

RANDOMISED TRIALS IN CHILD HEALTH IN DEVELOPING COUNTRIES

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Randomised trials in child health in developing countries 2008-09

SEARCH STRATEGY

Pubmed Hayne's strategy, search: ((Developing countries; Developing country; Countries, developing; Developed countries; Country, developing; Countries, developed; Developed country; Country, developed; Nations, developing; Developing nations OR India OR Africa OR Asia OR South America OR Papua New Guinea OR Asia-Pacific) and (Child*)) AND (randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract])).

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Introduction

This booklet is compiled annually to summarize the evidence on child health derived from randomized trials in developing countries over the previous year. The aim is to make this information widely available to paediatricians, nurses, other health workers and administrators in resource poor settings where up-to-date information is hard to find. It is hoped that such information will be helpful in reviewing treatment policies, clinical practice and public health strategies.

The method of searching for studies to include uses Pubmed, a search engine that is freely available and widely used in most countries throughout the world. The search strategy has been chosen to try to capture as many relevant studies as possible, although it is possible that some are missed. If you know of a relevant RCT that has not been included in this year's review, please let me know. The search strategy is reproducible by anyone with access to the Internet, through <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi>

Randomized controlled trials (RCTs) are far from the only valuable scientific evidence, and some RCTs, because of problems with design or implementation have limited value. However the method of the Randomized Trial is the Gold Standard for determining attributable benefit or harm from clinical and public health interventions. When appropriately performed they eliminate bias and confounding. However their results should not be accepted uncritically and they should be evaluated for quality and validity. Before the result of an RCT can be generalized to another setting there must be consideration of the wider applicability, feasibility and potential for sustainability.

This year there were 157 studies identified. These came from all regions of the world, mostly from developing country researchers. Several trials from 2008-09 will lead to significant changes in child health approaches or clinical recommendations.

We have again included the web-link for papers that are freely available in full-text on the Internet. More importantly, through HINARI (<http://www.who.int/hinari/en/>) a program set up by WHO in collaboration with major publishers, the full-text version of over 6400 journal titles are now available to health institutions in 108 countries. If your health institution (medical school, teaching hospital, nursing school, government office) has not registered with HINARI, you can check your eligibility and register online.

Please feel free to distribute this booklet to any colleagues. Previous editions (2002-2008) are available at: www.ichrc.org

Some of the important outcomes from studies in 2008-09 include:

- Mortality rates among HIV exposed but uninfected children are higher than among HIV-non-exposed children, and part of this excess mortality relates to early cessation of breast feeding. Abrupt cessation of breast feeding at 4-6 months, a previously recommended approach, may have detrimental effects
- Highly active antiretroviral therapy given to mothers decreases the risk of breast milk transmission of HIV, and can enable more prolonged safe breast feeding
- The 11-valent pneumococcal conjugate vaccine (PCV) reduced the incidence of radiologic pneumonia by 22% among children in Philippines
- Ceramic water filters significantly decrease rates of diarrhoea and dystentery
- Community-based delivery of essential newborn care in India reduced neonatal mortality
- Sublingual sugar is effective in preventing and treating hypoglycaemia in children with severe malaria

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- Intermittant preventative treatment of malaria in infants (IPTi) reduces the incidence of malaria and anaemia, and *doesn't* significantly increase the risk of severe malaria after the age of one year (a paradoxical effect that was previously reported)
- Two doses of IPT given in older children during peak transmission seasons reduces the risk of malaria, and IPT given to school age children also reduces anaemia and improves attention and cognition.
- IPTi has reduced effectiveness in malnourished children.
- This year there were 5 randomized trials on the use of ready-to-use fortified spread (lipid-based nutritional supplement with multivitamins). In Malawi and Nigeria, short term (6-12 weeks) administration of fortified spread reduced wasting. In Malawi, taking FS for 12 months was beneficial for the most severely stunted children, and had a sustained effect over the next 2 years.
- Micronutrient fortification of food given in schools was associated with improved linear growth in India, reduced rates of anaemia and zinc deficiency in Vietnam and China, and enhanced effect of deworming with albendazole in Vietnam.
- Zinc improved the rate of recovery for children with Shigella dysentery in Bangladesh, improved growth in stunted children in Iran, and reduced the risk of acute lower respiratory tract infection in a population of children with high rates of nasopharyngeal carriage of *Streptococcus pneumoniae* in Nepal

Dedication: Prof David Morley

This year's RCT booklet is dedicated to Professor David Morley. David died in June, aged 86. He was a paediatrician, teacher, author and innovator who founded Teaching Aids at Low Cost (TALC) in 1965 after working for many years in Nigeria. David worked tirelessly to make useful information and appropriate technology available to health workers and teachers in developing countries. In 1973 he wrote *Paediatric Priorities in the Developing World*, which was a wonderful description of how health priorities for children can be effectively addressed through primary care and district health services. He designed the Road-to-Health growth charts, and was one of the first to use measles vaccine to eradicate the infection in a community in Africa.

David was very supportive of previous editions of this small booklet. He encouraged me to produce it each year, and he helped distribute it by including it with other health information in CD-ROMs produced by the TALC. TALC has distributed over 60,000 copies of 10 editions of their health information CD-ROMs to health workers in developing countries where internet access is limited.

For more information about the extraordinary life and work of Professor David Morley, see: <http://www.talcuk.org/about/professor-david-morley.htm>, and Ebrahim and Waterston. *Journal of Tropical Paediatrics*; 2009; 55 (4): 213.

Trevor Duke
August 2009

Acute respiratory infection

(See also Zinc, Pneumococcal vaccine)

[J Trop Pediatr.](#) 2008 Dec;54(6):382-9. Epub 2008 Jul 8.



Effectiveness of 3-day amoxicillin vs. 5-day co-trimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age: a multi-centric open labeled trial.

[Awasthi S](#), [Agarwal G](#), [Singh JV](#), [Kabra SK](#), [Pillai RM](#), [Singhi S](#), [Nongkynrih B](#), [Dwivedi R](#), [More VB](#), [Kulkarni M](#), [Niswade AK](#), [Bharti B](#), [Ambast A](#), [Dhasmana P](#); [ICMR-IndiaClen Pneumonia Project Group](#). Collaborators (35)

[Awasthi S](#), [Agarwal GG](#), [Dhasmana P](#), [Pandey T](#), [Verma T](#), [Tripathi S](#), [Mittal SC](#), [Gupta D](#), [Raman R](#), [Patil A](#), [Randive M](#), [Purnima](#), [Goyal S](#), [Gakare RN](#), [Sawant DK](#), [Jayakumar S](#), [Gupta V](#), [Yadav K](#), [Lodha R](#), [Kapoor SK](#), [Kathal R](#), [Induria](#), [Nigam M](#), [Wakhlu I](#), [Reddy DC](#), [Pandey CM](#), [Saxena NC](#), [Rasaily R](#), [Misra N](#), [Bhatia VL](#), [Bhushan V](#), [Saxena NC](#), [Rasaily R](#), [Roy M](#), [Kapoor AN](#).

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This cluster randomized, open labeled trial was conducted to compare the **effectiveness of 3 days of oral amoxicillin and 5 days of co-trimoxazole treatment in terms of clinical failure in children with World Health Organization (WHO) defined non-severe pneumonia** in primary health centers in rural India. Participants were children aged 2-59 months with WHO defined non-severe pneumonia, with or without wheeze, who were accessible to follow up. From seven primary health centers in each arm, **2009 cases were randomized, 993 and 1016 in treatment with amoxicillin and co-trimoxazole, respectively**. Fever was present in 1247 (62.1%) and wheeze in 443 (22.1%). There was good adherence and low loss to follow-up. **Clinical failure on amoxicillin and co-trimoxazole on intention to treat analysis was 137 and 97, respectively (absolute difference = 0.04, 95% confidence interval: - 0.035-0.12)**. We conclude that there was no difference in effectiveness of oral co-trimoxazole or amoxicillin in treating non-severe pneumonia.

Comment

As in many of these trials of non-severe pneumonia, a high proportion of patients is likely to have viral pneumonia, as evidenced by the high percentage of children with wheeze (22% overall in this study). Surprisingly over 80% of the 2009 children in this study had vomiting prior to presentation, and more than 30% had diarrhoea. Why only 14% (277/1972) of children had cough (see Table 2 in full-text article) further raises questions about the illnesses that are being classified as non-severe pneumonia.

[Expert Opin Pharmacother.](#) 2008 Nov;9(16):2751-7.

Comparative evaluation of efficacy and safety of cefotaxime-sulbactam with amoxicillin-clavulanic acid in children with lower respiratory tract infections.

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OBJECTIVE: Beta-lactamase producing bacteria present a major problem in treating lower respiratory tract infections. The objective of this study was to evaluate efficacy and safety of cefotaxime-sulbactam combination versus amoxicillin-clavulanic acid injection as an alternative therapeutic option for treatment of lower respiratory tract infections in pediatric patients. **METHODS:** This randomized, multicentric, comparative study enrolled **102 inpatients with lower respiratory tract infections, in the age range of 3 months - 12 years**. Patients received **cefotaxime-sulbactam or amoxicillin-clavulanic acid injection intravenously for up to 7 days**. **RESULTS:** There was no difference between the two groups in demography or disease characteristics ($p > 0.05$) at baseline. Efficacy was evaluated in a total of 96 patients. Both the treatment groups were comparable in response rate at the end of the therapy ($p > 0.05$). **Clinical success rate was 93.6% and 89.8%, respectively for cefotaxime-sulbactam and co-amoxiclav**. One patient from the cefotaxime-sulbactam group reported convulsions, which were probably not related to the study medication in the opinion of the investigator. Except for this serious adverse event, both the study medications were safe and well tolerated in the study population. **CONCLUSION: In conclusion, cefotaxime-sulbactam administered 3 times a day for up to 7 days was found to be as effective as co-amoxiclav therapy**. However, further studies with a large number of patients are required to confirm these findings with more robust microbiological evaluation.

[Lancet.](#) 2008 Sep 6;372(9641):822-30. Epub 2008 Aug 18.

Care at first-level facilities for children with severe pneumonia in Bangladesh: a cohort study.

[Chowdhury EK](#), [El Arifeen S](#), [Rahman M](#), [Hoque DE](#), [Hossain MA](#), [Begum K](#), [Siddik A](#), [Begum N](#), [Sadeq-ur Rahman Q](#), [Akter T](#), [Haque TM](#), [Al-Helal ZM](#), [Baqui AH](#), [Bryce J](#), [Black RE](#).

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BACKGROUND: Guidelines on integrated management of childhood illness (IMCI) for severe pneumonia recommend referral to hospitals. However, in many settings, children who are referred do not actually attend hospital, which severely limits appropriate care. We aimed to assess the safety and effectiveness of modified guidelines that allowed most children with severe pneumonia to be treated locally in first-level facilities, with referral only for those with danger

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signs or other severe classifications. **METHODS:** We did an observational cohort study in ten first-level health facilities in Matlab, rural Bangladesh that had implemented IMCI guidelines. We assessed children with severe pneumonia who were aged between 2 and 59 months, and for whom we could obtain complete information, in two cohorts: **261 children who presented to these facilities between May, 2003, and April, 2004 (before implementation of the modified guidelines) and 1271 children between September, 2004, and August, 2005 (after full implementation).** We obtained information about the characteristics and management of their illness, including referrals and admissions to hospital, from facility records. Staff visited households to obtain details of treatment, socioeconomic information, and final outcome, including mortality data. **FINDINGS: 245 (94%) of 261 children who had severe pneumonia were referred to hospital before the guidelines were modified, compared with 107 (8%) of 1271 after implementation (p<0.0001). 94 (36%) children with severe pneumonia received correct management before the guidelines were modified, compared with 1145 (90%) children after implementation (p<0.0001).** Before modification of the guidelines, three children with severe pneumonia who presented at first-level facilities died, with a case-fatality rate of 1.1%; after modification, seven children died, with a case-fatality rate of 0.6% (p=0.39). **INTERPRETATION:** Local adaptation of the IMCI guidelines, with appropriate training and supervision, could allow safe and effective management of severe pneumonia, especially if compliance with referral is difficult because of geographic, financial, or cultural barriers.

[Indian Pediatr.](#) 2008 Jul;45(7):547-53.



Oral salbutamol for symptomatic relief in mild bronchiolitis a double blind randomized placebo controlled trial.

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OBJECTIVES: To determine the efficacy of oral salbutamol for providing symptomatic relief in mild bronchiolitis. **DESIGN:** Randomized double-blind placebo controlled trial. **SETTING:** Pediatric Outpatient Department of a tertiary care hospital. **SUBJECTS:** 140 infants (of 310 approached) with a clinical diagnosis of acute bronchiolitis with respiratory rate ≤ 70 breath/min, heart rate ≤ 200 beats/min, hemoglobin oxygen saturation (SpO₂) $\geq 95\%$ in room air, no or mild accessory muscle use, and respiratory distress assessment instrument (RDAI) score ≤ 10 . Children were followed up for 14 days. **INTERVENTION:** Oral salbutamol (0.1 mg/kg/dose) (n=70) or placebo (n=70) three times a day for 7 days or till complete resolution of symptoms, whichever was earlier. **OUTCOME VARIABLES:** Time for resolution of illness (ROI), duration of fever, cough, coryza, noisy breathing, time to achieve normal feeding and normal sleep, and frequency of hospitalization and adverse effects. **RESULTS: Median (SE, 95% CI) duration of resolution of overall illness was similar in the two groups [6 (0, 5 to 7) d in the salbutamol group vs. 5 (1, 4 to 6) days in placebo group; P=0.21].** There was no significant difference in mean duration of fever, cough, coryza, noisy breathing, time to achieve normal feeding and normal sleep; and frequency of hospitalization or adverse effects, between the two groups. However, tremors were observed in 5 infants in the

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salbutamol group. **CONCLUSION: Oral salbutamol is not superior to placebo in reducing the duration of symptoms in mild cases of acute bronchiolitis in children.**

Comment

For several reasons it is not surprising that oral salbutamol is ineffective in acute viral bronchiolitis in infants. In several studies of asthma oral salbutamol has been shown to be less effective and have more side effects than inhaled salbutamol, and in recent years there have been moves to remove the oral preparation from the WHO Essential Medicines List. However, a review in 2008 concluded that oral salbutamol may still have a role in some settings: where salbutamol inhalers are not available or too expensive; in young children who have difficulty learning to use spacers; possibly as an adjunct to inhaled salbutamol (as the combination of inhaled and oral salbutamol leads to greater increases in FEV1 than inhaled salbutamol alone); and in some children who are reluctant to carry a spacer and inhaler. See http://www.who.int/selection_medicines/committees/subcommittee/2/Salbutamol_review.pdf Oral salbutamol has stayed as an option for treating asthma in the WHO Pocket Book of Hospital Care for Children, although inhaled salbutamol and the use of spacers is the preferred option.

Anaemia

(See also Nutrition and Micronutrients, and Maternal Health sections)

[Gastroenterology](#). 2008 Nov;135(5):1534-42. Epub 2008 Aug 5.

Causal relationship of Helicobacter pylori with iron-deficiency anemia or failure of iron supplementation in children.

[Sarker SA](#), [Mahmud H](#), [Davidsson L](#), [Alam NH](#), [Ahmed T](#), [Alam N](#), [Salam MA](#), [Beglinger C](#), [Gyr N](#), [Fuchs GJ](#).

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BACKGROUND & AIMS: We investigated Helicobacter pylori (H pylori)-infection as a cause of iron deficiency (ID) and iron-deficiency anemia (IDA) or treatment failure of iron supplementation. **METHODS:** We randomized 200 Hp-infected children (positive urea breath test) 2-5 years of age with IDA (hemoglobin level <110 g/L; serum ferritin level <12 microg/L; and soluble transferrin receptor >8.3 mg/L) or ID (serum ferritin level <12 microg/L or soluble transferrin receptor level >8.3 mg/L) to 1 of 4 regimens: **2-week anti-Hp therapy (amoxicillin, clarithromycin, and omeprazole) plus 90-day oral ferrous sulfate (anti-Hp plus iron), 2-week anti-Hp therapy alone, 90-day oral iron alone, or placebo.** Sixty noninfected children with IDA received iron treatment as negative control. **RESULTS:** Hp-infected children receiving iron had significantly less frequent treatment failure compared with those with no iron in correcting IDA (11% [95% confidence interval (CI), 2%-20%] for anti-Hp plus iron, 0% for iron alone vs 33% [95% CI, 26%-46%] for anti-Hp and 45% [95% CI, 31%-59%] for placebo;

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chi(2) = 127; P < .0001), ID (19% [95% CI, 8%-30%] for anti-Hp plus iron, 7% [95% CI, 0%-14%] for iron alone vs 65% [95% CI, 52%-78%] for anti-Hp alone, and 78% [95% CI, 66%-90%] for placebo; chi(2) = 124; P < .0001), or anemia (34% [95% CI, 20%-40%] for anti-Hp plus iron, 27% [95% CI, 14%-40%] for iron alone vs 65% [95% CI, 52%-78%] for anti-Hp alone and 78% [95% CI, 66%-90%] for placebo; chi(2) = 46; P < .0001). Cure rates of IDA, ID, or anemia with iron were comparable with that of the negative control group. Improvements in iron status also were significantly greater in groups with iron. **CONCLUSIONS: H pylori is neither a cause of IDA/ID nor a reason for treatment failure of iron supplementation in young Bangladeshi children.**

[Trop Med Int Health](#), 2008 Oct;13(10):1257-66. Epub 2008 Aug 24.



Effect of iron or multiple micronutrient supplements on the prevalence of anaemia among anaemic young children of a malaria-endemic area: a randomized double-blind trial.

[Ouédraogo HZ](#), [Dramaix-Wilmet M](#), [Zeba AN](#), [Hennart P](#), [Donnen P](#).

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OBJECTIVE: To assess the effect of supplementation with iron or multiple micronutrients (MM) on the prevalence of anaemia in a malaria-endemic area. **METHODS:** A community-based randomized double-blind trial was conducted in rural Burkina Faso, including **children aged 6-23 months with haemoglobin (Hb) concentrations of 70-109 g/l who were randomized into an iron group (Fe, n = 96), an iron and zinc group (IZ, n = 100) or an MM group (MM, n = 100), 5 days/week for 6 months.** All children were provided with insecticide-treated bednets; those who had a Plasmodium falciparum (PF) positive-smear at baseline and/or at each monthly checking received antimalarial therapy. **RESULTS:** The mean (SD) endpoint Hb concentration was higher in the MM group [113.2 (13.6) g/l] than in the IZ group [106.3 (15.6) g/l] and the Fe group [107.1 (12.9) g/l] (P = 0.001). Children in the MM group were more likely to recover from anaemia than those in the Fe group [prevalence rate ratios, PRR (95% confidence interval, CI) = 1.62 (1.22-2.15), P < 0.001]. The IZ group did not differ from the Fe group [PRR (95% CI) = 0.94 (0.65-1.35), P = 0.72]. None of the interactions on the effect of supplementation of baseline age (0.13), or baseline height-for-age z-score (P = 0.33), or incident PF parasitemia (P = 0.99), was significant. **CONCLUSION: In this malaria-endemic area, in combination with malaria management, the MM supplement was more efficacious than the Fe supplement and the IZ supplement for reducing anaemia.** Further investigation into limiting factors and amounts of micronutrients that would be more efficacious for reducing anaemia is recommended.

Comment

The micronutrient mixture used in this study was a fortified energy-dense plumpy-nut like mixture, containing vitamins, A, C, D, E, K, B₁, B₆, B₁₂, Folic acid, niacin, iron, copper, iodine and electrolytes

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[Rev Saude Publica](#). 2008 Oct;42(5):786-95. Epub 2008 Aug 8.

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Effectiveness of daily and weekly iron supplementation in the prevention of anemia in infants.

[Engstrom EM](#), [Castro IR](#), [Portela M](#), [Cardoso LO](#), [Monteiro CA](#).

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OBJECTIVE: To evaluate the effectiveness of universal prophylactic targeting with iron sulfate on daily or weekly basis in the prevention of anemia in infants. **METHODS:** Randomized clinical field trial with children between ages six and 12 months seen at primary health care units in the municipality of Rio de Janeiro, Brazil, between 2004 and 2005. Three concurrent cohorts were compared: **daily group (n=150; 12.5mg Fe/day); weekly group (n=147; 25mg Fe/week) and control group. The intervention consisted of universal supplementation with iron sulfate for 24 weeks, combined with educational adherence-promoting measures.**

Outcome: mean serum hemoglobin concentration, distribution and prevalence of anemia (Hb<110.0 g/l) at age 12 months. Effectiveness was evaluated considering both intent to treat and adherence to protocol, using multiple regression analysis (linear and Poisson). **RESULTS:** Groups were homogeneous in terms of descriptive variables. The intervention was implemented successfully, with high adhesion to protocol in both groups, and no statistical difference between them. **After adjustment, only the daily regimen showed a protective effect.** Adherence analysis demonstrated an evident dose-response effect on mean Hb and prevalence of anemia only for the daily regimen. No protective effect was detected for the weekly regimen.

CONCLUSIONS: Universal supplementation with iron sulfate from six to 12 months of age was effective in increasing serum Hb and decreasing risk of anemia only when administered on a daily basis

[J Trop Pediatr](#). 2008 Aug;54(4):243-7. Epub 2007 Dec 21.

FULL FINAL TEXT
OXFORD JOURNALS

Anemia reduction in preschool children with the addition of low doses of iron to school meals.

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BACKGROUND: In developing countries there is high prevalence of iron deficiency anemia, which causes negative impact on growth, development and quality of life for infant population. Currently several strategies are being elaborated and tested to tackle this problem. **OBJECTIVE:** To measure anemia prevalence in preschool children. To evaluate fortification effectiveness

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with 5 or 10 mg of elemental iron/daily added to school meals by increasing hemoglobin levels in anemic children. **METHODS:** Double-blind, cluster randomized intervention study with 728 students from public network. Blood count was taken at beginning of study, to evaluate anemia prevalence, those anemic were selected for intervention, after intervention new blood count was taken to evaluate fortification effectiveness. **Ferrous Sulphate was added in individual dosage of 5 or 10 mg of elemental iron/daily to usual school meal.** From 35 schools 3 were randomized to receive 5 mg/daily (group A) and 3 to receive 10 mg/daily (group B). Hemoglobin and hematocrit averages before and after intervention were compared in each group and between them. **RESULTS: In group A, the anemia prevalence reduced 34.9 to 12.4%, and in group B 39.0 to 18.7%. In both groups a significant increase in hemoglobin was observed: in group A from 10.1 to 11.5 g/dl ($p < 0.01$) and in group B from 10.0 to 11.0 g/dl ($p < 0.01$).** There was no statistically significant difference in final levels of hemoglobin among groups. **CONCLUSIONS: Both dosages of elemental iron were equally effective in increasing hemoglobin levels, and reducing anemia prevalence. Fortification of school meals was shown to be an effective, low cost and easy to manage intervention.**

[Am J Clin Nutr.](#) 2009 Jun;89(6):1815-20. Epub 2009 Apr 29.



Regular consumption of a complementary food fortified with ascorbic acid and ferrous fumarate or ferric pyrophosphate is as useful as ferrous sulfate in maintaining hemoglobin concentrations >105 g/L in young Bangladeshi children.

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BACKGROUND: Non-water-soluble iron compounds have been reported to be less well absorbed than ferrous sulfate in young children, and concern has been raised about their usefulness as food fortificants. **OBJECTIVE:** The objective was to evaluate the usefulness of ferrous fumarate and ferric pyrophosphate, compared with ferrous sulfate, in maintaining hemoglobin concentrations >105 g/L in Bangladeshi children. **DESIGN: Two hundred thirty-five children aged 7-24 mo (hemoglobin >105 g/L) were randomly assigned in a double-blind study to receive an infant cereal fortified with ferrous fumarate, ferric pyrophosphate, or ferrous sulfate.** One serving of cereal (9.3 mg Fe; molar ratio of ascorbic acid to iron of 3:1) was consumed per day, 6 d/wk, for 9 mo. Blood samples were drawn at 4.5 and 9 mo. **RESULTS:** Raw data were reformatted, and a "time to event" was calculated that corresponded to reaching the following thresholds: hemoglobin <105 g/L, plasma ferritin <12 microg/L, or plasma C-reactive protein >10 mg/L at baseline, 4.5 mo, or 9 mo. Data were censored when children did not reach the threshold or were lost to follow-up. A Kaplan-Meier approach was used to compare the 3 groups. **No statistically significant differences were observed for hemoglobin <105 g/L ($P = 0.943$), plasma ferritin <12 microg/L ($P = 0.601$), or plasma C-reactive protein >10 mg/L ($P = 0.508$).** **CONCLUSIONS: Contrary to earlier concerns, these results do not indicate differences in usefulness between water-soluble and non-water-soluble iron compounds in maintaining hemoglobin concentrations and preventing iron deficiency. These data will be important in the development of food-fortification strategies to combat anemia and iron deficiency in highly vulnerable population groups.**

Anaesthesia and intensive care

[Anesth Analg.](#) 2009 Jun;108(6):1967-70.

Does ultrasound guidance improve the success rate of infraclavicular brachial plexus block when compared with nerve stimulation in children with radial club hands?

[Ponde VC](#), [Diwan S](#).

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BACKGROUND: The classical response to nerve stimulation may be altered in cases of radial club hand. Ultrasound guidance may prove to be a useful tool in such situations. In this study, we compared the success rate of ultrasound-guided infraclavicular brachial plexus block with nerve stimulation for children undergoing radial club hand repair. **METHODS:** **Fifty children, aged 1-2 yr, undergoing radial club hand repair were randomly assigned to receive infraclavicular brachial plexus block guided by nerve stimulator (Group NS) or ultrasound (Group U) in combination with light general anesthetic.** Bupivacaine 0.5 mL/kg of 0.5% was injected in both groups. Pain response to surgical stimulus was considered as block failure. The Children's Hospital Eastern Ontario Pain Scale pain score was recorded at 1, 4, 6, 8, and 10 postoperative hours. **RESULTS:** In Group NS, the blocks were successful in 16 of 25 patients (64%), whereas in Group U, 24 of 25 patients had successful blocks ($P = 0.0053$). There was no difference in the time to first analgesia or analgesic consumption in the 10-h study period. **CONCLUSION:** **Ultrasound-guided infraclavicular brachial plexus block improves the success rate in patients with radial club hands when compared with nerve stimulation in patients undergoing radial club hand correction.**

[Anesth Analg.](#) 2009 Apr;108(4):1132-8.

Subtenon block compared to intravenous fentanyl for perioperative analgesia in pediatric cataract surgery.

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BACKGROUND: General anesthesia with opioids provides good operative conditions for ocular surgery in children; however, postoperative pain management remains a significant problem. Regional anesthesia is commonly used as an adjunct to general anesthesia in children. **We compared the efficacy and safety of subtenon block (SB) versus IV fentanyl for perioperative analgesia in pediatric cataract surgery.** We hypothesized that perioperative analgesia using SB may reduce the requirement of postoperative rescue analgesia compared with fentanyl. **METHODS:** This was a prospective, randomized, controlled, double-blind trial. One hundred fourteen ASA I and II children (6 mo-6 yr) undergoing elective cataract surgery in

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one eye under general anesthesia were studied. Children were randomly allocated to one of the two groups, i.e., Group SB (n = 58) or Group F (n = 56) after securing the airway. Children in Group SB received SB with 0.06-0.08 mL/kg of 2% lidocaine and 0.5% bupivacaine (50:50) mixture and simultaneous 0.2 mL/kg normal saline IV, whereas children in Group F received 1 microg/kg (0.2 mL/kg of 5 microg/kg) of fentanyl IV and simultaneous subtenon injection with normal saline (0.06-0.08 mL/kg). Surgery started after 5 min of study drug administration. Postoperative assessment for pain, sedation, and nausea/vomiting was done at 0.5, 1, 2, 3, 4, and 24 h. The primary outcome was number of patients requiring rescue analgesia during the 24-h study period. Secondary outcomes assessed were pain and sedation scores, time to first rescue analgesia, incidence of oculocardiac reflex, and nausea/vomiting. **RESULTS:** The number of patients requiring rescue analgesia during the 24 h was significantly less in Group SB (n = 17/58, 29.3%) compared with Group F (n = 39/56, 69.6%, $P < 0.001$). The postoperative pain scores were statistically lower in Group SB at all time intervals. The median (range) time to first analgesic requirement was significantly prolonged in Group SB (16 [2-13] vs 4 [0.5-8.5] h in Group F) ($P < 0.001$). Sedation scores at (1/2) h were comparable, after which significantly more children were anxious or crying in Group F compared with Group SB in which more children were calm, sitting, or lying with eyes open and relaxed ($P < 0.05$). A significantly higher incidence of oculocardiac reflex was recorded in Group F versus Group SB ($P = 0.019$). No complication related to SB was noticed. **CONCLUSIONS: SB is a safe and superior alternative to IV fentanyl for perioperative analgesia in pediatric cataract surgery.**

[Reg Anesth Pain Med.](#) 2009 Mar-Apr;34(2):106-9.

A comparison between EMLA cream application versus lidocaine infiltration for postoperative analgesia after inguinal herniotomy in children.

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BACKGROUND: EMLA cream (eutectic mixture of local anesthetics) has been shown to penetrate intact skin and provide analgesia of superficial layers. There are no studies on the effects of topical application of EMLA cream for postoperative pain relief after inguinal hernia repair. **OBJECTIVE::** This randomized, double-blind, placebo-controlled study compared the efficacy of topical application of 5% EMLA cream before surgery, with wound infiltration with 1% lidocaine for postoperative analgesia in children. **METHODS:** Ninety children, aged 4 to 12 years, undergoing elective inguinal hernia repair under general anesthesia were enrolled in the study. **Patients were randomly assigned to receive either placebo cream (group1), 5% EMLA cream (group 2), or placebo cream followed by 0.5 mL/kg 1% lidocaine (group 3) in the wound after induction of anesthesia.** The anesthetic technique and monitoring were standardized, and postoperative pain was assessed using a 10-point objective pain scale. Fentanyl was used as rescue analgesic in immediate postoperative period, and acetaminophen was administered for postoperative pain in surgical ward. **RESULTS:** The number of patients requiring fentanyl in the immediate postoperative period was significantly less in the study groups compared with the placebo group. Sixty-seven percent of patients in the placebo group required more than 1 dose of acetaminophen in the first 6 hrs compared with 23% (EMLA group) and 20% (lidocaine group). Four patients (two in the lidocaine group, one in the EMLA group, and one in the control group) developed subcutaneous

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infection at the site of incision 10 to 15 days postoperatively. **CONCLUSION: Topical application of EMLA (5%) provides postoperative analgesia comparable to infiltration with 1% lidocaine after inguinal hernia repair in children.**

[Turk J Pediatr.](#) 2008 Nov-Dec;50(6):566-71.

The effects of maternal presence during anesthesia induction on the mother's anxiety and changes in children's behavior.

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This study aimed to evaluate whether maternal presence during induction has additional beneficial effects on a mother's anxiety or changes in the child's behavior when an information booklet was given to all mothers and premedication was given to all patients. One hundred children, aged 2-10 years, scheduled for ambulatory surgery were randomly assigned to a mother-present (Group M) or mother-absent group (Group C) after premedication with intranasal midazolam. All mothers were informed about general anesthesia with a detailed information booklet. Preoperatively (pre) and one week after the operation (post), maternal anxiety was assessed using State-Trait Anxiety Inventory (STAI), and Posthospitalization Behavior Questionnaire (PHBQ) was used to measure changes in children's behavior. Anesthesia was induced using sevoflurane-oxygen-nitrous oxide inhalation. The anesthesiologist graded the level of the children's stress at anesthesia induction with a four-point scale. There were no differences between the two groups regarding demographics, anxiety levels of the mothers and postoperative behavioral changes and stress scores of the children ($p > 0.05$ between the groups * $p < 0.005$ within groups). **In summary, maternal presence during induction in addition to premedication for children and information booklets for mothers had no additive effects in terms of reducing the mother's or the child's anxiety or postoperative behavioral changes.**

[J Indian Soc Pedod Prev Dent.](#) 2008 Sep;26(3):97-101.

Journal of Indian Society of
Pedodontics and Preventive
Dentistry Free Fulltext

Comparison of oral ketamine and oral midazolam as sedative agents in pediatric dentistry.

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The safe and effective treatment of uncooperative or combative preschool children with extensive dental needs is one of pediatric dentist's ongoing challenges. The traditional methods of behavior management are no longer acceptable to parents as they are not ready to spare more time for dental treatment of their children. Keeping this in mind, the present study was designed

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and carried out to evaluate the sedative effects of oral ketamine and oral midazolam prior to general anesthesia. Twenty uncooperative children in the age-group of 2-6 years were selected after thorough medical examination and investigations. Informed consent was obtained from the parent. This was a randomized double-blind study. **An anesthesiologist administered either 0.5 mg/kg midazolam or 5 mg/kg ketamine orally.** The heart rate, respiratory rate, and oxygen saturation were recorded at regular intervals. The sedation and anxiolysis scores were also recorded. The parents were asked to answer a questionnaire at the follow-up session the next day on the surgical experience of the parent and the child and side effects experienced, if any. **When the data was subjected to statistical analysis, it was observed that both drugs resulted in adequate sedation at the end of 30 min, with oral midazolam providing significantly better anxiolysis. The heart rate and respiratory rate were marginally higher with oral ketamine. The questionnaire revealed a better response with oral midazolam; side effects were more prominent with oral ketamine.**

[Ann Card Anaesth.](#) 2009 Jan-Jun;12(1):27-33.



Caudal epidural sufentanil and bupivacaine decreases stress response in paediatric cardiac surgery.

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Surgery and anaesthesia are known to cause stress response. Attenuation of stress response can decrease morbidity, postoperative hospital length of stay and, thus, cost. Intrathecal and epidural techniques produce reliable analgesia in patients undergoing surgery along with stress response attenuation. **The present study was undertaken to evaluate the efficacy of caudal sufentanil and bupivacaine combination on perioperative stress response in paediatric patients undergoing open heart surgery.** Thirty patients (ASA grade II-III) undergoing elective corrective cardiac surgery for acyanotic congenital heart disease, were randomly allocated to two groups. In group GA (n = 15), patients received balanced general anaesthesia. In group GC (n = 15), in addition to general anaesthesia, caudal block with bupivacaine and sufentanil combination was given after endotracheal intubation. Monitoring included electrocardiography, invasive arterial pressure, end-tidal carbon dioxide, pulse oximetry, arterial blood gases including serum electrolytes, blood glucose, serum cortisol, urine output, central venous pressure and temperature. Haemodynamic responses in both groups were statistically similar. Serum cortisol levels were significantly lower in GC group than GA group (P < 0.05) after sternotomy (9.8+/-7.5 vs. 34.74+/-27.35), on cardiopulmonary bypass (CPB) (12.17 +/- 6.2 vs. 35.36 +/- 24.15), after sternal closure (14.03 +/- 5.1 vs. 37.62 +/- 20.69), 4 hours (26.64 +/- 14.61 vs. 37.62 +/- 9.13) and 24 hours (14.30 +/- 8.11 vs. 28.12 +/- 16.31) after intubation. Blood glucose levels were significantly higher in GA group as compared to GC group at sternal closure (277.46 +/- 77.25 vs. 197.73 +/- 42.17) and 4 hours (255.26 +/- 73.73 vs. 185.26 +/- 57.41) after intubation (P < 0.05). To conclude, supplementation of caudal epidural bupivacaine and sufentanil could effectively attenuate the stress response in paediatric patients undergoing cardiac surgery under CPB in acyanotic congenital heart anomaly.

[Pediatr Crit Care Med](#). 2008 Sep;9(5):484-9.

A prospective, randomized, controlled trial of noninvasive ventilation in pediatric acute respiratory failure.

[Yañez LJ](#), [Yunge M](#), [Emilfork M](#), [Lapadula M](#), [Alcántara A](#), [Fernández C](#), [Lozano J](#), [Contreras M](#), [Conto L](#), [Arevalo C](#), [Gayan A](#), [Hernández F](#), [Pedraza M](#), [Feddersen M](#), [Bejares M](#), [Morales M](#), [Mallea F](#), [Glasinovic M](#), [Cavada G](#).

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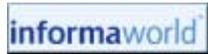
OUTCOMES: To compare the benefits of noninvasive ventilation (NIV) plus standard therapy vs. standard therapy alone in children with acute respiratory failure; assess method effectiveness in improving gas exchange and vital signs; and assess method safety. **DESIGN:** Prospective, randomized, controlled study. **SITE:** Two pediatric intensive care units in Santiago, Chile, at Clínica Santa María and Clínica Dávila, respectively. **PATIENTS AND METHODS:** Fifty patients with acute respiratory failure admitted to pediatric intensive care units were recruited; 25 patients were randomly allocated to noninvasive inspiratory positive airway pressure and expiratory positive airway pressure plus standard therapy (study group); the remaining 25 were given standard therapy (control group). Both groups were comparable in demographic terms. **INTERVENTIONS AND MEASUREMENTS:** **The study group received NIV under inspiratory positive airway pressure ranging between 12 cm and 18 cm H₂O and expiratory positive airway pressure between 6 cm and 12 cm H₂O.** Vital signs (cardiac and respiratory frequency), Po₂, Pco₂, pH, and Po₂/Fio₂ were recorded at the start and 1, 6, 12, 24, and 48 hrs into the study. **RESULTS:** Heart rate and respiratory rate improved significantly with NIV. Heart rate and respiratory rate were significantly lower after 1 hr of treatment compared with admission ($p = 0.0009$ and $p = 0.004$, respectively). The trend continued over time, heart rate being significantly lower than control after the first hour and heart rate after 6 hrs. With NIV, Po₂/Fio₂ improved significantly from the first hour. **The endotracheal intubation was significantly lower (28%) in the NIV group than in the control group (60%; $p = 0.045$).** **CONCLUSIONS:** **NIV improves hypoxemia and the signs and symptoms of acute respiratory failure.** NIV seems to afford these patients protection from endotracheal intubation.

Comment

This study provides a useful experience of the value of non-invasive ventilation, suggesting that early initiation of NIV may reduce the need for endotracheal intubation and mechanical ventilation. The method of NIV in this study were conventional ventilators and BIPAP machines, but in settings where endotracheal intubation is not possible and mechanical ventilators are unavailable, there are many new methods of providing positive end expiratory pressure. These include bubble-CPAP and humidified "high-flow" air-oxygen mix through nasal prongs.

Asthma

[J Asthma](#). 2009 Mar;46(2):156-9.



Effect of desloratadine on patients with allergic rhinitis and exercise-induced bronchoconstriction: a placebo controlled study.

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BACKGROUND: Exercise induced broncho-constriction (EIB) is a significant problem in asthmatic patients. The link between allergic rhinitis and asthma is now well established. Patients with allergic rhinitis may have EIB. **OBJECTIVE: This study compared the effects of desloratadine and placebo on EIB in a group of patients with allergic rhinitis and EIB.** **METHODS:** This was a double blind placebo controlled, randomized, crossover study. Exercise challenge tests were performed before and after 7 days of treatment with either 5 mg desloratadine or placebo. Patients then underwent a washout period for 7 days and were crossed over to receive either 5mg desloratadine or placebo. The exercise challenge tests were repeated. **RESULTS:** Desloratadine had no effect on the reduction in percentage fall in FEV(1), the AUC (0-60 min) and the time to recovery. **CONCLUSIONS: Desloratadine has no effect in attenuating the broncho-constriction caused by exercise in patients with allergic rhinitis and exercise induced broncho-constriction.** **CLINICAL IMPLICATIONS:** Patients with allergic rhinitis and exercise induced broncho-constriction must be treated with either a beta(2)-agonist or LRTA for relief or prophylaxis of their EIB. **CAPSULE SUMMARY: Desloratadine does not have an effect on exercise induced bronchoconstriction. Patients with allergic rhinitis with exercise induced bronchoconstriction who are on desloratadine will still require treatment with beta(2) agonist or leukotriene receptor antagonist for their symptoms.**

[Allergol Immunopathol \(Madr\)](#). 2008 Jul-Aug;36(4):196-200.

