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Newsletter of the Nigerian Branch of the South African Cochrane Centre
Calabar Institute of Tropical Diseases Research and Prevention, University of Calabar Teaching Hospital

Male Circumcision for The Prevention of HIV *in Heterosexual Men*

The Human Immunodeficiency Virus (HIV) is a retrovirus that infects cells of the immune system, resulting in destruction of the cells or impairment of their function. This infection leads to a progressive weakening of the immune system of the affected individual. In 2013, approximately 35 million people worldwide were living with HIV while 1.5 million people died from HIV-related causes. Sub-Saharan Africa is mostly affected accounting for 71% of cases of HIV.[1]

The symptoms of HIV infection vary and depend on the stage of the disease. In the first few weeks of infection, symptoms may include fever, headache, rash or sore throat. As the infection progresses, the individual may experience other symptoms such as swollen lymph nodes, weight loss, fever, diarrhoea and cough. If left untreated, the individual may develop life-threatening infections such as tuberculosis, cryptococcal meningitis, or cancers such as lymphomas and Kaposi's sarcoma.[1]

HIV can be treated by using antiretroviral therapy (ART). This consists of a combination of three of more antiretroviral drugs. Antiretroviral drugs do not cure the infection but suppress the virus and enable the individual live a healthy and productive life.

The World Health Organization (WHO), advocates a number of measures for the prevention of HIV infection. These include HIV counselling and testing, correct and consistent use of female or male condoms; treatment for sexually transmitted infections; promotion of safer sexual practices, pre-exposure prophylaxis, and prevention of mother-to-child transmission among others. In addition to these, WHO has recently recommended voluntary medical male circumcision for prevention of HIV in heterosexual men.

Male circumcision is the surgical removal of all or part of the foreskin of the penis. It may be performed for religious reasons shortly after birth or in childhood, or for medical reasons to treat infections, injuries or correct anomalies of the foreskin. Traditionally, it may also be performed as a ritual for initiation into manhood.

Three large randomized controlled trials were conducted between 2002 and 2006 to assess the effectiveness of medical circumcision for preventing HIV in heterosexual men (circumcision was performed by skilled practitioners in a sterile clinic environment). These trials, involving a total of 11,054 men, were conducted in Orange Farm, South Africa (3,274 participants), Rakai, Uganda (4,996 participants), and Kisumu, Kenya (2784 participants). The participants in the South African and Kenyan trials were men aged 18 to 24 years while ages of participants in the Ugandan trial ranged between 15 and 49 years. A Cochrane systematic review[2] of the research evidence from these three trials was carried out by Nandi Siegfried and associates. The results of the review show that there is strong evidence that medical male circumcision reduces the acquisition of HIV by heterosexual men by between 38% and 66% over 24 months.

When used in priority settings, such as countries with high HIV prevalence, generalized heterosexual HIV epidemics and low levels of male circumcision, WHO states that medical male circumcision offers excellent value for money[3] as it has the potential to save substantial costs by averting new HIV infections. It is therefore recommended that male circumcision should be used as part of a comprehensive strategy for prevention of HIV in conjunction with other methods of prevention such as male and female condoms.

References
1. http://www.who.int/mediacentre/factsheets/fs360/en/
2. Siegfried N, Muller M, Deeks JJ, Volmink J. Male circumcision for prevention of heterosexual acquisition of HIV in men. Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD003362. DOI: 10.1002/14651858. CD003362.pub2.

EVIDENCE AT YOUR FINGERTIPS

(From the Cochrane Library)

TECHNICAL SUMMARY

RAPID DIAGNOSTIC TESTS VERSUS CLINICAL DIAGNOSIS FOR MANAGING PEOPLE WITH FEVER IN MALARIA ENDEMIC SETTINGS

Background

Malaria is a febrile illness caused by infection with the *Plasmodium* parasite. The World health organization recommends that all suspected cases of malaria should be confirmed by parasitological diagnosis. The gold standard for confirming diagnosis of malaria is light microscopy. However, the vast majority of malaria episodes and deaths occur in rural parts of Africa where diagnostic services are limited. Consequently diagnosis of malaria is often based on clinical symptoms alone.

