



HPV vaccination of immunocompromised hosts

S.M. Garland^{a,b,c,*}, J.M.L. Brotherton^{d,e}, A.B. Moscicki^f, A.M. Kaufmann^g, M. Stanley^h,
N. Bhatlaⁱ, R. Sankaranarayanan^j, S. de Sanjosé^k, J.M. Palefsky^l, on behalf of IPVS

^a Department of Microbiology and Infectious Diseases, Royal Women's Hospital, 30 Flemington Road, Parkville 3052, Australia

^b Murdoch Childrens Research Institute, 50 Flemington Road, Parkville 3052, Australia

^c Department of Obstetrics and Gynaecology, University of Melbourne, Parkville 3052, Australia

^d VCS Registries, Victorian Cytology Service, Level 6, 176 Wellington Parade, East Melbourne 3002, Australia

^e School of Population and Global Health, University of Melbourne, Parkville 3052, Australia

^f Department of Pediatrics, David Geffen School of Medicine, University of California, Los Angeles, 10833 Le Conte Ave. MDCC 22-432, MC:175217, Los Angeles, CA 90095, United States

^g Gynäkologische Tumorummunologie, R. 4503 Gynäkologie, Charite-Universitätsmedizin Berlin, Campus Benjamin Franklin, Hindenburgdamm 30, 12200 Berlin, Germany

^h Department of Pathology, Tennis Court Road, Cambridge CB2 1QP, United Kingdom

ⁱ Department of Obstetrics & Gynaecology, All India Institute of Medical Sciences, New Delhi 110029, India

^j Screening Group, Section of Early Detection and Prevention, International Agency for Research on Cancer, World Health Organization, 150 cours Albert Thomas, 69372 Lyon CEDEX 08, France

^k Cancer Epidemiology Research Programme, IDIBELL, CIBERESP, Institut Català d'Oncologia, Av. Gran Via de l'Hospitalet 199-203, 08908 L'Hospitalet de Llobregat, Spain

^l University of California, San Francisco, 513 Parnassus Ave Box 0654, San Francisco, CA 94143, United States

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ABSTRACT

It is well-established that immunocompromised people are at increased risk of HPV-related disease compared with those who are immunocompetent. Prophylactic HPV sub-unit vaccines are safe and immunogenic in immunocompromised people and it is strongly recommended that vaccination occur according to national guidelines. When delivered to immunocompromised populations, HPV vaccines should be given as a 3-dose regimen.

1. Introduction

For the immunocompetent host, there are clear guidelines on the use of prophylactic human papillomavirus [HPV] vaccines (bivalent [2vHPV], quadrivalent [4vHPV] and nonavalent [9vHPV]) available from various international public health authorities, regulatory agencies and societies. These include the World Health Organisation (WHO) [1,2], European Medicines Agency (EMA) [3,4], as well as numerous national advisory committees worldwide, such as the Food and Drug Administration (FDA), US Advisory Committee on Immunisation Practices (ACIP) [5–10] American Society of Clinical Oncology [ASCO], Australian Therapeutic Goods Administration (TGA), Australian Technical Advisory Group on Immunisation [11], National Advisory Committee on Immunisation (NACI) in Canada [12], and International Papillomavirus Society (IPVS) [13]. The

currently licensed vaccines are viral-like-particles, which are subunit, non-replicating, and do not contain any infectious component. There is good evidence that HPV 16 and 18 contribute globally to 70% of cervical cancers [14], 78% of HPV related vulvar cancer [15], 65% of vaginal [16] and 90% of anal cancers in both sexes [17], as well as a geographically variable proportion of oropharyngeal cancers. Hence, the expected reduction in disease is substantial for those vaccinated with the 2vHPV or 4vHPV vaccine when given prior to HPV infection. Moreover, with the new 9vHPV vaccine, the proportion of the cancer burden that is potentially preventable in women rises an incremental amount to approximately 90% [18,19], 92% [15], 86% [16] and 95% [17], respectively, for cervical, vulvar, vaginal and vulvar cancer. These guidelines generally focus attention on vaccination of female preadolescents (target age is country-specific and dependent upon delivery strategy) from 9 to 14 years of age and prior to sexual debut, although

* Corresponding author at: Department of Microbiology and Infectious Diseases, Royal Women's Hospital, 30 Flemington Road, Parkville 3052, Australia.

E-mail addresses: Suzanne.Garland@thewomens.org.au (S.M. Garland), jbrother@vcs.org.au (J.M.L. Brotherton), AMoscicki@mednet.ucla.edu (A.B. Moscicki), Andreas.Kaufmann@charite.de (A.M. Kaufmann), mas1001@cam.ac.uk (M. Stanley), neerja.bhatla07@gmail.com (N. Bhatla), sankar@iarc.fr (R. Sankaranarayanan), desanjose.silvia@gmail.com (S. de Sanjosé), joel.palefsky@ucsf.edu (J.M. Palefsky).