Equivalence of a single saline nebulised dose of formoterol powder vs three doses of nebulised Albuterol every twenty minutes in acute asthma in children: a suitable cost effective approach for developing nations.

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BACKGROUND: An increase in asthma prevalence is reported from developed as well as developing nations, with rising costs from acute asthma and great expenditures to health care systems. Venezuela's Ministry of Health ambulatory facilities care for 80 % or more of a mostly urban and impoverished population of 26 million inhabitants, registering close to a million acute asthma visits per year; a nebulised fixed fenoterol-ipratropium bromide combination (Bero-dual, Boehringer-Ingelheim) in repeated dosing is the standard treatment. **OBJECTIVES:** to simplify acute asthma care and management in a cost effective manner employing Formoterol Fumarate powder, a long acting beta agonist with immediate bronchodilator effects. **METHODOLOGY: Fifty acute asthmatic children (5-12 years old) were randomly assigned (25 patients in**

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each group) to receive either a nebulised single dose (US \$1.35) of two 12 microg Formoterol Fumarate capsules (Foradil 12 microg/cap, Novartis Pharma AG, Basel, Switzerland) diluted in 2.5 ml of sterile saline solution; or 3 doses of Albuterol (US \$ 6.73) every twenty minutes for one hour (Glaxo Smith Kline Albuterol ampoules, 2.5 mg/2.5 ml, at a dose of 0.15 mg/kg/dose, maximum dose 2.5 mg). Symptoms score, oxygen saturation and lung function testing were recorded before and one hour after commencing treatments. RESULTS: Both groups improved significantly on all parameters, except for FEV(1) in the Albuterol group. CONCLUSIONS: **Single dose nebulised Formoterol Fumarate (dry powder) in sterile saline solution, as depicted in this trial, is equivalent to three doses of Albuterol every twenty minutes for one hour in acute asthma in children, simplifying acute care management and at one fifth of medication costs.** A pursuit of simpler and more cost effective approaches is found wanting in developing nations with depressed economies and unique cultural and socio-medical contexts; also, in countries where pharmaco-economics orients quality of health policies, novel approaches like this are worth exploring.

[Allergy](#). 2008 Jul;63(7):932-8.



Stability of asthma control with regular treatment: an analysis of the Gaining Optimal Asthma control (GOAL) study.

[Bateman ED](#), [Bousquet J](#), [Busse WW](#), [Clark TJ](#), [Gul N](#), [Gibbs M](#), [Pedersen S](#); [GOAL Steering Committee and Investigators](#).

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BACKGROUND: Uncontrolled asthma is characterized by variability. Current asthma guidelines recommend focussing on the achievement and maintenance of control but few studies have examined in detail, using composite measures of control, the stability and potential duration of control once achieved. In this post-hoc analysis of the results of the Gaining Optimal Asthma control (GOAL) study, we examine the association between the level of asthma control achieved during the step-up phase of the study and the stability of control experienced during the maintenance phase. METHODS: **GOAL was a 1-year, randomized, stratified, double-blind study of 3421 patients with uncontrolled asthma, which compared salmeterol/fluticasone propionate combination with fluticasone propionate in achieving two composite, guideline-based measures of control: totally controlled and well-controlled asthma.** We analysed the proportion and duration of time spent in control, the effect of treatment on asthma stability, and the impact of asthma control stability on unscheduled use of healthcare resources. RESULTS: In patients achieving well-controlled or totally controlled asthma, at least well-controlled asthma was maintained for a median of almost 3 and 6 months, and for more than 85% and 95% of weeks of follow-up, respectively. A high level of stability was confirmed in a Markov analysis investigating transitional probability of change in control status. Variability in control was associated with increased probability of an unscheduled healthcare resource use (odds ratio: 1.06, $P < 0.001$). CONCLUSIONS: **Most patients achieving guideline-defined control can maintain at least a similar level of control with regular, stable dosing, with little likelihood of losing control.**

Cardiology

(see also Neonatal Care)

[Eur J Cardiothorac Surg.](#) 2009 Mar;35(3):505-10. Epub 2009 Feb 1.

Neuropsychological function in children with cyanotic heart disease undergoing corrective cardiac surgery: effect of two different rewarming strategies.

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OBJECTIVE: Hypothermia conventionally used in cardiopulmonary bypass necessitates rewarming to normothermic temperatures, which has been shown to be associated with neuropsychological injury. We studied the effects of two different rewarming strategies on postoperative neuropsychological function in cyanotic paediatric patients undergoing elective primary intracardiac repair of tetralogy of Fallot with the aid of cardiopulmonary bypass. **METHODS:** This was a randomised clinical study undertaken in the cardiothoracic centre of a tertiary level referral and teaching hospital. **Eighty children, aged 6-15 years undergoing elective primary intracardiac repair of tetralogy of Fallot using cardiopulmonary bypass under moderate hypothermia at 28 degrees C were included in this study. The patients were randomly allocated into two groups of 40 each. Group 1 patients were rewarmed to a nasopharyngeal temperature of 33 degrees C while group 2 patients were rewarmed to a nasopharyngeal temperature of 37 degrees C before weaning them off cardiopulmonary bypass.** The anaesthetic and bypass management was standardised for both the groups. All patients were assessed for neuropsychological function preoperatively and on the fifth postoperative day using the MISIC tests. The amount of blood loss and need for blood and blood product transfusion postoperatively, need for pacing, increased inotropes or vasodilator use and time to extubation were also noted. Serum s-100beta levels were measured post anaesthetic induction and at 24h postoperatively. **RESULTS: There was a significant deterioration in neuropsychological function postoperatively in the patients in group 2 (37 degrees C) as compared to their preoperative function.** This was associated with higher s-100beta levels 24h postoperatively in group 2 (37 degrees C) compared to group 1 (33 degrees C) patients. The time to extubation was longer in group 1 (33 degrees C). No significant differences were noted in the amount of postoperative blood loss, blood and blood product use, inotrope or vasodilator use and the need for pacing. **CONCLUSION: Weaning off bypass at 33 degrees C is associated with lesser postoperative neuropsychological dysfunction compared to rewarming to 37 degrees C before weaning off bypass. This may be used as a tool to decrease neurologic morbidity following cardiac surgery in children with congenital cyanotic heart disease.**

Development and mental health

[Indian Pediatr.](#) 2009 Jan;46 Suppl:s20-6.

Effect of Child Development Centre model early stimulation among at risk babies--a randomized controlled trial.

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OBJECTIVE: To study the effectiveness of Child Development Centre (CDC) model early stimulation therapy done in the first year of postnatal life, in improving the developmental outcome of at-risk neonates at one and two years of age. **DESIGN:** Randomized controlled trial. **SETTING AND SUBJECTS:** The study participants included a consecutive sample of 800 babies discharged alive from the level II nursery of Medical College, Thiruvananthapuram. **INTERVENTION:** **The control group received routine postnatal check-up as per hospital practice. Intervention group in addition received CDC model early stimulation therapy (home-based).** **RESULTS:** The intervention group of babies had a statistically significant higher score for mental developmental index (MDI) and psychomotor developmental index (PDI) at one and two years of age. After adjusting all significant risk factors for development, the babies who had intervention had significantly higher Bayley scores, 5.8 units at one year and 2.8 units at two year, as compared to control babies. **CONCLUSION:** Early stimulation therapy was effective at one year. The beneficial effect also persisted at two years, without any additional interventions in the second year.

[BMJ.](#) 2009 Apr 14;338:b974. doi: 10.1136/bmj.b974.



Improving quality of mother-infant relationship and infant attachment in socioeconomically deprived community in South Africa: randomised controlled trial.

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OBJECTIVE: To assess the efficacy of an intervention designed to improve the mother-infant relationship and security of infant attachment in a South African peri-urban settlement with marked adverse socioeconomic circumstances. **DESIGN:** Randomised controlled trial. **SETTING:** Khayelitsha, a peri-urban settlement in South Africa. **PARTICIPANTS:** 449 pregnant women. **INTERVENTIONS:** The intervention was delivered from late pregnancy and for six months postpartum. **Women were visited in their homes by previously untrained lay community workers who provided support and guidance in parenting. The purpose of the intervention was to promote sensitive and responsive parenting and secure infant**

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attachment to the mother. Women in the control group received no therapeutic input from the research team. MAIN OUTCOME MEASURES: Primary outcomes: quality of mother-infant interactions at six and 12 months postpartum; infant attachment security at 18 months. Secondary outcome: maternal depression at six and 12 months. RESULTS: The intervention was associated with significant benefit to the mother-infant relationship. **At both six and 12 months, compared with control mothers, mothers in the intervention group were significantly more sensitive (6 months: mean difference=0.77 (SD 0.37), $t=2.10$, $P<0.05$, $d=0.24$; 12 months: mean difference=0.42 (0.18), $t=-2.04$, $P<0.05$, $d=0.26$) and less intrusive (6 months: mean difference=0.68 (0.36), $t=2.28$, $P<0.05$, $d=0.26$; 12 months: mean difference=-1.76 (0.86), $t=2.28$, $P<0.05$, $d=0.24$) in their interactions with their infants. The intervention was also associated with a higher rate of secure infant attachments at 18 months (116/156 (74%) v 102/162 (63%); Wald=4.74, odds ratio=1.70, $P<0.05$).** Although the prevalence of maternal depressive disorder was not significantly reduced, the intervention had a benefit in terms of maternal depressed mood at six months ($z=2.05$, $P=0.04$) on the Edinburgh postnatal depression scale). CONCLUSIONS: **The intervention, delivered by local lay women, had a significant positive impact on the quality of the mother-infant relationship and on security of infant attachment, factors known to predict favourable child development.** If these effects persist, and if they are replicated, this intervention holds considerable promise for use in the developing world. TRIAL REGISTRATION: Current Controlled Trials ISRCTN25664149.

[J Pediatr.](#) 2009 Apr;154(4):546-50. Epub 2009 Feb 20.

Influence of adapted environment on the anxiety of medically treated children with developmental disability.

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OBJECTIVES: To examine the influence of a sensory adapted environment (SAE) on the behavior and arousal levels of children with developmental disability in comparison with typical children, during a stress-provoking medical situation. STUDY DESIGN: Sixteen children (6-11 years old) with developmental disability and 19 age-matched typical children participated in a cross-over trial measuring behavioral and psychophysiological variables, performed during a dental intervention. RESULTS: Both groups performed better in the SAE compared with the regular environment (RE), by comparing: the mean duration of anxious behaviors in the SAE and RE (5.26 and 13.56 minutes; $P \leq .001$); the mean electrodermal activity for arousal levels, before commencement of treatment in the SAE and RE (784 and 349 Kohms; $P= .002$); and the mean electrodermal activity during treatment in the SAE and RE (830 and 588 Kohms; $P= .001$). A significant group by environment interaction was revealed, indicating that the difference in the 2 environments was greater in children with developmental disability than typical children in all 3 measures. CONCLUSIONS: **These findings indicate the importance of environment in determining the comfort level of all children.** The greater difference in the 2 environments observed in children with developmental disability suggests that this group benefits more from sensory adapted environments.

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[J Trop Pediatr.](#) 2009 Apr;55(2):116-21. Epub 2009 Feb 8.



Randomised controlled study-efficacy of clonidine versus carbamazepine in children with ADHD.

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BACKGROUND: Attention deficit hyperactivity disorder (ADHD) is one of the most common childhood psychiatric disorder with a prevalence of 8-12%. **Even though psychostimulants remain the treatment of choice, its cost and availability in developing countries limits the usage of the drug.** In view of free availability and low cost, a Randomized controlled study was carried out using two second line drugs (clonidine and carbamazepine) in a tertiary care hospital, Pondicherry, South India. **OBJECTIVE: To compare the efficacy of clonidine and carbamazepine in children with ADHD.** **METHOD:** With approval of ethics committee, a prospective, Double-blind, Randomized controlled study of clonidine and carbamazepine was conducted with 50 children with ADHD (age group 4-12 years), over a period of 2 years (2005-07) in a tertiary care hospital, Pondicherry, South India. **RESULTS: Clonidine was effective in improving the hyperactivity and impulsivity symptoms in children with ADHD as compared to carbamazepine. Statistical significant improvement was not noted with respect to inattention symptoms and other comorbid conditions.** **CONCLUSION:** Clonidine can be a safer and cheaper alternative in treatment of children with ADHD, with a predominant effect on their hyperactivity and impulsivity symptoms.

Comment

There are dangers with clonidine use in children, particularly the risk of overdose: associated with bradycardia, hypotension and unconsciousness: [J Paediatr Child Health.](#) 1998 Dec;34(6):508-12; [J Paediatr Child Health.](#) 1998 Jun;34(3):280-2.

[JAMA.](#) 2008 Aug 13;300(6):655-62.



School-based mental health intervention for children affected by political violence in Indonesia: a cluster randomized trial.

[Tol WA](#), [Komproe IH](#), [Susanty D](#), [Jordans MJ](#), [Macy RD](#), [De Jong JT](#).

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CONTEXT: Little is known about the efficacy of mental health interventions for children exposed to armed conflicts in low- and middle-income settings. Childhood mental health problems are difficult to address in situations of ongoing poverty and political instability.

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OBJECTIVE: To assess the efficacy of a school-based intervention designed for conflict-exposed children, implemented in a low-income setting. **DESIGN, SETTING, AND PARTICIPANTS:** A cluster randomized trial involving 495 children (81.4% inclusion rate) who were a mean (SD) age of 9.9 (1.3) years, were attending randomly selected schools in political violence-affected communities in Poso, Indonesia, and were screened for exposure (> or = 1 events), posttraumatic stress disorder, and anxiety symptoms compared with a wait-listed control group. Nonblinded assessment took place before, 1 week after, and 6 months after treatment between March and December 2006. **INTERVENTION:** Fifteen sessions, over 5 weeks, of a manualized, school-based group intervention, including trauma-processing activities, cooperative play, and creative-expressive elements, implemented by locally trained paraprofessionals. **MAIN OUTCOME MEASURES:** We assessed psychiatric symptoms using the Child Posttraumatic Stress Scale, Depression Self-Rating Scale, the Self-Report for Anxiety Related Disorders 5-item version, and the Children's Hope Scale, and assessed function impairment as treatment outcomes using standardized symptom checklists and locally developed rating scales. **RESULTS:** **Correcting for clustering of participants within schools, we found significantly more improvement in posttraumatic stress disorder symptoms (mean change difference, 2.78; 95% confidence interval [CI], 1.02 to 4.53) and maintained hope (mean change difference, -2.21; 95% CI, -3.52 to -0.91) in the treatment group than in the wait-listed group.** Changes in traumatic idioms (stress-related physical symptoms) (mean change difference, 0.50; 95% CI, -0.12 to 1.11), depressive symptoms (mean change difference, 0.70; 95% CI, -0.08 to 1.49), anxiety (mean change difference, 0.12; 95% CI, -0.31 to 0.56), and functioning (mean change difference, 0.52; 95% CI, -0.43 to 1.46) were not different between the treatment and wait-listed groups. **CONCLUSIONS:** **In this study of children in violence-affected communities, a school-based intervention reduced posttraumatic stress symptoms and helped maintain hope, but did not reduce traumatic-stress related symptoms, depressive symptoms, anxiety symptoms, or functional impairment.** **TRIAL REGISTRATION:** isrctn.org Identifier: ISRCTN25172408.

Diarrhoea

(see also Zinc)

Water purification

[Am J Trop Med Hyg.](#) 2008 Nov;79(5):696-701.



Use of ceramic water filtration in the prevention of diarrheal disease: a randomized controlled trial in rural South Africa and zimbabwe.

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To determine the effectiveness of ceramic filters in reducing diarrhea, we conducted a randomized controlled trial in Zimbabwe and South Africa, in which **61 of 115 households received ceramic filters. Incidence of non-bloody and bloody diarrhea was recorded daily over 6 months using pictorial diaries for children 24-36 months of age.** Poisson regression

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was used to compare incidence rates in intervention and control households. **Adjusted for source quality, intervention household drinking water showed reduced Escherichia coli counts (relative risk, 0.67; 95% CI, 0.50-0.89). Zero E. coli were obtained for drinking water in 56.9% of intervention households. The incidence rate ratio for bloody diarrhea was 0.20 (95% CI, 0.09-0.43; P < 0.001) and for non-bloody diarrhea was 0.17 (95% CI, 0.08-0.38; P < 0.001), indicating much lower diarrhea incidence among filter users.** The results suggest that ceramic filters are effective in reducing diarrheal disease incidence.

[Am J Trop Med Hyg.](#) 2008 Sep;79(3):394-400.



Local drinking water filters reduce diarrheal disease in Cambodia: a randomized, controlled trial of the ceramic water purifier.

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A randomized, controlled intervention trial of two household-scale drinking water filters was conducted in a rural village in Cambodia. After collecting four weeks of baseline data on household water quality, diarrheal disease, and other data related to water use and handling practices, households were randomly assigned to one of three groups of 60 households: those receiving a ceramic water purifier (CWP), those receiving a second filter employing an iron-rich ceramic (CWP-Fe), and a control group receiving no intervention. Households were followed for 18 weeks post-baseline with biweekly follow-up. **Households using either filter reported significantly less diarrheal disease during the study compared with a control group of households without filters as indicated by longitudinal prevalence ratios CWP: 0.51 (95% confidence interval [CI]: 0.41-0.63); CWP-Fe: 0.58 (95% CI: 0.47-0.71)**, an effect that was observed in all age groups and both sexes after controlling for clustering within households and within individuals over time.

Comment

The above 2 studies, involving households in South Africa, Zimbabwe and Cambodia add to the evidence of effectiveness of ceramic water purifiers from RCTs in recent years. These studies consistently show that ceramic water purifiers result in much lower risk of exposure to water borne enteric pathogens and are associated with substantial reductions in diarrhoea and dysentery.

Probiotics

[J Clin Gastroenterol.](#) 2008 Sep;42 Suppl 3 Pt 1:S126-9.

Use of VSL[sharp]3 in the treatment of rotavirus diarrhea in children: preliminary results.

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We conducted a double-blind randomized placebo-controlled study to evaluate efficacy and tolerability of VSL[sharp]3 (CD Pharma India) in the treatment of acute rotavirus diarrhea in children. The patients were randomly assigned to receive **4 days of oral treatment with VSL[sharp]3 probiotic mixture or placebo in addition to usual care for diarrhea.**

RESULTS: Out of 230 rotavirus-positive acute diarrhea children, 224 children completed the study, (113 in the drug group and 111 in the placebo group). At recruitment on Day 1, there were no significant differences between the 2 groups in terms of frequency of vomiting, mean loose stool frequency, stool consistency, and mean frequency of oral rehydration salts (ORS) and intravenous fluids administered. On Day 2, a lower mean stool frequency and improved stool consistency was noted in the drug group, which achieved statistical significance. This was also reflected in the lower volume of ORS administration in the drug group. Even on Day 3, mean loose stool frequency and frequency of ORS use and frequency of intravenous fluid use was significantly lower in the drug group. **The differences in the frequency of loose stools persisted till 8 hours of Day 4.** After this, as the placebo group also showed spontaneous improvement the difference between the 2 groups in terms of the overall stools frequency became comparable. However, the overall ORS requirement continued to be significantly lower in the drug group even on Day 4. The overall recovery rates were significantly better in the drug group compared with placebo. No side effects were noted with the use of the probiotic mixture. **Use of probiotic mixture VSL[sharp]3 in acute rotavirus diarrhea resulted in earlier recovery and reduced frequency of ORS administration reflecting decreased stool volume losses during diarrhea.**

[J Clin Gastroenterol.](#) 2008 Sep 22. [Epub ahead of print]

Efficacy of High-dose Lactobacillus rhamnosus GG in Controlling Acute Watery Diarrhea in Indian Children: A Randomized Controlled Trial.

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AIM: To evaluate the effective dose of Lactobacillus rhamnosus GG (LGG) as probiotic in acute watery diarrhea (AWD) in Indian children. **SETTING:** Hospital-based study. **DESIGN:** Randomized, controlled, blinded trial. **METHODS:** All patients of AWD admitted over 1 year were included in the study. **They were randomized into 3 groups to receive either only oral rehydration solution (ORS) (group A/control), ORS+LGG powder containing 10 colony forming units (CFU) (group B), or ORS+LGG powder containing 10 CFU (group C) twice daily for a minimum period of 7 days or until diarrhea stopped along with correction of dehydration.** None of them received any other drug such as antibiotic or antidiarrheal

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medication. The duration and frequency of diarrhea and vomiting were studied. Data were analyzed by SPSS-10 software. RESULTS: The study comprised of 559 patients, group A/controls (n=185), group B (n=188), and group C (n=186). All the groups were similar with respect to age, number of breastfed infants, presentation with dehydration, degree of protein energy malnutrition, and rotavirus infection. **The frequency and duration of diarrhea, requirement for intravenous therapy, and hospital stay were significantly lower in both the intervention groups compared with the controls.** There was no significant difference between the 2 intervention groups. No complication was observed from the doses of LGG used. CONCLUSIONS: Both the doses of LGG (10 and 10 CFU) were equally effective to decrease the frequency and duration of diarrhea and reduction in hospital stay in patients of AWD.

[Indian J Pediatr.](#) 2008 Jul;75(7):709-13. Epub 2008 Aug 21.

Randomized double blinded controlled trial to evaluate the efficacy and safety of Bifilac in patients with acute viral diarrhea.

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OBJECTIVE: To evaluate the efficacy and safety of Bifilac on reducing the episodes (frequency) and duration of diarrhea induced by rotaviral infection and to evaluate the efficacy of Bifilac to ameliorate the associated symptoms like dehydration and duration of rotaviral shedding in faeces. METHODS: 80 children aged between 3 months and 3 years were enrolled and divided into 2 groups, one group received standard therapy + placebo, the other group received standard therapy + probiotic (Bifilac) randomly. Children assessed for frequency and duration of diarrhea. Degree of dehydration, duration and volume of oral rehydration salt [ORS] therapy, duration and volume of Intra venous fluids and duration of rotaviral shedding. RESULTS: When compared to the placebo, Bifilac showed clinical as well as statistically significant reduction in Number of episodes (frequency) of diarrhea in a day, mean duration of diarrhea (in days) degree of dehydration, duration and volume of oral rehydration salt [ORS] therapy, duration and volume of intravenous fluid [IVF] therapy, duration of rotaviral shedding ($P<0.01$). CONCLUSION: The synbiotic, bifilac, appears to be a safe and very effective adjuvant in the management of acute rotaviral diarrhea.

Other adjuvative treatments

[BMC Infect Dis.](#) 2009 Mar 3;9:24.



Antimicrobial drugs for persistent diarrhoea of unknown or non-specific cause in children under six in low and middle income countries: systematic review of randomized controlled trials.

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BACKGROUND: A high proportion of children with persistent diarrhoea in middle and low income countries die. The best treatment is not clear. We conducted a systematic review to evaluate the effectiveness of antimicrobial drug treatment for persistent diarrhoea of unknown or non-specific cause. **METHODS:** We included randomized comparisons of antimicrobial drugs for the treatment of persistent diarrhoea of unknown or non-specific cause in children under the age of six years in low and middle income countries. We searched the electronic databases MEDLINE, EMBASE, LILACS, WEB OF SCIENCE, and the Cochrane Central Register of Controlled Trials (CENTRAL) to May 2008 for relevant randomized or quasi randomized controlled trials. We summarised the characteristics of the eligible trials, assessed their quality using standard criteria, and extracted relevant outcomes data. Where appropriate, we combined the results of different trials. **RESULTS: Three trials from South East Asia and one from Guatemala were included, all were small, and three had adequate allocation concealment.** Two were in patients with diarrhoea of unknown cause, and two were in patients in whom known bacterial or parasitological causes of diarrhoea had been excluded. **No difference was demonstrated for oral gentamicin compared with placebo (presence of diarrhoea at 6 or 7 days; 2 trials, n = 151); and for metronidazole compared with placebo (presence of diarrhoea at 3, 5 and 7 days; 1 trial, n = 99). In one small trial, sulphamethoxazole-trimethoprim appeared better than placebo in relation to diarrhoea at seven days and total stool volume (n = 55).** **CONCLUSION: There is little evidence as to whether or not antimicrobials help treat persistent diarrhoea in young children in low and middle income countries.**

[Eur J Clin Nutr.](#) 2009 Jan 28. [Epub ahead of print]



Effect of micronutrient supplementation on diarrhoeal disease among stunted children in rural South Africa.

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Background/Objective:The efficacy of zinc combined with vitamin A or multiple micronutrients in preventing diarrhoea is unclear in African countries with high prevalence of human immunodeficiency virus (HIV)-exposed children. Potential modifying factors, such as stunting, need to be addressed. The objective of this study was to determine whether adding zinc or zinc plus multiple micronutrients to vitamin A reduces diarrhoea incidence, and whether this differs between the strata of stunted or HIV-infected children.**Methods:**We analyzed data from a randomized, controlled, double-blinded trial (ClinicalTrials.gov NCT00156832) of prophylactic micronutrient supplementation to children aged 6-24 months. Three cohorts of children: **32 HIV-infected children, 154 HIV-uninfected children born to HIV-infected mothers and 187 uninfected children born to HIV-uninfected mothers, received vitamin A, vitamin A plus zinc or multiple micronutrients, which included vitamin A and zinc. The main**

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outcome was incidence of diarrhoea. Poisson regression was used in intent-to-treat analyses. Stratified analyses followed testing for statistical interaction between intervention and stunting. Results: **We observed no significant differences in overall diarrhoea incidence among treatment arms. Stunting modified this effect with stunted HIV-uninfected children having significantly lower diarrhoea incidence when supplemented with zinc or multiple micronutrients compared with vitamin A alone (2.04 and 2.23 vs 3.92 episodes/year, respectively, P=0.024).** No meaningful subgroup analyses could be done in the cohort of HIV-infected children. Conclusions: **Compared with vitamin A alone, supplementation with zinc and with zinc and multiple micronutrients, reduced diarrhoea morbidity in stunted rural South African children.** Efficacy of zinc supplementation in HIV-infected children needs confirmation in studies that represent the spectrum of disease severity and age groups. European Journal of Clinical Nutrition advance online publication, 28 January 2009; doi:10.1038/ejcn.2008.78.

[Clin Gastroenterol Hepatol.](#) 2009 Apr;7(4):456-62. Epub 2008 Dec 13.

Oral diosmectite reduces stool output and diarrhea duration in children with acute watery diarrhea.

[Dupont C](#), [Foo JL](#), [Garnier P](#), [Moore N](#), [Mathiex-Fortunet H](#), [Salazar-Lindo E](#); [Peru and Malaysia Diosmectite Study Groups](#). Collaborators (46)

[Quintanilla DF](#), [Echeccaya PH](#), [Rubio CH](#), [Asencio LC](#), [Martinez LA](#), [Valiente VR](#), [Ichiyanagui CH](#), [Acosta IR](#), [Jares MI](#), [Arias JL](#), [Sanchez CC](#), [Ponte HV](#), [Tegashira SG](#), [Ruiz CH](#), [Tirado JC](#), [Woo EC](#), [Saito AM](#), [Raez PC](#), [Foo JL](#), [Abu Bakar RB](#), [Hwang TK](#), [Chern LM](#), [Sithampanathan Y](#), [Nachal N](#), [Theranirajan E](#), [Hong SM](#), [Mahani N](#), [Gaik CL](#), [Ching HK](#), [Rivai AM](#), [Neezam N](#), [Nallusamy R](#), [Kaur J](#), [Kee TK](#), [Cheng WP](#), [Hong NS](#), [bin Muhamad SR](#), [Nyok CC](#), [Kumar S](#), [Abdul Wahab NH](#), [Jamli FM](#), [Lan KG](#), [Hin CE](#), [Yuen NS](#), [Ming CC](#), [Hang NS](#).

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BACKGROUND & AIMS: Diosmectite is a clay used to treat children with acute watery diarrhea. However, its effects on stool output reduction, the key outcome for pediatric antidiarrheal drugs, have not been shown. **METHODS:** Two parallel, double-blind studies of diosmectite efficacy on stool reduction were conducted in children 1 to 36 months old in Peru (n = 300) and Malaysia (n = 302). Inclusion criteria included 3 or more watery stools per day for less than 72 hours and weight/height ratios of 0.8 or greater. Exclusion criteria were the need for intravenous rehydration, gross blood in stools, fever higher than 39 degrees C, or current treatment with antidiarrheal or antibiotic medications. Rotavirus status was determined. **Diosmectite dosage was 6 g/day (children 1-12 months old) or 12 g/day (children 13-36 months old), given for at least 3 days, followed by half doses until complete recovery. Patients were assigned randomly to groups given diosmectite or placebo, in addition to oral rehydration solution (World Health Organization).** **RESULTS:** Children in each study had comparable average ages and weights. The frequencies of rotavirus infection were 22% in Peru and 12% in Malaysia. Similar amounts of oral rehydration solution were given to children in the diosmectite and placebo groups. **Stool output was decreased significantly by diosmectite in both studies, especially among rotavirus-positive children. In pooled data, children had a mean stool output of 94.5 +/- 74.4 g/kg of body weight in the diosmectite group versus 104.1 +/- 94.2 g/kg in the placebo group (P = .002). Diarrhea duration was reduced by diosmectite, which was well tolerated.** **CONCLUSIONS:** These results show that

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diosmectite significantly decreased stool output in children with acute watery diarrhea, especially those who were rotavirus-positive.

Comment

Diosmectite is a purified clay consisting of a double aluminum and magnesium silicate, it has been used in preventing diarrhoea in patients undergoing pelvic irradiation. A previous RCT by the same authors in children in Peru (http://www.accessmylibrary.com/coms2/summary_0286-32147783_ITM) showed similar results as this current trial: a significant improvement with diosmectite was seen for time to recovery of diarrhoea. There there may have been some overlap in the patient groups in these two studies.

Emergency care

[Pediatr Emerg Care](#). 2008 Oct;24(10):647-55.

A prospective randomized controlled study of two fluid regimens in the initial management of septic shock in the emergency department.

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OBJECTIVES: To compare the impact of 40 mL/kg of fluid over 15 minutes followed by dopamine and further titration of therapy to achieve therapeutic goals (study protocol) versus 20 mL/kg over 20 minutes up to a maximum of 60 mL/kg over 1 hour followed by dopamine (control protocol) in septic shock. **DESIGN AND SETTING:** Prospective randomized controlled study in the emergency department of a public hospital in India. **PATIENTS:** One hundred forty-seven children older than 1 month presenting with septic shock were enrolled into the study. **OUTCOME MEASURES:** Hospital mortality (primary outcome), 72-hour survival, achievement of therapeutic goals of shock resolution, incidence of hypoxia, hepatomegaly, intubation at 20, 40, and 60 minutes (secondary outcomes) were compared between the arms. **RESULTS:** Seventy-four and 73 children were assigned to the study and control group, respectively. Overall mortality was 17.6%, 26 deaths with 13 in each arm. Mortality in the study cohort was lower than our historical mortality of 50% ($P < 0.0001$), 95% confidence interval (CI), 11.9-24.8. **Cumulative survival at 72 hours was 72.5% (95% CI, 58.9-86.1) and 77.6% (95% CI, 66.0%-89.2%) in the control and study groups, respectively.** Resolution of shock in the emergency department was associated with survival odds ratio (OR) 9.2 (95% CI, 2.1-40.8). Rapidity of achieving therapeutic goals was not significantly different between groups. Intubation rates were also the same (46.5% in the control group versus 55% in the study group; $P = 0.28$). **At 20 minutes, 35.6% of the control group and 70% of the study group had hepatomegaly ($P < 0.01$).** **CONCLUSION:** There was no difference in the overall mortality, rapidity of shock resolution, or incidence of complications between the groups. The occurrence of hepatomegaly at 20 minutes following 40 mL/kg is of concern in settings with limited access to post-resuscitation ventilator care.

[Pediatr Crit Care Med.](#) 2009 Jan;10(1):121-5.

Low-dose hydrocortisone in pediatric septic shock: an exploratory study in a third world setting.

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OBJECTIVE: To study the efficacy of low-dose intravenous hydrocortisone therapy in the management of pediatric septic shock with respect to the time taken for shock reversal and requirement of inotropes. **DESIGN:** Open label randomized pilot study. **SETTING:** Pediatric intensive care unit of a tertiary care pediatric center in a third world country. **PATIENTS:** Thirty-eight children, 2 months-12 yrs of age, with septic shock unresponsive to fluid therapy alone. **INTERVENTION:** **Intravenous hydrocortisone 5 mg/kg/day in four divided doses followed by half the dose for a total duration of 7 days or normal saline (similar amount in a similar manner) for the same duration.** **RESULTS:** There was a trend toward earlier reversal of shock (median 49.5 vs. 70 hrs, $p = 0.65$, Mann-Whitney U test) and lower inotropes requirement (median [10th-90th centile] inotropes score: 20 [15-60] vs. 50 [20-80], $p = 0.15$) in the hydrocortisone-treated patients as compared with controls, although the difference was not statistically significant. **Mortality rate was similar in both groups.** **CONCLUSIONS:** Our data, although, inconclusive favor the need for a study with a larger sample size to clearly define role of low-dose hydrocortisone in pediatric septic shock in developing countries, while taking in consideration effect of malnutrition, delayed presentations, and their interactions with the hypothalamic-pituitary-adrenocortical axis.

[Malar J.](#) 2008 Nov 23;7:242.



Sublingual sugar for hypoglycaemia in children with severe malaria: a pilot clinical study.

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BACKGROUND: Hypoglycaemia is a poor prognostic indicator in severe malaria. Intravenous infusions are rarely feasible in rural areas. The efficacy of sublingual sugar (SLS) was assessed in a pilot randomized controlled trial among hypoglycaemic children with severe malaria in Mali. **METHODS:** Of 151 patients with presumed severe malaria, **23 children with blood glucose concentrations < 60 mg/dl (< 3.3 mmol/l) were assigned randomly to receive either intravenous 10% glucose (IVG; n = 9) or sublingual sugar (SLS; n = 14).** In SLS, a teaspoon of sugar, moistened with a few drops of water, was gently placed under the tongue every 20 minutes. The child was put in the recovery position. Blood glucose concentration (BGC) was measured every 5-10 minutes for the first hour. All children were treated for malaria with

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intramuscular artemether. The primary outcome measure was treatment response, defined as reaching a BGC of ≥ 3.3 mmol/l (60 mg/dl) within 40 minutes after admission. Secondary outcome measures were early treatment response at 20 minutes, relapse (early and late), maximal BGC gain (CG_{max}), and treatment delay. **RESULTS: There was no significant difference between the groups in the primary outcome measure. Treatment response occurred in 71% and 67% for SLS and IVG, respectively. Among the responders, relapses occurred in 30% on SLS at 40 minutes and in 17% on IVG at 20 minutes.** There was one fatality in each group. Treatment failures in the SLS group were related to children with clenched teeth or swallowing the sugar, whereas in the IVG group, they were due to unavoidable delays in beginning an infusion (median time 17.5 min (range 3-40)). Among SLS, the BGC increase was rapid among the nine patients who really kept the sugar sublingually. All but one increased their BGC by 10 minutes with a mean gain of 44 mg/dl (95%CI: 20.5-63.4). **CONCLUSION: Sublingual sugar appears to be a child-friendly, well-tolerated and effective promising method of raising blood glucose in severely ill children. More frequent repeated doses are needed to prevent relapse.** Children should be monitored for early swallowing which leads to delayed absorption, and in this case another dose of sugar should be given. **Sublingual sugar could be proposed as an immediate "first aid" measure while awaiting intravenous glucose.** In many cases it may avert the need for intravenous glucose.

Comment

This adds to a previous RCT in Burkino Faso by the same authors (Pediatrics. 2005 Nov;116(5):e648-53) of sublingual sugar, showing similar results. Sublingual sugar can be recommended for use in the community and in health centres, and in hospitals when infusions are not available (or until they are put in place) in any child with reduced conscious state. Where children have both severe anaemia requiring transfusion and hypoglycaemia, sublingual sugar carries a lower risk of fluid overload than intravenous glucose, and therefore might be useful even in well resourced settings. Sub-lingual sugar should probably be given wherever IM quinine is used as treatment for severe malaria prior to referral where intravenous therapy is not possible (although recent studies have shown rectal artesunate is a non-IV antimalarial that is highly effective with fewer side effects in the vomiting child).

Epilepsy

[Eur J Paediatr Neurol](#). 2009 Mar 16. [Epub ahead of print]



Lorazepam versus diazepam-phenytoin combination in the treatment of convulsive status epilepticus in children: A randomized controlled trial.

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BACKGROUND: Convulsive status epilepticus demands urgent and appropriate management with anticonvulsants. Intravenous diazepam is an established drug in the management of convulsive status epilepticus in adults as well as in children. The efficacy of intravenous

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lorazepam has not been well established in children. **OBJECTIVE:** To determine whether intravenous lorazepam is as efficacious as diazepam-phenytoin combination in the treatment of convulsive status epilepticus in children. **STUDY DESIGN:** Randomized controlled trial. **METHODS:** A total of 178 children were enrolled in the study; 90 in the lorazepam group and 88 in the diazepam-phenytoin combination group. **Enrolled subjects were between 1 and 12 years with a clinical diagnosis of convulsive status epilepticus, presenting in pediatric emergency of a tertiary care hospital. They were randomized to receive either intravenous lorazepam (0.1mg/kg) or intravenous diazepam (0.2mg/kg)-phenytoin (18mg/kg) combination at admission and were followed up for subsequent 18h.** **RESULTS:** The overall success rate of therapy was 100% in both the groups. There was no statistically significant difference in the two groups (lorazepam versus diazepam-phenytoin combination) in the median time taken to stop the seizure [20s in both groups], the number of subjects requiring more than one dose of the study drug to stop the presenting seizure [lorazepam 6(6.7%) versus diazepam-phenytoin combination: 14 (15.9%); adjusted RR (95% CI)=0.377 (0.377, 1.046); P=0.061] and the number (%) of patients having respiratory depression [lorazepam 4(4.4%) versus diazepam-phenytoin combination 5 (5.6%)]. None of the patients in the two groups required additional anticonvulsant drug to stop the presenting seizure. No patient required mechanical ventilation and none of the patients in the two groups required cross-over to the alternative regimen. **CONCLUSION:** Lorazepam is as efficacious and safe as diazepam-phenytoin combination. We recommend use of lorazepam as a single drug to replace the two drug combination of diazepam-phenytoin combination to control the initial seizure in pediatric convulsive status epilepticus.

[Brain Dev.](#) 2008 Dec 27. [Epub ahead of print]

Efficacy of buccal midazolam compared to intravenous diazepam in controlling convulsions in children: A randomized controlled trial.

