

RANDOMISED TRIALS IN CHILD AND ADOLESCENT HEALTH IN DEVELOPING COUNTRIES

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Please send suggestions about this booklet to:

Prof Trevor Duke
Centre for International Child Health
University of Melbourne, Department of Paediatrics
Royal Children's Hospital
Parkville, 3052, Victoria, Australia
Telephone: (613) 9345 5968
Email: trevor.duke@rch.org.au

Randomised trials in child health in developing countries 2015-16

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Introduction

Each year this booklet is compiled to summarize the evidence on child and adolescent health derived from randomized or controlled 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. We hope 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 capture as many relevant studies as possible, although it is possible that I have missed some. If you know of a relevant RCT or meta-analysis 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/sites/entrez>

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 done properly 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 188 studies were identified. These came from all regions of the world, mostly from developing country researchers. Several trials from 2015-16 will lead to significant changes in child health approaches or clinical recommendations.

We have included the web-link for papers that are available in full-text on the Internet free of charge (75 with free on-line access). Through HINARI (<http://www.who.int/hinari/en/>) a program set up by WHO in collaboration with publishers, the full-text versions of over 14,000 journal titles and 30,000 e-books are available to health institutions in over 100 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. The previous editions (2002-2015) are available at: www.ichrc.org

Two years ago we published a summary of the first 11 years of the controlled trials. The reference for this is: Duke T, Fuller D. Arch Dis Child 2014, 99:615–620, and you may download it at: <http://adc.bmj.com/content/99/7/615.full.pdf+html>

A brief summary of some of the important results in 2015-16

- In 1118 Indian children with acute respiratory infection, fast breathing and chest indrawing outpatient care with oral amoxicillin was equivalent to hospital based treatment with oral amoxicillin in regard clinical treatment failure at 7 days, and hospital-based treatment was cheaper.

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- Among hospitalised children with community-acquired pneumonia in Thailand switching from IV to oral antibiotics within 24 hours after symptom improvement and defervescence of fever was as effective as conventional hospital IV antibiotic treatment.
- In 2 large trials of pneumonia treatment, stunting increased the risk of treatment failure.
- Among 225 children with severe pneumonia and hypoxaemia in Dhaka, Bangladesh, use of bubble-CPAP was associated with a lower risk of treatment failure and death than the use of standard flow oxygen therapy.
- Among children with fluid-refractory septic shock in Brazil, early peripheral adrenaline infusion was associated with a significantly lower mortality than for children who received dopamine.
- Among children with severe malarial anaemia, transfusion of long-stored blood did not increase blood lactate or impair cerebral oxygenation or 30-day survival compared to blood stored for less than 10 days.
- In Zambia and in Thailand, cognitive behavioural therapy for trauma reduced levels of stress in children who had exposure to traumatic events
- Among Indian children with acute diarrhoea and vomiting, a single dose of ondansetron prior to commencing oral rehydration solution reduced the likelihood of failure of ORT to rehydrate, and reduced the need for intravenous rehydration.
- In a meta-analysis involving over 14,000 participants in low and middle income countries, hand-washing promotion in communities reduces diarrhoea rates by about 30%.
- Improving water quality in communities in Ghana by drilling bores reduced diarrhoea prevalence in children by 11%.
- In Nigerian children with calcium-deficient rickets, the daily dose of calcium needed to correct bone deformity was 1000-2000mg, and this bone recovery was equally achieved using ground fish or limestone as the calcium source.
- In rural India efforts to improve sanitation and reduce open defecation were only partially successful in reducing faecal bacterial loads in homes and cases of diarrhoea, and additional home interventions are needed.
- In the very different environment of Chinese homes and kindergartens, use of hand hygiene and surface disinfectant reduced diarrhoea and other infections.
- In a large meta-analysis of deworming it was found that although treating children known to have worm infection may have some nutritional benefits for the individual, in mass treatment of all children in endemic areas, there is substantial evidence that this does not improve average nutritional status, haemoglobin, cognition, school performance, or survival.
- In Burkina Faso, for seasonal malaria chemoprevention sulfadoxine-pyrimethamine plus amodiaquine (WHO's current recommendation) and dihydroartemisinin-piperaquine were both highly effective in reducing the risk of malaria infection.

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- In 8 African hospitals for children, adolescents and adults with uncomplicated malaria, ferroquine combined with artesunate was associated with high cure rates.
- In Burkina Faso, unsupervised treatment of uncomplicated malaria with artesunate-amodiaquine or artemether-lumefantrine resulted in lower cure rates (78-84%) compared to controlled clinical trials where treatment is supervised. WHO recommends a critical threshold of 90% cure for an anti-malarial drug in a treatment policy, but effectiveness in a field situation is less than trial efficacy.
- In 5 African countries, among 1047 children with severe malaria, a simplified three-dose intramuscular regimen was non-inferior to the more complex WHO-recommended regimen of 5 days treatment, based on the proportion of children with $\geq 99\%$ reduction in parasitemia at 24 h from admission values. Artesunate was associated with a risk of delayed anaemia.
- In an efficacy trial designed to reproduce mass drug administration (MDA), among 524 children in Papua New Guinea, use of drugs active against blood (chloroquine and artemether-lumefantrine) and liver (primaquine) resulted in much fewer episodes of *P. vivax* and *P. ovale* infections in the subsequent 8 months. However the primaquine was given for 20 days, raising questions about how effective such a MDA would be outside a clinical trial.
- In Malaysian children with *P. vivax* infection, chloroquine resistance was common, leading to high rates of treatment failure. Artemether-lumefantrine resulted in much more rapid parasite clearance and higher 28-day cure rates.
- Among Tanzanian children enrolled in a vitamin A RCT, height-for-age z-score was linearly associated with cognitive, communication, and motor development z-scores, that is, stunting has measurable and significant effects on many aspects of child development.
- Among pregnant Tanzanian women, iron supplementation commenced at or before 27 weeks gestation did not increase the risk of placental malaria, and reduced the risk of anaemia at delivery by 40% (RR, 0.60; 95% CI, 0.51-0.71).
- Among 300 pregnant adolescent girls and women in Uganda, placental malaria and malaria infection in pregnancy was significantly lower in those received intermittent preventive treatment with dihydroartemisinin-piperaquine than those who received sulfadoxine-pyrimethamine. Monthly treatment with dihydroartemisinin-piperaquine was superior to three-dose dihydroartemisinin-piperaquine.
- In South Africa, a monthly community health worker visit to pregnant women who were at risk of depression improved infant growth. Focusing on maternal caretaking of infants, even when mothers are depressed improved infant growth.
- In the treatment of hyperbilirubinemia in term and late-preterm neonates in Nigeria, filtered sunlight was effective in controlling bilirubin levels on 93% of days, and conventional phototherapy was effective in 90% of days. Temperatures higher than 38.0°C occurred in 5% of the infants receiving filtered sunlight and in 1% of those receiving conventional phototherapy.
- Among preterm Indian neonates with a patent ductus arteriosus, enteral paracetamol was as effective as intravenous indomethacin in closing the PDA: 100% (36/36) versus 94.6% (35/37) respectively.

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- Among Indian very low birth weight neonates, high-dose (loading 40 mg/kg/day and maintenance of 20 mg/kg/day) caffeine citrate was more effective than low-dose (loading 20 mg/kg/day and maintenance of 10 mg/kg/day) in reducing apnoea of prematurity within the first 10 days of life.
- In preterm neonates (27-34 weeks gestation), 1000 IU of vitamin D resulted in much lower rates of vitamin D deficiency than 400 IU (2% vs 64.6%, respectively).
- Among Kenyan children eating yellow cassava, compared with eating the more common white cassava, led to a modest increase in serum retinol concentration but a marked increase (5-fold) in serum β -carotene concentration, so use of yellow cassava is a good source of dietary vitamin A.
- In Asia myopia is an increasing problem. In a study of 1903 6-year old children in 12 primary schools in Guangzhou, China, an extra 40 minutes of outdoor activities each day reduced myopia rates by 9%: the cumulative incidence rate of myopia over the next 3 years was 30.4% in the intervention group and 39.5% in the control group.
- Among teachers and students in Zambia, a Teachers Diploma Program on Psychosocial Care, Support, and Protection was designed to reduce stigma, and abuse among vulnerable orphan children. Teachers who underwent the course showed positive changes in the areas of safety, social support, and gender equity. Students whose teachers underwent the course reported positive changes, including in areas of respect, future prospects, support, safety, sexual abuse, and bullying. And in Uganda, a trial of family-level economic support for AIDS-orphaned adolescents resulted in better educational outcomes, lower levels of hopelessness, and higher levels of self-concept compared to participants in the control group.
- In a large cluster RCT of mass drug administration (MDA) for scabies in Fiji, children given ivermectin had a significantly greater reduction in scabies and impetigo (the secondary skin infection due to *Streptococcus* and *Staphylococcus*) than children given permethrin cream, and both groups had a lower prevalence than children only treated if they were symptomatic. Using ivermectin MDA to control may reduce the secondary consequences including bacterial skin sepsis and rheumatic fever.
- When a baby is nursed on the side with the legs are gently flexed in a tucked position they experience less pain when receiving a vaccine in the thigh than when the baby is lying on her back with the leg held in a straight position.
- Among low birth weight babies in Guinea-Bissau having a scar and a TST response after BCG vaccination is associated with lower mortality risk. The adjusted mortality rate ratio comparing children with a BCG scar with those without was 0.42 (95% CI = 0.19; 0.93).
- In Bangladesh a single dose oral whole-cell cholera vaccine was 63% efficacious in older children (5-14 years) and adults in a setting with a high level of cholera endemicity. Using routine government services in Bangladesh, in urban areas involving over 200,000 people, the vaccine efficacy was 37-45%. When tested in a phase I study in Ethiopia, seroconversion occurred in 77% of children at 14 days after 2 doses of the vaccine.
- In Indian adolescent girls, serum antibodies to HPV 16 and 18 were similar at 7 months after 2 doses or 3 doses of quadrivalent HPV vaccine, but at 18 months after vaccination serum antibodies were higher after 3 doses.

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- A Dengue vaccine JENVAC, a Vero cell-derived vaccine developed using an Indian strain of JE virus resulted in protective antibodies in >90% of people; with a single dose of JENVAC, seroprotection titres lasted at least 12 months in >80% of people. Following 2 doses, 61% of subjects retained seroprotection titres at 24 months.
- In Africa the RTS,S/AS01 vaccine had protective activity against malaria parasites that depended on genetic alleles at the protein locus; it had greater efficacy against parasites with the matched circumsporozoite protein allele than those which were mismatched. In that trial, less than 10% of all infections were from parasites had matched alleles, leading to an efficacy of 33.4% (95% CI, 29.3 to 37.2) against unmatched alleles. In a large efficacy trial the vaccine efficacy against malaria infection was 28% with 3 doses (0,1,2 months), and 36% after 3 doses plus a booster at 20 months. Because malaria is so common the numbers of cases averted per 1000 young infants were 983 (95% CI 592-1337) in the 3 plus booster group and 558 (158-926) in the 3 dose only group.
- 2 TB vaccines underwent Phase II trials in 2016: M72/AS01E and H4:IC31. Both induced CD-4 T cell and antibody or cytokine responses, including interferon gamma and TNF-alpha.
- In Benin a novel way to provide zinc was a point-of-use water ultrafiltration device configured with glass zinc plates to produce zinc-fortified, potable water. Use of this increased plasma zinc concentration 7-fold compared with zinc-fortified maize. Consumption of filtered water fortified with a low dose of highly bioavailable zinc is an effective intervention in children from rural areas.

Again this year many studies had small sample sizes; the terms or phrases: ‘no difference’, non-inferiority, and equivalence were used in some papers with insufficient consideration to the possibility of a type II error. This can be misleading, and may result in the discarding of an effective intervention, or numerous inadequate trials of the same intervention.

Randomised trials often report the “average effect”, that is the effect on the overall population. However, depending on how specifically that population is defined, within that population may be children who will benefit from the therapy or intervention, children for whom the therapy will have no effect, and some children for whom it may be harmful. The “average” of these effects may be “no overall effect”, but it is increasingly important that researchers try to understand the effects for individuals or sub-groups within trials, and the context in which benefit or not occurs.

Some of the context differences that influence the results of a trial include: individual or population characteristics, comorbidities, the health care environment and health care providers, geographical factors, other interventions, the delivery mechanism for the drug, vaccine or other intervention, the disease stage and specific aetiology, economic, social and cultural characteristics of the population and individuals within it...and other unknown factors. This can be even more complex in understanding systematic reviews of randomised trials (where heterogeneity is often incompletely reported, and where there will be heterogeneity *within and between* studies).

Incorporating a detailed understanding of the observed effect in context requires a nuanced approach, and the randomised trial design may not be the best method for all interventions. This is especially the case for complex interventions (i.e. a complex clinical therapy or a health system improvement program).

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In the last 14 years there have been **2183 trial publications** summarised in the various editions of this booklet. The public health benefits that have come from the trials on malaria, for example can be seen in the uptake of new interventions and reductions in malaria in each affected country in the world. The funding of comprehensive programs of research to “roll-back” malaria and implement the results of trials is a good example of the optimum benefit of research. The changes to HIV treatment is another example of public health which has benefited remarkably from randomised trials: the improvements to prevention of mother-to-child transmission being a primary example. While malaria and HIV rates are falling reductions of similar magnitudes are not being seen in pneumonia, malnutrition or neonatal illness – and taking similar comprehensive approaches to the research agenda and to research-driven public health interventions are needed.

It is encouraging to see the increased evaluation of the developmental, psychological and mental health effects of interventions. Also encouraging are the increased trials that include adolescents, and trials of school-based health and trials of various ways to improve education.

In 2015-16 showed further the impact of economic transition, Western morbidities and high-technology research, with clinical trials this year from India and China on issues related to non-communicable diseases, including myopia, obesity, oral health, cancer, allergy, and modifying risk factors for adult cardiovascular disease.

More support is needed for developing public health research capacity in low income countries. The flourishing research output from transitional countries is welcome as it reflects the ‘grand convergence’, but may mean that the child health inequalities in the countries with the greatest health burdens are over-shadowed. Ongoing efforts to reduce inequity in child health are especially important in this era when disparities fuel conflict. Appropriate research and training that leads to improvements in child, adolescent and maternal health in the world’s poorest countries will help reduce inequality.

Trevor Duke
July 2016

Acknowledgement

Thanks to Charlotte for help with editing

Acute respiratory infection

(See also: Zinc; Vaccines - Pneumococcal vaccine; Hygiene and environmental health)

Treatment of pneumonia

[BMC Pediatr.](#) 2015 Nov 17;15:186. doi: 10.1186/s12887-015-0510-9.

[A randomized controlled trial of hospital versus home based therapy with oral amoxicillin for severe pneumonia in children aged 3 - 59 months: The IndiaCLEN Severe Pneumonia Oral Therapy \(ISPOT\) Study.](#)

[Patel AB](#), [Bang A](#), [Singh M](#), [Dhande L](#), [Chelliah LR](#), [Malik A](#), [Khadse S](#); [ISPOT Study Group](#).

Abstract

BACKGROUND:

Pneumonia is the leading cause of child mortality under five years of age worldwide. For pneumonia with chest indrawing in children aged 3-59 months, injectable penicillin and hospitalization was the recommended treatment. This increased the health care cost and exposure to nosocomial infections. We compared the clinical and cost outcomes of a seven day treatment with oral amoxicillin with the first 48 h of treatment given in the hospital (hospital group) or at home (home group).

METHODS:

We conducted an open-label, multi-center, two-arm randomized clinical trial at six tertiary hospitals in India. **Children aged 3 to 59 months with chest indrawing pneumonia were randomized to home or hospital group.** Clinical outcomes, treatment adherence, and patient safety were monitored through home visits on day 3, 5, 8, and 14 with an additional visit for the home group at 24 h. **Clinical outcomes included treatment failure rates up to 7 days (primary outcome)** and between 8-14 days (secondary outcome) using the intention to treat and per protocol analyses. Cost outcomes included direct medical, direct non-medical and indirect costs for a random 17% subsample using the micro-costing technique.

RESULTS:

1118 children were enrolled and randomized to home (n = 554) or hospital group (n = 564). Both groups had similar baseline characteristics. Overall treatment failure rate was 11.5% (per protocol analysis). The hospital group was significantly more likely to fail treatment than the home group in the intention to treat analysis. **Predictors with increased risk of treatment failure at any time were age 3-11 months, receiving antibiotics within 48 h prior to enrolment and use of high polluting fuel.** Death rates at 7 or 14 days did not differ significantly. (Difference -0.0%; 95% CI -0.5 to 0.5). The median total treatment cost was Rs. 399 for the home group versus Rs. 602 for the hospital group (p < 0.001), for the same effect of 5% failure rate at the end of 7 days of treatment in the random subsample.

CONCLUSIONS:

Home based oral amoxicillin treatment was equivalent to hospital treatment for first 48 h in selected children of chest indrawing pneumonia and was cheaper. Consistent with the recent WHO simplified guidelines, management with home based oral amoxicillin for select children with only fast breathing and chest-indrawing can be a cost effective intervention.

<http://bmcpediatr.biomedcentral.com/articles/10.1186/s12887-015-0510-9>

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Comment

There were over 6000 children screened for the above study of “chest indrawing” pneumonia, and over 3000 were excluded for clinical reasons, including likely asthma or bronchodilator responsive wheeze (1010), chronic cough or other chronic condition (419), severe malnutrition (163), presence of danger signs (412). 308 could not be a part of the study because they lived too far away to be followed up. So this gives some idea of the overall case mix and epidemiology of the populations presenting with respiratory disease. In translating the evidence from these community-based antibiotic trials into practice, the message should not be that “severe pneumonia can be managed at home”, but that if comorbidities and risk factors for severity and poor outcomes can be identified and excluded, then for very low risk children, home management of ARI with chest indrawing is safe. There were only 2 deaths in this study, one on each hospital and home care group.

[J Med Assoc Thai.](#) 2015 Sep;98(9):858-63.

[Comparison between the Efficacy of Switch Therapy and Conventional Therapy in Pediatric Community-Acquired Pneumonia.](#)

[In-iw S](#), [Winijkul G](#), [Sonjaipanich S](#), [Manaboriboon B](#).

Abstract

OBJECTIVE:

Compare the treatment outcomes of switch therapy and conventional therapy in pediatric patients aged one month to five years old, diagnosed with community-acquired pneumonia who required hospitalization.

MATERIAL AND METHOD:

The present study was performed and approved by the Siriraj Research Ethics Committee. With informed consent, 57 patients who fitted the inclusion criteria were randomized into two groups, 1) the switch therapy group (SWT), who **switched their method of receiving antibiotics from IV to oral within 24 hours after clinical improvement and body temperature under 37.8 °C at least eight hours**, and 2) the control group, the group treated as routine general practice. Chi-square tests, Fisher's exact tests, unpaired t-tests, and Mann-Whitney U tests were used in analysis. A non-inferiority analysis to estimate 1-sided 95% CIs was performed to determine the greatest difference (worst case) between groups.

RESULTS:

There were no significant differences in age, sex, clinical presentations, and antibiotics provided between the two groups. **A statistically significant reduction in length of hospital stay was found in the SWT group (P = 0.019), whereas the readmission rate for both groups was not significantly different (p = 0.66).** Morbidity and mortality were not found in either groups. The SWT group demonstrated non-inferior efficacy comparing to control group (difference 20%; $p < 0.001$).

CONCLUSION:

In pediatric community-acquired pneumonia, early switching from administer IV antimicrobial agents to oral form when clinical signs improved were safe and effective. Switch therapy showed non-inferiority outcomes compared to conventional therapy, and had advantages in shortening the length of stay and indirectly lowering the cost of hospitalization.

[Lancet](#). 2015 Sep 12;386(9998):1057-65. doi: 10.1016/S0140-6736(15)60249-5. Epub 2015 Aug 19.

Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial.

[Chisti MJ](#), [Salam MA](#), [Smith JH](#), [Ahmed T](#), [Pietroni MA](#), [Shahunja KM](#), [Shahid AS](#), [Faruque AS](#), [Ashraf H](#), [Bardhan PK](#), [Sharifuzzaman](#), [Graham SM](#), [Duke T](#).

Abstract

BACKGROUND:

In developing countries, mortality in children with very severe pneumonia is high, even with the provision of appropriate antibiotics, standard oxygen therapy, and other supportive care. We assessed whether oxygen therapy delivered by bubble continuous positive airway pressure (CPAP) improved outcomes compared with standard low-flow and high-flow oxygen therapies.

METHODS:

This open, randomised, controlled trial took place in Dhaka Hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh. **We randomly assigned children younger than 5 years with severe pneumonia and hypoxaemia to receive oxygen therapy by either bubble CPAP (5 L/min starting at a CPAP level of 5 cm H₂O), standard low-flow nasal cannula (2 L/min), or high-flow nasal cannula (2 L/kg per min up to the maximum of 12 L/min).** Randomisation was done with use of the permuted block methods (block size of 15 patients) and Fisher and Yates tables of random permutations. **The primary outcome was treatment failure (ie, clinical failure, intubation and mechanical ventilation, death, or termination of hospital stay against medical advice) after more than 1 h of treatment.** Primary and safety analyses were by intention to treat. We did two interim analyses and stopped the trial after the second interim analysis on Aug 3, 2013, as directed by the data safety and monitoring board.

FINDINGS:

Between Aug 4, 2011, and July 17, 2013, 225 eligible children were recruited. **We randomly allocated 79 (35%) children to receive oxygen therapy by bubble CPAP, 67 (30%) to low-flow oxygen therapy, and 79 (35%) to high-flow oxygen therapy.** Treatment failed for 31 (14%) children, of whom five (6%) had received bubble CPAP, 16 (24%) had received low-flow oxygen therapy, and ten (13%) had received high-flow oxygen therapy. Significantly fewer children in the bubble CPAP group had treatment failure than in the low-flow oxygen therapy group (relative risk [RR] 0.27, 99.7% CI 0.07-0.99; p=0.0026). No difference in treatment failure was noted between patients in the bubble CPAP and those in the high-flow oxygen therapy group (RR 0.50, 99.7% CI 0.11-2.29; p=0.175). **23 (10%) children died. Three (4%) children died in the bubble CPAP group, ten (15%) children died in the low-flow oxygen therapy group, and ten (13%) children died in the high-flow oxygen therapy group.** Children who received oxygen by bubble CPAP had significantly lower rates of death than the children who received oxygen by low-flow oxygen therapy (RR 0.25, 95% CI 0.07-0.89; p=0.022).

INTERPRETATION:

Oxygen therapy delivered by bubble CPAP improved outcomes in Bangladeshi children with very severe pneumonia and hypoxaemia compared with standard low-flow oxygen therapy. Use of bubble CPAP oxygen therapy could have a large effect in hospitals in developing countries where the only respiratory support for severe childhood pneumonia and hypoxaemia is low-flow oxygen therapy. The trial was stopped early because of higher mortality in the low-flow oxygen group than in the bubble CPAP group, and we acknowledge that the early cessation of the trial reduces the certainty of the findings. Further research is needed to test

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the feasibility of scaling up bubble CPAP in district hospitals and to improve bubble CPAP delivery technology.

Comment

WHO has recently published a manual of **Oxygen Therapy for Children**, which describes how to make low-cost CPAP (<http://apps.who.int/iris/handle/10665/204584>). Other descriptions are in **CPAP: a guide for clinicians in developing countries**

<http://www.tandfonline.com/doi/pdf/10.1179/2046905513Y.0000000102>

[Trop Med Int Health](#). 2015 Oct;20(10):1320-8. doi: 10.1111/tmi.12557. Epub 2015 Jul 15.

Stunting is associated with poor outcomes in childhood pneumonia.

[Moschovis PP](#), [Addo-Yobo EO](#), [Banajeh S](#), [Chisaka N](#), [Christiani DC](#), [Hayden D](#), [Jeena P](#), [MacLeod WB](#), [Mino G](#), [Patel A](#), [Qazi S](#), [Santosham M](#), [Thea DM](#), [Hibberd PL](#).

Abstract

OBJECTIVE:

Stunting affects 26.7% of children worldwide, and little is known about its effects on the outcomes of childhood pneumonia. We evaluated the effect of stunting on the outcomes of pneumonia among children enrolled in two large clinical trials.

METHODS:

We analysed data from two WHO and USAID-sponsored inpatient treatment trials, the Severe Pneumonia Evaluation Antimicrobial Research study (n = 958) and the Amoxicillin Penicillin Pneumonia International Study (n = 1702), which enrolled children aged 2-59 months across 16 sites in LMICs. We assessed the effect of stunting (height-for-age Z score < -2) on treatment outcome and time to resolution of hypoxaemic pneumonia.

RESULTS:

Among 2542 (96%) children with valid data for height, 28% were stunted and 12.8% failed treatment by 5 days. **The failure rate among stunted patients was 16.0% vs. 11.5% among non-stunted patients [unadjusted RR = 1.24 (95% CI 1.08, 1.41); adjusted RR = 1.28 (95% CI 1.10, 1.48)].** An inverse relationship was observed between height and failure rates, even among non-stunted children. Among 845 patients with hypoxaemic pneumonia, stunting was associated with a lower probability of normalisation of respiratory rate [HR = 0.63 (95% CI 0.52, 0.75)] and oxygen saturation [HR = 0.74 (95% CI 0.61, 0.89)].

CONCLUSIONS:

Stunting increases the risk of treatment failure and is associated with a longer course of recovery in children with pneumonia. Strategies to decrease stunting may decrease the burden of adverse outcomes in childhood pneumonia in low-resource settings.

Otitis media

(This year, where sub-headings from previous years have had no trials published, I have left the sub-heading in the book, so you can see the topics where no studies were published in 2015-16. Obviously not all topic sub-headings have equal importance in the overall burden of childhood disease, but perhaps over time this may raise awareness of gaps)

Bronchiolitis

Upper respiratory tract infections, tonsillitis

Adolescent health

(See also Vaccines - HPV vaccine and Injury prevention)

[Sex Transm Infect.](#) 2015 Sep;91(6):395-400. doi: 10.1136/sextrans-2015-052025. Epub 2015 Jul 2.

[Disclosure of HSV-2 serological test results in the context of an adolescent HIV prevention trial in Kenya.](#)

[Hallfors DD](#), [Cho H](#), [Mbai II](#), [Millimo BW](#), [Atieno C](#), [Okumu D](#), [Luseno WK](#), [Hartman S](#), [Halpern CT](#), [Hobbs MM](#).

Abstract

OBJECTIVES:

Herpes simplex virus type 2 (HSV-2) biomarkers are often used in adolescent sub-Saharan HIV prevention studies, but evaluations of test performance and disclosure outcomes are rare in the published literature. Therefore, we investigated the proportion of ELISA-positive and indeterminate samples confirmed by western blot (WB), the psychosocial response to disclosure and whether reports of sexual behaviour and HSV-2 symptoms are consistent with WB confirmatory results among adolescent orphans in Kenya.

METHODS:

In 2011, 837 Kenyan orphan youth in grades 7 and 8 enrolled in an HIV prevention clinical trial with HSV-2 biomarker outcomes. We used a modified algorithm for the Kalon HSV-2 ELISA to improve specificity; positive and indeterminate results were WB tested.

We developed culturally sensitive protocols for disclosing positive results, and documented psychosocial responses, reports of sexual contact and HSV-2 symptoms.

RESULTS:

28 adolescents (3.3%) were identified as HSV-2 seropositive, six as indeterminate. Of these, 22 positive and all indeterminates were WB tested; 20 and 5, respectively, were confirmed positive. Most youth reported moderate brief stress after disclosure; 22% reported longer and more severe distress. Boys were more likely to be in the latter category. Self-reported virginity was highly inconsistent with WB-confirmed positives.

CONCLUSIONS:

The higher than manufacturer's cut-off for Kalon ELISA modestly reduced the rate of false-positive test results, but also increased false negatives. Investigators should consider the risk:benefit ratio in deciding whether or not to disclose HSV-2 results to adolescent participants under specific field conditions.

[BMC Public Health.](#) 2015 Jul 4;15:608. doi: 10.1186/s12889-015-1963-3.

[Reaching the hard to reach: longitudinal investigation of adolescents' attendance at an after-school sexual and reproductive health programme in Western Cape, South Africa.](#)

Randomised trials in child health in developing countries 2015-16

[Mathews C](#), [Eggers SM](#), [de Vries PJ](#), [Mason-Jones AJ](#), [Townsend L](#), [Aarø LE](#), [De Vries H](#).

Abstract

BACKGROUND:

Adolescents need access to effective sexual and reproductive health (SRH) interventions, but face barriers accessing them through traditional health systems. School-based approaches might provide accessible, complementary strategies. **We investigated whether a 21-session after-school SRH education programme and school health service attracted adolescents most at risk for adverse SRH outcomes and explored motivators for and barriers to attendance.**

METHODS:

Grade 8 adolescents (average age 13 years) from 20 schools in the intervention arm of an HIV prevention cluster randomised controlled trial in the Western Cape Province of South Africa, were invited to participate in an after-school SRH program and to attend school health services. Using a longitudinal design, we surveyed participants at baseline, measured their attendance at weekly after-school sessions for 6 months and surveyed them post-intervention. We examined factors associated with attendance using bivariate and multiple logistic and Poisson regression analyses, and through thematic analysis of qualitative data.

RESULTS:

The intervention was fully implemented in 18 schools with 1576 trial participants. The mean attendance of the 21-session SRH programme was 8.8 sessions (S.D. 7.5) among girls and 6.9 (S.D. 7.2) among boys. School health services were visited by 17.3 % (14.9 % of boys and 18.7 % of girls). Adolescents who had their sexual debut before baseline had a lower rate of session attendance compared with those who had not (6.3 vs 8.5, $p < .001$). Those who had been victims of sexual violence or intimate partner violence (IPV), and who had perpetrated IPV also had lower rates of attendance. Participants were motivated by a wish to receive new knowledge, life coaching and positive attitudes towards the intervention. The unavailability of safe transport and domestic responsibilities were the most common barriers to attendance. Only two participants cited negative attitudes about the intervention as the reason they did not attend.

CONCLUSIONS:

Reducing structural barriers to attendance, after-school interventions are likely to reach adolescents with proven-effective SRH interventions. However, special attention is required to reach vulnerable adolescents, through offering different delivery modalities, improving the school climate, and providing support for adolescents with mental health problems and neurodevelopmental academic problems.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26141155/>

[Health Policy Plan](#). 2016 May;31(4):415-24. doi: 10.1093/heapol/czv078. Epub 2015 Sep 7.

Costs and cost-effectiveness of a mental health intervention for war-affected young persons: decision analysis based on a randomized controlled trial.

[McBain RK](#), [Salhi C](#), [Hann K](#), [Salomon JA](#), [Kim JJ](#), [Betancourt TS](#).

Abstract

BACKGROUND:

One billion children live in war-affected regions of the world. We conducted the first cost-effectiveness analysis of an intervention for war-affected youth in sub-Saharan Africa, as well as a broader cost analysis.

METHODS:

The Youth Readiness Intervention (YRI) is a behavioural treatment for reducing functional impairment associated with psychological distress among war-affected young

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persons. A randomized controlled trial was conducted in Freetown, Sierra Leone, from July 2012 to July 2013. **Participants (n = 436, aged 15-24) were randomized to YRI (n = 222) or care as usual (n = 214).** Functional impairment was indexed by the World Health Organization Disability Assessment Scale; scores were converted to quality-adjusted life years (QALYs). An 'ingredients approach' estimated financial and economic costs, assuming a societal perspective. Incremental cost-effectiveness ratios (ICERs) were also expressed in terms of gains across dimensions of mental health and schooling. Secondary analyses explored whether intervention effects were largest among those worst-off (upper quartile) at baseline.

RESULTS:

Retention at 6-month follow-up was 85% (n = 371). The estimated economic cost of the intervention was \$104 per participant. Functional impairment was lower among YRI recipients, compared with controls, following the intervention but not at 6-month follow-up, and yielded an ICER of \$7260 per QALY gained. **At 8-month follow-up, teachers' interviews indicated that YRI recipients observed higher school enrolment** [P < 0.001, odds ratio (OR) 8.9], denoting a cost of \$431 per additional school year gained, as well as better school attendance (P = 0.007, OR 34.9) and performance (P = 0.03, effect size = -1.31). Secondary analyses indicated that the intervention was cost-effective among those worst-off at baseline, yielding an ICER of \$3564 per QALY gained.

CONCLUSIONS:

The YRI is not cost-effective at a willingness-to-pay threshold of three times average gross domestic product per capita. However, results indicate that the YRI translated into a range of benefits, such as improved school enrolment, not captured by cost-effectiveness analysis. We also outline areas for modification to improve cost-effectiveness in future trials.

[Soc Sci Med.](#) 2015 Sep;141:36-45. doi: 10.1016/j.socscimed.2015.07.024. Epub 2015 Jul 26.

[Impact of the Kenya Cash Transfer for Orphans and Vulnerable Children on early pregnancy and marriage of adolescent girls.](#)

[Handa S](#), [Peterman A](#), [Huang C](#), [Halpern C](#), [Pettifor A](#), [Thirumurthy H](#).

Abstract

There is promising evidence that poverty-targeted cash transfer programs can have positive impacts on adolescent transitions to adulthood in resource poor settings, however existing research is typically from small scale programs in diverse geographic and cultural settings. We provide estimates of the impact of a national unconditional cash transfer program, the Kenya Cash Transfer for Orphans and Vulnerable Children, on pregnancy and early marriage among females aged 12 to 24, four years after program initiation. The evaluation was designed as a clustered randomized controlled trial and ran from 2007 to 2011, capitalizing on the existence of a control group, which was delayed entry to the program due to budget constraints. Findings indicate that, among 1549 females included in the study, while the program reduced the likelihood of pregnancy by five percentage points, there was no significant impact on likelihood of early marriage. Program impacts on pregnancy appear to work through increasing the enrollment of young women in school, financial stability of the household and delayed age at first sex. The Kenyan program is similar in design to most other major national cash transfer programs in Eastern and Southern Africa, suggesting a degree of generalizability of the results reported here. Although the objective of the program is primarily poverty alleviation, it appears to have an important impact on facilitating the successful transition of adolescent girls into adulthood.

[BMC Public Health](#). 2015 Sep 22;15:942. doi: 10.1186/s12889-015-2274-4.

[School-based intervention on healthy behaviour among Ecuadorian adolescents: effect of a cluster-randomized controlled trial on screen-time.](#)

[Andrade S](#), [Verloigne M](#), [Cardon G](#), [Kolsteren P](#), [Ochoa-Avilés A](#), [Verstraeten R](#), [Donoso S](#), [Lachat C](#).

Abstract

BACKGROUND:

Effective interventions on screen-time behaviours (television, video games and computer time) are needed to prevent non-communicable diseases in low- and middle-income countries. The present manuscript investigates the effect of a school-based health promotion intervention on screen-time behaviour among 12- to 15-year-old adolescents. We report the effect of the trial on screen-time after two stages of implementation.

METHODS:

We performed a cluster-randomised pair matched trial in urban schools in Cuenca-Ecuador. Participants were adolescents of grade eight and nine (mean age 12.8 ± 0.8 years, $n = 1370$, control group $n = 684$) from 20 schools (control group $n = 10$). The intervention included an individual and environmental component tailored to the local context and resources. The first intervention stage focused on diet, physical activity and screen-time behaviour, while the second stage focused only on diet and physical activity. Screen-time behaviours, primary outcome, were assessed at baseline, after the first (18 months) and second stage (28 months). Mixed linear models were used to analyse the data.

RESULTS:

After the first stage (data from $n = 1224$ adolescents; control group $n = 608$), the intervention group had a lower increase in TV-time on a week day ($\beta = -15.7$ min; $P = 0.003$) and weekend day ($\beta = -18.9$ min; $P = 0.005$), in total screen-time on a weekday ($\beta = -25.9$ min; $P = 0.03$) and in the proportion of adolescents that did not meet the screen-time recommendation ($\beta = -4$ percentage point; $P = 0.01$), compared to the control group. After the second stage (data from $n = 1078$ adolescents; control group $n = 531$), the TV-time on a weekday ($\beta = 13.1$ min; $P = 0.02$), and total screen-time on a weekday ($\beta = 21.4$ min; $P = 0.03$) increased more in adolescents from the intervention group. No adverse effects were reported.

DISCUSSION AND CONCLUSION:

A multicomponent school-based intervention was only able to mitigate the increase in adolescents' television time and total screen-time after the first stage of the intervention or in other words, when the intervention included specific components or activities that focused on reducing screen-time. After the second stage of the intervention, which only included components and activities related to improve healthy diet and physical activity and not to decrease the screen-time, the adolescents increased their screen-time again. Our findings might imply that reducing screen-time is only possible when the intervention focuses specifically on reducing screen-time.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26395439/>

[Cad Saude Publica](#). 2015 Jul;31(7):1381-94. doi: 10.1590/0102-311X00136014.

[The "Healthy Habits, Healthy Girls" randomized controlled trial for girls: study design, protocol, and baseline results.](#)

[Leme AC](#), [Philippi ST](#).

Randomised trials in child health in developing countries 2015-16

Abstract

The purpose of this article is to describe the study design, protocol, and baseline results of the "Healthy Habits, Healthy Girls" program. The intervention is being evaluated through a randomized controlled trial in 10 public schools in the city of São Paulo, Brazil. Data on the following variables were collected and assessed at baseline and will be reevaluated at 7 and 12 months: body mass index, waist circumference, dietary intake, nutrition, physical activity, social cognitive mediators, physical activity level, sedentary behaviors, self-rated physical status, and overall self-esteem. According to the baseline results, 32.4% and 23.4% of girls were overweight in the intervention and control groups, respectively, and in both groups a higher percentage failed to meet daily recommendations for moderate and vigorous physical activity and maximum screen time (TV, computer, mobile devices). There were no significant differences between the groups for most of the variables, except age ($p = 0.000$) and waist circumference ($p = 0.014$). The study showed a gap in the Brazilian literature on protocols for randomized controlled trials to prevent obesity among youth. The current study may thus be an important initial contribution to the field.

http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-311X2015000701381&lng=en&nrm=iso&tlng=en

[Am J Public Health](#). 2016 May 19:e1-e3. [Epub ahead of print]

Formative Work and Community Engagement Approaches for Implementing an HIV Intervention in Botswana Schools.

[Miller KS](#), [Cham HJ](#), [Taylor EM](#), [Berrier FL](#), [Duffy M](#), [Vig J](#), [Chipazi L](#), [Chakalisa C](#), [Sidibe S](#), [Swart K](#), [Tau NS](#), [Clark LF](#).

Abstract

Providing adolescents with evidence-based sexual risk reduction interventions is critical to addressing the HIV/AIDS epidemic among adolescents in sub-Saharan Africa. Project AIM (Adult Identity Mentoring) is an innovative, evidence-based, youth development intervention that is being evaluated for the first time in Botswana through a 3-year (2015-2017), 50-school cluster randomized controlled trial, including testing for herpes simplex virus type 2 as a sexual activity biomarker. Conducting a trial of this magnitude requires the support and collaboration of government and community stakeholders. All school staff, including teachers, must be well informed about the study; dedicated staff placed at each school can help to improve school and community familiarity with the study, improve the information flow, and relieve some of the burden study activities places on schools. (*Am J Public Health*. Published online ahead of print May 19, 2016: e1-e3. doi:10.2105/AJPH.2016.303225)

Allergy

(See Vitamin D, skin disease)

Anaemia and iron deficiency

[Food Nutr Bull](#). 2015 Sep;36(3):264-75. doi: 10.1177/0379572115596253.

Impact of Cowpea-Based Food Containing Fish Meal Served With Vitamin C-Rich Drink on Iron Stores and Hemoglobin Concentrations in Ghanaian Schoolchildren in a Malaria Endemic Area.

Egbi G, Ayi I, Saalia FK, Zotor F, Adom T, Harrison E, Ahorlu CK, Steiner-Asiedu M.

Abstract

BACKGROUND:

Nutritional anemia is a public health problem among Ghanaian schoolchildren. There is need to employ dietary modification strategies to solve this problem through school and household feeding programs.

OBJECTIVE:

To evaluate the effectiveness of cowpea-based food containing fish meal served with vitamin C-rich drink to improve iron stores and hemoglobin concentrations in Ghanaian schoolchildren.

METHODS:

The study involved cross-sectional baseline and nutrition intervention phases. There were 150 participants of age 6 to 12 years. They were randomly assigned to **3 groups, fish meal -vitamin C (n = 50), vitamin C (n = 50), and control (n = 50), and given different cowpea-based diets for a 6-month period.** Height and weight measurements were done according to the standard procedures, dietary data were obtained by 24-hour recall and food frequency questionnaire, hemoglobin concentrations were determined by Hemocue Hemoglobinometer, and serum ferritin and complement-reactive protein (CRP) were determined by enzyme-linked immunosorbent assay. Participants' blood samples were examined for malaria parasitemia and stools for helminthes using Giemsa stain and Kato-Katz techniques, respectively.

RESULTS:

Mean ferritin concentration was not significantly different among groups. **End line mean or change in hemoglobin concentrations between fish meal-vitamin C group ($128.4 \pm 7.2/8.3 \pm 10.6$ g/L) and control ($123.1 \pm 6.6/4.2 \pm 10.4$ g/L) were different, $P < .05$. Change in prevalence of anemia in fish meal-vitamin C group (19.5%) was different compared to those of vitamin C group (9.3%) and the control (12.2%).** Levels of malaria parasitemia and high CRP among study participants at baseline and end line were 58% and 80% then 55% and 79%, respectively. Level of hookworm infestation was 13%.

CONCLUSION:

Cowpea-based food containing 3% fish meal and served with vitamin C-rich drink improved hemoglobin concentration and minimized the prevalence of anemia among the study participants.

Food Nutr Bull. 2015 Dec;36(4):481-92. doi: 10.1177/0379572115615234. Epub 2015 Nov 26.

A Blinded, Cluster-Randomized, Placebo-Controlled School Feeding Trial in Burundi Using Rice Fortified With Iron, Zinc, Thiamine, and Folic Acid.

Parker ME, Mosites E, Reider K, Ndayishimiye N, Waring M, Nyandimbane G, Masumbuko D, Ndikuriyo L, Matthias D.

Abstract

BACKGROUND:

Iron-deficiency anemia is a major public health problem among school-aged children in sub-Saharan Africa.

