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HPV VACCINE FOR PREVENTING CERVICAL CANCER

Cervical cancer is an abnormal growth of cells in the cervix. It is the second most common cancer that affects women in developing countries. In 2012, approximately 270,000 women died from cervical cancer worldwide, with more than 85% of these deaths occurring in low and middle-income countries.[1] In these countries, cervical cancers account for about 12% of all cancers in women[2] compared to less than 1% in more developed regions.

Cervical cancers are caused by the human papilloma virus (HPV). Human papilloma virus is a type of virus belonging to the family *Papillomaviridae.* It is the most common sexually transmitted virus. More than 200 types of HPV have been identified.[3] These viruses can be classified into low-risk and high-risk types based on their ability to cause cancer. While most of the HPV types are low risk (non-cancer causing), at least twelve have been known to cause cancers and are classified as high-risk types. Of these, HPV types 16 and 18 are the most infectious. Seventy-one percent of cervical cancers worldwide are caused by HPV types 16 and 18. Persistent infection of women with HPV types 16 and 18 can lead to precancerous lesions, which if left untreated can progress to cervical cancer. Progression of the disease from precancerous lesions to cervical cancer can take many years.

There may be no symptoms until the disease has progressed to an advanced stage. This is why early detection is important. Symptoms at this stage may include pain in the back, leg or pelvic region; abnormal vaginal bleeding between menstrual periods or vaginal discharge; a single swollen leg, or fatigue. The World Health Organization (WHO) recommends cervical screening of women aged 30-49 years who are most at risk, for prevention or early detection of cervical cancer. More importantly, WHO recommends vaccination of girls aged 9-13 years, before they become sexually active, to protect them against cervical cancer and other HPV infections.

The efficacy of HPV vaccines in adolescent girls and women against high risk HPV types was assessed in a Cochrane systematic review of randomized controlled trials conducted by Arbyn and colleagues.[4] The study included 26 trials involving a total of 73,428 participants. Most of the participants were below 26 years of age.

Vaccines assessed in the review were monovalent, bivalent and quadrivalent vaccines.

The results of the research showed that, in women aged 15-25 who were not infected with any high risk HPV types, HPV vaccines reduced the risk of cervical precancer associated with HPV16/18 as well as the risk of precancer caused by any HPV type (**high certainty evidence)**. The results were also similar when the vaccines were assessed in women aged 15-26 who were not infected with HPV 16/18. In women above 25 years who were free from HPV 16/18, HPV vaccine reduced the risk of precancer associated with HPV16/18 (moderate certainty evidence). In all women aged 15-26, regardless of HPV status (with or without HPV infection), HPV vaccines were also found to be effective in reducing the risk of precancer associated with HPV16/18 and any precancer (**high certainty evidence**). HPV vaccination also reduced the risk of precancer associated with HPV16/18 in older women who received the vaccine between 25 to 45 years of age. However, the effect was much smaller in the older women, probably due to previous exposure to HPV. In this age group, the risk of any precancer is probably similar between unvaccinated and vaccinated women (**moderate certainty evidence**). The vaccine was not associated with an increased risk of serious adverse events. In pregnant women, the vaccines were not associated with an increased risk of miscarriage. The effect on the risk of babies being born with malformations and still births was uncertain.

Although cervical cancer is one of the most preventable and treatable cancers, unfortunately, many women, still die from this disease due to lack of facilities for the prevention and early detection of the disease. Furthermore, although, HPV vaccine has been shown to be safe and effective in preventing cervical cancer, vaccination rates in many sub-Saharan countries including Nigeria remain low. There is a need for Nigeria to include this vaccine in its National immunization programme and take steps to improve the provision and uptake of cancer screening.

References

1. http://www.who.int/news-room/fact-sheets/detail/human-papillomavirus-(hpv)-and-cervical-cancer
2. http://www.who.int/immunization/diseases/hpv/en/
3. World Health Organization. Human papillomavirus vaccines: WHO position paper, May 2017–Recommendations. Vaccine. 2017 Oct 13;35(43):5753-5.
4. Arbyn M, Xu L, Simoens C, Martin-Hirsch PPL. Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors. Cochrane Database of Systematic Reviews 2018, Issue 5. Art. No.: CD009069. DOI: 10.1002/14651858.CD009069.pub3

EVIDENCE AT YOUR FINGERTIPS
(FROM THE COCHRANE LIBRARY)

TECHNICAL SUMMARY

CORTICOSTEROIDS FOR PNEUMONIA

Acute pneumonia ranks among the top 10 most common causes of death in people of all ages and can be classified as community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP) ventilator-associated pneumonia (VAP), and healthcare-associated pneumonia (HCAP). There are approximately 5.16 to 6.11 cases of CAP per 1000 persons per year among adults and this number increases with age. The incidence of HAP ranges between 5 to >20 episodes per 1000 hospitalizations while the rate of development of VAP ranges between 10-30% in patients receiving more than 48 hours of mechanical

ventilation. The most common cause of CAP worldwide is *Streptococcus pneumonia* while HAP, VAP and HCAP may be caused by a broad variety of pathogens and can be polymicrobial.

