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University of Calabar Teaching Hospital



INTERMITTENT PREVENTIVE TREATMENT OF CHILDREN LIVING IN AREAS WITH SEASONAL MALARIA TRANSMISSION

Malaria is one of the leading causes of mortality in under-five year olds in sub-Saharan Africa and other tropical countries.¹ This is mostly due to infection of the children by *Plasmodium falciparum*, the most pathogenic species of the Plasmodium genus. In 2017, there were 219 million cases of malaria and approximately 435000 deaths from malaria. Almost half of the cases of malaria worldwide occurred in five countries: Nigeria (25%), the Democratic Republic of the Congo (11%), Mozambique (5%), India (4%) and Uganda (4%).

Initial symptoms of malaria include fever, headaches and chills. If left untreated, malaria can progress to serious illness and death. Children under five years of age are among those most vulnerable to malaria and its negative consequences. Due to the vulnerability of under-five children, who lack adequate immunity against malaria, the World Health Organization recommends

multi-faceted interventions to protect children from the severe outcomes of malaria. These interventions include prompt diagnosis and treatment, malaria prevention by sleeping under insecticide treated bed net, chemoprophylaxis and intermittent preventive treatment (IPT).²

Malaria chemoprophylaxis is the administration of anti-malaria drugs daily or weekly for the main purpose of interrupting the life cycle of the malaria parasite; thus preventing the outcomes of the disease. Intermittent preventive treatment differs from chemoprophylaxis in that it is "the administration of a full therapeutic course of an antimalarial or antimalarial combination to a selected, target population at specified times without determining whether or not the subject is infected"³. Intermittent preventive treatment in children (IPTc) is currently called Seasonal Malaria Chemoprevention (SMC).

What is the evidence supporting IPTc

A Cochrane systematic review⁴ titled "Intermittent preventive treatment for children living in areas with seasonal transmission" showed that in areas with seasonal transmission, IPTc reduces the incidence of clinical malaria in children, and severe malaria by as much as 75% during malaria season. This high quality evidence was derived from seven trials that involved 12,589 children from West African countries. In most of the trials, Amodiaquine plus sulphadoxine-pyrimethamine was the most studied drug. This drug was found to be effective although with mild adverse events such as increased vomiting.

According to Meremikwu and his colleagues⁴ there is no need to reassess the effectiveness of IPTc in areas with seasonal malaria transmission because of the high quality of the evidence. However, there is a need to assess the effectiveness of IPTc in children living in areas where malaria occurs throughout the year because there is no clear evidence to support its use in these settings.

In countries with seasonal transmission of malaria or in which parts of the country have seasonal transmission such as the Northern part of Nigeria, it is important for policy makers to incorporate IPTc into their treatment guidelines to reduce deaths from malaria among young children.

References:

1. <https://www.afro.who.int/health-topics/child-health>
2. https://www.who.int/malaria/areas/high_risk_groups/children/en/
3. Greenwood B. Anti-malarial drugs and the prevention of malaria

in the population of malaria endemic areas. *Malaria Journal* 2010;9 (Suppl 3):S2.

4. Meremikwu MM, Donegan S, Sinclair D, Esu E, Oringanje C. Intermittent preventive treatment of malaria in children living in areas with seasonal transmission. *Cochrane Database of Systematic Reviews* 2012, Issue 2. Art. No. : CD003756. DOI : 10.1002/14651858.CD003756.pub4.



EVIDENCE AT YOUR FINGERTIPS

(From the Cochrane Library)

TECHNICAL SUMMARY

OMEGA-3 FATTY ACIDS FOR THE PRIMARY AND SECONDARY PREVENTION OF CARDIOVASCULAR DISEASES

Background:

Cardiovascular diseases (CVDs) are disorders of the heart and blood vessels. Thirty-one per cent of all deaths globally are due to CVDs. In 2015, non-communicable diseases accounted for 17 million premature deaths; the majority of these deaths (82%) occurred in low- and middle-income countries and 37% were caused by CVDs.