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some have included a catch-up period up to 26 years of age. In some countries, there is a gender-neutral approach including boys. Based on immunogenicity data, and following endorsement from the WHO in 2014, a two-dose regimen is now recommended in many countries for immunocompetent individuals aged under 15 years at receipt of the first vaccine dose, with a dose interval of at least 6 months. Those who are 15 years or older at first dose, or those who are immunocompromised, require the standard three-dose vaccination schedule [1].

Guidelines for HPV vaccination of the immunocompromised host are provided in some countries by specialist immunisation advisory groups or societies [20–24]. In many countries immunisation for these groups is recommended, regardless of age, but not nationally funded. In this position statement, we outline the rationale for ensuring that clinicians, patients and policy makers explicitly consider the potential role of HPV vaccination in immunocompromised individuals.

2. Immunocompromised hosts

Immunocompromised hosts include those with infections affecting immune competency such as human immunodeficiency virus (HIV), and those on immunosuppressive and/or immunomodulatory treatment for autoimmune conditions (e.g. multiple sclerosis, inflammatory bowel disease, systemic lupus erythematosus (SLE)), or for prevention of graft rejection among those who are post-transplantation.

It has been well documented that HIV-positive women, have an overall higher prevalence of HPV DNA two or threefold higher than HIV negative women [25] (60–70%), have a higher prevalence of high-risk-HPV DNA (20–35%) [26], types that are known to cause cancer, more likely to have multiple HPV types present (35–50%) [25], higher HPV viral loads (45–60%) [25] and persistent HR-HPV infections (45% vs 15%) [25–29]. Notably a lower CD4 count in female patients is strongly associated with cervical and anal high grade squamous intraepithelial lesions (HSIL). There is also a greater risk of vulvar HSIL [30], a 10-fold greater risk of anal cancer [31] and a three to five fold higher risk for cervical SIL, with invasive cervical cancer being an AIDS-defining illness [32–36]. In addition for males and females who are HIV-positive there is a higher risk of HR-HPV anal infection, anal HSIL and anal cancer [37,38]. Although this association is presumably due to impaired ability to clear HPV and increased reactivation of latent infection [39–45], other mechanisms may be involved that result in cellular immune dysfunction [46,47].

Those who are immunocompromised for reasons other than HIV infection are also at increased risk of HPV infection, HSIL and cancer compared with immunocompetent individuals [25–36,39,40,43,45, 48–54]. For example, prior to prophylactic vaccines being available, bone marrow transplantation patients had a higher rate of cervical HSIL than in the age-adjusted general population [48]. Moreover, it was recognised that allogeneic transplant recipients had a higher rate of cervical abnormalities than did patients receiving autologous transplants [48,54]. Higher rates of cervical abnormalities have also been found in studies of women with SLE, rheumatoid arthritis and inflammatory bowel disease when on immunosuppressant medications [43,45].

Individuals who are HIV positive remain at risk for acquiring new HPV infections which likely can be prevented by HPV vaccination. This includes prevention of HR infections that can progress to HSIL. It is to be noted that highly active antiretroviral therapy (HAART) has modest effect or no effect on HPV carriage, clearance or persistence [28] although recent reports suggest a decline in cervical HSIL [55]. Recent studies show that management guidelines for women on HAART with HIV viral suppression, can parallel guidelines for healthy women [56]. Moreover, immunosuppressed patients are also at a higher risk of HSIL due to low risk HPV types [57–59]. In those who are HIV-positive, as all immunosuppressed peoples, there is also greater risk of genital warts being recalcitrant to treatment [30].

2.1. A growing evidence base: HPV vaccine studies in immunocompromised people

The increased risk of HPV infection and associated diseases in immunocompromised men and women warrants a strong emphasis on vaccinating these individuals according to the relevant national guidelines. Individuals who meet these guidelines may be vaccinated while immunocompromised or ideally, prior to the development of immunocompromised status.

The 4vHPV vaccine has been administered to HIV-positive children 7–12 years of age with seroconversion rates greater than 96% [60]. Antibody titres for HPV 6/11/16/18, were 30–50% lower compared with historical age-matched controls, but higher than natural infections and in the range where clinical efficacy is seen in adults [60]. Studies in vertically-acquired HIV-positive adolescents adult men and women show high rates of seroconversion (95–100%), with no adverse effects on CD4 or plasma HIV RNA levels [61–68]. We currently await efficacy data, although 4vHPV vaccine will likely benefit immunocompromised men and women when vaccinated in the recommended age range, despite the lower titres seen in this population.