Corticosteroids include steroid hormones that are naturally produced in the adrenal cortex of vertebrates and their synthetic analogues. They are important components in the treatment of many inflammatory, allergic, immunologic, and malignant disorders. Corticosteroids have been proposed for the treatment of various kinds of infections such as meningitis, tuberculosis, pneumocystis pneumonia, other bacterial pneumonia, and septic shock.

Clinically significant adverse effects have been associated with corticosteroids and are related to dose and duration of the therapy. Many of these effects, however, occur mainly with prolonged administration. The use of corticosteroids for treatment of pneumonia in clinical practice remains variable. There is need to combine data from all relevant trials in order to be able to reach more definitive conclusions.

Objectives:

To assess the efficacy and safety of corticosteroids in the treatment of pneumonia. Specifically, whether systemic steroid treatment:

1. reduces all-cause mortality among people with pneumonia;
2. reduces morbidity among people with pneumonia;
3. increases complication rates among people with pneumonia.

Main Results

Seventeen randomized controlled trials were included in the review.

- The participants were 2264 persons, most of whom were adults (1954)
- Eleven of the trials were conducted in high income countries, three in upper middle-income countries and three in lower middle-income countries.
- Interventions assessed included prednisone, intravenous dexamethasone, hydrocortisone and methylprednisolone and duration of treatments ranged from 2-10 days.
- All included trials assessed only participants with CAP with or without HCAP treated as inpatients.

Effects of interventions:

- ***All-Cause Mortality in Adults:*** Eleven studies (n=1863) showed that there was a significant reduction in all-cause mortality among adults with severe pneumonia (RR 0.58, 95% CI 0.40 to 0.84; moderate-quality evidence), but not in adults with non-severe pneumonia (RR 0.95, 95% CI 0.45 to 2.00; moderate-quality evidence).

- ***Early Clinical failure rates - adults:*** Corticosteroids significantly reduced early clinical failure rates in both adults with severe and non-severe pneumonia (RR 0.32, 95% CI 0.15 to 0.7; I^2 = 74% - 5 trials; and RR 0.68, 95% CI 0.56 to 0.83- I^2 = 0% 2 trials, respectively; high-quality evidence).

- ***Early Clinical failure rates - children:*** This outcome was reported in two small trials (n=88). Among children with bacterial pneumonia, corticosteroids led to a reduction in early clinical failure rates in intervention group compared to control (RR 0.41, 95% CI 0.24 to 0.70, I^2 = 25%; high-quality evidence).

- ***Adverse events:***
  - Adults: Overall there was no significant difference the number of adverse events between adults receiving corticosteroids and those in the control group.
  - Hyperglycaemia: Hyperglycaemia developed more often in those receiving corticosteroids compared to control arm (RR 1.72, 95% CI 1.38 to 2.14; 7 trials, 1578 participants, I^2 = 0%).
  - Children: No adverse events in were reported in children (2 trials)

- Corstocosteroids reduced time to clinical cure, length of hospital and intensive care unit stays, development of respiratory failure or shock not present at pneumonia onset, and rates of pneumonia complications.

Conclusion

Corticosteroids reduce mortality, clinical failure, complication rates, length of hospitalisation, and time to clinical cure in adults with severe community-acquired pneumonia (CAP). For non-severe CAP Corticosteroids reduce morbidity in adults and children but not mortality. More adverse events were associated with Corticosteroid especially hyperglycaemia, but the harm does not seem to outweigh the benefits.

MEFLOQUINE FOR PREVENTING MALARIA IN PREGNANT WOMEN

What is the aim of this review?
The aim of this Cochrane Review was to find out whether the antimalarial drug mefloquine is efficacious and safe for prevention of malaria in pregnant women living in stable transmission areas. We found six relevant studies to help us answer this question.

Key messages
The antimalarial drug mefloquine is efficacious for malaria prevention in pregnant women. The drug has been found to be safe in terms of adverse pregnancy outcomes, such as low birth weight, prematurity, stillbirths and abortions, and congenital malformations. However, it is worse tolerated than other antimalarial drugs.