Omega-3 fats include longer chain omega-3 fats from fish such as eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and docosapentaenoic acid and Alpha-linolenic acid (ALA shorter chain omega-3 fats found in plants). Some researchers have suggested that omega-3 fatty acids may have a protective effect against Cardiovascular disease. There may also however be some potentially harmful effects of omega-3 fats for example through extension of bleeding times or suppression of normal immune responses.

Objectives:

To assess effects of increased intake of fish- and plant-based omega-3 for all-cause mortality, cardiovascular (CVD) events, adiposity and lipids.

Main Results:

- A total of 79 randomized controlled trials (N=112,059) were included in the review.
- Most of the trials assessed the effects of longer chain omega-3 fatty acids. Only a few trials assessed effects of ALA on cardiovascular outcomes.
- The majority of the studies were conducted in high-income countries. Although a few were conducted in upper-middle-income countries, none of the studies was conducted in low or lower middle income



countries.

- Participants were adults (male and/or female) 18 years or older, at any risk of cardiovascular disease (with or without existing cardiovascular disease)

Effects of longer chain omega-3 fats (LCn3) on primary health outcomes.

The results of the review showed that increasing LCn3 has little or no effect on:

- All-cause mortality (RR 0.98, 95% CI 0.93 to 1.03; $I^2 = 12%$; high-quality evidence, 39 trials, 92,653 participants).
- Cardiovascular mortality (RR 0.95, 95% CI 0.87 to 1.03; $I^2 = 24%$, moderate quality evidence, 67,772 participants; 4544 CVD deaths in 25 trials),
- Cardiovascular events (RR 0.99, 95% CI 0.94 to 1.04; $I^2 = 37%$, high-quality evidence, 90,378 participants; 14,737 people experienced events in 38 trials),
- Coronary heart disease (CHD) mortality (RR 0.93, 95% CI 0.79 to 1.09, $I^2 = 35%$ moderate-quality evidence, 73,491 participants; 1596 CHD deaths in 21 trials).
- Stroke (RR 1.06, 95% CI 0.96 to 1.16; $I^2 = 0%$, moderate-quality evidence, 89,358 participants; 1822 strokes in 28 trials)
- Arrhythmia (RR 0.97, 95% CI 0.90 to 1.05, $I^2 = 43%$, moderate quality evidence, 53,796 participants; 3788 people experienced arrhythmia in 28 trials).

CHD events: There was a suggestion that LCn3 reduced **CHD events** (RR 0.93, 95% CI 0.88 to 0.97, 84,301 participants; 5469 people experienced CHD events in 28 trials); however, this was not maintained in sensitivity analyses – LCn3 probably makes little or no difference to CHD event risk.

Effects of Increasing ALA on primary outcomes

Increasing ALA:

- Probably makes little or no difference to **All-cause mortality** (RR 1.01, 95% CI 0.84 to 1.20, $I^2 = 0\%$, moderate quality evidence, 19,327 participants; 459 deaths, 5 RCTs) OR
- **Cardiovascular mortality** (RR 0.96, 95% CI 0.74 to 1.25, $I^2 = 0\%$, moderate quality evidence, 18,619 participants; 219 cardiovascular deaths, 4 RCTs).
- May make **little or no difference to CHD events** (RR 1.00, 95% CI 0.80 to 1.22, $I^2 = 2\%$, low-quality evidence, 19,061 participants, 397 CHD events, 4 RCTs).
- May slightly **reduce risk of cardiovascular events** (from 4.8% to 4.7%, RR 0.95, 95% CI 0.83 to

1.07, $I^2 = 0\%$, low-quality evidence, 19,327 participants; 884 CVD events, 5 RCTs),