Rapid diagnostic tests (RDTs) offer a reliable alternative to microscopy especially in rural areas. The introduction of RDTs has the potential to substantially reduce the over-prescription of antimalarial drugs, by reducing the misclassification of fevers, especially in low prevalence areas. It may also reduce the development and spread of antimalarial resistance which is believed to result from widespread overuse of antimalarial drugs.

Objectives

To evaluate whether introducing RDTs into algorithms for diagnosing and treating people with fever improves health outcomes, reduces antimalarial prescribing, and is safe compared to algorithms using clinical diagnosis.

Main Results

- The review included seven RCTs (two individually RCTs, two published cluster-randomized controlled trials (RCTs) and three unpublished cluster-RCTs).
- All studies were conducted in rural settings in Africa – specifically Ghana, Burkina Faso, Zambia, Kenya, and Uganda.
- The total number of

participants were 17,505 including adults and children.

- **Patients still unwell at day 4+ follow-up -** There was no significant difference between participants remaining unwell after four to seven days for clinical and RDT-supported diagnosis (RR 0.90, 95% CI 0.69 to 1.17, 6990 participants, five trials; Low quality evidence).
- **Patients with fever prescribed antimalarials -** The use of RDTs reduced prescription of antimalarials significantly up to three quarters) however there was substantial heterogeneity between trials (17,287 participants, seven trials, I^2 = 98%; moderate quality evidence). Reduction in prescribing of antimalarials varied with health workers adherence to RDT-supported protocol with greater reductions where adherence to protocol was high and also where malaria endemicity was low.
- **Patients with fever prescribed antibiotics -** The five trials that reported the proportion of patients prescribed antibiotics showed very variable results (13,573 participants, five trials, *very low quality evidence*). Some trials showed increase in antibiotic prescription with RDTs, some showed a reduction and others showed no statistically significant difference between RDT and clinical diagnosis.
- **Microscopy positive patients not prescribed antimalarials:** *Only one trial carried out microscopy on patients in both intervention arms to identify' false negatives'. The trial found no statistical significance in the proportion of slide-positive patients not prescribed antimalarials in the RDT group. (One trial, 1280 participants, low quality evidence).*

Conclusion

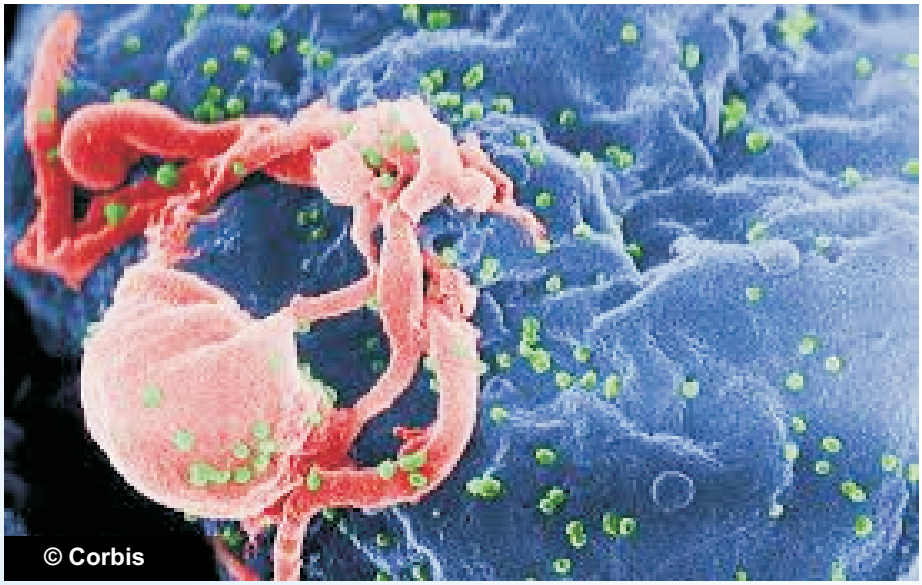
Although RDTs supported algorithms do not lead to improvement in health outcomes for patients, they can lead to a substantial reduction in prescribing of antimalarials if health workers adhere to test results. Further research is needed on how to improve the care of RDT negative patients.