OBJECTIVE:

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To evaluate the effectiveness of **micronutrient-fortified rice to increase hemoglobin (Hb)** concentration and reduce the prevalence of anemia among schoolchildren.

METHODS:

Nine hundred four school children participated in this cluster-randomized trial during a 7-month intervention period. The study was conducted in 12 primary schools in rural Burundi.

Hemoglobin, socioeconomic status, febrile illness, and dietary diversity were measured at baseline and follow-up. The changes in Hb concentration and anemia status were analyzed using linear and logistic mixed models, respectively. **The micronutrient formulation contained an iron-to-zinc molar ratio of approximately 2.2.**

RESULTS:

There was no significant difference in Hb concentration between the intervention and control groups ($\beta = .09$ g/dL; 95% confidence interval: -0.21 to 0.38) following the 7-month intervention. Nearly half the children reported having a fever within 2 weeks prior to baseline or follow-up. Children with febrile illness preceding follow-up were less than half as likely to show improvement in anemia status (odds ratio = 0.47, $P < .001$), with an average 0.56 g/dL smaller improvement in Hb at follow-up ($P < .001$).

CONCLUSION:

The high prevalence of fever and low iron-to-zinc molar ratio of the Ultra Rice formulation may have contributed to the lack of improvement in Hb. Alternatively, the detected anemia may not have been due to nutrient deficiencies. Anemia interventions in Burundi should implement multiple strategies to eliminate both iron deficiency and infectious causes of anemia.

[JAMA](#). 2015 Dec 15;314(23):2514-23. doi: 10.1001/jama.2015.13977.

[Effect of Transfusion of Red Blood Cells With Longer vs Shorter Storage Duration on Elevated Blood Lactate Levels in Children With Severe Anemia: The TOTAL Randomized Clinical Trial.](#)

[Dhabangi A](#), [Ainomugisha B](#), [Cserti-Gazdewich C](#), [Ddungu H](#), [Kyeyune D](#), [Musisi E](#), [Opoka R](#), [Stowell CP](#), [Dzik WH](#).

Abstract

IMPORTANCE:

Although millions of transfusions are given annually worldwide, the effect of red blood cell (RBC) unit storage duration on oxygen delivery is uncertain.

OBJECTIVE:

To determine if longer-storage RBC units are not inferior to shorter-storage RBC units for tissue oxygenation as measured by reduction in blood lactate levels and improvement in cerebral tissue oxygen saturation among children with severe anemia.

DESIGN, SETTING, AND PARTICIPANTS:

Randomized noninferiority trial of 290 children (aged 6-60 months), most with malaria or sickle cell disease, presenting February 2013 through May 2015 to a university-affiliated national referral hospital in Kampala, Uganda, with a hemoglobin level of 5 g/dL or lower and a lactate level of 5 mmol/L or higher.

INTERVENTIONS:

Patients were randomly assigned to receive RBC units stored 25 to 35 days (longer-storage group; n = 145) vs 1 to 10 days (shorter-storage group; n = 145). All units were leukoreduced prior to storage. All patients received 10 mL/kg of RBCs during hours 0 through 2 and, if indicated per protocol, an additional 10 mL/kg during hours 4 through 6.

MAIN OUTCOMES AND MEASURES:

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The primary outcome was the proportion of patients with a lactate level of 3 mmol/L or lower at 8 hours using a margin of noninferiority equal to an absolute difference of 25%. Secondary measures included noninvasive cerebral tissue oxygen saturation during the first transfusion, clinical and laboratory changes up to 24 hours, and survival and health at 30 days after transfusion. Adverse events were monitored up to 24 hours.

RESULTS:

In the total population of 290 children, the mean (SD) presenting hemoglobin level was 3.7 g/dL (1.3) and mean lactate level was 9.3 mmol/L (3.4). Median (interquartile range) RBC unit storage was 8 days (7-9) for shorter storage vs 32 days (30-34) for longer storage without overlap. **The proportion achieving the primary end point was 0.61 (95% CI, 0.52 to 0.69) in the longer-storage group vs 0.58 (95% CI, 0.49 to 0.66) in the shorter-storage group (between-group difference, 0.03 [95% CI, -0.07 to ∞], P < .001), meeting the prespecified margin of noninferiority. Mean lactate levels were not statistically different between the 2 groups at 0, 2, 4, 6, 8, or 24 hours.** Kaplan-Meier analysis and global nonlinear regression revealed no statistical difference in lactate reduction between the 2 groups. Clinical assessment, cerebral oxygen saturation, electrolyte abnormalities, adverse events, survival, and 30-day recovery were also not significantly different between the groups.

CONCLUSIONS AND RELEVANCE:

Among children with lactic acidosis due to severe anemia, transfusion of longer-storage compared with shorter-storage RBC units did not result in inferior reduction of elevated blood lactate levels. These findings have relevance regarding the efficacy of stored RBC transfusion for patients with critical tissue hypoxia and lactic acidosis due to anemia.

<http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2015.13977>

[Malar J.](#) 2015 Sep 17;14:347. doi: 10.1186/s12936-015-0872-3.

[The effect of iron-fortified complementary food and intermittent preventive treatment of malaria on anaemia in 12- to 36-month-old children: a cluster-randomised controlled trial.](#)

[Glinz D](#), [Hurrell RF](#), [Ouattara M](#), [Zimmermann MB](#), [Brittenham GM](#), [Adiossan LG](#), [Righetti AA](#), [Seifert B](#), [Diakité VG](#), [Utzinger J](#), [N'Goran EK](#), [Wegmüller R](#).

Abstract

BACKGROUND:

Iron deficiency (ID) and malaria co-exist in tropical regions and both contribute to high rates of anaemia in young children. It is unclear whether iron fortification combined with intermittent preventive treatment (IPT) of malaria would be an efficacious strategy for reducing anaemia in young children.

METHODS:

A 9-month cluster-randomised, single-blinded, placebo-controlled intervention trial was carried out in children aged 12-36 months in south-central Côte d'Ivoire, an area of intense and perennial malaria transmission. The study groups were: group 1: normal diet and IPT-placebo (n = 125); group 2: consumption of porridge, an iron-fortified complementary food (CF) with optimised composition providing 2 mg iron as NaFeEDTA and 3.8 mg iron as ferrous fumarate 6 days per week (CF-FeFum) and IPT-placebo (n = 126); group 3: IPT of malaria at 3-month intervals, using sulfadoxine-pyrimethamine and amodiaquine and no dietary intervention (n = 127); group 4: both CF-FeFum and IPT (n = 124); and group 5: consumption of porridge, an iron-fortified CF with the composition currently on the Ivorian market providing 2 mg iron as NaFeEDTA and 3.8 mg iron as ferric pyrophosphate 6 days per week (CF-FePP) and IPT-placebo (n = 127). The primary outcome was haemoglobin (Hb) concentration. Linear and

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logistic regression mixed-effect models were used for the comparison of the five study groups, and a 2 × 2 factorial analysis was used to assess treatment interactions of CF-FeFum and IPT (study groups 1-4).

RESULTS:

After 9 months, the Hb concentration increased in all groups to a similar extent with no statistically significant difference between groups. In the 2 × 2 factorial analysis after 9 months, no treatment interaction was found on Hb (P = 0.89). The adjusted differences in Hb were 0.24 g/dl (95 % CI -0.10 to 0.59; P = 0.16) in children receiving IPT and -0.08 g/dl (95 % CI -0.42 to 0.26; P = 0.65) in children receiving CF-FeFum. At baseline, anaemia (Hb <11.0 g/dl) was 82.1 %. After 9 months, IPT decreased the odds of anaemia (odds ratio [OR], 0.46 [95 % CI 0.23-0.91]; P = 0.023), whereas iron-fortified CF did not (OR, 0.85 [95 % CI 0.43-1.68]; P = 0.68), although ID (plasma ferritin <30 µg/l) was decreased markedly in children receiving iron fortified CF (OR, 0.19 [95 % CI 0.09-0.40]; P < 0.001).

CONCLUSIONS:

IPT alone only modestly decreased anaemia, but neither IPT nor iron fortified CF significantly improved Hb concentration after 9 months. Additionally, IPT did not augment the effect of the iron fortified CF. CF fortified with highly bioavailable iron improved iron status but not Hb concentration, despite three-monthly IPT of malaria. Thus, **further research is necessary to develop effective combination strategies to prevent and treat anaemia in malaria endemic regions.**

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26377199/>

J Nutr. 2015 Jul;145(7):1576-81. doi: 10.3945/jn.114.208009. Epub 2015 May 6.

[A Randomized Trial of Iron-Biofortified Pearl Millet in School Children in India.](#)

[Finkelstein JL](#), [Mehta S](#), [Udipi SA](#), [Ghugre PS](#), [Luna SV](#), [Wenger MJ](#), [Murray-Kolb LE](#), [Przybylski EM](#), [Haas JD](#).

Abstract

BACKGROUND:

Iron deficiency is the most widespread nutritional deficiency in the world.

OBJECTIVE:

The objective of this randomized efficacy trial was to determine the effects of iron-biofortified pearl millet (Fe-PM) on iron status compared with control pearl millet (Control-PM).

METHODS:

A randomized trial of **biofortified pearl millet (*Pennisetum glaucum*), bred to enhance iron content, was conducted in 246 children (12-16 y) for 6 mo in Maharashtra, India.** Iron status [hemoglobin, serum ferritin (SF), soluble transferrin receptor (sTfR), and total body iron (TBI)], inflammation (C-reactive protein and α -1 acid glycoprotein), and anthropometric indices were evaluated at enrollment and after 4 and 6 mo. Hodges-Lehmann-Sen 95% CIs were used to examine the effect of the Fe-PM on iron status compared with commercially available Control-PM. Linear and binomial regression models were used to evaluate the effects of Fe-PM on iron status and incidence of anemia and iron deficiency, compared with Control-PM.

RESULTS:

At baseline, 41% of children were iron deficient (SF <15 µg/L) and 28% were anemic (hemoglobin <12.0 g/dL). **Fe-PM significantly increased SF concentrations and TBI after 4 mo compared with Control-PM.** Among children who were iron deficient at baseline, those who received Fe-PM were 1.64 times more likely to become iron replete by 6 mo than were those receiving Control-PM (RR: 1.64, 95% CI: 1.07, 2.49, P = 0.02). The effects of Fe-PM on

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iron status were greater among children who were iron deficient at baseline than among children who were not iron deficient at baseline.

CONCLUSIONS:

Fe-PM significantly improved iron status in children by 4 mo compared with Control-PM.

This study demonstrated that feeding Fe-PM is an efficacious approach to improve iron status in school-age children and it should be further evaluated for effectiveness in a broader population context.

[Trials](#). 2015 Dec 30;16:599. doi: 10.1186/s13063-015-1135-x.

[The Karnataka Anemia Project 2--design and evaluation of a community-based parental intervention to improve childhood anemia cure rates: study protocol for a cluster randomized controlled trial.](#)

[Shet AS](#), [Zwarenstein M](#), [Mascarenhas M](#), [Risbud A](#), [Atkins S](#), [Klar N](#), [Galanti MR](#).

Abstract

BACKGROUND:

Childhood anemia is highly prevalent worldwide. Improving the hemoglobin level of preschool age children could yield substantial benefits in cognitive and psychosocial development and overall health. While evidence-based recommendations for reducing childhood anemia in high anemia prevalence countries are available, there is no experimental evidence of community centered education and counseling programs, as a route to improved acceptance of iron supplements, demonstrating beneficial effects on anemia outcomes. We report on the evaluation protocol of a complex educational intervention led by the community lay health worker (LHW) and delivered to mothers of 12-59-month-old anemic children living in and visiting village day care centers in a large district of southern India.

METHODS AND DESIGN:

The study is designed as a cluster randomized controlled trial. The intervention is based on the social cognitive theory and aims to promote among mothers, anemia awareness, dietary modifications to increase iron intake in the child, and recognition of the need for enhanced adherence to supplemental iron in the anemic child. From 270 eligible villages in the study area, a sample of 60 villages will be randomized to intervention [$n = 30$] or to treatment as usual [$n = 30$] of the study. LHWs in the intervention arm will be trained to administer the following intervention components to mothers of anemic children: 1] monthly distribution of Iron and folic acid (IFA) supplements to mothers of anemic children, and 2] five monthly counseling sessions of mothers of anemic children covering: a) anemia awareness education b) IFA adherence counseling and assessment, c) dietary modification to improve iron intake, and d) hygiene and sanitation. LHWs in the control arm will distribute IFA to mothers of anemic children as in the intervention arm but will not provide monthly education and counseling support. The primary outcome is the difference between the two experimental groups in anemia cure rates of children found to be anemic at baseline. Secondary outcomes, assessed as differences between all participants in both experimental groups, are: change in mothers' knowledge regarding anemia; 24 hour dietary iron intake; net improvement in individual hemoglobin values; serum ferritin; and the difference in overall cluster level childhood anemia prevalence. All outcomes will be measured 6 months after the start of the intervention. Multilevel linear and logistic regression models will be used to analyze differences between intervention and control groups in outcome variables.

DISCUSSION:

This trial is designed to evaluate the effectiveness of an intervention intended to improve anemia cure rates in anemic children living in villages of Chamarajnagar, Karnataka a large district

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in southIndia. The extensive study of secondary endpoints will be used to identify possible weak points in the compliance to intervention delivery and uptake. This evaluation is one of the few large randomized trials evaluating the impact of an education and counseling intervention to reduce childhood anemia prevalence.

<http://trialsjournal.biomedcentral.com/articles/10.1186/s13063-015-1135-x>

Anaesthesia and intensive care

[Anaesthesia](#). 2016 Jan;71(1):50-7. doi: 10.1111/anae.13230. Epub 2015 Oct 7.

[A comparison of single dose dexmedetomidine with propofol for the prevention of emergence delirium after desflurane anaesthesia in children.](#)

[Makkar JK](#), [Bhatia N](#), [Bala I](#), [Dwivedi D](#), [Singh PM](#).

Abstract

Emergence delirium is a common problem in children recovering from general anaesthesia. We performed a study comparing emergence characteristics in 100 patients who were randomly allocated to receive either 0.3 µg.kg(-1) dexmedetomidine, 1 mg.kg(-1) propofol or saline 0.9% and undergoing infra-umbilical surgery. The Pediatric Anesthesia Emergence Delirium scale was used to grade emergence delirium. Emergence delirium occurred in 9.4% of children in the dexmedetomidine group compared with 13.9% in the propofol group and 40.6% in the control group (p = 0.004). In the dexmedetomidine group, sedation occurred in 62.5% of children at 10 min after transfer to the recovery area, compared with 44.4% in the propofol group and 12.5% in the control group (p = 0.010). We conclude that dexmedetomidine significantly reduced the incidence of emergence delirium but this was at the expense of a greater incidence of sedation in the recovery period.

[Otolaryngol Head Neck Surg](#). 2015 Dec;153(6):1042-50. doi: 10.1177/0194599815599381. Epub 2015 Aug 18.

[A Randomized Controlled Trial Comparing Intranasal Midazolam and Chloral Hydrate for Procedural Sedation in Children.](#)

[Stephen MC](#), [Mathew J](#), [Varghese AM](#), [Kurien M](#), [Mathew GA](#).

Abstract

OBJECTIVES:

To evaluate the efficacy and safety of intranasal midazolam and chloral hydrate syrup for procedural sedation in children.

STUDY DESIGN:

Prospective randomized placebo-controlled trial (double blind, double dummy).

SETTING:

Tertiary care hospital over 18 months.

SUBJECTS AND METHODS:

Eighty-two children, 1 to 6 years old, undergoing auditory brainstem response testing were randomized to receive either intranasal midazolam with oral placebo or chloral hydrate syrup with placebo nasal spray. Intranasal midazolam was delivered at 0.5 mg/kg (100 mcg per spray) and oral syrup at 50 mg/kg. Children not sedated at 30 minutes had a second dose at half the initial dose. The primary outcomes measured were safety and efficacy. Secondary outcomes

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were time to onset of sedation, parental separation, nature of parental separation, parental satisfaction, audiologist's satisfaction, time to recovery, and number of attempts.

RESULTS:

Forty-one children were in each group, and no major adverse events were noted. **The chloral hydrate group showed earlier onset of sedation (66%) compared with the intranasal midazolam group (33%).** Significant difference in time to recovery was noted in the chloral hydrate group (78 minutes) versus the intranasal midazolam group (108 minutes). The parents' and audiologist's satisfaction was higher for chloral hydrate (95% and 75%) than for intranasal midazolam (49% and 29%, respectively). Overall, sedation was 95% with chloral hydrate versus 51% with intranasal midazolam. Both drugs maintained sedation.

CONCLUSIONS:

Intranasal midazolam and chloral hydrate are both safe and efficacious for pediatric procedural sedation. Chloral hydrate was superior to intranasal midazolam, with an earlier time to onset of sedation, a faster recovery, better satisfaction among parents and the audiologist, and successful sedation.

<http://oto.sagepub.com/cgi/pmidlookup?view=long&pmid=26286872>

[Pain Manag Nurs.](#) 2015 Dec;16(6):938-43. doi: 10.1016/j.pmn.2015.08.004. Epub 2015 Nov 3.

The Effect of Entonox, Play Therapy and a Combination on Pain Relief in Children: A Randomized Controlled Trial.

[Mohan S](#), [Nayak R](#), [Thomas RJ](#), [Ravindran V](#).

Abstract

Pediatric pain is often undertreated/neglected due to time constraints, difficulties in timing of oral analgesics, fear of side effects of opioids and anxiolytics, and apprehension of additional pain in the use of local anesthetic injections. In this study, the researcher was prompted to choose rapidly acting interventions that were low dose and allowed the child to stay alert, suitable for a quick discharge. The purpose of this study was to evaluate the effects of Entonox, play therapy, and a combination to relieve procedural pain in children aged 4-15 years. The study was designed as a randomized controlled trial; the subjects were divided into four groups using a sequential allocation plan from 123 total subjects. Group A received Entonox, Group B received play therapy, Group C received both Entonox and play therapy, and Group D received existing standard interventions. The study was vetted by the departmental study review committee. The pain level was assessed using FLACC scale for children aged 4-9 years and the Wong Bakers Faces Pain Scale for children aged 10-15 years; scores ranged from 0 to 10. All the data were analyzed using SPSS 16.0 with descriptive statistics and inferential statistics. The mean pain scores were as follows: Entonox group, 2.87; Play therapy group, 4; combination group, 3; and control group, 5.87. When statistical testing was applied, a significant reduction in the pain score in all the three experimental groups when compared to the control group was found ($p = .002$), but not in the pain score among the three experimental groups ($p = .350$). The findings of this study indicated that all three interventions were effective in lowering pain scores when compared to the control group. Play therapy is as potent as Entonox in relieving procedural pain, though there was no additive effect on pain relief when play therapy and Entonox were combined. A protocol for age-related choice between play therapy and Entonox administration was introduced as a standing order in the Pediatric Surgery department for acute procedural pain relief.

[Indian J Pediatr.](#) 2016 Mar;83(3):209-13. doi: 10.1007/s12098-015-1917-x. Epub 2015 Oct 19.

MRI Customized Play Therapy in Children Reduces the Need for Sedation – A Randomized Controlled Trial.

[Bharti B](#), [Malhi P](#), [Khandelwal N](#).

Abstract

OBJECTIVE:

To evaluate the effectiveness of an MRI-specific play therapy intervention on the need for sedation in young children.

METHODS:

All children in the age group of 4-10 y, who were advised an MRI scan over a period of one year were randomized. Exclusion criteria included children with neurodevelopmental disorders impairing cognition and children who had previously undergone diagnostic MRI. A total of 79 children were randomized to a control or an intervention condition. The intervention involved familiarizing the child with the MRI model machine, listing the steps involved in the scan to the child in vivid detail, training the child to stand still for 5 min, and conducting several dry runs with a doll or a favorite toy. The study was approved by the Institute ethical committee.

RESULTS:

The need for sedation was 41 % (n = 16) in the control group and this declined to 20 % (n = 8) in the intervention group ($\chi^2 = 4.13$; $P = 0.04$). The relative risk of sedation decreased by 49 % in the intervention group as compared to the control group (RR 0.49; 95 % CI: 0.24-1.01) and this difference was statistically significant ($P = 0.04$). The absolute risk difference in sedation use between intervention and control group was 21 % (95 % CI 1.3 %-40.8 %). Even on adjusting for age, relative risk of sedation remained significantly lower in children undergoing play therapy as compared to the control (RR 0.57, 95 % CI: 0.32-0.98) with P value of 0.04.

CONCLUSIONS:

The use of an MRI customized play therapy with pediatric patients undergoing diagnostic MRI resulted in significant reduction of the use of sedation.

[J Clin Exp Dent.](#) 2015 Oct 1;7(4):e513-8. doi: 10.4317/jced.52542. eCollection 2015.

Cartridge syringe vs computer controlled local anesthetic delivery system: Pain related behaviour over two sequential visits - a randomized controlled trial.

[Thoppe-Dhamodhara YK](#), [Asokan S](#), [John BJ](#), [Pollachi-Ramkrishnan G](#), [Ramachandran P](#), [Vilvanathan P](#).

Abstract

BACKGROUND:

Local anesthetic injection is one of the most anxiety provoking procedure in dentistry. Knowledge about change in pain related behaviour during consecutive visits helps in and scheduling of treatment procedures and management of children in dental clinic.

AIM:

To compare the pain perception, behavioural response and the associated change in physiological parameters while receiving local anesthesia injection with cartridge syringe and computer controlled local anesthetic delivery system (CCLAD) over two consecutive visits.

MATERIAL AND METHODS:

In this randomized controlled cross over trial, 120 children aged 7 - 11 years were randomly divided into group A: receiving injections with CCLAD during first visit; group B: receiving

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injections with cartridge syringe during first visit. The physiological parameters (heart rate and blood pressure) were recorded before and during injection procedure. Objective evaluation of disruptive behaviour and subjective evaluation of pain perceived were done using Face Legs Activity Cry Consolability (FLACC) scale and modified facial image scale (FIS) respectively.

RESULTS:

No statistical difference in pain response ($p = 0.164$) and disruptive behaviour ($p = 0.120$) between cartridge syringe and CCLAD injections were seen during the first visit although the latter showed lesser scores. However, during the second visit there were significant increase in pain response ($p = 0.004$) and disruptive behaviour ($p = 0.006$) in cartridge syringe group with an associated increase in heart rate.

CONCLUSIONS:

Injections with CCLAD produced lesser pain ratings and disruptive behaviour than cartridge syringe in children irrespective of order of visit.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26535099/>

Intensive care

(See also: Treatment of severe malaria; Intravenous fluids)

Crit Care Med. 2015 Nov;43(11):2292-302. doi: 10.1097/CCM.0000000000001260.

Double-Blind Prospective Randomized Controlled Trial of Dopamine Versus Epinephrine as First-Line Vasoactive Drugs in Pediatric Septic Shock.

Ventura AM, Shieh HH, Bousso A, Góes PF, de Cássia F O Fernandes I, de Souza DC, Paulo RL, Chagas F, Gilio AE.

Abstract

OBJECTIVES:

The primary outcome was to compare the effects of dopamine or epinephrine in severe sepsis on 28-day mortality; secondary outcomes were the rate of healthcare-associated infection, the need for other vasoactive drugs, and the multiple organ dysfunction score.

DESIGN:

Double-blind, prospective, randomized controlled trial from February 1, 2009, to July 31, 2013.

SETTING:

PICU, Hospital Universitário da Universidade de São Paulo, Brazil.

PATIENTS:

Consecutive children who are 1 month to 15 years old and met the clinical criteria for fluid-refractory septic shock. Exclusions were receiving vasoactive drug(s) prior to hospital admission, having known cardiac disease, having already participated in the trial during the same hospital stay, refusing to participate, or having do-not-resuscitate orders.

INTERVENTIONS:

Patients were randomly assigned to receive either dopamine (5-10 $\mu\text{g}/\text{kg}/\text{min}$) or epinephrine (0.1-0.3 $\mu\text{g}/\text{kg}/\text{min}$) through a peripheral or intraosseous line. Patients not reaching predefined stabilization criteria after the maximum dose were classified as treatment failure, at which point the attending physician gradually stopped the study drug and started another catecholamine.

MEASUREMENTS AND MAIN RESULTS:

Physiologic and laboratory data were recorded. Baseline characteristics were described as proportions and mean (\pm SD) and compared using appropriate statistical tests. Multiple regression analysis was performed, and statistical significance was defined as a p value of less

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than 0.05. Baseline characteristics and therapeutic interventions for the 120 children enrolled (63, dopamine; 57, epinephrine) were similar. **There were 17 deaths (14.2%): 13 (20.6%) in the dopamine group and four (7%) in the epinephrine group (p=0.033).** Dopamine was associated with death (odds ratio, 6.5; 95% CI, 1.1-37.8; p=0.037) and healthcare-associated infection (odds ratio, 67.7; 95% CI, 5.0-910.8; p=0.001). The use of epinephrine was associated with a survival odds ratio of 6.49.

CONCLUSIONS:

Dopamine was associated with an increased risk of death and healthcare-associated infection. Early administration of peripheral or intraosseous epinephrine was associated with increased survival in this population. Limitations should be observed while interpreting these results.

[Zhonghua Yi Xue Za Zhi](#). 2015 Nov 3;95(41):3347-50.

Pulmonary ultrasound guidance of congenital heart disease postoperative ventilator applications

[Han X](#), [Tian Q](#), [Chen F](#), [Wang Y](#), [Chen H](#).

Abstract

OBJECTIVE:

To investigate the pulmonary ultrasound in children with congenital heart disease postoperative invasive ventilator time, non-invasive ventilator use the guide.

METHODS:

Using prospective clinical observation research methods, Randomly divide 100 cases ranged from 6 months to 3 years old in cardiopulmonary bypass after congenital heart disease surgery patients into ultrasound group and control group, 50 cases in each group. All postoperative give positive cardiac function maintenance, diuresis, etc. Ultrasound group adopted the pulmonary ultrasound in children with pulmonary interstitial pulmonary edema monitoring and guide to extubation, enable the timing of the noninvasive ventilator support; Control group based on the bedside chest X-ray lung condition. Compare two groups of children with mechanical ventilation time (including the invasive and noninvasive ventilator support), noninvasive ventilator utilization rate and its accuracy, start the noninvasive ventilator time, the incidence of ventilator associated pneumonia (VAP), secondary tracheal intubation cases and ICU stay time, etc.

RESULTS:

The ultrasound group compared with the control group in Invasive ventilator time [(15.0 ± 11.0) vs (20.0 ± 13.5, P=0.043)], noninvasive ventilation time [(38.5 ± 11.8) vs (48.6 ± 21.9, P=0.032)], the number of cases of the use of noninvasive ventilation (10 cases vs 22 cases, P=0.041), the correct use of the number of cases (10 vs 14, P=0.034) and VAP cases (3 vs 8, P=0.044), there was statistical significance, P< 0.05. The ultrasound group of children with ICU stay time was significantly lower than the control group [(66.0 ± 38.9) vs (82.0 ± 42.4, P=0.038)]; Control group had 2 cases with secondary tracheal intubation, ultrasound group one, comparing the two groups has no statistical significance (P> 0.05).

CONCLUSION:

Postoperative children with congenital heart disease using pulmonary ultrasound evaluation of pulmonary interstitial edema, guide the ventilator, it can effectively shorten (invasive and noninvasive mechanical ventilation time and ICU length of hospital stay, lung ultrasound has instant, noninvasive, No radiation, repeatable, pulmonary ultrasound will be important after cardiopulmonary bypass interstitial lung edema diagnosis, evaluation of treatment means and helps to treat critically ill children.

http://zhyyzz.yiigle.com/CN112137201541/727402.htm?locale=zh_CN

(In Chinese)

[J Trop Pediatr.](#) 2015 Oct;61(5):339-50. doi: 10.1093/tropej/fmv033. Epub 2015 Jun 30.

High-dose Oral Ambroxol for Early Treatment of Pulmonary Acute Respiratory Distress Syndrome: an Exploratory, Randomized, Controlled Pilot Trial.

[Baranwal AK](#), [Murthy AS](#), [Singhi SC](#).

Abstract

OBJECTIVE:

To evaluate efficacy of high-dose oral ambroxol in acute respiratory distress syndrome (ARDS) with respect to ventilator-free days (VFD).

DESIGN:

Prospective, randomized, placebo-controlled, blinded pilot trial.

PATIENTS:

Sixty-six mechanically ventilated patients (1 month to 12 years) with ARDS who were hand-ventilated for <24 hr before pediatric intensive care unit admission.

INTERVENTIONS:

Patients randomized to oral ambroxol (40 mg/kg/day, in four divided doses) (n = 32) or placebo (n = 34) until 10 days, extubation or death whichever is earlier.

MEASUREMENTS AND MAIN RESULTS:

Majority (91%) had pneumonia and bronchiolitis. Two study groups were similar in baseline characteristics. Mean partial pressure of arterial oxygen/fraction of inspired oxygen and oxygenation index were >175 and <10, respectively, with no difference in the two study groups. VFD were similar in the two study groups. Overall mortality was 26%. No adverse events were noted with ambroxol.

CONCLUSIONS:

Among ventilated pulmonary ARDS patients with oxygenation index of <10, mortality was 26%. **Ambroxol did not improve VFD.** Study with higher and more frequently administered doses of ambroxol in larger sample is suggested after having generated relevant pharmacokinetic data among critically ill children.

Comment

Ambroxol is a mucolytic agent used in respiratory diseases associated with increased mucus production like acute or chronic bronchitis. It has a variety of anti-inflammatory properties, including inhibition or scavenging of oxidative stress, increase of local defence molecules involved in respiratory virus replication, reduction of proinflammatory cytokines and arachidonic acid metabolites, and reducing inflammatory cell chemotaxis and lipid peroxidation of tissues (Beeh KM, Eur J Med Res 2008; 13: 557-562). But in this study there was no benefit.

Antibiotic resistance

[J Matern Fetal Neonatal Med.](#) 2015 Aug;28(12):1491-4. doi: 10.3109/14767058.2014.958462. Epub 2014 Sep 19.

[A new risk factor for neonatal vancomycin-resistant Enterococcus colonisation: bacterial probiotics.](#)

[Topcuoglu S](#), [Gursoy T](#), [Ovalı F](#), [Serce O](#), [Karatekin G](#).

Abstract

OBJECTIVE:

Vancomycin-resistant Enterococcus (VRE) colonisation can be controlled with strict adherence to infection control measures. We describe a VRE outbreak coincident with bacterial probiotic trial. Relationship between probiotic and VRE colonisation, and other possible risk factors were investigated.

METHODS:

Two hundred and ten infants with gestational age less than 32 weeks had been randomised for a trial with probiotic preparation containing Lactobacillus casei, Lactobacillus rhamnosus, Lactobacillus plantarum, Bifidobacterium lactis, fructooligosaccharide, galactooligosaccharide, colostrums and lactoferrin (NBL probiotic ATP®; Nobel, Istanbul, Turkey) between February 2012 and August 2013 when a VRE outbreak also took place. The existence of a relationship between this probiotic preparation and VRE colonisation was investigated.

RESULTS:

The beginning and end of the outbreak were coincident with the beginning and end of the probiotic trial. Demographic and clinical features of neonates did not differ between VRE colonised (n = 94) and non-colonised infants (n = 116) except for vancomycin (p = 0.012) and probiotic (p < 0.001) use.

CONCLUSIONS:

Probiotic and vancomycin exposure were significant risk factors for VRE colonisation. The acquisition and transfer of resistance genes of bacteria may be mediated by probiotics. Therefore, the safety of probiotics is a concern and should be investigated further.

Asthma and chronic lung disease

[Respir Care](#). 2015 Dec;60(12):1743-8. doi: 10.4187/respcare.03213. Epub 2015 Jun 16.

[A Randomized Controlled Trial of 2 Inhalation Methods When Using a Pressurized Metered Dose Inhaler With Valved Holding Chamber.](#)

[Stephen D](#), [Vatsa M](#), [Lodha R](#), [Kabra SK](#).

Abstract

BACKGROUND:

Information on the comparative efficacy of single deep breathing versus tidal breathing for inhaled asthma medications is limited, although such information can be of much use for the treatment of patients suffering from asthma. The objective of the present study was to compare the relative difference in improvement in peak expiratory flow (PEF) with single maximal inhalation with breath-holding versus 5 tidal breaths during inhalation of salbutamol from a pressurized metered dose inhaler (pMDI) with valved holding chamber (VHC) in children 5-15 y of age with asthma.

METHODS:

The randomized controlled trial was carried out on children with asthma between 5 and 15 y of age using a pMDI with a VHC either by a single deep breath with breath-hold or 5 tidal breaths. The experimental group received 200 µg of salbutamol from the pMDI with VHC with a single

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maximal inhalation and breath-hold technique, whereas the control group received 200 µg of salbutamol from pMDI with VHC using the 5 tidal breaths technique. The outcome variable, PEF, was reassessed 30 min after salbutamol use.

RESULTS:

Eighty-two subjects (mean age 8.79 ± 2.5 y, 65 boys and 17 girls) were analyzed. There was significant improvement in the PEF, from baseline (pre-intervention) to post-intervention within the single maximal inhalation with breath-hold group and tidal breathing group independently ($P < .001$). **The mean difference in improvement in PEF between the single maximal inhalation with a breath-hold and 5 tidal breaths group was 30.0 ± 18.16 and 28.29 ± 13.94 L/min, respectively, and was not statistically significant ($P = .88$).**

CONCLUSIONS:

Single maximal inhalation with a breath-hold technique is not superior to tidal breathing for improvement in PEF following salbutamol inhalation. Either method may be used in children between 5 and 15 y of age.

[Respir Care](#). 2016 Jan;61(1):78-84. doi: 10.4187/respcare.04038. Epub 2015 Oct 6.

Zinc Supplementation for One Year Among Children with Cystic Fibrosis Does Not Decrease Pulmonary Infection.

[Sharma G](#), [Lodha R](#), [Shastri S](#), [Saini S](#), [Kapil A](#), [Singla M](#), [Mukherjee A](#), [Jat KR](#), [Kabra M](#), [Kabra SK](#).

Abstract

BACKGROUND:

Children with cystic fibrosis may have a deficiency of micronutrients, including zinc, which may affect their susceptibility to infections. There is a paucity of data on zinc supplementation among children with cystic fibrosis. We hypothesized that a pharmacologic dose of zinc administered daily for 12 months would reduce the need for antibiotics by 50%.

METHODS:

This double-blind randomized placebo-controlled trial was conducted among children with cystic fibrosis to assess the effect of zinc supplementation on the need for antibiotics and pulmonary function tests. **The children, age 5-15 y, of either sex, received either 30-mg zinc tablets or similar looking placebo tablets daily in addition to standard care.** They were followed up every month for a period of 12 months and whenever they had pulmonary exacerbations. Their serum zinc was estimated at baseline and at 12 months of enrollment. During each visit, the children underwent a pulmonary function test and sputum culture.

RESULTS:

Of a total of 43 children screened, 40 were enrolled, and of them, 37 completed the study. **The median (interquartile range) number of days of the administration of antibiotics over 12 months of follow-up among the children receiving zinc was 42 (14-97) d. In the placebo group, it was 38 (15-70) d ($P = .79$).** There were no significant differences in the percent-of-predicted FEV1 or change in FEV1 values at 12 months ($P = .44$). The number of children in whose respiratory specimens *Pseudomonas* was isolated was similar for the 2 groups at different time intervals. The adverse events reported were similar in the 2 groups.

CONCLUSION:

We did not find any significant difference in the need for antibiotics, pulmonary function tests, hospitalization, colonization with *Pseudomonas*, or the need for antibiotics for children with cystic fibrosis receiving zinc supplementation of 30 mg/d.

Community paediatrics and social support

(see also Environmental health)

Dengue

(see Vaccines - dengue)

[Am J Trop Med Hyg.](#) 2015 Dec;93(6):1330-7. doi: 10.4269/ajtmh.15-0096. Epub 2015 Oct 26.

Dengue Knowledge and Preventive Practices in Iquitos, Peru.

[Paz-Soldán VA](#), [Morrison AC](#), [Cordova Lopez JJ](#), [Lenhart A](#), [Scott TW](#), [Elder JP](#), [Sihuincha M](#), [Kochel TJ](#), [Halsey ES](#), [Astete H](#), [McCall PJ](#).

Abstract

As part of a cluster-randomized trial to evaluate insecticide-treated curtains for dengue prevention in Iquitos, Peru, we surveyed 1,333 study participants to examine knowledge and reported practices associated with dengue and its prevention. Entomological data from 1,133 of these households were linked to the survey. **Most participants knew that dengue was transmitted by mosquito bite (85.6%), but only few (18.6%) knew that dengue vectors bite during daytime.** Most commonly recognized dengue symptoms were fever (86.6%), headache (76.4%), and muscle/joint pain (67.9%). Most commonly reported correct practices for mosquito control were cleaning homes (61.6%), using insecticide sprays (23%), and avoiding having standing water at home (12.3%). Higher education was associated with higher knowledge about dengue, including transmission and vector control. Higher socioeconomic status was associated with increased reported use of preventive practices requiring money expenditure. We were less likely to find *Aedes aegypti* eggs, larvae, or pupae in households that had < 5-year-old children at home. Although dengue has been transmitted in Iquitos since the 1990s and the Regional Health Authority routinely fumigates households, treats domestic water containers with larvicide, and issues health education messages through mass media, knowledge of dengue transmission and household practices for prevention could be improved.

<http://www.ajtmh.org/cgi/pmidlookup?view=long&pmid=26503276>

Development, cerebral palsy and mental health

(See also: School health programs; and Nutrition – micronutrients; Adolescent health)

[Dev Med Child Neurol.](#) 2016 Mar;58(3):270-6. doi: 10.1111/dmcn.12873. Epub 2015 Aug 25.

Randomized controlled trial of a home-visiting intervention on infant cognitive development in peri-urban South Africa.

[Murray L](#), [Cooper P](#), [Arteche A](#), [Stein A](#), [Tomlinson M](#).

Abstract

AIM:

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To determine whether, in an impoverished South African community, an intervention that benefitted infant attachment also benefitted cognitive development.

METHOD:

Pregnant females were randomized to intervention (n=220) and no-treatment control groups (n=229). **The intervention was home-based parenting support for attachment, delivered until 6 months postpartum.** At 18 months, infants were assessed on attachment and cognitive development (Bayley Scales Mental Development Index [MDI]) (n=127 intervention, n=136 control participants). Infant MDI was examined in relation to intervention, socio-economic risk, antenatal depression, and infant sex and attachment.

RESULTS:

Overall, there was little effect of the intervention on MDI (p=0.094, d=0.20), but there was an interaction between intervention and risk (p=0.03, $\eta^2=0.02$). MDI scores of infants of lower risk intervention group mothers were, on average, 4.84 points higher than those of other infants (p=0.002, d=0.41). Antenatal depression was not significant once intervention and risk were controlled (p=0.08); there was no association between infant MDI and either sex (p=0.41) or attachment (p=0.56).

INTERPRETATION:

Parenting interventions for infant cognitive development may benefit from inclusion of specific components to support infant cognition beyond those that support attachment, and may be most effective for infants over 6 months. They may need augmentation with other input where adversity is extreme

[J Child Psychol Psychiatry](#). 2015 Aug;56(8):865-73. doi: 10.1111/jcpp.12352. Epub 2014 Nov 17.

[The impact of dialogic book-sharing training on infant language and attention: a randomized controlled trial in a deprived South African community.](#)

[Vally Z](#), [Murray L](#), [Tomlinson M](#), [Cooper PJ](#).

Abstract

BACKGROUND:

Dialogic book-sharing is an interactive form of shared reading. It has been shown in high income countries (HICs) to be of significant benefit to child cognitive development. Evidence for such benefit in low and middle income countries (LMICs) is scarce, although a feasibility study of our own produced encouraging findings. Accordingly, we aimed to establish the impact on child language and attention of providing training in dialogic booksharing to carers of infants in an impoverished South African community.

METHODS:

We conducted a randomized controlled trial in Khayelitsha, an informal settlement in South Africa. Mothers of infants aged between 14 and 16 months were recruited and randomized to either 8 weeks of manualized training in dialogic book-sharing or a no-intervention control group. Independent assessments were made of infant language and attention at baseline and following training. The trial was registered (ISRCTN39953901).

RESULTS:

Ninety one carer-infant dyads were recruited and randomized to the intervention group (n = 49) or the control group (n = 42), 82 (90%) of whom were available for follow-up assessments. **On a standardized carer report of infant vocabulary, compared to those in the control group, carers who received the intervention reported a significantly greater increase in the number of words understood by their infants as well as a larger increase in the number of**

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words that their infant understood and could vocalize. Intervention group children also showed substantially greater gains on a measure of sustained attention.

CONCLUSIONS:

In line with evidence from HICs, a dialogic book-sharing programme delivered to an impoverished South African sample was shown to be of considerable benefit to the development of child language and focussed attention. The training programme, which is simple and inexpensive to deliver, has the potential to benefit child cognitive development in LMIC contexts where such development is commonly compromised.

Comment

“To learn to read is to light a fire” Victor Hugo, Les Miserables

“You are never too old, too wacky or too wild to pick up a book and read to a child” Dr Suess

[Transl Psychiatry](#). 2016 Apr 12;6:e781. doi: 10.1038/tp.2016.45.

[Training sensory signal-to-noise resolution in children with ADHD in a global mental health setting.](#)

[Mishra J](#), [Sagar R](#), [Joseph AA](#), [Gazzaley A](#), [Merzenich MM](#).

Abstract

Children with attention deficit/hyperactivity disorder (ADHD) have impaired focus on goal-relevant signals and fail to suppress goal-irrelevant distractions. To address both these issues, we developed a novel neuroplasticity-based training program that adaptively trains the resolution of challenging sensory signals and the suppression of progressively more challenging distractions. We evaluated this sensory signal-to-noise resolution training in a small sample, global mental health study in Indian children with ADHD. The children trained for 30 h over 6 months in a double-blind, randomized controlled trial. Training completers showed steady and significant improvements in ADHD-associated behaviors from baseline to post training relative to controls, and benefits sustained in a 6-month follow-up. Post-training cognitive assessments showed significant positive results for response inhibition and Stroop interference tests in training completers vs controls, while measures of sustained attention and short-term memory showed nonsignificant improvement trends. Further, training-driven improvements in distractor suppression correlated with the improved ADHD symptoms. This initial study suggests utility of signal-to-noise resolution training for children with ADHD; it emphasizes the need for further research on this intervention and substantially informs the design of a larger trial.

