

# VACCINES FOR THE PREVENTION OF ROTAVIRUS DIARRHOEA

Diarrhoeal disease is the second leading cause of death in children under five years of age globally. In Nigeria, diarrhoea is among the top three causes of post-neonatal childhood deaths along with malaria and pneumonia. Rotavirus is one of the major causes of childhood diarrhoea and the leading cause of severe, dehydrating diarrhoea in children under five years. In 2013, an estimated 215,000 children below five years of age died from rotavirus infection globally.<sup>1</sup> Approximately 90% of these deaths occurred in low-income countries in Africa and Asia.<sup>2</sup> Four countries - India, Nigeria, Pakistan and the Democratic Republic of the Congo - accounted for about half of the rotavirus deaths among under-fives in 2013.<sup>1</sup>

Rotavirus infection is acquired through ingestion of contaminated food or drinks which may be by handling food with contaminated hands. Rotavirus has an incubation period of 1-3 days following

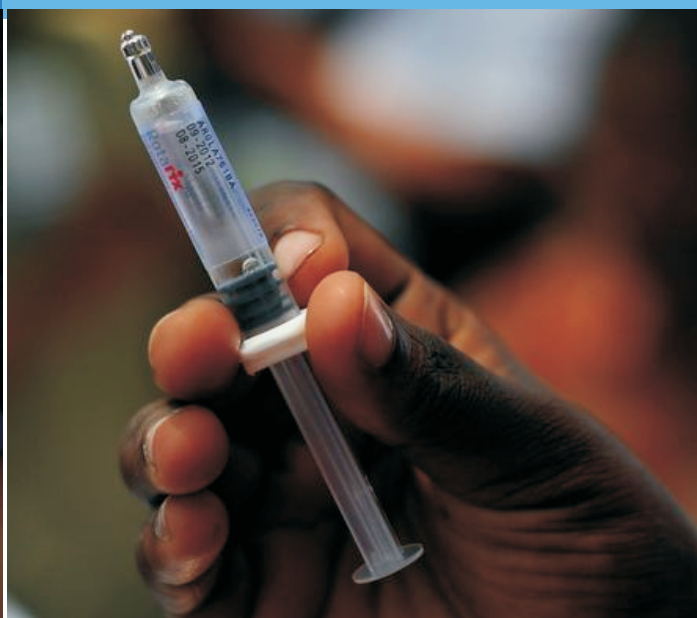
infection. Typical symptoms include passage of frequent watery stools (diarrhoea) and vomiting with fever. There is currently no specific treatment for rotavirus infection but oral rehydration solution and zinc are effective supportive treatments used to treat or prevent dehydration and decrease the severity and duration of the diarrhoea.<sup>2</sup>

Rotavirus diarrhoea often leads to severe dehydration and may be fatal if rehydration is delayed or given inappropriately. Universal hygiene practice at home and particularly in the preparation and handling of foods given to children reduces the risk and incidences of diarrhoea-causing infections including rotavirus.

One of the primary measures for preventing rotavirus diarrhoea is the use of rotavirus vaccines. There are currently two rotavirus vaccines which are licenced for use internationally; Rotarix® (RV1) the monovalent rotavirus vaccine developed by GlaxoSmithKline Biologicals, Belgium, and RotaTeq® (RV5) the pentavalent vaccine developed by Merck & Co. Inc., USA. These vaccines are developed using attenuated rotavirus strains of human and/or animal origin and are administered orally.

The efficacy and safety of rotavirus vaccines currently in use were assessed in a Cochrane systematic review by Soares-Weiser and others.<sup>3</sup> The systematic review assessed the effectiveness of three vaccines namely: RV1, RV5 and Lanzhou lamb rotavirus vaccine (LLR). RV1 is a human rotavirus vaccine which is administered to infants in two doses at least four weeks apart. This vaccine is approved in over 116 countries and has been included in the national immunization programmes in more than 20 countries.