For the 2vHPV vaccine, similar studies in HIV-positive women demonstrated high seroconversion rates, and sustained positivity for anti-HPV 16 and 18 over 12 months. Although lower antibody titres were seen than in HIV-negative controls, the titres remained well above levels seen following natural infection [69]. As with the 4vHPV vaccine, the 2vHPV vaccine showed no adverse effect on CD4 count over time, nor effect on HIV viral load over time: however these studies have been performed in largely HIV positive subjects enrolled with reasonably high CD4 counts.

Vaccination in other immunocompromised groups, including patients with solid organ transplants and autoimmune disorders have demonstrated lower titres of antibodies in these patients compared with controls. These included patients with juvenile idiopathic arthritis, SLE, juvenile dermatomyositis, and kidney and lung transplant [70–73]. One study noted that titres appeared to differ by type of immunosuppressive drug treatment, with patients on mycophenolate producing lower HPV antibody titres than patients on other drugs [73]. Another study indicated that lung transplant patients had much lower antibodies than other solid organ transplant recipients [70]. However, these studies all showed that the vaccines were safe and consistently found that HPV vaccination was not associated with significant adverse effects and importantly, the clinical course of these diseases were also not affected [73–75].

Given that the recommendation for two dose schedules of HPV vaccines is currently based upon bridging data, showing equivalent immunogenicity in immunocompetent young adolescents as three doses in older persons in whom efficacy has been assessed, there is no current evidence to support equivalence in immunocompromised individuals. Consequently, the recommendations for those who are immunosuppressed or HIV-positive should be for 3 doses, within the recommended age guidelines and as early as possible prior to the onset of immunocompromise. Continued research in this group of vaccine recipients is necessary.

3. Screening remains important

Currently screening remains a critical component of cervical cancer prevention for all women, regardless of HPV vaccination status. Because of their increased risk of cervical HSIL and cervical cancer, risk of disease due to non-vaccine HPV types and the lack of efficacy studies post-vaccination, secondary prevention through screening remains critical for immunocompromised women, regardless of HPV vaccination status. Most countries recommend more frequent screening for these women than for the general population on the basis of their higher risk [76–79]. Studies are in progress to determine whether screening for, and treatment of, anal HSIL is of value in preventing anal cancer in at-risk populations [80–82].

4. Key points

IPVS statement on HPV vaccination and immunocompromised hosts

- Immunocompromised people are at increased risk of HPV-related disease, compared with immunocompetent people.
HPV vaccination is safe in immunocompromised people (e.g., HIV-positive [+] individuals, transplant recipients).
- Current vaccines are simple, non-replicating subunit vaccines and hence, not infectious.
- Given current knowledge, HPV vaccines will likely benefit immunocompromised men and women, especially when vaccinated in the recommended age range.
- It is ideal to vaccinate everyone according to national guidelines, before people become immunocompromised.
- For those who are immunocompromised at the time of vaccination, 3 doses are currently recommended.
- Antibody titres in response to vaccination are often lower than those in immunocompetent people, but the clinical relevance of this is yet unknown. Efficacy data following vaccination in immunocompromised people are very limited to date.
- Vaccines that have broad coverage or cross-coverage should be encouraged for HIV (+) men and women given growing evidence that the distribution of HPV types in cancers may be broader than that seen in the immunocompetent population.
- Cervical cancer screening remains an important public health complement to HPV vaccination for the prevention of cervical cancer.