<http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/27070409/>

[Pediatrics](#). 2016 Mar 14. pii: peds.2015-3766. [Epub ahead of print]

[Home-Based Early Intervention and the Influence of Family Resources on Cognitive Development.](#)

[Bann CM](#), [Wallander JL](#), [Do B](#), [Thorsten V](#), [Pasha O](#), [Biasini FJ](#), [Bellad R](#), [Goudar S](#), [Chomba E](#), [McClure E](#), [Carlo WA](#).

Abstract

OBJECTIVE:

To investigate whether early developmental intervention (EDI) can positively affect the trajectories of cognitive development among children from low-resource families.

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METHODS:

Longitudinal analyses were conducted of data from 293 children in the Brain Research to Ameliorate Impaired Neurodevelopment Home-based Intervention Trial, a randomized controlled trial of a home-based EDI program, to examine trajectories of Bayley Scales of Infant Development-Second Edition Mental Development Index (MDI) scores from 12 to 36 months of age among young children from high- and low-resource families in 3 low- to middle-resource countries.

RESULTS:

A 3-way interaction among family resources, intervention group, and age was statistically significant after controlling for maternal, child, and birth characteristics (Wald $\chi^2(1) = 9.41$, $P = .002$). Among children of families with high resources, both the intervention and control groups had significant increases in MDI scores over time ($P < .001$ and $P = .002$, respectively), and 36-month MDI scores for these 2 groups did not differ significantly ($P = .602$). However, in families with low resources, the EDI group displayed greater improvement, resulting in significantly higher 36-month MDI scores than the control group ($P < .001$). In addition, the 36-month MDI scores for children in families with low resources receiving EDI did not differ significantly from children from high-resource families in either the EDI ($P = .509$) or control ($P = .882$) groups.

CONCLUSIONS:

A home-based EDI during the first 3 years of life can substantially decrease the developmental gap between children from families with lower versus higher resources, even among children in low- to middle-resource countries.

[JAMA Pediatr.](#) 2015 Aug;169(8):761-9. doi: 10.1001/jamapediatrics.2015.0580.

[Effectiveness of Trauma-Focused Cognitive Behavioral Therapy Among Trauma-Affected Children in Lusaka, Zambia: A Randomized Clinical Trial.](#) Murray LK, Skavenski S, Kane JC, Mayeya J, Dorsey S, Cohen JA, Michalopoulos LT, Imasiku M, Bolton PA.

Abstract

IMPORTANCE:

Orphans and vulnerable children (OVC) are at high risk for experiencing trauma and related psychosocial problems. Despite this, no randomized clinical trials have studied evidence-based treatments for OVC in low-resource settings.

OBJECTIVE:

To evaluate the effectiveness of lay counselor-provided trauma-focused cognitive behavioral therapy (TF-CBT) to address trauma and stress-related symptoms among OVC in Lusaka, Zambia.

DESIGN, SETTING, AND PARTICIPANTS:

This randomized clinical trial compared TF-CBT and treatment as usual (TAU) (varying by site) for children recruited from August 1, 2012, through July 31, 2013, and treated until December 31, 2013, for trauma-related symptoms from 5 community sites within Lusaka, Zambia. Children were aged 5 through 18 years and had experienced at least one traumatic event and reported significant trauma-related symptoms. Analysis was with intent to treat.

INTERVENTIONS:

The intervention group received 10 to 16 sessions of TF-CBT ($n = 131$). The TAU group ($n = 126$) received usual community services offered to OVC.

MAIN OUTCOMES AND MEASURES:

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The primary outcome was mean item change in trauma and stress-related symptoms using a locally validated version of the UCLA Posttraumatic Stress Disorder Reaction Index (range, 0-4) and functional impairment using a locally developed measure (range, 0-4). Outcomes were measured at baseline and within 1 month after treatment completion or after a waiting period of approximately 4.5 months after baseline for TAU.

RESULTS:

At follow-up, the mean item change in trauma symptom score was -1.54 (95% CI, -1.81 to -1.27), a reduction of 81.9%, for the TF-CBT group and -0.37 (95% CI, -0.57 to -0.17), a reduction of 21.1%, for the TAU group. The mean item change for functioning was -0.76 (95% CI, -0.98 to -0.54), a reduction of 89.4%, and -0.54 (95% CI, -0.80 to -0.29), a reduction of 68.3%, for the TF-CBT and TAU groups, respectively. The difference in change between groups was statistically significant for both outcomes ($P < .001$). The effect size (Cohen d) was 2.39 for trauma symptoms and 0.34 for functioning. Lay counselors participated in supervision and assessed whether the intervention was provided with fidelity in all 5 community settings.

CONCLUSIONS AND RELEVANCE:

The TF-CBT adapted for Zambia substantially decreased trauma and stress-related symptoms and produced a smaller improvement in functional impairment among OVC having experienced high levels of trauma.

<http://archpedi.jamanetwork.com/article.aspx?doi=10.1001/jamapediatrics.2015.0580>

[Behav Cogn Psychother](#). 2015 Sep;43(5):549-61. doi: 10.1017/S1352465813001197. Epub 2014 Apr 8.

Randomized Controlled Trial of Group Cognitive Behavioural Therapy for Post-Traumatic Stress Disorder in Children and Adolescents Exposed to Tsunami in Thailand.

[Pityaratstian N](#), [Piyasil V](#), [Ketumarn P](#), [Sitdhiraksa N](#), [Ularntinon S](#), [Pariwatcharakul P](#).

Abstract

BACKGROUND:

Post-traumatic stress disorder (PTSD) is a common and debilitating consequence of natural disaster in children and adolescents. Accumulating data show that cognitive behavioural therapy (CBT) is an effective treatment for PTSD. However, application of CBT in a large-scale disaster in a setting with limited resources, such as when the tsunami hit several Asian countries in 2004, poses a major problem.

AIMS:

This randomized controlled trial aimed to test for the efficacy of the modified version of CBT for children and adolescents with PTSD.

METHOD:

Thirty-six children (aged 10-15 years) who had been diagnosed with PTSD 4 years after the tsunami were randomly allocated to either CBT or wait list. CBT was delivered in 3-day, 2-hour-daily, group format followed by 1-month posttreatment self-monitoring and daily homework.

RESULTS:

Compared to the wait list, participants who received CBT demonstrated significantly greater improvement in symptoms of PTSD at 1-month follow-up, although no significant improvement was observed when the measures were done immediately posttreatment.

CONCLUSIONS:

Brief, group CBT is an effective treatment for PTSD in children and adolescents when delivered in conjunction with posttreatment self-monitoring and daily homework

Comment

Cognitive behavioural therapy for trauma includes relaxation training such as deep breathing and muscle relaxation skills, identifying feelings, discussing the trauma and overwhelming events and associated feelings, and cognitive coping strategies, such as identifying and replacing negative thoughts.

https://en.wikipedia.org/wiki/Trauma_focused_cognitive_behavioral_therapy

Diarrhoea

(See also: Vaccines and immunization - Rotavirus vaccine, Hygiene and Environmental health, Malnutrition)

[J Trop Pediatr.](#) 2015 Dec;61(6):435-41. doi: 10.1093/tropej/fmv054. Epub 2015 Aug 27.

[Safety and Efficacy of Low-osmolarity ORS vs. Modified Rehydration Solution for Malnourished Children for Treatment of Children with Severe Acute Malnutrition and Diarrhea: A Randomized Controlled Trial.](#)

[Kumar R](#), [Kumar P](#), [Aneja S](#), [Kumar V](#), [Rehan HS](#).

Abstract

World Health Organization-recommended rehydration solution for malnourished children (ReSoMal) for rehydrating severe acute malnourished children is not available in India. In present study, 110 consecutive children aged 6-59 months with severely acute malnourishment and acute diarrhea were randomized to low-osmolarity oral rehydration solution (ORS) (osmolarity: 245, sodium: 75) with added potassium (20 mmol/l) or modified ReSoMal (osmolarity: 300, sodium: 45). **In all, 15.4% of modified ReSoMal group developed hyponatremia as compared with 1.9% in low-osmolarity ORS**, but none developed severe hyponatremia or hypernatremia. Both groups had equal number of successful rehydration (52 each). Both types of ORS were effective in correcting hypokalemia and dehydration, but rehydration was achieved in shorter duration with modified ReSoMal.

[J Pediatr.](#) 2016 Feb;169:105-9.e3. doi: 10.1016/j.jpeds.2015.10.006. Epub 2015 Dec 1.

[Oral Ondansetron in Management of Dehydrating Diarrhea with Vomiting in Children Aged 3 Months to 5 Years: A Randomized Controlled Trial.](#)

[Danewa AS](#), [Shah D](#), [Batra P](#), [Bhattacharya SK](#), [Gupta P](#).

Abstract

OBJECTIVES:

To evaluate the role of oral ondansetron in facilitating successful rehydration of under-5-year-old children suffering from acute diarrhea with vomiting and some dehydration.

STUDY DESIGN:

Children (n = 170) aged 3 months to 5 years with acute diarrhea with vomiting and some dehydration were enrolled in this double blind, randomized, placebo-controlled trial. The **participants were randomized to receive either single dose of oral ondansetron (n = 85) or placebo (n = 85) in addition to standard management of dehydration according to World**

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Health Organization guidelines. Failure of oral rehydration therapy (ORT), administration of unscheduled intravenous fluids, and amount of oral rehydration solution intake in 4 hours were the primary outcomes. Secondary outcome measures included duration of dehydration correction, number of vomiting episodes, adverse effects, and caregiver satisfaction.

RESULTS:

Failure of ORT was significantly less in children receiving ondansetron compared with those receiving placebo (31% vs 62%; $P < .001$; relative risk 0.50, 95% CI 0.35-0.72).

Almost one-half of the children in the ondansetron group received intravenous fluids compared with those in the placebo group, but it was not statistically significant ($P = .074$; relative risk 0.56, 95% CI 0.30-1.07). **The oral rehydration solution consumption was significantly more in the ondansetron group (645 mL vs 554 mL; mean difference 91 mL; 95% CI: 35-148 mL). Patients in the ondansetron group also showed faster rehydration, lesser number of vomiting episodes, and better caregiver satisfaction.**

CONCLUSION:

A single oral dose of ondansetron, given before starting ORT to children <5 years of age with acute diarrhea and vomiting results in better oral rehydration

[Cochrane Database Syst Rev.](#) 2015 Sep 3;(9):CD004265. doi: 10.1002/14651858.CD004265.pub3.

[Hand washing promotion for preventing diarrhoea.](#)

[Ejemot-Nwadiaro RI](#), [Ehiri JE](#), [Arikpo D](#), [Meremikwu MM](#), [Critchley JA](#).

Abstract

BACKGROUND:

Diarrhoea accounts for 1.8 million deaths in children in low- and middle-income countries (LMICs). One of the identified strategies to prevent diarrhoea is hand washing.

OBJECTIVES:

To assess the effects of hand washing promotion interventions on diarrhoeal episodes in children and adults.

SEARCH METHODS:

We searched the Cochrane Infectious Diseases Group Specialized Register (27 May 2015); CENTRAL (published in the Cochrane Library 2015, Issue 5); MEDLINE (1966 to 27 May 2015); EMBASE (1974 to 27 May 2015); LILACS (1982 to 27 May 2015); PsycINFO (1967 to 27 May 2015); Science Citation Index and Social Science Citation Index (1981 to 27 May 2015); ERIC (1966 to 27 May 2015); SPECTR (2000 to 27 May 2015); Bibliomap (1990 to 27 May 2015); RoRe, The Grey Literature (2002 to 27 May 2015); World Health Organization (WHO) International Clinical Trial Registry Platform (ICTRP), metaRegister of Controlled Trials (mRCT), and reference lists of articles up to 27 May 2015. We also contacted researchers and organizations in the field.

SELECTION CRITERIA:

Individually randomized controlled trials (RCTs) and cluster-RCTs that compared the effects of hand washing interventions on diarrhoea episodes in children and adults with no intervention.

DATA COLLECTION AND ANALYSIS:

Three review authors independently assessed trial eligibility, extracted data, and assessed risk of bias. We stratified the analyses for child day-care centres or schools, community, and hospital-based settings. Where appropriate, incidence rate ratios (IRR) were pooled using the generic inverse variance method and random-effects model with 95% confidence intervals (CIs). We used the GRADE approach to assess the quality of evidence.

MAIN RESULTS:

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We included 22 RCTs: 12 trials from child day-care centres or schools in mainly high-income countries (54,006 participants), **nine community-based trials in LMICs (15,303 participants)**, and one hospital-based trial among people with acquired immune deficiency syndrome (AIDS) (148 participants). Hand washing promotion (education activities, sometimes with provision of soap) at child day-care facilities or schools prevents around one-third of diarrhoea episodes in high income countries (rate ratio 0.70; 95% CI 0.58 to 0.85; nine trials, 4664 participants, high quality evidence), and **may prevent a similar proportion in LMICs but only two trials from urban Egypt and Kenya have evaluated this (rate ratio 0.66, 95% CI 0.43 to 0.99; two trials, 45,380 participants, low quality evidence)**. Only three trials reported measures of behaviour change and the methods of data collection were susceptible to bias. In one trial from the USA hand washing behaviour was reported to improve; and in the trial from Kenya that provided free soap, hand washing did not increase, but soap use did (data not pooled; three trials, 1845 participants, low quality evidence). **Hand washing promotion among communities in LMICs probably prevents around one-quarter of diarrhoea episodes (rate ratio 0.72, 95% CI 0.62 to 0.83; eight trials, 14,726 participants, moderate quality evidence)**. However, six of these eight trials were from Asian settings, with only single trials from South America and sub-Saharan Africa. In six trials, soap was provided free alongside hand washing education, and the overall average effect size was larger than in the two trials which did not provide soap (soap provided: rate ratio 0.66, 95% CI 0.56 to 0.78; six trials, 11,422 participants; education only: rate ratio: 0.84, 95% CI 0.67 to 1.05; two trials, 3304 participants). There was increased hand washing at major prompts (before eating/cooking, after visiting the toilet or cleaning the baby's bottom), and increased compliance to hand hygiene procedure (behavioural outcome) in the intervention groups than the control in community trials (data not pooled: three trials, 3490 participants, high quality evidence). Hand washing promotion for the one trial conducted in a hospital among high-risk population showed significant reduction in mean episodes of diarrhoea (1.68 fewer) in the intervention group (Mean difference 1.68, 95% CI 1.93 to 1.43; one trial, 148 participants, moderate quality evidence). There was increase in hand washing frequency, seven times per day in the intervention group versus three times in the control in this hospital trial (one trial, 148 participants, moderate quality evidence). We found no trials evaluating or reporting the effects of hand washing promotions on diarrhoea-related deaths, all-cause-under five mortality, or costs.

AUTHORS' CONCLUSIONS:

Hand washing promotion probably reduces diarrhoea episodes in both child day-care centres in high-income countries and among communities living in LMICs by about 30%. However, less is known about how to help people maintain hand washing habits in the longer term.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26346329/>

J Trop Pediatr. 2016 Jun 9. pii: fmw032. [Epub ahead of print]

Efficacy and Safety of Saccharomyces boulardii in Acute Rotavirus Diarrhea: Double Blind Randomized Controlled Trial from a Developing Country.

Das S, Gupta PK, Das RR.

Abstract

OBJECTIVE:

To study the efficacy and safety of *Saccharomyces boulardii* (SB) in acute childhood rotavirus diarrhea.

METHODS:

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Children (3 months to 5 years) with WHO-defined acute watery diarrhea and stool rotavirus positive (n = 60) were randomized into intervention (n = 30) and control (n = 30) groups. The intervention group received SB (500 mg/day) for 5 days.

RESULTS:

The median duration (hours) of diarrhea was significantly shorter in the intervention group (60 vs. 89; 95% CI: -41.2 to -16.8). A significantly shorter duration of hospitalization (74 vs. 91; 95% CI: -33.46 to -0.54) was also seen in the intervention group, but no significant difference was seen for fever and vomiting. There was also no difference between the two groups in the proportion of children requiring parenteral rehydration and persistence of diarrhea lasting beyond day 7. There was no report of any adverse events.

CONCLUSIONS:

The present trial showed that SB is effective and safe in acute rotavirus diarrhea.

Water purification

[Int J Environ Res Public Health](#). 2015 Sep 25;12(10):12127-43. doi: 10.3390/ijerph121012127.
The Effect of Improved Water Supply on Diarrhea Prevalence of Children under Five in the Volta Region of Ghana: A Cluster-Randomized Controlled Trial.

[Cha S](#), [Kang D](#), [Tuffuor B](#), [Lee G](#), [Cho J](#), [Chung J](#), [Kim M](#), [Lee H](#), [Lee J](#), [Oh C](#).

Abstract

Although a number of studies have been conducted to explore the effect of water quality improvement, the majority of them have focused mainly on point-of-use water treatment, and the studies investigating the effect of improved water supply have been based on observational or inadequately randomized trials. We report the results of a **matched cluster randomized trial investigating the effect of improved water supply on diarrheal prevalence of children under five living in rural areas of the Volta Region in Ghana**. We compared the diarrheal prevalence of 305 children in 10 communities of intervention with 302 children in 10 matched communities with no intervention (October 2012 to February 2014). A modified Poisson regression was used to estimate the prevalence ratio. An intention-to-treat analysis was undertaken. **The crude prevalence ratio of diarrhea in the intervention compared with the control communities was 0.85 (95% CI 0.74-0.97) for Krachi West, 0.96 (0.87-1.05) for Krachi East, and 0.91 (0.83-0.98) for both districts**. Sanitation was adjusted for in the model to remove the bias due to residual imbalance since it was not balanced even after randomization. The adjusted prevalence ratio was 0.82 (95% CI 0.71-0.96) for Krachi West, 0.95 (0.86-1.04) for Krachi East, and 0.89 (0.82-0.97) for both districts. This study provides a basis for a better approach to water quality interventions.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26404337/>

Comment

This intervention involved drilling and rehabilitating boreholes, constructing latrines for schools and markets, and hygiene education and campaigns. The reductions were significant in some areas but minimal in others; overall the reduction in diarrhea prevalence was 11%. The authors point out that the effect of water quality improvement depends on the pre-intervention water quality, as well as the risk factors for diarrhea such as sanitation coverage and hygienic practices. So if it is bad to begin with, the impact will be greater.

Endocrine disorders and bone health

[J Pediatr.](#) 2015 Jul;167(1):148-54.e1. doi: 10.1016/j.jpeds.2015.02.008. Epub 2015 Mar 19.

[Comparison of Limestone and Ground Fish for Treatment of Nutritional Rickets in Children in Nigeria.](#)

[Thacher TD](#), [Bommersbach TJ](#), [Pettifor JM](#), [Isichei CO](#), [Fischer PR](#).

Abstract

OBJECTIVE:

To determine whether children with calcium-deficiency rickets respond better to treatment with calcium as limestone or as ground fish.

STUDY DESIGN:

Nigerian children with active rickets (n = 96) were randomized to receive calcium as powdered limestone (920 mg of elemental calcium) or ground fish (952 mg of elemental calcium) daily for 24 weeks. Radiographic healing was defined as achieving a score of 1.5 or less on a 10-point scale.

RESULTS:

The median (range) age of enrolled children was 35 (6-151) months. Of the 88 children who completed the study, 29 (66%) in the ground fish group and 24 (55%) in the limestone group achieved the primary outcome of a radiographic score of 1.5 or less within 6 months (P = .39).

The mean radiographic score improved from 6.2 ± 2.4 to 1.8 ± 2.2 in the ground fish group and from 6.3 ± 2.2 to 2.1 ± 2.4 in the limestone group (P = .68 for group comparison). In an intention to treat analysis adjusted for baseline radiographic score, age, milk calcium intake, and serum 25-hydroxyvitamin D concentration, the response to treatment did not differ between the 2 groups (P = .39). Younger age was associated with more complete radiographic healing in the adjusted model (aOR 0.74 [95% CI 0.57-0.92]). After 24 weeks of treatment, serum alkaline phosphatase had decreased, calcium and 25-hydroxyvitamin D increased, and bone mineral density increased in both groups, without significant differences between treatment groups.

CONCLUSION:

In children with calcium-deficiency rickets, treatment with calcium as either ground fish or limestone for 6 months healed rickets in the majority of children.

[J Bone Miner Res.](#) 2016 Jun 17. doi: 10.1002/jbmr.2886. [Epub ahead of print]

[Optimal Dose of Calcium for Treatment of Nutritional Rickets: A Randomized Controlled Trial.](#)

[Thacher TD](#), [Smith L](#), [Fischer PR](#), [Isichei CO](#), [Cha SS](#), [Pettifor JM](#).

Abstract

Calcium supplementation is indicated for the treatment of nutritional rickets. Our aim was to determine the optimal dose of calcium for treatment of children with rickets. Sixty-five Nigerian children with radiographically-confirmed rickets were randomized to daily supplemental calcium intake of 500 mg (n = 21), 1000 mg (n = 23), or 2000 mg (n = 21). Venous blood, radiographs, and forearm areal bone density (aBMD) were obtained at baseline and at 8, 16, and 24 weeks after enrollment. The primary outcome was radiographic healing, using a 10-point radiographic severity score. The radiographic severity scores improved in all three groups,

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but the rate of radiographic healing (points per month) was significantly more rapid in the 1000 mg (-0.29; 95%CI -0.13 to -0.45) and 2000 mg (-0.36; -0.19 to -0.53) supplementation groups relative to the 500 mg group. The 2000 mg group did not heal more rapidly than the 1000 mg group. After 24 weeks, 12 (67%), 20 (87%), and 14 (67%) in the 2000 mg, 1000 mg, and 500 mg groups, respectively, had achieved a radiographic score of 1.5 or less ($P = 0.21$). Serum alkaline phosphatase decreased and calcium increased similarly in all groups. Forearm diaphyseal aBMD improved significantly more rapidly in the 2000 mg group than in the 500 mg and 1000 mg groups ($P < 0.001$). **Daily calcium intakes of 1000 mg or 2000 mg produced more rapid radiographic healing of rickets than 500 mg, but 2000 mg did not have greater benefit than 1000 mg. Some children require longer than 24 weeks for complete healing of nutritional rickets.**

Enterovirus infections

[Trials](#). 2016 Feb 19;17:98. doi: 10.1186/s13063-016-1215-6.

[Intravenous magnesium sulfate for the management of severe hand, foot, and mouth disease with autonomic nervous system dysregulation in Vietnamese children: study protocol for a randomized controlled trial.](#)

[Qui PT](#), [Khanh TH](#), [Trieu HT](#), [Giang PT](#), [Bich NN](#), [Thoa le PK](#), [Nhan le NT](#), [Sabanathan S](#), [Van Doorn R](#), [Toan ND](#), [Merson L](#), [Dung NT](#), [Khanh LP](#), [Wolbers M](#), [Hung NT](#), [Chau NV](#), [Wills B](#).

Abstract

BACKGROUND:

Over the last 15 years, hand, foot, and mouth disease (HFMD) has emerged as a major public health burden across the Asia-Pacific region. A small proportion of HFMD patients, typically those infected with enterovirus 71 (EV71), develop brainstem encephalitis with autonomic nervous system (ANS) dysregulation and may progress rapidly to cardiopulmonary failure and death. Although milrinone has been reported to control hypertension and support myocardial function in two small studies, in practice, a number of children still deteriorate despite this treatment. Magnesium sulfate ($MgSO_4$) is a cheap, safe, and readily available medication that is effective in managing tetanus-associated ANS dysregulation and has shown promise when used empirically in EV71-confirmed severe HFMD cases.

METHODS/DESIGN:

We describe the protocol for a randomized, placebo-controlled, double-blind trial of intravenous $MgSO_4$ in Vietnamese children diagnosed clinically with HFMD plus ANS dysregulation with systemic hypertension. A loading dose of $MgSO_4$ or identical placebo is given over 20 min followed by a maintenance infusion for 72 h according to response, aiming for Mg levels two to three times the normal level in the treatment arm. The primary endpoint is a composite of disease progression within 72 h defined as follows: development of pre-specified blood pressure criteria necessitating the addition of milrinone, the need for ventilation, shock, or death.

Secondary endpoints comprise these parameters singly, plus other clinical endpoints including the following: requirement for other inotropic agents; duration of hospitalization; presence of neurological sequelae at discharge in survivors; and neurodevelopmental status assessed 6 months after discharge. The number and severity of adverse events observed in the two treatment arms will also be compared. Based on preliminary data from a case series, and allowing for some losses, 190 patients (95 in each arm) will allow detection of a 50 % reduction in disease progression with 90 % power at a two-sided 5 % significance level.

DISCUSSION:

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Given the large numbers of HFMD cases currently being seen in hospitals in Asia, if MgSO₄ is shown to be effective in controlling ANS dysregulation and preventing severe HFMD complications, this finding would be important to pediatric care throughout the region

Epilepsy and acute seizures

Hygiene, sanitation and environmental health

(See also Environmental enteropathy)

[Water Res.](#) 2016 May 4;100:232-244. doi: 10.1016/j.watres.2016.05.015. [Epub ahead of print]

Human fecal and pathogen exposure pathways in rural Indian villages and the effect of increased latrine coverage.

[Odagiri M](#), [Schriewer A](#), [Daniels ME](#), [Wuertz S](#), [Smith WA](#), [Clasen T](#), [Schmidt WP](#), [Jin Y](#), [Torondel B](#), [Misra PR](#), [Panigrahi P](#), [Jenkins MW](#).

Abstract

Efforts to eradicate open defecation and improve sanitation access are unlikely to achieve health benefits unless interventions reduce microbial exposures. This study assessed human fecal contamination and pathogen exposures in rural India, and the effect of increased sanitation coverage on contamination and exposure rates. In a cross-sectional study of 60 villages of a cluster-randomized controlled sanitation trial in Odisha, India, human and domestic animal fecal contamination was measured in community tubewells and ponds (n = 301) and via exposure pathways in homes (n = 354), using Bacteroidales microbial source tracking fecal markers validated in India. Community water sources were further tested for diarrheal pathogens (rotavirus, adenovirus and *Vibrio cholerae* by quantitative PCR; pathogenic *Escherichia coli* by multiplex PCR; *Cryptosporidium* and *Giardia* by immunomagnetic separation and direct fluorescent antibody microscopy). Exposure pathways in intervention and control villages were compared and relationships with child diarrhea examined. Human fecal markers were rarely detected in tubewells (2.4%, 95% CI: 0.3-4.5%) and ponds (5.6%, 95% CI: 0.8-10.3%), compared to homes (35.4%, 95% CI: 30.4-40.4%). In tubewells, *V. cholerae* was the most frequently detected pathogen (19.8%, 95% CI: 14.4-25.2%), followed by *Giardia* (14.8%, 95% CI: 10.0-19.7%). In ponds, *Giardia* was most often detected (74.5%, 95% CI: 65.7-83.3%), followed by pathogenic *E. coli* (48.1%, 95% CI: 34.8-61.5%) and rotavirus (44.4%, 95% CI: 34.2-54.7%). **At village-level, prevalence of fecal pathogen detection in community drinking water sources was associated with elevated prevalence of child diarrhea within 6 weeks of testing (RR 2.13, 95% CI: 1.25-3.63) while within homes, higher levels of human and animal fecal marker detection were associated with increased risks of subsequent child diarrhea (P = 0.044 and 0.013, respectively).** There was no evidence that the intervention, which increased functional latrine coverage and use by 27 percentage points, reduced human fecal contamination in any tested pathway, nor the prevalence of pathogens in water sources. In conclusion, the study demonstrates that **(1) improved sanitation alone may be insufficient and further interventions needed in the domestic domain to reduce widespread human and animal fecal contamination observed in homes, (2) pathogens detected in tubewells indicate these sources are microbiologically unsafe for drinking and were associated with child diarrhea, (3) domestic use of ponds heavily contaminated with multiple pathogens presents an under-recognized health risk, and (4) a 27 percentage**

point increase in improved sanitation access at village-level did not reduce detectable human fecal and pathogen contamination in this setting.

[http://linkinghub.elsevier.com/retrieve/pii/S0043-1354\(16\)30333-5](http://linkinghub.elsevier.com/retrieve/pii/S0043-1354(16)30333-5)

[J Health Econ.](#) 2016 Apr 20;48:135-148. doi: 10.1016/j.jhealeco.2016.03.003. [Epub ahead of print]

[Village sanitation and child health: Effects and external validity in a randomized field experiment in rural India.](#)

[Hammer J](#), [Spears D](#).

Abstract

Over a billion people worldwide defecate in the open, with important consequences for early-life health and human capital accumulation in developing countries. We report a cluster randomized controlled trial of a village sanitation intervention conducted in rural Maharashtra, India designed to identify an effect of village sanitation on average child height, an outcome of increasing importance to economists. **We find an effect of approximately 0.3 height-for-age standard deviations**, which is consistent with observations and hypotheses in economic and health literatures. We further exploit details of the planning and implementation of the experiment to study treatment heterogeneity and external validity.

[http://linkinghub.elsevier.com/retrieve/pii/S0167-6296\(16\)30003-0](http://linkinghub.elsevier.com/retrieve/pii/S0167-6296(16)30003-0)

[Biomed Environ Sci.](#) 2015 Nov;28(11):779-87. doi: 10.3967/bes2015.109.

[Effects of Multiple Cleaning and Disinfection Interventions on Infectious Diseases in Children: A Group Randomized Trial in China.](#)

[Ban HQ](#), [Li T](#), [Shen J](#), [Li J](#), [Peng PZ](#), [Ye HP](#), [Zhang LB](#).

Abstract

OBJECTIVE:

To assess the effectiveness of multiple cleaning and disinfection interventions in the homes and kindergartens, in reducing gastrointestinal and respiratory illnesses of children.

METHODS:

From October 2010 to September 2011, we performed a prospective, controlled study in China. 408 children under 5 years old were recruited and group randomized into intervention and control groups. **Families and kindergartens in the intervention group were provided with antibacterial products for hand hygiene and surface cleaning or disinfection for one year.** Each child's illness symptoms and sick leave were recorded every day.

RESULTS:

A total of 393 children completed the study, with similar baseline demographics in each of the 2 groups. Except for abdominal pain, the odds of symptoms (fever, cough and expectoration, runny nose and nasal congestion, diarrhea), illness (acute respiratory illness and gastrointestinal illness), and sick leave per person each month were significantly reduced by interventions. The rates of fever, diarrhea, acute respiratory illness, gastrointestinal illness and sick leave per person per year were significantly decreased as well.

CONCLUSION:

Not only the acute respiratory and gastrointestinal illness but the sick leave rate in children were significantly reduced by multiple interventions.

<http://dx.doi.org/10.3967/bes2015.109>

Health services

Soc Sci Med. 2015 Nov;144:96-103. doi: 10.1016/j.socscimed.2015.09.021. Epub 2015 Sep 14.

[The indirect effects of subsidised healthcare in rural Ghana.](#)

[Powell-Jackson T](#), [Ansah EK](#).

Abstract

Social networks provide a channel through which health policies and programmes can affect those with close social ties to the intended beneficiaries. We provide experimental evidence on the indirect effects of heavily subsidised healthcare. By exploiting data on 2151 households from a randomised study conducted in a rural district of Ghana in 2005, we estimate the extent to which social networks, defined by religion, influence the uptake of primary care services. We find that people socially connected to households with subsidised care are less likely to use primary care services despite the fact that the direct effect of the intervention is positive. We extend the empirical analysis to consider the implications of these changes in behaviour for welfare but find no evidence of indirect effects on child health and healthcare spending. In the context of this study, the findings highlight the potential for healthcare subsidies to have unintended consequences.

Trials. 2015 Aug 18;16:361. doi: 10.1186/s13063-015-0897-5.

[Health allowance for improving the nutritional status and development of 3-5-year-old left-behind children in poor rural areas of China: study protocol for a cluster randomised trial.](#)

[Lin Q](#), [Adab P](#), [Hemming K](#), [Yang L](#), [Qin H](#), [Li M](#), [Deng J](#), [Shi J](#), [Chen J](#).

Abstract

BACKGROUND:

Left-behind children (LBC) are recognised as a new social group in China. LBC are young children who are abandoned in rural villages whilst their parents travel to distant urban centres for employment (a new generation of migrant workers). Following the rapid growth in the number of migrant workers, the LBC population is also rapidly increasing. These children are usually left to be raised by elderly grandparents, a single parent, or sometimes distant relatives or neighbours who have limited resources, tend to have a poor education and sometimes are in frail health. Over 40 % of the 61 million LBC in China who are under 5 years old are undernourished, which affects their long-term health and abilities. An intervention that combines a conditional cash transfer (CCT) with nutrition education offers a potential solution.

METHODS/DESIGN:

A cluster randomised controlled trial design will be used to allocate 40 villages to the intervention arm (20 villages) or control arm (20 villages). The caregivers and all of the 3-5-year-old LBC will be the target population. Caregivers in the intervention arm will receive a cash allowance conditional on attending nutrition education sessions, ensuring that the LBC will use basic public health services over a 12-month period. At the baseline, midterm (month 6) and end (month 12) of the intervention period, evaluations will be conducted in all 40 villages.

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Multilevel generalised linear models will be used to analyse the impact of the intervention on nutrition status and other outcomes, adjusting for baseline levels using an analysis of covariance approach. The cost of the intervention will also be estimated.

DISCUSSION:

If found to be cost-effective, the findings will inform the development of a sustainable model to improve nutrition status among LBC in rural areas of China.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26282845/>

Haematological disorders

(See also Anaemia and iron deficiency, Malaria: treatment of uncomplicated malaria for study in sickle-cell disease patients)

[N Engl J Med.](#) 2016 Feb 18;374(7):625-35. doi: 10.1056/NEJMoa1512021. Epub 2015 Dec 8.

[A Multinational Trial of Prasugrel for Sickle Cell Vaso-Occlusive Events.](#)

[Heeney MM](#), [Hoppe CC](#), [Abboud MR](#), [Inusa B](#), [Kanter J](#), [Ogutu B](#), [Brown PB](#), [Heath LE](#), [Jakubowski JA](#), [Zhou C](#), [Zamoryakhin D](#), [Agbenyega T](#), [Colombatti R](#), [Hassab HM](#), [Nduba VN](#), [Oyieko JN](#), [Robitaille N](#), [Segbefia CI](#), [Rees DC](#); [DOVE Investigators](#).

Abstract

BACKGROUND:

Sickle cell anemia is an inherited blood disorder that is characterized by painful vaso-occlusive crises, for which there are few treatment options. Platelets mediate intercellular adhesion and thrombosis during vaso-occlusion in sickle cell anemia, which suggests a role for antiplatelet agents in modifying disease events.

METHODS:

Children and adolescents 2 through 17 years of age with sickle cell anemia were randomly assigned to receive oral prasugrel or placebo for 9 to 24 months. The primary end point was the rate of vaso-occlusive crisis, a composite of painful crisis or acute chest syndrome. The secondary end points were the rate of sickle cell-related pain and the intensity of pain, which were assessed daily with the use of pain diaries.

RESULTS:

A total of 341 patients underwent randomization at 51 sites in 13 countries across the Americas, Europe, Asia, and Africa. The rate of vaso-occlusive crisis events per person-year was 2.30 in the prasugrel group and 2.77 in the placebo group (rate ratio, 0.83; 95% confidence interval, 0.66 to 1.05; $P=0.12$). There were no significant differences between the groups in the secondary end points of diary-reported events. The safety end points, including the frequency of bleeding events requiring medical intervention, of hemorrhagic and nonhemorrhagic adverse events that occurred while patients were taking prasugrel or placebo, and of discontinuations due to prasugrel or placebo, did not differ significantly between the groups.

CONCLUSIONS:

Among children and adolescents with sickle cell anemia, the rate of vaso-occlusive crisis was not significantly lower among those who received prasugrel than among those who received placebo. There were no significant between-group differences in the safety findings

[Pediatr Blood Cancer.](#) 2016 Feb;63(2):299-305. doi: 10.1002/pbc.25771. Epub 2015 Sep 24.

Design of the DOVE (Determining Effects of Platelet Inhibition on Vaso-Occlusive Events) trial: A global Phase 3 double-blind, randomized, placebo-controlled, multicenter study of the efficacy and safety of prasugrel in pediatric patients with sickle cell anemia utilizing a dose titration strategy.

[Hoppe CC](#), [Styles L](#), [Heath LE](#), [Zhou C](#), [Jakubowski JA](#), [Winters KJ](#), [Brown PB](#), [Rees DC](#), [Heeney MM](#).

Abstract

BACKGROUND:

Sickle cell disease (SCD) is an inherited blood disorder characterized by painful vaso-occlusive crises (VOC) with limited treatment options, particularly for children. Emerging knowledge of the pathophysiology of SCD suggests antiplatelet therapies may hold promise for treatment of VOC. Multiple small studies have evaluated antiplatelet agents on the frequency of VOC with varying results, but there has not been an adequately powered study to definitively determine the effect of antiplatelet agents on VOC. Prasugrel, a third-generation thienopyridine that irreversibly inhibits platelet activation and aggregation, is approved in adults with acute coronary syndrome managed with percutaneous coronary intervention.

PROCEDURE:

Determining Effects of Platelet Inhibition on Vaso-Occlusive Events (DOVE) is a double-blind, randomized study with planned enrollment of >220 children from 14 countries across the Americas, Europe, Asia, and Africa, designed to test the hypothesis that prasugrel reduces the rate of VOC in children with sickle cell anemia (SCA) (homozygous hemoglobin S [HbSS] and hemoglobin S β (0) thalassemia [HbS β (0)]). Secondary study endpoints include reductions in rate and intensity of vaso-occlusive pain as recorded in daily electronic diaries. Safety assessments include incidence of hemorrhagic events requiring medical intervention and treatment-emergent adverse events. DOVE incorporates a dose-titration strategy to reduce potential bleeding risks inherent with antiplatelet therapy while maintaining blinded treatment assignment.

CONCLUSIONS:

DOVE presents a unique opportunity to determine whether antiplatelet therapy reduces frequency of patient-reported VOC and daily vaso-occlusive pain in a global study of children with SCA

HIV / AIDS

Ante-retroviral therapy (ART)

[JAMA](#). 2015 Nov 3;314(17):1808-17. doi: 10.1001/jama.2015.13631.

Efavirenz-Based Antiretroviral Therapy Among Nevirapine-Exposed HIV-Infected Children in South Africa: A Randomized Clinical Trial.

[Coovadia A](#), [Abrams EJ](#), [Strehlau R](#), [Shiau S](#), [Pinillos F](#), [Martens L](#), [Patel F](#), [Hunt G](#), [Tsai WY](#), [Kuhn L](#).

Abstract

IMPORTANCE:

Randomised trials in child health in developing countries 2015-16

Advantages of using efavirenz as part of treatment for children infected with human immunodeficiency virus (HIV) include once-daily dosing, simplification of co-treatment for tuberculosis, preservation of ritonavir-boosted lopinavir for second-line treatment, and harmonization of adult and pediatric treatment regimens. However, there have been concerns about possible reduced viral efficacy of efavirenz in children exposed to nevirapine for prevention of mother-to-child transmission.

OBJECTIVE:

To evaluate whether nevirapine-exposed children achieving initial viral suppression with ritonavir-boosted lopinavir-based therapy can transition to efavirenz-based therapy without risk of viral failure.

DESIGN, SETTING, AND PARTICIPANTS:

Randomized, open-label noninferiority trial conducted at Rahima Moosa Mother and Child Hospital, Johannesburg, South Africa, from June 2010 to December 2013, enrolling 300 HIV-infected children exposed to nevirapine for prevention of mother-to-child transmission who were aged 3 years or older and had plasma HIV RNA of less than 50 copies/mL during ritonavir-boosted lopinavir-based therapy; 298 were randomized and 292 (98%) were followed up to 48 weeks after randomization.

INTERVENTIONS:

Participants were randomly assigned to switch to efavirenz-based therapy (n = 150) or continue ritonavir-boosted lopinavir-based therapy (n = 148).

MAIN OUTCOMES AND MEASURES:

Risk difference between groups in (1) viral rebound (ie, ≥ 1 HIV RNA measurement of >50 copies/mL) and (2) viral failure (ie, confirmed HIV RNA >1000 copies/mL) with a noninferiority bound of -0.10 . Immunologic and clinical responses were secondary end points.

RESULTS:

The Kaplan-Meier probability of viral rebound by 48 weeks was 0.176 (n = 26) in the efavirenz group and 0.284 (n = 42) in the ritonavir-boosted lopinavir group. Probabilities of viral failure were 0.027 (n = 4) in the efavirenz group and 0.020 (n = 3) in the ritonavir-boosted lopinavir group. The risk difference for viral rebound was 0.107 (1-sided 95% CI, 0.028 to ∞) and for viral failure was -0.007 (1-sided 95% CI, -0.036 to ∞). We rejected the null hypothesis that efavirenz is inferior to ritonavir-boosted lopinavir ($P < .001$) for both end points. By 48 weeks, CD4 cell percentage was 2.88% (95% CI, 1.26%–4.49%) higher in the efavirenz group than in the ritonavir-boosted lopinavir group.

CONCLUSIONS AND RELEVANCE:

Among HIV-infected children exposed to nevirapine for prevention of mother-to-child transmission and with initial viral suppression with ritonavir-boosted lopinavir-based therapy, switching to efavirenz-based therapy compared with continuing ritonavir-boosted lopinavir-based therapy did not result in significantly higher rates of viral rebound or viral failure. This therapeutic approach may offer advantages in children such as these.

<http://jama.jamanetwork.com/article.aspx?articleid=2467551>

[Lancet Infect Dis.](#) 2015 Jul;15(7):803-9. doi: 10.1016/S1473-3099(15)00087-0. Epub 2015 Jun 1.

Reactivity of routine HIV antibody tests in children who initiated antiretroviral therapy in early infancy as part of the Children with HIV

Early Antiretroviral Therapy (CHER) trial: a retrospective analysis.

[Payne H](#), [Mkhize N](#), [Otwombe K](#), [Lewis J](#), [Panchia R](#), [Callard R](#), [Morris L](#), [Babiker A](#), [Violari A](#), [Cotton MF](#), [Klein NJ](#), [Gibb DM](#).