RV5 is a live human-bovine reassortant multivalent rotavirus vaccine. It is



administered in three doses to children who are 6-32 weeks old. RV5 has been approved in over 97 countries and has been included in the national immunization programmes of over 10 countries including the European Union and the USA.

The third vaccine, LLR, developed by Lanzhou Institute of Biomedical Products, China, has only been licensed in China. It is a live attenuated monovalent vaccine derived from a lamb and is administered orally in three doses.

The primary objective of the review was to determine the efficacy of vaccines which have been approved for use in preventing rotavirus diarrhoea, all cause diarrhoea and death in children aged 1-2 years living in low and high mortality countries. In addition the review sought to determine whether serious adverse events including intussusceptions, are associated with use of these vaccines in the age group studied.

The authors identified a total of 41 randomized controlled trials (with a total of 186,263 participants) conducted in several countries around the world. Twenty-nine of these trials (involving 101,671 participants) assessed RV1 vaccine and 12 trials (involving 84,592

participants) evaluated RV5. The review authors identified no trials that evaluated LLR.

The results of the study showed that in countries with low mortality rates, RVI vaccine prevents more than 80% of severe cases of rotavirus diarrhoea in the first two years of life and up to 40% of severe rotavirus diarrhoea cases in high mortality countries. In low mortality countries, RV1 vaccine reduced severe cases of diarrhoea from all causes by 35-40% and by 15-30% in high mortality countries. RV5 vaccine reduced severe cases of rotavirus diarrhoea in the first two years of life by more than 80% in low mortality countries and by 40-57% in high mortality countries. In low mortality countries, RV5 vaccine reduced severe cases of diarrhoea from all causes by 73-96%, and by 15% per cent in high mortality countries.

No increased risk of serious adverse events, particularly intussusception, was observed with the use of RV1 or RV5 vaccines when compared with placebo.

Although results of the review indicate that the efficacy of the vaccine is lower in high mortality countries, the absolute benefit is higher considering the higher burden of disease in these settings. Nigeria



and other countries with high incidence of rotavirus deaths, stand to benefit from inclusion of these vaccines in their national immunization programmes.

## References

1. [http://www.who.int/immunization/monitoring\\_surveillance/burden/estimates/rotavirus/en/](http://www.who.int/immunization/monitoring_surveillance/burden/estimates/rotavirus/en/)
2. Vaccines R. WHO Position Paper- January 2013. Releve Epidemiologique Hebdomadaire/Section d'Hygiene du Secretariat de la Societe des Nations. Weekly Epidemiological Record/Health Section of the Secretariat of the League of Nations. 2013;88:49-64.
3. Soares-Weiser K, MacLehose H, Bergman H, Ben-Aharon I, Nagpal S, Goldberg E, Pitan F, Cunliffe N. Vaccines for preventing rotavirus diarrhoea: vaccines in use. Cochrane Database of Systematic Reviews 2012, Issue 11. Art. No.: CD008521. DOI: 10.1002/14651858.CD008521.pub3.



# EVIDENCE AT YOUR FINGERTIPS

(From the Cochrane Library)

## TECHNICAL SUMMARY



# DAILY IRON SUPPLEMENTATION

FOR IMPROVING ANAEMIA, IRON STATUS AND HEALTH IN MENSTRUATING WOMEN

### Background

Anaemia is a condition in which haemoglobin production is diminished. Over 1.6 billion people worldwide have anaemia. Women of menstruating age account for approximately a third of all cases of anaemia across the globe. Iron deficiency is believed to contribute to at least half the global burden of anaemia, especially in non-malaria-endemic countries.

Iron deficiency and iron-deficiency anaemia have been associated with a range of adverse physical, psychological, and cognitive effects. When anaemia is severe, it may cause lethargy, fatigue, irritability, pallor, breathlessness and reduced tolerance for exertion. Alleviation of iron-deficiency anaemia among menstruating women is thus considered a major public health priority, both to improve their existing health status and to enhance their health in preparation for future pregnancies.

