategies. However, further large-scale quantitative studies are needed.

Hosaka M, Fujita H, Hanley SJB, Sasaki T, Shirakawa Y, Kudo M, Kaneuchi M, Watari H, Kikuchi K, Sakuragi N. **Incidence risk of cervical intraepithelial neoplasia 3 or more severe lesions is a function of human papillomavirus genotypes and severity of cytological and histological abnormalities in adult Japanese women**, *Int J Cancer* 132(2): 327-34, 2013.

We examined incidence probabilities of cervical intraepithelial neoplasia 3 (CIN3) or more severe lesions (CIN3+) in 1,467 adult Japanese women with abnormal cytology in relation to seven common human papillomavirus (HPV) infections (16/18/31/33/35/52/58) between April 2000 and March 2008. Sixty-seven patients with multiple HPV infection were excluded from the risk factor analysis. Incidence of CIN3+ in 1,400 patients including 68 with ASCUS, 969 with low grade squamous intraepithelial lesion (LSIL), 132 with HSIL without histology-proven CIN2 (HSIL/CIN2(-)) and 231 with HSIL with histology-proven CIN2 (HSIL/CIN2(+)) was investigated. In both high grade squamous intraepithelial lesion (HSIL)/CIN2(-) and HSIL/CIN2(+), HPV16/18/33 was associated with a significantly earlier and higher incidence of CIN3+ than HPV31/35/52/58 ($p = 0.049$ and $p = 0.0060$, respectively). This association was also observed in LSIL ($p = 0.0002$). The 1-year cumulative incidence rate (CIR) of CIN3+ in HSIL/CIN2(-) and HSIL/CIN2(+) according to HPV genotypes (16/18/33 vs. 31/35/52/58) were 27.1% vs. 7.5% and 46.6% vs. 19.2%, respectively. In contrast, progression of HSIL/CIN2(+) to CIN3+ was infrequent when HPV DNA was undetected: 0% of 1-year CIR and 8.1% of 5-year CIR. All cervical cancer occurred in HSIL cases of seven high-risk HPVs (11/198) but not in cases of other HPV or undetectable/negative-HPV (0/165) ($p = 0.0013$). In conclusion, incidence of CIN3+ depends on HPV genotypes, severity of cytological abnormalities and histology of CIN2. HSIL/CIN2(+) associated with HPV16/18/33 may justify early therapeutic intervention, while HSIL/CIN2(-) harboring these HPV genotypes needs close observation to detect incidence of CIN3+. A therapeutic intervention is not indicated for CIN2 without HPV DNA.

Hayashi Y, Shimizu Y, Netsu S, Hanley SJB, Konno R. **High HPV vaccination uptake rates for adolescent girls after regional governmental funding in Shiki City, Japan**. *Vaccine*. 2012; 30(37): 5547-50.

BACKGROUND: In Japan, the bivalent HPV vaccine was approved in October, 2009 and became available as a non-routine vaccine from December, 2009. While routine vaccinations are free, the cost and responsibility for non-routine vaccinations are left to the individual. In exceptional circumstances regional governments fund non-routine vaccinations. This was the case in Shiki City, Saitama Prefecture, where a high uptake rate for individual (non-school based) HPV vaccination was obtained. **MATERIALS:** On January 20, 2010, the mayor of Shiki City announced to the media his decision to vaccinate adolescent girls in Shiki City against HPV. A project team for HPV vaccination was set up in the city's Health Promotion Center. To gain mutual consent for HPV vaccination, senior health professionals, city officials, the head of the board of education, school principals and health-care teachers met several times. The cohort to be vaccinated was 1254 girls aged 12-15 years. Individual notifications were mailed to each girl on April 23, 2010, along with information about the HPV vaccine. **CONCLUSIONS:** As of April 10th, 2011, the uptake rate for girls aged 15 years old was 90.7% for the 1st dose. The vaccine registry is managed by the health care system of the city. The success of the HPV vaccination program and high uptake rates in Shiki City is a good model for the nationwide HPV vaccination program that started in February, 2011.

Hanley SJB, Yoshioka E, Ito Y, Konno R, Hayashi Y, Kishi R, Sakuragi N. **Acceptance of and attitudes towards human papillomavirus vaccination in Japanese mothers of adolescent girls**. *Vaccine* 2012; 30(39): 5740-7.

To better understand how to achieve high uptake rates of human papillomavirus (HPV) vaccination in Japan, we investigated acceptance of and attitudes towards HPV vaccination in 2192 mothers of girls aged 11-14 yrs. A school-based survey was conducted in five elementary and fourteen junior high schools in Sapporo, Japan. Responses from 862 participants were analyzed. Ninety-three

percent of mothers would accept the vaccine for their daughter if free, but only 1.5% was willing to pay the minimum recommended price of ¥ 40,000. Vaccine acceptance was higher in mothers who had heard of HPV vaccine (adjusted odds ratio, aOR=2.58, confidence interval, CI=1.47-4.53), and who believed susceptibility to (aOR=2.30, CI=1.34-3.92) and severity of (aOR=3.73, CI=1.41-9.88) HPV to be high. Recommendations from a doctor (aOR=12.60, CI=7.06-21.48) and local health board (aOR=27.80, CI=13.88-55.86) were also positively associated with increased HPV vaccine acceptance. Concerns about side effects of both the HPV vaccine (aOR=0.03, CI=0.01-0.08) and routine childhood vaccines in general (aOR=0.11, CI=0.02-0.78) emerged as barriers to vaccination. Not participating in routine cervical screening also emerged as a deterrent (aOR=0.49, CI=0.27-0.91). While most mothers (66.8%) agreed that 10-14 yr was an appropriate age for vaccination, a further 30.6% believed >15 yr to be more appropriate. In conclusion, attitudes of Japanese mothers toward HPV vaccination are encouraging. While lower vaccine acceptance in mothers who do not undergo regular cervical screening needs further investigation, this study indicates that high uptake may be possible in a publically funded HPV vaccination program if physicians actively address safety concerns and justify why the vaccine is needed at a particular age.

Hanley SJB, Konno R. **HPV catch-up vaccination: The benefits of vaccinating Japanese women in their forties.** *Obstet Gynecol.* 2010; 77 (9): 1016-1022 (In Japanese).

No abstract available

Konno R, Sagae S, Yoshikawa H, Basu PS, Hanley SJB, Tan JH, Shin HR. **Cervical Cancer Working Group report.** 2010; *Jpn J Clin Oncol* 40 Suppl 1: i44-50.

Disease burden of cervical cancer in Asia was summarized. Human papillomavirus 16 is the most oncogenic human papillomavirus type. Korea's national cervical cancer screening program targets women aged 30 or over, with coverage of almost 80%. Japan has a long history (50 years) of cervical cancer screening, and cytological screening programs have reduced the incidence/mortality of cervical cancer by 70%. But, recent cervical cancer screening coverage is ~24%. Modeling suggested that vaccination of all 12-year-old girls would reduce cervical cancer cases by 73% in Japan. India has no cervical cancer screening program, as well as a serious lack of awareness in the general population, medical professionals and policy-makers. A realistic, affordable approach would be a low-volume, once-in-a-lifetime human papillomavirus-based screening program. In Australia, the national cervical cancer program has been very successful in reducing the incidence and mortality of cervical cancer. Australia was the first country to implement free, national human papillomavirus immunization (April 2007), expected to reduce human papillomavirus 16 infections by 56% in 2010 and 92% in 2050. A comparison of the UK and Japan was demonstrated that in the UK, cervical cancer screening and human papillomavirus vaccination uptakes are high because the government provides adequate education/funding. The Japanese government needs to put more emphasis on women's health and preventative medicine. Our conclusion and recommendations are that heightened public awareness of cervical cancer prevention, focusing on screening and vaccination will lead to improved survival and a better quality of life.

Implementing the HPV programme in England – what mattered?
Joanne Yarwood, National Infection Service, Public Health England

HPV Vaccination in the United States, the First 10 Years: Policy, Program and Monitoring.
Lauri Markowitz, Centre for Disease Control & Prevention (CDC) (US)

Reagan-Steiner S, Yankey D, Jeyarajah J, Elam-Evans L, Singleton J, Curtis R, MacNeil J, Markowitz LE, Stokley S. **National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 Years — United States, 2014.** MMWR. 2015; 64:784-91.

Routine immunization is recommended for adolescents aged 11-12 years by the Advisory Committee on Immunization Practices (ACIP) for protection against diseases including pertussis, meningococcal disease, and human papillomavirus (HPV)-associated cancers. To assess vaccination coverage among adolescents, CDC analyzed data collected regarding 20,827 adolescents through the 2014 National Immunization Survey-Teen (NIS-Teen). From 2013 to 2014, coverage among adolescents aged 13-17 years increased for all routinely recommended vaccines: from 84.7% to 87.6% for ≥1 tetanus-diphtheria-acellular pertussis (Tdap) vaccine dose, from 76.6% to 79.3% for ≥1 meningococcal conjugate (MenACWY) vaccine dose, from 56.7% to 60.0% and from 33.6% to 41.7% for ≥1 HPV vaccine dose among females and males, respectively.† Coverage differed by state and local area. Despite overall progress in vaccination coverage among adolescents, HPV vaccination coverage continues to lag behind Tdap and MenACWY coverage at state and national levels. Seven public health jurisdictions achieved significant increases in ≥1- or ≥3-dose HPV vaccination coverage among females in 2014, demonstrating that substantial improvement in HPV vaccination coverage is feasible.

Markowitz LE, Liu G, Hariri S, Steinau M, Dunne EF, Unger ER. **Prevalence of HPV after introduction of the vaccination program in the United States.** Pediatrics. 2016; 137:1-9.

BACKGROUND: Since mid-2006, human papillomavirus (HPV) vaccination has been recommended for females aged 11 to 12 years and through 26 years if not previously vaccinated. **METHODS:** HPV DNA prevalence was analyzed in cervicovaginal specimens from females aged 14 to 34 years in NHANES in the prevaccine era (2003-2006) and 4 years of the vaccine era (2009-2012) according to age group. Prevalence of quadrivalent HPV vaccine (4vHPV) types (HPV-6, -11, -16, and -18) and other HPV type categories were compared between eras. Prevalence among sexually active females aged 14 to 24 years was also analyzed according to vaccination history. **RESULTS:** Between the prevaccine and vaccine eras, 4vHPV type prevalence declined from 11.5% to 4.3% (adjusted prevalence ratio [aPR]: 0.36 [95% confidence interval (CI): 0.21-0.61]) among females aged 14 to 19 years and from 18.5% to 12.1% (aPR: 0.66 [95% CI: 0.47-0.93]) among females aged 20 to 24 years. There was no decrease in 4vHPV type prevalence in older age groups. Within the vaccine era, among sexually active females aged 14 to 24 years, 4vHPV type prevalence was lower in vaccinated (≥1 dose) compared with unvaccinated females: 2.1% vs 16.9% (aPR: 0.11 [95% CI: 0.05-0.24]). There were no statistically significant changes in other HPV type categories that indicate cross-protection. **CONCLUSIONS:** Within 6 years of vaccine introduction, there was a 64% decrease in 4vHPV type prevalence among females aged 14 to 19 years and a 34% decrease among those aged 20 to 24 years. This finding extends previous observations of population impact in the United States and demonstrates the first national evidence of impact among females in their 20s.

Shimabukuro T, Nguyen M, Martin D, DeStefano F. **Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS).** Vaccine. 2015 Aug 26;33(36):4398-405.

The Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA) conduct post-licensure vaccine safety monitoring using the Vaccine Adverse Event Reporting System (VAERS), a spontaneous (or passive) reporting system. This means that after a vaccine is approved, CDC and FDA continue to monitor safety while it is distributed in the marketplace for use by collecting and analyzing spontaneous reports of adverse events that occur in persons following vaccination. Various methods and statistical techniques are used to analyze VAERS data, which CDC and FDA use to guide

further safety evaluations and inform decisions around vaccine recommendations and regulatory action. VAERS data must be interpreted with caution due to the inherent limitations of passive surveillance. VAERS is primarily a safety signal detection and hypothesis generating system. Generally, VAERS data cannot be used to determine if a vaccine caused an adverse event. VAERS data interpreted alone or out of context can lead to erroneous conclusions about cause and effect as well as the risk of adverse events occurring following vaccination. CDC makes VAERS data available to the public and readily accessible online. We describe fundamental vaccine safety concepts, provide an overview of VAERS for healthcare professionals who provide vaccinations and might want to report or better understand a vaccine adverse event, and explain how CDC and FDA analyze VAERS data. We also describe strengths and limitations, and address common misconceptions about VAERS. Information in this review will be helpful for healthcare professionals counselling patients, parents, and others on vaccine safety and benefit-risk balance of vaccination.

Belgium

Geert Top, Agentschap Zorg en Gezondheid (Belgium)

Romania

Patriciu Achimas, The Oncology Institute "Prof. Dr. Ion Chiricuta" (Romania)

HPV vaccination experience in 45 low and middle-income countries: lessons learnt

Kate Gallagher (presenting on behalf of Deborah Watson-Jones), London School of Hygiene and Tropical Medicine (UK)

Gallagher KE, Baisley K, Grosskurth H, Vallely A, Kapiga AS, Vandepitte J, Kamali A, de Sanjosé S, Changalucha J, Hayes R, Watson-Jones D. **The Association Between Cervical Human Papillomavirus Infection and Subsequent HIV Acquisition in Tanzanian and Ugandan Women: A Nested Case-Control Study** *J Infect Dis.* 2016. 214(1):87-95.

OBJECTIVE: This study was performed to analyze the associations between cervical human papillomavirus (HPV) infection and human immunodeficiency virus (HIV) acquisition, using cervical samples from previous studies in Tanzania and Uganda. **METHODS:** A total of 161 adult women who acquired HIV infection during follow-up and 464 individually matched HIV-seronegative controls were selected from 5 cohorts of women working in bars and recreational facilities. Stored cervical samples were tested for 37 HPV genotypes, using a polymerase chain reaction assay (Roche Linear Array genotyping assay). Multivariate matched analysis using conditional logistic regression was performed to evaluate HPV infection, persistence, and clearance as predictors of HIV acquisition. **RESULTS:** HIV seroconverters were significantly more likely than controls to frequently drink alcohol and to be infected with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or herpes simplex virus type 2. There was no evidence of an association between HIV acquisition and any detectable HPV at the visit prior to HIV seroconversion (adjusted odds ratio, 1.02; 95% confidence interval, .66-1.57) or between HIV acquisition and persistent HPV infection (defined as 2 positive HPV genotype-specific test results at least 6 months apart), cleared HPV infection (defined as a positive HPV test result followed by negative HPV genotype-specific test result), or newly acquired HPV infection, compared with HPV-negative women. **CONCLUSIONS:** There was no evidence of association between HPV infection status and subsequent HIV acquisition. These results stand in contrast to other observational studies.

Gallagher KE, Griffiths UK, Burchett HED, et al. **Lessons learnt from human papillomavirus vaccine delivery in low and middle-income countries.** Abstract presented at 30th International Papillomavirus Conference, Lisbon, Portugal 17th-21st September 2015 (Abstract HPV15-0130) 2015.

Gallagher KE, Kadokura E, Eckert LO, et al. **Factors influencing completion of multi-dose vaccine schedules in adolescents: a systematic review.** BMC public health 2016;16(1):172.

BACKGROUND: Completion of multiple dose vaccine schedules is crucial to ensure a protective immune response, and maximise vaccine cost-effectiveness. While barriers and facilitators to vaccine uptake have recently been reviewed, there is no comprehensive review of factors influencing subsequent adherence or completion, which is key to achieving vaccine effectiveness. This study identifies and summarises the literature on factors affecting completion of multi-dose vaccine schedules by adolescents. **METHODS:** Ten online databases and four websites were searched (February 2014). Studies with analysis of factors predicting completion of multi-dose vaccines were included. Study participants within 9-19 years of age were included in the review. The defined outcome was completion of the vaccine series within 1 year among those who received the first dose. **RESULTS:** Overall, 6159 abstracts were screened, and 502 full texts were reviewed. Sixty one studies were eligible for this review. All except two were set in high-income countries. Included studies evaluated human papillomavirus vaccine, hepatitis A, hepatitis B, and varicella vaccines. Reported vaccine completion rates, among those who initiated vaccination, ranged from 27% to over 90%. Minority racial or ethnic groups and inadequate health insurance coverage were risk factors for low completion, irrespective of initiation rates. Parental healthcare seeking behaviour was positively associated with completion. Vaccine delivery in schools was associated with higher completion than delivery in the community or health facilities. Gender, prior healthcare use and socio-economic status rarely remained significant risks or protective factors in multivariate analysis. **CONCLUSIONS:** Almost all studies investigating factors affecting completion have been carried out in developed countries and investigate a limited range of variables. Increased understanding of barriers to completion in adolescents will be invaluable to future new vaccine introductions and the further development of an adolescent health platform.

Kabakama S, Gallagher KE, Howard N, et al. **Social mobilisation, consent procedures, and acceptability: a study of human papillomavirus vaccination in low and middle-income countries.** (Accepted; BMC PH) 2016.

No abstract available.

E-learning initiative on vaccine safety assessment focused in HPV vaccines.
Xavier Bosch, Catalanian Institute of Oology (Spain)

Denmark

*Kåre Mølbak, Anders Koch, Statens Serum Institute, Division of Epidemiology
and Disease Surveillance (Denmark)*

Session 5 **Barriers and opportunities in HPV screening programs**

Using behavioural science to increase participation in cervical cancer prevention.

Laura Marlow, Department of Epidemiology and Public Health, UCL (UK)

Waller J, Jackowska M, Marlow LAV & Wardle J. **Exploring age differences in reasons for nonattendance for cervical screening: a qualitative study.** *BJOG.* 2012; 119 (1), 26-32.

OBJECTIVES: To explore differences in barriers to attendance at cervical screening across age groups because coverage of the cervical screening programme in England has been falling, particularly among women in the youngest age group (25-29 years). **DESIGN:** A qualitative study. **SETTING:** A university in London. **SAMPLE:** Professionals working in the screening field (n=12) and women of varying ages who had either never attended for cervical screening or did not attend regularly (n=46). **METHODS:** In Study 1 we interviewed professionals to elicit their views on the reasons for lower screening attendance in young women. In Study 2, we carried out four focus groups (n=27) and 19 individual interviews with under-screened women to explore their barriers to attendance. Verbatim transcripts were analysed using Framework Analysis. **RESULTS:** Reasons for nonattendance were many and varied. Health professionals identified population-level factors, service provision issues, time pressures, risk perceptions, lack of knowledge and psychological barriers. The nonattenders fell into two groups: those who had made an active decision not to take part (who tended to be older), and those who intended to be screened but did not attend (predominantly younger women). Practical barriers were raised more often by younger women whereas older women had more negative attitudes to screening. **CONCLUSION:** This study provides rich data on the complex reasons why women do not attend for cervical screening. It points to age differences in barriers to screening, and suggests that addressing practical issues such as appointment systems and clinic times may have a positive impact on attendance in young women.

Sheeran P. **Intention—Behavior Relations: A Conceptual and Empirical Review.** *European Review of Social Psychology.* 2002; 12 (1), 1-6.

This chapter addresses two questions; how big is the “gap” between intentions and behavior, and what psychological variables might be able to “bridge” the intention-behavior gap? A meta-analysis of meta-analyses is used to quantify the gap and a conceptual analysis of intention-behavior discrepancies is presented. Research is described on the extent to which four groups of variables behavior type, intention type, properties of intention, and cognitive and personality variables-moderate intention-behavior relations. Finally, the scope of the intention construct is discussed in the light of recent evidence concerning the role of habits and automaticity in human behavior.

Chorley AJ, Marlow L AV, Forster AS, Haddrell JB & Waller J. **Experiences of cervical screening and barriers to participation in the context of an organised programme: A systematic review and thematic synthesis.** *Psycho-Oncology.* 2016; doi: 10.1002/pon.4126 (Online ahead of print).

OBJECTIVE: As uptake of cervical screening continues to decline, this systematic review synthesises the qualitative literature on women's perceptions and experiences of cervical screening in the context of an organised call-recall programme, in order to understand the barriers to informed uptake. **METHODS:** We searched nine databases for English language peer-reviewed publications reporting on qualitative data from screening-eligible women, exploring barriers to cervical screening in countries that offer a nationally organised call-recall programme. Evidence was integrated using thematic synthesis.

RESULTS: Thirty-nine papers from the UK, Australia, Sweden and Korea were included. The majority of participants had attended screening at least once. Two broad themes were identified: (a) should I go for screening? and (b) screening is a big deal. In considering whether to attend, women discussed the personal relevance and value of screening. Women who had previously attended described how it was a big deal, physically and emotionally, and the varied threats that screening presents. Practical barriers affected whether women translated screening intentions into action. CONCLUSIONS: The variation in women's understanding and perceptions of cervical screening suggests that interventions tailored to decisional stage may be of value in increasing engagement with the invitation and uptake of screening in those who wish to take part. There is also a need for further research with women who have never attended screening, especially those who remain unaware or unengaged, as their perspectives are lacking in the existing literature.

Weinstein ND, Sandman PM, Blalock SJ. [The Precaution Adoption Process Model](#). In: Glanz K, Rimer BK & Viswanath K (eds.) Health Behaviour and Health Education, 4th edn. Jossey-Bass: San Francisco. 2008: 123-47.

No abstract available.

Mobilizing resources for scale-up of vaccination and screening/preventive treatment: Cervical Cancer Action and the new global Initiative.
Scott Wittet, PATH (US)

Progress in Cervical Cancer Prevention: The CCA Report Card 2015

http://www.cervicalcanceraction.org/pubs/CCA_reportcard_low-res_2015.pdf

Over the past decade, the world has seen extraordinary advances in cervical cancer prevention. Until recently, the knowledge and tools needed to effectively tackle the disease in low-resource settings had not been developed or validated. Today, following extraordinary scientific breakthroughs, strategic field research, and tireless efforts by governments and their partners, a new reality is emerging. We now have the knowledge and tools to bring cervical cancer prevention to every country and to dramatically scale interventions that are proven to save women's lives. Ramping up global commitment to cervical cancer prevention is critical to achieve current and emerging global health and development targets and the reduction of NCDs worldwide. Cervical cancer prevention should be a core component of an integrated approach to protecting women, children, and adolescents throughout the life-course. We must support the integration of vaccination, screening, and preventive treatment into school health, women's health, and HIV/ AIDS prevention and treatment programs. It is time for international agencies, governments, and donors to step up their efforts to support national initiatives. Engagement in cervical cancer prevention could result in one of the most significant "easy wins" in global public health today. By working to improve and scale current prevention programs, we have the unique opportunity to strengthen health systems and expand equity

Investing in Cervical Cancer Prevention 2015–2020: Meeting report, London, November 3 & 4, 2015

http://www.cervicalcanceraction.org/pubs/CCA_london_meeting_report_2015.pdf

Cervical Cancer Prevention: Practical Experience from PATH

<http://www.rho.org/HPV-practical-experience.htm>

From 2006 to 2011, PATH conducted demonstration projects in four low- to middle-income countries—India, Peru, Uganda, and Vietnam—to provide evidence for decision-making about public-sector introduction of human papillomavirus (HPV) vaccines. The Cervical Cancer Prevention: Practical Experience Series summarizes lessons learned from these projects that can help guide future cervical cancer prevention program planning, especially in low-resource settings around the globe.

HPV Vaccine Lessons Learnt

<http://www.rho.org/HPVlessons/>

To aid decision-makers interested in HPV vaccine introduction or scale-up, in 2014–2015 the [London School of Hygiene & Tropical Medicine](#) and [PATH](#) conducted the first comprehensive review of HPV vaccine delivery experiences across 37 low- and middle-income countries. These experiences have helped countries learn valuable lessons about effective methods for garnering parental acceptance and reaching young adolescent girls with the vaccine, at relatively low delivery costs. The lessons learnt from these countries can provide critical information for policymakers and programme planners on how best to prepare, deliver, and sustain HPV vaccines. Highlights include key findings and lessons from HPV vaccination experience across five themes: preparation, communications, delivery, achievements, and sustainability. Also addressed are the value of demonstration projects and potential HPV vaccination pitfalls.

Reducing cervical cancer inequities worldwide

http://www.rho.org/files/PATH_Cervical_cancer_inequities_2015.pdf

Social determinants of health associated with cervical cancer screening; focus on barriers/challenges/facilitators with vulnerable or marginalized women.

Pamela Wakewich, Lakehead University (Canada)

Maar, M., P. Wakewich, B. Wood, A. Severini, J. Little, A. N. Burchell, G. Ogilvie and I. Zehbe. **Strategies for Increasing Cervical Cancer Screening Amongst First Nations Communities in Northwest Ontario, Canada.** *Health Care Women Int.* 2016; 37(4): 478-495.

The high burden of cervical cancer in Indigenous populations worldwide is due to underscreening and inadequate follow-up. Using qualitative, participatory action research, we interviewed health care staff to identify ways to increase screening recruitment in First Nations communities in Northwest Ontario, Canada. Our findings suggest the value of a multilevel social-ecological model to promote behavioral changes at the community, health care service and stakeholder, and decision-maker level. Participants emphasized the central role of First Nations women as nurturers of life and for the well-being of their family members. They stressed the importance of building awareness and motivation for cervical cancer screening through various activities including continuous education, hosting screening events specifically for women, improving the attitude and service of health care providers, and promoting screening tools and policies that complement and are respectful of First Nations women.

Wakewich, P., Wood, B., Davey, C., Laframboise, A., Zehbe, I. and on behalf of the ACCSS group. **Colonial legacy and the experience of First Nations women in cervical cancer screening: a Canadian multi-community study.** *Critical Public Health.* 2015; DOI: 10.1080/09581596.2015.1067671.

Regular Papanicolaou (Pap) screening has dramatically reduced cervical cancer incidence in Canada since the 1950s. However, Indigenous women's rates of cervical cancer remain disproportionately high, a factor which is not acknowledged in national media or in educational materials reporting Canada's new cervical cancer screening guidelines. Here, we present findings from a cervical cancer screening initiative in Northwestern Ontario. Based on participatory action research, we worked with 10 First Nations communities in the Robinson Superior Treaty area to increase awareness of cervical cancer risk, develop culturally sensitive tools for screening and education and test the efficacy of human papillomavirus (HPV) self-sampling as an alternative to Pap cytology. We conducted 16 interviews with health care professionals and 9 focus groups with 69 women from the communities. A central theme for both health care providers (HCPs) and community members was the colonial legacy and its influence on women's experiences of cervical cancer screening. This was evidenced by a strong sense of body shyness, including shame related to sexuality and sexually transmitted infections, concerns about confidentiality in clinical encounters and distrust or caution around HCPs. Reaffirming women's traditional caregiving and educational roles, enhancing mother and daughter communication, improving cultural sensitivity in health care and education and adoption of HPV self-sampling to increase women's privacy and control of the cervical cancer screening experience were endorsed. We argue that education and screening initiatives must reflect the cultural preferences of Indigenous women, empowering them to take control of their experiences of health and body in cervical cancer screening.

Zehbe, I., Wood, B., Wakewich, P., Maar, M., Escott, N., Jumah, N., Little, J. and on behalf of the ACCSS group. **Teaching tools to engage Anishinaabek First Nations women in cervical cancer screening: report of an educational workshop.** *Health Education Journal.* 2015; 1-12. DOI: 10.1177/0017896915580446.

OBJECTIVE: To explore educational strategies for engaging First Nations women in Canada to attend cervical cancer screening. DESIGN: Within a participatory action research framework, semi-structured interviews with health-care providers in First Nations communities revealed that education

about the value of screening is perceived as being a key factor to promote cervical cancer screening. SETTING: To obtain feedback from workshop informants, a 1-day educational workshop was held to identify appropriate educational intervention strategies, which would be applied in a forthcoming randomised controlled cervical screening trial. METHODS: Common discussion and discussion groups, which were facilitated by a First Nations workshop moderator and a note taker. RESULTS: This workshop helped to strengthen the ethical space dialogue with the First Nations communities with whom the study team had established research partnerships. The workshop atmosphere was relaxed and the invited informants decided that an educational health promotion event for community women needed to be held prior to inviting them to the cervical screening trial. Such an event would provide an opportunity to communicate the importance of attending regular cervical screening allowing women to make informed decisions about screening participation. Complementary promotional items, including an eye-catching pamphlet and storytelling, were also suggested. CONCLUSION: The key messages from the events and promotional items can help to de-stigmatise women who develop a type of cancer that is caused by a sexually transmitted virus that affects both men and women. Developing and implementing positive health education that respectfully depicts female bodies, sexuality and health behaviours through a First Nations lens is strongly warranted.

HPV screening barriers in Romania.

Patriciu Achimas, The Oncology Institute "Prof. Dr. Ion Chiricuta" (Romania)

Session 6 *HPV-faster: Broadening the scope for prevention of HPV-related cancer.*

Session organised by Xavier Bosch

After an introduction of the proposed strategy we will have an extended discussion on topics below. As part of the introduction

Acceptability of HPV vaccination in adult women: Coheahr study
Silvia de Sanjose, Catalanian Institute of Ocology (Spain)

HPV and cervical cancer control: epidemiological modelling
Iacopo Baussano, International Agency for Research on Cancer (France)

Bosch FX, Robles C, Díaz M, Arbyn M, Baussano I, Clavel C, Ronco G, Dillner J, Lehtinen M, Petry KU, Poljak M, Kjaer SK, Meijer CJ, Garland SM, Salmerón J, Castellsagué X, Bruni L, de Sanjosé S, Cuzick J., **HPV-FASTER: broadening the scope for prevention of HPV-related cancer HPV-FASTER: broadening the scope for prevention of HPV-related cancer.** *Nat Rev Clin Oncol.* Feb;13(2):119-32, 2016.

Human papillomavirus (HPV)-related screening technologies and HPV vaccination offer enormous potential for cancer prevention, notably prevention of cervical cancer. The effectiveness of these approaches is, however, suboptimal owing to limited implementation of screening programmes and restricted indications for HPV vaccination. Trials of HPV vaccination in women aged up to 55 years have shown almost 90% protection from cervical precancer caused by HPV16/18 among HPV16/18-DNA-negative women. We propose extending routine vaccination programmes to women of up to 30 years of age (and to the 45-50-year age groups in some settings), paired with at least one HPV-screening test at age 30 years or older. Expanding the indications for HPV vaccination and much greater use of HPV testing in screening programmes has the potential to accelerate the decline in cervical cancer incidence. Such a combined protocol would represent an attractive approach for many health-care systems, in particular, countries in Central and Eastern Europe, Latin America, Asia, and some more-developed parts of Africa. The role of vaccination in women aged >30 years and the optimal number of HPV-screening tests required in vaccinated women remain important research issues. Cost-effectiveness models will help determine the optimal combination of HPV vaccination and screening in public health programmes, and to estimate the effects of such approaches in different populations.

Franceschi, S., M. Chantal Umulisa, U. Tshomo, T. Gheit, I. Baussano, V. Tenet, T. Tshokey, M. Gatera, F. Ngabo, P. Van Damme, P. J. Snijders, M. Tommasino, A. Vorsters and G. M. Clifford. **Urine testing to monitor the impact of HPV vaccination in Bhutan and Rwanda.** *Int J Cancer.* 2016; 139(3): 518-526.

Bhutan (2010) and Rwanda (2011) were the first countries in Asia and Africa to introduce national, primarily school-based, human papillomavirus (HPV) vaccination programmes. These target 12 year-old girls and initially included catch-up campaigns (13-18 year-olds in Bhutan and ninth school grade in Rwanda). In 2013, to obtain the earliest indicators of vaccine effectiveness, we performed two school-based HPV urine surveys; 973 female students (median age: 19 years, 5th-95th percentile: 18-22) were recruited in Bhutan and 912 (19 years, 17-20) in Rwanda. Participants self-collected a first-void urine sample using a validated protocol. HPV prevalence was obtained using two PCR assays that differ in sensitivity and type spectrum, namely GP5+/GP6+ and E7-MPG. 92% students in Bhutan and 43% in Rwanda reported to have been vaccinated (median vaccination age = 16, 5th-95th: 14-18). HPV positivity in urine was significantly associated with sexual activity measures. In Rwanda, HPV6/11/16/18 prevalence

was lower in vaccinated than in unvaccinated students (prevalence ratio, PR = 0.12, 95% confidence interval, CI: 0.03-0.51 by GP5+/GP6+, and 0.45, CI: 0.23-0.90 by E7-MPG). For E7-MPG, cross-protection against 10 high-risk types phylogenetically related to HPV16 or 18 was of borderline significance (PR = 0.68; 95% CI: 0.45-1.01). In Bhutan, HPV6/11/16/18 prevalence by GP5+/GP6+ was lower in vaccinated than in unvaccinated students but CIs were broad. In conclusion, our study supports the feasibility of urine surveys to monitor HPV vaccination and quantifies the effectiveness of the quadrivalent vaccine in women vaccinated after pre-adolescence. Future similar surveys should detect increases in vaccine effectiveness if vaccination of 12 year-olds continues.

Baussano I, Lazzarato F, Ronco G, Dillner J and Franceschi S. **Benefits of catch-up in vaccination against human papillomavirus in medium- and low-income countries.** *Int J Cancer.* 2013; 133 (8): 1876-1881.

Human papillomavirus (HPV) vaccination of a birth cohort of girls in the 9-13 age range is recommended as a priority, but decreases in HPV vaccine cost may make catch-up of a few additional cohorts more attractive not only in high-income countries. We assessed the reduction in HPV16 and 18 infections that could be achieved in a medium- (Poland) and a low-income (Guinea) country by adding one-time catch-up of 12- to 19-year-old girls to the vaccination of 11-year-old girls. According to our ad hoc adapted dynamic model of HPV infection transmission, the addition of catch-up was estimated to bring forward the 50% reduction of HPV16/18 prevalence due to vaccination in women ≤ 35 by as much as 5 years. Catch-up of 12- to 15-year olds reduced the cumulative probability of HPV16/18 infections by age 35 in the relevant cohorts by about 30% in both countries. Catch-up of 16- to 19-year-old girls added little. Regardless of the chosen catch-up strategy, 16 to 20% of HPV16/18 prevention from vaccination was attributable to herd immunity. Assuming a sufficiently low vaccine cost, the addition of a catch-up round is, therefore, worth considering in medium/low-income countries to extend vaccine benefits to less young adolescent girls whose future access to cervical screening is uncertain.

Elfstrom KM, Lazzarato F, Franceschi S, Dillner J and Baussano I. **Human Papillomavirus Vaccination of Boys and Extended Catch-up Vaccination: Effects on the Resilience of Programs.** *J Infect Dis.* 2016; 213 (2): 199-205.

BACKGROUND: Decreasing human papillomavirus (HPV) vaccine prices makes scaling up of vaccination programs attractive for countries that initially targeted 1 or a few birth cohorts of girls and/or achieved low coverage. This article aims to compare the impact of alternative HPV vaccination strategies, using data from Sweden, a high-income country that has experienced vaccine price changes. **METHODS:** Using an HPV transmission model, we compared the existing vaccination program to alternatives, accounting for a 1-time catch-up vaccination of 22-26-year-old women, with or without routine vaccination of school-age boys, and for a 1-time catch-up vaccination of males aged 13-26 years. We also assessed the resilience of vaccination alternatives to coverage reduction. **RESULTS:** On the basis of an HPV16/18 prevalence of 12% before the HPV vaccine era, extended catch-up vaccination for females and males yielded relative reductions in the HPV prevalence of 49.4% and 55.6%, respectively, during the first 10 years after the start of each vaccination strategy, whereas the existing program yielded a relative reduction of 38.6% during the same period. The increased prevalence reduction due to catch-up vaccination continued for about 30 years. As compared to female-only routine and extended catch-up vaccination, routine vaccination of males with or without catch-up was, respectively, 12.6-fold and 7.2-fold more resilient to coverage reduction. **CONCLUSIONS:** Vaccination strategies based on catch-up vaccination of females and males are effective for accelerating HPV prevalence reduction. Inclusion of routine male vaccination improves the resilience of vaccination programs.

Lehtinen M, Apter D, Baussano I, Eriksson T, Natunen K, Paavonen J, Vanska S, Bi D, David MP, Datta S, Struyf F, Jenkins D, Pukkala E, Garnett G and Dubin G. **Characteristics of a cluster-randomized phase IV human papillomavirus vaccination effectiveness trial.** *Vaccine*. 2015; 33 (10): 1284-1290.

High-risk human papillomaviruses (hrHPV) cause anogenital and oropharyngeal cancers. HPV-16/18 virus-like particle vaccine formulated with an AS04 adjuvant is very efficacious against hrHPV associated precancers but the herd effects of different vaccination scenarios are not known. Our cluster randomized trial (NCT00534638) assesses the overall and herd effects of vaccinating girls vs. girls and boys. In two school-years (2007-2008 and 2008-2009) we invited 80,272 1992-1995 born early adolescents to a CRT in 33 communities a priori stratified by low, intermediate and high HPV-16/18 seroprevalence. In 11 Arm A communities 90% of participating girls and boys were assigned to receive HPV-16/18 vaccine, in 11 Arm B communities 90% of girls were assigned to receive HPV-16/18 vaccine - boys were assigned to receive hepatitis B-virus (HBV) vaccine, and in 11 Arm C communities all were assigned to receive HBV-vaccine. Prevalence of HPV in vaccinated and unvaccinated girls is studied at age 18.5 years. Recruitment resulted in equal enrolment of four birth cohorts (born 1992-1995) comprising altogether 32,175 (40% response) early adolescents: 20,514 girls (50.5-53.0% response by arm) and 11,661 boys (21.9-31.6% response by arm). At the age of 15 years, 79.3% of the vaccinees completed a questionnaire. Among them >98% were living at, and during the week-ends 1.3-1.6% stayed outside, the study site communities. Smoking habit and alcohol consumption were similar in the different trial arms, also mean-age of menarche (12.4 years) and 1st ejaculation (12.6 years), and sexual behaviour (among those <25%, who had had sexual debut) did not differ by arm: mean-age at the sexual debut 14.3 and 14.4 in girls and boys, and proportions of those with multiple (>=5) life-time sexual partners (6.5-7.5%) at the age of 15 years. Uniform residential, life-style and sexual behaviour characteristics indicate successful randomization/enrolment of the CRT. Our CRT will verify modelled predictions on up to 31% herd effect of vaccinating both girls and boys with moderate vaccine coverage - quantifying overall effectiveness of different strategies which will soon guide how to implement HPV vaccination.

Part 2: References based on a Pubmed search, by session

Session 2 *Interpretation of safety data*

A Pubmed search was performed with the following selection criteria: HPV [title/abstract] AND vaccine AND safety [title/abstract] published in the last 5 years: 74 items were retrieved. References were imported in EndNote. Herein, a relevant manual selection of publications between 2013-2016 based on title and abstract was made. References are sorted by first authors name.

Human papillomavirus vaccination coverage among adolescent girls, 2007-2012, and postlicensure vaccine safety monitoring, 2006-2013 - United States. MMWR Morb Mortal Wkly Rep. 2013; 62(29): 591-595.

Since mid-2006, the Advisory Committee on Immunization Practices (ACIP) has recommended routine vaccination of adolescent girls at ages 11 or 12 years with 3 doses of human papillomavirus (HPV) vaccine. Two HPV vaccines are currently available in the United States. Both the quadrivalent (HPV4) and bivalent (HPV2) vaccines protect against HPV types 16 and 18, which cause 70% of cervical cancers and the majority of other HPV-associated cancers; HPV4 also protects against HPV types 6 and 11, which cause 90% of genital warts.* This report summarizes national HPV vaccination coverage levels among adolescent girls aged 13-17 yearsdagger from the 2007-2012 National Immunization Survey-Teen (NIS-Teen) and national postlicensure vaccine safety monitoring. Although vaccination coverage with ≥ 1 dose of any HPV vaccine increased from 25.1% in 2007 to 53.0% in 2011, coverage in 2012 (53.8%) was similar to 2011. If HPV vaccine had been administered during health-care visits when another vaccine was administered, vaccination coverage for ≥ 1 dose could have reached 92.6%. Safety monitoring data continue to indicate that HPV4 is safe. Despite availability of safe and effective vaccines and ample opportunities for vaccine delivery in the health-care setting, HPV vaccination coverage among adolescent girls failed to increase from 2011 to 2012.

Akioka, S. **Bivalent HPV vaccine safety depending on subtypes of juvenile idiopathic arthritis.** Ann Rheum Dis. 2014; 73(12): e75.

Baker, M. A., et al. **Post-licensure rapid immunization safety monitoring program (PRISM) data characterization.** Vaccine. 2013; 31 Suppl 10: K98-112.

BACKGROUND: The Post-Licensure Rapid Immunization Safety Monitoring (PRISM) program is the immunization safety monitoring component of FDA's Mini-Sentinel project, a program to actively monitor the safety of medical products using electronic health information. FDA sought to assess the surveillance capabilities of this large claims-based distributed database for vaccine safety surveillance by characterizing the underlying data. **METHODS:** We characterized data available on vaccine exposures in PRISM, estimated how much additional data was gained by matching with select state and local immunization registries, and compared vaccination coverage estimates based on PRISM data with other available data sources. We generated rates of computerized codes representing potential health outcomes relevant to vaccine safety monitoring. Standardized algorithms including ICD-9 codes, number of codes required, exclusion criteria and location of the encounter were used to obtain the background rates. **RESULTS:** The majority of the vaccines routinely administered to infants, children, adolescents and adults were well captured by claims data. Immunization registry data in up to seven states comprised between 5% and 9% of data for all vaccine categories with the exception of 10% for hepatitis B and 3% and 4% for rotavirus and zoster respectively. Vaccination coverage estimates based on PRISM's computerized data were similar to but lower than coverage estimates from the National Immunization Survey and Healthcare Effectiveness Data and Information Set. For the 25 health outcomes of interest studied, the rates of potential outcomes based on ICD-9 codes were generally higher than rates described

in the literature, which are typically clinically confirmed cases. **CONCLUSION:** PRISM program's data on vaccine exposures and health outcomes appear complete enough to support robust safety monitoring.

Basu, P., et al. **Efficacy and safety of human papillomavirus vaccine for primary prevention of cervical cancer: A review of evidence from phase III trials and national programs.** South Asian J Cancer. 2013; 2(4): 187-192.

The Human Papillomavirus (HPV) vaccines have been widely introduced in the national immunization programs in most of the medium and high income countries following endorsement from national and international advisory bodies. HPV vaccine is unique and its introduction is challenging in many ways - it is the first vaccine developed to prevent any cancer, the vaccine is gender specific, it targets adolescent females who are difficult to reach by any health intervention programs. It is not unusual for such a vaccine to face scepticism and reservations not only from lay public but also from professionals in spite of the clinical trial results convincingly and consistently proving their efficacy and safety. Over the last few years millions of doses of the HPV vaccine have been administered round the world and the efficacy and safety data have started coming from the real life programs. A comprehensive cervical cancer control program involving HPV vaccination of the adolescent girls and screening of the adult women has been proved to be the most cost-effective approach to reduce the burden of cervical cancer. The present article discusses the justification of HPV vaccination in the backdrop of natural history of cervical cancer, the mechanism of action of the vaccines, efficacy and safety data from phase III randomized controlled trials as well as from the national immunization programs of various countries.

Blaisdell, L. L., et al. **Unknown Risks: Parental Hesitation about Vaccination.** Med Decis Making. 2016; 36(4): 479-489.

OBJECTIVE: This qualitative study of a select sample of vaccine-hesitant parents (VHPs) explores perceived and constructed personal judgments about the risks and uncertainties associated with vaccines and vaccine-preventable diseases (VPDs) and how these subjective risk judgments influence parents' decisions about childhood vaccination. **METHODS:** The study employed semistructured focus group interviews with 42 VHPs to elicit parents' perceptions and thought processes regarding the risks associated with vaccination and nonvaccination, the sources of these perceptions, and their approach to decision making about vaccination for their children. **RESULTS:** VHPs engage in various reasoning processes and tend to perceive risks of vaccination as greater than the risks of VPDs. At the same time, VHPs engage in other reasoning processes that lead them to perceive ambiguity in information about the harms of vaccination-citing concerns about the missing, conflicting, changing, or otherwise unreliable nature of information. **CONCLUSIONS:** VHPs' refusal of vaccination may reflect their aversion to both the risk and ambiguity they perceive to be associated with vaccination. Mitigating this vaccine hesitancy likely requires reconstructing the risks and ambiguities associated with vaccination-a challenging task that requires providing parents with meaningful evidence-based information on the known risks of vaccination versus VPDs and explicitly acknowledging the risks that remain truly unknown.

Bloom, B. R., et al. **Addressing vaccine hesitancy.** Science. 2014; 344(6182): 339.

Burki, T. **The many shades of vaccine hesitancy.** Lancet Infect Dis 2015; 15(10): 1138-1139.

Cameron, R. L., et al. **Adverse event monitoring of the human papillomavirus vaccines in Scotland.** Intern Med J. 2016; 46(4): 452-457.

BACKGROUND: Human papillomavirus (HPV) vaccines are currently utilised globally in national immunisation programmes. While evidence from clinical trials and epidemiological studies suggest that the HPV vaccines are both effective and safe, concerns about the safety of the vaccine and scientifically

unproven associations with severe adverse events following immunisation have led to dramatic decreases in vaccine uptake in Japan and acceptance issues in other countries. **AIM:** In Scotland, we utilised hospital admissions data to assess the impact of the HPV immunisation programme on the incidence of 60 diagnoses between 2004 and 2014 in both girls and boys; with boys acting as a comparator group. **METHODS:** Tabular and graphical outputs of the number of admissions, the incidence and the incidence ratio of 59 diagnoses were created to assess trends before and after the introduction of the HPV vaccine. Data linkage was utilised to investigate further the increase in Bell palsy diagnoses. **RESULTS:** Fifty-four diagnoses showed no change in incidence following the introduction of the national immunisation programme, and while small increases in incidence were observed for Bell palsy, coeliac disease, ovarian dysfunction, juvenile onset of type 1 diabetes, demyelinating disease and juvenile rheumatoid arthritis, none was statistically significant. **CONCLUSIONS:** Consistent with previous evidence, we present disaggregate data that reiterate the safety of both HPV vaccines.

Gee, J., et al. **Quadrivalent HPV vaccine safety review and US safety monitoring plans for nine-valent HPV vaccine.** Hum Vaccin Immunother. 2016: 1-12.

Quadrivalent human papillomavirus (4vHPV) vaccine was licensed for use in the United States in 2006 and through 2015 was the predominate HPV vaccine used. With the exception of syncope, a known preventable adverse event after any injected vaccination, both pre-licensure and post-licensure 4vHPV safety data have been reassuring with no confirmed safety signals identified. Nine-valent HPV vaccine (9vHPV) was licensed in 2014. This review includes post-licensure 4vHPV safety findings published to date that have informed the US vaccination program; these data will inform US safety monitoring and evaluation for 9vHPV.

Goncalves, A. K., et al. **Safety, tolerability and side effects of human papillomavirus vaccines: a systematic quantitative review.** Braz J Infect Dis. 2014; 18(6): 651-659.

Recently, many studies have evaluated HPV vaccine safety and adverse effects. Two vaccines have been recently evaluated in randomized controlled trials: the bivalent vaccine for HPV 16 and 18 (Cervarix, GlaxoSmithKline Biologicals, Rixensart, Belgium) and the quadrivalent vaccine for HPV 6, 11, 16, and 18 (Gardasil, Merck and Co., Inc., Whitehouse Station, NJ). We have performed a systematic review of all randomized controlled trials in which HPV vaccines were compared with placebo regarding safety, tolerability and adverse effects. Studies were searched up to March 2013 in the databases: Pubmed, Embase, Scielo and Cancerlit. Odds Ratios (OR) of most incident adverse effects were obtained. Twelve reports, involving 29,540 subjects, were included. In the HPV 16/18 group, the most frequently reported events related to the vaccine were pain (OR 3.29; 95% CI: 3.00-3.60), swelling (OR 3.14; 95% CI: 2.79-3.53) and redness (OR 2.41; 95% CI: 2.17-2.68). For the HPV 6/11/16/18 group the events were pain (OR 2.88; 95% CI: 2.42-3.43) and swelling (OR 2.65; 95% CI: 2.0-3.44). Concerning the HPV 16/18 vaccine, pain was the most common outcome detected. These effects can be due to a possible VLP-related inflammation process. Fatigue was the most relevant general effect observed followed by fever, gastrointestinal symptoms, and headache. In the HPV 6/11/16/18 group, only general symptoms, pain and swelling were observed. Pain and swelling were the most frequent. Comparing HPV 16/18 to HPV 6/11/16/18 vaccines, the former presented more adverse effects, perhaps because there are many more trials evaluating the bivalent vaccine. Other studies are needed to clarify this issue.

Grimaldi-Bensouda, L., et al. **Autoimmune disorders and quadrivalent human papillomavirus vaccination of young female subjects.** J Intern Med. 2014; 275(4): 398-408.

OBJECTIVES: The aim of this study was to investigate whether the quadrivalent human papillomavirus (HPV) vaccine Gardasil is associated with a change in the risk of autoimmune disorders (ADs) in young female subjects. **DESIGN:** Systematic case-control study of incident ADs associated with

quadrivalent HPV vaccination in young women across France. **PARTICIPANTS AND SETTING:** A total of 113 specialised centres recruited (from December 2007 to April 2011) females aged 14-26 years with incident cases of six types of ADs: idiopathic thrombocytopenic purpura (ITP), central demyelination/multiple sclerosis (MS), Guillain-Barre syndrome, connective tissue disorders (systemic lupus erythematosus, rheumatoid arthritis/juvenile arthritis), type 1 diabetes mellitus and autoimmune thyroiditis. Control subjects matched to cases were recruited from general practice. **ANALYSIS:** Multivariate conditional logistic regression analysis; factors included age, geographical origin, smoking, alcohol consumption, use of oral contraceptive(s) or vaccine(s) other than Gardasil received within 24 months before the index date and personal/family history of ADs. **RESULTS:** Overall, 211 definite cases of ADs were matched to 875 controls. The adjusted odds ratio (OR) for any quadrivalent HPV vaccine use was 0.9 [95% confidence interval (CI) 0.5-1.5]. The individual ORs were 1.0 (95% CI 0.4-2.6) for ITP, 0.3 (95% CI 0.1-0.9) for MS, 0.8 (95% CI 0.3-2.4) for connective disorders and 1.2 (95% CI 0.4-3.6) for type 1 diabetes. No exposure to HPV vaccine was observed in cases with either Guillain-Barre syndrome or thyroiditis. **CONCLUSIONS:** No evidence of an increase in the risk of the studied ADs was observable following vaccination with Gardasil within the time periods studied. There was insufficient statistical power to allow conclusions to be drawn regarding individual ADs.

Herrero, R., et al. **Present status of human papillomavirus vaccine development and implementation.** *Lancet Oncol.* 2015; 16(5): e206-216.

Oncogenic human papillomavirus (HPV) infection is the cause of nearly all cervical cancers and a proportion of other anogenital and oropharyngeal cancers. A bivalent vaccine containing HPV 16 and 18 and a quadrivalent vaccine containing HPV 6, 11, 16, and 18 antigens are in use in vaccination programmes around the world. In clinical trials, three vaccine doses provided 90-100% protection against cervical infection and pre-cancer related to HPV 16 and 18 in women aged 15-26 years who were not infected at vaccination. Partial cross-protection against other HPV types has been reported but its duration is unknown. The vaccines were also efficacious at the prevention of HPV 16 and 18 infections at other anatomical sites in both sexes. Immunobridging studies allowed licensing of the vaccines for use starting at age 9 years for both sexes. Two-dose schedules elicit high antibody concentrations, leading to the recommendation of two-dose schedules for girls aged 9-14 years. Pre-licensure and post-licensure studies have provided data supporting vaccine safety. In 2014, a nonavalent vaccine containing HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58 antigens was licensed by the US Food and Drug Administration. HPV vaccination was first introduced in high-income countries owing to vaccine cost, logistic challenges, and competing health priorities. Since 2011, vaccine prices have lowered, allowing the introduction of the vaccine in some middle-income countries. Funding of the vaccine by the GAVI Alliance in 2012 led to demonstration projects in some low-income countries. By 2014, more than 57 countries had included the HPV vaccine in their national health programmes. Data from several countries have shown the effect of vaccination on HPV infection and associated disease, and provided evidence of herd immunity. Expansion of programmes to countries with the highest burden of disease is beginning, but further efforts are needed to realise the potential of HPV vaccines.

Jacobsen, S. J. and Poland, G. A. **Methods in vaccine effectiveness and safety studies: a critical need for vaccine confidence.** *Vaccine.* 2011; 29(52): 9573-9574.

Levi, M., et al. **Evaluation of bivalent human papillomavirus (HPV) vaccine safety and tolerability in a sample of 25 year old Tuscan women.** *Hum Vaccin Immunother.* 2013; 9(7): 1407-1412.

The aim of this study was to gather data on the safety of the HPV-16/18 AS04-adjuvated vaccine among women aged 25, evaluating the frequency and severity of adverse events reported after vaccination and to compare the results obtained with previously published data regarding a sample of

Italian preadolescents. Every woman residing in the province of Florence and in the age group targeted by the cervical cancer screening was invited to participate. Participants registered daily, for 14 d post-vaccination, solicited local and systemic reactions, as well as unsolicited adverse events in a developed ad hoc safety diary card. Data were collected in a database in Access and analyzed using STATA 11 SE statistical software. A total of 271 participants were recruited in the study group. All three diary cards were completed and delivered by 186 subjects (85.7% of participants). In all, a total of 616 diary cards were collected: 216 after the 1st dose, 209 after the 2nd dose and 191 after the 3rd dose. No severe symptoms were registered. The most frequently reported adverse reaction proved to be pain at the site of injection (83.4% of doses), followed by local swelling (20.8%) and pyrexia (14.6%). The safety and tolerability of the HPV-16/18 AS04-adjuvated vaccine in this sample of adult women aged 25 did not differ much from that previously observed in a sample of preadolescents Italian girls. Fever and local pain were however more frequently registered in our sample of adult women.

Markowitz, L. E., et al. **Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP)**. MMWR Recomm Rep. 2014; 63(Rr-05): 1-30.

This report summarizes the epidemiology of human papillomavirus (HPV) and associated diseases, describes the licensed HPV vaccines, provides updated data from clinical trials and postlicensure safety studies, and compiles recommendations from CDC's Advisory Committee on Immunization Practices (ACIP) for use of HPV vaccines. Persistent infection with oncogenic HPV types can cause cervical cancer in women as well as other anogenital and oropharyngeal cancers in women and men. HPV also causes genital warts. Two HPV vaccines are licensed in the United States. Both are composed of type-specific HPV L1 protein, the major capsid protein of HPV. Expression of the L1 protein using recombinant DNA technology produces noninfectious virus-like particles (VLPs). Quadrivalent HPV vaccine (HPV4) contains four HPV type-specific VLPs prepared from the L1 proteins of HPV 6, 11, 16, and 18. Bivalent HPV vaccine (HPV2) contains two HPV type-specific VLPs prepared from the L1 proteins of HPV 16 and 18. Both vaccines are administered in a 3-dose series. ACIP recommends routine vaccination with HPV4 or HPV2 for females aged 11 or 12 years and with HPV4 for males aged 11 or 12 years. Vaccination also is recommended for females aged 13 through 26 years and for males aged 13 through 21 years who were not vaccinated previously. Males aged 22 through 26 years may be vaccinated. ACIP recommends vaccination of men who have sex with men and immunocompromised persons (including those with HIV infection) through age 26 years if not previously vaccinated. As a compendium of all current recommendations for use of HPV vaccines, information in this report is intended for use by clinicians, vaccination providers, public health officials, and immunization program personnel as a resource. ACIP recommendations are reviewed periodically and are revised as indicated when new information and data become available.

Nakalembe, M., et al. **Vaccines against human papillomavirus in low and middle income countries: a review of safety, immunogenicity and efficacy**. Infect Agent Cancer. 2015; 10: 17.

Currently, there is limited data on the immunogenicity and efficacy of human papillomavirus vaccines in Low and Middle income countries (LMIC). The review aims to summarize the current status from published HPV vaccine safety, immunogenicity and efficacy studies in low and middle income countries (LMIC). Electronic databases (PubMed/MEDLINE and HINARI) were searched for peer reviewed English language articles on HPV vaccination in LMIC that have so far been published from 1st January 2006 up to 30th January 2015. Eligible studies were included if they had used the bivalent (bHPV) or quadrivalent HPV (qHPV) vaccines in a LMIC and investigated safety, immunogenicity and/or efficacy. The main findings were extracted and summarized. A total of fourteen HPV vaccine studies assessing safety, Immunogenicity and efficacy of the bivalent or quadrivalent vaccines in LMIC were included. There are only ten published clinical trials where a LMIC has participated. There was no published study so far that assessed efficacy of the HPV vaccines in Sub-Saharan Africa. From these studies, vaccine induced immune

response was comparable to that from results of HICs for all age groups. Studies assessing HPV vaccine efficacy of the bivalent or quadrivalent vaccine within LMIC were largely missing. Only three studies were found where a LMIC was part of a multi center clinical trial. In all the studies, there were no vaccine related serious adverse events. The findings from the only study that investigated less than three doses of the bivalent HPV-16/18 vaccine suggest that even with less than three doses, antibody levels were still comparable with older women where efficacy has been proven. The few studies from LMIC in this review had comparable safety, Immunogenicity and efficacy profiles like in HIC. Overall, the LMIC of Africa where immune compromising/modulating situations are prevalent, there is need for long term immunogenicity as well as surveillance studies for long term clinical effectiveness after two and three dose regimens.

Nicol, A. F., et al. **HPV vaccines: their pathology-based discovery, benefits, and adverse effects.** Ann Diagn Pathol. 2015; 19(6): 418-422.

The discovery of the human papillomavirus (HPV) vaccine illustrates the power of in situ-based pathologic analysis in better understanding and curing diseases. The 2 available HPV vaccines have markedly reduced the incidence of cervical intraepithelial neoplasias, genital warts, and cervical cancer throughout the world. Concerns about HPV vaccine safety have led some physicians, health care officials, and parents to refuse providing the recommended vaccination to the target population. The aims of the study were to discuss the discovery of HPV vaccine and review scientific data related to measurable outcomes from the use of HPV vaccines. The strong type-specific immunity against HPV in humans has been known for more than 25 years. Multiple studies confirm the positive risk benefit of HPV vaccination with minimal documented adverse effects. The most common adverse effect, injection site pain, occurred in about 10% of girls and was less than the rate reported for other vaccines. Use of HPV vaccine should be expanded into more diverse populations, mainly in low-resource settings.

Schwarz, T. F., et al. **Long-term immunogenicity and safety of the HPV-16/18 AS04-adjuvanted vaccine in 10- to 14-year-old girls: open 6-year follow-up of an initial observer-blinded, randomized trial.** Pediatr Infect Dis J. 2014; 33(12): 1255-1261.

BACKGROUND: Immunogenicity and safety of the HPV-16/18 AS04-adjuvanted vaccine were evaluated up to 6 years postvaccination (month 72) in preteen/adolescent girls. METHODS: Participants, who had received 3 HPV-16/18 AS04-adjuvanted vaccine doses at 10-14 years of age in an initial controlled, observer-blinded, randomized study (NCT00196924) and participated in the open 3-year follow-up (NCT00316706), were invited to continue the follow-up for up to 10 years postvaccination (NCT00877877). Anti-HPV-16 and -18 antibody titers were measured by enzyme-linked immunosorbent assays at yearly visits and were used to fit the modified power-law and piecewise models, predicting long-term immunogenicity. Serious adverse events (SAEs) and pregnancy information were recorded. RESULTS: In the according-to-protocol immunogenicity cohort, all participants (N = 505) with data available remained seropositive for anti-HPV-16 and -18 antibodies at month 72. In initially seronegative participants, anti-HPV-16 and -18 antibody geometric mean titers were 65.8- and 33.0-fold higher than those associated with natural infection (NCT00122681) and 5.0- and 2.5-fold higher than those measured at month 69-74 in a study demonstrating vaccine efficacy in women aged 15-25 years (NCT00120848). Exploratory antibody modeling, based on the 6-year data, predicted that vaccine-induced population anti-HPV-16 and -18 antibody geometric mean titers would remain above those associated with natural infection for at least 20 years postvaccination. The HPV-16/18 AS04-adjuvanted vaccine safety profile was clinically acceptable. CONCLUSIONS: In preteen/adolescent girls, the HPV-16/18 AS04-adjuvanted vaccine induced high anti-HPV-16 and -18 antibody levels up to 6 years postvaccination, which were predicted to remain above those induced by natural infection for at least 20 years.

Stillo, M., et al. **Safety of human papillomavirus vaccines: a review.** *Expert Opin Drug Saf.* 2015; 14(5): 697-712.

INTRODUCTION: Between 2006 and 2009, two different human papillomavirus virus (HPV) vaccines were licensed for use: a quadrivalent (qHPVv) and a bivalent (bHPVv) vaccine. Since 2008, HPV vaccination programmes have been implemented in the majority of the industrialized countries. Since 2013, HPV vaccination has been part of the national programs of 66 countries including almost all countries in North America and Western Europe. Despite all the efforts made by individual countries, coverage rates are lower than expected. Vaccine safety represents one of the main concerns associated with the lack of acceptance of HPV vaccination both in the European Union/European Economic Area and elsewhere. **AREAS COVERED:** Safety data published on bivalent and quadrivalent HPV vaccines, both in pre-licensure and post-licensure phase, are reviewed. **EXPERT OPINION:** Based on the latest scientific evidence, both HPV vaccines seem to be safe. Nevertheless, public concern and rumors about adverse events (AE) represent an important barrier to overcome in order to increase vaccine coverage. Passive surveillance of AEs is an important tool for detecting safety signals, but it should be complemented by activities aimed at assessing the real cause of all suspect AEs. Improved vaccine safety surveillance is the first step for effective communication based on scientific evidence.

Subelj, M., et al. **Adverse events following school-based vaccination of girls with quadrivalent human papillomavirus vaccine in Slovenia, 2009 to 2013.** *Euro Surveill.* 2016; 21(14).

Adverse events following immunisation (AEFIs) with qHPV reported to the Slovenian AEFI Registry for the first four school years of the vaccination programme were analysed. We calculated annual reporting rates for 11-14 year-old vaccinees with AEFIs, using the number of qHPV doses distributed within the school-based vaccination programme as the denominator. Between September 2009 and August 2013, 211 AEFIs that occurred in 89 vaccinees were reported, a rate of 149.5 vaccinees with AEFI per 100,000 qHPV doses distributed. For five vaccinees, serious AEFIs (8.4 per 100,000 doses distributed) were reported. The highest reporting rates were for fatigue, headache, and fever ($\geq 38.0(0)$) (53.8, 40.3, and 35.3 per 100,000 qHPV doses distributed, respectively). As no AEFI resulted in permanent sequelae and they all were categorised as serious only due to the criterion of a minimum of one day of hospitalisation, this provides reassurance for the safety of our school-based HPV vaccination programme. Further AEFI surveillance is warranted to provide data for HPV vaccination programme monitoring and evaluation of its safety.

Tomljenovic, L., et al. **Human papillomavirus (HPV) vaccines as an option for preventing cervical malignancies: (how) effective and safe?** *Curr Pharm Des.* 2013; 19(8): 1466-1487.

We carried out a systematic review of HPV vaccine pre- and post-licensure trials to assess the evidence of their effectiveness and safety. We find that HPV vaccine clinical trials design, and data interpretation of both efficacy and safety outcomes, were largely inadequate. Additionally, we note evidence of selective reporting of results from clinical trials (i.e., exclusion of vaccine efficacy figures related to study subgroups in which efficacy might be lower or even negative from peer-reviewed publications). Given this, the widespread optimism regarding HPV vaccines long-term benefits appears to rest on a number of unproven assumptions (or such which are at odd with factual evidence) and significant misinterpretation of available data. For example, the claim that HPV vaccination will result in approximately 70% reduction of cervical cancers is made despite the fact that the clinical trials data have not demonstrated to date that the vaccines have actually prevented a single case of cervical cancer (let alone cervical cancer death), nor that the current overly optimistic surrogate marker-based extrapolations are justified. Likewise, the notion that HPV vaccines have an impressive safety profile is only supported by highly flawed design of safety trials and is contrary to accumulating evidence from vaccine safety surveillance databases and case reports which continue to link HPV vaccination to serious adverse

outcomes (including death and permanent disabilities). We thus conclude that further reduction of cervical cancers might be best achieved by optimizing cervical screening (which carries no such risks) and targeting other factors of the disease rather than by the reliance on vaccines with questionable efficacy and safety profiles.

Van Ganse, E., et al. **Health problems most commonly diagnosed among young female patients during visits to general practitioners and gynecologists in France before the initiation of the human papillomavirus vaccination program.** *Pharmacoepidemiol Drug Saf.* 2012; 21(3): 261-268.

PURPOSE: Background rates for common health problems have seldom been estimated to facilitate interpretation of signals that may occur after a new public health intervention. Background rates of diagnoses from general practitioners (GPs) and gynecologists (GYNs) were assessed before the implementation of human papillomavirus (HPV) immunization program. **METHODS:** This cross-sectional study used data collected in 2006 in France. All visits of women (aged 11-23 years) to a GP or a GYN participating in the longitudinal patient data (LPD) network were considered. Diagnoses and symptoms were retrieved and classified according to the International Classification of Primary Care. Only diagnoses made in $\geq 1\%$ of visits were reported in primary analyses. Independent analyses were performed for visits to GPs and GYNs and for adolescents and young adults. Finally, the rates of pre-specified health problems of interest (e.g., because of their potential identification as signals after HPV immunization) were computed from processed diagnostic data, using time windows consistent with HPV vaccination scheme. **RESULTS:** About 380,813 GP and 36,329 GYN visits were analyzed. Acute upper respiratory infections were the most frequently recorded diagnoses by GPs, accounting for 11,783 per 100,000 visits per year. Visits related to the respiratory system accounted for 10 of the 23 most frequent diagnoses by GPs. Genital candidiasis was the most frequent GYN diagnosis, accounting for 4746 per 100,000 visits per year. Most GYN visits were for pregnancy-related issues or menstrual problems. The main diagnoses were similar in adolescents compared with young adults in both GP and GYN settings. Pre-specified health problems occurred at high rates, as exemplified by acne that was diagnosed in 0.8% of patients during time windows consistent with HPV immunization. **CONCLUSION:** Diagnostic data processed from electronic health records identified the rates of common health events experienced by young female patients routinely visiting their GP or GYN before HPV immunization. Such rates may prove useful in interpreting adverse events reported after the launch of new medical interventions.

Vesikari, T., et al. **A Randomized, Double-Blind, Phase III Study of the Immunogenicity and Safety of a 9-Valent Human Papillomavirus L1 Virus-Like Particle Vaccine (V503) Versus Gardasil(R) in 9-15-Year-Old Girls.** *Pediatr Infect Dis J.* 2015; 34(9): 992-998.

BACKGROUND: A 9-valent human papillomavirus (9vHPV) vaccine has been developed to prevent infections and diseases related to HPV 6/11/16/18 [as per the licensed quadrivalent HPV (qHPV) vaccine], as well as 5 additional oncogenic HPV types (HPV 31/33/45/52/58). Compared with the qHPV vaccine, the 9vHPV vaccine potentially increases the coverage of protection from 70% to 90% of cervical cancers. We compared the immunogenicity and safety of the 9vHPV vaccine versus the qHPV vaccine in 9-15-year-old girls. **METHODS:** Participants (n = 600) were randomized to receive 9vHPV or qHPV vaccines on day 1, month 2 and month 6. Serology testing was performed on day 1 and month 7. HPV type-specific antibody titers (anti-HPV 6/11/16/18/31/33/45/52/58) were determined by competitive Luminex immunoassay and expressed as geometric mean titers and seroconversion rates. Vaccine safety was also assessed. **RESULTS:** The HPV 6/11/16/18 immune responses elicited by the 9vHPV vaccine were comparable with those elicited by the qHPV vaccine. All participants (except 1 for HPV 45) receiving the 9vHPV vaccine seroconverted for HPV 31/33/45/52/58. The 9vHPV and qHPV vaccines showed comparable safety profiles, although the incidence of injection-site swelling was higher in the 9vHPV vaccine group. **CONCLUSIONS:** In addition to immune responses to HPV 31/33/45/52/58, a 3-dose regimen of the 9vHPV

vaccine elicited a similar immune response to HPV 6/11/16/18 when compared with the qHPV vaccine in girls aged 9-15 years. The safety profile was also similar for the 2 vaccines.

Vichnin, M., et al. **An Overview of Quadrivalent Human Papillomavirus Vaccine Safety: 2006 to 2015.** *Pediatr Infect Dis J.* 2015; 34(9): 983-991.

BACKGROUND: A quadrivalent human papillomavirus (HPV4) type 6/11/16/18 vaccine (GARDASIL/SILGARD(R)) has been licensed in many countries around the world for the prevention of cervical, vulvar, vaginal, and anal cancers and precancers, as well as external genital warts causally related to HPV types 6/11/16/18. Across 7 phase 3 clinical trials involving more than 29,000 males and females ages 9-45 years, vaccination was generally well tolerated. Because of its expected public health benefit in reducing cervical cancer and other HPV-related diseases, the vaccine has been implemented in the national vaccination programs of several countries, with over 178 million doses distributed worldwide. **METHODS:** Extensive efforts to assess the safety of the vaccine in routine practice have been conducted over the past 9 years since licensure, including more than 15 studies in more than 1 million preadolescents, adolescents and adults from various countries. Most have been performed in the general population although there have been some in special populations (pregnant women, HIV-infected individuals and those with systemic lupus erythematosus). **RESULTS:** We present a summary of the published, postlicensure safety data from active and passive surveillance. Only syncope, and possibly skin infections were associated with vaccination in the postlicensure setting. Serious adverse events, such as adverse pregnancy outcomes, autoimmune diseases (including Guillain-Barre Syndrome and multiple sclerosis), anaphylaxis, venous thromboembolism and stroke, were extensively studied, and no increase in the incidence of these events was found compared with background rates. **CONCLUSIONS:** These results, along with the safety data from the prelicensure clinical trials, confirm that the HPV4 vaccine has a favorable safety profile. Key policy, medical and regulatory organizations around the world have independently reviewed these data and continue to recommend routine HPV vaccination.

Whitaker, J. A., et al. **Adversomics: a new paradigm for vaccine safety and design.** *Expert Rev Vaccines.* 2015; 14(7): 935-947.

Despite the enormous population benefits of routine vaccination, vaccine adverse events (AEs) and reactions, whether real or perceived, have posed one of the greatest barriers to vaccine acceptance--and thus to infectious disease prevention--worldwide. A truly integrated clinical, translational, and basic science approach is required to understand the mechanisms behind vaccine AEs, predict them, and then apply this knowledge to new vaccine design approaches that decrease, or avoid, these events. The term 'adversomics' was first introduced in 2009 and refers to the study of vaccine adverse reactions using immunogenomics and systems biology approaches. In this review, we present the current state of adversomics research, review known associations and mechanisms of vaccine AEs/reactions, and outline a plan for the further development of this emerging research field.

Session 3

Vaccine confidence

A Pubmed search was performed with the following selection criteria: Vaccine AND confidence [title/abstract] OR vaccine And hesitancy [title/abstract] OR vaccine And acceptance [title/abstract] published in the last 5 years: 314 items were retrieved. References were imported in EndNote. Herein, a relevant manual selection of publications between 2012-2016 based on title and abstract was made. References are sorted by first authors name.

Assessing the State of Vaccine Confidence in the United States: Recommendations from the National Vaccine Advisory Committee: Approved by the National Vaccine Advisory Committee on June 9, 2015 [corrected]. Public Health Rep. 2015; 130(6): 573-595.

Allen, J. D., et al. **Decision-Making about the HPV Vaccine among Ethnically Diverse Parents: Implications for Health Communications.** J Oncol. 2012: 401979.

OBJECTIVE: To describe parents' knowledge, attitudes, and decision-making with regard to obtaining the HPV vaccine for their daughters. METHODS: White, Black, and Hispanic parents of daughters who were age eligible to receive the HPV vaccine (9-17 years) were recruited from community settings to participate in focus groups. Parents were asked about knowledge and awareness of HPV, decision-making about HPV vaccine, as well as preferred and actual sources of HPV information. RESULTS: Seven focus groups (n = 64 participants) were conducted. Groups were segmented by gender (women = 72%) and race/ethnicity (Black = 59%; White = 23%; Hispanic = 19%). Prevalent themes included: insufficient information to make informed decisions; varied preferences for involvement in decision-making; concerns about vaccine safety; mistrust of medical providers and pharmaceutical companies; and mismatch between actual and preferred sources of information. DISCUSSION: Improving communication between providers and caregivers and helping parents to access information necessary for informed decision-making, while alleviating concerns about vaccine safety, may help to improve vaccine acceptance.

Arwanire, E. M., et al. **Communicating vaccine safety in the context of immunization programs in low resource settings.** Curr Drug Saf. 2015; 10(1): 68-75.

Vaccines are effective in preventing infectious diseases and their complications, hence reducing morbidity and infectious disease mortality. Successful immunization programs, however, depend on high vaccine acceptance and coverage rates. In recent years there has been an increased level of public concern towards real or perceived adverse events associated with immunizations, leading to many people in high- as well as low-resource settings to refuse vaccines. Health care workers therefore must be able to provide parents and guardians of children with the most current and accurate information about the benefits and risks of vaccination. Communicating vaccine safety using appropriate channels plays a crucial role in maintaining public trust and confidence in vaccination programs. Several factors render this endeavor especially challenging in low-resource settings where literacy rates are low and access to information is often limited. Many languages are spoken in most countries in low-resource settings, making the provision of appropriate information difficult. Poor infrastructure often results in inadequate logistics. Recently, some concerned consumer groups have been able to propagate misinformation and rumors. To successfully communicate vaccine safety in a resource limited setting it is crucial to use a mix of communication channels that are both culturally acceptable and effective. Social mobilization through cultural, administrative and political leaders, the media or text messages (SMS) as well as the adoption of the Village Health Team (VHT) strategy whereby trained community members (Community Health Workers (CHWs)) are providing primary healthcare, can all be effective in increasing the demand for immunization.

Atkinson, K. M., et al. **Vaccination attitudes and mobile readiness: A survey of expectant and new mothers.** *Hum Vaccin Immunother.* 2015; 11(4): 1039-1045.