Odaga J, Sinclair D, Lokong JA, Donegan S, Hopkins H, Garner P. Rapid diagnostic tests versus clinical diagnosis for managing people with fever in malaria endemic settings. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD008998. DOI: 10.1002/14651858.CD008998.pub2.

PLAIN LANGUAGE SUMMARIES

Using Antiretroviral Drugs to treat Children under 3 years Old who have HIV Infection

Children under 3 years of age who have HIV infection have a high risk of dying without antiretroviral therapy (ART). However, treatment in this age group is challenging because there are high levels of virus in the blood and few suitable drug choices. Results from this systematic review show that ART soon after birth is preferable to delaying treatment, because infants are less likely to die or become sick. Starting a first-line treatment regimen that includes lopinavir/ritonavir rather than nevirapine is preferable, because infants and young children are less likely to have to stop treatment, whether or not they had previously been exposed to nevirapine. However, lopinavir/ritonavir is more expensive than nevirapine. It is also currently only available as an inconvenient liquid, which tastes bitter and has to be refrigerated, making it challenging to implement in all parts of the world. While waiting for better formulations to become available, it may be possible to switch from lopinavir/ritonavir to nevirapine



once the HIV virus levels become undetectable. However, based on the evidence currently available, a viral load test would be required to identify those children who could safely substitute lopinavir/ritonavir with nevirapine. Viral loads are expensive and not widely available in most countries in sub-Saharan Africa. An alternative treatment approach is to give a stronger drug combination (four different drugs together) when treatment is first started, then reduce down to three drugs after a short while. However, this strategy did not appear to have long-term benefits. A 'treatment interruption' strategy, in which infants start ART soon after birth but then stop medication after 1-2 years, is difficult to implement. Children stopping ART need to restart it very quickly to prevent them becoming sick, and monitoring a child off treatment is challenging in settings with few resources.

Penazzato M, Prendergast AJ, Muhe LM, Tindyebwa D, Abrams E. Optimisation of antiretroviral therapy in HIV-infected children under 3 years of age. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD004772. DOI: 10.1002/14651858.CD004772.pub4.

Early Referral to a Specialist Doctor for People with Kidney Disease

Some degree of kidney failure affects about 15% to 25% of people and is a silent disease that creeps up on an individual with symptoms and signs developing only very late. When kidney failure becomes end-stage, life supporting therapy in the form of dialysis or transplantation is the only option available for the patient. This form of therapy is very expensive and highly intrusive into the patients' life. Measures to prevent progression to this terminal stage are of great importance to prevent this catastrophe.

Our analyses of 40 studies of people with chronic kidney disease shows that people referred earlier to a specialist kidney doctor lived longer. Death rates in people referred early were about half of those referred late and these benefits were seen as early as three months and lasted for at least five years. People referred early also spent less time in hospital and were better prepared for dialysis. Dialysis first requires surgical placement of a fistula and early referral to specialist services often means better preparation, a lower risk of infection and other complications.

We did not discover any adverse effects from early specialist referral. Randomised controlled trials provide the most reliable information of all study designs, so it should be noted that all 40 studies analysed for this review used a cohort design. Cohort studies are the next best level of evidence and the only available evidence. For ethical reasons it is unlikely that a randomised controlled trial that deliberately assigns patients to late specialist referral will ever be conducted.

Smart NA, Dieberg G, Ladhani M, Titus T. Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD007333. DOI:

10.1002/14651858.CD007333.pub2.