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A study was done to examine the efficacy of **buccal midazolam in controlling convulsion in children by comparing it with intravenous diazepam**, a standard mode of treating convulsions. One hundred and twenty cases presenting with convulsions to emergency were treated randomly with either buccal midazolam (in a dose of 0.2mg/kg) or intravenous diazepam (in a dose of 0.3mg/kg). Partial seizures, generalized tonic, clonic and tonic-clonic convulsions were included irrespective of duration or cause. One episode per child only was included. **The frequency of overall control of convulsive episodes within 5min were 85% and 93.3% in buccal midazolam and intravenous diazepam groups, respectively; the difference was, however, not statistically significant (p=0.142).** The mean time needed for controlling the convulsive episodes after administration of the drugs was significantly less with intravenous diazepam (p<0.001). The mean time for initiation of treatment was significantly less with buccal midazolam (p<0.001). The mean time for controlling the convulsive episodes after noticing these first were significantly less with buccal midazolam than with intravenous diazepam (p=0.004) that is likely to be due to longer time needed for initiating treatment with intravenous diazepam in preparing the injection and establishing an IV line. There was no significant side effect in both the groups. **The findings suggest that buccal midazolam can be used as an alternative to intravenous diazepam especially when getting an IV line becomes**

difficult. In situations where establishing an IV line is a problem, buccal midazolam may be the first choice.

Comment

This is another useful study showing the efficacy of treatments that can be used where intravenous therapy is not immediately available. Rectal diazepam is another alternative, which can also be given rapidly and is effective. A trial of buccal midazolam compared with rectal (rather than IV) diazepam might better inform which anticonvulsant (and route) is best to use in resource limited circumstances.

Fever

[Indian Pediatr.](#) 2009 Feb;46(2):133-6.



Comparative effectiveness of tepid sponging and antipyretic drug versus only antipyretic drug in the management of fever among children: a randomized controlled trial.

[Thomas S](#), [Vijaykumar C](#), [Naik R](#), [Moses PD](#), [Antonisamy B](#).

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OBJECTIVE: To compare the effectiveness of tepid sponging and antipyretic drug versus only antipyretic drug among febrile children. **DESIGN:** Randomized controlled trial. **SETTING:** Tertiary care hospital. **PARTICIPANTS:** **150 children 6 mo - 12 yr age with axillary temperature 101F.** **INTERVENTION:** Tepid sponging and antipyretic drug (Paracetamol) (n=73) or only antipyretic drug (Paracetamol) (n=77). **MAIN OUTCOME MEASURES:** Reduction of body temperature and level of comfort. **RESULTS:** **The reduction of body temperature in the tepid sponging and antipyretic drug group was significantly faster than only antipyretic group; however, by the end of 2 hours both groups had reached the same degree of temperature. The children in tepid sponging and antipyretic drug had significantly higher discomfort than only antipyretic group, but the discomfort was mostly mild.** **CONCLUSION:** Apart from the initial rapid temperature reduction, addition of tepid sponging to antipyretic administration does not offer any advantage in ultimate reduction of temperature; moreover it may result in additional discomfort.

Filariasis

[Trans R Soc Trop Med Hyg.](#) 2009 Mar;103(3):274-9. Epub 2008 Dec 9.

A randomised, double-blind field trial of ivermectin alone and in combination with albendazole for the treatment of Mansonella perstans infections in Uganda.

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The effect of a single dose of ivermectin alone (150-200microg/kg body weight) or in combination with albendazole (total of 400mg) in Mansonella perstans infection was assessed in a randomised, double-blind field trial in two endemic communities in Mukono and Luwero districts of Uganda. No side effects were observed or reported during the first 7 days after treatment. The effect on microfilaraemia was analysed among individuals with ≥ 20 microfilariae (mf) per 100mul of blood at baseline, who took the treatment and who attended follow-up examinations at 6 months and 12 months after treatment (48 and 46 in Mukono and 48 and 40 in Luwero for the ivermectin and combination treatment, respectively). **In both communities, the combination treatment appeared slightly more effective than ivermectin alone, but the difference was not statistically significant.** Both drug regimens were more effective in Luwero than in Mukono, probably owing to different diets in the two areas. However, in general both treatment regimens in both communities had limited effect on microfilarial intensities, and only one individual (given combination treatment in Luwero) was mf-negative at 6 months and 12 months after treatment. [ClinicalTrials.gov identifier: NCT00215280].

Gastrointestinal infections and helminths

[BMC Infect Dis.](#) 2009 Feb 19;9:20.



Patterns of soil-transmitted helminth infection and impact of four-monthly albendazole treatments in preschool children from semi-urban communities in Nigeria: a double-blind placebo-controlled randomised trial.

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BACKGROUND: Children aged between one and five years are particularly vulnerable to disease caused by soil-transmitted helminths (STH). Periodic deworming has been shown to improve growth, micronutrient status (iron and vitamin A), and motor and language development in preschool children and justifies the inclusion of this age group in deworming programmes. Our objectives were to describe the prevalence and intensity of STH infection and to investigate the effectiveness of repeated four-monthly albendazole treatments on STH infection in children aged one to four years. **METHODS:** The study was carried out in four semi-urban villages situated near Ile-Ife, Osun State, Nigeria. The study was a double-blind placebo-controlled randomised trial. Children aged one to four years were randomly assigned to receive either albendazole or placebo every four months for 12 months with a follow-up at 14 months. **RESULTS:** The results presented here revealed that 50% of the preschool children in these semi-urban communities were infected by one or more helminths, the most prevalent STH

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being *Ascaris lumbricoides* (47.6%). **Our study demonstrated that repeated four-monthly anthelmintic treatments with albendazole were successful in reducing prevalence and intensity of *A. lumbricoides* infections. At the end of the follow-up period, 12% and 43% of the children were infected with *A. lumbricoides* and mean epg was 117 (S.E. 50) and 1740 (S.E. 291) in the treatment and placebo groups respectively compared to 45% and 45% of the children being infected with *Ascaris* and mean epg being 1095 (S.E. 237) and 1126 (S.E. 182) in the treatment and placebo group respectively at baseline.**

CONCLUSION: Results from this study show that the moderate prevalence and low intensity of STH infection in these preschool children necessitates systematic treatment of the children in child health programmes.

Comment

WHO recommends deworming 2 to 3 times per year in areas where the prevalence of geohelminths exceeds 50% (Savioli L, Montresor A, Gyorkos TW, et al. Helminth control in school-age children. A guide for managers of control programs . Geneva: World Health Organization, 2002). This study supports deworming every 4 months.

[Helicobacter](#). 2008 Dec;13(6):550-6.



Evaluation of two triple-therapy regimens with metronidazole or clarithromycin for the eradication of *H. pylori* infection in Vietnamese children: a randomized, double-blind clinical trial.

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BACKGROUND: Eradication of *Helicobacter pylori* infection in children in developing countries needs further investigations upon which to base treatment recommendations. The aim of the study was to compare two 2-week triple therapies in a randomized double-blind trial. MATERIALS AND METHODS: In order not to exceed recommended dosages, the 238 *H. pylori*-infected children, aged 3 to 15 years (mean 8.6), were divided in two weight categories receiving at weights 13-22 kg: **lansoprazole 15 mg once-daily and amoxicillin 500 mg twice-daily with metronidazole 250 mg twice-daily or clarithromycin 250 mg once-daily**; at weights 23-45 kg: lansoprazole 15 mg and amoxicillin 750 mg with metronidazole 500 mg or clarithromycin 250 mg, all administered twice daily. *H. pylori* status was assessed by culture and a monoclonal-based antigen-in-stool test (Premier Platinum HpSA PLUS) and side effects by structured questionnaires. RESULTS: **The overall per-protocol eradication (n = 233) was similar in the two treatment regimens, 62.1% for the metronidazole and 54.7% for the clarithromycin-containing therapy.** Eradication rate was higher in children \geq 23 kg (70.9%) than in children $<$ 23 kg (45.7%). In children \geq 23 kg (n = 117) that received twice-daily administration of all drugs, efficacy of the metronidazole and clarithromycin-containing treatments were 69.5% and 72.4%, respectively. CONCLUSIONS: The two treatments gave similar eradication rates. Significant differences for both treatments were found by weight,

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which could be the result of the once-daily proton pump inhibitor and clarithromycin and/or more antibiotic resistant strains in younger children.

[Bull World Health Organ.](#) 2008 Oct;86(10):788-95.

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available at [SciELO.org](#)



A randomized, double-blind, placebo-controlled trial of safety and efficacy of combined praziquantel and artemether treatment for acute schistosomiasis japonica in China.

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Hunan Institute of Parasitic Diseases, WHO Collaborating Centre for Research and Control on Schistosomiasis in Lake Region, Yueyang, China.

OBJECTIVE: To evaluate the safety and efficacy of combining artemether (AM) and praziquantel (PZQ) in different regimens for treating acute schistosomiasis japonica.

METHODS: We undertook a randomized, double-blind, placebo-controlled trial within four specialized schistosomiasis hospitals in the Dongting Lake region, Hunan province, China, between May 2003 and December 2005. Study participants were randomized into one of four treatment regimes: **group A received 60 mg/kg PZQ + 6 mg/kg AM; group B received 60 mg/kg PZQ + AM placebo; group C received 120 mg/kg PZQ + 6 mg/kg AM; and group D received 120 mg/kg PZQ + AM placebo.** All participants were followed up over a 45-day period. The primary endpoint of the trial was human infection status (determined by positive stool examination). Secondary endpoints involved clinical observations and blood biochemistry, including monitoring haemoglobin and alanine aminotransferase levels over time. **FINDINGS:** Treatment efficacies of the four different treatment regimens were 98.0%, 96.4%, 97.7% and 95.7% for group A, B, C, and D respectively ($P > 0.05$). The group B had a greater treatment efficacy (96.4%) than the group D (95.7%) ($P > 0.05$). Group A treatment was better for clearance of fever ($P < 0.05$) and resulted in a shorter hospitalization time ($P < 0.05$).

CONCLUSION: This is the first report of a randomized, double-blind, placebo-controlled trial for evaluating combined chemotherapy with AM and two different dosages (60 mg/kg and 120 mg/kg) of PZQ in the treatment of acute schistosomiasis japonica in China. **The combination of AM and PZQ chemotherapy did not improve treatment efficacy compared with PZQ alone.** PZQ given as a dosage of 60 mg/kg (1 day, 3 x 20 mg/kg doses at 4-5 hour intervals) may be as effective as a dosage of 120 mg/kg (6 days, 20 mg/kg for each day split into 3 doses at 4-5 hour intervals).

[Trans R Soc Trop Med Hyg.](#) 2009 Mar;103(3):229-36. Epub 2008 Oct 19.



The effect of iron and multi-micronutrient supplementation on *Ascaris lumbricoides* reinfection among Zambian schoolchildren.

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A randomised, placebo-controlled, double-blind trial was conducted among schoolchildren in Chawama, Lusaka, Zambia, to determine the effect of iron and multi-micronutrients on reinfection with *Ascaris lumbricoides*. Supplementation was given on every school day for 10 months. Baseline *A. lumbricoides* prevalence and geometric mean intensity among positives were 43.4% and 2526 eggs per gram (epg) faeces, respectively. Serum ferritin <12microg/l was associated with higher egg counts than serum ferritin ≥12microg/l (4728 vs. 2036epg, P=0.033). Of 406 children recruited, 378 (93.1%) were examined at baseline and all infected children were treated and cure ascertained. The mean number of tablets taken per week was 2.5, giving 50% compliance. **At six months 283 (74.9%) children complied, and reinfection intensities in those receiving iron were lower than in those receiving placebo (1600 vs. 3085epg, P=0.056).** This effect disappeared at 10 months, where 215 (56.9%) complied. Iron had no effect on *A. lumbricoides* reinfection rates and multi-micronutrients had no effect on reinfection rates or intensities. Iron appears to affect reinfection intensity with *A. lumbricoides*, but further investigations are required to confirm this effect and elucidate the mechanisms involved.

HIV / AIDS

[Soc Sci Med.](#) 2009 Mar;68(6):1038-43. Epub 2009 Jan 21.

Peer-group support intervention improves the psychosocial well-being of AIDS orphans: cluster randomized trial.

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Accumulating evidence suggests that AIDS orphanhood status is accompanied by increased levels of psychological distress such as anxiety, depression, intense guilt, shame, and anger. However, few studies have examined the possible reduction of psychological distress in AIDS orphans through the help of interventions that promote well-being. The objective of the study was to evaluate the effects of a school-based peer-group support intervention combined with periodic somatic health assessments and treatment on the psychosocial well-being of AIDS orphans in the Mbarara District of southwestern Uganda. In a cluster randomized controlled design, 326 AIDS orphans aged 10-15 years were assigned to either peer-group support intervention combined with monthly somatic healthcare (n=159) or control group (n=167) for follow-up assessment. Baseline and 10 week follow-up psychological assessments were conducted in both groups using self-administered Beck Youth Inventories. Complete data were available for 298 orphans. After adjusting for baseline scores, follow-up scores for the intervention group in comparison with controls showed significant improvement in depression, anger, and anxiety but not for self-concept. This study demonstrated that peer-group support intervention decreased psychological distress, particularly symptoms of depression, anxiety and

anger. Thus, the use of peer-group support interventions should be incorporated into existing school health programs.

Clinical management and anti-retroviral therapy

(see also Vaccines, Pneumococcal vaccine and Diarrhoea)

*** [N Engl J Med](#). 2008 Nov 20;359(21):2233-44.



Early antiretroviral therapy and mortality among HIV-infected infants.

[Violari A](#), [Cotton MF](#), [Gibb DM](#), [Babiker AG](#), [Steyn J](#), [Madhi SA](#), [Jean-Philippe P](#), [McIntyre JA](#); [CHER Study Team](#).

[Violari A](#), [McIntyre J](#), [Pelser W](#), [Steyn J](#), [Madhi S](#), [Naeem-Sheik A](#), [Budge M](#), [Saleh M](#), [Cassimjee S](#), [Lazarus E](#), [Mashinini S](#), [Dlamini S](#), [Kemese V](#), [Bolton J](#), [Cotton MF](#), [Rabie H](#), [van Rensburg AJ](#), [Dobbels E](#), [Fourie G](#), [Bester M](#), [Orange W](#), [Arendze R](#), [Andrea C](#), [Smuts M](#), [Smith K](#), [Louw T](#), [Abrahams A](#), [Kelly K](#), [Bohle A](#), [Mong I](#), [Howard J](#), [Cyster T](#), [Solomon G](#), [Benjamin G](#), [Mkalipi J](#), [Barnes E](#), [Sanne I](#), [Gray G](#), [Panchia R](#), [Davies C](#), [Cornell M](#), [Stevens W](#), [Glencross D](#), [Spector S](#), [van der Horst C](#), [Babiker AG](#), [Gibb DM](#), [Steens JM](#), [Snowden WX](#), [Thoofer N](#), [Loeliger E](#), [Handelsman E](#), [Reese K](#), [Jean-Phillipe P](#), [Nadler J](#), [McNamara J](#), [Hoff R](#), [Lehrman S](#), [Oster C](#), [Peto T](#), [Levin L](#), [Gibb D](#), [Ellenberg S](#), [DerSimonian R](#), [Dodoo A](#), [Harrington D](#), [Kamali A](#), [Katabira E](#), [Lombard C](#), [Luo C](#), [Marshall MF](#), [Mokgathe L](#), [Mwinga A](#), [Nunn A](#), [Saloojee H](#), [Sande M](#), [Schoeman J](#), [Singh J](#), [Boss-Victoria R](#), [Chipato T](#), [Emerson S](#), [Mfutso-Bengo J](#), [Mwaba P](#).

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BACKGROUND: In countries with a high seroprevalence of human immunodeficiency virus type 1 (HIV-1), HIV infection contributes significantly to infant mortality. We investigated antiretroviral-treatment strategies in the Children with HIV Early Antiretroviral Therapy (CHER) trial. **METHODS:** HIV-infected infants 6 to 12 weeks of age with a CD4 lymphocyte percentage (the CD4 percentage) of 25% or more were randomly assigned to receive antiretroviral therapy (lopinavir-ritonavir, zidovudine, and lamivudine) when the CD4 percentage decreased to less than 20% (or 25% if the child was younger than 1 year) or clinical criteria were met (the deferred antiretroviral-therapy group) or to immediate initiation of limited antiretroviral therapy until 1 year of age or 2 years of age (the early antiretroviral-therapy groups). We report the early outcomes for infants who received deferred antiretroviral therapy as compared with early antiretroviral therapy. **RESULTS:** At a median age of 7.4 weeks (interquartile range, 6.6 to 8.9) and a CD4 percentage of 35.2% (interquartile range, 29.1 to 41.2), 125 infants were randomly assigned to receive deferred therapy, and 252 infants were randomly assigned to receive early therapy. After a median follow-up of 40 weeks (interquartile range, 24 to 58), antiretroviral therapy was initiated in 66% of infants in the deferred-therapy group. **Twenty infants in the deferred-therapy group (16%) died versus 10 infants in the early-therapy groups (4%) (hazard ratio for death, 0.24; 95% confidence interval [CI], 0.11 to 0.51; P<0.001).** In 32 infants in the deferred-therapy group (26%) versus 16 infants in the early-therapy groups (6%), disease progressed to Centers for Disease Control and Prevention stage C or severe stage B (hazard ratio for disease progression, 0.25; 95% CI, 0.15 to 0.41; P<0.001). Stavudine was substituted for zidovudine in four infants in the early-therapy groups because of neutropenia in three infants and anemia in one infant; no

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drugs were permanently discontinued. After a review by the data and safety monitoring board, the deferred-therapy group was modified, and infants in this group were all reassessed for initiation of antiretroviral therapy. **CONCLUSIONS: Early HIV diagnosis and early antiretroviral therapy reduced early infant mortality by 76% and HIV progression by 75%.** (ClinicalTrials.gov number, NCT00102960.) 2008 Massachusetts Medical Society

Comment

This paper is very important, showing the benefits of early definitive diagnosis of HIV and early initiation of ART. In many parts of the world HIV PCR testing and CD-4 testing are not available, but this study clearly shows the survival benefits that can result from such monitoring and early treatment.

Prevention of parent to child transmission

[Antivir Ther.](#) 2009;14(1):117-22.

Perinatal zidovudine prophylaxis in HIV type-1-infected pregnant women with thalassaemia carriage in Thailand.

[Briand N](#), [Pornprasert S](#), [Ngo-Giang-Huong N](#), [Galactéros F](#), [Pissard S](#), [Tatu T](#), [Sanguanserm Sri T](#), [Jourdain G](#), [Lallemant M](#), [Le Coeur S](#).

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BACKGROUND: To investigate a possible interaction between alpha-thalassaemia, beta-thalassaemia and haemoglobin-E trait and the haematological parameters of HIV type-1 (HIV-1)-infected pregnant women receiving zidovudine prophylaxis for the prevention of mother-to-child HIV-1 transmission in Thailand. **METHODS:** The study sample was composed of HIV-1-infected pregnant women receiving zidovudine (300 mg twice daily) from 28 weeks of gestational age to delivery as part of the Perinatal HIV Prevention Trial (PHPT-1), a large trial investigating zidovudine use in pregnancy. These women were randomly selected and screened for haemoglobin abnormalities. Haemoglobin levels, haematocrit and erythrocyte, leukocyte, absolute neutrophil and absolute lymphocyte counts were measured at 26, 32 and 35 weeks of gestation and at delivery. PCR genotyping techniques were used to screen for haemoglobin abnormalities, which included alpha-thalassaemia-1 Southeast Asian type deletion, beta-thalassaemia mutation (codons 41/42 [-TCTT], codon 17 [A-->T], intervening sequence-I nucleotide 1 [G-->T], codons 71/72 [+A]) and haemoglobin-E trait. The evolution of haematological parameters between 26 weeks and delivery was compared according to thalassaemia carriage using linear mixed models adjusted for baseline sociodemographic characteristics, HIV clinical stage, CD4+ T-cell count and viral load. **RESULTS: At baseline, women with thalassaemia or haemoglobin-E trait had significantly lower haemoglobin level and red blood cell counts than women with no haemoglobin abnormalities, whereas absolute neutrophil and leukocyte counts were significantly higher. Exposure to zidovudine until delivery did not increase this difference. CONCLUSIONS: Zidovudine exposure did not appear to have increased haematological toxicity in HIV-1-infected pregnant women with thalassaemia.**

[J Infect Dis.](#) 2009 Feb 1;199(3):414-8.



Risk factors for early and late transmission of HIV via breast-feeding among infants born to HIV-infected women in a randomized clinical trial in Botswana.

[Shapiro RL](#), [Smeaton L](#), [Lockman S](#), [Thior I](#), [Rossenkhan R](#), [Wester C](#), [Stevens L](#), [Moffat C](#), [Arimi P](#), [Ndase P](#), [Asmelash A](#), [Leidner J](#), [Novitsky V](#), [Makhema J](#), [Essex M](#).

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Risk factors for mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV) via breast-feeding were evaluated in a randomized trial. **HIV-infected women and their infants received zidovudine as well as single-dose nevirapine or placebo. Infants were randomized to formula-feed (FF) or breast-feed (BF) in combination with zidovudine prophylaxis. Of 1116 at-risk infants, 6 (1.1%) in the FF group and 7 (1.3%) in the BF group were infected between birth and 1 month (P=.99).** Maternal receipt of nevirapine did not predict early MTCT in the BF group (P=.45). Of 547 infants in the BF group at risk for late MTCT, 24 (4.4%) were infected. Maternal HIV-1 RNA levels in plasma (P<.001) and breast milk (P<.001) predicted late MTCT. **These findings support the safety of 1 month of breast-feeding in combination with maternal and infant antiretroviral prophylaxis.** Trial registration. ClinicalTrials.gov identifiers: NCT00197691 and NCT00197652.

[Int J Epidemiol.](#) 2009 Apr;38(2):569-76. Epub 2008 Nov 30.



Role of breastfeeding cessation in mediating the relationship between maternal HIV disease stage and increased child mortality among HIV-exposed uninfected children.

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BACKGROUND: Maternal CD4 count predicts child mortality in HIV-uninfected children born to HIV-infected women. METHODS: To explore the mediating role of breastfeeding cessation in this relationship, we compared marginal structural models of maternal CD4 count on child death with and without adjustment for breastfeeding. RESULTS: **In crude analyses, children of mothers with CD4<200 during pregnancy were 3.2 times more likely to die by 18 months (CI 1.3-8.1) as children whose mothers had CD4>500. Earlier breastfeeding cessation was also associated with low CD4 (HR 1.8; CI 1.2-2.7). After adjusting for breastfeeding and low birth weight using a marginal structural model, the low CD4 count-child mortality association through 18 months was reduced 17%.** The change was overestimated using a traditional Cox proportional hazards model (35% reduction in HR from

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3.4 to 2.5). **CONCLUSIONS: Our analysis suggests that only a small part of the effect of low vs high CD4 count on child mortality through 18 months is mediated through breastfeeding cessation.** Our results must be taken into account when deciding whether or not to recommend breastfeeding for infants of HIV-infected mothers.

Comment

The authors point out that besides earlier cessation of breast feeding, there are several other factors in the increased morbidity and mortality among HIV-exposed but uninfected infants, including increased exposure to infectious diseases, low birth weight and poor growth, and general inability to care for the child. The finding that infants of mothers with low CD-4 counts are particularly at risk of death, despite being uninfected with HIV is important. The more widespread availability of HAART should allow mothers to breast-feed their infants without a substantial risk of HIV transmission, and therefore afford their infants the substantial protection of breast-feeding.

*** [N Engl J Med.](#) 2008 Jul 10;359(2):130-41. Epub 2008 Jun 4.



Effects of early, abrupt weaning on HIV-free survival of children in Zambia.

[Kuhn L](#), [Aldrovandi GM](#), [Sinkala M](#), [Kankasa C](#), [Semrau K](#), [Mwiya M](#), [Kasonde P](#), [Scott N](#), [Vwalika C](#), [Walter J](#), [Bulterys M](#), [Tsai WY](#), [Thea DM](#); [Zambia Exclusive Breastfeeding Study](#).

[Abrams E](#), [Colton T](#), [Fawzi W](#), [Kapiga S](#), [Chomba E](#), [Allen S](#), [Luo C](#), [Mofenson L](#), [Piwoz E](#), [Ryan K](#), [Simon J](#), [Stein Z](#), [Stringer J](#), [Vermund S](#).

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BACKGROUND: In low-resource settings, many programs recommend that women who are infected with the human immunodeficiency virus (HIV) stop breast-feeding early. **We conducted a randomized trial to evaluate whether abrupt weaning at 4 months as compared with the standard practice has a net benefit for HIV-free survival of children.** **METHODS:** We enrolled 958 HIV-infected women and their infants in Lusaka, Zambia. All the women planned to breast-feed exclusively to 4 months; **481 were randomly assigned to a counseling program that encouraged abrupt weaning at 4 months, and 477 to a program that encouraged continued breast-feeding for as long as the women chose. The primary outcome was either HIV infection or death of the child by 24 months.** **RESULTS:** **In the intervention group, 69.0% of the mothers stopped breast-feeding at 5 months or earlier; 68.8% of these women reported the completion of weaning in less than 2 days. In the control group, the median duration of breast-feeding was 16 months.** In the overall cohort, there was no significant difference between the groups in the rate of HIV-free survival among the children; 68.4% and 64.0% survived to 24 months without HIV infection in the intervention and control groups, respectively (P=0.13). Among infants who were still being breast-fed and were not infected with HIV at 4 months, there was no significant difference between the groups in HIV-free survival at 24 months (83.9% and 80.7% in the intervention and control groups, respectively; P=0.27). **Children who were infected with HIV by 4 months had a higher mortality by 24 months if they had been assigned to the intervention group than if they**

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had been assigned to the control group (73.6% vs. 54.8%, $P=0.007$). CONCLUSIONS: Early, abrupt cessation of breast-feeding by HIV-infected women in a low-resource setting, such as Lusaka, Zambia, does not improve the rate of HIV-free survival among children born to HIV-infected mothers and is harmful to HIV-infected infants. (ClinicalTrials.gov number, NCT00310726.) 2008 Massachusetts Medical Society

Comment

This study and the one below were included in last year's summary of RCTs, as they were published on-line in June, but are reproduced here because they were published in the hard copy journal in July 2009. The study above is an important trial, adding to the evidence from Botswana published in 2006 showing that although formula feeding is associated with lower risk of mother-to-child HIV transmission, it was associated with a higher mortality (JAMA. 2006 Aug 16;296(7):794-805). Among HIV-affected infants in Zambia, mortality is higher if there is abrupt weaning at 4 months of age. This shows that evidence on breast-feeding in HIV is highly context specific, as are the results of most RCTs!

[N Engl J Med.](#) 2008 Jul 10;359(2):119-29. Epub 2008 Jun 4.



Extended antiretroviral prophylaxis to reduce breast-milk HIV-1 transmission.

[Kumwenda NI](#), [Hoover DR](#), [Mofenson LM](#), [Thigpen MC](#), [Kafulafula G](#), [Li Q](#), [Mipando L](#), [Nkanaunena K](#), [Mebrahtu T](#), [Bulterys M](#), [Fowler MG](#), [Taha TE](#).

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BACKGROUND: Effective strategies are urgently needed to reduce mother-to-child transmission of human immunodeficiency virus type 1 (HIV-1) through breast-feeding in resource-limited settings. METHODS: Women with HIV-1 infection who were breast-feeding infants were enrolled in a randomized, phase 3 trial in Blantyre, Malawi. At birth, the infants were randomly assigned to one of three regimens: **single-dose nevirapine plus 1 week of zidovudine (control regimen) or the control regimen plus daily extended prophylaxis either with nevirapine (extended nevirapine) or with nevirapine plus zidovudine (extended dual prophylaxis) until the age of 14 weeks.** Using Kaplan-Meier analyses, we assessed the risk of HIV-1 infection among infants who were HIV-1-negative on DNA polymerase-chain-reaction assay at birth. RESULTS: Among 3016 infants in the study, the control group had consistently higher rates of HIV-1 infection from the age of 6 weeks through 18 months. At 9 months, the estimated rate of HIV-1 infection (the primary end point) was 10.6% in the control group, as compared with 5.2% in the extended-nevirapine group ($P<0.001$) and 6.4% in the extended-dual-prophylaxis group ($P=0.002$). There were no significant differences between the two extended-prophylaxis groups. The frequency of breast-feeding did not differ significantly among the study groups. Infants receiving extended dual prophylaxis had a significant increase in the number of adverse events (primarily neutropenia) that were deemed to be possibly related to a study drug. CONCLUSIONS: **Extended prophylaxis with nevirapine or with nevirapine and zidovudine for the first 14 weeks of life significantly reduced postnatal HIV-1 infection in 9-month-old infants.** (ClinicalTrials.gov number, NCT00115648.) 2008 Massachusetts Medical Society

Comment

This too is important information, worth repeating, confirming there are effective strategies to make prolonged breast feeding safer in HIV affected infants in settings where abrupt cessation of breast feeding may be dangerous. 90% of infants in this trial were breast fed to 6 months, one-quarter to one-third up to 9 months, and almost 20% to 15 months.

[Pediatr Infect Dis J.](#) 2008 Sep;27(9):808-14.

Morbidity and mortality among a cohort of human immunodeficiency virus type 1-infected and uninfected pregnant women and their infants from Malawi, Zambia, and Tanzania.

[Chilongozi D](#), [Wang L](#), [Brown L](#), [Taha T](#), [Valentine M](#), [Emel L](#), [Sinkala M](#), [Kafulafula G](#), [Noor RA](#), [Read JS](#), [Brown ER](#), [Goldenberg RL](#), [Hoffman I](#); [HIVNET 024 Study Team](#).

[Taha TE](#), [Goldenberg R](#), [Kumwenda N](#), [Kafulafula G](#), [Martinson F](#), [Msamanga G](#), [Sinkala M](#), [Stringer J](#), [Hoffman I](#), [Fawzi W](#), [Broadhead R](#), [Liomba G](#), [Kumwenda J](#), [Mebrahtu T](#), [Katunda P](#), [Dahab M](#), [Kazembe P](#), [Chilongozi D](#), [Chasela C](#), [Joaki G](#), [Dzinyemba W](#), [Kamanga S](#), [Lyamuya E](#), [Kilewo C](#), [Manji K](#), [Kaaya S](#), [Aboud S](#), [Sheriff M](#), [Saathoff E](#), [Satow P](#), [Ballonzi I](#), [Antelman G](#), [Basheka E](#), [Mudenda V](#), [Kaseba C](#), [Njobvu M](#), [Kabaso M](#), [Kapina M](#), [Yeta A](#), [Kaminsa S](#), [Malama C](#), [Potter D](#), [Ukwimi M](#), [Taylor A](#), [Chipaila P](#), [Mwale B](#), [Joshi P](#), [Cachafeiro A](#), [Greene S](#), [Turner M](#), [Kerkau M](#), [Alabanza P](#), [James A](#), [Siharath S](#), [Tribull T](#), [Kapiga S](#), [Seage G](#), [Vermud S](#), [Andrews W](#), [Lyon D](#), [Adenivi-Jones S](#), [Read JS](#), [Estep S](#), [Brown ER](#), [Fleming TR](#), [Mwatha A](#), [Wang L](#), [Chen YQ](#), [Fiscus S](#), [Emel L](#), [Lands DJ](#), [Dominique CJ](#), [Fisher AH](#), [Doyle M](#), [Valentine M](#).

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BACKGROUND: Morbidity and mortality patterns among pregnant women and their infants (before antiretroviral therapy was widely available) determines HIV-1 diagnostic, monitoring, and care interventions. METHODS: Data from mothers and their infants enrolled in a trial of antibiotics to reduce mother-to-child-transmission of HIV-1 at 4 sub-Saharan African sites were analyzed. Women were enrolled during pregnancy and follow-up continued until the infants reached 12 months of age. We describe maternal and infant morbidity and mortality in a cohort of HIV-1-infected and HIV-1-uninfected mothers. Maternal and infant factors associated with mortality risk in the infants were assessed using Cox proportional hazard modeling. RESULTS: Among 2292 HIV-1-infected mothers, 166 (7.2%) had a serious adverse event (SAE) and 42 (1.8%) died, whereas no deaths occurred among the 331 HIV-1 uninfected mothers. Four hundred twenty-four (17.8%) of 2383 infants had an SAE and 349 (16.4%) died before the end of follow-up. Infants with early HIV-1 infection (birth to 4-6 weeks) had the highest mortality. Among infants born to HIV-1-infected women, maternal morbidity and mortality ($P = 0.0001$), baseline CD4 count ($P = 0.0002$), and baseline plasma HIV-1 RNA concentration ($P < 0.0001$) were significant predictors of infant mortality in multivariate analyses. CONCLUSIONS: **The high mortality among infants with early HIV-1 infection supports access to HIV-1 diagnostics and appropriate early treatment for all infants of HIV-1-infected mothers.** The significant association between stage of maternal HIV-1 infection and infant mortality supports routine CD4 counts at the time of prenatal HIV-1 testing.

Haematology

[J Pediatr Hematol Oncol](#). 2008 Aug;30(8):598-601.

A single dose of anti-D immunoglobulin raises platelet count as efficiently as intravenous immunoglobulin in newly diagnosed immune thrombocytopenic purpura in Korean children.

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OBJECTIVE: The aim of this study is to compare the efficacy and safety of a single dose of anti-D immunoglobulin (anti-D) at 50 mug/kg to intravenous immunoglobulin (IVIG) in Korean children with acute immune thrombocytopenic purpura (ITP). **METHODS:** We performed this study prospectively by randomly administering **2 consecutive doses of IVIG at a dose of 1.0 g/kg/dor a single dose of anti-D at 50 microg/kg to children upon initial diagnosis of acute ITP. The platelet count and adverse events, including hemoglobin concentration, were then serially evaluated, and the responses were compared.** **RESULTS:** **The likelihood of having a platelet count greater than 20x10/mm after 3 days of treatment in the IVIG and anti-D group was 93% and 92%, respectively.** In addition, hemoglobin concentration in the anti-D group had declined more than that of the IVIG group (1.49 g/dL vs. 0.80 g/dL, P=0.014) 3 days after treatment. Fever, chills, and headache occurred less frequently in the anti-D group than the IVIG group, however, this difference was not statistically significant (25% vs. 45%, P=0.494). **CONCLUSIONS:** **A single dose of 50 microg/kg of anti-D raised platelet count as efficiently as IVIG in newly diagnosed cases of ITP in Korean children.** Although 50 microg/kg of anti-D had a greater effect on the hemoglobin concentration than IVIG, the adverse effects were found to be acceptable, and no serious events were observed.

[Ann Hematol](#). 2008 Jul;87(7):545-50. Epub 2008 Mar 20.

Iron chelation in thalassemia: combined or monotherapy? The Egyptian experience.

[El-Beshlawy A](#), [Manz C](#), [Naja M](#), [Eltagui M](#), [Tarabishi C](#), [Youssry I](#), [Sobh H](#), [Hamdy M](#), [Sharaf I](#), [Mostafa A](#), [Shaker O](#), [Hoffbrand AV](#), [Taher A](#).

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Patients with thalassemia major requiring regular blood transfusions accumulate iron that is toxic to the heart, liver, and endocrine systems. The following prospective, randomized trial was carried out to determine the effectiveness, in children and young adults, of combined deferiprone (DFP) and deferoxamine (DFO) in reducing transfusional iron overload compared to either drug alone and to assess the safety and tolerability of DFP. **Sixty-six patients were**

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randomized into three treatment arms: daily DFP combined with DFO twice weekly; daily DFP only; and DFO only 5 days/week. Fifty-six patients completed the 54 weeks and were assessed by different indices. A significant reduction of liver iron concentration and serum ferritin was observed in all three arms while significant reduction of liver iron score was observed in patients on combination therapy only. Cardiac function did not significantly change in any arm. Compliance improved in patients who received combined therapy. Toxicity of DFP was mild to moderate and acceptable; most commonly, transient arthropathy and nausea/vomiting were observed. Thus, combination therapy has shown to be effective in reducing iron overload in thalassemia patients.

Injury prevention

[Accid Anal Prev](#). 2009 Jan;41(1):183-90. Epub 2008 Nov 14.

The impact of a home visitation programme on household hazards associated with unintentional childhood injuries: a randomised controlled trial.

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BACKGROUND: The continued high mortality and morbidity rates for unintentional childhood injuries remain a public health concern. This article reports on the influence of a home visitation programme (HVP) on household hazards associated with unintentional childhood injuries in a South African low-income setting. **METHODS:** A randomised controlled trial (n=211 households) was conducted in a South African informal settlement. **Community members were recruited and trained as paraprofessional visitors. Four intervention visits were conducted over 3 months, focusing on child development, and the prevention of burn, poison, and fall injuries.** The HVP, a multi-component intervention, included educational inputs, provision of safety devices, and an implicit enforcement strategy. The intervention effect (IE) was measured with a standardised risk assessment index that compared post-intervention scores for intervention and control households. **RESULTS: A significant reduction was observed in the hazards associated with electrical and paraffin appliances, as well as in hazards related to poisoning. Non-significant changes were observed for burn safety household practices and fall injury hazards.** **CONCLUSIONS:** This study confirmed that a multi-component HVP effectively reduced household hazards associated with electrical and paraffin appliances and poisoning among children in a low-income South African setting.

Integrated management of childhood illness

[Am J Public Health](#). 2009 May;99(5):837-46. Epub 2009 Mar 19.



A multifaceted intervention to improve health worker adherence to integrated management of childhood illness guidelines in Benin.

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OBJECTIVES: We evaluated an intervention to support health workers after training in Integrated Management of Childhood Illness (IMCI), a strategy that can improve outcomes for children in developing countries by encouraging workers' use of evidence-based guidelines for managing the leading causes of child mortality. **METHODS:** We conducted a randomized trial in Benin. We administered a survey in 1999 to assess health care quality before IMCI training. Health workers then received training plus either **study supports (job aids, nonfinancial incentives, and supervision of workers and supervisors)** or usual supports. Follow-up surveys conducted in 2001 to 2004 assessed recommended treatment, recommended or adequate treatment, and an index of overall guideline adherence. **RESULTS:** We analyzed 1244 consultations. Performance improved in both intervention and control groups, with no significant differences between groups. However, **training proceeded slowly, and low-quality care from health workers without IMCI training diluted intervention effects. Per-protocol analyses revealed that workers with IMCI training plus study supports provided better care than did those with training plus usual supports (27.3 percentage-point difference for recommended treatment; $P < .05$), and both groups outperformed untrained workers.** **CONCLUSIONS:** IMCI training was useful but insufficient. Relatively inexpensive supports can lead to additional improvements.

Comment

Many countries are struggling to sustain IMCI. It has become clear that IMCI training will not be sustained by in-service training, which is the original method of implementation in many countries. For IMCI to evolve into a sustainable part of the health culture, program simplification, more support for incorporation into health training colleges and existing MCH systems, and a greater understanding of how to support the ongoing education of health workers must occur. This study suggests some ways to achieve this.

Leishmaniasis

[Am J Trop Med Hyg.](#) 2009 Feb;80(2):172-5.



Efficacy of cryotherapy versus intralesional meglumine antimoniate (glucantime) for treatment of cutaneous leishmaniasis in children.

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We compared intralesional glucantime and cryotherapy for treatment of children with cutaneous leishmaniasis in Iran. We observed that cryotherapy is an effective treatment for cutaneous leishmaniasis in children. No serious post-treatment side effects were observed in either group. At six months of follow-up, no recurrence of disease was observed in cured patients in either group. Because of its simplicity, lower cost, low rate of serious complications, and greater tolerability, cryotherapy should be recommended as an appropriate alternative treatment for leishmaniasis in children.