Supplementation is probably the most widespread intervention practiced clinically and in public health for treatment of iron deficiency. Daily iron and folic acid supplementation for three months should be considered for the

prophylaxis of iron deficiency in populations where the prevalence of anaemia exceeds 40%.

### Objectives

To establish the evidence for effects of daily supplementation with iron on anaemia and iron status, as well as on physical, psychological and neurocognitive health in menstruating women.

### Main Results

- Sixty-Seven studies were included in the review. These studies were conducted in numerous countries with different economic backgrounds.

- Participants (N= 8506) were menstruating women, most of whom were aged between 13 and 45 years. Only three studies included women below 13 years and six studies included women above 45 years.

- The intervention consisted of various oral iron formulations, the most common being ferrous sulphate in thirty-three of the studies. The doses of elemental iron ranged from 1 mg of elemental iron to approximately 300 mg of elemental iron a day. The duration of

intervention varied significantly among studies ranging from 1-24 weeks.

- Primary outcomes were anaemia, haemoglobin, iron deficiency, iron deficiency anaemia, all-cause mortality, adverse side effects and cognitive function. All-cause mortality, however, was not reported by any of the studies. Secondary outcomes reported by the studies were iron status, psychological health, adherence, anthropometric measures, physical exercise performance and serum/plasma zinc.

### Effects of Interventions

#### Primary Outcomes

**Anaemia:** Ten studies (n = 3273 women) measured this outcome. At the end of the intervention women that received iron were significantly less likely to be anaemic compared to women in the control group. (RR 0.39, 95% CI 0.25 to 0.60,  $I^2 = 93\%$ ; moderate quality evidence).

**Haemoglobin:** Fifty-one trials (n=6861 women) measured haemoglobin at the end of the intervention. Women that received iron had a higher haemoglobin concentration compared with women receiving control. (MD 5.30, 95% CI 4.14 to 6.45;  $I^2 = 86\%$ ; high quality evidence).

**Iron Deficiency:** This outcome was reported in seven studies (n=1088 women). At the end of the intervention, women receiving iron had reduced risk of iron deficiency compared to controls (RR 0.62, 95%CI 0.50 to 0.76;  $I^2 = 28\%$ ; moderate quality evidence).

**Iron deficiency anaemia:** One study (n=55 women) measured this outcome. There were no events in the intervention or control group.

#### Adverse side effects

**Any side effect:** Seven studies (n = 901 women) reported this outcome. The studies did not identify an overall increased prevalence of side effects from iron supplements (RR 2.14, 95% CI 0.94 to 4.86;  $I^2 = 88\%$ , low quality evidence).

**Gastrointestinal side effects:** Five studies (n=521 women) showed increased prevalence of gastrointestinal side effects in women taking iron (RR 1.99, 95% CI 1.26 to 3.12;  $I^2 = 45\%$ ; low quality evidence).

**Loose stools/diarrhoea:** Six studies (n=604 women) identified increased



prevalence of loose stools/diarrhoea: (RR 2.13, 95% CI 1.10 to 4.11;  $I^2 = 17\%$ ; high quality evidence).

**Hard stools/constipation:** Eight studies (n=1036 women) identified an increased prevalence of hard stools/constipation (RR 2.07, 95% CI 1.35 to 3.17;  $I^2 = 0\%$ ; high quality evidence).

**Abdominal pain:** Seven studies (n=1190 women) showed no definitive increase in abdominal pain (RR 1.55, 95% CI 0.99 to 2.41;  $I^2 = 0\%$ ; low quality evidence).

**Nausea:** Eight studies (n=1214 women) provided no evidence of increased

prevalence of nausea (RR 1.19, 95% CI 0.78 to 1.82;  $I^2 = 0\%$ ).