Interventions to Reduce Haemorrhage during Myomectomy for Treating Fibroids

Background

Some women have non-cancerous growths of the uterus, called fibroids. In a third of cases the fibroids produce symptoms, such as vaginal bleeding, that warrant treatment. The surgical removal of the fibroids, called myomectomy, is one of the treatment options for fibroids. It can be accomplished by either laparotomy (through an incision into the abdomen) or laparoscopy (keyhole surgery). The procedure is associated with heavy bleeding. Many

interventions have been used by doctors to reduce bleeding during an operation for removing fibroids but it is unclear whether or not the interventions are effective.

Study characteristics

The evidence is current to June 2014. The review included 18 studies with a total of 1250 women who had myomectomy for uterine fibroids. All studies compared an intervention to reduce bleeding during myomectomy with either a placebo or no such treatment.

Key results

The data available suggest that vaginal insertion of misoprostol and infiltration of vasopressin into the uterine muscle are effective in reducing bleeding during myomectomy. Limited data available also suggest that chemical dissection (such as with mesna), vaginal insertion of dinoprostone, a gelatin-thrombin matrix, tranexamic acid, infusion of vitamin C (ascorbic acid) during surgery, infiltration of a mixture of bupivacaine and epinephrine into the uterine muscles, or the use of fibrin sealant patch (a surgical patch that improves blood clotting) may be effective in reducing bleeding during myomectomy. We found limited information on the harms (adverse effects) of the different interventions.

Quality of the evidence

There is moderate-quality evidence that misoprostol reduces blood loss by between 70.24 ml and 125.52 ml; with a laparotomy vasopressin reduces blood loss by between 392.51 and 507.49 ml during myomectomy, and by between 121.73 ml and 172.17 ml during laparoscopic myomectomy. There is low-quality evidence for the rest of the interventions (chemical dissection, dinoprostone, gelatin-thrombin matrix, tranexamic acid, vitamin C, mixture of bupivacaine and epinephrine and a fibrin sealant patch).

Kongnyuy EJ, Wiysonge CS. Interventions to reduce haemorrhage during myomectomy for fibroids. Cochrane Database of Systematic Reviews 2014, Issue 8. Art. No.: CD005355. DOI: 10.1002/14651858.CD005355.pub5.

Zinc supplementation for preventing death and disease, and for growth, in children aged six months to 12 years of age

Review question

This review investigated the effectiveness of zinc supplementation for preventing illness and mortality, and for promoting growth, in children between six months and 12 years of age.

Background

Zinc is an essential micronutrient and zinc deficiency is an important public health problem in low- and middle-income countries. Zinc deficiency impairs growth and contributes to numerous child deaths per year due to diarrhoea, pneumonia, and malaria. This review aimed to determine if giving children zinc supplements would help prevent child death, disease, and growth deficits.

Study characteristics

We searched a wide range of electronic databases for studies that randomly assigned children aged six months to 12 years to either zinc supplementation or a control group that did not receive zinc. Eighty randomised studies with 205,401 eligible participants were included in this review. The evidence is current to December 2012.

Key results and the quality of the evidence

Giving children zinc supplements might reduce their risk of death in general, and their risk of death due to diarrhoea, lower respiratory tract infection (LRTI), or malaria. The quality of evidence for overall mortality was high, though evidence for other critical outcomes was only moderate. Children given zinc experience less diarrhoeal disease than children not given zinc; however, zinc does not seem to reduce children's risk of respiratory infection or malaria. Zinc supplementation may have a very small effect on growth, but eating more calories would probably have a larger effect for many malnourished children. Children who take zinc supplements may experience vomiting as a side effect.

Mayo-Wilson E, Junior JA, Imdad A, Dean S, Chan XHS, Chan ES, Jaswal A, Bhutta ZA. Zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years of age. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD009384. DOI: 10.1002/14651858.CD009384.pub2.