Sub-optimal vaccination coverage and recent outbreaks of vaccine-preventable diseases serve as a reminder that vaccine hesitancy remains a concern. ImmunizeCA, a new smartphone app to help track immunizations, may address several reasons for not vaccinating. We conducted a study to describe demographic variables, attitudes, beliefs and information sources regarding pediatric vaccination in a sample of childbearing women who were willing to download an immunization app. We also sought to measure their current mobile usage behaviors and determine if there is an association between participant demographics, attitudes, beliefs and information sources regarding pediatric vaccination and mobile usage. We recruited participants using a combination of passive and active methods at a tertiary care hospital in Ottawa, Canada. We used surveys to collect demographic information, examine attitudes, behavior, and information sources regarding immunization and self-reported mobile phone usage. A total of 54 women participated. The majority had positive attitudes toward vaccination (96%) and intended to vaccinate their children (98%). Participants were interested in information on pediatric vaccination (94%), and found information from public health the most reliable and accessible (78%). Participants also trusted immunization information from their doctor or nurse and public health (83%) more than other sources. There was variability in participant use of mobile apps for other purposes. The median participant mobile readiness score was 3.2. We found no significant associations between participant age, behavior and attitudes regarding vaccination and mobile readiness scores. This is the first evaluation of mobile readiness for a smartphone app to track immunizations. Our findings suggest that there exists an opportunity to provide reliable information on vaccination through mobile devices to better inform the public, however predictors of individual engagement with these technologies merits further study.

Attwell, K. and Freeman, M. **I Immunise: An evaluation of a values-based campaign to change attitudes and beliefs.** *Vaccine.* 2015; 33(46): 6235-6240.

This paper presents results of a study determining the efficacy of a values based approach to changing vaccination attitudes. It reports an evaluation survey of the "I Immunise" campaign, conducted in Fremantle, Western Australia, in 2014. "I Immunise" explicitly engaged with values and identity; formulated by locals in a community known for its alternative lifestyles and lower-than-national vaccine coverage rates. Data was collected from 304 online respondents. The campaign polarised attitudes towards vaccination and led some to feel more negatively. However, it had an overall positive response with 77% of participants. Despite the campaign only resonating positively with a third of parents who had refused or doubted vaccines, it demonstrates an important in-road into this hard-to-reach group.

Bahk, C. Y., et al. **Publicly Available Online Tool Facilitates Real-Time Monitoring Of Vaccine Conversations And Sentiments.** *Health Aff (Millwood).* 2016; 35(2): 341-347.

Real-time monitoring of mainstream and social media can inform public health practitioners and policy makers about vaccine sentiment and hesitancy. We describe a publicly available platform for monitoring vaccination-related content, called the Vaccine Sentimeter. With automated data collection from 100,000 mainstream media sources and Twitter, natural-language processing for automated filtering, and manual curation to ensure accuracy, the Vaccine Sentimeter offers a global real-time view of vaccination conversations online. To assess the system's utility, we followed two events: polio vaccination in Pakistan after a news story about a Central Intelligence Agency vaccination ruse and subsequent attacks on health care workers, and a controversial episode in a television program about adverse events following human papillomavirus vaccination. For both events, increased online activity was detected and characterized. For the first event, Twitter response to the attacks on health care workers decreased drastically after the first attack, in contrast to mainstream media coverage. For the second

event, the mainstream and social media response was largely positive about the HPV vaccine, but antivaccine conversations persisted longer than the provaccine reaction. Using the Vaccine Sentimeter could enable public health professionals to detect increased online activity or sudden shifts in sentiment that could affect vaccination uptake.

Betsch, C. and Bohm, R. **Detrimental effects of introducing partial compulsory vaccination: experimental evidence.** *Eur J Public Health.* 2016; 26(3): 378-381.

BACKGROUND: During outbreaks of vaccine-preventable diseases, compulsory vaccination is sometimes discussed as a last resort to counter vaccine refusal. Besides ethical arguments, however, empirical evidence on the consequences of making selected vaccinations compulsory is lacking. Such evidence is needed to make informed public health decisions. This study therefore assesses the effect of partial compulsory vaccination on the uptake of other voluntary vaccines. **METHOD:** A total of 297 (N) participants took part in an online experiment that simulated two sequential vaccination decisions using an incentivized behavioural vaccination game. The game framework bases on epidemiological, psychological and game-theoretical models of vaccination. Participants were randomized to the compulsory vaccination intervention (n = 144) or voluntary vaccination control group (n = 153), which determined the decision architecture of the first of two decisions. The critical second decision was voluntary for all participants. We also assessed the level of anger, vaccination attitude and perceived severity of the two diseases. **RESULTS:** Compulsory vaccination increased the level of anger among individuals with a rather negative vaccination attitude, whereas voluntary vaccination did not. This led to a decrease in vaccination uptake by 39% in the second voluntary vaccination (reactance). **CONCLUSION:** Making only selected vaccinations compulsory can have detrimental effects on the vaccination programme by decreasing the uptake of voluntary vaccinations. As this effect occurred especially for vaccine hesitant participants, the prevalence of vaccine hesitancy within a society will influence the damage of partial compulsory vaccination.

Butler, R. and MacDonald, N. E. **Diagnosing the determinants of vaccine hesitancy in specific subgroups: The Guide to Tailoring Immunization Programmes (TIP).** *Vaccine.* 2015; 33(34): 4176-4179.

Despite relatively high vaccination coverage rates in the European Region, vaccine hesitancy is undermining individual and community protection from vaccine preventable diseases. At the request of its European Technical Advisory Group of Experts on Immunization (ETAGE), the Vaccine-preventable Diseases and Immunization Programme of the WHO Regional Office for Europe (WHO/EURO) developed tools to help countries address hesitancy more effectively. The Guide to Tailoring Immunization Programmes (TIP), an evidence and theory based behavioral insight framework, issued in 2013, provides tools to (1) identify vaccine hesitant population subgroups, (2) diagnose their demand- and supply-side immunization barriers and enablers and (3) design evidence-informed responses to hesitancy appropriate to the subgroup setting, context and vaccine. The Strategic Advisory Group of Experts on Immunization (SAGE) through its Working Group on Vaccine Hesitancy has closely followed the development, implementation, use and evolution of TIP concluding that TIP, with local adaptation, could be a valuable tool for use in all WHO regions, to help address countries' vaccine hesitancy problems. The TIP principles are applicable to communicable, noncommunicable and emergency planning where behavioral decisions influence outcomes.

Buttenheim, A. M., et al. **Provider dismissal policies and clustering of vaccine-hesitant families: an agent-based modeling approach.** *Hum Vaccin Immunother.* 2013; 9(8): 1819-1824.

Many pediatric practices have adopted vaccine policies that require parents who refuse to vaccinate according to the ACIP schedule to find another health care provider. Such policies may inadvertently cluster unvaccinated patients into practices that tolerate non vaccination or alternative

schedules, turning them into risky pockets of low herd immunity. The objective of this study was to assess the effect of provider zero-tolerance vaccination policies on the clustering of intentionally unvaccinated children. We developed an agent-based model of parental vaccine hesitancy, provider non-vaccination tolerance, and selection of patients into pediatric practices. We ran 84 experiments across a range of parental hesitancy and provider tolerance scenarios. When the model is initialized, all providers accommodate refusals and intentionally unvaccinated children are evenly distributed across providers. As provider tolerance decreases, hesitant children become more clustered in a smaller number of practices and eventually are not able to find a practice that will accept them. Each of these effects becomes more pronounced as the level of hesitancy in the population rises. Heterogeneity in practice tolerance to vaccine-hesitant parents has the unintended result of concentrating susceptible individuals within a small number of tolerant practices, while providing little if any compensatory protection to adherent individuals. These externalities suggest an agenda for stricter policy regulation of individual practice decisions.

Byington, C. L. **Vaccines: can transparency increase confidence and reduce hesitancy?** *Pediatrics*. 2014; 134(2): 377-379.

Callender, D. **Vaccine hesitancy: More than a movement."** *Hum Vaccin Immunother*. 2016: 1-5.

Vaccines are some of if not the most successful public health endeavors ever put into practice. Countless lives have been saved and the occurrences of vaccine preventable diseases are at a fraction of the rate experienced before vaccines. Vaccines and the realization of their compulsory scheduling are highly studied, safe, and purposeful. Despite these realities, there are an alarming number of parents who do not permit the vaccination of their children as scheduled. This is known in the health community as vaccine hesitancy and commonly portrayed in popular media as anti-vaccination sentiment. This analysis opens with the topic as it was addressed during a September 2015 debate for the Republic Party's 2016 presidential nomination. Some key historical aspects of vaccine hesitancy are presented. This history leads to a description of the 2014-2015 measles outbreak in California. The factors that aide in the recruitment of under vaccination are then explored. Finally, select strategies to control, combat, and potentially attenuate vaccine hesitancy are presented.

Casciotti, D. M., et al. **Topics associated with conflict in print news coverage of the HPV vaccine during 2005 to 2009.** *Hum Vaccin Immunother* 2014; 10(12): 3466-3474.

HPV vaccines represent a significant advancement for cancer prevention, but vaccination against a sexually transmitted infection and possible vaccine mandates have created considerable negative publicity. We sought to understand media portrayal of vaccine-related controversy, and potential influences on attitudes and vaccine acceptance. We analyzed characteristics of media coverage of the HPV vaccine in 13 US newspapers between June 2005-May 2009, as well as relationships between conflict and pro-vaccine tone and specific story characteristics. The four-year timeframe was selected to capture coverage during the development of the vaccine, the period immediately pre- and post-approval, and the time of widespread recommendation and initial uptake. This allowed the exploration of a range of issues and provided an understanding of how coverage changed over time. Analysis included 447 news stories and opinion pieces, the majority of which were published in 2007. Most articles were positive (pro-vaccine) in tone, prompted by research/scientific advancement or legislative activities. We deemed 66% of all stories conflict-containing. Fewer articles from 2005-2006 and 2008-2009 contained conflict than those from 2007, suggesting a peak period of concern, followed by gradual acceptance of the HPV vaccine. Legislative activities and content related to sexual activity were sources of conflict in HPV vaccine media messages. Health communication strategies can be improved by understanding and addressing potential sources of conflict in news coverage of public health initiatives.

Casciotti, D. M., et al. **Discussions of adolescent sexuality in news media coverage of the HPV vaccine.** *J Adolesc.* 2014; 37(2): 133-143.

Given the sexually transmitted nature of human papillomavirus (HPV), some worry the HPV vaccine will create a false sense of security and promote adolescent sexual activity. Media coverage of vaccines can influence social norms, parental attitudes, and vaccine acceptance; in this paper we examine U.S. news media messages related to sexuality and HPV vaccination. Drawing on a structured analysis of 447 articles published during 2005-2009, we qualitatively analyzed a purposive sample of 49 articles discussing adolescent health behaviors related to HPV vaccination. Commonly, articles discussed vaccination in the context of abstinence-only versus comprehensive sexual health education; cited research findings to support vaccination or sex education; argued against connecting vaccination to promiscuous behavior; but included fear-inducing messages. Media messages concerning health behaviors related to HPV vaccination tended to support government and parental involvement in sex education, and dismiss concerns linking vaccination to sexual activity, while also presenting the vaccine as lifesaving.

Cates, J. R. and Coyne-Beasley, T. **Social marketing to promote HPV vaccination in pre-teenage children: talk about a sexually transmitted infection.** *Hum Vaccin Immunother.* 2015; 11(2): 347-349.

A significant barrier to the delivery of HPV vaccine is reluctance by both healthcare providers and parents to vaccinate at age 11 or 12, which may be considered a young age. This barrier has been called "vaccine hesitancy" in recent research. In this commentary, we suggest using social marketing strategies to promote HPV vaccination at the recommended preteen ages. We emphasize a critical public health message of a sexually transmitted infection (STI) as preventable and vaccination against HPV as a way to protect against its consequences. The message tackles the issue of vaccine hesitancy head on, by saying that most people are at risk for HPV and there is a way to prevent HPV's serious consequences of cancer. Our approach to this conversation in the clinical setting is also to engage the preteen in a dialog with the parent and provider. We expect our emphasis on the risk of STI infection will not only lead to increased HPV vaccination at preteen ages but also lay important groundwork for clinical adoption of other STI vaccines in development (HIV, HSV, Chlamydia, and Gonorrhea) as well as begin conversations to promote sexual health.

Chen, B., et al. **Media and public reactions toward vaccination during the 'hepatitis B vaccine crisis' in China.** *Vaccine.* 2015; 33(15): 1780-1785.

BACKGROUND: Public disputations affected vaccine confidence and vaccine rates particularly when adverse events occur. The vigorous development of Internet in China provides an opportunity to observe public reaction and sentiment toward vaccination when Kangtai Hepatitis B vaccine crisis happened and evolved to a widespread debate on the internet from December 12, 2013 to January 3, 2014. **METHODS:** This study conducted Internet surveillance by examining three daily indicators including the daily number of relevant online news article, Sina Weibo posts and Baidu search index during the crisis. We also analyzed the sentiments of relevant original microblog posts collected from Sina Weibo platform in the crisis. **RESULTS:** A total of 17 infant deaths were reported to associated with Hepatitis B vaccination. Three major waves of high media and public attention were detected. The daily indicators reached their peaks in the second wave after the relevant vaccine was suspended by the authority (from December 20 to December 29, 2013) with 23,200 daily online news reports, 34,018 Sina Weibo posts and 17,832 Baidu search indices. There were significant correlations between the daily amount of online news, Weibo posts, and Baidu searches ($p < .001$). The contents analysis suggested 1343 out of 1608 (83.5%) original Weibo posts expressed negative sentiment with almost 90% in the second wave. **CONCLUSION:** This study found the Kangtai vaccine crisis raised great public attention and negative sentiment toward

vaccinations on the internet in China. Policy change such as suspension of the suspected vaccine might trigger even greater reaction and more negative sentiment. The government should provide ways to address emerging public concerns after policy change to avoid misinformation and misunderstanding during such a vaccine crisis.

Chen, N. T. **Predicting Vaccination Intention and Benefit and Risk Perceptions: The Incorporation of Affect, Trust, and Television Influence in a Dual-Mode Model.** *Risk Anal.* 2015; 35(7): 1268-1280.

Major health behavior change models tend to consider health decisions as primarily resulting from a systematic appraisal of relevant beliefs, such as the perceived benefits and risks of a pharmacological intervention. Drawing on research from the disciplines of risk management, communication, and psychology, this study proposed the inclusion of a heuristic route in established theory and tested the direction of influence between heuristic and systematic process variables. Affect and social trust were included as key heuristics in the proposed dual-mode framework of health decision making. Furthermore, exposure to health-related coverage on television was considered potentially influential over both heuristic and systematic process variables. To test this framework, data were collected from a national probability sample of 584 adults in the United States in 2012 regarding their decision to vaccinate against a hypothetical avian flu. The results provided some support for the bidirectional influence between heuristic and systematic processing. Affect toward flu vaccination and trust in the Food and Drug Administration were found to be powerful predictors of vaccination intention, enhancing intention both directly and indirectly via certain systematic process variables. The direction of influence between perceived susceptibility and severity, on the one hand, and affect, on the other, is less clear, suggesting the need for further research. Contrary to the opinion of media critics, exposure to televised health coverage was negatively associated with the perceived risks of vaccination. Results from this study carry theoretical and practical implications, and applying this model to the acceptance of different health interventions constitutes an area for future inquiries.

Clark, S. J., et al. **Understanding Non-Completion of the Human Papillomavirus Vaccine Series: Parent-Reported Reasons for Why Adolescents Might Not Receive Additional Doses, United States, 2012.** *Public Health Rep.* 2016; 131(3): 390-395.

Completion rates of the human papillomavirus (HPV) vaccine series among U.S. adolescents are below public health targets. We explored parent-reported reasons for their children's non-completion of the HPV vaccine series using a nationally representative online survey of parents of children aged 9-17 years, fielded in October 2012. Among the 1,653 parents who responded, the proportion reporting that their child would definitely continue with the HPV vaccine series among those who had started the series ranged from 28% to 54%. The most common reason cited by parents for non-completion of the series was their child's fear of needles, followed by lack of awareness about additional doses and safety concerns. These findings demonstrate the need to encourage adoption of strategies addressing needle fears, utilize reminders for parents about subsequent doses, and emphasize recent HPV vaccine safety data in discussions with parents.

Closser, S., et al. **The Global Context of Vaccine Refusal: Insights from a Systematic Comparative Ethnography of the Global Polio Eradication Initiative.** *Med Anthropol Q.* 2016.

Many of medical anthropology's most pressing research questions require an understanding how infections, money, and ideas move around the globe. The Global Polio Eradication Initiative (GPEI) is a \$9 billion project that has delivered 20 billion doses of oral polio vaccine in campaigns across the world. With its array of global activities, it cannot be comprehensively explored by the traditional anthropological method of research at one field site. This article describes an ethnographic study of the GPEI, a collaborative effort between researchers at eight sites in seven countries. We developed a methodology

grounded in nuanced understandings of local context but structured to allow analysis of global trends. Here, we examine polio vaccine acceptance and refusal to understand how global phenomena-in this case, policy decisions by donors and global health organizations to support vaccination campaigns rather than building health systems-shape local behavior.

Danchin, M. and Nolan, T. **A positive approach to parents with concerns about vaccination for the family physician.** *Aust Fam Physician* 2014; 43(10): 690-694.

BACKGROUND: Vaccine hesitancy is becoming increasingly recognised as an issue in Australia and globally, as concerns about vaccines and their safety predominate over concerns about the risk of vaccine-preventable diseases. **OBJECTIVE:** This review provides an approach for primary care physicians to enable effective communication with parents who have different levels of concerns about vaccinations and awareness of currently available resources that may be used to support discussions. **DISCUSSION:** Clear and flexible communication strategies for healthcare providers to undertake effective discussions with vaccine-hesitant parents or clear referral pathways are the key to addressing concerns about vaccination in both primary and secondary care.

Diekema, D. S. **Provider dismissal of vaccine-hesitant families: misguided policy that fails to benefit children.** *Hum Vaccin Immunother.* 2013; 9(12): 2661-2662.

Some health care providers have adopted the policy of refusing to accept into their practices families who refuse to vaccinate their children according to the standard vaccine schedule. While the frustration that drives these policies is understandable, the practice of refusing to see these families is misguided. Such a strategy does not benefit the child or the health of the community, and may have a negative impact on both. Physicians represent the best opportunity to influence the vaccine-hesitant parent, but only if physicians are willing to care for these families will that be possible. Maintaining a relationship of open communication and trust remains the best strategy for addressing the problem of parental vaccine hesitancy.

Domachowske, J. B. and Suryadevara, M. **Practical approaches to vaccine hesitancy issues in the United States: 2013.** *Hum Vaccin Immunother.* 2013; 9(12): 2654-2657.

The intention to delay or avoid vaccines that are recommended by the Advisory Committee on Immunization Practices can be described as "vaccine hesitancy." While outright refusal of all vaccines is uncommon, hesitancy is seen on a regular basis in most primary care offices, resulting in immunization delay and prolonged susceptibility to preventable disease. The consequences of vaccine hesitancy include the potential for resurgence of vaccine preventable infections. Open, honest, and frank discussions with hesitant patients and their families can assist in their understanding of the importance of vaccines. While many experienced providers are able to do so in an intuitive manner, others may benefit from developing a systemic framework for such discussions. An understanding of the history and rationale for vaccine hesitancy is a first step in regaining lost public confidence in our robust immunization programs.

Dube, E., et al. **Strategies intended to address vaccine hesitancy: Review of published reviews.** *Vaccine.* 2015; 33(34): 4191-4203.

When faced with vaccine hesitancy, public health authorities are looking for effective strategies to address this issue. In this paper, the findings of 15 published literature reviews or meta-analysis that have examined the effectiveness of different interventions to reduce vaccine hesitancy and/or to enhance vaccine acceptance are presented and discussed. From the literature, there is no strong evidence to recommend any specific intervention to address vaccine hesitancy/refusal. The reviewed studies included interventions with diverse content and approaches that were implemented in different settings and targeted various populations. Few interventions were directly targeted to vaccine hesitant individuals.

Given the paucity of information on effective strategies to address vaccine hesitancy, when interventions are implemented, planning a rigorous evaluation of their impact on vaccine hesitancy/vaccine acceptance will be essential.

Dube, E., et al. **Mapping vaccine hesitancy--country-specific characteristics of a global phenomenon.** *Vaccine*. 2014; 32(49): 6649-6654.

The term vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite the availability of vaccination services. Different factors influence vaccine hesitancy and these are context-specific, varying across time and place and with different vaccines. Factors such as complacency, convenience and confidence are involved. Acceptance of vaccines may be decreasing and several explanations for this trend have been proposed. The WHO Strategic Advisory Group of Experts (SAGE) on Immunization has recognized the global importance of vaccine hesitancy and recommended an interview study with immunization managers (IMs) to better understand the range of vaccine hesitancy determinants that are encountered in different settings. Interviews with IMs in 13 selected countries were conducted between September and December 2013 and various factors that discourage vaccine acceptance were identified. Vaccine hesitancy was not defined consistently by the IMs and most interpreted the term as meaning vaccine refusal. Although vaccine hesitancy existed in all 13 countries, some IMs considered its impact on immunization programmes to be a minor problem. The causes of vaccine hesitancy varied in the different countries and were context-specific, indicating a need to strengthen the capacity of national programmes to identify the locally relevant causal factors and to develop adapted strategies to address them.

Dube, E., et al. **Understanding Vaccine Hesitancy in Canada: Results of a Consultation Study by the Canadian Immunization Research Network.** *PLoS One*. 2016; 11(6): e0156118.

"Vaccine hesitancy" is a concept now frequently used in vaccination discourse. The increased popularity of this concept in both academic and public health circles is challenging previously held perspectives that individual vaccination attitudes and behaviours are a simple dichotomy of accept or reject. A consultation study was designed to assess the opinions of experts and health professionals concerning the definition, scope, and causes of vaccine hesitancy in Canada. We sent online surveys to two panels (1- vaccination experts and 2- front-line vaccine providers). Two questionnaires were completed by each panel, with data from the first questionnaire informing the development of questions for the second. Our participants defined vaccine hesitancy as an attitude (doubts, concerns) as well as a behaviour (refusing some / many vaccines, delaying vaccination). Our findings also indicate that both vaccine experts and front-line vaccine providers have the perception that vaccine rates have been declining and consider vaccine hesitancy an important issue to address in Canada. Diffusion of negative information online and lack of knowledge about vaccines were identified as the key causes of vaccine hesitancy by the participants. A common understanding of vaccine hesitancy among researchers, public health experts, policymakers and health care providers will better guide interventions that can more effectively address vaccine hesitancy within Canada.

Dube, E., et al. **Parental Vaccine Hesitancy in Quebec (Canada).** *PLoS Curr* 2016; 8.

INTRODUCTION: "Vaccine hesitancy" is a concept frequently used in the discourse around vaccine acceptance. This study aims to contribute to the ongoing reflections on tools and indicators of vaccine hesitancy by providing results of a knowledge, attitudes and beliefs (KAB) survey conducted among parents. **METHODS:** Data were collected in 2014 through a computer-assisted telephone interview survey administered to a sample of parents of children aged between 2 months and 17 years of age. **RESULTS:** The majority of the 589 parents included in the analyses agreed on the importance of vaccination to protect their children's health and to prevent the spread of diseases in the community. The majority of

the parents (81%) reported that their child had received all doses of recommended vaccines and 40% of parents indicated having hesitated to have their child vaccinated. Fear of adverse events and low perceived vulnerability of the child or severity of the disease were the most frequent reasons mentioned by these vaccine-hesitant parents. In multivariate analyses, KAB items remaining significantly associated both with an incomplete vaccination status of the child and parents' vaccine hesitancy were: not thinking that it is important to have the child vaccinated to prevent the spreading of diseases in the community; not trusting the received vaccination information and having felt pressure to have the child vaccinated. DISCUSSION: Further researches will be needed to better understand when, how and why these beliefs are formed in order to prevent the onset of vaccine hesitancy.

Dube, E., et al. **Vaccine hesitancy: an overview.** Hum Vaccin Immunother. 2013; 9(8): 1763-1773.

Despite being recognized as one of the most successful public health measures, vaccination is perceived as unsafe and unnecessary by a growing number of individuals. Lack of confidence in vaccines is now considered a threat to the success of vaccination programs. Vaccine hesitancy is believed to be responsible for decreasing vaccine coverage and an increasing risk of vaccine-preventable disease outbreaks and epidemics. This review provides an overview of the phenomenon of vaccine hesitancy. First, we will characterize vaccine hesitancy and suggest the possible causes of the apparent increase in vaccine hesitancy in the developed world. Then we will look at determinants of individual decision-making about vaccination.

Dube, E. and MacDonald N. E. **Managing the risks of vaccine hesitancy and refusals.** Lancet Infect Dis. 2016.

Dube, E., et al. **Vaccine hesitancy, vaccine refusal and the anti-vaccine movement: influence, impact and implications.** Expert Rev Vaccines. 2015; 14(1): 99-117.

Despite being recognized as one of the most successful public health measures, vaccination is perceived as unsafe and unnecessary by a growing number of parents. Anti-vaccination movements have been implicated in lowered vaccine acceptance rates and in the increase in vaccine-preventable disease outbreaks and epidemics. In this review, we will look at determinants of parental decision-making about vaccination and provide an overview of the history of anti-vaccination movements and its clinical impact.

Dube, E., et al. **Nature Does Things Well, Why Should We Interfere?": Vaccine Hesitancy Among Mothers.** Qual Health Res. 2016; 26(3): 411-425.

Parents' decision to use vaccination services is complex and multi-factorial. Of particular interest are "vaccine-hesitant" parents who are in the middle of the continuum between vaccine acceptance and refusal. The objective of this qualitative longitudinal study was to better understand why mothers choose to vaccinate-or not-their newborns. Fifty-six pregnant mothers living in different areas of Quebec (Canada) were interviewed. These interviews gathered information on mothers' views about health and vaccination. Almost half of the mothers were categorized as vaccine-hesitant. A second interview was conducted with these mothers 3 to 11 months after birth to look at their actual decision and behavior concerning vaccination. Our results show the heterogeneity of factors influencing vaccine decision making. Although the majority of vaccine-hesitant mothers finally chose to follow the recommended vaccine schedule for their child, they were still ambivalent and they continued to question their decision.

Eskola, J., et al. **How to deal with vaccine hesitancy?** Vaccine. 2015; 33(34): 4215-4217.

Based on the concerns about vaccine hesitancy and its impact on vaccine uptake rates and the performance of national immunization programmes, the Strategic Advisory Group of Experts (SAGE) on Immunization Working Group on Vaccine Hesitancy [1], carried out a review, and proposed a set of

recommendations directed to the public health community, to WHO and its partners, and to the World Health Organization (WHO) member states. The final recommendations issued by SAGE in October 2014 fall into three categories: (1) those focused on the need to increase the understanding of vaccine hesitancy, its determinants and the rapidly changing challenges it entails; (2) those focused on dealing with the structures and organizational capacity to decrease hesitancy and increase acceptance of vaccines at the global, national and local levels; (3) and those focused on the sharing of lessons learnt and effective practices from various countries and settings as well as the development, validation and implementation of new tools to address hesitancy.

Feemster, K. A. **Overview: special focus vaccine acceptance.** Hum Vaccin Immunother. 2013; 9(8): 1752-1754.

At the World Economic Forum in 2010, The Gates Foundation announced the "Decade of Vaccines," a \$10 billion commitment to increase access to existing and new childhood vaccines. It is estimated that this effort could save 6.4 million lives and avert 426 million illnesses [1, 2] Achieving these goals will require a significant effort among global health agencies, non-governmental organizations, industry and national governments to support vaccine development and ensure a strong infrastructure for sustainable vaccine delivery. Vaccines are one of the most important public health achievements in history, resulting in significant decreases in the prevalence of many childhood diseases. However, persistent disparities exist in the adoption of new vaccines and sustained vaccination rates in both developed and developing countries. Decreasing vaccination rates in some communities have resulted in outbreaks of vaccine-preventable diseases. Disparities may be due to vaccine supply, poor infrastructure, or low prioritization of vaccines for public health spending. However, another crucial contributor to the success of vaccination programs is vaccine acceptance.

Feinberg, Y., et al. **Understanding Public Perceptions of the HPV Vaccination Based on Online Comments to Canadian News Articles.** PLoS One. 2015; 10(6): e0129587.

BACKGROUND: Given the variation in human papillomavirus (HPV) vaccine coverage across Canada, and debate regarding delivery of HPV vaccines in Catholic schools, we studied online comments on Canadian news websites to understand public perceptions of HPV and HPV vaccine. **METHODS:** We searched English- and French-language Canadian news websites for 2012 articles that contained the terms "HPV" or "human papillomavirus." Articles about HPV vaccinations that contained at least one comment were included. Two researchers independently coded comments, analyzing them for emerging themes. **RESULTS:** We identified 3073 comments from 1198 individuals in response to 71 news articles; 630 (52.6%) individuals expressed positive sentiments about HPV vaccination (2.5 comments/individual), 404 (33.7%) were negative (3.0 comments/individual), 34 (2.8%) were mixed (1.5 comments/individual) and 130 (10.8%) were neutral (1.6 comments/individual). Vaccine-supportive commenters believed the vaccine is safe and effective. Common themes in negative comments included concerns regarding HPV vaccine safety and efficacy, distrust of pharmaceutical companies and government, and belief that school-age children are too young for HPV vaccine. Many comments focused on whether the Catholic Church has the right to inform health policy for students, and discussion often evolved into debates regarding HPV and sexual behaviour. We noted that many individuals doubted the credibility of vaccine safety information. **CONCLUSION:** The majority of commenters do not appear to be against HPV vaccination, but public health messaging that focuses on both the vaccine's safety profile, and its use as a means to prevent cancer rather than sexually transmitted HPV infection may facilitate its acceptance.

Gargano, L. M., et al. **Impact of a physician recommendation and parental immunization attitudes on receipt or intention to receive adolescent vaccines.** Hum Vaccin Immunother. 2013; 9(12): 2627-2633.

Four vaccines are recommended by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices for adolescents. Parental attitudes may play a key role in vaccination uptake in this age group. In 2011, we conducted a cross-sectional survey among parents of adolescents in one county in Georgia to identify parental attitudes toward adolescent vaccination, reasons for vaccine acceptance or refusal, and impact of a physician recommendation for vaccination. Physician recommendation was reported as one of the top reasons for receipt or intent to receive any of the vaccines. Physician recommendation of any of the four vaccines was associated with receipt of Tdap ($p < 0.001$), MCV4 ($p < 0.001$), and HPV ($p = 0.03$) and intent to receive Tdap ($p = 0.05$), MCV4 ($p = 0.005$), and HPV ($p = 0.05$). Compared with parents who did not intend to have their adolescent vaccinated with any of the vaccines, parents who did intend reported higher perceived susceptibility (3.12 vs. 2.63, $p = 0.03$) and severity of disease (3.89 vs. 3.70, $p = 0.02$) and higher perceived benefit of vaccination (8.48 vs. 7.74, $p = 0.02$). These findings suggest that future vaccination efforts geared toward parents may benefit from addressing the advantages of vaccination and enhancing social norms. Physicians can play a key role by providing information on the benefits of adolescent vaccination.

Gargano, L. M., et al. **Development, theoretical framework, and evaluation of a parent and teacher-delivered intervention on adolescent vaccination.** *Health Promot Pract.* 2014; 15(4): 556-567.

The Advisory Committee on Immunization Practices recommended immunization schedule for adolescents includes three vaccines (tetanus, diphtheria, and acellular pertussis [Tdap]; human papillomavirus [HPV] vaccine; and meningococcal conjugate vaccine [MCV4]) and an annual influenza vaccination. Given the increasing number of recommended vaccines for adolescents and health and economic costs associated with nonvaccination, it is imperative that effective strategies for increasing vaccination rates among adolescents are developed. This article describes the development, theoretical framework, and initial first-year evaluation of an intervention designed to promote vaccine acceptance among a middle and high school-based sample of adolescents and their parents in eastern Georgia. Adolescents, parents, and teachers were active participants in the development of the intervention. The intervention, which consisted of a brochure for parents and a teacher-delivered curriculum for adolescents, was guided by constructs from the health belief model and theory of reasoned action. Evaluation results indicated that our intervention development methods were successful in creating a brochure that met cultural relevance and the literacy needs of parents. We also demonstrated an increase in student knowledge of and positive attitudes toward vaccines. To our knowledge, this study is the first to extensively engage middle and high school students, parents, and teachers in the design and implementation of key theory-based educational components of a school-based, teacher-delivered adolescent vaccination intervention.

Gerend, M. A., et al. **The multidimensional nature of perceived barriers: global versus practical barriers to HPV vaccination.** *Health Psychol.* 2013; 32(4): 361-369.

OBJECTIVE: Perceived barriers are one of the strongest determinants of health behavior. The current study presents a novel conceptualization of perceived barriers by testing the following hypotheses: (a) perceived barriers are multidimensional and thus should cluster into distinct factors; (b) practical barriers should be salient for individuals intending to engage in a particular health behavior, whereas global barriers should be salient for individuals not intending to enact the behavior; and (c) whereas global barriers should be negatively associated with behavioral intentions, practical barriers should be positively related to intentions. **METHODS:** The context for this investigation was young adult women's perceived barriers to human papillomavirus (HPV) vaccination. Two months after viewing an educational video about HPV vaccination, women (aged 18-26) who had not received any doses of the HPV vaccine ($n = 703$) reported their perceived barriers to HPV vaccination and intentions to receive the vaccine. **RESULTS:** Relative to the conventional single-factor approach, a five-factor model provided a

better fit to the data and accounted for a larger proportion of variance in vaccination intentions. The relative salience of different perceived barriers varied as a function of women's intentions. Participants who were not intending to get vaccinated cited global concerns about vaccine safety and low perceived need for the vaccine. In contrast, participants intending to get vaccinated cited practical concerns (cost, logistical barriers) related to carrying out their intentions. Moreover, whereas global perceived barriers were associated with lower intentions, practical barriers were associated with higher intentions. **CONCLUSIONS:** Perceived barriers are multidimensional and vary systematically as a function of people's behavioral intentions.

Gilkey, M. B., et al. **The Vaccination Confidence Scale: a brief measure of parents' vaccination beliefs.** *Vaccine*. 2014; 32(47): 6259-6265.

PURPOSE: The success of national immunization programs depends on the public's confidence in vaccines. We sought to develop a scale for measuring confidence about adolescent vaccination in diverse populations of parents. **METHODS:** Data came from 9623 parents who completed the 2010 National Immunization Survey-Teen, an annual, population-based telephone survey. Parents reported on a 13- to 17-year-old child in their households. We used exploratory and confirmatory factor analysis to identify latent constructs underlying parents' responses to 8 vaccination belief survey items (response scale 0-10) conceptualized using the Health Belief Model. We assessed the scale's psychometric properties overall and across demographic subgroups. **RESULTS:** Parents' confidence about adolescent vaccination was generally high. Analyses provided support for three factors assessing benefits of vaccination (mean=8.5), harms of vaccination (mean=3.3), and trust in healthcare providers (mean=9.0). The model showed good fit both overall (comparative fit index=0.97) and across demographic subgroups, although internal consistency was variable for the three factors. We found lower confidence among several potentially vulnerable subpopulations, including mothers with lower levels of education and parents whose children were of Hispanic ethnicity (both $p < 0.05$). **CONCLUSIONS:** Our brief, three-factor scale offers an efficient way to measure confidence in adolescent vaccination across demographic subgroups. Given evidence of lower confidence by educational attainment and race/ethnicity, program planners should consider factors such as health literacy and cultural competence when designing interventions to promote adolescent vaccination to ensure these programs are fully accessible.

Gilkey, M. B., et al. **Validation of the Vaccination Confidence Scale: A Brief Measure to Identify Parents at Risk for Refusing Adolescent Vaccines.** *Acad Pediatr*. 2016; 16(1): 42-49.

OBJECTIVE: To validate a brief measure of vaccination confidence using a large, nationally representative sample of parents. **METHODS:** We analyzed weighted data from 9018 parents who completed the 2010 National Immunization Survey-Teen, an annual, population-based telephone survey. Parents reported on the immunization history of a 13- to 17-year-old child in their households for vaccines including tetanus, diphtheria, and acellular pertussis (Tdap), meningococcal, and human papillomavirus vaccines. For each vaccine, separate logistic regression models assessed associations between parents' mean scores on the 8-item Vaccination Confidence Scale and vaccine refusal, vaccine delay, and vaccination status. We repeated analyses for the scale's 4-item short form. **RESULTS:** One quarter of parents (24%) reported refusal of any vaccine, with refusal of specific vaccines ranging from 21% for human papillomavirus to 2% for Tdap. Using the full 8-item scale, vaccination confidence was negatively associated with measures of vaccine refusal and positively associated with measures of vaccination status. For example, refusal of any vaccine was more common among parents whose scale scores were medium (odds ratio, 2.08; 95% confidence interval, 1.75-2.47) or low (odds ratio, 4.61; 95% confidence interval, 3.51-6.05) versus high. For the 4-item short form, scores were also consistently associated with vaccine refusal and vaccination status. Vaccination confidence was inconsistently associated with vaccine delay.

CONCLUSIONS: The Vaccination Confidence Scale shows promise as a tool for identifying parents at risk for refusing adolescent vaccines. The scale's short form appears to offer comparable performance.

Goldstein, S., et al. **Health communication and vaccine hesitancy.** *Vaccine* 2015; 33(34): 4212-4214.

Health communication is an evolving field. There is evidence that communication can be an effective tool, if utilized in a carefully planned and integrated strategy, to influence the behaviours of populations on a number of health issues, including vaccine hesitancy. Experience has shown that key points to take into account in devising and implementing a communication plan include: (i) it is necessary to be proactive; (ii) communication is a two-way process; (iii) knowledge is important but not enough to change behaviour; and (iv) communication tools are available and can be selected and used creatively to promote vaccine uptake. A communication strategy, incorporating an appropriate selection of the available communication tools, should be an integral part of every immunization programme, addressing the specific factors that influence hesitancy in the target populations.

Gottvall, M., et al. **Trust versus concerns-how parents reason when they accept HPV vaccination for their young daughter.** *Ups J Med Sci.* 2013; 118(4): 263-270.

BACKGROUND: From spring of 2012, human papillomavirus (HPV) vaccine against cervical cancer is offered free of charge to all girls aged 10-12 years through a school-based vaccination programme in Sweden. The aim of this study was to explore how parents reason when they accept HPV vaccination for their young daughter and also their views on HPV-related information. **METHODS:** Individual interviews with parents (n = 27) of 11-12-year-old girls. The interviews were recorded, transcribed verbatim, and analysed using thematic content analysis. **RESULTS:** Three themes emerged through the analysis: Trust versus concern, Responsibility to protect against severe disease, and Information about HPV and HPV vaccination is important. The parents expressed trust in recommendations from authorities and thought it was convenient with school-based vaccination. They believed that cervical cancer was a severe disease and felt a responsibility to protect their daughter from it. Some had certain concerns regarding side effects and vaccine safety, and wished for a dialogue with the school nurse to bridge the information gaps. **CONCLUSIONS:** Trust in the recommendations from authorities and a wish to protect their daughter from a severe disease outweighed concerns about side effects. A school-based vaccination programme is convenient for parents, and the school nurse has an important role in bridging information gaps. The findings from this qualitative study cannot be generalized; however, it can provide a better understanding of how parents might reason when they accept the HPV vaccination for their daughter.

Grabenstein, J. D. **What the world's religions teach, applied to vaccines and immune globulins.** *Vaccine.* 2013; 31(16): 2011-2023.

For millennia, humans have sought and found purpose, solace, values, understanding, and fellowship in religious practices. Buddhist nuns performed variolation against smallpox over 1000 years ago. Since Jenner developed vaccination against smallpox in 1796, some people have objected to and declined vaccination, citing various religious reasons. This paper reviews the scriptural, canonical basis for such interpretations, as well as passages that support immunization. Populous faith traditions are considered, including Hinduism, Buddhism, Jainism, Judaism, Christianity, and Islam. Subjects of concern such as blood components, pharmaceutical excipients of porcine or bovine origin, rubella strain RA 27/3, and cell-culture media with remote fetal origins are evaluated against the religious concerns identified. The review identified more than 60 reports or evaluations of vaccine-preventable infectious-disease outbreaks that occurred within religious communities or that spread from them to broader communities. In multiple cases, ostensibly religious reasons to decline immunization actually reflected concerns about vaccine safety or personal beliefs among a social network of people organized around a faith community, rather than theologically based objections per se. Themes favoring vaccine acceptance included

transformation of vaccine excipients from their starting material, extensive dilution of components of concern, the medicinal purpose of immunization (in contrast to diet), and lack of alternatives. Other important features included imperatives to preserve health and duty to community (e.g., parent to child, among neighbors). Concern that 'the body is a temple not to be defiled' is contrasted with other teaching and quality-control requirements in manufacturing vaccines and immune globulins. Health professionals who counsel hesitant patients or parents can ask about the basis for concern and how the individual applies religious understanding to decision-making about medical products, explain facts about content and processes, and suggest further dialog with informed religious leaders. Key considerations for observant believers for each populous religion are described.

Hardt, K., et al. **Sustaining Vaccine Confidence in the 21st Century**. *Vaccines* (Basel). 2013; 1(3): 204-224.

Vaccination provides many health and economic benefits to individuals and society, and public support for immunization programs is generally high. However, the benefits of vaccines are often not fully valued when public discussions on vaccine safety, quality or efficacy arise, and the spread of misinformation via the internet and other media has the potential to undermine immunization programs. Factors associated with improved public confidence in vaccines include evidence-based decision-making procedures and recommendations, controlled processes for licensing and monitoring vaccine safety and effectiveness and disease surveillance. Community engagement with appropriate communication approaches for each audience is a key factor in building trust in vaccines. Vaccine safety/quality issues should be handled rapidly and transparently by informing and involving those most affected and those concerned with public health in effective ways. Openness and transparency in the exchange of information between industry and other stakeholders is also important. To maximize the safety of vaccines, and thus sustain trust in vaccines, partnerships are needed between public health sector stakeholders. Vaccine confidence can be improved through collaborations that ensure high vaccine uptake rates and that inform the public and other stakeholders of the benefits of vaccines and how vaccine safety is constantly assessed, assured and communicated.

Hausman, B. L., et al. **'Poisonous, filthy, loathsome, damnable stuff': the rhetorical ecology of vaccination concern**. *Yale J Biol Med*. 2014; 87(4): 403-416.

In this article, we analyze newspaper articles and advertisements mentioning vaccination from 1915 to 1922 and refer to historical studies of vaccination practices and attitudes in the early 20th century in order to assess historical continuities and discontinuities in vaccination concern. In the Progressive Era period, there were a number of themes or features that resonated with contemporary issues and circumstances: 1) fears of vaccine contamination; 2) distrust of medical professionals; 3) resistance to compulsory vaccination; and 4) the local nature of vaccination concern. Such observations help scholars and practitioners understand vaccine skepticism as longstanding, locally situated, and linked to the sociocultural contexts in which vaccination occurs and is mandated for particular segments of the population. A rhetorical approach offers a way to understand how discourses are engaged and mobilized for particular purposes in historical contexts. Historically situating vaccine hesitancy and addressing its articulation with a particular rhetorical ecology offers scholars and practitioners a robust understanding of vaccination concerns that can, and should, influence current approaches to vaccination skepticism.

Healy, C. M., et al. **Parent and provider perspectives on immunization: are providers overestimating parental concerns?** *Vaccine*. 2014; 32(5): 579-584.

OBJECTIVES: Data are limited on whether providers understand parental attitudes to recommended childhood immunizations. We determined parental attitudes and assessed how accurately providers estimated parental opinions. **METHODS:** Survey of parents and providers (pediatricians, nurses, medical assistants) in randomly selected practices in Houston, Texas. Surveys assessed demographics,

perceptions of immunization importance, safety and efficacy, and acceptability of vaccine delivery. Providers estimated parental responses. RESULTS: 401 parents (82% mothers, 12% fathers, 6% other) and 105 providers participated. Parents thought vaccines were important for health (median score 9.5; 0=not important, 10=extremely important) but also were concerned regarding vaccine safety and side effects (8.9 on 0-10 scale). 309 (77%) agreed that vaccines effectively prevent disease. Route of administration mattered to 147 (37%), who preferred injection (9.0) over oral (7.3) or intranasal (4.8) routes. Although parents would prefer three or fewer injections per visit, preventing more diseases (189 [47.6%]) was more important than number of injections (167 [42.3%]) when deciding the number of vaccines allowed per visit. White parents rated vaccines less important in preventing some illnesses than did non-white ($P<=0.006$ for meningitis, hepatitis, HPV, influenza and rotavirus) and rated number of injections per visit more important than number of diseases prevented (51.6% white versus 34.2% non-white; $P 0.002$). Providers underestimated parental attitudes toward vaccine importance (particularly influenza and HPV), and overestimated the proportion of parents who thought route of administration mattered (63%) and that number of injections per visit was the most important factor (76%) around parental vaccine decisions ($P<0.001$ for parent-provider mismatch). CONCLUSIONS: Most surveyed parents believe vaccines are important for child health and rate disease prevention higher than number of injections entailed. Providers underestimate the importance of some vaccines to parents and overestimate parental concerns regarding route of administration. Future research should focus on how this mismatch impacts parental vaccine decisions.

Hendry, M., et al. **"HPV? Never heard of it!": a systematic review of girls' and parents' information needs, views and preferences about human papillomavirus vaccination.** *Vaccine* 2013; 31(45): 5152-5167.

BACKGROUND AND OBJECTIVE: Two human papillomavirus vaccines were licenced in 2006/2007 for cervical cancer prevention. National vaccination programmes for schoolgirls were subsequently introduced in some European countries, North America and Australia. To understand factors influencing vaccine uptake and to inform the development of appropriate UK educational materials, we aimed to synthesise evidence of girls' and parents' information needs, views and preferences regarding HPV vaccination. DESIGN: Systematic review and mixed method synthesis of qualitative and survey data. DATA SOURCES: Twelve electronic databases; bibliographies of included studies 1980 to August 2011. REVIEW METHODS: Two reviewers independently screened papers and appraised study quality. Studies were synthesised collaboratively using framework methods for qualitative data, and survey results integrated where they supported, contrasted or added to the themes identified. RESULTS: Twenty-eight qualitative studies and 44 surveys were included. Where vaccination was offered, uptake was high. Intention to decline was related to a preference for vaccinating later to avoid appearing to condone early sexual activity, concerns about vaccine safety and low perception of risk of HPV infection. Knowledge was poor and there were many misconceptions; participants tried to assess the potential benefits and harms of vaccination but struggled to interpret limited information about HPV in the context of existing knowledge about sexually transmitted infections and cancer. Conclusion Many girls and their parents have limited understanding to an extent that impinges on their ability to make informed choices about HPV vaccination and could impact on future uptake of cervical screening. This is a considerable challenge to those who design and provide information, but getting the messages right for this programme could help in developing patient information about other HPV related cancers.

Hickler, B., et al. **Vaccine Special Issue on Vaccine Hesitancy.** *Vaccine*. 2015; 33(34): 4155-4156.

Jacobson, R. M. **Making the C.A.S.E. for the human papillomavirus vaccine: how to talk to parents and adolescents.** *Minn Med*. 2014; 97(2): 38-42.

Human papillomavirus (HPV) vaccination rates have been stagnant or falling for females, and vaccination efforts are off to a poor start for males. Despite recommendations by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices and other authorities that all adolescents receive the vaccine at 11 to 12 years of age, the latest data indicate no more than 32% of females ages 13 to 17 years have completed all three doses; the rate for males is less than 8%. Most parents are unfamiliar with HPV and are unaware that their children may one day become infected. In addition, they may not know that the vaccine is recommended. Others may question its safety and whether their child needs it; or they may think their child is too young to be vaccinated. Whether adolescents get the vaccine depends largely on their clinician: A clinician who directs a parent to have their child vaccinated will be more successful in ensuring that child is vaccinated than those who merely tell parents the vaccine is available. The Minnesota Chapter of the American Academy of Pediatrics teaches clinicians to address vaccine hesitancy among parents using the C.A.S.E. approach. This approach is not just for parents; it also can be used to address adolescents' concerns in a persuasive manner.

Jacobson, R. M., et al. **Vaccine Hesitancy**. *Mayo Clin Proc.* 2015; 90(11): 1562-1568.

Vaccine refusal received a lot of press with the 2015 Disneyland measles outbreak, but vaccine refusal is only a fraction of a much larger problem of vaccine delay and hesitancy. Opposition to vaccination dates back to the 1800s, Edward Jenner, and the first vaccine ever. It has never gone away despite the public's growing scientific sophistication. A variety of factors contribute to modern vaccine hesitancy, including the layperson's heuristic thinking when it comes to balancing risks and benefits as well as a number of other features of vaccination, including falling victim to its own success. Vaccine hesitancy is pervasive, affecting a quarter to a third of US parents. Clinicians report that they routinely receive requests to delay vaccines and that they routinely acquiesce. Vaccine rates vary by state and locale and by specific vaccine, and vaccine hesitancy results in personal risk and in the failure to achieve or sustain herd immunity to protect others who have contraindications to the vaccine or fail to generate immunity to the vaccine. Clinicians should adopt a variety of practices to combat vaccine hesitancy, including a variety of population health management approaches that go beyond the usual call to educate patients, clinicians, and the public. Strategies include using every visit to vaccinate, the creation of standing orders or nursing protocols to provide vaccination without clinical encounters, and adopting the practice of stating clear recommendations. Up-to-date, trusted resources exist to support clinicians' efforts in adopting these approaches to reduce vaccine hesitancy and its impact.

Jarrett, C., et al. **Strategies for addressing vaccine hesitancy - A systematic review**. *Vaccine.* 2015; 33(34): 4180-4190.

The purpose of this systematic review is to identify, describe and assess the potential effectiveness of strategies to respond to issues of vaccine hesitancy that have been implemented and evaluated across diverse global contexts. METHODS: A systematic review of peer reviewed (January 2007-October 2013) and grey literature (up to October 2013) was conducted using a broad search strategy, built to capture multiple dimensions of public trust, confidence and hesitancy concerning vaccines. This search strategy was applied and adapted across several databases and organizational websites. Descriptive analyses were undertaken for 166 (peer reviewed) and 15 (grey literature) evaluation studies. In addition, the quality of evidence relating to a series of PICO (population, intervention, comparison/control, outcomes) questions defined by the SAGE Working Group on Vaccine Hesitancy (WG) was assessed using Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria; data were analyzed using Review Manager. RESULTS: Across the literature, few strategies to address vaccine hesitancy were found to have been evaluated for impact on either vaccination uptake and/or changes in knowledge, awareness or attitude (only 14% of peer reviewed and 25% of grey literature). The majority of evaluation studies were based in the Americas and primarily focused on influenza, human

papillomavirus (HPV) and childhood vaccines. In low- and middle-income regions, the focus was on diphtheria, tetanus and pertussis, and polio. Across all regions, most interventions were multi-component and the majority of strategies focused on raising knowledge and awareness. Thirteen relevant studies were used for the GRADE assessment that indicated evidence of moderate quality for the use of social mobilization, mass media, communication tool-based training for health-care workers, non-financial incentives and reminder/recall-based interventions. Overall, our results showed that multicomponent and dialogue-based interventions were most effective. However, given the complexity of vaccine hesitancy and the limited evidence available on how it can be addressed, identified strategies should be carefully tailored according to the target population, their reasons for hesitancy, and the specific context.

Kalichman, S. C. and Kegler, C. **Vaccine-related internet search activity predicts H1N1 and HPV vaccine coverage: implications for vaccine acceptance.** J Health Commun. 2015; 20(3): 259-265.

The Internet is a primary source for health-related information, and Internet search activity is associated with infectious disease outbreaks. The authors hypothesized that Internet search activity for vaccine-related information would predict vaccination coverage. They examined Internet search activity for H1N1 and human papilloma virus (HPV) disease and vaccine information in relation to H1N1 and HPV vaccine uptake. Google Insight for Search was used to assess the volume of Internet search queries for H1N1- and vaccine-related terms in the United States in 2009, the year of the H1N1 pandemic. Vaccine coverage data were also obtained from the Centers for Disease Control and Prevention at the state level for H1N1 vaccinations in 2009. These same measures were collected at the state level for HPV- and vaccine-related search terms in 2010 as well as HPV vaccine uptake in that year. Analyses showed that the search terms H1N1 and vaccine were correlated with H1N1 vaccine uptake; ordinal regression found the H1N1 search term was independently associated with H1N1 vaccine coverage. Similarly, the correlation between vaccine search volume and HPV coverage was significant; ordinal regression showed the search term vaccine independently predicted HPV vaccination coverage. This is among the first studies to show that Internet search activity is associated with vaccination coverage. The Internet should be exploited as an opportunity to dispel vaccine misinformation by providing accurate information to support vaccine decision making.

Kestenbaum, L. A. and Feemster, K. A. **Identifying and addressing vaccine hesitancy.** Pediatr Ann. 2015; 44(4): e71-75.

In the 20th century, the introduction of multiple vaccines significantly reduced childhood morbidity, mortality, and disease outbreaks. Despite, and perhaps because of, their public health impact, an increasing number of parents and patients are choosing to delay or refuse vaccines. These individuals are described as "vaccine hesitant." This phenomenon has developed due to the confluence of multiple social, cultural, political, and personal factors. As immunization programs continue to expand, understanding and addressing vaccine hesitancy will be crucial to their successful implementation. This review explores the history of vaccine hesitancy, its causes, and suggested approaches for reducing hesitancy and strengthening vaccine acceptance.

Kumar, D., et al. **Vaccine hesitancy: understanding better to address better.** Isr J Health Policy Res. 2016; 5: 2.

Vaccine hesitancy is an emerging term in the socio-medical literature which describes an approach to vaccine decision making. It recognizes that there is a continuum between full acceptance and outright refusal of some or all vaccines and challenges the previous understanding of individuals or groups, as being either anti-vaccine or pro-vaccine. The behaviours responsible for vaccine hesitancy can be related to confidence, convenience and complacency. The causes of vaccine hesitancy can be described by the epidemiological triad i.e. the complex interaction of environmental- (i.e. external), agent- (i.e. vaccine)

and host (or parent)- specific factors. Vaccine hesitancy is a complex and dynamic issue; future vaccination programs need to reflect and address these context-specific factors in both their design and evaluation. Many experts are of the view that it is best to counter vaccine hesitancy at the population level. They believe that it can be done by introducing more transparency into policy decision-making before immunization programs, providing up-to-date information to the public and health providers about the rigorous procedures undertaken before introduction of new vaccines, and through diversified post-marketing surveillance of vaccine-related events.

Kundi, M., et al. **The impact of the parent-physician relationship on parental vaccine safety perceptions.** *Curr Drug Saf.* 2015; 10(1): 16-22.

In times of declining immunization rates among children in many countries and an increasing threat of potentially vaccine-preventable diseases, there is a strong need for new strategies to improve trust in vaccinations and acceptance of recommendations, especially in parents of infants and children. A survey to evaluate vaccination acceptance has been conducted in Vienna, Austria, based on a US CDC survey, applying a cross-sectional approach with districts and public as well as private kindergartens and preschools as selection base. The survey aimed to investigate the impact of parent satisfaction with, and overall trust in the physician on vaccine acceptance, as well as the impact of quality and completeness of safety information delivered during the vaccination consultation. Overall 1101 parents, predominantly (84.2%) mothers, participated in the survey. The majority (82.7%) of participants had a generally positive view concerning childhood vaccination. However, 25.1% refused at least one of the recommended vaccinations. In multivariate analysis, confidence in vaccinations was significantly influenced by education (lower confidence at higher levels of education), gender (higher confidence in females), and positively associated with trust in physician, smooth vaccination procedure, and information about vaccine risks. Similar results were obtained for compliance with recommended vaccinations with information about vaccine benefits being the most important predictor. This large survey indicates an important role of the physician in communicating balanced information about benefits and risks associated with childhood vaccinations. A trustworthy parent-physician relationship is crucial for vaccination decisions of parents.

Larson, H., et al. **A Multidisciplinary Research Agenda for Understanding Vaccine-Related Decisions.** *Vaccines (Basel).* 2013; 1(3): 293-304.

There is increasingly broad global recognition of the need to better understand determinants of vaccine acceptance. Fifteen social science, communication, health, and medical professionals (the "Motors of Trust in Vaccination" (MOTIV) think tank) explored factors relating to vaccination decision-making as a step to building a multidisciplinary research agenda. One hundred and forty seven factors impacting decisions made by consumers, professionals, and policy makers on vaccine acceptance, delay, or refusal were identified and grouped into three major categories: cognition and decision-making; groups and social norms; and communication and engagement. These factors should help frame a multidisciplinary research agenda to build an evidence base on the determinants of vaccine acceptance to inform the development of interventions and vaccination policies.

Larson, H. J. **Negotiating vaccine acceptance in an era of reluctance.** *Hum Vaccin Immunother.* 2013; 9(8): 1779-1781.

Studies to better understand the determinants of vaccine acceptance have expanded to include more investigation into dynamics of individual decision-making as well as the influences of peers and social networks. Vaccine acceptance is determined by a range of factors, from structural issues of supply, costs and access to services, as well as the more demand-side determinants. The term vaccine hesitancy is increasingly used in the investigation of demand-side determinants, moving away from the more polarized framing of pro- and anti-vaccine groups to recognizing the importance of understanding and

engaging those who are delaying vaccination, accepting only some vaccines, or who are yet undecided, but reluctant. As hesitancy is a state of indecision, it is difficult to measure, but the stage of indecision is a critical time to engage and support the decision-making process. This article suggests modes of investigating the determinants of vaccine confidence and levers of vaccine acceptance toward better engagement and dialogue early in the process of decision-making. Pressure to vaccinate can be counter-productive. Listening and dialog can support individual decision-making and more effectively inform the public health community of the issues and concerns influencing vaccine hesitancy.

Larson, H. J., et al. **Addressing the vaccine confidence gap.** *Lancet.* 2011; 378(9790): 526-535.

Vaccines--often lauded as one of the greatest public health interventions--are losing public confidence. Some vaccine experts have referred to this decline in confidence as a crisis. We discuss some of the characteristics of the changing global environment that are contributing to increased public questioning of vaccines, and outline some of the specific determinants of public trust. Public decision making related to vaccine acceptance is neither driven by scientific nor economic evidence alone, but is also driven by a mix of psychological, sociocultural, and political factors, all of which need to be understood and taken into account by policy and other decision makers. Public trust in vaccines is highly variable and building trust depends on understanding perceptions of vaccines and vaccine risks, historical experiences, religious or political affiliations, and socioeconomic status. Although provision of accurate, scientifically based evidence on the risk-benefit ratios of vaccines is crucial, it is not enough to redress the gap between current levels of public confidence in vaccines and levels of trust needed to ensure adequate and sustained vaccine coverage. We call for more research not just on individual determinants of public trust, but on what mix of factors are most likely to sustain public trust. The vaccine community demands rigorous evidence on vaccine efficacy and safety and technical and operational feasibility when introducing a new vaccine, but has been negligent in demanding equally rigorous research to understand the psychological, social, and political factors that affect public trust in vaccines.

Larson, H. J., et al. **Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: a systematic review of published literature, 2007-2012.** *Vaccine.* 2014; 32(19): 2150-2159.

Vaccine "hesitancy" is an emerging term in the literature and discourse on vaccine decision-making and determinants of vaccine acceptance. It recognizes a continuum between the domains of vaccine acceptance and vaccine refusal and de-polarizes previous characterization of individuals and groups as either anti-vaccine or pro-vaccine. The primary aims of this systematic review are to: 1) identify research on vaccine hesitancy; 2) identify determinants of vaccine hesitancy in different settings including its context-specific causes, its expression and its impact; and 3) inform the development of a model for assessing determinants of vaccine hesitancy in different settings as proposed by the Strategic Advisory Group of Experts Working Group (SAGE WG) for dealing with vaccine hesitancy. A broad search strategy, built to capture multiple dimensions of public trust, confidence and hesitancy around vaccines, was applied across multiple databases. Peer-reviewed studies were selected for inclusion if they focused on childhood vaccines [≤ 7 years of age], used multivariate analyses, and were published between January 2007 and November 2012. Our results show a variety of factors as being associated with vaccine hesitancy but they do not allow for a complete classification and confirmation of their independent and relative strength of influence. Determinants of vaccine hesitancy are complex and context-specific - varying across time, place and vaccines.

Larson, H. J., et al. **Measuring vaccine hesitancy: The development of a survey tool.** *Vaccine.* 2015; 33(34): 4165-4175.

In March 2012, the SAGE Working Group on Vaccine Hesitancy was convened to define the term "vaccine hesitancy", as well as to map the determinants of vaccine hesitancy and develop tools to measure

and address the nature and scale of hesitancy in settings where it is becoming more evident. The definition of vaccine hesitancy and a matrix of determinants guided the development of a survey tool to assess the nature and scale of hesitancy issues. Additionally, vaccine hesitancy questions were piloted in the annual WHO-UNICEF joint reporting form, completed by National Immunization Managers globally. The objective of characterizing the nature and scale of vaccine hesitancy issues is to better inform the development of appropriate strategies and policies to address the concerns expressed, and to sustain confidence in vaccination. The Working Group developed a matrix of the determinants of vaccine hesitancy informed by a systematic review of peer reviewed and grey literature, and by the expertise of the working group. The matrix mapped the key factors influencing the decision to accept, delay or reject some or all vaccines under three categories: contextual, individual and group, and vaccine-specific. These categories framed the menu of survey questions presented in this paper to help diagnose and address vaccine hesitancy.

Larson, H. J., et al. **Measuring vaccine confidence: introducing a global vaccine confidence index.** PLoS Curr. 2015; 7.

BACKGROUND: Public confidence in vaccination is vital to the success of immunisation programmes worldwide. Understanding the dynamics of vaccine confidence is therefore of great importance for global public health. Few published studies permit global comparisons of vaccination sentiments and behaviours against a common metric. This article presents the findings of a multi-country survey of confidence in vaccines and immunisation programmes in Georgia, India, Nigeria, Pakistan, and the United Kingdom (UK) - these being the first results of a larger project to map vaccine confidence globally. **METHODS:** Data were collected from a sample of the general population and from those with children under 5 years old against a core set of confidence questions. All surveys were conducted in the relevant local-language in Georgia, India, Nigeria, Pakistan, and the UK. We examine confidence in immunisation programmes as compared to confidence in other government health services, the relationships between confidence in the system and levels of vaccine hesitancy, reasons for vaccine hesitancy, ultimate vaccination decisions, and their variation based on country contexts and demographic factors. **RESULTS:** The numbers of respondents by country were: Georgia (n=1000); India (n=1259); Pakistan (n=2609); UK (n=2055); Nigerian households (n=12554); and Nigerian health providers (n=1272). The UK respondents with children under five years of age were more likely to hesitate to vaccinate, compared to other countries. Confidence in immunisation programmes was more closely associated with confidence in the broader health system in the UK (Spearman's $\rho=0.5990$), compared to Nigeria ($\rho=0.5477$), Pakistan ($\rho=0.4491$), and India ($\rho=0.4240$), all of which ranked confidence in immunisation programmes higher than confidence in the broader health system. Georgia had the highest rate of vaccine refusals (6 %) among those who reported initial hesitation. In all other countries surveyed most respondents who reported hesitating to vaccinate went on to receive the vaccine except in Kano state, Nigeria, where the percentage of those who ultimately refused vaccination after initially hesitating was as high as 76%) Reported reasons for hesitancy in all countries were classified under the domains of "confidence," "convenience," or "complacency," and confidence issues were found to be the primary driver of hesitancy in all countries surveyed.

Larson, H. J., et al. **Measuring vaccine confidence: analysis of data obtained by a media surveillance system used to analyse public concerns about vaccines.** Lancet Infect Dis. 2013; 13(7): 606-613.

BACKGROUND: The intensity, spread, and effects of public opinion about vaccines are growing as new modes of communication speed up information sharing, contributing to vaccine hesitancy, refusals, and disease outbreaks. We aimed to develop a new application of existing surveillance systems to detect and characterise early signs of vaccine issues. We also aimed to develop a typology of concerns and a way to assess the priority of each concern. **METHODS:** Following preliminary research by The Vaccine Confidence Project, media reports (eg, online articles, blogs, government reports) were obtained using

the HealthMap automated data collection system, adapted to monitor online reports about vaccines, vaccination programmes, and vaccine-preventable diseases. Any reports that did not meet the inclusion criteria--any reference to a human vaccine or vaccination campaign or programme that was accessible online--were removed from analysis. Reports were manually analysed for content and categorised by concerns, vaccine, disease, location, and source of report, and overall positive or negative sentiment towards vaccines. They were then given a priority level depending on the seriousness of the reported event and time of event occurrence. We used descriptive statistics to analyse the data collected during a period of 1 year, after refinements to the search terms and processes had been made. FINDINGS: We analysed data from 10,380 reports (from 144 countries) obtained between May 1, 2011, and April 30, 2012. 7171 (69%) contained positive or neutral content and 3209 (31%) contained negative content. Of the negative reports, 1977 (24%) were associated with impacts on vaccine programmes and disease outbreaks; 1726 (21%) with beliefs, awareness, and perceptions; 1371 (16%) with vaccine safety; and 1336 (16%) with vaccine delivery programmes. We were able to disaggregate the data by country and vaccine type, and monitor evolution of events over time and location in specific regions where vaccine concerns were high. INTERPRETATION: Real-time monitoring and analysis of vaccine concerns over time and location could help immunisation programmes to tailor more effective and timely strategies to address specific public concerns. FUNDING: Bill & Melinda Gates Foundation.

Larson, H. J., et al. **Tracking the global spread of vaccine sentiments: the global response to Japan's suspension of its HPV vaccine recommendation.** *Hum Vaccin Immunother.* 2014; 10(9): 2543-2550.

In June 2013 the Japanese Ministry of Health, Labor, and Welfare (MHLW) suspended its HPV vaccination recommendation after a series of highly publicized alleged adverse events following immunization stoked public doubts about the vaccine's safety. This paper examines the global spread of the news of Japan's HPV vaccine suspension through online media, and takes a retrospective look at non-Japanese media sources that were used to support those claiming HPV vaccine injury in Japan. METHODS: Two searches were conducted. One searched relevant content in an archive of Google Alerts on vaccines and vaccine preventable diseases. The second search was conducted using Google Search on January 6th 2014 and on July 18th 2014, using the keywords, "HPV vaccine Japan" and "cervical cancer vaccine Japan." Both searches were used as Google Searches render more (and some different) results than Google Alerts. RESULTS: Online media collected and analyzed totalled 57. Sixty 3 percent were published in the USA, 23% in Japan, 5% in the UK, 2% in France, 2% in Switzerland, 2% in the Philippines, 2% in Kenya and 2% in Denmark. The majority took a negative view of the HPV vaccine, the primary concern being vaccine safety. DISCUSSION: The news of Japan's suspension of the HPV vaccine recommendation has traveled globally through online media and social media networks, being applauded by anti-vaccination groups but not by the global scientific community. The longer the uncertainty around the Japanese HPV vaccine recommendation persists, the further the public concerns are likely to travel.

Lavail, K. H. and Kennedy, A. M. **The role of attitudes about vaccine safety, efficacy, and value in explaining parents' reported vaccination behavior.** *Health Educ Behav.* 2013; 40(5): 544-551.

OBJECTIVES: To explain vaccine confidence as it related to parents' decisions to vaccinate their children with recommended vaccines, and to develop a confidence measure to efficiently and effectively predict parents' self-reported vaccine behaviors. METHOD: A sample of parents with at least one child younger than 6 years ($n = 376$) was analyzed using data from the HealthStyles 2010 survey. Questions were grouped into block variables to create three confidence constructs: value, safety, and efficacy. Regression equations controlling for demographic characteristics were used to identify the confidence construct(s) that best predicted parents' self-reported vaccination decisions (accept all, some, or none of the recommended childhood vaccines). RESULTS: Among the three constructs evaluated, confidence in the value of vaccines, that is the belief that vaccines are important and vaccinating one's children is the

right thing to do, was the best predictor of parents' vaccine decisions, $F(2, 351) = 119.199$, $p < .001$. When combined into a block variable for analysis, two survey items measuring confidence in the value of vaccines accounted for 40% of the variance in parents' self-reported vaccine decisions. Confidence in the safety or efficacy of vaccines failed to account for additional significant variance in parent-reported vaccination behavior. **CONCLUSIONS:** Confidence in the value of vaccines is a helpful predictor of parent-reported vaccination behavior. Attitudinal constructs of confidence in the safety and efficacy of vaccines failed to account for additional significant variance in parents' vaccination behaviors. Future research should assess the role of vaccine knowledge and tangible barriers, such as access and cost, to further explain parents' vaccination behaviors.

Leask, J. **Should we do battle with antivaccination activists?** *Public Health Res Pract.* 2015; 25(2): e2521515.

Antivaccination activists have existed since variolation was introduced in Europe in the 18th century. Today, they continue to attempt to influence the vaccination decisions of parents. Commentators have expressed concern about the impact of such activists on vaccination rates and disease outbreaks. Some argue that public health advocates should engage in adversarial approaches involving public attempts to discredit or stop an antivaccination group or individual. This article argues that such adversarial advocacy may not be the most effective way to support vaccine programs. It argues this on the basis of what is known to influence vaccination attitudes and uptake, and the unintended negative consequences that can arise from an adversarial approach. These include drawing attention to such activists and their arguments, and potentially alienating the most important audience - hesitant parents - where the primary goal is to establish trust. The exception is when the antivaccination activists' actions may cause direct harm, such as encouraging a 'disease party' or illegal activities. Generally, however, advocacy should focus on areas where real gains can be made - on policies that directly address determinants of low coverage such as lack of opportunity to vaccinate and lack of acceptance of vaccination. This includes advocacy for accessible and affordable vaccines. In addressing the global problem of vaccine hesitancy, public health has a responsibility to better monitor public attitudes, support health professionals in communication, and develop and test strategies that engage vaccine-hesitant parents and communities.

Leask, J., et al. **The big picture in addressing vaccine hesitancy.** *Hum Vaccin Immunother.* 2014; 10(9): 2600-2602.

Public acceptance of vaccination has never been a given. Today there is a set of societal circumstances that may contribute to a growing parental hesitancy about vaccination. These include: increasingly 'crowded' vaccination schedules; lower prevalence of vaccine-preventable diseases; greater access to, and more rapid dissemination of, vaccine-critical messages via digital networks; hyper-vigilance of parents in relation to children and risk; and an increasingly consumerist orientation to healthcare.

MacDonald, N. E. **Vaccine hesitancy: Definition, scope and determinants.** *Vaccine* 2015; 33(34): 4161-4164.

The SAGE Working Group on Vaccine Hesitancy concluded that vaccine hesitancy refers to delay in acceptance or refusal of vaccination despite availability of vaccination services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence. The Working Group retained the term 'vaccine' rather than 'vaccination' hesitancy, although the latter more correctly implies the broader range of immunization concerns, as vaccine hesitancy is the more commonly used term. While high levels of hesitancy lead to low vaccine demand, low levels of hesitancy do not necessarily mean high vaccine demand. The Vaccine Hesitancy Determinants Matrix displays the factors influencing the behavioral decision to accept, delay or

reject some or all vaccines under three categories: contextual, individual and group, and vaccine/vaccination-specific influences.

MacDonald, N. E. and Dube, E. **Unpacking Vaccine Hesitancy Among Healthcare Providers**. EBioMedicine. 2015; 2(8): 790-791.

Marshall, G. S. **Roots of vaccine hesitancy**. S D Med Spec 2013; no: 52-57.

McKee, C. and Bohannon, K. **Exploring the Reasons Behind Parental Refusal of Vaccines**. J Pediatr Pharmacol Ther. 2016; 21(2): 104-109.

Parental refusal of vaccines is a growing concern for the increased occurrence of vaccine preventable diseases in children. A number of studies have looked into the reasons that parents refuse, delay, or are hesitant to vaccinate their child(ren). These reasons vary widely between parents, but they can be encompassed in 4 overarching categories. The 4 categories are religious reasons, personal beliefs or philosophical reasons, safety concerns, and a desire for more information from healthcare providers. Parental concerns about vaccines in each category lead to a wide spectrum of decisions varying from parents completely refusing all vaccinations to only delaying vaccinations so that they are more spread out. A large subset of parents admits to having concerns and questions about childhood vaccinations. For this reason, it can be helpful for pharmacists and other healthcare providers to understand the cited reasons for hesitancy so they are better prepared to educate their patients' families. Education is a key player in equipping parents with the necessary information so that they can make responsible immunization decisions for their children.

McRee, A. L., et al. **HPV vaccine hesitancy: findings from a statewide survey of health care providers**. J Pediatr Health Care. 2014; 28(6): 541-549.

INTRODUCTION: Health care provider recommendations are critical for human papillomavirus (HPV) vaccine uptake. We sought to describe providers' HPV vaccine recommendation practices and explore their perceptions of parental hesitancy. **METHOD:** A statewide sample (n = 575) of Minnesota health care providers (20% pediatricians, 47% family medicine physicians, and 33% nurse practitioners) completed our online survey in April 2013. **RESULTS:** Only 76% of health care providers reported routinely recommending HPV vaccine for girls ages 11 to 12 years, and far fewer (46%) did so for boys (p < .001). A majority of providers reported asking questions about parents' concerns (74%), but many lacked time to probe reasons (47%) or believed that they could not change parents' minds (55%). Higher levels of self-efficacy and outcome expectations were associated with routine recommendations (p < .05). **DISCUSSION:** Findings suggest that providers' perceptions of hesitancy may discourage them from routinely recommending the HPV vaccine. Improving providers' self-efficacy to address hesitancy may be important for improving vaccination rates.

Mesch, G. S. and Schwirian, K. P. **Social and political determinants of vaccine hesitancy: Lessons learned from the H1N1 pandemic of 2009-2010**. Am J Infect Control. 2015; 43(11): 1161-1165.

BACKGROUND: Public acceptance of vaccination programs is essential for vaccine preventable diseases. However, increasing sectors of the population have expressed hesitancy about participating in such programs, leading to the re-emergence of vaccine preventable diseases. In this study we rely on a re-creancy hypothesis to test the association between confidence in the government and local hospitals and the willingness to take the vaccine. **METHODS:** A secondary analysis of a survey that used a large sample of the U.S. population conducted in October 2009 was used (N = 968). **RESULTS:** The results indicate that 36.1% of the respondents expressed willingness to be vaccinated. Those with the greatest trust in the government were the most likely to be vaccinated (43.4%), and those least confident were the

least willing (15.8%). From the ones reporting being confident in the local health system, 38.4% were willing to be vaccinated, and from those not confident, only 23.5% were willing to be vaccinated. **CONCLUSION:** The decision to get vaccinated in the midst of a contagious outbreak involves many considerations. Trust in the government's technical and organization skill to deal with the infectious outbreak along with trust in medical organizations predict the adoption of recommended protection measures. The results indicate that public compliance with vaccination plans in health crisis requires the development of social and institutional trust.

Nawa, N., et al. **Listening to public concerns on vaccinations in order to provide information in a timely manner.** Vaccine. 2016.