What was studied in the review?
Pregnant women are vulnerable to malaria infection, especially if they are living with HIV. The consequences of malaria during pregnancy can be severe and include poor health outcomes for both women and their children. For this reason, in malaria-endemic areas of stable transmission, women are recommended to prevent malaria infection by sleeping under mosquito bed-nets and by taking effective drugs (such as sulphadoxine-pyrimethamine or cotrimoxazole in case of HIV infection) as chemoprevention against malaria throughout pregnancy.

This Cochrane Review looked at the effects of mefloquine for prevention of malaria in both HIV-uninfected and HIV-infected pregnant women.

What are the main results of the review?
We found five relevant studies conducted in sub-Saharan Africa and one in Thailand between 1987 and 2013. These studies compared mefloquine with placebo or other antimalarial drugs currently recommended for prevention of malaria in pregnant women. The review shows the following:

- Compared with sulfadoxine-pyrimethamine, mefloquine chemoprevention in HIV-uninfected women:
  - reduces risks of maternal peripheral parasitaemia (presence of malaria parasites in the blood of women) and anaemia at delivery;
  - makes no difference in the prevalence of adverse maternal outcomes (such as low birth weight, prematurity, stillbirths and abortions, and congenital malformations) and in the incidence of clinical malaria episodes during pregnancy; and
  - increases risks of drug-related adverse events including vomiting, fatigue/weakness, and dizziness.
- Compared with cotrimoxale prophylaxis alone, mefloquine chemoprevention plus cotrimoxazole in HIV-infected women:
  - reduces the risk of maternal peripheral parasitaemia at delivery and the risk of placental malaria;
  - makes no difference in the prevalence of adverse pregnancy outcomes (such as low birth weight, prematurity, stillbirths and abortions, and congenital malformations) and in the incidence of clinical malaria episodes during pregnancy; and
  - increases the risk of drug-related adverse events such as vomiting and dizziness.

Overall, the high proportion of mefloquine-related adverse events constitutes an important barrier to its effectiveness for malaria preventive treatment in pregnant women.

How up-to-date is this review?
The review authors searched for studies up to 31 January 2018.

WHAT FACTORS INFLUENCE THE DELIVERY OF CARE BY SKILLED BIRTH ATTENDANTS IN LOW- AND MIDDLE-INCOME COUNTRIES?

Review aim
The aim of this Cochrane synthesis of qualitative evidence was to identify factors that influence the provision of care by skilled birth attendants. To answer this question, we searched for and analysed qualitative studies of skilled birth attendants' views, experiences, and behaviour.

This synthesis complements another Cochrane Review assessing the effect of strategies to promote women's use of healthcare facilities when giving birth.

Key messages
Many factors influence the care that skilled birth attendants provide to mothers during childbirth. These include access to training and

supervision; staff numbers and workloads; salaries and living conditions; and access to well-equipped, well-organised healthcare facilities with water, electricity, and transport. Other factors that may play a role include the existence of teamwork, trust, collaboration, and communication between health workers and with mothers. Skilled birth attendants reported many problems tied to these factors.

What did we study in the synthesis?
In low- and middle-income countries, many mothers still die during childbirth. Women are encouraged to give birth in health facilities rather than at home so they can receive care from skilled birth attendants. A skilled birth attendant is a health worker such as a midwife, doctor, or nurse who is trained to manage a normal pregnancy and childbirth, and refer the mother and newborn when complications arise.

By exploring skilled birth attendants' views, experiences, and behaviour, this synthesis aimed to identify factors that can influence their ability to provide quality care.

Main findings
We included 31 studies conducted in Africa, Asia, and Latin America. Participants were skilled birth attendants including doctors, midwives, nurses, auxiliary nurses and their managers.

Our synthesis pointed to several factors that affected skilled birth attendants' provision of quality care. The following factors are based on evidence assessed as of moderate to high confidence. Skilled birth attendants reported that they sometimes had insufficient training during their education or after they had begun work. Where facilities lacked staff, skilled birth attendants' workloads could increase, it could become difficult to provide supervision, and mothers could receive poorer care. In addition, skilled birth attendants did not always believe that their salaries and benefits reflected their tasks and responsibilities and the personal risks they undertook. Together with poor living and working conditions, these issues could lead to stress and affect skilled birth attendants' family life. Some skilled birth attendants felt that managers lacked capacity and skills, and they felt unsupported when their workplace concerns were not addressed.