References

- [1] World Health Organisation Meeting of the Strategic Advisory Group of Experts on Immunisation April 2014 – Conclusions and Recommendations. *Weekly Epidemiological Record*, 21(89), 2014, pp. 221–236.
- [2] Human Papillomavirus Vaccines: WHO Position Paper, October 2014. *Weekly Epidemiological Record*, 89(43), 2014, pp. 456–492.
- [3] EPAR Summary for the Public Gardasil 9 (http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/003852/WC500189114.pdf).
- [4] European Medicines Agency 21 November 2013 EMA/789820/2013 Committee for Medicinal Products for Human Use (CHMP) Assessment Report Cervarix (http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Assessment_Report_-_Variation/human/000721/WC500160885.pdf).
- [5] Centers for Disease Control Prevention, FDA licensure of bivalent human papillomavirus vaccine (HPV2, Cervarix) for use in females and updated HPV vaccination recommendations from the Advisory Committee on Immunization Practices (ACIP), *MMWR Morb. Mortal. Wkly. Rep.* 59 (20) (2010) 626.
- [6] LE Markowitz, EF Dunne, M Saraiya, HW Lawson, H Chesson, ER Unger, Centers for Disease C, Prevention, Advisory Committee on Immunization P: Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity & Mortality Weekly Report Recommendations & Reports*, 2007, 56(RR-2), pp. 1–24.
- [7] L.E. Markowitz, E.F. Dunne, M. Saraiya, H.W. Chesson, C. Robinette Curtis, J. Gee, J.A. Bocchini Jr., E.R. Unger, Human papillomavirus vaccination recommendations of the Advisory Committee on Immunisation Practices (ACIP), *Cent. Dis. Control Prev. MMWR* 63 (5) (2014) 1–30.
- [8] Centers for Disease Control and Prevention Recommendations on the Use of Quadrivalent Human Papillomavirus Vaccine in Males – Advisory Committee on Immunisation Practices (ACIP), *Morbidity and Mortality Weekly Report*, 2011, 60(50), pp. 1705–1708.
- [9] E. Petrosky, J.A. Bocchini Jr., S. Hariri, H. Chesson, C.R. Curtis, M. Saraiya, E.R. Unger, L.E. Markowitz, Control CfD, prevention: use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the advisory committee on immunization practices, *MMWR Morb. Mortal. Wkly. Rep.* 64 (11) (2015) 300–304.
- [10] ACIP Recommends Two-dose Regimen for HPV Vaccines. (<http://www.aafp.org/news/health-of-the-public/20161026acipoctmtg.html>).
- [11] The Australian Immunisation Handbook 10th edition. (<http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/handbook10-home>).
- [12] An Advisory Committee Statement (ACS) National Advisory Committee on Immunisation (NACI), Update on the recommended Human Papillomavirus (HPV) vaccine immunisation schedule. (http://www.phac-aspc.gc.ca/naci-ccni/acs-dcc-2015/hpv-vph_0215-eng.php).
- [13] S.M. Garland, M. Stanley, J. Brotherton, A.B. Moscicki, N. Bhatla, A.M. Kaufmann, R. Sankaranarayanan, IPVS PJobo: IPVS policy statement on safety of HPV vaccines, *Papillomavirus Res.* 2 (2016) 9–10.
- [14] D. Forman, C. de Martel, C.J. Lacey, I. Soerjomataram, J. Lortet-Tieulent, L. Bruni, J. Vignat, J. Ferlay, F. Bray, M. Plummer, Global burden of human papillomavirus and related diseases, *Vaccine* 30 (2012) F12–F23.
- [15] S. de Sanjosé, L. Alemany, J. Ordi, S. Tous, M. Alejo, S.M. Bigby, E.A. Joura, P. Maldonado, J. Laco, I.G. Bravo, Worldwide human papillomavirus genotype attribution in over 2000 cases of intraepithelial and invasive lesions of the vulva, *Eur. J. Cancer* 49 (16) (2013) 3450–3461.
- [16] L. Alemany, M. Saunier, L. Tinoco, B. Quirós, I. Alvarado-Cabrero, M. Alejo, E. Joura, P. Maldonado, J. Klaustermeier, J. Salmerón, Large contribution of human papillomavirus in vaginal neoplastic lesions: a worldwide study in 597 samples, *Eur. J. Cancer* 50 (16) (2014) 2846–2854.
- [17] L. Alemany, M. Saunier, I. Alvarado-Cabrero, B. Quirós, J. Salmeron, H.R. Shin, E.C. Pirog, N. Guimerà, G. Hernandez-Suarez, A. Felix, Human papillomavirus DNA prevalence and type distribution in anal carcinomas worldwide, *Int. J. Cancer* 136 (1) (2015) 98–107.
- [18] E.A. Joura, A.R. Giuliano, O.-E. Iversen, C. Bouchard, C. Mao, J. Mehlsen, E.D. Moreira Jr., Y. Ngan, L.K. Petersen, E. Lazcano-Ponce, A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women, *N. Engl. J. Med.* 372 (8) (2015) 711–723.
- [19] B. Serrano, L. Alemany, S. Tous, L. Bruni, G.M. Clifford, T. Weiss, F.X. Bosch, S. de Sanjosé, Potential impact of a nine-valent vaccine in human papillomavirus related cervical disease, *Infect. Agents Cancer* 7 (1) (2012) 1.