Nicol, A. F., et al. **HPV vaccines: a controversial issue?** Braz J Med Biol Res. 2016; 49(5): e5060.

Controversy still exists over whether the benefits of the available HPV vaccines outweigh the risks and this has suppressed uptake of the HPV vaccines in comparison to other vaccines. Concerns about HPV vaccine safety have led some physicians, healthcare officials and parents to withhold the recommended vaccination from the target population. The most common reason for not administering the prophylactic HPV vaccines are concerns over adverse effects. The aim of this review is the assessment of peer-reviewed scientific data related to measurable outcomes from the use of HPV vaccines throughout the world with focused attention on the potential adverse effects. We found that the majority of studies continue to suggest a positive risk-benefit from vaccination against HPV, with minimal documented adverse effects, which is consistent with other vaccines. However, much of the published scientific data regarding the safety of HPV vaccines appears to originate from within the financially competitive HPV vaccine market. We advocate a more independent monitoring system for vaccine immunogenicity and adverse effects to address potential conflicts of interest with regular systematic literature reviews by qualified individuals to vigilantly assess and communicate adverse effects associated with HPV vaccination. Finally, our evaluation suggests that an expanded use of HPV vaccine into more diverse populations, particularly those living in low-resource settings, would provide numerous health and social benefits.

Noel, M., et al. **HELPinKids&Adults Knowledge Synthesis of the Management of Vaccination Pain and High Levels of Needle Fear: Limitations of the Evidence and Recommendations for Future Research.** Clin J Pain. 2015; 31(10 Suppl): S124-131.

The HELPinKids&Adults knowledge synthesis for the management of vaccination-related pain and high levels of needle fear updated and expanded upon the 2010 HELPinKIDS knowledge synthesis and clinical practice guideline for pain mitigation during vaccine injections in childhood. Interventions for vaccine pain management in adults and treatment of individuals with high levels of needle fear, phobias, or both were included, thereby broadening the reach of this work. The present paper outlines the overarching limitations of this diverse evidence base and provides recommendations for future research. Consistent with the framing of clinical questions in the systematic reviews, the Participants, Intervention, Comparison, Outcome, Study design (PICOAS) framework was used to organize these predominant issues and research directions. The major limitations we identified across systematic reviews were an overall dearth of trials on vaccination, lack of methodological rigor, failure to incorporate important outcomes, poor study reporting, and various sources of heterogeneity. Future research directions in terms of conducting additional trials in the vaccination context, improving methodological quality and rigor, assessment of global acceptability and feasibility of interventions, and inclusion of outcomes that stakeholders consider to be important (eg, compliance) are recommended. Given concerns about pain and fear are known contributors to vaccine hesitancy, improving and expanding this evidence base will be integral to broader efforts to improve vaccine compliance and public health worldwide.

Nowak, G. J., et al. **Addressing vaccine hesitancy: The potential value of commercial and social marketing principles and practices.** *Vaccine*. 2015; 33(34): 4204-4211.

Many countries and communities are dealing with groups and growing numbers of individuals who are delaying or refusing recommended vaccinations for themselves or their children. This has created a need for immunization programs to find approaches and strategies to address vaccine hesitancy. An important source of useful approaches and strategies is found in the frameworks, practices, and principles used by commercial and social marketers, many of which have been used by immunization programs. This review examines how social and commercial marketing principles and practices can be used to help address vaccine hesitancy. It provides an introduction to key marketing and social marketing concepts, identifies some of the major challenges to applying commercial and social marketing approaches to immunization programs, illustrates how immunization advocates and programs can use marketing and social marketing approaches to address vaccine hesitancy, and identifies some of the lessons that commercial and non-immunization sectors have learned that may have relevance for immunization. While the use of commercial and social marketing practices and principles does not guarantee success, the evidence, lessons learned, and applications to date indicate that they have considerable value in fostering vaccine acceptance.

Odone, A. and Signorelli, C. **When vaccine hesitancy makes headlines.** *Vaccine*. 2015.

Opel, D. J. and Marcuse, E. K. **Rethinking vaccine policy making in an era of vaccine hesitancy: time to rebuild, not remodel?** *Hum Vaccin Immunother*. 2013; 9(12): 2672-2673.

Recently in this journal, David Ropeik argued for imposing additional burdens upon individuals who refused vaccines for themselves or for their children. Specifically, Ropeik advocated for policies that would decrease the ease of claiming vaccine exemptions and restricting unvaccinated children participation in social activities. We argue that, in order to derive the optimal societal benefit from modern vaccinology in an era of vaccine hesitancy, we need to consider doing more than conventional remodeling of current policies. We may need to fundamentally redesign and rebuild.

Ozawa, S. and Stack, M. L. **Public trust and vaccine acceptance--international perspectives.** *Hum Vaccin Immunother* 2013; 9(8): 1774-1778.

Vaccines save millions of lives every year. They are one of the safest and most effective public health interventions in keeping populations healthy while bringing numerous social and economic benefits. Vaccines play an important role in ensuring that children, regardless of where they live, can have a healthy start to life. New financing mechanisms that allow poorer countries to gain access to vaccines faster than ever mean additional deaths and disabilities are projected to be saved during the Decade of Vaccines (2011-2020). Trust in vaccines and in the health system is an important element of public health programs that aim to deliver life-saving vaccines. Indeed, understanding the contributors and threats to trust is essential to explaining vaccine acceptance, particularly as they vary across epidemiologic conditions, specific vaccines and cultural and sociopolitical settings. Greater efforts to communicate the benefits and risks of vaccines and address issues with evidence-based information will help improve and sustain public trust in vaccines and health systems worldwide. Measuring and monitoring trust levels and focusing on deliberate efforts to build trust in vaccines are important steps to reducing vaccine confidence gaps when they occur.

Peretti-Watel, P., et al. **Vaccine hesitancy: clarifying a theoretical framework for an ambiguous notion.** *PLoS Curr* 2015; 7.

Today, according to many public health experts, public confidence in vaccines is waning. The term "vaccine hesitancy" (VH) is increasingly used to describe the spread of such vaccine reluctance. But VH is

an ambiguous notion and its theoretical background appears uncertain. To clarify this concept, we first review the current definitions of VH in the public health literature and examine its most prominent characteristics. VH has been defined as a set of beliefs, attitudes, or behaviours, or some combination of them, shared by a large and heterogeneous portion of the population and including people who exhibit reluctant conformism (they may either decline a vaccine, delay it or accept it despite their doubts) and vaccine-specific behaviours. Secondly, we underline some of the ambiguities of this notion and argue that it is more a catchall category than a real concept. We also call into question the usefulness of understanding VH as an intermediate position along a continuum ranging from anti-vaccine to pro-vaccine attitudes, and we discuss its qualification as a belief, attitude or behaviour. Thirdly, we propose a theoretical framework, based on previous literature and taking into account some major structural features of contemporary societies, that considers VH as a kind of decision-making process that depends on people's level of commitment to healthism/risk culture and on their level of confidence in the health authorities and mainstream medicine.

Poland, C. M. and Brunson, E. K. **The need for a multi-disciplinary perspective on vaccine hesitancy and acceptance.** *Vaccine*. 2015; 33(2): 277-279.

Prashanth, G. P. **Measurement of vaccine confidence using media surveillance system.** *Lancet Infect Dis*. 2014; 14(3): 187-188.

Rambout, L., et al. **Self-reported barriers and facilitators to preventive human papillomavirus vaccination among adolescent girls and young women: a systematic review.** *Prev Med*. 2014; 58: 22-32.

OBJECTIVE: Widespread uptake of preventive human papillomavirus vaccination among target groups is an important public health goal. To evaluate barriers and facilitators to human papillomavirus vaccination, we conducted a systematic review of self-reported views of adolescent girls and young women. **METHODS:** Twenty-two studies including 8079 females aged 9-26 years in North America, published between 2008 and 2011 (representing studies conducted post-vaccine availability), were included. Two reviewers performed all levels of screening and data abstraction in duplicate. We collated findings pertaining to vaccination barriers and facilitators, study characteristics, and study quality. **RESULTS:** Participants were mainly unvaccinated (70%) and sexually active. Twenty-one barriers to vaccination were identified. Cost was the most frequently reported barrier, followed by feelings that vaccination was unnecessary, and concerns regarding vaccine safety and side effects. Facilitators included perceived benefit of vaccination, health care provider recommendations, and social norms. Few studies specifically sought to isolate the views of adolescents, though not being sexually active was the most commonly reported barrier among this group. **CONCLUSION:** Understanding factors which arbitrate in vaccination decisions among key target groups can improve the success of health promotion interventions. Additional studies of superior methodological quality are needed to produce reliable data to inform health promotion strategies.

Raude, J., et al. **Opening the 'Vaccine Hesitancy' black box: how trust in institutions affects French GPs' vaccination practices.** *Expert Rev Vaccines*. 2016; 1-12.

BACKGROUND: In recent years, vaccine hesitancy among health professionals has emerged as an important issue on public health agendas. However, we do not yet know very much about whether, and if so how, trust in institutions affects their practices. **METHODS:** A path analysis model explaining the influence of trust on GPs' vaccine hesitancy was applied to a cross-sectional survey of 1,582 French GPs performed in 2014. We hypothesized that distrust in public health institutions influences GPs' concerns about the safety of various vaccines, their perceptions about the importance of vaccination, their self-efficacy in the doctor-patient relationship, and ultimately their vaccination recommendations to patients.

RESULTS: GPs' trust in institutions was found to be significantly associated with lower vaccine hesitancy, an association mediated to a large extent by the vaccine's perceived safety ($\beta = 0.09$, $P < 0.01$) and the importance of vaccination ($\beta = 0.46$, $P < 0.001$). **CONCLUSION:** These results suggest that restoration of high vaccination coverage may require the re-establishment of a significant degree of trust in the public health system among health professionals.

Rawson, S. J., et al. **Addressing vaccine hesitancy in the pharmacy.** *J Am Pharm Assoc* (2003). 2016; 56(2): 209-210.

Roberts, J. R., et al. **Vaccine hesitancy among parents of adolescents and its association with vaccine uptake.** *Vaccine*. 2015; 33(14): 1748-1755.

BACKGROUND: Addressing parental vaccine hesitancy may increase adolescent vaccination acceptance. However, no validated measure exists to identify parents hesitant toward adolescent vaccines. **OBJECTIVE:** To determine if a modified version of the Parent Attitudes about Childhood Vaccines (PACV) survey, a previously validated tool to identify parental hesitancy toward vaccines in infants, predicts adolescent vaccine uptake at office visits. **METHODS:** We modified the PACV for use in the adolescent setting and distributed it to a convenience sample of parents of adolescents aged 11 to 17 presenting for care at a diverse group of six pediatric practices in Oklahoma and South Carolina. We determined the vaccination status of the parents' adolescents for 3 vaccines (Tetanus-diphtheria-acellular pertussis [Tdap], meningococcal conjugate [MCV4], and human papillomavirus [HPV] vaccines). We used Fisher's exact tests to compare vaccination status with each survey item and with an overall general hesitancy scale that we constructed. **RESULTS:** We analyzed 363 surveys. At the time of the visit, vaccination coverage was 84% for Tdap, 73% for MCV, and 45% for any dose of HPV. Thirty-nine percent of parents expressed concern about vaccine efficacy and 41% expressed concern about side effects. Forty-five percent of parents disagreed with the statement that "teens can get all of the vaccines that are due at a single visit." Two individual items were associated with not receiving a dose of HPV vaccine that was due. The overall modified PACV score failed to predict adolescent vaccine uptake at an office visit. **CONCLUSION:** Several individual items were associated with vaccine uptake. The cumulative modified PACV, a general measure of vaccine hesitancy, was not associated with vaccination status despite illuminating parental hesitancy. We need to better understand vaccine-specific concerns for the adolescent population.

Ropeik, D. **How society should respond to the risk of vaccine rejection.** *Hum Vaccin Immunother*. 2013; 9(8): 1815-1818.

While vaccine acceptance remains high in general, fear of vaccines has grown dramatically in the past several years in many developed countries. In some communities, this fear has led to significantly increased rates of vaccine refusal which are associated with increases in illness and death from vaccine-preventable diseases, and large economic costs for health care and society. Despite overwhelming evidence supporting the safety and benefits of vaccination, this fear has proven resistant to information campaigns, a phenomenon well-explained by psychological research which has established that risk perception is subjective, a product of both the facts and how those facts feel. Given the innately emotional and instinctive nature of risk perception, and the risks to public health these perceptions produce, and consistent with well-established legal principles supporting government action to protect the common good, society has the right and responsibility to establish laws, regulations, and choice frameworks that discourage vaccine refusal.

Sadaf, A., et al. **A systematic review of interventions for reducing parental vaccine refusal and vaccine hesitancy.** *Vaccine*. 2013; 31(40): 4293-4304.

Unvaccinated individuals pose a public health threat to communities. Research has identified many factors associated with parental vaccine refusal and hesitancy toward childhood and adolescent immunizations. However, data on the effectiveness of interventions to address parental refusal are limited. We conducted a systematic review of four online databases to identify interventional studies. We used criteria recommended by the WHO's Strategic Advisory Group of Experts on immunization (SAGE) for the quality assessment of studies. Intervention categories and outcomes were evaluated for each body of evidence and confidence in overall estimates of effect was determined. There is limited evidence to guide implementation of effective strategies to deal with the emerging threat of parental vaccine refusal. There is a need for appropriately designed, executed and evaluated intervention studies to address this gap in knowledge.

Salmon, D. A., et al. **Vaccine hesitancy: Causes, consequences, and a call to action.** *Vaccine.* 2015; 33 Suppl 4: D66-71.

Vaccine hesitancy reflects concerns about the decision to vaccinate oneself or one's children. There is a broad range of factors contributing to vaccine hesitancy, including the compulsory nature of vaccines, their coincidental temporal relationships to adverse health outcomes, unfamiliarity with vaccine-preventable diseases, and lack of trust in corporations and public health agencies. Although vaccination is a norm in the U.S. and the majority of parents vaccinate their children, many do so amid concerns. The proportion of parents claiming non-medical exemptions to school immunization requirements has been increasing over the past decade. Vaccine refusal has been associated with outbreaks of invasive *Haemophilus influenzae* type b disease, varicella, pneumococcal disease, measles, and pertussis, resulting in the unnecessary suffering of young children and waste of limited public health resources. Vaccine hesitancy is an extremely important issue that needs to be addressed because effective control of vaccine-preventable diseases generally requires indefinite maintenance of extremely high rates of timely vaccination. The multifactorial and complex causes of vaccine hesitancy require a broad range of approaches on the individual, provider, health system, and national levels. These include standardized measurement tools to quantify and locate clustering of vaccine hesitancy and better understand issues of trust; rapid, independent, and transparent review of an enhanced and appropriately funded vaccine safety system; adequate reimbursement for vaccine risk communication in doctors' offices; and individually tailored messages for parents who have vaccine concerns, especially first-time pregnant women. The potential of vaccines to prevent illness and save lives has never been greater. Yet, that potential is directly dependent on parental acceptance of vaccines, which requires confidence in vaccines, healthcare providers who recommend and administer vaccines, and the systems to make sure vaccines are safe.

Scherer, L. D., et al. **Can the vaccine adverse event reporting system be used to increase vaccine acceptance and trust?** *Vaccine* 2016; 34(21): 2424-2429.

Vaccine refusal has an impact on public health, and the human papillomavirus (HPV) vaccine is particularly underutilized. Research suggests that it may be difficult to change vaccine-related attitudes, and there is currently no good evidence to recommend any particular intervention strategy. One reason for vaccine hesitancy is lack of trust that vaccine harms are adequately documented and reported, yet few communication strategies have explicitly attempted to improve this trust. This study tested the possibility that data from the vaccine adverse event reporting system (VAERS) can be used to increase trust that vaccine harms are adequately researched and that potential harms are disclosed to the public, and thereby improve perceptions of vaccines. In the study, participants were randomly assigned to one of three communication interventions. All participants read the Centers for Disease Control (CDC) vaccine information statement (VIS) for the HPV vaccine. Two other groups were exposed to additional information about VAERS, either summary data or full detailed reports of serious adverse events from 2013. Results showed that the CDC's VIS alone significantly increased perceptions of vaccine benefits and

decreased perceived risks. Participants who were also educated about VAERS and given summary data about the serious adverse events displayed more trust in the CDC and greater HPV vaccine acceptance relative to the VIS alone. However, exposure to the detailed VAERS reports significantly reduced trust in the CDC and vaccine acceptance. Hence, general information about the VAERS data slightly increased trust in the CDC and improved vaccine acceptance, but the specific VAERS reports negatively influenced both trust and acceptance. Implications for communicating about vaccines are discussed.

Schuster, M., et al. **Review of vaccine hesitancy: Rationale, remit and methods.** *Vaccine*. 2015; 33(34): 4157-4160.

Despite a wide array of safe and effective vaccines in use globally, with major impacts on health worldwide, the WHO Strategic Advisory Group of Experts (SAGE) on Immunization has been repeatedly confronted with reports of hesitancy towards accepting specific vaccines or vaccination programmes. This paper summarizes the rationale for a SAGE review of the issue of vaccine hesitancy, its impact and ways to address it, and the convening of a Vaccine Hesitancy Working Group in March 2012 to prepare for the SAGE review. It describes the methods used and mode of operations, and advances in the relatively new field of research on vaccine hesitancy. It further elaborates and references the work conducted, including a series of products, conclusions and recommendations that emerged from the SAGE review in October 2014.

Shelby, A. and Ernst, K. **Story and science: how providers and parents can utilize storytelling to combat anti-vaccine misinformation.** *Hum Vaccin Immunother*. 2013; 9(8): 1795-1801.

With little or no evidence-based information to back up claims of vaccine danger, anti-vaccine activists have relied on the power of storytelling to infect an entire generation of parents with fear of and doubt about vaccines. These parent accounts of perceived vaccine injury, coupled with Andrew Wakefield's fraudulent research study linking the MMR vaccine to autism, created a substantial amount of vaccine hesitancy in new parents, which manifests in both vaccine refusal and the adoption of delayed vaccine schedules. The tools used by the medical and public health communities to counteract the anti-vaccine movement include statistics, research, and other evidence-based information, often delivered verbally or in the form of the CDC's Vaccine Information Statements. This approach may not be effective enough on its own to convince vaccine-hesitant parents that vaccines are safe, effective, and crucial to their children's health. Utilizing some of the storytelling strategies used by the anti-vaccine movement, in addition to evidence-based vaccine information, could potentially offer providers, public health officials, and pro-vaccine parents an opportunity to mount a much stronger defense against anti-vaccine messaging.

Shelton, R. C., et al. **HPV vaccine decision-making and acceptance: does religion play a role?** *J Relig Health* 2013; 52(4): 1120-1130.

We conducted a web-based survey among 476 white, Black, and Hispanic parents or caregivers with daughter(s) between the ages of 9-17 to better understand how religion influences HPV vaccine acceptance. Catholic parents were more likely than nonaffiliated parents to have already vaccinated their daughters (vs. being undecided) (OR = 3.26, 95% CI = 1.06, 10.06). Parents with frequent attendance at religious services were more likely than parents who do not attend services to have decided against vaccination (vs. being undecided) (OR = 2.92, 95% CI = 1.25, 6.84). Directions for research and implications for interventions are addressed.

Shoup, J. A., et al. **Development of an interactive social media tool for parents with concerns about vaccines.** *Health Educ Behav* 2015; 42(3): 302-312.

OBJECTIVE: Describe a process for designing, building, and evaluating a theory-driven social media intervention tool to help reduce parental concerns about vaccination. **METHOD:** We developed an interactive web-based tool using quantitative and qualitative methods (e.g., survey, focus groups, individual interviews, and usability testing). **RESULTS:** Survey results suggested that social media may represent an effective intervention tool to help parents make informed decisions about vaccination for their children. Focus groups and interviews revealed four main themes for development of the tool: Parents wanted information describing both benefits and risks of vaccination, transparency of sources of information, moderation of the tool by an expert, and ethnic and racial diversity in the visual display of people. Usability testing showed that parents were satisfied with the usability of the tool but had difficulty with performing some of the informational searches. Based on focus groups, interviews, and usability evaluations, we made additional revisions to the tool's content, design, functionality, and overall look and feel. **CONCLUSION:** Engaging parents at all stages of development is critical when designing a tool to address concerns about childhood vaccines. Although this can be both resource- and time-intensive, the redesigned tool is more likely to be accepted and used by parents. Next steps involve a formal evaluation through a randomized trial.

Shrivastava, S. R., et al. **The Growing Global Problem of Vaccine Hesitancy: Time to Take Action.** *Int J Prev Med.* 2016; 7: 18.

Siddiqui, M., et al. **Epidemiology of vaccine hesitancy in the United States.** *Hum Vaccin Immunother.* 2013; 9(12): 2643-2648.

Vaccines are among the most effective public health interventions against infectious diseases. However, there is evidence in the United States for parents either delaying or refusing recommended childhood vaccination. Exemptions to school immunization laws and use of alternative schedule from those recommended by the Advisory Committee on Immunization Practices and the American Academy of Pediatrics cannot only increase the risk of children contracting vaccine-preventable diseases but also increases the risk of infecting others who are either too young to be vaccinated, cannot be vaccinated for medical reasons or did not develop a sufficient immunological response to the vaccine. Healthcare providers are cited as the most influential source by parents on vaccine decision-making. Vaccine hesitancy needs to be addressed by healthcare providers and the scientific community by listening to the parental concerns and discussing risks associated with either delaying or refusing vaccines.

Signorelli, C. and Odone, A. **Advocacy communication, vaccines and the role of scientific societies.** *Ann Ig.* 2015; 27(5): 737-747.

In 1986 the Ottawa Charter underlined the importance of advocacy in health. This article analyzes the role of advocacy in Public Health making the case of immunization, whose coverage rates are decreasing in many countries. An effective advocacy action could counteract the growing phenomenon of the vaccine hesitancy within both the general population and an increasing share of healthcare providers as well as contrast antivax movements' action. We identify who are the advocates focusing on Italy and on the crucial role of scientific societies which share the responsibility of making the latest scientific evidence and most effective infectious diseases' control strategies available to health policy makers. The Italian Society of Hygiene (SItI) has been actively engaged for several years in a number of initiatives of advocacy communication and vaccines including research, training, media exposure and a dedicated website portal (vaccinarSi).

Small, S. L., et al. **Modifiable influences on female HPV vaccine uptake at the clinic encounter level: a literature review.** *J Am Assoc Nurse Pract.* 2014; 26(9): 519-525.

PURPOSE: A review of the literature to identify modifiable influences on female human papillomavirus (HPV) vaccine uptake relevant to clinical practice in order to support nurse practitioners (NPs) in the prevention of cervical cancer. **DATA SOURCES:** PubMed, CINAHL, reference lists of publications that surfaced in the electronic search. **CONCLUSIONS:** Six influences are modifiable and potentially amenable to being addressed at the clinic encounter level: (a) cost and insurance coverage, (b) provider recommendation, (c) vaccination opportunity, (d) HPV and HPV vaccine knowledge, (e) vaccine safety concerns, and (f) HPV risk. **IMPLICATIONS FOR PRACTICE:** NPs have an important role in improving HPV vaccine uptake and research suggests several areas they can address to increase vaccination during clinic visits.

Smith, J. C., et al. **Building confidence in vaccines.** *Adv Exp Med Biol.* 2013; 764: 81-98.

Despite significant efforts by governments, organizations and individuals to maintain public trust in vaccines, concerns persist and threaten to undermine the effectiveness of immunization programs. Vaccine advocates have traditionally focused on education based on evidence to address vaccine concerns and hesitancy. However, being informed of the facts about immunization does not always translate into support for immunization. While many are persuaded by scientific evidence, others are more influenced by cognitive shortcuts, beliefs, societal pressure and the media, with the latter group more likely to hesitate over immunization. Understanding evidence from the behaviour sciences opens new doors to better support individual decision-making about immunization. Drawing on heuristics, this overview explores how individuals find, process and utilize vaccine information and the role health care professionals and society can play in vaccine decision-making. Traditional, evidence-based approaches aimed at staunching the erosion of public confidence in vaccines are proving inadequate and expensive. Enhancing public confidence in vaccines will be complex, necessitating a much wider range of strategies than currently used. Success will require a shift in how the public, health care professionals and media are informed and educated about vaccine benefits, risks and safety; considerable introspection and change in current academic and vaccine decision-making practices; development of proactive strategies to broadly address current and potential future concerns, as well as targeted interventions such as programs to address pain with immunization. This overview outlines ten such opportunities for change to improve vaccine confidence.

Smith, M. J. **Promoting Vaccine Confidence.** *Infect Dis Clin North Am.* 2015; 29(4): 759-769.

Vaccine hesitancy incorporates a wide range of parental attitudes and behaviors surrounding vaccines. Ironically, the very success of the immunization program has fueled vaccine concerns; because vaccine-preventable diseases are no longer prevalent, attention has shifted to the safety and necessity of vaccines themselves. This article reviews some of the underlying themes of vaccine hesitancy as well as specific vaccine safety concerns. Strategies for discussing vaccines with concerned parents are also discussed.

Stahl, J. P., et al. **The impact of the web and social networks on vaccination. New challenges and opportunities offered to fight against vaccine hesitancy.** *Med Mal Infect* 2016; 46(3): 117-122.

OBJECTIVE: Vaccine hesitancy is a growing and threatening trend, increasing the risk of disease outbreaks and potentially defeating health authorities' strategies. We aimed to describe the significant role of social networks and the Internet on vaccine hesitancy, and more generally on vaccine attitudes and behaviors. **METHODS:** Presentation and discussion of lessons learnt from: (i) the monitoring and analysis of web and social network contents on vaccination; (ii) the tracking of Google search terms used by web users; (iii) the analysis of Google search suggestions related to vaccination; (iv) results from the Vaccinoscopie((c)) study, online annual surveys of representative samples of 6500 to 10,000 French mothers, monitoring vaccine behaviors and attitude of French parents as well as vaccination coverage of

their children, since 2008; and (v) various studies published in the scientific literature. RESULTS: Social networks and the web play a major role in disseminating information about vaccination. They have modified the vaccination decision-making process and, more generally, the doctor/patient relationship. The Internet may fuel controversial issues related to vaccination and durably impact public opinion, but it may also provide new tools to fight against vaccine hesitancy. CONCLUSION: Vaccine hesitancy should be fought on the Internet battlefield, and for this purpose, communication strategies should take into account new threats and opportunities offered by the web and social networks.

Suk, J. E., et al. **Hesitancy, trust and individualism in vaccination decision-making**. PLoS Curr 2015; 7.

Thomson, A. and Watson, M. **Vaccine hesitancy: A vade mecum v1.0**. Vaccine 2016; 34(17): 1989-1992.

Vasilevska, M., et al. **Factors associated with healthcare worker acceptance of vaccination: a systematic review and meta-analysis**. Infect Control Hosp Epidemiol. 2014; 35(6): 699-708.

BACKGROUND AND OBJECTIVE: Healthcare workers experience occupational risk of infection and may transmit infections to patients. Vaccination provides an efficient means of protecting workers and patients, but uptake may be low. We sought to identify factors influencing vaccine acceptance by healthcare workers in order to obtain insights leading to more effective vaccination programs in this population. DESIGN: Systematic review and meta-analysis. METHODS: We searched Medline, Embase, and CINAHL databases to identify studies published up to May 2012. Factors influencing vaccination acceptance were devised a priori. Random-effects meta-analysis was performed to generate summary estimates of effect. Heterogeneity and publication bias were explored using statistical tools. RESULTS: Thirty-seven studies evaluating a variety of vaccines (against influenza, pertussis, smallpox, anthrax, and hepatitis B) were included. Homogeneous effects on vaccine acceptance were identified with desire for self-protection (odds ratio [OR], 3.42 [95% confidence interval (CI), 2.42-4.82]) and desire to protect family and friends (OR, 3.28 [95% CI, 1.10-9.75]). Concern that vaccine transmits the illness it was meant to prevent decreased acceptance (OR, 0.42 [95% CI, 0.30-0.58]). Differences in physician and nurse acceptance of immunization were seen between Asian and non-Asian studies. CONCLUSIONS: Consideration of self-protection (rather than absolute disease risk or protection of patients) appears the strongest and most consistent driver of healthcare workers' decisions to accept vaccination, though other factors may also be impactful, and reasons for between-study divergence in effects is an important area for future research. This finding has important implications for the design of programs to enhance healthcare worker vaccine uptake.

Velan, B. **Vaccine hesitancy as self-determination: an Israeli perspective**. Isr J Health Policy Res. 2016; 5: 13.

Vaccine hesitancy can be portrayed as a broad spectrum of phenomena, ranging from a genuine call for help to complete defiance of authorities. The emphasis here is made on mid-spectrum hesitancy; hesitancy as an act of personal exploration and deliberation whether to get vaccinated or not. This form of vaccine hesitancy can be identified in the attitude of the Israeli public towards routine childhood vaccination programs, seasonal flu vaccination, newly introduced vaccines, such as human papilloma virus vaccine, as well as towards the emergency vaccination programs against poliovirus and H1N1 pandemic influenza. Vaccine hesitancy in Israel appears to be a process where individuals exercise self-determination and self-empowerment and make their own decisions based on assessment, reflection, choosing between various options and dealing with considerable complexities. Addressing this form of vaccine hesitancy could be challenging, but ultimately fruitful. This would require change of attitudes on the part of policymakers. The first steps should involve the realization that deliberative hesitancy is here to stay, and that hesitant individuals should be respected. This could pave the way for designing

appropriate intervention strategies for convincing the hesitant public about the advantages of vaccination.

Voysey, M., et al. **Update on barriers to human papillomavirus vaccination and effective strategies to promote vaccine acceptance.** *BMJ Open.* 2016; 28(3): 407-412.

PURPOSE OF REVIEW: This article provides a clinically relevant review and analysis of the latest research regarding barriers to human papillomavirus (HPV) vaccination and strategic efforts to promote this vaccine. **RECENT FINDINGS:** HPV vaccines are safe, effective, and could prevent the majority of HPV-attributable cancers, if vaccination coverage is high. However, uptake of HPV vaccine lags behind other vaccines recommended for 11 to 12-year olds. A lack of provider recommendation has consistently been found to be a key barrier to increasing vaccination rates. Lack of knowledge about the vaccine among parents coupled with an overestimation of parental vaccine hesitancy among providers also hinder vaccine uptake. Strongly recommending the vaccine as a safe, routine immunization that prevents cancer, and coadministering it with tetanus, diphtheria, and acellular pertussis vaccine and quadrivalent meningococcal conjugate vaccine, enhance vaccine uptake. In some cases, reminder and recall systems result in additional increases in vaccination rates. **SUMMARY:** Recent publications reveal new information about the implementation of HPV vaccines. Provider recommendation is a key approach, as is offering it routinely at the same time as other universally recommended adolescent immunizations. With the integration of these concepts into the clinical setting, adolescents can be better protected against HPV and its associated diseases.

Wang, E., et al. **"Everybody just wants to do what's best for their child": Understanding how pro-vaccine parents can support a culture of vaccine hesitancy.** *Vaccine* 2015; 33(48): 6703-6709.

BACKGROUND: Although a large majority of parents vaccinate their children, vaccine hesitancy has become more widespread. It is not well understood how this culture of vaccine hesitancy has emerged and how it influences parents' decisions about vaccine schedules. **OBJECTIVE:** We sought to examine how attitudes and beliefs of parents who self-report as pro-vaccine are developed and contribute to immunization decisions, including delaying or spacing vaccines. **METHODS:** Open-ended, in-depth interviews (N=23) were conducted with upper-middle class parents with young children living in Philadelphia. Interview data were coded and key themes identified related to vaccine decision-making. **RESULTS:** Parents who sought out vaccine information were often overwhelmed by the quantity and ambiguity when interpreting that information, and, consequently, had to rely on their own instinct or judgment to make vaccine decisions. In particular, while parents in this sample did not refuse vaccines, and described themselves as pro-vaccine, they did frequently delay or space vaccines. This experience also generated sympathy for and tolerance of vaccine hesitancy in other parents. Parents also perceived minimal severe consequences for deviating from the recommended immunization schedule. **CONCLUSION:** These findings suggest that the rise in and persistence of vaccine hesitancy and refusal are, in part, influenced by the conflicts in the information parents gather, making it difficult to interpret. Considerable deviations from the recommended vaccination schedule may manifest even within a pro-vaccine population due to this perceived ambiguity of available information and resulting tolerance for vaccine hesitancy.

Ward, J. K., et al. **Vaccine-criticism on the internet: new insights based on French-speaking websites.** *Vaccine.* 2015; 33(8): 1063-1070.

The internet is playing an increasingly important part in fueling vaccine related controversies and in generating vaccine hesitant behaviors. English language Antivaccination websites have been thoroughly analyzed, however, little is known of the arguments presented in other languages on the internet. This study presents three types of results: (1) Authors apply a time tested content analysis methodology to

describe the information diffused by French language vaccine critical websites in comparison with English speaking websites. The contents of French language vaccine critical websites are very similar to those of English language websites except for the relative absence of moral and religious arguments. (2) Authors evaluate the likelihood that internet users will find those websites through vaccine-related queries on a variety of French-language versions of google. Queries on controversial vaccines generated many more vaccine critical websites than queries on vaccination in general. (3) Authors propose a typology of vaccine critical websites. Authors distinguish between (a) websites that criticize all vaccines ("antivaccine" websites) and websites that criticize only some vaccines ("vaccine-selective" websites), and between (b) websites that focus on vaccines ("vaccine-focused" websites) and those for which vaccines were only a secondary topic of interest ("generalist" websites). The differences in stances by groups and websites affect the likelihood that they will be believed and by whom. This study therefore helps understand the different information landscapes that may contribute to the variety of forms of vaccine hesitancy. Public authorities should have better awareness and understanding of these stances to bring appropriate answers to the different controversies about vaccination.

Wiemken, T. L., et al. **Understanding why low-risk patients accept vaccines: a socio-behavioral approach.** BMC Res Notes. 2015; 8: 813.

BACKGROUND: Vaccines are one of the most important public health interventions. Understanding factors associated with vaccine acceptance is critical. The objectives of this study were to evaluate the impact of the three constructs of the Theory of Planned Behavior (TPB) on the intention to be vaccinated among healthy individuals being seen for pre-travel care, and to evaluate if behavioral intention was associated with vaccine acceptance. **METHODS:** We surveyed individuals seeking vaccination at the University of Louisville Vaccine and International Health and Travel Clinic. Linear and two stage least squares regression models were used to define the associations between constructs of the TPB and the intention to be vaccinated, as well as the association between the intention to be vaccinated and vaccine acceptance. **RESULTS:** A total of 183 individuals were included in the analysis. None of the constructs of the TPB were associated with intention to be vaccinated. Behavioral intention was not associated with vaccination acceptance. **CONCLUSIONS:** This study suggests that the TPB does not predict the intention to get vaccinated among individuals attending our Vaccine and International Health and Travel Clinic. It will be critical to define better predictors of vaccine uptake in healthy, low-risk individuals to increase vaccine acceptance.

Williams, S. E. **What are the factors that contribute to parental vaccine-hesitancy and what can we do about it?** Hum Vaccin Immunother. 2014; 10(9): 2584-2596.

Parental refusal or delay of childhood vaccines is increasing. Barriers to vaccination among this population have been described, yet less is known regarding motivating factors. Researchers are beginning to evaluate various approaches to address the concerns of "vaccine-hesitant" parents, but few studies have evaluated the effect of interventions on timely vaccine uptake. Several models for communicating with vaccine-hesitant parents have been reported for healthcare providers; however, the effectiveness and utility of these strategies has not been quantified. This article reviews the known barriers to vaccination reported by vaccine-hesitant parents and the current evidence on strategies to address parental vaccine hesitancy.

Wilson, K., et al. **Opportunities for utilizing new technologies to increase vaccine confidence.** Expert Rev Vaccines. 2014; 13(8): 969-977.

The emergence of new digital technologies has 'disrupted' traditional vaccine information communication. This article reviews the impact of the Internet, social media, digital detection and mobile applications on both fueling anti-vaccine sentiment and providing a mechanism by which to address

vaccine hesitancy. While the anti-vaccine community has leveraged the Internet and social media to bypass traditional sources of information and communicate with susceptible parents, digital surveillance and mobile apps offer an important opportunity for public health officials to develop new strategies to identify and address concerns in a real-time manner.

Witteman, H. O. **Addressing Vaccine Hesitancy With Values**. *Pediatrics*. 2015; 136(2): 215-217.

Zimet, G. D., et al. **Beliefs, behaviors and HPV vaccine: correcting the myths and the misinformation**. *Prev Med*. 2013; 57(5): 414-418.

OBJECTIVE: Human papillomavirus (HPV) vaccine uptake in many countries has been sub-optimal. We examine several issues associated with non-vaccination that have received particular attention, including fears about sexual risk compensation, concerns about vaccine safety, inadequate vaccination recommendations by health care providers (HCPs), and distrust due to the perceived "newness" of HPV vaccines. **METHODS:** Selective review of behavioral and social science literature on HPV vaccine attitudes and uptake. **RESULTS:** There is no evidence of post-vaccination sexual risk compensation, HPV vaccines are quite safe, and they can no longer be considered "new". Nonetheless, research findings point to these issues and, most importantly, to the failure of HCPs to adequately recommend HPV vaccine as major drivers of non-vaccination. **CONCLUSION:** Most fears related to HPV vaccine are more related to myth than reality. In the absence of major health policy initiatives, such as those implemented in Canada, the U.K., and Australia, a multi-level, multi-faceted approach will be required to achieve high rates of HPV vaccination. It will be essential to focus on the education of HCPs regarding indications for HPV vaccination and approaches to communicating most effectively with parents and patients about the safety and benefits of vaccination and the risks associated with non-vaccination.

Session 4 HPV vaccination programs: country experiences and lessons learnt.

A Pubmed search was performed with the following selection criteria: HPV [title/abstract] AND vaccination [title/abstract] AND program [title/abstract] published in the last 5 years: 348 items were retrieved. References were imported in EndNote. Herein, a relevant manual selection of publications between 2014-2016 based on title and abstract was made. References are sorted by first authors name. References were sorted by WHO region and first authors name. Articles about vaccination programmes in low- and middle-income countries and those not region specific are presented in a separate category.

African Region

Adejuyigbe, F. F., et al. **Cervical Cancer and Human Papilloma Virus Knowledge and Acceptance of Vaccination among Medical Students in Southwest Nigeria.** *Afr J Reprod Health.* 2015; 19(1): 140-148.

Human papillomavirus (HPV) is the commonest viral sexually transmitted infection in the world and the leading cause of cervical cancer. Medical students as future healthcare providers will play a role in influencing patients' decision to receive HPV vaccination. This study was aimed at determining the knowledge of cervical cancer and HPV as well as the acceptance of HPV vaccination among medical students of the University of Lagos. A descriptive cross-sectional study was carried out among 280 medical students sampled using stratified sampling technique. Self-administered questionnaires were used to collect relevant data. Most respondents were aware of cervical cancer (95.4%), HPV (85.4%) and HPV vaccination (69.3%) and the most common source of information was school teaching. Good knowledge of cervical cancer, HPV and HPV vaccination was demonstrated by 51.8%, 67.1% and 21.1% respectively; only 39.6% fully accepted HPV vaccination. Inadequate information and high costs were the obstacles identified to receiving vaccine and recommending it to others. Older age and higher levels of study were significantly associated with good knowledge of HPV. Good knowledge of HPV and HPV vaccination respectively were significantly associated with full acceptance of vaccination. There is need for more education on cervical cancer, HPV infection and HPV vaccination for the medical students via school teaching and other media, and inclusion of the HPV vaccine in the National Program on Immunization to improve access.

Friedman, A. L., et al. **Preparing for human papillomavirus vaccine introduction in Kenya: implications from focus-group and interview discussions with caregivers and opinion leaders in Western Kenya.** *BMC Public Health.* 2014; 14: 855.

BACKGROUND: Cervical cancer claims the lives of 275,000 women each year; most of these deaths occur in low-or middle-income countries. In Kenya, cervical cancer is the leading cause of cancer-related mortality among women of reproductive age. Kenya's Ministry of Public Health and Sanitation has developed a comprehensive strategy to prevent cervical cancer, which includes plans for vaccinating preteen girls against human papillomavirus (HPV) by 2015. To identify HPV vaccine communication and mobilization needs, this research sought to understand HPV vaccine-related perceptions and concerns of male and female caregivers and community leaders in four rural communities of western Kenya. **METHODS:** We conducted five focus groups with caregivers (n = 56) and 12 key-informant interviews with opinion leaders to explore cervical cancer-related knowledge, attitudes and beliefs, as well as acceptability of HPV vaccination for 9-12 year-old girls. Four researchers independently reviewed the data and developed codes based on questions in interview guides and topics that emerged organically, before comparing and reconciling results through a group consensus process. **RESULTS:** Cervical cancer was not commonly recognized, though it was understood generally in terms of its symptoms. By association with cancer and genital/reproductive organs, cervical cancer was feared and stigmatized. Overall acceptability

of a vaccine that prevents cervical cancer was high, so long as it was endorsed by trusted agencies and communities were sensitized first. Some concerns emerged related to vaccine safety (e.g., impact on fertility), program intent, and health equity. **CONCLUSION:** For successful vaccine introduction in Kenya, there is a need for communication and mobilization efforts to raise cervical cancer awareness; prompt demand for vaccination; address health equity concerns and stigma; and minimize potential resistance. Visible endorsement by government leaders and community influencers can provide reassurance of the vaccine's safety, efficacy and benefits for girls and communities. Involvement of community leadership, parents and champions may also be critical for combatting stigma and making cervical cancer relevant to Kenyan communities. These findings underscore the need for adequate planning and resources for information, education and communication prior to vaccine introduction. Specific recommendations for communication and social-marketing strategies are made.

Morhason-Bello, I. O., et al. **Willingness of reproductive-aged women in a Nigerian community to accept human papillomavirus vaccination for their children.** *J Obstet Gynaecol Res.* 2015; 41(10): 1621-1629.

AIM: The aim of this study was to determine the willingness of reproductive-aged women in a Nigerian community to allow human papillomavirus (HPV) vaccination in their children and the associated factors with this decision. **MATERIAL AND METHODS:** A multistage household survey of 1002 women who participated in the HPV Vaccine and Cervical Cancer Prevention Survey from 26 August to 29 September 2012 at Ibadan North Local Government Area, Mokola Ibadan, Nigeria. Descriptive, bivariate and multivariable analyses were performed, and statistical significance was set at 95% confidence level (CI). **RESULTS:** There was high willingness (88.6%) to vaccinate, and this attitude was associated with previous history of genital discharge or sores (adjusted odds ratio, 1.91; 95%CI, 1.05-3.45), and knowledge that cervical cancer is preventable (adjusted odds ratio, 1.67; 95%CI, 1.07-2.59). On the likely acceptability of Nigerian HPV vaccine policy, about two-thirds strongly agreed to its incorporation into the routine immunization program (66.9%), it being free (66.7%) and mandatory (64.3%), amongst other factors. The commonest concerns raised were cost/expenses (10.2%), that it might encourage promiscuity (9.9%), or stimulate early sexual debut (6.7%), and fear of infertility (6.3%). **CONCLUSION:** This study found that the majority of Nigerian women are willing to vaccinate their children against HPV infection and would prefer free universal HPV vaccination with regulation to ensure better uptake. The concerns expressed would need to be addressed by policy-makers to increase its acceptability.

Mugisha, E., et al. **Feasibility of delivering HPV vaccine to girls aged 10 to 15 years in Uganda.** *Afr Health Sci.* 2015; 15(1): 33-41.

BACKGROUND: Cervical cancer is a leading cause of mortality among women in Uganda. The availability of the human papillomavirus (HPV) vaccine presents an opportunity to prevent cervical cancer. The Government of Uganda conducted a demonstration project exploring the feasibility of two delivery strategies. **OBJECTIVE:** To explore the feasibility of two HPV vaccine delivery strategies: 1) a stand-alone school-based strategy that selected girls based on their enrolment in grade 5 (known as the "grade-based" strategy; and 2) an age-based strategy that delivered the HPV vaccine based on the girls' age (10-year-olds). This strategy combined the delivery of the vaccine with the distribution of deworming medication and vitamin A through an existing Child Days Plus program. **METHODS:** A qualitative study that explored the feasibility of the two delivery strategies from the perspective of health workers, district leaders, and staff of the Uganda National Expanded Programme on Immunization, utilizing in-depth interviews and focus group discussions. **RESULTS:** Coverage data showed that more girls (88%) were vaccinated using the grade-based strategy and completed all three doses compared to those (73%) vaccinated using the age-based strategy. Health workers and teachers indicated that determining vaccination eligibility was easier by grade than by age and there were minor disruptions to health services and school programs during vaccinations, as reported by health workers and teachers using the grade-based strategy. **CONCLUSION:**

HPV vaccine delivery at schools using grade eligibility was more feasible than selecting girls by age. Lessons learned in Uganda could be relevant for countries considering implementing HPV vaccinations.

Muhwezi, W. W., et al. **Parents' knowledge, risk perception and willingness to allow young males to receive human papillomavirus (HPV) vaccines in Uganda.** PLoS One 2014; 9(9): e106686.

The Ministry of Health in Uganda in collaboration with the Program for Appropriate Technology for Health (PATH) supported by Bill and Melinda Gates Foundation in 2008-2009 vaccinated approximately 10,000 girls with the bivalent humanpapilloma virus (HPV) vaccine. We assessed parent's knowledge, risk perception and willingness to allow son(s) to receive HPV vaccines in future through a cross-sectional survey of secondary school boys aged 10-23 years in 4 districts. 377 questionnaires were distributed per district and 870 were used in analysis. Parents that had ever heard about cervical cancer and HPV vaccines; those who would allow daughter(s) to be given the vaccine and those who thought that HPV infection was associated with genital warts were more willing to allow son(s) to receive the HPV vaccine. Unwilling parents considered HPV vaccination of boys unimportant ($p = 0.003$), believed that only females should receive the vaccine ($p = 0.006$), thought their son(s) couldn't contract HPV ($p = 0.010$), didn't know about HPV sexual transmissibility ($p = 0.002$), knew that males could not acquire HPV ($p = 0.000$) and never believed that the HPV vaccines could protect against HPV ($p = 0.000$). Acceptance of HPV vaccination of daughters and likelihood of recommending HPV vaccines to son(s) of friends and relatives predicted parental willingness to allow sons to receive HPV vaccines. Probable HPV vaccination of boys is a viable complement to that of girls. Successfulness of HPV vaccination relies on parental acceptability and sustained sensitization about usefulness of HPV vaccines even for boys is vital.

Torres-Rueda, S., et al. **HPV vaccine introduction in Rwanda: Impacts on the broader health system.** Sex Reprod Health. 2016; 7: 46-51.

OBJECTIVES: Rwanda was the first country in Africa to introduce the human papillomavirus (HPV) vaccine. This was achieved through multi-year school-based campaigns. Our study evaluated the impact of the HPV vaccine introduction on the country's immunisation programme and health system. **METHODS:** Thirty key informants were interviewed at national and district levels, and in participating schools. Twenty-seven health facilities completed a questionnaire exploring the effects of the new vaccine introduction on six health system building blocks, as defined by the World Health Organization. Routine service activity data were collected during a 90-day period around the introduction. **RESULTS:** Routine vaccination activities were not disrupted during the delivery, likely due to a strong Expanded Program on Immunization, appropriate planning and a well-resourced operation. Opportunities were seized to co-deliver other interventions targeted at children and adolescents, such as health promotion. Collaboration with the Ministry of Education was strengthened at national level. Although there were some temporary increases in staff workload, no major negative effects were reported. **CONCLUSION:** Despite its delivery through school-based campaigns, the HPV vaccine integrated well into the immunisation programme and health system. The introduction had no major negative effects. Some opportunities were seized to expand services and collaborations.

Tracy, J. K., et al. **Planning for human papillomavirus (HPV) vaccination in sub-Saharan Africa: a modeling-based approach.** Vaccine. 2014; 32(26): 3316-3322.

BACKGROUND: Human papillomavirus (HPV) vaccines have the potential to reduce cervical cancer incidence and mortality, particularly in the parts of the developing world that bear the greatest burden of disease. This research sought to predict the impact and cost-effectiveness of an HPV vaccination program in an example low-resource country with a high burden of cervical cancer: Mali, West Africa. **METHODS:** Novel compartmental mathematical models projected the impact of adolescent HPV vaccination in urban and rural areas of Mali. The models accounted for two high-risk vaccine-types: HPV 16 and 18. We then

attached comprehensive real cost and cost-effectiveness estimates. **RESULTS:** Our models predict that HPV vaccination in Mali will reduce cervical cancer burden by a factor roughly equal to vaccine coverage. A point vaccination program was simulated in a cohort of 333,146 urban and 588,982 rural Malian women, age 10-14. Vaccination of 50% of girls reduced the peak prevalence of HPV 16/18 to 5.0% in the urban setting and 9.6% in the rural setting, down from 11.7% and 22.0%, respectively, with no vaccination. The 50% vaccination scenario averted 1145 cervical cancer deaths in the urban group and 2742 in the rural group. The cost per discounted life-year saved in this scenario was 1030 US dollars (urban) and 725 dollars (rural). The cost per life-year saved was higher at 90% coverage, but was still in the range of a "cost-effective" public health intervention. **CONCLUSIONS:** This research yielded the most comprehensive real cost estimates of HPV vaccination yet published for sub-Saharan Africa. Our models indicate that HPV vaccination in Mali will be cost-effective when introduced. To maximize the benefit using limited resources, vaccination programs may begin with a target coverage of about 50%. We anticipate that costs of reaching late adopters after the First Vaccinated Wave of vaccination will be higher, but worthwhile.

Vermandere, H., et al. **Implementation of an HPV vaccination program in Eldoret, Kenya: results from a qualitative assessment by key stakeholders.** BMC Public Health. 2015; 15: 875.

BACKGROUND: Cervical cancer strikes hard in low-resource regions yet primary prevention is still rare. Pilot projects have however showed that Human Papillomavirus (HPV) vaccination programs can attain high uptake. Nevertheless, a study accompanying a vaccination demonstration project in Eldoret, Kenya, revealed less encouraging outcomes: uptake during an initial phase targeting ten schools (i.e., 4000 eligible girls), was low and more schools had to be included to reach the proposed number of 3000 vaccinated girls. The previously conducted study also revealed that many mothers had not received promotional information which had to reach them through schools: teachers were sensitized by health staff and asked to invite students and parents for HPV vaccination in the referral hospital. In this qualitative study, we investigate factors that hampered promotion and vaccine uptake. **METHODS:** Focus group discussions (FGD) with teachers (4) and fathers (3) were organized to assess awareness and attitudes towards the vaccination program, cervical cancer and the HPV vaccine, as well as a FGD with the vaccinators (1) to discuss the course of the program and potential improvements. Discussions were recorded, transcribed, translated, and analyzed using thematic analysis. In addition, a meeting with the program coordinator was set up to reflect upon the program and the results of the FGD, and to formulate recommendations for future programs. **RESULTS:** Cervical cancer was poorly understood by fathers and teachers and mainly linked with nonconforming sexual behavior and modern lifestyle. Few had heard about the vaccination opportunity: feeling uncomfortable to discuss cervical cancer and not considering it as important had hampered information flow. Teachers requested more support from health staff to address unexpected questions from parents. Non-uptake was also the result of distrust towards new vaccines. Schools entering the program in the second phase reacted faster: they were better organized, e.g., in terms of transport, while the community was already more familiarized with the vaccine. **CONCLUSIONS:** Close collaboration between teachers and health staff is crucial to obtain high HPV vaccine uptake among schoolgirls. Promotional messages should, besides providing correct information, tackle misbeliefs, address stigma and stress the priority to vaccinate all, regardless of lifestyle. Monitoring activities and continuous communication could allow for detection of rumors and unequal uptake in the community.

Vermandere, H., et al. **Determinants of acceptance and subsequent uptake of the HPV vaccine in a cohort in Eldoret, Kenya.** PLoS One. 2014; 9(10): e109353.

The development of Human Papillomavirus (HPV) vaccines provides new opportunities in the fight against cervical cancer. Many acceptability studies have revealed high interest in these vaccines, but acceptance is only a precursor of behavior, and many factors, at personal, community and provider level,

may inhibit the translation of willingness to vaccinate into actual uptake. Through a longitudinal study in Eldoret, Kenya, HPV vaccine acceptability was measured before a vaccination program (n = 287) and vaccine uptake, as reported by mothers, once the program was finished (n = 256). In between baseline and follow-up, a pilot HPV vaccination program was implemented via the GARDASIL Access Program, in which parents could have their daughter vaccinated for free at the referral hospital. The program was promoted at schools: Health staff informed teachers who were then asked to inform students and parents. Even though baseline acceptance was very high (88.1%), only 31.1% of the women reported at follow-up that their daughter had been vaccinated. The vaccine was declined by 17.7%, while another 51.2% had wanted the vaccination but were obstructed by practical barriers. Being well-informed about the program and baseline awareness of cervical cancer were independently associated with vaccine uptake, while baseline acceptance was correlated in bivariate analysis. Side effects were of great concern, even among those whose daughter was vaccinated. Possible partner disapproval lowered acceptance at baseline, and women indeed reported at follow-up that they had encountered his opposition. In Kenya, women prove to be very willing to have their daughter vaccinated against cervical cancer. However, in this study, uptake was more determined by program awareness than by HPV vaccine acceptance. School-based vaccination might improve coverage since it reduces operational problems for parents. In addition, future HPV vaccination campaigns should address concerns about side effects, targeting men and women, given both their involvement in HPV vaccination decision-making.

Eastern Mediterranean Region

Majidi, A., et al. **Priority Setting for Improvement of Cervical Cancer Prevention in Iran.** *Int J Health Policy Manag.* 2015; 5(4): 225-232.

BACKGROUND: Cervical cancer is the fourth most common cancer among women worldwide. Organized cervical screening and vaccination against human papilloma virus (HPV) have been successful interventions for prevention of invasive cervical cancer (ICC). Because of cultural and religious considerations, ICC has low incidence in Iran and many other Muslim countries. There is no organized cervical screening in these countries. Therefore, ICC is usually diagnosed in advanced stages with poor prognosis in these countries. We performed a priority setting exercise and suggested priorities for prevention of ICC in this setting. **METHODS:** We invited experts and researchers to a workshop and asked them to list important suggestions for ICC prevention in Iran. After merging similar items and removing the duplicates, we asked the experts to rank the list of suggested items. We used a strategy grid and Go-zone analysis to determine final list of priorities for ICC prevention in Iran. **RESULTS:** From 26 final items suggested as priorities for prevention of ICC, the most important priorities were developing national guidelines for cervical screening and quality control protocol for patient follow-up and management of precancerous lesions. In addition, we emphasized considering insurance coverage for cervical screening, public awareness, and research priorities, and establishment of a cervical screening registry. **CONCLUSION:** A comprehensive approach and implementation of organized cervical screening program is necessary for prevention of ICC in Iran and other low incidence Muslim countries. Because of high cost for vaccination and low incidence of cervical cancer, we do not recommend HPV vaccination for the time being in Iran.

Masika, M. M., et al. **Knowledge on HPV Vaccine and Cervical Cancer Facilitates Vaccine Acceptability among School Teachers in Kitui County, Kenya.** *PLoS One* 2015; 10(8): e0135563.

BACKGROUND: Vaccines against human papillomavirus (HPV) infection have the potential to reduce the burden of cervical cancer. School-based delivery of HPV vaccines is cost-effective and successful uptake depends on school teachers' knowledge and acceptability of the vaccine. The aim of this study is to assess primary school teachers' knowledge and acceptability of HPV vaccine and to explore facilitators and barriers of an ongoing Gavi Alliance-supported vaccination program in Kitui County, Kenya. **METHODS:** This was a cross-sectional, mixed methods study in Central Division of Kitui County where the Ministry of Health is offering the quadrivalent HPV vaccine to grade four girls. Data on primary school teachers' awareness, knowledge and acceptability of HPV vaccine as well as facilitators and barriers to the project was collected through self-administered questionnaires and two focus group discussions. **RESULTS:** 339 teachers (60% female) completed the survey (62% response rate) and 13 participated in 2 focus group discussions. Vaccine awareness among teachers was high (90%), the level of knowledge about HPV and cervical cancer among teachers was moderate (48%, SD = 10.9) and females scored higher than males (50% vs. 46%, $p = 0.002$). Most teachers (89%) would recommend the vaccine to their daughter or close relatives. Those who would recommend the vaccine had more knowledge than those who would not ($p = <0.001$). The main barriers were insufficient information about the vaccine, poor accessibility of schools, absenteeism of girls on vaccine days, and fear of side effects. **CONCLUSIONS:** Despite low to moderate levels of knowledge about HPV vaccine among school teachers, vaccine acceptability is high. Teachers with little knowledge on HPV vaccine are less likely to accept the vaccine than those who know more; this may affect uptake if not addressed. Empowering teachers to be vaccine champions in their community may be a feasible way of disseminating information about HPV vaccine and cervical cancer.

Ortashi, O., et al. **Acceptability of human papilloma virus vaccination among women in the United Arab Emirates.** Asian Pac J Cancer Prev. 2014; 15(5): 2007-2011.

BACKGROUND: Human papilloma virus (HPV) is a common sexually transmitted infectious agent. It is estimated that 10% of all women worldwide are infected with HPV, that is some 660 million each year. HPV vaccination has a reported efficacy of more than 98% for protection against infection in females. In 2008 the Abu Dhabi Health Authority in the United Arab Emirates (UAE) introduced free HPV vaccination for all eligible schoolgirls in both public and private schools. **METHODS:** A cross-sectional study of 640 women aged 18-50 years in the Emirate of Abu Dhabi in UAE from April 2012 to October 2012 was conducted. **RESULTS:** Thirty-seven percent of the women in our sample had heard about HPV vaccination, and 80% of these would consider getting vaccinated themselves, and 87% would recommend vaccination to relatives or friends. Most women in the study (69%) had a favorable opinion about the vaccine. Only 17% of the women felt it might not be culturally acceptable, and 1% felt that there might be religious objections to HPV vaccination. Vaccine safety and recommendation by a doctor (36% each) were the factors identified most frequently by our sample of women which would enhance the uptake of the HPV vaccination. **CONCLUSIONS:** Knowledge about HPV vaccination among women in our sample was below average (37%); however, 80% of those who had heard about HPV vaccination were willing to be vaccinated themselves, and 87% would recommend vaccination to relatives and friends.

European Region

Cameron, R. L., et al. **Human Papillomavirus Prevalence and Herd Immunity after Introduction of Vaccination Program, Scotland, 2009-2013.** *Emerg Infect Dis.* 2016; 22(1): 56-64.

In 2008, a national human papillomavirus (HPV) immunization program using a bivalent vaccine against HPV types 16 and 18 was implemented in Scotland along with a national surveillance program designed to determine the longitudinal effects of vaccination on HPV infection at the population level. Each year during 2009-2013, the surveillance program conducted HPV testing on a proportion of liquid-based cytology samples from women undergoing their first cervical screening test for precancerous cervical disease. By linking vaccination, cervical screening, and HPV testing data, over the study period we found a decline in HPV types 16 and 18, significant decreases in HPV types 31, 33, and 45 (suggesting cross-protection), and a nonsignificant increase in HPV 51. In addition, among nonvaccinated women, HPV types 16 and 18 infections were significantly lower in 2013 than in 2009. Our results preliminarily indicate herd immunity and sustained effectiveness of the bivalent vaccine on virologic outcomes at the population level.

Collange, F., et al. **General practitioners' attitudes and behaviors toward HPV vaccination: A French national survey.** *Vaccine* 2016; 34(6): 762-768.

OBJECTIVE: General practitioners (GPs) play a crucial role in human papillomavirus (HPV) vaccine acceptance in France. We sought to study: (1) GPs' perceptions of its risks and efficacy and their recommendation behavior; (2) the relative importance of factors associated with the frequency of their recommendations. **METHODS:** Cross-sectional observational study in 2014 nested in a national panel of 1712 randomly selected GPs in private practice in France (response rate: 92.4%). We used model averaging to analyze the associations of self-reported frequency of GPs' HPV vaccine recommendations with their perception of its risk-benefit balance and their opinions about the utility of vaccines in general. **RESULTS:** Overall, 72% of participants reported frequently recommending HPV vaccination; 60% considered that not enough is known about its risks. The model averaging showed that the factors most associated with infrequent recommendation of this vaccine by GPs were: unfavorable perceptions of its risk-benefit balance (OR=0.13; 95%CI=0.09-0.21; partial R(2)=0.10), a decision not to vaccinate one's own daughter(s) with this vaccine (OR=0.13; 95%CI=0.07-0.24; partial R(2)=0.05), and doubts about vaccine utility in general (OR=0.78; 95%CI=0.71-0.86; partial R(2)=0.03). **CONCLUSION:** Although nearly three-quarters of French GPs frequently recommended the HPV vaccine, our findings indicate that a substantial percentage of them are hesitant about it. Doubts about its risks and efficacy strongly influence their recommendation behavior. More research is warranted to help design and evaluate tailored tools and multicomponent intervention strategies to address physician's hesitancy about this vaccine.

Elfstrom, K. M., et al. **Organization and quality of HPV vaccination programs in Europe.** *Vaccine.* 2015; 33(14): 1673-1681.

BACKGROUND: HPV vaccination is underway in most European countries, but there are limited efforts toward optimization and standardization of organization, monitoring and evaluation. Our Europe-wide survey sought to identify how programs are currently organized, the costs associated with the organizing and ensuring quality of the program and how quality and effectiveness measurements are carried out. **METHODS:** A comprehensive questionnaire was developed through systematic literature review and the European guidelines for quality assurance in cervical screening. The survey was piloted in a sub-set of countries and then sent to program organizers, Ministries of Health, and key experts in 34 EU and EFTA countries (including countries within the UK). Detailed information on program organization and target population, monitoring and evaluation (including indicators used for evaluating the impact of

vaccination), and associated costs were collected. In addition, documentation of program guidelines, protocols, and publications were requested. **RESULTS:** Of the 34 countries contacted, 27 responded. The majority of countries had some level of vaccination activity, with approximately half of the countries reporting an organized vaccination program. Centralized vaccine registries were in place in the majority of countries with an organized program, allowing for monitoring of key indicators at the national level. Costs of organization and monitoring were difficult to estimate and varied significantly, as some countries were able to use existing infrastructures while others had to create new systems, incurring greater costs. **CONCLUSIONS:** The organization and quality of HPV vaccination programs differ across countries and, in some instances, even across regions within the same country. The monitoring being performed varies across programs with regard to level of detail but engagement in the survey from the participating countries demonstrates that there is strong interest in reflecting on and improving program performance. This survey could serve as a basis for strengthening surveillance of HPV vaccination programs.

Elfstrom, K. M., et al. **Human Papillomavirus Vaccination of Boys and Extended Catch-up Vaccination: Effects on the Resilience of Programs.** *J Infect Dis* 2016; 213(2): 199-205.

BACKGROUND: Decreasing human papillomavirus (HPV) vaccine prices makes scaling up of vaccination programs attractive for countries that initially targeted 1 or a few birth cohorts of girls and/or achieved low coverage. This article aims to compare the impact of alternative HPV vaccination strategies, using data from Sweden, a high-income country that has experienced vaccine price changes. **METHODS:** Using an HPV transmission model, we compared the existing vaccination program to alternatives, accounting for a 1-time catch-up vaccination of 22-26-year-old women, with or without routine vaccination of school-age boys, and for a 1-time catch-up vaccination of males aged 13-26 years. We also assessed the resilience of vaccination alternatives to coverage reduction. **RESULTS:** On the basis of an HPV16/18 prevalence of 12% before the HPV vaccine era, extended catch-up vaccination for females and males yielded relative reductions in the HPV prevalence of 49.4% and 55.6%, respectively, during the first 10 years after the start of each vaccination strategy, whereas the existing program yielded a relative reduction of 38.6% during the same period. The increased prevalence reduction due to catch-up vaccination continued for about 30 years. As compared to female-only routine and extended catch-up vaccination, routine vaccination of males with or without catch-up was, respectively, 12.6-fold and 7.2-fold more resilient to coverage reduction. **CONCLUSIONS:** Vaccination strategies based on catch-up vaccination of females and males are effective for accelerating HPV prevalence reduction. Inclusion of routine male vaccination improves the resilience of vaccination programs.

Firenze, A., et al. **Facilitators and barriers HPV unvaccinated girls after 5 years of program implementation.** *Hum Vaccin Immunother.* 2015; 11(1): 240-244.

Understanding perceptions and characteristics of human papillomavirus (HPV) vaccinated and non-vaccinated girls can inform communication activities and vaccine delivery strategies. The purpose of this study was to evaluate knowledge and factors associated with HPV unvaccinated girls after five years of vaccination program implementation in Sicily, an Italian region with low vaccination coverage (<50.0%). A cross-sectional study was conducted through a questionnaire designed to assess knowledge and vaccination status of girls of 1997, 1998, 1999, and 2000 birth cohorts. The sample consisted of 350 girls who attended three high schools. Multivariable logistic regression analysis was conducted to examine predictors of vaccine refusal. The survey sample of girls shows that the 43.1% were HPV unvaccinated. A significant increased risk of being unvaccinated originated from the belief that the vaccine was too new (AdjOR = 21.08, CI95% = 2.57-172.97) and that it may cause cervical cancer (AdjOR = 4.36, CI95% = 1.26-15.07), along with having friends as a source of information on the vaccine (AdjOR = 3.67, CI95% = 1.63-8.25). A significant inverse association was observed between being unvaccinated and having Pediatrician/General practitioner as a source of information on HPV vaccine (AdjOR = 0.40, CI95% = 0.24-

0.68). Many girls lack the fundamental knowledge about the HPV vaccine. The key issue is the promotion and implementation of information programs to raise awareness of girls on the importance of the vaccine.

Fonteneau, L., et al. **The use of reimbursement data for timely monitoring of vaccination coverage: the example of human papillomavirus vaccine following public concerns about vaccine safety.** BMC Public Health. 2015; 15: 1233.

BACKGROUND: Since 2011 public concerns about Human Papillomavirus (HPV) vaccination safety and efficacy arose in France. We explored the relevance of using vaccines reimbursement data to assess the impact of those public concerns on vaccination coverage. **METHODS:** We used the Permanent Sample of Beneficiaries which was, at the time of the study, a representative sample of 1/97(th) health insurance beneficiaries of the main Social Security scheme, the General Health Insurance Scheme, covering approximately 77 % of the French resident population. We estimated HPV vaccination coverage among girls born between 1995 and 1999 at their 15(th), 16(th) and 17(th) birthday. **RESULTS:** The coverage for complete vaccination among 16 years old girls decreased from 26.5 % in the first semester of 2011 to 18.6 % in the first semester of 2014. **CONCLUSIONS:** HPV vaccination coverage was already low in 2011 and continued to decrease thereafter. Vaccines reimbursement data allowed us to reactively monitor the impact of the controversy on vaccination coverage and design counteracting measures.

Gottvall, M., et al. **Informed consent for HPV vaccination: a relational approach.** Health Care Anal 2015; 23(1): 50-62.

The aim of this study was to explore the relational aspects of the consent process for HPV vaccination as experienced by school nurses, based on the assumption that individuals have interests related to persons close to them, which is not necessarily to be apprehended as a restriction of autonomy; rather as a voluntary and emotionally preferred involvement of their close ones. Thirty Swedish school nurses were interviewed in five focus groups, before the school based vaccination program had started in Sweden. The empirical results were discussed in light of theories on relational autonomy. The school nurses were convinced that parental consent was needed for HPV vaccination of 11-year-old girls, but problems identified were the difficulty to judge when a young person is to be regarded as autonomous and what to do when children and parents do not agree on the decision. A solution suggested was that obtaining informed consent in school nursing is to be seen as a deliberative process, including the child, the parents and the nurse. The nurses described how they were willing to strive for a dialogue with the parents and negotiate with them in the consent process. Seeing autonomy as relational might allow for a more dialogical approach towards how consent is obtained in school based vaccination programs. Through such an approach, conflicts of interests can be made visible and become possible to deal with in a negotiating dialogue. If the school nurses do not focus exclusively on accepting the individual parent's choice, but strive to engage in a process of communication and deliberation, the autonomy of the child might increase and power inequalities might be reduced.

Guzzetta, G., et al. **The impact of HPV female immunization in Italy: model based predictions.** PLoS One. 2014; 9(3): e91698.

The Human Papillomavirus (HPV) is a sexually transmitted virus that causes cervical cancer. Since 2008 a vaccination program targeting 12-year-old girls has been initiated in Italy, backing up the cervical screening program already active since 1996. We propose a mathematical model of HPV transmission dynamics with the aim of evaluating the impact of these prevention strategies. The model considers heterosexual transmission of HPV types 16 and 18, structured by sex, age and sexual activity level, where transition to sexual activity is explicitly modeled from recent survey data. The epidemiological structure is a hybrid SIS/SIR, where a fraction of individuals recovering from infection develops permanent immunity against reinfection. Infections may progress to cervical lesions and cancer and heal spontaneously or upon

treatment. Women undergoing hysterectomy (either after treatment of HPV lesions or by other causes) also transmit HPV infection. The model fits well both the age-specific prevalence of HPV infections and the incidence of cervical cancers in Italy, and accurately reproduces the decreasing trend in cancer incidence due to the introduction of the screening program. The model predicts that if the screening coverage is maintained at current levels, even in the absence of vaccination, such trend will continue in the next few decades, eventually plateauing at 25% below the current level. The additional initiation of routine vaccination targeting 12-year-old girls will further reduce cervical cancer incidence by two thirds at equilibrium, under realistic assumptions of 70% coverage and a duration of protective immunity of 50 years. If catch-up immunization of 25-year-old women at first cervical screening is also introduced, about 3,000 cervical cancer cases overall can be averted, corresponding to 9.6% of all cases expected in the scenario without catch-up. We conclude that HPV vaccination in addition to cervical screening will significantly reduce the burden of cervical cancer in Italy.

Hequet, D., et al. **Age impact on human papillomavirus vaccination in France in 2014: A study from the National Health Insurance Database.** Bull Cancer. 2015; 102(11): 892-897.

INTRODUCTION: Human papillomavirus (HPV) is the main cause of cervical cancer. In France, since March 2007, HPV vaccination has been recommended for girls aged 14, in addition to a catch-up program for girls aged 15 to 23. In October 2012, the target population was changed to 11- to 14-year-old girls. The main objective of the present study was to evaluate the impact of the recommendation change on HPV vaccination coverage and compliance. **METHODS:** We conducted a descriptive study of the Echantillon Generaliste des Beneficiaires (EGB), which is a random 1/97 permanent sample from the French National Health Insurance Database. We focused our analyses on girls aged 11 to 17 years who were covered by the main insurance scheme (which covers 77% of the French population). **RESULTS:** We included 16,195 girls in this analysis. At the last update of the database (06/15/2014), 42% of 17-year-old girls had been vaccinated, with more than 50% of them having been vaccinated at age 14. Between January 2012 and June 2014, patients were reimbursed for a total of 7698 doses of the HPV vaccine. During the first trimester of 2013, the number of vaccinated 11- to 13-year-old girls increased, growing by more than 20-fold between the last trimester of 2012 (n=8) and the last trimester of 2013 (n=178). Less than 60% of the vaccinated patients received 3 injections. **DISCUSSION:** Implementation of the new recommendations was rapid but had only a slight impact on vaccination coverage.

Hofman, R., et al. **Have preferences of girls changed almost 3 years after the much debated start of the HPV vaccination program in The Netherlands? A discrete choice experiment.** PLoS One. 2014; 9(8): e104772.

OBJECTIVES: To assess how girls' preferences have changed almost 3 years after the much debated start of the human papillomavirus (HPV) vaccination program. **METHODS:** A discrete choice experiment (DCE) was conducted among girls aged 11-15 years who were invited, or were not yet invited, to get vaccinated. A panel latent class model was used to determine girls' preferences for vaccination based on five characteristics: degree of protection against cervical cancer; duration of protection; risk of mild side-effects; age of vaccination; and the number of required doses of the vaccine. **RESULTS:** The response rate was 85% (500/592). Most girls preferred vaccination at age 14 years (instead of at age 9 years) and a 2-dose scheme (instead of the current 3-dose scheme). Girls were willing to trade-off 7% (CI: 3.2% to 10.8%) of the degree of protection to have 10% less risk of mild side-effects, and 4% (CI: 1.2% to 5.9%) to receive 2 doses instead of 3 doses. Latent class analyses showed that there was preference heterogeneity among girls, i.e., higher educated girls and HPV vaccinated girls had a higher probability to opt for HPV vaccination at a higher age than lower educated girls or non-vaccinated girls. **CONCLUSIONS:** Three years after the start of HPV vaccination program the risk of mild side-effects and age at vaccination seem to have become less important. For the Dutch national immunization program, we recommend not

to lower the current target age of 12 years. A 2-dose scheme may result in a higher uptake and we recommend that if this scheme is introduced, it needs to receive adequate publicity.

Jeannot, E., et al. **Successful implementation and results of an HPV vaccination program in Geneva Canton, Switzerland.** Public Health Rep. 2015; 130(3): 202-206.

We describe a human papillomavirus (HPV) vaccination program implemented since 2007 in Geneva Canton, Switzerland, that used school services, a public hospital, and private physicians as vaccination providers. We assessed program performance with the evolution of immunization coverage during the first four years of program implementation. We measured vaccination coverage of the target population using individual records of vaccination status collected by service providers and transmitted to the Geneva Canton Medical Office. The target population was 20,541 adolescent girls aged 11-19 years as of September 1, 2008, who resided in the canton when the program began. As of June 30, 2012, HPV vaccination coverage was 72.6% and 74.8% in targeted cohorts for three and two doses, respectively. The global coverage for three doses increased by 27 percentage points from December 2009 to June 2012. Coverage for girls aged 16-18 years at the beginning of the program reached 80% or more four years into the program. High coverage by this HPV vaccination program in Geneva was likely related to free vaccination and easy access to the vaccine using a combination of delivery services, including school health services, a public hospital, and private physicians, covering most eligible adolescent girls.

Kose, D., et al. **Mothers' knowledge and attitudes about HPV vaccination to prevent cervical cancers.** Asian Pac J Cancer Prev. 2014; 15(17): 7263-7266.