Abstract

BACKGROUND:

Early antiretroviral therapy (ART) and virological suppression can affect evolving antibody responses to HIV infection. We aimed to assess frequency and predictors of seronegativity in infants starting early ART.

METHODS:

We compared HIV antibody results between two of three treatment groups of the Children with HIV Early Antiretroviral Therapy (CHER) trial, done from July, 2005, until July, 2011, in which **infants with HIV infection aged 5·7-12·0 weeks with a percentage of CD4-positive T lymphocytes of at least 25% were randomly assigned to immediate ART for 96 weeks (ART-96W) or deferred ART until clinical or immunological progression (ART-Def)**. We measured antibody from all available stored samples for ART-96W and ART-Def at trial week 84 using three assays: fourth-generation enzyme immunoassay HIV antigen-antibody combination, HIV-1 and HIV-2 rapid antibody test, and quantitative anti-gp120 IgG ELISA. We also assessed odds of seropositivity with respect to age of ART initiation and cumulative viral load. The CHER trial was registered with ClinicalTrials.gov, number [NCT00102960](https://clinicaltrials.gov/ct2/show/study/NCT00102960).

FINDINGS:

The median age of the infants from when samples were taken (184 samples from 268 infants) was 92 weeks (IQR 90·6-93·4). **More specimens from the ART-96W group were seronegative than from the ART-Def group by enzyme immunoassay (ART-96W 49 [46%] of 107 vs ART-Def eight [11%] of 75; $p<0\cdot0001$) and rapid antibody test (54 [53%] of 101 vs eight [11%] of 74; $p<0\cdot0001$).** Median anti-gp120 IgG concentration was lower in the ART-96W group (230 $\mu\text{g}/\mu\text{L}$ [IQR 133-13 129]) than in the ART-Def group (6870 $\mu\text{g}/\mu\text{L}$ [1706-53 645]; $p<0\cdot0001$). If ART was started between 12 and 24 weeks of age, odds of seropositivity were increased 13·7 times (95% CI 3·1-60·2; $p=0\cdot001$) compared with starting it between 0 and 12 weeks. All children starting ART aged older than 24 weeks were seropositive. Cumulative viral load to week 84 correlated with anti-gp120 IgG concentrations (coefficient 0·54; $p<0\cdot0001$) and increased odds of seropositivity (odds ratio 1·59 [95% CI 1·1-2·3]) adjusted for ART initiation age.

INTERPRETATION:

About half of children starting ART before 12 weeks of age were HIV seronegative by almost 2 years of age. **HIV antibody tests cannot be used to reconfirm HIV diagnosis in children starting early ART.** Long-term effects of seronegativity need further study. Clear guidelines are needed for retesting alongside improved diagnostic tests.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26043884/>

Comment

An important study that informs us of the interpretation of HIV serology in children on ART, the earlier ART is commenced the more likely children are to be seronegative later.

Early infant diagnosis

(See also: Vaccines – BCG vaccine and delayed administration in HIV exposed infants)

[Implement Sci.](https://doi.org/10.1186/s13012-015-0284-3) 2015 Jul 9;10:96. doi: 10.1186/s13012-015-0284-3.

[Improving early infant HIV diagnosis in Kenya: study protocol of a cluster-randomized efficacy trial of the HITSsystem.](https://doi.org/10.1186/s13012-015-0284-3)

Randomised trials in child health in developing countries 2015-16

[Finocchiaro-Kessler S](#), [Goggin K](#), [Khamadi S](#), [Gautney B](#), [Dariotis JK](#), [Bawcom C](#), [Cheng AL](#), [Nazir N](#), [Martin C](#), [Ruff A](#), [Sweat M](#), [Okoth V](#).

Abstract

BACKGROUND:

Early infant diagnosis among human immunodeficiency virus (HIV)-exposed infants is a critical component of prevention of mother-to-child transmission programs. Barriers to early infant diagnosis include poor uptake, low retention at designated re-testing intervals, delayed test results, passive systems of communication, and poor linkage to treatment. This study will evaluate the HIV Infant Tracking System (HITSsystem), an eHealth intervention that streamlines communication and accountability between the key early infant diagnosis stakeholders: HIV+ mothers and their HIV-exposed infants, healthcare providers, and central laboratory personnel. It is hypothesized that the HITSsystem will significantly improve early infant diagnosis retention at 9 and 18 months postnatal and the timely provision of services.

METHODS/DESIGN:

Using a phased cluster-randomized controlled trial design, we will evaluate the impact of the HITSsystem on eight primary benchmarks in the 18-month long cascade of care for early infant diagnosis. Study sites are six government hospitals in Kenya matched on geographic region, resource level, and patient volume. Early infant diagnosis outcomes of mother-infant dyads (n = 120 per site) at intervention hospitals (n = 3) where the HITSsystem is deployed at baseline will be compared to the matched control sites providing standard care. After allowing for sufficient time for enrollment and 18-month follow-up of dyads, the HITSsystem will be deployed at the control sites in the end of Year 3. Primary outcomes are retention among mother-infant dyads, initiation of antiretroviral therapy among HIV-infected infants, and the proportion of services delivered within the optimal time window indicated by national and study guidelines. Satisfaction interviews with participants and providers will inform intervention improvements. Cost-effectiveness analyses will be conducted to inform the sustainability of the HITSsystem. Hypothesized outcomes include significantly higher retention throughout the 18-month early infant diagnosis process, significantly more services provided on-time at intervention sites, and a potential savings to the healthcare system.

DISCUSSION:

This study will evaluate the public health impact of the HITSsystem to improve critical early infant diagnosis outcomes in low-resource settings. Cost-effectiveness analyses will inform the feasibility of scale-up in other settings.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26155932/>

Management of HIV-related conditions

Nutrition, growth and development of children with HIV

[Public Health Nutr.](#) 2016 Jul;19(10):1904-12. doi: 10.1017/S1368980015003456. Epub 2015 Dec 7.

[**Leaf concentrate compared with skimmed milk as nutritional supplementation for HIV-infected children: a randomized controlled trial in Burundi.**](#)

[Collin SM](#), [Leclercq B](#), [Twungubumwe N](#), [Andréoletti L](#), [Richardier FC](#), [Bertin E](#).

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Abstract

OBJECTIVE:

The effectiveness of leaf concentrate powder (LCP) as a nutritional supplement was established in trials conducted among adolescent girls and pregnant women in India. Here we evaluate LCP, compared with skimmed milk powder (SMP), as a supplement for antiretroviral-naïve children living with HIV in a sub-Saharan African country.

DESIGN:

Randomized controlled, two-arm, 6-month trial comparing effects of isoproteic (5 g) LCP (10 g daily) and SMP (15 g daily) on HIV-1 viral load, CD4+ cell count/percentage, weight/height-for-age, general blood parameters, diarrhoea, respiratory and HIV-related opportunistic infections.

SETTING:

Bujumbura and Kirundo, Burundi.

SUBJECTS:

Eighty-three HIV-positive, antiretroviral-naïve children aged 5-14 years: median (range) CD4+ count, 716 (361-1690) cells/mm³; log₁₀ HIV-1 viral load, 4.39 (1.79-6.00).

RESULTS:

LCP was equivalent to SMP in relation to HIV-specific blood parameters and did not demonstrate superiority over SMP in relation to Hb. Three children in each arm (LCP, 7.1 % (3/42); SMP, 7.3 % (3/41)) proceeded to antiretroviral therapy because their CD4+ counts fell below 350 cells/mm³. Children in the LCP group reported higher levels of appetite and overall health at 6 months. There were no differences in clinical events or any other outcome measures. LCP was less palatable than SMP to the children in this population, but there were few negative perceptions of appearance, texture and taste.

CONCLUSIONS:

LCP appears to be equivalent to SMP as a nutritional supplement in this population, despite slightly lower palatability. In relation to viral load and CD4+ count, equivalence may indicate no effect in either group. Effectiveness relative to no supplementation remains to be determined.

[Indian J Pediatr.](#) 2016 Mar;83(3):232-7. doi: 10.1007/s12098-015-1873-5. Epub 2015 Sep 4.

[Effect of Nutrition Supplementation in Children Living with HIV at ART Centre.](#)

[Thakur HS](#), [Gottapu GS](#), [Kadali SP](#), [Kulkarni B](#), [Mamidi RS](#).

Abstract

OBJECTIVE:

To assess the benefits of nutrition supplementation in children living with HIV (CLHIV).

METHODS:

A prospective observational study was carried out at antiretroviral therapy (ART)/pediatric centre of excellence (PCOE), Niloufer hospital for a period of one year in CLHIV (N = 164) aged 1 to 18 y referred to ART/PCOE. Nutrition supplementation was given in the form of Ready to Use Food (About 350 kcal and 12 g of protein per day) supplementation to assess improvement in Height for age Z (HAZ), Weight for Age Z (WAZ), Weight for Height Z (WHZ) and Body Mass Index for age Z (BMIZ) scores over a period of one year.

RESULTS:

At baseline, 65.5 % and 57.5 % of children below and above 5 y respectively were stunted. 24.1 % and 45.3 % children below and above 5 y respectively were wasted/thin (as assessed by

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BMI for age). Mean BMIZ score significantly improved in both the age groups (0.96 Z score, $P < 0.001$) in below and above 5 (0.37 Z score, $P < 0.001$) respectively at the end of 12 mo. Mean HAZ score also significantly improved in children above 5 y (0.09 Z score, $P < 0.05$) with non-significant improvement below 5 y (0.14 Z score, $P < 0.57$) by the end of 12 mo.

CONCLUSIONS:

Nutrition supplementation over one year resulted in moderate improvement in the nutritional status of CLHIV. However, it is unclear, whether the improvement in nutritional status was due to regular visits to ART centre that may have resulted in better adherence to treatment or an additional benefit of nutrition intervention. This warrants a well-designed randomized controlled trial to examine the benefits of nutrition supplementation in CLHIV attending ART centre.

Prevention of parent to child transmission of HIV

[Lancet](#). 2016 Feb 6;387(10018):566-73. doi: 10.1016/S0140-6736(15)00984-8. Epub 2015 Nov 19.

[Extended pre-exposure prophylaxis with lopinavir-ritonavir versus lamivudine to prevent HIV-1 transmission through breastfeeding up to 50 weeks in infants in Africa \(ANRS 12174\): a randomised controlled trial.](#)

[Nagot N](#), [Kankasa C](#), [Tumwine JK](#), [Meda N](#), [Hofmeyr GJ](#), [Vallo R](#), [Mwiya M](#), [Kwagala M](#), [Traore H](#), [Sunday A](#), [Singata M](#), [Siuluta C](#), [Some E](#), [Rutagwera D](#), [Neboua D](#), [Ndeezi G](#), [Jackson D](#), [Maréchal V](#), [Neveu D](#), [Engebretsen IM](#), [Lombard C](#), [Blanche S](#), [Sommerfelt H](#), [Rekacewicz C](#), [Tylleskär T](#), [Van de Perre P](#); ANRS 12174 Trial Group.

Abstract

BACKGROUND:

Strategies to prevent postnatal mother-to-child transmission of HIV-1 in Africa, including infant prophylaxis, have never been assessed past 6 months of breastfeeding, despite breastfeeding being recommended up to 12 months after birth. **We aimed to compare the efficacy and safety of infant prophylaxis with the two drug regimens (lamivudine or lopinavir-ritonavir) to prevent postnatal HIV-1 transmission up to 50 weeks of breastfeeding.**

METHODS:

We did a randomised controlled trial in four sites in Burkina Faso, South Africa, Uganda, and Zambia in **children born to HIV-1-infected mothers not eligible for antiretroviral therapy (CD4 count >350 cells per μ L)**. An independent researcher electronically generated a randomisation schedule; we then used sequentially numbered envelopes to randomly assign (1:1) HIV-1-uninfected breastfed infants aged 7 days to either lopinavir-ritonavir or lamivudine (paediatric liquid formulations, twice a day) up to 1 week after complete cessation of breastfeeding or at the final visit at week 50. We stratified the randomisation by country and used permuted blocks of four and six. We used a study label on drug bottles to mask participants, study physicians, and assessors to the treatment allocation. The primary outcome was infant HIV-1 infection between age 7 days and 50 weeks, diagnosed every 3 months with HIV-1 DNA PCR, in the modified intention-to-treat population (all who attended at least one follow-up visit). This trial is registered with ClinicalTrials.gov, number [NCT00640263](#).

FINDINGS:

Between Nov 16, 2009, and May 7, 2012, we enrolled and randomised 1273 infants and analysed 1236; 615 assigned to lopinavir-ritonavir or 621 assigned to lamivudine. 17 HIV-1 infections were diagnosed in the study period (eight in the lopinavir-ritonavir group and nine in the lamivudine group), resulting in cumulative HIV-1 infection of 1.4% (95% CI 0.4-2.5) and

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1.5% (0.7-2.5), respectively. Infection rates did not differ between the two drug regimens (hazard ratio [HR] of lopinavir-ritonavir versus lamivudine of 0.90, 95% CI 0.35-2.34; p=0.83). Clinical and biological severe adverse events did not differ between groups; 251 (51%) infants had a grade 3-4 event in the lopinavir-ritonavir group compared with 246 (50%) in the lamivudine group.

INTERPRETATION:

Infant HIV-1 prophylaxis with lopinavir-ritonavir was not superior to lamivudine and both drugs led to very low rates of HIV-1 postnatal transmission for up to 50 weeks of breastfeeding. Infant pre-exposure prophylaxis should be extended until the end of HIV-1 exposure and mothers should be informed about the persistent risk of transmission throughout breastfeeding.

Comment

Using the now WHO recommended ART regimen of Option B Plus, mothers who test positive for HIV would be commenced on ART, regardless of their CD-4 level. With this regimen it is likely that the risk of breast milk transmission of HIV would be even less. It is encouraging even that in the absence of maternal treatment, transmission rates through breast feeding can be very low with lamivudine or lopinavir-ritonavir.

[J Acquir Immune Defic Syndr.](#) 2015 Aug 15;69(5):e164-71. doi: 10.1097/QAI.0000000000000656.

[Implementation and Operational Research: Effect of Integration of HIV Care and Treatment Into Antenatal Care Clinics on Mother-to-Child HIV Transmission and Maternal Outcomes in Nyanza, Kenya: Results From the SHAIIP Cluster Randomized Controlled Trial.](#)

[Washington S](#), [Owuor K](#), [Turan JM](#), [Steinfeld RL](#), [Onono M](#), [Shade SB](#), [Bukusi EA](#), [Ackers ML](#), [Cohen CR](#).

Abstract

BACKGROUND:

Many HIV-infected pregnant women identified during antenatal care (ANC) do not enroll in long-term HIV care, resulting in deterioration of maternal health and continued risk of HIV transmission to infants.

METHODS:

We performed a cluster randomized trial to evaluate the effect of integrating HIV care into ANC clinics in rural Kenya. Twelve facilities were randomized to provide either integrated services (ANC, prevention of mother-to-child transmission, and HIV care delivered in the ANC clinic; n = 6 intervention facilities) or standard ANC services (including prevention of mother-to-child transmission and referral to a separate clinic for HIV care; n = 6 control facilities).

RESULTS:

There were high patient attrition rates over the course of this study. Among study participants who enrolled in HIV care, there was 12-month follow-up data for 256 of 611 (41.8%) women and postpartum data for only 325 of 1172 (28%) women. By 9 months of age, 382 of 568 (67.3%) infants at intervention sites and 338 of 594 (57.0%) at control sites had tested for HIV [odds ratio (OR) 1.45, 95% confidence interval (CI): 0.71 to 2.82]; 7.3% of infants tested HIV positive at intervention sites compared with 8.0% of infants at control sites (OR 0.89, 95% CI: 0.56 to 1.43). The composite clinical/immunologic progression into AIDS was similar in both arms (4.9% vs. 5.1%, OR 0.83, 95% CI: 0.41 to 1.68).

CONCLUSIONS:

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Despite the provision of integrated services, patient attrition was substantial in both arms, suggesting barriers beyond lack of service integration. Integration of HIV services into the ANC clinic was not associated with a reduced risk of HIV transmission to infants and did not appear to affect short-term maternal health outcomes.

Maternal HIV prevention strategies

[Curr Opin HIV AIDS](#). 2016 Jan;11(1):18-26. doi: 10.1097/COH.0000000000000207.

[Tenofovir-based oral preexposure prophylaxis prevents HIV infection among women.](#)

[Thomson KA](#), [Baeten JM](#), [Mugo NR](#), [Bekker LG](#), [Celum CL](#), [Heffron R](#).

Abstract

PURPOSE OF REVIEW:

Despite tremendous promise as a female-controlled HIV prevention strategy, implementation of preexposure prophylaxis (PrEP) among women has been limited, in part because of disparate efficacy results from randomized trials in this population. This review synthesizes existing evidence regarding PrEP efficacy for preventing HIV infection in women and considerations for delivering PrEP to women.

RECENT FINDINGS:

In three efficacy trials, conducted among men and women, tenofovir-based oral PrEP reduced HIV acquisition in subgroups of women by 49-79% in intent-to-treat analyses, and by >85% when accounting for PrEP adherence. Two trials did not demonstrate an HIV prevention benefit from PrEP in women, but substantial evidence indicates those results were compromised by very low adherence to the study medication. Qualitative research has identified risk perception, stigma, and aspects of clinical trial participation as influencing adherence to study medication. Pharmacokinetic studies provide supporting evidence that PrEP offers HIV protection in women who are adherent to the medication.

SUMMARY:

Tenofovir-based daily oral PrEP prevents HIV acquisition in women. Offering PrEP as an HIV prevention option for women at high risk of HIV acquisition is a public health imperative and opportunities to evaluate implementation strategies for PrEP for women are needed.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4705855/>

[N Engl J Med](#). 2016 Feb 22. [Epub ahead of print]

[Use of a Vaginal Ring Containing Dapivirine for HIV-1 Prevention in Women.](#)

[Baeten JM](#), [Palanee-Phillips T](#), [Brown ER](#), [Schwartz K](#), [Soto-Torres LE](#), [Govender V](#), [Mgodi NM](#), [Matovu Kiweewa F](#), [Nair G](#), [Mhlanga F](#), [Siva S](#), [Bekker LG](#), [Jeenarain N](#), [Gaffoor Z](#), [Martinson F](#), [Makanani B](#), [Pather A](#), [Naidoo L](#), [Husnik M](#), [Richardson BA](#), [Parikh UM](#), [Mellors JW](#), [Marzinke MA](#), [Hendrix CW](#), [van der Straten A](#), [Ramjee G](#), [Chirenje ZM](#), [Nakabiito C](#), [Taha TE](#), [Jones J](#), [Mayo A](#), [Scheckter R](#), [Berthiaume J](#), [Livant E](#), [Jacobson C](#), [Ndase P](#), [White R](#), [Patterson K](#), [Germuga D](#), [Galaska B](#), [Bunge K](#), [Singh D](#), [Szydlo](#)

Randomised trials in child health in developing countries 2015-16

[DW](#), [Montgomery ET](#), [Mensch BS](#), [Torjesen K](#), [Grossman CI](#), [Chakhtoura N](#), [Nel A](#), [Rosenberg Z](#), [McGowan I](#), [Hillier S](#); [MTN-020–ASPIRE Study Team](#).

Abstract

Background Antiretroviral medications that are used as prophylaxis can prevent acquisition of human immunodeficiency virus type 1 (HIV-1) infection. However, in clinical trials among African women, the incidence of HIV-1 infection was not reduced, probably because of low adherence. Longer-acting methods of drug delivery, such as vaginal rings, may simplify use of antiretroviral medications and provide HIV-1 protection.

Methods We conducted a **phase 3, randomized, double-blind, placebo-controlled trial of a monthly vaginal ring containing dapivirine, a non-nucleoside HIV-1 reverse-transcriptase inhibitor**, involving women between the ages of 18 and 45 years in Malawi, South Africa, Uganda, and Zimbabwe.

Results Among the 2629 women who were enrolled, 168 HIV-1 infections occurred: 71 in the dapivirine group and 97 in the placebo group (incidence, 3.3 and 4.5 per 100 person-years, respectively). **The incidence of HIV-1 infection in the dapivirine group was lower by 27% (95% confidence interval [CI], 1 to 46; P=0.05) than that in the placebo group.** In an analysis that excluded data from two sites that had reduced rates of retention and adherence, the incidence of HIV-1 infection in the dapivirine group was lower by 37% (95% CI, 12 to 56; P=0.007) than that in the placebo group. In a post hoc analysis, higher rates of HIV-1 protection were observed among women over the age of 21 years (56%; 95% CI, 31 to 71; P<0.001) but not among those 21 years of age or younger (-27%; 95% CI, -133 to 31; P=0.45), a difference that was correlated with reduced adherence. The rates of adverse medical events and antiretroviral resistance among women who acquired HIV-1 infection were similar in the two groups.

Conclusions A monthly vaginal ring containing dapivirine reduced the risk of HIV-1 infection among African women, with increased efficacy in subgroups with evidence of increased adherence.

HIV vaccine

(see Vaccine – HIV vaccine)

Integrated approaches to HIV care and prevention

[A Livelihood Intervention to Reduce the Stigma of HIV in Rural Kenya: Longitudinal Qualitative Study.](#)

[Tsai AC](#), [Hatcher AM](#), [Bukusi EA](#), [Weke E](#), [Lemus Hufstedler L](#), [Dworkin SL](#), [Kodish S](#), [Cohen CR](#), [Weiser SD](#).

Abstract

The scale-up of effective treatment has partially reduced the stigma attached to HIV, but HIV still remains highly stigmatized throughout sub-Saharan Africa. Most studies of anti-HIV stigma interventions have employed psycho-educational strategies such as information provision, counseling, and testimonials, but these have had varying degrees of success. Theory suggests that livelihood interventions could potentially reduce stigma by weakening the instrumental and symbolic associations between HIV and premature morbidity, economic incapacity, and death, but this hypothesis has not been directly examined. **We conducted a longitudinal qualitative study among 54 persons with HIV participating in a 12-month randomized controlled**

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trial of a livelihood intervention in rural Kenya. Our study design permitted assessment of changes over time in the perspectives of treatment-arm participants (N = 45), as well as an understanding of the experiences of control arm participants (N = 9, interviewed only at follow-up). Initially, participants felt ashamed of their seropositivity and were socially isolated (internalized stigma). **They also described how others in the community discriminated against them, labeled them as being "already dead," and deemed them useless and unworthy of social investment (perceived and enacted stigma). At follow-up, participants in the treatment arm described less stigma and voiced positive changes in confidence and self-esteem. Concurrently, they observed that other community members perceived them as active, economically productive, and contributing citizens.** None of these changes were noted by participants in the control arm, who described ongoing and continued stigma. In summary, our findings suggest a theory of stigma reduction: livelihood interventions may reduce internalized stigma among persons with HIV and also, by targeting core drivers of negative attitudes toward persons with HIV, positively change attitudes toward persons with HIV held by others. Further research is needed to formally test these hypotheses, assess the extent to which these changes endure over the long term, and determine whether this class of interventions can be implemented at scale.

Helminth and other gastrointestinal disorders

(See also Anaemia, Diarrhoea, Micronutrients and food fortification, Malaria and HIV)

[Cochrane Database Syst Rev.](#) 2015 Jul 23;(7):CD000371. doi: 10.1002/14651858.CD000371.pub6.

[Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin, and school performance.](#)

[Taylor-Robinson DC](#), [Maayan N](#), [Soares-Weiser K](#), [Donegan S](#), [Garner P](#).

Abstract

BACKGROUND:

The World Health Organization (WHO) recommends treating all school children at regular intervals with deworming drugs in areas where helminth infection is common. As the intervention is often claimed to have important health, nutrition, and societal effects beyond the removal of worms, we critically evaluated the evidence on benefits.

OBJECTIVES:

To summarize the effects of giving deworming drugs to children to treat soil-transmitted helminths on weight, haemoglobin, and cognition; and the evidence of impact on physical well-being, school attendance, school performance, and mortality.

SEARCH METHODS:

We searched the Cochrane Infectious Diseases Group Specialized Register (14 April 2015); Cochrane Central Register of Controlled Trials (CENTRAL), published in the Cochrane Library (2015, Issue 4); MEDLINE (2000 to 14 April 2015); EMBASE (2000 to 14 April 2015); LILACS (2000 to 14 April 2015); the metaRegister of Controlled Trials (mRCT); and reference lists, and registers of ongoing and completed trials up to 14 April 2015.

SELECTION CRITERIA:

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We included randomized controlled trials (RCTs) and quasi-RCTs comparing deworming drugs for soil-transmitted helminths with placebo or no treatment in children aged 16 years or less, reporting on weight, haemoglobin, and formal tests of intellectual development. We also sought data on school attendance, school performance, and mortality. We included trials that combined health education with deworming programmes.

DATA COLLECTION AND ANALYSIS:

At least two review authors independently assessed the trials, evaluated risk of bias, and extracted data. We analysed continuous data using the mean difference (MD) with 95% confidence intervals (CIs). Where data were missing, we contacted trial authors. We used outcomes at time of longest follow-up. The evidence quality was assessed using GRADE. This edition of the Cochrane Review adds the DEVTA trial from India, and draws on an independent analytical replication of a trial from Kenya.

MAIN RESULTS:

We identified 45 trials, including nine cluster-RCTs, that met the inclusion criteria. One trial evaluating mortality included over one million children, and the remaining 44 trials included a total of 67,672 participants. Eight trials were in children known to be infected, and 37 trials were carried out in endemic areas, including areas of high (15 trials), moderate (12 trials), and low prevalence (10 trials). **Treating children known to be infected with a single dose of deworming drugs (selected by screening, or living in areas where all children are infected) may increase weight gain over the next one to six months (627 participants, five trials, low quality evidence). The effect size varied across trials from an additional 0.2 kg gain to 1.3 kg.** There is currently insufficient evidence to know whether treatment has additional effects on haemoglobin (247 participants, two trials, very low quality evidence); school attendance (0 trials); cognitive functioning (103 participants, two trials, very low quality evidence), or physical well-being (280 participants, three trials, very low quality evidence). Community deworming programmes. **Treating all children living in endemic areas with a dose of deworming drugs probably has little or no effect on average weight gain (MD 0.04 kg less, 95% CI 0.11 kg less to 0.04 kg more; trials 2719 participants, seven trials, moderate quality evidence),** even in settings with high prevalence of infection (290 participants, two trials). A single dose also probably has no effect on average haemoglobin (MD 0.06 g/dL, 95% CI -0.05 lower to 0.17 higher; 1005 participants, three trials, moderate quality evidence), or average cognition (1361 participants, two trials, low quality evidence). Similarly, regularly treating all children in endemic areas with deworming drugs, given every three to six months, may have little or no effect on average weight gain (MD 0.08 kg, 95% CI 0.11 kg less to 0.27 kg more; 38,392 participants, 10 trials, low quality evidence). The effects were variable across trials; one trial from a low prevalence setting carried out in 1995 found an increase in weight, but nine trials carried out since then found no effect, including five from moderate and high prevalence areas. There is also reasonable evidence that regular treatment probably has no effect on average height (MD 0.02 cm higher, 95% CI 0.14 lower to 0.17 cm higher; 7057 participants, seven trials, moderate quality evidence); average haemoglobin (MD 0.02 g/dL lower; 95% CI 0.08 g/dL lower to 0.04 g/dL higher; 3595 participants, seven trials, low quality evidence); formal tests of cognition (32,486 participants, five trials, moderate quality evidence); exam performance (32,659 participants, two trials, moderate quality evidence); or mortality (1,005,135 participants, three trials, low quality evidence). There is very limited evidence assessing an effect on school attendance and the findings are inconsistent, and at risk of bias (mean attendance 2% higher, 95% CI 4% lower to 8% higher; 20,243 participants, two trials, very low quality evidence). In a sensitivity analysis that only included trials with adequate allocation concealment, there was no evidence of any effect for the main outcomes.

AUTHORS' CONCLUSIONS:

Treating children known to have worm infection may have some nutritional benefits for the individual. However, in mass treatment of all children in endemic areas, there is now

substantial evidence that this does not improve average nutritional status, haemoglobin, cognition, school performance, or survival.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26202783/>

[PLoS Negl Trop Dis.](#) 2015 Sep 25;9(9):e0004057. doi: 10.1371/journal.pntd.0004057. eCollection 2015.

Assessment of Efficacy and Quality of Two Albendazole Brands Commonly Used against Soil-Transmitted Helminth Infections in School Children in Jimma Town, Ethiopia.

[Belew S](#), [Getachew M](#), [Suleman S](#), [Mohammed T](#), [Deti H](#), [D'Hondt M](#), [Wynendaele E](#), [Mekonnen Z](#), [Vercruyssen J](#), [Duchateau L](#), [De Spiegeleer B](#), [Levecke B](#).

Abstract

BACKGROUND:

There is a worldwide upsurge in mass drug administration (MDA) programs to control the morbidity caused by soil-transmitted helminths (STHs): *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm. Although anthelmintic drugs which are used for MDA are supplied by two pharmaceutical companies through donation, there is a wide range of brands available on local markets for which the efficacy against STHs and quality remain poorly explored. In the present study, we evaluated the drug efficacy and quality of two albendazole brands (Bendex and Ovis) available on the local market in Ethiopia.

METHODOLOGY/PRINCIPAL FINDINGS:

A randomized clinical trial was conducted according to the World Health Organization (WHO) guidelines to assess drug efficacy, by means of egg reduction rate (ERR), of Bendex and Ovis against STH infections in school children in Jimma, Ethiopia. In addition, the chemical and physicochemical quality of the drugs was assessed according to the United States and European Pharmacopoeia, encompassing mass uniformity of the tablets, amount of active compound and dissolution profile. Both drugs were highly efficacious against *A. lumbricoides* (>97%), but showed poor efficacy against *T. trichiura* (~20%). For hookworms, Ovis was significantly ($p < 0.05$) more efficacious compared to Bendex (98.1% vs. 88.7%). Assessment of the physicochemical quality of the drugs revealed a significant difference in dissolution profile, with Bendex having a slower dissolution than Ovis.

CONCLUSION/SIGNIFICANCE:

The study revealed that differences in efficacy between the two brands of albendazole (ABZ) tablets against hookworm are linked to the differences in the in-vitro drug release profile. Differences in uptake and metabolism of this benzimidazole drug among different helminth species may explain that this efficacy difference was only observed in hookworms and not in the two other species. The results of the present study underscore the importance of assessing the chemical and physicochemical quality of drugs before conducting efficacy assessment in any clinical trials to ensure appropriate therapeutic efficacy and to exclude poor drug quality as a factor of reduced drug efficacy other than anthelmintic resistance. Overall, this paper demonstrates that "all medicines are not created equal".

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26406600/>

[J Infect Dis.](#) 2016 Jan 15;213(2):266-75. doi: 10.1093/infdis/jiv382. Epub 2015 Jul 13.

Effect of Repeated Anthelmintic Treatment on Malaria in School Children in Kenya: A Randomized, Open-Label, Equivalence Trial.

Kepha S, Nuwaha F, Nikolay B, Gichuki P, Mwandawiro CS, Mwinzi PN, Odiere MR, Edwards T, Allen E, Brooker SJ.

Abstract

BACKGROUND:

School children living in the tropics are often concurrently infected with plasmodium and helminth parasites. It has been hypothesized that immune responses evoked by helminths may modify malaria-specific immune responses and increase the risk of malaria.

METHODS:

We performed a randomized, open-label, equivalence trial among 2436 school children in western Kenya. Eligible children were randomized to receive either 4 repeated doses or a single dose of albendazole and were followed up during 13 months to assess the incidence of clinical malaria. Secondary outcomes were Plasmodium prevalence and density, assessed by repeat cross-sectional surveys over 15 months. Analysis was conducted on an intention-to-treat basis with a prespecified equivalence range of 20%.

RESULTS:

During 13 months of follow-up, the incidence rate of malaria was 0.27 episodes/person-year in the repeated treatment group and 0.26 episodes/person-year in the annual treatment group (incidence difference, 0.01; 95% confidence interval, -.03 to .06). The prevalence and density of malaria parasitemia did not differ by treatment group at any of the cross-sectional surveys.

CONCLUSIONS:

Our findings suggest that repeated deworming does not alter risks of clinical malaria or malaria parasitemia among school children and that school-based deworming in Africa may have no adverse consequences for malaria.

<http://www.jid.oxfordjournals.org/cgi/pmidlookup?view=long&pmid=26170395>

[Cochrane Database Syst Rev.](#) 2016 Apr 14;4:CD006419. doi:

10.1002/14651858.CD006419.pub4.

Anthelmintics in helminth-endemic areas: effects on HIV disease progression.

Means AR, Burns P, Sinclair D, Walson JL.

Abstract

BACKGROUND:

Helminth infections, such as soil-transmitted helminths, schistosomiasis, onchocerciasis, and lymphatic filariasis, are prevalent in many countries where human immunodeficiency virus (HIV) infection is also common. There is some evidence from observational studies that HIV and helminth co-infection may be associated with higher viral load and lower CD4+ cell counts. Treatment of helminth infections with anthelmintics (deworming drugs) may have benefits for people living with HIV beyond simply clearance of worm infections. This is an update of a Cochrane Review published in 2009 and we have expanded it to include outcomes of anaemia and adverse events.

OBJECTIVES:

To evaluate the effects of deworming drugs (anthelmintic therapy) on markers of HIV disease progression, anaemia, and adverse events in children and adults.

SEARCH METHODS:

In this review update, we searched online for published and unpublished studies in the Cochrane Library, MEDLINE, EMBASE, CENTRAL, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), ClinicalTrials.gov, and the WHO Global Health Library up to 29 September 2015. We also searched databases listing conference abstracts, scanned reference lists of articles, and contacted the authors of included studies.

SELECTION CRITERIA:

We searched for randomized controlled trials (RCTs) that compared antihelminthic drugs with placebo or no intervention in HIV-positive people.

DATA COLLECTION AND ANALYSIS:

Two review authors independently extracted data and assessed trials for eligibility and risk of bias. The primary outcomes were changes in HIV viral load and CD4+ cell count, and secondary outcomes were anaemia, iron deficiency, adverse events, and mortality events. We compared the effects of deworming using mean differences, risk ratios (RR), and 95% confidence intervals (CIs). We assessed the quality of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

MAIN RESULTS:

Eight trials met the inclusion criteria of this review, enrolling a total of 1612 participants. Three trials evaluated the effect of providing antihelminthics to all adults with HIV without knowledge of their helminth infection status, and five trials evaluated the effects of providing deworming drugs to HIV-positive individuals with confirmed helminth infections. Seven trials were conducted in sub-Saharan Africa and one in Thailand. Antihelminthics for people with unknown helminth infection status. **Providing antihelminthics (albendazole and praziquantel together or separately) to HIV-positive adults with unknown helminth infection status may have a small suppressive effect on mean viral load at six weeks but the 95% CI includes the possibility of no effect** (difference in mean change $-0.14 \log_{10}$ viral RNA/mL, 95% CI -0.35 to 0.07 , $P = 0.19$; one trial, 166 participants, low quality evidence). Repeated dosing with deworming drugs over two years (albendazole every three months plus annual praziquantel), probably has little or no effect on mean viral load (difference in mean change $0.01 \log_{10}$ viral RNA, 95% CI: -0.03 to -0.05 ; one trial, 917 participants, moderate quality evidence), and little or no effect on mean CD4+ count (difference in mean change 2.60 CD4+ cells/ μ L, 95% CI -10.15 to 15.35 ; $P = 0.7$; one trial, 917 participants, low quality evidence). Antihelminthics for people with confirmed helminth infections. **Treating confirmed helminth infections in HIV-positive adults may have a small suppressive effect on mean viral load at six to 12 weeks following deworming** (difference in mean change $-0.13 \log_{10}$ viral RNA, 95% CI -0.26 to -0.00 ; $P = 0.04$; four trials, 445 participants, low quality evidence). However, this finding is strongly influenced by a single study of praziquantel treatment for schistosomiasis. There may also be a small favourable effect on mean CD4+ cell count at 12 weeks after deworming in HIV-positive populations with confirmed helminth infections (difference in mean change 37.86 CD4+ cells/ μ L, 95% CI 7.36 to 68.35 ; $P = 0.01$; three trials, 358 participants, low quality evidence). Adverse events and mortality. There is no indication that antihelminthic drugs impart additional risks in HIV-positive populations. However, adverse events were not well reported (very low quality evidence) and trials were underpowered to evaluate effects on mortality (low quality evidence).

AUTHORS' CONCLUSIONS:

There is low quality evidence that treating confirmed helminth infections in HIV-positive adults may have small, short-term favourable effects on markers of HIV disease progression. Further studies are required to confirm this finding. Current evidence suggests that deworming with antihelminthics is not harmful, and this is reassuring for the routine treatment of confirmed or suspected helminth infections in people living with HIV in co-endemic areas. Further long-term studies are required to make confident conclusions regarding the impact of

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presumptively deworming all HIV-positive individuals irrespective of helminth infection status, as the only long-term trial to date did not demonstrate an effect.

[Indian Pediatr.](#) 2015 Oct;52(10):847-51.

Efficacy and Safety of Drotaverine Hydrochloride in Children with Recurrent Abdominal Pain: A Randomized Placebo Controlled Trial.

[Narang M](#), [Shah D](#), [Akhtar H](#).

Abstract

OBJECTIVE:

To evaluate the efficacy and safety of Drotaverine hydrochloride in children with recurrent abdominal pain.

DESIGN:

Double blind, randomized placebo-controlled trial.

SETTING:

Pediatric Gastroenterology clinic of a teaching hospital.

PARTICIPANTS:

132 children (age 4-12 y) with recurrent abdominal pain (Apley Criteria) randomized to received drotaverine (n=66) or placebo (n=66) orally.

INTERVENTION:

Children between 4-6 years of age received 10 mL syrup orally (20 mg drotaverine hydrochloride or placebo) thrice daily for 4 weeks while children >6 years of age received one tablet orally (40 mg drotaverine hydrochloride or placebo) thrice daily for 4 weeks.

OUTCOME MEASURES:

Primary: Number of episodes of pain during 4 weeks of use of drug/placebo and number of pain-free days. Secondary: Number of school days missed during the study period, parental satisfaction (on a Likert scale), and occurrence of solicited adverse effects.

RESULTS:

Reduction in number of episodes of abdominal pain [mean (SD) number of episodes 10.3 (14) vs 21.6 (32.4); P=0.01] and lesser school absence [mean (SD) number of school days missed 0.25 (0.85) vs 0.71 (1.59); P=0.05] was noticed in children receiving drotaverine in comparison to those who received placebo. The number of pain-free days, were comparable in two groups [17.4 (8.2) vs 15.6 (8.7); P=0.23]. Significant improvement in parental satisfaction score was noticed on Likert scale by estimation of mood, activity, alertness, comfort and fluid intake. Frequency of adverse events during follow-up period was comparable between children receiving drotaverine or placebo (46.9% vs 46.7%; P=0.98).

CONCLUSION:

Drotaverine hydrochloride is an effective and safe pharmaceutical agent in the management of recurrent abdominal pain in children.

<http://www.indianpediatrics.net/oct2015/847.pdf>

Injury prevention

Integrated management of Childhood Illness (IMCI)

[BMC Pediatr.](#) 2015 Aug 28;15:103. doi: 10.1186/s12887-015-0410-z.

[Effect of integrated infectious disease training and on-site support on the management of childhood illnesses in Uganda: a cluster randomized trial.](#)

[Imani P](#), [Jakech B](#), [Kirunda I](#), [Mbonye MK](#), [Naikoba S](#), [Weaver MR](#).

Abstract

BACKGROUND:

The Integrated Infectious Disease Capacity-Building Evaluation (IDCAP) was designed to test the effects of two interventions, Integrated Management of Infectious Disease (IMID) training and on-site support (OSS), on clinical practice of mid-level practitioners. This article reports the effects of these interventions on clinical practice in management of common childhood illnesses.

METHODS:

Two trainees from each of 36 health facilities participated in the IMID training. IMID was a three-week core course, two one-week boost courses, and distance learning over nine months. Eighteen of the 36 health facilities were then randomly assigned to arm A, and participated in OSS, while the other 18 health facilities assigned to arm B did not. Clinical faculty assessed trainee practice on clinical practice of six sets of tasks: patient history, physical examination, laboratory tests, diagnosis, treatment, and patient/caregiver education. The effects of IMID were measured by the post/pre adjusted relative risk (aRR) of appropriate practice in arm B. The incremental effects of OSS were measured by the adjusted ratio of relative risks (aRRR) in arm A compared to arm B. All hypotheses were tested at a 5% level of significance.

RESULTS:

Patient samples were comparable across arms at baseline and endline. The majority of children were aged under five years; 84% at baseline and 97% at endline. The effects of IMID on patient history (aRR = 1.12; 95% CI = 1.04-1.21) and physical examination (aRR = 1.40; 95% CI = 1.16-1.68) tasks were statistically significant. OSS was associated with incremental improvement in patient history (aRRR = 1.18; 95% CI = 1.06-1.31), and physical examination (aRRR = 1.27; 95% CI = 1.02-1.59) tasks. Improvements in laboratory testing, diagnosis, treatment, and patient/caregiver education were not statistically significant.

CONCLUSION:

IMID training was associated with improved patient history taking and physical examination, and OSS further improved these clinical practices. On-site training and continuous quality improvement activities support transfer of learning to practice among mid-level practitioners. <http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26315284/>

Intravenous fluids

[Indian J Pediatr.](#) 2016 Jan;83(1):27-32. doi: 10.1007/s12098-015-1791-6. Epub 2015 Jun 2.

[Isotonic versus Hypotonic Parenteral Maintenance Fluids in Very Severe Pneumonia.](#)

[Ramanathan S](#), [Kumar P](#), [Mishra K](#), [Dutta AK](#).

Abstract

OBJECTIVE:

To compare the risk of hyponatremia between hypotonic and isotonic parenteral maintenance solutions (PMS) administered to children with very severe pneumonia, admitted in the general pediatric ward.

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METHODS:

A randomized controlled open label trial was conducted in the pediatrics department of a tertiary care medical college hospital including euvoletic children 2 mo to 5 y of age, fulfilling the WHO clinical definition of very severe pneumonia and requiring PMS. They were randomized to receive either isotonic PMS (0.9% saline in 5% dextrose and potassium chloride 20 meq/L) or hypotonic PMS (0.18% saline in 5% dextrose and potassium chloride 20 meq/L) at standard rates for next 24 h.