**Cognitive function:** Five studies reported this but the results could not be put into a meta-analysis because the studies reported varying outcomes and used different cognitive tests.

### Secondary Outcomes

**Physical exercise performance:** Both peak and submaximal exercise performance were improved by iron supplementation.

**Fatigue:** Data from studies that measured fatigue could not be meta-analysed due to variations in reporting. However, women with symptomatic fatigue appeared to experience improvement while in asymptomatic women the effects were less evident.

**Adherence:** Due to heterogeneous methods of reporting adherence, the data from the studies could not put into a meta-analysis. However, in general, participants who received iron did not have poorer adherence than those that had placebo.

**Anthropometric measures:** The studies did not identify any effect of iron on height (Four studies, n=302 women) or weight (Eight studies, n= 593 women). However iron led to increased body mass index (6 studies, n=520 women).

### Conclusion

From the results of the review, daily iron supplementation appears to be effective in reducing anaemia and iron deficiency as well as symptomatic fatigue. It also increases haemoglobin and iron stores and improves physical performance. However these benefits come at the risk of some adverse effects, notably gastrointestinal side effects.

Further research is needed on the effect of iron on important outcomes such as cognitive function, psychological health, well-being and economic productivity as limited data is available on these outcomes. In addition research is needed on the risk-benefit of iron interventions as well as the effect of iron on future pregnancy outcomes.

*Low MSY, Speedy J, Styles CE, De-Regil LM, Pasricha SR. Daily iron supplementation for improving anaemia, iron status and health in menstruating women. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD009747. DOI: 10.1002/14651858.CD009747.pub2.*

## PLAIN LANGUAGE SUMMARIES

### DRUGS THAT AIM TO REDUCE THE LOSS OF WATER FROM RED BLOOD CELLS IN PEOPLE WITH SICKLE CELL DISEASE

#### Review question

We reviewed the evidence to assess the relative risks and benefits of drugs to rehydrate sickled red blood cells.

#### Background

Sickle cell disease is an inherited condition that causes red blood cells to become sickle shaped when they lose water. This leads to a high risk of the blood vessels becoming blocked. Such blockages can cause pain, stroke and damage to organs. Recent therapies aim to stop the cells becoming sickle shaped by preventing them losing water.

#### Search date

The evidence is current to: 28 November 2015.

#### Study characteristics

The review included three studies with 524 people with sickle cell disease aged between 12 and 65 years of age. The intervention in one study was zinc sulphate and in two studies was senicapoc. Each study was compared to a placebo group (a substance which contains no medication). For each study people were selected for one treatment or the other randomly. The studies lasted from three months to 18 months.

#### Key results

The study with zinc sulphate showed that this drug may be able to reduce the number of sickle cell crises without causing toxic effects. There were 145 participants in this study and results

showed a significant reduction in the total number of serious sickle-related crises over one and a half years, mean difference -2.83 (95% confidence interval -3.51 to -2.15). However, our analysis was limited since not all data were reported. Changes to red cell measurements and blood counts were not consistent. No serious adverse events were noted in the study. The two studies with senicapoc demonstrated that this drug increases the red blood survival and has a role in the prevention on red blood cell dehydration in people with sickle cell disease. The higher dose of the drug was more effective compared to the lower dose. But these changes in the red blood cells did not translate into positive clinical outcomes in terms of reduction in the number of sickle cell crises. Senicapoc had a favourable safety profile. More longer-term research is needed on these drugs and others that might prevent water loss in red blood cells.

We will continue to run searches to identify any potentially relevant trials;

however, we do not plan to update other sections of the review until new trials are published.

### Quality of the evidence

All the studies appeared to be well run and we do not think any factors will influence the results in a negative way.

*Nagalla S, Ballas SK. Drugs for preventing red blood cell dehydration in people with sickle cell disease. Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD003426. DOI: 10.1002/14651858.CD003426.pub5*

## PHYSICAL FITNESS TRAINING FOR STROKE SURVIVORS

### Review question

We reviewed the evidence that examines whether physical fitness training is beneficial for a range of health and function outcomes in people with stroke.