BACKGROUND: Cervical cancer which is one of the most preventable cancers is an important public health problem worldwide, and especially in developing countries. The aim of this study was to determine knowledge and attitudes about the HPV vaccination of mothers with 0- to 18-year old children. **MATERIALS AND METHODS:** Written approval was taken from the local authorities. The study subjects consisted of 799 mothers who agreed to participate. The data were collected via a "Personal Information Form" which included 30 questions that were prepared by the researchers themselves in line with the literature. The data were collected by face to face interviews with the mothers. Analyses were performed using commercial software. **RESULTS:** The mean age of the mothers who participated in the study was 32.0 +/- 6.52, and 88.1% reported no information about HPV, and 83.5% no information about HPV vaccination. Only 0.7% of the mothers had daughters who had HPV vaccination, and 44.3% of the mothers who had sons were found out to be indecisive about having HPV vaccination. There was a significant correlation between the educational status of the mothers and their knowledge about HPV vaccination ($p < 0.05$). However, there was no significant correlation in terms of economic conditions ($p > 0.05$). **CONCLUSIONS:** This study suggested that mothers had very little information on HPV and HPV vaccination. Knowledge of the disease and its vaccination is an essential factor for the success of the vaccination program. It is of great importance that mothers are trained in this subject by health professionals.

Leeson, S. C., et al. **HPV testing and vaccination in Europe.** J Low Genit Tract Dis. 2014; 18(1): 61-69.

Current cytology-based screening has a moderate sensitivity to detect cervical intraepithelial neoplasia grade 3 (CIN 3) and cervical cancer even in those states providing rigorous quality control of their cervical screening programs. The impact of vaccination against human papillomavirus (HPV) types 16 and 18 as well as the incorporation of HPV testing on the detection of CIN 3 and cancer is discussed. HPV testing used as a triage for atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesions, test of cure after treatment, and HPV-based primary screening may improve current cervical screening programs. HPV testing as a triage test for ASCUS seems to offer an improved sensitivity, with a similar specificity as compared to repeat cytology for diagnosing high-grade CIN and has been recommended throughout most EU states. HPV testing as a triage test for low-grade

squamous intraepithelial lesions has a low specificity and is not recommended in most member states. HPV test of cure offers an improved sensitivity compared to cytology for women with persistent cervical precancer after treatment. HPV-based cervical cancer screening is more effective than screening with cytology. The effects of HPV-based screening depend on the organization of the program and on adherence to algorithms for screening triage. Otherwise, it is likely that HPV-based screening will increase the referral rate to colposcopy including more women with no detectable cervical lesion. HPV vaccination will require many years to evaluate any beneficial effects on cervical cancer incidence and mortality.

Mantzari, E., et al. **Financial incentives for increasing uptake of HPV vaccinations: a randomized controlled trial.** *Health Psychol.* 2015; 34(2): 160-171.

OBJECTIVE: Uptake of human papillomavirus (HPV) vaccinations by 17- to 18-year-old girls in England is below (<35%) target (80%). This trial assesses (a) the impact of financial incentives on uptake and completion of an HPV vaccination program, and (b) whether impacts are moderated by participants' deprivation level. It also assesses the impact of incentives on decision quality to get vaccinated, as measured by attitudes toward the vaccination and knowledge of its consequences. **METHOD:** One thousand 16- to 18-year-old girls were invited to participate in an HPV vaccination program: 500 previously uninvited, and 500 unresponsive to previous invitations. Girls randomly received either a standard invitation letter or a letter including the offer of vouchers worth pound 45 (euro 56; \$73) for undergoing 3 vaccinations. Girls attending their first vaccination appointment completed a questionnaire assessing decision quality to be vaccinated. Outcomes were uptake of the first and third vaccinations and decision quality. **RESULTS:** The intervention increased uptake of the first (first-time invitees: 28.4% vs. 19.6%, odds ratio [OR] = 1.63, 95% confidence interval [CI]; 1.08, 2.47]; previous nonattenders: 23.6% vs. 10.4%, OR = 2.65, 95% CI [1.61, 4.38]) and third (first-time invitees: 22.4% vs. 12%, OR = 2.15, 95% CI [1.32, 3.50]; previous nonattenders: 12.4% vs. 3%, OR = 4.28, 95% CI [1.92, 9.55]) vaccinations. Impacts were not moderated by deprivation level. Decision quality was unaffected by the intervention. **CONCLUSIONS:** Although the intervention increased completion of HPV vaccinations, uptake remained lower than the national target, which, in addition to cost effectiveness and acceptability issues, necessitates consideration of other ways of achieving it.

Michail, G., et al. **Female students receiving post-secondary education in Greece: the results of a collaborative human papillomavirus knowledge survey.** *Public Health* 2014; 128(12): 1099-1105.

OBJECTIVES: Contrary to the optimistic forecasts, existing until 2008 and despite the incorporation of the vaccine into the Greek National Immunization Program, six years later, the percentage of HPV vaccination coverage in Greece remains disappointingly low. The aim of this extended study was to investigate the knowledge, behaviour and attitude of a representative sample of the initial target group; young female students of Greek higher education institutions to Pap cervical screening, biology of HPV infection and principles of HPV vaccination. **STUDY DESIGN:** Cross-sectional study. **METHODS:** One thousand two hundred ten (1210) questionnaires were completed by young female students aged 17-24 years. The survey questionnaire sought data relating to sociodemographic characteristics, health behaviour and knowledge about HPV, as well as vaccination status. **RESULTS:** 79.6% of the sample reported at least one annual gynaecologic examination and 92.6% were familiar with the rationale of cervical screening; however only 52.9% had undergone a Pap smear. 69.7% reported adequate knowledge about HPV and 89.3% were aware of the possible course of HPV infection. Despite most (95.9%) were aware of vaccine availability, vaccinated students represented only 33.1%. According to the multivariate analysis, vaccination status was associated with university studies (OR 1.96; 95% CI: 1.19-3.20), parental area of expertise (OR 2.77; 95% CI: 1.18-6.53, OR 2.03; 95% CI: 1.05-3.94), and adequate knowledge of the reasons for which women should undergo regular cervical screening (OR 4.23; 85% CI: 1.55-11.55). Fear of side-effects and equivocal information were the main reasons of non-vaccination (52.2% and

33.1% respectively). Finally, the majority of unvaccinated individuals showed a positive attitude towards prospective HPV vaccination, providing they received well-documented advising. **CONCLUSIONS:** Young women attending Greek higher education exhibit a good level of knowledge about HPV and its correlation with cervical cancer. These data highlight the need for further sensitization of the general population.

Mollers, M., et al. **Equity in human papilloma virus vaccination uptake?: sexual behaviour, knowledge and demographics in a cross-sectional study in (un)vaccinated girls in the Netherlands.** BMC Public Health. 2014; 14: 288.

BACKGROUND: In the Netherlands, human papillomavirus (HPV) vaccination is part of a national program equally accessible for all girls invited for vaccination. To assess possible inequalities in vaccine uptake, we investigated differences between vaccinated and unvaccinated girls with regard to various characteristics, including education and ethnicity, (both associated with non-attendance to the national cervical screening program), sexual behaviour and knowledge of HPV. **METHODS:** In 2010, 19,939 nationwide randomly-selected 16-17 year-old girls (2009 vaccination campaign) were invited to fill out an online questionnaire. A knowledge scale score and multivariable analyses identified variables associated with vaccination status. **RESULTS:** 2989 (15%) of the selected girls participated (65% vaccinated, 35% unvaccinated). The participants were comparable with regard to education, ethnicity, most sexual risk behaviour and had similar knowledge scores on HPV transmission and vaccination. However, unvaccinated girls lived in more urbanised areas and were more likely to have a religious background. Irrespective of vaccination status, 81% of the girls were aware of the causal relationship between HPV and cervical cancer, but the awareness of the necessity of cervical screening despite being vaccinated was limited. **CONCLUSIONS:** HPV vaccine uptake was not associated with knowledge of HPV and with factors that are known to be associated with non-attendance to the cervical cancer screening program in the Netherlands. Furthermore, most sexual behaviour was not related to vaccination status meaning that teenage unvaccinated girls were not at a disproportionately higher risk of being exposed to HPV. Routine HPV vaccination may reduce the social inequity of prevention of cervical cancer.

Paul, K. T. **"Saving lives": Adapting and adopting Human Papilloma Virus (HPV) vaccination in Austria.** Soc Sci Med. 2016; 153: 193-200.

Vaccination against the sexually transmitted Human Papilloma Virus (HPV), a necessary agent for the development of cervical cancer, has triggered much debate. In Austria, HPV policy turned from "lagging behind" in 2008 into "Europe's frontrunner" by 2013. Drawing on qualitative research, the article shows how the vaccine was transformed and made "good enough" over the course of five years. By means of tinkering and shifting storylines, policy officials and experts disassociated the vaccine from gender, vaccine manufacturers, and youth sexuality. Ultimately, the HPV vaccine functioned to strengthen the national immunization program. To this end, preventing an effective problematization of the extant screening program was essential.

Rehn, M., et al. **Highest Vaccine Uptake after School-Based Delivery - A County-Level Evaluation of the Implementation Strategies for HPV Catch-Up Vaccination in Sweden.** PLoS One. 2016; 11(3): e0149857.

BACKGROUND: The Swedish school-based vaccination programme offers HPV vaccine to girls born ≥ 1999 in 5-6th grade. In 2012, all counties introduced free-of-charge catch-up vaccination campaigns targeting girls born 1993-1998. Varying vaccine uptake in the catch-up group by December 2012 suggested that some implementation strategies were more successful than others. In order to inform future vaccination campaigns, we assessed the impact of different implementation strategies on the county-level catch-up vaccine uptake. **METHODS:** We conducted an ecological study including all Swedish counties ($n = 21$), asking regional health offices about the information channels they used and where vaccination of the catch-up target group took place in their counties. The uptake of ≥ 1 dose by 30

September 2014 was estimated using data from the voluntary national vaccination register. We investigated associations between counties' catch-up vaccine uptake, information channels and vaccination settings by calculating incidence rate ratios (IRR) and 95% confidence intervals (CI), using negative binomial regression models. RESULTS: County level catch-up vaccine uptake varied between 49-84%. All counties offered vaccination through primary health care settings. Apart from this eight (34%) also offered the vaccine in some of their schools, four (19%) in all their schools, and two (10%) in other health care centres. The information channels most frequently used were: information at the national on-line health care consulting web-page (100%), letter/invitations (90%), and advertisement (81%). Counties offering vaccination to girls in all schools and counties offering vaccination in some of their schools, reached higher vaccine uptake compared to counties not offering vaccination in any of their schools (all schools adjusted IRR: 1.3, 95% CI: 1.1-1.5, some schools adjusted IRR: 1.2, 95% CI: 1.1-1.3). CONCLUSION: Counties offering HPV vaccination to catch-up groups in schools reached the highest vaccine uptake. No information channel explained differences in county-level vaccine uptake. Our findings suggest that catch-up vaccination outside the national vaccination program can reach a high uptake at the population level if it is implemented primarily with an organized delivery (e.g. in schools).

Saeterdal, I., et al. **Expansion of the Norwegian HPV Vaccination Program**. Value Health. 2014; 17(7): A636.

Slattelid Schreiber, S. M., et al. **Socioeconomic predictors of human papillomavirus vaccination among girls in the Danish childhood immunization program**. J Adolesc Health. 2015; 56(4): 402-407.

PURPOSE: In 2009, human papillomavirus (HPV) vaccination was introduced in the Danish national childhood immunization program targeting all 12-year-old girls. Previous findings suggest that 10%-13% of girls born in 1996-1997 have not initiated vaccination despite free access. This study aims to identify socioeconomic predictors of initiation and completion of HPV vaccination. METHODS: Girls born in 1996-1997 and their guardians were identified through the Danish Civil Registration System. Information on socioeconomic variables and HPV vaccination status was obtained by linkage to Statistics Denmark and the Danish National Health Insurance Service Register. Through logistic regression, we examined associations between socioeconomic variables and HPV vaccine initiation (N = 65,926) and completion (N = 61,162). RESULTS: Girls with immigrant ethnicity (odds ratio [OR] = .49; 95% confidence interval [CI], .42-.57) had lower HPV vaccine initiation than Danish girls. Girls of mothers with basic education (OR = .75; 95% CI, .69-.82) or low disposable income (OR = .67; 95% CI, .61-.73) had decreased initiation compared with girls of mothers with higher education/income. Girls of unemployed mothers (OR = .75; 95% CI, .69-.82) or mothers being unmarried (OR = .70; 95% CI, .65-.76) had lower initiation than girls of employed or married mothers. Finally, vaccine initiation varied depending on place of residence. The predictors of HPV vaccine completion were similar to those of initiation. CONCLUSIONS: We found social inequality in the initiation and completion of HPV vaccination despite free access. As socioeconomic risk factors identified for cervical cancer also are associated with decreased HPV vaccination, social inequalities in cervical cancer have the potential to increase.

Thierry, P., et al. **Human Papillomavirus vaccination in general practice in France, three years after the implementation of a targeted vaccine recommendation based on age and sexual history**. Hum Vaccin Immunother. 2016; 12(2): 528-533.

In France, vaccination against human papilloma virus (HPV) was recommended in 2007 for all 14-year-old girls as well as "catch-up" vaccination for girls between 15-23 y of age either before or within one year of becoming sexually active. We evaluated the vaccine coverage according to the eligibility for vaccination in a sample of young girls aged 14 to 23 years, who were seen in general practices. A survey was proposed to 706 general practitioners (GPs) and carried out from July to September 2010. GPs, also

called "family doctor," are physicians whose practice is not restricted to a specific field of medicine but instead covers a variety of medical problems in patients of all ages. Each participating GP included, retrospectively, the last female patient aged 14-17 y and the last female patient aged 18-23 y whom he had seen. A questionnaire collected information regarding the GP and the patients' characteristics. The vaccine coverage was determined according to the eligibility for vaccination, i.e. the coverage among younger women (14-17) and among those sexually active in the second age range (18-23). Sexual activity status was assessed by GP, according to information stated in the medical record. The 363 participating physicians (response rate 51.4%) included 712 patients (357 in the 14- to 17-year-old group and 355 in the 18- to 23-year-old group) in their responses. The rate of the vaccination coverage in the 14- to 17-year-old group was 55%. Among the girls in the 18- to 23-year-old group, 126 were eligible, and their vaccination coverage rate was 82%. The evaluation of the eligibility by the GPs was incorrect in 36% of the cases. Of the 712 patients, 6% of the girls had been vaccinated without a need for the vaccination, and 26% of the girls had not been vaccinated, although they needed to be vaccinated. Regarding the vaccine uptake, vaccination at the age of 14 was not as effective as vaccinating the older population for which vaccination was indicated as a catch-up program, based on sexual history. However, in more than one-third of the older population, difficulties remained regarding the determination of eligibility, according to the sexual history of the patient.

Topan, A., et al. **Knowledge level of working and student nurses on cervical cancer and human papilloma virus vaccines.** *Asian Pac J Cancer Prev.* 2015; 16(6): 2515-2519.

PURPOSE: To determine knowledge levels of working and student nurses about cervical cancer and prophylactic cancer vaccines. **MATERIALS AND METHODS:** This study was performed on 259 nursing students in the Department of Nursing and 137 nurses working in Health Research and Practice Center, approved to participate in the study between April-June 2012. The study was performed universally without selecting a sample. A questionnaire that was prepared for evaluating participants' knowledge and attitudes about human papilloma virus (HPV) vaccine was distributed to the nurses and data obtained from the forms were transferred to SPSS 15.00 program and statistically analyzed. **RESULTS:** It was found that 54.8% of the student nurses were between 21-24 years old and 13.1% of working students were between 25-28 years old. When student nurses and working nurses were compared in terms of their knowledge about the causes of cervical cancer, their ideas about prevention from cervical cancer with HPV vaccine, their ideas about possible risks of HPV vaccine and conservation ratios of HPV vaccine, it was observed that there were no statistically significant differences ($p > 0.05$). When student nurses and working nurses were compared in terms of the information-source about HPV, ways of HPV contamination, awareness about people who are susceptible to HPV contamination and age of HPV vaccination, it was determined that there was a statistically significant difference ($p < 0.05$). **CONCLUSIONS:** It was found that all nurses had some knowledge about cervical cancer and HPV vaccine, but this was not sufficient. Therefore; it is recommended to use verbal, written and visual communication tools intensively in order to have topics on cervical cancer, early diagnosis and prevention in bachelor and master programs for nurses, to inform society about cervical cancer and HPV vaccine for public health and to teach precautions for its prevention.

Verger, P., et al. **Vaccine Hesitancy Among General Practitioners and Its Determinants During Controversies: A National Cross-sectional Survey in France.** *EBioMedicine.* 2015; 2(8): 889-895.

BACKGROUND: This study aimed to assess: 1) vaccine hesitancy (VH) prevalence among French general practitioners (GPs) through the frequency of their vaccine recommendations, and 2) the determinants of these recommendations. **METHODS:** Cross-sectional observational study in 2014 nested in a national panel of 1712 randomly selected GPs in private practice in France. We constructed a score of self-reported recommendation frequency for 6 specific vaccines to target populations. **RESULTS:** 16%

to 43% of GPs sometimes or never recommended at least one specific vaccine to their target patients. Multivariable logistic regressions of the dichotomized score showed that GPs recommended vaccines frequently when they felt comfortable explaining their benefits and risks to patients (OR = 1.87; 1.35-2.59), or trusted official sources of information highly (OR = 1.40; 1.01-1.93). They recommended vaccines infrequently when they considered that adverse effects were likely (OR = 0.71; 0.52-0.96) or doubted the vaccine's utility (OR = 0.21; 0.15-0.29). INTERPRETATION: Our findings show that after repeated vaccine controversies in France, some VH exists among French GPs, whose recommendation behaviors depend on their trust in authorities, their perception of the utility and risks of vaccines, and their comfort in explaining them. Further research is needed to confirm these results among health care workers in other countries.

Region of the Americas

Ahken, S., et al. **HPV awareness in higher-risk young women: the need for a targeted HPV catch-up vaccination program.** J Obstet Gynaecol Can. 2015; 37(2): 122-128.

OBJECTIVE: To determine levels of HPV awareness and knowledge in higher-risk young women and their attitudes toward HPV vaccination and catch-up programs. **METHODS:** An anonymous, cross-sectional, Internet-based, self-reported questionnaire was completed by women ages 13 to 25 attending two outreach clinics. Primary outcomes were HPV infection/vaccine awareness, vaccination rates, and catch-up program acceptability. Chi-square, Fisher exact test, and logistic regression analyses were performed. **RESULTS:** Of 105 respondents (mean age 19.32), 66.7% received social assistance and 54.3% relied on walk-in clinics. Overall HPV awareness was 81.0% and vaccine awareness was 76.2%. HPV awareness was significantly higher in women < 20 years old ($P = 0.032$) and with past sexually transmitted infection (STI) history ($P = 0.039$) but didn't differ by education level. Vaccine awareness differed significantly with STI history ($P = 0.031$) but not by age or education level. Awareness of HPV's association with genital warts and cervical cancer was low (30.0%, 41.9%) and didn't differ by education level or sexually transmitted infection history. Thirty percent had been vaccinated (of those, 42% had received 3 doses), mainly in school-based programs (71%). Odds of vaccination were significantly higher in those with a family doctor (OR 8.08). Reasons for not being vaccinated included: "Did not know about it" (28.5%) and "Don't know" (28.5%). Catch-up program acceptability was high (92.8%, 95.2% if free) and did not differ significantly by age or education level. **CONCLUSION:** Higher-risk young women may have high levels of HPV infection/vaccine awareness but lack knowledge of HPV consequences. Those who missed or did not complete HPV vaccination opportunities would support free catch-up vaccination programs in accessible, youth-friendly centres.

Aragones, A., et al. **Parental education and text messaging reminders as effective community based tools to increase HPV vaccination rates among Mexican American children.** Prev Med Rep 2015; 2: 554-558.

OBJECTIVE: Latino populations, particularly Mexican-Americans who comprise 65% of the Latinos in the U.S., are disproportionately affected by HPV-related diseases. The HPV vaccination completion rates remain low, well below the Healthy People 2020 goal. In this study we assessed the effect of parental education and a text messaging reminder service on HPV vaccine completion rates among eligible children of Mexican American parents. **STUDY DESIGN:** Nonequivalent group study of Mexican parents of HPV vaccine eligible children attended the Health Window program at the Mexican Consulate in New York City, a non-clinical, trusted community setting, during 2012-2013. 69 parents received HPV education onsite, 45 of whom also received a series of text message vaccination reminders. We measured HPV vaccination completion of the youngest eligible children of Mexican parents as the main outcome. **RESULTS:** 98% of those in the education plus text messaging group reported getting the first dose of the vaccine for their child and 87% among those in the educational group only ($p = 0.11$). 88% of those receiving the 1st dose in the text messaging group reported completing the three doses versus 40% in the educational group only ($p = 0.004$). **CONCLUSIONS:** Parental text messaging plus education, implemented in a community based setting, was strongly associated with vaccine completion rates among vaccine-eligible Mexican American children. Although pilot in nature, the study achieved an 88% series completion rate in the children of those who received the text messages, significantly higher than current vaccination levels.

Baker, M. L., et al. **Paving pathways: Brazil's implementation of a national human papillomavirus immunization campaign.** Rev Panam Salud Publica 2015; 38(2): 163-166.

In 2014, Brazil introduced an HPV immunization program for girls 9-13 years of age as part of the Unified Health System's (SUS) National Immunization Program. The first doses were administered in March 2014; the second ones, in September 2014. In less than 3 months more than 3 million girls received the first dose of quadrivalent HPV vaccine, surpassing the target rate of 80%. This paper examines three elements that may influence the program's long-term success in Brazil: sustaining effective outreach, managing a large technology-transfer collaboration, and developing an electronic immunization registry, with a focus on the State of Sao Paulo. If these three factors are managed, the Government of Brazil is primed to serve as a model of success for other countries interested in implementing a national HPV vaccination program to decrease HPV-related morbidity and mortality.

Barnack-Tavlaris, J. L., et al. **Human Papillomavirus Vaccination Awareness and Acceptability Among U.S.-Born and U.S. Foreign-Born Women Living in California.** *Health Care Women Int.* 2016; 37(4): 444-462.

We examined human papillomavirus vaccine awareness and acceptance between U.S.-born and U.S. foreign-born women by utilizing California Health Interview Survey data from 1,672 women (ages 18-27) and 2,994 mothers (ages 28-65). Foreign-born women and mothers had lower vaccine awareness. Foreign-born young adult Latinas had greater vaccine acceptance than U.S.-born Latinas. Other factors associated with young adult women's vaccine acceptability were being younger, unmarried, and sexually active in the past year; having poorer self-reported health; and having heard of the vaccine. Variables associated with mothers' vaccine acceptability were being White, insured, and unmarried; having had a Pap test in past 3 years; being less educated; and being impoverished.

Berenson, A. B., et al. **Assessing the need for and acceptability of a free-of-charge postpartum HPV vaccination program.** *Am J Obstet Gynecol.* 2014; 210(3): 213.e211-217.

OBJECTIVE: Human papillomavirus (HPV) vaccine uptake rate among young adult US women was only 23% in 2010. One way to improve this low rate is to administer the vaccine postpartum. We examined whether this population requires vaccination and whether they would be agreeable to receiving it free of charge after delivery. STUDY DESIGN: Women 26 years of age or younger seeking prenatal care in publicly funded clinics in southeast Texas were interviewed in 2012 regarding their HPV vaccination status, barriers to vaccination, and whether they would be willing to receive this vaccine postpartum if offered free of charge. Medical charts were reviewed to extract additional information. RESULTS: Overall, 13.0% (65 of 500) stated they had initiated and 7.6% (38 of 500) completed the 3-dose vaccine series. Ethnic differences were noted with 21.0% of non-Hispanic whites, 14.6% of blacks, and 9.3% of Hispanics ($P = .002$) initiating the vaccine and 13.5%, 7.8%, and 5.2% ($P = .006$) completing all 3 doses, respectively. Lowest initiation (4.2%) and completion (1.4%) rates were observed among recently immigrated Hispanic women. Those who had not graduated from high school and older women were less likely to have been vaccinated. Almost 83% of those who had not received any HPV doses or completed the series were willing to receive the injection free of charge in the hospital after their delivery. CONCLUSION: HPV vaccine uptake rates are very low among women receiving prenatal care in southeast Texas. Offering this vaccine free of charge to postpartum women could be an effective strategy in this population because 5 of 6 women favored receiving it in this setting.

Berenson, A. B., et al. **A human papillomavirus vaccination program for low-income postpartum women.** *Am J Obstet Gynecol.* 2016.

BACKGROUND: Effective interventions are needed to address the low rate of human papillomavirus (HPV) vaccination in the United States, particularly among girls and women 16-26 years old. Counseling and offering the vaccine to postpartum patients could be an effective strategy to increase

uptake among young women who did not complete the 3-dose series at an earlier age. **OBJECTIVE:** The purpose of this evaluation was to assess the effectiveness of a multicomponent program designed for postpartum women that used patient navigators (PNs) and reminders for follow-up visits to improve uptake and completion of the HPV vaccine series. **STUDY DESIGN:** As part of standard care, patients ≤ 26 years of age from Galveston County, Texas, who delivered an infant from November 2012 through June 2014 at a public hospital were counseled and offered the HPV vaccine postpartum. PNs assisted with scheduling follow-up injections during postpartum or well-child visits. A program evaluation was conducted after 20 months. **RESULTS:** Of 1038 patients approached, only 161 (15.5%) had previously completed the vaccine series. Of the 877 patients who had not completed the series, 661 (75.4%) received at least 1 dose postpartum, with 575 patients receiving their first dose and 86 receiving their second or third doses. By April 2015, initiation rates had increased as a result of this program from 25.4% before the program was initiated to 80.8% and completion rates from 15.5-65.1%. Missed appointments for injections were less likely among those who received text message reminders and more likely among those with ≥ 2 prior pregnancies. Those who were Hispanic or had received an influenza vaccination in the last year were more likely to initiate and complete the series through this program. Patients who missed ≥ 1 follow-up appointments were less likely to complete the vaccine series. **CONCLUSION:** Offering the HPV vaccine postpartum dramatically increased initiation rates among postpartum patients. PN and text messages ensured that a high percentage completed all 3 doses.

Berkowitz, Z., et al. **Providers' beliefs about the effectiveness of the HPV vaccine in preventing cancer and their recommended age groups for vaccination: Findings from a provider survey, 2012.** *Prev Med.* 2015; 81: 405-411.

BACKGROUND: The human papillomavirus (HPV) vaccine was recommended in 2007 by the Advisory Committee on Immunization Practices (ACIP) to preadolescent and adolescent girls. Vaccination initiation was recommended at age 11-12 years with the option to start at age 9. Catchup vaccination was recommended to females aged 13-26 previously not vaccinated. However, vaccination coverage remains low. Studies show that the HPV vaccine can prevent cervical, vulvar, vaginal, anal and some oropharyngeal cancers and that provider recommendation of vaccines can improve low vaccination rates. **METHODS:** Using data from 2012 DocStyles, an annual, web-based survey of U.S. healthcare professionals including physicians and nurse practitioners ($n=1753$), we examined providers' knowledge about the effectiveness of the HPV vaccine in preventing cancer and their vaccine recommendation to all age-eligible females (9-26 years). Descriptive statistics and Chi-square tests were used to assess differences across specialties. **RESULTS:** Knowledge about HPV vaccine effectiveness in preventing cervical cancer was highly prevalent (96.9%), but less so for anal, vaginal, vulvar and oropharyngeal cancers. Only 14.5% of providers recommended the vaccine to all age-eligible females and 20.2% recommended it to females aged 11-26 years. Knowledge assessment of cancers associated with HPV and vaccination recommendations varied significantly among providers ($p<0.01$). Providers more frequently recommended the vaccine to girls older than 11-12 years. **CONCLUSIONS:** Improving providers' knowledge about HPV-associated cancers and the age for vaccination initiation, communicating messages focusing on the vaccine safety and benefits in cancer prevention and on the importance of its delivery prior to sexual onset, may improve HPV vaccine coverage.

Berkowitz, Z., et al. **Providers' practice, recommendations and beliefs about HPV vaccination and their adherence to guidelines about the use of HPV testing, 2007 to 2010.** *Prev Med.* 2016; 87: 128-131.

Human papillomavirus (HPV) vaccines prevent cervical pre-cancer lesion and can potentially reduce abnormal Papanicolaou (Pap) results among vaccinated females. However, current U.S. cervical screening guidelines recommend no change in screening initiation and frequency based on vaccination status. We examined providers' practices and beliefs about HPV vaccination to evaluate their adherence

to guidelines. We used 4-year data (2007-2010) from two nationally representative samples totaling 2119 primary-care providers from the Cervical Cancer Screening Supplement to the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS). Providers in each survey were stratified to obstetrician/gynecologist (OB/GYNs) and non-OB/GYNs. Descriptive statistics and chi-square tests were performed to assess differences between providers' types in each survey. Approximately 60% of providers believed that HPV vaccination will result in fewer abnormal Pap tests and fewer referrals to colposcopy and over 92% would not change their cervical cancer screening practices for fully vaccinated females. NAMCS OB/GYNs were more likely ($p < 0.05$) than non-OB/GYNs to rarely/never use the number of sexual partners to determine who gets the HPV vaccine (68.4% vs. 59.1%), more likely to recommend the vaccine to females with history of abnormal Pap (79.6% vs. 68.4%) and to females with a history of HPV positive test result (75.3% vs. 62.8%). Consistent with guidelines, most providers would not change cervical cancer screening practices based on patients' vaccination history. However, some providers used inappropriate tests for making vaccination decisions. Improving HPV vaccine knowledge and recommendations for its use is warranted to implement a successful vaccine program.

Calo, W. A., et al. **Exploring the role of ethnic identity on the attitudes towards HPV vaccine advertising among Puerto Ricans: a qualitative analysis.** *J Immigr Minor Health.* 2015; 17(1): 314-317.

Despite the existence of guidelines recommending vaccination against the human papillomavirus (HPV) and widespread availability of the vaccine through the Vaccines for Children program, HPV vaccination rates among island Puerto Ricans are suboptimal. Advertising plays a central role in promoting HPV vaccination by increasing awareness of and knowledge about the vaccine; however, little is known about the influence of cultural factors on the impact of HPV messages delivered through the media. The aim of this qualitative study was to explore the role of ethnic identity on the attitudes towards HPV vaccine advertising among island Puerto Ricans. Five focus groups ($n = 23$) were conducted with parents and non-vaccinated females. Our analysis found several themes that may influence attitudes towards HPV vaccine advertising among this population: physical ethnic similarity, relevance of information, and sociocultural congruence. Findings may assist in developing culturally appropriate health promotion programs and media to promote HPV vaccination among Puerto Ricans.

Chau, J., et al. **HPV knowledge and vaccine acceptance in an uninsured Hispanic population in Providence, RI.** *R I Med J* (2013) 2014; 97(5): 35-39.

The Food and Drug Administration has approved two human papillomavirus (HPV) vaccines for use by men and women in the United States. The vaccines not only protect against HPV infection, but also reduce the risk of cervical cancer in women. Despite the widespread availability of these vaccines, vulnerable populations such as those with low incomes have been reported to have limited access to and knowledge about HPV vaccines. In order to evaluate and improve HPV vaccination uptake in a population of uninsured, low-income Spanish-speaking individuals attending a free clinic in Rhode Island, we administered a questionnaire regarding knowledge, attitudes, and practices (KAP) and performed an education intervention. We found that knowledge of HPV infection and cervical cancer among the patients sampled was low when comparing Hispanics to non-Hispanics (47.2%, 85.7%, respectively) but willingness to vaccinate oneself or one's child was very high after a brief video-based intervention.

Drolet, M., et al. **Can high overall human papillomavirus vaccination coverage hide sociodemographic inequalities? An ecological analysis in Canada.** *Vaccine.* 2016; 34(16): 1874-1880.

BACKGROUND: Human papillomavirus (HPV) vaccination programs have been implemented in more than 50 countries. These programs offer tremendous promise of reducing HPV-related disease burden. However, failure to achieve high coverage among high-risk groups may mitigate program success

and increase inequalities. We examined sociodemographic inequalities in HPV vaccination coverage in 4 Canadian provinces (Quebec (QC), Ontario (ON), Manitoba (MB), British Columbia (BC)). **METHODS:** We obtained annual HPV vaccination coverage of pre-adolescent girls at provincial and regional levels, from the start of programs to 2012/2013. Regions refer to administrative areas responsible for vaccine implementation and monitoring (there are 18/36/10/16 regions in QC/ON/MB/BC). We obtained regions' sociodemographic characteristics from Statistics Canada Census. We used univariate weighted linear regression to examine the associations between regions' sociodemographic characteristics and HPV vaccination coverage. **RESULTS:** Provincial HPV vaccination coverage is generally high (QC:78%; ON:80%; MB:64%, BC:69%, 2012/13). QC had the highest provincial vaccination coverage since the program start, but had the greatest inequalities. In QC, regional HPV vaccination coverage was lower in regions with higher proportions of socially deprived individuals, immigrants, and/or native English speakers ($p < 0.0001$). These inequalities remained stable over time. Regional-level analysis did not reveal inequalities in ON, MB and BC. **CONCLUSION:** School-based HPV vaccination programs have resulted in high vaccination coverage in four Canadian provinces. Nonetheless, high overall coverage did not necessarily translate into equality in coverage. Future work is needed to understand underlying causes of inequalities and how this could impact existing inequalities in HPV-related diseases and overall program success.

Fiks, A. G., et al. **Improving HPV Vaccination Rates Using Maintenance-of-Certification Requirements." *Pediatrics*. 2016; 137(3): 1-11.**

BACKGROUND: Many pediatricians are now required to participate in American Board of Pediatrics Maintenance of Certification (MOC) Part IV programs focused on improving health care quality, but the benefits of participation are unproven. **METHODS:** Twenty-seven primary care pediatricians from 11 primary care practices participated in a 1-year MOC program for human papillomavirus (HPV) vaccine. Participants received education and electronic health record (EHR)-generated performance feedback reports with their rates of captured HPV immunization opportunities (dose given at eligible visit) and those of peers. In each of 3 cycles, clinicians collectively identified a goal for improvement. Rates of captured opportunities among adolescents 11 to <18 years old were tabulated, and statistical process control charts were created to evaluate changes over time among participants compared with 200 nonparticipants. Provider perceptions of the program and time invested were recorded via survey. **RESULTS:** Participating clinicians missed fewer opportunities for HPV vaccination than nonparticipants. MOC participants significantly increased their captured opportunities relative to nonparticipating clinicians by 5.7 percentage points for HPV dose 1 at preventive visits and by 0.7 and 5.6 percentage points for doses 1 and 2, respectively, at acute visits. There were no significant differences for other doses. The estimated program cost was \$662/participant. Of the participating pediatricians, 96% felt the effort to participate was warranted, and half would not have joined the project without the MOC requirement. **CONCLUSIONS:** Participation in MOC Part IV improved vaccination at modest cost and with high pediatrician satisfaction, demonstrating benefits of the program that may help to inform future initiatives.

Galbraith, K. V., et al. **Parental acceptance and uptake of the HPV vaccine among African-Americans and Latinos in the United States: A literature review.** *Soc Sci Med* 2016; 159: 116-126.

BACKGROUND: African-Americans and Latinos suffer the highest cervical cancer burden compared to other populations and have sub-optimal HPV vaccination rates. **OBJECTIVE:** To condense research findings of studies conducted with African-Americans and Latinos on factors associated with HPV vaccine acceptability and uptake. **METHODS:** Standards for conducting an integrative review were used. PubMed, Cumulative Index to Nursing and Allied Health Literature, and PsycINFO databases were searched. **RESULTS:** Awareness about HPV and the HPV vaccine varied by demographics of parents. For Latino parents, acculturation and awareness were associated. However, findings were mixed regarding the association between acculturation and knowledge. Among African-Americans, higher socioeconomic

status (SES) and awareness were associated. Sexuality-related concerns, concerns about safety and low perceived risk of daughter's acquiring HPV emerged as barriers to vaccination among Latinos and African-Americans. Among Latinos, vaccine acceptability was associated with the vaccine's cancer prevention benefits and a provider's recommendation. Among African-Americans, acceptability was associated with awareness, perceived risk of acquiring HPV, religion, and a provider's recommendation. Few interventions have been developed to increase HPV vaccine acceptance. Importantly, few studies assessed the influence of culture on vaccine acceptance and uptake. **CONCLUSIONS:** Future research should be informed by culture-centered theories as this is the first step to inform the development of culturally-grounded interventions.

Harris, T., et al. **Adverse events following immunization in Ontario's female school-based HPV program. Vaccine.** 2014; 32(9): 1061-1066.

BACKGROUND: In September 2007, a school-based human papillomavirus (HPV) vaccination program targeting grade 8 girls (approximately 13 years old) and delivered by public health was implemented in Ontario, Canada. We assessed reports of adverse events following immunization (AEFI) from the school-based program as part of quadrivalent HPV (HPV4) vaccine safety surveillance and to contribute to a comprehensive HPV vaccine program evaluation. **METHODS:** AEFIs following HPV4 vaccine (Gardasil((R))) administered between September 1, 2007 and December 31, 2011 were extracted from the province's reportable disease system. Confirmed AEFI reports among females 12-15 years old (i.e. assumed to have received vaccine through the program) were included. Events were grouped according to provincial AEFI case definitions. Rates were calculated using doses distributed as the denominator. **RESULTS:** Between 2007 and 2011, 133 confirmed AEFIs were reported while 691,994 HPV4 vaccine doses were distributed in the school-based program. The overall reporting rate was 19.2 HPV4 AEFI per 100,000 doses distributed. Annual reporting rates decreased from 30.0 to 18.3 per 100,000 doses distributed. Frequently reported events included 'allergic reaction-dermatologic/mucosa' (25%), 'rash' (22%), and 'local/injection site reaction' (20%); 26% of reports had a non-specific event of 'other severe/unusual events' selected. Ten serious AEFIs were reported (7.5% of reports) including 2 anaphylaxis, 2 seizures, 1 thrombocytopenia and 1 death. Further review found that the reports of anaphylaxis did not meet the Brighton anaphylaxis definition and the death was attributed to a preexisting cardiac condition. **CONCLUSIONS:** Overall these findings are consistent with the safety profile of HPV4 vaccine from pre-licensure clinical trials and post-marketing surveillance reports and importantly, no new safety signals were identified, especially no reports of VTE in this younger female population. Continued assessment of HPV4 AEFI surveillance data may be important to detect and investigate safety signals.

Khurana, S., et al. **HPV vaccine acceptance among adolescent males and their parents in two suburban pediatric practices. Vaccine.** 2015; 33(13): 1620-1624.

PURPOSE: To measure HPV vaccine acceptance among unvaccinated adolescent males and parents and correlate acceptance with knowledge, awareness, and personal experience. **METHODS:** Adolescent males ages 11-21 years old and their parents completed questionnaires measuring attitudes and knowledge about HPV vaccination and personal experience. Acceptance was defined as wanting the vaccine and conditional acceptance as wanting the vaccine if it would protect against genital warts or cervical cancer. **RESULTS:** Adolescent (n=154) and parent (n=121) vaccine acceptance was low (16% and 34%, respectively); however, conditional acceptance was higher. While adolescents had similar conditional acceptance for a vaccine against genital warts and cervical cancer, parents reported higher conditional acceptance for protection against genital warts. Independent predictors of acceptance included personal experience and demographic variables. **CONCLUSIONS:** HPV vaccine acceptance among adolescents and parents was low. Conditional acceptance levels highlight the importance of education about a few important benefits of HPV vaccination, which may increase vaccination rates.

Krawczyk, A., et al. **Parents' decision-making about the human papillomavirus vaccine for their daughters: I. Quantitative results.** *Hum Vaccin Immunother.* 2015; 11(2): 322-329.

Vaccination against the human papillomavirus (HPV) is an effective primary prevention measure for HPV-related diseases. For children and young adolescents, the uptake of the vaccine is contingent on parental consent. This study sought to identify key differences between parents who obtain (acceptors) and parents who refuse (non-acceptors) the HPV vaccine for their daughters. In the context of a free, universal, school-based HPV vaccination program in Quebec, 774 parents of 9-10 year-old girls completed and returned a questionnaire by mail. The questionnaire was based on the theoretical constructs of the Health Belief Model (HBM), along with constructs from other theoretical frameworks. Of the 774 parents, 88.2% reported their daughter having received the HPV vaccine. Perceived susceptibility of daughters to HPV infection, perceived benefits of the vaccine, perceived barriers (including safety of the vaccine), and cues to action significantly distinguished between parents whose daughters had received the HPV vaccine and those whose daughters had not. Other significant factors associated with daughter vaccine uptake were parents' general vaccination attitudes, anticipated regret, adherence to other routinely recommended vaccines, social norms, and positive media influence. The results of this study identify a number of important correlates related to parents' decisions to accept or refuse the HPV vaccine uptake for their daughters. Future work may benefit from targeting such factors and incorporating other health behavior theories in the design of effective HPV vaccine uptake interventions.

Krawczyk, A., et al. **Parents' decision-making about the human papillomavirus vaccine for their daughters: II. Qualitative results.** *Hum Vaccin Immunother.* 2015; 11(2): 330-336.

The goal of the study was to examine the reasons given by parents who accepted or refused the HPV vaccine for their daughters in the context of a free provincial school-based vaccination program. A random sample of parents of 9-10 y old girls completed a mail-in questionnaire. Parents' responses to 2 open-ended questions were assessed using content analysis. Coding themes were derived from the Health Belief Model. 806 parents returned and answered the relevant items. 88% of these parents decided to vaccinate their daughter. The primary reasons for parents' acceptance was the perceived benefits (e.g., health protection, cancer/HPV prevention) and cues to action (e.g., physician recommendation, trusting the school vaccine program). Reasons for parental refusal included barriers (e.g., fear of side effects) and low susceptibility (e.g., their daughter is not at risk). Both groups of parents had unanswered questions, doubts and often inaccurate information. This study provides unique insight into parents' perspectives concerning the decision making process for their daughter. There appears to be a need for accurate and complete information to assure informed HPV vaccine decision-making by parents and to increase HPV vaccine uptake.

Liu, X. C., et al. **Adverse events following HPV vaccination, Alberta 2006-2014.** *Vaccine* 2016; 34(15): 1800-1805.

BACKGROUND: In Canada, private purchase of human papilloma virus (HPV) vaccines has been possible since 2006. In Alberta, Canada, a publicly funded quadrivalent HPV vaccine program began in the 2008/2009 school year. There have been concerns about adverse events, including venous thromboembolism (VTE) associated with HPV vaccines. We describe the frequencies of adverse events following HPV vaccination among Alberta females aged 9 years or older and look at VTE following HPV vaccination. **METHODS:** We used the Alberta Immunization and Adverse Reaction to Immunization (Imm/ARI) repository (publicly funded vaccine), the population-based Pharmaceutical Information Network (PIN) information system (dispensing of a vaccine), and the Alberta Morbidity and Ambulatory Care Abstract reporting system (MACAR) for June 1, 2006-November 19, 2014. Deterministic data linkage used unique personal identifiers. We identified all reported adverse events following immunization (AEFI)

and all emergency department (ED) utilization or hospitalizations within 42 days of immunization. We calculated the frequency of AEFI by type, rates per 100,000 doses of HPV vaccine administered and the frequencies of ICD-10-CA codes for hospitalizations and emergency department visits. RESULTS: Over the period 195,270 females received 528,913 doses of HPV vaccine. Of those receiving at least one dose, 192 reported one or more AEFI events (198 AEFI events), i.e., 37.4/100,000 doses administered (95% CI 32.5-43.0). None were consistent with VTE. Of the women who received HPV vaccine 958 were hospitalized and 19,351 had an ED visit within 42 days of immunization. Four women who had an ED visit and hospitalization event were diagnosed with VTE. Three of these had other diagnoses known to be associated with VTE; the fourth woman had VTE among ED diagnoses but not among those for the hospitalization. CONCLUSIONS: Rates of AEFI after HPV immunization in Alberta are low and consistent with types of events seen elsewhere.

Manthiram, K., et al. **Sustaining motivation to immunize: exchanging lessons between India and the United States.** Hum Vaccin Immunother. 2014; 10(10): 2930-2934.

In our recent study on vaccine uptake and parental attitudes toward immunizations in urban South India, we found strong support for vaccination due to fear of vaccine-preventable diseases and confidence in the recommendations made by health care professionals. In this commentary, we will characterize the reasons behind strong parental motivation to immunize in South India and consider ways these motivators can be enhanced in the United States, where vaccine hesitancy has led to outbreaks of vaccine-preventable disease. In addition, we will also discuss lessons that can be learned from the hesitancy movements in the United States and applied in India to maintain strong support for vaccination.

McClure, C. A., et al. **Human papillomavirus vaccine uptake in boys and girls in a school-based vaccine delivery program in Prince Edward Island, Canada.** Vaccine. 2015; 33(15): 1786-1790.

BACKGROUND: In 2013, Prince Edward Island was the first province to introduce HPV vaccine universally to grade six boys in a school-based program. Because uptake rates in boys are unknown in this type of vaccination program, uptake of HPV vaccination in boys was measured and compared with uptake rates in girls and then analyzed with factors such as county, urban-rural location of the school, and school board to identify where the vaccine program could be improved. METHODS: HPV vaccination records from the provincial childhood immunization registry in PEI were merged with Department of Education data containing all grade six girls and boys in PEI. Vaccine uptakes between years and between sexes were compared using two sample tests of proportions. Logistic regression modeling which accounted for the hierarchical nature of the data was used to analyze associations between factors and uptake rates. RESULTS: Although uptake was high in boys and girls, a significantly greater proportion of girls (85%) received all three doses of the HPV vaccine compared to boys (79%; $p=0.004$). The odds of grade six girls being fully vaccinated for HPV were 1.5 times greater than of grade six boys, and the odds of students in the English Language School Board receiving all three doses were more than twice as great as the odds of French Language School Board students. CONCLUSIONS: HPV vaccination for boys in PEI has had a successful launch, almost reaching the Canadian Immunization Committee recommendations of >80% for the early years of a program. PEI has a highly organized Public Health Nursing program that is involved in all childhood and school-based vaccinations in PEI and in this context very high coverage rates were obtained. Areas to target for improving uptake include the boys and the students in the French Language School Board.

Moran, M. B., et al. **Information scanning and vaccine safety concerns among African American, Mexican American, and non-Hispanic White women.** Patient Educ Couns. 2016; 99(1): 147-153.

OBJECTIVE: A significant number of parents delay or refuse vaccinating their children. Incidental exposure to vaccine information (i.e., scanned information) may be an important contributor to anti-

vaccine sentiment. This study examines the association between scanned information, trust in health information sources and vaccine safety concerns among African American, Mexican American, and non-Hispanic White women. **METHODS:** Women (N=761) in Los Angeles County were sampled via random digit dial and surveyed regarding use of and trust in health information resources and vaccine safety concerns. **RESULTS:** Analyses indicate that the sources of information associated with vaccine safety concerns varied by ethnicity. Each ethnic group exhibited different patterns of association between trust in health information resources and vaccine safety concerns. **CONCLUSIONS:** Information scanning is associated with beliefs about vaccine safety, which may lead parents to refuse or delay vaccinating their children. These relationships vary by ethnicity. **PRACTICE IMPLICATIONS:** These findings help inform practitioners and policy makers about communication factors that influence vaccine safety concerns. Knowing these sources of information will equip practitioners to better identify women who may have been exposed to anti-vaccine messages and counter these beliefs with effective, vaccine-promoting messages via the most relevant information sources.

Nan, X., et al. **Parental cancer beliefs and trust in health information from medical authorities as predictors of HPV vaccine acceptability.** *J Health Commun.* 2014; 19(1): 100-114.

This research examines parental cancer beliefs and trust in health information from medical authorities as predictors of HPV vaccine acceptability. Specifically, the authors investigated how parents' perceived susceptibility to and severity of cancer, fatalistic beliefs about cancer prevention, and trust in health information from doctors/health professionals and government health agencies are related to willingness to vaccinate their daughters ages 11-12 years against HPV. The authors analyzed data from the 2007 Health Information National Trends Survey. The authors found that parents were more likely to accept the vaccine if they perceived a higher risk of getting cancer themselves and if they had a higher level of trust in health information from medical authorities. Perceived severity of cancer and fatalistic beliefs about cancer prevention did not predict vaccine acceptance.

Nodulman, J. A., et al. **Investigating stakeholder attitudes and opinions on school-based human papillomavirus vaccination programs.** *J Sch Health.* 2015; 85(5): 289-298.

BACKGROUND: In several countries worldwide, school-based human papillomavirus (HPV) vaccination programs have been successful; however, little research has explored US stakeholders' acceptance toward school-based HPV vaccination programs. **METHODS:** A total of 13 focus groups and 12 key informant interviews (N = 117; 85% females; 66% racial/ethnic minority) were conducted with 5 groups of stakeholders: parents of adolescent girls, parents of adolescent boys, adolescent girls, middle school nurses, and middle school administrators throughout the 5 public health regions of New Mexico. **RESULTS:** All groups of stakeholders lacked knowledge on HPV and HPV vaccines. Stakeholders were interested in--but apprehensive about--the benefits of HPV vaccination. Despite previous literature showing the benefits of using middle schools as an HPV vaccination site, stakeholders did not deem middle schools as a viable site for vaccination. Nurses reported that using the school as an HPV vaccination site had not occurred to them; parents and adolescents stated they were uncertain about using this type of program. School administrators indicated that they lacked implementation authority. **CONCLUSIONS:** Our study uncovered barriers to using middle schools as a site of HPV vaccination. Resources should be directed toward increased support and education for middle school nurses who function as opinion leaders relevant to the uptake of HPV vaccination.

Paiva, A. L., et al. **Evaluation of the acceptability and feasibility of a computer-tailored intervention to increase human papillomavirus vaccination among young adult women.** *J Am Coll Health.* 2014; 62(1): 32-38.

OBJECTIVE: To examine acceptability and feasibility of a Transtheoretical Model (TTM)-based computer-tailored intervention (CTI) for increasing human papillomavirus (HPV) vaccination in college-aged women. **PARTICIPANTS:** Two hundred forty-three women aged 18-26 were recruited between February and May of 2011. **METHODS:** Participants completed the intervention and a 14-item evaluation of intervention content and delivery. **RESULTS:** Most participants had heard of HPV (91%), but the majority (57%) of participants were in Precontemplation for getting vaccinated. Eighty-nine percent of participants rated the CTI positively across all acceptability items, and 91% endorsed intention to get vaccinated after intervention. Although average ratings in each demographic subgroup were positive, Hispanic women and participants in more advanced stages of change rated the program more favorably than non-Hispanic and earlier-stage participants. Additionally, HPV knowledge was higher among white/non-Hispanic participants. **CONCLUSIONS:** Initial acceptability and feasibility data for this intervention are promising. Its computer-based, individually tailored format is state of the art and ideal for inexpensive dissemination.

Palfrey, S. **New initiatives to improve HPV vaccination rates.** Hum Vaccin Immunother. 2016; 1-5.

Patel, H., et al. **Argentina's Successful Implementation Of A National Human Papillomavirus Vaccination Program.** Health Aff (Millwood). 2016; 35(2): 301-308.

Every year around fourteen million people globally are infected with human papillomavirus (HPV), the sexually transmitted virus that is the cause of most cervical cancers. A number of vaccines have been developed to protect against HPV, but in many countries, HPV vaccination rates have been low compared with rates for other recommended vaccines. Parental concerns, cost, and lack of information and awareness among both health professionals and parents are cited as important barriers to HPV vaccination. In Argentina the HPV vaccine has been provided to all eleven-year-old girls since 2011 as part of a comprehensive national program to prevent cervical cancer. Coverage increased from negligible levels before 2011 to a national average of 87.9 percent for the first dose, 71.6 percent for the second dose, and 52.2 percent for the third dose in 2013. There was a large variance in HPV vaccine coverage across the country's provinces. This article describes key strategies to overcome barriers to implementation of HPV vaccination and provides recommendations for policy makers.

Pierre Joseph, N., et al. **Ethnic differences in perceived benefits and barriers to HPV vaccine acceptance: a qualitative analysis of young African American, Haitian, Caucasian, and Latino men.** Clin Pediatr (Phila). 2014; 53(2): 177-185.

PURPOSE: To examine the attitudes toward human papillomavirus (HPV) vaccination among young men from African American, Haitian, Caucasian, and Latino backgrounds. **METHODS:** We used in-person surveys at an urban teaching hospital from 2010 to 2012 to examine the racial and ethnic differences in the perceived benefits and barriers to HPV vaccination and vaccine mandate acceptance among 18- to 22-year-old African American, Haitian, Caucasian, and Latino men. **RESULTS:** A total of 89 men participated (35% African American, 29% Haitian, 20% Latino, and 16% white). Participants from all ethnic groups perceived benefits to HPV vaccination but differed in their perceptions of barriers to vaccination as well as their acceptance of a vaccine mandate. **CONCLUSIONS:** Culturally competent educational messages may overcome ethnic differences in the attitudes, beliefs, and behaviors regarding vaccination among college-aged men from an urban population.

Reiter, P. L. and McRee, A. L. **Correlates of receiving recommended adolescent vaccines among youth with special health care needs: Findings from a statewide survey.** Vaccine. 2016; 34(27): 3125-3131.

BACKGROUND: Many youth with special health care needs (YSHCN) have not received recommended adolescent vaccines, yet data are lacking on correlates of vaccination among this population. Such information can identify subgroups of YSHCN that may be at risk for under-immunization

and strategies for increasing vaccination. **METHODS:** We analyzed weighted data from a population-based sample of parents with an 11- to 17-year-old child with a special health care need from the 2010-2012 North Carolina Child Health Assessment and Monitoring Program (n=604). We used ordinal logistic regression to identify correlates of how many recommended vaccines (tetanus booster, meningococcal, and HPV [at least one dose] vaccines) adolescents had received. **RESULTS:** Only 12% of YSHCN (18% of females and 7% of males) had received all three vaccines. More YSHCN had received tetanus booster vaccine (91%) than meningococcal (28%) or HPV vaccines (32%). In multivariable analyses, YSHCN who were female (OR=2.59, 95% CI: 1.57-4.24), ages 16-17 (OR=2.06, 95% CI: 1.10-3.87), or who had a preventive check-up in the past year (OR=2.98, 95% CI: 1.24-7.21) had received a greater number of the vaccines. YSHCN from households that contained a person with at least some college education had received fewer of the vaccines (OR=0.57, 95% CI: 0.33-0.96). Vaccine coverage did not differ by type of special health care need. **CONCLUSIONS:** Vaccine coverage among YSHCN is lacking and particularly low among those who are younger or male. Reducing missed opportunities for vaccination at medical visits and concomitant administration of adolescent vaccines may help increase vaccine coverage among YSHCN.

Remes, O., et al. **Individual- and regional-level determinants of human papillomavirus (HPV) vaccine refusal: the Ontario Grade 8 HPV vaccine cohort study.** BMC Public Health. 2014; 14: 1047.

BACKGROUND: Studies on the determinants of human papillomavirus (HPV) vaccine use have generally focused on individual-level characteristics, despite the potentially important influence of regional-level characteristics. Therefore, we undertook a population-based, retrospective cohort study to identify individual- and regional-level determinants of HPV vaccine refusal (non-receipt) in Ontario's (Canada) Grade 8 HPV Immunization Program. **METHODS:** Ontario's administrative health and immunization databases were used to identify girls eligible for free HPV vaccination in 2007-2011 and to ascertain individual-level characteristics of cohort members (socio-demographics, vaccination history, health care utilization, medical history). The social and material characteristics of the girl's region (health unit) were derived from the 2006 Canadian Census. Generalized estimating equations (binomial distribution, logit link) were used to estimate the population-average effects of individual- and regional-level characteristics on HPV vaccine refusal. **RESULTS:** Our cohort consisted of 144,047 girls, 49.3% of whom refused HPV vaccination. Factors associated with refusal included a previous diagnosis of Down's syndrome (OR = 1.37, 95% CI 1.16-1.63) or autism (OR = 1.60, 95% CI 1.34-1.90), few physician visits (OR = 1.45, 95% CI 1.35-1.55), and previous refusal of mandatory (OR = 2.23, 95% CI 2.07-2.40) and optional (OR = 3.96, 95% CI 3.87-4.05) vaccines. Refusal was highest among the lowest and highest income levels. Finally, a previous diagnosis of obesity and living in an area of high deprivation were associated with lower refusal (OR = 0.87, 95% CI 0.83-0.92 and OR = 0.82 95%, CI 0.79-0.86, respectively). **CONCLUSIONS:** Studies on HPV vaccine determinants should consider regional-level factors. Efforts to increase HPV vaccine acceptance should include vulnerable populations (such as girls of low income) and girls with limited contact with the healthcare system.

Sussman, A. L., et al. **Catching Up With the HPV Vaccine: Challenges and Opportunities in Primary Care.** Ann Fam Med. 2015; 13(4): 354-360.

PURPOSE: Data confirm that high rates of human papillomavirus (HPV) vaccination have not been achieved despite strong clinician endorsement of the vaccine. We conducted a study of primary care clinicians to assess the broad range of health care delivery, health policy, and attitudinal factors influencing vaccination uptake and opportunities for informed decision making. **METHODS:** We implemented a mixed methods study in RIOS Net, a primary care practice-based research network in New Mexico. We first conducted qualitative, in-depth interviews with primary care clinicians, health policy makers, and immunization experts, and followed up with a confirmatory survey distributed to RIOS Net

clinician members. **RESULTS:** Health service delivery challenges emerged as the greatest barrier to HPV vaccination, specifically the lack of capacity to track and distribute reminders to eligible patients. Clinicians also reported variations in counseling approaches attributable to both age and emphasis on the cancer prevention benefits of the vaccine. There was no evidence of sociocultural influences on vaccine decision making, nor did concerns about perceived overprotection emerge. **CONCLUSIONS:** Our findings, based on a long-term program of research, suggest that both patients' attributes and health system delivery are most influential in HPV vaccination coverage challenges. Interventions targeting innovative communication techniques, as well as health system changes that build on efforts toward coordinated care and utilization of other venues to promote vaccination, will be necessary to address these challenges.

Vanderpool, R. C., et al. **Implementation and Evaluation of a School-Based Human Papillomavirus Vaccination Program in Rural Kentucky.** *Am J Prev Med.* 2015; 49(2): 317-323.

INTRODUCTION: Human papillomavirus (HPV) vaccination rates remain marginal across the U.S., including Kentucky, a state recognized for increased HPV-related cancer burden. School-based HPV immunization programs may be a viable approach to improving vaccination initiation and completion rates among youth. Therefore, the purpose of this study was to design, implement, and evaluate a school-based HPV vaccination program conducted in rural south-central Kentucky. **METHODS:** Guided by evidence-based approaches to increasing immunization rates, the practical expertise of school nursing staff, and a detailed study protocol, academic and health department-based investigators implemented an HPV vaccination project in two high schools during the 2012-2013 academic year; data were analyzed in 2013-2014. Rates of returned parental consent forms, parental consent/declination, and HPV vaccination rates were documented. **RESULTS:** At the beginning of the school year, all 935 students at the two schools were given HPV vaccination parental consent forms. Five hundred eleven students returned consent forms (55% return rate), and 447 of these students were HPV vaccine naive (87%). Of these students, 315 (70%) initiated the vaccine series, with 276 (62%) completing the entire three-dose series, so that 88% of students initiating the vaccine series successfully completed the series. In estimating rates for the entire school body, 45% of students had received all three doses by the end of the project. **CONCLUSIONS:** Despite study design limitations, results of this project provide further evidence about school-based immunization programs as an effective strategy for improving HPV vaccination rates among Kentucky and U.S. adolescents.

South-East Asia Region

Asiedu, G. B., et al. **Vietnamese Health Care Providers' Preferences Regarding Recommendation of HPV Vaccines.** *Asian Pac J Cancer Prev.* 2015; 16(12): 4895-4900.

Physician recommendation is an important predictor of HPV vaccine acceptance; however, physician willingness and preferences regarding HPV vaccination may be influenced by factors including patient age, vaccine type, and cost. A cross-sectional survey was administered to a convenience sample of health care providers in Da Nang, Vietnam, to evaluate awareness, perceptions about HPV and HPV vaccines, and willingness to vaccinate a female patient. Willingness to vaccinate was evaluated using a full-factorial presentation of scenarios featuring the following factors: vaccine cost (free vs 1,000,000 VND), patient age (12, 16, or 22 years), and HPV vaccine type (bivalent vs quadrivalent). Responses from 244 providers were analyzed; providers had a mean age of 34+/-11.9 years; a majority were female, married, and had children of their own. Thirty-six percent specialized in obstetrics/gynecology and 24% were providers in family medicine. Of the three factors considered in conjoint analysis, vaccine cost was the most important factor in willingness to vaccinate, followed by patient age, and vaccine type. The most favorable scenario for vaccinating a female patient was when the vaccine was free, the patient was 22

years of age, and the HPV4 vaccine was described. In multivariable analysis, older age, being a physician, being married, and having children were all associated with increased willingness to recommend HPV vaccination ($p < 0.05$). Provider willingness is an important aspect of successful HPV vaccination programs; identifying preferences and biases in recommendation patterns will highlight potential areas for education and intervention.

Barbaro, B. and J. M. Brotherton **Assessing HPV vaccine coverage in Australia by geography and socioeconomic status: are we protecting those most at risk?** *Aust N Z J Public Health* 2014; 38(5): 419-423.

OBJECTIVE: To determine whether HPV vaccine coverage in 12-13-year-olds varies by geographical area, remoteness and ecological level indicators of socioeconomic status (SES). **METHOD:** Data from the National HPV Vaccination Program Register (NHVPR) were analysed at Statistical Local Area (SLA) level, by the Index of Relative Disadvantage (IRSD) and the Australian Standard Geographical Classification Remoteness Structure. **RESULTS:** Nationally, 73% of females aged 12-13 years in 2007 were fully vaccinated against HPV. Coverage in low SES areas (71.5%) was 4.1 percentage points lower than coverage in high SES areas (75.6%). Uptake of the first two doses was higher in the very remote parts of Australia (dose 1 - 88.5%, dose 2 - 81.8%) than in major cities (dose 1 - 83.4%, dose 2 - 80.2%), but not for dose 3 where coverage in major cities was 3% higher (73.6% versus 71.4%). **CONCLUSION:** Notifications of HPV vaccine doses delivered to females aged 12-13 through schools suggest a high and relatively equal uptake across socioeconomic groups. Females in remote regions have the highest uptake of dose 1 but are least likely to complete the course. This may be due to particular challenges in vaccine delivery to residents of remote areas.

Dorji, T., et al. **Introduction of a National HPV vaccination program into Bhutan.** *Vaccine*. 2015; 33(31): 3726-3730.

BACKGROUND: Cervical cancer is the most common cancer in Bhutanese women. To help prevent the disease, the Ministry of Health (MoH) developed a national human papillomavirus (HPV) vaccine program. **METHODS:** MoH considerations included disease incidence, the limited reach of cervical screening, poor outcomes associated with late diagnosis of the disease, and Bhutan's ability to conduct the program. For national introduction, it was decided to implement routine immunization for 12 year-old girls with the quadrivalent HPV6/11/16/18 (QHPV) vaccine and a one-time catch-up campaign for 13-18 year-old girls in the first year of the program (2010). Health workers would administer the vaccine in schools, with out-of-school girls to receive the vaccine at health facilities. From 2011, HPV vaccination would enter into the routine immunization schedule using health-center delivery. **RESULTS:** During the initial campaign in 2010, over 130,000 doses of QHPV were administered and QHPV 3-dose vaccination coverage was estimated to be around 99% among 12 year-olds and 89% among 13-18 year-olds. QHPV vaccine was well tolerated and no severe adverse events were reported. In the three following years, QHPV vaccine was administered routinely to 12 year-olds primarily through health centers instead of schools, during which time the population-level 3-dose coverage decreased to 67-69%, an estimate which was confirmed by individual-level survey data in 2012 (73%). In 2014, when HPV delivery was switched back to schools, 3-dose coverage rose again above 90%. **DISCUSSION:** The rapid implementation and high coverage of the national HPV vaccine program in Bhutan were largely attributable to the strength of political commitment, primary healthcare and support from the education system. School-based delivery appeared clearly superior to health centers in achieving high-coverage among 12 year-olds. **CONCLUSIONS:** Bhutan's lessons for other low/middle-income countries include the superiority of school-based vaccination and the feasibility of a broad catch-up campaign in the first year.

Hussain, S., et al. **Perception of human papillomavirus infection, cervical cancer and HPV vaccination in North Indian population.** PLoS One. 2014; 9(11): e112861.

BACKGROUND: Human Papillomavirus (HPV) -associated cervical cancer is the second-most common cancer in women worldwide but it is the most frequent gynaecological cancer and cancer associated death in India women. The objective of this study was to assess knowledge about cervical cancer, HPV, HPV vaccine, HPV vaccine acceptance among school and undergraduates students and their parent's perception about acceptance of HPV vaccine in Northern part of India (Delhi and NCR regions). **MATERIALS AND METHODS:** A qualitative questionnaire based survey among 2500 urban/rural students aged 12-22 years was conducted. **RESULTS:** Overall, a low frequency (15%) of HPV and cervical cancer awareness was observed in students and their parents. However, the awareness was much higher in females belonging to urban setup compared to boys with a perception that HPV causes cervical cancer in women only. Additionally, only (13%) participants who were aware of cervical cancer and HPV) were willing to accept HPV vaccination. Apparently, parents of female students were two times more willing to accept HPV vaccination for their ward than male students ($p < 0.001$; OR 95%CI = 2.09 (1.58-2.76)). **CONCLUSION:** Cervical cancer and HPV awareness among school, undergraduate students and also to their parents was found to be very low in this part of India. The level of awareness and education appears to be insignificant determinants in rural compared to urban setup. Better health education will be needed to maximize public awareness for cervical cancer prevention.

Kruiroongroj, S., et al. **Knowledge, acceptance, and willingness to pay for human papilloma virus (HPV) vaccination among female parents in Thailand.** Asian Pac J Cancer Prev. 2014; 15(13): 5469-5474.

BACKGROUND: This study aimed to examine the level of knowledge, attitude, acceptance, and willingness to pay (WTP) for HPV vaccination among female parents of girls aged 12-15 years in Thailand. **MATERIALS AND METHODS:** A cross-sectional survey was conducted in eight schools across Bangkok. **RESULTS:** Of 1,200 questionnaires sent out, a total of 861 questionnaires were received. Knowledge regarding the HPV vaccine among parents was quite low. Only half of the parents knew about the link between HPV and cervical cancer while one-third of them knew that the vaccine should be administered to the children before they become sexually active. Nevertheless, vaccine acceptance was high if it was offered for free: 76.9% for the bivalent and 74.4% for the quadrivalent vaccine. The proportion of respondents who were willing to copay for the vaccine if it was not totally free was also high, ranging from 68.9% for the bivalent to 67.3% for the quadrivalent vaccine. No significant difference between bivalent and quadrivalent vaccines in terms of prevalence of acceptance and willingness to pay was found. About one-third of the participants, who were willing to copay for the vaccine if it was not offered for free, indicated that they would copay less than 500 baht (30 baht = approx US\$1) for three doses of bivalent vaccine. **CONCLUSIONS:** Substantial effort should be made to educate parents prior to introduction of a national HPV vaccination program. In terms of acceptance, either bivalent or quadrivalent vaccines can be recommended.

LaMontagne, D. S., et al. **Qualitative study of the feasibility of HPV vaccine delivery to young adolescent girls in Vietnam: evidence from a government-implemented demonstration program.** BMC Public Health 2014; 14: 556.

BACKGROUND: Introduction of human papillomavirus (HPV) vaccine in national programs has proceeded apace since 2006, mostly in high-income countries. Recently concluded pilots of HPV vaccination in low-income countries have provided important lessons learned for these settings; however, rigorous evaluations of the feasibility of these delivery strategies that effectively reach young adolescents have been few. This paper presents results from a qualitative evaluation of a demonstration program which implemented school-based and health center-based HPV vaccinations to all girls in grade 6, or 11 years of age, for two years in four districts of Vietnam. **METHODS:** Using semi-structured interviews of

131 health and education staff from local, district, province, and national levels and 26 focus-group discussions with local project implementers (n = 153), we conducted a qualitative two-year evaluation to measure the impact of HPV vaccinations on the health and education systems. RESULTS: HPV vaccine delivery at schools or health centers was made feasible by: a. close collaboration between the health and education sectors, b. detailed planning for implementation, c. clearly defined roles and responsibilities for project implementers, d. effective management and supervision of vaccinations during delivery, and e. engagement with community organizations for support. Both the health and education systems were temporarily challenged with the extra workload, but the disruptions were short-lived (a few days for each of three doses) and perceived as worth the longer-term benefit of cervical cancer prevention. CONCLUSION: The learning from Vietnam has identified critical elements for successful vaccine delivery that can provide a model for other countries to consider during their planning of national rollout of HPV vaccine.

Manthiram, K., et al. **Sustaining motivation to immunize: exchanging lessons between India and the United States.** Hum Vaccin Immunother. 2014; 10(10): 2930-2934.

In our recent study on vaccine uptake and parental attitudes toward immunizations in urban South India, we found strong support for vaccination due to fear of vaccine-preventable diseases and confidence in the recommendations made by health care professionals. In this commentary, we will characterize the reasons behind strong parental motivation to immunize in South India and consider ways these motivators can be enhanced in the United States, where vaccine hesitancy has led to outbreaks of vaccine-preventable disease. In addition, we will also discuss lessons that can be learned from the hesitancy movements in the United States and applied in India to maintain strong support for vaccination.

Rajiah, K., et al. **Awareness and acceptance of human papillomavirus vaccination among health sciences students in Malaysia.** Virusdisease. 2015; 26(4): 297-303.

The major cause of cervical cancer is human papillomavirus (HPV) for which vaccination is available. The success HPV vaccination programme largely depend on the degree of knowledge of the healthcare providers who can recommend to the public. Health sciences students as future healthcare providers play a major role in HPV vaccination initiatives. The objective of this study was to evaluate the knowledge, attitude, practice and to find out the willingness to pay for HPV vaccination among the health sciences students in a private university. The cross-sectional study was conducted among the university students studying health sciences program using a validated questionnaire to measure their awareness and acceptance of HPV vaccination. The students demonstrated moderate knowledge about HPV infection and vaccination with mean knowledge scores of 9.3 out of 17. Students were showing positive attitude towards HPV vaccination with mean scores of 3.80 out of 5. However, low HPV vaccination uptake rate was reported among the students. Most of the students were willing to recommend HPV vaccine. The participants felt that the cost is the major barrier towards HPV vaccination and they felt the government should cover the cost of vaccination for all. The results of this study may be helpful in establishing educational policies on cervical cancer-related topics in the universities.

Western Pacific Region

Brotherton, J. M., et al. **Estimating human papillomavirus vaccination coverage among young women in Victoria and reasons for non-vaccination.** *Sex Health.* 2015.

Background: Adult Australian women aged 18 to 26 years were offered human papillomavirus (HPV) vaccine in a mass catch up campaign between 2007 and 2009. Not all doses administered were notified to Australia's HPV vaccine register and not all young women commenced or completed the vaccine course. Methods: We surveyed vaccine age-eligible women as part of the Victorian Population Health Survey 2011-2012, a population based telephone survey, to ascertain self-reported vaccine uptake and reasons for non-vaccination or non-completion of vaccination among young women resident in the state of Victoria, Australia. Results: Among 956 women surveyed, 62.3 per cent (57.8-66.6%) had been vaccinated against HPV and coverage with three doses was estimated at 53.7 per cent (49.1-58.2%). These estimates are higher than register-based estimates for the same cohort, which were 57.8 per cent and 37.2 per cent respectively. A lack of awareness about needing three doses and simply forgetting, rather than fear or experience of side effects, were the most common reasons for failure to complete all three doses. Among women who were not vaccinated, the most frequent reasons were not knowing the vaccine was available, perceiving they were too old to benefit, or not being resident in Australia at the time. Conclusions: It is likely that at least half of Victoria's young women were vaccinated during the catch-up program. This high level of coverage is likely to explain the marked reductions in HPV infection, genital warts and cervical disease already observed in young women in Victoria.

Canfell, K., et al. **Factors related to vaccine uptake by young adult women in the catch-up phase of the National HPV Vaccination Program in Australia: Results from an observational study.** *Vaccine.* 2015; 33(20): 2387-2394.

BACKGROUND: Australia commenced a publically-funded, National Human Papillomavirus (HPV) Vaccination Program in 2007 with a two year catch-up phase for females aged 12-26 years. OBJECTIVE: To identify the factors associated with the uptake of the HPV vaccine (which has a recommended 3-dose schedule in Australia) by young adult women vaccinated by general practitioners and community-based programs within the catch-up phase. METHODS: 1139 women who were eligible to receive the free HPV vaccine during the catch-up period were recruited in 2008-2009 (age 20-29 years at recruitment), in New South Wales, after having a normal (negative) cervical smear result recorded on the NSW Pap Test Register. Participants completed a self-administered questionnaire providing information on vaccination status, and sociodemographic and other factors. RESULTS: Overall, 880 (77%) women reported receiving ≥ 1 dose of the vaccine and 777 women (68%) reported receiving ≥ 2 doses. In multivariable analysis (adjusting for the period for which each woman was eligible for free HPV vaccination), uptake of ≥ 1 dose of the vaccine was significantly associated with being born in Australia ($p < 0.01$), being single ($p = 0.02$), being nulliparous ($p < 0.01$), living in a higher socioeconomic status area (p -trend = 0.03), living in more remote areas ($p = 0.03$), drinking alcohol ($p < 0.01$) and using hormonal contraceptives ($p < 0.01$). Although vaccinated women were more likely to have fewer sexual partners than unvaccinated women (p -trend = 0.02), they were also more likely to report a prior sexually transmitted infection (STI) ($p = 0.03$). Similar factors were associated with receiving ≥ 2 doses. CONCLUSIONS: In this group, women living in higher socioeconomic status areas were more likely to be vaccinated against HPV in the catch-up phase of the national program. Although vaccinated women tended to have fewer sexual partners, they also reported prior STIs, which may be a marker of increased risk of prior exposure to HPV. The findings of this study reinforce the continuing need to prioritise equitable delivery of vaccination to various population subgroups.

Egawa-Takata, T., et al. **Survey of Japanese mothers of daughters eligible for human papillomavirus vaccination on attitudes about media reports of adverse events and the suspension of governmental recommendation for vaccination.** *J Obstet Gynaecol Res.* 2015; 41(12): 1965-1971.