- Probably makes little or no difference to **CHD mortality** (1.1% to 1.0%, RR 0.95, 95% CI 0.72 to 1.26, $I^2 = 0\%$, moderate quality evidence, 18,353 participants, 193 CHD deaths, 3 RCTs)
- Probably reduces the risk of **arrhythmias** (3.3% to 2.6%, RR 0.79, 95% CI 0.57 to 1.10, 4,837 participants; 141 events, 1 RCT moderate quality).
- The effects of increasing ALA on stroke are unclear.
- For all LCn3 primary outcomes except arrhythmias, conducting a sensitivity analysis including only trials at low risk of bias caused the effect sizes to move towards the null (RR 1.0). For most of the ALA outcomes, however, the effect sizes moved to suggest protection.

Conclusion:

Moderate- and high-quality evidence suggests that increasing EPA and DHA has little or no effect on mortality or cardiovascular health. This evidence comes mainly from trials of

capsules of fish oil (supplement trials). Low-quality evidence suggests that ALA may slightly reduce CVD event and arrhythmia risk.

There is need for further large and high-quality trials of ALA conducted in lower and higher income countries which assess baseline ALA intake and use biomarkers to assess compliance, in order to clarify the cardiovascular effects of ALA. Additional trials assessing dietary fish are also desirable.

Abdelhamid AS, Brown TJ, Brainard JS, Biswas P, Thorpe GC, Moore HJ, Deane KHO, AlAbdulghafoor FK, Summerbell CD, Worthington HV, Song F, Hooper L. Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease. *Cochrane Database of Systematic Reviews* 2018, Issue 11. Art. No.: CD003177. DOI: 10.1002/14651858.CD003177.pub4.

PLAIN LANGUAGE SUMMARIES

WHICH DRUG IS BEST FOR REDUCING EXCESSIVE BLOOD LOSS AFTER BIRTH?

What is the issue?

The aim of this Cochrane Review was to find out which drug is most effective in preventing excessive blood loss at childbirth and has the least side effects. We collected and analysed all the relevant studies to answer this question (date of search: 24 May 2018).

Why is this important?

Excessive bleeding after birth is the most common reason why mothers

die in childbirth worldwide. Although most women will have moderate bleeding at birth, others may bleed excessively, and this can pose a serious risk to their health and life. To reduce excessive bleeding at birth, the routine administration of a drug to contract the uterus (uterotonic) has become standard practice across the world.

Different drugs given routinely at birth have been used for reducing excessive bleeding. They include oxytocin, misoprostol, ergometrine, carbetocin, injectable prostaglandins and combinations of these drugs, each with different effectiveness and side effects. Some of the side effects

identified include: vomiting, high blood pressure and fever. Currently, oxytocin is recommended as the standard drug to reduce excessive bleeding. We analysed all the available evidence to compare the effectiveness and side-effect profiles for each drug.

What evidence did we find?

We found 196 studies involving 135,559 women. We compared seven uterotonic agents against each other and against women receiving no uterotonic. Studies were conducted across 53 countries. In most studies women were giving birth normally and in a hospital.

The analysis suggests that all drugs are effective for preventing blood loss that equals or exceeds 500 mL when compared with no routine uterotonic treatment. Compared with oxytocin (the standard recommended drug), the three best drugs for this outcome were a combination of ergometrine plus oxytocin, carbetocin, and a combination of misoprostol plus oxytocin. We found the other drugs misoprostol, injectable prostaglandins, and ergometrine may make little or no difference to this outcome compared with oxytocin.

All drugs except ergometrine and injectable prostaglandins are effective for preventing blood loss that equals or exceeds 1000 mL when compared with no treatment. Ergometrine plus oxytocin and misoprostol plus oxytocin make little or no difference in this outcome compared with oxytocin. It is uncertain whether carbetocin and ergometrine alone make any difference to this outcome. However, misoprostol is less effective in preventing blood loss that equals or exceeds 1000 mL compared with oxytocin.