### Background

Physical fitness is important to allow people to carry out everyday activities such as walking and climbing stairs. Physical fitness varies among everyone. For example, fitness in men tends to be a little higher than in women and everyone's fitness becomes reduced as we get older and if we become less physically active. Physical fitness is often particularly low in stroke survivors. It may limit their ability to perform everyday activities and also worsen any stroke-related disability. For this reason fitness training has been proposed as a beneficial approach for people with stroke. However, taking part in fitness training could have a range of other benefits important to people with stroke such as improving cognitive function (thinking skills), improving mood, and quality of life, and it could reduce the chance of having another stroke.

### Study characteristics

By February 2015 we identified 58 trials for inclusion in the review. The trials involved at total of 2797 participants at all stages of care including being in hospital or back living at home. Most of the people who took part were able to walk on their own. The trials tested different forms of fitness training; these included 1) cardiorespiratory or 'endurance' training, 2) resistance or 'strength' training, or 3) mixed training, which is a combination of cardiorespiratory plus resistance training.

### Key results

We found that cardiorespiratory fitness training, particularly involving walking, can improve exercise ability and walking after stroke. Mixed training improves walking ability and improves balance. However, there was not enough information to draw reliable conclusions about the impact of fitness training on other areas such as quality of life, mood, or cognitive function. Cognitive function is under-investigated despite being a key outcome of interest for stroke survivors. There was no evidence that any of the different types of fitness training caused injuries or other health problems; exercise appears to be a safe intervention. We need more studies to examine the benefits that are important to stroke survivors, in particular for those with more severe stroke who are unable to walk.

### Quality of the evidence

Studies of fitness training can be difficult to carry out. This means most of the studies were small and of moderate quality. However, some consistent findings did emerge with different studies all tending to show the same effect.

*Saunders DH, Sanderson M, Hayes S, Kilrane M, Greig CA, Brazzelli M, Mead GE. Physical fitness training for stroke patients. Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD003316. DOI: 10.1002/14651858.CD003316.pub6.*

## DOES LEGISLATION TO BAN SMOKING REDUCE EXPOSURE TO SECOND-HAND SMOKE AND SMOKING BEHAVIOUR?

Since the first national legislation banning indoor smoking in all public places was introduced in 2004, there has been an increase in the number of countries, states and regions adopting similar smoke-free legislation banning smoking in public places and work places since this review was first published. The main reason is to protect nonsmokers from the harmful health effects of exposure to secondhand smoke. Another reason is to provide a supportive environment for people who want to quit smoking.

### Study characteristics

We searched for studies that investigated the effect of introducing a ban on any measures of health, or on smoking

behaviour (up to February 2015). Since the previous version of this review had shown clear evidence that introducing legislation to ban smoking in public places does reduce exposure to secondhand smoke (SHS) in those places, we did not include studies that only reported exposure to SHS. We included 77 studies from 21 countries in this updated review. Studies of health outcomes typically used data from hospitals to look for changes in rates of admissions, discharges or deaths. Most studies looked at illnesses related to the cardiovascular system (heart or blood vessels), such as heart attacks and strokes. Studies also looked at effects on respiratory health, including chronic obstructive pulmonary disease (e.g. bronchitis), asthma and lung function. Seven studies looked at the health of newborn children. Eleven studies reported death rates. The best-quality studies collected data at multiple time points before and after the introduction of a ban in order to adjust for existing time trends. Some studies could compare events rates in areas with and without bans, or where bans were introduced at different times.

### Key results

There is evidence that countries and their populations benefit from improved health after introducing smoking bans, importantly to do with the heart and blood vessels. We found evidence of reduced deaths. The impact of bans on respiratory health, on the health of newborn children, and on reducing the number of smokers and their cigarette use is not as clear, with some studies not detecting any reduction.