AIM: Following media reports of adverse medical events surrounding human papillomavirus (HPV) vaccination and the suspension of Japanese governmental recommendation, most adolescents have refrained from receiving the vaccine. This represents a national critical event, because the incidence of cervical cancer in Japan continues to increase. **METHODS:** We conducted an Internet survey to investigate why Japanese adolescent girls decline, continue or discontinue their HPV vaccination, how their mothers influence their decision, and the mothers' feelings about future HPV vaccination for their daughters. One thousand mothers with daughters 10-18 years of age were recruited for our questionnaire. **RESULTS:** Our results suggest that acceptance of the HPV vaccine was determined predominantly by the mother's perceptions of risk versus benefits, rather than the daughter's wishes. The mothers' knowledge of the benefits of the prophylactic HPV vaccine and their attitude toward cervical cancer screening influenced their decision whether to allow their daughter to receive future vaccinations. The tenor of survey responses of those mothers who were anti-vaccine changed significantly to the positive in response to a proposed scenario where the governmental recommendation for the HPV vaccine was reinstated, whereas a hypothetical educational intervention sheet did not significantly change their attitude. **CONCLUSIONS:** Promotion of the HPV vaccine through comprehensive education for both mothers and daughters, not only on the vaccine itself, but also about cervical cancer and screening, is required for any successful program to prevent cervical cancer.

Forbes, T. A., et al. **Vaccination uptake by vaccine-hesitant parents attending a specialist immunization clinic in Australia.** *Hum Vaccin Immunother.* 2015; 11(12): 2895-2903.

Vaccine hesitancy (VH) is an issue of global concern. The quality of communication between healthcare providers and parents can influence parental immunization acceptance. We aimed to describe immunization uptake following specialist immunization clinic (SIC) consultation for Australian children of VH parents as a cohort, and according to pre-clinic parental position on immunization. At a single tertiary pediatric SIC (RCH, Melbourne) a retrospective descriptive study classified VH families according to 3 proposed parental positions on immunization at initial clinic attendance. Immunization status at follow up was ascertained via the Australian Children's Immunization Register and National HPV Program Register and compared between groups. Of the VH cohort, 13/38 (34%) families were classified as hesitant, 21 (55%) as late/selective vaccinators and 4 (11%) as vaccine refusers. Mean follow up post-SIC attendance was 14.5 months. For the overall VH cohort, the majority chose selective immunization (42%) following SIC consultation. When analyzed by pre-clinic parental position on immunization, there was a trend for hesitant families to proceed with full immunization, selective families to continue selective immunization and refusing families to remain unimmunised ($p < 0.0001$). The most commonly omitted vaccines were hepatitis B (66%) and Haemophilus influenzae type B (55%), followed by the meningococcal C conjugate vaccine (53%) and measles, mumps and rubella vaccine (53%). Immunization outcome appears to correlate with pre-clinic parental position on immunization for the majority of families attending a SIC in Australia, with selective immunization the most common outcome. Tailored communication approaches based on parental position on immunization may optimise clinic resources and engagement of families, but require prospective research evaluation.

Garland, S. M. **The Australian experience with the human papillomavirus vaccine.** *Clin Ther.* 2014; 36(1): 17-23.

OBJECTIVE: The goal of this study was to review the current human papillomavirus (HPV) vaccine program and its outcomes to date in Australia. **METHODS:** This was a review of the published data relating to the introduction and subsequent measurable outcomes of the quadrivalent vaccine, which became

part of the Australian national HPV immunization program in 2007. Australia commenced an ongoing, schoolbased, government-funded, HPV vaccination program using the quadrivalent vaccine from April 2007 for adolescent female subjects aged 12 to 13 years, together with a catch-up program for female subjects 13 to 26 years of age from July 2007 to December 31, 2009. RESULTS: The Australian community (lay and clinical) have embraced the program, resulting in high coverage with >70% for 3 doses in the 12- to 13-year-old ongoing target population. Vaccine effectiveness (outcomes of vaccination in a real-world setting) is already being seen. This effectiveness has been noted in significant reductions in HPV vaccine-related infections in vaccine eligible age female subjects (77% fall in prevalence), rapid reduction of >90% in genital warts (first marker of disease reduction, as well as herd immunity), and reduction in high-grade cervical lesions in this age group. These remarkable changes so soon after implementation of the vaccine in the country occurred faster, and to a greater extent, than anyone could have predicted. CONCLUSIONS: These findings from Australia should encourage other countries to follow suit, with the ultimate aim of translating treatment into reductions in HPV-related neoplasia globally. The greatest success from such an approach will only be realized when prophylactic vaccines are rolled out effectively, with high coverage and at affordable costs, to those areas of the world with the highest burden of disease. To achieve this outcome requires government endorsement and commitment; education of the community at large; realization of the safety, efficacy, and immunogenicity of the available prophylactic vaccines in reducing HPV-related infections and disease, especially neoplasia; and governments procuring vaccines at affordable prices through the various options now available (eg, support from the GAVI Alliance to eligible countries, tiered pricing, negotiation with pharmaceutical manufacturers). We have the tools to reach this goal, and it is time these tools were implemented.

Hanley, S. J., et al. **An exploratory study of Japanese fathers' knowledge of and attitudes towards HPV and HPV vaccination: does marital status matter?** Asian Pac J Cancer Prev. 2014; 15(4): 1837-1843.

BACKGROUND: No studies on male attitudes towards HPV and HPV vaccination have been conducted in Japan, and little is known globally whether attitudes of single fathers differ to those living with a female partner. This exploratory study assessed whether Japanese fathers were likely to have their daughter vaccinated against HPV in a publically funded program and whether any differences existed regarding attitudes and knowledge about HPV according to marital status. MATERIALS AND METHODS: Subjects were 27 fathers (16 single; 11 married) who took part in a study on HPV vaccine acceptability aimed at primary caregivers of girls aged 11-14 yrs in three Japanese cities between July and December 2010. RESULTS: Knowledge about HPV was extremely poor (mean score out of 13 being 2.74 +/- 3.22) with only one (3.7%) participant believing he had been infected with HPV and most (81.4%) believing they had no or low future risk. No difference existed regarding knowledge or awareness of HPV according to marital status. Concerning perceived risk for daughters, single fathers were significantly more likely to believe their daughter was at risk for both HPV (87.5% versus 36.4%; p=0.01) and cervical cancer (75.0% versus 27.3%; p=0.02). Acceptability of free HPV vaccination was high at 92% with no difference according to marital status, however single fathers were significantly more likely (p=0.01) to pay when vaccination came at a cost. Concerns specific to single fathers included explaining the sexual nature of HPV and taking a daughter to a gynecologist to be vaccinated. CONCLUSIONS: Knowledge about HPV among Japanese fathers is poor, but HPV vaccine acceptability is high and does not differ by marital status. Providing sexual health education in schools that addresses lack of knowledge about HPV as well as information preferences expressed by single fathers, may not only increase HPV vaccine acceptance, but also actively involve men in cervical cancer prevention strategies. However, further large-scale quantitative studies are needed.

La Vincente, S. F., et al. **Implementation of a national school-based Human Papillomavirus (HPV) vaccine campaign in Fiji: knowledge, vaccine acceptability and information needs of parents.** BMC Public Health. 2015; 15: 1257.

BACKGROUND: In 2008 Fiji implemented a nationwide Human Papillomavirus (HPV) vaccine campaign targeting all girls aged 9-12 years through the existing school-based immunisation program. Parents of vaccine-eligible girls were asked to provide written consent for vaccination. The purpose of this study was to describe parents' knowledge, experiences and satisfaction with the campaign, the extent to which information needs for vaccine decision-making were met, and what factors were associated with vaccine consent. **METHODS:** Following vaccine introduction, a cross-sectional telephone survey was conducted with parents of vaccine-eligible girls from randomly selected schools, stratified by educational district. Factors related to vaccine consent were explored using Generalised Estimating Equations. **RESULTS:** There were 560 vaccine-eligible girls attending the participating 19 schools at the time of the campaign. Among these, 313 parents could be contacted, with 293 agreeing to participate (93.6%). Almost 80% of participants reported having consented to HPV vaccination (230/293, 78.5%). Reported knowledge of cervical cancer and HPV prior to the campaign was very low. Most respondents reported that they were satisfied with their access to information to make an informed decision about HPV vaccination (196/293, 66.9%). and this was very strongly associated with provision of consent. Despite their young age, the vaccine-eligible girls were often involved in the discussion and decision-making. Most consenting parents were satisfied with the campaign and their decision to vaccinate, with almost 90% indicating they would consent to future HPV vaccination. However, negative media reports about the vaccine campaign created confusion and concern. Local health staff were cited as a trusted source of information to guide decision-making. Just over half of the participants who withheld consent cited vaccine safety fears as the primary reason (23/44, 52.3%). **CONCLUSION:** This is the first reported experience of HPV introduction in a Pacific Island nation. In a challenging environment with limited community knowledge of HPV and cervical cancer, media controversy and a short lead-time for community education, Fiji has implemented an HPV vaccine campaign that was largely acceptable to the community and achieved a high level of participation. Community sensitisation and education is critical and should include a focus on the local health workforce and the vaccine target group.

Mahajan, D., et al. Surveillance of adverse events following immunisation in Australia annual report, 2013. *Commun Dis Intell Q Rep.* 2015; 39(3): E369-386.

This report summarises Australian passive surveillance data for adverse events following immunisation (AEFI) for 2013 reported to the Therapeutic Goods Administration (TGA) for 2013 and describes reporting trends over the 14-year period 1 January 2000 to 31 December 2013. There were 3,161 AEFI records for vaccines administered in 2013. This is an annual AEFI reporting rate of 13.9 per 100,000 population, the 2nd highest since 2000 and an increase of 59% compared with 2012 (1,994 AEFI records; 8.8 per 100,000 population). The increase was partly due to implementation of enhancements to vaccine safety reporting. This included stimulated reporting of AEFI as part of the extension of national human papillomavirus (HPV) vaccination under the National Immunisation Program to males aged 12-13 years, along with a catch-up program for males aged 14 and 15 years in February 2013 (n=785; includes males and females), in which certain events, such as syncope, were closely monitored. Eighty-two per cent (n=341/414) of the syncope reports were following HPV vaccination and of these 57% (n=195) were males and 43% (n=146) were females. In addition, reporting rates for most other the vaccines were higher in 2013 compared with 2012. The majority of AEFI reports described non-serious events while 5% (n=158) were classified as serious. There were 4 reports of death; however, all deaths were investigated by the TGA and no clear causal relationship with vaccination was found. The most commonly reported reactions were injection site reaction (13%), rash (10%), pyrexia (8%), and syncope (7%).

Miyagi, E., et al. **Web-based recruiting for a survey on knowledge and awareness of cervical cancer prevention among young women living in Kanagawa prefecture, Japan.** *Int J Gynecol Cancer.* 2014; 24(7): 1347-1355.

OBJECTIVES: Cervical cancer (CC) incidence and mortality among young women have been increasing in Japan. To develop effective measures to combat this, we assessed the feasibility of using a social networking site (SNS) to recruit a representative sample of young women to conduct a knowledge and attitude study about CC prevention via an internet-based questionnaire. **METHODS:** From July 2012 to March 2013, advertising banners targeting women aged 16 to 35 years in Kanagawa Prefecture were placed on Facebook in a similar manner as an Australian (AUS) study conducted in 16- to 25-year-olds in 2010 and on a homepage to advertise our CC advocacy activities. Eligible participants were emailed instructions for accessing our secure Web site where they completed an online survey including demographics, awareness, and knowledge of human papillomavirus (HPV) and CC. Data for the study population were compared with the general Japanese population and the AUS study. **RESULTS:** Among 394 women who expressed interest, 243 (62%) completed the survey, with 52% completing it via Facebook. Women aged 26 to 35 years, living in Yokohama City, with an education beyond high school, were overrepresented. Participants had high awareness and knowledge of HPV and CC, comparable with the AUS study participants. However, the self-reported HPV vaccination rate (22% among participants aged 16-25 years) and the recognition rate of the link between smoking and CC (31%) were significantly lower than in the AUS study (58% and 43%, respectively) ($P < 0.05$). Significant predictors of high knowledge scores about HPV included awareness of HPV vaccine ($P < 0.001$) and self-reported HPV vaccination ($P < 0.05$). **CONCLUSIONS:** The SNS and homepage are efficient methods to recruit young women into health surveys, which can effectively be performed online. A nationwide survey using SNSs would be an appropriate next step to better understand the current lack of uptake of the national HPV vaccine program by young women in Japan.

Saville, A. M. **Cervical cancer prevention in Australia: Planning for the future.** *Cancer Cytopathol.* 2016; 124(4): 235-240.

The high rate of coverage that has been achieved to date by the Australian government's Human Papillomavirus (HPV) Vaccination Program has already led to profound reductions in the prevalence of biopsy-confirmed, high-grade abnormalities and of vaccine-preventable HPV types in Australia. Declines in the prevalence of vaccine preventable HPV have occurred not only in vaccinated women but also in unvaccinated women, suggesting a herd-immunity effect. These declines were anticipated on the basis of modelling and were the major drivers for the changes proposed to the Australian National Cervical Screening Program. The federal and state-based Australian governments established a "Renewal Steering Committee," which conducted a literature search and a review of the available evidence to assess its applicability and quality. Together with this information the committee also used modeling to determine the optimal screening pathway for cervical cancer screening and constructed a plan for implementing the changes that will be required to transition from the currently successful screening program to the renewed program. The committee recommended that Australia move to a screening program based on testing every 5 years using an HPV test with partial genotyping with reflex liquid-based cytology (LBC) triage for HPV-vaccinated and unvaccinated women ages 25 to 69 years, and an additional exit test for women up to age 74 years. Primary HPV testing and reflex LBC will be funded by government. Symptomatic women outside the screening program will also be able to access government funded testing. The new screening program, to be rolled out in 2017, will also provide a cost-effective framework for an evaluation of the national HPV vaccination program, enabling ongoing monitoring of HPV genotypes and cervical lesions in screened women.

Skinner, S. R., et al. **HPV.edu study protocol: a cluster randomised controlled evaluation of education, decisional support and logistical strategies in school-based human papillomavirus (HPV) vaccination of adolescents.** BMC Public Health. 2015; 15: 896.

BACKGROUND: The National Human Papillomavirus (HPV) Vaccination Program in Australia commenced in 2007 for females and in 2013 for males, using the quadrivalent HPV vaccine (HPV 6,11,16,18). Thus far, we have demonstrated very substantial reductions in genital warts and in the prevalence of HPV among young Australian women, providing early evidence for the success of this public health initiative. Australia has a long history of school-based vaccination programs for adolescents, with comparatively high coverage. However, it is not clear what factors promote success in a school vaccination program. The HPV.edu study aims to examine: 1) student knowledge about HPV vaccination; 2) psychosocial outcomes and 3) vaccination uptake. **METHODS/DESIGN:** HPV.edu is a cluster randomised trial of a complex intervention in schools aiming to recruit 40 schools with year-8 enrolments above 100 students (approximately 4400 students). The schools will be stratified by Government, Catholic, and Independent sectors and geographical location, with up to 20 schools recruited in each of two states, Western Australia (WA) and South Australia (SA), and randomly allocated to intervention or control (usual practice). Intervention schools will receive the complex intervention which includes an adolescent intervention (education and distraction); a decisional support tool for parents and adolescents and logistical strategies (consent form returns strategies, in-school mop-up vaccination and vaccination-day guidelines). Careful process evaluation including an embedded qualitative evaluation will be undertaken to explore in depth possible mechanisms for any observed effect of the intervention on primary and secondary outcomes. **DISCUSSION:** This study is the first to evaluate the relative effectiveness of various strategies to promote best practice in school-based vaccination against HPV. The study aims to improve vaccination-related psychosocial outcomes, including adolescent knowledge and attitudes, decision-making involvement, self-efficacy, and to reduce fear and anxiety. The study also aims to improve school vaccination program logistics including reduction in time spent vaccinating adolescents and increased number of consent forms returned (regardless of decision). Less anxiety in adolescents will likely promote more efficient vaccination, which will be more acceptable to teachers, nurses and parents. Through these interventions, it is hoped that vaccination uptake will be increased. **TRIAL REGISTRATION:** Australian and New Zealand Clinical Trials Registry, ACTRN12614000404628 , 14.04.2014.

Sukegawa, A., et al. **Three-year questionnaire survey on human papillomavirus vaccination targeting new female college students.** J Obstet Gynaecol Res. 2015; 41(1): 99-106.

AIM: A questionnaire survey was conducted at fixed points to describe changes over a 3-year period in the human papillomavirus (HPV) vaccination uptake rate among young women. Several factors obtained from the questionnaire were investigated in relation to HPV vaccination. **METHODS:** The study was conducted at two universities in Yokohama City, Japan. Newly enrolled female students of the universities were recruited to participate in this study in 2011, 2012 and 2013. The study participants were asked about their HPV vaccination status. They were also questioned about factors that potentially influenced HPV vaccination, such as current age, place of residence during high school, and knowledge related to cervical cancer and HPV vaccination. **RESULTS:** The proportion of vaccinated participants dramatically increased in 2013 (48.7%) in comparison to 2011 (5.4%) and 2012 (13.5%). Three factors were positively related to HPV vaccination: being 18 years old in 2013, which means that they were eligible for a financial support program ($P < 0.001$); living in the study city, in which HPV vaccination was well conducted ($P < 0.001$); and proper knowledge of cervical cancer and HPV vaccination ($P < 0.001$). **CONCLUSION:** The HPV vaccination uptake rate in 2013 dramatically increased from that in 2011. Official financial support and publicity work were likely to have had an effect on the HPV vaccination uptake rate.

Wang, S. M., et al. **Human papillomavirus vaccine awareness, acceptability, and decision-making factors among Chinese college students.** *Asian Pac J Cancer Prev.* 2014; 15(7): 3239-3245.

BACKGROUND: College students are recommended as the target groups for catch-up human papillomavirus (HPV) vaccination. Systematical exploration of awareness, acceptability, and decision-making factors of HPV vaccination among Chinese college students has been limited. **MATERIALS AND METHODS:** A multi-center survey was conducted in mainland China between November 2011 and May 2012. College students aged 18-22 years were stratified by their grade, gender, and major for sampling. Socio-demographic and HPV-related information such as knowledge, perceptions, acceptability, and attitudes were collected through a questionnaire. **RESULTS:** A total of 3,497 undergraduates completed the questionnaire, among which 1,686 were males. The acceptability of the HPV vaccine was high (70.8%). Undergraduates from high-level universities, at lower grade, or with greater prior knowledge of HPV vaccines showed higher acceptability of HPV vaccination (ptrend <0.001). Additionally, undergraduates with vaccination experience outside the National Expanded Program on Immunization (OR=1.29; 95%CI: 1.10-1.51) or fear of HPV-related diseases (OR=2.79; 95%CI: 2.28-3.41) were more willing to accept HPV vaccination. General knowledge of HPV vaccine was low among undergraduates, and safety was a major concern (71.05%). The majority of students wished to pay less than 300RMB for HPV vaccine and chose the Chinese Center for Disease Control and Prevention as the most appropriate venue for vaccination. **CONCLUSIONS:** Although most undergraduates demonstrate positive attitudes towards HPV vaccination, challenges pertaining to introduction exist in China. Corresponding proactive education and governmental subsidy to do so are urgently needed by this age-group population. Suggestions and potential strategies indicated may help shape the future HPV vaccination program in China.

Yuji, K. and Nakada, H. **Compensation programs after withdrawal of the recommendation for HPV vaccine in Japan.** *Hum Vaccin Immunother.* 2016; 12(5): 1321-1324.

HPV vaccinations were recommended with the backing of a Japanese government subsidy program in 2010, and were included in the National Immunization Program in April 2013. However, the Ministry of Health, Labour, and Welfare withdrew the recommendation for the HPV vaccination in June 2013. We investigated HPV vaccine injury compensation programs for both the national and local governments. Approximately 3.38 million girls were vaccinated, and 2,584 complained of health problems. The majority of these received the vaccine shot as a non-routine vaccination. In total, 98 people developed health problems and applied for assistance from 2011 to 2014, but no cases have been processed since October 2014. Several local governments are providing their own compensation program for cases of vaccine adverse reactions, but the number is extremely low (16 of 1,741 municipalities and 1 of 47 prefectures). The local governments that are providing compensation are largely those where HPV vaccine victim support groups are prominent. The confusion regarding the national program for HPV vaccine injury was caused by the discrepancy between the compensation programs for those vaccinated under the immunization law and for those who received voluntary vaccinations. The establishment of a new compensation program might be key to finding a lasting resolution.

Zhang, S. K., et al. **Knowledge of human papillomavirus vaccination and related factors among parents of young adolescents: a nationwide survey in China.** *Ann Epidemiol.* 2015; 25(4): 231-235.

PURPOSE: To investigate the human papillomavirus (HPV) vaccine-related knowledge and factors associated with the knowledge among parents of young adolescents in China. **METHODS:** The study was based on data of a survey carried out in seven geographic regions of China. Parents of students in junior middle school were surveyed during parents' meetings. **RESULTS:** A total of 2895 parents were included in the analyses. Of parents, 38.3% responded with "yes" to more than three of the six knowledge questions, among whom only 4.5% of them correctly answered all six questions. Social benefit programs (41.3%), doctors and/or nurses (39.7%), and newspapers and/or magazines (36.5%) were selected as the

top three sources of HPV-related knowledge. Mothers, parents who work in the health care sector, and parents with a higher annual income or with vaccination experience outside the expanded program on immunization showed a better knowledge base. Parents who consented to sex education for children or showed fear of cervical cancer were likely to have more HPV-related knowledge. In particular, the knowledge level of parents with prior consultation regarding HPV vaccines was higher. **CONCLUSIONS:** Parents of young adolescents in China possessed a low level of HPV vaccine-related knowledge. Findings highlight the need for tailored health education through different channels to improve HPV-related knowledge among parents.

Low- and middle-income countries

Cobos Munoz, D., et al. **Exposing concerns about vaccination in low- and middle-income countries: a systematic review.** *Int J Public Health* 2015; 60(7): 767-780.

OBJECTIVES: Concerns about vaccination lead to under- and no-vaccination. Our objective is to synthesise and expose evidence on individuals' and communities' concerns about vaccination to influence current debates on strategies to improve vaccination coverage in low- and middle-income countries. **METHODS:** Systematic literature review till February 2014, following standard methods. Published and grey literature that focused on individuals and community concerns on childhood vaccinations were selected. **RESULTS:** 44 quantitative, qualitative and mixed-methods studies were included. Main reported concerns referred to perceptions of vaccine harms (e.g. attribution of fatal events). Other concerns included programme distrust (mainly due to rumours and conspiracies) and health system unfriendliness. **CONCLUSIONS:** Concerns about vaccination are widespread and further worsen the challenges related to programmatic and health system barriers to vaccination. There is a disconnection between qualitative and quantitative research which misses the opportunity to quantify what is reported in the former. Strikingly, there is a wealth of evidence on concerns but much lesser evidence on interventions to address them. We welcome World Health Organization initiative to tackle vaccine hesitancy and call for the synthesis of evidence and production of guidance on strategies to address concerns on vaccination.

Hanson, C. M., et al. **Gavi HPV Programs: Application to Implementation.** *Vaccines (Basel)* 2015; 3(2): 408-419.

Developing countries disproportionately suffer from the burden of cervical cancer yet lack the resources to establish systematic screening programs that have resulted in significant reductions in morbidity and mortality in developed countries. Human Papillomavirus (HPV) vaccination provides an opportunity for primary prevention of cervical cancer in low-resource settings through vaccine provision by Gavi The Vaccine Alliance. In addition to the traditional national introduction, countries can apply for a demonstration program to help them make informed decisions for subsequent national introduction. This article summarizes information from approved Gavi HPV demonstration program proposals and preliminary implementation findings. After two rounds of applications, 23 countries have been approved targeting approximately 400,000 girls for vaccination. All countries are proposing primarily school-based strategies with mixed strategies to locate and vaccinate girls not enrolled in school. Experiences to date include: Reaching marginalized girls has been challenging; Strong coordination with the education sector is key and overall acceptance has been high. Initial coverage reports are encouraging but will have to be confirmed in population based coverage surveys that will take place later this year. Experiences from these countries are consistent with existing literature describing other HPV vaccine pilots in low-income settings.

Ladner, J., et al. **Performance of 21 HPV vaccination programs implemented in low and middle-income countries, 2009-2013.** BMC Public Health. 2014; 14: 670.

BACKGROUND: Cervical cancer is the third most common cancer in women worldwide, with high incidence in lowest income countries. Vaccination against Human Papilloma Virus (HPV) may help to reduce the incidence of cervical cancer. The aim of the study was to analyze HPV vaccination programs performance implemented in low and middle-income countries. **METHODS:** The Gardasil Access Program provides HPV vaccine at no cost to help national institutions gain experience implementing HPV vaccination. Data on vaccine delivery model, number of girls vaccinated, number of girls completing the three-dose campaign, duration of vaccination program, community involvement and sensitization strategies were collected from each program upon completion. Vaccine Uptake Rate (VUR) and Vaccine Adherence between the first and third doses (VA) rate were calculated. Multivariate linear regressions analyses were fitted. **RESULTS:** Twenty-one programs were included in 14 low and middle-income countries. Managing institutions were non-governmental organizations (NGOs) (n = 8) or Ministries of Health (n = 13). Twelve programs were school-based, five were health clinic-based and four utilized a mixed model. A total of 217,786 girls received a full course of vaccination. Mean VUR was 88.7% (SD = 10.5) and VA was 90.8% (SD = 7.3). The mean total number of girls vaccinated per program-month was 2,426.8 (SD = 2,826.6) in school model, 335.1 (SD = 202.5) in the health clinic and 544.7 (SD = 369.2) in the mixed models ($p = 0.15$). Community involvement in the follow-up of girls participating in the vaccination campaign was significantly associated with VUR. Multivariate analyses identified school-based (beta = 13.35, $p = 0.001$) and health clinic (beta = 13.51, $p = 0.03$) models, NGO management (beta = 14.58, $p < 10(-3)$) and duration of program vaccination (beta = -1.37, $p = 0.03$) as significant factors associated with VUR. **CONCLUSION:** School and health clinic-based models appeared as predictive factors for vaccination coverage, as was management by an NGO; program duration could play a role in the program's effectiveness. Results suggest that HPV vaccine campaigns tailored to meet the needs of communities can be effective. These results may be useful in the development of national HPV vaccination policies in low and middle-income countries.

Sridhar, S., et al. **A systematic literature review of missed opportunities for immunization in low- and middle-income countries.** Vaccine. 2014; 32(51): 6870-6879.

BACKGROUND: Missed opportunities for immunization (MOIs) may contribute to low coverage in diverse settings, including developing countries. **METHODS:** We conducted a systematic literature review on MOIs among children and women of childbearing age from 1991 to the present in low- and middle-income countries. We searched multiple databases and the references of retrieved articles. Meta-analysis provided a pooled prevalence estimate and both univariate and multivariate meta-regression analysis was done to explore heterogeneity of results across studies. **RESULTS:** We found 61 data points from 45 studies involving 41,310 participants. Of the 45 studies, 41 involved children and 10 involved women. The pooled MOI prevalence was 32.2% (95% CI: 26.8-37.7) among children - with no change during the study period - and 46.9% (95% CI: 29.7-64.0%) among women of child-bearing age. The prevalence varied by region and study methodology but these two variables together accounted for only 12% of study heterogeneity. Among 352 identified reasons for MOIs, the most common categories were health care practices, false contraindications, logistic issues related to vaccines, and organizational limitations, which did not vary by time or geographic region. **CONCLUSIONS:** MOI prevalence was high in low- and middle-income settings but the large number of identified reasons precludes standardized solutions.

Tsu, V. D., et al. **Lessons learned from HPV vaccine delivery in low-resource settings and opportunities for HIV prevention, treatment, and care among adolescents.** J Acquir Immune Defic Syndr. 2014; 66 Suppl 2: S209-216.

BACKGROUND: Human papillomavirus (HPV) vaccines to prevent cervical cancer have become available in recent years and presented a new challenge to health systems, since they prevent a sexually transmitted virus and are most effective if they are delivered to young adolescent girls, a group not widely served by other health programs. Demonstration and pilot HPV vaccination programs undertaken in the past 7-8 years in low-resource settings have produced lessons that may be more broadly applied to other adolescent health interventions, particularly to those that attempt to reduce human immunodeficiency virus (HIV) infection. **METHODS:** A systematic literature review was undertaken to identify formal and informal evaluations of HPV vaccine use in low- and middle-income countries. Special attention was devoted to the detailed evaluations carried out on large demonstration projects in India, Peru, Uganda, and Vietnam. **RESULTS:** These lessons fall into 2 main categories: service delivery operations and community outreach and mobilization. Operational issues included venue and timing of vaccinations, definition of target population, micro-planning and coordination, integration with other services, and training. Community issues included consent, messages and channels, endorsement and support, and timing of mobilization efforts. **DISCUSSION:** Careful planning, good coordination across sectors and levels, and sensitive attention to the expressed needs for information and preferences for communication channels among youth, parents, and communities more broadly were among the key lessons that are relevant for HIV interventions, but many of the smaller details were also important. **CONCLUSIONS:** Applying or adapting these lessons to adolescent HIV services could accelerate effective program design and enhance success.

Not region specific

Lee, A., et al. **A home-school-doctor model to break the barriers for uptake of human papillomavirus vaccine.** BMC Public Health. 2015; 15: 935.

BACKGROUND: A high coverage of human papillomavirus (HPV) vaccination is required to achieve a clinically significant reduction in disease burden. Countries implementing free-of-charge national vaccination program for adolescent girls are still challenged by the sub-optimal uptake rate. Voluntary on-site school-based mass vaccination programs have demonstrated high coverage. Here, we tested whether this could be an option for countries without a government-supported vaccination program as in Hong Kong. **METHOD:** A Home-School-Doctor model was evolved based on extensive literature review of various health promotion models together with studies on HPV vaccination among adolescent girls. The outcome measure was uptake of vaccination. Factors associated with the outcome were measured by validated surveys in which 4,631 students from 24 school territory wide participated. Chi-square test was used to analyze association between the categorical variables and the outcome. Multivariate analysis was performed to identify independent variables associated with the outcome with vaccine group as case and non-vaccine group as control. **RESULTS:** In multivariate analysis, parental perception of usefulness of the Home-School-Doctor model had a very high odds ratio for uptake of HPV vaccination (OR 26.6, 95% CI 16.4, 41.9). Paying a reasonable price was another independent factor associated with increased uptake (OR 1.71, 95% CI 1.39, 2.1 for those with parents willing to pay US\$125-250 for vaccination). For parents and adolescents who were not sure where to get vaccination, this model was significantly associated with improved uptake rate (OR 1.66, 95% CI 1.23, 2.23). Concerns with side effects of vaccine (OR 0.70, 95% CI 0.55, 0.88), allowing daughters to make their own decisions (OR 0.49, 95% CI 0.38, 0.64) and not caring much about daughters' social life (95% CI 0.45, 0.92) were factors associated with a lower uptake. **DISCUSSION:** The findings of this study have added knowledge on how a school-based vaccination program would improve vaccine uptake rate even when the users need to pay. Our findings are consistent with other study that the most acceptable way to achieve high uptake of HPV vaccine is to offer voluntary school-based vaccination. **CONCLUSION:** A model of care incorporating the efforts and expertise of

academics and health professionals working closely with school can be applied to improve the uptake of vaccine among adolescent girls. Subsidized voluntary school-based vaccination scheme can be an option.

Paul, P. and Fabio, A. **Literature review of HPV vaccine delivery strategies: considerations for school- and non-school based immunization program.** *Vaccine*. 2014; 32(3): 320-326.

School-based vaccination is becoming a more widely considered method of delivering HPV immunizations to an adolescent population; however, many countries do not have experience with delivering adolescent vaccines or school-based programs. This literature review will summarize the experiences from countries implementing non-health facility-based and health facility-based vaccination programs and assess HPV vaccine coverage. In October 2012, a systematic search in PubMed for studies related to the evaluation of national/regional, pilot, or demonstration HPV immunization programs that worked within existing health system yielded nine articles, representing seventeen countries. School-based programs achieved high HPV vaccination coverage rates in 9 to 13-year-old girls across the different studies and geographic locations, suggesting non-health facility-based programs are possible for HPV vaccine introduction. Grade-based, compared to age-based, eligibility criteria may be easier to implement in school settings. More studies are needed to explore the methods to standardize estimates for HPV vaccine coverage so that programs can be appropriately evaluated.

Session 5 Barriers and opportunities in HPV screening programs

A Pubmed search was performed with the following selection criteria: HPV [title/abstract] AND screening [title/abstract] AND program [title/abstract] published in the last 5 years: 298 items were retrieved. A second pubmed search with the following selection criteria was performed: barriers [title/abstract] AND cervical cancer [title/abstract] AND screening[title/abstract] published in the last 5 years: 60 items were retrieved. References were imported in EndNote. Herein, a relevant manual selection of publications between 2013-2016 based on title and abstract was made. References are sorted by first authors name.

Abuelo, C. E., et al. **The Peru Cervical Cancer Screening Study (PERCAPS): the design and implementation of a mother/daughter screen, treat, and vaccinate program in the Peruvian jungle.** J Community Health. 2014; 39(3): 409-415.

Peru struggles to prevent cervical cancer (CC). In the jungle, prevention programs suffer from significant barriers although technology exists to detect CC precursors. This study used community based participatory research (CBPR) methods to overcome barriers. The objective was to evaluate the utility of CBPR techniques in a mother-child screen/treat and vaccinate program for CC prevention in the Peruvian jungle. The CC prevention program used self-sampling for human papillomavirus (HPV) for screening, cryotherapy for treatment and the HPV vaccine Gardasil for vaccination. Community health leaders (HL) from around Iquitos participated in a two half day educational course. The HLs then decided how to implement interventions in their villages or urban sectors. The success of the program was measured by: (1) ability of the HLs to determine an implementation plan, (2) proper use of research forms, (3) participation and retention rates, and (4) participants' satisfaction. HLs successfully registered 320 women at soup kitchens, schools, and health posts. Screening, treatment, and vaccination were successfully carried out using forms for registration, consent, and results with minimum error. In the screen/treat intervention 100% of participants gave an HPV sample and 99.7% reported high satisfaction; 81% of HPV + women were treated, and 57% returned for 6-month followup. Vaccine intervention: 98% of girls received the 1st vaccine, 88% of those received the 2nd, and 65% the 3rd. CBPR techniques successfully helped implement a screen/treat and vaccinate CC prevention program around Iquitos, Peru. These techniques may be appropriate for large-scale preventive health-care interventions.

Alfaro, K. M., et al. **Factors affecting attendance to cervical cancer screening among women in the Paracentral Region of El Salvador: a nested study within the CAPE HPV screening program.** BMC Public Health. 2015; 15: 1058.

BACKGROUND: Cervical cancer is the third most commonly occurring cancer among women and the fourth leading cause of cancer-related deaths in women worldwide, with more than 85 % of these cases occurring in developing countries. These global disparities reflect the differences in cervical cancer screening rates between high-income and medium- and low-income countries. At 19 %, El Salvador has the lowest reported screening coverage of all Latin American countries. The purpose of this study is to identify factors affecting public sector HPV DNA-based cervical cancer screening participation in El Salvador. **METHODS:** This study was nested within a public sector screening program where health promoters used door-to-door outreach to recruit women aged 30-49 years to attend educational sessions about HPV screening. A subgroup of these participants was chosen randomly and questioned about demographic factors, healthcare utilization, previous cervical cancer screening, and HPV knowledge. Women then scheduled screening appointments at their public health clinics. Screening participants were adherent if they attended their scheduled appointment or rescheduled and were screened within 6 months. The association between non-adherence and demographic variables, medical history, history of cancer, sexual history, birth control methods, and screening barriers was assessed using Chi-square tests

of significance and logistic regression. RESULTS: All women (n = 409) enrolled in the study scheduled HPV screening appointments, and 88 % attended. Non-adherence was associated with a higher number of lifetime partners and being under-screened-defined as not having participated in cervical cancer screening within the previous 3 years (p = 0.03 and p = 0.04, respectively); 22.8 % of participants in this study were under-screened. CONCLUSIONS: Adherence to cervical cancer screening after educational sessions was higher than expected, in part due to interactions with the community-based health promoters as well as the educational session itself. More effective recruitment methods targeted toward under-screened women are required.

Almobarak, A. O., et al. **Knowledge, Attitudes and Practices of Sudanese Women Regarding the Pap Smear Test and Cervical Cancer.** Asian Pac J Cancer Prev. 2016; 17(2): 625-630.

BACKGROUND: Despite the established role of the Pap smear test (PST) in prevention and early detection of cervical cancer, it is still rarely practiced in Sudan. Many challenges hinder the establishment of an effective cervical cancer screening program, including socio-cultural factors. Therefore, this study aimed to investigate the knowledge, attitudes and practices (KAP) of Sudanese women with regard to the Pap smear test and cervical cancer. MATERIALS AND METHODS: A total of 500 married women aged 14 to 58 years were recruited from obstetric clinics, hospitals and universities in Khartoum in 2014. Data were collected using a standardized, pretested questionnaire that inquired socio-demographic characteristics and their KAP about cervical cancer and the PST. RESULTS: More than 52% of participating women were above 30 years of age, and the majority (78.8%) were university degree holders. A total of 486 (97.2 %) of participants were resident in urban areas of Khartoum State. However about 48% of the respondents had never heard about PST, and only 15.8% of the participants had undergone a Pap smear test previously; 46.6% (233/500) knew that the human papilloma virus (HPV) was the causative agent, but only 39.2% (196/500) had heard about HPV vaccination, and only 11.4% (57/500) had received the vaccine. However 68% of the respondents agreed to do Pap smear if properly informed about the test and 75.4% of the respondents agreed to participate in a cervical cancer screening program. CONCLUSIONS: Despite a high educational level, less than half of our participants had accurate knowledge about cervical cancer, HPV, and cervical cancer screening. Health education about cervical cancer, HPV and sexually transmitted infections and the role of PST in cervical cancer prevention are crucial when designing interventions aimed at improving cervical cancer screening for Sudanese women.

Arbyn, M. and Castle, P. E. **Offering Self-Sampling Kits for HPV Testing to Reach Women Who Do Not Attend in the Regular Cervical Cancer Screening Program.** Cancer Epidemiol Biomarkers. 2015; Prev 24(5): 769-772.

In 2016, the Netherlands will switch, as first European country, from cytology-based to HPV-based cervical cancer screening, with cytology triage for those with a positive HPV test. The new Dutch program includes sending self-sampling devices to women who do not respond to an invitation to have a cervical sample taken by their general practitioner. The cost-effectiveness of this additional strategy will depend on its capacity to recruit nonscreened women and in particular those at increased risk of cervical (pre)cancer, the possible switch of previous responders to self-sampling, the accuracy and cost of the HPV assay-self-sampler combination, and the compliance of women being self-sample HPV-positive with further follow-up. Validated PCR-based assays, detecting high-risk HPV DNA, are as accurate on self-samples as on clinician-collected samples. On the contrary, HPV assays, based on signal amplification, are less sensitive and specific on self-samples. The introduction of self-sampling strategies should be carefully prepared and evaluated in pilot studies integrated in well-organized settings before general rollout. Opt-in procedures involving a request for a self-sampler may reduce response rates. Therefore, an affordable device that can be included with the invitation to all nonattendees may yield a stronger effect on participation.

Arrossi, S., et al. Implementation of HPV-testing for cervical cancer screening in programmatic contexts: The Jujuy demonstration project in Argentina. Int J Cancer. 2015; 137(7): 1709-1718.

The aim of this article is to present results of programmatic introduction of HPV testing with cytologic triage among women 30 years and older in the province of Jujuy, Argentina, including description of the planning phase and results of program performance during the first year. We describe the project implementation process, and calculate key performance indicators using SITAM, the national screening information system. We also compare disease detection rates of HPV testing in 2012 with cytology as performed during the previous year. HPV testing with cytology triage was introduced through a consensus-building process. Key activities included establishment of algorithms and guidelines, creating the HPV laboratory, training of health professionals, information campaigns for women and designing the referral network. By the end of 2012, 100% (n = 270) of public health care centers were offering HPV testing and 22,834 women had been HPV tested, 98.5% (n = 22,515) were 30+. HPV positivity among women over 30 was 12.7%, 807 women were HPV+ and had abnormal cytology, and 281 CIN2+ were identified. CIN2+ detection rates was 1.25 in 2012 and 0.62 in 2011 when the program was cytology based ($p = 0.0002$). This project showed that effective introduction of HPV testing in programmatic contexts of low-middle income settings is feasible and detects more disease than cytology.

Augusto, E. F., et al. Barriers to cervical cancer screening in women attending the Family Medical Program in Niteroi, Rio de Janeiro. Arch Gynecol Obstet. 2013; 287(1): 53-58.

BACKGROUND: The Family Medical Program is a health care system in the Rio de Janeiro state. Women's health services offered by the Family Medical Program include preventive exams and screening, family planning, and prenatal follow-up. Although cervical cancer screening is offered, barriers to care still hinder the full success of the program, and we are attempting to identify these barriers. **METHODS:** We undertook a cross-sectional and prospective study involving 351 women who were referred to the Family Medical Program between March 2009 and November 2010. Demographic data were obtained through a structured household questionnaire. The dependent variable was defined as the non-realization of the Pap smear test following the protocol of the Health Ministry. Cervical samples for screening were collected after clinical examination. **RESULTS:** Women who had undergone Pap smear testing at least once every 3 years comprised 282 of the participants (80.3 %). Most of the women had normal or inflammatory cytology (96.3 %). Illiteracy and the absence of symptomatic episodes of sexually transmitted disease were independent barriers to having cancer screening at regular intervals. Illiterate women were more likely to be older, not to be using any contraceptive method, and on average had more than two children, more than four pregnancies, and more than two abortions. Embarrassment was the greatest barrier to seeking professional care reported by all women, regardless of level of educational attainment. Other important barriers to seeking care and/or screening included time constraints, due to work or childcare. **CONCLUSION:** This study indicates that the Family Medical Program effectively provides cervical cancer screening coverage for its eligible population, at the level mandated by the WHO and the Brazilian Health Ministry. Fully 96.3 % of the women in our study had normal or benign inflammation on cytology. Understanding of barriers to care-seeking behavior that limit program adherence is one way to facilitate communication between providers and patients regarding the benefits of cancer screening.

Bahmani, A., et al. Factors Affecting Cervical Cancer Screening Behaviors Based On the Precaution Adoption Process Model: A Qualitative Study. Glob J Health Sci. 2015; 8(5): 51253.

One of the most preventable cancers in women is cervical cancer. Pap smear test is an effective screening program; however, it is not conducted very frequently. The aim of this study is explaining the determinants affecting women's participation in the Pap smear test based on precaution adoption process model with a qualitative approach. This study was a qualitative approach using a Directed Content Analysis

methodology which was conducted in 2014. Participants were 30 rural women who participated in this study voluntarily in sarvabad, Iran. Purposive sampling was initiated and continued until data saturation. Semi-structured interviews were the primary method of data collection. Data were analyzed using qualitative content analysis and continuous comparisons. Women's information and awareness about cervical cancer and Pap smear is insufficient and most of them believed that they were not at risk; however, they perceived the severity of the disease. Some of them had no adequate understanding of the test benefits. They pointed to the lack of time, financial difficulties, fear of test result and lack of awareness as the main barriers against the Pap smear test; however, they did not say that they were not willing to do the test. Findings could help health policy makers to find the right area and purpose to facilitate the participation of women in the Pap smear test.

Baussano, I., et al. **Cervical cancer screening program in Thimphu, Bhutan: population coverage and characteristics associated with screening attendance.** BMC Womens Health. 2014; 14: 147.

BACKGROUND: Bhutan has been engaged in good-quality cytology-based cervical screening since 2000 and has vaccinated >90% girls against human papillomavirus (HPV) since 2010. We explored the characteristics associated with lack of previous screening and screening coverage in women age ≥ 25 years. **METHODS:** Women were invited at home or during their attendance at 2 outpatient clinics, in the capital, Thimphu, and nearby Lungthenphu. Age-adjusted odds ratios for lack of previous screening by selected characteristics were computed among 1,620 participating women. In Thimphu an invitation registry allowed to estimate screening history not only among participating women but also among additional 500 women who did not accept to join our study. **RESULTS:** Among women who had a Pap smear, lack of previous screening was associated with age < 35 or ≥ 45 years. It was also associated with some occupations; being single, or widowed/separated; and presence of HPV infection. Multiparity and use of contraceptive methods were associated with having been screened. In women invited at home in Thimphu screening history substantially differed by participation. Past screening attendance was 59% among women recruited in the 2 clinics, 53% in women who were invited from home and accepted the invitation, but only 25% in those who refused it. Based on all women recruited from home the estimate of population-based coverage in Thimphu is 34% (95% CI: 31-37). **CONCLUSIONS:** Transition from an opportunistic screening to an all-reaching population-based screening is yet to be achieved in Bhutan, even in the capital. Better ways to target never-screened women are needed.

Blake, S. C., et al. **Facilitators and barriers to cervical cancer screening, diagnosis, and enrollment in Medicaid: experiences of Georgia's Women's Health Medicaid Program enrollees.** J Cancer Educ. 2015; 30(1): 45-52.

Although cervical cancer incidence and mortality rates have declined in the USA, African American women have a higher incidence rate of cervical cancer and a higher percentage of late-stage diagnosis than white women. Previous analyses by the authors showed that, even after adjusting for age, provider location, and availability, African American women were almost half as likely as white women to be diagnosed or enter Medicaid while at an early stage of their cervical cancer. To understand why these differences exist, we undertook a qualitative examination of the cervical cancer experiences of women enrolled in Georgia's Women's Health Medicaid Program (WHMP). Life history interviews were conducted with 24 WHMP enrollees to understand what factors shaped their cervical cancer experiences, from screening through enrollment in Medicaid. We also examined whether these factors differed by race in order to identify opportunities for increasing awareness of cervical cancer screening among underserved women. Results suggest that many women, especially African Americans, lacked understanding and recognition of early symptoms of cervical cancer, which prevented them from receiving a timely diagnosis. Additionally, participants responded positively to provider support and good communication but wished that their doctors explained their diagnosis more clearly. Finally, women were able to enroll in Medicaid

without difficulty due largely to the assistance of clinical staff. These findings support the need to strengthen provider education and public health efforts to reach low-income and minority communities for screening and early detection of cervical cancer.

Boehm, J. E., et al. **Recruiting patients into the CDC's Colorectal Cancer Screening Demonstration Program: strategies and challenges across 5 sites.** *Cancer* 2013; 119 Suppl 15: 2914-2925.

BACKGROUND: In 2005, the Centers for Disease Control and Prevention (CDC) funded 5 sites as part of the Colorectal Cancer Screening Demonstration Program (CRCDSP) to provide colorectal cancer screening to low-income, uninsured, and underinsured individuals. Funded sites experienced unexpected challenges in recruiting patients for services. **METHODS:** The authors conducted a longitudinal, qualitative case study of all 5 sites to document program implementation, including recruitment. Data were collected during 3 periods over the 4-year program and included interviews, document review, and observations. After coding and analyzing the data, themes were identified and triangulated across the research team. Patterns were confirmed through member checking, further validating the analytic interpretation. **RESULTS:** During early implementation, patient enrollment was low at 4 of the 5 CRCDSP sites. Evaluators found 3 primary challenges to patient recruitment: overreliance on in-reach to National Breast and Cervical Cancer Early Detection Program patients, difficulty keeping colorectal cancer screening and the program a priority among staff at partnering primary care clinics responsible for patient recruitment, and a lack of public knowledge about the need for colorectal cancer screening among patients. To address these challenges, site staff expanded partnerships with additional primary care networks for greater reach, enhanced technical support to primary care providers to ensure more consistent patient enrollment, and developed tailored outreach and education. **CONCLUSIONS:** Removing financial barriers to colorectal cancer screening was necessary but not sufficient to reach the priority population. To optimize colorectal cancer screening, public health practitioners must work closely with the health care sector to implement evidence-based, comprehensive strategies across individual, environmental, and systems levels of society.

Broberg, G., et al. **Increasing participation in cervical cancer screening: offering a HPV self-test to long-term non-attendees as part of RACOMIP, a Swedish randomized controlled trial.** *Int J Cancer.* 2014; 134(9): 2223-2230.

RACOMIP is a population-based, randomized trial of the effectiveness and cost-effectiveness of different interventions aimed at increasing participation in a well-run cervical cancer screening program in western Sweden. In this article, we report results from one intervention, offering non-attendees a high-risk human papillomavirus (HPV) self-test. Comparison was made with standard screening invitation routine or standard routine plus a telephone call. Women (8,800), aged 30-62, were randomly selected among women without a registered Pap smear in the two latest screening rounds. These women were randomized 1:5:5 to one of three arms: 800 were offered a high-risk HPV self-test, 4,000 were randomized to a telephone call (reported previously) and 4,000 constituted a control group (standard screening invitation routine). Results were based on intention to treat analysis and cost-effectiveness was calculated as marginal cost per cancer case prevented. The endpoint was the frequency of testing. The total response rate in the self-testing arm was 24.5%, significantly higher than in the telephone arm (18%, RR 1.36, 95% CI 1.19-1.57) and the control group (10.6%, RR 2.33, 95% CI 2.00-2.71). All nine women who tested positive for high-risk HPV attended for a cervical smear and colposcopy. From the health-care sector perspective, the intervention will most likely lead to no additional cost. Offering a self-test for HPV as an alternative to Pap smears increases participation among long-term non-attendees. Offering various screening options can be a successful method for increasing participation in this group.

Brotherton, J. M., et al. **HPV vaccine impact in Australian women: ready for an HPV-based screening program.** *Med J Aust.* 2016; 204(5): 184.

Brown, S. R., et al. **Cancer Screening on the Hopi Reservation: A Model for Success in a Native American Community.** *J Community Health.* 2015; 40(6): 1165-1172.

American Indian women have lower cancer survival rates compared to non-Hispanic White women. Increased cancer screening fostered by culturally sensitive education and community programs may help decrease this disparity. This study assesses the effectiveness of Hopi Cancer Support Services (HCSS) in maintaining high rates of breast and cervical cancer screening among Hopi women and evaluates the impact of participation in HCSS programs on colorectal cancer (CRC) screening. A population-based survey was conducted on the Hopi reservation in 2012 (n = 252 women). Frequency of breast, cervical, and colorectal cancer screenings, participation in HCSS programs and barriers to screening were evaluated. Unconditional multiple logistic regression estimated the independent effect of the HCSS program on CRC screening. Approximately 88 % of Hopi women 40+ reported ever having had a mammogram; 71 % did so within the past 2 years. Approximately 66 % of women 50+ were ever screened for colorectal cancer (FOBT and/or colonoscopy). Women who had their last mammogram through HCSS were 2.81 (95 % CI 1.12, 7.07) times more likely to have been screened for CRC. Breast and cervical cancer screening continues at a high rate among Hopi women and is substantially greater than that reported prior to the inception of HCSS. Furthermore, participation in programs offered by HCSS is strongly associated with increased colorectal cancer screening. This tribal health program (HCSS) has strongly influenced cancer screening among Hopi women and is a model of a tribally run cancer prevention program.

Brun-Micaleff, E., et al. **Cervical cancer screening by cytology and human papillomavirus testing during pregnancy in French women with poor adhesion to regular cervical screening.** *J Med Virol.* 2014; 86(3): 536-545.

In France, cervical screening is opportunistic and approximately 40% of women do not attend regular screening programs. The aim of this study was (1) to assess the prevalence of human papillomavirus (HPV) cervical infection and of cytological abnormalities in a population of young pregnant women with poor adherence to cervical cancer screening and (2) to evaluate the adherence to a screening strategy combining HPV testing and cytology during pregnancy. For this purpose, pregnant women benefited from a cervical smear associated with HPV DNA detection. High-risk HPV types were detected and identified using the HC2 assay and the INNO-LiPA HPV genotyping Extra assay. Two hundred forty-seven women (mean age 26.6 +/- 5.1 years) were enrolled. Among them, 76.8% did not attend regular cervical cancer screening programs. High-risk HPV types were detected in 50 (20.2%) samples, HPV 16 being the most frequent (N = 12; 14.5%), with multiple HPV infection in 17 samples (27%). Nine (3.6%) abnormal cervical smears were diagnosed. Follow-up of women with abnormal cytology and/or infection with high-risk HPV was obtained in 29 cases (55.8%), showing 12 persistent high-risk HPV infections. Nine women had colposcopy with a final diagnosis of four normal cervixes, three cervical intraepithelial neoplasia grade 1 and two cervical intraepithelial neoplasia grade 2. Overall, women adherence to the free post-partum follow-up visit was 53.5%. This study suggests that a screening program combining HPV testing with cervical cytology during pregnancy may be one option to target young women with poor adhesion to regular cervical cancer screening.

Budd, A. C., et al. **Cervical screening rates for women vaccinated against human papillomavirus.** *Med J Aust.* 2014; 201(5): 279-282.

OBJECTIVE: To compare cervical screening rates for women vaccinated with a quadrivalent human papillomavirus (HPV) vaccine with those for unvaccinated women, to address concerns that vaccinated

women may not be participating in cervical screening. DESIGN, SETTING AND PARTICIPANTS: Cross-sectional analysis of linked data from the Victorian Cervical Cytology Registry and the National HPV Vaccination Program Register for 20-29-year-old women in Victoria, Australia, for the period 1 January 2009 to 31 December 2011. MAIN OUTCOME MEASURES: Screening participation rates for vaccinated and unvaccinated women. RESULTS: Participation in cervical screening during the 2-year period 2010-2011 was significantly lower in 20-24-year-old vaccinated women compared with unvaccinated women of the same age (37.6% v 47.7%, a 10.1 percentage point difference [95% CI, 9.7-10.6]; $P < 0.001$) and significantly lower in 25-29-year-old vaccinated women compared with unvaccinated women of the same age (45.2% v 58.7%, a 13.5 percentage point difference [95% CI, 13.1%-13.9%]; $P < 0.001$). Similar results were observed for participation during the 3-year period 2009-2011. CONCLUSIONS: Despite education messages provided to young women, our results suggest that vaccinated women are being screened at lower rates than unvaccinated women in Australia. While some degree of undermatching of women in the study may have occurred, this cannot wholly explain our findings. Effective implementation of Individual Healthcare Identifiers to health records, including registry records, is needed to prevent potential undermatching of individuals in future linkage studies. In the meantime, efforts to increase participation in cervical screening by vaccinated women are needed.

Caster, M. M., et al. **Assessing the Acceptability, Feasibility, and Effectiveness of a Tablet-Based Cervical Cancer Educational Intervention.** J Cancer Educ. 2015.

Cervical cancer is a common and deadly disease, especially in developing countries. We developed and implemented an interactive, tablet-based educational intervention to improve cervical cancer knowledge among women in rural Malawi. Chichewa-speaking adult women in six rural villages participated. Each woman took a pretest, participated in the lesson, and then took a posttest. The lesson included information on cervical cancer symptoms, causes, risk factors, prevention, and treatment. Over the 6-month study period, 243 women participated. Women ranged in age from 18 to 77 years. Only 15 % had education beyond primary school. Nearly half of participants (48 %) had heard of cervical cancer prior to viewing the lesson. For these women, the median number of correct responses on the pretest was 11 out of 20; after the lesson, they had a median of 18 correct responses ($p < 0.001$). After the intervention, 93 % of women indicated a desire for cervical cancer screening. Despite lack of familiarity with computers (96 %), most women (94 %) found the tablet easy to use. A tablet-based educational program was an effective, feasible, and acceptable strategy to disseminate cervical cancer information to women with low education in rural Malawi. This method may be appropriate to distribute health information about other health topics in low-resource settings.

Catarino, R., Jr., et al. **Feasibility of at-home self-sampling for HPV testing as an appropriate screening strategy for nonparticipants in Switzerland: preliminary results of the DEPIST study.** J Low Genit Tract Dis. 2015; 19(1): 27-34.

OBJECTIVE: Nonattendees to cervical cancer screening are at a higher risk of developing cervical cancer. This study assessed women's willingness to perform a home-based self-sampling for human papillomavirus testing (Self-HPV) and explored the feasibility of establishing a home-based Self-HPV screening strategy in Switzerland. MATERIALS AND METHODS: Underscreened women ($n = 158$) who had not undergone a Pap test in the preceding 3 years were recruited between September 2011 and September 2013. Participants completed 2 questionnaires evaluating reasons for non-attendance at a screening program, sociodemographic issues, and satisfaction with and acceptability of the Self-HPV. Descriptive data and multivariate logistic regression were used to identify variables associated with women's willingness to perform at-home self-sampling for HPV testing. RESULTS: Lack of time because of work or childcare was the most common reason for nonattendance at a screening program. One hundred six women (82%) preferred the Self-HPV because it is easy to perform, convenient, comfortable, and

private. Women were more likely to accept the Self-HPV as a future screening strategy if they had missed cervical cancer screening in the past because of lack of time (odds ratio [OR] = 6.2, 95% confidence interval [CI] = 1.6-23.6; $p < .01$). Twenty-six women felt pain during self-sampling. Previous negative experiences with screening and stress during sampling were associated with higher risk for pain (OR = 7.14, 95% CI = 2.0-25.3, $p < .01$ and OR = 4.73, 95% CI = 1.5-14.5, $p < .01$, respectively). **CONCLUSIONS:** The Self-HPV was accepted by nonattendees of cervical cancer screening programs. Self-sampling may promote screening among the unscreened and underscreened population of women in Switzerland while overcoming some practical barriers.

Catarino, R. R., et al. **Barriers to Cervical Cancer Screening in Geneva (DEPIST Study)**. *J Low Genit Tract Dis*. 2016; 20(2): 135-138.

OBJECTIVES: Cervical screening is only efficient if a large part of eligible women participate. Our aim was to identify sociodemographic barriers to cervical screening and consider self-reported reasons to postpone screening. **METHODS:** Between September 2011 and June 2015, a questionnaire addressing reasons for nonparticipation in cervical screening was completed by 556 women who had not undergone a Pap test in the preceding 3 years. Pearson chi test was used to analyze differences between subgroups. Logistic regression was used to explore the association between sociodemographic characteristics and reasons for nonparticipation. **RESULTS:** The main reasons for nonparticipation in cervical cancer screening were practical barriers, such as lack of time and the cost of screening. These barriers were more likely to be reported by working women, women who were not sexually active, and those without health insurance. Younger women, non-European women living in Switzerland, and childless women were more likely to have never participated in a screening program before (adjusted odds ratio [aOR], 3.15; 95% CI, 1.41-6.98; aOR, 2.76; 95% CI, 1.48-5.16; aOR, 1.74; 95% CI, 1.03-2.99, respectively). **CONCLUSIONS:** Practical considerations seem to play a more important role in screening participation than emotional reasons and other beliefs. Particular attention should be paid to immigrant communities, where women seem more likely to skip cervical screening.

Choma, K. and McKeever, A. E. **Cervical cancer screening in adolescents: an evidence-based internet education program for practice improvement among advanced practice nurses**. *Worldviews Evid Based Nurs*. 2015; 12(1): 51-60.

BACKGROUND: The literature reports great variation in the knowledge levels and application of the recent changes of cervical cancer screening guidelines into clinical practice. Evidence-based screening guidelines for the prevention and early detection of cervical cancer offers healthcare providers the opportunity to improve practice patterns among female adolescents by decreasing psychological distress as well as reducing healthcare costs and morbidities associated with over-screening. **PURPOSE:** The purpose of this pilot intervention study was to determine the effects of a Web-based continuing education unit (CEU) program on advanced practice nurses' (APNs) knowledge of current cervical cancer screening evidence-based recommendations and their application in practice. This paper presents a process improvement project as an example of a way to disseminate updated evidence-based practice guidelines among busy healthcare providers. **METHODS:** This Web-based CEU program was developed, piloted, and evaluated specifically for APNs. The program addressed their knowledge level of cervical cancer and its relationship with high-risk human papillomavirus. It also addressed the new cervical cancer screening guidelines and the application of those guidelines into clinical practice. **FINDINGS:** Results of the study indicated that knowledge gaps exist among APNs about cervical cancer screening in adolescents. However, when provided with a CEU educational intervention, APNs' knowledge levels increased and their self-reported clinical practice behaviors changed in accordance with the new cervical cancer screening guidelines. **LINKING EVIDENCE TO PRACTICE:** Providing convenient and readily accessible up-to-date electronic content that provides CEU enhances the adoption of clinical practice guidelines, thereby

decreasing the potential of the morbidities associated with over-screening for cervical cancer in adolescents and young women.

Eder, M. M. and Firke, C. **Stand against cancer: evaluating a breast and cervical cancer screening program for uninsured patients.** *Prog Community Health Partnersh.* 2015; 9(1): 129-134.

BACKGROUND: Stand Against Cancer (SAC) is a long-running, community-based, organization-led program that addresses breast and cervical cancer disparities. Managed by Access Community Health Network (ACCESS), ongoing program evaluation reports on program performance over 5 years and public health implications. **OBJECTIVES:** To reduce disparities by making free cancer screening readily accessible to uninsured women and by connecting women to nurse case management to resolve abnormal screening results. Evaluation supports program management by assessing operations and outcomes. **METHODS:** Health center staff completes patient applications that start the clock to achieve a resolution for all women who screen. All women with abnormal screens are referred to nurse case management and entered into a database for tracking. Program evaluation tracks the extent to which the predominantly minority women successfully reach resolution points, specifically the return of screening results and diagnostic resolution of abnormal results, including initiation of treatment. **RESULTS:** A 5-year average of 10,400 women received SAC-supported screening at ACCESS. Through nurse case management, 90% of patients with abnormal screening results received a diagnosis. Women increasingly return and screen in subsequent years, contributing to a lower rate of late-stage cancers. Uninsured patients receiving SAC screening made additional nonscreening visits. Evaluation determined that SAC participant outcomes approximate or exceed a comparable national cohort and that program outcomes demonstrate effectiveness, equity, and optimality. **CONCLUSIONS:** Annual SAC evaluation illustrates that removing access barriers and providing nurse case management support to patients with abnormal results produced non-disparate outcomes for uninsured women.

Fabrizio, C. S. and Shea, C. M. **Disseminating a cervical cancer screening program through primary physicians in Hong Kong: a qualitative study.** *BMC Health Serv Res.* 2014; 14: 85.

BACKGROUND: Organized screening programs are more effective and equitable than opportunistic screening, yet governments face challenges to implement evidence-based programs. The objective of this study was to identify reasons for low levels of adoption among primary care physicians of a government sponsored Cervical Screening Program (CSP). **METHODS:** We conducted in-depth interviews with a snowball sample of primary care private and public primary care physicians in Hong Kong. Rogers' theory of diffusion of innovation was used to understand the factors that influenced the physicians' practice decisions. **RESULTS:** Our study found that Hong Kong physicians made the decision to encourage cervical screening and to participate in the CSP based primarily upon their clinical and business practice needs rather than upon the scientific evidence. The low rates of adoption of the CSP can be attributed to the physicians' perceptions that the program's complexity and incompatibility exceeded its relative advantages. Furthermore, women's knowledge, attitudes and practices, identified as barriers by physicians, were also barriers to physicians adopting the CSP. **CONCLUSIONS:** In both private and public health care systems, screening programs that rely on physicians must align program incentives with the physicians' motivators or pursue additional demand creation policies to achieve objectives.

Ferris, D. G., et al. **The Impact of Accessible Cervical Cancer Screening in Peru-The Dia del Mercado Project.** *J Low Genit Tract Dis.* 2015; 19(3): 229-233.

OBJECTIVE: The purpose of this study was to determine the potential impact of accessible secondary cervical cancer prevention efforts in indigenous Peruvian women living in the rural Andes Mountain region of Peru. **METHODS:** Peruvian women presenting for a Pap test or visiting a local marketplace, clinic, or public facility were asked to complete a questionnaire that assessed their response

to the rural Pap screening program. We identified the following: 1) barriers to care, 2) patient knowledge of cervical cancer and Pap tests, and 3) perceptions of and reactions to the market clinic model. Chi-square or Fisher exact tests, t tests and 1-way ANOVA were used to examine differences between locations. RESULTS: Of 4,560 women enrolled, those examined in tents indicated it was easier to get a Pap test (98.7%, $P = 0.001$) compared with women seen in buildings (96.8%) or CerviCusco (98.0%), and they felt it was more important to have a Pap test close to their home more often (99.3%) than those seen at CerviCusco (97.8%) or buildings (98.8%). Women examined in tents felt the market was a good place to have a Pap test more often (67.0%, $P < 0.001$) than women who went to buildings (46.0%) or CerviCusco (29.2%). CONCLUSIONS: Many poor indigenous women living in isolated regions are unable to travel to distant health-care facilities. Using a novel mobile clinic model, the "Dia del Mercado Project" successfully reduced barriers to cervical cancer screening by using local marketplaces.

Figueroa-Munoz Ledo, A. A., et al. **Individual and community effectiveness of a cervical cancer screening program for semi-urban Mexican women.** J Community Health. 2014; 39(3): 423-431.

The effectiveness at the individual and community level of an educational intervention to increase cervical cancer screening self-efficacy among semi-urban Mexican women was evaluated and changes in reported community barriers were measured after the intervention was implemented. The educational intervention was evaluated with a quasi-experimental pre-test/post-test design and a control group, based on the Integrative Model of Behavior Prediction and AMIGAS project materials. For the intervention group, increased self-efficacy increased requests to obtain a Pap ($p < 0.05$). Barriers to obtaining a Pap were embarrassment and lack of time at the individual level, and lack of time, test conditions and fear of social rejection in the community's cultural domain. At both the individual and community levels, having more information about the test and knowing it would be performed by a woman were primary facilitators. Few women used medically precise information when referring to the Pap and cervical uterine cancer. Although the level of self-efficacy of the participants increased, barriers in the health system affect the women's perceived ability to get a Pap. Better care for users is needed to increase consistent use of the test. The study shows the importance of using culturally adapted, multilevel, comprehensive interventions to achieve successful results in target populations.

Fornos, L. B., et al. **Increasing cervical cancer screening for a multiethnic population of women in South Texas.** J Cancer Educ. 2014; 29(1): 62-68.

Cervical cancer is a preventable disease. Precancers can be identified and treated through cervical screenings. The HPV vaccine prevents precancers from becoming cancers. The aim of the A Su Salud Cervical Cancer Prevention Program was to apply well-understood health promotion techniques and increase the rate of cervical cancer screening among a high-risk, multiethnic, low-income population in South Texas. Qualitative research was used to identify uptake barriers and tailor media messaging. Using existing resources, we applied evidence-based strategies in novel ways that changed personal behaviors, leading to cancer screening, risk reduction, and early detection. We created a database to track a cohort of 32,807 women and measured cervical cancer screenings over 3 years. Our analysis revealed an increase in cervical cancer screenings after use of highly targeted automated telephone reminders and media dissemination on multiple platforms. Those women at low risk for cervical cancer obtained the highest proportion of Pap tests. This innovative, theory-based program increased overall Pap tests up to 9% among women enrolled in a safety net hospital financial assistance plan. This study fills a gap in research on Pap test compliance in uninsured, mostly Hispanic women by building on cultural strengths and tailored messaging.

Herweijer, E., et al. **The Participation of HPV-Vaccinated Women in a National Cervical Screening Program: Population-Based Cohort Study.** PLoS One. 2015; 10(7): e0134185.

BACKGROUND: Concerns have been raised that HPV-vaccination might affect women's cervical screening behavior. We therefore investigated the association between opportunistic HPV-vaccination and attendance after invitation to cervical screening. **METHODS:** A cohort of all women resident in Sweden, born 1977-1987 (N=629,703), and invited to cervical screening, was followed October 2006 - December 2012. Invitations to screening were identified via the National Quality Register for Cervical Cancer Prevention, as was the primary outcome of a registered smear. Vaccination status was obtained from two nationwide health data registers. Hazard ratios (HR) were estimated using Cox regression adjusted for age, education level and income (HR_{adj}). Women were individually followed for up to 6 years, of which the first and second screening rounds were analyzed separately. **RESULTS:** Screening attendance after three years of follow-up was 86% in vaccinated women (N=4,897) and 75% in unvaccinated women (N=625,804). The crude HR of screening attendance in vaccinated vs. unvaccinated women was 1.31 (95% CI 1.27-1.35) in the first screening round. Adjustment for education and income reduced but did not erase this difference (HR_{adj}=1.09, 95% CI 1.05-1.13). In the second screening round, attendance was likewise higher in HPV-vaccinated women (crude HR=1.26, 95% CI 1.21-1.32; HR_{adj}=1.15, 95% CI 1.10-1.20). **CONCLUSIONS:** HPV-vaccination is so far associated with equal or higher attendance to cervical screening in Sweden in a cohort of opportunistically vaccinated young women. Most but not all of the difference in attendance was explained by socioeconomic differences between vaccinated and unvaccinated women. HPV vaccine effectiveness studies should consider screening attendance of HPV-vaccinated women when assessing incidence of screen-detected cervical lesions.

Jia, Y., et al. **Knowledge about cervical cancer and barriers of screening program among women in Wufeng County, a high-incidence region of cervical cancer in China.** PLoS One 2013; 8(7): e67005.

PURPOSE: Cervical cancer screening is an effective method for reducing the incidence and mortality of cervical cancer, but the screening attendance rate in developing countries is far from satisfactory, especially in rural areas. Wufeng is a region of high cervical cancer incidence in China. This study aimed to investigate the issues that concern cervical cancer and screening and the factors that affect women's willingness to undergo cervical cancer screening in the Wufeng area. **PARTICIPANTS AND METHODS:** A cross-sectional survey of women was conducted to determine their knowledge about cervical cancer and screening, demographic characteristics and the barriers to screening. **RESULTS:** Women who were willing to undergo screenings had higher knowledge levels. "Anxious feeling once the disease was diagnosed" (47.6%), "No symptoms/discomfort" (34.1%) and "Do not know the benefits of cervical cancer screening" (13.4%) were the top three reasons for refusing cervical cancer screening. Women who were younger than 45 years old or who had lower incomes, positive family histories of cancer, secondary or higher levels of education, higher levels of knowledge and fewer barriers to screening were more willing to participate in cervical cancer screenings than women without these characteristics. **CONCLUSION:** Efforts are needed to increase women's knowledge about cervical cancer, especially the screening methods, and to improve their perceptions of the screening process for early detection to reduce cervical cancer incidence and mortality rates.

Karjalainen, L., et al. **Self-sampling in cervical cancer screening: comparison of a brush-based and a lavage-based cervicovaginal self-sampling device.** BMC Cancer. 2016; 16(1): 221.

BACKGROUND: High coverage and attendance is essential for cervical cancer screening success. We investigated whether the previous positive experiences on increasing screening attendance by self-sampling in Finland are sampler device dependent. **METHODS:** All women identified to cervical cancer screening in 2013 in 28 Finnish municipalities were randomised to receive a lavage- (n = 6030) or a brush type of self-sampling device (n = 6045) in case of non-attendance after two invitation letters. Seven hundred seventy non-attending women in the lavage device group and 734 in the brush group received the self-sampling offer. Women's experiences were enquired with an enclosed questionnaire. **RESULTS:**

Total attendance in the lavage group increased from 71.0 to 77.7 % by reminder letters and further to 80.5 % by self-sampling. Respective increase in the brush group was from 72.2 to 78.6 % and then to 81.5 %. The participation by self-sampling was 21.7 % (95 % CI 18.8-24.6) in the lavage group and 23.8 % (95 % CI 20.8-26.9) in the brush group. Women's self-sampling experiences were mainly positive and the sampler devices were equally well accepted by the women. **CONCLUSION:** Our study shows that the lavage device and brush device perform similarly in terms of uptake by non-attending women and user comfort. If self-sampling is integrated to the routine screening program in Finland, either of the devices can be chosen without the fear of losing participants due to a less acceptable device.

Kress, C. M., et al. **Knowledge, attitudes, and practices regarding cervical cancer and screening among Ethiopian health care workers.** *Int J Womens Health.* 2015; 7: 765-772.

BACKGROUND: Though cervical cancer incidence has dramatically decreased in resource rich regions due to the implementation of universal screening programs, it remains one of the most common cancers affecting women worldwide and has one of the highest mortality rates. The vast majority of cervical cancer-related deaths are among women that have never been screened. Prior to implementation of a screening program in Addis Ababa University-affiliated hospitals in Ethiopia, a survey was conducted to assess knowledge of cervical cancer etiology, risk factors, and screening, as well as attitudes and practices regarding cervical cancer screening among women's health care providers. **METHODS:** Between February and March 2012 an anonymous, self-administered survey to assess knowledge, attitudes, and practices related to cervical cancer and its prevention was distributed to 334 health care providers at three government hospitals in Addis Ababa, Ethiopia and three Family Guidance Association clinics in Awassa, Adama, and Bahir Dar. Data were analyzed using SPSS software and chi-square test was used to test differences in knowledge, attitudes, and practices across provider type. **RESULTS:** Overall knowledge surrounding cervical cancer was high, although awareness of etiology and risk factors was low among nurses and midwives. Providers had no experience performing cervical cancer screening on a routine basis with <40% having performed any type of cervical cancer screening. Reported barriers to performing screening were lack of training (52%) and resources (53%); however the majority (97%) of providers indicated cervical cancer screening is an essential part of women's health care. **CONCLUSION:** There is a clear need among women's health care providers for education regarding cervical cancer etiology, risk factors and for training in low-tech, low-cost screening methods. Meeting these needs and improving the infrastructure necessary to implement appropriate screening programs is essential to reduce the burden of cervical cancer in Ethiopia.

Laranjeira, C. A. **Portuguese women's knowledge and health beliefs about cervical cancer and its screening.** *Soc Work Public Health.* 2013; 28(2): 150-157.

Currently little is known about Portuguese women's knowledge and beliefs about cervical cancer screening, so this information is crucial to the success of cervical cancer screening programs. The intention of this study was to describe the knowledge and beliefs of women in Portugal. In-depth, face-to-face, individual interviews were conducted. Twenty-five females were recruited, the age range was 30 to 60. The results showed a lack of knowledge on cervical cancer and the Pap smear test. From a public policy point of view, it may be important to further explore the extent to which perceived barriers to screening will affect screening uptake when a national screening program is implemented.

Leniz, J., et al. **HPV vaginal self-sampling among women non-adherent to Papanicolaou screening in Chile.** *Salud Publica. Mex* 2013; 55(2): 162-169.

OBJECTIVE: To evaluate acceptance, preference and compliance with referral of vaginal self-sampling for the detection of Human papillomavirus (HPV) among women non-adherent to Papanicolaou (Pap) screening in Santiago, Chile. **MATERIALS AND METHODS:** Using multistage sampling we identified

women aged 30-64 years who reported not receiving a Pap test in the previous three years and offered them Pap testing at the health center or vaginal self-sampling for HPV testing at home. Self-collected samples were analyzed with hybrid capture. All HPV+ women were referred for colposcopy, biopsy and treatment when needed. RESULTS: 1 254 eligible women were contacted; 86.5% performed self-sampling and 8.1% refused; 124 women were HPV+ (11.4%: 95%CI 9.6-13.5) of whom 85.5% attended colposcopy; 12 had CIN2+ (1.1%: 95 %CI 0.5-1.7). CONCLUSION: HPV vaginal self-sampling can be easily implemented in Chile and could improve coverage, successfully reaching women who drop out of the screening program.