Possible causes of staff shortages included problems with hiring and assigning health workers to health facilities; lack of funding; poor management and bureaucratic systems; and low salaries. Skilled birth attendants and their managers suggested factors that could help recruit, keep, and motivate health workers, and improve the quality of their work; these included good-quality housing, allowances for extra work, paid vacations, continued education, proper assessments of their work, and rewards.

Skilled birth attendants' ability to provide quality care was also limited by a lack of equipment, drugs, and supplies; blood and the infrastructure to manage blood transfusions; electricity and water supplies; and adequate space and amenities on maternity wards. These factors were seen to reduce skilled birth attendants' morale, increase their workload and infection risk, and make them less efficient in their work.

A lack of transport sometimes made it difficult for skilled birth attendants to refer women to higher levels of care. In addition, women's negative perceptions of the health system could make them reluctant to accept referral.

We identified some other factors that also may have affected the quality of care, which were based on findings assessed as of low or very low confidence. Poor teamwork and lack of trust and collaboration between health workers appeared to negatively influence care. In contrast, good collaboration and teamwork appeared to increase skilled birth attendants' motivation, their decision-making abilities, and the quality of care. Skilled birth attendants' workloads and staff shortages influenced their interactions with mothers. In addition, poor communication undermined trust between skilled birth attendants and mothers.

How up-to-date is this review?
We searched for studies published before November 2016.

EVIDENCE BASED HEALTH CARE REPORTING WORKSHOP

Group photo of participants with Ebony State Commissioner for Health and other officials from the Ministry of Health.

As part of a weeklong of activities to mark the World Malaria Day, Cochrane Nigeria collaborated with the Jhpiego to hold a workshop on Evidence-based health care reporting from 23-25 April 2018. The aim of the workshop was to teach the participants what evidence based health (EBHC) reporting means and how they can practice EBHC reporting. A total of 24 participants attended the workshop. This comprised of journalists, ministry of health staff, and Jhpiego staff. Facilitators at the event were Dr. Ifeanyichukwu Ezebialu, Mrs. Moriam Chibuzor, Dr. Bartholomew Odio and Mr. Banji Olawole.

The first day of the workshop began with a press briefing by the Commissioner for Health, Ebony State – Dr. Daniel Howard Akuna Umezuruike on the World malaria day. The theme of this year's World Malaria Day was ''Ready to beat Malaria – together we can'' in which he highlighted the problem posed by malaria and thus the need for increased measures to fight malaria. He intimated the press on the ongoing efforts by the Ebonyi State Ministry of Health to fight malaria and noted that the one-week celebration was part of this effort to create awareness of about malaria, its prevention and control. The press briefing was followed by a media chat during which the Commissioner fielded questions from the journalists. The remaining part of the day and the following two days were used for the workshop. Sessions at the workshop included Introduction to Evidence based medicine (EBM), finding evidence, evidence-based health care reporting and critical appraisal of Randomized controlled trials and systematic reviews. Other sessions focused on how to navigate, read and interpret a systematic review and twitter sessions for communicating evidence. Most of the participants were appreciative of the workshop and indicated that they had learnt new skills from the workshop.

Dr. Daniel Umuzuruike, Ebonyi State Commisioner for Health (second from left) giving a press briefing as part of World Malaria Day celebrations.

Dr. Ezebialu (facilitator) with participants during a practical exercise on levels of evidence.

The following new and updated reviews, published recently in the Cochrane Library, were authored or co-authored by Nigerians.

New or Updated Reviews

- Educational interventions for improving primary caregiver complementary feeding practices for children aged 24 months and under **by** *Dachi Arikpo, Ededet Sewanu Edet, Moriam T Chibuzor, Fridey Odey* and *Deborah M Caldwell.* Issue 5 2018.
- Phytomedicines (medicines derived from plants) for sickle cell disease **by** *Oluseyi Oniyangi* and *Damian H Cohall*. Issue 2, 2018.
- Honey for acute cough in children **by** *Olabisi Oduwole, Ekong E Udoh, Angela Oyo-Ita* and *Martin M Meremikwu*. Issue 4, 2018.
- Contracting out to improve the use of clinical health services and health outcomes in low- and middle-income countries **by** *Willem A Odendaal, Kim Ward, Jesse Uneke, Henry Uro-Chukwu, Dereck Chitama, Yusentha Balakrishna* and *Tamara Kredo.* Issue 4, 2018.
- Stiripentol add-on therapy for focal refractory epilepsy **by** *Francesco Brigo, Stanley C Igwe* and *Nicola Luigi Bragazzi.* Issue 5, 2018.

