Full citation: *"Impact of the Pharmacist-Led Intervention on the Control of Medical Cardiovascular Risk Factors for the Primary Prevention of Cardiovascular Disease in General Practice: A Systematic Review and Meta-Analysis of Randomized Controlled Trials." Abdullah Alshehri, Zahraa Jalal, Ejaz Cheema, M Haque, Duncan Jenkins, and Asma Yahyouche. British Journal of Clinical Pharmacology. Published Online: November 28, 2019, DOI: 10.1111/bcp.14164. URL Upon Publication: http://doi.wiley.com/10.1111/bcp.14164*

NEW COCHRANE REVIEW ASSESSES DIFFERENT HPV VACCINES AND VACCINE SCHEDULES IN ADOLESCENT GIRLS AND BOYS

AUGUST 16, 2019 - New evidence published in the Cochrane Library today provides further information on the benefits and harms of different human papillomavirus (HPV) vaccines and vaccine schedules in young women and men.

HPV is the most common viral infection of the reproductive tract in both women and men globally (WHO 2017). Most people who have sexual contact will be exposed to HPV at some point in their life. In most people, their own immune system will clear the HPV infection.

HPV infection can sometimes persist if the immune system does not clear the virus. Persistent infection with some 'high-risk' strains of HPV can lead to the development of cancer. High-risk HPV strains cause almost all cancers of the cervix and anus, and some cancers of the vagina, vulva, anus, penis, and head and neck. Other 'low risk', HPV strains cause genital warts but do not cause cancer. Development of cancer due to HPV happens gradually, over many years, through a number of pre-cancer stages, called intra-epithelial neoplasia. In the cervix (neck of the womb) these changes are called cervical intraepithelial neoplasia (CIN). High-grade CIN changes have a 1 in 3 chance of developing into cervical cancer, but many CIN lesions regress and do not develop into cancer. HPV-related cancers accounted for an estimated 4.5% of cancers worldwide in 2012 (de Martel 2017).

Vaccination aims to prevent future HPV infection and the cancers caused by high-risk HPV infection. HPV vaccines are mainly targeted towards adolescent girls because cancer of the cervix is the most common HPV-associated cancer. For the prevention of cervical cancer, the World Health Organization recommends vaccinating girls aged 9-14 years with HPV vaccine using a two-dose schedule (0, 6 months) as the most effective strategy. A three-dose schedule is recommended for older girls ≥15 years of age or for people with human immunodeficiency virus (HIV) infection or other causes of immunodeficiency (WHO 2017).

Three HPV vaccines are currently in use: a bivalent vaccine that is targeted at the two most common high-risk HPV types; a quadrivalent vaccine targeted at four HPV types, and a nonavalent vaccine targeted at nine HPV types. In women, the bivalent and quadrivalent vaccines have been shown to protect against pre-cancer of the cervix caused by the HPV types contained in the vaccine if given before natural infection with HPV (Arbyn 2018).
This Cochrane Review summarizes the results from 20 randomized controlled trials involving 31,940 people conducted across all continents. In most studies, the outcome reported was the production of

HPV antibodies by the vaccine recipient's immune system. HPV antibody responses predict protection against the HPV-related diseases and cancers the vaccines are intended to prevent. Antibody response is often used as a surrogate in HPV vaccine studies because it takes many years for pre-cancer to develop after HPV infection, so it is difficult for studies to follow participants over such long periods of time. Moreover, because trial participants were tested for HPV infection and offered treatment, if HPV-related precancer was found, progression to cervical cancer in this group would be expected to be very low, even without vaccination.

Four studies compared a two-dose vaccine schedule with a three-dose schedule in 2,317 adolescent girls and three studies compared different time intervals between the first two vaccine doses in 2,349 girls and boys. Antibody responses were similar after two-dose and three-dose HPV vaccine schedules in girls. Antibody responses in girls and boys were stronger when the interval between the first two doses of HPV vaccine was longer.

There was evidence from one study of 16 to 26-year old men that the quadrivalent HPV vaccine reduces the incidence of external genital lesions and genital warts compared with a group who did not receive the HPV vaccine.

There was also evidence from a study of 16 to 26-year old women that compared the nonavalent and quadrivalent vaccines that they provide a similar level of protection against cervical, vaginal, and vulval pre-cancerous lesions.

There was evidence from seven studies about HPV vaccines in people living with HIV. HPV antibody responses in children living with HIV were higher after vaccination with either bivalent or quadrivalent vaccine than with a non-HPV control vaccine. These antibody responses against HPV could be maintained up to two years. The evidence about clinical outcomes and harms for HPV vaccines in people with HIV was very limited.

Evidence suggested that up to 90% of males and females who received an HPV vaccine experienced local minor adverse events such as redness, swelling and pain at the injection site. Due to the low rates of serious adverse events in quadrivalent and nonavalent vaccine groups, and the broad definition of these events used in the trials, we cannot really determine the relative safety of different vaccine schedules.

The lead editor of this review and Consultant in Gynaecological Oncology, Musgrove Park Hospital, Somerset, UK, Dr. Jo Morrison said: "We need long-term population-level studies to provide data on the effects of dosing intervals, schedules and vaccines on HPV-related cancers, as well as giving us a more complete picture of rare harms. However, with fewer doses having a similar antibody response, and more extensive evidence from vaccine studies in boys, policy makers are now in a better position to determine how local vaccination programmes can be designed. It would be interesting to see how different schedules and vaccines influence immunisation coverage, but this review, and the studies within it, were not designed to be able to answer that question."

Full citation: *"Bergman H, Buckley BS, Villanueva G, Petkovic J, Garritty C, Lutje V, Riveros-Balta AX, Low N, Henschke N. Comparison of different human papillomavirus (HPV) vaccine types and dose schedules for prevention of HPV-related disease in females and males. Published Online: November 22, 2019 (DOI: 10.1002/anie.201904467). URL Upon Publication: https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.30716*