Malaria

(see also Vitamin A)

Malaria vaccine

[PLoS One.](#) 2009;4(3):e4708. Epub 2009 Mar 5.



Blood stage malaria vaccine eliciting high antigen-specific antibody concentrations confers no protection to young children in Western Kenya.

[Ogutu BR](#), [Apollo OJ](#), [McKinney D](#), [Okoth W](#), [Siangla J](#), [Dubovsky F](#), [Tucker K](#), [Waitumbi JN](#), [Diggs C](#), [Wittes J](#), [Malkin E](#), [Leach A](#), [Soisson LA](#), [Milman JB](#), [Otieno L](#), [Holland CA](#), [Polhemus M](#), [Remich SA](#), [Ockenhouse CF](#), [Cohen J](#), [Ballou WR](#), [Martin SK](#), [Angov E](#), [Stewart VA](#), [Lyon JA](#), [Heppner DG](#), [Withers MR](#); [MSP-1 Malaria Vaccine Working Group](#). Collaborators (13)

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OBJECTIVE: The antigen, falciparum malaria protein 1 (FMP1), represents the 42-kDa C-terminal fragment of merozoite surface protein-1 (MSP-1) of the 3D7 clone of *P. falciparum*. Formulated with AS02 (a proprietary Adjuvant System), it constitutes the FMP1/AS02 candidate malaria vaccine. We evaluated this vaccine's safety, immunogenicity, and efficacy in African children. **METHODS:** A randomised, double-blind, Phase IIb, comparator-controlled trial. The trial was conducted in 13 field stations of one mile radii within Kombewa Division,

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Nyanza Province, Western Kenya, an area of holoendemic transmission of *P. falciparum*. We enrolled 400 children aged 12-47 months in general good health. **Children were randomised in a 1:1 ratio to receive either FMP1/AS02 (50 microg) or Rabipur(R) rabies vaccine. Vaccinations were administered on a 0, 1, and 2 month schedule. The primary study endpoint was time to first clinical episode of *P. falciparum* malaria (temperature ≥ 37.5 degrees C with asexual parasitaemia of $\geq 50,000$ parasites/microL of blood) occurring between 14 days and six months after a third dose.** Case detection was both active and passive. Safety and immunogenicity were evaluated for eight months after first immunisations; vaccine efficacy (VE) was measured over a six-month period following third vaccinations. **RESULTS:** 374 of 400 children received all three doses and completed six months of follow-up. FMP1/AS02 had a good safety profile and was well-tolerated but more reactogenic than the comparator. Geometric mean anti-MSP-1(42) antibody concentrations increased from 1.3 microg/mL to 27.3 microg/mL in the FMP1/AS02 recipients, but were unchanged in controls. 97 children in the FMP1/AS02 group and 98 controls had a primary endpoint episode. **Overall VE was 5.1% (95% CI: -26% to +28%; p-value = 0.7).** **CONCLUSIONS: FMP1/AS02 is not a promising candidate for further development as a monovalent malaria vaccine.** Future MSP-1(42) vaccine development should focus on other formulations and antigen constructs. TRIAL REGISTRATION: Clinicaltrials.gov NCT00223990.

Intermittent preventative treatment

[Antimicrob Agents Chemother.](#) 2009 May;53(5):1753-9. Epub 2009 Feb 17.

Reduced efficacy of intermittent preventive treatment of malaria in malnourished children.

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Intermittent preventive treatment in infants with sulfadoxine-pyrimethamine (IPTi-SP) reduces malaria episodes by 20 to 59% across Africa. This protective efficacy, however, may be affected by the high frequency of malnutrition in African infants. **We analyzed the impact of malnutrition as defined by anthropometry on the incidence of malaria and on the protective efficacy of IPTi in a cohort of 1,200 children in northern Ghana, where malaria is hyperendemic. These children received IPTi-SP or placebo at 3, 9, and 15 months of age and were monitored until 24 months of age. Malnutrition was present in 32, 40, and 50% of children at ages 3, 9, and 15 months, respectively.** It was associated with increased risks of severe anemia and death but not an increased risk of malaria. Although malaria slightly contributed to chronic malnutrition, IPTi did not substantially improve child growth. **Importantly, the protective efficacies of IPTi in malnourished children were roughly half or even less of those observed in nonmalnourished children. In the first year of life, IPTi reduced the incidence of malaria to a significantly lesser extent in infants who received both doses in a malnourished condition (25%; 95% confidence interval [CI], -7 to 48%) compared to that of nonmalnourished children (46%; 95% CI, 30 to 58%; P = 0.049).** Moreover, in contrast to nutritionally advantaged children, the rate of severe malaria appeared to

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be increased in malnourished children who took IPTi. IPTi might exhibit reduced efficacy in regions of abundant malnutrition. Concomitant nutrition programs may be needed in these places to achieve the desired impact.

[PLoS One](#). 2008;3(12):e4000. Epub 2008 Dec 22.



Seasonal intermittent preventive treatment for the prevention of anaemia and malaria in Ghanaian children: a randomized, placebo controlled trial.

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BACKGROUND: Malaria and anaemia are the leading causes of morbidity and mortality in children in sub-Saharan Africa. We have investigated the effect of intermittent preventive treatment with sulphadoxine-pyrimethamine or artesunate plus amodiaquine on anaemia and malaria in children in an area of intense, prolonged, seasonal malaria transmission in Ghana. **METHODS:** 2451 children aged 3-59 months from 30 villages were individually randomised to receive placebo or artesunate plus amodiaquine (AS+AQ) monthly or bimonthly, or sulphadoxine-pyrimethamine (SP) bimonthly over a period of six months. The primary outcome measures were episodes of anaemia (Hb<8.0 g/dl) or malaria detected through passive surveillance. **FINDINGS:** Monthly artesunate plus amodiaquine reduced the incidence of malaria by 69% (95% CI: 63%, 74%) and anaemia by 45% (95% CI: 25%,60%), bimonthly sulphadoxine-pyrimethamine reduced the incidence of malaria by 24% (95% CI: 14%,33%) and anaemia by 30% (95% CI: 6%, 49%) and bimonthly artesunate plus amodiaquine reduced the incidence of malaria by 17% (95% CI: 6%, 27%) and anaemia by 32% (95% CI: 7%, 50%) compared to placebo. There were no statistically significant reductions in the episodes of all cause or malaria specific hospital admissions in any of the intervention groups compared to the placebo group. **There was no significant increase in the incidence of clinical malaria in the post intervention period in children who were >1 year old when they received IPTc compared to the placebo group.** However the incidence of malaria in the post intervention period was higher in children who were <1 year old when they received AS+AQ monthly compared to the placebo group. **INTERPRETATION:** IPTc is safe and efficacious in reducing the burden of malaria in an area of Ghana with a prolonged, intense malaria transmission season. **TRIAL REGISTRATION:** ClinicalTrials.gov NCT00119132.

[Malar J](#). 2008 Oct 1;7:198.



Therapeutic and prophylactic effect of intermittent preventive anti-malarial treatment in infants (IPTi) from Ghana and Gabon.

[May J](#), [Adjei S](#), [Busch W](#), [Gabor JJ](#), [Issifou S](#), [Kobbe R](#), [Kreuels B](#), [Lell B](#), [Schwarz NG](#), [Adjei O](#), [Kremsner PG](#), [Grobusch MP](#).

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BACKGROUND: Intermittent preventive treatment in infants (IPTi) with sulphadoxine-pyrimethamine (SP) reduces the incidence of malaria episodes in young children. The exact mechanism by which the protective effect is mediated needs to be defined. This study aimed to investigate therapeutic, prophylactic, and possible exceeding effects of SP-based IPTi in two clinical trials. **METHODS:** Protective efficacies from two IPTi trials performed in Kumasi, Ghana, and Lambaréné, Gabon, were assessed for overlapping time series of 61 days. For six-months periods after each of three IPTi doses a multivariate Poisson regression model with the respective cohort as co-variate was generated and effect modification of protective efficacy with time strata was evaluated by log-likelihood tests. **RESULTS:** Protective efficacies were not significantly different between the two study cohorts. Study-cohort corrected protective efficacy was highest for the first 61 days after each IPTi application and decreased continuously. For the first 61 days after IPTi-1, IPTi-2, and IPTi-3 the protective efficacy was 71%, 44%, and 43%, respectively. A reduction of the malaria incidence rate was detectable for the first 60, 30 and 40 days after IPTi-1, IPTi-2 and IPTi-3 drug application, respectively. After IPTi-3 a higher risk for malaria could be seen after day 60. This effect was mainly based on the overwhelming influence of the Kumasi cohort. **CONCLUSION: The results suggest that SP-based IPTi mainly works through a therapeutic and prophylactic effect over 30 to 60 days after drug application and that a sustained effect beyond post-treatment prophylaxis might be very low.** **TRIAL REGISTRATION:** Data analysis from clinical trials NCT ID # 00206739 (Kumasi Trial) and NCT ID # 00167843 (Lambaréné Trial), <http://www.clinicaltrials.gov>.

[Malar J.](#) 2008 Jul 8;7:123.



Impact of intermittent preventive treatment with sulphadoxine-pyrimethamine targeting the transmission season on the incidence of clinical malaria in children in Mali.

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BACKGROUND: Recent studies have shown that intermittent preventive malaria treatment (IPT) in infants in areas of stable malaria transmission reduces malaria and severe anaemia incidence. However in most areas malaria morbidity and mortality remain high in older children. **METHODS:** To evaluate the effect of seasonal IPT with sulphadoxine pyrimethamine (SP) on incidence of malaria disease in area of seasonal transmission, **262 children 6 months-10 years in Kambila, Mali were randomized to receive either IPT with SP twice at eight weeks interval or no IPT during the transmission season of 2002 and were followed up for 12 months.** Subjects were also followed during the subsequent transmission season in 2003 to assess possible rebound effect. Clinical malaria cases were treated with SP and followed to assess the in vivo response during both periods. **RESULTS:** The incidence rate of malaria

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disease per 1,000 person-months during the first 12 months was 3.2 episodes in the treatment group vs. 5.8 episodes in the control group with age-adjusted Protective Efficacy (PE) of 42.5% [95% CI 28.6%-53.8%]. When the first 16 weeks of follow up is considered age-adjusted PE was 67.5% [95% CI 55.3% - 76.6%]. During the subsequent transmission season, the incidence of clinical malaria per 1000 persons-days was similar between the two groups (23.0 vs 21.5 episodes, age-adjusted IRR = 1.07 [95% CI, 0.90-1.27]). No significant difference was detected in in vivo response between the groups during both periods. **CONCLUSION: Two malaria intermittent treatments targeting the peak transmission season reduced the annual incidence rate of clinical malaria by 42.5% in an area with intense seasonal transmission.** This simple strategy is likely to be one of the most effective in reducing malaria burden in such areas. TRIAL REGISTRATION: Clinicaltrials.gov NCT00623155.

[Lancet](#). 2008 Jul 12;372(9633):127-38.



Effect of intermittent preventive treatment of malaria on health and education in schoolchildren: a cluster-randomised, double-blind, placebo-controlled trial.

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BACKGROUND: Malaria is a major cause of morbidity and mortality in early childhood, yet its consequences for health and education during the school-age years remain poorly understood. **We examined the effect of intermittent preventive treatment (IPT) in reducing anaemia and improving classroom attention and educational achievement in semi-immune schoolchildren in an area of high perennial transmission.** **METHODS:** A stratified, cluster-randomised, double-blind, placebo-controlled trial of IPT was done in 30 primary schools in western Kenya. Schools were randomly assigned to treatment (sulfadoxine-pyrimethamine in combination with amodiaquine or dual placebo) by use of a computer-generated list. Children aged 5-18 years received three treatments at 4-month intervals (IPT n=3535, placebo n=3223). **The primary endpoint was the prevalence of anaemia, defined as a haemoglobin concentration below 110 g/L.** This outcome was assessed through cross-sectional surveys 12 months post-intervention. Analysis was by both intention to treat, excluding children with missing data, and per protocol. This study is registered with ClinicalTrials.gov, number NCT00142246. **FINDINGS: 2604 children in the IPT group and 2302 in the placebo group were included in the intention-to-treat analysis of the primary outcome;** the main reason for exclusion was loss to follow-up. **Prevalence of anaemia at 12 months averaged 6.3% in the IPT group and 12.6% in the placebo group (adjusted risk ratio 0.52, 95% CI 0.29-0.93; p=0.028).** Significant improvements were also seen in two of the class-based tests of sustained attention, with a mean increase in code transmission test score of 6.05 (95% CI 2.83-9.27; p=0.0007) and counting sounds test score of 1.80 (0.19-3.41; p=0.03), compared with controls. No effect was shown for inattentive or hyperactive-compulsive behaviours or on educational achievement. The per-protocol analysis yielded similar results. 23 serious adverse events were reported within 28 days of any treatment (19 in the IPT group and four in the placebo group); the main side-effects were problems of balance, dizziness, feeling faint, nausea, and/or vomiting shortly after treatment. **INTERPRETATION: IPT of**

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malaria improves the health and cognitive ability of semi-immune schoolchildren. Effective malaria interventions could be a valuable addition to school health programmes.

Comment

This year several studies have consolidated the knowledge of IPTi and its effect on malaria, anaemia and other complications. Studies have clearly shown that IPTi reduces the incidence of malaria and anaemia. Encouragingly its use in infancy doesn't significantly increase the risk of severe malaria after the age of 1 year. Two doses of IPT given in older children during peak transmission season reduced the malaria incidence significantly. IPT in school age children also reduces anaemia and improves attention and cognition. IPTi has reduced effectiveness in malnourished children.

Diagnostic tests

[East Afr Med J](#). 2008 Nov;85(11):544-9.

Comparison of blood smear microscopy to a rapid diagnostic test for in-vitro testing for *P. falciparum* malaria in Kenyan school children.

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OBJECTIVE: To compare the diagnostic performance of microscopy using Giemsa-stained thick and thin blood smears to a rapid malaria dipstick test (RDT) in detecting *P. falciparum* malaria in Kenyan school children. **DESIGN:** Randomised, controlled feeding intervention trial from 1998-2001. **SETTING:** Rural Embu district, Kenya. The area is considered endemic for malaria, with four rainy seasons per year. Chloroquine resistance was estimated in 80% of patients. Children had a spleen rate of 45%. **SUBJECTS:** A sample of 515 rural Kenyan primary school children, aged 7-11 years, who were enrolled in a feeding intervention trial from 1998-2001. **MAIN OUTCOME MEASURES:** Percent positive and negative *P. falciparum* malaria status, sensitivity, specificity and positive and negative predictive values of RDT. **RESULTS:** For both years, the RDT yielded positive results of 30% in children compared to microscopy (17%). With microscopy as the "gold standard", RDT yielded a sensitivity of 81.3% in 1998 and 79.3% in 2000. Specificity was 81.6% in 1998 and 78.3% in 2000. Positive predictive value was 47.3% in 1998 and 42.6% in 2000, and negative predictive value was 95.6% in 1998 and 94.9% in 2000. **CONCLUSION:** Rapid diagnostic testing is a valuable tool for diagnosis and can shorten the interval for starting treatment, particularly where microscopy may not be feasible due to resource and distance limitations.

Malar J. 2008 Oct 2;7:199.



Impact of training in clinical and microscopy diagnosis of childhood malaria on antimalarial drug prescription and health outcome at primary health care level in Tanzania: a randomized controlled trial.

[Ngasala B](#), [Mubi M](#), [Warsame M](#), [Petzold MG](#), [Massele AY](#), [Gustafsson LL](#), [Tomson G](#), [Premji Z](#), [Bjorkman A](#).

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BACKGROUND: Prescribing antimalarial medicines based on parasite confirmed diagnosis of malaria is critical to rational drug use and optimal outcome of febrile illness. The impact of microscopy-based versus clinical-based diagnosis of childhood malaria was assessed at primary health care (PHC) facilities using a cluster randomized controlled training intervention trial. **METHODS:** Sixteen PHC facilities in rural Tanzania were randomly allocated to training of health staff in clinical algorithm plus microscopy (Arm-I, n = 5) or clinical algorithm only (Arm-II, n = 5) or no training (Arm-III, n = 6). Febrile under-five children presenting at these facilities were assessed, treated and scheduled for follow up visit after 7 days. Blood smears on day 0 were only done in Arm-I but on Day 7 in all arms. Primary outcome was antimalarial drug prescription. Other outcomes included antibiotic prescription and health outcome. Multilevel regression models were applied with PHC as level of clustering to compare outcomes in the three study arms. **RESULTS:** A total of 973, 1,058 and 1,100 children were enrolled in arms I, II and III, respectively, during the study period. **Antimalarial prescriptions were significantly reduced in Arm-I (61.3%) compared to Arms-II (95.3%) and III (99.5%)** (both $P < 0.001$), whereas antibiotic prescriptions did not vary significantly between the arms (49.9%, 54.8% and 34.2%, respectively). **In Arm-I, 99.1% of children with positive blood smear readings received antimalarial prescriptions and so did 11.3% of children with negative readings.** Those with positive readings were less likely to be prescribed antibiotics than those with negative (relative risk = 0.66, 95% confidence interval: 0.55, 0.72). On day 7 follow-up, more children reported symptoms in Arm-I compared to Arm-III, but fewer children had malaria parasitaemia ($p = 0.049$). The overall sensitivity of microscopy reading at PHC compared to reference level was 74.5% and the specificity was 59.0% but both varied widely between PHCs. **CONCLUSION: Microscopy based diagnosis of malaria at PHC facilities reduces prescription of antimalarial drugs, and appears to improve appropriate management of non-malaria fevers, but major variation in accuracy of the microscopy readings was found. Lack of qualified laboratory technicians at PHC facilities and the relatively short training period may have contributed to the shortcomings.** **TRIAL REGISTRATION:** This study is registered at Clinicaltrials.gov with the identifier NCT00687895.

Insecticide treated materials

[Indian J Med Res.](#) 2008 Sep;128(3):262-70.



Impact of lambda-cyhalothrin capsule suspension treated bed nets on malaria in tribal villages of Malkangiri district, Orissa, India.

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BACKGROUND & OBJECTIVE: Insecticide treated mosquito nets are increasingly being used in malaria control programmes. **One of the problems with the treatment of bed nets with conventional formulations of insecticides was that regular washing of treated nets diminish insecticidal effect.** Lambda-cyhalothrin 2.5 capsule suspension (CS) (2.5% a.i., w/v), a new water-based microencapsulated formulation is reported to have wash-resistant property and longer persistence on the netting material than other formulations. We evaluated the impact of the use of nylon bed nets treated with lambda-cyhalothrin 2.5 CS at 10 mg (a.i.)/m² in comparison to untreated nets and no nets on malaria in tribal villages in Orissa. **METHODS:** Nine foothill villages, highly endemic for falciparum malaria, from the Primary Health Centre (PHC) areas of Khairput and Kudumulgumma of Malkangiri district, Orissa, were divided into three groups, each with a population of about 500 and allocated randomly for treated (TN) and untreated nets (UN) and no nets (NN). Bed nets were distributed in September 2001 and retreatment was done in June 2002. The impact was assessed based on the changes in vector density, parous rate, malaria incidence and parasite rates. Indoor-resting collections of *Anopheles fluviatilis* and *An. culicifacies* were made at fortnightly intervals from fixed human dwellings. Mass blood surveys before and after distribution of nets and fortnightly active surveillance were carried out to assess the change in parasite rates and malaria incidence. Bioassays were conducted at fortnightly intervals on the bed nets supplied to the villagers. **RESULTS: The reductions in indoor resting catches of *An. fluviatilis* and *An. culicifacies* were 96 and 38 per cent in villages with treated nets and 2.6 and 23 per cent in villages with untreated nets respectively compared to no net villages.** For six months following treatment, 100 per cent mortality of *An. fluviatilis* was observed on the unwashed nets and on the nets washed once or twice. **After re-treatment, 100 per cent mortality of *An. fluviatilis* or *An. culicifacies* was observed for nine months even after two washes.** Usage rates of treated and untreated nets varied seasonally; 58.9 and 46.3 per cent in rainy season, 48.6 and 37.1 per cent in winter season and 38.1 and 31.6 per cent in summer season respectively. **Reductions in malaria parasite rates were about 65 per cent in the treated net villages and 39 per cent in the untreated net villages compared to no net villages. About 75 per cent of treated nets and 60 per cent of untreated nets were in usable condition 19 months after distribution.** **INTERPRETATION & CONCLUSION:** The estimated protection factor based on malaria incidence was 86 per cent for the treated nets during both post-treatment and post-retreatment periods and 34 and 51 per cent for untreated nets for the corresponding periods compared to no

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nets. The results of the study showed that the use of bed nets treated nets with CS formulation of lambda-cyhalothrin at 10 mg (a.i.)/m² was acceptable to the community and re-treatment of nets at nine-monthly intervals can significantly reduce density and survival of *An. fluviatilis* and incidence of falciparum malaria.

Treatment of uncomplicated malaria

[Lancet](#). 2009 May 9;373(9675):1623-31. Epub 2009 Apr 9.

Home management of malaria with artemether-lumefantrine compared with standard care in urban Ugandan children: a randomised controlled trial.

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BACKGROUND: Home management of malaria—the presumptive treatment of febrile children with antimalarial drugs—is advocated to ensure prompt effective treatment of the disease. We assessed the effect of home delivery of artemether-lumefantrine on the incidence of antimalarial treatment and on clinical outcomes in children from an urban setting with fairly low malaria transmission. **METHODS:** In Kampala, Uganda, 437 children aged between 1 and 6 years from 325 households were randomly assigned by a computer-generated sequence to receive home delivery of prepackaged artemether-lumefantrine for presumptive treatment of febrile illnesses (n=225) or current standard of care (n=212). Randomisation was done by household after a pilot period of 1 month. After randomisation, study participants were followed up for an additional 12 months and information on their health and treatment of illnesses was obtained by use of monthly questionnaires and household diaries, which were completed by the participants' carers. The primary outcome was treatment incidence density per person-year. Analysis of the primary outcome was done on the modified intention-to-treat population, which included all participants apart from those excluded before data collection. This trial is registered with ClinicalTrials.gov, number NCT00115921. **FINDINGS:** Eight participants in the home management group and four in the standard care group were excluded before data collection; therefore, the primary analysis was done in 217 and 208 participants, respectively. **The home management group received nearly twice the number of antimalarial treatments as the standard care group (4.66 per person-year vs 2.53 per person-year; incidence rate ratio [IRR] 1.72, 95% CI 1.43-2.06, p<0.0001), and nearly five times the number given to children with microscopically confirmed malaria in a comparable cohort of children (4.66 per person-year vs 1.03 per person-year, IRR 5.19, 95% CI 4.24-6.35, p<0.0001).** Clinical data were available for 189 children in the home management group and 176 in the control group at study end; the main reasons for exclusion were movement out of the study area or loss to follow-up. **The proportion of participants with parasitaemia at final assessment in the intervention group was lower than in the control group (four [2%] vs 17 [10%], p=0.006), but there were no other differences in standard malariometric indices, including anaemia. Serious adverse events were captured retrospectively.** One child died in each group (home management—severe pneumonia and possible septicaemia; standard care—presumed respiratory failure). **INTERPRETATION: Although home management of malaria led to prompt treatment of fever, there was little effect on clinical outcomes. The substantial over-treatment suggests**

that artemether-lumefantrine provided in the home might not be appropriate for large urban areas or settings with fairly low malaria transmission. FUNDING: Gates Malaria Partnership.

[Malar J.](#) 2009 Mar 16;8:48.



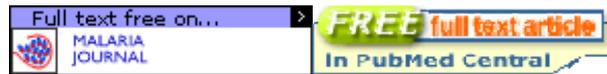
The efficacy and safety of a new fixed-dose combination of amodiaquine and artesunate in young African children with acute uncomplicated *Plasmodium falciparum*.

[Sirima SB](#), [Tiono AB](#), [Gansané A](#), [Diarra A](#), [Ouédraogo A](#), [Konaté AT](#), [Kiechel JR](#), [Morgan CC](#), [Olliaro PL](#), [Taylor WR](#).

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BACKGROUND: Artesunate (AS) plus amodiaquine (AQ) is one artemisinin-based combination (ACT) recommended by the WHO for treating *Plasmodium falciparum* malaria. Fixed-dose AS/AQ is new, but its safety and efficacy are hitherto untested. **METHODS:** **A randomized, open-label trial was conducted comparing the efficacy (non-inferiority design) and safety of fixed (F) dose AS (25 mg)/AQ (67.5 mg) to loose (L) AS (50 mg) + AQ (153 mg) in 750, *P. falciparum*-infected children from Burkina Faso aged 6 months to 5 years. Dosing was by age.** Primary efficacy endpoint was Day (D) 28, PCR-corrected, parasitological cure rate. Recipients of rescue treatment were counted as failures and new infections as cured. Documented, common toxicity criteria (CTC) graded adverse events (AEs) defined safety. **RESULTS:** Recruited and evaluable children numbered 750 (375/arm) and 682 (90.9%), respectively. There were 8 (AS/AQ) and 6 (AS+AQ) early treatment failures and one D7 failure (AS+AQ). Sixteen (AS/AQ) and 12 (AS+AQ) patients had recurrent parasitaemia (PCR new infections 10 and 6, respectively). Fourteen patients per arm required rescue treatment for vomiting/spitting out study drugs. Efficacy rates were 92.1% in both arms: AS/AQ = 315/342 (95% CI: 88.7-94.7) vs. AS+AQ = 313/340 (95% CI: 88.6-94.7). **Non-inferiority was demonstrated at two-sided alpha = 0.05: Delta (AS+AQ - AS/AQ) = 0.0% (95% CI: -4.1% to 4.0%). D28, Kaplan Meier PCR-corrected cure rates (all randomized children) were similar: 93.7% (AS/AQ) vs. 93.2% (AS+AQ) Delta = -0.5 (95% CI -4.2 to 3.0%). By D2, both arms had rapid parasite (F & L, 97.8% aparasitaemic) and fever (97.2% [F], 96.0% [L] afebrile) clearances.**Both treatments were well tolerated. Drug-induced vomiting numbered 8/375 (2.1%) and 6/375 (1.6%) in the fixed and loose arms, respectively (p = 0.59). One patient developed asymptomatic, CTC grade 4 hepatitis (AST 1052, ALT 936). Technical difficulties precluded the assessment and risk of neutropaenia for all patients. **CONCLUSION:** Fixed dose AS/AQ was efficacious and well tolerated. **These data support the use of this new fixed dose combination for treating *P. falciparum* malaria with continued safety monitoring.** TRIAL REGISTRATION: Current Controlled Trials ISRCTN07576538.

[Malar J.](#) 2009 Mar 3;8:37.



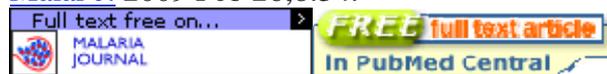
Extended high efficacy of the combination sulphadoxine-pyrimethamine with artesunate in children with uncomplicated falciparum malaria on the Benin coast, West Africa.

[Nahum A](#), [Erhart A](#), [Ahounou D](#), [Bonou D](#), [Van Overmeir C](#), [Menten J](#), [Akogbeto M](#), [Coosemans M](#), [Massougbdji A](#), [D'Alessandro U](#).

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BACKGROUND: A study carried out in 2003-2005 in Southern Benin showed a day-28 sulphadoxine-pyrimethamine (SP) monotherapy failure rate greater than 40%, while for SP combined with artesunate (SP-AS) the failure rate was 5.3%. Such a large difference could be explained by the relatively short 28-day follow-up period, with a substantial number of recurrent infections possibly occurring after day 28. This paper reports the treatment outcome observed in the same study cohort beyond the initial 28-day follow-up. **METHODS:** After the 28-day follow-up, children treated with either chloroquine alone (CQ), SP or SP-AS, were visited at home twice a week until day 90 after treatment. A blood sample was collected if the child had fever (axillary temperature ≥ 37.5 degrees C). Total clinical failure for each treatment group was estimated by combining all the early treatment failures and late clinical failures that occurred over the whole follow-up period, i.e. from day 0 up to day 90. Pre-treatment randomly selected blood samples were genotyped for the dhfr gene (59) and the dhps gene (437 and 540) point mutations related to SP resistance. **RESULTS:** The PCR-corrected clinical failure at day 90 was significantly lower in the SP-AS group (SP-AS: 2.7%, SP alone: 38.2%; CQ: 41.1%) (Log-Rank $p < 0,001$). The most prevalent haplotype was dhfr Arg-59 with the dhps Gly-437 mutant and the dhps 540 wild type (85.5%). The dhps 540 mutation could be found in only three (8.3%) samples. **CONCLUSION: Combining artesunate to SP dramatically increased the treatment efficacy, even when extending the follow-up to day 90 post-treatment, and despite the high percentage of failures following treatment with SP alone.** Such a good performance may be explained by the low prevalence of the dhps 540 mutation, by the rapid parasite clearance with artesunate and by the level of acquired immunity.

[Malar J.](#) 2009 Feb 26;8:34.



Efficacy of chloroquine, amodiaquine and sulphadoxine-pyrimethamine for the treatment of uncomplicated falciparum malaria: revisiting molecular markers in an area of emerging AQ and SP resistance in Mali.

[Tekete M](#), [Djimde AA](#), [Beavogui AH](#), [Maiga H](#), [Sagara I](#), [Fofana B](#), [Ouologuem D](#), [Dama S](#), [Kone A](#), [Dembele D](#), [Wele M](#), [Dicko A](#), [Doumbo OK](#).

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Randomised trials in child health in developing countries 2008-09

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BACKGROUND: To update the National Malaria Control Programme of Mali **on the efficacy of chloroquine, amodiaquine and sulphadoxine-pyrimethamine in the treatment of uncomplicated falciparum malaria.** **METHODS:** During the malaria transmission seasons of 2002 and 2003, 455 children--between six and 59 months of age, with uncomplicated malaria in Kollo, Mali, were randomly assigned to one of three treatment arms. In vivo outcomes were assessed using WHO standard protocols. Genotyping of msp1, msp2 and CA1 polymorphisms were used to distinguish reinfection from recrudescence parasites (molecular correction). **RESULTS: Day 28 adequate clinical and parasitological responses (ACPR) were 14.1%, 62.3% and 88.9% in 2002 and 18.2%, 60% and 85.2% in 2003 for chloroquine, amodiaquine and sulphadoxine-pyrimethamine, respectively.** After molecular correction, ACPRs (cACPR) were 63.2%, 88.5% and 98.0% in 2002 and 75.5%, 85.2% and 96.6% in 2003 for CQ, AQ and SP, respectively. Amodiaquine was the most effective on fever. Amodiaquine therapy selected molecular markers for chloroquine resistance, while in the sulphadoxine-pyrimethamine arm the level of dhfr triple mutant and dhfr/dhps quadruple mutant increased from 31.5% and 3.8% in 2002 to 42.9% and 8.9% in 2003, respectively. No infection with dhps 540E was found. **CONCLUSION: In this study, treatment with sulphadoxine-pyrimethamine emerged as the most efficacious on uncomplicated falciparum malaria followed by amodiaquine. The study demonstrated that sulphadoxine-pyrimethamine and amodiaquine were appropriate partner drugs that could be associated with artemisinin derivatives in an artemisinin-based combination therapy.**

[J Infect Dis.](#) 2009 Mar 1;199(5):750-7.

The University of
Chicago Press

In vivo selection of Plasmodium falciparum parasites carrying the chloroquine-susceptible pfprt K76 allele after treatment with artemether-lumefantrine in Africa.

[Sisowath C](#), [Petersen I](#), [Veiga MI](#), [Mårtensson A](#), [Premji Z](#), [Björkman A](#), [Fidock DA](#), [Gil JP](#).

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BACKGROUND: Artemether-lumefantrine (AL) is a major and highly effective artemisinin-based combination therapy that is becoming increasingly important as a new first-line therapy against Plasmodium falciparum malaria. However, recrudescences occurring after AL treatment have been reported. Identification of drug-specific parasite determinants that contribute to treatment failures will provide important tools for the detection and surveillance of AL resistance. **METHODS:** The findings from a 42-day follow-up efficacy trial in Tanzania that compared AL with sulfadoxine-pyrimethamine (SP) were analyzed to identify candidate markers for lumefantrine tolerance/resistance in the chloroquine resistance transporter gene (pfprt) and multidrug resistance gene 1 (pfmdr1). The findings were corroborated in vitro with genetically modified isogenic P. falciparum parasite lines. **RESULTS: Treatment with AL selected for the chloroquine-susceptible pfprt K76 allele (P < .0001) and, to a lesser extent, the pfmdr1 N86 (P = .048) allele among recurrent infections.** These genotypes were not selected during SP treatment. No pfmdr1 gene amplifications were observed. Isogenic pfprt-

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modified parasite lines demonstrated a 2-fold increase in susceptibility to lumefantrine, which was directly attributable to the K76T mutation. **CONCLUSIONS: Our findings suggest that the pfcr K76T mutation is a drug-specific contributor to enhanced P. falciparum susceptibility to lumefantrine in vivo and in vitro, and they highlight the benefit of using AL in areas affected by chloroquine-resistant P. falciparum malaria.**

[J Infect Dis.](#) 2009 Mar 1;199(5):758-65.

The University of
Chicago Press

Decreasing efficacy of antimalarial combination therapy in Uganda is explained by decreasing host immunity rather than increasing drug resistance.

[Greenhouse B](#), [Slater M](#), [Njama-Meya D](#), [Nzarubara B](#), [Maiteki-Sebuguzi C](#), [Clark TD](#), [Staedke SG](#), [Kamya MR](#), [Hubbard A](#), [Rosenthal PJ](#), [Dorsey G](#).

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BACKGROUND: Improved control efforts are reducing the burden of malaria in Africa but may result in decreased antimalarial immunity. **METHODS:** A cohort of 129 children aged 1-10 years in Kampala, Uganda, were treated with amodiaquine plus sulfadoxine-pyrimethamine for 396 episodes of uncomplicated malaria over a 29-month period as part of a longitudinal clinical trial. **RESULTS:** The risk of treatment failure increased over the course of the study from 5% to 21% (hazard ratio [HR], 2.4 per year [95% confidence interval {CI}, 1.3-4.3]). Parasite genetic polymorphisms were associated with an increased risk of failure, but their prevalence did not change over time. **Three markers of antimalarial immunity were associated with a decreased risk of treatment failure: increased age (HR, 0.5 per 5-year increase [95% CI, 0.2-1.2]), living in an area of higher malaria incidence (HR, 0.26 [95% CI, 0.11-0.64]), and recent asymptomatic parasitemia (HR, 0.06 [95% CI, 0.01-0.36]).** In multivariate analysis, adjustment for recent asymptomatic parasitemia, but not parasite polymorphisms, removed the association between calendar time and the risk of treatment failure (HR, 1.5 per year [95% CI, 0.7-3.4]), suggesting that worsening treatment efficacy was best explained by decreasing host immunity. **CONCLUSION: Declining immunity in our study population appeared to be the primary factor underlying decreased efficacy of amodiaquine plus sulfadoxine-pyrimethamine. With improved malaria-control efforts, decreasing immunity may unmask resistance to partially efficacious drugs.**

[PLoS One.](#) 2009;4(2):e4364. Epub 2009 Feb 5.

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Submicroscopic gametocytes and the transmission of antifolate-resistant Plasmodium falciparum in Western Kenya.

[Oesterholt MJ](#), [Alifrangis M](#), [Sutherland CJ](#), [Omar SA](#), [Sawa P](#), [Howitt C](#), [Gouagna LC](#),

[Sauerwein RW](#), [Bousema T](#).

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BACKGROUND: Single nucleotide polymorphisms (SNPs) in the dhfr and dhps genes are associated with sulphadoxine-pyrimethamine (SP) treatment failure and gametocyte carriage. This may result in enhanced transmission of mutant malaria parasites, as previously shown for chloroquine resistant parasites. In the present study, we determine the association between parasite mutations, submicroscopic *P. falciparum* gametocytemia and malaria transmission to mosquitoes. **METHODOLOGY/PRINCIPAL FINDINGS:** **Samples from children treated with SP alone or in combination with artesunate (AS) or amodiaquine were genotyped for SNPs in the dhfr and dhps genes.** Gametocytemia was determined by microscopy and Pfs25 RNA-based quantitative nucleic acid sequence-based amplification (Pfs25 QT-NASBA). Transmission was determined by membrane-feeding assays. We observed no wild type infections, 66.5% (127/191) of the infections expressed mutations at all three dhfr codons prior to treatment. The presence of all three mutations was not related to higher Pfs25 QT-NASBA gametocyte prevalence or density during follow-up, compared to double mutant infections. The proportion of infected mosquitoes or oocyst burden was also not related to the number of mutations. Addition of AS to SP reduced gametocytemia and malaria transmission during follow-up. **CONCLUSIONS/SIGNIFICANCE:** In our study population where all infections had at least a double mutation in the dhfr gene, additional mutations were not related to increased submicroscopic gametocytemia or enhanced malaria transmission. The absence of wild-type infections is likely to have reduced our power to detect differences. **Our data further support the use of ACT to reduce the transmission of drug-resistant malaria parasites.**

[Am J Trop Med Hyg.](#) 2009 Feb;80(2):199-201.

Short report: comparison of chlorproguanil-dapsone with a combination of sulfadoxine-pyrimethamine and chloroquine in children with malaria in northcentral Nigeria.

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Effective and affordable treatment of malaria is critical in the face of resistance of *Plasmodium falciparum* to chloroquine (CQ) and sulfadoxine-pyrimethamine (SP). **We conducted a randomized controlled trial comparing the efficacy of chlorproguanil-dapsone (CD) with a combination SP plus CQ in children in Nigeria less than five years of age with malaria.** Of 264 children enrolled, 122 (89.7%) and 118 (92.2%) completed the study in the SP + CQ and CD groups, respectively. By day 3, 96 (78.7%) and 94 (79.7%) had cleared their parasitemia ($P = 0.79$), and 107 (87.7%) and 109 (92.4%) were symptom free ($P = 0.32$) in the SP + CQ and CD groups, respectively. Adequate clinical and parasitologic response at day 14 occurred in 111 (94.1%; 95% confidence interval [CI] = 91.6-95.7%) in the CD group and 113 (92.6%; 95% CI = 89.9-94.3%) in the SP + CQ group ($P = 0.85$). **SP + CQ and CD had similar antimalarial efficacy and still provide affordable treatment of uncomplicated malaria in northcentral Nigeria.**

[Malar J.](#) 2009 Jan 7;8:5.



Artemisinin-based combinations versus amodiaquine plus sulphadoxine-pyrimethamine for the treatment of uncomplicated malaria in Faladje, Mali.

[Kayentao K](#), [Maiga H](#), [Newman RD](#), [McMorrow ML](#), [Hoppe A](#), [Yattara O](#), [Traore H](#), [Kone Y](#), [Guirou EA](#), [Save R](#), [Traore B](#), [Djimde A](#), [Doumbo OK](#).