Misoprostol plus oxytocin reduces the use of additional uterotonics and probably also reduces the risk of blood transfusion when compared with oxytocin. Carbetocin, injectable prostaglandins and ergometrine plus oxytocin may also reduce the use of additional uterotonics but the certainty of the evidence is low. No meaningful differences could be detected between all agents for maternal deaths or severe birth complication as these are rare in such studies.

The two combinations of drugs were associated with important side effects. When compared with oxytocin, women receiving misoprostol plus oxytocin combination are more likely to suffer vomiting and fever. Women receiving ergometrine plus oxytocin are also more likely to suffer vomiting and may make little or no difference to the risk of hypertension, however the certainty of the evidence was low for this outcome.

The analyses gave similar results irrespective of whether women were giving birth normally or by caesarean, in a hospital or in the communi-

ty, were at high or low risk for bleeding excessively after birth, whether they received a high or a low dose of misoprostol and whether they received a bolus or an infusion of oxytocin or both.

What does this mean?

All agents were generally effective for preventing excessive bleeding when compared with no uterotonic drug treatment. Ergometrine plus oxytocin combination, carbetocin, and misoprostol plus oxytocin combination may have some additional benefits compared with the current standard oxytocin. The two combination drugs, however, are associated with significant side effects that women might find disturbing compared with oxytocin. Carbetocin may have some additional benefits compared with oxytocin and appears to be without an increase in side effects.

Reference:

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, Williams MJ, Diaz V, Pasquale J, Chamillard M, Widmer M, Tunçalp Ö, Hofmeyr GJ, Althabe F, Gülmezoglu AM, Vogel JP, Oladapo OT, Coomarasamy A. *Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis*. *Cochrane Database of Systematic Reviews* 2018, Issue 12. Art. No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.

ANTIBIOTICS FOR PROLONGED MOIST COUGH IN CHILDREN

Background

Cough is the most common symptom which presents to doctors. Current recommendations suggest treating prolonged wet cough with antibiotics. We examined whether antibiotics are useful in treating children who have an ongoing persistent wet cough.

Study characteristics

We included randomised controlled trials that compared antibiotics with a placebo (pretend treatment) or control group. The children included in the trials had wet cough lasting more than 10 days. The evidence is current to September 2017.

We found three studies that varied in a number of ways including

different antibiotics (two studies used amoxicillin/clavulanate acid and one used erythromycin) and length of treatment was seven or 14 days.

The mean ages of the children ranged from 21 months to six years.

Key results

This review, involving 190 children with persistent wet cough, found that antibiotics were beneficial in curing the cough. The cure rate was one child cured for every three children treated. Antibiotics also prevented the illness from getting worse, thus avoiding a further course of antibiotics, for one in every four children treated. We found no clear evidence about whether antibiotics were associated with more side effects. We could not assess long-term results.

Reliability of the evidence

The reliability of the evidence was moderate when using antibiotics to cure cough and for illness progression, while it was only low for side effects of medicines.

Take home message

Antibiotics are effective in treating children with chronic (greater than four weeks) wet cough and could be considered when they present to doctors.

Reference: Marchant JM, Petsky HL, Morris PS, Chang AB. *Antibiotics for prolonged wet cough in children*. *Cochrane Database of Systematic Reviews* 2018, Issue 7. Art. No.: CD004822. DOI: 10.1002/14651858.CD004822.pub3.

VAGINAL CLEANSING WITH ANTISEPTIC SOLUTION BEFORE CESAREAN DELIVERY TO REDUCE POST-CESAREAN INFECTIONS

What is the issue?

We set out to determine if cleansing the vagina with an antiseptic solution before a caesarean delivery decreases the risk of maternal infections, including infection of the lining of the uterus and wound complications. Cleansing the vagina

before the cesarean delivery can reduce the number of bacteria in the vagina. Bacteria are naturally present in the vagina and cervix and can move up to infect the uterus during the procedure. Antibiotics are routinely given before or during the surgery to reduce the risk of infections, but some women still suffer from these complications. Some antibiotics do not consistently eradicate all bacteria and antibiotic-resistant bacteria may also be present.