- [20] Human Papillomavirus (HPV) ACIP Vaccine Recommendations. (<https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hpv.html>).
- [21] Human Papillomavirus (HPV): The Green Book, Chapter 18a. (<https://www.gov.uk/government/publications/human-papillomavirus-hpv-the-green-book-chapter-18a>).
- [22] L.G. Rubin, M.J. Levin, P. Ljungman, E.G. Davies, R. Avery, M. Tomblyn, A. Bousvaros, S. Dhanireddy, L. Sung, H. Keyserling, 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host, *Clin. Infect. Dis.* (2013) (cit684).
- [23] J.L. Klosky, H.L. Gamble, S.L. Spunt, M.E. Randolph, D.M. Green, M.M. Hudson, Human papillomavirus vaccination in survivors of childhood cancer, *Cancer* 115 (24) (2009) 5627–5636.
- [24] Cancer Immunisation Guideline: Chemotherapy and Post Hematopoietic Stem Cell Transplant. (<http://www.mvec.vic.edu.au/immunisation-references/cancer-immunisation-guideline-chemotherapy-and-post-hematopoietic-stem-cell-transplant/>).
- [25] D.J. Jamieson, A. Duerr, R. Burk, R.S. Klein, P. Paramsothy, P. Schuman, S. Cu-Uvin, K. Shah, Group HERSCharacterization of genital human papillomavirus infection in women who have or who are at risk of having HIV infection, *Am. J. Obstet. Gynecol.* 186 (1) (2002) 21–27.
- [26] J.M. Palefsky, H. Minkoff, L.A. Kalish, A. Levine, H.S. Sacks, P. Garcia, M. Young, S. Melnick, P. Miotti, R. Burk, Cervicovaginal human papillomavirus infection in human immunodeficiency virus-1 (HIV)-positive and high-risk HIV-negative women, *J. Natl. Cancer Inst.* 91 (3) (1999) 226–236.
- [27] L. Ahdieh, R.S. Klein, R. Burk, S. Cu-Uvin, P. Schuman, A. Duerr, M. Safaiean, J. Astemborski, R. Daniel, K. Shah, Prevalence, incidence, and type-specific persistence of human papillomavirus in human immunodeficiency virus (HIV)-positive and HIV-negative women, *J. Infect. Dis.* 184 (6) (2001) 682–690.
- [28] S. Shrestha, S.L. Sudenga, J.S. Smith, L.H. Bachmann, C.M. Wilson, M.C. Kempf, The impact of highly active antiretroviral therapy on prevalence and incidence of cervical human papillomavirus infections in HIV-positive adolescents, *BMC Infect. Dis.* 10 (1) (2010) 1.
- [29] I. Heard, J.-M. Tassie, V. Schmitz, L. Mandelbrot, M.D. Kazatchkine, G. Orth, Increased risk of cervical disease among human immunodeficiency virus-infected women with severe immunosuppression and high human papillomavirus load, *Obstet. Gynecol.* 96 (3) (2000) 403–409.
- [30] L.J. Conley, T.V. Ellerbrock, T.J. Bush, M.A. Chiasson, D. Sawo, T.C. Wright, HIV-1 infection and risk of vulvovaginal and perianal condylomata acuminata and intraepithelial neoplasia: a prospective cohort study, *Lancet* 359 (9301) (2002) 108–113.
- [31] M. Frisch, R.J. Biggar, J.J. Goedert, Group ACMRSHuman papillomavirus-associated cancers in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome, *J. Natl. Cancer Inst.* 92 (18) (2000) 1500–1510.
- [32] P. Schuman, S.E. Ohmit, R.S. Klein, A. Duerr, S. Cu-Uvin, D.J. Jamieson, J. Anderson, K.V. Shah, Longitudinal study of cervical squamous intraepithelial lesions in human immunodeficiency virus (HIV)-seropositive and at-risk HIV-seronegative women, *J. Infect. Dis.* 188 (1) (2003) 128–136.
- [33] A. Duerr, B. Kieke, D. Warren, K. Shah, R. Burk, J.F. Peipert, P. Schuman, R.S. Klein, Human papillomavirus-associated cervical cytologic abnormalities among women with or at risk of infection with human immunodeficiency virus, *Am. J. Obstet. Gynecol.* 184 (4) (2001) 584–590.
- [34] L.S. Massad, E.C. Seaberg, D.H. Watts, H. Minkoff, A.M. Levine, D. Henry, C. Colie, T.M. Darragh, N.A. Hessol, Long-term incidence of cervical cancer in women with human immunodeficiency virus, *Cancer* 115 (3) (2009) 524–530.
- [35] C. Six, I. Heard, C. Bergeron, G. Orth, J.-D. Poveda, P. Zagury, P. Cesbron, C. Crenn-Hébert, R. Pradinaud, M. Sobesky, Comparative prevalence, incidence and short-term prognosis of cervical squamous intraepithelial lesions amongst HIV-positive and HIV-negative women, *AIDS* 12 (9) (1998) 1047–1056.
- [36] T.C. Wright, T.V. Ellerbrock, M.A. Chiasson, N. Van Devanter, X.-W. Sun, Cervical intraepithelial neoplasia in women infected with human immunodeficiency virus: prevalence, risk factors, and validity of Papanicolaou smears, *Obstet. Gynecol.* 84