Leon-Maldonado, L., et al. **Perceptions and Experiences of Human Papillomavirus (HPV) Infection and Testing among Low-Income Mexican Women.** PLoS One. 2016; 11(5): e0153367.

BACKGROUND: HPV infection causes cervical cancer, a major contributor to morbidity and mortality among low-income Mexican women. Human papillomavirus (HPV) DNA testing is now a primary screening strategy in Mexico's early cervical cancer detection program (ECDP). Research on Mexican women's perceptions of HPV and testing is necessary for establishing culturally appropriate protocols and educational materials. Here, we explore perceptions about HPV and HPV-related risk factors among low-income Mexican ECDP participants. METHODS: We conducted semi-structured interviews with 24 ECDP participants from two primary care health clinics in Michoacan state, Mexico. Interviews addressed women's understandings of and experiences with HPV and HPV testing. Analysis was inductive and guided by the Health Belief Model with a focus on gender. RESULTS: Women's confusion about HPV and HPV screening caused emotional distress. They understood HPV to be a serious disease that would always cause severe symptoms, often characterizing it as analogous to HIV or inevitably carcinogenic. Women also attributed it to men's sexual behaviors, specifically infidelity and poor hygiene. Women described both sexes' desire for sex as natural but understood men's negative practices of masculinity, like infidelity, as the causes of women's HPV infection. Some women believed dirty public bathrooms or heredity could also cause HPV transmission. CONCLUSIONS: These results are consistent with prior findings that geographically and economically diverse populations lack clear understandings of the nature, causes, or symptoms of HPV, even among those receiving HPV testing. Our findings also reveal that local cultural discourse relating to masculinity, along with failure to provide sufficient education to low-income and indigenous-language speaking patients, exacerbate women's negative emotions surrounding HPV testing. While negative emotions did not deter women from seeking testing, they could be ameliorated with better health education and communication.

Levano, W., et al. **Public education and targeted outreach to underserved women through the National Breast and Cervical Cancer Early Detection Program.** Cancer. 2014; 120 Suppl 16: 2591-2596.

The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) was established to provide low-income, uninsured, and underinsured women access to cancer screening and diagnostic services with the goal of increasing the early detection and prevention of breast and cervical cancer. Although this is a valuable resource for women who might not have the means to get screened otherwise, providing services at no cost, by itself, does not guarantee uptake of screening services. Public education and targeted outreach facilitate the critical link between public service programs and the communities they serve. The purpose of public education and outreach in the NBCCEDP is to increase the number of women who use breast and cervical cancer screening services by raising awareness, providing education, addressing barriers, and motivating women to complete screening exams and follow-up. Effective strategies focus on helping to remove structural, physical, interpersonal, financial, and cultural barriers; educate women about the importance of screening and inform women about the services available to them. This article provides an overview of the importance of public education and targeted outreach activities for cancer screening through community-based programs including examples from NBCCEDP

grantees that highlight successes, challenges, and solutions, encountered when conducting these types of interventions.

Levinson, K. L., et al. **The Peru Cervical Cancer Prevention Study (PERCAPS): the technology to make screening accessible.** *Gynecol Oncol.* 2013; 129(2): 318-323.

OBJECTIVE: This study utilized a combination of HPV self-sampling, iFTA elute specimen cards, and long distance transport for centralized processing of specimens to determine the feasibility of large-scale screening in remote and transient populations. **METHODS:** This study was performed in two locations in Peru (Manchay and Iquitos). The "Just For Me" cervico-vaginal brush and iFTA elute cards were used for the collection and transport of specimens. Samples were shipped via FedEx to China and tested for 14 types of high-risk HPV using PCR based MALDI-TOF. HPV positive women were treated with cryotherapy after VIA triage, and followed-up with colposcopy, biopsy, ECC, and repeat HPV testing at 6 months. **RESULTS:** Six hundred and forty three women registered, and 632 returned a sample over a 10 day period. Within 2 weeks, specimens were shipped, samples tested, and results received by study staff. Sixty-eight women (10.8%) tested positive, and these results were delivered over 4 days. Fifty-nine HPV positive women (87%) returned for evaluation and treatment, and 2 had large lesions not suitable for cryotherapy. At 6 months, 42 women (74%) returned for follow-up, and 3 had CIN 2 (all positive samples from the endocervical canal). Ninety eight percent of participants reported that they would participate in this type of program again. **CONCLUSIONS:** Utilizing HPV self-sampling, solid media specimen cards for long distance transport, and centralized high throughput processing, we achieved rapid delivery of results, high satisfaction levels, and low loss to follow-up for cervical cancer screening in remote and transient populations.

Lorenzi, A. T., et al. **Can the careHPV test performed in mobile units replace cytology for screening in rural and remote areas?** *Cancer Cytopathol.* 2016.

BACKGROUND: Human papillomavirus (HPV) DNA testing can be crucial for women who have limited access to traditional screening. The current study compared the results obtained through HPV DNA testing with those obtained through cytology-based screening. **METHODS:** A total of 3068 women aged 18 to 85 years were enrolled in an opportunistic cervical cancer screening program developed by the Barretos Cancer Hospital and performed by a team of health professionals working within a mobile unit from March to December 2012, followed by statistical analyses. For each patient, 2 different cervical samples were collected and preserved in a careHPV assay and SurePath medium, respectively. **RESULTS:** High-risk HPV (hr-HPV) DNA was detected in 10.0% of women, with the majority (86.7%) demonstrating no abnormal Papanicolaou test results. The following cytological samples were found to be hr-HPV positive: 8.2% of the normal samples; 39.4% of the samples with atypical squamous/glandular cells of undetermined significance; 38.5% of the samples with atypical squamous/glandular cells of undetermined significance, cannot exclude high-grade lesion; 55.3% of the samples with low-grade squamous intraepithelial lesions; and 100% of the samples with high-grade squamous intraepithelial lesions. Colposcopy examinations were performed among 33.4% of the women with positive results on at least 1 of the tests (HPV DNA positive and/or cytology with atypical squamous/glandular cells of undetermined significance, cannot exclude high-grade lesion or high-grade squamous intraepithelial lesions), and 59.5% of these women underwent biopsies. Among these samples, 18.2% were confirmed as cervical intraepithelial neoplasia. **CONCLUSIONS:** The careHPV test was demonstrated to be a feasible alternative to primary screening in low-resource settings accessed through the use of mobile units. *Cancer Cytopathol* 2016. (c) 2016 American Cancer Society.

Mandigo, M., et al. **Pairing community health workers with HPV self-sampling for cervical cancer prevention in rural Haiti.** *Int J Gynaecol Obstet.* 2015; 128(3): 206-210.

OBJECTIVE: To assess a program in which community health workers (CHWs) provided women with self-sampling devices to detect high-risk human papillomavirus (HPV). **METHODS:** In a cross-sectional study, 13 CHWs visited homes in a rural area in Haiti's Central Plateau to recruit premenopausal women aged 30-50 years between July 2009 and April 2010. Eligible women had not undergone a cervical smear in the previous 3 years. Participants learned about cervical cancer and self-sampling for HPV testing before using a self-sampler in private. They then completed a questionnaire. CHWs later returned to provide results and advice about follow-up care. **RESULTS:** CHWs enrolled 493 women. Among the 485 women for whom questionnaires were received, 468 (96.5%) were comfortable using the self-sampler and 484 (99.8%) stated they would recommend it to others. Among 426 analyzed samples, 54 (12.7%) were positive for high-risk HPV, of whom 46 (85.2%) received follow-up care and 17 (31.5%) had precursor lesions and were treated. **CONCLUSION:** Using a CHW-led intervention, women at high risk for developing cervical cancer were identified and navigated to preventive care. Therefore, pairing CHWs with HPV self-sampling is a promising strategy to combat cervical cancer in rural Haiti and similar settings.

Maseko, F. C., et al. **Cervical cancer control and prevention in Malawi: need for policy improvement.** Pan Afr Med J. 2015; 22: 247.

INTRODUCTION: Malawi has the highest incidents of cervical cancer followed by Mozambique and Comoros thus according to the 2014 Africa cervical cancer multi indicator incidence and mortality score card. Despite having an established cervical cancer prevention program, there is low screening coverage. Studies have been carried out to determine socio-cultural and economical barriers to cervical cancer prevention services utilization and very few have concentrated on health system and policy related barriers to cervical cancer prevention and control. The paper presents finding on a qualitative study which carried out to determine the suitability of the national sexual and reproductive health and rights [SRHR] in mitigating challenges in cervical cancer control and prevention. **METHODS:** a desk review of the Malawi National Sexual and Reproductive Health and Rights [SRHR] policy 2009 was done with an aim of understanding its context, goal and objectives. Analysis of the policy history provided insight into the conditions that led to the policy. Policies from countries within the region were referred in the review. Government officials were interviewed to solicit information on the policy. **RESULTS:** Malawi does not have a standalone policy on cervical cancer; however, cervical cancer is covered under reproductive cancer theme in the SRHR. Unlike some policies within the region, the Malawian SRHR policy does not mention the age at which the women should be screened, the frequency and who is to do the screening. The policy does not stipulate policy implications on the ministry of health, the SRH programs and health service providers on cervical cancer. Furthermore the policy does not include HPV vaccination as a key component of cervical cancer control and prevention. **CONCLUSION:** the policy does not reflect fairly the best attempt to reduce the incidence and mortality of cervical cancer as such we recommend that the Reproductive Health Directorate to consider developing a standalone policy on cervical cancer control and prevention.

McCree, R., et al. **Expanding Cervical Cancer Screening and Treatment in Tanzania: Stakeholders' Perceptions of Structural Influences on Scale-Up.** Oncologist. 2015; 20(6): 621-626.

Tanzania has the highest burden of cervical cancer in East Africa. This study aims to identify perceived barriers and facilitators that influence scale-up of regional and population-level cervical cancer screening and treatment programs in Tanzania. Convenience sampling was used to select participants for this qualitative study among 35 key informants. Twenty-eight stakeholders from public-sector health facilities, academia, government, and nongovernmental organizations completed in-depth interviews, and a seven-member municipal health management team participated in a focus group discussion. The investigation identified themes related to the infrastructure of health services for cervical cancer prevention, service delivery, political will, and sociocultural influences on screening and treatment.

Decentralizing service delivery, improving access to screening and treatment, increasing the number of trained health workers, and garnering political will were perceived as key facilitators for enhancing and initiating screening and treatment services. In conclusion, participants perceived that system-level structural factors should be addressed to expand regional and population-level service delivery of screening and treatment. **IMPLICATIONS FOR PRACTICE:** Tanzanian women have a high burden of cervical cancer. Understanding the perceived structural factors that may influence screening coverage for cervical cancer and availability of treatment may be beneficial for program scale-up. This study showed that multiple factors contribute to the challenge of cervical cancer screening and treatment in Tanzania. In addition, it highlighted systematic developments aimed at expanding services. This study is important because the themes that emerged from the results may help inform programs that plan to improve screening and treatment in Tanzania and potentially in other areas with high burdens of cervical cancer.

Mittal, S., et al. **HPV detection-based cervical cancer screening program in low-resource setting: lessons learnt from a community-based demonstration project in India.** 2016; 27(3): 351-358.

PURPOSE: A demonstration project was conducted to assess feasibility of implementing HPV detection-based cervical cancer screening in primary care settings in India and to generate local evidence on feasibility and effectiveness of HPV detection in primary screening. **METHODS:** The project was implemented by setting up screening clinics at primary health centers. Eligible women were screened by HPV DNA test (Hybrid capture 2). All samples were processed and tested in a single laboratory. Colposcopy services were provided to screen-positive women at the same community clinics. Project utilized services of community health workers for community mobilization, recall of screen-positive and disease-positive women. Women with \geq CIN2 diagnosis were treated at tertiary hospital. **RESULTS:** Totally, 44,110 women were screened and HPV positivity was 4.7 %. Compliance to recall of HC2-positive women for colposcopy was 78 %. Detection rate of CIN3+ by HPV test was 3.9/1,000 women. Compliance of women to treatment was 80.1 %. However, compliance of HPV-positive women for follow-up at 1 year was poor (23.2 %). Concurrent use of VIA to screen the women did not have any advantage but increased number of unnecessary colposcopies and biopsies. **CONCLUSIONS:** Our project demonstrated that it was possible to implement HPV detection-based screening using existing primary healthcare infrastructure. Performing colposcopy at primary setting is feasible, improves compliance and reduces over-treatment. In settings with low to moderately high HPV prevalence, direct referral of HPV-positive women is advisable. Community health workers can be effectively used for recalling the positive women.

Miyagi, E., et al. **Attitudes toward cervical cancer screening among women receiving human papillomavirus vaccination in a university-hospital-based community: interim 2-year follow-up results.** J Obstet Gynaecol Res. 2014; 40(4): 1105-1113.

AIM: This study investigated the status of cervical cancer screening among women in a university hospital-based community who received catch-up human papillomavirus (HPV) vaccinations as a basic element of our community-based cervical cancer prevention advocacy. **METHODS:** Self-administered questionnaires were distributed to 173 women working or studying in the community at their first HPV vaccination in 2010, at the third vaccination, and 2 years later. Their demographics and attitudes toward the Pap test were analyzed. **RESULTS:** The median age of the participants was 27.5 years and 88.2% were sexually active. Before the first vaccination, 38.5% (57/148) of the screening targets had never had a Pap test. Among the women who completed the third vaccination, Pap test experiences within the recent 2 years increased from 45.3% (63/139) at the first vaccination to 71.2% (99/137) at the third vaccination, and 67.5% (54/80) 2 years later. In 45.3% of the screening targets who had never had a Pap test at the time of their first HPV vaccination, their first Pap test was followed by their vaccination. **CONCLUSIONS:** Having biennial Pap tests in accordance with the Japanese national cancer screening guideline was shown to be difficult even for the women in the medical community; however, education about the Pap test and

the efficacy of HPV vaccination in providing opportunistic screening encouraged them to have their first or suspended Pap test. Our interim data suggest the need for urgently changing the cervical cancer prevention strategy for young adult women who are excluded from the national HPV vaccine program.

Mojahed, S., et al. **Attitude and knowledge of Iranian female nurses about human papillomavirus infection and cervical cancer: a cross sectional survey.** J Prev Med Hyg. 2013; 54(3): 187-190.

BACKGROUND AND AIM: Human Papillomavirus (HPV) is one of the most widespread sexually transmitted diseases is highly related to cervical cancer in women. Cervical cancer's crude incidence rate in Iran is 6-8 per 100,000. The HPV vaccine provides a chance to considerably decrease the transmission of most types of HPV. The aim of this study was to evaluate awareness and knowledge of HPV infection and vaccines and to assess the attitude and approach toward these vaccines among female nurses at Shahid Sadoughi University of Medical Sciences, Yazd, Iran. **MATERIALS AND METHODS:** This cross-sectional, descriptive study was performed among 380 female nurses. Data were collected using a questionnaire consisted in demographic variables and questions on knowledge of participants about HPV infection, HPV vaccine and cervical cancer and also questions on attitude of nurses towards HPV vaccination. The validity and internal consistency of questionnaire was confirmed during experts consents and pilot testing ($\alpha = 0.79$). Data analysis was performed using SPSS15 using chi2-test or Fisher's exact test. **RESULTS:** Three hundred and eighty questionnaires were distributed and 357 female nurses completed and returned their questionnaires: Only one hundred and thirty-one of the nurses (36.7%) knew about HPV infection and how it can cause abnormal pap Smear results. about 147 (41.2%) of the nurses stated they would want to be vaccinated. About 146 (40.9%) of respondents supported vaccination of preadolescent girls. **CONCLUSION:** The results of this study confirm the lack of knowledge about HPV vaccine and its relation to cervical cancer and also the ways of this cancer prevention. Our study shows an urgent need to design similar studies in other regions of Iran and draw a broad estimation on knowledge of different target groups to make a national program to increase the knowledge of women on this matter and help to decrease the rate of cervical cancer in Iranian population.

Munro, A., et al. **The role of general practitioners in the continued success of the National Cervical Screening Program.** Aust Fam Physician. 2014; 43(5): 293-296.

BACKGROUND: As the gateway to healthcare for Australian women, general practitioners (GPs) are critical to the success of the National Cervical Screening Program (NCSP). Despite an enviable record - halving the incidence and mortality of cervical cancer - in 2010-2011 more than 2.7 million women did not comply with the recommended 2-yearly screening interval. **OBJECTIVE:** General practice strategies are presented to assist GPs in encouraging all women, in particular, high-risk and vulnerable women, to participate in cervical screening. **DISCUSSION:** GPs play a crucial part in addressing the demographic, psychosocial and healthcare barriers that prevent women's participation in cervical screening. Encouraging uptake of the human papillomavirus vaccine and educating all patients on the importance of continued participation in cervical screening is essential for further decreasing the prevalence of this disease through early detection and treatment of cervical abnormalities.

Ogilvie, G. S., et al. **Correlates of women's intentions to be screened for human papillomavirus for cervical cancer screening with an extended interval.** BMC Public Health. 2016; 16(1): 213.

BACKGROUND: High-risk HPV DNA testing has been proposed as a primary tool for cervical cancer screening (HPV-CCS) as an alternative to the Papanicolaou cytology- method. This study describes factors associated with women's intentions to attend cervical cancer screening if high-risk HPV DNA testing (HPV-CCS) was implemented as a primary screening tool, and if screening were conducted every 4 years starting after age 25. **METHODS:** This online survey was designed using the Theory of Planned Behaviour to assess factors that impact women's intentions to attend HPV-CCS among women aged 25-69 upon exit of the

HPV FOCAL trial. Univariate and regression analyses were performed to compare the demographic, sexual history, and smoking characteristics between women willing and unwilling to screen, and scales for intention to attend HPV-CCS. A qualitative analysis was performed by compiling and coding the comments section of the survey. RESULTS: Of the 981 women who completed the survey in full, only 51.4 % responded that they intended to attend HPV-CCS with a delayed start age and extended screening interval. Women who intended to screen were more likely to have higher education (AOR 0.59, 95 % CI [0.37, 0.93]), while both positive attitudes (AOR 1.26, 95 % CI [1.23, 1.30]) and perceived behavior control (AOR 1.06, 95 % CI [1.02, 1.10]) were significant predictors of intention to screen. Among women who provided comments in the survey, a large number of women expressed fears about not being checked more than every 4 years, but 12 % stated that these fears may be alleviated by having more information. CONCLUSIONS: Acceptability of increased screening intervals and starting age could be improved through enhanced education of benefits. Program planners should consider measures to assess and improve women's knowledge, attitudes and beliefs prior to the implementation of new screening programs to avoid unintended consequences.

Ogilvie, G. S., et al. **Results of a community-based cervical cancer screening pilot project using human papillomavirus self-sampling in Kampala, Uganda.** *Int J Gynaecol Obstet.* 2013; 122(2): 118-123.

OBJECTIVE: To examine the feasibility of a community-based screening program using human papillomavirus (HPV) self-sampling in a low-income country with a high burden of cervical cancer. METHODS: A pilot study was conducted among 205 women aged 30-69 years in the Kisenyi district of Kampala, Uganda, from September 5 to October 30, 2011. Women were invited to provide a self-collected specimen for high-risk oncogenic HPV testing by outreach workers at their homes and places of gathering in their community. Specimens were tested for HPV, *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Women who tested positive for HPV were referred for colposcopy, biopsy, and treatment at a regional hospital. RESULTS: Of the 199 women who provided a specimen, 35 (17.6%) tested positive for HPV. The outreach workers were able to provide results to 30 women (85.7%). In all, 26 (74.3%) of the women infected with HPV attended their colposcopy appointments and 4 (11.4%) women were diagnosed with grade 3 cervical intraepithelial neoplasia. CONCLUSION: Self-collection of samples for community-based HPV testing was an acceptable option; most women who tested positive attended for definitive treatment. Self-sampling could potentially allow for effective recruitment to screening programs in limited-resource settings.

Olsson, E., et al. **Community collaboration to increase foreign-born women's participation in a cervical cancer screening program in Sweden: a quality improvement project.** *Int J Equity Health.* 2014; 13: 62.

INTRODUCTION: The prevailing inequities in healthcare have been well addressed in previous research, especially screening program participation, but less attention has been paid to how to overcome these inequities. This paper explores a key factor of a successful improvement project: collaboration with local doulas to raise cervical cancer screening participation by more than 40 percent in an area with a large number of foreign-born residents. METHODS: Data was collected through two focus group discussions with the doulas in order to design interventions and debrief after interventions had been carried out in the community. Various tools were used to analyze the verbal data and monitor the progress of the project. RESULTS: Three major themes emerged from the focus group discussions: barriers that prevent women from participating in the cervical cancer screening program, interventions to increase participation, and the role of the doulas in the interventions. CONCLUSIONS: This paper suggests that several barriers make participation in cervical cancer screening program more difficult for foreign-born women in Sweden. Specifically, these barriers include lack of knowledge concerning cancer and the importance of preventive healthcare services and practical obstacles such as unavailable child care and language skills. The overarching approach to surmount these barriers was to engage persons with a shared

cultural background and mother tongue as the target audience to verbally communicate information. The doulas who helped to identify barriers and plan and execute interventions gained increased confidence and a sense of pride in assisting to bridge the gap between healthcare providers and users.

Ostensson, E., et al. **Barriers to and facilitators of compliance with clinic-based cervical cancer screening: population-based cohort study of women aged 23-60 years.** PLoS One 2015; 10(5): e0128270.

OBJECTIVE: This study aims to identify possible barriers to and facilitators of cervical cancer screening by (a) estimating time and travel costs and other direct non-medical costs incurred in attending clinic-based cervical cancer screening, (b) investigating screening compliance and reasons for noncompliance, (c) determining women's knowledge of human papillomavirus (HPV), its relationship to cervical cancer, and HPV and cervical cancer prevention, and (d) investigating correlates of HPV knowledge and screening compliance. **MATERIALS AND METHODS:** 1510 women attending the clinic-based cervical cancer screening program in Stockholm, Sweden were included. Data on sociodemographic characteristics, time and travel costs and other direct non-medical costs incurred in attending (e.g., indirect cost of time needed for the screening visit, transportation costs, child care costs, etc.), mode(s) of travel, time, distance, companion's attendance, HPV knowledge, and screening compliance were obtained via self-administered questionnaire. **RESULTS:** Few respondents had low socioeconomic status. Mean total time and travel costs and direct non-medical cost per attendance, including companion (if any) were euro55.6. Over half (53%) of the respondents took time off work to attend screening (mean time 147 minutes). A large portion (44%) of the respondents were noncompliant (i.e., did not attend screening within 1 year of the initial invitation), 51% of whom stated difficulties in taking time off work. 64% of all respondents knew that HPV vaccination was available; only 34% knew it was important to continue to attend screening following vaccination. Age, education, and income were the most important correlates of HPV knowledge and compliance; and additional factors associated with compliance were time off work, accompanying companion and HPV knowledge. **CONCLUSION:** Time and travel costs and other direct non-medical costs for clinic-based screening can be considerable, may affect the cost-effectiveness of a screening program, and may constitute barriers to screening while HPV knowledge may facilitate compliance with screening.

Paul, P., et al. **Screen-and-treat approach to cervical cancer prevention using visual inspection with acetic acid and cryotherapy: experiences, perceptions, and beliefs from demonstration projects in Peru, Uganda, and Vietnam.** Oncologist 2013; 18 Suppl: 6-12.

Cervical cancer is preventable but continues to cause the deaths of more than 270,000 women worldwide each year, most of them in developing countries where programs to detect and treat precancerous lesions are not affordable or available. Studies have demonstrated that screening by visual inspection of the cervix using acetic acid (VIA) is a simple, affordable, and sensitive test that can identify precancerous changes of the cervix so that treatment such as cryotherapy can be provided. Government partners implemented screening and treatment using VIA and cryotherapy at demonstration sites in Peru, Uganda, and Vietnam. Evaluations were conducted in the three countries to explore the barriers and facilitating factors for the use of services and for incorporation of screen-and-treat programs using VIA and cryotherapy into routine services. Results showed that use of VIA and cryotherapy in these settings is a feasible approach to providing cervical cancer prevention services. Activities that can help ensure successful programs include mobilizing and educating communities, organizing services to meet women's schedules and needs, and strengthening systems to track clients for follow-up. Sustainability also depends on having an adequate number of trained providers and reducing staff turnover. Although some challenges were found across all sites, others varied from country to country, suggesting that careful assessments before beginning new secondary prevention programs will optimize the probability of success.

Primeau, S. W., et al. **Social service barriers delay care among women with abnormal cancer screening.** *J Gen Intern Med* 2014; 29(1): 169-175.

BACKGROUND: Inequity in cancer outcomes for minorities and vulnerable populations has been linked to delays in cancer care that arise from barriers to accessing care. Social service barriers represent those obstacles related to meeting life's most basic needs, like housing and income, which are often supported by public policy, regulation and services. **OBJECTIVE:** To examine the association between social service barriers and timely diagnostic resolution after a cancer screening abnormality. **DESIGN:** Secondary analysis of the intervention arm of Boston Patient Navigation Research Program (2007-2008) conducted across six urban community health centers. Subjects with no barriers, other barriers, and social service barriers were compared on their time to diagnostic resolution. **SUBJECTS:** Women \geq 18 years of age with a breast or cervical cancer screening abnormality. **MAIN MEASURES:** Social service barriers included: income supports, housing and utilities, education and employment, and personal/family stability and safety. Time to event analyses compared across five groups: those with no barriers, one barrier (other), one barrier (social service), two or more barriers (all other), and two or more barriers (at least one social service). **KEY RESULTS:** 1,481 navigated women; 31 % Hispanic, 27 % Black, 32 % White; 37 % non-English speakers and 28 % had private health insurance. Eighty-eight women (6 %) had social service barriers. Compared to those without social service barriers, those with were more likely to be Hispanic, younger, have public/no health insurance, and have multiple barriers. Those with two or more barriers (at least one social service barrier), had the longest time to resolution compared to the other four groups (aHR resolution $<$ 60 days = 0.27, \geq 60 days = 0.37). **CONCLUSION:** Vulnerable women with multiple barriers, when at least one is a social service barrier, have delays in care despite navigation. The impact of patient navigation may never be fully realized if social service barriers persist without being identified or addressed.

Ramachandran, A., et al. **Multiple barriers delay care among women with abnormal cancer screening despite patient navigation.** *J Womens Health (Larchmt)* 2015; 24(1): 30-36.

BACKGROUND: While there is widespread dissemination of patient navigation programs in an effort to reduce delays in cancer care, little is known about the impact of barriers to care on timely outcomes. **METHODS:** We conducted a secondary analysis of the Boston Patient Navigation Research Program (PNRP) to examine the effect that the presence of barriers had on time to diagnostic resolution of abnormal breast or cervical cancer screening tests. We used multivariable Cox proportional hazards regression with time to diagnostic resolution as the outcome to examine the effect of the number of barriers, controlling for demographic covariates and clustered by patients' primary navigator. **RESULTS:** There were 1481 women who received navigation; mean age was 39 years; 32% were White, 27% Black, and 31% Hispanic; 28% had private health insurance; and 38% did not speak English. Overall, half (n=745, 50%) had documentation of one or more barriers to care. Women with barriers were more likely to be older, non-White, non-English language speakers, and on public or no health insurance compared with women without barriers. In multivariable analyses, we found less timely diagnostic resolution as the number of barriers increased (one barrier, adjusted hazard ratio [aHR] 0.81 [95% CI 0.56-1.17], $p=0.26$; two barriers, aHR 0.55 [95% CI 0.37-0.81], $p=0.0025$; three or more barriers, aHR 0.31 [95% CI 0.21-0.46], $p<0.0001$). **CONCLUSION:** Within a patient navigation program proven to reduce delays in care, we found that navigated patients with documented barriers to care experience less timely resolution of abnormal cancer screening tests.

Ramachandran, A., et al. **Barriers to health care contribute to delays in follow-up among women with abnormal cancer screening: Data from the Patient Navigation Research Program.** *Cancer* 2015; 121(22): 4016-4024.

BACKGROUND: There is limited understanding of the association between barriers to care and clinical outcomes within patient navigation programs. **METHODS:** Secondary analyses of data from the intervention arms of the Patient Navigation Research Program were performed, which included navigated participants with abnormal breast and cervical cancer screening tests from 2007 to 2010. Independent variables were: 1) the number of unique barriers to care (0, 1, 2, or ≥ 3) documented during patient navigation encounters; and 2) the presence of socio-legal barriers originating from social policy (yes/no). The median time to diagnostic resolution of index screening abnormalities was estimated using Kaplan-Meier cumulative incidence curves. Multivariable Cox proportional hazards regression examined the impact of barriers on time to resolution, controlling for sociodemographics and stratifying by study center. **RESULTS:** Among 2600 breast screening participants, approximately 75% had barriers to care documented (25% had 1 barrier, 16% had 2 barriers, and 34% had ≥ 3 barriers). Among 1387 cervical screening participants, greater than one-half had barriers documented (31% had 1 barrier, 11% had 2 barriers, and 13% had ≥ 3 barriers). Among breast screening participants, the presence of barriers was associated with less timely resolution for any number of barriers compared with no barriers. Among cervical screening participants, only the presence of ≥ 2 barriers was found to be associated with less timely resolution. Both types of barriers, socio-legal and other barriers, were found to be associated with delay among breast and cervical screening participants. **CONCLUSIONS:** Navigated women with barriers resolved cancer screening abnormalities at a slower rate compared with navigated women with no barriers. Further innovations in navigation care are necessary to maximize the impact of patient navigation programs nationwide.

Smith, M., et al. **Impact of HPV sample self-collection for underscreened women in the renewed Cervical Screening Program.** *Med J Aust.* 2016; 204(5): 194.

OBJECTIVES: In 2017, the National Cervical Screening Program in Australia will transition to 5-yearly primary HPV screening for all women, irrespective of human papillomavirus (HPV) vaccination status. As an adjunct to the mainstream program, HPV testing on self-collected samples will be offered under practitioner supervision to all unscreened and underscreened women aged 30-74 years. We quantified how different screening decisions affect the future risk of cervical cancer. **DESIGN:** Simulation of outcomes for 100 000 previously unscreened women, aged 30 years and eligible for self-collection, using a well-established model of HPV natural history and cervical screening. **MAIN OUTCOME MEASURES:** Cumulative cancer diagnoses and deaths averted (compared with remaining unscreened) to age 84, number needed to treat for pre-cancer (NNT) to avert each cancer diagnosis. **RESULTS:** One round of self-collected HPV screening at age 30 years would avert 908 cancer diagnoses and 364 cancer deaths in the cohort by age 84 (NNT, 5.8). Benefits would still be achieved were self-collected screening delayed to age 40 (922 fewer diagnoses; 426 fewer deaths; NNT, 3.7) or 50 (684 fewer diagnoses; 385 fewer deaths; NNT, 3.2). However, the benefits associated with joining the mainstream screening program would be substantially larger (2002, 1623 or 1091 fewer diagnoses and NNT of 4.9, 3.7 or 3.4 by joining at age 30, 40 or 50 years respectively). The relative benefits of joining the mainstream program were similar for cohorts who had been offered vaccination. **CONCLUSIONS:** Offering HPV self-collection has the potential to considerably improve outcomes for unscreened and underscreened women. Nevertheless, these findings underscore the need for concerted strategies to encourage these women to join the mainstream HPV screening program.

Smith, L. W., et al. **Women's intentions to self-collect samples for human papillomavirus testing in an organized cervical cancer screening program.** *BMC Public Health.* 2014; 14: 1060.

BACKGROUND: Mounting evidence affirms HPV testing as an effective cervical cancer screening tool, and many organized screening programs are considering adopting it as primary testing. HPV self-collection has comparable sensitivity to clinician collected specimens and is considered a feasible option

in hard-to-reach women. We explored women's intentions to HPV self-collect for cervical cancer screening from a cohort participating in a Canadian randomized controlled cervical cancer screening trial. **METHODS:** Women aged 25-65 were invited to complete an online survey assessing intentions to be screened with HPV testing instead of the Pap smear. The survey was based in the Theory of Planned Behaviour and questions were included to assess women's intentions to self-collect for HPV. Demographic characteristics of women who intended to self-collect were compared with those who did not. Demographic and scale variables achieving a p-value <0.1 in the univariate and bivariate analyses were included in the stepwise logistic regression model. The final model was created to predict factors associated with women's intentions to self-collect an HPV specimen for cervical cancer. Odds ratios were calculated with 95% confidence intervals to identify variables associated with a woman's intention to self-collect for cervical cancer screening. **RESULTS:** The overall survey response rate was 63.8% (981/1538) with 447 (45.6%) reporting they intended to self-collect, versus 534 (54.4%) reporting they did not. In the univariate analysis, women with more than high school education were more likely to self-collect. Women who intended to receive HPV testing versus the Pap smear were 1.94 times as likely to be in favour of self-collection and those who intended to self-collect had significantly higher attitudinal scores towards HPV self-collection. The adjusted odds ratio and 95% confidence interval from the multivariate analysis demonstrated attitude towards self-collection was the only significant variable predicting a woman's intention to self-collect (OR 1.25; 95% CI: 1.22, 1.29). **CONCLUSIONS:** The primary predictor of a woman's intention to HPV self-collect for cervical cancer screening was her attitude towards the procedure. From a program planning perspective, these results indicate that education and awareness may be significant contributing factors to improving acceptance of self-collection and subsequently, improving screening attendance rates.

Smith, J. L., et al. **AMIGAS: building a cervical cancer screening intervention for public health practice.** *J Womens Health (Larchmt)*. 2013; 22(9): 718-723.

BACKGROUND: Many barriers to cervical cancer screening for Hispanic women have been documented, but few effective interventions exist. The Community Preventive Services Task Force recommends increasing cervical cancer screening through various methods. Building on this evidence, the Centers for Disease Control and Prevention funded the research and testing phases for an evidence-based and theoretically grounded intervention designed to increase cervical cancer screening among never and rarely screened Hispanic women of Mexican descent. In this article, we describe the development process of the AMIGAS (Ayudando a las Mujeres con Informacion, Guia, y Amor para su Salud) intervention, highlight the integration of scientific evidence and community-based participatory research principles, and identify opportunities for dissemination, adaptation, and implementation of this intervention. **METHODS:** The AMIGAS team was a collaboration among researchers, promotoras (community health workers), and program administrators. The multiyear, multiphase project was conducted in Houston, Texas; El Paso, Texas; and Yakima, Washington. The team completed several rounds of formative research, designed intervention materials and methodology, conducted a randomized controlled trial, created a guide for program administrators, and developed an intervention dissemination plan. **RESULTS:** Trial results demonstrated that AMIGAS was successful in increasing cervical cancer screening among Hispanic women. Adaptation of AMIGAS showed minimal reduction of outcomes. Dissemination efforts are underway to make AMIGAS available in a downloadable format via the Internet. **CONCLUSIONS:** Developing a community-based intervention that is evidence-based and theoretically grounded is challenging, time-intensive, and requires collaboration among multiple disciplines. Inclusion of key stakeholders-in particular program deliverers and administrators-and planning for dissemination and translation to practice are integral components of successful intervention design. By providing explicit directions for adaptation for program deliverers, relevant information for program administrators, and

access to the intervention via the Internet, AMIGAS is available to help increase cervical cancer screening among Hispanic women and other women disproportionately affected by cervical cancer.

Snijders, P. J., et al. **High-risk HPV testing on self-sampled versus clinician-collected specimens: a review on the clinical accuracy and impact on population attendance in cervical cancer screening.** *Int J Cancer.* 2013; 132(10): 2223-2236.

This review elaborates on the accuracy and feasibility of human papillomavirus (HPV) self-sampling, i.e., offering self-sampling of (cervico-)vaginal cell material by women themselves in nonclinical settings for high-risk HPV (hrHPV) detection in the laboratory, for cervical screening. To that end a bibliographic database search (PubMed) was performed to identify studies (published between January 1992 and January 2012) that compared clinical accuracy of HPV testing on self-sampled material with that of cytology or HPV testing on clinician-taken samples, and studies comparing response to offering HPV self-sampling with a recall invitation. Overall, hrHPV testing on self-samples appeared to be at least as, if not more, sensitive for cervical intraepithelial neoplasia grade 2 or worse (CIN2+) as cytology on clinician-obtained cervical samples, though often less specific. In most studies, hrHPV testing on self- and clinician-sampled specimens is similarly accurate with respect to CIN2+ detection. Variations in clinical performance likely reflect the use of different combinations of collection devices and HPV tests. Because it is known that underscreened women are at increased risk of cervical cancer, targeting non-attendees of the screening program could improve the effectiveness of cervical screening. In developed countries offering self-sampling has shown to be superior to a recall invitation for cytology in re-attracting original non-attendees into the screening program. Additionally, self-testing has shown to facilitate access to cervical screening for women in low resource areas. This updated review of the literature suggests that HPV self-sampling could be an additional strategy that can improve screening performance compared to current cytology-based call-recall programs.

Steens, A., et al. **Association between human papillomavirus vaccine uptake and cervical cancer screening in the Netherlands: implications for future impact on prevention.** *Int J Cancer.* 2013; 132(4): 932-943.

Several countries recently added human papillomavirus (HPV) vaccination to cervical cancer screening in the effort to prevent cervical cancer. They include the Netherlands, where both programs are free. To estimate their combined future impact on cancer prevention, information is needed on the association between participation in vaccination now and in screening in the future and on what groups are at risk for nonparticipation. We studied the association between participation in screening by mothers and in vaccination by their daughters. Girls' vaccination status was matched by house-address with their mothers' screening participation. We estimated the effect on cancer incidence by means of computer simulation. We investigated risk groups for nonparticipation using multivariable multilevel logistic regression and calculated population-attributable fractions. Our results, based on 89% of girls invited for vaccination in 2009 ($n = 337,368$), show that vaccination status was significantly associated with mothers' screening participation (odds ratio: 1.54 [95% confidence interval: 1.51-1.57]). If a mother's screening is taken as proxy of a girl's future screening, only 13% of the girls will not participate in either program compared to 23% if screening alone is available. The positive association between vaccination and screening resulted in slightly lower model estimates of the impact of vaccination on cancer incidence, compared to estimates assuming no association. Girls with nonwestern ethnicities, with young mothers, who live in urban areas with low socioeconomic status, are at risk for nonparticipation. A significant part of potential nonscreeners may be reached through HPV vaccination. Estimates made before vaccination was introduced only slightly overestimated its impact on cervical cancer incidence.

Stormo, A. R., et al. **Cervical cancer-related knowledge, attitudes, and practices of health professionals working in Brazil's network of primary care units.** *Oncologist* 2014; 19(4): 375-382.

INTRODUCTION: Brazil's national strategy for cervical cancer screening includes using the Papanicolaou (Pap) test every 3 years among women aged 25-64 years. Comprehensive primary care services are provided through a network of primary health units, but little is known about cervical cancer-related knowledge, attitudes, and practices among health professionals and coordinators working in these facilities. **METHODS:** In 2011, we conducted a cross-sectional nationally representative phone survey of 1,600 primary health care units to interview one unit coordinator and one health care professional per unit (either nurse, physician, or community health worker). Responses were obtained from 1,251 coordinators, 182 physicians, 347 nurses, and 273 community health workers. Questionnaires were administered to assess health units' characteristics and capacity for cervical cancer-related services as well as health professionals' perceived effectiveness of the Pap test, preparedness to talk to women about cervical cancer, adherence with screening guidelines, and willingness to recommend human papillomavirus (HPV) vaccination to females. **RESULTS:** Most units conducted screening (91.9%), used home visits to conduct recruitment and outreach (83.4%), and provided follow-up to women who did not return to discuss Pap test results (88.1%). Approximately 93% of health professionals stated that Pap testing was effective in decreasing death rates from cervical cancer and 65% stated that national guidelines for cervical cancer screening are very influential; 93% of nurses and physicians reported screening women annually and 75% reported beginning to screen women younger than 25 years old. Regarding HPV vaccination, almost 90% of nurses and physicians would recommend the HPV vaccine to their female patients if it were available. A larger proportion of physicians and nurses recommended the HPV vaccine to older girls (13-18 years) and women (19-26 years and even older than 26 years) than to younger girls (12 years or younger). **CONCLUSION:** Although Brazil's network of primary care units has significantly increased access to cervical cancer screening, effective strategies are needed to ensure that women get screened at the appropriate ages and intervals. Additionally, this study's baseline data on HPV vaccination may be useful as Brazil embarks on a national HPV vaccination program in 2014.

Stormo, A. R., et al. **Bolivian health providers' attitudes toward alternative technologies for cervical cancer prevention: a focus on visual inspection with acetic acid and cryotherapy.** *J Womens Health (Larchmt)*. 2012; 21(8): 801-808.

BACKGROUND: Little is known about health providers' attitudes toward visual inspection with acetic acid (VIA) and cryotherapy in the prevention of cervical cancer, as most research in Latin America and the Caribbean (LAC) has examined attitudes of the general population. This study describes attitudes of Bolivian health professionals toward new technologies for cervical cancer prevention, focusing on VIA and cryotherapy. **METHODS:** Between February 2011 and March 2012, we surveyed 7 nurses and 35 physicians who participated in 5-day workshops on VIA and cryotherapy conducted in Bolivia. Multiple choice and open-ended questions were used to assess participants' acceptability of these procedures and the feasibility of their implementation in the context of perceived barriers for the early detection of cervical cancer in this country. **RESULTS:** Most believed that cultural factors represent the main barrier for the early detection of cervical cancer (70%), although all stated that VIA and cryotherapy would be accepted by women, citing the advantages of VIA over cytology for this belief. Most also believed their colleagues would accept VIA and cryotherapy (71%) and that VIA should replace Pap testing (61%), reiterating the advantages of VIA for these beliefs. Those who believed the contrary expressed a general resistance to change associated with an already existing cytology program and national norms prioritizing Pap testing. **CONCLUSIONS:** Most participants had favorable attitudes toward VIA and cryotherapy; however, a sizable minority cited challenges to their adoption by colleagues and believed VIA should not replace cytology. This report can inform the development of strategies to expand the use of alternative cervical cancer screening methods in LAC and Bolivia.

Tavasoli, S. M., et al. **Impact of invitation and reminder letters on cervical cancer screening participation rates in an organized screening program.** *Prev Med* 2016; 88: 230-236.

Study's Objective was to explore the impact of invitation and reminder letters on cervical cancer screening participation among eligible Ontario women 30 to 69 years of age. A cross-sectional study was used to describe factors and screening patterns for 1,150,783 eligible women. A cohort design was used to compare the impact of invitation and reminder letters on Pap uptake comparing women who received the intervention (n=99,278) with a historical non-intervention group (n=130,181). Factors that might influence screening participation were included as covariates in a multivariable logistic regression models. Overall, 26.7% of women who had a Pap test 3 to 5 years prior and 9.8% of women with no Pap test in the previous 5 years were screened within 9 months after the intervention. On cohort analysis, 14.1% of women in the intervention group and 8.5% of women in the non-intervention group were screened within 9 months. Being mailed an invitation letter was associated with greater likelihood of screening (OR=1.8, CI 1.7-1.8). Controlling for covariates, the letter intervention was associated with 9 month screening for both women with a Pap test 3 to 5 years prior (AOR=1.7, CI 1.6-1.8) and those with no Pap test in the previous 5 years (AOR=1.8, CI 1.7-1.9). There was a significant effect of all covariates on the participation. The invitation and reminder letter strategy increased cervical cancer screening participation. Additional strategies that could encourage eligible women to participate and/or removing barriers to screening for eligible women may be necessary.

Tejeda, S., et al. **Patient barriers to follow-up care for breast and cervical cancer abnormalities.** *J Womens Health (Larchmt)*. 2013; 22(6): 507-517.

BACKGROUND: Women with breast or cervical cancer abnormalities can experience barriers to timely follow-up care, resulting in delays in cancer diagnosis. Patient navigation programs that identify and remove barriers to ensure timely receipt of care are proliferating nationally. The study used a systematic framework to describe barriers, including differences between African American and Latina women; to determine recurrence of barriers; and to examine factors associated with barriers to follow-up care. **METHODS:** Data originated from 250 women in the intervention arm of the Chicago Patient Navigation Research Program (PNRP). The women had abnormal cancer screening findings and navigator encounters. Women were recruited from a community health center and a publicly owned medical center. After describing proportions of African American and Latina women experiencing particular barriers, logistic regression was used to explore associations between patient characteristics, such as race/ethnicity, and type of barriers. **RESULTS:** The most frequent barriers occurred at the intrapersonal level (e.g., insurance issues and fear), while institutional-level barriers such as system problems with scheduling care were the most commonly recurring over time (29%). The majority of barriers (58%) were reported in the first navigator encounter. Latinas (81%) reported barriers more often than African American women (19%). Differences in race/ethnicity and employment status were associated with types of barriers. Compared to African American women, Latinas were more likely to report an intrapersonal level barrier. Unemployed women were more likely to report an institutional level barrier. **CONCLUSION:** In a sample of highly vulnerable women, there is no single characteristic (e.g., uninsured) that predicts what kinds of barriers a woman is likely to have. Nevertheless, navigators appear able to easily resolve intrapersonal-level barriers, but ongoing navigation is needed to address system-level barriers. Patient navigation programs can adopt the PNRP barriers framework to assist their efforts in assuring timely follow-up care.

Townsend, J. S., et al. **Current cervical cancer screening knowledge, awareness, and practices among U.S. affiliated pacific island providers: opportunities and challenges.** *Oncologist* 2014; 19(4): 383-393.

BACKGROUND: Cervical cancer is a leading cause of cancer mortality in nearly all U.S. Affiliated Pacific Island Jurisdictions (USAPIJ); however, most jurisdictions are financially and geographically limited in their capacity to deliver routine screening. **METHODS:** We conducted a cross-sectional survey of 72 health care providers from five of the six USAPIJ in 2011 to assess knowledge, beliefs, practices, and perceived barriers regarding routine cervical cancer screening. We compared the responses of providers from jurisdictions that were funded by the Centers for Disease Control and Prevention's National Breast and Cervical Cancer Early Detection Program (NBCCEDP) with those that were not funded. **RESULTS:** Most providers reported cervical cancer prevention as a priority in their clinical practices (90.3%) and use the Papanicolaou test for screening (86.1%). Many providers reported knowledge of screening guidelines (76.4%); however, more than half reported that annual screening is most effective (56.9%). Providers in non-NBCCEDP-funded jurisdictions reported greater acceptance of visual inspection with acetic acid (93.9%) and self-sampling for human papillomavirus testing (48.5%) compared with NBCCEDP-funded jurisdictions (15.4% and 30.8% respectively). Providers from non-NBCCEDP-funded jurisdictions reported inadequate technological resources for screening women (42.4%), and approximately 25% of providers in both groups believed that screening was cost-prohibitive. **CONCLUSION:** Although cervical cancer screening is a priority in clinical practice, beliefs about annual screening, costs associated with screening, and varying levels of support for alternative screening tests pose barriers to providers throughout the USAPIJ. Further exploration of using evidence-based, lower cost, and sustainable screening technologies is warranted in addition to emphasizing timely follow-up of all positive cases.

Vassilakos, P., et al. **Use of swabs for dry collection of self-samples to detect human papillomavirus among Malagasy women.** *Infect Agent Cancer.* 2016; 11: 13.

BACKGROUND: Most women in developing countries have never attended cervical screening programmes and often little information exists on type-specific human papillomavirus (HPV) prevalence among these populations. Self-sampling for HPV testing (self-HPV) using a dry swab may be useful for establishing a screening program and evaluating HPV prevalence. Our aim was to evaluate self-HPV using a dry swab stored at room temperature. **METHODS:** This community-based study in Madagascar consisted of 449 women aged 30-65. Eligible women were provided a dry swab to perform self-HPV. HPV analysis was accomplished by two different real-time PCR tests using the same extracted DNA from the samples. **RESULTS:** Overall, 52 (11.6 %) specimens were invalid for HPV detection. The delay between sampling and laboratory processing of DNA extraction considerably increased invalid results. Overall HPV prevalence of 14 hrHPV types detected by the two PCR tests was found to be 38.2 % (n = 152). Distribution of 19 hrHPV and 9 low-risk HPV (lrHPV) types revealed most frequently 53 and 68 among hrHPV and HPV 54, HPV 70 and HPV 42 among lrHPV. Agreement between the two PCR methods for any of the 14 high-risk HPV (hrHPV) strains detected was 89.9 % (kappa = 0.77, 95 % CI: 0.71-0.84). In 385 (85.7 %) samples the DNA load of ss-globin demonstrated a signal with medium or high level copies. Conversely, in 28 (60.9 %) invalid samples the signal was undetectable. The HPV-DNA load signal was predominantly of intermediate level (58.5 %, n = 218). **CONCLUSIONS:** Self-HPV using a dry swab stored at room temperature could be a useful method for HPV screening and for conducting population-based surveys on HPV prevalence in resource-poor settings.

Virtanen, A., et al. **Improving cervical cancer screening attendance in Finland.** *Int J Cancer* 2015; 136(6): E677-684.

High attendance is essential to cervical cancer screening results. Attendance in the Finnish program is currently at 70%, but extensive opportunistic screening occurs beside the organized. A shift from opportunistic to organized screening is imperative to optimize the costs and impact of screening and minimize potential harms. We evaluated the effect of reminder letters (1st reminder) and self-sampling test (2nd reminder) on program attendance. The study population consisted of 31,053 screening invitees

in 31 Finnish municipalities. 8,284 non-attendees after one invitation received a reminder letter and 4,536 further non-attendees were offered a self-sampling option. Socioeconomic factors related to participation were clarified by combining screening data to data from Statistics Finland. Reminder letters increased participation from 72.6% (95% CI 72.1, 73.1) to 79.2% (95% CI 78.8, 79.7) and self-sampling further to 82.2% (95% CI 81.8, 82.7). Reminder letters with scheduled appointments resulted in higher increase than open invitations (10 vs. 6%). Screening of original non-attendees increased the yield of CIN3+ lesions by 24%. Non-attendance was associated with young age, immigrant background, lower education level and having never been married. We showed that a total attendance of well over 80% can be achieved within an organized program when the invitational protocol is carefully arranged.

Virtanen, A., et al. **Self-sampling experiences among non-attendees to cervical screening.** *Gynecol Oncol* 2014; 135(3): 487-494.

OBJECTIVE: High coverage and attendance is essential to positive cervical cancer screening results. Offering self-sampling for HPV-testing to the non-attendees of the program may improve attendance rates. Information on women's perceptions and experiences with self-sampling (acceptability) is needed to further optimize attendance by this method. **METHODS:** A questionnaire study focusing on women's experiences on the screening method was embedded in a trial investigating the effects and feasibility of self-sampling among non-attendees of cervical screening in 31 Finnish municipalities in 2011-2012 (n=4688). Reasons for non-attendance in routine screening were also surveyed. **RESULTS:** Response rate to the questionnaire was 98.8% (909/920) among women who performed self-sampling. Self-sampling participants reported mainly good experiences. Negative experiences (difficulties in sample taking, pain, fear, anxiety, insecurity) were reported rarely, but more commonly among women with a mother tongue other than Finnish or Swedish (immigrants). Most common reason for non-attendance in routine screening was a recent Pap-smear elsewhere (opportunistic screening). Practical reasons (pregnancy, scheduling difficulties) were reported by 42%, emotional or attitudinal reasons by 17%, and 16% forgot to take part. Response yield to questionnaire was unsatisfactory among those women who declined the self-sampling option. **CONCLUSIONS:** Optimizing the practical aspects of screening and offering a self-sampling option to non-attendees can help to overcome a large variety of both practical and emotional barriers to traditional screening. More research is needed among the non-attendees to routine screening who decline also the self-sampling option.

Yap, D., et al. **Clinicians' attitude towards changes in Australian National Cervical Screening Program.** *J Clin Virol* 2016; 76 Suppl 1: S81-87.

BACKGROUND: Australian guidelines for cervical cancer screening are being revised under the "renewal program". Physicians' willingness to accept these changes will play a pivotal role in its success. **OBJECTIVE:** To understand the willingness and acceptance of, as well as barriers and facilitators for Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) affiliates to screening using human papillomavirus (HPV) testing, starting at 25 years of age, every 5 years. **STUDY DESIGN:** An electronic survey of RANZCOG affiliates was undertaken April-June 2014, while renew was announced April 28th 2014. Responses used a 7 point Likert scale, which was dichotomized as ≤ 4 , indicating 'unwilling' and > 4 , indicating 'willing' to adopt revised practices. **RESULTS:** Response rate was 22% (n=956): 60% were obstetricians and gynaecologists (OG); 27% general practitioner diplomates; 13% OG trainees. Overall, 60% (n=526/874) were willing to revise their screening practice. This correlated with awareness of new guidelines ($p < 0.001$). Fifty percent (n=438/869) of respondents were concerned about delaying to 25 years, and 48% (n=421/869) concerned cervical cancers would be missed. Reasons respondents gave for wishing to continue screening from 18 years contrary to guidelines included: women not being vaccinated (65.6%), immunosuppressed women (92.2%) and women who had been victims of childhood sexual assault (73.9%). **CONCLUSIONS:** The majority of RANZCOG affiliates were willing to change

screening practice however, a number of barriers to delaying onset of screening age to age 25 years were reported. Effective change management strategies will need to be implemented to address the concerns raised to ensure best practice for cervical screening.

Session 6 HPV-faster: Broadening the scope for prevention of HPV-related cancer.

Bosch FX, Robles C, Díaz M, Arbyn M, Baussano I, Clavel C, Ronco G, Dillner J, Lehtinen M, Petry KU, Poljak M, Kjaer SK, Meijer CJ, Garland SM, Salmerón J, Castellsagué X, Bruni L, de Sanjosé S, Cuzick J., **HPV-FASTER: broadening the scope for prevention of HPV-related cancer.** Nat Rev Clin Oncol. Feb;13(2):119-32, 2016.

Human papillomavirus (HPV)-related screening technologies and HPV vaccination offer enormous potential for cancer prevention, notably prevention of cervical cancer. The effectiveness of these approaches is, however, suboptimal owing to limited implementation of screening programmes and restricted indications for HPV vaccination. Trials of HPV vaccination in women aged up to 55 years have shown almost 90% protection from cervical precancer caused by HPV16/18 among HPV16/18-DNA-negative women. We propose extending routine vaccination programmes to women of up to 30 years of age (and to the 45-50-year age groups in some settings), paired with at least one HPV-screening test at age 30 years or older. Expanding the indications for HPV vaccination and much greater use of HPV testing in screening programmes has the potential to accelerate the decline in cervical cancer incidence. Such a combined protocol would represent an attractive approach for many health-care systems, in particular, countries in Central and Eastern Europe, Latin America, Asia, and some more-developed parts of Africa. The role of vaccination in women aged >30 years and the optimal number of HPV-screening tests required in vaccinated women remain important research issues. Cost-effectiveness models will help determine the optimal combination of HPV vaccination and screening in public health programmes, and to estimate the effects of such approaches in different populations.

Part 3: Bibliography of Speakers

List obtained via speaker forms or (if speaker form was not available) via a Pubmed search on Name of the speaker. (Ten) most recent articles are shown.

Patriciu Achimas, The Oncology Institute "Prof. Dr. Ion Chiricuta" (Romania)

(Based on a pubmed search)

Zaharie, F., G. Ciorogar, R. Zaharie, T. Mocan, C. Zdrehus, L. Mocan, I. Berindan-Neagoe, P. Achimas, C. Iancu and C. Tomus. **Laparoscopic rectal resection versus conventional open approach for rectal cancer - a 4-year experience of a single center.** J buon. 2015; 20(6): 1447-1455.

PURPOSE: This study was carried out to compare the therapeutic outcomes and complications of the laparoscopic and the conventional open surgery technique used for treating rectal cancer. Another goal was to find the fastest and most accurate method of treatment for rectal cancer, along with establishing the advantages and disadvantages of the two surgical techniques, depending on cancer location and its stage. **METHODS:** A total of 172 patients diagnosed with rectal cancer and hospitalized in the Department of Surgery III between January 1st 2008 and December 31st 2011 were studied. The laparoscopic approach was performed on 29 (16.8%) patients, and the remaining 143 (83.2%) underwent the conventional Miles/Lloyd-Davies abdominoperineal resection. A longitudinal study was conducted on patients with rectal resection, the used data being obtained from the database of the Department of Surgery III, hospital records, protocols and clinical charts of rectal cancer cases. **RESULTS:** There were no statistically significant differences regarding symptoms, gender, age, body mass index (BMI), tumor site, TNM stage, intraoperative accidents, operative time, and postoperative mortality between the two groups. The laparoscopic group presented advantages regarding antibiotic and analgesic therapy, early mobilization, hospital stay, intraoperative blood loss, resuming oral nutrition, bowel transit resumption, postoperative complications and wound complications. **CONCLUSION:** Laparoscopic abdominoperineal resection for rectal cancer is feasible, safe and effective. It can be safely performed by an experienced team, reducing the rate of postoperative complications, the need for blood transfusions, the administration of antibiotics and painkillers, allowing faster bowel transit resumption, shortening hospital stay and providing superior aesthetic results.

Marc Arbyn, Scientific Institute of Public Health (Belgium)

Arbyn M, Buntinx F, Van Ranst M, Paraskevaidis E, Martin-Hirsch P, Dillner J. **Virologic versus cytologic triage of women with equivocal Pap smears: a meta-analysis of the accuracy to detect high-grade intraepithelial neoplasia.** J Natl Cancer Inst. 2004; 96: 280-93.

BACKGROUND: The appropriate management of women with minor cytologic lesions in their cervix is unclear. We performed a meta-analysis to assess the accuracy of human papillomavirus (HPV) DNA testing as an alternative to repeat cytology in women who had equivocal results on a previous Pap smear. **METHODS:** Data were extracted from articles published between 1992 and 2002 that contained results of virologic and cytologic testing followed by colposcopically directed biopsy in women with an index smear showing atypical cells of undetermined significance (ASCUS). Fifteen studies were identified in which HPV triage and the histologic outcome (presence or absence of a cervical intraepithelial neoplasia of grade II or worse [CIN2+]) was documented. Nine, seven, and two studies also documented the accuracy of repeat cytology when the cutoff for abnormal cytology was set at a threshold of ASCUS or worse, low-grade squamous intraepithelial lesion (LSIL) or worse, or high-grade squamous intraepithelial lesion (HSIL) or worse, respectively. Random-effects models were used for pooling of accuracy parameters in case of interstudy heterogeneity. Differences in accuracy were assessed by pooling the ratio of the sensitivity (or specificity) of HPV testing to that of repeat cytology. **RESULTS:** The sensitivity and specificity were 84.4% (95% confidence interval [CI] = 77.6% to 91.1%) and 72.9% (95% CI = 62.5% to 83.3%), respectively, for HPV testing overall and 94.8% (95% CI = 92.7% to 96.9%) and 67.3% (95% CI = 58.2% to 76.4%), respectively, for HPV testing in the eight studies that used the Hybrid Capture II assay. Sensitivity and specificity of repeat cytology at a threshold for abnormal cytology of ASCUS or worse was 81.8% (95% CI = 73.5% to 84.3%) and 57.6% (95% CI = 49.5% to 65.7%), respectively. Repeat cytology that used higher cytologic thresholds yielded substantially lower sensitivity but higher specificity than triage with the Hybrid Capture II assay. The ratio of the sensitivity of the Hybrid Capture II assay to that of repeat cytology at a threshold of ASCUS or worse pooled from the four studies that used both triage tests was 1.16 (95% CI = 1.04 to 1.29). The specificity ratio was not statistically different from unity. **CONCLUSION:** The published literature indicates that the Hybrid Capture II assay has improved accuracy (higher sensitivity, similar specificity) than the repeat Pap smear using the threshold of ASCUS for an outcome of CIN2+ among women with equivocal cytologic results. The sensitivity of triage at higher cytologic cutoffs is poor.

Arbyn M, Sasieni P, Meijer CJ, Clavel C, Koliopoulos G, Dillner J. **Chapter 9: Clinical applications of HPV testing: a summary of meta-analyses.** Vaccine. 2006; 24 (SUPPL. 3): S78-S89.

BACKGROUND: More than ever, clinicians need regularly updated reviews given the continuously increasing amount of new information regarding innovative cervical cancer prevention methods. **MATERIAL AND METHODS:** A summary is given from recently published meta-analyses on three possible clinical applications of human papillomavirus (HPV)-DNA testing: triage of women with equivocal or low-grade cytological abnormalities; prediction of the therapeutic outcome after treatment of cervical intraepithelial neoplasia (CIN) lesions, and last not but not least, primary screening for cervical cancer and pre-cancer. **RESULTS:** Consistent evidence is available indicating that HPV-triage with the Hybrid Capture-2 assay (HC2) is more accurate (significantly higher sensitivity, similar specificity) than repeat cytology to triage women with equivocal Pap smear results. When triaging women with low-grade squamous intraepithelial lesions (LSIL), a reflex HC2 test does not show a significantly higher sensitivity, but a significantly lower specificity compared to a repeat Pap smear. After treatment of cervical lesions, HPV testing easily detects (with higher sensitivity and not lower specificity) residual or recurrent CIN than follow-up cytology. Primary screening with HC2 generally detects 23% (95% confidence interval, CI: 13-23%) more CIN-2, CIN-3, or cancer compared to cytology at cut-off atypical squamous cells of

undetermined significance (ASCUS) or LSIL, but is 6% (95% CI: 4-8%) less specific. By combined HPV and cytology screening, a further 4% (95% CI: 3-5%) more CIN-3 lesions can be identified but at the expense of a 7% (95% CI: 5-9%) loss in specificity, in comparison with isolated HC2 screening. **CONCLUSIONS:** Sufficient evidence exists to recommend HPV testing in triage of women with atypical cytology and in surveillance after treatment of CIN lesions. In the United States, recently reviewed knowledge has resulted in the approval of combined cytology and HC2 primary screening in women older than 30 years. However, in Europe, cytology-based screening still remains the standard screening method. The European screening policy will be reviewed based on the longitudinal results of randomised population trials which are currently underway.

Kyrgiou M, Koliopoulos G, Martin-Hirsch P, Arbyn M, Prendiville W, Paraskevaidis E. **Obstetric outcomes after conservative treatment for intra-epithelial or early invasive cervical lesions: a systematic review and meta-analysis of the literature.** *Lancet.* 2006; 367: 489-98.

Arbyn M, Kyrgiou M, Simoens C, Raifu AO, Koliopoulos G, Martin-Hirsch P et al. **Peri-natal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: a meta-analysis.** *BMJ.* 2008; 337: a1284.

OBJECTIVE: To assess the relative risk of perinatal mortality, severe preterm delivery, and low birth weight associated with previous treatment for precursors of cervical cancer. **DATA SOURCES:** Medline and Embase citation tracking from January 1960 to December 2007. Selection criteria Eligible studies had data on severe pregnancy outcomes for women with and without previous treatment for cervical intraepithelial neoplasia. Considered outcomes were perinatal mortality, severe preterm delivery (<32/34 weeks), extreme preterm delivery (<28/30 weeks), and low birth weight (<2000 g, <1500 g, and <1000 g). Excisional and ablative treatment procedures were distinguished. **RESULTS:** One prospective cohort and 19 retrospective studies were retrieved. Cold knife conisation was associated with a significantly increased risk of perinatal mortality (relative risk 2.87, 95% confidence interval 1.42 to 5.81) and a significantly higher risk of severe preterm delivery (2.78, 1.72 to 4.51), extreme preterm delivery (5.33, 1.63 to 17.40), and low birth weight of <2000 g (2.86, 1.37 to 5.97). Laser conisation, described in only one study, was also followed by a significantly increased chance of low birth weight of <2000 g and <1500 g. Large loop excision of the transformation zone and ablative treatment with cryotherapy or laser were not associated with a significantly increased risk of serious adverse pregnancy outcomes. Ablation by radical diathermy was associated with a significantly higher frequency of perinatal mortality, severe and extreme preterm delivery, and low birth weight below 2000 g or 1500 g. **CONCLUSIONS:** In the treatment of cervical intraepithelial neoplasia, cold knife conisation and probably both laser conisation and radical diathermy are associated with an increased risk of subsequent perinatal mortality and other serious pregnancy outcomes, unlike laser ablation and cryotherapy. Large loop excision of the transformation zone cannot be considered as completely free of adverse outcomes.

Arbyn M, Bergeron C, Klinkhamer P, Martin-Hirsch P, Siebers AG, Bulten J. **Liquid compared with conventional cervical cytology: a systematic review and meta-analysis.** *Obstet Gynecol.* 2008; 111: 167-77.

OBJECTIVE: To compare test performance characteristics of conventional Pap tests and liquid-based cervical cytology samples. **DATA SOURCES:** Eligible studies, published between 1991 and 2007, were retrieved through PubMed/EmBase searching and completed by consultation of other sources. **METHODS OF STUDY SELECTION:** Studies were selected if a conventional and a liquid-based sample were prepared from the same woman or when one or the other type of sample was taken from a separate but similar cohort. The current systematic review and meta-analysis is restricted to studies where all subjects were

submitted to gold standard verification, based on colposcopy and histology of colposcopy-targeted biopsies, allowing computation of absolute and relative test validity for cervical intraepithelial neoplasia grade 2 or worse. Randomized trials were selected as well if all test-positive cases were verified with the same gold standard, allowing computation of the relative sensitivity. Impact of study characteristics on accuracy was assessed by subgroup meta-analyses, meta-regression, and summary receiver operating characteristic curve regression. **TABULATION, INTEGRATION, AND RESULTS:** The relative sensitivity, pooled from eight studies, with complete gold standard verification and from one randomized clinical trial, did not differ significantly from unity. Also, the specificity, considering high-grade and low-grade squamous intraepithelial lesions as cutoff, was similar in conventional and liquid cytology. However, a lower pooled specificity was found for liquid-based cytology when presence of atypical squamous cells of undetermined significance was the cutoff (ratio 0.91, 95% confidence interval 0.84-0.98). Differences in study characteristics did not explain interstudy heterogeneity. **CONCLUSION:** Liquid-based cervical cytology is neither more sensitive nor more specific for detection of high-grade cervical intraepithelial neoplasia compared with the conventional Pap test.

Siebers AG, Klinkhamer PJ, Grefte JMM, Massuger LF, Vedder JEM, Arbyn M. **Comparison of liquid-based cytology with conventional cytology for detection of cervical cancer precursors: a randomized controlled trial.** JAMA. 2009; 302: 1757-64.

CONTEXT: Liquid-based cytology has been developed as an alternative for conventional cervical cytology. Despite numerous studies and systematic reviews, controversy remains about its diagnostic accuracy. **OBJECTIVE:** To assess the performance of liquid-based cytology compared with conventional cytology in terms of detection of histologically confirmed cervical intraepithelial neoplasia (CIN). **DESIGN, SETTING, AND PARTICIPANTS:** Cluster randomized controlled trial involving 89,784 women aged 30 to 60 years participating in the Dutch cervical screening program at 246 family practices. One hundred twenty-two practices were assigned to use liquid-based cytology and screened 49,222 patients and 124 practices were assigned to use the conventional Papanicolaou (Pap) test and screened 40,562 patients between April 2004 and July 1, 2006. Patients were followed up for 18 months through January 31, 2008. **INTERVENTION:** Screening for CIN using liquid-based cytology or conventional papanicolaou (Pap) test and the blinded review of all follow-up of screen-positive women (blinded to the type of cytology and the initial result). **MAIN OUTCOME MEASURES:** Intention-to-treat and per-protocol analysis of the detection rates of and positive predictive values for histologically verified CIN in both cytology systems. Outcomes are presented as crude and adjusted rate ratios (adjustment for age, urbanization, study site, and period). **RESULTS:** The adjusted detection rate ratios for CIN grade 1+ was 1.01 (95% confidence interval [CI], 0.85-1.19); for CIN grade 2+, 1.00 (95% CI, 0.84-1.20); for CIN grade 3+, 1.05 (95% CI, 0.86-1.29); and for carcinoma, 1.69 (95% CI, 0.96-2.99). The adjusted positive predictive value (PPV) ratios, considered at several cytological cutoffs and for various outcomes of CIN did not differ significantly from unity. **CONCLUSION:** This study indicates that liquid-based cytology does not perform better than conventional Pap tests in terms of relative sensitivity and PPV for detection of cervical cancer precursors.

Arbyn M, Anttila A, Jordan J, Ronco G, Schenck U, Segnan N, Wiener H, Herbert A, von Karsa L. **European Guidelines for Quality Assurance in Cervical Cancer Screening. Second Edition – Summary Document.** Ann Oncol. 2010; 21: 448-58.

European Guidelines for Quality Assurance in Cervical Cancer Screening have been initiated in the Europe Against Cancer Programme. The first edition established the principles of organised population-based screening and stimulated numerous pilot projects. The second multidisciplinary edition was published in 2008 and comprises approximately 250 pages divided into seven chapters prepared by 48 authors and contributors. Considerable attention has been devoted to organised, population-based programme policies which minimise adverse effects and maximise benefits of screening. It is hoped that this expanded guidelines edition will have a greater impact on countries in which screening programmes are still lacking and in which opportunistic screening has been preferred in the past. Other methodological aspects such as future prospects of human papillomavirus testing and vaccination in cervical cancer control have also been examined in the second edition; recommendations for integration of the latter technologies into European guidelines are currently under development in a related project supported by the European Union Health Programme. An overview of the fundamental points and principles that should support any quality-assured screening programme and key performance indicators are presented here in a summary document of the second guidelines edition in order to make these principles and standards known to a wider scientific community.

Arbyn M, Castellsagué X, de Sanjosé S, Bruni L, Saraiya M, Bray F, Ferlay J. **Worldwide burden of cervical cancer in 2008.** Ann Oncol. 2011; 22: 2675-86.

BACKGROUND: The knowledge that persistent human papillomavirus infection is the main cause of cervical cancer has resulted in the development of assays that detect nucleic acids of the virus and prophylactic vaccines. Up-to-date and reliable data are needed to assess impact of existing preventive measures and to define priorities for the future. **MATERIALS AND METHODS:** Best estimates on cervical cancer incidence and mortality are presented using recently compiled data from cancer and mortality registries for the year 2008. **RESULTS:** There were an estimated 530,000 cases of cervical cancer and 275,000 deaths from the disease in 2008. It is the third most common female cancer ranking after breast (1.38 million cases) and colorectal cancer (0.57 million cases). The incidence of cervical cancer varies widely among countries with world age-standardised rates ranging from <1 to >50 per 100,000. Cervical cancer is the leading cause of cancer-related death among women in Eastern, Western and Middle Africa; Central America; South-Central Asia and Melanesia. The highest incidence rate is observed in Guinea, with ~6.5% of women developing cervical cancer before the age of 75 years. India is the country with the highest disease frequency with 134,000 cases and 73 000 deaths. Cervical cancer, more than the other major cancers, affects women <45 years. **CONCLUSIONS:** In spite of effective screening methods, cervical cancer continues to be a major public health problem. New methodologies of cervical cancer prevention should be made available and accessible for women of all countries through well-organised programmes.

Arbyn M, Verdoordt F, Snijders PJF, Verhoef VM, Suonio E, Dillner J, Minozzi S, Bellisario C, Banzi R et al. **Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis.** *Lancet Oncol.* 2014; 15: 172-83.

BACKGROUND: Screening for human papillomavirus (HPV) infection is more effective in reducing the incidence of cervical cancer than screening using Pap smears. Moreover, HPV testing can be done on a vaginal sample self-taken by a woman, which offers an opportunity to improve screening coverage. However, the clinical accuracy of HPV testing on self-samples is not well-known. We assessed whether HPV testing on self-collected samples is equivalent to HPV testing on samples collected by clinicians. **METHODS:** We identified relevant studies through a search of PubMed, Embase, and CENTRAL. Studies were eligible for inclusion if they fulfilled all of the following selection criteria: a cervical cell sample was self-collected by a woman followed by a sample taken by a clinician; a high-risk HPV test was done on the self-sample (index test) and HPV-testing or cytological interpretation was done on the specimen collected by the clinician (comparator tests); and the presence or absence of cervical intraepithelial neoplasia grade 2 (CIN2) or worse was verified by colposcopy and biopsy in all enrolled women or in women with one or more positive tests. The absolute accuracy for finding CIN2 or worse, or CIN grade 3 (CIN3) or worse of the index and comparator tests as well as the relative accuracy of the index versus the comparator tests were pooled using bivariate normal models and random effect models. **FINDINGS:** We included data from 36 studies, which altogether enrolled 154 556 women. The absolute accuracy varied by clinical setting. In the context of screening, HPV testing on self-samples detected, on average, 76% (95% CI 69-82) of CIN2 or worse and 84% (72-92) of CIN3 or worse. The pooled absolute specificity to exclude CIN2 or worse was 86% (83-89) and 87% (84-90) to exclude CIN3 or worse. The variation of the relative accuracy of HPV testing on self-samples compared with tests on clinician-taken samples was low across settings, enabling pooling of the relative accuracy over all studies. The pooled sensitivity of HPV testing on self-samples was lower than HPV testing on a clinician-taken sample (ratio 0.88 [95% CI 0.85-0.91] for CIN2 or worse and 0.89 [0.83-0.96] for CIN3 or worse). Also specificity was lower in self-samples versus clinician-taken samples (ratio 0.96 [0.95-0.97] for CIN2 or worse and 0.96 [0.93-0.99] for CIN3 or worse). HPV testing with signal-based assays on self-samples was less sensitive and specific than testing on clinician-based samples. By contrast, some PCR-based HPV tests generally showed similar sensitivity on both self-samples and clinician-based samples. **INTERPRETATION:** In screening programmes using signal-based assays, sampling by a clinician should be recommended. However, HPV testing on a self-sample can be suggested as an additional strategy to reach women not participating in the regular screening programme. Some PCR-based HPV tests could be considered for routine screening after careful piloting assessing feasibility, logistics, population compliance, and costs.

Ronco G, Dillner J, Elfstrom KM, Tunesi S, Snijders PJ, Arbyn M. **Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials.** *Lancet.* 2014; 383: 524-32.