Why is this important?

Cesarean deliveries are common, with almost one in three babies born by cesarean in some countries such as the USA. Between one in four and one in 10 women having a cesarean delivery develop an infection of the uterus (endometritis) or a problem with their skin incision, respectively. The risk of infection is greater if a woman's waters have already broken or she is in labor before the cesarean section. These complications slow a woman's recovery from the surgery and may affect her ability to take care of her baby. This is a Cochrane Review first published in 2010 and then subsequently updated in 2012 and twice in 2014.

What evidence did we find?

We searched for evidence on July 10, 2017. In this update, we have

included 11 randomized controlled studies, involving a total of 3403 women undergoing cesarean section. Eight studies used povidone-iodine for vaginal cleansing, two chlorhexidine, and one benzalkonium chloride. The quality of the evidence using GRADE was moderate for the reported outcomes.

We found that cleansing the vagina with an antiseptic solution compared to not cleansing or using saline or water immediately before the cesarean delivery more than halved the risk of post-cesarean infection of the uterus from a rate of 8.7% down to a rate of 3.8% (10 studies, 3283 women). While we should be cautious about results found for women in certain groups, we did also find that the benefit was also seen if the woman's waters had already broken (from 17.9% to 4.3% with vaginal cleansing; three studies, 272 women) and if women were already in labor at the time of the cesarean delivery (from a rate of 11.1% down to 4.7% with vaginal cleansing four studies, 960 women). The benefits were similar using both povidone-iodine and chlorhexidine.

The risk of experiencing a fever (eight studies, 3109 women) or wound infection (eight studies, 2839 women) after the cesarean delivery may be slightly lowered by antiseptic preparation, but the

results were not entirely clear. Only the composite outcome of wound complication or endometritis was reduced overall for women receiving preoperative vaginal cleansing (two studies, 499 women).

None of the reports mentioned that any women had adverse events such as an allergic reaction to the cleansing solution or irritation.

What does this mean?

Cleansing the vagina immediately before a cesarean delivery with either an iodine-based or chlorhexidine-based solution probably reduces the risk of infection of the uterus after a cesarean section. This benefit may be greater for women who have their cesarean delivery after their membranes have already ruptured or they are already in labor. This is a generally simple, well-tolerated way to lower the chances of developing an infection after having a baby by cesarean.

Reference

Haas DM, Morgan S, Contreras K, Enders S. Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections. *Cochrane Database of Systematic Reviews* 2018, Issue 7. Art. No.: CD007892. DOI: 10.1002/14651858.CD007892.pub6.

RECENT EVENTS

CAPACITY BUILDING INTRODUCTION TO COCHRANE SYSTEMATIC REVIEWS



Group photograph of participants and facilitators

Cochrane Nigeria recently held an introduction to Cochrane systematic reviews workshop in Calabar, Cross River State. The workshop, which held from 11-13 March 2019, had twenty persons in attendance. The participants came from different institutions in Nigeria and included doctors, nurses and a student of medicine and surgery. The three-day workshop was facilitated by a number of Cochrane authors/staff including Prof. Angela Oyo-Ita (Co-Director Cochrane Nigeria), Dr. Emmanuel Effa

(training Coordinator, Cochrane Nigeria), Dr. Ekpereonne Esu (Lecturer, Department of Public Health, University of Calabar) and Mrs. Dachi Arikpo and Moriam Chibuzor (Research Officers, Cochrane Nigeria).

Topics covered at the workshop included Introduction to Systematic Reviews and Evidence Based Medicine, Writing a Systematic Review Protocol, Navigating the Cochrane library, searching for studies, Risk of Bias Assessment, Introduction to RevMan 5, Data Collection and Introduction to Meta Analysis.