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BACKGROUND: Because of the emergence of chloroquine resistance in Mali, artemether-lumefantrine (AL) or artesunate-amodiaquine (AS+AQ) are recommended as first-line therapy for uncomplicated malaria, but have not been available in Mali until recently because of high costs. **METHODS:** From July 2005 to January 2006, a randomized open-label trial of three oral antimalarial combinations, namely AS+AQ, artesunate plus sulphadoxine-pyrimethamine (AS+SP), and amodiaquine plus sulphadoxine-pyrimethamine (AQ+SP), was conducted in Faladje, Mali. Parasite genotyping by polymerase chain reaction (PCR) was used to distinguish new from recrudescence Plasmodium falciparum infections. **RESULTS:** **397 children 6 to 59 months of age with uncomplicated Plasmodium falciparum malaria were enrolled, and followed for 28 days to assess treatment efficacy. Baseline characteristics were similar in all three treatment groups. The uncorrected rates of adequate clinical and parasitologic response (ACPR) were 55.7%, 90.8%, and 97.7% in AS+AQ, AS+SP, and AQ+SP respectively (p < 0.001); after PCR correction ACPR rates were similar among treatment groups: 95.4%, 96.9%, and 99.2% respectively (p = 0.17).** Mean haemoglobin concentration increased across all treatment groups from Day 0 (9.82 +/- 1.68 g/dL) to Day 28 (10.78 +/- 1.49 g/dL) (p < 0.001), with the greatest improvement occurring in children treated with AQ+SP. On Day 2, the prevalence of parasitaemia was significantly greater among children treated with AQ+SP (50.8%) than in children treated with AS+AQ (10.5%) or AS+SP (10.8%) (p < 0.001). No significant difference in gametocyte carriage was found between groups during the follow-up period. **CONCLUSION:** **The combination of AQ+SP provides a potentially low cost alternative for treatment of uncomplicated P. falciparum infection in Mali and appears to have the added value of longer protective effect against new infection.**

Comment

Most countries have changed to artemisinin-based combination therapy, with the added cost and need to improve point-of-care malaria diagnostics to ensure efficient use of an expensive new drug. In Mali, as in many countries, the implementation of artemisinin-based combination therapy has been hampered by cost and limited drug availability in remote rural areas. This study shows that the combination of AQ-SP remains highly effective among children in Mali with uncomplicated malaria.

[Malar J.](#) 2008 Dec 22;7:262.



A randomized, open-label, comparative efficacy trial of artemether-lumefantrine suspension versus artemether-lumefantrine tablets for treatment of uncomplicated Plasmodium falciparum malaria in children in western Kenya.

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BACKGROUND: Artemether/lumefantrine (AL) has been adopted as the treatment of choice for uncomplicated malaria in Kenya and other countries in the region. Six-dose artemether/lumefantrine tablets are highly effective and safe for the treatment of infants and children weighing between five and 25 kg with uncomplicated Plasmodium falciparum malaria. However, oral paediatric formulations are urgently needed, as the tablets are difficult to administer to young children, who cannot swallow whole tablets or tolerate the bitter taste of the crushed tablets. **METHODS:** A randomized, controlled, open-label trial was conducted comparing day 28 PCR corrected cure-rates in 245 children aged 6-59 months, treated over three days with either six-dose of artemether/lumefantrine tablets (Coartem) or three-dose of artemether/lumefantrine suspension (Co-artesiane) for uncomplicated falciparum malaria in western Kenya. The children were followed-up with clinical, parasitological and haematological evaluations over 28 days. **RESULTS:** Ninety three percent (124/133) and 90% (121/134) children in the AL tablets and AL suspension arms respectively completed followed up. **A per protocol analysis revealed a PCR-corrected parasitological cure rate of 96.0% at Day 28 in the AL tablets group and 93.4% in the AL suspension group, p = 0.40.** Both drugs effectively cleared gametocytes and were well tolerated, with no difference in the overall incidence of adverse events. **CONCLUSION:** The once daily three-dose of artemether-lumefantrine suspension (Co-artesiane(R)) was not superior to six-dose artemether-lumefantrine tablets (Coartem) for the treatment of uncomplicated malaria in children below five years of age in western Kenya.

[Malar J.](#) 2008 Dec 19;7:261.



A randomized trial on effectiveness of artemether-lumefantrine versus artesunate plus amodiaquine for unsupervised treatment of uncomplicated Plasmodium falciparum malaria in Ghanaian children.

[Kobbe R](#), [Klein P](#), [Adjei S](#), [Amemasor S](#), [Thompson WN](#), [Heidemann H](#), [Nielsen MV](#), [Vohwinkel J](#), [Hogan B](#), [Kreuels B](#), [Bührlen M](#), [Loag W](#), [Ansong D](#), [May J](#).

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BACKGROUND: Numerous trials have demonstrated high efficacy and safety of artemisinin-based combination therapy (ACT) under supervised treatment. In contrast, effectiveness studies comparing different types of ACT applied unsupervised are scarce. **The aim of this study was to compare effectiveness, tolerability and acceptance of artesunate plus amodiaquine (ASAQ) against that of artemether-lumefantrine (AL) in Ghanaian children with uncomplicated Plasmodium falciparum malaria.** **METHODS:** A randomized open-label trial was conducted at two district hospitals in the Ashanti region, Ghana, an area of intense malaria transmission. **A total of 246 children under five years of age were randomly assigned to either ASAQ (Arsucam) or AL (Coartem).** Study participants received their first weight-adjusted dose under supervision. After the parent/guardian was advised of times and mode of administration the respective three-day treatment course was completed unobserved at home. Follow-up visits were performed on days 3, 7, 14 and 28 to evaluate clinical and parasitological outcomes, adverse events, and haematological recovery. Length polymorphisms of variable regions of msp1 and msp2 were determined to differentiate recrudescences from reinfections. Acceptance levels of both treatment regimens were assessed by means of standardized interviews. **RESULTS: Adequate clinical and parasitological responses after AL and ASAQ treatment were similar (88.3% and 91.7%, respectively). Interestingly, more late clinical failures until day 28 occurred in AL-treated children than in those who received ASAQ (17.5% and 7.3%, respectively; Hazard Ratio 2.41, 95% CI 1.00-5.79, p < 0.05).** Haematological recovery and drug tolerability were not found to be significantly different in both study arms. The acceptance of treatment with ASAQ was higher than that with AL (rank-scores 10.6 and 10.3, respectively; p < 0.05). **CONCLUSION: Unobserved AL and ASAQ treatment showed high adequate clinical and parasitological responses, though AL was inferior in preventing late clinical failures.**

[N Engl J Med.](#) 2008 Dec 11;359(24):2545-57. Epub 2008 Dec 8.



A trial of combination antimalarial therapies in children from Papua New Guinea.

[Karunajeewa HA](#), [Mueller I](#), [Senn M](#), [Lin E](#), [Law I](#), [Gomorra PS](#), [Oa O](#), [Griffin S](#), [Kotab K](#), [Suano P](#), [Tarongka N](#), [Ura A](#), [Lautu D](#), [Page-Sharp M](#), [Wong R](#), [Salman S](#), [Siba P](#), [Ilett KF](#), [Davis TM](#).

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BACKGROUND: Malaria control is difficult where there is intense year-round transmission of multiple plasmodium species, such as in Papua New Guinea. **METHODS:** Between April 2005 and July 2007, we conducted an open-label, randomized, parallel-group study of conventional chloroquine-sulfadoxine-pyrimethamine and artesunate-sulfadoxine-pyrimethamine, dihydroartemisinin-piperaquine, and artemether-lumefantrine in children in Papua New Guinea 0.5 to 5 years of age who had falciparum or vivax malaria. The primary end point was the rate of adequate clinical and parasitologic response at day 42 after the start of treatment with regard to Plasmodium falciparum, after correction for reinfections identified through polymerase-chain-

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reaction (PCR) genotyping of polymorphic loci in parasite DNA. Secondary end points included the rate of adequate clinical and parasitologic response at day 42 with regard to *P. vivax* without correction through PCR genotyping. RESULTS: Of 2802 febrile children screened, 482 with falciparum malaria and 195 with vivax malaria were included. **The highest rate of adequate clinical and parasitologic response for *P. falciparum* was in the artemether-lumefantrine group (95.2%), as compared with 81.5% in the chloroquine-sulfadoxine-pyrimethamine group (P=0.003), 85.4% in the artesunate-sulfadoxine-pyrimethamine group (P=0.02), and 88.0% in the dihydroartemisinin-piperaquine group (P=0.06). The rate of adequate clinical and parasitologic response for *P. vivax* in the dihydroartemisinin-piperaquine group (69.4%) was more than twice that in each of the other three treatment groups.** The in vitro chloroquine and piperaquine levels that inhibited growth of local *P. falciparum* isolates by 50% correlated significantly (P<0.001). Rash occurred more often with artesunate-sulfadoxine-pyrimethamine and dihydroartemisinin-piperaquine than with chloroquine-sulfadoxine-pyrimethamine (P=0.004 for both comparisons). CONCLUSIONS: **The most effective regimens were artemether-lumefantrine against *P. falciparum* and dihydroartemisinin-piperaquine against *P. vivax*.** The relatively high rate of treatment failure with dihydroartemisinin-piperaquine against *P. falciparum* may reflect cross-resistance between chloroquine and piperaquine. (Australian New Zealand Clinical Trials Registry number, ACTRN12605000550606.) 2008 Massachusetts Medical Society

[Trop Med Int Health](#). 2008 Nov;13(11):1384-91.



dhfr and dhps genotype and sulfadoxine-pyrimethamine treatment failure in children with falciparum malaria in the Democratic Republic of Congo.

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OBJECTIVE: To determine the relationship between mutations in dhfr and dhps and SP treatment failure in Plasmodium falciparum malaria in the Democratic Republic of the Congo (DRC). METHODS: Therapeutic efficacy trial was conducted in Rutshuru, Eastern DRC, between June and September 2002, comparing **sulfadoxine-pyrimethamine (SP), SP plus amodiaquine (AQSP) and artesunate plus SP (ASSP) regimens for treating malaria in children under 5 years old.** We genotyped 212 samples for mutations associated with SP resistance and investigated their association with treatment failure. RESULTS: In the SP arm, 61% of the subjects experienced treatment failure after 14 days. The failure rate was lower in the combination arms (AQSP: 32%, ASSP: 21%). The dhfr-108 and dhfr-51 mutations were nearly universal while 89% of the samples had at least one additional mutation at dhfr-59, dhps-437 or dhps-540. Dhps mutations had a bigger impact on treatment failure in children with high parasite density: for children with a parasite density <45 000 parasites/microl, the risk of treatment failure was 37% for mutations at dhps-437 and dhps-540 mutation and 21% for neither mutation [risk difference (RD) = 17%, 95% CI: -3%, 36%]. In children with a parasite density >45 000 parasites/microl, the treatment failure risk was 58% and 8% for children with both mutations or neither mutation, respectively (RD = 51%, 95% CI: 34%, 67%). CONCLUSIONS: **Dhps-437 and dhps-540 are strongly associated with SP treatment failure and should be evaluated further as a method for surveillance of SP-based therapy in DRC.**

[Malar J.](#) 2008 Nov 18;7:237.



A randomized trial to monitor the efficacy and effectiveness by QT-NASBA of artemether-lumefantrine versus dihydroartemisinin-piperaquine for treatment and transmission control of uncomplicated Plasmodium falciparum malaria in western Kenya.

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BACKGROUND: Many countries have implemented artemisinin-based combination therapy (ACT) for the first-line treatment of malaria. Although many studies have been performed on efficacy and tolerability of the combination arthemeter-lumefantrine (AL) or dihydroartemisinin-piperaquine (DP), less is known of the effect of these drugs on gametocyte development, which is an important issue in malaria control. **METHODS AND RESULTS:** In this two-arm randomized controlled trial, 146 children were treated with either AL or DP. Both groups received directly observed therapy and were followed for 28 days after treatment. Blood samples were analysed with microscopy and NASBA. In comparison with microscopy NASBA detected much more gametocyte positive individuals. **Moreover, NASBA showed a significant difference in gametocyte clearance in favour of AL compared to DP.** The decline of parasitaemia was slower and persistence or development of gametocytes was significantly higher and longer at day 3, 7 and 14 in the DP group but after 28 days no difference could be observed between both treatment arms. **CONCLUSION:** Although practical considerations could favour the use of one drug over another, the effect on gametocytogenesis should also be taken into account and studied further using molecular tools like NASBA. This also applies when a new drug is introduced. **TRIAL REGISTRATION:** Current controlled trials ISRCTN36463274.

[Acta Trop.](#) 2009 Jan;109(1):55-60. Epub 2008 Oct 17.

Effects of amodiaquine, artesunate, and artesunate-amodiaquine on Plasmodium falciparum malaria-associated anaemia in children.

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The effects of amodiaquine, artesunate and artesunate-amodiaquine on Plasmodium falciparum malaria-associated anaemia (PfMAA) and the recovery from PfMAA were evaluated in 328 children with uncomplicated malaria randomized to the standard dose regimens of the three drug treatments. Overall, malaria-attributable fall in haematocrit (MAFH) before treatment was

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4.8+/-2.8%, 95% confidence interval (CI) 4.4-5.2%, and was not significantly different between the treatment groups (P=0.31). An age <5 years and a history of illness >3d were independent predictors of MAFH before treatment >4%. **Following treatment, drug-attributable fall in haematocrit (DAFH) was significantly higher in amodiaquine-treated children (4.6+/-2.9%, 2.8+/-1.8%, 3.0+/-1.8% for amodiaquine, artesunate, artesunate-amodiaquine, respectively, P<0.0001).** The rate of DAFH was significantly lower in artesunate-treated children (1.4+/-0.9%, 0.7+/-0.6%, 1.0+/-0.6% per day for amodiaquine, artesunate and artesunate-amodiaquine, respectively, P<0.0001). The rate of rise in haematocrit from the nadir on days 3-7 was significantly higher in amodiaquine treated children (P=0.045). In anaemic children (n=68), the time elapsing from treatment to the attainment of a haematocrit > or =30%, the anaemia resolution time, and the proportion of anaemic children with complete resolution on day 14 were similar in all treatment groups (P=0.17 and 0.65, respectively). Artemisinin drugs may reduce the extent and rate of fall in PfMAA during treatment and may attenuate malaria-associated anaemia in children.

[Lancet](#). 2008 Nov 22;372(9652):1819-27. Epub 2008 Oct 14.

Efficacy and safety of artemether-lumefantrine dispersible tablets compared with crushed commercial tablets in African infants and children with uncomplicated malaria: a randomised, single-blind, multicentre trial.

[Abdulla S](#), [Sagara I](#), [Borrmann S](#), [D'Alessandro U](#), [González R](#), [Hamel M](#), [Ogutu B](#), [Mårtensson A](#), [Lyimo J](#), [Maiga H](#), [Sasi P](#), [Nahum A](#), [Bassat Q](#), [Juma E](#), [Otieno L](#), [Björkman A](#), [Beck HP](#), [Andriano K](#), [Cousin M](#), [Lefèvre G](#), [Ubben D](#), [Premji Z](#).

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BACKGROUND: Combination treatments, preferably containing an artemisinin derivative, are recommended to improve efficacy and prevent *Plasmodium falciparum* drug resistance. Our aim was to show non-inferiority of a new dispersible formulation of artemether-lumefantrine to the conventional crushed tablet in the treatment of young children with uncomplicated malaria. **METHODS:** We did a randomised non-inferiority study on children weighing 5-35 kg with uncomplicated *P. falciparum* malaria in Benin, Kenya, Mali, Mozambique, and Tanzania. The primary outcome measure was PCR-corrected 28-day parasitological cure rate. We aimed to show non-inferiority (with a margin of -5%) of dispersible versus crushed tablet. We constructed an asymptotic one-sided 97.5% CI on the difference in cure rates. A computer-generated randomisation list was kept centrally and investigators were unaware of the study medication administered. We used a modified intention-to-treat analysis. This trial is registered with ClinicalTrials.gov, number NCT00386763. **FINDINGS:** 899 children aged 12 years or younger were randomly assigned to either dispersible (n=447) or crushed tablets (n=452). More than 85% of patients in each treatment group completed the study. 812 children qualified for the modified intention-to-treat analysis (n=403 vs n=409). **The PCR-corrected day-28 cure rate was 97.8% (95% CI 96.3-99.2) in the group on dispersible formulation and 98.5% (97.4-99.7) in the group on crushed formulation.** The lower bound of the one-sided 97.5% CI was -2.7%. The most common drug-related adverse event was vomiting (n=33 [7%] and n=42 [9%], respectively). No signs of ototoxicity or relevant cardiotoxicity were seen. **INTERPRETATION:** **A six-dose regimen of artemether-lumefantrine with the new dispersible formulation is as**

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efficacious as the currently used crushed tablet in infants and children, and has a similar safety profile.

[Ann Trop Med Parasitol](#). 2008 Oct;102(7):565-76.

A randomized, comparative study of supervised and unsupervised artesunate-amodiaquine, for the treatment of uncomplicated malaria in Ghana.

[Oduro AR](#), [Anyorigiya T](#), [Anto F](#), [Amenga-Etego L](#), [Ansah NA](#), [Atobrah P](#), [Ansah P](#), [Koram K](#), [Hodgson A](#).

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Although the use of artesunate-amodiaquine treatment is growing in Africa, data on its effectiveness are limited. In only the second published comparison of supervised and unsupervised treatments with this combination, Ghanaian children with uncomplicated malaria have recently been investigated in an open-label, randomized, comparative study. Children aged 6-120 months attending the Navrongo War Memorial hospital between November 2005 and December 2006 were enrolled if they had uncomplicated *Plasmodium falciparum* malaria and at least one of their parents/guardians gave their informed consent. Overall, 638 patients were screened, 357 were found to have *P. falciparum* infection, and 308 of these satisfied the other selection criteria and were enrolled. The subjects were divided randomly into two treatment arms. **All the children were scheduled to receive 10 mg amodiaquine/kg and 4 mg artesunate/kg daily for 3 days but only 154 (the 'supervised') were given all their treatments in hospital, with each dose directly observed. Although the other 154 children (the 'unsupervised') were given their first dose in hospital, under supervision, they were then sent home with the tablets they required to complete treatment.** Study participation lasted for 28 days, with follow-up on days 3, 7, 14, 21 and 28. During follow-up, axillary temperatures, any emergent signs and symptoms, and concomitant drug consumption were recorded and haemoglobin concentrations and malarial parasitaemias and gametocytaemias were measured. All but seven of the 308 subjects completed the study. At enrolment the subjects had a mean age of 45.0 months, a mean weight of 14.8 kg, a mean axillary temperature of 37.9 degrees C and a geometric mean parasitaemia of 11,367 asexual stages/microl. About 55% of the children investigated were girls. There were no significant baseline difference between the two treatment arms. **Although there was also no difference in the clearance of fever and parasitaemia between the two arms by day 14, a supervised child was significantly more likely to show an adequate clinical and parasitological response, by day 21 (91.3% v. 84.1%; P= 0.05) or day 28 (80.0% v. 64.9%; P<0.01), than an unsupervised child.** The reported adverse effects following treatment and the trend in haemoglobin recovery were, however, similar in the two arms. **Although artesunate-amodiaquine appeared very effective in the treatment of uncomplicated *P. falciparum* malaria in children, whether supervised or not, it appears that supervised treatment provided stronger prevention against re-infection and recrudescence.** At least in the present study, treatment at home, without medical supervision, probably led to relatively poor compliance.

PLoS One. 2008 Aug 6;3(8):e2861.



A randomised trial of an eight-week, once weekly primaquine regimen to prevent relapse of plasmodium vivax in Northwest Frontier Province, Pakistan.

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BACKGROUND: Vivax malaria remains a major cause of morbidity in the subtropics. To undermine the stability of the disease, drugs are required that prevent relapse and provide reservoir reduction. **A 14-day course of primaquine (PQ) is effective but cannot safely be used in routine practice because of its interaction with glucose-6-phosphate dehydrogenase (G6PD) deficiency for which testing is seldom available.** Safe and effective use of PQ without the need for G6PD testing would be ideal. The efficacy and safety of an 8-week, once weekly PQ regimen was compared with current standard treatment (chloroquine alone) and a 14-day PQ regimen. METHODS AND PRINCIPAL FINDINGS: **200 microscopically confirmed Plasmodium vivax patients were randomly assigned to either once weekly 8-week PQ (0.75 mg/kg/week), once weekly 8-week placebo, or 14-day PQ (0.5mg/kg/day) in North West Frontier Province, Pakistan.** All patients were treated with a standard chloroquine dose and tested for G6PD deficiency. Deficient patients were assigned to the 8-week PQ group. Failure was defined as any subsequent episode of vivax malaria over 11 months of observation. **There were 22/71 (31.0%) failures in the placebo group and 1/55 (1.8%) and 4/75 (5.1%) failures in the 14-day and 8-week PQ groups, respectively.** Adjusted odds ratios were: for 8-week PQ vs. placebo-0.05 (95%CI: 0.01-0.2, $p<0.001$) and for 14-day PQ vs. placebo-0.01 (95%CI: 0.002-0.1, $p<0.001$). Restricted analysis allowing for a post-treatment prophylactic effect confirmed that the 8-week regimen was superior to current treatment. Only one G6PD deficient patient presented. There were no serious adverse events. CONCLUSIONS: A practical radical treatment for vivax malaria is essential for control and elimination of the disease. **The 8-week PQ course is more effective at preventing relapse than current treatment with chloroquine alone.** Widespread use of the 8-week regimen could make an important contribution to reservoir reduction or regional elimination where G6PD testing is not available. TRIAL REGISTRATION: ClinicalTrials.gov NCT00158587.

[Malar J](#). 2008 Jul 11;7:127.



Amodiaquine-artesunate vs artemether-lumefantrine for uncomplicated malaria in Ghanaian children: a randomized efficacy and safety trial with one year follow-up.

[Adjei GO](#), [Kurtzhals JA](#), [Rodrigues OP](#), [Alifrangis M](#), [Hoegberg LC](#), [Kitcher ED](#), [Badoe EV](#), [Lamprey R](#), [Goka BQ](#).

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BACKGROUND: Artesunate-amodiaquine (AS+AQ) and artemether-lumefantrine (AM-L) are efficacious artemisinin combination therapy (ACT) regimens that have been widely adopted in sub-Saharan Africa. However, there is little information on the efficacy of these regimens on subsequent episodes beyond 28 days, or on the safety of repeated treatments. **METHODS:** Children aged six months to 14 years with uncomplicated malaria were randomly assigned to treatment with AS+AQ (n = 116), or AM-L (n = 111). Recruited subjects were followed-up, initially for 28 days, and then monthly for up to one year. All subsequent attacks of uncomplicated malaria after 28 days were treated with the same regimen as at randomization. Investigations aimed at determining efficacy and side effects were conducted. **RESULTS:** **Adequate clinical and parasitological response in subjects with evaluable end-points were, 97.1% (100/103) and 98.2% (107/109) on day 14, and 94.2% (97/103) and 95.3% (102/107) on day 28 in the AM-L and AS+AQ groups, respectively.** Similar results were obtained after PCR correction. The incidence of malaria attacks in the year following recruitment was similar between the two treatment groups (p = 0.93). There was a high incidence of potentially AQ-resistant parasites in the study area. The incidence of adverse events, such as pruritus, fatigue and neutropaenia were similar in the two treatment groups. No patient showed signs of hearing impairment, and no abnormal neurological signs were observed during one year of follow-up. Other adverse events were mild in intensity and overlapped with known malaria symptomatology. No adverse event exacerbation was observed in any of the subjects who received multiple treatment courses with these ACT regimens during one year follow-up. **CONCLUSION:** AS+AQ and AM-L were efficacious for treatment of children with uncomplicated malaria in Ghana and drug-related adverse events were rare in treated subjects during one year of follow-up. The high prevalence of potentially AQ resistant parasites raises questions about the utility of AQ as a partner drug for ACT in Ghana. The efficacy of AS+AQ in Ghana requires, therefore, continuous monitoring and evaluation. **TRIAL REGISTRATION:** NCT 00406146 <http://www.clinicaltrials.gov>.

Treatment of severe or complicated malaria

(See also Emergency Care, for treatment of hypoglycaemia associated with severe malaria)

[Malar J.](#) 2008 Oct 17;7:210.



Artemisinin derivatives versus quinine in treating severe malaria in children: a systematic review.

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BACKGROUND: The efficacy of intravenous quinine, which is the mainstay for treating severe malaria in children, is decreasing in South East Asia and Africa. Artemisinin derivatives are a potential alternative to quinine. However, their efficacy compared to quinine in treating severe malaria in children is not clearly understood. **The objective of this review was to assess the efficacy of parenteral artemisinin derivatives versus parenteral quinine in treating severe**

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malaria in children. METHODS: All randomized controlled studies comparing parenteral artemisinin derivatives with parenteral quinine in treating severe malaria in children were included in the review. Data bases searched were: The Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 4, 2007), MEDLINE (1966 to February 2008), EMBASE (1980 to February 2008), and LILACS (1982 to February 2008). Dichotomous variables were compared using risk ratios (RR) and the continuous data using weighted mean difference (WMD). RESULTS: **Twelve trials were included (1,524 subjects). There was no difference in mortality between artemisinin derivatives and quinine (RR = 0.90, 95% CI 0.73 to 1.12). The artemisinin derivatives resolved coma faster than quinine (WMD = -4.61, 95% CI: -7.21 to -2.00, fixed effect model), but when trials with adequate concealment only were considered this differences disappeared. There was no statistically significant difference between the two groups in parasite clearance time, fever clearance time, incidence of neurological sequelae and 28th day cure rate. One trial reported significantly more local reactions at the injection site with intramuscular quinine compared to artemether. None of the trials was adequately powered to demonstrate equivalence. CONCLUSION: There was no evidence that treatment of children with severe malaria with parenteral artemisinin derivatives was associated with lower mortality or long-term morbidity compared to parenteral quinine.** Future studies require adequately powered equivalence trial design to decide whether both drugs are equally effective.

Malnutrition

Comment

This year there were 5 randomized trials on the use of ready-to-use fortified spread (lipid-based nutritional supplement with multivitamins). In Malawi and Nigeria, short term (6-12 weeks) administration of fortified spread reduces wasting. In Malawi, taking FS for 12 weeks was insufficient for any substantial improvement in stunting, but 12 months seems to be beneficial, especially for the most severely stunted children, and had a sustained effect over the next 2 years. The mixute was made of peanut butter, milk powder, sugar, vegetable oil, and pre-mixed micronutrient supplement.

[Arch Pediatr Adolesc Med.](#) 2008 Jul;162(7):619-26.

Complementary feeding with fortified spread and incidence of severe stunting in 6- to 18-month-old rural Malawians.

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OBJECTIVE: To compare growth and incidence of malnutrition in infants receiving long-term dietary supplementation with ready-to-use fortified spread (FS) or micronutrient-fortified maize-soy flour (likuni phala [LP]). DESIGN: Randomized, controlled, single-blind trial. SETTING:

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Rural Malawi. PARTICIPANTS: A total of 182 six-month-old infants. INTERVENTION: **Participants were randomized to receive 1 year of daily supplementation with 71 g of LP (282 kcal), 50 g of FS (FS50) (256 kcal), or 25 g of FS (FS25) (130 [corrected] kcal).** OUTCOME MEASURES: Weight and length gains and the incidences of severe stunting, underweight, and wasting. RESULTS: Mean weight and length gains in the LP, FS50, and FS25 groups were 2.37, 2.47, and 2.37 kg ($P = .66$) and 12.7, 13.5, and 13.2 cm ($P = .23$), respectively. In the same groups, the cumulative 12-month incidence of severe stunting was 13.3%, 0.0%, and 3.5% ($P = .01$), of severe underweight was 15.0%, 22.5%, and 16.9% ($P = .71$), and of severe wasting was 1.8%, 1.9%, and 1.8% ($P > .99$). Compared with LP-supplemented infants, those given FS50 gained a mean of 100 g more weight and 0.8 cm more length. There was a significant interaction between baseline length and intervention ($P = .04$); **in children with below-median length at enrollment, those given FS50 gained a mean of 1.9 cm more than individuals receiving LP.** CONCLUSION: **One-year-long complementary feeding with FS does not have a significantly larger effect than LP on mean weight gain in all infants, but it is likely to boost linear growth in the most disadvantaged individuals and, hence, decrease the incidence of severe stunting.**

[Matern Child Nutr.](#) 2009 Apr;5(2):159-70.

Supplementary feeding with fortified spread among moderately underweight 6-18-month-old rural Malawian children.

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We aimed to analyse growth and recovery from undernutrition among **moderately underweight ambulatory children receiving micronutrient-fortified maize-soy flour (Likuni Phala, LP) or ready-to-use fortified spread (FS) supplementary diet.** One hundred and seventy-six 6-18-month-old individuals were randomized to receive 500 g LP or 350 g FS weekly for 12 weeks. Baseline and end of intervention measurements were used to calculate anthropometric gains and recovery from underweight, wasting and stunting. Mean weight-for-age increased by 0.22 (95% CI 0.07-0.37) and 0.28 (0.18-0.40) Z-score units in the LP and FS groups respectively. Comparable increase for mean weight-for-length was 0.39 (0.20-0.57) and 0.52 (0.38-0.65) Z-score units. Recovery from underweight and wasting was 20% and 93% in LP group and 16% and 75% in FS group. Few individuals recovered from stunting and mean length-for-age was not markedly changed. There were no statistically significant differences between the outcomes in the two intervention groups. **In a poor food-security setting, underweight infants and children receiving supplementary feeding for 12 weeks with ready-to-use FS or maize-soy flour porridge show similar recovery from moderate wasting and underweight. Neither intervention, if limited to a 12-week duration, appears to have significant impact on the process of linear growth or stunting.**

[Am J Clin Nutr.](#) 2009 Jan;89(1):382-90. Epub 2008 Dec 3.

Postintervention growth of Malawian children who received 12-mo dietary complementation with a lipid-based nutrient supplement or maize-soy flour.

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BACKGROUND: Therapeutic feeding with micronutrient-fortified lipid-based nutrient supplements (LNSs) has proven useful in the rehabilitation of severely malnourished children. We recently reported that complementary feeding of 6-18-mo-old infants with an LNS known as FS50 was associated with improved linear growth and a reduction in the incidence of severe stunting during the supplementation period. **OBJECTIVE:** **Our objective was to assess whether a reduction in stunting seen with 12-mo LNS supplementation was sustained over a subsequent 2-y nonintervention period.** **DESIGN:** One hundred eighty-two 6-mo-old healthy rural Malawian infants were randomly assigned to receive daily supplementation for 12 mo with 71 g of maize-soy flour [likuni phala (LP); control group, 282 kcal] or either 50 g of FS50 (264 kcal; main intervention group), or 25 g of FS25 (130 kcal). Main outcome measures were incidence of severe stunting and mean z score changes in weight-for-age, length-for-age, and weight-for-length during a 36-mo follow-up period. **RESULTS:** **The cumulative 36-mo incidence of severe stunting was 19.6% in LP, 3.6% in FS50, and 10.3% in FS25 groups (P = 0.03).** Mean weight-for-age changes were -1.09, -0.76, and -1.22 (P = 0.04); mean length-for-age changes were -0.47, -0.37, and -0.71 (P = 0.10); and mean weight-for-length changes were -1.52, -1.18, and -1.48 (P = 0.27). All differences were more marked among individuals with baseline length-for-age below the median. Differences in length developed during the intervention at age 10-18 mo, whereas weight differences continued to increase after the intervention. **CONCLUSIONS:** **Twelve-month-long complementary feeding with 50 g/d FS50 is likely to have a positive and sustained impact on the incidence of severe stunting in rural Malawi.** Half-dose intervention may not have the same effect. This trial was registered at (clinicaltrials.gov) as NCT00131209.

[J Nutr.](#) 2009 Apr;139(4):773-8. Epub 2009 Feb 18.

Supplementary feeding with fortified spreads results in higher recovery rates than with a corn/soy blend in moderately wasted children.

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Moderate childhood wasting is defined as having a weight-for-height Z-score (WHZ) < -2, but > or = -3. These children are typically given fortified corn/soy blended flour (CSB), but this intervention has shown limited effectiveness. **Fortified spreads (FS) can be used as supplementary foods instead; they are energy-dense, lipid-based pastes with added powdered micronutrients.** In this randomized clinical effectiveness trial, the recovery rates were compared among children with moderate wasting who received either milk/peanut FS,

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soy/peanut FS, or CSB. Children received isoenergetic quantities of food, 314 kJ x kg(-1) x d(-1), for up to 8 wk with biweekly follow-up. The primary outcome was recovery, defined as having a WHZ > -2. Time-event analysis was used to compare the recovery rate. A total of 1362 children were enrolled in the study. Children receiving soy/peanut FS had a similar recovery rate to those receiving milk/peanut FS and children in either FS group were more likely to recover than those receiving CSB (80% in both FS groups vs. 72% in the CSB group; P < 0.01). The rate of weight gain in the first 2 wk was greater among children receiving milk/peanut FS (2.6 g x kg(-1) x d(-1), n = 465) or children receiving soy/peanut FS (2.4 g x kg(-1) x d(-1), n = 450) than among children receiving CSB (2.0 g x kg(-1) x d(-1), n = 447; P < 0.05). Rates of length gain did not differ among the 3 groups. **A total of 8% of children in each feeding group developed edema, indicative of severe malnutrition, while receiving supplemental feeding. We conclude that FS are superior supplementary foods to CSB for moderately wasted Malawian children.**

[JAMA](#). 2009 Jan 21;301(3):277-85.



Effect of preventive supplementation with ready-to-use therapeutic food on the nutritional status, mortality, and morbidity of children aged 6 to 60 months in Niger: a cluster randomized trial.

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CONTEXT: Ready-to-use therapeutic foods (RUTFs) are an important component of effective outpatient treatment of severe wasting. However, their effectiveness in the population-based prevention of moderate and severe wasting has not been evaluated. OBJECTIVE: **To evaluate the effect of a 3-month distribution of RUTF on the nutritional status, mortality, and morbidity of children aged 6 to 60 months in Niger.** DESIGN, SETTING, AND PARTICIPANTS: A cluster randomized trial of 12 villages in Maradi, Niger. Six villages were randomized to intervention and 6 to no intervention. All children in the study villages aged 6 to 60 months were eligible for recruitment. INTERVENTION: **Children with weight-for-height 80% or more of the National Center for Health Statistics reference median in the 6 intervention villages received a monthly distribution of 1 packet per day of RUTF (92 g [500 kcal/d]) from August to October 2006. Children in the 6 nonintervention villages received no preventive supplementation.** Active surveillance for conditions requiring medical or nutritional treatment was conducted monthly in all 12 study villages from August 2006 to March 2007. MAIN OUTCOME MEASURES: Changes in weight-for-height z score (WHZ) according to the World Health Organization Child Growth Standards and incidence of wasting (WHZ < -2) over 8 months of follow-up. RESULTS: The number of children with height and weight measurements in August, October, December, and February was 3166, 3110, 2936, and 3026, respectively. The WHZ difference between the intervention and nonintervention groups was -0.10 z (95% confidence interval [CI], -0.23 to 0.03) at baseline and 0.12 z (95% CI, 0.02 to

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0.21) after 8 months of follow-up. The adjusted effect of the intervention on WHZ from baseline to the end of follow-up was thus 0.22 z (95% CI, 0.13 to 0.30). The absolute rate of wasting and severe wasting, respectively, was 0.17 events per child-year (140 events/841 child-years) and 0.03 events per child-year (29 events/943 child-years) in the intervention villages, compared with 0.26 events per child-year (233 events/895 child-years) and 0.07 events per child-year (71 events/1029 child-years) in the nonintervention villages. **The intervention thus resulted in a 36% (95% CI, 17% to 50%; P < .001) reduction in the incidence of wasting and a 58% (95% CI, 43% to 68%; P < .001) reduction in the incidence of severe wasting.** There was no reduction in mortality, with a mortality rate of 0.007 deaths per child-year (7 deaths/986 child-years) in the intervention villages and 0.016 deaths per child-year (18 deaths/1099 child-years) in the nonintervention villages (adjusted hazard ratio, 0.51; 95% CI, 0.25 to 1.05).

CONCLUSION: Short-term supplementation of nonmalnourished children with RUTF reduced the decline in WHZ and the incidence of wasting and severe wasting over 8 months. TRIAL

REGISTRATION: clinicaltrials.gov Identifier: NCT00682708.

Maternal health, education and nutrition

[Pediatrics](#). 2009 Apr;123(4):e685-92.

Effects of maternal multimicronutrient supplementation on the mental development of infants in rural western China: follow-up evaluation of a double-blind, randomized, controlled trial.

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OBJECTIVE: We investigated the benefits of maternal multimicronutrient supplementation during gestation on the mental and psychomotor development of infants. METHODS: In a double-blind, randomized, controlled trial, pregnant women (N = 5828) in 2 rural counties in western China were assigned randomly to receive multimicronutrient (**5 minerals and 10 vitamins at levels approximating the recommended daily allowance**), **folic acid plus iron, or folic acid supplementation daily from approximately 14 weeks of gestation until delivery**. We assessed a subset of the newborns (N = 1305) from the 3 supplementation groups by measuring their mental and psychomotor development with the Bayley Scales of Infant Development, at 3, 6, and 12 months of age. Multilevel analyses were used to compare the mental development and psychomotor development raw scores at 3, 6, and 12 months.

RESULTS: **Multimicronutrient supplementation was associated with mean increases in mental development raw scores for infants at 1 year of age of 1.00 and 1.22 points, compared with folic acid only and folic acid plus iron supplementation, respectively.**

However, supplementation did not increase significantly the psychomotor development raw scores up to 1 year of age. CONCLUSION: Compared with iron and folic acid supplementation,

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the administration of multimicronutrients to pregnant women improved the mental development of their children at 1 year of age.

[Am J Clin Nutr.](#) 2009 Mar;89(3):946S-950S. Epub 2009 Jan 21.

Iron deficiency and child and maternal health.

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BACKGROUND: Iron deficiency is most commonly found in women of reproductive age and infants worldwide, but the influence of maternal iron deficiency on infant development is underexplored. **OBJECTIVE:** The objective was to examine the relation between maternal iron status and mother-child interactions in a randomized, double-blind, intervention trial conducted in South Africa. **DESIGN:** Women were recruited into the study from a health clinic at 6-8 wk postpartum and were classified as either iron-deficient anemic (IDA) or iron-sufficient after blood analysis. IDA mothers received iron supplements of 125 mg FeSO₄ (IDA-Fe; n = 34) or placebo (IDA-PL; n = 30) daily from 10 wk to 9 mo postpartum. The control group (n = 31) consisted of iron-sufficient mothers. Free-play mother-child interaction sessions were videotaped in the clinic at 10 wk (n = 80) and 9 mo (n = 66) postpartum and coded per the Emotional Availability Scales (4 maternal scales: sensitivity, structuring, nonintrusiveness, and nonhostility; 2 infant scales: responsiveness and involvement). **RESULTS:** **At 10 wk, scores for maternal sensitivity and child responsiveness were significantly greater in the control group than in the IDA groups (P = 0.028 and 0.009, respectively). At 9 mo, the control and IDA-Fe groups no longer differed. These 2 groups scored significantly better on the maternal sensitivity, structuring, and nonhostility scales and on the child responsiveness scale than did the IDA-PL group (P = 0.007-0.032), whose iron status remained low.** **CONCLUSION:** These data indicate that maternal iron deficiency negatively affects mother-child interactions and that iron supplementation protects against these negative effects.

[J Nutr.](#) 2008 Dec;138(12):2468-73.



Dietary supplementation of rural Gambian women during pregnancy does not affect body composition in offspring at 11-17 years of age.