### Quality of the evidence

Legislative bans have not been evaluated by randomized trials, and the quality of the evidence from the types of studies contributing to this review is lower. Changes in health outcomes could be due to other things, such as change in healthcare practices. However, many of the studies used methods of analysis that could control for underlying trends, and increase our confidence that any changes are caused by the introduction of bans.

*Frazer K, Callinan JE, McHugh J, van Baarsel S, Clarke A, Doherty K, Kelleher C. Legislative smoking bans for reducing harms from secondhand smoke exposure, smoking prevalence and tobacco consumption. Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD005992. DOI: 10.1002/14651858.CD005992.pub3.*



## RECENT EVENTS

### Cochrane Systematic Review and EBM Workshop at LUTH



**Group photograph of participants and facilitators**

Cochrane Nigeria recently headed down to Idi-Araba, Surulere, Lagos to hold a two-day workshop on Evidence based-Medicine and Systemic reviews at the Lagos University Teaching Hospital. The workshop took place from 29-30 March 2016 at the Surgery Training Centre LUTH and was a joint collaboration between the LUTH and Cochrane Nigeria. Thirty-one participants, from the College of Medicine University of Lagos, Igbinedion University and Babcock University attended the workshop. Most of the participants, however, were from the College of Medicine, University of Lagos.

The workshop was facilitated by Dr. Olabisi Oduwole (Cochrane Nigeria), Mr. Ekpereonne Esu (Department of Public Health, University of Calabar), Dr. Babasola Okusanya (College of Medicine, University of Lagos) and Dr. Daniel Odebiyi (College of Medicine, University of Lagos) and comprised of a blend of learning activities such as presentations by facilitators, practical sessions, and group work/ presentations. The sessions were very interactive and participants asked a lot of questions. The participants were able to come up with a number of interesting new review titles.

The Chief Medical Director of LUTH, Prof. Christopher Bode, represented by the Chairman Medical and Advisory Committee, Dr. Olufemi Fasanmade, gave the opening remarks at the workshop. He indicated great pleasure over the workshop and expressed the hope that Cochrane workshops would become an annual event at the LUTH. Professor Afolabi Lesi (Dean, Faculty of Clinical Sciences) and Professor Bosede Afolabi (Professor/ Consultant Obstetrician & Gynaecologist, College of Medicine, University of Lagos, Nigeria) who are seasoned and long-standing Cochrane review authors were also present. They told the participants that they were very proud to be part of Cochrane and enthusiastically encouraged the participants to come on board. They also expressed their willingness to mentor the review authors.

At the end of the workshop most of the participants indicated that they found the presentations useful and that they had learnt a great deal. They however desired that the workshop would be for a longer duration – up to three days.



**Dr. Olabisi Oduwole making a presentation**



**Interactive small group sessions**



**Presentation of group work by a participant**



# MEDIA ROUNDTABLE ON CHRONIC KIDNEY DISEASE

Cochrane Nigeria held a media roundtable discussion with 20 media practitioners from the Nigerian Union of Journalists, Cross River State (NUJ, CRS) Chapter on 12 January 2016. The focus of the discussion was Chronic Kidney Disease (CKD). Dr. Emmanuel Effa, (Consultant Nephrologist, Department of Internal Medicine, University of Calabar Teaching Hospital) made a presentation to give the participants a background to Chronic kidney Disease. He defined chronic kidney disease as "progressive deterioration in kidney functions usually over a period of months to years leading eventually to complete inability of the kidneys to carry out their normal functions". He highlighted the number of people affected by the disease in Nigeria as well as the

symptoms, risk factors and management of CKD. Part of the treatment for CKD is lifestyle modifications. One of these is dietary modifications.