The workshop included a lot of practical and group sessions and the participants were very actively involved in all the sessions. The next introduction to Cochrane Reviews Workshop is expected to hold in the Western part of Nigeria in Oyo State.



Dr. Esu facilitating a session during the workshop



Cochrane Nigeria



Some of the participants during a group exercise



Cochrane Nigeria



Participants during a practical exercise on levels of evidence.



New and Updated Reviews from the Cochrane Library

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

New or Updated Review

Reviews by Nigerian Authors

- Vaccines for preventing invasive salmonella infections in people with sickle cell disease by Friday Odey, Uduak Okomo, and Angela Oyo-Ita. Issue 12, 2018.
- Palliative interventions for controlling vaginal bleeding in advanced cervical cancer by George U Eleje, Ahizechukwu C Eke, Gabriel O Igherase, Anthony O Igwegbe, and Lydia I Eleje. Issue 3, 2019.

OTHER RECENT 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, Friday 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 Urochukwu, Dereck Chitama, Yusen-tha Balakrishna and Tamara Kreda. Issue 4, 2018
- **Stiripentol add-on therapy for focal refractory epilepsy** by Francesco Brigo, Stanley C Igwe and Nicola Luigi Bragazzi Issue 5, 2018.

WHAT'S NEW!

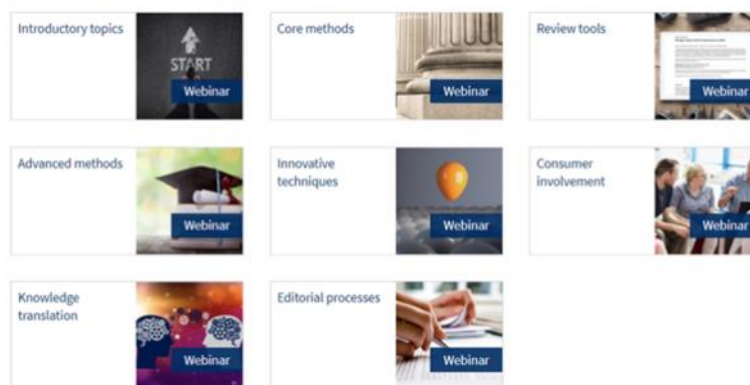
SPOTLIGHT ON COCHRANE TRAINING

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 ten self-directed and interactive learning modules on conducting systematic reviews. The courses are free for all **Cochrane Authors and residents of WHO Hinari Group A and B Countries**.

Live Webinars: “Cochrane Training” includes a wide range of webinars.

Cochrane Learning Live webinar archive



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.

Upcoming webinars:

April 11, 2019

Visualising Cochrane Evidence in practice: experience from the Cochrane Common Mental Disorders group

May 7, 2019

How RevMan Web can improve your experience of writing a systematic review

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

- **Cochrane Colloquium Santiago – Registration Open**

Registration has opened for the 26th Cochrane Colloquium which will take place at the CasaPiedra in Santiago, Chile from the 22-25 October 2019. The theme of the Colloquium is “Embracing Diversity”.

For more information and key dates, visit the Colloquium site: <https://colloquium2019.cochrane.org/>

- **Cochrane Colloquium - Call for Stipends Applications:** A number of stipends are being made available to consumers and residents of developing countries to attend the Cochrane Colloquium in Santiago (22-25 October 2019). For more details on the criteria for applications and how to apply see: <https://colloquium2019.cochrane.org/news/we-are-now-accepting-applications-cochrane-stipends>

- **Cochrane Interactive learning – New Module on Network Meta-analysis:** Cochrane training has recently included a new module (Module 10) on Network Meta-analysis in its Online Interactive training modules. You can have free access to this and other modules if you are a Cochrane Author or if you are resident in a WHO Hinari Group A or B country (Nigeria included). To access these course: <https://training.cochrane.org/interactivelearning>



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