BACKGROUND: In four randomised trials, human papillomavirus (HPV)-based screening for cervical cancer was compared with cytology-based cervical screening, and precursors of cancer were the endpoint in every trial. However, direct estimates are missing of the relative efficacy of HPV-based versus cytology-based screening for prevention of invasive cancer in women who undergo regular screening, of modifiers (eg, age) of this relative efficacy, and of the duration of protection. We did a follow-up study of the four randomised trials to investigate these outcomes. **METHODS:** 176,464 women aged 20-64 years were randomly assigned to HPV-based (experimental arm) or cytology-based (control arm) screening in Sweden (Swedescreen), the Netherlands (POBASCAM), England (ARTISTIC), and Italy (NTCC). We followed up these women for a median of 6.5 years (1,214,415 person-years) and identified 107 invasive cervical carcinomas by linkage with screening, pathology, and cancer registries, by masked review of histological specimens, or from reports. Cumulative and study-adjusted rate ratios (experimental vs control) were calculated for incidence of invasive cervical carcinoma. **FINDINGS:** The rate ratio for invasive cervical carcinoma among all women from recruitment to end of follow-up was 0.60 (95% CI 0.40-0.89), with no heterogeneity between studies ($p=0.52$). Detection of invasive cervical carcinoma was similar between screening methods during the first 2.5 years of follow-up (0.79, 0.46-1.36) but was significantly lower in the experimental arm thereafter (0.45, 0.25-0.81). In women with a negative screening test at entry, the rate ratio was 0.30 (0.15-0.60). The cumulative incidence of invasive cervical carcinoma in women with negative entry tests was 4.6 per 10(5) (1.1-12.1) and 8.7 per 10(5) (3.3-18.6) at 3.5 and 5.5 years, respectively, in the experimental arm, and 15.4 per 10(5) (7.9-27.0) and 36.0 per 10(5) (23.2-53.5), respectively, in the control arm. Rate ratios did not differ by cancer stage, but were lower for adenocarcinoma (0.31, 0.14-0.69) than for squamous-cell carcinoma (0.78, 0.49-1.25). The rate ratio was lowest in women aged 30-34 years (0.36, 0.14-0.94). **INTERPRETATION:** HPV-based screening provides 60-70% greater protection against invasive cervical carcinomas compared with cytology. Data of large-scale randomised trials support initiation of HPV-based screening from age 30 years and extension of screening intervals to at least 5 years.

Iacopo Baussano, International Agency for Research on Cancer (France)

Baussano I, Elfstrom KM, Lazzarato F, Gillio-Tos A, De Marco L, Carozzi F, Del Mistro A, Dillner J, Franceschi S and Ronco G. **Type-specific human papillomavirus biological features: validated model-based estimates.** PLoS One. 2013; 8 (11): e81171.

Infection with high-risk (hr) human papillomavirus (HPV) is considered the necessary cause of cervical cancer. Vaccination against HPV16 and 18 types, which are responsible of about 75% of cervical cancer worldwide, is expected to have a major global impact on cervical cancer occurrence. Valid estimates of the parameters that regulate the natural history of hrHPV infections are crucial to draw reliable projections of the impact of vaccination. We devised a mathematical model to estimate the probability of infection transmission, the rate of clearance, and the patterns of immune response following the clearance of infection of 13 hrHPV types. To test the validity of our estimates, we fitted the same transmission model to two large independent datasets from Italy and Sweden and assessed finding consistency. The two populations, both unvaccinated, differed substantially by sexual behaviour, age distribution, and study setting (screening for cervical cancer or Chlamydia trachomatis infection). Estimated transmission probability of hrHPV types (80% for HPV16, 73%-82% for HPV18, and above 50% for most other types); clearance rates decreasing as a function of time since infection; and partial protection against re-infection with the same hrHPV type (approximately 20% for HPV16 and 50% for the other types) were similar in the two countries. The model could accurately predict the HPV16 prevalence observed in Italy among women who were not infected three years before. In conclusion, our models inform on biological parameters that cannot at the moment be measured directly from any empirical data but are essential to forecast the impact of HPV vaccination programmes.

Baussano, I., F. Lazzarato, M. Brisson and S. Franceschi. **Human Papillomavirus Vaccination at a Time of Changing Sexual Behavior.** Emerg Infect. 2016; Dis 22(1): 18-23.

Human papillomavirus (HPV) prevalence varies widely worldwide. We used a transmission model to show links between age-specific sexual patterns and HPV vaccination effectiveness. We considered rural India and the United States as examples of 2 heterosexual populations with traditional age-specific sexual behavior and gender-similar age-specific sexual behavior, respectively. We simulated these populations by using age-specific rates of sexual activity and age differences between sexual partners and found that transitions from traditional to gender-similar sexual behavior in women <35 years of age can result in increased (2.6-fold in our study) HPV16 prevalence. Our model shows that reductions in HPV16 prevalence are larger if vaccination occurs in populations before transitions in sexual behavior and that increased risk for HPV infection attributable to transition is preventable by early vaccination. Our study highlights the importance of using time-limited opportunities to introduce HPV vaccination in traditional populations before changes in age-specific sexual patterns occur.

Baussano I, Franceschi S and Plummer M. **Infection transmission and chronic disease models in the study of infection-associated cancers.** Br J Cancer. 2014; 110 (1): 7-11.

In the last three decades, the appreciation of the role of infections in cancer aetiology has greatly expanded. Among the 13 million new cancer cases that occurred worldwide in 2008, around 2 million (16%) were attributable to infections. Concurrently, the approach to prevention of infection-related cancers is shifting from cancer control to infection control, for example, vaccination and the detection of infected individuals. In support of this change, the use of infection transmission models has entered the field of infection-related cancer epidemiology. These models are useful to understand the infection

transmission processes, to estimate the key parameters that govern the spread of infection, and to project the potential impact of different preventive measures. However, the concepts, terminology, and methods used to study infection transmission are not yet well known in the domain of cancer epidemiology. This review aims to concisely illustrate the main principles of transmission dynamics, the basic structure of infection transmission models, and their use in combination with empirical data. We also briefly summarise models of carcinogenesis and discuss their specificities and possible integration with models of infection natural history.

Franceschi S and Baussano I. **Naturally acquired immunity against human papillomavirus (HPV): why it matters in the HPV vaccine era.** J Infect Dis. 2014; 210 (4): 507-509.

No abstract available.

Baussano I, Tshomo U, Clifford GM, Tenet V, Tshokey T and Franceschi S. **Cervical cancer screening program in Thimphu, Bhutan: population coverage and characteristics associated with screening attendance.** BMC Womens Health. 2014; 14: 147.

BACKGROUND: Bhutan has been engaged in good-quality cytology-based cervical screening since 2000 and has vaccinated >90% girls against human papillomavirus (HPV) since 2010. We explored the characteristics associated with lack of previous screening and screening coverage in women age ≥ 25 years. **METHODS:** Women were invited at home or during their attendance at 2 outpatient clinics, in the capital, Thimphu, and nearby Lungthenphu. Age-adjusted odds ratios for lack of previous screening by selected characteristics were computed among 1,620 participating women. In Thimphu an invitation registry allowed to estimate screening history not only among participating women but also among additional 500 women who did not accept to join our study. **RESULTS:** Among women who had a Pap smear, lack of previous screening was associated with age <35 or ≥ 45 years. It was also associated with some occupations; being single, or widowed/separated; and presence of HPV infection. Multiparity and use of contraceptive methods were associated with having been screened. In women invited at home in Thimphu screening history substantially differed by participation. Past screening attendance was 59% among women recruited in the 2 clinics, 53% in women who were invited from home and accepted the invitation, but only 25% in those who refused it. Based on all women recruited from home the estimate of population-based coverage in Thimphu is 34% (95% CI: 31-37). **CONCLUSIONS:** Transition from an opportunistic screening to an all-reaching population-based screening is yet to be achieved in Bhutan, even in the capital. Better ways to target never-screened women are needed.

Xavier F. Bosch, Catalanian Institute of Ocology (Spain)

(Based on pubmed search)

Aleman, L., A. Cubilla, G. Halec, E. Kasamatsu, B. Quiros, E. Masferrer, S. Tous, B. Lloveras, G. Hernandez-Suarez, R. Lonsdale, L. Tinoco, M. Alejo, I. Alvarado-Cabrero, J. Laco, N. Guimera, E. Poblet, L. E. Lombardi, C. Bergeron, O. Clavero, H. R. Shin, A. Ferrera, A. Felix, J. Germar, V. Mandys, C. Clavel, M. Tzardi, L. E. Pons, V. Wain, E. Cruz, C. Molina, J. D. Mota, R. Jach, J. Velasco, C. Carrilho, R. Lopez-Revilla, M. T. Goodman, W. G. Quint, X. Castellsague, I. Bravo, M. Pawlita, N. Munoz, F. X. Bosch and S. de Sanjose. **Role of Human Papillomavirus in Penile Carcinomas Worldwide.** *Eur Urol.* 2016; 69(5): 953-961.

BACKGROUND: Invasive penile cancer is a rare disease with an approximately 22 000 cases per year. The incidence is higher in less developed countries, where penile cancer can account for up to 10% of cancers among men in some parts of Africa, South America, and Asia. **OBJECTIVE:** To describe the human papillomavirus (HPV) DNA prevalence, HPV type distribution, and detection of markers of viral activity (ie, E6*I mRNA and p16(INK4a)) in a series of invasive penile cancers and penile high-grade squamous intraepithelial lesions (HGSILs) from 25 countries. A total of 85 penile HGSILs and 1010 penile invasive cancers diagnosed from 1983 to 2011 were included. **DESIGN, SETTING, AND PARTICIPANTS:** After histopathologic evaluation of formalin-fixed paraffin-embedded samples, HPV DNA detection and genotyping were performed using the SPF-10/DEIA/LiPA25 system, v.1 (Laboratory Biomedical Products, Rijswijk, The Netherlands). HPV DNA-positive cases were additionally tested for oncogene E6*I mRNA and all cases for p16(INK4a) expression, a surrogate marker of oncogenic HPV activity. **OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS:** HPV DNA prevalence and type distributions were estimated. **RESULTS AND LIMITATIONS:** HPV DNA was detected in 33.1% of penile cancers (95% confidence interval [CI], 30.2-36.1) and in 87.1% of HGSILs (95% CI, 78.0-93.4). The warty-basaloid histologic subtype showed the highest HPV DNA prevalence. Among cancers, statistically significant differences in prevalence were observed only by geographic region and not by period or by age at diagnosis. HPV16 was the most frequent HPV type detected in both HPV-positive cancers (68.7%) and HGSILs (79.6%). HPV6 was the second most common type in invasive cancers (3.7%). The p16(INK4a) upregulation and mRNA detection in addition to HPV DNA positivity were observed in 69.3% of HGSILs, and at least one of these HPV activity markers was detected in 85.3% of cases. In penile cancers, these figures were 22.0% and 27.1%, respectively. **CONCLUSIONS:** About a third to a fourth of penile cancers were related to HPV when considering HPV DNA detection alone or adding an HPV activity marker, respectively. The observed HPV type distribution reinforces the potential benefit of current and new HPV vaccines in the reduction of HPV-related penile neoplastic lesions. **PATIENT SUMMARY:** About one-third to one-quarter of penile cancers were related to human papillomavirus (HPV). The observed HPV type distribution reinforces the potential benefit of current and new HPV vaccines to prevent HPV-related penile neoplastic lesions.

Bosch, F. X., C. Robles, M. Diaz, M. Arbyn, I. Baussano, C. Clavel, G. Ronco, J. Dillner, M. Lehtinen, K. U. Petry, M. Poljak, S. K. Kjaer, C. J. Meijer, S. M. Garland, J. Salmeron, X. Castellsague, L. Bruni, S. de Sanjose and J. Cuzick; **HPV-FASTER: broadening the scope for prevention of HPV-related cancer.** *Nat Rev Clin Oncol.* 2016; 13(2): 119-132.

Human papillomavirus (HPV)-related screening technologies and HPV vaccination offer enormous potential for cancer prevention, notably prevention of cervical cancer. The effectiveness of these approaches is, however, suboptimal owing to limited implementation of screening programmes and restricted indications for HPV vaccination. Trials of HPV vaccination in women aged up to 55 years have shown almost 90% protection from cervical precancer caused by HPV16/18 among HPV16/18-DNA-negative women. We propose extending routine vaccination programmes to women of up to 30 years of

age (and to the 45-50-year age groups in some settings), paired with at least one HPV-screening test at age 30 years or older. Expanding the indications for HPV vaccination and much greater use of HPV testing in screening programmes has the potential to accelerate the decline in cervical cancer incidence. Such a combined protocol would represent an attractive approach for many health-care systems, in particular, countries in Central and Eastern Europe, Latin America, Asia, and some more-developed parts of Africa. The role of vaccination in women aged >30 years and the optimal number of HPV-screening tests required in vaccinated women remain important research issues. Cost-effectiveness models will help determine the optimal combination of HPV vaccination and screening in public health programmes, and to estimate the effects of such approaches in different populations.

Company, A., M. Montserrat, F. X. Bosch and S. de Sanjose. **Training in the prevention of cervical cancer: advantages of e-learning.** *Ecancermedicalscience*. 2016; 9: 580.

Cervical cancer remains the second most common cancer for women worldwide and is the cancer priority in most low- and middle-income countries (LMIC). The development of vaccines against the human papilloma virus (HPV) and the impact of technology both for the detection of HPV and cervical cancer represent milestones and new opportunities in prevention. New internet-based technologies are generating mass access to training programmes. This article presents the methodology for developing an online training programme for the prevention of cervical cancer as well as the results obtained during the four year period wherein the same programme was delivered in Latin America.

Garland, S. M., A. K. Subasinghe, Y. L. Jayasinghe, J. D. Wark, A. B. Moscicki, A. Singer, X. Bosch, K. Cusack and M. Stanley. **HPV vaccination for victims of childhood sexual abuse.** *Lancet*. 2015; 386(10007): 1919-1920.

Georgalis, L., S. de Sanjose, M. Esnaola, F. X. Bosch and M. Diaz. **Present and future of cervical cancer prevention in Spain: a cost-effectiveness analysis.** *Eur J Cancer Prev*. 2015.

Human papillomavirus (HPV) vaccination within a nonorganized setting creates a poor cost-effectiveness scenario. However, framed within an organized screening including primary HPV DNA testing with lengthening intervals may provide the best health value for invested money. To compare the effectiveness and cost-effectiveness of different cervical cancer (CC) prevention strategies, including current status and new proposed screening practices, to inform health decision-makers in Spain, a Markov model was developed to simulate the natural history of HPV and CC. Outcomes included cases averted, life expectancy, reduction in the lifetime risk of CC, life years saved, quality-adjusted life years (QALYs), net health benefits, lifetime costs, and incremental cost-effectiveness ratios. The willingness-to-pay threshold is defined at 20 000€/QALY. Both costs and health outcomes were discounted at an annual rate of 3%. A strategy of 5-year organized HPV testing has similar effectiveness, but higher efficiency than 3-year cytology. Screening alone and vaccination combined with cytology are dominated by vaccination followed by 5-year HPV testing with cytology triage (12 214€/QALY). The optimal age for both ending screening and switching age from cytology to HPV testing in older women is 5 years later for unvaccinated than for vaccinated women. Net health benefits decrease faster with diminishing vaccination coverage than screening coverage. Primary HPV DNA testing is more effective and cost-effective than current cytological screening. Vaccination uptake improvements and a gradual change toward an organized screening practice are critical components for achieving higher effectiveness and efficiency in the prevention of CC in Spain.

Rossi, P. G., G. Ronco, J. Dillner, K. M. Elfstrom, P. J. Snijders, M. Arbyn, J. Berkhof, F. Carozzi, A. Del Mistro, S. De Sanjose, X. Bosch, K. U. Petry, M. Poljak, C. Naldoni and C. J. Meijer). Why follow-back studies should be interpreted cautiously: The case of an HPV-negative cervical lesion. *Cancer Cytopathol* 124(1): 66-67.

Roura, E., N. Travier, T. Waterboer, S. de Sanjose, F. X. Bosch, M. Pawlita, V. Pala, E. Weiderpass, N. Margall, J. Dillner, I. T. Gram, A. Tjonneland, C. Munk, D. Palli, K. T. Khaw, K. Overvad, F. Clavel-Chapelon, S. Mesrine, A. Fournier, R. T. Fortner, J. Ose, A. Steffen, A. Trichopoulou, P. Lagiou, P. Orfanos, G. Masala, R. Tumino, C. Sacerdote, S. Polidoro, A. Mattiello, E. Lund, P. H. Peeters, H. B. Bueno-de-Mesquita, J. R. Quiros, M. J. Sanchez, C. Navarro, A. Barricarte, N. Larranaga, J. Ekstrom, D. Lindquist, A. Idahl, R. C. Travis, M. A. Merritt, M. J. Gunter, S. Rinaldi, M. Tommasino, S. Franceschi, E. Riboli and X. Castellsague. **The Influence of Hormonal Factors on the Risk of Developing Cervical Cancer and Pre-Cancer: Results from the EPIC Cohort.** *PLoS One*. 2016; 11(1): e0147029.

BACKGROUND: In addition to HPV, high parity and hormonal contraceptives have been associated with cervical cancer (CC). However, most of the evidence comes from retrospective case-control studies. The aim of this study is to prospectively evaluate associations between hormonal factors and risk of developing cervical intraepithelial neoplasia grade 3 (CIN3)/carcinoma in situ (CIS) and invasive cervical cancer (ICC). **METHODS AND FINDINGS:** We followed a cohort of 308,036 women recruited in the European Prospective Investigation into Cancer and Nutrition (EPIC) Study. At enrollment, participants completed a questionnaire and provided serum. After a 9-year median follow-up, 261 ICC and 804 CIN3/CIS cases were reported. In a nested case-control study, the sera from 609 cases and 1,218 matched controls were tested for L1 antibodies against HPV types 11,16,18,31,33,35,45,52,58, and antibodies against *Chlamydia trachomatis* and Human herpesvirus 2. Multivariate analyses were performed to estimate hazard ratios (HR), odds ratios (OR) and corresponding 95% confidence intervals (CI). The cohort analysis showed that number of full-term pregnancies was positively associated with CIN3/CIS risk (p -trend = 0.03). Duration of oral contraceptives use was associated with a significantly increased risk of both CIN3/CIS and ICC (HR = 1.6 and HR = 1.8 respectively for ≥ 15 years versus never use). Ever use of menopausal hormone therapy was associated with a reduced risk of ICC (HR = 0.5, 95%CI: 0.4-0.8). A non-significant reduced risk of ICC with ever use of intrauterine devices (IUD) was found in the nested case-control analysis (OR = 0.6). Analyses restricted to all cases and HPV seropositive controls yielded similar results, revealing a significant inverse association with IUD for combined CIN3/CIS and ICC (OR = 0.7). **CONCLUSIONS:** Even though HPV is the necessary cause of CC, our results suggest that several hormonal factors are risk factors for cervical carcinogenesis. Adherence to current cervical cancer screening guidelines should minimize the increased risk of CC associated with these hormonal risk factors.

Sanchez, G. I., L. E. Bravo, G. Hernandez-Suarez, S. Tous, L. Alemany, S. de Sanjose, F. X. Bosch and N. Munoz. **Secular trends of HPV genotypes in invasive cervical cancer in Cali, Colombia 1950-1999.** *Cancer Epidemiol.* 2016; 40: 173-178.

Aim To estimate relative contribution and time trends of HPV types in cervical cancer in Cali, Colombia over a 50 years' period. **METHODS:** Paraffin blocks of 736 cervical cancer histological confirmed cases were retrieved from the pathology laboratory at Hospital Universitario del Valle (Cali, Colombia) and HPV genotyped using SPF10-PCR/DEIA/LiPA25 (version 1) assay. Marginal effect of age and year of diagnosis in secular trends of HPV type prevalence among HPV+ cases were assessed by robust Poisson regression analysis. **RESULTS:** 64.7% (95%CI: 59.9-69.2) of squamous cell carcinomas (SCCs) were attributed to HPV 16 and 18, 78.2% (95%CI: 74-82) to HPV 16, 18, 31, 33 and 45 and 84.8% (95%CI: 81-88.1) to HPV 16, 18, 31, 33, 45, 52 and 58 while ninety-three percent of adenocarcinomas (ADCs) were attributed to HPV 16, 18 and 45 only. The prevalence of specific HPV types did not change over the 50-year period. A significant downward trend of prevalence ratios of HPV16 ($P=0.017$) and alpha7 but HPV

18 (i.e., HPV 39, 45, 68, 70, $P=0.024$) with increasing age at diagnosis was observed. In contrast, the prevalence ratio to other HPV genotypes of alpha9 but HPV 16 genotypes (i.e., HPV 31, 33, 35, 52, 58, 67, $P=0.002$) increased with increasing age at diagnosis. **CONCLUSION:** No changes were observed in the relative contribution of HPV types in cervical cancer in Cali, Colombia during the 50 years. In this population, an HPV vaccine including the HPV 16, 18, 31, 33, 45, 52 and 58 genotypes may have the potential to prevent approximately 85% and 93% of SCC and ADC cases respectively.

Schutze, D. M., O. Krijgsman, P. J. Snijders, B. Ylstra, J. Weischenfeldt, B. R. Mardin, A. M. Stutz, J. O. Korbel, J. P. de Winter, C. J. Meijer, W. G. Quint, L. Bosch, S. M. Wilting and R. D. Steenbergen. **Immortalization capacity of HPV types is inversely related to chromosomal instability.** *Oncotarget*. 2016;

High-risk human papillomavirus (hrHPV) types induce immortalization of primary human epithelial cells. Previously we demonstrated that immortalization of human foreskin keratinocytes (HFKs) is HPV type dependent, as reflected by the presence or absence of a crisis period before reaching immortality. This study determined how the immortalization capacity of ten hrHPV types relates to DNA damage induction and overall genomic instability in HFKs. Twenty five cell cultures obtained by transduction of ten hrHPV types (i.e. HPV16/18/31/33/35/45/51/59/66/70 E6E7) in two or three HFK donors each were studied. All hrHPV-transduced HFKs showed an increased number of double strand DNA breaks compared to controls, without exhibiting significant differences between types. However, immortal descendants of HPV-transduced HFKs that underwent a prior crisis period (HPV45/51/59/66/70-transduced HFKs) showed significantly more chromosomal aberrations compared to those without crisis (HPV16/18/31/33/35-transduced HFKs). Notably, the hTERT locus at 5p was exclusively gained in cells with a history of crisis and coincided with increased expression. Chromothripsis was detected in one cell line in which multiple rearrangements within chromosome 8 resulted in a gain of MYC. Together we demonstrated that upon HPV-induced immortalization, the number of chromosomal aberrations is inversely related to the viral immortalization capacity. We propose that hrHPV types with reduced immortalization capacity in vitro, reflected by a crisis period, require more genetic host cell aberrations to facilitate immortalization than types that can immortalize without crisis. This may in part explain the observed differences in HPV-type prevalence in cervical cancers and emphasizes that changes in the host cell genome contribute to HPV-induced carcinogenesis.

Van Damme, P., P. Bonanni, F. X. Bosch, E. Joura, S. K. Kjaer, C. J. Meijer, K. U. Petry, B. Soubeyrand, T. Verstraeten and M. Stanley. **Use of the nonavalent HPV vaccine in individuals previously fully or partially vaccinated with bivalent or quadrivalent HPV vaccines.** *Vaccine*. 2016; 34(6): 757-761.

With the availability of the nonavalent human papillomavirus (HPV) vaccine, vaccinees, parents and healthcare providers need guidance on how to complete an immunization course started with the bi- or quadrivalent vaccine and whether to revaccinate individuals who have completed a full immunization course with the bi- or quadrivalent vaccine. To answer these questions three parameters should be considered: age at the start of vaccination (9 to 14 years of age versus 15 years and older, the cut-off for 2 or 3 doses schedule), the number of doses already received and the time interval between doses. Based on a number of scenarios, we propose that the 9-valent vaccine can be used to complete an incomplete vaccination regimen or might be added to a previous completed schedule to extend protection.

Monica Chaturvedi, Monica Chaturvedi, Public Health Foundation (India)

VSQ, [Communication guidelines for building vaccine confidence around AEFI](#), Vaccine Safety Quarterly 4/214.

Immunization Technical Support Unit. [Communication guidelines for building vaccine confidence around AEFI](#). Government of India. 2013.

Immunization Technical Support Unit. [Communication plan a model approach](#). Ministry of Health & Family Welfare (India).

Immunization Technical Support Unit. [AEFI media response protocol](#). Ministry of Health & Family Welfare (India).

Silvia de Sanjose, Catalanian Institute of Oncology (Spain)

Bosch FX, Robles C, Díaz M, Arbyn M, Baussano I, Clavel C, Ronco G, Dillner J, Lehtinen M, Petry KU, Poljak M, Kjaer SK, Meijer CJ, Garland SM, Salmerón J, Castellsagué X, Bruni L, de Sanjosé S, Cuzick J. **HPV-FASTER: broadening the scope for prevention of HPV-related cancer.** *Nat Rev Clin Oncol.* 2015. . *Nat Rev Clin Oncol.* Feb;13(2):119-32, 2016.

Human papillomavirus (HPV)-related screening technologies and HPV vaccination offer enormous potential for cancer prevention, notably prevention of cervical cancer. The effectiveness of these approaches is, however, suboptimal owing to limited implementation of screening programmes and restricted indications for HPV vaccination. Trials of HPV vaccination in women aged up to 55 years have shown almost 90% protection from cervical precancer caused by HPV16/18 among HPV16/18-DNA-negative women. We propose extending routine vaccination programmes to women of up to 30 years of age (and to the 45-50-year age groups in some settings), paired with at least one HPV-screening test at age 30 years or older. Expanding the indications for HPV vaccination and much greater use of HPV testing in screening programmes has the potential to accelerate the decline in cervical cancer incidence. Such a combined protocol would represent an attractive approach for many health-care systems, in particular, countries in Central and Eastern Europe, Latin America, Asia, and some more-developed parts of Africa. The role of vaccination in women aged >30 years and the optimal number of HPV-screening tests required in vaccinated women remain important research issues. Cost-effectiveness models will help determine the optimal combination of HPV vaccination and screening in public health programmes, and to estimate the effects of such approaches in different populations.

Serrano B, de Sanjosé S, Tous S, Quiros B, Muñoz N, Bosch X, Alemany L. **Human papillomavirus genotype attribution for HPVs 6, 11, 16, 18, 31, 33, 45, 52 and 58 in female anogenital lesions.** *Eur J Cancer.* 2015; 51(13):1732-41.

OBJECTIVE: Human papillomavirus (HPV) vaccines can potentially control cervical cancer and help to reduce other HPV-related cancers. We aimed to estimate the relative contribution (RC) of the nine types (HPVs 16/18/31/33/45/52/58/6/11) included in the recently approved 9-valent HPV vaccine in female anogenital cancers and precancerous lesions (cervix, vulva, vagina and anus). **METHODS:** Estimations were based on an international study designed and coordinated at the Catalan Institute of Oncology (Barcelona-Spain), including information on 10,575 invasive cervical cancer (ICC), 1709 vulvar, 408 vaginal and 329 female anal cancer cases and 587 Vulvar Intraepithelial Neoplasia grade 2/3 (VIN2/3), 189 Vaginal Intraepithelial Neoplasia grade 2/3 (VaIN2/3) and 29 Anal Intraepithelial Neoplasia grade 2/3 (AIN2/3) lesions. Consecutive histologically confirmed paraffin-embedded cases were obtained from hospital pathology archives from 48 countries worldwide. HPV DNA-detection and typing was performed by SPF10-DEIA-LiPA25 system and RC was expressed as the proportion of type-specific cases among HPV positive samples. Multiple infections were added to single infections using a proportional weighting attribution. **RESULTS:** HPV DNA prevalence was 84.9%, 28.6%, 74.3% and 90.0% for ICC, vulvar, vaginal and anal cancers, respectively, and 86.7%, 95.8% and 100% for VIN2/3, VaIN2/3 and AIN2/3, respectively. RC of the combined nine HPV types was 89.5% (95% confidence interval (CI): 88.8-90.1)-ICC, 87.1% (83.8-89.9)-vulvar, 85.5% (81.0-89.2)-vaginal, 95.9% (93.0-97.9)-female anal cancer, 94.1% (91.7-96.0)-VIN2/3, 78.7% (71.7-84.2)-VaIN2/3 and 86.2% (68.3-96.1)-AIN2/3. HPV16 was the most frequent type in all lesions. Variations in the RC of HPVs 31/33/45/52/58 by cancer site were observed, ranging from 7.8% (5.0-11.4)-female anal cancer to 20.5% (16.1-25.4)-vaginal cancer. **CONCLUSIONS:** The addition of HPVs 31/33/45/52/58 to HPV types included in current vaccines (HPV16/18) could prevent almost 90% of HPV positive female anogenital lesions worldwide. Taking into account that most HPV-related cancers are ICC ones, the 9-valent HPV vaccine could potentially avoid almost 88% of all female anogenital cancers.

Quesada P, Whitby D, Benavente Y, Miley W, Labo N, Chichareon S, Trong N, Shin HR, Anh PT, Thomas J, Matos E, Herrero R, Muñoz N, Molano M, Franceschi S, de Sanjosé S. **Hepatitis C virus seroprevalence in the general female population from 8 countries.** *J Clin Virol.* 2015; 68:89-93.

BACKGROUND: Hepatitis C virus (HCV) infection is a significant global health issue because it is widespread and persistent and can cause serious liver diseases. **OBJECTIVES:** The aim of this study is to estimate HCV prevalence in women from the general population in different geographical areas worldwide and to assess the potential role of sexual behaviour in the virus transmission. **STUDY DESIGN:** Each participating centre recruited a random sample of women from the general population aged from less than 20 to more than 75 years. The study included 8130 women from 8 countries with information on sociodemographic factors, reproductive and sexual behaviour, smoking habit and HPV DNA through individual interviews. A blood sample was also collected to perform serological tests. We estimated the prevalence ratios associated to HCV to evaluate the effect of sexual behaviour in viral transmission. **RESULTS:** Women were reactive to a minimum of two HCV antigens, including at least one nonstructural protein were considered as positive (33% of the samples were classified as positive, 40% as negative, and 27% as indeterminate (N=402), that were considered as not positive). The age-adjusted HCV seroprevalence varied significantly by regions (0.3% in Argentina to 21.1% in Nigeria). We found no association between HCV prevalence and age, educational level, smoking habit and any of the available variables for sexual behaviour and reproductive history. **CONCLUSIONS:** This large study showed heterogeneous distribution of HCV seroprevalence in female and provides evidence of the null impact of sexual behaviour in HCV transmission.

Ndiaye C, Mena M, Alemany L, Arbyn M, Castellsagué X, Laporte L, Bosch FX, de Sanjosé S, Trottier H. **HPV DNA, E6/E7 mRNA, and p16INK4a detection in head and neck cancers: a systematic review and meta-analysis.** *Lancet Oncol.* 2014; 15(12):1319-31.

BACKGROUND: We aimed to provide updated information about the global estimates of attributable fraction and type distribution of human papillomavirus (HPV) in head and neck squamous cell carcinomas by doing a systematic review and meta-analysis. **METHODS:** We did a literature search on PubMed to identify studies that used PCR for detection of HPV DNA in head and neck squamous cell carcinomas with information about HPV genotype distribution. We included studies that tested 20 or more biopsies per cancer site and were published between July 15, 1990, and Feb 29, 2012. We collected information about sex, risk factors, HPV detection methods, and biomarkers of potentially HPV-induced carcinogenesis (E6/E7 mRNA and p16(INK4a)). If it was not possible to abstract the required information directly from the paper, we contacted the authors. We did a meta-analysis to produce pooled prevalence estimates including a meta-regression to explore sources of heterogeneity. **FINDINGS:** 148 studies were included, contributing data for 12 163 cases of head and neck squamous cell carcinoma from 44 countries. HPV DNA was detected in 3837 cases. HPV16 accounted for 82.2% (95% CI 77.7-86.4) of all HPV DNA positive cases. By cancer site, pooled HPV DNA prevalence estimates were 45.8% (95% CI 38.9-52.9) for oropharynx, 22.1% (16.4-28.3) for larynx (including hypopharynx), and 24.2% (18.7-30.2) for oral cavity. The percent positivity of p16(INK4a) positive cases in HPV-positive oropharyngeal cancer cases was 86.7% (95% CI 79.2-92.9) and of E6/E7 mRNA positive cases was 86.9% (73.2-96.8). The estimate of HPV attributable fraction in oropharyngeal cancer defined by expression of positive cases of E6/E7 mRNA was 39.8% and of p16(INK4a) was 39.7%. Of subsites, tonsils (53.9%, 95% CI 46.4-61.3) had the highest HPV DNA prevalence. HPV DNA prevalence varied significantly by anatomical site, geographic region, but not by sex or tobacco or alcohol consumption. **INTERPRETATION:** The contribution of HPV prevalence in head

and neck squamous cell carcinoma and in particular that of HPV16 in the oropharynx shows the potential benefit of prophylactic vaccines.

Serrano B, Alemany L, Ruiz PA, Tous S, Lima MA, Bruni L, Jain A, Clifford GM, Qiao YL, Weiss T, Bosch FX, de Sanjosé S. **Potential impact of a 9-valent HPV vaccine in HPV-related cervical disease in 4 emerging countries (Brazil, Mexico, India and China)**. *Cancer Epidemiol.* 2014; 38(6):748-56.

BACKGROUND: We estimated the potential impact of an investigational 9-valent human papillomavirus (HPV) vaccine (HPVs 6/11/16/18/31/33/45/52/58) in HPV-related cervical disease in Brazil, Mexico, India and China, to help to formulate recommendations on cervical cancer prevention and control. **METHODS:** Estimations for invasive cervical cancer (ICC) were based on an international study including 1356 HPV-positive cases for the four countries altogether, and estimations for precancerous cervical lesions were extracted from a published meta-analysis including 6 025 HPV-positive women from the four mentioned countries. Globocan 2012 and 2012 World Population Prospects were used to estimate current and future projections of new ICC cases. **RESULTS:** Combined proportions of the 9 HPV types in ICC were 88.6% (95%CI: 85.2-91.3) in Brazil, 85.7% (82.3-88.8) in Mexico, 92.2% (87.9-95.3) in India and 97.3% (93.9-99.1) in China. The additional HPV 31/33/45/52/58 proportions were 18.8% (15.3-22.7) in Brazil, 17.6% (14.2-21.2) in Mexico, 11.3% (7.5-16.1) in India and 11.9% (7.5-17.2) in China. HPV6 and 11 single types were not identified in any of the samples. Proportion of the individual 7 high risk HPV types included in the vaccine varied by cytological and histological grades of HPV-positive precancerous cervical lesions. HPV 16 was the dominant type in all lesions, with contributions in low grade lesions ranging from 16.6%(14.3-19.2) in Mexico to 39.8% (30.0-50.2) in India, and contributions in high grade lesions ranging from 43.8% (36.3-51.4) in Mexico to 64.1% (60.6-67.5) in Brazil. After HPV 16, variations in other majors HPV types were observed by country, with an under representation of HPV 18 and 45 compared to ICC. **CONCLUSION:** The addition of HPVs 31/33/45/52/58 to HPV types included in current vaccines could increase the ICC preventable fraction in a range of 12 to 19% across the four countries, accounting the 9-types altogether 90% of ICC cases. Assuming the same degree of efficacy of current vaccines, the implementation of the 9-valent HPV vaccine in Brazil, Mexico, India and China would substantially impact on the reduction of the world cervical cancer burden.

Kate Gallagher, London school of Hygiene and Tropical Medicine (UK)

Gallagher KE, Baisley K, Grosskurth H, Vallely A, Kapiga AS, Vandepitte J, Kamali A, de Sanjosé S, Chagalucha J, Hayes R, Watson-Jones D. **The Association Between Cervical Human Papillomavirus Infection and Subsequent HIV Acquisition in Tanzanian and Ugandan Women: A Nested Case-Control Study** *J Infect Dis.* 2016. 214(1):87-95.

OBJECTIVE: This study was performed to analyze the associations between cervical human papillomavirus (HPV) infection and human immunodeficiency virus (HIV) acquisition, using cervical samples from previous studies in Tanzania and Uganda. **METHODS:** A total of 161 adult women who acquired HIV infection during follow-up and 464 individually matched HIV-seronegative controls were selected from 5 cohorts of women working in bars and recreational facilities. Stored cervical samples were tested for 37 HPV genotypes, using a polymerase chain reaction assay (Roche Linear Array genotyping assay). Multivariate matched analysis using conditional logistic regression was performed to evaluate HPV infection, persistence, and clearance as predictors of HIV acquisition. **RESULTS:** HIV seroconverters were significantly more likely than controls to frequently drink alcohol and to be infected with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or herpes simplex virus type 2. There was no evidence of an association between HIV acquisition and any detectable HPV at the visit prior to HIV seroconversion (adjusted odds ratio, 1.02; 95% confidence interval, .66-1.57) or between HIV acquisition and persistent HPV infection (defined as 2 positive HPV genotype-specific test results at least 6 months apart), cleared HPV infection (defined as a positive HPV test result followed by negative HPV genotype-specific test result), or newly acquired HPV infection, compared with HPV-negative women. **CONCLUSIONS:** There was no evidence of association between HPV infection status and subsequent HIV acquisition. These results stand in contrast to other observational studies.

Gallagher KE, Griffiths UK, Burchett HED, et al. **Lessons learnt from human papillomavirus vaccine delivery in low and middle-income countries.** Abstract presented at 30th International Papillomavirus Conference, Lisbon, Portugal 17th-21st September 2015 (Abstract HPV15-0130) 2015.

Gallagher KE, Kadokura E, Eckert LO, et al. **Factors influencing completion of multi-dose vaccine schedules in adolescents: a systematic review.** BMC public health 2016;16(1):172.

BACKGROUND: Completion of multiple dose vaccine schedules is crucial to ensure a protective immune response, and maximise vaccine cost-effectiveness. While barriers and facilitators to vaccine uptake have recently been reviewed, there is no comprehensive review of factors influencing subsequent adherence or completion, which is key to achieving vaccine effectiveness. This study identifies and summarises the literature on factors affecting completion of multi-dose vaccine schedules by adolescents. **METHODS:** Ten online databases and four websites were searched (February 2014). Studies with analysis of factors predicting completion of multi-dose vaccines were included. Study participants within 9-19 years of age were included in the review. The defined outcome was completion of the vaccine series within 1 year among those who received the first dose. **RESULTS:** Overall, 6159 abstracts were screened, and 502 full texts were reviewed. Sixty one studies were eligible for this review. All except two were set in high-income countries. Included studies evaluated human papillomavirus vaccine, hepatitis A, hepatitis B, and varicella vaccines. Reported vaccine completion rates, among those who initiated vaccination, ranged from 27% to over 90%. Minority racial or ethnic groups and inadequate health insurance coverage were risk factors for low completion, irrespective of initiation rates. Parental healthcare seeking behaviour was positively associated with completion. Vaccine delivery in schools was associated with higher completion than delivery in the community or health facilities. Gender, prior healthcare use and socio-economic status rarely remained significant risks or protective factors in multivariate analysis. **CONCLUSIONS:** Almost all studies investigating factors affecting completion have been carried out in developed countries and investigate a limited range of variables. Increased understanding of barriers to completion in adolescents will be invaluable to future new vaccine introductions and the further development of an adolescent health platform.

Kabakama S, Gallagher KE, Howard N, et al. **Social mobilisation, consent procedures, and acceptability: a study of human papillomavirus vaccination in low and middle-income countries.** (Accepted; BMC PH) 2016.

Sharon Hanley, Hokkaido University Graduate School of Medicine (Japan)

Hanley SJB, Fujita H, Yokoyama S, Kunisawa S, Tamakoshi A, Dong P, Kobayashi N, Watari H, Kudo M and Sakuragi N. **HPV self-sampling in Japanese women: A feasibility study in a population with limited experience of tampon use**, *J Med Screen*, 2016.

OBJECTIVES: Cervical cancer incidence and mortality is increasing in Japanese women under age 50. Screening uptake is low and proactive recommendations for human papillomavirus vaccination have been suspended. Other cervical cancer prevention initiatives are urgently needed. We assessed whether human papillomavirus self-sampling might be an acceptable alternative to physician-led screening, particularly in women with limited experience of tampon use. We also sought to identify any practical, logistical, or safety issues in women already attending for screening, before carrying out further large-scale studies in non-responders. **METHODS:** In total, 203 women aged 20-49 attending their annual workplace healthcheck in Sapporo, northern Japan, performed unsupervised human papillomavirus self-sampling before undergoing a physician-led cervical smear and human papillomavirus test, and completing a measure of acceptability for both tests. **RESULTS:** Ninety per cent of participants stated they would use self-sampling again. They found instructions easy to follow and reported no issues with the usability of the self-sampling device. Compared with physician-led testing, women found self-sampling significantly less painful, less embarrassing and could relax more ($p < 0.001$), regardless of history of tampon use, which was associated with negative experiences in physician sampling ($p = 0.034$). Women lacked confidence the test had been performed correctly, despite no unsatisfactory samples. No safety issues were reported. **CONCLUSIONS:** Self-sampling was highly acceptable in this population of women. They could perform the test safely unsupervised, but lacked confidence the test has been carried out correctly. Japanese women need to be educated about the accuracy of human papillomavirus self-sampling and further large-scale studies are necessary in non-responders.

Hanley SJB, Yoshioka E, Ito Y, Kishi R. **HPV vaccination crisis in Japan**, *Lancet*. 2015; 385 (9987): 2571.
No abstract available

Hanley SJB, Pollock KG, Cuschieri K. **Peripheral sympathetic nerve dysfunction in adolescent Japanese girls following immunization with the human papillomavirus vaccine**. *Intern Med*. 2015; 54(15): 1953.
No abstract available

Larson HJ, Wilson R, Hanley SJB, Parys A & Paterson P. **Tracking the global spread of vaccine sentiments: The global response to Japan's suspension of its HPV vaccine recommendation**. *Hum Vaccin Immunother*. 2014; 10(9): 2543-50.

BACKGROUND: In June 2013 the Japanese Ministry of Health, Labor, and Welfare (MHLW) suspended its HPV vaccination recommendation after a series of highly publicized alleged adverse events following immunization stoked public doubts about the vaccine's safety. This paper examines the global spread of the news of Japan's HPV vaccine suspension through online media, and takes a retrospective look at non-Japanese media sources that were used to support those claiming HPV vaccine injury in Japan. **METHODS:** Two searches were conducted. One searched relevant content in an archive of Google Alerts on vaccines and vaccine preventable diseases. The second search was conducted using Google Search on January 6th 2014 and on July 18th 2014, using the keywords, "HPV vaccine Japan" and "cervical cancer vaccine Japan." Both searches were used as Google Searches render more (and some different) results than Google Alerts. **RESULTS:** Online media collected and analyzed totalled 57. Sixty 3 percent were published in the USA, 23% in Japan, 5% in the UK, 2% in France, 2% in Switzerland, 2% in the Philippines, 2% in Kenya and 2% in Denmark. The majority took a negative view of the HPV vaccine, the primary

concern being vaccine safety. DISCUSSION: The news of Japan's suspension of the HPV vaccine recommendation has traveled globally through online media and social media networks, being applauded by anti-vaccination groups but not by the global scientific community. The longer the uncertainty around the Japanese HPV vaccine recommendation persists, the further the public concerns are likely to travel.

Hanley SJB, Yoshioka E, Ito Y, Konno R, Sasaki Y, Kishi R, Sakuragi N. **An exploratory study of Japanese fathers' knowledge of and attitudes towards HPV and HPV vaccination: does marital status matter?**, *Asian Pac J Cancer Prev*. 2014; 15(4): 1837-43.

BACKGROUND: No studies on male attitudes towards HPV and HPV vaccination have been conducted in Japan, and little is known globally whether attitudes of single fathers differ to those living with a female partner. This exploratory study assessed whether Japanese fathers were likely to have their daughter vaccinated against HPV in a publically funded program and whether any differences existed regarding attitudes and knowledge about HPV according to marital status. MATERIALS AND METHODS: Subjects were 27 fathers (16 single; 11 married) who took part in a study on HPV vaccine acceptability aimed at primary caregivers of girls aged 11-14 yrs in three Japanese cities between July and December 2010. RESULTS: Knowledge about HPV was extremely poor (mean score out of 13 being 2.74 +/- 3.22) with only one (3.7%) participant believing he had been infected with HPV and most (81.4%) believing they had no or low future risk. No difference existed regarding knowledge or awareness of HPV according to marital status. Concerning perceived risk for daughters, single fathers were significantly more likely to believe their daughter was at risk for both HPV (87.5% versus 36.4%; $p=0.01$) and cervical cancer (75.0% versus 27.3%; $p=0.02$). Acceptability of free HPV vaccination was high at 92% with no difference according to marital status, however single fathers were significantly more likely ($p=0.01$) to pay when vaccination came at a cost. Concerns specific to single fathers included explaining the sexual nature of HPV and taking a daughter to a gynecologist to be vaccinated. CONCLUSIONS: Knowledge about HPV among Japanese fathers is poor, but HPV vaccine acceptability is high and does not differ by marital status. Providing sexual health education in schools that addresses lack of knowledge about HPV as well as information preferences expressed by single fathers, may not only increase HPV vaccine acceptance, but also actively involve men in cervical cancer prevention strategies. However, further large-scale quantitative studies are needed.

Hosaka M, Fujita H, Hanley SJB, Sasaki T, Shirakawa Y, Kudo M, Kaneuchi M, Watari H, Kikuchi K, Sakuragi N. **Incidence risk of cervical intraepithelial neoplasia 3 or more severe lesions is a function of human papillomavirus genotypes and severity of cytological and histological abnormalities in adult Japanese women**, *Int J Cancer* 132(2): 327-34, 2013.

We examined incidence probabilities of cervical intraepithelial neoplasia 3 (CIN3) or more severe lesions (CIN3+) in 1,467 adult Japanese women with abnormal cytology in relation to seven common human papillomavirus (HPV) infections (16/18/31/33/35/52/58) between April 2000 and March 2008. Sixty-seven patients with multiple HPV infection were excluded from the risk factor analysis. Incidence of CIN3+ in 1,400 patients including 68 with ASCUS, 969 with low grade squamous intraepithelial lesion (LSIL), 132 with HSIL without histology-proven CIN2 (HSIL/CIN2(-)) and 231 with HSIL with histology-proven CIN2 (HSIL/CIN2(+)) was investigated. In both high grade squamous intraepithelial lesion (HSIL)/CIN2(-) and HSIL/CIN2(+), HPV16/18/33 was associated with a significantly earlier and higher incidence of CIN3+ than HPV31/35/52/58 ($p = 0.049$ and $p = 0.0060$, respectively). This association was also observed in LSIL ($p = 0.0002$). The 1-year cumulative incidence rate (CIR) of CIN3+ in HSIL/CIN2(-) and HSIL/CIN2(+) according to HPV genotypes (16/18/33 vs. 31/35/52/58) were 27.1% vs. 7.5% and 46.6% vs. 19.2%, respectively. In contrast, progression of HSIL/CIN2(+) to CIN3+ was infrequent when HPV DNA was undetected: 0% of 1-year CIR and 8.1% of 5-year CIR. All cervical cancer occurred in HSIL cases of seven high-risk HPVs (11/198)

but not in cases of other HPV or undetectable/negative-HPV (0/165) ($p = 0.0013$). In conclusion, incidence of CIN3+ depends on HPV genotypes, severity of cytological abnormalities and histology of CIN2. HSIL/CIN2(+) associated with HPV16/18/33 may justify early therapeutic intervention, while HSIL/CIN2(-) harboring these HPV genotypes needs close observation to detect incidence of CIN3+. A therapeutic intervention is not indicated for CIN2 without HPV DNA.

Hayashi Y, Shimizu Y, Netsu S, Hanley SJB, Konno R. **High HPV vaccination uptake rates for adolescent girls after regional governmental funding in Shiki City, Japan.** *Vaccine*. 2012; 30(37): 5547-50.

BACKGROUND: In Japan, the bivalent HPV vaccine was approved in October, 2009 and became available as a non-routine vaccine from December, 2009. While routine vaccinations are free, the cost and responsibility for non-routine vaccinations are left to the individual. In exceptional circumstances regional governments fund non-routine vaccinations. This was the case in Shiki City, Saitama Prefecture, where a high uptake rate for individual (non-school based) HPV vaccination was obtained. **MATERIALS:** On January 20, 2010, the mayor of Shiki City announced to the media his decision to vaccinate adolescent girls in Shiki City against HPV. A project team for HPV vaccination was set up in the city's Health Promotion Center. To gain mutual consent for HPV vaccination, senior health professionals, city officials, the head of the board of education, school principals and health-care teachers met several times. The cohort to be vaccinated was 1254 girls aged 12-15 years. Individual notifications were mailed to each girl on April 23, 2010, along with information about the HPV vaccine. **CONCLUSIONS:** As of April 10th, 2011, the uptake rate for girls aged 15 years old was 90.7% for the 1st dose. The vaccine registry is managed by the health care system of the city. The success of the HPV vaccination program and high uptake rates in Shiki City is a good model for the nationwide HPV vaccination program that started in February, 2011.

Hanley SJB, Yoshioka E, Ito Y, Konno R, Hayashi Y, Kishi R, Sakuragi N. **Acceptance of and attitudes towards human papillomavirus vaccination in Japanese mothers of adolescent girls.** *Vaccine* 2012; 30(39): 5740-7.

To better understand how to achieve high uptake rates of human papillomavirus (HPV) vaccination in Japan, we investigated acceptance of and attitudes towards HPV vaccination in 2192 mothers of girls aged 11-14 yrs. A school-based survey was conducted in five elementary and fourteen junior high schools in Sapporo, Japan. Responses from 862 participants were analyzed. Ninety-three percent of mothers would accept the vaccine for their daughter if free, but only 1.5% was willing to pay the minimum recommended price of ¥ 40,000. Vaccine acceptance was higher in mothers who had heard of HPV vaccine (adjusted odds ratio, aOR=2.58, confidence interval, CI=1.47-4.53), and who believed susceptibility to (aOR=2.30, CI=1.34-3.92) and severity of (aOR=3.73, CI=1.41-9.88) HPV to be high. Recommendations from a doctor (aOR=12.60, CI=7.06-21.48) and local health board (aOR=27.80, CI=13.88-55.86) were also positively associated with increased HPV vaccine acceptance. Concerns about side effects of both the HPV vaccine (aOR=0.03, CI=0.01-0.08) and routine childhood vaccines in general (aOR=0.11, CI=0.02-0.78) emerged as barriers to vaccination. Not participating in routine cervical screening also emerged as a deterrent (aOR=0.49, CI=0.27-0.91). While most mothers (66.8%) agreed that 10-14 yr was an appropriate age for vaccination, a further 30.6% believed >15 yr to be more appropriate. In conclusion, attitudes of Japanese mothers toward HPV vaccination are encouraging. While lower vaccine acceptance in mothers who do not undergo regular cervical screening needs further investigation, this study indicates that high uptake may be possible in a publically funded HPV vaccination program if physicians actively address safety concerns and justify why the vaccine is needed at a particular age.

Hanley SJB, Konno R. **HPV catch-up vaccination: The benefits of vaccinating Japanese women in their forties.** *Obstet Gynecol*. 2010; 77 (9): 1016-1022 (In Japanese).

No abstract available

Konno R, Sagae S, Yoshikawa H, Basu PS, Hanley SJB, Tan JH, Shin HR. **Cervical Cancer Working Group report.** 2010; Jpn J Clin Oncol 40 Suppl 1: i44-50.

Disease burden of cervical cancer in Asia was summarized. Human papillomavirus 16 is the most oncogenic human papillomavirus type. Korea's national cervical cancer screening program targets women aged 30 or over, with coverage of almost 80%. Japan has a long history (50 years) of cervical cancer screening, and cytological screening programs have reduced the incidence/mortality of cervical cancer by 70%. But, recent cervical cancer screening coverage is ~24%. Modeling suggested that vaccination of all 12-year-old girls would reduce cervical cancer cases by 73% in Japan. India has no cervical cancer screening program, as well as a serious lack of awareness in the general population, medical professionals and policy-makers. A realistic, affordable approach would be a low-volume, once-in-a-lifetime human papillomavirus-based screening program. In Australia, the national cervical cancer program has been very successful in reducing the incidence and mortality of cervical cancer. Australia was the first country to implement free, national human papillomavirus immunization (April 2007), expected to reduce human papillomavirus 16 infections by 56% in 2010 and 92% in 2050. A comparison of the UK and Japan was demonstrated that in the UK, cervical cancer screening and human papillomavirus vaccination uptakes are high because the government provides adequate education/funding. The Japanese government needs to put more emphasis on women's health and preventative medicine. Our conclusion and recommendations are that heightened public awareness of cervical cancer prevention, focusing on screening and vaccination will lead to improved survival and a better quality of life.

Emilie Karafillakis, London School of Hygiene and Tropical Medicine (UK)

(Submitted to Vaccine) Karafillakis E, Dinca I, Apfel F, Cecconi S, Würz A, Takacs J, Suk J, Celentano LP, Kramarz P, and Larson HJ. **Vaccine Hesitancy among healthcare workers in Europe: A qualitative study.**

(Submitted to Health Policy and Planning) Shoman H, Karafillakis E, Rawaf S. **The link between the West African Ebola outbreak and health systems in Guinea, Liberia, and Sierra Leone: a systematic review.**

(Submitted to BMJ Global Health): Karafillakis E, Jalloh MF, Nuriddin A, Larson H, Whitworth J, Lees S, Hageman KM, Sengeh P, Jalloh MB, Bunnell R, Carroll DD, Morgan O. **Once there is life, there is hope: Ebola survivors' experiences, behaviours and attitudes in Sierra Leone, 2015.**

Karafillakis, E., Hassounah, S., & Atchison, C. **Effectiveness and impact of rotavirus vaccines in Europe, 2006-2014.** Vaccine. 2015; 33 (18):2097-2107.

Prior to the introduction of rotavirus vaccines in 2006, rotavirus was the leading cause of severe gastroenteritis among European children <5 years of age. We conducted a systematic review of the published literature to examine the effectiveness and impact of rotavirus vaccines in Europe following the first eight years of routine use. Four publication databases were searched, yielding 276 unique citations from February 1st, 2006 to July 31st, 2014. Twenty four studies on effectiveness (n=9) and impact (n=15) met the inclusion criteria. Across Europe, vaccine effectiveness against rotavirus-related healthcare utilisation ranged from 68% to 98%, consistent with efficacy data from clinical trials. Reductions in rotavirus hospitalisations ranged from 65% to 84%, consistent with findings from post-marketing studies from the US and Latin America. We confirm the significant public health benefit of rotavirus vaccination in Europe and provide further evidence to support implementation of universal rotavirus vaccination in all European countries.

European Centre for Disease Prevention and Control. **Vaccine hesitancy among healthcare workers and their patients in Europe – A qualitative study.** Stockholm: ECDC; 2015.

The research described in this report was conducted to assess potential concerns among hesitant healthcare workers in Europe as part of an ECDC project entitled 'Comprehensive expert opinion on motivating hesitant population groups to vaccinate'. The aim of this research project is to have a better understanding of vaccine hesitancy and safety concerns among healthcare vaccine providers and their patients in Europe and to explore the link and potential influence between the two groups.

The knowledge gained from this study will help public health professionals in Europe to develop more targeted and effective public health measures to prevent and respond to vaccine hesitancy, especially among healthcare professionals. It should be noted that the views of the healthcare workers interviewed in this study may not be representative of the views of the general population of healthcare workers and must therefore be interpreted with caution. The views expressed in this publication do not necessarily reflect the views of the European Centre for Disease Prevention and Control (ECDC).

European Centre for Disease Prevention and Control. **Rapid literature review on motivating hesitant population groups in Europe to vaccinate.** Stockholm: ECDC; 2015.

The aim of this rapid literature review is to bring together knowledge and research related to vaccine hesitancy in EU /EEA countries into a format that is easy to understand and follow. The review focuses on identifying what is known about:

- who the hesitant populations are
- what are enablers and barriers to vaccination uptake for these hesitant populations
- what is known about successful interventions targeting these populations; especially, interventions provided for and by healthcare providers.

European Centre for Disease Prevention and Control. **Let's talk about hesitancy.** Stockholm: ECDC; 2016.

<http://ecdc.europa.eu/en/publications/Publications/lets-talk-about-hesitancy-vaccination-guide.pdf>

This guide provides practical evidence-based and peer-reviewed advice for public health programme managers and communicators involved with immunisation services. It identifies ways to enhance people's confidence in vaccination and addresses common issues which underlie vaccination hesitancy. The guide serves as a supplement to the ECDC guide [Let's talk about protection](#), which focuses on strengthening the capacities of healthcare providers to better address concerns about vaccination and tackle obstacles to vaccination uptake.

Karafillakis, E. **Implementation of HPV vaccination programmes in the Netherlands and abroad.** Public Health Genomics: the Implementation of Vaccination Programs against Human Papilloma Virus. Maastricht: IPHG. 2010.

In the last two years, the implementation of Human Papilloma Virus (HPV) vaccination programs started in many countries around the globe. Years after a causal link between HPV and cervical cancer was proven, Public Health systems offer vaccines to young girls. The vast majority of countries opted for the vaccination of 12 year old girls and offered catch-up programs for girls between 13 and 16. The costs for the HPV vaccination differ with a median of 300 Euros for the vaccine. The coverage rate is lower than expected in most countries and substantial variations can be observed. Despite the financial burden in some countries like Poland, also cultural and gender specific issues need to be better reflected to ensure a higher coverage rate. From a biological and gender perspective more efforts are needed to assess the need for a vaccination of boys. A vaccination of boys may not be costeffective based on the existing data but latest publications link HPV also to other cancer types like throat and penis. The discourse on the vaccination of boys should also address the disease burden related to genital warts which are often neglected. Within the study we observed a general weakness of Public Health systems to respond to upcoming and emerging genome-based knowledge in the field of HPV. Within the last ten years research groups have developed strategies which aim to accelerate and foster the process of translational research. The case of HPV demonstrates that these concepts have not been transposed into practice yet. Based on the weak uptake of new knowledge, substantial problems have also been observed in the communication strategy and the way parents, and in particular groups with specific needs are addressed. The HPV vaccination programs in many countries need further improvement and successful examples like the Australian school-based implementation concept need further exploration.

Heidi Larson,

(Based on pubmed search)

Jarrett, C., R. Wilson, M. O'Leary, E. Eckersberger and H. J. Larson. **Strategies for addressing vaccine hesitancy - A systematic review.** *Vaccine.* 2015; 33(34): 4180-4190.

The purpose of this systematic review is to identify, describe and assess the potential effectiveness of strategies to respond to issues of vaccine hesitancy that have been implemented and evaluated across diverse global contexts. **METHODS:** A systematic review of peer reviewed (January 2007-October 2013) and grey literature (up to October 2013) was conducted using a broad search strategy, built to capture multiple dimensions of public trust, confidence and hesitancy concerning vaccines. This search strategy was applied and adapted across several databases and organizational websites. Descriptive analyses were undertaken for 166 (peer reviewed) and 15 (grey literature) evaluation studies. In addition, the quality of evidence relating to a series of PICO (population, intervention, comparison/control, outcomes) questions defined by the SAGE Working Group on Vaccine Hesitancy (WG) was assessed using Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria; data were analyzed using Review Manager. **RESULTS:** Across the literature, few strategies to address vaccine hesitancy were found to have been evaluated for impact on either vaccination uptake and/or changes in knowledge, awareness or attitude (only 14% of peer reviewed and 25% of grey literature). The majority of evaluation studies were based in the Americas and primarily focused on influenza, human papillomavirus (HPV) and childhood vaccines. In low- and middle-income regions, the focus was on diphtheria, tetanus and pertussis, and polio. Across all regions, most interventions were multi-component and the majority of strategies focused on raising knowledge and awareness. Thirteen relevant studies were used for the GRADE assessment that indicated evidence of moderate quality for the use of social mobilization, mass media, communication tool-based training for health-care workers, non-financial incentives and reminder/recall-based interventions. Overall, our results showed that multicomponent and dialogue-based interventions were most effective. However, given the complexity of vaccine hesitancy and the limited evidence available on how it can be addressed, identified strategies should be carefully tailored according to the target population, their reasons for hesitancy, and the specific context.

Larson, H. The world must accept that the HPV vaccine is safe. *Nature.* 2015; 528(7580): 9.

Hawkes, S., E. Kismodi, H. Larson and K. Buse. **Vaccines to promote and protect sexual health: policy challenges and opportunities.** *Vaccine.* 2014; 32(14): 1610-1615.

Vaccines aim to improve the well-being of everyone and are seen as a public health success story in the prevention and control of communicable infections. However, decisions to use vaccinations are not without controversy, and the introduction of vaccines targeting sexually transmitted infections (STIs) is particularly contentious. In this paper we investigate the underlying policy challenges and opportunities for rolling out STI vaccines. Looking in detail at the experience of delivering HPV vaccine, we explore the lessons that can be learnt, including policy and human rights dimensions, for future STI vaccine introduction and scale up. Policies arise from the interaction of ideas, interests and institutions. In the case of HPV vaccine, ideas have been particularly contested, although interests and institutions have impacted on policy too. A review of human rights in relation to STI vaccine policies highlights the specific needs and rights of adolescents, and the paper details concepts of consent and evolving capacity which can be used to ensure that adolescents have full access to health interventions. Policy options for vaccines include mandatory approaches - and these have been utilized in some settings for HPV vaccines. The paper argues, and outlines the rationale, against adopting mandatory STI vaccine policy approaches. The paper concludes by identifying policy opportunities for introducing new vaccines targeting STIs.

Larson, H. J., R. Wilson, S. Hanley, A. Parys and P. Paterson. **Tracking the global spread of vaccine sentiments: the global response to Japan's suspension of its HPV vaccine recommendation.** Hum Vaccin Immunother. 2014; 10(9): 2543-2550.

In June 2013 the Japanese Ministry of Health, Labor, and Welfare (MHLW) suspended its HPV vaccination recommendation after a series of highly publicized alleged adverse events following immunization stoked public doubts about the vaccine's safety. This paper examines the global spread of the news of Japan's HPV vaccine suspension through online media, and takes a retrospective look at non-Japanese media sources that were used to support those claiming HPV vaccine injury in Japan. METHODS: Two searches were conducted. One searched relevant content in an archive of Google Alerts on vaccines and vaccine preventable diseases. The second search was conducted using Google Search on January 6th 2014 and on July 18th 2014, using the keywords, "HPV vaccine Japan" and cervical cancer vaccine Japan. Both searches were used as Google Searches render more (and some different) results than Google Alerts. RESULTS: Online media collected and analyzed totalled 57. Sixty 3 percent were published in the USA, 23% in Japan, 5% in the UK, 2% in France, 2% in Switzerland, 2% in the Philippines, 2% in Kenya and 2% in Denmark. The majority took a negative view of the HPV vaccine, the primary concern being vaccine safety. DISCUSSION: The news of Japan's suspension of the HPV vaccine recommendation has traveled globally through online media and social media networks, being applauded by anti-vaccination groups but not by the global scientific community. The longer the uncertainty around the Japanese HPV vaccine recommendation persists, the further the public concerns are likely to travel.

Pier Luigi Lopalco, University of Pisa (Italy)

Di Mario S, Basevi V, Lopalco PL, Balduzzi S, D'Amico R, Magrini N. **Are the Two Human Papillomavirus Vaccines Really Similar? A Systematic Review of Available Evidence: Efficacy of the Two Vaccines against HPV.** *J Immunol Res.* 2015; 2015:435141. Review

Stillo M, Carrillo Santistevé P, Lopalco PL. **Safety of human papillomavirus vaccines: a review.** *Expert Opin Drug Saf.* 2015;1-16.

INTRODUCTION: Between 2006 and 2009, two different human papillomavirus virus (HPV) vaccines were licensed for use: a quadrivalent (qHPVv) and a bivalent (bHPVv) vaccine. Since 2008, HPV vaccination programmes have been implemented in the majority of the industrialized countries. Since 2013, HPV vaccination has been part of the national programs of 66 countries including almost all countries in North America and Western Europe. Despite all the efforts made by individual countries, coverage rates are lower than expected. Vaccine safety represents one of the main concerns associated with the lack of acceptance of HPV vaccination both in the European Union/European Economic Area and elsewhere. **AREAS COVERED:** Safety data published on bivalent and quadrivalent HPV vaccines, both in pre-licensure and post-licensure phase, are reviewed. **EXPERT OPINION:** Based on the latest scientific evidence, both HPV vaccines seem to be safe. Nevertheless, public concern and rumors about adverse events (AE) represent an important barrier to overcome in order to increase vaccine coverage. Passive surveillance of AEs is an important tool for detecting safety signals, but it should be complemented by activities aimed at assessing the real cause of all suspect AEs. Improved vaccine safety surveillance is the first step for effective communication based on scientific evidence.

Lopalco PL, DeStefano F. **The complementary roles of Phase 3 trials and post-licensure surveillance in the evaluation of new vaccines.** *Vaccine.* 2014; 33(13):1541-8. Review

Vaccines have led to significant reductions in morbidity and saved countless lives from many infectious diseases and are one of the most important public health successes of the modern era. Both vaccines' effectiveness and safety are keys for the success of immunisation programmes. The role of post-licensure surveillance has become increasingly recognised by regulatory authorities in the overall vaccine development process. Safety, purity, and effectiveness of vaccines are carefully assessed before licensure, but some safety and effectiveness aspects need continuing monitoring after licensure; Post-marketing activities are a necessary complement to pre-licensure activities for monitoring vaccine quality and to inform public health programmes. In the recent past, the availability of large databases together with data-mining and cross-linkage techniques have significantly improved the potentialities of post-licensure surveillance. The scope of this review is to present challenges and opportunities offered by vaccine post-licensure surveillance. While pre-licensure activities form the foundation for the development of effective and safe vaccines, post-licensure monitoring and assessment, are necessary to assure that vaccines are effective and safe when translated in real world settings. Strong partnerships and collaboration at an international level between different stakeholders is necessary for finding and optimally allocating resources and establishing robust post-licensure processes.

European Centre for Disease Prevention and Control. **Introduction of HPV vaccines in EU countries – an update.** Stockholm: ECDC. 2012.

In January 2008, a panel of ECDC experts produced the Guidance for the introduction of HPV vaccines in EU countries (document below). Since then, most countries have implemented national vaccination programmes for adolescent girls and a significant number have also introduced catch-up

programmes for young women. Literature published since 2008 has provided new evidence and filled some knowledge gaps. Meanwhile, new questions have arisen: one of the main issues is whether vaccination protocols should include boys as well as girls, while another pressing concern is the unsatisfactory immunisation coverage rate achieved in most countries. The report reviews the main developments in relation to HPV vaccination.

Dorleans F, Giambi C, Dematte L, Cotter S, Stefanoff P, Mereckiene J, O'Flanagan D, Lopalco PL, D'Ancona F, Levy-Bruhl D; VENICE 2 project gatekeepers group. **The current state of introduction of human papillomavirus vaccination into national immunisation schedules in Europe: first results of the VENICE2 2010 survey.** Euro Surveill. 2010; 15(47). pii: 19730

The Venice 2 human papillomavirus vaccination survey evaluates the state of introduction of the HPV vaccination into the national immunisation schedules in the 29 participating countries. As of July 2010, 18 countries have integrated this vaccination. The vaccination policy and achievements vary among those countries regarding target age groups, delivery infrastructures and vaccination coverage reached. Financial constraints remain the major obstacle for the 11 countries who have not yet introduced the vaccination.

King LA, Lévy-Bruhl D, O'Flanagan D, Bacci S, Lopalco PL, Kudjawu Y, Salmaso S; VENICE Country Specific Gate Keepers and Contact Points. **Introduction of human papillomavirus (HPV) vaccination into national immunisation schedules in Europe: Results of the VENICE 2007 survey.** Euro Surveill. 2008;13(33).

The European Union Member States are simultaneously considering introducing HPV vaccination into their national immunisation schedules. The Vaccine European New Integrated Collaboration Effort (VENICE) project aims to develop a collaborative European vaccination network. A survey was undertaken to describe the decision status and the decision-making process regarding the potential introduction of human papillomavirus (HPV) vaccination into their national immunisation schedules. A web-based questionnaire was developed and completed online in 2007 by 28 countries participating in VENICE. As of 31 October 2007, five countries had decided to introduce HPV vaccination into the national immunisation schedule, while another seven had started the decision-making process with a recommendation favouring introduction. Varying target populations were selected by the five countries which had introduced the vaccination. Half of the surveyed countries had undertaken at least one ad hoc study to support the decision-making process. According to an update of the decision status from January 2008, the number of countries which had made a decision or recommendation changed to 10 and 5 respectively. This survey demonstrates the rapidly evolving nature of HPV vaccine introduction in Europe and the existence of expertise and experience among EU Member States. The VENICE network is capable of following this process and supporting countries in making vaccine introduction decisions. A VENICE collaborative web-space is being developed as a European resource for the decision-making process for vaccine introduction.

European Centre for Disease Prevention and Control. **Guidance for the introduction of HPV vaccines in EU countries.** Stockholm: ECDC; 2008

The purpose of the report is to lay down the scientific basis for the potential introduction of human papillomavirus (HPV) vaccines in order to help European Union (EU) Member States to make policy choices. It highlights issues to be considered and provides a list of policy options for each of these issues.

Lauri Markowitz, Centre for Disease Control & Prevention (CDC) (US)

Hariri S, Bennett NM, Niccolai LM, Schafer S, Park IU, Bloch KC, Unger ER, Whitney E, Julian P, Scahill MW, Abdullah N, Levine D, Johnson ML, Steinau M, Markowitz LE. HPV-IMPACT Working Group. **Reduction in HPV 16/18-associated high grade cervical lesions following HPV vaccine introduction in the United States - 2008-2012.** *Vaccine.* 2015; 33:1608-13.

BACKGROUND: Prevention of pre-invasive cervical lesions is an important benefit of HPV vaccines, but demonstrating impact on these lesions is impeded by changes in cervical cancer screening. Monitoring vaccine-types associated with lesions can help distinguish vaccine impact from screening effects. We examined trends in prevalence of HPV 16/18 types detected in cervical intraepithelial neoplasia 2, 3, and adenocarcinoma in situ (CIN2+) among women diagnosed with CIN2+ from 2008 to 2012 by vaccination status. We estimated vaccine effectiveness against HPV 16/18-attributable CIN2+ among women who received ≥ 1 dose by increasing time intervals between date of first vaccination and the screening test that led to detection of CIN2+ lesion. **METHODS:** Data are from a population-based sentinel surveillance system to monitor HPV vaccine impact on type-specific CIN2+ among adult female residents of five catchment areas in California, Connecticut, New York, Oregon, and Tennessee. Vaccination and cervical cancer screening information was retrieved. Archived diagnostic specimens were obtained from reporting laboratories for HPV DNA typing. **RESULTS:** From 2008 to 2012, prevalence of HPV 16/18 in CIN2+ lesions statistically significantly decreased from 53.6% to 28.4% among women who received at least one dose ($P_{trend} < .001$) but not among unvaccinated women (57.1% vs 52.5%; $P_{trend} = .08$) or women with unknown vaccination status (55.0% vs 50.5%; $P_{trend} = .71$). Estimated vaccine effectiveness for prevention of HPV 16/18-attributable CIN2+ was 21% (95% CI: 1-37), 49% (95% CI: 28-64), and 72% (95% CI: 45-86) in women who initiated vaccination 25-36 months, 37-48 months, and >48 months prior to the screening test that led to CIN2+ diagnosis. **CONCLUSIONS:** Population-based data from the United States indicate significant reductions in CIN2+ lesions attributable to types targeted by the vaccines and increasing HPV vaccine effectiveness with increasing interval between first vaccination and earliest detection of cervical disease.

Hariri S, Johnson ML, Bennett NM, Bauer HM, Park IU, Schafer S, Niccolai LM, Unger ER, Markowitz LE; HPV-IMPACT Working Group. **Population-based trends in high-grade cervical lesions in the early human papillomavirus vaccine era in the United States.** *Cancer.* 2015; 121:2775-81.

BACKGROUND: Cervical intraepithelial neoplasia grade 2, 3, and adenocarcinoma in situ (CIN2+) lesions can be monitored as early indicators of human papillomavirus (HPV) vaccine impact. Changes to screening utilization will affect observed reductions in CIN2+ rates and complicate the interpretation of vaccine impact. **METHODS:** From 2008 to 2012, 9119 cases of CIN2+ among 18- to 39-year-old residents of catchment areas in California, Connecticut, New York, and Oregon were reported to the HPV-IMPACT Project, a sentinel system for monitoring the population impact of HPV vaccine. Age-stratified CIN2+ incidence rates were calculated for each catchment. Annual cervical screening was estimated for California, New York, and Oregon catchments with administrative and survey data. The Cochran-Armitage test was used to examine trends. **RESULTS:** From 2008 to 2012, the incidence of CIN2+ significantly decreased among 18- to 20-year-olds (California, from 94 to 5 per 100,000 women; Connecticut, from 450 to 57 per 100,000 women; New York, from 299 to 43 per 100,000 women; and Oregon, from 202 to 37 per 100,000 women; $P_{trend} < .0001$) and among 21- to 29-year-olds in Connecticut (from 762 to 589 per 100,000 women) and New York (from 770 to 465 per 100,000 women; $P_{trend} < .001$); rates did not differ among 30- to 39-year-olds. During the same period, screening rates also declined, with the largest decreases among 18- to 20-year-olds (from 67% in Oregon to 88% in California) and with smaller declines among 21- to 29-year-olds (13%-27%) and 30- to 39-year-olds (3%-21%). **CONCLUSIONS:** The declines in

CIN2+ detection in young women were likely due to reduced screening but could also reflect the impact of vaccination. These data illustrate challenges in interpreting CIN2+ ecologic trends in the new era of cervical cancer prevention and emphasize the importance of information such as HPV types detected in lesions to assess the impact of HPV vaccine on cervical precancers.

Brisson M, Laprise JF, Chesson HW, Drolet M, Malagón T, Boily MC, Markowitz LE. **Health and economic impact of switching from a 4-valent to a 9-valent HPV vaccination program in the United States.** J Natl Cancer Inst. 2015; 108.

BACKGROUND: Randomized clinical trials have shown the 9-valent human papillomavirus (HPV) vaccine to be highly effective against types 31/33/45/52/58 compared with the 4-valent. Evidence on the added health and economic benefit of the 9-valent is required for policy decisions. We compare population-level effectiveness and cost-effectiveness of 9- and 4-valent HPV vaccination in the United States. **METHODS:** We used a multitype individual-based transmission-dynamic model of HPV infection and disease (anogenital warts and cervical, anogenital, and oropharyngeal cancers), 3% discount rate, and societal perspective. The model was calibrated to sexual behavior and epidemiologic data from the United States. In our base-case, we assumed 95% vaccine-type efficacy, lifelong protection, and a cost/dose of \$145 and \$158 for the 4- and 9-valent vaccine, respectively. Predictions are presented using the mean (80% uncertainty interval [UI] = 10(th)-90(th) percentiles) of simulations. **RESULTS:** Under base-case assumptions, the 4-valent gender-neutral vaccination program is estimated to cost \$5500 (80% UI = 2400-9400) and \$7300 (80% UI = 4300-11 000)/quality-adjusted life-year (QALY) gained with and without cross-protection, respectively. Switching to a 9-valent gender-neutral program is estimated to be cost-saving irrespective of cross-protection assumptions. Finally, the incremental cost/QALY gained of switching to a 9-valent gender-neutral program (vs 9-valent girls/4-valent boys) is estimated to be \$140 200 (80% UI = 4200->1 million) and \$31 100 (80% UI = 2100->1 million) with and without cross-protection, respectively. Results are robust to assumptions about HPV natural history, screening methods, duration of protection, and healthcare costs. **CONCLUSIONS:** Switching to a 9-valent gender-neutral HPV vaccination program is likely to be cost-saving if the additional cost/dose of the 9-valent is less than \$13. Giving females the 9-valent vaccine provides the majority of benefits of a gender-neutral strategy.