RESULTS:

A total of 119 children were randomized (59: Isotonic; 60: Hypotonic PMS). **Nine (15%) children in the isotonic PMS group and 29 (48%) in the hypotonic PMS group developed hyponatremia during the study period, ($p < 0.001$) with a relative risk being 3.16 (95% CI 1.64 to 6.09).** Mean serum sodium was significantly lower in the hypotonic group compared to the isotonic group ($p < 0.001$ each at 6, 12 and 24 h). The difference in mean change in serum sodium from baseline was also significant at 12 and 24 h (5.4 and 5.8 meq/L respectively; $p < 0.001$ each).

CONCLUSIONS:

This study demonstrates the rationality of the use of isotonic PMS in children with respiratory infections, a condition regularly encountered by most pediatricians.

[Indian Pediatr.](#) 2015 Nov;52(11):965-72.

Mortality and Other Outcomes in Relation to First Hour Fluid Resuscitation Rate: A Systematic Review.

[Tripathi A](#), [Kabra SK](#), [Sachdev HP](#), [Lodha R](#).

Abstract

OBJECTIVE:

To determine the effect of different regimen of first hour fluid administration rates on mortality and severe consequences of impaired circulation in 2 to 60 months old children with impaired circulation.

DESIGN:

Systematic review of randomized controlled trials.

DATA SOURCES:

Various databases including PubMed, Cochrane Library and EMBASE were searched.

RESULTS:

We found only two relevant trials; one was excluded as there was no comparator arm. Only one study (The FEAST Trial) compared boluses with maintenance fluid alone in children with severe febrile illness and one or more signs of impaired perfusion. The 48 hour mortality was more in the bolus group (RR 1.45, 95% CI 1.13, 1.86). The quality of evidence is rated as moderate. For the children who met the WHO criteria for shock (severely impaired circulation) ($n=65$ children), those receiving boluses had higher mortality (RR 2.40, 95% CI 0.84, 6.88); the quality of evidence was rated as very low.

CONCLUSION:

A single large randomized controlled trial conducted in low-resource settings indicates that administration of fluid bolus is associated with higher mortality in comparison to the maintenance fluids alone in children with severe febrile illness and one or more signs of impaired perfusion. The findings are not generalizable to contexts with different severity of and different causes of shock and in centers with better facilities. There is urgent need for research in different settings to determine the optimal rate of fluid resuscitation in the first hour in children presenting with impaired circulation, particularly with severely impaired circulation.

<http://www.indianpediatrics.net/nov2015/965.pdf>

Kidney disease

[Br J Clin Pharmacol](#). 2015 Aug;80(2):242-52. doi: 10.1111/bcp.12607. Epub 2015 Jun 5.

Population pharmacokinetics of levamisole in children with steroid-sensitive nephrotic syndrome.

[Kreeftmeijer-Vegter AR](#), [Dorlo TP](#), [Gruppen MP](#), [de Boer A](#), [de Vries PJ](#).

Abstract

AIM:

The aim was to investigate the population pharmacokinetics of levamisole in children with steroid-sensitive nephrotic syndrome.

METHODS:

Non-linear mixed effects modelling was performed on samples collected during a randomized controlled trial. Samples were collected from children who were receiving 2.5 mg kg⁻¹ levamisole (or placebo) orally once every other day. One hundred and thirty-six plasma samples were collected from 38 children from India and Europe and included in the analysis. A one compartment model described the data well.

RESULTS:

The apparent clearance rate (CL/F) and distribution volume (V/F) were 44 l h⁻¹ 70 kg⁻¹ and 236 l 70 kg⁻¹, respectively; estimated interindividual variability was 32-42%. In addition to allometric scaling of CL/F and V/F to body weight, we identified a significant proportional effect of age on CL/F (-10.1% per year). The pharmacokinetics parameters were not affected by gender, tablet strength or study centre. The median (interquartile range) maximum plasma concentration of levamisole was 438.3 (316.5-621.8) ng ml⁻¹, and the median area under the concentration-time curve was 2847 (2267-3761) ng ml⁻¹ h. Median t_{max} and t_{1/2} values were 1.65 (1.32-2.0) h and 2.60 (2.06-3.65) h, respectively.

CONCLUSIONS:

Here, we present the first pharmacokinetic data regarding levamisole in children with steroid-sensitive nephrotic syndrome. The pharmacokinetic profile of levamisole in children was similar to findings reported in adults, although the elimination rate was slightly higher in children.

Leishmaniasis

[Am J Trop Med Hyg](#). 2016 Jan;94(1):93-8. doi: 10.4269/ajtmh.14-0657. Epub 2015 Nov 2.

Short-Course Treatment Regimen of Indian Visceral Leishmaniasis with an Indian Liposomal Amphotericin B Preparation (Fungisome™).

[Goswami RP](#), [Goswami RP](#), [Das S](#), [Satpati A](#), [Rahman M](#).

Abstract

India bears the burden of about half of global visceral leishmaniasis (VL) cases with emerging problems of stibionate resistance. Liposomal preparations have improved treatment outcome through shorter duration of therapy and lower toxicity compared with conventional amphotericin B. We report the efficacy of two short-course regimens of an Indian preparation of liposomal amphotericin B (Fungisome™) for VL caused by *Leishmania donovani* in India. An open-label, randomized, single-center comparative study was undertaken from 2008 to 2011,

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involving 120 treatment naive non-human immunodeficiency virus VL patients randomly allocated to two groups. Fungisome™ was given, in groups A (N = 60), 5 mg/kg daily for 2 days and B (N = 60), 7.5 mg/kg daily for 2 days, as intravenous infusion. Initial cure rate was 100% in both the groups after 1 month posttreatment. **At 6 months after completion of treatment, definitive cure rate was group A 90% (54/60, 95% confidence interval (CI): 80.55-95.72%); group B: 100% (95% CI: 95.92-100%); (P = 0.027).** No serious adverse events occurred in either group. The short-course, 2-day regimen of 15 mg/kg Fungisome™ infusion is easy to administer, effective, and safe for treatment of VL caused by *L. donovani* in India.

[Am J Trop Med Hyg.](#) 2015 Oct;93(4):767-9. doi: 10.4269/ajtmh.14-0721. Epub 2015 Jul 14.
[Inadequacy of 12-Week Miltefosine Treatment for Indian Post-Kala-Azar Dermal Leishmaniasis.](#)

[Ghosh S](#), [Das NK](#), [Mukherjee S](#), [Mukhopadhyay D](#), [Barbhuiya JN](#), [Hazra A](#), [Chatterjee M](#).

Abstract

Post-kala-azar dermal leishmaniasis (PKDL) is a chronic dermatosis that generally occurs after apparent cure of visceral leishmaniasis caused by *Leishmania donovani*. In view of the prolonged treatment regimens necessary for PKDL, noncompliance is a major limitation; an optimal regimen is yet to be defined, but 12 weeks of therapy with miltefosine is generally recommended. We performed a single-arm open-label trial of miltefosine administered daily for 16 weeks in 27 patients in Kolkata with PKDL. After 4 weeks of treatment, nine patients were lost to follow-up because of unacceptable side effects, including severe abdominal pain, nausea, and vomiting. Of the 18 remaining patients, seven completed 12 weeks of therapy and 11 completed 16 weeks of therapy. Three of the seven who received 12 weeks of therapy and none of the 11 who received 16 weeks of therapy experienced disease relapse. Our results suggest that **a 16-week course of miltefosine is required for reliable cure of PKDL.** Further, the study highlighted the urgent need for a multicentric randomized controlled trial of 12 versus 16 weeks of treatment with miltefosine for PKDL so as to achieve the goal of elimination of leishmaniasis in south Asia.

Leprosy

[Indian J Dermatol Venereol Leprol.](#) 2015 Jul-Aug;81(4):356-62. doi: 10.4103/0378-6323.159929.

[A randomized controlled trial to compare cure and relapse rate of paucibacillary multidrug therapy with monthly rifampicin, ofloxacin, and minocycline among paucibacillary leprosy patients in Agra District, India.](#)

[Kumar A](#), [Girdhar A](#), [Girdhar BK](#).

Abstract

OBJECTIVES:

To study cure rate and relapse rate of **standard World Health Organization paucibacillary multidrug therapy (PB-MDT) with monthly rifampicin, ofloxacin, and minocycline for six months (ROM-6)** among paucibacillary leprosy patients.

METHODS:

Randomised trials in child health in developing countries 2015-16

A total of 268 patients, detected during active search in Agra district during 2001-2004, who had paucibacillary (PB) leprosy having 1-5 skin lesions and/or one nerve thickening/tenderness, were allocated, using random number tables, to two treatment groups; PB-MDT and ROM-6. On the first day of the month, dose of PB-MDT and of the ROM were given under supervision for 6 months. After completion of drug therapy, patients were followed every 6 months for first 5 years and later annually for next 3 years for monitoring disease status, cure rates, reactions and relapses.

RESULTS:

The cure rate at 2 years was 99% in ROM-6 and 97.0% in PB-MDT group, of those who completed treatment and the difference was statistically not significant. At 5 years, only 88 patients in PB-MDT group and 90 patients in ROM-6 group could be followed; all were observed to be cured. However, during the period of 5-8 years, 3 of 67 patients in PB-MDT group and 1 of 73 in ROM-6 group were observed to have relapsed. In all, 10 relapses were noted (3 in ROM-6 and 7 in PB-MDT group) giving a relapse rate of 1.10/100 person years in PB-MDT and 0.435/100 person years in ROM groups ($P = 0.053$; statistically not significant). Of the 10 relapses, 5 occurred within 5 years (3 in PB-MDT group and 2 in ROM-6), 4 during 5-8 years (3 in PB-MDT and 1 in ROM-6), and 1 occurred in MDT group after 8 years.

LIMITATION:

A number of patients were lost to follow up after release from treatment and thus actual number of relapses in the study could not be assessed. Additionally, diagnosis was purely clinical and histology could not be done for reasons related to functional difficulties in the field.

CONCLUSION:

The study shows that PB-MDT and ROM-6 have almost similar acceptability, cure rate and relapse rate.

Malaria

(See also Maternal health, Anaemia)

Diagnosis

[PLoS One](#). 2016 Apr 7;11(4):e0152960. doi: 10.1371/journal.pone.0152960. eCollection 2016.

[Effect of Test-Based versus Presumptive Treatment of Malaria in Under-Five Children in Rural Ghana - A Cluster-Randomised Trial.](#)

[Baiden F](#), [Bruce J](#), [Webster J](#), [Tivura M](#), [Delmini R](#), [Amengo-Etego S](#), [Owusu-Agyei S](#), [Chandramohan D](#).

Abstract

BACKGROUND:

Malaria-endemic countries in sub-Saharan Africa are shifting from the presumptive approach that is based on clinical judgement (CJ) to the test-based approach that is based on confirmation through test with rapid diagnostic tests (RDT). It has been suggested that the loss of the prophylactic effect of presumptive-administered ACT in children who do not have malaria will result in increase in their risk of malaria and anaemia.

METHODS AND FINDINGS:

We undertook a cluster-randomized controlled trial to compare the effects of the presumptive approach using clinical judgment (CJ-arm) and the test-based approach using RDTs (RDT-arm) in a high-transmission setting in Ghana. **A total of 3046 eligible children (1527 in the RDT**

Randomised trials in child health in developing countries 2015-16

arm and 1519 in the CJ- arm) living around 32 health centres were enrolled. Nearly half were female (48.7%) and 47.8% were below the age of 12 months as at enrolment. **Over 24-months, the incidence of all episodes of malaria following the first febrile illness was 0.64 (95% CI 0.49-0.82) and 0.76 (0.63-0.93) per child per year in the RDT and CJ arms respectively (adjusted rate ratio 1.13 (0.82-1.55)).** After the first episode of febrile illness, the incidence of severe anaemia was the same in both arms (0.11 per child per year) and that of moderate anaemia was 0.16 (0.13-0.21) vs. 0.17 (0.14-0.21) per child year respectively. The incidence of severe febrile illness was 0.15 (0.09, 0.24) in the RDT arm compared to 0.17 (0.11, 0.28) per child per year respectively. The proportion of fever cases receiving ACT was lower in the RDT arm (72% vs 81%; $p = 0.02$).

CONCLUSION:

The test-based approach to the management of malaria did not increase the incidence of malaria or anaemia among under-five children in this setting.

Insecticide-treated bed nets

Other preventative interventions

(See also: Vaccines – malaria vaccine)

[Antimicrob Agents Chemother.](#) 2015 Aug;59(8):4387-96. doi: 10.1128/AAC.04923-14. Epub 2015 Apr 27.

[Randomized Noninferiority Trial of Dihydroartemisinin-Piperaquine Compared with Sulfadoxine-Pyrimethamine plus Amodiaquine for Seasonal Malaria Chemoprevention in Burkina Faso.](#)

[Zongo I](#), [Milligan P](#), [Compaore YD](#), [Some AF](#), [Greenwood B](#), [Tarning J](#), [Rosenthal PJ](#), [Sutherland C](#), [Nosten F](#), [Ouedraogo JB](#).

Abstract

The WHO recommends that children living in areas of highly seasonal malaria transmission in the Sahel subregion should receive seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine plus amodiaquine (SPAQ). **We evaluated the use of dihydroartemisinin-piperaquine (DHAPQ) as an alternative drug that could be used if SPAQ starts to lose efficacy.** A total of 1,499 children 3 to 59 months old were randomized to receive SMC with SPAQ or DHAPQ over 3 months. The primary outcome measure was the risk of clinical malaria (fever or a history of fever with a parasite density of at least 3,000/ μ l). A cohort of 250 children outside the trial was followed up as a control group. Molecular markers of drug resistance were assessed. **The risk of a malaria attack was 0.19 in the DHAPQ group and 0.15 in the SPAQ group, an odds ratio of 1.33 (95% confidence interval [CI], 1.02 to 1.72).** Efficacy of SMC compared to the control group was 77% (67% to 84%) for DHAPQ and 83% (74% to 89%) for SPAQ. *pf*dhfr and *pf*dhps mutations associated with antifolate resistance were more prevalent in parasites from children who received SPAQ than in children who received DHAPQ. Both regimens were highly efficacious and well tolerated. DHAPQ is a potential alternative drug for SMC. (This trial is registered at ClinicalTrials.gov under registration no. [NCT00941785](#)).

<http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/25918149/>

[Trials](#). 2015 Aug 13;16:347. doi: 10.1186/s13063-015-0862-3.

Assessing the effectiveness of household-level focal mass drug administration and community-wide mass drug administration for reducing malaria parasite infection prevalence and incidence in Southern Province, Zambia: study protocol for a community randomized controlled trial.

[Eisele TP](#), [Silumbe K](#), [Finn T](#), [Chalwe V](#), [Kamuliwo M](#), [Hamainza B](#), [Moonga H](#), [Bennett A](#), [Yukich J](#), [Keating J](#), [Steketee RW](#), [Miller JM](#).

Abstract

BACKGROUND:

Mass drug administration (MDA) and focal MDA (fMDA) using dihydroartemisinin plus piperazine (DHAp), represent two strategies to maximize the use of existing information to achieve greater clearance of human infection and reduce the parasite reservoir, and provide longer chemoprophylactic protection against new infections. The primary aim of this study is to quantify the relative effectiveness of MDA and fMDA with DHAp against no mass treatment (standard of care) for reducing *Plasmodium falciparum* prevalence and incidence.

METHODS/DESIGN:

The study will be conducted along Lake Kariba in Southern Province, Zambia; an area of low to moderate malaria transmission and high coverage of vector control. A community randomized controlled trial (CRCT) of 60 health facility catchment areas (HFCAs) will be used to evaluate the impact of two rounds of MDA and fMDA interventions, relative to a control of no mass treatment, stratified by high and low transmission. Community residents in MDA HFCAs will be treated with DHAp at the end of the dry season (round one: November to December 2014) and the beginning of the rainy season (round two: February to March 2015). Community residents in fMDA HFCAs will be tested during the same two rounds for malaria parasites with a rapid diagnostic test; all positive individuals and all individuals living in their household will be treated with DHAp. Primary outcomes include malaria parasite prevalence (n = 5,640 children aged one month to under five-years-old), as measured by pre- and post-surveys, and malaria parasite infection incidence (n = 2,250 person-years among individuals aged three months and older), as measured by a monthly longitudinal cohort. The study is powered to detect approximately a 50 % relative reduction in these outcomes between each intervention group versus the control.

DISCUSSION:

Strengths of this trial include: a robust study design (CRCT); cross-sectional parasite surveys as well as a longitudinal cohort; and stratification of high and low transmission areas. Primary limitations include: statistical power to detect only a 50 % reduction in primary outcomes within high and low transmission strata; potential for contamination; and potential for misclassification of exposure.

<http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26268804/>

Treatment of uncomplicated malaria

[Lancet Infect Dis](#). 2015 Dec;15(12):1409-19. doi: 10.1016/S1473-3099(15)00079-1. Epub 2015 Sep 3.

Ferroquine and artesunate in African adults and children with Plasmodium falciparum malaria: a phase 2, multicentre, randomised, double-blind, dose-ranging, non-inferiority study.

[Held J](#), [Supan C](#), [Salazar CL](#), [Tinto H](#), [Bonkian LN](#), [Nahum A](#), [Moulero B](#), [Sié A](#), [Coulibaly B](#), [Sirima SB](#), [Siribie M](#), [Otsyula N](#), [Otieno L](#), [Abdallah AM](#), [Kimutai R](#), [Bouyou-Akotet M](#), [Kombila M](#), [Koiwai K](#), [Cantalloube C](#), [Din-Bell C](#), [Djeriou E](#), [Waitumbi J](#), [Mordmüller B](#), [Ter-Minassian D](#), [Lell B](#), [Kremsner PG](#).

Abstract

BACKGROUND:

Artemisinin-based combination therapies (ACTs) are the recommended first-line treatment for uncomplicated Plasmodium falciparum malaria. **Ferroquine is a new combination partner for fast-acting ACTs such as artesunate.** We aimed to assess different doses of ferroquine in combination with artesunate against uncomplicated P falciparum malaria in a heterogeneous population in Africa.

METHODS:

We did a phase 2, multicentre, parallel-group, double-blind, randomised, dose-ranging non-inferiority trial at eight African hospitals (two in Gabon, three in Burkina Faso, one in Benin, and two in Kenya). We recruited patients presenting with acute P falciparum mono-infection (1000-200,000 parasites per μL), and a central body temperature of at least 37.5°C or history of fever in the past 24 h. We assessed patients in two sequential cohorts: cohort 1 contained adults (bodyweight >50 kg) and adolescents (aged ≥ 14 years, >30 kg), and cohort 2 contained children (aged 2-13 years, 15-30 kg). **We randomly assigned patients (1:1:1:1) to receive artesunate 4 mg/kg per day plus ferroquine 2 mg/kg, 4 mg/kg, or 6 mg/kg, given double-blind once per day for 3 days, or ferroquine monotherapy 4 mg/kg per day given single-blind (ie, allocation was only masked from the patient) once per day for 3 days.** We did 14 patient visits (screening, 3 treatment days and 48 h post-treatment surveillance, a visit on day 7, then one follow-up visit per week until day 63). The primary endpoint was non-inferiority of treatment in terms of PCR-corrected cure rate against a reference value of 90%, with a 10% non-inferiority margin, assessed in patients treated without major protocol deviations for parasitologically confirmed malaria. We assessed safety in all treated patients. This study is registered with ClinicalTrials.gov, number [NCT00988507](#), and is closed.

FINDINGS:

Between Oct 16, 2009, and Sept 22, 2010, we randomly assigned 326 eligible patients to treatment groups, with last follow-up visit on Dec 1, 2010. 284 patients (87%) were available for per-protocol analyses. At day 28, PCR-confirmed cure was noted in 68 (97%, 95% CI 90-100) of 70 patients treated with ferroquine 2 mg/kg plus artesunate, 73 (99%, 93-100) of 74 with ferroquine 4 mg/kg plus artesunate, 71 (99%, 93-100) of 72 with ferroquine 6 mg/kg plus artesunate, and 54 (79%, 68-88) of 68 with ferroquine 4 mg/kg monotherapy. The three dose groups of ferroquine plus artesunate met the non-inferiority hypothesis. The most common adverse events were headache in cohort 1 (30 [19%] of 162 patients) and worsening malaria in cohort 2 (23 [14%] of 164 patients); occurrences were similar between treatment groups.

INTERPRETATION:

Ferroquine combined with artesunate was associated with high cure rates and was safe at all doses tested, and could be a promising new drug combination for the treatment of P falciparum malaria. Ferroquine could also partner other drugs to establish a new generation of antimalarial combinations, especially in regions that have developed resistance to ACTs.

[http://linkinghub.elsevier.com/retrieve/pii/S1473-3099\(15\)00079-1](http://linkinghub.elsevier.com/retrieve/pii/S1473-3099(15)00079-1)

[Malar J.](#) 2015 Aug 20;14:325. doi: 10.1186/s12936-015-0843-8.

Effectiveness and safety of artemether-lumefantrine versus artesunate-amodiaquine for unsupervised treatment of uncomplicated falciparum malaria in patients of all age groups in Nanoro, Burkina Faso: a randomized open label trial.

[Sondo P](#), [Derra K](#), [Diallo-Nakanabo S](#), [Tarnagda Z](#), [Zampa O](#), [Kazienga A](#), [Valea I](#), [Sorgho H](#), [Owusu-Dabo E](#), [Ouedraogo JB](#), [Guiguemde TR](#), [Tinto H](#).

Abstract

BACKGROUND:

Several studies have reported high efficacy and safety of artemisinin-based combination therapy (ACT) mostly under strict supervision of drug intake and limited to children less than 5 years of age. Patients over 5 years of age are usually not involved in such studies. Thus, the findings do not fully reflect the reality in the field. This study aimed to assess the effectiveness and safety of ACT in routine treatment of uncomplicated malaria among patients of all age groups in Nanoro, Burkina Faso.

METHODS:

A randomized open label trial comparing artesunate-amodiaquine (ASAQ) and artemether-lumefantrine (AL) was carried out from September 2010 to October 2012 at two primary health centres (Nanoro and Nazoanga) of Nanoro health district. **A total of 680 patients were randomized to receive either ASAQ or AL without any distinction by age.** Drug intake was not supervised as pertains in routine practice in the field. Patients or their parents/guardians were advised on the time and mode of administration for the 3 days treatment unobserved at home. Follow-up visits were performed on days 3, 7, 14, 21, and 28 to evaluate clinical and parasitological resolution of their malaria episode as well as adverse events. PCR genotyping of merozoite surface proteins 1 and 2 (msp-1, msp-2) was used to differentiate recrudescence and new infection.

RESULTS:

By day 28, the PCR corrected adequate clinical and parasitological response was 84.1 and 77.8 % respectively for ASAQ and AL. The cure rate was higher in older patients than in children under 5 years old. The risk of re-infection by day 28 was higher in AL treated patients compared with those receiving ASAQ ($p < 0.00001$). Both AL and ASAQ treatments were well tolerated.

CONCLUSION:

This study shows a lowering of the efficacy when drug intake is not directly supervised. This is worrying as both rates are lower than the critical threshold of 90% required by the WHO to recommend the use of an anti-malarial drug in a treatment policy.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26289949/>

[Malar J.](#) 2015 Aug 19;14:320. doi: 10.1186/s12936-015-0825-x.

Development of a text-messaging intervention to improve treatment adherence and post-treatment review of children with uncomplicated malaria in western Kenya.

[Githinji S](#), [Jones C](#), [Malinga J](#), [Snow RW](#), [Talisuna A](#), [Zurovac D](#).

Abstract

BACKGROUND:

Randomised trials in child health in developing countries 2015-16

Patients' low adherence to artemisinin-based combination therapy has been reported in areas of Kenya bordering the Lake Victoria region, where the burden of malaria remains high.

A randomized controlled trial is underway to determine the efficacy of short message service (SMS) text reminders on adherence to artemether-lumefantrine and post-treatment review of children under the age of five. This paper reports on the iterative process of intervention and delivery system development.

METHODS:

An intervention development workshop involving the research team and other stakeholders was held to determine the content of the text messages. Three focus group discussions were conducted to test caregivers' understanding of the messages developed during the workshop. The tested messages were refined and incorporated into an automated SMS distribution system and piloted with 20 caregivers drawn from facilities neighbouring the study sites. The automated SMS distribution system was repeatedly refined following the pilot and implemented at the start of the trial.

RESULTS:

The content of SMS messages underwent major revisions following the focus group discussions. Technical terms and abbreviations were replaced with simplified general terms. Message sign-off was modified to reflect the name of health facility, removing references to health workers. Day 3 post-treatment review visit reminder was modified to state the purpose of the visit while wording 'day 28' was added to the last post-treatment review visit reminder to help the caregiver recall the appointment date. The unscheduled visit prompt was modified to reflect flexibility and practicality of taking the child back to the facility if unwell. Reception of SMS reminders during the pilot was low with only 169/240 (70%) of scheduled messages delivered to the caregivers. The automated distribution system underwent major refinement and repeated testing following the pilot until effective delivery of all scheduled messages was achieved and sustained over a period of 3 months.

CONCLUSIONS:

Text message interventions should be carefully developed, tested and refined before implementation to ensure they are written in the most appropriate way for their target population. SMS distribution systems should be rigorously tested to ensure efficient delivery of the messages before they are deployed.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26283229/>

Treatment of severe or complicated malaria

PLoS Med. 2016 Jan 12;13(1):e1001938. doi: 10.1371/journal.pmed.1001938. eCollection 2016.

Intramuscular Artesunate for Severe Malaria in African Children: A Multicenter Randomized Controlled Trial.

[Kremsner PG](#), [Adegnika AA](#), [Hounkpatin AB](#), [Zinsou JF](#), [Taylor TE](#), [Chimalizeni Y](#), [Liomba A](#), [Kombila M](#), [Bouyou-Akotet MK](#), [Mawili Mboumba DP](#), [Agbenyega T](#), [Ansong D](#), [Sylverken J](#), [Ogotu BR](#), [Otieno GA](#), [Wangwe A](#), [Bojang KA](#), [Okomo U](#), [Sanya-Isijola F](#), [Newton CR](#), [Njuguna P](#), [Kazungu M](#), [Kerb R](#), [Geditz M](#), [Schwab M](#), [Velavan TP](#), [Nguetse C](#), [Köhler C](#), [Issifou S](#), [Bolte S](#), [Engleitner T](#), [Mordmüller B](#), [Krishna S](#).

Abstract

BACKGROUND:

Randomised trials in child health in developing countries 2015-16

Current artesunate (ARS) regimens for severe malaria are complex. Once daily intramuscular (i.m.) injection for 3 d would be simpler and more appropriate for remote health facilities than the current WHO-recommended regimen of five intravenous (i.v.) or i.m. injections over 4 d. We compared both a three-dose i.m. and a three-dose i.v. parenteral ARS regimen with the standard five-dose regimen using a non-inferiority design (with non-inferiority margins of 10%).

METHODS AND FINDINGS:

This randomized controlled trial included children (0.5-10 y) with severe malaria at seven sites in five African countries to assess whether the efficacy of simplified three-dose regimens is non-inferior to a five-dose regimen. **We randomly allocated 1,047 children to receive a total dose of 12 mg/kg ARS as either a control regimen of five i.m. injections of 2.4 mg/kg (at 0, 12, 24, 48, and 72 h) (n = 348) or three injections of 4 mg/kg (at 0, 24, and 48 h) either i.m. (n = 348) or i.v. (n = 351), both of which were the intervention arms. The primary endpoint was the proportion of children with $\geq 99\%$ reduction in parasitemia at 24 h from admission values, measured by microscopists who were blinded to the group allocations.** Primary analysis was performed on the per-protocol population, which was 96% of the intention-to-treat population. Secondary analyses included an analysis of host and parasite genotypes as risks for prolongation of parasite clearance kinetics, measured every 6 h, and a Kaplan-Meier analysis to compare parasite clearance kinetics between treatment groups. A post hoc analysis was performed for delayed anemia, defined as hemoglobin ≤ 7 g/dl 7 d or more after admission. The per-protocol population was 1,002 children (five-dose i.m.: n = 331; three-dose i.m.: n = 338; three-dose i.v.: n = 333); 139 participants were lost to follow-up. **In the three-dose i.m. arm, 265/338 (78%) children had a $\geq 99\%$ reduction in parasitemia at 24 h compared to 263/331 (79%) receiving the five-dose i.m. regimen, showing non-inferiority of the simplified three-dose regimen to the conventional five-dose regimen (95% CI -7, 5; p = 0.02).** In the three-dose i.v. arm, 246/333 (74%) children had $\geq 99\%$ reduction in parasitemia at 24 h; hence, non-inferiority of this regimen to the five-dose control regimen was not shown (95% CI -12, 1; p = 0.24). Delayed parasite clearance was associated with the N86YPfmdr1 genotype. **In a post hoc analysis, 192/885 (22%) children developed delayed anemia, an adverse event associated with increased leukocyte counts.** There was no observed difference in delayed anemia between treatment arms. A potential limitation of the study is its open-label design, although the primary outcome measures were assessed in a blinded manner.

CONCLUSIONS:

A simplified three-dose i.m. regimen for severe malaria in African children is non-inferior to the more complex WHO-recommended regimen. Parenteral ARS is associated with a risk of delayed anemia in African children.

<http://dx.plos.org/10.1371/journal.pmed.1001938>

Treatment of vivax malaria

PLoS Med. 2015 Oct 27;12(10):e1001891. doi: 10.1371/journal.pmed.1001891. eCollection 2015.

[Strategies for understanding and reducing the Plasmodium vivax and Plasmodium ovale hypnozoite reservoir in Papua New Guinean children: a randomised placebo-controlled trial and mathematical model.](#)

Randomised trials in child health in developing countries 2015-16

[Robinson LJ](#), [Wampfler R](#), [Betuela I](#), [Karl S](#), [White MT](#), [Li Wai Suen CS](#), [Hofmann NE](#), [Kinboro B](#), [Waltmann A](#), [Brewster J](#), [Lorry L](#), [Tarongka N](#), [Samol L](#), [Silkey M](#), [Bassat Q](#), [Siba PM](#), [Schofield L](#), [Felger I](#), [Mueller I](#).

Abstract

BACKGROUND:

The undetectable hypnozoite reservoir for relapsing *Plasmodium vivax* and *P. ovale* malariae presents a major challenge for malaria control and elimination in endemic countries. This study aims to directly determine the contribution of relapses to the burden of *P. vivax* and *P. ovale* infection, illness, and transmission in Papua New Guinean children.

METHODS AND FINDINGS:

From 17 August 2009 to 20 May 2010, 524 children aged 5-10 y from East Sepik Province in Papua New Guinea (PNG) participated in a randomised double-blind placebo-controlled trial of **blood- plus liver-stage drugs (chloroquine [CQ], 3 d; artemether-lumefantrine [AL], 3 d; and primaquine [PQ], 20 d, 10 mg/kg total dose) (261 children) or blood-stage drugs only (CQ, 3 d; AL, 3 d; and placebo [PL], 20 d) (263 children)**. Participants, study staff, and investigators were blinded to the treatment allocation. Twenty children were excluded during the treatment phase (PQ arm: 14, PL arm: 6), and 504 were followed actively for 9 mo. During the follow-up time, 18 children (PQ arm: 7, PL arm: 11) were lost to follow-up. **Main primary and secondary outcome measures were time to first *P. vivax* infection (by qPCR), time to first clinical episode, force of infection, gametocyte positivity, and time to first *P. ovale* infection (by PCR)**. A basic stochastic transmission model was developed to estimate the potential effect of mass drug administration (MDA) for the prevention of recurrent *P. vivax* infections. **Targeting hypnozoites through PQ treatment reduced the risk of having at least one qPCR-detectable *P. vivax* or *P. ovale* infection during 8 mo of follow-up** (*P. vivax*: PQ arm 0.63/y versus PL arm 2.62/y, HR = 0.18 [95% CI 0.14, 0.25], $p < 0.001$; *P. ovale*: 0.06 versus 0.14, HR = 0.31 [95% CI 0.13, 0.77], $p = 0.011$) and the risk of having at least one clinical *P. vivax* episode (HR = 0.25 [95% CI 0.11, 0.61], $p = 0.002$). PQ also reduced the molecular force of *P. vivax* blood-stage infection in the first 3 mo of follow-up (PQ arm 1.90/y versus PL arm 7.75/y, incidence rate ratio [IRR] = 0.21 [95% CI 0.15, 0.28], $p < 0.001$). **Children who received PQ were less likely to carry *P. vivax* gametocytes (IRR = 0.27 [95% CI 0.19, 0.38], $p < 0.001$)**. PQ had a comparable effect irrespective of the presence of *P. vivax* blood-stage infection at the time of treatment ($p = 0.14$). Modelling revealed that mass screening and treatment with highly sensitive quantitative real-time PCR, or MDA with blood-stage treatment alone, would have only a transient effect on *P. vivax* transmission levels, while MDA that includes liver-stage treatment is predicted to be a highly effective strategy for *P. vivax* elimination. The inclusion of a directly observed 20-d treatment regime maximises the efficiency of hypnozoite clearance but limits the generalisability of results to real-world MDA programmes.

CONCLUSIONS:

These results suggest that **relapses cause approximately four of every five *P. vivax* infections and at least three of every five *P. ovale* infections in PNG children and are important in sustaining transmission**. MDA campaigns combining blood- and liver-stage treatment are predicted to be a highly efficacious intervention for reducing *P. vivax* and *P. ovale* transmission. <http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26505753/>

[Clin Infect Dis](#). 2016 Jun 1;62(11):1403-11. doi: 10.1093/cid/ciw121. Epub 2016 Apr 22.

[Efficacy of Artesunate-mefloquine for Chloroquine-resistant Plasmodium vivax Malaria in Malaysia: An Open-label, Randomized, Controlled Trial.](#)

Randomised trials in child health in developing countries 2015-16

[Grigg MJ](#), [William T](#), [Menon J](#), [Barber BE](#), [Wilkes CS](#), [Rajahram GS](#), [Edstein MD](#), [Auburn S](#), [Price RN](#), [Yeo TW](#), [Anstey NM](#).

Abstract

BACKGROUND:

Chloroquine (CQ)-resistant *Plasmodium vivax* is increasingly reported throughout southeast Asia. The efficacy of CQ and alternative artemisinin combination therapies (ACTs) for vivax malaria in Malaysia is unknown.

METHODS:

A randomized, controlled trial of CQ vs artesunate-mefloquine (AS-MQ) for uncomplicated vivax malaria was conducted in 3 district hospitals in Sabah, Malaysia. Primaquine was administered on day 28. The primary outcome was the cumulative risk of treatment failure by day 28 by Kaplan-Meier analysis.

RESULTS:

From 2012 to 2014, 103 adults and children were enrolled. **Treatment failure by day 28 was 61.1% (95% confidence interval [CI], 46.8-75.6) after CQ and 0% (95% CI, 0-.08) following AS-MQ (P < .001)**, of which 8.2% (95% CI, 2.5-9.6) were early treatment failures. All patients with treatment failure had therapeutic plasma CQ concentrations at day 7. Compared with CQ, AS-MQ was associated with faster parasite clearance (normalized clearance slope, 0.311 vs 0.127; P < .001) and fever clearance (mean, 19.0 vs 37.7 hours; P = .001) and with lower risk of anemia at day 28 (odds ratio = 3.7; 95% CI, 1.5-9.3; P = .005). Gametocytes were present at day 28 in 23.8% (10/42) of patients following CQ vs none with AS-MQ (P < .001). AS-MQ resulted in lower bed occupancy: 4037 vs 6510 days/1000 patients (incidence rate ratio 0.62; 95% CI, .60-.65; P < .001). One patient developed severe anemia not regarded as related to their AS-MQ treatment.

CONCLUSIONS:

High-grade CQ-resistant *P. vivax* is prevalent in eastern Malaysia. AS-MQ is an efficacious ACT for all malaria species. Wider CQ-efficacy surveillance is needed in vivax-endemic regions with earlier replacement with ACT when treatment failure is detected. Clinical Trials

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4872287/>

Malnutrition

(Papers listed in this section refer to the management of protein-energy malnutrition. For other relevant studies of nutrition see also Nutrition, Vitamin A, Vitamin D, Zinc, Maternal health, Anaemia and iron deficiency)

[J Nutr](#). 2015 Nov;145(11):2604-9. doi: 10.3945/jn.115.214957. Epub 2015 Sep 30.

Severe and Moderate Acute Malnutrition Can Be Successfully Managed with an Integrated Protocol in Sierra Leone.

[Maust A](#), [Koroma AS](#), [Abla C](#), [Molokwu N](#), [Ryan KN](#), [Singh L](#), [Manary MJ](#).

Abstract

BACKGROUND:

Global acute malnutrition (GAM) is the sum of moderate acute malnutrition (MAM) and severe acute malnutrition (SAM). The use of different foods and protocols for MAM and SAM treatment can be cumbersome in emergency settings.

OBJECTIVE:

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Our objective was to determine the recovery and coverage rates for GAM of an integrated protocol with a single food product, ready-to-use therapeutic food (RUTF), compared with standard management.

METHODS:

This was a cluster-randomized controlled trial in Sierra Leone conducted in 10 centers treating GAM in children aged 6-59 mo. **The integrated protocol used mid-upper arm circumference (MUAC) as the criterion for admission and discharge, with a MUAC <12.5 cm defining malnutrition.** The protocol included a decreasing ration of RUTF and health maintenance messages delivered by peers. Standard therapy treated MAM with a fortified blended flour and SAM with RUTF and used weight-for-height to determine admission to the treatment program. Coverage rates were the number of children who received treatment/number of children in the community eligible for treatment.

RESULTS:

Most of the children receiving integrated management had MAM (774 of 1100; 70%), whereas among those receiving standard management, SAM predominated (537 of 857; 63%; $P = 0.0001$). Coverage was 71% in the communities served by integrated management and 55% in the communities served by standard care ($P = 0.0005$). GAM recovery in the integrated management protocol was 910 of 1100 (83%) children and was 682 of 857 (79%) children in the standard therapy protocol.

CONCLUSION:

Integrated management of GAM in children is an acceptable alternative to standard management and provides greater community coverage

[J Pediatr Gastroenterol Nutr.](#) 2015 Jul;61(1):138-43. doi: 10.1097/MPG.0000000000000741.

[High-Oleic Ready-to-Use Therapeutic Food Maintains Docosahexaenoic Acid Status in Severe Malnutrition.](#)

[Hsieh JC](#), [Liu L](#), [Zeilani M](#), [Ickes S](#), [Trehan I](#), [Maleta K](#), [Craig C](#), [Thakwalakwa C](#), [Singh L](#), [Brenna JT](#), [Manary MJ](#).

Abstract

OBJECTIVES:

Ready-to-use therapeutic food (RUTF) is the preferred treatment for uncomplicated severe acute malnutrition. It contains large amounts of linoleic acid and little α -linolenic acid, which may reduce the availability of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) to the recovering child. A novel high-oleic RUTF (HO-RUTF) was developed with less linoleic acid to determine its effect on DHA and EPA status.

METHODS:

We conducted a prospective, randomized, double-blind clinical effectiveness trial treating rural Malawian children with severe acute malnutrition. **Children were treated with either HO-RUTF or standard RUTF.** Plasma phospholipid fatty acid status was measured on enrollment and after 4 weeks and compared between the 2 intervention groups.

RESULTS:

Among the 141 children enrolled, **48 of 71 receiving HO-RUTF and 50 of 70 receiving RUTF recovered.** Plasma phospholipid samples were analyzed from 43 children consuming HO-RUTF and 35 children consuming RUTF. The change in DHA content during the first 4 weeks was +4% and -25% in the HO-RUTF and RUTF groups, respectively ($P=0.04$). For EPA, the change in content was 63% and -24% in the HO-RUTF and RUTF groups, respectively ($P<0.001$). For arachidonic acid, the change in content was -3% and 13% in the HO-RUTF and RUTF groups, respectively ($P<0.009$).

CONCLUSIONS:

The changes in DHA and EPA seen in the children treated with HO-RUTF warrant further investigation because they suggest that HO-RUTF support improved polyunsaturated fatty acid status, necessary for neural development and recovery.

[J Nutr.](#) 2015 Dec;145(12):2705-14. doi: 10.3945/jn.115.215996. Epub 2015 Oct 7.

Malnutrition and Its Determinants Are Associated with Suboptimal Cognitive, Communication, and Motor Development in Tanzanian Children.

[Sudfeld CR](#), [McCoy DC](#), [Fink G](#), [Muhimi A](#), [Bellinger DC](#), [Masanja H](#), [Smith ER](#), [Danaei G](#), [Ezzati M](#), [Fawzi WW](#).

Abstract

BACKGROUND:

A large volume of literature has shown negative associations between stunting and child development; however, there is limited evidence for associations with milder forms of linear growth faltering and determinants of malnutrition in developing countries.

OBJECTIVE:

The objective of this study was to assess the association between anthropometric growth indicators across their distribution and determinants of malnutrition with development of Tanzanian children.

METHODS:

We used the Bayley Scales of Infant Development III to assess a cohort of 1036 Tanzanian children between 18 and 36 mo of age who were previously enrolled in a neonatal vitamin A trial. Linear regression models were used to assess standardized mean differences in child development for anthropometry z scores, along with pregnancy, delivery, and early childhood factors.

RESULTS:

Height-for-age z score (HAZ) was linearly associated with cognitive, communication, and motor development z scores across the observed range in this population (all P values for linear relation < 0.05). **Each unit increase in HAZ was associated with +0.09 (95% CI: 0.05, 0.13), +0.10 (95% CI: 0.07, 0.14), and +0.13 (95% CI: 0.09, 0.16) higher cognitive, communication, and motor development z scores, respectively.** The relation of weight-for-height z score (WHZ) was nonlinear with only wasted children (WHZ < -2) experiencing deficits (P values for nonlinear relation < 0.05). Wasted children had -0.63 (95% CI: -0.97, -0.29), -0.32 (95% CI: -0.64, 0.01), and -0.54 (95% CI: -0.86, -0.23) z score deficits in cognitive, communication, and motor development z scores, respectively, relative to nonwasted children. Maternal stature and flush toilet use were associated with higher cognitive and motor z scores, whereas being born small for gestational age (SGA) was associated with a -0.16 (95% CI: -0.30, -0.01) z score deficit in cognition.