- (4, Part1) (1994) 591–597.
- [37] J.M. Palefsky, E.A. Holly, C.J. Hogeboom, M.L. Ralston, M.M. DaCosta, R. Botts, J.M. Berry, N. Jay, T.M. Darragh, Virologic, immunologic, and clinical parameters in the incidence and progression of anal squamous intraepithelial lesions in HIV-positive and HIV-negative homosexual men, *J. Acquir. Immune Defic. Syndr.* 17 (4) (1998) 314–319.
- [38] D.A. Machalek, M. Poynten, F. Jin, C.K. Fairley, A. Farnsworth, S.M. Garland, R.J. Hillman, K. Petoumenos, J. Roberts, S.N. Tabrizi, et al., Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis, *Lancet Oncol.* 13 (5) (2012) 487–500.
- [39] N.M. Reusser, C. Downing, J. Guidry, S.K. Tyring, HPV carcinomas in immunocompromised patients, *J. Clin. Med.* 4 (2) (2015) 260–281.
- [40] W. Likes, J.T. Santoso, J. Wan, A cross-sectional analysis of lower genital tract intraepithelial neoplasia in immune-compromised women with an abnormal Pap, *Arch. Gynecol. Obstet.* 287 (4) (2013) 743–747.
- [41] I.H.R. Grein, N. Groot, M.I. Lacerda, N. Wulffraat, G. Pileggi, HPV infection and vaccination in Systemic Lupus Erythematosus patients: what we really should know, *Pediatr. Rheumatol.* 14 (1) (2016) 12.
- [42] E. Zard, L. Arnaud, A. Mathian, Z. Chakhtoura, M. Hie, P. Touraine, I. Heard, Z. Amoura, Increased risk of high grade cervical squamous intraepithelial lesions in systemic lupus erythematosus: a meta-analysis of the literature, *Autoimmun. Rev.* 13 (7) (2014) 730–735.
- [43] M. Cottone, S. Renna, IBD: incidence of HSV and HPV with azathioprine, *Nat. Rev. Gastroenterol. Hepatol.* 6 (8) (2009) 444–445.
- [44] C.H. Feldman, J. Liu, S. Feldman, D.H. Solomon, S.C. Kim, Risk of high-grade cervical dysplasia and cervical cancer in women with systemic lupus erythematosus receiving immunosuppressive drugs, *Lupus* (2016) (0961203316672928).
- [45] S.C. Kim, R.J. Glynn, E. Giovannucci, S. Hernández-Díaz, J. Liu, S. Feldman, E.W. Karlson, S. Schneeweiss, D.H. Solomon, Risk of high-grade cervical dysplasia and cervical cancer in women with systemic inflammatory diseases: a population-based cohort study, *Ann. Rheum. Dis.* 74 (7) (2015) 1360–1367.
- [46] L.E. Bennetts, M. Wagner, A.R. Giuliano, J.M. Palefsky, M. Steben, T.W. Weiss, Associations of anogenital low-risk human papillomavirus infection with cancer and acquisition of HIV, *Sex. Transm. Dis.* 42 (10) (2015) 541–544.
- [47] K.K. Smith-McCune, S. Shiboski, M.Z. Chirenje, T. Magure, J. Tuveson, Y. Ma, M. Da Costa, A.-B. Moscicki, J.M. Palefsky, R. Makunike-Mutasa, Type-specific cervico-vaginal human papillomavirus infection increases risk of HIV acquisition independent of other sexually transmitted infections, *PLoS One* 5 (4) (2010) e10094.
- [48] J. Sasadeusz, H. Kelly, J. Szer, A. Schwarzer, H. Mitchell, A. Grigg, Post-Transplant Complications—Abnormal cervical cytology in bone marrow transplant recipients, *Bone Marrow Transplant.* 28 (4) (2001) 393–398.
- [49] C.K. Fairley, S. Chen, S.N. Tabrizi, J. McNeil, G. Becker, R. Walker, R.C. Atkins, N. Thomson, P. Allan, C. Woodburn, et al., Prevalence of HPV DNA in cervical specimens in women with renal transplants: a comparison with dialysis-dependent patients and patients with renal impairment, *Nephrol. Dial. Transplant.* 9 (4) (1994) 416–420.
- [50] C.K. Fairley, S. Chen, S.N. Tabrizi, R. Walker, R.C. Atkins, S.M. Garland, Prospective study of HPV DNA in cervical specimens from women with renal transplants, *Nephrol. Dial. Transplant.* 9 (10) (1994) 1520–1521.
- [51] M. Alloub, B. Barr, K. McLaren, I. Smith, M. Bunney, G. Smart, Human papillomavirus infection and cervical intraepithelial neoplasia in women with renal allografts, *Br. Med. J.* 298 (6667) (1989) 153–156.
- [52] R. Halpert, R.G. Fruchter, A. Sedlis, K. Butt, J.G. Boyce, F. Sillman, Human papillomavirus and lower genital neoplasia in renal transplant patients, *Obstet. Gynecol.* 68 (2) (1986) 251–258.