A Cochrane review by Fouque and Laville has assessed the effect of low protein diets on CKD in non-diabetic adults. This review formed the focal point for the media roundtable. Mr. Ekpereonne Esu (Lecturer, Department of Public Health, University of Calabar) presented the results of this review. The review indicates that, in people with kidney disease, low protein diet can delay end-stage kidney disease (kidney failure).



Group Photo of Participants



Question and Answer Session with Participants



Journalists interviewing one of the resource persons (Dr. Emmanuel Effa)



**Cochrane  
Library**

## New and Updated Reviews from the Cochrane Library

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

### Updated Reviews

- Interventions for preventing unintended pregnancies among adolescents **by** Chioma Oringanje, Martin M Meremikwu, Hokehe Eko, Ekpereonne Esu, Anne Meremikwu, John E Ehiri. Issue 2, 2016.
- Melatonin as add-on treatment for epilepsy **by** Francesco Brigo, Stanley C Igwe. Issue 3, 2016.

### Other Recent Reviews

- Adjuvant corticosteroids for reducing death in neonatal bacterial meningitis **by** Tinuade A Ogunlesi, Chibuzo C Odigwe and Olufemi T Oladapo. Issue 11, 2015.

- Surgical versus non-surgical management of abdominal injury **by** Angela Oyo-Ita, Paul Chinnock and Ikpeme A Ikpeme. Issue 11, 2015.
- Hand washing promotion for preventing diarrhoea **by** Regina I Ejemot-Nwadiaro, John E Ehiri, Dachi Arikpo, Martin M Meremikwu and Julia A Critchley. Issue 9, 2015.
- Peribulbar versus retrobulbar anaesthesia for cataract surgery **by** Mahmoud B Alhassan, Fatima Kyari and Henry OD Ejere. Issue 7, 2015.
- Methods for assessing pre-induction cervical ripening **by** Ifeanyichukwu U Ezebialu, Ahizechukwu C Eke, George U Eleje and Chukwuemeka E Nwachukwu. Issue 6, 2015.
- Vaccines for preventing invasive salmonella infections in people with sickle cell disease **by** Friday Odey, Uduak Okomo and Angela Oyo-Ita. Issue 6, 2015.
- Topical antifungals for seborrhoeic dermatitis **by** Enembe O Okokon, Jos H Verbeek, Jani H Ruotsalainen, Olumuyiwa A Ojo and Victor Nyange Bakhoya. Issue 5, 2015.

# ANNOUNCEMENTS

- **Aubrey Sheiham Evidence-based Health Care in Africa Leadership Award- Call for Applications:**

This scholarship is offered annually by Cochrane to an individual from Africa to support the conduct and dissemination of a high-impact Cochrane Review focusing on a topic relevant to resource-constrained settings. The award is administered by Cochrane South Africa (SA).

For full details, eligibility criteria and instructions on how to apply please visit: <http://community-archive.cochrane.org/about-us/awards-scholarships-funding-initiatives/fellowships-scholarships-and-bursaries#ASPHPCS>

**Deadline for applications: 31 July 2016**

- **Kenneth Warren Prize – Call for Nominations:** Cochrane is currently accepting nominations for the Kenneth

Warren Prize. This prize is awarded annually to the principal *author who is a national living in a developing country of a published Cochrane Review which is of high methodological quality and relevant to health problems in developing countries*. Authors may also self-select their review(s).  
*For more details see: <https://colloquium.cochrane.org/kenneth-warren-prize>*

- **24<sup>th</sup> Cochrane Colloquium:** The 24<sup>th</sup> Cochrane Colloquium will hold in Seoul Korea from 23<sup>rd</sup>-27<sup>th</sup> October

2016. The theme for this year's colloquium is "Challenges to Evidence Based Medicine. For more details please visit the Colloquium Site: <https://colloquium.cochrane.org>

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## **Cochrane Nigeria**

Calabar Institute of Tropical Diseases Research and Prevention  
University of Calabar Teaching Hospital, Moore Road  
GPO Box 3134, Calabar, Cross River State

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