CONCLUSIONS:

Mild to severe chronic malnutrition was associated with increasing developmental deficits in Tanzanian children, whereas only wasted children exhibited developmental delays during acute malnutrition. Interventions to reduce SGA, improve sanitation, and increase maternal stature may have positive effects on child development.

Maternal health

(see also Malaria)

[JAMA Pediatr.](#) 2015 Oct;169(10):947-55. doi: 10.1001/jamapediatrics.2015.1480.

Iron Supplementation in Iron-Replete and Nonanemic Pregnant Women in Tanzania: A Randomized Clinical Trial.

[Etheredge AJ](#), [Premji Z](#), [Gunaratna NS](#), [Abioye AI](#), [Aboud S](#), [Duggan C](#), [Mongi R](#), [Meloney L](#), [Spiegelman D](#), [Roberts D](#), [Hamer DH](#), [Fawzi WW](#).

Abstract

IMPORTANCE:

Anemia is common in pregnancy and increases the risk of adverse outcomes. Iron deficiency is a leading cause of anemia in sub-Saharan Africa, and iron supplementation is the standard of care during pregnancy; however, recent trials among children have raised concerns regarding the safety of iron supplementation in malaria-endemic regions. There is limited evidence on the safety of iron supplementation during pregnancy in these areas.

OBJECTIVE:

To evaluate the safety and efficacy of iron supplementation during pregnancy in a malaria-endemic region.

DESIGN, SETTING, AND PARTICIPANTS:

We conducted a randomized, double-blind, placebo-controlled clinical trial among pregnant women presenting for antenatal care in Dar es Salaam, Tanzania, from September 28, 2010, through October 4, 2012. **Iron-replete, nonanemic women were eligible if they were uninfected with human immunodeficiency virus, primigravidae or secundigravidae**, and at or before 27 weeks of gestation. Screening of 21,316 women continued until the target enrollment of 1500 was reached. Analyses followed the intent-to-treat principle and included all randomized participants.

INTERVENTIONS:

Participants were randomized to receive 60 mg of iron or placebo, returning every 4 weeks for standard prenatal care, including malaria screening, prophylaxis with the combination of sulfadoxine and pyrimethamine, and treatment, as needed.

MAIN OUTCOMES AND MEASURES:

The primary outcomes were placental malaria, maternal hemoglobin level at delivery, and birth weight.

RESULTS:

Among 1500 study participants (750 randomized for each group), 731 in iron group and 738 in placebo group had known birth outcomes and 493 in iron group and 510 in placebo group had placental samples included in the analysis. Maternal characteristics were similar at baseline in the iron and placebo groups, and 1354 (91.7%) used malaria control measures. **The risk of placental malaria was not increased by maternal iron supplementation (relative risk [RR], 1.03; 95% CI, 0.65-1.65), and iron supplementation did not significantly affect birth weight (3155 vs 3137 g, P = .89).** Compared with placebo, iron supplementation significantly improved the mean increase from baseline to delivery for hemoglobin (0.1 vs -0.7 g/dL, P < .001) and serum ferritin (41.3 vs 11.3 µg/L, P < .001). Iron supplementation significantly decreased the risk of anemia at delivery by 40% (RR, 0.60; 95% CI, 0.51-0.71) but not severe anemia (RR, 0.68; 95% CI, 0.41-1.14). Iron supplementation significantly reduced the risk of maternal iron deficiency at delivery by 52% (RR, 0.48; 95% CI, 0.32-0.70) and the risk of iron deficiency anemia by 66% (RR, 0.34; 95% CI, 0.19-0.62).

CONCLUSIONS AND RELEVANCE:

Prenatal iron supplementation among iron-replete, nonanemic women was not associated with an increased risk of placental malaria or other adverse events in the context of good malaria control. Participants receiving supplementation had improved hematologic and iron status at delivery compared with the placebo group. These findings provide support for continued administration of iron during pregnancy in malaria-endemic regions.

<http://archpedi.jamanetwork.com/article.aspx?doi=10.1001/jamapediatrics.2015.1480>

[N Engl J Med.](#) 2016 Mar 10;374(10):928-39. doi: 10.1056/NEJMoa1509150.

[Dihydroartemisinin-Piperaquine for the Prevention of Malaria in Pregnancy.](#)

[Kakuru A](#), [Jagannathan P](#), [Muhindo MK](#), [Natureeba P](#), [Awori P](#), [Nakalembe M](#), [Opira B](#), [Olwoch P](#), [Ategeka J](#), [Nayebare P](#), [Clark TD](#), [Feeney ME](#), [Charlebois ED](#), [Rizzuto G](#), [Muehlenbachs A](#), [Havilir DV](#), [Kamya MR](#), [Dorsey G](#).

Abstract

BACKGROUND:

Intermittent treatment with sulfadoxine-pyrimethamine is widely recommended for the prevention of malaria in pregnant women in Africa. However, with the spread of resistance to sulfadoxine-pyrimethamine, new interventions are needed.

METHODS:

We conducted a double-blind, randomized, controlled trial involving 300 human immunodeficiency virus (HIV)-uninfected pregnant adolescents or women in Uganda, where sulfadoxine-pyrimethamine resistance is widespread. **We randomly assigned participants to a sulfadoxine-pyrimethamine regimen (106 participants), a three-dose dihydroartemisinin-piperaquine regimen (94 participants), or a monthly dihydroartemisinin-piperaquine regimen (100 participants).** The primary outcome was the prevalence of histopathologically confirmed placental malaria.

RESULTS:

The prevalence of histopathologically confirmed placental malaria was significantly higher in the sulfadoxine-pyrimethamine group (50.0%) than in the three-dose dihydroartemisinin-piperaquine group (34.1%, P=0.03) or the monthly dihydroartemisinin-piperaquine group (27.1%, P=0.001). The prevalence of a composite adverse birth outcome was lower in the monthly dihydroartemisinin-piperaquine group (9.2%) than in the sulfadoxine-pyrimethamine group (18.6%, P=0.05) or the three-dose dihydroartemisinin-piperaquine group (21.3%, P=0.02). During pregnancy, the incidence of symptomatic malaria was significantly higher in the sulfadoxine-pyrimethamine group (41 episodes over 43.0 person-years at risk) than in the three-dose dihydroartemisinin-piperaquine group (12 episodes over 38.2 person-years at risk, P=0.001) or the monthly dihydroartemisinin-piperaquine group (0 episodes over 42.3 person-years at risk, P<0.001), as was the prevalence of parasitemia (40.5% in the sulfadoxine-pyrimethamine group vs. 16.6% in the three-dose dihydroartemisinin-piperaquine group [P<0.001] and 5.2% in the monthly dihydroartemisinin-piperaquine group [P<0.001]). In each treatment group, the risk of vomiting after administration of any dose of the study agents was less than 0.4%, and there were no significant differences among the groups in the risk of adverse events.

CONCLUSIONS:

The burden of malaria in pregnancy was significantly lower among adolescent girls or women who received intermittent preventive treatment with dihydroartemisinin-piperaquine than among those who received sulfadoxine-pyrimethamine, and monthly treatment with dihydroartemisinin-piperaquine was superior to three-dose dihydroartemisinin-piperaquine with regard to several outcomes

[BJOG](#). 2016 Jan;123(1):120-7. doi: 10.1111/1471-0528.13540. Epub 2015 Sep 1.

Misoprostol for primary versus secondary prevention of postpartum haemorrhage: a cluster-randomised non-inferiority community trial.

[Raghavan S](#), [Geller S](#), [Miller S](#), [Goudar SS](#), [Anger H](#), [Yadavannavar MC](#), [Dabash R](#), [Bidri SR](#), [Gudadinni MR](#), [Ud giri R](#), [Koch AR](#), [Bellad MB](#), [Winikoff B](#).

Abstract

OBJECTIVE:

To assess whether secondary prevention, which preemptively treats women with above-average postpartum bleeding, is non-inferior to universal prophylaxis.

DESIGN:

A cluster-randomised non-inferiority community trial.

SETTING:

Health sub-centres and home deliveries in the Bijapur district of Karnataka, India.

POPULATION:

Women with low-risk pregnancies who were eligible for delivery with an Auxiliary Nurse Midwife at home or sub-centre and who consented to be part of the study.

METHODS:

Auxiliary Nurse Midwives were randomised to secondary prevention using 800 mcg sublingual misoprostol administered to women with postpartum blood loss ≥ 350 ml or to universal prophylaxis using 600 mcg oral misoprostol administered to all women during the third stage of labour.

MAIN OUTCOME MEASURES:

Postpartum haemoglobin ≤ 7.8 g/dl, mean postpartum blood loss and postpartum haemoglobin, postpartum haemorrhage rate, transfer to higher-level facilities, acceptability and feasibility of the intervention.

RESULTS:

Misoprostol was administered to 99.7% of women as primary prevention. In secondary prevention, 92 (4.7%) women had postpartum bleeding ≥ 350 ml, of which 90 (97.8%) received misoprostol. The proportion of women with postpartum haemoglobin ≤ 7.8 g/dl was 5.9 and 8.8% in secondary and primary prevention clusters, respectively [difference -2.9%, one-sided 95% confidence interval (CI) $< 1.3\%$]. Postpartum transfer and haemorrhage rates were low ($< 1\%$) in both groups. Shivering was more common in primary prevention clusters ($P = 0.013$).

CONCLUSION:

Secondary prevention of postpartum haemorrhage with misoprostol is non-inferior to universal prophylaxis based on the primary outcome of postpartum haemoglobin. Secondary prevention could be a good alternative to universal prophylaxis as it medicates fewer women and is an acceptable and feasible strategy at the community level.

[BMC Pregnancy Childbirth](#). 2015 Sep 14;15:219. doi: 10.1186/s12884-015-0650-9.

The MamaMiso study of self-administered misoprostol to prevent bleeding after childbirth in rural Uganda: a community-based, placebo-controlled randomised trial.

[Weeks AD](#), [Ditai J](#), [Ononge S](#), [Faragher B](#), [Frye LJ](#), [Durocher J](#), [Mirembe FM](#), [Byamugisha J](#), [Winikoff B](#), [Alfirevic Z](#).

Abstract

BACKGROUND:

600 mcg of oral misoprostol reduces the incidence of postpartum haemorrhage (PPH), but in previous research this medication has been administered by health workers. It is unclear whether it is also safe and effective when self-administered by women.

METHODS:

This placebo-controlled, double-blind randomised trial enrolled consenting women of at least 34 weeks gestation, recruited over a 2-month period in Mbale District, Eastern Uganda.

Participants had their haemoglobin measured antenatally and were given either 600 mcg misoprostol or placebo to take home and use immediately after birth in the event of delivery at home. The primary clinical outcome was the incidence of fall in haemoglobin of over 20% in home births followed-up within 5 days.

RESULTS:

748 women were randomised to either misoprostol (374) or placebo (374). Of those enrolled, 57% delivered at a health facility and 43% delivered at home. **82% of all medicine packs were retrieved at postnatal follow-up and 97% of women delivering at home reported self-administration of the medicine.** Two women in the misoprostol group took the study medication antenatally without adverse effects. There was no significant difference between the study groups in the drop of maternal haemoglobin by >20% (misoprostol 9.4% vs placebo 7.5%, risk ratio 1.11, 95% confidence interval 0.717 to 1.719). There was significantly more fever and shivering in the misoprostol group, but women found the medication highly acceptable.

CONCLUSIONS:

This study has shown that antenatally distributed, self-administered misoprostol can be appropriately taken by study participants. The rarity of the primary outcome means that a very large sample size would be required to demonstrate clinical effectiveness.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26370443/>

[Acta Obstet Gynecol Scand.](#) 2016 Feb;95(2):173-81. doi: 10.1111/aogs.12815. Epub 2015 Nov 30.

[Home use of misoprostol for early medical abortion in a low resource setting: secondary analysis of a randomized controlled trial.](#)

[Iyengar K](#), [Klingberg-Allvin M](#), [Iyengar SD](#), [Paul M](#), [Essén B](#), [Gemzell-Danielsson K](#).

Abstract

INTRODUCTION:

Although home use of misoprostol for early medical abortion is considered to be safe, effective and feasible, it has not become standard service delivery practice. The aim of this study was to compare the efficacy, safety, and acceptability of home use of misoprostol with clinic misoprostol in a low-resource setting.

MATERIAL AND METHODS:

This was a secondary analysis of a randomized controlled trial conducted in six primary care clinics in India. Women seeking medical abortion within up to nine gestational weeks (n = 731) received mifepristone in the clinic and were allocated either to home or clinic administration of misoprostol. Follow-up contact was after 10-15 days.

RESULTS:

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Of 731 participants, 73% were from rural areas and 55% had no formal education. Complete abortion rates in the home and clinic misoprostol groups were 94.2 and 94.4%, respectively. The rate of adverse events was similar in both groups (0.3%). A greater proportion of home users (90.2%) said that they would opt for misoprostol at home in the event of a future abortion compared with clinic users (79.7%) who would opt for misoprostol at the clinic in a similar situation ($p = 0.0002$). Ninety-six percent women using misoprostol at home or in the clinic were satisfied with their abortion experience.

CONCLUSIONS:

Home-use of misoprostol for early medical abortion is as effective and acceptable as clinic use, in low resource settings. Women should be offered a choice of this option regardless of distance of their residence from the clinic and communication facilities

[Am J Prev Med.](#) 2015 Nov;49(5):715-25. doi: 10.1016/j.amepre.2015.05.004. Epub 2015 Jul 29.

Alcohol Use, Partner Violence, and Depression: A Cluster Randomized Controlled Trial Among Urban South African Mothers Over 3 Years.

[Rotheram-Borus MJ](#), [Tomlinson M](#), [Le Roux I](#), [Stein JA](#).

Abstract

INTRODUCTION:

Pregnant South African women with histories of drinking alcohol, abuse by violent partners, depression, and living with HIV are likely to have their post-birth trajectories over 36 months significantly influenced by these risks.

DESIGN:

All pregnant women in 24 Cape Town neighborhoods were recruited into a cluster RCT by neighborhood to either: (1) a standard care condition (n=12 neighborhoods, n=594 mothers); or (2) a home-visiting intervention condition (n=12 neighborhoods, n=644 mothers).

SETTING/PARTICIPANTS:

Pregnant women residing in urban, low-income neighborhoods in Cape Town, South Africa.

INTERVENTION:

Home visiting included prenatal and postnatal visits by community health workers (Mentor Mothers) focusing on general maternal and child health, HIV/tuberculosis, alcohol use, and nutrition.

MAIN OUTCOME MEASURES:

Mothers were assessed in pregnancy and at 18 and 36 months post birth: 80.6% of mothers completed all assessments between 2009 and 2014 and were included in these analyses performed in 2014. Longitudinal structural equation modeling examined alcohol use, partner violence, and depression at the baseline and 18-month interviews as predictors of maternal outcomes at 36 months post birth.

RESULTS:

Relative to standard care, intervention mothers were significantly less likely to report depressive symptoms and more positive quality of life at 36 months. Alcohol use was significantly related to use over time, but was also related to depression and HIV status at each assessment and partner violence at 36 months.

CONCLUSIONS:

Alcohol, partner violence, and depression are significantly related over time. A home-visiting intervention improved the emotional health of low-income mothers even when depression was not initially targeted.

[BMC Psychiatry](#). 2015 Sep 23;15:225. doi: 10.1186/s12888-015-0606-7.

Community health workers can improve child growth of antenatally-depressed, South African mothers: a cluster randomized controlled trial.

[Tomlinson M](#), [Rotheram-Borus MJ](#), [Harwood J](#), [le Roux IM](#), [O'Connor M](#), [Worthman C](#).

Abstract

BACKGROUND:

Maternal antenatal depression has long-term consequences for children's health. We examined if home visits by community health workers (CHW) can improve growth outcomes for children of mothers who are antenatally depressed.

METHODS:

A cluster randomized controlled trial of all pregnant, neighbourhood women in Cape Town, South Africa. Almost all pregnant women (98 %, N = 1238) were recruited and assessed during pregnancy, two weeks post-birth (92 %) and 6 months post-birth (88 %). **Pregnant women were randomized to either: 1) Standard Care (SC), which provided routine antenatal care; or 2) an intervention**, The Philani Intervention Program (PIP), which included SC and home visits by CHW trained as generalists (M = 11 visits). Child standardized weight, length, and weight by length over 6 months based on maternal antenatal depression and intervention condition.

RESULTS:

Depressed mood was similar across the PIP and SC conditions both antenatally (16.5 % rate) and at 6 months (16.7 %). **The infants of depressed pregnant women in the PIP group were similar in height (height-for-age Z scores) to the children of non-depressed mothers in both the PIP and the SC conditions, but significantly taller at 6 months of age than the infants of pregnant depressed mothers in the SC condition.** The intervention did not moderate children's growth. Depressed SC mothers tended to have infants less than two standard deviations in height on the World Health Organization's norms at two weeks post-birth compared to infants of depressed PIP mothers and non-depressed mothers in both conditions.

CONCLUSIONS:

A generalist, CHW-delivered home visiting program improved infant growth, even when mothers' depression was not reduced. **Focusing on maternal caretaking of infants, even when mothers are depressed, is critical in future interventions.**

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26400691/>

[Implement Sci](#). 2015 Aug 14;10:117. doi: 10.1186/s13012-015-0309-y.

Learning before leaping: integration of an adaptive study design process prior to initiation of BetterBirth, a large-scale randomized controlled trial in Uttar Pradesh, India.

[Hirschhorn LR](#), [Semrau K](#), [Kodkany B](#), [Churchill R](#), [Kapoor A](#), [Spector J](#), [Ringer S](#), [Firestone R](#), [Kumar V](#), [Gawande A](#).

Abstract

BACKGROUND:

Pragmatic and adaptive trial designs are increasingly used in quality improvement (QI) interventions to provide the strongest evidence for effective implementation and impact prior to broader scale-up. We previously showed that an on-site coaching intervention focused on the

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World Health Organization Safe Childbirth Checklist (SCC) improved performance of essential birth practices (EBPs) in one facility in Karnataka, India. We report on the process and outcomes of adapting the intervention prior to larger-scale implementation in a randomized controlled trial in Uttar Pradesh (UP), India.

METHODS:

Initially, we trained a local team of physicians and nurses to coach birth attendants in SCC use at two public facilities for 4-6 weeks. Trained observers evaluated adherence to EBPs before and after coaching. Using mixed methods and a systematic adaptation process, we modified and strengthened the intervention. The modified intervention was implemented in three additional facilities. Pre/post-change in EBP prevalence aggregated across facilities was analyzed.

RESULTS:

In the first two facilities, limited improvement was seen in EBPs with the exception of post-partum oxytocin. Checklists were used <25 % of observations. We identified challenges in physicians coaching nurses, need to engage district and facility leadership to address system gaps, and inadequate strategy for motivating SCC uptake. Revisions included change to peer-to-peer coaching (nurse to nurse, physician to physician); strengthened coach training on behavior and system change; adapted strategy for effective leadership engagement; and an explicit motivation strategy to enhance professional pride and effectiveness. These modifications resulted in improvement in multiple EBPs from baseline including taking maternal blood pressure (0 to 16 %), post-partum oxytocin (36 to 97 %), early breastfeeding initiation (3 to 64 %), as well as checklist use (range 32 to 88 %), all $p < 0.01$. Further adaptations were implemented to increase the effectiveness prior to full trial launch.

CONCLUSIONS:

The adaptive study design of implementation, evaluation, and feedback drove iterative redesign and successfully developed a SCC-focused coaching intervention that improved EBPs in UP facilities. This work was critical to develop a replicable BetterBirth package tailored to the local context. The multi-center pragmatic trial is underway measuring impact of the BetterBirth program on EBP and maternal-neonatal morbidity and mortality.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26271331/>

Maternal nutrition and micronutrient supplementation

[Matern Child Nutr.](#) 2015 Jul;11(3):297-304. doi: 10.1111/mcn.12018. Epub 2012 Dec 17.

Effect of multivitamin supplements on weight gain during pregnancy among HIV-negative women in Tanzania.

[Changamire FT](#), [Mwiru RS](#), [Peterson KE](#), [Msamanga GI](#), [Spiegelman D](#), [Petraro P](#), [Urassa W](#), [Fawzi WW](#).

Abstract

Multivitamin supplementation has been shown to reduce the risk of low birthweight. This effect could be mediated through gestational weight gain. However, the effect of multivitamin supplementation on weight gain during pregnancy has not been fully studied. **The objective of this study was to examine the effects of multivitamins on pregnancy weight gain. We enrolled 8468 HIV-negative women from Dar es Salaam, Tanzania, in a randomised, placebo-controlled trial of multivitamins on birth outcomes. Women were randomly assigned to receive either a daily oral dose of multivitamin tablets or a placebo and were weighed every 4 weeks from enrolment until the last visit before delivery. Intent-to-treat analyses**

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were carried out to examine the effects of multivitamins on pregnancy weight gain. Multivariate linear and binomial regression models with the log-link function were used to examine the association of weight gain during pregnancy to birthweight. **The overall total weight gain was 253 g (SE: 69, P: 0.0003) more, while the overall 4 weekly weight gain was 59 g greater (SE: 18, P: 0.005) among women who received multivitamins compared to placebo.** Women in the lowest quartile of gestational weight gain had babies with an average birthweight of 3030 g (SD: 524), while women in the highest quartile had babies weighing 3246 g (SD: 486), on average. **Prenatal multivitamin supplements increased gestational weight gain, which was a significant predictor of birthweight.**

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC23253638/>

[Matern Child Nutr.](#) 2015 Jul;11(3):385-97. doi: 10.1111/mcn.12021. Epub 2012 Dec 13.

Early invitation to food and/or multiple micronutrient supplementation in pregnancy does not affect body composition in offspring at 54 months: follow-up of the MINIMat randomised trial, Bangladesh.

[Khan AI](#), [Kabir I](#), [Hawkesworth S](#), [Ekström EC](#), [Arifeen S](#), [Frongillo EA](#), [Persson LÅ](#).

Abstract

Growth patterns in early life are associated with later health. The effect of nutrition during in utero development on later body composition is unclear. We evaluated whether prenatal early invitation to food and/or multiple micronutrient supplementation (MMS) in pregnancy has an effect on offspring body composition at 54 months of age. In Maternal and Infant Nutrition Interventions in Matlab trial (ISRCTN16581394) in Bangladesh, 4436 pregnant women were randomised into six equally sized groups: double-masked supplementation with capsules of either 30 mg Fe and 400 µg folic acid, or 60 mg Fe and 400 µg folic acid, or MMS (15 micronutrients), was combined with a randomised early invitation (around 9 weeks) or a usual invitation (around 20 weeks) to start food supplementation (608 kcal 6 days per week). At 54 months, the body composition of the offspring was assessed by leg-to-leg bioelectrical impedance analysis. Of the 3267 live singletons with birth anthropometry, 2290 children were measured at 54 months, representing 70% of the live births. There was no interaction between the food and micronutrient supplementation on body composition outcomes. There were no significant differences in a range of anthropometric and body composition measurements, including weight, height, mid-upper arm circumference, head circumference, skinfold thickness, and fat mass and fat-free mass between the different prenatal food and micronutrient groups using an intention-to-treat analysis. This analysis shows that early invitation to food supplementation and MMS provided to rural Bangladeshi women during pregnancy did not affect offspring body composition at 54 months of age.

[J Nutr.](#) 2016 May;146(5):1109-17. doi: 10.3945/jn.115.224261. Epub 2016 Apr 13.

A 2-Year Integrated Agriculture and Nutrition Program Targeted to Mothers of Young Children in Burkina Faso Reduces Underweight among Mothers and Increases Their Empowerment: A Cluster-Randomized Controlled Trial.

[Olney DK](#), [Bliznashka L](#), [Pedehombga A](#), [Dillon A](#), [Ruel MT](#), [Heckert J](#).

Abstract

BACKGROUND:

Randomised trials in child health in developing countries 2015-16

Recent evidence demonstrates the benefits of integrated agriculture and nutrition programs for children's health and nutrition outcomes. These programs may also improve mothers' nutrition and empowerment outcomes. However, evidence from rigorous evaluations is scarce.

OBJECTIVE:

We examined impacts of Helen Keller International's 2-y enhanced-homestead food production (E-HFP) program in Burkina Faso on the secondary impact measures of mothers' nutrition and empowerment.

METHODS:

We used a cluster-randomized controlled trial whereby **55 villages with 1767 mothers of youngchildren were randomly assigned to 3 groups: 1) control, 2) E-HFP with the behavior change communication (BCC) strategy implemented by older women leaders, or 3) E-HFP with BCC implemented by health committee members.** Data for the treatment groups were pooled for this analysis because no differences were found between the 2 groups in key mothers' outcomes. We used difference-in-differences (DID) estimates to assess impacts on mothers' dietary intake, diversity, body mass index (BMI; in kg/m²), prevalence of underweight (BMI <18.5), and empowerment.

RESULTS:

The E-HFP program significantly increased mothers' intake of fruit (DID = 15.8 percentage points; P = 0.02) and marginally increased their intake of meat/poultry (DID = 7.5 percentage points; P = 0.08) and dietary diversity (DID = 0.3 points; P = 0.08). The prevalence of underweight was significantly reduced among mothers in treatment compared with control villages by 8.7 percentage points (P < 0.01). Although the changes in BMI did not differ between mothers in treatment and control villages, there was a marginally significant interaction (baseline underweight × change in BMI; P-interaction = 0.07), indicating that underweight mothers had a greater increase in BMI than did mothers who were not underweight. The E-HFP program also positively affected mothers' overall empowerment score (DID = 3.13 points out of 37 possible points; P < 0.01) and 3 components of empowerment: meeting with women (DID = 1.21 points out of 5 possible points; P < 0.01), purchasing decisions (DID = 0.86 points out of 8 possible points; P = 0.01), and health care decisions (DID = 0.24 points out of 2 possible points; P = 0.05).

CONCLUSIONS:

Helen Keller International's E-HFP program in Burkina Faso substantially improved mothers' nutrition and empowerment outcomes. These positive impacts benefit the mothers themselves and may also improve their ability to care for their children.

[Am J Clin Nutr.](#) 2015 Dec;102(6):1450-9. doi: 10.3945/ajcn.113.072413. Epub 2015 Nov 11.

[Periconceptional multiple-micronutrient supplementation and placental function in rural Gambian women: a double-blind, randomized, placebo-controlled trial.](#)

[Owens S](#), [Gulati R](#), [Fulford AJ](#), [Sosseh F](#), [Denison FC](#), [Brabin BJ](#), [Prentice AM](#).

Abstract

BACKGROUND:

Maternal micronutrient deficiencies are commonly associated with clinical indicators of placental dysfunction.

OBJECTIVE:

We tested the hypothesis that periconceptional multiple-micronutrient supplementation (MMS) affects placental function.

DESIGN:

Randomised trials in child health in developing countries 2015-16

We conducted a double-blind, randomized, placebo-controlled trial of MMS in 17- to 45-y-old Gambian women who were menstruating regularly and within the previous 3 mo. Eligible subjects were pre-randomly assigned to supplementation with the UNICEF/WHO/United Nations University multiple micronutrient preparation (UNIMMAP) or placebo on recruitment and until they reached their first antenatal check-up or for 1 y if they failed to conceive. Primary outcome measures were midgestational indexes of utero-placental vascular-endothelial function [ratio of plasminogen-activator inhibitor (PAI) 1 to PAI-2 and mean uterine-artery resistance index (UtARI)] and placental active transport capacity at delivery [fetal to maternal measles antibody (MMA) ratio].

RESULTS:

We recruited 1156 women who yielded 415 pregnancies, of which 376 met all of the inclusion criteria. With adjustment for gestational age at sampling, there were no differences in PAI-1 to PAI-2 or MMA ratios between trial arms, but there was a 0.02-unit reduction in UtARI between 18 and 32 wk of gestation (95% CI: -0.03, -0.00; P = 0.040) in women taking UNIMMAP.

CONCLUSIONS:

Placental vascular function was modifiable by periconceptional micronutrient supplementation. However, the effect was small and supplementation did not further affect other variables of placental function.

<http://ajcn.nutrition.org/cgi/pmidlookup?view=long&pmid=26561613>

[BMC Pregnancy Childbirth](#). 2015 Aug 18;15:175. doi: 10.1186/s12884-015-0605-1.

[Effectiveness of a normative nutrition intervention \(diet, physical activity and breastfeeding\) on maternal nutrition and offspring growth: the Chilean maternal and infant nutrition cohort study \(CHiMINCs\).](#)

[Garmendia ML](#), [Corvalan C](#), [Araya M](#), [Casanello P](#), [Kusanovic JP](#), [Uauy R](#).

Abstract

BACKGROUND:

Maternal obesity before and during pregnancy predicts maternal and infant risks of obesity and its associated metabolic conditions. Dietary and physical activity recommendations during pregnancy as well as weight monitoring are currently available in the Chilean primary health care system. However some of these recommendations are not updated and most of them are poorly implemented. We seek to assess the effectiveness of an intervention that enhances the implementation of updated nutrition health care standards (diet, physical activity, and breastfeeding promotion) during pregnancy on maternal weight gain and infant growth.

METHODS:

DESIGN & SETTING:

Cluster randomized controlled trial. The cluster units will be 12 primary health care centers from two counties (La Florida and Puente Alto) from the South-East Area of Santiago randomly allocated to: 1) enhanced nutrition health care standards (intervention group) or 2) routine care (control group).

PARTICIPANTS:

Women seeking prenatal care before 15 weeks of gestation, residing within a catchment area of selected health centers, and who express that they are not planning to change residence will be invited to participate in the study. Pregnant women classified as high risk according to the Chilean norms (i.e age <16 or >40 years, multiple gestation, pre-gestational medical conditions, previous pregnancy-related issues) and/or underweight will be excluded.

INTERVENTION:

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Pregnant women who attend intervened health care centers starting at their first prenatal visit will receive advice regarding optimal weight gain during pregnancy and diet and physical activity counseling-support. Pregnant women who attend control health clinics will receive routine antenatal care according to national guidelines. We plan to recruit 200 women in each health center. Assuming a 20% loss to follow up, we expect to include 960 women per arm.

MAIN OUTCOME MEASURES:

1) Achievement of adequate weight gain based on IOM 2009 recommendations and adequate glycaemic control at 24-28 weeks of pregnancy according to ADA 2011, and 2) healthy infant growth during the first year of age based on WHO standards.

DISCUSSION:

We expect that the intervention will benefit the participants in achieving adequate weight gain & metabolic control during pregnancy as well as adequate infant growth as a result of an increased impact of standard nutrition and health care practices. Gathered information should contribute to a better understanding of how to develop effective interventions to halt the maternal obesity epidemic and its associated co-morbidities in the Chilean population.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26283529/>

Meningitis and encephalitis

Newborn care

[N Engl J Med. 2015 Sep 17;373\(12\):1115-24. doi: 10.1056/NEJMoa1501074.](#)

[A Randomized Trial of Phototherapy with Filtered Sunlight in African Neonates.](#)

[Slusher TM](#), [Olusanya BO](#), [Vreman HJ](#), [Brearley AM](#), [Vaucher YE](#), [Lund TC](#), [Wong RJ](#), [Emokpae AA](#), [Stevenson DK](#).

Abstract

BACKGROUND:

Sequelae of severe neonatal hyperbilirubinemia constitute a substantial disease burden in areas where effective conventional phototherapy is unavailable. We previously found that the use of filtered sunlight for the purpose of phototherapy is a safe and efficacious method for reducing total bilirubin. However, its relative safety and efficacy as compared with conventional phototherapy are unknown.

METHODS:

We conducted a **randomized, controlled noninferiority trial in which filtered sunlight was compared with conventional phototherapy for the treatment of hyperbilirubinemia in term and late-preterm neonates in a large, urban Nigerian maternity hospital.** The primary end point was efficacy, which was defined as a rate of increase in total serum bilirubin of less than 0.2 mg per deciliter per hour for infants up to 72 hours of age or a decrease in total serum bilirubin for infants older than 72 hours of age who received at least 5 hours of phototherapy; we prespecified a noninferiority margin of 10% for the difference in efficacy rates between groups. The need for an exchange transfusion was a secondary end point. We also assessed safety, which was defined as the absence of the need to withdraw therapy because of hyperthermia, hypothermia, dehydration, or sunburn.

RESULTS:

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We enrolled 447 infants and randomly assigned 224 to filtered sunlight and 223 to conventional phototherapy. Filtered sunlight was efficacious on 93% of treatment days that could be evaluated, as compared with 90% for conventional phototherapy, and had a higher mean level of irradiance (40 vs. 17 μW per square centimeter per nanometer, $P<0.001$). Temperatures higher than 38.0°C occurred in 5% of the infants receiving filtered sunlight and in 1% of those receiving conventional phototherapy ($P<0.001$), but no infant met the criteria for withdrawal from the study for reasons of safety or required an exchange transfusion.

CONCLUSIONS:

Filtered sunlight was noninferior to conventional phototherapy for the treatment of neonatal hyperbilirubinemia and did not result in any study withdrawals for reasons of safety

http://www.nejm.org/doi/abs/10.1056/NEJMoal501074?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dwww.ncbi.nlm.nih.gov

[Eur J Pediatr.](#) 2015 Sep;174(9):1159-67. doi: 10.1007/s00431-015-2511-y. Epub 2015 Mar 24.

Comparison of two types of intervention to enhance placental redistribution in term infants: randomized control trial.

[Jaiswal P,](#) [Upadhyay A,](#) [Gothwal S,](#) [Singh D,](#) [Dubey K,](#) [Garg A,](#) [Vishnubhatala S.](#)

Abstract

The objective of the study was to **compare the effect of umbilical cord milking (UCM) and delayed cord clamping (DCC) on hematological parameters (serum ferritin and hemoglobin) at 6 weeks of life in term neonates.** It was a randomized controlled trial conducted at a teaching hospital in North India during August 2012 to August 2013. Babies born at >36 weeks of gestation were randomized in two groups, UCM and DCC (100 in each group). **Umbilical cord milking was done after cutting and clamping the cord at 25 cm from the umbilicus. In DCC group, clamping was delayed by 60 to 90 s before cutting the cord.** The baseline characteristics were comparable in the two groups. Mean serum ferritin (134.0 ng/ml [89.8]) and mean hemoglobin (11.0 gm/dl [2.4]) in umbilical cord milking group was comparable to mean serum ferritin (142.7 ng/ml [87.1]) and hemoglobin (11.3 gm/dl [2.6]) in DCC group at 6 weeks of age. There was no difference in hemodynamic status, cranial Doppler indices, and adverse neonatal outcomes among the two groups.

CONCLUSION:

In term neonates, the DCC and UCM had comparable effect on hematological parameters at 6 weeks of life.

[Arch Dis Child Fetal Neonatal Ed.](#) 2015 Jul;100(4):F309-12. doi: 10.1136/archdischild-2014-306269. Epub 2015 Mar 19.

Keeping babies warm: a non-inferiority trial of a conductive thermal mattress.

[Bhat SR,](#) [Meng NF,](#) [Kumar K,](#) [Nagesh KN,](#) [Kawale A,](#) [Bhutani VK.](#)

Abstract

BACKGROUND:

External thermal support is critical for preterm or ill infants due to altered thermoregulation. Incubators are the gold standard for long-term support and have been adopted successfully in many countries. Alternatives such as radiant warmers, blankets and others are often used as

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standard of care (SoC) in resource-limited settings when infants are otherwise not in Kangaroo Mother Care (KMC).

METHODS:

In this pilot study, we evaluate the feasibility of a **conductive thermal mattress (CTM)** using phase change materials as a low-cost warmer. We conducted a prospective multicentre open-label randomised controlled trial to determine non-inferiority of this CTM to SoC warming practices in low birthweight infants. The primary outcome was maintenance of axillary temperature.

RESULTS:

We equally randomised 160 infants to CTM or SoC. The latter cohort continued to receive warmth by radiant warmers (n=48), blankets (n=18), warmed cradles (n=7) or KMC (n=7) before, during and subsequent to the study. **CTM was deemed non-inferior since warmed babies had higher axillary temperature compared with SoC** (mean increase $0.11 \pm 0.03^\circ\text{C}$ SEM; $p < 0.001$). Post hoc comparison to radiant warmers alone showed that CTM led to a higher axillary temperature (mean increase by $0.14 \pm 0.03^\circ\text{C}$ SEM; $p < 0.001$).

CONCLUSIONS:

Short-term use of CTM compared with radiant warmers and other modes of warming is non-inferior to SoC and efficacious in maintaining body temperature. No adverse effects were reported. An extended multinational trial, preferably one that demonstrates longer-term thermoregulation, is warranted.

[Indian Pediatr.](#) 2015 Jul;52(7):573-8.

Enteral paracetamol or Intravenous Indomethacin for Closure of Patent Ductus Arteriosus in Preterm Neonates: A Randomized Controlled Trial.

[Dash SK](#), [Kabra NS](#), [Avasthi BS](#), [Sharma SR](#), [Padhi P](#), [Ahmed J](#).

Abstract

OBJECTIVE:

To compare the efficacy of enteral paracetamol and intravenous indomethacin for closure of patent ductus arteriosus (PDA) in preterm neonates.

DESIGN:

Randomized controlled trial.

SETTING:

Level III neonatal intensive care unit.

PARTICIPANTS:

77 preterm neonates with birth weight < 1500 g and PDA size < 1.5 mm, with left to right ductal flow with left atrium to aortic root ratio $> 1.5:1$; diagnosed by 2D-Echo within first 48 hours of life.

INTERVENTION:

Paracetamol drops through the infant feeding tube (15 mg/kg/dose 6 hourly for 7 days) or intravenous indomethacin (0.2 mg/kg/dose once daily for 3 days).

OUTCOME MEASURES:

Primary: PDA closure rate assessed by echocardiography. Secondary: need for surgical closure of PDA, renal impairment, gastrointestinal bleed, necrotising enterocolitis, hepatotoxicity, pulmonary hemorrhage, sepsis, hypothermia, retinopathy of prematurity, intraventricular hemorrhage, bronchopulmonary dysplasia and mortality.

RESULTS:

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PDA closure rate was 100% (36/36) in enteral paracetamol group as compared to 94.6% (35/37) in intravenous indomethacin group (P=0.13). The secondary outcomes were also similar between the two groups. There was no occurrence of hepatotoxicity.

CONCLUSIONS:

Enteral paracetamol is safe but not superior to intravenous indomethacin in the treatment of PDA in preterm neonates.

<http://www.indianpediatrics.net/july2015/573.pdf>

[PLoS Med.](#) 2015 Sep 29;12(9):e1001881. doi: 10.1371/journal.pmed.1001881. eCollection 2015.

[Effectiveness of a Home-Based Counselling Strategy on Neonatal Care and Survival: A Cluster-Randomised Trial in Six Districts of Rural Southern Tanzania.](#)

[Hanson C](#), [Manzi F](#), [Mkumbo E](#), [Shirima K](#), [Penfold S](#), [Hill Z](#), [Shamba D](#), [Jaribu J](#), [Hamisi Y](#), [Soremekun S](#), [Cousens S](#), [Marchant T](#), [Mshinda H](#), [Schellenberg D](#), [Tanner M](#), [Schellenberg J](#).

Abstract

BACKGROUND:

We report a cluster-randomised trial of a home-based counselling strategy, designed for large-scale implementation, in a population of 1.2 million people in rural southern Tanzania. We hypothesised that the strategy would improve neonatal survival by around 15%.

METHODS AND FINDINGS:

In 2010 we **trained 824 female volunteers to make three home visits to women and their families during pregnancy and two visits to them in the first few days of the infant's life in 65 wards, selected randomly from all 132 wards in six districts in Mtwara and Lindi regions, constituting typical rural areas in Southern Tanzania.** The remaining wards were comparison areas. Participants were not blinded to the intervention. The primary analysis was an intention-to-treat analysis comparing the neonatal mortality (day 0-27) per 1,000 live births in intervention and comparison wards based on a representative survey in 185,000 households in 2013 with a response rate of 90%. **We included 24,381 and 23,307 live births between July 2010 and June 2013 and 7,823 and 7,555 live births in the last year in intervention and comparison wards, respectively.** We also compared changes in neonatal mortality and newborn care practices in intervention and comparison wards using baseline census data from 2007 including 225,000 households and 22,243 births in five of the six intervention districts. Amongst the 7,823 women with a live birth in the year prior to survey in intervention wards, 59% and 41% received at least one volunteer visit during pregnancy and postpartum, respectively. Neonatal mortality reduced from 35.0 to 30.5 deaths per 1,000 live births between 2007 and 2013 in the five districts, respectively. **There was no evidence of an impact of the intervention on neonatal survival (odds ratio [OR] 1.1, 95% confidence interval [CI] 0.9-1.2, p = 0.339).** Newborn care practices reported by mothers were better in intervention than in comparison wards, including immediate breastfeeding (42% of 7,287 versus 35% of 7,008, OR 1.4, CI 1.3-1.6, p < 0.001), feeding only breast milk for the first 3 d (90% of 7,557 versus 79% of 7,307, OR 2.2, 95% CI 1.8-2.7, p < 0.001), and clean hands for home delivery (92% of 1,351 versus 88% of 1,799, OR 1.5, 95% CI 1.0-2.3, p = 0.033). Facility delivery improved dramatically in both groups from 41% of 22,243 in 2007 and was 82% of 7,820 versus 75% of 7,553 (OR 1.5, 95% CI 1.2-2.0, p = 0.002) in intervention and comparison wards in 2013. Methodological limitations include our inability to rule out some degree of leakage of the intervention into the comparison areas and response bias for newborn care behaviours.

CONCLUSION:

Neonatal mortality remained high despite better care practices and childbirth in facilities becoming common. Public health action to improve neonatal survival in this setting should include a focus on improving the quality of facility-based childbirth care.

<http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26418813/>

[Matern Child Health J.](#) 2015 Dec;19(12):2698-706. doi: 10.1007/s10995-015-1792-0.

[An Intervention to Enhance Obstetric and Newborn Care in India: A Cluster Randomized-Trial.](#)

[Goudar SS](#), [Derman RJ](#), [Honnungar NV](#), [Patil KP](#), [Swamy MK](#), [Moore J](#), [Wallace DD](#), [McClure EM](#), [Kodkany BS](#), [Pasha O](#), [Sloan NL](#), [Wright LL](#), [Goldenberg RL](#).