Liu G, Markowitz LE, Hariri S, Panicker G, Unger ER. **Seroprevalence of 9 human papillomavirus types in the United States, 2005-2006.** J Infect Dis. 2016;213:191-8.

BACKGROUND: A 9-valent human papillomavirus (HPV) vaccine, licensed in 2014, prevents 4 HPV types targeted by the quadrivalent vaccine (6/11/16/18) and 5 additional high-risk (HR) types (31/33/45/52/58). Measuring seropositivity before vaccine introduction provides baseline data on exposure to types targeted by vaccines. **METHODS:** We determined seroprevalence of HPV 6/11/16/18/31/33/45/52/58 among 4943 persons aged 14-59 years who participated in the National Health and Nutrition Examination Survey, 2005-2006. **RESULTS:** Among females, seroprevalence was 40.5% for any of the 9 vaccine types, 30.0% for any 7 HR types (16/18/31/33/45/52/58), 19.0% for any 5 additional types (31/33/45/52/58), and 18.3% for 16/18. Compared with non-Hispanic whites, non-Hispanic blacks had higher seroprevalence of 31/33/45/52/58 (36.8% vs 15.9%) and 16/18 (30.1% vs 17.8%), while Mexican Americans had higher seroprevalence of 31/33/45/52/58 (23.6% vs 15.9%) (P < .05 for all). In multivariable analyses of data from females, race/ethnicity, number of sex partners, and age were associated with 16/18 and 31/33/45/52/58 seropositivity. Seropositivity was lower among males than among females (P < .001 for all type categories). **CONCLUSIONS:** In 2005-2006, about 40% of females and 20% of males had serological evidence of exposure to ≥ 1 of 9 HPV types. Seroprevalence of all type categories, especially HPV 31/33/45/52/58 among females, varied by race/ethnicity.

Markowitz LE, Liu G, Hariri S, Steinau M, Dunne EF, Unger ER. **Prevalence of HPV after introduction of the vaccination program in the United States.** *Pediatrics*. 2016; 137:1-9.

BACKGROUND: Since mid-2006, human papillomavirus (HPV) vaccination has been recommended for females aged 11 to 12 years and through 26 years if not previously vaccinated. **METHODS:** HPV DNA prevalence was analyzed in cervicovaginal specimens from females aged 14 to 34 years in NHANES in the prevaccine era (2003-2006) and 4 years of the vaccine era (2009-2012) according to age group. Prevalence of quadrivalent HPV vaccine (4vHPV) types (HPV-6, -11, -16, and -18) and other HPV type categories were compared between eras. Prevalence among sexually active females aged 14 to 24 years was also analyzed according to vaccination history. **RESULTS:** Between the prevaccine and vaccine eras, 4vHPV type prevalence declined from 11.5% to 4.3% (adjusted prevalence ratio [aPR]: 0.36 [95% confidence interval (CI): 0.21-0.61]) among females aged 14 to 19 years and from 18.5% to 12.1% (aPR: 0.66 [95% CI: 0.47-0.93]) among females aged 20 to 24 years. There was no decrease in 4vHPV type prevalence in older age groups. Within the vaccine era, among sexually active females aged 14 to 24 years, 4vHPV type prevalence was lower in vaccinated (≥ 1 dose) compared with unvaccinated females: 2.1% vs 16.9% (aPR: 0.11 [95% CI: 0.05-0.24]). There were no statistically significant changes in other HPV type categories that indicate cross-protection. **CONCLUSIONS:** Within 6 years of vaccine introduction, there was a 64% decrease in 4vHPV type prevalence among females aged 14 to 19 years and a 34% decrease among those aged 20 to 24 years. This finding extends previous observations of population impact in the United States and demonstrates the first national evidence of impact among females in their 20s.

Chesson HW, Laprise JF, Brisson M, Markowitz LE. **Impact and Cost-effectiveness of 3 Doses of 9-Valent Human Papillomavirus (HPV) Vaccine Among US Females Previously Vaccinated With 4-Valent HPV Vaccine.** *J Infect Dis.* 2016; 213:1694-700.

BACKGROUND: We estimated the potential impact and cost-effectiveness of providing 3-doses of nonavalent human papillomavirus (HPV) vaccine (9vHPV) to females aged 13-18 years who had previously completed a series of quadrivalent HPV vaccine (4vHPV), a strategy we refer to as "additional 9vHPV vaccination." **METHODS:** We used 2 distinct models: (1) the simplified model, which is among the most basic of the published dynamic HPV models, and (2) the US HPV-ADVISE model, a complex, stochastic, individual-based transmission-dynamic model. **RESULTS:** When assuming no 4vHPV cross-protection, the incremental cost per quality-adjusted life-year (QALY) gained by additional 9vHPV vaccination was \$146 200 in the simplified model and \$108 200 in the US HPV-ADVISE model (\$191 800 when assuming 4vHPV cross-protection). In 1-way sensitivity analyses in the scenario of no 4vHPV cross-protection, the simplified model results ranged from \$70 300 to \$182 000, and the US HPV-ADVISE model results ranged from \$97 600 to \$118 900. **CONCLUSIONS:** The average cost per QALY gained by additional 9vHPV vaccination exceeded \$100 000 in both models. However, the results varied considerably in sensitivity and uncertainty analyses. Additional 9vHPV vaccination is likely not as efficient as many other potential HPV vaccination strategies, such as increasing primary 9vHPV vaccine coverage.

Gee J, Weinbaum C, Sukumaran L, Markowitz LE. **Quadrivalent HPV vaccine safety review and US safety monitoring plans for nine-valent HPV vaccine.** *Hum Vaccin Immunother.* 2016; 12:1406-17.

Quadrivalent human papillomavirus (4vHPV) vaccine was licensed for use in the United States in 2006 and through 2015 was the predominate HPV vaccine used. With the exception of syncope, a known preventable adverse event after any injected vaccination, both pre-licensure and post-licensure 4vHPV safety data have been reassuring with no confirmed safety signals identified. Nine-valent HPV vaccine (9vHPV) was licensed in 2014. This review includes post-licensure 4vHPV safety findings published to date that have informed the US vaccination program; these data will inform US safety monitoring and evaluation for 9vHPV.

Laura Marlow, Department of Epidemiology and Public Health, UCL (UK)

Chorley, A. J., Marlow, L. A. V., Forster, A. S., Haddrell, J. B., & Waller, J. **Experiences of cervical screening and barriers to participation in the context of an organised programme: A systematic review and thematic synthesis.** *Psycho-Oncology*. 2016. doi:10.1002/pon.4126

OBJECTIVE: As uptake of cervical screening continues to decline, this systematic review synthesises the qualitative literature on women's perceptions and experiences of cervical screening in the context of an organised call-recall programme, in order to understand the barriers to informed uptake. **METHODS:** We searched nine databases for English language peer-reviewed publications reporting on qualitative data from screening-eligible women, exploring barriers to cervical screening in countries that offer a nationally organised call-recall programme. Evidence was integrated using thematic synthesis. **RESULTS:** Thirty-nine papers from the UK, Australia, Sweden and Korea were included. The majority of participants had attended screening at least once. Two broad themes were identified: (a) should I go for screening? and (b) screening is a big deal. In considering whether to attend, women discussed the personal relevance and value of screening. Women who had previously attended described how it was a big deal, physically and emotionally, and the varied threats that screening presents. Practical barriers affected whether women translated screening intentions into action. **CONCLUSIONS:** The variation in women's understanding and perceptions of cervical screening suggests that interventions tailored to decisional stage may be of value in increasing engagement with the invitation and uptake of screening in those who wish to take part. There is also a need for further research with women who have never attended screening, especially those who remain unaware or unengaged, as their perspectives are lacking in the existing literature.

Forster A. S., Waller, J., Bowyer, H. L., & Marlow, L. A. V. **Girls' explanations for being unvaccinated or under vaccinated against human papillomavirus: a content analysis of survey responses.** *BMC Public Health*. 2015: 15 (1): 1278.

BACKGROUND: In England HPV vaccination is offered to all girls age 12-13 years, free-at-the-point-of-receipt, mostly in schools. Coverage is good, but around 20% of girls remain unvaccinated. This research sought to explore reasons for being un-/under vaccinated. **METHODS:** An ethnically diverse sample of girls aged 15-16 years attending one of twelve London schools completed a survey three years after being offered HPV vaccination. Girls reported their HPV vaccine status and those who were unvaccinated (had not received any doses of the vaccine) or under vaccinated (had not completed the recommended 3-dose course) recorded reasons for their un-/under vaccinated status. Reasons were reported using free-text and content analysis was used to analyse responses. **RESULTS:** Around 74% of un-/under vaccinated girls provided a reason for their vaccination status (n = 259). Among unvaccinated girls, the most common reasons related to lack of perceived need for vaccination, concerns about safety and lack of parental consent. Girls who were under vaccinated gave practical reasons, including the need for more information (e.g. not knowing that multiple doses were needed), administrative issues (e.g. school absence), health and procedural concerns (e.g. fear of needles). Descriptively, there were few differences in the reasons given between girls from different ethnic backgrounds. Girls from Black and Asian backgrounds more commonly thought that the vaccine was not needed. Lack of parental consent without providing further explanation was most often cited by girls from Black backgrounds. **CONCLUSIONS:** Safety concerns and lack of perceived need should be addressed to encourage informed uptake of HPV vaccination. Immunisation programme coordinators may be able to increase series completion by tackling practical problems facing under vaccinated girls.

Dodd, R. H., Waller, J., & Marlow, L. A. V. **Human Papillomavirus and Head and Neck Cancer: Psychosocial Impact in Patients and Knowledge of the Link - A Systematic Review.** *Clinical Oncology*. 2016; 28(7):421-39.

Head and neck cancer (HNC) currently affects approximately 11 200 people in the UK, with an increasing proportion known to be caused by the human papillomavirus (HPV). We undertook a systematic review of studies measuring the psychosocial impact of HPV-related HNC and also studies measuring knowledge about the link between HPV and HNC among different populations. Searches were conducted on MEDLINE, Embase, PsycINFO, CINAHL Plus and Web of Science, with reference and forward citation searches also carried out on included studies. Studies were selected if they (i) were original peer-reviewed research (qualitative or quantitative), (ii) mentioned HPV and HNC, (iii) measured an aspect of the psychosocial impact of the diagnosis of HPV-related HNC as the dependent variable and/or (iv) measured knowledge of the association between HPV and HNC. In total, 51 papers met the inclusion criteria; 10 measuring psychosocial aspects and 41 measuring knowledge of the link between HPV and HNC. Quality of life in those with HPV-positive HNC was found to be higher, lower or equivalent to those with HPV-negative HNC. Longitudinal studies found quality of life in patients was at its lowest 2-3 months after diagnosis and some studies found quality of life almost returned to baseline levels after 12 months. Knowledge of the link between HPV and HNC was measured among different populations, with the lowest knowledge in the general population and highest in medical and dental professionals. Due to the limited studies carried out with patients measuring the psychosocial impact of a diagnosis of HPV-positive HNC, future work is needed with the partners of HPV-positive HNC patients and health professionals caring for these patients. The limited knowledge of the association between HPV and HNC among the general population also indicates the need for research to explore the information that these populations are receiving.

Marlow, L. A. V., Wardle, J., & Waller, J. (2015). **Understanding cervical screening non-attendance among ethnic minority women in England.** *British Journal of Cancer*, 113 (5), 833-839.

BACKGROUND: Women from Black, Asian and Minority Ethnic (BAME) backgrounds are less likely to attend cervical screening than White British women. This study explored sociodemographic and attitudinal correlates of cervical screening non-attendance among BAME women. **METHODS:** Women (30-60 years) were recruited from Indian, Pakistani, Bangladeshi, Caribbean, African and White British backgrounds (n=720). Participants completed structured interviews. **RESULTS:** BAME women were more likely to be non-attenders than white British women (44-71% vs 12%) and fell into two groups: the disengaged and the overdue. Migrating to the United Kingdom, speaking a language other than English and low education level were associated with being disengaged. Being overdue was associated with older age. Three attitudinal barriers were associated with being overdue for screening among BAME women: low perceived risk of cervical cancer due to sexual inactivity, belief that screening is unnecessary without symptoms and difficulty finding an appointment that fits in with other commitments. **CONCLUSIONS:** BAME non-attenders appear to fall into two groups, and interventions for these groups may need to be targeted and tailored accordingly. It is important to ensure that BAME women understand cancer screening is intended for asymptomatic women and those who have ceased sexual activity may still be at risk.

Bowyer, H. L., Dodd, R. H., Marlow, L. A. V., & Waller, J. **Association between human papillomavirus vaccine status and other cervical cancer risk factors.** *Vaccine*. 2014; 32 (34), 4310-4316.

Little is known about the relationship between HPV vaccine uptake and other risk factors for cervical cancer. This study aimed to measure the association between vaccine status and cervical cancer risk factors in adolescent girls. Girls (15-16 years) from the first two cohorts to be offered routine HPV

vaccination in the NHS immunisation programme completed a survey 3 years post-vaccination. Recruitment took place at 13 schools in London. Of 2768 girls registered in Year 11, 1912 (69%) took part and provided analysable data. Questions assessed vaccine status, demographic characteristics, smoking status, sexual behaviour and intention to attend cervical screening. Overall, 78% had completed the three-dose vaccine course. There was no association between vaccine status and smoking behaviour or sexual experience. In adjusted analyses, girls from black or 'other' ethnic backgrounds were less likely to be fully-vaccinated than those from white backgrounds. Those with low intentions to attend cervical screening were less likely to be fully vaccinated than those with high intentions. Efforts will be needed to ensure that unvaccinated women understand the importance of cervical screening when they reach the age that screening begins. Ethnic inequalities in vaccine coverage need to be explored further.

Marlow, L., Waller, J., & Wardle, J. **Barriers to cervical cancer screening among ethnic minority women: A qualitative study.** *Journal of Family Planning and Reproductive Health Care.* 2015; 41(4):248-54.

BACKGROUND: Ethnic minority women are less likely to attend cervical screening. **AIM:** To explore self-perceived barriers to cervical screening attendance among ethnic minority women compared to white British women. **DESIGN:** Qualitative interview study. **SETTING:** Community groups in ethnically diverse London boroughs. **METHODS:** Interviews were carried out with 43 women from a range of ethnic minority backgrounds (Indian, Pakistani, Bangladeshi, Caribbean, African, Black British, Black other, White other) and 11 White British women. Interviews were recorded, transcribed verbatim and analysed using Framework analysis. **RESULTS:** Fifteen women had delayed screening/had never been screened. Ethnic minority women felt that there was a lack of awareness about cervical cancer in their community, and several did not recognise the terms 'cervical screening' or 'smear test'. Barriers to cervical screening raised by all women were emotional (fear, embarrassment, shame), practical (lack of time) and cognitive (low perceived risk, absence of symptoms). Emotional barriers seemed to be more prominent among Asian women. Low perceived risk of cervical cancer was influenced by beliefs about having sex outside of marriage and some women felt a diagnosis of cervical cancer might be considered shameful. Negative experiences were well remembered by all women and could be a barrier to repeat attendance. **CONCLUSIONS:** Emotional barriers (fear, embarrassment and anticipated shame) and low perceived risk might contribute to explaining lower cervical screening coverage for some ethnic groups. Interventions to improve knowledge and understanding of cervical cancer are needed in ethnic minority communities, and investment in training for health professionals may improve experiences and encourage repeat attendance for all women.

Ekechi, C., Olaitan, A., Ellis, R., Koris, J., Amajuoyi, A., & Marlow, L. A. **Knowledge of cervical cancer and attendance at cervical cancer screening: a survey of Black women in London.** *BMC Public Health.* 2014; 14: 1096.

BACKGROUND: Women from ethnic minority backgrounds are less likely to attend cervical screening, but further understanding of ethnic inequalities in cervical screening uptake is yet to be established. This study aimed to explore the socio-demographic and ethnicity-related predictors of cervical cancer knowledge, cervical screening attendance and reasons for non-attendance among Black women in London. **METHODS:** A questionnaire was completed by women attending Black and ethnic hair and beauty specialists in London between February and April 2013. A stratified sampling frame was used to identify Black hair specialists in London subdivisions with >10% Black population (including UK and foreign-born). Fifty-nine salons participated. Knowledge of cervical cancer risk factors and symptoms, self-reported screening attendance and reasons for non-attendance at cervical screening were assessed. **RESULTS:** Questionnaires were completed by 937 Black women aged 18-78, describing themselves as being predominantly from African or Caribbean backgrounds (response rate 26.5%). Higher educational

qualifications ($p < .001$) and being born in the UK ($p = .011$) were associated with greater risk factor knowledge. Older age was associated with greater symptom knowledge ($p < .001$). Being younger, single, African (compared to Caribbean) and attending religious services more frequently were associated with being overdue for screening. Women who had migrated to the UK more than 10 years ago were less likely to be overdue than those born in the UK. Of those overdue for screening who endorsed a barrier (67/133), 'I meant to go but didn't get round to it' (28%), fear of the test procedure (18%) and low risk perception (1a8%) were the most common barriers. **CONCLUSIONS:** Ethnicity, migration and religiosity play a role in predicting cervical screening attendance among women from Black backgrounds. African women, those born in the UK and those who regularly attend church are most likely to put off attending. Additional research is needed to explore the attitudes, experiences and beliefs that explain why these groups might differ.

Bowyer, H. L., Forster, A. S., Marlow, L. A., & Waller, J. **Predicting human papillomavirus vaccination behaviour among adolescent girls in England: results from a prospective survey.** *J Fam Plann Reprod Health Care.* 2014; 40 (1), 14-22.

BACKGROUND: To maximise the benefits of human papillomavirus (HPV) vaccination, uptake needs to be high. We examined psychosocial predictors of HPV vaccine uptake and the association between vaccine intention and uptake 1 year later in adolescent girls (aged 16-17 years) in England. **METHOD:** Adolescent girls in the catch-up cohort were recruited from colleges in the South East of England in 2009 and 2010. Participants completed a questionnaire 6 months before ($n=606$) and 6 months after ($n=214$) being offered the vaccine, which assessed vaccine intention, vaccine uptake, demographics and attitudes based on the Health Belief Model and Theory of Planned Behaviour.

RESULTS: A number of demographic and psychological factors, including intention, showed associations with vaccine uptake in uni-variable analyses. In multi-variable analyses, only ethnicity was independently associated with vaccine uptake. Participants from Black or 'Other' ethnic backgrounds were less likely to have received the HPV vaccine than White participants. **CONCLUSIONS:** More research is needed to help understand variation in vaccine coverage between ethnic groups.

Bowyer, H. L., Marlow, L. A., Hibbitts, S., Pollock, K. G., & Waller, J. **Knowledge and awareness of HPV and the HPV vaccine among young women in the first routinely vaccinated cohort in England.** *Vaccine.* 2013; 31 (7), 1051-1056.

A national school-based human papillomavirus (HPV) vaccination programme has been available for 12-13 year old females in the UK since 2008, offering protection against HPV types 16 and 18, which are responsible for the majority of cervical cancer. Little is known about HPV knowledge in girls who have been offered the vaccine. Girls offered the school-based vaccine in the first routine cohort ($n=1033$) were recruited from 13 schools in London three years post-vaccination. Participants completed a questionnaire about HPV awareness, knowledge about HPV and the vaccine, and demographic characteristics including vaccine status. About a fifth of the girls reported they were unaware of the HPV infection. Among those who reported being aware of HPV ($n=759$) knowledge was relatively low. Approximately half of the participants knew that HPV infection causes cervical cancer, condoms can reduce the risk of transmission and that cervical screening is needed regardless of vaccination status. These results are helpful in benchmarking HPV-related knowledge in vaccinated girls and could be used in the development of appropriate educational messages to accompany the first cervical screening invitation in this cohort in the future.

Marlow, L. A., Zimet, G. D., McCaffery, K. J., Ostini, R., & Waller, J. (2013). **Knowledge of human papillomavirus (HPV) and HPV vaccination: an international comparison.** *Vaccine*. 2013; 31 (5), 763-769.

Since vaccination against human papillomavirus (HPV) became available, awareness of HPV has dramatically increased. Implementation of a vaccine program varies internationally yet no studies have explored the influence this has on the public's knowledge of HPV. The present study aimed to explore differences in awareness of HPV and HPV knowledge across three countries: The US, UK and Australia. Participants (n=2409) completed a validated measure of HPV knowledge as part of an online survey. There were higher levels of HPV awareness among men and women in the US than the UK and Australia. Being male and having a lower educational level was associated with lower HPV awareness in all three countries. Awareness of HPV vaccine was higher in women from the US than the UK and Australia. Women in the US scored significantly higher on general HPV knowledge (on a 15-item scale) than women in the UK and Australia, but there were no between country differences in HPV vaccine knowledge (on a 6-item scale). When asked about country-specific vaccine availability, participants in the US were less able to identify the correct answers than participants in the UK and Australia. More than half of participants did not know: HPV can cause genital warts; most sexually active people will get HPV at some point in their life; or HPV doesn't usually need treatment. Pharmaceutical advertising campaigns could explain why awareness of HPV and HPV vaccine is higher in the US and this has helped to get some important messages across. Significant gaps in HPV knowledge remain across all three countries.

Kåre Mølbak, Statens Serum Institute (Denmark)

(Based on pubmed search)

Dorleans, F., G. Falkenhorst, B. Bottiger, M. Howitz, S. Midgley, J. Nielsen and K. Molbak. **A case-control study of risk factors for rotavirus infections in adults, Denmark, 2005-2009.** *Epidemiol Infect.* 2016; 144(3): 560-566.

Rotavirus (RV) infections affect young children, but can also occur in adults. We sought to identify risk factors for RV infections in adults aged 18 years in Denmark, and to describe illness and genotyping characteristics. From March 2005 to February 2009, we recruited consecutive cases of laboratory-confirmed RV infection and compared them with healthy controls matched by age, gender and municipality of residence. We collected information on illness characteristics and exposures using postal questionnaires. We calculated univariable and multivariable matched odds ratios (mOR) with conditional logistic regression. The study comprised 65 cases and 246 controls. Illness exceeded 10 days in 31% of cases; 22% were hospitalized. Cases were more likely than controls to suffer serious underlying health conditions [mOR 5.6, 95% confidence interval (CI) 1.7-18], and to report having had close contact with persons with gastrointestinal symptoms (mOR 9.4, 95% CI 3.6-24), in particular young children aged 18 years. Close contact with young children or adults with gastrointestinal symptoms is the main risk factor for RV infection in adults in Denmark. RV vaccination assessments should consider that RV vaccination in children may indirectly reduce the burden of disease in adults.

Harboe, Z. B., T. Dalby, D. M. Weinberger, T. Benfield, K. Molbak, H. C. Slotved, C. H. Suppli, H. B. Konradsen and P. Valentiner-Branth. **Impact of 13-valent pneumococcal conjugate vaccination in invasive pneumococcal disease incidence and mortality.** *Clin Infect Dis.* 2014; 59(8): 1066-1073.

BACKGROUND: The impact of the 13-valent pneumococcal conjugate vaccine (PCV13) at the population level is unclear. We explored PCV13's effect in reducing invasive pneumococcal disease (IPD)-related morbidity and mortality, and whether serotype-specific changes were attributable to vaccination or expected as a part of natural, cyclical variations. **METHODS:** This was a Danish nationwide population-based cohort study based on the linkage of laboratory surveillance data and the Danish Civil Registration System. Changes in IPD incidence and mortality during baseline (2000-2007), 7-valent pneumococcal conjugate vaccine (PCV7) (2008-2010), and PCV13 (2011-2013) periods were estimated. Predicted incidences of serotypes were estimated controlling for cyclical trends from historical patterns observed during the past 20 years. **RESULTS:** We observed a 21% reduction (95% confidence interval [CI], 17%-25%) in IPD incidence in the total population after PCV13's introduction, and a 71% reduction (95% CI, 62%-79%) in children aged <2 years, considered as the vaccine effectiveness. We estimated a 28% reduction (95% CI, 18%-37%) in IPD-related 30-day mortality, from 3.4 deaths (95% CI, 3.2-3.6) per 100 000 population in the pre-PCV period to 2.4 (95% CI, 2.2-2.7) in the PCV13 period. The decline in mortality was observed across all age groups but was mainly related to mortality reductions in the nonvaccinated population. For serotypes 1 and 3, there were no significant changes in incidence beyond what would be expected from natural cyclical patterns. Serotype 19A significantly increased following PCV7's introduction, but the incidence declined toward baseline in 2012. **CONCLUSIONS:** PCV13 has brought greater benefits than we had expected in our setting. We observed a further decline on IPD incidence shortly after the shift from PCV7 to PCV13 in the national immunization program. This decline was accompanied by a substantial population-level decline in pneumococcal-related mortality of nearly 30% among nonvaccinated persons.

Helmuth, I. G., A. Poulsen, C. H. Suppli and K. Molbak. **Varicella in Europe-A review of the epidemiology and experience with vaccination.** *Vaccine.* 2015; 33(21): 2406-2413.

There is no consensus as regards the European varicella immunisation policy; some countries have introduced varicella vaccination in their routine childhood immunisation programs whereas others have decided against or are debating. With the aim of providing an overview of the epidemiology of varicella in Europe and addressing the different strategies and the experiences so far, we performed a review of epidemiological studies done in Europe from 2004 to 2014. Varicella is mainly a disease of childhood, but sero-epidemiological studies show regional differences in the proportion of susceptible adults. Hospitalisation due to varicella is not common, but complications and hospitalisation mainly affect previously healthy children, which underlines the importance of not dismissing varicella as a disease of little importance. The experience with universal vaccination in Europe shows that vaccination leads to a rapid reduction of disease incidence. Vaccine effectiveness is high and a protective herd effect is obtained. Experience with vaccination in Europe has not been long enough, though, to draw conclusions on benefits and drawbacks with vaccination as well as the capacity for national programs in Europe to maintain a sufficiently high coverage to prevent a change in age group distribution to older children and young adults or on the impact that varicella immunisation may have on the epidemiology of shingles.

Norheim, G., M. Sadarangani, O. Omar, L. M. Yu, K. Molbak, M. Howitz, P. Olcen, M. Haglund, A. van der Ende and A. J. Pollard. **Association between population prevalence of smoking and incidence of meningococcal disease in Norway, Sweden, Denmark and the Netherlands between 1975 and 2009: a population-based time series analysis.** *BMJ Open*. 2014; 4(2): e003312.

OBJECTIVE: To investigate the relationship between the prevalence of smoking in the population and incidence of invasive meningococcal disease (IMD) among children under 5 years of age. **DESIGN:** Retrospective, longitudinal, observational study. Poisson regression controlled for confounding factors. **SETTING:** Norway, Sweden, Denmark and the Netherlands between 1975 and 2009. **POPULATION:** Total population of approximately 35 million people in these four countries. **DATA SOURCES:** Data were collected from the Ministries of Health, National Statistics Bureaus and other relevant national institutes. **RESULTS:** In Norway, there was a significant positive relationship between the annual prevalence of daily smokers among individuals aged 25-49 years and the incidence of IMD in children under 5 years of age, unadjusted (RR=1.04-1.06, 95% CI 1.02 to 1.07, $p < 0.001$) and after adjustment for time of year (quarter), incidence of influenza-like illness and household crowding (RR=1.05-1.07, 95% CI 1.03 to 1.09, $p < 0.001$). Depending on age group, the risk of IMD increased by 5.2-6.9% per 1% increase in smoking prevalence among individuals aged 25-49 years in adjusted analyses. Using limited datasets from the three other countries, unadjusted analysis showed positive associations between IMD in children related to older smokers in Sweden and the Netherlands and negative associations related to younger smokers in Sweden. However, there were no demonstrable associations between incidence of IMD and prevalence of smoking, after adjustment for the same confounding variables. **CONCLUSIONS:** The reduced incidence of IMD in Norway between 1975 and 2009 may partly be explained by the reduced prevalence of smoking during this period. High-quality surveillance data are required to confirm this in other countries. Strong efforts to reduce smoking in the whole population including targeted campaigns to reduce smoking among adults may have a role to play in the prevention of IMD in children.

Pebody, R. G. and K. Molbak. **Importance of timely monitoring of seasonal influenza vaccine effectiveness.** *Euro Surveill*. 2016; 21(16).

Widgren, K., J. Simonsen, P. Valentiner-Branth and K. Molbak. **Uptake of the human papillomavirus-vaccination within the free-of-charge childhood vaccination programme in Denmark.** *Vaccine*. 2011; 29(52): 9663-9667.

BACKGROUND: Persistent infection with human papillomavirus (HPV) is a prerequisite for cervical cancer, which causes 175 yearly deaths and substantial morbidity in Denmark. In January 2009, HPV-vaccination for 12 year-old girls was introduced into the free-of-charge childhood vaccination programme. Due to concerns about potential poor compliance we determined the uptake and identified determinants for vaccination after the first year of the programme. **METHODS:** All vaccinations given within the vaccination programme are reported to a central register, which we linked to demographic information found in the Danish civil register. We calculated vaccination uptake and used Cox regression survival analysis to compare the uptake rates between demographic subgroups in the population, e.g. by number of siblings, age of mother (at the daughter's birth) and place of origin. **RESULTS:** The uptake among the 33,838 eligible girls was 80%, 75% and 62% respectively for the three HPV-doses. All subgroups had uptake above 68% for the first HPV-vaccination. Girls with mothers younger or older than the reference group of 25-34 years had a lower uptake rate (adjHR 0.94, 95% CI 0.91-0.97 and adjHR 0.91, 95% CI 0.88-0.94 respectively). Girls with 5 or more siblings had lower uptake rate than girls without siblings (adjHR 0.79, 95% CI 0.71-0.87). Girls born in other EU/EFTA-countries had lower uptake rate than Danish-born girls with Danish-born parents (adjHR 0.74, 95% CI 0.67-0.82). **CONCLUSIONS:** The introduction of routine HPV-vaccination in Denmark resulted in a relatively high uptake, indicating little reason for major concern about barriers towards the vaccination in Denmark. Population groups with reduced uptake were identified, but as they were small in number their effect on the overall vaccination coverage was marginal. Nonetheless, these groups should be targeted in future acceptance studies and vaccination awareness campaigns.

Hannah Nohynek, National Institute for Health and Welfare (Finland).

Lucero MG, [Nohynek H](#), Williams G, Tallo V, Simoes EAF, Lupisan S, Sanvictores D, Forsyth S, Puumalainen T, Ugpo J, Lechago M, de Campo M, Abucejo-Ladesma E, Sombrero L, Nissinen A, Soininen A, Ruutu P, Riley I, Mäkelä PH, ARIVAC consortium. **Efficacy of an 11-valent pneumococcal conjugate vaccine against radiologically confirmed pneumonia among children less than two years of age in the Philippines: a randomized, double-blind, placebo-controlled trial.** *Pediatr Infect Dis J* 2009;28:455-62. Epub 2009 May 28.

BACKGROUND: Pneumococcus is a leading cause of childhood pneumonia worldwide. Pneumococcal conjugate vaccines (PCV) have demonstrated efficacy against childhood invasive pneumococcal disease (IPD) and pneumonia in the United States and Africa. No information is available from Asia on the impact of PCV on childhood pneumonia. **METHODS:** We conducted a randomized, placebo-controlled, double-blind trial in Bohol, the Philippines (ISRCTN 62323832). Children 6 weeks to <6 months of age were randomly allocated to receive 3 doses of either an 11-valent PCV (11PCV, sanofi pasteur, Lyon, France) or a saline placebo, with a minimum interval of 4 weeks between doses to determine vaccine efficacy (VE) against the primary outcome of a child experiencing first episode of community-acquired radiologically defined pneumonia in the first 2 years of life. Secondary end points were clinical pneumonia, IPD, safety, and immunogenicity. **RESULTS:** Twelve thousand one hundred ninety-one children were enrolled. By per protocol (PP) analysis, 93 of 6013 fully vaccinated 11PCV recipient children had a first episode of radiologic pneumonia compared with 120 of 6018 placebo recipients. VE against radiologically defined pneumonia for the PP cohort of children 3 to 23 months old was 22.9% (95% CI: -1.1, 41.2; P = 0.06), for the prespecified subgroups of children 3 to 11 months of age, 34.0% (95% CI: 4.8, 54.3; P = 0.02), and of those 12 to 23 months old, 2.7% (95% CI: -43.5, 34.0; P = 0.88). By intent-to-treat (ITT) analysis, 119 of 6097 11PCV recipient children had an episode of radiologic pneumonia compared with 141 of 6094 placebo recipients. VE against radiologic pneumonia for the ITT cohort of children <2 years old was 16.0% (95% CI -7.3, 34.2; P = 0.16), for a subgroup of children <12 months of age, 19.8% (95% CI: -8.8, 40.8; P = 0.15). VE against clinical pneumonia by PP was not significant (VE 0.1%; 95% CI -9.4, 8.7; P = 0.99). IPD was rare: only 3 cases of IPD due to vaccine serotypes were observed during the study. 11PCV was immunogenic and well tolerated. Among 11PCV recipients, a small excess of serious adverse respiratory events was observed in the first 28 days after the first and second dose of vaccine, and of nonrespiratory events after the first dose. An excess of pneumonia episodes in 11PCV recipients in the month following the second dose of vaccination was the principal reason for lower VE by ITT analysis than by PP analysis. **CONCLUSIONS:** In PP analysis, a 22.9% reduction of community-acquired radiologically confirmed pneumonia in children younger than 2 years of age in the 11-valent tetanus-diphtheria toxoid-conjugated PCV vaccinated group was observed; a reduction similar as observed in other PCV trials. We could not demonstrate any VE against clinical pneumonia. Our finding confirms for the first time that in a low-income, low-mortality developing country in Asia, at least one-fifth of radiologically confirmed pneumonia is caused by pneumococcus, and thus preventable by PCV. Whether PCV should be included in national program in such settings, however, depends on careful country specific disease burden measurement and cost-effectiveness calculation.

Zuber PLF, Autran B, Asturias EJ, Evans S, Hartigan-Go K, Hussey G, John TJ, Lambert PH, Law B, Midthun K, Nohynek H, Salmaso S, Smith PG, Bentsi-Enchill A, Caric A, Pfeifer D, Duclos P, Wood D. **Global Advisory Committee on Vaccine Safety, World Health Organization secretariat. Global safety of vaccines: strengthening systems for monitoring, management and the role of GACVS.** *Expert Rev Vaccines* 2009;8:705-16.

Shann F, [Nohynek H](#), Scott JA, Hesselting A, Flanagan KL; Working Group on Non-specific Effects of Vaccines. **Randomised trials to study the non-specific effects of vaccines in children in low-income countries.** *Pediatr Infect Dis J* 2010;29:457-461

The Expanded Program on Immunization (EPI) has led to large reductions in morbidity and mortality among children in low-income countries. However, the basic EPI schedule may no longer be optimal because of changes in vaccines, programs, and epidemiologic circumstances. In addition, evidence has accumulated that some EPI vaccines may have nonspecific effects that increase or decrease mortality from subsequent infections with other unrelated organisms. There is therefore a need for randomized trials to evaluate the effects of alternative EPI schedules on all-cause mortality, as well as vaccine efficacy against the target diseases. We have reviewed the available literature on the nonspecific effects of vaccines on mortality, and compiled a list of potential trials that might address this issue. We have then ranked the trials based on the potential importance of the results and the ethical and practical considerations. Trials of early BCG vaccination in low-birth-weight babies, early measles vaccination, and altered timing of DTP vaccination all have a high priority.

[Nohynek H](#), Jokinen J, Partinen M, Vaarala O, Kirjavainen T, Sundman J, Himanen SL, Hublin C, Julkunen I, Olsén P, Saarenpää-Heikkilä O, Kilpi T. **AS03 adjuvanted AH1N1 vaccine associated with an abrupt increase in the incidence of childhood narcolepsy in Finland.** *PLoS ONE* 2012; 7(3): e33536.

BACKGROUND: Narcolepsy is a chronic sleep disorder with strong genetic predisposition causing excessive daytime sleepiness and cataplexy. A sudden increase in childhood narcolepsy was observed in Finland soon after pandemic influenza epidemic and vaccination with AS03-adjuvanted Pandemrix. No increase was observed in other age groups. **METHODS:** Retrospective cohort study. From January 1, 2009 to December 31, 2010 we retrospectively followed the cohort of all children living in Finland and born from January 1991 through December 2005. Vaccination data of the whole population was obtained from primary health care databases. All new cases with assigned ICD-10 code of narcolepsy were identified and the medical records reviewed by two experts to classify the diagnosis of narcolepsy according to the Brighton collaboration criteria. Onset of narcolepsy was defined as the first documented contact to health care because of excessive daytime sleepiness. The primary follow-up period was restricted to August 15, 2010, the day before media attention on post-vaccination narcolepsy started. **FINDINGS:** Vaccination coverage in the cohort was 75%. Of the 67 confirmed cases of narcolepsy, 46 vaccinated and 7 unvaccinated were included in the primary analysis. The incidence of narcolepsy was 9.0 in the vaccinated as compared to 0.7/100,000 person years in the unvaccinated individuals, the rate ratio being 12.7 (95% confidence interval 6.1-30.8). The vaccine-attributable risk of developing narcolepsy was 1:16,000 vaccinated 4 to 19-year-olds (95% confidence interval 1:13,000-1:21,000). **CONCLUSIONS:** Pandemrix vaccine contributed to the onset of narcolepsy among those 4 to 19 years old during the pandemic influenza in 2009-2010 in Finland. Further studies are needed to determine whether this observation exists in other populations and to elucidate potential underlying immunological mechanism. The role of the adjuvant in particular warrants further research before drawing conclusions about the use of adjuvanted pandemic vaccines in the future.

Poli F, Overeem S, Lammers GJ, Plazzi G, Lecendreux M, Bassetti CL, Dauvilliers Y, Keene D, Khatami R, Li Y, Mayer G, [Nohynek H](#), Pahud B, Paiva T, Partinen M, Scammell TE, Shimabukuro T, Sturkenboom M, van Dinther K, Wiznitzer M, Bonhoeffer J. **Narcolepsy as adverse event following immunization: case definition and guidelines for data collection, analysis and presentation.** *Vaccine* 2013;31(6):994-1007. No abstract available.

Melén K, Partinen M, Tynell J, Sillanpää M, Himanen SL, Saarenpää-Heikkila O, Hublin C, Olsen P, Ilonen J, Nohynek H, Syrjänen R, Kilpi T, Vuorela A, Kirjavainen T, Vaarala O, Julkunen I. **No serological evidence of influenza A H1N1pdm09 virus infection as a contributing factor in childhood narcolepsy after Pandemrix vaccination campaign in Finland.** PLoS One 2013 ;8(8):e68402.

BACKGROUND: Narcolepsy cataplexy syndrome, characterised by excessive daytime sleepiness and cataplexy, is strongly associated with a genetic marker, human leukocyte antigen (HLA) DQB1*06:02. A sudden increase in the incidence of childhood narcolepsy was observed after vaccination with AS03-adjuvanted Pandemrix influenza vaccine in Finland at the beginning of 2010. Here, we analysed whether the coinciding influenza A H1N1pdm pandemic contributed, together with the Pandemrix vaccination, to the increased incidence of childhood narcolepsy in 2010. The analysis was based on the presence or absence of antibody response against non-structural protein 1 (NS1) from H1N1pdm09 virus, which was not a component of Pandemrix vaccine. **METHODS:** Non-structural (NS) 1 proteins from recombinant influenza A/Udorn/72 (H3N2) and influenza A/Finland/554/09 (H1N1pdm09) viruses were purified and used in Western blot analysis to determine specific antibody responses in human sera. The sera were obtained from 45 patients who fell ill with narcolepsy after vaccination with AS03-adjuvanted Pandemrix at the end of 2009, and from controls. **FINDINGS:** Based on quantitative Western blot analysis, only two of the 45 (4.4%) Pandemrix-vaccinated narcoleptic patients showed specific antibody response against the NS1 protein from the H1N1pdm09 virus, indicating past infection with the H1N1pdm09 virus. Instead, paired serum samples from patients, who suffered from a laboratory confirmed H1N1pdm09 infection, showed high levels or diagnostic rises (96%) in H1N1pdm virus NS1-specific antibodies and very high cross-reactivity to H3N2 subtype influenza A virus NS1 protein. **CONCLUSION:** Based on our findings, it is unlikely that H1N1pdm09 virus infection contributed to a sudden increase in the incidence of childhood narcolepsy observed in Finland in 2010 after AS03-adjuvanted Pandemrix vaccination.

Nohynek H, Wichmann O, D'Ancona F, VENICE National Gatekeepers. **National Advisory Groups and their role in immunization policy making processes in European countries.** Clin Microbiol Infect. 2013; 19(12):1096-105.

During the twenty-first century, the development of national immunization programmes (NIP) has matured into robust processes where evidence-based methodologies and frameworks have increasingly been adopted. A key role in the decision-making and recommending processes is played by National Immunization Technical Advisory Groups (NITAGs). In a survey performed among European Union member states, Norway and Iceland, in February 2013, 85% of the 27 responding countries reported having established a NITAG, and of these, 45% have formal frameworks in place for the systematic development of vaccination recommendations. Independent of whether a formal framework is in place, common key factors are addressed by all NITAGs and also in countries without NITAGs. The four main factors addressed by all were: disease burden in the country, severity of the disease, vaccine effectiveness or efficacy, and vaccine safety at population level. Mathematical modelling and cost-effectiveness analyses are still not common tools. Differences in the relative weighting of these key factors, differences in data or assumptions on country-specific key factors, and differences in existing vaccination systems and financing, are likely to be reasons for differences in NITAG recommendations, and eventually NIPs, across Europe. Even if harmonization of NIPs is presently not a reasonable aim, systematic reviews and the development of mathematical/economic models could be performed at supranational level, thus sharing resources and easing the present work-load of NITAGs. Nevertheless, it has been argued that harmonization would ease central purchase of vaccines, thus reducing the price and increasing access to new vaccines.

Keller-Stanislawski B, Englund JA, Kang G, Mangtani P, Neuzil K, Nohynek H, Pless R, Lambach P, Zuber P. **Safety of immunization during pregnancy: A review of the evidence of selected inactivated and live attenuated vaccines.** *Vaccine*. 2014; 32(52): 7057-7064.

Vaccine-preventable infectious diseases are responsible for significant maternal, neonatal, and young infant morbidity and mortality. While there is emerging scientific evidence, as well as theoretical considerations, indicating that certain vaccines are safe for pregnant women and fetuses, policy formulation is challenging because of perceived potential risks to the fetus. This report presents an overview of available evidence on pregnant women vaccination safety monitoring in pregnant women, from both published literature and ongoing surveillance programs. Safety data were reviewed for vaccines against diseases which increase morbidity in pregnant women, their fetus or infant as well as vaccines which are used in mass vaccination campaigns against diseases. They include inactivated seasonal and pandemic influenza, mono- and combined meningococcal polysaccharide and conjugated vaccines, tetanus toxoid and acellular pertussis combination vaccines, as well as monovalent or combined rubella, oral poliomyelitis virus and yellow fever vaccines. No evidence of adverse pregnancy outcomes has been identified from immunization of pregnant women with these vaccines.

Vaarala O, Vuorela A, Partinen M, Baumann M, Freitag T, Meri S, Saavalainen P, Jauhiainen M, Soliymani R, Kirjavainen T, Olsen P, Saarenpää-Heikkilä O, Rouvinen J, Roivainen M, Nohynek H, Jokinen J, Julkunen I, Kilpi T. **Antigenic differences between AS03 adjuvanted influenza A (H1N1) pandemic vaccines: implications for Pandemrix-associated narcolepsy risk.** *PLoS One*. 2014; 9(12):e114361.

BACKGROUND: Narcolepsy results from immune-mediated destruction of hypocretin secreting neurons in hypothalamus, however the triggers and disease mechanisms are poorly understood. Vaccine-attributable risk of narcolepsy reported so far with the AS03 adjuvanted H1N1 vaccination Pandemrix has been manifold compared to the AS03 adjuvanted Arepanrix, which contained differently produced H1N1 viral antigen preparation. Hence, antigenic differences and antibody response to these vaccines were investigated. **METHODS AND FINDINGS:** Increased circulating IgG-antibody levels to Pandemrix H1N1 antigen were found in 47 children with Pandemrix-associated narcolepsy when compared to 57 healthy children vaccinated with Pandemrix. H1N1 antigen of Arepanrix inhibited poorly these antibodies indicating antigenic difference between Arepanrix and Pandemrix. High-resolution gel electrophoresis quantitation and mass spectrometry identification analyses revealed higher amounts of structurally altered viral nucleoprotein (NP) in Pandemrix. Increased antibody levels to hemagglutinin (HA) and NP, particularly to detergent treated NP, was seen in narcolepsy. Higher levels of antibodies to NP were found in children with DQB1*06:02 risk allele and in DQB1*06:02 transgenic mice immunized with Pandemrix when compared to controls. **CONCLUSIONS:** This work identified 1) higher amounts of structurally altered viral NP in Pandemrix than in Arepanrix, 2) detergent-induced antigenic changes of viral NP, that are recognized by antibodies from children with narcolepsy, and 3) increased antibody response to NP in association of DQB1*06:02 risk allele of narcolepsy. These findings provide a link between Pandemrix and narcolepsy. Although detailed mechanisms of Pandemrix in narcolepsy remain elusive, our results move the focus from adjuvant(s) onto the H1N1 viral proteins.

Ahmed SS, Volkmuth W, Duca J, Corti L, Pallaoro M, Pezzicoli A, Karle A, Rigat F, Rappuoli R, Narasimhan V, Julkunen I, Vuorela A, Vaarala O, Nohynek H, Laghi Pasini F, Montomoli E, Trombetta C., Adams CM, Rothbard J, Steinman L. **Cross-reactivity of antibodies to influenza nucleoprotein with hypocretin receptor.** *Sci Transl Med*. 2015; 7(294): 294ra105.

No abstract available.

Robert Pless, Public Health Agency of Canada

Global Advisory Committee on Vaccine Safety, 2-3 December 2015. [Wkly Epidemiol Rec. 2016 Jan 22](#); 91(3):21-31.

Global Advisory Committee on Vaccine Safety, 11–12 December 2013. [Wkly Epidemiol Rec. 2014 Feb 14](#); 89(7):53-60.

Global Advisory Committee on Vaccine Safety, 12–13 June 2013. [Wkly Epidemiol Rec. 2013 Jul 19](#); 88(29):301-12.

Global Advisory Committee on Vaccine Safety, 12-13 June 2007. Wkly Epidemiol Rec. 2007 Jul 20; 82(28-29):252-9.

Global Advisory Committee on Vaccine Safety, 17-18 December 2008. Wkly Epidemiol Rec. 2009 Jan 30; 84(5):37-40.

Global Advisory Committee on Vaccine Safety, report of meeting held 17-18 June 2009. Wkly Epidemiol Rec. 2009 Aug 7; 84(32):325-32.

Global Advisory Committee on Vaccine Safety, June 2012. Wkly Epidemiol Rec. 2012 Jul 27; 87(30):281-7.

Kevin Pollock, Health Protection (Scotland)

Cuschieri K, Kavanagh K, Moore C, Bhatia R, Love J, Pollock KG. **Impact of partial bivalent HPV vaccination on vaccine-type infection: a population-based analysis.** *Br J Cancer.* 2016; 114(11): 1261-4.

BACKGROUND: Data on the effectiveness of one dose of HPV vaccine are lacking, particularly in population-based settings. Data from a national HPV immunisation catch-up programme of 14-18-year-old girls were used to assess the effectiveness of <3 doses of the bivalent vaccine on vaccine-type and cross-reactive-type HPV infection. **METHODS:** Cervical samples from women attending for their first cervical smear, which had been genotyped for HPV as part of a longitudinal HPV surveillance programme were linked to immunisation records to establish the number of vaccine doses (0, 1, 2 and 3) administered. Vaccine effectiveness (VE) adjusted for deprivation and age at first dose, was assessed for prevalent HPV 16/18 and HPV 31/33/45 infection. **RESULTS:** VE for prevalent HPV 16/18 infection associated with 1, 2 and 3 doses was 48.2% (95% CI 16.8, 68.9), 54.8% (95% CI 30.7, 70.8) and 72.8% (95% CI 62.8, 80.3). Equivalent VE for prevalent HPV 31/33/45 infection was -1.62% (95% CI -85.1, 45.3), 48.3% (95% CI 7.6, 71.8) and 55.2% (95% CI 32.6, 70.2). **CONCLUSIONS:** Consistent with recent aggregated trial data, we demonstrate the potential effectiveness of even one dose of HPV vaccine on vaccine-type infection. Given that these women were immunised as part of a catch-up campaign, the VE observed in this study is likely to be an underestimate of what will occur in girls vaccinated at younger ages. Further population-based studies which look at the clinical efficacy of one-dose schedules are warranted.

Palmer TJ, McFadden M, Pollock KG, Kavanagh K, Cuschieri K, Cruickshank M, Cotton S, Nicoll S, Robertson C. **HPV immunisation and cervical screening-confirmation of changed performance of cytology as a screening test in immunised women: a retrospective population-based cohort study.** *Br J Cancer.* 2016; 114(5): 582-9.

BACKGROUND: To document the effect of bivalent HPV immunisation on cervical cytology as a screening test and assess the implications of any change, using a retrospective analysis of routinely collected data from the Scottish Cervical Screening Programme (SCSP). **METHODS:** Data were extracted from the Scottish Cervical Call Recall System (SCCRS), the Scottish Population Register and the Scottish Index of Multiple Deprivation. A total of 95 876 cytology records with 2226 linked histology records from women born between 1 January 1988 and 30 September 1993 were assessed. Women born in or after 1990 were eligible for the national catch-up programme of HPV immunisation. The performance of cervical cytology as a screening test was evaluated using the key performance indicators used routinely in the English and Scottish Cervical Screening Programmes (NHSCSP and SCSP), and related to vaccination status. **RESULTS:** Significant reductions in positive predictive value (16%) and abnormal predictive value (63%) for CIN2+ and the mean colposcopy score (18%) were observed. A significant increase (38%) in the number of women who had to be referred to colposcopy to detect one case of CIN2+ was shown. The negative predictive value of negative- or low-grade cytology for CIN2+ increased significantly (12%). Sensitivity and specificity, as used by the UK cervical screening programmes, were maintained. **CONCLUSIONS:** The lower incidence of disease in vaccinated women alters the key performance indicators of cervical cytology used to monitor the quality of the screening programme. These findings have implications for screening, colposcopy referral criteria, colposcopy practice and histology reporting.

Bhatia R, Kavanagh K, Cubie HA, Serrano I, Wennington H, Hopkins M, Pan J, Pollock KG, Palmer TJ, Cuschieri K. **Use of HPV testing for cervical screening in vaccinated women-Insights from the SHEVa (Scottish HPV Prevalence in Vaccinated Women) study.** *Int J Cancer.* 2016; 138(12): 2922-31.

The management of cervical disease is changing worldwide as a result of HPV vaccination and the increasing use of HPV testing for cervical screening. However, the impact of vaccination on the performance of HPV based screening strategies is unknown.

The SHEVa (Scottish HPV Prevalence in Vaccinated women) projects are designed to gain insight into the impact of vaccination on the performance of clinically validated HPV assays. Samples collated from women attending for first cervical smear who had been vaccinated as part of a national "catch-up" programme were tested with three clinically validated HPV assays (2 DNA and 1 RNA). Overall HR-HPV and type specific positivity was assessed in total population and according to underlying cytology and compared to a demographically equivalent group of unvaccinated women. HPV prevalence was significantly lower in vaccinated women and was influenced by assay-type, reducing by 23-25% for the DNA based assays and 32% for the RNA assay ($p = 0.0008$). All assays showed over 75% reduction of HPV16 and/or 18 ($p < 0.0001$) whereas the prevalence of non 16/18 HR-HPV was not significantly different in vaccinated vs unvaccinated women. In women with low grade abnormalities, the proportion associated with non 16/18 HR-HPV was significantly higher in vaccinated women ($p < 0.0001$). Clinically validated HPV assays are affected differentially when applied to vaccinated women, dependent on assay chemistry. The increased proportion of non HPV16/18 infections may have implications for clinical performance, consequently, longitudinal studies linking HPV status to disease outcomes in vaccinated women are warranted.

Palmer TJ, McFadden M, Pollock KG, Kavanagh K, Cuschieri K, Cruickshank M, Nicoll S, Robertson C. **HPV immunisation and increased uptake of cervical screening in Scottish women; observational study of routinely collected national data.** *Br J Cancer.* 2016; 114(5): 576-81.

BACKGROUND: To measure the uptake of first invitation to cervical screening by vaccine status in a population-based cohort offered HPV immunisation in a national catch-up campaign. **METHODS:** A retrospective observational study of routinely collected data from the Scottish Cervical Screening Programme. Data were extracted and linked from the Scottish Cervical Call Recall System, the Scottish Population Register and the Scottish Index of Multiple Deprivation. Records from 201 023 women born between 1 January 1988 and 30 September 1993 were assessed. Women born in or after 1990 were eligible for the national catch-up programme of HPV immunisation. Attendance for screening was within 12 months of the first invitation at age 20 years. **RESULTS:** There was a significant decline in overall attendance from the 1988 cohort to the 1993 cohort with the adjusted attendance ratio of the 1988 cohort being 1.49 times (95% CI 1.46-1.52) that of the 1993 cohort. Immunisation compensated for this decrease in uptake with unvaccinated individuals having a reduced ratio of attendance compared with those fully vaccinated (RR=0.65, 95% CI 0.64-0.65). Not taking up the opportunity for HPV immunisation was associated with an attendance for screening below the trend line for all women before the availability of HPV immunisation. **CONCLUSIONS:** HPV immunisation is not associated with the reduced attendance for screening that had been feared. Immunised women in the catch-up cohorts appear to be more motivated to attend than unimmunised women, but this may be a result of a greater awareness of health issues. These results, while reassuring, may not be reproduced in routinely immunised women. Continued monitoring of attendance for the first smear and subsequent routine smears is needed.

Cameron RL, Ahmed S, Pollock KG. **Adverse event monitoring of the human papillomavirus vaccines in Scotland.** *Intern Med J.* 2016; 46(4): 452-7.

AIM: In Scotland, we utilised hospital admissions data to assess the impact of the HPV immunisation programme on the incidence of 60 diagnoses between 2004 and 2014 in both girls and boys; with boys acting as a comparator group. **METHODS:** Tabular and graphical outputs of the number of admissions, the incidence and the incidence ratio of 59 diagnoses were created to assess trends before and after the introduction of the HPV vaccine. Data linkage was utilised to investigate further the increase in Bell palsy diagnoses. **RESULTS:** Fifty-four diagnoses showed no change in incidence following the introduction of the national immunisation programme, and while small increases in incidence were observed for Bell palsy, coeliac disease, ovarian dysfunction, juvenile onset of type 1 diabetes, demyelinating disease and juvenile rheumatoid arthritis, none was statistically significant. **CONCLUSIONS:** Consistent with previous evidence, we present disaggregate data that reiterate the safety of both HPV vaccines.

Cameron RL, Kavanagh K, Pan J, Love J, Cuschieri K, Robertson C, Ahmed S, Palmer T, Pollock KG. **Human Papillomavirus Prevalence and Herd Immunity after Introduction of Vaccination Program, Scotland, 2009-2013.** *Emerg Infect Dis.* 2016; 22(1): 56-64.

In 2008, a national human papillomavirus (HPV) immunization program using a bivalent vaccine against HPV types 16 and 18 was implemented in Scotland along with a national surveillance program designed to determine the longitudinal effects of vaccination on HPV infection at the population level. Each year during 2009-2013, the surveillance program conducted HPV testing on a proportion of liquid-based cytology samples from women undergoing their first cervical screening test for precancerous cervical disease. By linking vaccination, cervical screening, and HPV testing data, over the study period we found a decline in HPV types 16 and 18, significant decreases in HPV types 31, 33, and 45 (suggesting cross-protection), and a nonsignificant increase in HPV 51. In addition, among nonvaccinated women, HPV types 16 and 18 infections were significantly lower in 2013 than in 2009. Our results preliminarily indicate herd immunity and sustained effectiveness of the bivalent vaccine on virologic outcomes at the population level.

Hanley SJ, Pollock KG, Cuschieri K. **Peripheral Sympathetic Nerve Dysfunction in Adolescent Japanese Girls Following Immunization with the Human Papillomavirus Vaccine.** Intern Med. 2015; 54(15): 1953.

No abstract available.

Drolet M, Bénard É, Boily MC, Ali H, Baandrup L, Bauer H, Beddows S, Brisson J, Brotherton JM, Cummings T, Donovan B, Fairley CK, Flagg EW, Johnson AM, Kahn JA, Kavanagh K, Kjaer SK, Kliwer EV, Lemieux-Mellouki P, Markowitz L, Mboup A, Mesher D, Niccolai L, Oliphant J, Pollock KG, Soldan K, Sonnenberg P, Tabrizi SN, Tanton C, Brisson M. **Population-level impact and herd effects following human papillomavirus vaccination programmes: a systematic review and meta-analysis.** Lancet Infect Dis. 2015; 15(5): 565-80. Review.

BACKGROUND: Human papillomavirus (HPV) vaccination programmes were first implemented in several countries worldwide in 2007. We did a systematic review and meta-analysis to assess the population-level consequences and herd effects after female HPV vaccination programmes, to verify whether or not the high efficacy reported in randomised controlled clinical trials are materialising in real-world situations. **METHODS:** We searched the Medline and Embase databases (between Jan 1, 2007 and Feb 28, 2014) and conference abstracts for time-trend studies that analysed changes, between the pre-vaccination and post-vaccination periods, in the incidence or prevalence of at least one HPV-related endpoint: HPV infection, anogenital warts, and high-grade cervical lesions. We used random-effects models to derive pooled relative risk (RR) estimates. We stratified all analyses by age and sex. We did subgroup analyses by comparing studies according to vaccine type, vaccination coverage, and years since implementation of the vaccination programme. We assessed heterogeneity across studies using I^2 and χ^2 statistics and we did trends analysis to examine the dose-response association between HPV vaccination coverage and each study effect measure. **FINDINGS:** We identified 20 eligible studies, which were all undertaken in nine high-income countries and represent more than 140 million person-years of follow-up. In countries with female vaccination coverage of at least 50%, HPV type 16 and 18 infections decreased significantly between the pre-vaccination and post-vaccination periods by 68% (RR 0.32, 95% CI 0.19-0.52) and anogenital warts decreased significantly by 61% (0.39, 0.22-0.71) in girls 13-19 years of age. Significant reductions were also recorded in HPV types 31, 33, and 45 in this age group of girls (RR 0.72, 95% CI 0.54-0.96), which suggests cross-protection. Additionally, significant reductions in anogenital warts were also reported in boys younger than 20 years of age (0.66 [95% CI 0.47-0.91]) and in women 20-39 years of age (0.68 [95% CI 0.51-0.89]), which suggests herd effects. In countries with female vaccination coverage lower than 50%, significant reductions in HPV types 16 and 18 infection (RR 0.50, 95% CI 0.34-0.74) and in anogenital warts (0.86 [95% CI 0.79-0.94]) occurred in girls younger than 20 years of age, with no indication of cross-protection or herd effects. **INTERPRETATION:** Our results are promising for the long-term population-level effects of HPV vaccination programmes. However, continued monitoring is essential to identify any signals of potential waning efficacy or type-replacement.

King E, Ottensmeier C, Pollock KG. **Novel Approaches for Vaccination Against HPV-Induced Cancers.** *Curr Top Microbiol Immunol.* 2015.

To date, more than 5 % of all cancers are as a result of human papillomavirus (HPV) infection, and this incidence is increasing. Early recognition of disease is associated with good survival, but late presentation results in devastating consequences. Prevention is better than cure, and there are now successful prophylactic vaccination programmes in place. We discuss these and the prospect of therapeutic vaccinations in the near future to address a growing need for improved therapeutic options.

Meshor D, Cuschieri K, Hibbitts S, Jamison J, Sargent A, Pollock KG, Powell N, Wilson R, McCall F, Fiander A, Soldan K. **Type-specific HPV prevalence in invasive cervical cancer in the UK prior to national HPV immunisation programme: baseline for monitoring the effects of immunisation.** *J Clin Pathol.* 2015; 68(2): 135-40.

AIMS: To establish the human papillomavirus (HPV) type-specific prevalence in cervical cancer and high-grade cervical lesions in the UK prior to the introduction of national HPV vaccination. **METHODS:** Specimens of cervical cancer (n=1235) and cervical intraepithelial neoplasia (CIN)3 (n=2268) were tested for HPV genotypes in England, Scotland, Wales and Northern Ireland. Data were pooled and weighted estimates presented. **RESULTS:** Among cervical cancer cases, 95.8% were positive for at least one high-risk (HR) HPV type. Restricting to those with HR HPV, the proportion positive for HPV16 and/or HPV18 was similar across countries (weighted overall prevalence 83.0%). This proportion decreased with increasing age at diagnosis (p=0.0005). HPV31, HPV33, HPV45, HPV52 and/or HPV58 were detected in 16.1% of HR HPV-positive cervical cancers and there was no significant association with age for these types. For HR HPV-positive CIN3 cases, there was a similar age-specific pattern with the highest positivity of HPV16 and/or HPV18 in the youngest age group (77.2%). The proportion of HR HPV CIN3 cases positive for HPV31, HPV33, HPV45, HPV52 and/or HPV58 was 36.3% in those aged <30 years at diagnosis. **CONCLUSIONS:** The prevalence of HPV 16 and/or 18 was high in all UK countries and highest in those diagnosed at a younger age. The UK is well placed to monitor the impact of HPV vaccination on type-specific HPV prevalence in cervical disease.

Geert Top, Agentschap Zorg en Gezondheid (Belgium)

Pamela Wakewich, Lakehead University (Canada)

(Based on publications list on [Lakehead University website](#))

Sameshima P, Wakewich P, Slingerland, D., Morriseau, K. and Zehbe I. **Growing Well-being through Community Participatory Arts: A Canadian Anishinaabek First Nations Women Cervical Cancer Screening Study**, In G. Barton and M. Baguley, eds. *The Palgrave Handbook of Global Arts Education* (in press). *Palgrave Macmillan*.

This paper describes the successful use of wool felting to enhance cervical cancer screening education for Canadian Indigenous women. The Anishinaabek Cervical Cancer Screening Study (ACCSS) is a large mixed-methods study being conducted by a multi-disciplinary team in collaboration with ten Robinson-Superior Treaty First Nations communities in northwest Ontario, Canada, to address and ultimately improve cervical cancer screening in First Nations women. Despite significant decrease in cervical cancer deaths since the introduction of the Pap(anicolaou) test, Indigenous women in Canada have 2 to 20 times the risk of contracting cervical cancer. This chapter shares the research tenets underpinning this arts integrated work, the outcomes of needle felting in a pilot focus group, and an artist-researcher's learnings in creating the art pieces "Growing Wellbeing" in conjunction with this research project.

Moeller, H, Dowsley, M., Wakewich, P., Burnett, K., Bishop, L. and Churchill, M.E. **A Qualitative Assessment of Factors in the Uptake of Midwifery of Diverse Populations in Thunder Bay, Ontario**. *Canadian Journal of Midwifery Research and Practice - Revue Canadienne de la Recherche et de la Pratique Sage-femme*. 2015; 14(3):14-20.

Maar, M., P. Wakewich, B. Wood, A. Severini, J. Little, A. N. Burchell, G. Ogilvie and I. Zehbe. **Strategies for Increasing Cervical Cancer Screening Amongst First Nations Communities in Northwest Ontario, Canada**. *Health Care Women Int*. 2016; 37(4): 478-495.

The high burden of cervical cancer in Indigenous populations worldwide is due to underscreening and inadequate follow-up. Using qualitative, participatory action research, we interviewed health care staff to identify ways to increase screening recruitment in First Nations communities in Northwest Ontario, Canada. Our findings suggest the value of a multilevel social-ecological model to promote behavioral changes at the community, health care service and stakeholder, and decision-maker level. Participants emphasized the central role of First Nations women as nurturers of life and for the well-being of their family members. They stressed the importance of building awareness and motivation for cervical cancer screening through various activities including continuous education, hosting screening events specifically for women, improving the attitude and service of health care providers, and promoting screening tools and policies that complement and are respectful of First Nations women.

Wakewich, P., Wood, B., Davey, C., Laframboise, A., Zehbe, I. and on behalf of the ACCSS group. **Colonial legacy and the experience of First Nations women in cervical cancer screening: a Canadian multi-community study**. *Critical Public Health*. 2015; DOI: 10.1080/09581596.2015.1067671.

Regular Papanicolaou (Pap) screening has dramatically reduced cervical cancer incidence in Canada since the 1950s. However, Indigenous women's rates of cervical cancer remain disproportionately high, a factor which is not acknowledged in national media or in educational materials reporting Canada's new cervical cancer screening guidelines. Here, we present findings from a cervical cancer screening initiative in Northwestern Ontario. Based on participatory action research, we worked with 10 First Nations communities in the Robinson Superior Treaty area to increase awareness of cervical cancer risk, develop culturally sensitive tools for screening and education and test the efficacy of human

papillomavirus (HPV) self-sampling as an alternative to Pap cytology. We conducted 16 interviews with health care professionals and 9 focus groups with 69 women from the communities. A central theme for both health care providers (HCPs) and community members was the colonial legacy and its influence on women's experiences of cervical cancer screening. This was evidenced by a strong sense of body shyness, including shame related to sexuality and sexually transmitted infections, concerns about confidentiality in clinical encounters and distrust or caution around HCPs. Reaffirming women's traditional caregiving and educational roles, enhancing mother and daughter communication, improving cultural sensitivity in health care and education and adoption of HPV self-sampling to increase women's privacy and control of the cervical cancer screening experience were endorsed. We argue that education and screening initiatives must reflect the cultural preferences of Indigenous women, empowering them to take control of their experiences of health and body in cervical cancer screening.

Zehbe, I., Wood, B., Wakewich, P., Maar, M., Escott, N., Jumah, N., Little, J. and on behalf of the ACCSS group. **Teaching tools to engage Anishinaabek First Nations women in cervical cancer screening: report of an educational workshop.** Health Education Journal. 2015; 1-12. DOI: 10.1177/0017896915580446.

OBJECTIVE: To explore educational strategies for engaging First Nations women in Canada to attend cervical cancer screening. **DESIGN:** Within a participatory action research framework, semi-structured interviews with health-care providers in First Nations communities revealed that education about the value of screening is perceived as being a key factor to promote cervical cancer screening. **SETTING:** To obtain feedback from workshop informants, a 1-day educational workshop was held to identify appropriate educational intervention strategies, which would be applied in a forthcoming randomised controlled cervical screening trial. **METHODS:** Common discussion and discussion groups, which were facilitated by a First Nations workshop moderator and a note taker. **RESULTS:** This workshop helped to strengthen the ethical space dialogue with the First Nations communities with whom the study team had established research partnerships. The workshop atmosphere was relaxed and the invited informants decided that an educational health promotion event for community women needed to be held prior to inviting them to the cervical screening trial. Such an event would provide an opportunity to communicate the importance of attending regular cervical screening allowing women to make informed decisions about screening participation. Complementary promotional items, including an eye-catching pamphlet and storytelling, were also suggested. **CONCLUSION:** The key messages from the events and promotional items can help to de-stigmatise women who develop a type of cancer that is caused by a sexually transmitted virus that affects both men and women. Developing and implementing positive health education that respectfully depicts female bodies, sexuality and health behaviours through a First Nations lens is strongly warranted.

Scott Wittet, PATH (US)

Progress in Cervical Cancer Prevention: The CCA Report Card 2015

http://www.cervicalcanceraction.org/pubs/CCA_reportcard_low-res_2015.pdf

Over the past decade, the world has seen extraordinary advances in cervical cancer prevention. Until recently, the knowledge and tools needed to effectively tackle the disease in low-resource settings had not been developed or validated. Today, following extraordinary scientific breakthroughs, strategic field research, and tireless efforts by governments and their partners, a new reality is emerging. We now have the knowledge and tools to bring cervical cancer prevention to every country and to dramatically scale interventions that are proven to save women's lives. Ramping up global commitment to cervical cancer prevention is critical to achieve current and emerging global health and development targets and the reduction of NCDs worldwide. Cervical cancer prevention should be a core component of an integrated approach to protecting women, children, and adolescents throughout the life-course. We must support the integration of vaccination, screening, and preventive treatment into school health, women's health, and HIV/ AIDS prevention and treatment programs. It is time for international agencies, governments, and donors to step up their efforts to support national initiatives. Engagement in cervical cancer prevention could result in one of the most significant "easy wins" in global public health today. By working to improve and scale current prevention programs, we have the unique opportunity to strengthen health systems and expand equity

Investing in Cervical Cancer Prevention 2015–2020: Meeting report, London, November 3 & 4, 2015

http://www.cervicalcanceraction.org/pubs/CCA_london_meeting_report_2015.pdf

No abstract available

Cervical Cancer Prevention: Practical Experience from PATH

<http://www.rho.org/HPV-practical-experience.htm>

From 2006 to 2011, PATH conducted demonstration projects in four low- to middle-income countries—India, Peru, Uganda, and Vietnam—to provide evidence for decision-making about public-sector introduction of human papillomavirus (HPV) vaccines. The Cervical Cancer Prevention: Practical Experience Series summarizes lessons learned from these projects that can help guide future cervical cancer prevention program planning, especially in low-resource settings around the globe.

HPV Vaccine Lessons Learnt

<http://www.rho.org/HPVlessons/>

To aid decision-makers interested in HPV vaccine introduction or scale-up, in 2014–2015 the [London School of Hygiene & Tropical Medicine](#) and [PATH](#) conducted the first comprehensive review of HPV vaccine delivery experiences across 37 low- and middle-income countries. These experiences have helped countries learn valuable lessons about effective methods for garnering parental acceptance and reaching young adolescent girls with the vaccine, at relatively low delivery costs. The lessons learnt from these countries can provide critical information for policymakers and programme planners on how best to prepare, deliver, and sustain HPV vaccines. Highlights include key findings and lessons from HPV vaccination experience across five themes: preparation, communications, delivery, achievements, and sustainability. Also addressed are the value of demonstration projects and potential HPV vaccination pitfalls.

Reducing cervical cancer inequities worldwide

http://www.rho.org/files/PATH_Cervical_cancer_inequities_2015.pdf

Joanne Yarwood, National Infection Service, Public Health England

(Based on a pubmed search & Research gate)

Noakes, K., J. Yarwood and D. Salisbury. **Parental response to the introduction of a vaccine against human papilloma virus.** *Hum Vaccin.* 2016; 2(6): 243-248.

The introduction of a vaccine against human papillomavirus (HPV), a sexually transmitted virus that is the causal factor of at least 95% of invasive cervical cancer, could significantly reduce the number of cases of cervical cancer occurring in the UK each year. To ensure that individuals are protected before onset of sexual activity, it is likely that the vaccine will be offered to children around 10 years of age. It is important that parents' attitudes to HPV vaccination are taken into account, particularly as the subject relates to sexual health issues. In order to gauge parents' initial responses to the addition of HPV vaccine to the immunisation programme and identify the issues needing further research, in-depth interviews were held with parents of girls and boys aged 8-10 years. Our results show that most parents have not heard of HPV and were not aware of the role of HPV in cervical cancer. There were concerns about offering a vaccine that protects against a sexually transmitted infection to children and that the vaccine should be offered at an older age in conjunction with a sex education program. In order to avoid rejection of this vaccine, work needs to take place now to raise awareness of HPV as a cause of cervical cancer prior to any introduction of the vaccination program.

Stefanoff, P., S. E. Mamelund, M. Robinson, E. Netterlid, J. Tuells, M. A. Bergsaker, H. Heijbel and J. Yarwood. **Tracking parental attitudes on vaccination across European countries: The Vaccine Safety, Attitudes, Training and Communication Project (VACSATC).** *Vaccine.* 2010; 28(35): 5731-5737.

The paper presents the first results from the European project VACSATC which aimed to track parental attitudes on vaccinations across several European countries. We compared five cross-sectional surveys of parents with children less than 3 years of age in England, Norway, Poland, Spain and Sweden carried out during 2008-2009. Data were collected from 6611 respondents. Two countries used face-to face interviews, one used telephone interviews, and two other countries used mail-in questionnaires. In all countries health professionals were indicated as the most important and trusted source of information on vaccination. The study results also show that parental attitudes on vaccinations in the childhood vaccination programs are generally positive. However, there were differences in attitudes on vaccination between the five countries, possibly reflecting different methods of sampling the respondents, context-specific differences (e.g. level of activity of governmental agencies), but also individual-level parental variation in demographic and socioeconomic status variables.

Yarwood, J. **Communicating vaccine benefit and risk - lessons from the medical field.** *Vet Microbiol.* 2006; 117(1): 71-74.

The childhood immunisation programme in England aims to achieve and maintain high vaccine coverage so that no child needlessly suffers from a vaccine preventable disease. As part of the programme, parents must have appropriate support from health professionals and have information available to them to make informed decisions about their choices. Even though immunisation is voluntary in England, coverage is generally high. It has been estimated that only 0.33% of parents do not consent to their child being included in a computerised database that schedules immunisation appointments. Parental attitudes, experiences and social grade are influential in determining whether a child receives a vaccine. Personal experience and knowledge of diseases influence parental perceptions about the seriousness of diseases and their likelihood of being affected by it. In societies where immunisation programmes have

been successful, the challenge is maintaining high levels of vaccine coverage. In the absence of disease, the threat of that disease rapidly disappears and anxieties about the vaccine's safety may increase. A fall in vaccine coverage can lead to the return of disease as happened in the UK when rates of pertussis immunisation plummeted in the 1970s. Further perceived threats may also affect vaccine uptake, for example, the MMR controversy dating from 1998. The article outlines the MMR debate in the UK, the communication of risk and benefit and the management of information to the public. It will share lessons learned and examine how they might apply to the veterinary programme.

Yarwood, J., K. Noakes, D. Kennedy, H. Campbell and D. Salisbury. **Tracking mothers attitudes to childhood immunisation 1991-2001**. *Vaccine*. 2005; 23(48-49): 5670-5687.

This report presents the findings from a series of 20 surveys carried out between 1991 and 2001. The main objectives of the research were to: This unique body of more than 15,000 interviews was conducted as part of a routine programme of research supporting the national immunisation programme in England. These surveys show that the public wants clarity, consistency, factual information and openness from those delivering immunisation services.