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Fetal nutrition is thought to be an important determinant of later disease risk, although evidence from randomized-controlled trials in humans is lacking. **We followed children born during a**

protein-energy supplementation trial to investigate to what extent this maternal supplement, which improved birth weight, influenced offspring body composition in adolescence. Subjects were 1270 Gambian children (659 boys, 611 girls) aged 11-17 y whose mothers had participated in the original cluster-randomized trial and had received the supplement during pregnancy (intervention) or postpartum (control). **Basic anthropometry was measured using standard techniques and fatness was assessed by bioelectrical impedance analysis and population-specific prediction equations.** For boys, mean body fat was 12.6% for both intervention and control groups. Mean trunk fat was 11.9% in the intervention group and 12.0% in the control. Intervention girls had a mean body fat of 19.5% and trunk fat of 15.2%; for control girls, it was 19.3 and 14.8%, respectively. BMI, body fat, trunk fat, fat mass index, and fat-free mass index did not differ for either sex when analyzed with generalized estimating equations adjusted for age, maternal height, maternal parity, location, season of birth, and menarche in females. Neither infant-attained size nor the onset of menarche were affected by maternal supplementation. **These findings suggest that protein-energy supplements to pregnant women, compared with lactating women, do not affect offspring body composition during adolescence.**

[Am J Clin Nutr.](#) 2008 Nov;88(5):1330-40.



Effects of maternal multiple micronutrient supplementation on fetal growth: a double-blind randomized controlled trial in rural Burkina Faso.

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[Ki JP](#), [Koudougbo V](#), [Toe L](#), [Lanou H](#), [Da E](#), [Lougue G](#), [Negalo B](#), [Guebe O](#), [Hien B](#), [Ouattara S](#), [Bicaba B](#), [Yameogo CK](#), [Diallo N](#), [Sanou M](#), [Hien A](#), [Kusin J](#), [Delpeuch F](#), [Van Camp J](#), [Bourdoux P](#), [Diagbouga S](#), [Tapsoba S](#), [Boncougou M](#), [Nikiema P](#).

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BACKGROUND: Intrauterine growth retardation is a major predictor of child health in developing countries. OBJECTIVE: We tested whether providing pregnant women with the UNICEF/WHO/UNU international multiple micronutrient preparation (UNIMMAP), rather than iron and folic acid alone, improved fetal growth and its correlates. DESIGN: An intention-to-treat, double-blind, randomized controlled trial including 1426 pregnancies was carried out in rural Burkina Faso. Tablet intake was directly observed. RESULTS: Pregnancy outcome was known in 96.3% of the participants. **After adjustment for gestational age at delivery, both birth weight (52 g; 95% CI: 4, 100; P = 0.035) and birth length (3.6 mm; 95% CI: 0.8, 6.3; P = 0.012) were significantly higher in the UNIMMAP group.** UNIMMAP had a differential effect by percentiles of birth weight and length distributions: the risk of large-for-gestational-age infants was higher in the UNIMMAP group (OR: 1.58; 95% CI: 1.04, 2.38; P = 0.03), although the risk of low birth weight remained unchanged. The effect of UNIMMAP on birth size was modified by maternal body mass index at enrollment and could be more important in multiparous women and women taking sulfadoxine-pyrimethamine. **Unexpectedly, the risk of perinatal death was marginally significantly increased in the UNIMMAP group (OR: 1.78; 95% CI: 0.95, 3.32; P = 0.07), and this seemed to affect mainly primiparous women (OR: 3.44; 95% CI: 1.1, 10.7; P for interaction = 0.11).** CONCLUSIONS: Maternal UNIMMAP modestly but significantly increased fetal growth. The resulting benefit on infant growth

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and survival needs to be assessed. The possible lack of benefit and potential harm in primiparous women should be further investigated. This trial was registered at clinicaltrials.gov as NCT00642408.

Comment

There is uncertainty about the effect of maternal multivitamin supplementation on perinatal survival. A study from Indonesia showed an 18% reduction in post-natal mortality, but the pooled results of two studies from Nepal showed an increased risk of still birth with maternal micronutrient supplementation, as did this trial, particularly for primiparous women. Further research is necessary to clarify this issue.

[Int J Epidemiol](#). 2009 Feb;38(1):119-27. Epub 2008 Aug 2.



Maternal protein-energy supplementation does not affect adolescent blood pressure in The Gambia.

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BACKGROUND: Birthweight, and by inference maternal nutrition during pregnancy, is thought to be an important determinant of offspring blood pressure but the evidence base for this in humans is lacking data from randomized controlled trials. **METHODS:** **The offspring from a maternal prenatal protein-energy supplementation trial were enrolled into a follow-up study of chronic disease risk factors including blood pressure.** Subjects were 11-17 years of age and blood pressure was measured in triplicate using an automated monitor (Omron 705IT). One-thousand two-hundred sixty seven individuals (71% of potential participants) were included in the analysis. **RESULTS:** **There was no difference in blood pressure between those whose mothers had consumed protein-energy biscuits during pregnancy and those whose mothers had consumed the same supplement post-partum.** For systolic blood pressure the intention-to-treat regression coefficient was 0.46 (95% CI: -1.12, 2.04). Mean systolic blood pressure for control children was 110.2 (SD +/- 9.3) mmHg and for intervention children was 110.8 (SD +/- 8.8) mmHg. Mean diastolic blood pressure for control children was 64.7 (SD +/- 7.7) mmHg and for intervention children was 64.6 (SD +/- 7.6) mmHg. **CONCLUSIONS:** **We have found no association between maternal prenatal protein-energy supplementation and offspring blood pressure in adolescence amongst rural Gambians.** We found some evidence to suggest that offspring body composition may interact with the effect of maternal supplementation on blood pressure.

[Matern Child Nutr.](#) 2008 Oct;4(4):275-86.



Effectiveness of a community-based responsive feeding programme in rural Bangladesh: a cluster randomized field trial.

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Responsive complementary feeding, whereby the mother feeds her child in response to child cues of hunger state and psychomotor abilities, is a problem in some countries, and likely contributes to malnutrition. Interventions are needed to evaluate whether promoting responsive feeding would add any benefit. **Using a cluster randomized field trial, we evaluated a six-session educational programme that emphasized practice of two key behaviours, namely child self-feeding and maternal responsiveness.** One hundred mothers and their 12- to 24-month-olds attended the sessions as part of village clusters randomly assigned to the intervention group. A similar number of controls received sessions on foods to feed and nutritional disorders. Outcomes assessed at pre-test, 2-week post-intervention and again 5-months post-intervention included weight, mouthfuls of food taken, self-feeding and maternal responsiveness. Research assistants, blind to group assignment, observed and coded mother and child behaviours during the midday meal. Secondary measures included foods fed and feeding messages recalled. Analysis was based on intention to treat and accounted for clustering. Only 10% of each group was lost to follow-up. Weight ($d = 0.28$), weight gain ($d = 0.48$) and child self-feeding ($d = 0.30$) were significantly higher in the responsive feeding group. Mouthfuls of food eaten and maternal responsiveness were not significantly increased by the intervention. **Mothers in the intervention gave their children more vegetables, and spontaneously recalled more feeding messages at the 5-month follow-up.** These results provide evidence that self-feeding and weight gain can improve by targeting specific behaviours, while maternal responsiveness may require more intensive strategies.

Measles

(see also Vaccination, Measles)

[Cochrane Database Syst Rev.](#) 2008 Jul 16;(3):CD001477.



Antibiotics for preventing complications in children with measles.

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BACKGROUND: Measles is the leading killer among vaccine-preventable diseases, responsible for an estimated 44% of the 1.7 million vaccine-preventable deaths among children annually.

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OBJECTIVES: To assess the effects of antibiotics given to children with measles to prevent complications and reduce pneumonia, other morbidities and mortality. **SEARCH STRATEGY:** In this 2008 update we searched the Cochrane Central Register of Controlled Trials (The Cochrane Library 2008, Issue 1) MEDLINE (1966 to January week 1, 2008), EMBASE (1980 to December 2007) and the National Research Register (Issue 3, 2007). **SELECTION CRITERIA:** Randomized controlled trials (RCTs) and quasi-RCTs comparing antibiotics with placebo or no treatment to prevent complications in children with measles. **DATA COLLECTION AND ANALYSIS:** Two review authors independently extracted data and assessed trial quality. **MAIN RESULTS:** Seven trials with 1385 children were included. Pooled study data showed that the incidence of pneumonia was lower in the treatment group compared to the control group. However, the difference was not statistically significant. In children who received antibiotics, 1.9% developed pneumonia, while in the control group 6% developed pneumonia (OR 0.28; 95% CI 0.06 to 1.25). The one trial that showed an increase in the rate of pneumonia with antibiotics was conducted in 1942 and compared oral sulfathiazole with symptomatic treatment. **If the results of this trial are removed from the meta-analysis, and the remaining six studies are combined, there is a statistically significant reduction in the incidence of pneumonia in children receiving antibiotics (OR 0.17; 95% CI 0.05 to 0.65).** The number needed to treat to prevent one episode of pneumonia is 24 patients. **The incidence of other complications was significantly lower in children receiving antibiotics: purulent otitis media (OR 0.34; 95% CI 0.16 to 0.73) and tonsillitis (OR 0.08; 95% CI 0.01 to 0.72).** There was no difference in the incidence of conjunctivitis (OR 0.39; 95% CI 0.15 to 1.0), diarrhea (OR 0.53; 95% CI 0.23 to 1.22) or croup (OR 0.16; 95% CI 0.01 to 4.06). **AUTHORS' CONCLUSIONS:** **This review suggests a beneficial effect of antibiotics in preventing complications such as pneumonia, purulent otitis media and tonsillitis in children with measles.** On the basis of this review, it is not possible to give definitive guidelines on the type of antibiotic, duration, or the day of initiation. Use of penicillin or co-trimoxazole may be considered. There is a need to generate more evidence by well planned RCTs to answer these questions.

Meningitis and Encephalitis

[Pediatr Infect Dis J.](#) 2008 Oct;27(10):892-6.

Increase in serum osmolality is possible mechanism for the beneficial effects of glycerol in childhood bacterial meningitis.

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BACKGROUND: Oral glycerol reduces severe neurologic sequelae in childhood bacterial meningitis, but the mechanism awaits elucidation. We conducted a prospective, randomized, double-blind study in which the effects of glycerol and intravenous dexamethasone were compared with placebo recipients in an intensive care setting in India. **METHODS: Thirty-six children at age 2 months to 12 years with meningitis were treated with ceftriaxone and were randomized to receive also either dexamethasone intravenously, or glycerol orally, or both agents, or neither.** The illness was monitored with preset criteria. The primary outcome

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measures were the changes in plasma osmolality and in urine output. **RESULTS: Nine children received glycerol, 8 dexamethasone, 11 both agents, and 8 only placebo.** The leading agents identified were *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, and *Staphylococcus aureus*. **Only the glycerol recipients increased plasma osmolality by up to 3% from the mean baseline of 294 mOsm/kg in the glycerol and 295 mOsm/kg in the glycerol-dexamethasone group. This change occurred within 6 hours, the critical period of treatment, and lasted <24 hours. Blood pressure was not affected, nor did urine output increase. The dexamethasone-only and placebo-only recipients showed immediate decrease in serum osmolality.** **CONCLUSIONS:** Because excretion of the cerebrospinal fluid is inversely associated with plasma osmolality, we suggest that the glycerol-induced osmolality increase reduce the volume of cerebrospinal fluid, enhanced water movement back to the plasma by osmosis, increased cerebral blood flow, and thus, improved brain oxygenation.

Comment

This study build on the large RCT involving 654 children in 10 hospitals in 8 countries in South America that showed oral glycerol (1g per ml, at a dose of 1.5g/kg every 6 hours) reduced severe neurological sequelae, and the combined outcome of severe neurological sequelae and death (Clinical Infectious Diseases 2007;45:1277-1286). In that study children were not followed up beyond hospital discharge, so there were some study limitations, as with all multicentre trials. Glycerol should be considered for inclusion in the WHO Pocketbook of Hospital Care for Children as adjunctive therapy for bacterial meningitis, as it has proven efficacy in RCTs in resource limited settings, is safe, inexpensive, easily available, can be taken orally, and has no special storage requirements.

[Clin Infect Dis.](#) 2009 Jan 14. [Epub ahead of print]



Randomized, Controlled Trial of Oral Ribavirin for Japanese Encephalitis in Children in Uttar Pradesh, India.

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Background. Japanese encephalitis is associated with high rates of mortality and disabling sequelae. To date, no specific antiviral has proven to be of benefit for this condition. We attempted to determine the efficacy of oral ribavirin treatment for reducing early mortality among children with Japanese encephalitis in Uttar Pradesh, India. Methods. Children (age, 6 months to 15 years) who had been hospitalized with acute febrile encephalopathy (a ≤ 2-week history of fever plus altered sensorium) were tested for the presence of immunoglobulin M antibodies to Japanese encephalitis virus with commercial immunoglobulin M capture enzyme-linked immunosorbent assay. **Children with positive results were**

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randomized to receive either ribavirin (10 mg/kg per day in 4 divided doses for 7 days) or placebo syrup through nasogastric tube or by mouth. The primary outcome was early mortality; secondary outcome measures were early (at hospital discharge; normal or nearly normal, independent functioning, dependent, vegetative state, or death) outcome, time to resolution of fever, time to resumption of oral feeding, duration of hospitalization, and late outcome (≥ 3 months after hospital discharge). The study was double-blind, and analysis was by intention to treat. Results. @nbsp; **A total of 153 patients were enrolled during a 3-year period; 70 patients received ribavirin, and 83 received placebo. There was no statistically significant difference between the 2 groups in the early mortality rate: 19 (27.1%) of 70 ribavirin recipients and 21 (25.3%) of 83 placebo recipients died (odds ratio, 1.10; 95% confidence interval, 0.5-2.4). No statistically significant differences in secondary outcome measures were found.** Conclusions. @nbsp; For the dosage schedule used in our study, oral ribavirin has no effect in reducing early mortality associated with Japanese encephalitis. Trial registration. @nbsp; ClinicalTrials.gov identifier: NCT00216268

Neonatal care

[Indian Pediatr.](#) 2009 Jan;46 Suppl:s37-42.

Pyritinol for post asphyxial encephalopathy in term babies-- a randomized double-blind controlled trial.

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OBJECTIVE: To evaluate the efficacy of pyritinol in improving the neurodevelopmental outcome at one year of age among term babies with post-asphyxial encephalopathy. **SETTING:** Level II Neonatal Nursery and Child Development Centre, Medical College, Thiruvananthapuram. **Design:** Randomised placebo controlled double blind trial. **PARTICIPANTS:** 108 term babies with post-asphyxial encephalopathy, stratified into three grades based on clinical criteria. **INTERVENTION:** **The treatment group (n=54) received pyritinol and the control group (n=54) received placebo, in exactly the same increasing dosage schedule of 1 to 5 mL liquid drug (20-100 mg) from 8th postnatal day until the end of six months.** **OUTCOME VARIABLES:** Mean Mental Development Index (MDI) and mean Psychomotor Development Index (PDI) measured on Bayley Scales of Infant Development at one year of age. **RESULTS:** No statistically significant difference was observed in MDI or PDI scores at one year between the treatment and control groups. The confidence interval for the differences ranged from -6.3 to 8.7 for MDI and from - 4.1 to 12.7 for PDI. On multiple regression analysis using one year MDI and PDI scores, even after controlling for birthweight, there was no statistically significant difference between the treatment and control groups. **CONCLUSION:** **Pyritinol is not useful in improving the neurodevelopmental status of babies with post-asphyxial encephalopathy at one year of age.**

[J Med Assoc Thai](#). 2008 Oct;91 Suppl 3:S28-34.

Prophylaxis of symptomatic patent ductus arteriosus with oral ibuprofen in very low birth weight infants.

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BACKGROUND: Patent ductus arteriosus (PDA) is a common cause of mortality and morbidity among very low birth weight infants. Oral ibuprofen suspension has been shown to have the same efficacy and safety as intravenous indomethacin in the prevention and treatment of symptomatic PDA. With lower dosage, the prevalence of side effects may decrease without changes in efficacy. **OBJECTIVE: To evaluate the efficacy and side effects of low dose ibuprofen suspension for prevention of symptomatic PDA in very low birth weight infants.** **PATIENTS AND METHOD:** A prospective, double blind, randomized controlled trial was conducted on premature neonates with gestational ages between 28-32 weeks, birth weight 1500 grams or less, at the Neonatal Unit, Queen Sirikit National Institute of Child Health (QSNICH) during October 2005 to October 2006. Only infants who had PDA on echocardiogram were included in the study. **Three doses of ibuprofen suspension or placebo were randomly given at the dosage of 10, 5, 5 mg/kg every 24 hours.** Daily physical examination, serial laboratory evaluation and echocardiogram were used to evaluate symptomatic PDA, complications and side effects. **RESULTS:** Sixty-two infants were recruited in the study and randomly assigned into the study and control group. The gestational age and birthweight of the 2 groups were similar **The prevalence of symptomatic PDA was less in the ibuprofen group than in placebo group (9.86% vs. 35.48%; p = 0.015).** There were no differences in the prevalence of complications and adverse effects between the two groups. **CONCLUSION:** Prophylactic oral ibuprofen suspension at lower dosage results in less symptomatic PDA without significant side-effects.

Comment

Although this study showed the effectiveness of prophylactic ibuprofen in preventing PDA in premature infants, it is not large enough to conclude that adverse effects are minimal. Another study (from Canada) this year showed oral ibuprofen to be as effective as IV ibuprofen for treatment of PDA, but to have fewer side effects (9% vs 31%) (Cherif A, Pediatrics 2008; 122:e1256-1261). A small study in 1996 concluded that the net benefits of early duct closure was better (including shorter hospital stay, early establishment of feeding), but this study only included 34 babies. Before ibuprofen is recommended routinely to all very low birth weight babies in all settings, further trials would be necessary, large enough to evaluate safety issues.

Management of newborn infections in primary care settings: a review of the evidence and implications for policy?

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BACKGROUND: Long-term, sustainable programs to address high incidence and death rates from neonatal infections are required for improving child survival. There is an urgent need to define the role of community-based management for neonates with serious bacterial infections--both at home and at first-level facilities. **METHODS:** We reviewed available evidence for community-based antibiotic management strategies for serious neonatal infections. **RESULTS:** Nine distinct studies contributing data for community-based management of neonatal pneumonia and sepsis were identified. **In a pooled analysis of 5 controlled trials of community-based management of neonatal pneumonia (4 using cotrimoxazole, 1 ampicillin, or penicillin), all-cause neonatal mortality showed 27% [95% confidence interval (CI): 18%-35%] reduction and pneumonia-specific mortality, 42% (95% CI: 22%-57%). Substantial reductions in neonatal mortality have been demonstrated in a nonrandomized controlled study in rural India (62% reduction, $P < 0.001$) and in a cluster randomized trial in rural Bangladesh (34% reduction, 95% CI: 7%-53%). Reduced case fatalities (0%-3%) with community-based management of neonatal sepsis were observed in 2 small uncontrolled studies from India and Guatemala and a recent randomized trial from Pakistan.** **CONCLUSIONS:** Although methodological limitations preclude estimating the precise contribution of antibiotics toward neonatal mortality reduction in community settings in low income countries, available data suggest substantial benefit of case management approaches using antibiotics for neonatal sepsis in such settings

Comment

There could be little doubt that giving antibiotics to neonates with bacterial sepsis as early as possible will reduce mortality, compared with the situation where infants do not receive antibiotics because they have no access to hospitals. However community case management models differ and the implementation challenge is to understand how best to use resources to strengthen community care. On the one hand community care might mean a proper assessment using the Integrated Management of Childhood Illness (IMCI) guidelines and antibiotics given by a nurse with 2-3 years training in a well set up primary government, mission-run community health clinic, or during home visits. On the other hand, many studies have used a different model where antibiotics are given by a volunteer health worker with as little as 2-6 weeks training in a village setting, with variable but sometimes limited connection with the formal health system. There are important issues about community care by volunteers without formal qualifications and the context in which it is effective and appropriate. How much training is needed? What level of health worker is appropriate? How to ensure supervision on a large scale? Can village health volunteers give more than oral antibiotics? There is little evidence about the effectiveness of properly trained nurses working within the formal health system at the community level, because such studies have not been performed. There is therefore a risk that, in the apparent absence of evidence, less effort and resources will be put into formal nurse training and community health systems, in favour of programs for less trained volunteer village health workers. The World Health Report in 2008 called for the revitalization of primary care,

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but stressed that primary care in the 21st Century was not low technology substandard care given by untrained health workers, but by properly trained community health workers using appropriate technology.

[Lancet](#). 2008 Sep 27;372(9644):1151-62.***

Effect of community-based behaviour change management on neonatal mortality in Shivgarh, Uttar Pradesh, India: a cluster-randomised controlled trial.

[Kumar V](#), [Mohanty S](#), [Kumar A](#), [Misra RP](#), [Santosham M](#), [Awasthi S](#), [Baqui AH](#), [Singh P](#), [Singh V](#), [Ahuja RC](#), [Singh JV](#), [Malik GK](#), [Ahmed S](#), [Black RE](#), [Bhandari M](#), [Darmstadt GL](#); [Saksham Study Group](#). Collaborators (25)
[Ahuja RC](#), [Awasthi S](#), [Baqui AH](#), [Bhandari M](#), [Bharti N](#), [Black RE](#), [Darmstadt GL](#), [Gupta A](#), [Gupta S](#), [Kumar A](#), [Kumar V](#), [Malik GK](#), [Mehrotra H](#), [Misra RP](#), [Mohanty S](#), [Mitra MK](#), [Santosham M](#), [Singh JV](#), [Singh K](#), [Singh P](#), [Singh R](#), [Singh S](#), [Singh V](#), [Winch PJ](#), [Yadav R](#).

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BACKGROUND: In rural India, most births take place in the home, where high-risk care practices are common. We developed an intervention of behaviour change management, with a focus on prevention of hypothermia, aimed at modifying practices and reducing neonatal mortality. **METHODS:** We did a cluster-randomised controlled efficacy trial in Shivgarh, a rural area in Uttar Pradesh. 39 village administrative units (population 104,123) were allocated to one of three groups: a control group, which received the usual services of governmental and non-governmental organisations in the area; an intervention group, which received a preventive package of interventions for essential newborn care (birth preparedness, clean delivery and cord care, thermal care [including skin-to-skin care], breastfeeding promotion, and danger sign recognition); or another intervention group, which received the package of essential newborn care plus use of a liquid crystal hypothermia indicator (ThermoSpot). In the intervention clusters, community health workers delivered the packages via collective meetings and two antenatal and two postnatal household visitations. Outcome measures included changes in newborn-care practices and neonatal mortality rate compared with the control group. Analysis was by intention to treat. This study is registered as International Standard Randomised Control Trial, number NCT00198653. **FINDINGS:** Improvements in birth preparedness, hygienic delivery, thermal care (including skin-to-skin care), umbilical cord care, skin care, and breastfeeding were seen in intervention arms. There was little change in care-seeking.

Compared with controls, neonatal mortality rate was reduced by 54% in the essential newborn-care intervention (rate ratio 0.46 [95% CI 0.35-0.60], p<0.0001) and by 52% in the essential newborn care plus ThermoSpot arm (0.48 [95% CI 0.35-0.66], p<0.0001).

INTERPRETATION: A socioculturally contextualised, community-based intervention, targeted at high-risk newborn-care practices, can lead to substantial behavioural modification and reduction in neonatal mortality. This approach can be applied to behaviour change along the continuum of care, harmonise vertical interventions, and build community capacity for sustained development. **FUNDING:** USAID and Save the Children-US through a grant from the Bill & Melinda Gates Foundation.

Comment

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This is another important study from South Asia showing how community-based delivery of neonatal care reduces mortality. Last year a study from Sylhet, Bangladesh showed a similar effect on neonatal mortality ([Lancet](#), 2008 Jun 7;371(9628):1936-44). In that study, community health workers (CHWs) had 6 weeks training in communication, provision of essential newborn care, clinical assessment of neonates, and management of sick neonates with an algorithm adapted from IMCI. The CHWs identified pregnancies during visits to each household every 2 months, and provided 2 antenatal and 3 early postnatal home visits, and gave iron and folic acid supplements. The CHWs identified very sick newborns and gave IM antibiotics and referred babies on. A 34% reduction in neonatal mortality was observed. Such models of home based care have been successful in India, Bangladesh and Nepal particularly.

Neurocysticercosis

[Pediatr Infect Dis J](#). 2009 May;28(5):403-6.

Combination therapy with albendazole and praziquantel versus albendazole alone in children with seizures and single lesion neurocysticercosis: a randomized, placebo-controlled double blind trial.

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BACKGROUND: A combination of albendazole and praziquantel was more effective than albendazole alone in destroying *Taenia* cysts in an animal model. There are no such studies in humans. **OBJECTIVE:** To evaluate the efficacy and safety of a combination of albendazole and praziquantel in children with seizures and single small enhancing computerized tomographic lesions. **STUDY TYPE:** Prospective, interventional, randomized, placebo-controlled, double blind clinical trial at a tertiary hospital in North India. **SUBJECTS::** One hundred twelve children with seizures for <3 months and single lesion neurocysticercosis; 9 lost to follow-up. **INTERVENTION:** All children received albendazole (15 mg/kg/d) for 7 days with either praziquantel or placebo (75 mg/kg/d) for 1 day according to random allocation. Repeat CT scans were done after 1, 3, and 6 months. All children were followed up for at least 6 months. **RESULTS:** Fifty-three children received praziquantel (group A) and 50 placebo (group B). Complete resolution of lesions was seen in 60% and 72% of children at 3 and 6 months in group A versus 42% and 52% of children in group B. Nonresolution and calcification were higher in group B than in group A at 3 months (B: 28%, 14%; A: 12%, 8%) and 6 months (B: 16%, 22%; A: 6%, 9%), but the differences were not statistically significant. Seizure control and side effects were similar in the 2 groups. **CONCLUSIONS: A combination therapy for albendazole and praziquantel was statistically comparable to sole therapy with albendazole in eradicating lesions and preventing seizures.**

[J Neurol Sci](#). 2009 Jan 15;276(1-2):108-14. Epub 2008 Oct 11.

Randomized controlled trial of albendazole in new onset epilepsy and MRI confirmed solitary cerebral cysticercal lesion: effect on long-term seizure outcome.

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No trials to date have focused on long-term seizure outcome in solitary cerebral cysticercal lesion (SCCL), which is believed to produce a relatively benign form of epilepsy. This is a prospective randomized controlled study to evaluate the effect of Albendazole on long-term seizure outcome in patients with MRI-confirmed solitary cerebral cysticercal lesion (SCCL). One hundred and twenty-three patients with new-onset seizures and SCCL on contrast MRI were randomized to treatment with albendazole and followed for up to five years with serial MRI and clinical evaluation. At final analysis 103 patients (M-54, F-49) with a mean age of 18.6+/-10.7 years and follow-up period more than 12 months were included. The mean follow-up duration was 31.4+/-14.8 months (12-64). **At one month follow-up more patients receiving albendazole were seizure-free (62% versus 49% for controls). Subsequently there was no significant difference in overall seizure outcome between the two groups.** There was no correlation between seizure semiology, albendazole therapy and long-term seizure outcome. **Baseline MRI showed active lesions in all; 23% remained active at 12 months with no difference between the albendazole and control groups.** Patients whose lesions resolved at 12 months showed better seizure outcome. **Reduction in mean cyst area was greater in the albendazole group as compared to the controls and the difference at six months was significant (p<0.05). At three months follow-up perilesional edema also resolved faster in albendazole group (p<0.05). Thus, albendazole did not alter the long-term seizure outcome in patients with SCCL and epilepsy.** However, albendazole hastened resolution of SCCL on MRI, but interestingly 23% of lesions were still active 12 months after treatment.

Nutrition, micronutrients and breast feeding

(See also Diarrhoea, Anaemia)

Micronutrients and food fortification

(see also Anaemia)

Comment

This year micronutrient fortification of food given at schools or communities was associated with improved linear growth in India, reduced rates of anaemia, iron deficiency and zinc deficiency in Vietnam, China and Burkina Faso, and enhanced effect of deworming when given in conjunction with albendazole in Vietnam.

[Am J Clin Nutr](#). 2009 Jun;89(6):1766-75. Epub 2009 Apr 15.



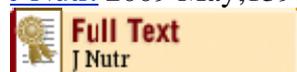
Effect of fortification with multiple micronutrients and n-3 fatty acids on growth and cognitive performance in Indian schoolchildren: the CHAMPION (Children's Health and Mental Performance Influenced by Optimal Nutrition) Study.

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BACKGROUND: Fortification with multiple micronutrients has been shown to improve growth and cognitive performance among children in developing countries, but it is unknown whether higher concentrations are more effective than lower concentrations. **OBJECTIVE:** We compared the effect of 2 different concentrations of a combination of micronutrients and n-3 (omega-3) fatty acids on indicators of growth and cognitive performance in low-income, marginally nourished schoolchildren in Bangalore, India. **DESIGN:** In a 2-by-2 factorial, double-blind, randomized controlled trial, **598 children aged 6-10 y were individually allocated to 1 of 4 intervention groups to receive foods fortified with either 100% or 15% of the Recommended Dietary Allowance of micronutrients in combination with either 900 mg alpha-linolenic acid plus 100 mg docosahexaenoic acid or 140 mg alpha-linolenic acid for 12 mo.** Anthropometric and biochemical assessments were performed at baseline and 12 mo. Cognitive performance was measured at baseline and at 6 and 12 mo. **RESULTS: The high micronutrient treatment significantly improved linear growth at 12 mo (0.19 cm; 0.01, 0.36) and short-term memory at 6 mo (0.11 SD; 0.01, 0.20) and was less beneficial on fluid reasoning at 6 (-0.10 SD; -0.17, -0.03) and 12 (-0.12 SD; -0.20, -0.04) mo than was the low micronutrient treatment, whereas no differences were observed on weight, retrieval ability, cognitive speediness, and overall cognitive performance.** No significant differences were found between the n-3 treatments. **CONCLUSIONS: The high micronutrient treatment was more beneficial for linear growth than was the low micronutrient treatment.** However, with some small differential effects, higher micronutrient concentrations were as effective as lower concentrations on cognitive performance. This trial was registered at clinicaltrials.gov as NCT00467909.

[J Nutr](#). 2009 May;139(5):1013-21. Epub 2009 Mar 25.



Multi-micronutrient-fortified biscuits decreased prevalence of anemia and improved micronutrient status and effectiveness of deworming in rural Vietnamese school children.

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Concurrent micronutrient deficiencies are prevalent among Vietnamese school children. A school-based program providing food fortified with multiple micronutrients could be a cost-effective and sustainable strategy to improve health and cognitive function of school children. However, the efficacy of such an intervention may be compromised by the high prevalence of parasitic infestation. To evaluate the efficacy of school-based intervention using multi-micronutrient-fortified biscuits with or without deworming on anemia and micronutrient status in Vietnamese schoolchildren, a randomized, double-blind, placebo-controlled trial was conducted among 510 primary schoolchildren, aged 6-8 y, in rural Vietnam. **Albendazole (Alb) (400 mg) or placebo was given at baseline. Nonfortified or multi-micronutrient-fortified biscuits including iron (6 mg), zinc (5.6 mg), iodine (35 microg), and vitamin A (300 microg retinol equivalents) were given 5 d/wk for 4 mo.** Multi-micronutrient fortification significantly improved the concentrations of hemoglobin (+1.87 g/L; 95% CI: 0.78, 2.96), plasma ferritin (+7.5 microg/L; 95% CI: 2.8, 12.6), body iron (+0.56 mg/kg body weight; 95% CI: 0.29, 0.84), plasma zinc (+0.61 micromol/L; 95% CI: 0.26, 0.95), plasma retinol (+0.041 micromol/L; 95% CI: 0.001, 0.08), and urinary iodine (+22.49 micromol/L; 95% CI: 7.68, 37.31). **Fortification reduced the risk of anemia and deficiencies of zinc and iodine by >40%.** Parasitic infestation did not affect fortification efficacy, whereas fortification significantly enhanced deworming efficacy, with the lowest reinfection rates in children receiving both micronutrients and Alb. **Multi-micronutrient fortification of biscuits is an effective strategy to improve the micronutrient status of Vietnamese schoolchildren and enhances effectiveness of deworming.**

[J Nutr Sci Vitaminol \(Tokyo\)](#). 2008 Dec;54(6):440-7.



Effects of vitamin A, vitamin A plus iron and multiple micronutrient-fortified seasoning powder on preschool children in a suburb of Chongqing, China.

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Preschool children in developing countries are likely to have multiple, concurrent micronutrient deficiencies. This study was designed to evaluate the effectiveness of different combinations of nutritional fortified diet to improve the blood levels of iron, vitamin A and other essential micronutrients in the preschool population of Banan District of Chongqing, China. From December 2005 to June 2006, a total of 226 2-6 y old preschool children were recruited from three nurseries in the area, and they were randomly assigned to three different fortified diet groups for 6 mo. **Group I was fortified with vitamin A; groups II and III were fortified with vitamin A plus iron and vitamin A plus iron, thiamine, riboflavin, folic acid, niacinamide, zinc and calcium, respectively.** Subjects' weight and height were measured for assessing the children's growth and development. Blood samples were taken at the beginning and the end of the 6-mo study period for measuring serum levels of micronutrients. **Group III with the multiple micronutrient fortified diet was the most effective to improve the serum level of retinol from [media (P25, P75): 1.06 (0.89, 1.32)] micromol/L to 1.29 (1.04, 1.39) micromol/L (p<0.05) and retinol binding protein from 17.0 (12.6, 25.6) mg/L to 31.6 (24.4, 44.0) mg/L (p<0.05) and to mobilize the stored iron in the liver (p<0.05).** In addition, the three groups' hemoglobin levels were elevated from 117.0 (109.0, 124.1) g/L, 114.0 (109.2,

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119.7) g/L and 115.0 (109.5, 122.7) g/L to 125.7 (119.2, 133.1) g/L, 126.5 (122.2, 135.9) g/L and 125.1 (119.8, 131.6) g/L over the 6 mo of intervention period, but there were no difference among the three groups ($p>0.05$). Nevertheless, unexpected results were obtained when comparing the effects on growth status among the different supplement groups. Our study has demonstrated that a multiple micronutrient fortified diet for 6 mo is more effective to improve the levels of hemoglobin, serum retinol, and RBP as well as to facilitate the mobilization of iron storage in preschool children.

[Am J Clin Nutr.](#) 2008 Nov;88(5):1378-87.



Dual fortification of salt with iodine and iron: a randomized, double-blind, controlled trial of micronized ferric pyrophosphate and encapsulated ferrous fumarate in southern India.

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BACKGROUND: Dual fortification of salt with iodine and iron could be a sustainable approach to combating iodine and iron deficiencies. **OBJECTIVE:** We compared the efficacy of **dual-fortified salt (DFS) made by using 2 proposed contrasting formulas-one fortifying with iron as micronized ground ferric pyrophosphate (MGFePP) and the other with iron as encapsulated ferrous fumarate (EFF)-with the efficacy of iodized salt (IS) in schoolchildren in rural southern India.** **DESIGN:** After stability and acceptability testing, a double-blind, household-based intervention was conducted in 5-15-y-old children ($n = 458$) randomly assigned into 3 groups to receive IS or DFS with iron as MGFePP or EFF, both at 2 mg/g salt. We measured hemoglobin, iron status, and urinary iodine at baseline, 5 mo, and 10 mo. **RESULTS:** Median serum ferritin and calculated median body iron improved significantly in the 2 groups receiving iron. After 10 mo, the prevalence of anemia decreased from 16.8% to 7.7% in the MGFePP group ($P < 0.05$) and from 15.1% to 5.0% in the EFF group ($P < 0.01$). The median urinary iodine concentration increased significantly in the IS and EFF groups ($P < 0.001$) but not in the MGFePP group. Losses of iodine in salt with 1.8% moisture were high for MGFePP, whereas the EFF segregated in salt with 0.5% moisture and caused color changes in some local foods. **CONCLUSIONS: Both DFSs were efficacious in reducing the prevalence of anemia and iron deficiency in school-age children.** Local salt characteristics should be taken into consideration when choosing an iron fortificant for DFS to achieve optimal iodine stability and color.

[J Food Sci.](#) 2008 Sep;73(7):S354-8. Epub 2008 Aug 18.



Acceptability of micronutrient fortified school meals by schoolchildren in rural Himalayan villages of India.

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This cross-sectional randomized controlled study assessed the social acceptability of micronutrient fortified cooked lunch meals by schoolchildren in rural Himalayan villages of India, in a program where the cooking and the micronutrient fortification were done at school. Subjects were randomly assigned to treatment (91) and control (90) groups. **The treatment group consumed a weighed amount of cooked lunch meals fortified with locally produced multi-micronutrient premix and the control group consumed a weighed amount of the same meals but without added micronutrient premix.** After having eaten, subjects were asked to rate, on a 3-point Likert scale using "smiley" faces, the pleasantness of smell, taste, and overall satisfaction with the food. The mean age of study children was 7.96 +/- 1.64 y and 48.6% were males. The average amounts of food consumed by the treatment and control groups were 345 +/- 114 and 360 +/- 102.4 g, respectively. Addition of the multi-micronutrient premix to school meals did not significantly affect the mean amount of food consumed by the schoolchildren ($P > 0.05$; independent sample t-test). **No significant differences were seen between treatment and control groups in terms of ratings for taste, smell, and the general acceptance of the micronutrient fortified or the unfortified school meals.** In conclusion, the addition of a multiple micronutrient premix to school meals was well liked by schoolchildren and did not adversely affect their food consumption.

[Indian J Pediatr.](#) 2008 Jul;75(7):671-8. Epub 2008 Aug 21.

Trial using multiple micronutrient food supplement and its effect on cognition.

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OBJECTIVE: To test the efficacy of a multiple micronutrient food supplement (MMFS) on the nutrition status of school children and its effect on cognition. **METHODS:** A MMFS was developed containing chelated ferrous sulphate and microencapsulated vitamin A, B2, B6, B12, folic acid, niacin, calcium pantothenate, vitamin C, vitamin E, lysine and calcium and the efficacy of the MMFS was assessed in 7-11 year old school children in Chennai, India by a pre-post test design. In the experimental group (N=51), the food in the school kitchen was cooked with the MMFS for the residential school children for a period of one year. The control group (N=72) consisted of day scholars who did not eat at the school. Hemoglobin, red blood cell count and hematocrit were measured at baseline and at the end of the study (after one year). A battery of 7 memory tests (The personal information test, the Mann-Suiter Visual memory screen for objects, The digit span forward test, The digit span backward test, The delayed response test, The Benton Visual Retention Test and The Cattells retentivity test), one test for attention and concentration (Letter cancellation test) and one test for intelligence (Ravens's coloured progressive matrices) were administered to all the children at baseline and endline. **RESULTS: It was seen that there was a significant ($P < 0.05$) improvement in the experimental group in hemoglobin, hematocrit and red cell count whereas in the control group there was a statistically significant decline ($P < 0.05$) in hemoglobin and red cell count. In 5 tests out of the 7 memory tests and in the letter cancellation test for attention, the mean change in scores in the experimental group is significantly more ($P < 0.05$) than the**

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control group. There was no significant improvement in the overall intelligence as seen in the Ravens progressive matrices between the experimental and control groups at endline.

CONCLUSION: The study shows that the MMFS is effective in improving the nutrition status and cognition in children.

Comment

This was a non-randomised trial where participants were selected on the basis of whether they were boarders at the school or day scholars, therefore there may have been other differences in the populations, introducing some bias.

Breastfeeding

[Am J Clin Nutr.](#) 2008 Jul;88(1):84-94.



Effects of energy density and feeding frequency of complementary foods on total daily energy intakes and consumption of breast milk by healthy breastfed Bangladeshi children.