- [53] O. Ogunbiyi, J. Scholefield, A. Raftery, J. Smith, S. Duffy, F. Sharp, K. Rogers, Prevalence of anal human papillomavirus infection and intraepithelial neoplasia in renal allograft recipients, *Br. J. Surg.* 81 (3) (1994) 365–367.
- [54] B.N. Savani, P. Stratton, A. Shenoy, E. Kozanas, S. Goodman, A.J. Barrett, Increased risk of cervical dysplasia in long-term survivors of allogeneic stem cell transplantation; implications for screening and HPV vaccination, *Biol. Blood Marrow Transplant.* 14(9), pp. 1072–1075.
- [55] G.M. Clifford, S. Franceschi, O. Keiser, F. Schöni-Affolter, M. Lise, S. Dehler, F. Levi, M. Mousavi, C. Bouchardy, A. Wolfensberger, Immunodeficiency and the risk of cervical intraepithelial neoplasia 2/3 and cervical cancer: a nested case-control study in the Swiss HIV cohort study, *Int. J. Cancer* 138 (7) (2016) 1732–1740.
- [56] L.S. Massad, X. Xie, G. D'Souza, T.M. Darragh, H. Minkoff, R. Wright, C. Colie, L. Sanchez-Keeland, H.D. Strickler, Incidence of cervical precancers among HIV-seropositive women, *Am. J. Obstet. Gynecol.* 212 (5) (2015) (606.e601–606.e608).
- [57] E. Kwak, K. Julian, Human papillomavirus infection in solid organ transplant recipients, *Am. J. Transplant.* 9 (s4) (2009).
- [58] R.H. Gormley, C. Kovarik, Human papillomavirus-related genital disease in the immunocompromised host, *J. Am. Acad. Dermatol.* 66(6), 867.e861–867.e814.
- [59] A.M. Cornall, J.M. Roberts, S.M. Garland, R.J. Hillman, A.E. Grulich, S.N. Tabrizi, Anal and perianal squamous carcinomas and high-grade intraepithelial lesions exclusively associated with “low-risk” HPV genotypes 6 and 11, *Int. J. Cancer* 133 (9) (2013) 2253–2258.
- [60] M.J. Levin, A.-B. Moscicki, L.-Y. Song, T. Fenton, W.A. Meyer III, J.S. Read, E.L. Handelsman, B. Nowak, C.A. Sattler, A. Saah, Safety and immunogenicity of a quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine in HIV-infected children 7 to 12 years old, *J. Acquir. Immune Defic. Syndr.* (1999) 55 (2) (2010) 197.
- [61] A.B. Moscicki, B. Karalius, D. Jacobson, K. Patel, M. Purswani, G. Seage, T.J. Yao, K.T.: HPV4, Vaccine immunogenicity/effectiveness in Perinatally HIV-Infected (PHIV) youth. In: Proceedings of the 31st International Papillomavirus Conference & Clinical and Public Health Workshops in Cape Town, South Africa, Abstract No. 317a, 2017.
- [62] T. Wilkin, J.Y. Lee, S.Y. Lensing, E.A. Stier, S.E. Goldstone, J.M. Berry, N. Jay, D. Aboulafia, D.L. Cohn, M.H. Einstein, Safety and immunogenicity of the quadrivalent human papillomavirus vaccine in HIV-1-infected men, *J. Infect. Dis.* 202 (8) (2010) 1246–1253.
- [63] L. Toft, M. Tolstrup, M. Storgaard, L. Østergaard, O.S. Søgaard, Vaccination against oncogenic human papillomavirus infection in HIV-infected populations: review of current status and future perspectives, *Sex. Health* 11 (6) (2014) 511–523.
- [64] V. Rainone, V. Giacomet, F. Penagini, V. Fabiano, F. Calascibetta, C. Mameli, S. Pisanelli, G.V. Zuccotti, M. Clerici, D. Trabattini, Human papilloma virus vaccination induces strong human papilloma virus specific cell-mediated immune responses in HIV-infected adolescents and young adults, *AIDS* 29 (6) (2015) 739–743.
- [65] D.M. Money, E. Moses, S. Blitz, S.M. Vandriel, N. Lipsky, S.L. Walmsley, M. Loufy, S. Trottier, F. Small, M.H. Yudin, HIV viral suppression results in higher antibody responses in HIV-positive women vaccinated with the quadrivalent human papillomavirus vaccine, *Vaccine* 34 (40) (2016) 4799–4806.
- [66] E.M. Kojic, M. Kang, M.S. Cespedes, T. Umbleja, C. Godfrey, R.T. Allen, C. Firnhaber, B. Grinsztejn, J.M. Palefsky, J.Y. Webster-Cyriaque, Immunogenicity and safety of the quadrivalent human papillomavirus vaccine in HIV-1-infected women, *Clin. Infect. Dis.* 59 (1) (2014) 127–135.