RECENT EVENTS

Nigerian Branch Hosts Review Authors on Fellowship

Group Photo of Fellows with facilitators;
L-R – Olabisi Oduwole, Philip Oshun, Bappa Adamu, Emmanuel Effa

The Nigerian Branch of the South African Cochrane Centre (NBofSACC) recently hosted two medical doctors, Dr. Bappa Adamu and Dr. Philip Oshun for a short fellowship to work on their Cochrane reviews. The fellowship, which took place at the Calabar Institute of Tropical Diseases Research and Prevention from 14-24th July 2014, was sponsored by the South African Cochrane Centre while technical support was provided by the Nigerian Branch. Dr. Adamu, an Associate Professor of Medicine/Nephrology at the Bayero University/Aminu Kano Teaching Hospital, worked on his review *'Adjunctive medical expulsive therapy for kidney and ureteral stone fragments following shock wave lithotripsy'* while Dr. Oshun (Consultant Microbiologist, Lagos University Teaching Hospital) worked on his review titled *'Antiviral therapy of genital herpes in HIV-infected individuals'.*

The fellowship consisted mainly of dedicated time for the fellows to work on their reviews and one-on-one mentoring sessions. These sessions were facilitated by Dr. Emmanuel Effa (Consultant Nephrologist, University of Calabar Teaching Hospital/Training Coordinator NBofSACC) and Mrs. Olabisi Oduwole (Research Officer, NBofSACC). At the end of the fellowship, both fellows expressed the fact that the fellowship had enabled them make significant progress on their reviews which might not have been possible in their usual places of abode.

WRITING A COCHRANE REVIEW: CHALLENGES NIGERIAN AUTHORS FACE

The article below was written by Dr. Adamu and Dr. Oshun, who recently attended a fellowship at the Nigerian Branch. It highlights some of the issues Nigerian, and probably African authors have to grapple with in trying to complete a Cochrane Review as well as possible solutions to some of these problems.

Dr. Bappa Adamu

The Nigerian author has to overcome several hurdles to be a successful Cochrane reviewer. Many consider it, and truly too, to be a Herculean task. The major challenges lie around finding the time, energy and resources to carry out a Cochrane review. The Nigerian author is typically busy with his daily schedule which is often quite packed with clinical and academic activities. These activities compete with many uncertainties related to power outages, erratic and slow internet services, and traffic jams in many urban settings where most of the authors reside. If the author resides in a conflict zone, as I do, this further complicates matters.

The few authors who are committed to writing a Cochrane review despite their busy schedules and competing uncertainties, will have to overcome the next hurdle, which is finding the extra time and resources to carry out the review. I typically come back exhausted from the hectic activities of the day and usually plan to wake up late at night or during the early hours of the morning to make some progress on my review: but then almost always it is pitch dark; 'put on your stand by generator and work', I tell myself. My better half tells me, don't draw the attention of armed robbers to your house. Typically, I just go back to sleep.

The author may squeeze out sometime during the day to work on his review: then he will be frustrated by slow internet connections, taking ages to check in or out a review, do searches, and download articles and so on and so forth. In the end, it takes ages to complete a review. So the Nigerian author may ask himself, is it worth it? On the positive side, initiatives such as the fellowship offered to us by the South African Cochrane centre to have time out at the Nigerian branch and work exclusively on our reviews for a number of days, act as spring-boards to catapult the Nigerian author to complete his review.

Dr. Philip Oshun

Writing a Cochrane review has its challenges like writing an article for submission to a peer reviewed journal. The greatest challenge for me has been dedicating time out of my busy schedule to write the review. Often I make plans to

block out some days in the month to focus on the review but most times other pressing issues take over. This delay may often mean reading the review all over again to remember where I left off.

Another challenge for me has been biostatistics. I have some crossover trials in my review and incorporating these into the review with issues of unit of analysis, how to combine them with parallel trials etc, has been a challenge. Other challenges are access to internet and power supply. Internet is now more available but may be slow and at other times one does not get access to journal articles due to non-subscription.

I am part of the Cochrane HIV/AIDS group and they have a mentoring programme which helps to guide new authors through the review process. This is a very good step and should be replicated by other groups. Review authors in Nigeria should network and collaborate with each other in writing reviews. The Nigerian Cochrane branch is doing well in this regard with the newsletters we get periodically. I encourage us all to read these newsletters and get to know each other so we can work together.