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BACKGROUND: Information is needed on the minimum energy density and feeding frequency of complementary foods that can provide adequate energy intakes (EIs) for healthy breastfed children. **OBJECTIVES:** The objectives of the study were to evaluate the effects of various energy densities and feeding frequencies of complementary foods on EI from these foods, breast milk consumption, and total EI from both sources. **DESIGN:** During 9 separate, randomly ordered dietary periods lasting 3-6 d each, we measured intakes of food and breast milk by 18 healthy breastfed children 8-11 mo of age who, 3, 4, or 5 times/d, were fed porridge with a coded energy density of 0.5, 1.0, or 1.5 kcal/g. Food intake was measured by weighing the feeding bowl before and after meals, and breast milk intake was measured by test weighing. **RESULTS:** The mean amounts of complementary foods consumed were inversely related to their energy density and positively related to the number of meals/d ($P < 0.001$ for both); EIs from foods were positively related to both factors. Breast milk intake decreased slightly but progressively, with greater energy density and feeding frequency of complementary foods; total EIs (kcal/d) increased in relation to both factors ($P < 0.001$ for both). **CONCLUSIONS:** The energy density and feeding frequency of complementary foods affect infants' total daily EI and breast milk consumption. Recommendations can be developed for the appropriate combinations of these dietary factors that are compatible with adequate EI, although longer-term effects of complementary feeding practices on breast milk intake and breastfeeding duration need further community-based studies.

[Rev Saude Publica.](#) 2008 Dec;42(6):1027-33.

Educational intervention on breastfeeding promotion to the Family Health Program team

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OBJECTIVE: Breastfeeding Friendly Primary Care Initiative comprises educational activities focused on primary care units. To evaluate the effectiveness of a strategy on breastfeeding promotion to the Family Health Program team. **METHODS:** A controlled intervention study was performed with 20 family health care teams randomly selected into intervention and control group in Montes Claros, Southeastern Brazil, in 2006. The teams randomly selected into intervention and control group, and the intervention group took part in a 24-hour training program on breastfeeding promotion for health providers, modeled on the Baby-Friendly Hospital Initiative. It was emphasized health provider's support for breastfeeding and management of major lactation problems. The control group received routine breastfeeding training. Mothers of all children under two cared by the teams were interviewed at home before (n=1,423) and 12 months after the intervention (n=1,491) and answered questions about breastfeeding practices. Survival curves of breastfeeding were plotted and compared for both time points studied using the log rank test. **RESULTS:** There was a significant increase in exclusive breastfeeding after the educational activities for the Family Health Program teams. Survival curves of exclusive breastfeeding at the first time point studied showed no statistical significance difference between the groups by log rank test (p=0.502). After the intervention, survival curves of exclusive breastfeeding were significantly different by the log rank test (p=0.001). **CONCLUSIONS:** The training of Family Health Program teams as proposed by the Baby-Friendly Hospital Initiative proved to be an effective, low-cost strategy for raising awareness among health providers, providing consistent information, and assuring the required support to mothers with breastfeeding issues.

Obesity

[Am J Clin Nutr](#). 2008 Sep;88(3):605-11.



Effects of replacing the habitual consumption of sugar-sweetened beverages with milk in Chilean children.

[Albala C](#), [Ebbeling CB](#), [Cifuentes M](#), [Lera L](#), [Bustos N](#), [Ludwig DS](#).

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BACKGROUND: During the nutrition transition in Chile, dietary changes were marked by increased consumption of high-energy, nutrient-poor products, including sugar-sweetened beverages (SSBs). Obesity is now the primary nutritional problem in posttransitional Chile.

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OBJECTIVE: We conducted a randomized controlled trial to examine the effects on body composition of delivering milk beverages to the homes of overweight and obese children to displace SSBs. **DESIGN:** We randomly assigned 98 children aged 8-10 y who regularly consumed SSBs to intervention and control groups. During a 16-wk intervention, children were instructed to drink 3 servings/d (approximately 200 g per serving) of the milk delivered to their homes and to not consume SSBs. Body composition was measured by dual-energy X-ray absorptiometry. Data were analyzed by multiple regression analysis according to the intention-to-treat principle. **RESULTS:** For the intervention group, milk consumption increased by a mean (+/- SEM) of 452.5 +/- 37.7 g/d (P < 0.0001), and consumption of SSBs decreased by -711.0 +/- 33.7 g/d (P < 0.0001). For the control group, milk consumption did not change, and consumption of SSBs increased by 71.9 +/- 33.6 g/d (P = 0.04). Changes in percentage body fat, the primary endpoint, did not differ between groups. Nevertheless, the mean (+/- SE) accretion of lean body mass was greater (P = 0.04) in the intervention (0.92 +/- 0.10 kg) than in the control (0.62 +/- 0.11 kg) group. The increase in height was also greater (P = 0.01) in the intervention group (2.50 +/- 0.21 cm) than in the control group (1.77 +/- 0.20 cm) for boys but not for girls. **CONCLUSION:** Replacing habitual consumption of SSBs with milk may have beneficial effects on lean body mass and growth in children, despite no changes in percentage body fat. This trial was registered at clinicaltrials.gov as NCT00149695.

Oncology

[Asian J Surg.](#) 2008 Oct;31(4):225-9.



Anterior intratumoural chemotherapy: a newer modality of treatment in advanced solid tumours in children.

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OBJECTIVE: Advanced and inoperable solid tumours in children have high mortality despite aggressive multimodal treatment. Intravenous chemotherapy is abandoned at times because of systemic toxicity. **This study investigated intratumoural chemotherapy and compared it with intravenous chemotherapy.** **METHODS:** Forty children with advanced inoperable solid tumours (Wilms' tumour and neuroblastoma) were randomly allocated into two groups of 20. Group A was given intratumoural chemotherapy and group B was given intravenous chemotherapy. Both groups were compared for reduction in tumour size and volume, tumour resectability, histopathological changes and drug side effects. **RESULTS:** **Intratumoural chemotherapy was superior to intravenous chemotherapy in terms of reducing tumour size and volume (63% in group A vs. 22% in group B). The resectability was 70% in the intratumoural group compared with 40% in the intravenous group. The overall good histopathological response was 71% in group A as opposed to 0% in group B. Moreover, the incidence and severity of drug side effects and morbidity were less with intratumoural chemotherapy. Mortality was also low in group A (5%) compared to group B (20%).**

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CONCLUSION: Intratumoural chemotherapy can be offered as an effective and safe alternative treatment modality for advanced and inoperable Wilms' tumour and neuroblastoma.

Comment

Intratumoural chemotherapy consisted of actinomycin D and adriamycin as single doses and vincristine weekly for 6 weeks, plus hyaluronidase to enhance the drugs local distribution. The drugs were administered using a 26G spinal needle under ultrasound control and full aseptic technique. Biopsy confirmation of diagnoses was made prior to enrolment in the study.

Ophthalmology

(see also Anaesthesia)

[Ophthalmic Epidemiol.](#) 2009 May-Jun;16(3):175-80.



Randomized trial of high dose azithromycin compared to standard dosing for children with severe trachoma in Tanzania.

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BACKGROUND: Children with a heavy load of *C. trachomatis* infection may continue to be infected following a single dose of 20 mg/kg of azithromycin. **We compared the *C. trachomatis* infection rates at six weeks post-treatment of children randomized to 30 mg/kg single dose of azithromycin versus 20 mg/kg single dose of azithromycin.** METHODS: **Ninety-nine children with severe trachoma (defined as either trachoma intense or follicular trachoma with ten or more follicles) were enrolled and randomly assigned.** Baseline data on age, sex, and trachoma status was obtained, and swabs for determination of *C. trachomatis* were taken. Dosing was weight-based and observed. Children were followed up at six weeks for trachoma and infection. The laboratory was masked to treatment assignment. RESULTS: Both groups experienced reductions in infection and in severe trachoma. Twelve percent of the 20 mg/kg group were PCR positive at 6 weeks, compared with 69% at baseline, an 82% reduction (p -value < .001). In the 30 mg/kg group, 15% were infected, compared with 62% at baseline, a 76% reduction (p < .001). **The rate of infection comparing treatment groups was not significantly different at 6 weeks ($p = 0.71$).** Analyses on children who were infected at baseline showed those remaining positive at six weeks were 18%, and 14% in the standard and high dose groups, respectively. CONCLUSION: **Increasing the single dose of azithromycin to 30 mg/kg in children with severe trachoma did not result in significantly less infection at six weeks post-treatment compared to 20 mg/kg.**

[Ophthalmic Physiol Opt.](#) 2009 Jan;29(1):41-8.



The effectiveness of progressive addition lenses on the progression of myopia in

Chinese children.

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PURPOSE: To evaluate the effectiveness of progressive addition lenses (PALs), with a near addition of +1.50 D, on the progression of myopia in Chinese children. **METHODS:** We enrolled 178 Chinese juvenile-onset acquired myopes (aged 7-13 years, -0.50 to -3.00 D spherical refractive error), who did not have moderately or highly myopic parents, for a 2-year prospective study. They were randomly assigned to the PAL group or single vision (SV) group. Primary measurements, which included myopia progression and ocular biometry, were performed every 6 months. Treatment effect was adjusted for important covariates, by using a multiple linear regression model. **RESULTS:** One hundred and forty-nine subjects (75 in SV and 74 in PAL) completed the 2-year study. The myopia progression (mean +/- S.D.) in the SV and PAL groups was -1.50 +/- 0.67 and -1.24 +/- 0.56 D, respectively. This difference of 0.26 D over 2 years was statistically significant ($p = 0.01$). The lens type ($p = 0.02$) and baseline spherical equivalent refraction ($p = 0.05$) were significant contributing factors to myopia progression. Mean increase in the depth of vitreous chamber was 0.70 +/- 0.40 and 0.59 +/- 0.24 mm, respectively. This difference of 0.11 mm was statistically significant ($p = 0.04$). Age ($p < 0.01$) was the only contributing factor to the elongation of vitreous chamber. Different near phoria ($p < 0.01$) and gender ($p = 0.02$) caused different treatment effects when wearing SV lenses. However, there were no factors found to influence the treatment effect of wearing PALs. **CONCLUSIONS:** Compared with SV lenses, myopia progression was found to be retarded by PALs to some extent in Chinese children without moderately or highly myopic parents, especially for subjects with near esophoria or females.

[JNMA J Nepal Med Assoc](#). 2008 Oct-Dec;47(172):179-85.

Safety of primary intraocular lens insertion in unilateral childhood traumatic cataract.

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This study analyzes the results of cataract surgery with primary intraocular lens implantation in unilateral childhood traumatic cataract following penetrating trauma and its long term follow up. It is a hospital based study of 114 children (age 3-10 years) with unilateral traumatic cataract who underwent extracapsular cataract extraction/ lens aspiration with implantation of posterior chamber intraocular lens (IOL). Primary posterior capsulotomy (PPC) was performed in 57 eyes and the rest 57 were without PPC (NPPC). The patients were followed up at regular intervals for a period of 3 years. Postoperative inflammation and pupillary capture were two frequent complications seen during postoperative period. Development of posterior capsular opacification (PCO) was 1/57, 4/57 at 8th week and 7/30 and 14/39 at 6 months, in PPC and NPPC group, respectively. Best corrected visual acuity (BCVA) $\geq 6/18$ was achieved in 50% of eyes at 8th week post operatively and the same at 3 years with/without

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membranectomy/capsulotomy was evident in 73.3% of eyes. Meticulous case selection with insertion of "in the bag IOL" and subjecting the traumatized cataractous eyes to primary posterior capsulotomy are factors responsible for optimal outcome in unilateral traumatic cataract in children.

[Clin Experiment Ophthalmol.](#) 2008 Oct;36(7):625-30.



Square-edge polymethylmethacrylate intraocular lens design for reducing posterior capsule opacification following paediatric cataract surgery: initial experience.

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PURPOSE: To compare the incidence and severity of development of posterior capsule opacification (PCO) following implantation of square-edged polymethylmethacrylate (PMMA) or hydrophobic acrylic intraocular lenses (IOLs) following paediatric cataract surgery. **DESIGN:** Prospective, consecutive, interventional, comparative, randomized and cross-sectional study of 40 eyes of 32 children aged between 4 and 12 years who underwent phacoemulsification and posterior chamber IOL implantation. **METHODS:** The patients were randomized into two groups of 20 eyes each. Group 1 eyes received a square-edge hydrophobic acrylic IOL (Acrysof SA 60 AT, Alcon Surgical, Fort Worth, Texas), and Group 2 eyes received a square-edge single-piece PMMA lens (Aurolab SQ 3600 Aurolab IOL Division, Madurai, India) in the capsular bag. No eye underwent a primary posterior capsulotomy. The PCO density was evaluated on slitlamp retroillumination photographs by using POCOMan software at 3, 6, 9 and 12 months post surgery. **RESULTS:** The average percentage PCO on POCOMan analysis was 51.23 for Group 1 and 49.49 for Group 2 ($P = 0.09$), and the average PCO severity grade was 1.34 in Group 1 and 1.12 in Group 2 ($P = 0.08$). Visual axis remained clear in 14 of 20 eyes with the acrylic lens as compared with 13 of 20 eyes with the PMMA lens. ($P = 0.32$). **CONCLUSIONS:** Square-edge PMMA IOLs offer a significant cost advantage over acrylic lenses at similar rates of PCO formation following paediatric cataract surgery, which is of significant value in developing countries.

[Ophthalmic Epidemiol.](#) 2008 Nov-Dec;15(6):410-7.



Barriers to spectacle use in Tanzanian secondary school students.

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PURPOSE: Screening school students for refractive errors is a component of many primary eye care programs. In 2004 a trial of two approaches of spectacle-delivery to Tanzanian secondary school students found that only one third of students were using their spectacles at three months.

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Barriers to spectacle use were investigated using questionnaires and focus group discussions. **METHODS:** At the three months follow-up survey a questionnaire explored satisfaction with spectacles and the attitudes of trial participants (median age 15 years). Attitudes and reactions of friends, teachers and families were also explored. Students also discussed their experience with spectacle use and reasons for non-use in 8 focus groups divided by intervention, sex and spectacle use. **RESULTS:** In general, students seemed happy with the appearance of their spectacles and the beneficial impact on their vision. Peer pressure and parental concerns about safety of spectacle use, cost of purchasing spectacles and difficulties in accessing good local optical services were identified as the main barriers. Students criticized prescribing practices of local opticians and favored alternative and traditional treatments for visual impairment. **CONCLUSION:** To increase the effectiveness of school vision screening in Tanzania, barriers such as peer pressure or concerns about safety need to be addressed, in addition to provision of affordable, good quality spectacles. Barriers to spectacle use in children are likely to exist in all populations, but may vary in their nature and importance and therefore should be investigated in existing and new screening programs.

[J Pediatr Ophthalmol Strabismus](#). 2009 Mar-Apr;46(2):87-90; quiz 91-2.

Levodopa/carbidopa in the treatment of amblyopia.

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PURPOSE: To evaluate the role of levodopa/carbidopa in the treatment of amblyopia. **METHODS:** Thirty patients with strabismic amblyopia between the ages of 3 and 12 years were part of this double-blind, randomized study. Patients were divided into two groups. **Group A received 0.50 mg + 1.25 mg of levodopa/carbidopa per kilogram body weight three times daily after meals, with a protein rich drink, whereas Group B received placebo.** Both groups received full-time conventional occlusion until a visual acuity of 6/6 was achieved or for a maximum of 3 months. **RESULTS: The authors observed more than two lines improvement in visual acuity that was greater in the levodopa group (15 of 15) than in the placebo group (9 of 15) (P < .005). Furthermore, improvement in visual acuity of more than two lines was greater in patients younger than 8 years (100%) than in patients older than 8 years of age (60%) (P = .0026). There was also no significant reversal of the improved visual acuity in up to 6 months of follow-up.** **CONCLUSION: Levodopa/carbidopa improves visual acuity in patients with amblyopia and maintains improved visual acuity, especially in patients younger than 8 years.**

[Indian J Ophthalmol](#). 2008 Nov-Dec;56(6):459-63.



Part-time occlusion therapy for amblyopia in older children.

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AIM: To compare the efficacy of part-time versus full-time occlusion for treatment of amblyopia in children aged 7-12 years. MATERIALS AND METHODS: Prospective interventional case series. **One hundred children between 7-12 years of age with anisometropic (57), strabismic (25) and mixed (18) unilateral amblyopia were randomized (simple randomization) into four groups (25 each) to receive two hours, four hours, six hours or full-time occlusion therapy.** Children were regularly followed up at six-weekly intervals for a minimum of three visits. STATISTICAL ANALYSIS: Intragroup visual improvement was analyzed using paired t-test while intergroup comparisons were done using ANOVA and unpaired t-test. RESULTS: **All four groups showed significant visual improvement after 18 weeks of occlusion therapy (P < 0.001). Seventy-three (73%) of the total 100 eyes responded to amblyopia therapy with 11 eyes (44%), 17 eyes (68%), 22 eyes (88%) and 23 eyes (92%) being amblyopia responders in the four groups respectively, with the least number of responders in the two hours group. In mild to moderate amblyopia (vision 20/30 to 20/80), there was no significant difference in visual outcome among the four groups (P =0.083). However, in severe amblyopia (vision 20/100 or worse), six hours (P =0.048) and full-time occlusion (P =0.027) treatment were significantly more effective than two hours occlusion.** CONCLUSION: All grades of part-time occlusion are comparable to full-time occlusion in effectiveness of treatment for mild to moderate amblyopia in children between 7-12 years of age unlike in severe amblyopia, where six hours and full-time occlusion were more effective than two hours occlusion therapy.

Comment

It seems levodopa adds something to full-time occlusion in severe amblyopia in children under the age of 8 years. There are several RCTs since 1999 showing a benefit of levodopa in this condition.

Organization, health financing and administration

[PLoS Med.](#) 2009 Jan 6;6(1):e1000007.



Effect of removing direct payment for health care on utilisation and health outcomes in Ghanaian children: a randomised controlled trial.

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BACKGROUND: Delays in accessing care for malaria and other diseases can lead to disease progression, and user fees are a known barrier to accessing health care. Governments are introducing free health care to improve health outcomes. Free health care affects treatment seeking, and it is therefore assumed to lead to improved health outcomes, but there is no direct trial evidence of the impact of removing out-of-pocket payments on health outcomes in developing countries. This trial was designed to test the impact of free health care on health outcomes directly. METHODS AND FINDINGS: **2,194 households containing 2,592 Ghanaian children under 5 y old were randomised into a prepayment scheme allowing**

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free primary care including drugs, or to a control group whose families paid user fees for health care (normal practice); 165 children whose families had previously paid to enrol in the prepayment scheme formed an observational arm. The primary outcome was moderate anaemia (haemoglobin [Hb] < 8 g/dl); major secondary outcomes were health care utilisation, severe anaemia, and mortality. At baseline the randomised groups were similar. **Introducing free primary health care altered the health care seeking behaviour of households; those randomised to the intervention arm used formal health care more and nonformal care less than the control group.** Introducing free primary health care did not lead to any measurable difference in any health outcome. The primary outcome of moderate anaemia was detected in 37 (3.1%) children in the control and 36 children (3.2%) in the intervention arm (adjusted odds ratio 1.05, 95% confidence interval 0.66-1.67). There were four deaths in the control and five in the intervention group. Mean Hb concentration, severe anaemia, parasite prevalence, and anthropometric measurements were similar in each group. Families who previously self-enrolled in the prepayment scheme were significantly less poor, had better health measures, and used services more frequently than those in the randomised group. **CONCLUSIONS:** In the study setting, removing out-of-pocket payments for health care had an impact on health care-seeking behaviour but not on the health outcomes measured.

Comment

This is an important study, the first RCT to investigate the effect of providing free health care on health outcomes. The study showed that provision of free health care resulted in increased care seeking behaviour, but did not affect the primary outcome, which was moderate anaemia. The investigators suggested several reasons for this, including the technical adequacy of the intervention to prevent or treat anaemia (predominantly artemisinin-based antimalarial agents), the lack of deworming as an intervention offered, the relatively small difference in health utilisation between the two arms of the study, the possibility that other non-measured health outcomes improved even though the prevalence of malaria did not, the lag-time to effect after free health care was provided, and other contextual factors. More studies are required to understand the effect of free health care on health outcomes.

Renal disease

[Am J Kidney Dis.](#) 2009 May;53(5):760-9. Epub 2009 Mar 5.

Efficacy and safety of tacrolimus versus cyclosporine in children with steroid-resistant nephrotic syndrome: a randomized controlled trial.

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BACKGROUND: To examine whether tacrolimus is more effective and safe than cyclosporine (CsA) in inducing remission in patients with steroid-resistant nephrotic syndrome (SRNS). **STUDY DESIGN:** Randomized controlled trial, nonblind, parallel group. **SETTINGS & PARTICIPANTS:** Tertiary-care hospital; 41 consecutive patients with idiopathic SRNS, estimated glomerular filtration rate greater than 60 mL/min/1.73 m², and histological

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characteristics showing minimal change disease, focal segmental glomerulosclerosis, or mesangioproliferative glomerulonephritis were randomly assigned to treatment with tacrolimus (n = 21) or CsA (n = 20). INTERVENTION: Tacrolimus (0.1 to 0.2 mg/kg/d) or CsA (5 to 6 mg/kg/d) for 1 year; cotreatment with alternate-day prednisolone and enalapril. OUTCOMES: Patients achieving complete remission (urinary protein-creatinine ratio < 0.2 g/g and serum albumin > or = 2.5 g/dL) or partial remission (urinary protein-creatinine ratio, 0.2 to 2 g/g, and serum albumin > or = 2.5 g/dL) at 6 and 12 months; time to remission; proportion with relapses; side effects. RESULTS: No patient was lost to follow-up. **After 6 months of therapy, remission occurred in 18 (85.7%) and 16 patients (80%) treated with tacrolimus and CsA, respectively (relative risk [RR], 1.07; 95% confidence interval [CI], 0.81 to 1.41).** Rates of remission at 12 months were also similar (RR, 1.14; 95% CI, 0.84 to 1.55). The proportion of patients who experienced relapse was significantly greater in those receiving CsA compared with tacrolimus (RR, 4.5; 95% CI, 1.1 to 18.2; P = 0.01). The decrease in blood cholesterol levels was greater with tacrolimus compared with CsA (difference in mean values, 45.1 mg/dL; 95% CI, 19.1 to 71.2). Persistent nephrotoxicity necessitating stoppage of medicine was seen in 4.7% and 10% patients, respectively. Cosmetic side effects (hypertrichosis and gum hypertrophy) were significantly more frequent in CsA-treated patients (P < 0.001). LIMITATIONS: Single-center study, small sample size, and short duration of follow-up. CONCLUSIONS: **Tacrolimus or CsA in combination with low-dose steroids show similar efficacy in inducing remission in patients with SRNS.** Therapy with tacrolimus is a promising alternative to CsA in view of the lower risk of relapses and lack of cosmetic side effects.

[Pediatr Nephrol.](#) 2008 Sep;23(9):1495-502. Epub 2008 Jun 20.

Efficacy of intravenous pulse cyclophosphamide treatment versus combination of intravenous dexamethasone and oral cyclophosphamide treatment in steroid-resistant nephrotic syndrome.

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We compared, in a randomized controlled trial, the efficacy of a regimen based on intravenous (i.v.) cyclophosphamide therapy with a combination of i.v. dexamethasone and oral cyclophosphamide therapy in inducing remission in patients with steroid-resistant nephrotic syndrome (SRNS). During April 2001 to December 2003, 52 consecutive patients with idiopathic SRNS, normal renal function and renal histology findings showing minimal change disease, focal segmental glomerulosclerosis or mesangioproliferative glomerulonephritis were enrolled into the study. Patients in group I received i.v. injection of cyclophosphamide once a month for 6 months and prednisolone on alternate days. Those in group II received i.v. treatment with dexamethasone (initially on alternate days, later fortnightly and monthly; total 14 doses), oral cyclophosphamide therapy (for 3 months) and prednisolone on alternate days. Data from 49 patients (26 in group I, 23 in group II) were analyzed; their clinical and biochemical features were similar at inclusion. Following treatment, complete remission was seen in 53.8% and 47.8% patients in groups I and II, respectively (P = 0.6). Long-term follow up showed favorable outcome in 14 (53.8%) patients in group I, and 9 (39.1%) in group II. Chief adverse effects, including cushingoid features and serious infections, were similar in both groups. Patients receiving i.v. dexamethasone therapy commonly showed hypertension and hypokalemia, while

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vomiting and reversible alopecia occurred in those receiving i.v. treatment with cyclophosphamide. **In patients with SRNS, the efficacy of treatment intravenously with cyclophosphamide and orally with prednisolone was similar to the combination of dexamethasone intravenously, orally administered cyclophosphamide and prednisolone.**

[Pediatr Nephrol.](#) 2009 Apr;24(4):775-82. Epub 2009 Jan 14.

Randomized cross-over trial comparing albumin and frusemide infusions in nephrotic syndrome.

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The contribution of hypoalbuminemia to impaired diuretic responsiveness can be overcome by administering larger doses of loop diuretics. However, the clinical efficacy of the combination of loop-acting diuretics with human albumin remains controversial. In the study reported here, 16 children with nephrotic syndrome and refractory edema were randomized in a cross-over trial to receive either the combination of 20% human albumin and frusemide infusion (HA+FU infusion group) or frusemide infusion alone (FU infusion group). At the end of study, median urine volume was 3.27 [95% confidence interval (CI) 2.04-4.50] ml/kg per hour in the HA+FU infusion group and 1.33 (95% CI 0.79-1.88) ml/kg per hour in the FU infusion group ($P = 0.01$); the median daily sodium excretion was 58 (95% CI 30-366) mEq and 30 (95% CI 10-122) mEq ($P = 0.08$), respectively. The changes in other variables included weight loss [HA+FU 5.2% (95% CI 3.1-8.8); FU 0.8% (95% CI -1.9 to 4.1); $P = 0.006$]; urine osmolality [HA+FU 315 (95% CI 220-426) mOsm/kg; FU 368 (95% CI 318-446) mOsm/kg; $P = 0.13$]; osmolal clearance [HA+FU 1600 (95% CI 916-4140) ml/day; FU 880 (95% CI 510-2105) ml/day; $P = 0.01$]; free water clearance [HA+FU -190 (95% CI -960 to 280) ml/day; FU -162 (95% CI -446 to -70) ml/day; $P = 0.18$]. **The findings from this study suggest that the co-administration of albumin and frusemide infusions is more effective than the administration of frusemide infusion alone in inducing diuresis and natriuresis in patients with nephrotic syndrome**

Comment

Giving frusemide alone to children with nephrotic syndrome can be dangerous, as despite being oedematous, many have borderline intravascular volume. Frusemide will mobilize intravascular water for excretion more quickly than interstitial water and this can lead to shock if patients are not monitored carefully.

[Trans R Soc Trop Med Hyg.](#) 2009 Jan;103(1):38-44. Epub 2008 Oct 5.

ELSEVIER
FULL-TEXT ARTICLE

Efficacy of a combination of praziquantel and artesunate in the treatment of urinary schistosomiasis in Nigeria.

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The combined effects of praziquantel and artesunate in the treatment of urinary schistosomiasis were assessed among 312 randomly selected schoolchildren aged 4-20 years in Adim community, Nigeria. In the preliminary screening, infection was confirmed in 327 (38.5%) of the 850 subjects screened. Infected subjects who reported for treatment were then divided into six treatment groups of 52 subjects each; 44 subjects in each group completed their treatment regimens and submitted their urine for post-treatment assessment. Praziquantel and artesunate were administered orally at 40 mg/kg and 4 mg/kg body weight, respectively. Adverse effects due to drug reactions were assessed 72 h after medication and all perceived episodes of illness were treated. Morbidity indicators were assessed 56 days after the final dose of the drug regimens. All treatment regimens were well tolerated. **The cure rates were 72.7% in the praziquantel plus placebo-treated group and 70.5% in the artesunate plus placebo group, while the artesunate plus praziquantel group had the highest cure rate (88.6%).** Haematuria and proteinuria were extensively reduced after treatment with the three drug regimens. **This study confirmed that the treatment of urinary schistosomiasis with the combination of praziquantel and artesunate is safe and more effective than treatment with either drug alone.**

Comment

*This study adds to the literature on the anti-schistosomal effects of artemisinin derivatives (see RCT from last year also: [Ann Trop Med Parasitol](#). 2008 Jan;102(1):39-44). The artemisinins and synthetic trioxolanes possess a broad spectrum of activity against trematodes. High worm-burden reductions were obtained with these drugs in experiments in rodents with infections of *Schistosoma japonicum*, *S. mansoni*, *Clonorchis sinensis*, *Fasciola hepatica* and *Opisthorchis viverrini*. Clinical from Africa, utilizing artemether or artesunate singly or as artemisinin-based combination therapies, following recommended malaria treatment schedules, found an effect against schistosomiasis (*Curr Opin Infect Dis*. 2007 Dec;20(6):605-12.) This study above confirms the usefulness of artesunate with praziquantel.*

School health

[J Adolesc Health](#). 2009 Feb;44(2):118-23. Epub 2008 Oct 18.

Effects of school health nursing education interventions on HIV/AIDS-related attitudes of students in Akwa Ibom State, Nigeria.

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PURPOSE: One of the greatest challenges facing school nurses is that of identifying and using appropriate strategies to meet the health education needs of adolescents in regard to prevention of human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS). This study examined the effects of HIV/AIDS preventive health education with parental involvement on students' attitude toward HIV/AIDS prevention in Akwa Ibom State, Nigeria. **METHODS:** The study population comprised students from three of nine secondary schools in the study area. The three schools were randomly assigned as Intervention Group 1 (IG1), involving nurses only; Intervention Group 2 (IG2), involving both nurses and parents (IG2); and a control group. A pretest/post-test intervention design was used. A 29-item, validated questionnaire was the instrument for data collection. Sampling involved multistage and stratified random technique to select 120 subjects from each of the three selected schools, with a total of 360 subjects representing 8.3% of the study population. From this number, 339 (94.2%) provided sufficient data for analysis. Data analysis involved analysis of covariance and the Scheffé post hoc test determined at the .05 significance level. **RESULTS:** Results show significant effect of intervention on students attitudes toward preventive measures ($F = 234.27$, $p < .001$ *). The intervention that involved nurses only was found to be a more potent strategy in providing favorable attitudes toward HIV/AIDS prevention (IG1 mean, 20.59; IG2 mean, 19.20; control mean, 12.34). Attitudes were influenced by older age but not by gender. **CONCLUSION:** Health education efforts aimed at improving HIV/AIDS-related attitudes should not only focus on children but also on parents so that they in turn could assist to improve on health workers' efforts in educating the children.

Skin disease

[Indian J Dermatol Venereol Leprol.](#) 2008 Sep-Oct;74(5):447-52.



Evening primrose oil is effective in atopic dermatitis: a randomized placebo-controlled trial.

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BACKGROUND: Atopic dermatitis (AD) is a chronic, relapsing, itchy dermatosis of multifactorial origin, which commonly starts in childhood. Defective metabolism of essential fatty acids leading to relative dominance of pro-inflammatory prostaglandins (PGE2 and PGF2) has been reported as an important factor in the pathogenesis of AD. Evening primrose oil (EPO) as a source of gamma-linolenic acid (GLA) has been of interest in the management of AD. **AIM:** To evaluate the efficacy and safety of EPO in atopic dermatitis in our patients. **METHODS:** **Consecutive new out-patient department (OPD) patients of a referral hospital in Kolkata clinically diagnosed as having AD were randomly allocated to two groups. To the first group, evening primrose oil was supplied as 500-mg oval clear unmarked capsules, while placebo capsules identical in appearance and containing 300 mg of sunflower oil were given to the other group.** Treatment continued for a period of 5 months. With pre-designed

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scoring system (based on four major parameters: extent, intensity, itching, and dryness), clinical evaluation was done at baseline and subsequent monthly visits. Data of the first 25 patients from each group who completed the 5 months of trial were compiled and analyzed. **RESULTS: At the end of the fifth month, 24 (96%) patients of EPO group and 8 (32%) patients of placebo group showed improvement. There was significant difference in outcome of treatment between two groups ($P < 0.00001$).** No significant adverse effect was reported by any patient/guardian at any point of assessment. **CONCLUSION: Evening primrose oil is a safe and effective medicine in management of AD. However, since not all researchers across the world have found the same good result, further large trials on Indian patients are needed.**

Snake-bite

[Ann Trop Med Parasitol](#). 2008 Oct;102(7):643-9.

The role of prednisolone in reducing limb oedema in children bitten by green pit vipers: a randomized, controlled trial.

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When green pit vipers (GPV), which are common venomous snakes in Thailand, bite humans they cause coagulopathy as well as local tissue oedema. The use of steroids to reduce such oedema is controversial. **The role of low, oral doses of prednisolone in the treatment of GPV bites in children has therefore now been assessed, in a randomized, double-blinded, placebo-controlled, clinical trial in Bangkok.** Overall, **43 children aged 3-15 years, each with a recent GPV bite to one limb, were randomly assigned to receive oral prednisolone (1 mg/kg.day) or placebo for 3 days, without antivenom or prophylactic antibiotics.** The degree of limb oedema was assessed, immediately before the first dose and then daily, by measuring the limb circumference around the fang marks. **By 72 h post-bite, both treatment groups showed significant decreases in the level of their limb oedema. Since, at each time-point, the patients in the two groups showed similar levels of limb oedema (and of reduction in such oedema), there appeared to be no benefit from the use of the prednisolone.**

Surgical problems

[Urol J](#). 2008 Fall;5(4):233-6.

Lubrication of circumcision site for prevention of meatal stenosis in children younger than 2 years old.

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INTRODUCTION: Circumcision is one of the most common surgical operations throughout the world, and meatal stenosis is one its late complications. We evaluated the topical use of a lubricant jelly after circumcision in boys in order to reduce the risk of meatal stenosis.

MATERIALS AND METHODS: A randomized control trial was performed, in which 2 groups of boys younger the 2 years old underwent circumcision according to the sleeve method. **The parents in the study group were instructed to use petroleum jelly on the circumcision site after each diaper change for 6 months.** In the control group, no topical medication was used. The children were followed up regularly and evaluated for meatal stenosis, bleeding, infection, and recovery time. **RESULTS:** **A total of 197 boys in each group completed the study. None of the children in the study group but 13 (6.6%) in the control group developed meatal stenosis (P < .001). Infection of the circumcision site was seen in 3 (1.5%) and 23 (11.7%) children of the lubricant and control groups, respectively (P < .001), and bleeding was seen in 6 (3.0%) and 37 (18.8%), respectively (P < .001). The mean time of recovery in the lubricant group was 3.8 +/- 1.2 days, while it was 6.9 +/- 4.2 days in the control group (P = .03).** **CONCLUSION:** Based on the findings of this study, it seems logical to use a lubricant jelly for reducing postcircumcision meatal stenosis and other complications

[Pediater Surg Int.](#) 2009 Jan;25(1):57-9. Epub 2008 Nov 7.

Comparison of topical versus parenteral testosterone in children with microphallic hypospadias.

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INTRODUCTION: Surgical correction of genital defects was formerly proposed when the size of the penis was sufficient to permit easy surgical repair. To enlarge penile size, temporary stimulation with testosterone either topical or parenteral has been reported. Parenteral testosterone has been found to be effective; however, variable results have been reported with topical testosterone. This study was taken up as an attempt to compare the efficacy of parenteral versus topical testosterone application. **MATERIALS AND METHODS:** **Twenty-one consecutive children with microphallic hypospadias were randomized to receive either topical or parenteral testosterone prior to surgery.** Penile length, glans circumference and secondary effects were recorded before and after therapy by the same observer. **RESULTS:** Significant penile growth was noticed in both the groups of children when compared with pre-therapy size. **CONCLUSIONS:** The desired therapeutic effect of significant penile growth following testosterone was achieved in both the groups of children. There was no significant difference between the two routes of administration.

[J Pediatr Surg.](#) 2008 Oct;43(10):1869-72.

Use of fibrin glue in preventing urethrocutaneous fistula after hypospadias

repair.

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Urethrocutaneous fistula is one of the most common complications after hypospadias surgery. The incidence of fistula development has varied from 4% to 20% in larger series. We sought to investigate the role of fibrin glue (Tisseel manufactured by Baxter India Pvt Ltd, Chennai, India) to reduce the chances of fistula formation in cases in proximal penile hypospadias. **METHOD:** A total of 120 patients with proximal penile hypospadias (patients having urethral meatus at posterior third of penile shaft and at penoscrotal junction) were included in the present study. Patients were randomly allocated into 2 groups of 60 each by using Strata 9 software random number table. In group A, fibrin glue was used as a sealant after hypospadias surgery, whereas in group B, no sealant was used. All the operations were performed by single surgeon using transverse preputial tubularized island flap urethroplasty. **RESULT:** Fistula formation occurred in 6 cases in group A (10%) and 19 cases in group B (32%) ($P = .027$). The fistulae observed in fibrin glue group A were single and small in size (<1 mm). Multiple (≥ 2 fistulae) and larger fistulae (>2 mm) were observed in group B. Overall complication was significantly higher in group B ($P = .006$). **CONCLUSION:** Fibrin glue in hypospadias repair does not eliminate fistula formation. However, it seems that it minimizes the incidence of fistula formation.

[Pediatr Surg Int](#). 2008 Oct;24(10):1181-5. Epub 2008 Aug 23.

The role of preoperative antibiotics in the prevention of wound infection after day case surgery for inguinal hernia in children in Ile Ife, Nigeria.

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PURPOSE: Day case surgery for inguinal hernia had been an established practice of the Paediatric Surgery Unit, OAUTHC, Ile Ife for about two decades. In a retrospective review of the practice from the same center, a high incidence of postoperative wound infection was noted, which was attributed to the poor personal hygiene of the patients. This prospective study, therefore, was performed to evaluate the role of a single dose of preoperative antibiotic (using gentamicin) in the prevention of these wound infections after day case surgery for inguinal hernia in children. **METHODS:** This was a prospective study carried out over a period of 8 months from 11 April 2004 to 20 December 2004. During this period, **88 children aged from birth to 15 years were randomized into two groups of equal numbers to undergo elective inguinal herniotomy. The children in the test group received prophylactic intravenous gentamicin, 30 min before a groin crease incision was made, while those in the control group did not. All patients were subsequently followed up for 32 days for any evidence of a wound infection.** **RESULTS:** There were 104 wounds in the ratio of 50:54 in the control and test groups, respectively. All 54 wounds of the children who received prophylactic

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gentamicin healed primarily and without complication. Five cases of wound infections occurred in the control group, giving an infection rate of 4.8% ($P < 0.041$). *Staphylococcus aureus* was the single pathogen isolated from the infected postherniotomy wounds and this organism was wholly sensitive to gentamicin. **CONCLUSION:** From the findings in this study, administration of preoperative gentamicin has a role in the prevention of wound infection after day case surgery for inguinal hernias in susceptible children. Preoperative intravenous gentamicin is therefore recommended as a prophylactic measure against wound infection after day case surgery for inguinal hernias in those children at risk of wound infection.

Vaccines and immunization

[Vaccine](#). 2009 Jan 14;27(3):467-72. Epub 2008 Nov 7.

Redesigned immunization card and center-based education to reduce childhood immunization dropouts in urban Pakistan: a randomized controlled trial.