Abstract

OBJECTIVES:

This study assessed whether community mobilization and interventions to improve emergency obstetric and newborn care reduced perinatal mortality (PMR) and neonatal mortality rates (NMR) in Belgaum, India.

METHODS:

The cluster-randomised controlled trial was conducted in Belgaum District, Karnataka State, India. Twenty geographic clusters were randomized to control or the intervention. The intervention engaged and mobilized community and health authorities to leverage support; strengthened community-based stabilization, referral, and transportation; and aimed to improve quality of care at facilities.

RESULTS:

17,754 Intervention births and 15,954 control births weighing ≥ 1000 g, respectively, were enrolled and analysed. Comparing the baseline period to the last 6 months period, the NMR was lower in the intervention versus control clusters (OR 0.60, 95% CI 0.34-1.06, $p = 0.076$) as was the PMR (OR 0.74, 95% CI 0.46-1.19, $p = 0.20$) although neither reached statistical significance. Rates of facility birth and caesarean section increased among both groups. There was limited influence on quality of care measures.

CONCLUSIONS FOR PRACTICE:

The intervention had large but not statistically significant effects on neonatal and perinatal mortality. Community mobilization and increased facility care may ultimately improve neonatal and perinatal survival, and are important in the context of the global transition towards institutional delivery.

[Arch Dis Child.](#) 2016 Feb;101(2):152-60. doi: 10.1136/archdischild-2014-307908. Epub 2015 Oct 29.

[Thermoregulatory effects of swaddling in Mongolia: a randomised controlled study.](#)

[Tsoqt B](#), [Manaseki-Holland S](#), [Pollock J](#), [Blair PS](#), [Fleming P](#).

Abstract

OBJECTIVE:

To investigate thermal balance of infants in a Mongolian winter, and compare the effects of traditional swaddling with an infant sleeping-bag in apartments or traditional tents (Gers).

Randomised trials in child health in developing countries 2015-16

DESIGN:

A substudy within a randomised controlled trial.

SETTING:

Community in Ulaanbaatar, Mongolia.

SUBJECTS:

A stratified randomly selected sample of 40 swaddled and 40 non-swaddled infants recruited within 48 h of birth.

INTERVENTION:

Sleeping-bags and baby outfits of total thermal resistance equivalent to that of swaddled babies.

OUTCOME MEASURE:

Digital recordings of infants' core, peripheral, environmental and microenvironmental temperatures at 30-s intervals over 24 h at ages 1 month and 3 months.

RESULTS:

In Gers, indoor temperatures varied greatly ($0-25^{\circ}\text{C}$), but remained between 20°C and 22°C , in apartments. Despite this, heavy wrapping, bed sharing and partial head covering, infant core and peripheral temperatures were similar and **no infants showed evidence of significant heat or cold stress whether they were swaddled or in sleeping-bags**. At 3 months, infants in sleeping-bags showed the 'mature' diurnal pattern of a fall in core temperature after sleep onset, accompanied by a rise in peripheral temperature, with a reverse pattern later in the night, just before awakening. This pattern was not related to room temperature, and was absent in the swaddled infants, suggesting that the mature diurnal pattern may develop later in them.

CONCLUSIONS:

No evidence of cold stress was found. **Swaddling had no identifiable thermal advantages over sleeping-bags during the coldest times, and in centrally heated apartments could contribute to the risk of overheating during the daytime.**

<http://adc.bmj.com/cgi/pmidlookup?view=long&pmid=26515228>

Low birth weight and prematurity

[J Trop Pediatr](#). 2015 Dec;61(6):414-20. doi: 10.1093/tropej/fmv049. Epub 2015 Sep 3.

[Topical Oil Application and Trans-Epidermal Water Loss in Preterm Very Low Birth Weight Infants-A Randomized Trial.](#)

[Nangia S](#), [Paul VK](#), [Deorari AK](#), [Sreenivas V](#), [Agarwal R](#), [Chawla D](#).

Abstract

OBJECTIVE:

Topical emollient application reduces **trans-epidermal water loss (TEWL) in preterm neonates**. Coconut oil used traditionally for infant massage in India has not been evaluated for the same.

PATIENTS AND METHODS:

Very low birth weight (VLBW) neonates were randomized at 12 h of age to Oil (n = 37) or Control (n = 37) groups. Oil group neonates received twice-daily coconut oil application without massage, and Control group received standard care. TEWL was measured every 12 h using an evaporimeter till Day 7 when skin swabs were obtained for bacterial growth and skin condition was assessed using a validated score.

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RESULTS:

Birth weight (g; mean \pm SD: 1213 + 214 vs. 1164 + 208, $p = 0.31$), gestation [week; median (interquartile range): 32 (31-33) vs. 32 (29-33), $p = 0.10$] and other baseline variables were comparable. **TEWL was significantly reduced (g/m(2)/h, mean difference: -6.80, 95% confidence interval: -3.48, -10.15; $p < 0.01$) with better skin condition and lower bacterial growth in the Oil group (20% vs. 60%, $p < 0.01$).**

CONCLUSION:

Coconut oil application reduced TEWL without increasing skin colonization in VLBW neonates.

[BMC Pregnancy Childbirth](#). 2016 May 17;16:110. doi: 10.1186/s12884-016-0900-5.

Risk factors for small-for-gestational-age and preterm births among 19,269 Tanzanian newborns.

[Muhihi A](#), [Sudfeld CR](#), [Smith ER](#), [Noor RA](#), [Mshamu S](#), [Briegleb C](#), [Bakari M](#), [Masanja H](#), [Fawzi W](#), [Chan GJ](#).

Abstract

BACKGROUND:

Few studies have differentiated risk factors for term-small for gestational age (SGA), preterm-appropriate for gestational age (AGA), and preterm-SGA, despite evidence of varying risk of child mortality and poor developmental outcomes.

METHODS:

We analyzed birth outcome data from singleton infants, who were enrolled in a large randomized, double-blind, placebo-controlled trial of neonatal vitamin A supplementation conducted in Tanzania. SGA was defined as birth weight <10th percentile for gestation age and sex using INTERGROWTH standards and preterm birth as delivery at <37 complete weeks of gestation. Risk factors for term-SGA, preterm-AGA, and preterm-SGA were examined independently using log-binomial regression.

RESULTS:

Among 19,269 singleton Tanzanian newborns included in this analysis, 68.3 % were term-AGA, 15.8 % term-SGA, 15.5 % preterm-AGA, and 0.3 % preterm-SGA. **In multivariate analyses, significant risk factors for term-SGA included maternal age <20 years, starting antenatal care (ANC) in the 3(rd) trimester, short maternal stature, being firstborn, and male sex (all $p < 0.05$).** Independent risk factors for preterm-AGA were maternal age <25 years, short maternal stature, firstborns, and decreased wealth (all $p < 0.05$). In addition, receiving ANC services in the 1(st) trimester significantly reduced the risk of preterm-AGA ($p = 0.01$). Significant risk factors for preterm-SGA included maternal age >30 years, being firstborn, and short maternal stature which appeared to carry a particularly strong risk (all $p < 0.05$).

CONCLUSION:

Over 30 % of newborns in this large urban and rural cohort of Tanzanian newborns were born preterm and/or SGA. Interventions to promote early attendance to ANC services, reduce unintended young pregnancies, increased maternal height, and reduce poverty may significantly decrease the burden of SGA and preterm birth in sub-Saharan Africa.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4869183/>

[Eur J Pediatr](#). 2015 Jul;174(7):949-56. doi: 10.1007/s00431-015-2494-8. Epub 2015 Feb 3.

[High versus low-dose caffeine for apnea of prematurity: a randomized controlled trial.](#)

[Mohammed S](#), [Nour I](#), [Shabaan AE](#), [Shouman B](#), [Abdel-Hady H](#), [Nasef N](#).

Abstract

The optimum caffeine dose in preterm infants has not been well investigated. We aimed to compare the efficacy and safety of high versus low-dose caffeine citrate on apnea of prematurity (AOP) and successful extubation of preterm infants from mechanical ventilation. **We compared high-dose (loading 40 mg/kg/day and maintenance of 20 mg/kg/day) versus low-dose (loading 20 mg/kg/day and maintenance of 10 mg/kg/day) caffeine citrate in preterm infants <32 weeks gestation, presented with AOP within the first 10 days of life.** A total of 120 neonates (60 in each group) were enrolled. **High-dose caffeine was associated with a significant reduction in extubation failure in mechanically ventilated preterm infants ($p<0.05$), the frequency of apnea ($p<0.001$), and days of documented apnea ($p<0.001$).** High-dose caffeine was associated with significant increase in episodes of tachycardia ($p<0.05$) without a significant impact on physician decision to withhold caffeine.

CONCLUSION:

The use of higher, than current standard, dose of caffeine may decrease the chance of extubation failure in mechanically ventilated preterm infants and frequency of AOP without significant side effects.

[J Perinatol](#). 2016 May 5. doi: 10.1038/jp.2016.70. [Epub ahead of print]

[A randomized double-blind controlled trial comparing two regimens of vitamin D supplementation in preterm neonates.](#)

[Tergestina M](#), [Rebekah G](#), [Job V](#), [Simon A](#), [Thomas N](#).

Abstract

OBJECTIVE:

To compare the efficacy of 400 vs 1000 IU oral vitamin D supplementation in preterm neonates of 27 to 34 weeks gestation.

METHODS:

This double-blind randomized controlled trial allocated preterm babies to receive either 400 or 1000 IU of vitamin D₃ (n=60 in each group). Primary outcome was prevalence of vitamin D insufficiency (serum vitamin D levels <20 ng ml⁻¹) at 40 weeks of corrected gestational age (CGA).

RESULTS:

At term CGA vitamin D insufficiency was significantly lower in the 1000 IU group than in the 400 IU group (2% vs 64.6%, $P\leq 0.001$). Although elevated vitamin D levels were seen in 9.8% of babies on 1000 IU per day, this was not associated with clinical or biochemical evidence of toxicity.

CONCLUSION:

Supplementing preterm babies with 1000 IU of vitamin D₃ daily decreases the prevalence of vitamin D insufficiency at term CGA. Excess levels of vitamin D may occur at this dose in some babies.

[BMJ Open](#). 2015 Jul 10;5(7):e006564. doi: 10.1136/bmjopen-2014-006564.

Role of probiotics VSL#3 in prevention of suspected sepsis in low birthweight infants in India: a randomised controlled trial.

Sinha A, Gupta SS, Chellani H, Maliye C, Kumari V, Arya S, Garg BS, Gaur SD, Gaind R, Deotale V, Taywade M, Prasad MS, Thavraj V, Mukherjee A, Roy M.

Abstract

OBJECTIVES:

To assess the effect of the probiotic VSL#3 in prevention of neonatal sepsis in low birthweight (LBW) infants.

DESIGN:

Randomised, double-blind, placebo-controlled trial.

SETTING:

Community setting in rural India.

PARTICIPANTS:

LBW infants aged 3-7 days.

INTERVENTIONS:

Infants were randomised to receive probiotic (VSL#3, 10 billion colony-forming units (cfu)) or placebo for 30 days, and were followed up for 2 months.

MAIN OUTCOME MEASURE:

Possible serious bacterial infection (PSBI) as per the Integrated Management of Neonatal Childhood Illnesses algorithm, as diagnosed by fieldworkers/physicians.

RESULTS:

668 infants were randomised to VSL#3 and 672 to placebo. By intention-to-treat analysis, the risk of PSBI among infants in the overall population of LBW infants was not statistically significant (RR 0.79 (95% CI 0.56 to 1.03)). Probiotics reduced median days of hospitalisation (6 days vs 3 days in probiotics) (p=0.018) but not the risk of hospitalisation (RR 0.66 (95% CI 0.42 to 1.04)). The onset of PSBI in 10% of infants occurred on the 40th day in the probiotics arm versus the 25th day in the control arm (p=0.063).

CONCLUSIONS:

Daily supplementation of LBW infants with probiotics VSL#3 (10 billion cfu) for 30 days led to a non-significant 21% reduction in risk of neonatal sepsis. A larger study with sufficient power and a more specific primary end point is warranted to confirm the preventive effect of VSL#3 on neonatal sepsis in LBW infants.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26163028/>

Trials. 2016 May 26;17(1):265. doi: 10.1186/s13063-016-1387-0.

Is a woolen cap effective in maintaining normothermia in low-birth-weight infants during kangaroo mother care? Study protocol for a randomized controlled trial.

Trevisanuto D, Putoto G, Pizzol D, Serena T, Manenti F, Varano S, Urso E, Massavon W, Tsegaye A, Wingo O, Onapa E, Segafredo G, Cavallin F.

Abstract

BACKGROUND:

Neonatal hypothermia is an important challenge associated with morbidity and mortality. Preventing neonatal hypothermia is important in high-resource countries, but is of fundamental importance in low-resource settings where supportive care is limited. Kangaroo mother care (KMC) is a low-cost intervention that, whenever possible, is strongly recommended for

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temperature maintenance. During KMC, the World Health Organization (WHO) guidelines recommend the use of a cap/hat, but its effect on temperature control during KMC remains to be established. In the hospitals participating in the projects of the non-governmental organization CUAMM, KMC represents a standard of care, but the heads of the babies often remain uncovered due to local habits or to the unavailability of a cap. The aim of the present study will be to assess the effectiveness and safety of using a woolen cap in maintaining normothermia in low-birth-weight infants (LBWI) during KMC.

METHODS/DESIGN:

This is a multicenter (three hospitals), multicountry (three countries), prospective, unblinded, randomized controlled trial of KMC treatment with and without a woolen cap in LBWI. After obtaining parental consent, all infants with a birth weight below 2500 g and who are candidates for KMC, based on the clinical decision of the attending physician, will be assigned to the KMC with a woolen cap group or to the KMC without a woolen cap group in a 1:1 ratio according to a computer-generated, randomized sequence. The duration of the study will be until the patient's discharge, with a maximum treatment duration of 7 days. The primary outcome measure will be whether the infants' temperatures remain within the normal range (36.5-37.5 °C) in the course of KMC during the intervention. In all participants, axillary temperature will be measured with a digital thermometer four times per day. In addition, maternal and room temperature will be recorded. Secondary outcome measures will be: episodes of apnea; sepsis; mortality before hospital discharge; in-hospital growth; and age at discharge.

DISCUSSION:

The findings of this study will be important for other units/settings in high- as well low-resource countries where KMC is routinely performed. Based on the results of the present study, we could speculate whether the use of a woolen cap may help to maintain the neonate within the normal thermal range. Furthermore, potential complications such as hyperthermia will be strictly monitored and collected.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4882808/>

Neonatal infection

[World J Pediatr.](#) 2016 Feb 1. [Epub ahead of print]

Feasibility and efficacy of gentamicin for treating neonatal sepsis in community-based settings: a systematic review.

[Jaiswal N](#), [Singh M](#), [Kondel R](#), [Kaur N](#), [Thumburu KK](#), [Kumar A](#), [Kaur H](#), [Chadha N](#), [Gupta N](#), [Agarwal A](#), [Malhotra S](#), [Shafiq N](#).

Abstract

BACKGROUND:

Neonatal sepsis is a leading cause of neonatal deaths in developing countries. The current recommended in-hospital treatment is parenteral ampicillin (or penicillin) and gentamicin in young infants for 10- 14 days; however, very few could access and afford. The current review is to evaluate the feasibility of gentamicin in community based settings.

METHODS:

Both observational and randomized controlled trials were included. Medline, Embase, Cochrane Central Register of Controlled Trials and Central Trial Register of India were searched until September 2013. We assessed the risk of bias by Cochrane Collaboration's "risk of bias" tool.

RESULTS:

Two observational studies indicated feasibility ensuring coverage of population, decrease in case fatality rate in the group treated by community health workers. In an RCT, no significant

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difference was observed in the treatment failure rates [odds ratio (OR)=0.88], and the mortality in the first and second week (OR=1.53; OR=2.24) between gentamicin and ceftriaxone groups. Within the gentamicin group, the combination of penicillin and gentamicin showed a lower rate of treatment failure (OR=0.44) and mortality at second week of life (OR=0.17) as compared to the combination of gentamicin and oral cotrimoxazole.

CONCLUSIONS:

Gentamicin for the treatment of neonatal sepsis is both feasible and effective in community-based settings and can be used as an alternative to the hospital based care in resource compromised settings. But there was less evidence in the management of neonatal sepsis in hospitals as was seen in this review in which we included only one RCT and three observational studies.

Nutrition, micronutrients and breast feeding

(see also Anaemia and iron deficiency, Zinc, Maternal nutrition, Vitamin A, Tuberculosis, Helminths and other gastrointestinal infections, HIV case management)

Micronutrients, multivitamins and food fortification

[Am J Clin Nutr.](#) 2016 May 11. pii: ajcn132571. [Epub ahead of print]

[Provitamin A-biofortified maize increases serum \$\beta\$ -carotene, but not retinol, in marginally nourished children: a cluster-randomized trial in rural Zambia.](#)

[Palmer AC](#), [Siamusantu W](#), [Chileshe J](#), [Schulze KJ](#), [Barffour M](#), [Craft NE](#), [Molobeka N](#), [Kalungwana N](#), [Arguello MA](#), [Mitra M](#), [Caswell B](#), [Klemm RD](#), [West KP Jr](#).

Abstract

BACKGROUND:

Vitamin A deficiency remains a nutritional concern in sub-Saharan Africa. Conventionally bred maize hybrids with high provitamin A carotenoid concentrations may have the potential to improve vitamin A status in maize-consuming populations.

OBJECTIVE:

We evaluated the efficacy of regular provitamin A carotenoid-biofortified "orange" maize meal (~15 μg β -carotene/g) consumption in improving vitamin A status and reducing vitamin A deficiency in children.

DESIGN:

This was a cluster-randomized controlled trial in the rural farming district of Mkushi, Zambia. All 4- to 8-y-old children in an ~400-km² area were identified and grouped by proximity into clusters of ~15-25 children. **We randomly assigned clusters to 1) orange maize meal (n = 25), 2) white maize meal (n = 25), or 3) a parallel, nonintervention group (n = 14).** Children in intervention clusters (n = 1024) received 200 g maize meal for 6 d/wk over 6 mo; the maize meal was prepared according to standardized recipes and served in cluster-level kitchens. Staff recorded attendance and leftovers. We collected venous blood before and after the intervention to measure serum retinol, β -carotene, C-reactive protein, and α_1 -acid glycoprotein.

RESULTS:

Intervention groups were comparable at baseline, and vitamin A status was better than anticipated (12.1% deficient on the basis of serum retinol <0.7 $\mu\text{mol/L}$). Although attendance at

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meals did not differ (85%), median daily maize intake was higher in white (154 g/d) than in orange (142 g/d) maize meal clusters. At follow-up, mean serum β -carotene was 0.14 $\mu\text{mol/L}$ (95% CI: 0.09, 0.20 $\mu\text{mol/L}$) higher in orange maize meal clusters ($P < 0.001$), but mean serum retinol (1.00 \pm 0.33 $\mu\text{mol/L}$ overall) and deficiency prevalence (17.1% overall) did not differ between arms.

CONCLUSION:

In this marginally nourished population, regular biofortified maize meal consumption increased serum β -carotene concentrations but did not improve serum retinol.

[Public Health Nutr.](#) 2016 Apr;19(5):935-45. doi: 10.1017/S1368980015002037. Epub 2015 Jul 6.

[Effect of African leafy vegetables on the micronutrient status of mildly deficient farm-school children in South Africa: a randomized controlled study.](#)

[van der Hoeven M](#), [Faber M](#), [Osei J](#), [Kruger A](#), [Smuts CM](#).

Abstract

OBJECTIVE:

A randomized controlled trial was conducted to assess the effect of African leafy vegetable (ALV) consumption on Fe, Zn and vitamin A status in children.

DESIGN:

Children were randomly allocated to receive either a 300 g cooked ALV dish and school meal starch (n 86) or the normal school meal (n 81) five times per week for three months. ALV in the dish consisted mainly of *Amaranthus cruentus* (at least 80 %) and the remainder of *Cleome gynandra*, *Cucurbita maxima* or *Vigna unguiculata*. Nutrient content and consumer acceptance of the ALV dish were also determined.

SETTING:

North West Province, South Africa.

SUBJECTS:

Grade R to grade 4 children (6-12 years old) of two farm schools.

RESULTS:

The ALV dish contributed 11.6-15.8 mg Fe and 1.4-3.7 mg Zn. At baseline, prevalence of deficiencies in the intervention group was 16.0 %, 16.3 %, 7.0 % and 75.6 %, respectively, for anaemia (Hb < 11.5 g/dl), Fe (serum ferritin < 15 $\mu\text{g/l}$), vitamin A (serum retinol < 20 $\mu\text{g/dl}$) and Zn (serum Zn < 65 $\mu\text{g/dl}$); and in the control group 10.5 %, 18.5 %, 2.5 % and 75.3 %, respectively. No significant estimated intervention effect was found.

CONCLUSIONS:

This randomized controlled trial showed that ALV were unable to improve serum retinol, serum ferritin or Hb if there are only mild deficiencies present. Furthermore, despite the low Zn status in the study population, ALV consumption did not improve serum Zn concentrations either.

[Am J Clin Nutr.](#) 2016 Jan;103(1):258-67. doi: 10.3945/ajcn.114.100164. Epub 2015 Dec 16.

[Biofortified yellow cassava and vitamin A status of Kenyan children: a randomized controlled trial.](#)

[Talsma EF](#), [Brouwer ID](#), [Verhoef H](#), [Mbera GN](#), [Mwangi AM](#), [Demir AY](#), [Maziya-Dixon B](#), [Boy E](#), [Zimmermann MB](#), [Melse-Boonstra A](#).

Abstract

BACKGROUND:

Whereas conventional white cassava roots are devoid of provitamin A, biofortified yellow varieties are naturally rich in β -carotene, the primary provitamin A carotenoid.

OBJECTIVE:

We assessed the effect of consuming yellow cassava on serum retinol concentration in Kenyan school children with marginal vitamin A status.

DESIGN:

We randomly allocated 342 children aged 5-13 y to receive daily, 6 d/wk, for 18.5 wk 1) **white cassava and placebo supplement (control group)**, 2) **provitamin A-rich cassava (mean content: 1460 μg β -carotene/d) and placebo supplement (yellow cassava group)**, and 3) **white cassava and β -carotene supplement (1053 $\mu\text{g}/\text{d}$; β -carotene supplement group)**. The **primary outcome was serum retinol concentration**; prespecified secondary outcomes were hemoglobin concentration and serum concentrations of β -carotene, retinol-binding protein, and prealbumin. Groups were compared by using ANCOVA, adjusting for inflammation, baseline serum concentrations of retinol and β -carotene, and stratified design.

RESULTS:

The baseline prevalence of serum retinol concentration $<0.7 \mu\text{mol}/\text{L}$ and inflammation was 27% and 24%, respectively. For children in the control, yellow cassava, and β -carotene supplement groups, the mean daily intake of cassava was 378, 371, and 378 g, respectively, and the total daily supply of provitamin A and vitamin A from diet and supplements was equivalent to 22, 220, and 175 μg retinol, respectively. **Both yellow cassava and β -carotene supplementation increased serum retinol concentration by 0.04 $\mu\text{mol}/\text{L}$ (95% CI: 0.00, 0.07 $\mu\text{mol}/\text{L}$); correspondingly, serum β -carotene concentration increased by 524% (448%, 608%) and 166% (134%, 202%).** We found no effect on hemoglobin concentration or serum concentrations of retinol-binding protein and prealbumin.

CONCLUSIONS:

In our study population, consumption of yellow cassava led to modest gains in serum retinol concentration and a large increase in β -carotene concentration. It can be an efficacious, new approach to improve vitamin A status.

<http://ajcn.nutrition.org/cgi/pmidlookup?view=long&pmid=26675768>

[Br J Nutr.](#) 2015 Dec 14;114(11):1829-37. doi: 10.1017/S0007114515003554. Epub 2015 Sep 28.

[Iodine status of young Burkinabe children receiving small-quantity lipid-based nutrient supplements and iodised salt: a cluster-randomised trial.](#)

[Hess SY](#), [Abbeddou S](#), [Yakes Jimenez E](#), [Ouédraogo JB](#), [Brown KH](#).

Abstract

The objective of the present study was to assess the impact of providing small-quantity lipid-based nutrient supplements (SQ-LNS) on the I status of young Burkinabe children. In total, thirty-four communities were assigned to intervention (IC) or non-intervention cohorts (NIC). **IC children were randomly assigned to receive 20 g lipid-based nutrient supplements (LNS)/d containing 90 μg I with 0 or 10 mg Zn from 9 to 18 months of age, and NIC children received no SQ-LNS.** All the children were exposed to iodised salt through the national salt iodization programme. Spot urinary iodine (UI), thyroid-stimulating hormone (TSH) and total thyroxine (T4) in dried blood spots as well as plasma thyroglobulin (Tg)

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concentrations were assessed at 9 and 18 months of age among 123 IC and fifty-six NIC children. At baseline and at 18 months, UI, TSH and T4 did not differ between cohorts. Tg concentration was higher in the NIC v. IC at baseline, but this difference did not persist at 18 months of age. In both cohorts combined, the geometric mean of UI was 339.2 (95% CI 298.6, 385.2) µg/l, TSH 0.8 (95% CI 0.7, 0.8) mU/l, T4 118 (95 % CI 114, 122) nmol/l and Tg 26.0 (95% CI 24.3, 27.7) µg/l at 18 months of age. None of the children had elevated TSH at 18 months of age. Marginally more children in NIC (8.9%) had low T4 (15 ppm). A reduction of SQ-LNS I content could be considered in settings with similarly successful salt iodisation programmes.

[Clin Nutr.](#) 2016 Feb;35(1):190-8. doi: 10.1016/j.clnu.2015.02.001. Epub 2015 Feb 21.

The effects of regular consumption of a multiple micronutrient fortified milk beverage on the micronutrient status of school children and on their mental and physical performance.

[Kuriyan R](#), [Thankachan P](#), [Selvam S](#), [Pauline M](#), [Srinivasan K](#), [Kamath-Jha S](#), [Vinoy S](#), [Misra S](#), [Finnegan Y](#), [Kurpad AV](#).

Abstract

Multiple micronutrient deficiencies exist in school going children in India and bridging the gap between nutrient intake and requirements is an effective way to combat the deficiencies. This study aimed to test the effect of a multi-micronutrient fortified malt and cocoa based milk beverage on the micronutrient status, cognition, physical performance and nutritional deficiencies of 7-10 years old south Indian children. A randomized, double blind placebo controlled study design was used with normal healthy children from low to middle income families, **aged 7-10 years randomly assigned to receive either a multi-micronutrient fortified or an unfortified milk based control drink. The drinks were provided 6 days/week for 5 months.** Assessments included anthropometry, blood biochemistry, physical performance and cognition at baseline and endline. The baseline characteristics of the study groups were similar. The changes in body weight and height were similar between the groups at the end of the study. **Levels of vitamin B12, red cell folate and vitamin B2 significantly improved in the intervention group, while vitamin D, selenium and body iron showed no difference. The Hemoglobin (Hb) and serum ferritin levels of the control group decreased at endline, while those in the intervention group maintained their levels.** The serum transferrin receptor levels increased in both the groups. **The prevalence of iron deficiency and Vitamin B2 deficiency were significantly lower in the intervention group at endline.** Overall improvement in cognitive and physical performance was seen in both the groups at endline, with no significant differences between the groups. The micronutrient fortified milk based drink was efficacious in improving the micronutrient status of Vitamin B2, Vitamin B12 and red cell folate and in preventing a decline in Hb level compared to an unfortified milk based drink. It also reduced anemia and the risk of deficiencies of iron, and B12, in apparently healthy children

[Nutrients.](#) 2015 Aug 7;7(8):6606-27. doi: 10.3390/nu7085302.

The Long Term Impact of Micronutrient Supplementation during Infancy on Cognition and Executive Function Performance in Pre-School Children.

[Warthon-Medina M](#), [Qualter P](#), [Zavaleta N](#), [Dillon S](#), [Lazarte F](#), [Lowe NM](#).

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Abstract

Brain growth and development are critically dependent on several micronutrients. During early development cellular activity may be sensitive to micronutrient deficiencies, however the evidence from human studies is equivocal. The objective of this study was to examine the long-term cognitive and social-emotional effects of multiple micronutrient supplementation compared with iron supplementation alone, administered during infancy. This study was a follow-up to an initial randomized, double-blind controlled trial (RCT) in 2010 in which 902 infants, aged 6-17 months, from Lima, Peru, were given daily supplements of either iron (Fe) or multiple micronutrients (MMN) including zinc (451 in each group). The supplementation period for both groups was six months. In 2012, a subsample of 184 children from the original cohort (now aged 36-48 months) was randomly selected to participate in a follow-up trial and was assessed for intelligence, working memory, inhibition, and executive function. The tests showed no significant differences between the supplementation groups though there were some gender differences, with girls displaying higher scores than boys across both groups on the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) Verbal IQ sentences subtest, the Day-Night cognitive test and on the Brief Infant-Toddler Social Emotional Assessment (BITSEA) social competency, and boys scoring higher than girls in problem behaviour. The results indicate that MMN supplementation had no long term additional effects on cognitive function compared with iron supplementation alone. The timing of supplement administration for maximum impact on a child's cognitive development requires further investigation.

<http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26262642/>

Environmental enteric dysfunction

[Trials](#). 2015 Nov 14;16:520. doi: 10.1186/s13063-015-1027-0.

[Common beans and cowpeas as complementary foods to reduce environmental enteric dysfunction and stunting in Malawian children: study protocol for two randomized controlled trials.](#)

[Trehan I](#), [Benzoni NS](#), [Wang AZ](#), [Bollinger LB](#), [Ngoma TN](#), [Chimimba UK](#), [Stephenson KB](#), [Agapova SE](#), [Maleta KM](#), [Manary MJ](#).

Abstract

BACKGROUND:

Interventions to decrease the burden of childhood malnutrition are urgently needed, as millions of children die annually owing to undernutrition and hundreds of millions more are left cognitively and physically stunted. Environmental enteric dysfunction (EED), a pervasive chronic sub-clinical inflammatory condition among children that develops when complementary foods are introduced, places them at high risk of stunting, malabsorption, and poor oral vaccine efficacy. Improved interventions to reduce the burden of EED and stunting are expected to markedly improve the nutritional status and survival of children throughout resource-limited settings.

METHODS/DESIGN:

We will conduct, in parallel, two prospective randomized controlled clinical trials to determine whether **common beans or cowpeas improve growth, ameliorate EED, and alter the intestinal microbiome during a high-risk period in the lives of rural Malawian children.** Study 1 will enroll children at 6 months of age and randomize them to receive common beans,

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cowpeas, or a standard complementary food for 6 months. Anthropometry will be compared among the three groups; EED will be assessed using a dual-sugar absorption test and by quantifying human intestinal mRNA for inflammatory messages; and the intestinal microbiota will be characterized by deep sequencing of fecal DNA, to enumerate host microbial populations and their metabolic capacity. Study 2 will enroll children 12-23 months old and follow them for 12 months, with similar interventions and assessments as Study 1.

DISCUSSION:

By amalgamating the power of rigorous clinical trials and advanced biological analysis, we aim to elucidate the potential of two grain legumes to reduce stunting and EED in a high-risk population. Legumes have potential as an affordable and effective complementary food intervention, given their cultural acceptability, nutritional content, and agricultural feasibility in sub-Saharan Africa.

<http://trialsjournal.biomedcentral.com/articles/10.1186/s13063-015-1027-0>

Comment

These above studies are yet to be done, but environmental enteropathy is important and neglected problem among children living in the poorest circumstances. Environmental enteropathy is a chronic inflammatory state of the duodenum and jejunum, associated with mucosal villus atrophy, crypt hyperplasia and inflammatory cell infiltrate (CD8+ T-cell lymphocytes). The villi are broad and flat with increases in the crypt depth between villi. The surface area available for nutrient absorption is markedly reduced. There is moderate malabsorption, often subclinical, often without diarrhoea. Absorption of essential fats, carbohydrates and vitamins is decreased. Because it is an indolent chronic condition it leads to stunting. Environmental enteropathy is likely to be caused by faecal bacteria ingested in large quantities by young children living in conditions of poor sanitation and hygiene. The solutions are likely to be water, sanitation and hygiene: toilets, handwashing, soap and running water, improved drinking water, exclusive breast feeding, properly prepared complementary feeding, and avoidance of bottle feeding.

Macronutrient nutrition and complementary feeding

(See also Vitamin A)

[Int J Epidemiol.](#) 2015 Dec;44(6):1862-76. doi: 10.1093/ije/dyv155. Epub 2015 Aug 14.

[Effect of fortified complementary food supplementation on child growth in rural Bangladesh: a cluster-randomized trial.](#)

[Christian P](#), [Shaikh S](#), [Shamim AA](#), [Mehra S](#), [Wu L](#), [Mitra M](#), [Ali H](#), [Merrill RD](#), [Choudhury N](#), [Parveen M](#), [Fuli RD](#), [Hossain MI](#), [Islam MM](#), [Klemm R](#), [Schulze K](#), [Labrique A](#), [de Pee S](#), [Ahmed T](#), [West KP Jr](#).

Abstract

BACKGROUND:

Growth faltering in the first 2 years of life is high in South Asia where prevalence of stunting is estimated at 40-50%. Although nutrition counselling has shown modest benefits, few

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intervention trials of food supplementation exist showing improvements in growth and prevention of stunting.

METHODS:

A cluster-randomized controlled trial was conducted in rural Bangladesh to **test the effect of two local, ready-to-use foods (chickpea and rice-lentil based) and a fortified blended food (wheat-soy-blend++, WSB++) compared with Plumpy'doz**, all with nutrition counselling vs nutrition counselling alone (control) on outcomes of linear growth (length and length-for-age z-score, LAZ), stunting (LAZ < -2), weight-for-length z-score (WLZ) and wasting (WLZ < -2) in children 6-18 months of age. Children (n = 5536) were enrolled at 6 months of age and, in the food groups, provided with one of the allocated supplements daily for a year.

RESULTS:

Growth deceleration occurred from 6 to 18 months of age but deceleration in LAZ was lower (by 0.02-0.04/month) in the Plumpy'doz (P = 0.02), rice-lentil (< 0.01), and chickpea (< 0.01) groups relative to control, whereas WLZ decline was lower only in Plumpy'doz and chickpea groups. WSB++ did not impact on these outcomes. The prevalence of stunting was 44% at 18 months in the control group, but lower by 5-6% (P ≤ 0.01) in those receiving Plumpy'doz and chickpea. Mean length and LAZ at 18 months were higher by 0.27-0.30 cm and 0.07-0.10 (all P < 0.05), respectively, in all four food groups relative to the control.

CONCLUSIONS:

In rural Bangladesh, small amounts of daily fortified complementary foods, provided for a year in addition to nutrition counselling, modestly increased linear growth and reduced stunting at 18 months of age.

<http://ije.oxfordjournals.org/cgi/pmidlookup?view=long&pmid=26275453>

[J Nutr.](#) 2016 Jan;146(1):124-32. doi: 10.3945/jn.115.218917. Epub 2015 Nov 25.

[A Randomized Controlled Trial Offering Higher- Compared with Lower-Dairy Second Meals Daily in Preschools in Guinea-Bissau Demonstrates an Attendance-Dependent Increase in Weight Gain for Both Meal Types and an Increase in Mid-Upper Arm Circumference for the Higher-Dairy Meal.](#)

[Batra P](#), [Schlossman N](#), [Balan I](#), [Pruzensky W](#), [Balan A](#), [Brown C](#), [Gamache MG](#), [Schleicher MM](#), [de Sa AB](#), [Saltzman E](#), [Wood L](#), [Roberts SB](#).

Abstract

BACKGROUND:

Controversy remains over the most effective approaches to prevent childhood malnutrition.

OBJECTIVES:

We tested the feasibility and effectiveness of delivering ready-to-use supplementary foods (RUSFs) as a second daily meal in preschool children aged 3-5 y in Guinea-Bissau, and compared RUSFs with different levels of dairy protein.

METHODS:

This study was a **3 mo cluster-randomized controlled pilot trial of 2 RUSFs differing in dairy protein in 533 boys and girls from 9 preschools**. Children receiving RUSFs were compared with wait-listed controls, and all students received a daily school lunch. The RUSFs were delivered 5 d/wk for 3 mo and contained 478 kcal and 11.5 g protein per 92-g daily serving. Deliveries included a ready-to-use supplementary food with 15% of protein from dairy sources (RUSF-15%) or one with 33% of protein from dairy sources (RUSF-33%). Intention-to-treat (ITT) and per-protocol analyses (>50 d of RUSF consumption) were conducted. Changes in the weight-for-age z score (WAZ) and height-for-age z score were primary outcomes.

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Additional outcomes included changes in mid-upper arm circumference (MUAC), hemoglobin, and retinol binding protein.

RESULTS:

Baseline anthropometry was not different between groups (WAZ, -0.48 ± 1.04) and increased significantly over time ($P < 0.01$) with no effects of the RUSFs in ITT analyses.

However, children consuming RUSFs for >50 d had a significantly greater increase in WAZ relative to the increase in controls ($+0.40$ and $+0.32$ for RUSF-15% and RUSF-33%, respectively, compared with $+0.24$ in controls, $P < 0.01$ and $P < 0.05$, respectively). RUSF-33%, but not RUSF-15%, also eliminated a decrease in MUAC observed in controls (-0.01 cm in RUSF-33% compared with -0.34 cm in controls, $P < 0.05$). The only difference between RUSF-15% and RUSF-33% was a mean decrease in hemoglobin in children receiving RUSF-15% (-0.5 compared with -0.002 g/dL, $P = 0.05$).

CONCLUSIONS:

Implementation of 2-meal preschool feeding programs is feasible in low-income countries, and there are measurable benefits relative to 1-meal programs in children attending preschool regularly. In addition, MUAC and hemoglobin measurements indicate that meals with 33% compared with 15% of protein from dairy may help prevent wasting and anemia.

[J Nutr.](#) 2015 Aug;145(8):1909-15. doi: 10.3945/jn.114.208181. Epub 2015 Jun 10.

[Provision of 10-40 g/d Lipid-Based Nutrient Supplements from 6 to 18 Months of Age Does Not Prevent Linear Growth Faltering in Malawi.](#)

[Maleta KM](#), [Phuka J](#), [Alho L](#), [Cheung YB](#), [Dewey KG](#), [Ashorn U](#), [Phiri N](#), [Phiri TE](#), [Vosti SA](#), [Zeilani M](#), [Kumwenda C](#), [Bendabenda J](#), [Pulakka A](#), [Ashorn P](#).

Abstract

BACKGROUND:

Complementing infant diets with lipid-based nutrient supplements (LNSs) has been suggested to improve growth and reduce morbidity, but the daily quantity and the milk content of LNSs affect their cost.

OBJECTIVE:

We tested the hypotheses that the change in mean length-for-age z score (LAZ) for infants provided with 10-40 g LNSs/d from ages 6 to 18 mo would be greater than that for infants receiving no dietary intervention at the same age and that provision of LNSs that did not contain milk would be as good as milk-containing LNSs in promoting linear growth.

METHODS:

We enrolled in a randomized single-blind trial 6-mo-old infants who were allocated to 1 of 6 groups to receive 10, 20, or 40 g LNSs/d containing milk powder; 20 or 40 g milk-free LNSs/d; or no supplement until 18 mo of age. The primary outcome was change in LAZ.

RESULTS:

Of the 1932 enrolled infants, 78 (4.0%) died and 319 (16.5%) dropped out during the trial. The overall reported supplement consumption was 71.6% of days, with no difference between the groups ($P = 0.26$). **The overall mean \pm SD length and LAZ changes were 13.0 ± 2.1 cm and -0.45 ± 0.77 z score units, respectively, which did not differ between the groups ($P = 0.66$ for length and $P = 0.74$ for LAZ).** The difference in mean LAZ change in the no-milk LNS group compared with the milk LNS group was -0.02 (95% CI: $-0.10, 0.06$; $P = 0.72$).

CONCLUSION:

Our results do not support the hypothesis that LNS supplementation during infancy and childhood promotes length gain or prevents stunting between 6 and 18 mo of age in Malawi.

[J Nutr.](#) 2015 Jul;145(7):1588-95. doi: 10.3945/jn.114.209593. Epub 2015 May 20.

Malawian Mothers Consider Lipid-Based Nutrient Supplements Acceptable for Children throughout a 1-Year Intervention, but Deviation from User Recommendations Is Common.

[Ashorn U](#), [Alho L](#), [Arimond M](#), [Dewey KG](#), [Maleta K](#), [Phiri N](#), [Phuka J](#), [Vosti SA](#), [Zeilani M](#), [Ashorn P](#).

Abstract

BACKGROUND:

Lipid-based nutrient supplements (LNSs) offer a vehicle to improve children's diets in low-income countries where complementary foods are typically deficient in essential nutrients. Sustained acceptability by the intended users is essential for achieving growth-promoting effects.

OBJECTIVE:

We aimed to determine the sustained acceptability of LNSs among 6- to 18-mo-old children in Malawi.

METHODS:

In the context of a trial testing the growth-promoting effect of different formulations and doses of LNSs, we delivered LNSs to the homes of the children biweekly according to the randomization protocol. We defined acceptability to include adherence to feeding recommendations and mothers' experiences of feeding LNSs to their child. We conducted brief interviews each week with the mothers. At 2 time points we conducted knowledge, attitudes, and practices (KAP) interviews. In addition, we conducted repeated in-depth interviews with a subset of mothers.

RESULTS:

Of the 1612 children who received the LNS intervention, we analyzed adherence data from 1478 (91.7%) children and KAP data at 2 time points (child's age of 12 and 18 mo) from 839 (52.1%) of the children. **The mean \pm SD overall adherence (proportion of days when the study child reportedly consumed LNSs considering only those weeks when the supplement had been successfully delivered to the home) was $92.4 \pm 9.6\%$, and there was no difference between children receiving milk-containing or milk-free LNSs.** There was also no increasing or decreasing trend over time in any of the groups. Sharing and deviation from other feeding recommendations were common. Maternal experiences were mostly very positive.