Other Recent Reviews

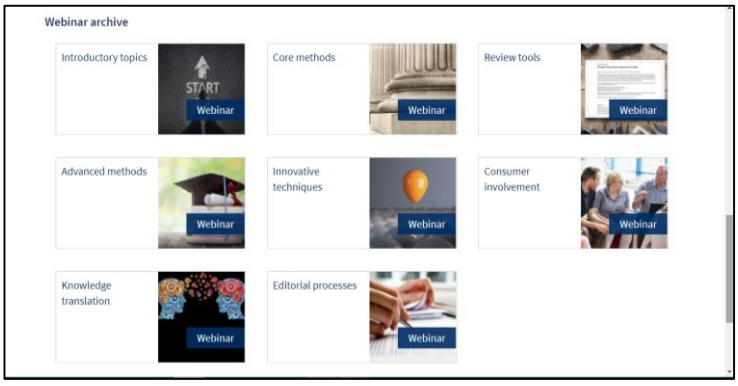
- Prophylactic intravenous calcium therapy for exchange blood transfusion in the newborn **by** *Tinuade A Ogunlesi, Foluso EA Lesi* and *Olabisi Oduwole.* Issue 10, 2017.
- Fluid replacement therapy for acute episodes of pain in people with sickle cell disease **by** *Uduak Okomo* and *Martin M Meremikwu*. Issue 7, 2017.
- Hepatitis B immunoglobulin during pregnancy for prevention of mother-to0child transmission of Hepatitis B virus **by** *Ahizechukwu C Eke, George U Eleje, Uzoamaka A Eke, Yun Xia* and *Jiao Liu.* Issue 2, 2017.
- Ethosuximide, sodium valproate or lamotrigine for absence seizures in children and adolescents **by** *Francesco Brigo* and *Stanley C Igwe.* Issue 2, 2017.
- Short-acting erythropoiesis-stimulating agents for anaemia in predialysis patients **by** *Deirdre Hahn, Christopher I Esezobar, Noha Elserafy, Angela C Webster* and *Elisabeth M Hodson.* Issue 1, 2017.

What's New!

SPOTLIGHT ON COCHRANE TRAINING

Cochrane has re-launched its training website. The site has been redesigned to be more user-friendly and contains many useful resources for new comers to Cochrane, new authors and existing authors. Available resources include:

- **Online interactive learning courses** – This consists of nine self-directed and interactive learning modules on conducting systematic reviews. The courses are free for all **registered Cochrane authors.**



- **Live Webinars:** "Cochrane Training" includes a wide range of webinars. These include upcoming live webinars on various aspects of review

methodology as well as recordings of past webinars (in webinars archive) which authors and other researchers will find very useful, e.g. *Allowing for uncertainty due to missing outcome data in meta-analysis, Undertaking a qualitative evidence synthesis to support decision-making in a Cochrane context.*

Upcoming webinars:

1. Meta-analysis of time-to-event data - July 3, 2018
2. Get to know RevMan Web – the new review writing tool - August 1, 2018
3. A research program on rapid reviews: where should we venture next? *Statistical Methods Group webinar* - August 21, 2018

To register for upcoming webinars see: http://training.cochrane.org/cll-webinars

- **Learning resources on Cochrane review methodology:** e.g. GRADE, and DTA reviews http://training.cochrane.org/cochrane-methodology
- **Author Starter Kit:** A review author starter kit which contains a collection of useful resources for new authors is also available on Cochrane Training.
- **Certificates on completion**: Printable certificates are available on completion of the courses.
- Explore the excellent training resources on Cochrane Training visit: http://training.cochrane.org

Announcements

- **25th Annual Cochrane Colloquium:** The 25th Annual Colloquium will be taking place in Edinburgh, Scotland from 16-18 September 2018 at the Edinburgh International Conference Centre. The theme of this year's colloquium is 'Cochrane for all – better evidence for better health decisions' and it will be a patients included event – co-designed, co-produced and co=presented with healthcare consumers.

For more information and key dates, visit the colloquium website: http://colloquium.cochrane.org/

- **Improved Cochrane training website:** Cochrane has re-launched its training website. The website has been redesigned, is more user friendly and has various new collections on different themes and topics. Most of the resources are free of charge. Visit Cochrane training at training.cochrane.org
- **Upcoming GRADE Training at Cochrane Nigeria:** Cohrane Nigeria Will be holding a 2-day GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach workshop from 4-5 October 2018 in Calabar, Cross River State, Nigeria. If you are interested in attending this workshop please write: cochranenigeria@yahoo.co.uk

• Impact Factor for Cochrane Database of Systematic Reviews now 6.754: The 2017 Journal Impact Factor for the Cochrane Database of Systematic Reviews has risen to 6.754 from 6.264 in 2016.

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