New and Updated Reviews from the Cochrane Library

The following reviews published between May and July 2014 in the Cochrane Library were authored or co-authored by Nigerians.

New Reviews

- Extra fluids for breastfeeding mothers for increasing milk production **by** *Chizoma M Ndikom, Bukola Fawole and Roslyn E Ilesanmi*. Issue 6, 2014.
- Topical anti-inflammatory agents for seborrhoeic dermatitis of the face or scalp **by** *Helena Kastarinen , Tuija Oksanen , Enembe O Okokon , Vesa V Kiviniemi , Kristiina Airola , Johanna Jyrkkä , Tuomas Oravilahti , Piia K Rannanheimo and Jos H Verbeek*. Issue 5, 2014
- Anticoagulation therapy versus placebo for pulmonary hypertension **by** *Ifeanyi R Ezedunukwe , Hilary Enuh , Jay Nfonoyim and Collins U Enuh*. Issue 6, 2014.

Updated Reviews

- Immediate postabortal insertion of intrauterine devices **by** *Babasola O Okusanya , Olabisi Oduwole and Emmanuel E Effa*. Issue 7, 2014.

Other Recent Reviews

- Antibiotic prophylaxis for preventing post-solid organ transplant tuberculosis **by** *Bappa Adamu , Aliyu Abdu ,Abdullahi A Abba , Musa M Borodo and Imad M Tleyjeh.* Issue 3, 2014.
- Prophylactic versus selective blood transfusion for sickle cell disease in pregnancy **by** *Babasola O Okusanya, Olufemi T Oladapo*. Issue 12, 2013.
- Interventions for the prevention of mycobacterium avium complex in adults and children with HIV **by** *Muhammed Mubashir B Uthman, Olalekan A Uthman and Ismail Yahaya. Issue 4, 2013.*
- Home or community-based programmes for treating Malaria **by** *Charles I Okwundu, Sukrti Nagpal, Alfred Musekiwa, David Sinclair. Issue 5, 2013.*
- Interventions for HIV-associated nephropathy **by** *Ismail Yahaya, Olalekan A Uthman, Muhammed Mubashir B Uthman. Issue 1, 2013.*
- Intramuscular versus intravenous anti-D for preventing Rhesus alloimmunization during pregnancy **by** *Charles I Okwundu, Bosede B Afolabi. Issue 1, 2013*.

ANNOUNCEMENTS

FELLOWSHIPS/GRANTS

- **British Council Newton Fund – Call for Applications:** The British Council has opened a call for proposals for travel grants. For full details and eligibility criteria please visit: http://www.britishcouncil.org/education/science/current-opportunities/travel-grants-2014. **Deadline for applications** - 30 September 2014

- **Schlumberger Foundation Call for Applications for the 2015-2016 Faculty for the Future Fellowships:** The Faculty for the Future program, launched in 2004, awards fellowships to women from developing and emerging economies to pursue PhD or Post-doctorate studies in science, technology, engineering and mathematics (STEM) disciplines at leading universities worldwide. **Applications open from September 10th to November 14th 2014 – For more information visit: http://www.facultyforthefuture.net**

COCHRANE NEW

- **Issue 7, 2014 is online** – The complete issue of Issue 7, 2014 is now online. Please visit www.thecochranelibrary.com
- The 2013 impact factor for the *Cochrane Database of Systematic Reviews* (CDSR) was recently released in Journal Citation Report (JCR) by Thomson ISI. Effective July 2014 the impact factor of the CDSR is **5.939**. This is an increase on the 2012 impact factor, which was 5.785.

- **22nd Annual Cochrane Colloquium** - The 22nd Annual Cochrane Colloquium will be hosted by the South Asian Cochrane Network and Centre and will take place at the Hyderabad International convention Centre, Hyderabad, India, 21-26 September 2014. Theme: '*Evidence-Informed Public Health: Opportunities and Challenges*'.

- **How can we serve you better** Please feel free to contact us and let us know how we can tailor the *Info Sheet* to better meet your needs. Send your emails to cochranenigeria@yahoo.co.uk

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