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In Pakistan during 2000-2004, about 11-13% of children who received the first dose of diphtheria-pertussis-tetanus (DPT1) failed to complete its third dose (DPT3). We assessed the effect of a redesigned immunization card and center-based education to mothers on DPT3 completion. We enrolled 1500 mother-child units at DPT1, randomized them to three intervention and one standard care groups, and recorded their DPT3 visits during a 90-day follow-up. In multivariable analysis, a significant increase of 31% (adjusted RR=1.31, 95% CI=1.18-1.46) in DPT3 completion was estimated in the group that received both redesigned card and center-based education compared with the standard care group.

Non-specific effects

[PLoS One](#). 2008;3(12):e4056. Epub 2008 Dec 29.



Sex-differential effect on infant mortality of oral polio vaccine administered with BCG at birth in Guinea-Bissau. A natural experiment.

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BACKGROUND: The policy to provide oral polio vaccine (OPV) at birth was introduced in low-income countries to increase coverage. The effect of OPV at birth on overall child mortality

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was never studied. During a trial of vitamin A supplementation (VAS) at birth in Guinea-Bissau, OPV was not available during several periods. We took advantage of this "natural experiment" to test the effect on mortality of receiving OPV at birth. **METHODOLOGY:** Between 2002 and 2004, **the VAS trial randomised normal-birth-weight infants to 50,000 IU VAS or placebo administered with BCG. Provision of OPV at birth was not part of the trial, but we noted whether the infants received OPV or not.** OPV was missing during several periods in 2004. We used Cox proportional hazards models to compute mortality rate ratios (MRR) of children who had received or not received OPV at birth. **PRINCIPAL FINDINGS:** A total of 962 (22.1%) of the 4345 enrolled children did not receive OPV at birth; 179 children died within the first year of life. Missing OPV at birth was associated with a tendency for decreased mortality (adjusted MRR = 0.69 (95% CI = 0.46-1.03)), the effect being similar among recipients of VAS and placebo. There was a highly significant interaction between OPV at birth and sex ($p = 0.006$). Not receiving OPV at birth was associated with a weak tendency for increased mortality in girls (1.14 (0.70-1.89)) but significantly decreased mortality in boys (0.35 (0.18-0.71)). **CONCLUSIONS:** In our study OPV at birth had a sex-differential effect on mortality. Poliovirus is almost eradicated and OPV at birth contributes little to herd immunity. A randomised study of the effect of OPV at birth on overall mortality in both sexes is warranted.

Comment

This study that adds more questions than answers to the debate on non-specific effects of vaccines. For a better understanding of such studies and this issue overall, see Fine PE, et al. "Epidemiological studies of the 'non-specific effects' of vaccines: I - data collection in observational studies." [Trop Med Int Health](#). 2009 Jun 15 (and look for subsequent publications in this series in the same journal throughout 2009).

Rotavirus vaccine

[J Infect Dis](#). 2009 Jun 22. [Epub ahead of print]

A Dose-Escalation Safety and Immunogenicity Study of Live Attenuated Oral Rotavirus Vaccine 116E in Infants: A Randomized, Double-Blind, Placebo-Controlled Trial.

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Background. Rotavirus infections cause approximately 122,000 deaths among Indian children annually. **Methods.** The neonatal rotavirus candidate vaccine 116E was tested in a double-blind, placebo-controlled dose-escalation trial in India. Two doses of the Vero cell-adapted vaccine were evaluated. One hundred eighty-seven infants received a vaccine dose of [Formula: see text] focus-forming units (ffu) and 182 received a dose of [Formula: see text] ffu in a 1:1 randomization with placebo recipients. Infants received the vaccine at 8, 12, and 16 weeks, separately from routine vaccines. **Results.** No significant differences in clinical adverse events or laboratory toxicity were observed between vaccine and placebo recipients. There were no

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vaccine-related serious adverse events. A 4-fold increase in rotavirus immunoglobulin A titer was observed in 66.7% and 64.5% of infants after the first administration and in 62.1% and 89.7% of infants after 3 administrations of doses of [Formula: see text] ffu and [Formula: see text] ffu, respectively; the differences between these groups and placebo recipients were statistically significant. Conclusions. Three administrations of vaccine doses of [Formula: see text] ffu and [Formula: see text] ffu were safe. The [Formula: see text]-ffu dose of 116E demonstrated a robust immune response after 3 administrations. These favorable results warrant further development of the vaccine candidate and provide optimism that vaccinating infants in the developing world will prevent serious sequelae of rotavirus infection. Clinical trials registration. NCT00439660 and ISRCTN57452882 .

[Ann Acad Med Singapore](#). 2008 Jul;37(7):546-53.



Immunogenicity, reactogenicity and safety of a diphtheria-tetanus-acellular pertussis-inactivated polio and Haemophilus influenzae type b vaccine in a placebo-controlled rotavirus vaccine study.

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INTRODUCTION: In recent years, acellular pertussis combination vaccines have facilitated compliance with and coverage of the national immunisation programme in Singapore. This phase-II study (Rota-007) evaluated the immunogenicity, reactogenicity and safety of a DTPa-IPV/Hib combined vaccine when co-administered with a rotavirus vaccine. **MATERIALS AND METHODS:** A total of 2464 children aged 3 months were vaccinated with DTPa-IPV/Hib together with a randomised 1:3 ratio of either placebo (n=653) or 1 of 3 different formulations of a rotavirus vaccine. Blood samples were collected for immunogenicity analysis 1 month after the third DTPa-IPV/Hib vaccine dose in a subset of subjects (n = 640). Local and general reactogenicity and unsolicited adverse events were recorded during the follow-up after each vaccination. **RESULTS:** Serological analysis showed >95% response for all antigens in the co-administered DTPa-IPV/Hib vaccine, with no difference between the rotavirus vaccine and placebo groups. No differences in adverse events and reactogenicity were reported in the rotavirus vaccine and placebo groups. Only 0.2% of the subjects reported Grade 3 adverse events. Three subjects (from the vaccine groups) died during the study, which were assessed by the investigators as unrelated to vaccination. No deaths were reported in the placebo group. **CONCLUSION:** The combined DTPa-IPV/Hib vaccine is safe, well tolerated and highly immunogenic when given alone or coadministered with the rotavirus vaccine for infants in Singapore.

Pneumococcal vaccine

[Pediatr Infect Dis J](#). 2009 Jun;28(6):455-62.

Efficacy of an 11-valent pneumococcal conjugate vaccine against radiologically confirmed pneumonia among children less than 2 years of age in the Philippines: a randomized, double-blind, placebo-controlled trial.

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BACKGROUND: Pneumococcus is a leading cause of childhood pneumonia worldwide. Pneumococcal conjugate vaccines (PCV) have demonstrated efficacy against childhood invasive pneumococcal disease (IPD) and pneumonia in the United States and Africa. No information is available from Asia on the impact of PCV on childhood pneumonia. **METHODS:** We conducted a randomized, placebo-controlled, double-blind trial in Bohol, the Philippines (ISRCTN 62323832). Children 6 weeks to <6 months of age were randomly allocated to receive 3 doses of either an 11-valent PCV (11PCV, sanofi pasteur, Lyon, France) or a saline placebo, with a minimum interval of 4 weeks between doses to determine vaccine efficacy (VE) against the primary outcome of a child experiencing first episode of community-acquired radiologically defined pneumonia in the first 2 years of life. Secondary end points were clinical pneumonia, IPD, safety, and immunogenicity. **RESULTS:** Twelve thousand one hundred ninety-one children were enrolled. By per protocol (PP) analysis, **93 of 6013 fully vaccinated 11PCV recipient children had a first episode of radiologic pneumonia compared with 120 of 6018 placebo recipients. VE against radiologically defined pneumonia for the PP cohort of children 3 to 23 months old was 22.9% (95% CI: -1.1, 41.2; P = 0.06), for the prespecified subgroups of children 3 to 11 months of age, 34.0% (95% CI: 4.8, 54.3; P = 0.02), and of those 12 to 23 months old, 2.7% (95% CI: -43.5, 34.0; P = 0.88).** By intent-to-treat (ITT) analysis, 119 of 6097 11PCV recipient children had an episode of radiologic pneumonia compared with 141 of 6094 placebo recipients. **VE against radiologic pneumonia for the ITT cohort of children <2 years old was 16.0% (95% CI -7.3, 34.2; P = 0.16), for a subgroup of children <12 months of age, 19.8% (95% CI: -8.8, 40.8; P = 0.15). VE against clinical pneumonia by PP was not significant (VE 0.1%; 95% CI -9.4, 8.7; P = 0.99).** IPD was rare: only 3 cases of IPD due to vaccine serotypes were observed during the study. 11PCV was immunogenic and well tolerated. Among 11PCV recipients, a small excess of serious adverse respiratory events was observed in the first 28 days after the first and second dose of vaccine, and of nonrespiratory events after the first dose. An excess of pneumonia episodes in 11PCV recipients in the month following the second dose of vaccination was the principal reason for lower VE by ITT analysis than by PP analysis. **CONCLUSIONS:** In PP analysis, a 22.9% reduction of community-acquired radiologically confirmed pneumonia in children younger than 2 years of age in the 11-valent tetanus-diphtheria toxoid-conjugated PCV vaccinated group was observed; a reduction similar as observed in other PCV trials. We could not demonstrate any VE against clinical pneumonia. Our finding confirms for the first time that in a low-income, low-mortality developing country in Asia, at least one-fifth of radiologically confirmed pneumonia is caused by pneumococcus, and thus preventable by PCV. Whether PCV should be included in national program in such settings, however, depends on careful country specific disease burden measurement and cost-effectiveness calculation.

Comment

This is a very important study, which adds evidence on which countries can base decisions about adding pneumococcal conjugate vaccine (PCV) to their vaccine schedule. Although these are expensive vaccines, a 22% reduction in radiologic pneumonia would be a major reduction

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in childhood illness, and would result in a substantial reduction in health care utilisation and costs. It is estimated that globally there are 150 million cases of pneumonia each year, of which 11-20 require hospitalization. Issues that countries need to consider in deciding to introduce PCV include: dose schedule (would one or two doses be sufficient? Can the first dose be given in the neonatal period?), the risk of sero-type replacement with non-vaccine strains, whether the vaccine contains appropriate serotypes for a given population, cost and sustainability after initial periods of global agency support.

[Vaccine](#). 2009 May 5;27(20):2680-8. Epub 2009 Feb 24.

IgG antibody concentrations after immunization with 11-valent mixed-carrier pneumococcal conjugate vaccine in efficacy trial against pneumonia among Filipino infants.

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BACKGROUND: Pneumococcal pneumonia is a major cause of morbidity and mortality worldwide. Efficacy of pneumococcal conjugate vaccines (PCV) in reducing childhood pneumonia has been estimated in four double-blind, randomized, controlled trials. An investigational 11-valent pneumococcal conjugate vaccine (11PCV) had an efficacy of 22.9% against radiologically defined pneumonia during first 2 years of life in Filipino infants. We report here the immunogenicity of the vaccine in a nested study of 1111 infants randomized 1:1 to receive 11PCV or placebo scheduled to be given according to the National EPI Program at 6, 10, and 14 weeks of age. **METHODS:** IgG antibody concentrations to pneumococcal capsular polysaccharides were measured by a standardized enzyme immuno-assay in serum samples drawn post-3rd dose for peak antibody response and at the time of measles vaccination at 9 months of age for persistence of the antibodies. **RESULTS:** The geometric mean concentrations (GMCs) of antibodies were significantly higher in 11PCV than in placebo recipients against vaccine serotypes at both sampling points. One month post-3rd dose, 93-100% of 11PCV recipients had ≥ 0.35 microg/ml for 9 serotypes, 76% for 6B, and 87% for 23F. The same proportions varied between 24% and 97% at 9.5 months of age due to antibody decrease. GMC to vaccine-related serotype 19A, but not to 6A, was higher in 11PCV than in placebo recipients. 7-12% of the 11PCV recipients had spontaneous antibody increases to serotypes 6B, 23F, and 14 between the two sampling points. These serotypes were common in nasopharyngeal samples of the infants. **CONCLUSION: The 11PCV demonstrated good immunogenicity after three doses and persistence of antibodies at least up to 9.5 months of age**, comparable to other PCVs that have been evaluated for efficacy against radiologically defined pneumonia in other populations.

[Vaccine](#). 2009 May 5;27(20):2723-9. Epub 2008 Oct 31.

Reactogenicity and tolerability of a non-adjuvanted 11-valent diphtheria-tetanus toxoid pneumococcal conjugate vaccine in Filipino children.

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In a phase three randomized, double-blind, saline-placebo controlled study conducted in Bohol, Philippines, we assessed the reactogenicity of an 11-valent PCV (11PCV) when given simultaneously with EPI vaccines at 6, 10 and 14 weeks of age in a subset of 252 and 126 children who were followed-up by passive and active surveillance, respectively. **In passive surveillance (parents' observation), redness was observed in 14.4% vs. 11.8%, swelling in 8% vs. 3.9%, induration in 13.6% vs. 8.6%, and pain in 54.4% vs. 47.2% of 11PCV and placebo infants, respectively, after the first dose of the vaccine. Redness at injection site was significantly more common with 11PCV than placebo infants after the third dose (13.6% vs. 3.2%, $p=0.005$). Crying (53.6% vs. 48%), irritability (48% vs. 46.4%), and fever (22.4% vs. 19.6%) were commonly observed in 11PCV and placebo infants, respectively, after the first dose.** Loss of appetite was significantly more common among 11PCV (12%) than placebo (4.7%) infants but only after the first dose of the vaccine ($P=0.04$). The number of reactions decreased in both groups with subsequent doses. The non-adjuvanted 11PCV vaccine was found to be well-tolerated among Filipino infants.

[J Infect Dis](#). 2009 Apr 15;199(8):1168-76.

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Quantitative and qualitative anamnestic immune responses to pneumococcal conjugate vaccine in HIV-infected and HIV-uninfected children 5 years after vaccination.

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BACKGROUND: Administration of pneumococcal conjugate vaccine (PCV) to HIV-infected children during infancy confers limited long-term protection in the absence of antiretroviral therapy. The objective of the present study was to determine the immune responses to PCV at 5 years of age in HIV-infected and HIV-uninfected children who had been primed with vaccine during infancy (i.e., previous vaccinees) and in those receiving their first dose of vaccine (i.e., control subjects). **METHODS:** Serotype-specific antibodies were quantified by enzyme immunoassay, and antibody functionality to serotypes 6B, 9V, and 19F were evaluated using an opsonophagocytic killing assay 1 month after vaccination. **RESULTS:** Of the HIV-infected children, 19.7% were receiving antiretroviral therapy, and 40.5% had a CD4(+) cell percentage <15%. **Geometric mean concentrations of antibody and the proportion with a concentration 0.35 microg/mL after vaccination were greater among HIV-uninfected children than among HIV-infected children for both previous vaccinees and control subjects. Antibody concentrations after vaccination were lower for 3 of 7 serotypes among HIV-infected previous vaccinees than among control subjects.** Detectable opsonophagocytic

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activity to all studied serotypes was lower among HIV-infected than among HIV-uninfected previous vaccinees and control subjects. Postvaccination antibody-mediated killing activity as determined by the opsonophagocytic killing assay was enhanced in control subjects compared with previous vaccinees among HIV-uninfected children. **CONCLUSION: HIV-infected vaccinees experience a partial loss of anamnestic responses to PCV. The optimal timing and frequency of booster vaccination as well as the responses to them among HIV-infected children need to be determined.**

[Vaccine](#). 2009 Feb 25;27(9):1340-7. Epub 2009 Jan 14.



Neonatal pneumococcal conjugate vaccine immunization primes T cells for preferential Th2 cytokine expression: a randomized controlled trial in Papua New Guinea.

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The effects of neonatal immunization with 7-valent pneumococcal conjugate vaccine (7vPCV) on development of T-cell memory and general immune maturation were studied in a cohort of Papua New Guinean newborns. Neonatal 7vPCV priming (followed by a dose at 1 and 2 months of age) was associated with enhanced Th2, but not Th1, cytokine responses to CRM(197) compared to 7vPCV at 1 and 2 months of age only. T cell responses to non-7vPCV vaccine antigens were similar in all groups, but TLR-mediated IL-6 and IL-10 responses were enhanced in 7vPCV vaccinated compared to controls. Neonatal 7vPCV vaccination primes T cell responses with a polarization towards Th2 with no bystander effects on other T cell responses.

[Vaccine](#). 2008 Jul 4;26(29-30):3719-26. Epub 2008 May 16.

Immunogenicity and serotype-specific efficacy of a 9-valent pneumococcal conjugate vaccine (PCV-9) determined during an efficacy trial in The Gambia.

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This study aimed to determine the immunogenicity of a 9-valent pneumococcal conjugate vaccine (PCV-9) in a subgroup of Gambian children enrolled in a large vaccine efficacy trial. To place the antibody results in context, in this paper we also report previously unpublished data on serotype-specific clinical vaccine efficacy from the main trial. In the sub-study, a single 2-4 ml venous blood specimen was collected from 212 Gambian children 4-6 weeks after the administration of a third dose of PCV-9 or placebo. IgG antibodies to pneumococcal serotype 1,

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4, 5, 6B, 9V, 14, 18C, 19F and 23F polysaccharides were measured by ELISA. The proportions of infants with antibody concentrations above 0.2, 0.35 and 1.0 microg/ml, and the geometric mean concentrations (GMCs) of anti-pneumococcal polysaccharide antibodies were substantially higher for each serotype in children who received three doses of PCV-9 than those in the placebo group. Among PCV-9 recipients, GMCs ranged between 2.61 and 11.09 microg/ml with the highest being against serotype 14 and the lowest against 9V polysaccharide. The estimated overall protective antibody level for all nine serotypes, based on the vaccine efficacy against vaccine-type invasive pneumococcal disease (IPD) of 77% (95% CI: 51, 90) observed in the trial, was 2.3 microg/ml (95% CI: 1.0, 5.0). The PCV-9 studied was immunogenic in a Gambian population where it was also found to be efficacious.

Rabies vaccine

[Pediatr Infect Dis J.](#) 2009 Apr;28(4):335-7.

A three-year clinical study on immunogenicity, safety, and booster response of purified chick embryo cell rabies vaccine administered intramuscularly or intradermally to 12- to 18-month-old Thai children, concomitantly with Japanese encephalitis vaccine.

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After concomitant administration of purified chick embryo cell rabies vaccine and Japanese encephalitis vaccine to toddlers, adequate rabies and Japanese encephalitis virus neutralizing antibodies concentrations were demonstrated by day 49, 7 days after a booster at 1 year, and in the majority at 3 years postvaccination. The inclusion of rabies vaccine in the expanded program on immunization should be considered in rabies endemic countries.

[Hum Vaccin.](#) 2008 Sep-Oct;4(5):365-9. Epub 2008 Oct 1.

Protecting Indian schoolchildren against rabies: pre-exposure vaccination with purified chick embryo cell vaccine (PCECV) or purified verocell rabies vaccine (PVRV).

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Although rabies can be effectively prevented by means of preexposure or post-exposure prophylaxis, in India, an estimated 17,000 to 20,000 human rabies deaths occur annually.

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Tragically, 50% of these victims are children under the age of 15. In addition to immediate post-exposure prophylaxis measures, including active and passive immunization, pre-exposure vaccination using tissue culture vaccines is a safe and effective but highly underutilized method of preventing rabies in humans living or working in areas at risk. This study assessed the safety and immunogenicity of Purified Chick Embryo Cell Vaccine (PCECV) and Purified Verocell Rabies Vaccine (PVRV), administered as a three-dose intramuscular pre-exposure regimen on days 0, 7 and 28 in 175 healthy schoolchildren. PCECV was administered after reconstitution using either 1.0 mL or 0.5 mL (half the diluent volume) and PVRV was given after reconstitution with 0.5 mL. Vaccine safety was assessed observer-blind, including pain assessment with a validated visual analogue scale for children. Rabies virus neutralizing antibody (RVNA) concentrations were measured on day 49 by RFFIT. All children developed adequate RVNA concentrations above 0.5 IU/mL. Solicited local and systemic reactions were within the range expected, pain after vaccination was reported in 2 to 12% of study subjects, fever was reported in 2 to 5%. There was no statistical difference by vaccination group or vaccination day. No unexpected or serious adverse event was reported during the study. In conclusion, **PCECV and PVRV are safe and immunogenic when administered intramuscularly for pre-exposure prophylaxis of rabies in children. A 1.0 mL dilution volume for PCECV was as well tolerated as PVRV or PCECV reconstituted in half the volume.**

Influenza vaccine

[PLoS One](#). 2008;3(12):e4028. Epub 2008 Dec 29.



Safety, humoral and cell mediated immune responses to two formulations of an inactivated, split-virion influenza A/H5N1 vaccine in children.

[Chotpitayasunondh T](#), [Thisyakorn U](#), [Pancharoen C](#), [Pepin S](#), [Nougarede N](#).

Queen Sirikit National Institute of Child Health, Bangkok, Thailand.

BACKGROUND: Highly pathogenic influenza A/H5N1 has caused outbreaks in wild birds and poultry in Asia, Africa and Europe. It has also infected people, especially children, causing severe illness and death. Although the virus shows limited ability to transmit between humans, A/H5N1 represents a potential source of the next influenza pandemic. **This study assesses the safety and immunogenicity of aluminium hydroxide adjuvanted (Al) and non adjuvanted influenza A/Vietnam/1194/2004 NIBRG-14 (H5N1) vaccine in children.** **METHODS AND FINDINGS:** In a Phase II, open, randomised, multicentre trial 180 children aged 6 months to 17 years received two injections, 21 days apart, of vaccine containing either: 30 microg haemagglutinin (HA) with adjuvant (30 microg+Al) or 7.5 microg HA without adjuvant. An additional 60 children aged 6-35 months received two "half dose" injections (ie 15 microg+Al or 3.8 microg). Safety was followed for 21 days after vaccination. Antibody responses were assessed 21 days after each injection and cellular immune responses were explored. Vaccination appeared well tolerated in all age groups. The 30 microg+Al formulation was more immunogenic than 7.5 microg in all age groups: in these two groups 79% and 46% had haemagglutination inhibition antibody titres > or =32 (1/dil). Among 6-35 month-olds, the full doses were more immunogenic than their half dose equivalents. Vaccination induced a predominantly Th2 response against H5 HA. **CONCLUSIONS: This influenza A(H5N1)**

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vaccine was well tolerated and immunogenic in children and infants, with AI adjuvant providing a clear immunogenic advantage. These results demonstrate that an H5N1 AI-adjuvanted vaccine, previously shown to be immunogenic and safe in adults, can also be used in children, the group most at risk for pandemic influenza

[Vaccine](#). 2008 Aug 18;26(35):4579-84. Epub 2008 Jun 17.

Safety and immunogenicity of two subunit influenza vaccines in healthy children, adults and the elderly: a randomized controlled trial in China.

[Zhu FC](#), [Zhou W](#), [Pan H](#), [Lu L](#), [Gerez L](#), [Nauta J](#), [Giezeman K](#), [de Bruijn I](#).

Jiangsu Provincial Center for Disease Control and Prevention, Nanjing, Jiangsu Province, People's Republic of China.

The burden of influenza is well known in the elderly and at-risk patients, but also in children. Especially in those under 5 years old, influenza may cause severe morbidity and mortality. Influenza infections and complications can be reduced by vaccination. **In a randomized, endpoint-blinded, parallel group trial the immunogenicity and safety was studied of two trivalent inactivated surface antigen (subunit) influenza vaccines Influvac and Agrippal in healthy children** as well as in adults and the elderly. An open safety part in 30 children aged 3-12 years and 30 adults aged 18-60 years vaccinated with Influvac was followed by an endpoint-blind, parallel group part in 300 healthy children aged 3-12 years, 300 healthy adults aged 18-59 years, and 240 healthy elderly persons aged 60 years or over, in which subjects were randomized 2:1 to vaccination with either Influvac or Agrippal. The primary immunogenicity endpoint was the geometric mean titer (GMT) 4 weeks after vaccination. Both Influvac and Agrippal induced high anti-hemagglutinin antibody titers in the children and in the adult and elderly subjects. **Seroprotection rates were >85% and seroconversion rates >70% for both vaccines in all three age groups for all three-virus strains.** The GMT ratios after vaccination indicated that the immunogenicity of Influvac was at least comparable with that of Agrippal in all three age groups. Both vaccines were well tolerated and safe. In this trial, Influvac and Agrippal were immunogenic, safe and well tolerated in healthy children as well as in adults and elderly people.

Measles vaccine

[J Infect Dis](#). 2008 Nov 15;198(10):1457-65.

The University of
Chicago Press

Evaluation of the immune response to a 2-dose measles vaccination schedule administered at 6 and 9 months of age to HIV-infected and HIV-uninfected children in Malawi.

[Helfand RF](#), [Witte D](#), [Fowlkes A](#), [Garcia P](#), [Yang C](#), [Fudzulani R](#), [Walls L](#), [Bae S](#), [Strebel P](#), [Broadhead R](#), [Bellini WJ](#), [Cutts F](#).

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BACKGROUND: The World Health Organization recommends that infants at high risk for developing measles before 9 months of age, including human immunodeficiency virus (HIV)-infected infants, receive measles vaccination (MV) at 6 and 9 months of age. **METHODS:** **Children born to HIV-infected mothers received MV at 6 and 9 months, and children of HIV-uninfected mothers were randomized to receive MV at 6 and 9 months, MV at 9 months, or routine MV without follow-up.** Blood samples were obtained before and 3 months after each MV. Data were collected on adverse events for 21 days after each MV, at all clinic visits, on any hospitalization, and for subjects who died. HIV-infection status was determined by antibody assays and polymerase chain reaction; the presence of measles IgG was determined by EIA. **RESULTS:** Twenty-two hundred mother-infant pairs were enrolled. **After the first and second doses of measles vaccine, respectively, the percentages of children who were measles seropositive were 59% (36 of 61) and 64% (29 of 45) among HIV-infected children, 68% (152 of 223) and 94% (189 of 202) among HIV-exposed but uninfected children, and 62% (288 of 467) and 92% (385 of 417) among HIV-unexposed children.** Of 521 HIV-unexposed children vaccinated only at 9 months, 398 (76%) were measles seropositive at 12 months. No serious vaccine-related adverse events were identified. **CONCLUSIONS:** **An early, 2-dose MV schedule was immunogenic, but a higher proportion of HIV-infected children remained susceptible to measles, compared with HIV-uninfected children (whether HIV exposed or HIV unexposed).**

[BMJ](#). 2008 Jul 24;337:a661. doi: 10.1136/bmj.a661.

Protective efficacy of standard Edmonston-Zagreb measles vaccination in infants aged 4.5 months: interim analysis of a randomised clinical trial.

[Martins CL](#), [Garly ML](#), [Balé C](#), [Rodrigues A](#), [Ravn H](#), [Whittle HC](#), [Lisse IM](#), [Aaby P](#).

Bandim Health Project, Indepth Network, Bissau, Guinea-Bissau.

OBJECTIVE: To examine the protective efficacy of measles vaccination in infants in a low income country before 9 months of age. **DESIGN:** Randomised clinical trial. **PARTICIPANTS:** 1333 infants aged 4.5 months: 441 in treatment group and 892 in control group. **SETTING:** Urban area in Guinea-Bissau. **INTERVENTION:** Measles vaccination using standard titre Edmonston-Zagreb vaccine at 4.5 months of age. **MAIN OUTCOME MEASURES:** **Vaccine efficacy against measles infection, admission to hospital for measles, and measles mortality before standard vaccination at 9 months of age.** **RESULTS:** 28% of the children tested at 4.5 months of age had protective levels of maternal antibodies against measles at enrolment. **After early vaccination against measles 92% had measles antibodies at 9 months of age.** A measles outbreak offered a unique situation for testing the efficacy of early measles vaccination. During the outbreak, 96 children developed measles; 19% of unvaccinated children had measles before 9 months of age. The monthly incidence of measles among the 441 children enrolled in the treatment arm was 0.7% and among the 892 enrolled in the control arm was 3.1%. **Early vaccination with the Edmonston-Zagreb measles vaccine prevented infection; vaccine efficacy for children with serologically confirmed measles and definite clinical measles was 94% (95% confidence interval 77% to 99%), for admissions to hospital for measles was 100% (46% to 100%), and for measles mortality was 100% (-42% to 100%).** The number

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needed to treat to prevent one case of measles between ages 4.5 months and 9 months during the epidemic was 7.2 (6.8 to 9.2). **The treatment group tended to have lower overall mortality (mortality rate ratio 0.18, 0.02 to 1.36) although this was not significant.** CONCLUSIONS: **In low income countries, maternal antibody levels against measles may be low and severe outbreaks of measles can occur in infants before the recommended age of vaccination at 9 months. Outbreaks of measles may be curtailed by measles vaccination using the Edmonston-Zagreb vaccine as early as 4.5 months of age.** TRIAL REGISTRATION CLINICAL TRIALS: NCT00168558 [ClinicalTrials.gov].

Comment

*This study demonstrates the safety and efficacy of measles vaccine at 4½ months of age. Achieving very high coverage at 9-12 months of age is the primary goal for measles control in every country. However there may still be considerable advantages in giving the first dose of measles vaccine earlier in some countries where mortality is high. These advantages include: the likely non-specific effects of measles vaccine on mortality; including data from Africa on lower overall mortality when measles vaccine is given before 9 months of age. The problem of non-seroconversion because of maternal antibodies in young infants also needs to be balanced against the **effective** coverage achieved (proportion of the population vaccinated and who have seroconverted). In some developing countries, where access to health services is difficult, there is a lower coverage achieved by immunizations scheduled for later infancy because of waning parental interest in bringing children to preventative health clinics as they get older. The protective effect of measles vaccine may be more complicated than just stimulation of antibody formation; there is evidence that when given to young infants there is priming of the immune system due to stimulation of cell mediated immunity, which can be followed by a later booster response.*

[Saudi Med J](#). 2008 Jul;29(7):1009-13.

Sero-response to measles vaccination at 12 months of age in Saudi infants in Qassim Province.

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OBJECTIVE: To evaluate the sero-response to measles component of the first measles, mumps and rubella MMR dose given at 12 months by measuring measles antibody before and one month after the vaccination. METHODS: A follow-up study where, 57 children at the age of 12 months were recruited randomly from the Primary Health Care Centers in Qassim, Saudi Arabia using a multistage sampling techniques. Fieldwork was conducted from October until December 2006. Blood samples were collected to measure measles IgG antibody before, and one month after giving MMR using enzyme linked immunosorbent assay. Data were compared before and after vaccination using geometric mean titer GMT and seroconversion. RESULTS: **In the 57 infants, positivity rate increased significantly from 3.5% (2/57) pre-vaccination to 100% one month after p=0.0001, and with a sero-conversion of 96.5% (55/57).** Also, GMT increased significantly from 0.014-2.172 IU/ML, after vaccination p=0.0001. CONCLUSION:

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Sero conversion and GMT are significantly high after the first MMR given at 12 months and this is supported by the surveillance data in Qassim.

Vitamin A

(See: Micronutrient and food fortification; diarrhoea; and deworming)

Zinc

(see also: Diarrhoea, Vitamin A)

[BMC Med.](#) 2009 May 5;7:22.



Zinc and copper supplementation in acute diarrhea in children: a double-blind randomized controlled trial.

[Patel A](#), [Dibley MJ](#), [Mamtani M](#), [Badhoniya N](#), [Kulkarni H](#).

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BACKGROUND: Diarrhea causes an estimated 2.5 million child deaths in developing countries each year, 35% of which are due to acute diarrhea. Zinc and copper stores in the body are known to be depleted during acute diarrhea. Our objectives were to evaluate the efficacy of zinc and copper supplementation when given with standard treatment to children with acute watery or bloody diarrhea. **METHODS:** We conducted a double-blind randomized controlled clinical trial in the Department of Pediatrics at Indira Gandhi Government Medical College Nagpur, India. **Eight hundred and eight children aged 6 months to 59 months with acute diarrhea were individually randomized to placebo (Pl), zinc (Zn) only, and zinc and copper (Zn+Cu) together with standard treatment for acute diarrhea.** **RESULTS:** The mean duration of diarrhea from enrollment and the mean stool weight during hospital stay were 63.7 hours and 940 grams, respectively, and **there were no significant differences in the adjusted means across treatment groups. Similarly, the adjusted means of the amount of oral rehydration solution or intravenous fluids used, the proportion of participants with diarrhea more than 7 days from onset, and the severity of diarrhea indicated by more than three episodes of some dehydration or any episode of severe dehydration after enrollment, did not differ across the three groups.** **CONCLUSION:** The expected beneficial effects of zinc supplementation for acute diarrhea were not observed. Therapeutic Zn or Zn and Cu supplementation may not have a universal beneficial impact on the duration of acute diarrhea in children.

[J Pediatr Gastroenterol Nutr.](#) 2009 Jan;48(1):89-93.

Zinc therapy for diarrhoea improves growth among Bangladeshi infants 6 to 11 months of age.

[Naheed A](#), [Walker Fischer CL](#), [Mondal D](#), [Ahmed S](#), [Arifeen SE](#), [Yunus M](#), [Black RE](#),

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OBJECTIVES: We assessed the effect of zinc for the treatment of diarrhoea implemented at the community level on physical growth among children 6 to 35 months of age. **METHODS:** The service areas of 30 community health workers in the Matlab field site of International Centre for Diarrhoeal Disease Research, Bangladesh, were randomly allocated to the intervention or comparison study arm. Between November 1998 and October 2000, caretakers of 3- to 59-month-old children with diarrhoea in both intervention and comparison areas were offered oral rehydration solution and feeding advice, and severe episodes were referred for facility-based care. **The caretakers of the children in the intervention area were additionally offered 20 mg/day elemental zinc for 14 days as adjunct treatment for each diarrhoea episode.** Weight and length of children who were 6 to 11 months of age at the beginning of the study were measured every 2 months for 2 years. Rates of length and weight gains were compared between children living in intervention and control arms using a latent growth model. **RESULTS:** Characteristics of children living in control and intervention areas were similar, except that more children living in intervention areas were underweight at baseline (44 vs 35%; $P = 0.02$). **Children living in intervention clusters gained slightly more weight and length than children in the control clusters (86.4 g/year and 2.8 mm/year, respectively).** **CONCLUSIONS:** **The therapeutic use of zinc along with oral rehydration solution for community-based diarrhoea management may have a small positive benefit on the rates of growth among children younger than 3 years of age.**

[Biol Trace Elem Res.](#) 2009 May;128(2):118-27. Epub 2008 Oct 28.

Effects of zinc supplementation on physical growth in 2-5-year-old children.

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Physical growth disorders in under 5-year-old children are a common health problem in many countries including Iran. The aim of this study was to determine effects of supplemental zinc on physical growth in preschool children with retarded linear growth. This study was a community-based randomized controlled trial on 2-5-year-old children with height-for-age below 25th percentile of National Center for Health Statistics growth chart. **Ninety children were randomly assigned in zinc group (ZG) or placebo group (PG).** After 6 months of zinc or placebo supplementation, we followed up the children for another 6 months. Anthropometric indicators were measured before the intervention and then monthly for 11 months. Forty children in ZG and 45 in PG concluded the study. Zinc supplementation increased weight gain in boys ($P = 0.04$) and girls ($P = 0.05$) compared to placebo but had no significant effect on mid-upper arm circumference increment in either sexes. **The most significant ($P = 0.001$) effect of Zinc supplementation was seen in boys' height increment at the end of follow-up period. Stunted growth rate in ZG changed significantly ($P = 0.01$) from 26.7% to 2.5% throughout the study. This study showed that daily supplementation of 5 mg elemental**

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zinc for 6 months improves physical growth in terms of height increment and weight gain in children with undesirable linear growth, especially in boys.

[Eur J Clin Nutr.](#) 2008 Jul;62(7):849-55. Epub 2007 Jun 6.



Zinc supplementation in the management of shigellosis in malnourished children in Bangladesh.

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OBJECTIVE: To assess the impact of zinc supplementation on clinical recovery, weight gain and subsequent growth and morbidity in moderately malnourished children with shigellosis. **DESIGN:** A randomized, double-blind, controlled trial. **SETTING:** Dhaka hospital of ICDDR,B: Centre for Health and Population Research, Dhaka, Bangladesh. **SUBJECTS:** Fifty-six moderately malnourished children, aged 12-59 months with culture-proven shigellosis. **METHODS:** **Subjects were randomly allocated to receive zinc (20 mg/day elemental) in multivitamin syrup (intervention) or multivitamin syrup without zinc (control) in two equally divided doses daily for 2 weeks.** All children received pivmecillinam in a dose of 15 mg/kg every 6 h for 5 days. After supplementation, children were followed in their respective homes every 2 weeks for 6 months. **RESULTS:** **Children receiving zinc recovered from acute illness significantly faster than the control children (P<0.05). The medians time (days) to recovery and disappearances of blood and mucous were significantly 50% shorter in the zinc-supplemented group compared to the control group.** The mean body weight of zinc supplemented children increased significantly from 8.8 kg on admission to 9.2 kg (P<0.01) at recovery, which was not observed in the control children (from 9.3 to 9.6 kg; P=0.12). During the 6-month follow-up period, zinc-supplemented children had significantly fewer mean episodes of diarrhoea compared to the control children (2.2 vs 3.3; P=0.03). **CONCLUSION:** Zinc supplementation significantly shortens the duration of acute shigellosis, promotes better weight gain during recovery and reduces diarrhoeal morbidity during the subsequent 6 months.

[J Nutr.](#) 2008 Dec;138(12):2462-7.

Zinc modifies the association between nasopharyngeal Streptococcus pneumoniae carriage and risk of acute lower respiratory infection among young children in rural Nepal.

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Nasopharyngeal (NP) carriage is necessary for *Streptococcus pneumoniae* (Spn) transmission and invasive infection. **This study evaluated the effect of zinc prophylaxis on the association between NP colonization with Spn and acute lower respiratory infection (ALRI) in children aged 1-35 mo living in a rural district in southern Nepal.** We compared carriage prevalence of Spn in 550 ALRI cases with that of healthy age- and season-matched controls. This study, conducted from December 2003 to July 2005, was nested in a community-randomized trial designed to evaluate the effect of zinc on morbidity and mortality in 1- to 36-month-old children. They were randomized to receive either 10-mg tablets of zinc or placebo daily until discharge. Approximately 75% of cases and controls were Spn carriers. There was an interaction between zinc and Spn carriage ($P = 0.091$). **Spn carriage increased the risk of ALRI in the placebo group [adjusted matched odds ratio (AMOR) = 2.57; $P = 0.025$] but not in the zinc group (AMOR = 0.95; $P = 0.890$). Among the subset of symptomatic cases and their controls, the odds of ALRI for Spn carriers in the placebo group was 30 times greater (AMOR = 78.09; $P = 0.006$) than in the zinc group (AMOR = 2.77; $P = 0.288$). These findings suggest that zinc prophylaxis may protect children against ALRI associated with carriage of Spn and that the effect may differ by infectious etiology.**

Comment

*This year, zinc was shown to improve the rate of recovery for children with *Shigella* dysentery in Bangladesh, improve growth in stunted children, and reduce the risk of acute lower respiratory tract infection in a population of children with high rates of nasopharyngeal carriage of *Streptococcus pneumoniae*. While some of these effects require daily supplementation, there are also preventative benefits on reduction in subsequent diarrhoea, and may be some benefit on subsequent growth, if zinc is given during an acute diarrhoeal episode. Therefore countries that are struggling with how to implement prophylactic zinc to all children might first ensure that all children with diarrhoea, dysentery, malnutrition, low birth weight or pneumonia receive a course of zinc during the treatment of their acute illness. This will have a strong curative, and also a preventative effect, and be a deliverable strategy.*