- [67] J.A. Kahn, J. Xu, B.G. Kapogiannis, B. Rudy, R. Gonin, N. Liu, C.M. Wilson, C. Worrell, K.E. Squires, Immunogenicity and safety of the human papillomavirus-6,-11,-16,-18 vaccine in HIV-infected young women, *Clin. Infect. Dis.* (2013) (cit319).
- [68] H. Faust, L. Toft, P. Sehr, M. Müller, J. Bonde, O. Forslund, L. Østergaard, M. Tolstrup, J. Dillner, Human Papillomavirus neutralizing and cross-reactive antibodies induced in HIV-positive subjects after vaccination with quadrivalent and bivalent HPV vaccines, *Vaccine* 34 (13) (2016) 1559–1565.
- [69] L. Denny, B. Hendricks, C. Gordon, F. Thomas, M. Hezareh, K. Dobbelaere, C. Durand, C. Hervé, D. Descamps, Safety and immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine in HIV-positive women in South Africa: a partially-blind randomised placebo-controlled study, *Vaccine* 31 (48) (2013) 5745–5753.
- [70] D. Kumar, E.R. Unger, G. Panicker, P. Medvedev, L. Wilson, A. Humar, Immunogenicity of quadrivalent human papillomavirus vaccine in organ transplant recipients, *Am. J. Transplant.* 13 (9) (2013) 2411–2417.
- [71] S. Esposito, F. Corona, L. Barzon, F. Cuomo, L. Squarzon, G. Marcati, M. Torcoletti, M. Gambino, G. Palù, N. Principi, Immunogenicity, safety and tolerability of a bivalent human papillomavirus vaccine in adolescents with juvenile idiopathic arthritis, *Expert Rev. Vaccin.* 13 (11) (2014) 1387–1393.
- [72] M.W. Heijstek, M. Scherpenisse, N. Groot, C. Tacke, R.M. Schepp, A.-M. Buisman, G.A. Berbers, F.R. van der Klis, N.M. Wulffraat, Immunogenicity and safety of the bivalent HPV vaccine in female patients with juvenile idiopathic arthritis: a prospective controlled observational cohort study, *Ann. Rheum. Dis.* 73 (8) (2014) 1500–1507.
- [73] C.C. Mok, L.Y. Ho, L.S. Fong, C.H. To, Immunogenicity and safety of a quadrivalent human papillomavirus vaccine in patients with systemic lupus erythematosus: a case-control study, *Ann. Rheum. Dis.* 72 (5) (2013) 659–664.
- [74] O. Grönlund, E. Herweijer, K. Sundström, L. Arnheim-Dahlström, Incidence of new-onset autoimmune disease in girls and women with pre-existing autoimmune disease after quadrivalent human papillomavirus vaccination: a cohort study, *J. Intern. Med.* 280 (6) (2016) 618–626.
- [75] L. Grimaldi-Bensouda, M. Rossignol, I. Koné-Paut, A. Krivitzky, C. Lebrun-Frenay, J. Clet, D. Brassat, C. Papeix, M. Nicolino, P.-Y. Benhamou, et al., Risk of autoimmune diseases and human papilloma virus (HPV) vaccines: six years of case-referent surveillance, *J. Autoimmun.* 79 (2017) 84–90.
- [76] Secondary Prevention of Cervical Cancer: ASCO Resource-Stratified Clinical Practice Guideline. (www.asco.org/irs-cervical-cancer-secondary-prev-guideline).
- [77] Cervical Screening: Professional Guidance. (<https://www.gov.uk/government/collections/cervical-screening-professional-guidance>).
- [78] NHMRC Screening to Prevent Cervical Cancer: Guidelines for the Management of Asymptomatic Women with Screen Detected Abnormalities. (www.nhmrc.gov.au/publications).
- [79] European Guidelines for Quality Assurance in Cervical Cancer Screening. (http://screening.iarc.fr/doc/ND7007117ENC_002.pdf).
- [80] D.A. Machalek, I.M. Poynten, F. Jin, R.J. Hillman, D.J. Templeton, C. Law, J.M. Roberts, S.N. Tabrizi, S.M. Garland, A. Farnsworth, A composite cytology-histology endpoint allows a more accurate estimate of anal high grade squamous intraepithelial lesion prevalence, *Cancer Epidemiol. Prev. Biomark.* 1106 (2016) 2015.
- [81] D.A. Machalek, A.E. Grulich, R.J. Hillman, F. Jin, D.J. Templeton, S.N. Tabrizi, S.M. Garland, G. Prestage, K. McCaffery, K. Howard, et al., The Study of the Prevention of Anal Cancer (SPANC): design and methods of a three-year prospective cohort study, *BMC Public Health* 13 (2013) (946–946).
- [82] ANCHOR: Anal Cancer/HSIL Outcomes Research Study. (https://jcto.weill.cornell.edu/open_clinical_trials/anchor-anal-cancerhsil-outcomes-research-study).