CONCLUSIONS:

The acceptability of LNS products was good and was sustained for 12 mo in this rural Malawian population. However, sharing of the products with family members and deviation from other feeding recommendations were frequent, which means that individually targeted children were likely to receive less than the intended dose of the LNS

[J Nutr.](#) 2015 Dec;145(12):2749-55. doi: 10.3945/jn.115.212134. Epub 2015 Oct 21.

Promotion of Weight Gain in Early Childhood Does Not Increase Metabolic Risk in Adolescents: A 15-Year Follow-Up of a Cluster-Randomized Controlled Trial.

[Santos IS](#), [Matijasevich A](#), [Assunção MC](#), [Valle NC](#), [Horta BL](#), [Gonçalves HD](#), [Gigante DP](#), [Martines JC](#), [Pelto G](#), [Victora CG](#).

Abstract

Randomised trials in child health in developing countries 2015-16

BACKGROUND:

A rapid gain in weight for length may put children at a higher risk of noncommunicable diseases later in life.

OBJECTIVE:

The objective of this study was to assess the long-term effects of nutrition counseling delivered in the first 2 y of life in Pelotas, a city in Southern Brazil.

METHODS:

The original cluster-randomized controlled trial was conducted in 1998. Nutrition counseling (breastfeeding promotion and increased intake of micronutrient-rich and energy-dense foods) was delivered to mothers of children aged 0-17.9 mo attending primary care. Six months later, weight gain was higher in the intervention group than in the control group for children ≥ 12 mo of age at enrollment. In 2013 (mean age 15 y), assessments included anthropometric measurements, body composition (air-displacement plethysmography), body shape (3-dimensional photonic scan), and plasma total, LDL, and HDL cholesterol, triglycerides, C-reactive protein, and glucose.

RESULTS:

A total of 363 of the 424 original participants were assessed. An a priori decision was made to prioritize analyses of subjects aged 12-17.9 mo at enrollment (51 from the intervention group and 45 from the control group). **In this subgroup, boys in the intervention group were [mean (95% CI)] 3.4 (0.8, 6.0) cm taller than those in the control group.** Systolic blood pressure tended to be 5.2 (-0.8, 11.1) mm Hg higher in male subjects from the intervention group than in those in the control group. Lipid profiles tended to be healthier in the intervention group. The plasma total cholesterol concentration was -17.8 (-29.8, -5.7) mg/dL lower in boys in the intervention group than in those in the control group. The total-to-HDL cholesterol ratio and triglyceride concentration in the girls in the intervention group were -0.4 (-0.6, -0.1) and -26.3 (-46.3, -6.3) mg/dL, respectively, lower than in the control group. There was no difference between the groups in terms of body composition.

CONCLUSIONS:

Promotion of weight gain in children between 12.0-17.9 mo of age was not associated with higher metabolic risk 15 y later. On the contrary, there was some evidence of reduced metabolic risk in the intervention group.

Breastfeeding

[Lancet Glob Health](#). 2015 Sep;3(9):e546-55. doi: 10.1016/S2214-109X(15)00012-1. Epub 2015 Aug 2.

[Ten Steps to Successful Breastfeeding programme to promote early initiation and exclusive breastfeeding in DR Congo: a cluster-randomised controlled trial.](#)

[Yotebieng M](#), [Labbok M](#), [Soeters HM](#), [Chalachala JL](#), [Lapika B](#), [Vitta BS](#), [Behets F](#).

Abstract

BACKGROUND:

Optimisation of breastfeeding practices could reduce high mortality rates in children younger than 5 years, but in DR Congo, despite near-universal breastfeeding initiation and nine of ten children still breastfeeding at 1 year of age, exclusivity remains a difficulty. We assessed the effect on breastfeeding outcomes of a short-cut implementation of a programme called the Ten

Randomised trials in child health in developing countries 2015-16

Steps to Successful Breastfeeding, the key component of the Baby-Friendly Hospital Initiative (BFHI).

METHODS:

We did a cluster-randomised controlled trial and randomly assigned health-care clinics in Kinshasa, DR Congo, to standard care (control group), BFHI steps 1-9 (steps 1-9 group), or BFHI steps 1-9 plus additional support during well-child visits (steps 1-10 group) with computer-generated random numbers used to assign matched pairs to study groups.

Mothers at these clinics who had given birth to one healthy baby during enrolment, and who expressed their intentions of visiting a well-baby session at the same clinic, were eligible and received the treatment assigned to their clinic. Mother-infant pairs were excluded if the mothers intended to attend well-baby clinic visits at a different health facility, or to travel before the child was aged at least 6 months. Participants and independent interviewers were masked to group assignment (ie, they were recruited after randomisation and training of the clinic staff and were not informed of the study scheme), but clinical staff were unmasked. **BFHI steps 1-9 and 1-10 were given by health-care staff trained with the WHO/UNICEF BFHI course.** The primary outcomes were breastfeeding initiation within 1 h of birth and exclusive breastfeeding at age 14 and 24 weeks, assessed at face-to-face interviews in the clinic. Analysis was by intention to treat. Prevalence ratios (PR) were adjusted for cluster effects and baseline characteristics. This trial is registered at ClinicalTrials.gov, number [NCT01428232](https://clinicaltrials.gov/ct2/show/study/NCT01428232), and is closed to new participants.

FINDINGS:

Between May 24, and Aug 25, 2012, we randomly assigned two eligible clinics to control, two to BFHI steps 1-9, and two to BFHI steps 1-10. We enrolled 975 eligible mother-infant pairs (304 in the control group, 363 in the steps 1-9 group, and 308 in the steps 1-10 group). 230 (76%) of infants in the control group, 263 (72%) in the steps 1-9 group, and 220 (71%) in the steps 1-10 group were breastfed within 1 h of birth; these results did not differ significantly between groups. Prevalence of exclusive breastfeeding at age 14 weeks was 89 (29%) in the control group, 237 (65%) in the steps 1-9 group (adjusted PR 2.20, 95% CI 1.73-2.77), and 129 (42%) in the steps 1-10 group (1.40, 1.13-1.74). At age 24 weeks, the prevalence of exclusive breastfeeding was 36 (12%) in the control group, 131 (36%) in the steps 1-9 group (3.50, 2.76-4.43), and 43 (14%) in the steps 1-10 group (1.31, 0.91-1.89).

INTERPRETATION:

In the setting of health-care clinics in DR Congo with a high proportion of mothers initiating breastfeeding, implementation of basic training in BFHI steps 1-9 had no additional effect on initiation of breastfeeding but significantly increased exclusive breastfeeding at 6 months of age. Additional support based on the same training materials and locally available breastfeeding support materials, offered during well-child visits (ie, step 10) did not enhance this effect, and might have actually lessened it.

[http://linkinghub.elsevier.com/retrieve/pii/S2214-109X\(15\)00012-1](http://linkinghub.elsevier.com/retrieve/pii/S2214-109X(15)00012-1)

Comment

The 10 steps of the Baby Friendly Hospital Initiative are:

1. *Have a written breastfeeding policy that is routinely communicated to all health care staff.*
2. *Train all health care staff in skills necessary to implement this policy.*
3. *Inform all pregnant women about the benefits and management of breastfeeding.*
4. *Help mothers initiate breastfeeding within a half-hour of birth.*
5. *Show mothers how to breastfeed and how to maintain lactation, even if they should be separated from their infants.*
6. *Give newborn infants no food or drink other than breast milk unless medically indicated.*
7. *Practice rooming-in - allow mothers and infants to remain together - 24 hours a day.*

Randomised trials in child health in developing countries 2015-16

8. *Encourage breastfeeding on demand.*
9. *Give no artificial teats or pacifiers (also called dummies or soothers) to breastfeeding infants.*
10. *Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or clinic.*

Community nutrition and agriculture

[BMC Public Health](#). 2015 Oct 12;15:1044. doi: 10.1186/s12889-015-2380-3.

[The REFANI Pakistan study--a cluster randomised controlled trial of the effectiveness and cost-effectiveness of cash-based transfer programmes on child nutrition status: study protocol.](#)

Fenn B, Sangrasi GM, Puett C, Trenouth L, Pietzsch S.

Abstract

BACKGROUND:

Cash-based transfer programmes are an emerging strategy in the prevention of wasting in children, especially targeted at vulnerable households during periods of food insecurity or during emergencies. However, the evidence surrounding the use of either cash or voucher transfer programmes in the humanitarian context and on nutritional outcomes is elusive. More evidence is needed not only to inform the global community of practice on best practices in humanitarian settings, but also to help strengthen national mitigation responses.

METHODS/DESIGN:

The Research for Food Assistance on Nutrition Impact Pakistan study (REFANI-P) sets out to evaluate the impact of **three cash-based interventions on nutritional outcomes in children aged less than five years from poor and very poor households in Dadu District**. This four-arm parallel cluster randomised controlled trial is set among Action Against Hunger (ACF) programme villages in Dadu District, Sindh Province. Mothers are the target recipients of either seasonal unconditional cash transfers or fresh food vouchers. A comparison group receives 'standard care' provided by the ACF programme to which all groups have the same access. The primary outcomes are prevalence of wasting and mean weight-for-height Z-score (WHZ) in children. Impact will be assessed at 6 months and at 1 year from baseline. Using a theory-based approach we will determine 'how' the different interventions work by looking at the processes involved and the impact pathways following the theory of change developed for this context. Quantitative and qualitative data are collected on morbidity, health seeking, hygiene and nutrition behaviours, dietary diversity, haemoglobin concentration, women's empowerment, household food security and expenditures and social capital. The direct and indirect costs of each intervention borne by the implementing organisation and their partners as well as by beneficiaries and their communities are also assessed.

DISCUSSION:

The results of this trial will provide robust evidence to help increase knowledge about the predictability of how different modalities of cash-based transfer work best to reduce the risk of child wasting during a season where food insecurity is at its highest. Evidence on costing and cost-effectiveness will further aid decisions on choice of modality in terms of effectiveness and sustainability.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26459336/>

[BMC Public Health](#). 2015 Aug 8;15:762. doi: 10.1186/s12889-015-2060-3.

[The MAM'Out project: a randomized controlled trial to assess multiannual and seasonal cash transfers for the prevention of acute malnutrition in children under 36 months in Burkina Faso.](#)

[Tonguet-Papucci A](#), [Huybregts L](#), [Ait Aissa M](#), [Huneau JF](#), [Kolsteren P](#).

Abstract

BACKGROUND:

Wasting is a public health issue but evidence gaps remain concerning preventive strategies not primarily based on food products. Cash transfers, as part of safety net approach, have potential to prevent under-nutrition. However, most of the cash transfer programs implemented and scientifically evaluated do not have a clear nutritional objective, which leads to a lack of evidence regarding their nutritional benefits.

METHODS/DESIGN:

The MAM'Out research project aims at evaluating a seasonal and multiannual cash transfer program to prevent acute malnutrition in children under 36 months, in terms of effectiveness and cost-effectiveness in the Tapoa province (Eastern region of Burkina Faso, Africa). The program is targeted to economically vulnerable households with children less than 1 year old at the time of inclusion. Cash is distributed to mothers and the transfers are unconditional, leading to beneficiaries' self-determination on the use of cash. The study is designed as a two-arm cluster randomized intervention trial, based on the randomization of rural villages. One group receives cash transfers via mobile phones and one is a control group. The main outcomes are the cumulative incidence of acute malnutrition and the cost-effectiveness. Child anthropometry (height, weight and MUAC) is followed, as well as indicators related to dietary diversity, food security, health center utilization, families' expenses, women empowerment and morbidities. 24 h-food recalls are also carried out. Individual interviews and focus group discussions allow collecting qualitative data. Finally, based on a theory framework built a priori, the pathways used by the cash to have an effect on the prevention of under-nutrition will be assessed.

DISCUSSION:

The design chosen will lead to a robust assessment of the effectiveness of the proposed intervention. Several challenges appeared while implementing the study and discrepancies with the research protocol, mainly due to unforeseen events, can be highlighted, such as delay in project implementation, switch to e-data collection and implementation of a supervision process.

<http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26253152/>

Obesity

Oncology

(see also HIV – management of HIV related conditions)

[Support Care Cancer](#). 2015 Nov;23(11):3229-37. doi: 10.1007/s00520-015-2714-9. Epub 2015 Apr 8.

[Aprepitant as an add-on therapy in children receiving highly emetogenic chemotherapy: a randomized, double-blind, placebo-controlled trial.](#)

[Bakhshi S](#), [Batra A](#), [Biswas B](#), [Dhawan D](#), [Paul R](#), [Sreenivas V](#).

Abstract

BACKGROUND:

Aprepitant, a neurokinin-1 receptor antagonist, in combination with 5 HT-3 antagonist and dexamethasone is recommended in adults receiving moderately and highly emetogenic chemotherapy to reduce chemotherapy-induced vomiting (CIV). Data for use of aprepitant in children is limited and hence aprepitant is not recommended by Pediatric Oncology Group of Ontario guidelines for prevention of CIV in children <12 years.

METHODS:

A randomized, double-blind, placebo-controlled trial was conducted at a single center in chemotherapy naïve children (5-18 years) receiving highly emetogenic chemotherapy. All patients received intravenous ondansetron (0.15 mg/kg) and dexamethasone (0.15 mg/kg) prior to chemotherapy followed by oral ondansetron and dexamethasone. Patients randomly assigned to aprepitant arm received oral aprepitant (15-40 kg = days 1-3, 80 mg; 41-65 kg = day 1, 125 mg and days 2-3, 80 mg) 1 h before chemotherapy. Control group received placebo as add-on therapy. **Primary outcome measure was the incidence of acute moderate to severe vomiting**, which was defined as more than two vomiting episodes within 24 h after the administration of the first chemotherapy dose until 24 h after the last chemotherapy dose in the block. Complete response (CR) was defined as absence of vomiting and retching during the specified phase.

RESULTS:

Of the 96 randomized patients, three were excluded from analysis; 93 patients were analyzed (50 in aprepitant arm and 43 in placebo arm). **Acute moderate and severe vomiting was reported in 72 % patients receiving placebo and 38 % patients receiving aprepitant** ($p = 0.001$). Complete response rates during acute phase were significantly higher in aprepitant arm (48 vs. 12 %, $p < 0.001$). No major adverse effects were reported by patients/guardians.

CONCLUSIONS:

This double-blind, randomized, placebo-controlled trial shows that aprepitant significantly decreases the incidence of CIV during acute phase when used as an add-on drug with ondansetron and dexamethasone in children receiving highly emetogenic chemotherapy.

Ophthalmology

[JAMA](#). 2015 Sep 15;314(11):1142-8. doi: 10.1001/jama.2015.10803.

[Effect of Time Spent Outdoors at School on the Development of Myopia Among Children in China: A Randomized Clinical Trial.](#)

[He M](#), [Xiang F](#), [Zeng Y](#), [Mai J](#), [Chen Q](#), [Zhang J](#), [Smith W](#), [Rose K](#), [Morgan IG](#).

Abstract

IMPORTANCE:

Myopia has reached epidemic levels in parts of East and Southeast Asia. However, there is no effective intervention to prevent the development of myopia.

OBJECTIVE:

To assess the efficacy of increasing time spent outdoors at school in preventing incident myopia.

DESIGN, SETTING, AND PARTICIPANTS:

Cluster randomized trial of children in grade 1 from 12 primary schools in Guangzhou, China, conducted between October 2010 and October 2013.

INTERVENTIONS:

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For 6 intervention schools (n = 952 students), 1 additional 40-minute class of outdoor activities was added to each school day, and parents were encouraged to engage their children in outdoor activities after school hours, especially during weekends and holidays. Children and parents in the 6 control schools (n = 951 students) continued their usual pattern of activity.

MAIN OUTCOMES AND MEASURES:

The primary outcome measure was the 3-year cumulative incidence rate of myopia (defined using the Refractive Error Study in Children spherical equivalent refractive error standard of ≤ -0.5 diopters [D]) among the students without established myopia at baseline. Secondary outcome measures were changes in spherical equivalent refraction and axial length among all students, analyzed using mixed linear models and intention-to-treat principles. Data from the right eyes were used for the analysis.

RESULTS:

There were 952 children in the intervention group and 951 in the control group with a mean (SD) age of 6.6 (0.34) years. **The cumulative incidence rate of myopia was 30.4% in the intervention group (259 incident cases among 853 eligible participants) and 39.5% (287 incident cases among 726 eligible participants) in the control group (difference of -9.1% [95% CI, -14.1% to -4.1%]; $P < .001$).** There was also a significant difference in the 3-year change in spherical equivalent refraction for the intervention group (-1.42 D) compared with the control group (-1.59 D) (difference of 0.17 D [95% CI, 0.01 to 0.33 D]; $P = .04$). Elongation of axial length was not significantly different between the intervention group (0.95 mm) and the control group (0.98 mm) (difference of -0.03 mm [95% CI, -0.07 to 0.003 mm]; $P = .07$).

CONCLUSIONS AND RELEVANCE:

Among 6-year-old children in Guangzhou, China, **the addition of 40 minutes of outdoor activity at school compared with usual activity resulted in a reduced incidence rate of myopia over the next 3 years.** Further studies are needed to assess long-term follow-up of these children and the generalizability of these findings.

<http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2015.10803>

Comment

This is an impressive study, focusing (no pun intended) on a major problem in China and many countries in East Asia. Myopia not only is inconvenient, necessitating the wearing of glasses, but it can lead to an elongation of the eyeball, which means that the lens focuses light from far objects slightly in front of the retina, rather than on it. In severe cases, myopia stretches the inner parts of the eye, which increases the risk of retinal detachment, cataracts, glaucoma. If you are reading this booklet inside on a computer, follow the public health message in Singapore...



[Am J Ophthalmol](#). 2015 Nov;160(5):897-904. doi: 10.1016/j.ajo.2015.08.013. Epub 2015 Aug 15.

[Safety of Spectacles for Children's Vision: A Cluster-Randomized Controlled Trial.](#)

[Ma X](#), [Congdon N](#), [Yi H](#), [Zhou Z](#), [Pang X](#), [Meltzer ME](#), [Shi Y](#), [He M](#), [Liu Y](#), [Rozelle S](#).

Abstract

PURPOSE:

To study safety of children's glasses in rural China, where fear that glasses harm vision is an important barrier for families and policy makers.

DESIGN:

Exploratory analysis from a cluster-randomized, investigator-masked, controlled trial.

METHODS:

Among primary schools ($n = 252$) in western China, children were randomized by school to 1 of 3 interventions: free glasses provided in class, vouchers for free glasses at a local facility, or glasses prescriptions only (Control group). The main outcome of this analysis is uncorrected visual acuity after 8 months, adjusted for baseline acuity.

RESULTS:

Among 19 934 children randomly selected for screening, 5852 myopic (spherical equivalent refractive error ≤ -0.5 diopters) eyes of 3001 children (14.7%, mean age 10.5 years) had VA $\leq 6/12$ without glasses correctable to $>6/12$ with glasses, and were eligible. Among these, 1903 (32.5%), 1798 (30.7%), and 2151 (36.8%) were randomized to Control, Voucher, and Free

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Glasses, respectively. Intention-to-treat analyses were performed on all 1831 (96.2%), 1699 (94.5%), and 2007 (93.3%) eyes of children with follow-up in Control, Voucher, and Free Glasses groups. Final visual acuity for eyes of children in the treatment groups (Free Glasses and Voucher) was significantly better than for Control children, adjusting only for baseline visual acuity (difference of 0.023 logMAR units [0.23 vision chart lines, 95% CI: 0.03, 0.43]) or for other baseline factors as well (0.025 logMAR units [0.25 lines, 95% CI 0.04, 0.45]).

CONCLUSION:

We found no evidence that spectacles promote decline in uncorrected vision with aging among children.

[Am J Ophthalmol](#). 2015 Nov;160(5):889-896.e1. doi: 10.1016/j.ajo.2015.08.006. Epub 2015 Aug 12.

[Impact of Free Glasses and a Teacher Incentive on Children's Use of Eyeglasses: A Cluster-Randomized Controlled Trial.](#)

[Yi H](#), [Zhang H](#), [Ma X](#), [Zhang L](#), [Wang X](#), [Jin L](#), [Naidoo K](#), [Minto H](#), [Zou H](#), [Lu L](#), [Rozelle S](#), [Congdon N](#).

Abstract

PURPOSE:

To study the effect of free glasses combined with teacher incentives on in-school glasses wear among Chinese urban migrant children.

DESIGN:

Cluster-randomized controlled trial.

METHODS:

Children with visual acuity (VA) $\leq 6/12$ in either eye owing to refractive error in 94 randomly chosen primary schools underwent randomization by school to receive free glasses, education on their use, and a teacher incentive (Intervention), or glasses prescriptions only (Control).

Intervention group teachers received a tablet computer if $\geq 80\%$ of children given glasses wore them during unannounced visits 6 weeks and 6 months (main outcome) after intervention.

RESULTS:

Among 4376 children, 728 (16.7%, mean age 10.9 years, 51.0% boys) met enrollment criteria and were randomly allocated, 358 (49.2%, 47 schools) to Intervention and 370 (50.8%, 47 schools) to Control. Among these, 693 children (95.2%) completed the study and underwent analysis. Spectacle wear was significantly higher at 6 months among Intervention children (Observed [main outcome]: 68.3% vs 23.9%, adjusted odds ratio [OR] = 11.5, 95% confidence interval [CI] 5.91-22.5, $P < .001$; Self-reported: 90.6% vs 32.1%, OR = 43.7, 95% CI = 21.7-88.5, $P < .001$). Other predictors of observed wear at 6 months included baseline spectacle wear ($P < .001$), uncorrected VA $< 6/18$ ($P = .01$), and parental spectacle wear ($P = .02$). The 6-month observed wear rate was only 41% among similar-aged children provided free glasses in our previous trial without teacher incentives.

CONCLUSIONS:

Free spectacles and teacher incentives maintain classroom wear in the large majority of children needing glasses over a school year. Low wear among Control children demonstrates the need for interventions.

[Acta Ophthalmol](#). 2015 Aug;93(5):e366-71. doi: 10.1111/aos.12634. Epub 2015 Jan 4.

Is viscotrabeculotomy superior to conventional trabeculotomy in the management of Egyptian infants with congenital glaucoma?

ElSheikha OZ, Abdelhakim MA, Elhilali HM, Kassem RR.

Abstract

PURPOSE:

The aim of this study was to assess the efficacy of viscotrabeculotomy in the management of congenital glaucoma as compared to conventional trabeculotomy, in Egyptian infants.

METHODS:

This is a prospective interventional randomized comparative study in which patients with primary congenital glaucoma were randomly allocated to either group A or B; viscotrabeculotomy (VT); and trabeculotomy (T), respectively. Patients were followed up regarding intra-ocular pressure (IOP), cup/disc (C/D) ratio and horizontal corneal diameter (HCD) for 6 months. A probability value (p value) <0.05 was considered significant.

RESULTS:

Twenty-one eyes in group A and 20 eyes in group B were enrolled in the study. The mean preoperative IOP was 23.5 and 24.3 mmHg in the VT and T groups, respectively. Postoperatively, IOP dropped at six months to 14.7 and 17 mmHg in the VT and T groups, respectively. That was significant in either group when compared to preoperative IOP, but not significant between both groups at the same point of comparison.

CONCLUSIONS:

Both techniques were equally effective in the reduction in IOP in the management of congenital glaucoma, but viscotrabeculotomy did not appear to add more benefit to the surgical outcome than classic trabeculotomy.

Trachoma

(See also Hygiene)

[Am J Trop Med Hyg.](#) 2015 Nov;93(5):1106-9. doi: 10.4269/ajtmh.15-0106. Epub 2015 Sep 21.

The Effect of Mass Azithromycin Distribution on Childhood Mortality: Beliefs and Estimates of Efficacy.

See CW, O'Brien KS, Keenan JD, Stoller NE, Gaynor BD, Porco TC, Lietman TM.

Abstract

A cluster-randomized trial demonstrated that mass oral azithromycin distribution reduced childhood mortality 49.6% (Trachoma Amelioration in Northern Amhara [TANA]). The relative risk of childhood mortality was then estimated using two approaches: an expert survey and a Bayesian analysis. The survey asked public health experts to estimate the true effect of mass azithromycin distribution on childhood mortality. The Bayesian estimation used the TANA study's results and prior estimates of the efficacy of other effective population-level interventions. The experts believed mass azithromycin reduces childhood mortality (relative risk = 0.83, 95% credible intervals [CrI] = 0.70-1.00). The Bayesian analysis estimated a relative risk of 0.71 (95% CrI = 0.39-0.93). Both estimates suggest that azithromycin may have a true mortality benefit, though of a smaller magnitude than found in the single available trial. Prior information about nonantibiotic, population-level interventions may have informed the expert's opinions. Additional trials are needed to confirm a mortality benefit from mass azithromycin.

Oral health / dentistry

[Int Endod J.](#) 2016 May;49(5):413-21. doi: 10.1111/iej.12478. Epub 2015 Jul 4.

[Pulpectomies in primary mandibular molars: a comparison of outcomes using three root filling materials.](#)

[Pramila R](#), [Muthu MS](#), [Deepa G](#), [Farzan JM](#), [Rodrigues SJ](#).

Abstract

AIM:

To evaluate the outcome of root canal treatment in primary teeth using three root canal filling materials - RC Fill, Vitapex and Pulpdent root canal sealer.

METHODOLOGY:

The study was a single-centre, double-blind, randomized controlled trial carried out on 129 primary mandibular molars with necrotic pulps or irreversible pulpitis in 4- to 9-year-old children. Participants were selected based on specific inclusion and exclusion criteria and were randomly allocated into 3 groups: Group I - RC Fill [zinc oxide-eugenol (ZOE) with iodoform]; Group II - Vitapex (calcium hydroxide with iodoform); and Group III - Pulpdent root canal sealer (ZOE). The outcome measures were evaluated both clinically and radiographically at 6, 12 and 30 months according to modified American Association of Endodontists (AAE) criteria. The radiographic outcomes were assessed by two blinded and calibrated evaluators. Pearson's chi-square analysis was performed for both intention-to-treat (ITT) and per-protocol population.

RESULT:

The success rates of RC Fill, Vitapex and Pulpdent were 94%, 90% and 97%, respectively, at 30 months and the differences were not significant ($P = 0.137$).

CONCLUSION:

All three materials were found to be equally effective root filling materials for primary molars with necrotic pulps and irreversible pulpitis at 30 months. However, long-term follow-up until the eruption of the permanent successor teeth is needed for more definitive assessments.

[Contemp Clin Dent.](#) 2016 Jan-Mar;7(1):45-50. doi: 10.4103/0976-237X.177110.

[In vivo comparison of cavity disinfection efficacy with APF gel, Propolis, Diode Laser, and 2% chlorhexidine in primary teeth.](#)

[Mohan PV](#), [Uloopi KS](#), [Vinay C](#), [Rao RC](#).

Abstract

BACKGROUND:

The survival of atraumatic restorative treatment (ART) restorations would be enhanced if near total elimination of cariogenic microorganisms could be done in the process of cavity cleaning before placing a restoration. Thus, use of disinfecting agents for achieving this goal could herald a new beginning in the field of contemporary dentistry.

AIM:

To assess and compare the cavity disinfection efficacy of APF gel, Brazilian Propolis, Diode Laser, and 2% chlorhexidine (CHX).

MATERIALS AND METHODS:

Randomised trials in child health in developing countries 2015-16

The study was a randomized, single blinded, parallel grouped, active controlled trial. Eighty primary molars in 68 children with cavitated dentinal occlusal caries were randomly assigned into four groups (20 teeth each) Group I: APF gel; Group II: Propolis; Group III: Diode Laser, and Group IV: 2% CHX (control). After cavity preparation using ART procedure, dentinal samples collected before and after disinfection with respective agent of the group. These samples were subjected to microbiological evaluation, for total viable count (TVC) on blood agar, Streptococcus mutans on mutans-sanguis (MS) agar, and Lactobacilli (LB) on Rogosa agar.

RESULTS:

Intragroup comparison (Wilcoxon signed rank test) showed significant reductions in TVC, MS, and LB counts in all the groups. Pairwise Mann-Whitney test showed APF gel had least bacterial reductions among the agents tested.

CONCLUSION:

This study illustrated the need for cavity disinfection. Diode Laser and Brazilian Propolis are equally effective as 2% CHX in cavity disinfection.

[Anesth Prog.](#) 2016 Spring;63(1):3-7. doi: 10.2344/0003-3006-63.1.3.

[Evaluation of 2-Stage Injection Technique in Children.](#)

[Sandeep V](#)¹, [Kumar M](#)², [Jyostna P](#)³, [Duggi V](#)¹.

Abstract

Effective pain control during local anesthetic injection is the cornerstone of behavior guidance in pediatric dentistry. The aim of this study was to evaluate the practical efficacy of a 2-stage injection technique in reducing injection pain in children. This was a split-mouth, randomized controlled crossover trial. One hundred cooperative children aged 7 to 13 years in need of bilateral local anesthetic injections (inferior alveolar nerve block, posterior superior alveolar nerve block, or maxillary and mandibular buccal infiltrations) for restorative, endodontic, and extraction treatments were recruited for the study. Children were randomly allocated to receive either the 2-stage injection technique or conventional technique at the first appointment. The other technique was used at the successive visit after 1 week. Subjective and objective evaluation of pain was done using the Wong-Baker FACES Pain Rating Scale (FPS) and Sound Eye Motor (SEM) scale, respectively. The comparison of pain scores was done by Wilcoxon sign-rank test. Both FPS and SEM scores were significantly lower when the 2-stage injection technique of local anesthetic nerve block/infiltration was used compared with the conventional technique. The 2-stage injection technique is a simple and effective means of reducing injection pain in children.

[J Clin Diagn Res.](#) 2016 Apr;10(4):ZC13-7. doi: 10.7860/JCDR/2016/16645.7533. Epub 2016 Apr 1.

[Effect of ACP-CPP Chewing Gum and Natural Chewable Products on Plaque pH, Calcium and Phosphate Concentration.](#)

[Sultan S](#), [Telgi CR](#), [Chaudhary S](#), [Manuja N](#), [Kaur H](#), [Amit SA](#), [Lingesha RT](#).

Abstract

INTRODUCTION:

Randomised trials in child health in developing countries 2015-16

Numerous epidemiological studies have documented dental caries as the major public health problems throughout the world. It is gradually increasing in the underdeveloped and developing countries especially in children due to increasing popularity of refined sugars.

AIM:

The aim of the study was to evaluate the effect of natural chewable products (Tulsi, sesame seeds, fennel seeds, coconut) and ACP-CPP chewing gum on plaque pH, calcium and phosphate concentration.

MATERIALS AND METHODS:

A randomized controlled trial, with a cross-over study design, was conducted. Ten subjects aged 15-17 years who agreed to refrain from oral hygiene practice for 48 hours prior to the sample collection were selected for the study. The baseline plaque pH, calcium and phosphate was measured and repeated after 5 and 30 minutes. It was ensured that each study participant was subjected to all the products making an effective sample of ten subjects per product. The data was statistically analysed.

RESULTS:

The mean pH in all the study groups increased after 5 minutes and 30 minutes compared to baseline, except for coconut group at 30 minutes and fennel group at 5 minutes. Highest increase in plaque calcium concentration was found in fennel group followed by recaldent and sesame, respectively. Whereas, the highest increase in plaque phosphate was found in recaldent group followed by sesame group and fennel group respectively.

CONCLUSION:

Plant products can be effective, inexpensive, easily accessible methods of maintaining oral health. Further studies are recommended to confirm long term effects.

[J Indian Soc Pedod Prev Dent.](#) 2016 Jan-Mar;34(1):60-4. doi: 10.4103/0970-4388.175516.

Effect of the video output of the dental operating microscope on anxiety levels in a pediatric population during restorative procedures.

[Sayed A](#), [Ranna V](#), [Padawe D](#), [Takate V](#).

Abstract

BACKGROUND:

Adapting a child to the alien settings of a dental operatory is a major challenge to the dentist. Fear of the unknown and preconceived notions of dental pain causes anxiety in the pediatric patient. This often leads to disruptive and uncooperative behavior in the dental operatory. Many methods of behavior management have been described, of which the Tell-Show-Do (TSD) is an established and time-tested technique of behavior management.

AIM:

To determine if a live visual output of the dental operating microscope (DOM) could be used as an adjunct to the TSD technique, to involve the child more completely in the procedure and reduce the fear of the unknown.

MATERIALS AND METHODS:

The study was a randomized, controlled, crossover, and cross-sectional clinical trial. Data were obtained from two visits. 90 children having carious lesions on both lower first molars, in the 7-9 years age group were selected and divided randomly into two groups. Restorative procedures were performed on one tooth per visit, with visits 1 week apart. Live display of the procedure was shown to the patient using video output of the DOM displayed on a 72 inch LCD monitor, angled for best visibility of the child. Anxiety levels were evaluated using Venhams picture selection test and pulse oximetry.

STATISTICAL ANALYSIS:

Randomised trials in child health in developing countries 2015-16

Student's t-test was used to compare the anxiety scores obtained from the two groups.

RESULTS:

The results showed there was a decrease in the anxiety from the first visit to the second visit. ($P = 0.05$ for Group A and $P = 0.003$ for Group B). The patients preferred the visit in which the DOM was used. The operator reported an increased patient compliance and reduced patient movement in the visits in which the DOM was used.

CONCLUSION:

There is a reduction in anxiety from the first visit to the second visit for restorative treatment when the DOM is used.

[J Dent \(Tehran\)](#). 2015 Oct;12(10):729-38.

Comparative Evaluation of Commercially Available Freeze Dried Powdered Probiotics on Mutans Streptococci Count: A Randomized, Double Blind, Clinical Study.

[Yousuf A](#), [Nagaraj A](#), [Ganta S](#), [Sidiq M](#), [Pareek S](#), [Vishnani P](#), [Acharya S](#), [Singh K](#).

Abstract

OBJECTIVES:

Probiotic approaches are being considered to eliminate pathogenic microorganisms and are an alternative and promising way to combat infections by using harmless bacteria to displace pathogenic microorganisms. The aim of this study was to evaluate the effectiveness of commercially available freeze dried powdered probiotics on mutans streptococci count among 12-15 year-old Indian schoolchildren.

MATERIALS AND METHODS:

The study was conducted in two phases of in-vitro (phase I) and in-vivo (phase II) study, which was a double blind, randomized and placebo controlled clinical trial. A total of 33 school children between 12-15 years were included in the study. They were randomly allocated to three groups. **Group A included 11 children using freeze dried Lactobacillus acidophilus, Bifidobacterium longum, Bifidobacterium bifidum and Bifidobacterium lactis. Group B included 11 children using freeze dried lactic acid bacillus only. Group C included 11 children using placebo powder.** The study was conducted over a period of three weeks and examination and sampling of the subjects were done on days 0 (baseline), seven, 14 and 21.

RESULTS:

For both the intervention groups A and B, statistically significant reduction ($P < 0.05$) in salivary mutans streptococci counts was recorded up to the second week.

CONCLUSION:

Oral administration of probiotics showed a short-term effect on reduction of mutans streptococci count and showed a preventive role in caries development.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC27252756/>

Poisoning and toxins

Quality of care

Research methods

Schistosomiasis

School health and education

(See Adolescent health)

[Psychol Health Med.](#) 2016 Mar 10:1-12. [Epub ahead of print]

[**A randomized-control trial for the teachers' diploma programme on psychosocial care, support and protection in Zambian government primary schools.**](#)

[Kaljee L](#), [Zhang L](#), [Langhaug L](#), [Munjile K](#), [Tembo S](#), [Menon A](#), [Stanton B](#), [Li X](#), [Malungo J](#).

Abstract

Orphaned and vulnerable children (OVC) experience poverty, stigma, and abuse resulting in poor physical, emotional, and psychological outcomes. The Teachers' Diploma Programme on Psychosocial Care, Support, and Protection is a child-centered 15-month long-distance learning program focused on providing teachers with the knowledge and skills to enhance their school environments, foster psychosocial support, and facilitate school-community relationships. A randomized controlled trial was implemented in 2013-2014. Both teachers (n=325) and students (n=1378) were assessed at baseline and 15-months post-intervention from randomly assigned primary schools in Lusaka and Eastern Provinces, Zambia. Multilevel linear mixed models (MLM) indicate positive significant changes for intervention teachers on outcomes related to self-care, teaching resources, safety, social support, and gender equity. Positive outcomes for intervention students related to future orientation, respect, support, safety, sexual abuse, and bullying. Outcomes support the hypothesis that teachers and students benefit from a program designed to enhance teachers' psychosocial skills and knowledge.

[Prev Sci.](#) 2016 Jan;17(1):134-43. doi: 10.1007/s11121-015-0580-9.

[**Applying a Family-Level Economic Strengthening Intervention to Improve Education and Health-Related Outcomes of School-Going AIDS-Orphaned Children: Lessons from a Randomized Experiment in Southern Uganda.**](#)

[Ssewamala FM](#)^{1,2}, [Karimli L](#)^{3,4}, [Torsten N](#)⁵, [Wang JS](#)^{6,3}, [Han CK](#)⁷, [Ilic V](#)^{6,3}, [Nabunya P](#)⁴.

Abstract

Children comprise the largest proportion of the population in sub-Saharan Africa. Of these, millions are orphaned. Orphanhood increases the likelihood of growing up in poverty, dropping out of school, and becoming infected with HIV. Therefore, programs aimed at securing a healthy developmental trajectory for these orphaned children are desperately needed. We conducted a two-arm cluster-randomized controlled trial to **evaluate the effectiveness of a family-level economic strengthening intervention with regard to school attendance, school grades, and self-esteem in AIDS-orphaned adolescents aged 12-16 years from 10 public rural primary schools in southern Uganda.** Children were randomly assigned to receive usual

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care (counseling, school uniforms, school lunch, notebooks, and textbooks), "bolstered" with mentorship from a near-peer (control condition, n = 167), or to receive bolstered usual care plus a family-level economic strengthening intervention in the form of a matched Child Savings Account (Suubi-Maka treatment arm, n = 179). The two groups did not differ at baseline, but **24 months later, children in the Suubi-Maka treatment arm reported significantly better educational outcomes, lower levels of hopelessness, and higher levels of self-concept compared to participants in the control condition.** Our study contributes to the ongoing debate on how to address the developmental impacts of the increasing numbers of orphaned and vulnerable children and adolescents in sub-Saharan Africa, especially those affected by HIV/AIDS. Our findings indicate that innovative family-level economic strengthening programs, over and above bolstered usual care that includes psychosocial interventions for young people, may have positive developmental impacts related to education, health, and psychosocial functioning.

[Trials](#). 2015 Dec 16;16:574. doi: 10.1186/s13063-015-1081-7.

Remedial after-school support classes offered in rural Gambia (The SCORE trial): study protocol for a cluster randomized controlled trial.

[Boone P](#), [Camara A](#), [Eble A](#), [Elbourne D](#), [Fernandes S](#), [Frost C](#), [Jayanty C](#), [Lenin M](#), [Silva AF](#).

Abstract

BACKGROUND:

Low education levels are endemic in much of the developing world, particularly in rural areas where traditional government-provided public services often have difficulty reaching beneficiaries. Providing trained para-teachers to teach regular after-school remedial education classes has been shown to improve literacy and numeracy in children of primary school age residing in such areas in India. This trial investigates whether such an intervention can also be effective in a West African setting with similarly low learning levels and difficult geographic access.

METHODS/DESIGN:

DESIGN:

cluster-randomized controlled trial. Clusters: villages or groups of villages with 15-300 households and at least 15 eligible children in the Lower River and North Bank Regions of The Gambia.

PARTICIPANTS:

children born between 1 September 2007 and 31 August 2009 planning to enter the first grade, for the first time, in the 2015-2016 school year in eligible villages. We anticipate enrolling approximately 150 clusters of villages with approximately 6000 children as participants.

INTERVENTION:

a program providing remedial after-school lessons, focusing on literacy and numeracy, 5 to 6 days a week for 3 years to eligible children, based on the intervention evaluated in the Support To Rural India's Public Education System (STRIPES) trial (PLoS ONE 8(7):e65775).

CONTROL:

both the intervention and control groups will receive small bundles of useful materials during annual data collection as recompense for their time. If the education intervention is shown to be cost-effective at raising learning levels, it is expected that the control group villages will receive the intervention for several years after the trial results are available.

OUTCOMES:

the primary outcome of the trial is a composite mathematics and language test score. Secondary outcomes include school attendance, enrollment, performance on nationally administered exams, parents' spending on education, spillover learning to siblings and family members, and

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school-related time use of parents and children. Subgroup analyses of the primary outcome will also be carried out based on ethnic group, gender, distance from the main highway, parents' education level, and school type. The trial will run by independent research and implementation teams and supervised by a Trial Steering Committee.

DISCUSSION:

Along with the overall impact of the intervention, we will conduct a cost-effectiveness analysis. There are no major ethical issues for this study.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26671345/>

[Eur Child Adolesc Psychiatry](#). 2015 Aug;24(8):931-40. doi: 10.1007/s00787-014-0642-8. Epub 2014 Nov 14.

[A randomised controlled trial of a web-based educational program in childmental health for schoolteachers.](#)

[Pereira CA](#), [Wen CL](#), [Miguel EC](#), [Polanczyk GV](#).

Abstract

Children affected by mental disorders are largely unrecognised and untreated across the world. Community resources, including the school system and teachers, are important elements in actions directed to promoting child mental health and preventing and treating mental disorders, especially in low- and middle-income countries. We developed a **web-based program to educate primary school teachers on mental disorders in childhood** and conducted a cluster-randomised controlled trial to test the effectiveness of the web-based program intervention in comparison with the same program based on text and video materials only and to a waiting-list control group. **All nine schools of a single city in the state of São Paulo, Brazil, were randomised to the three groups, and teachers completed the educational programs during 3 weeks.** Data were analysed according to complete cases and intention-to-treat approaches. In terms of gains of knowledge about mental disorders, the web-based program intervention was superior to the intervention with text and video materials, and to the waiting-list control group. In terms of beliefs and attitudes about mental disorders, the web-based program intervention group presented less stigmatised concepts than the text and video group and more non-stigmatised concepts than the waiting-list group. No differences were detected in terms of teachers' attitudes. This study demonstrated initial data on the effectiveness of a web-based program in educating schoolteachers on child mental disorders. Future studies are necessary to replicate and extend the findings.

[BMJ Open](#). 2015 Aug 25;5(8):e008749. doi: 10.1136/bmjopen-2015-008749.

[Children Learning About Secondhand Smoke \(CLASS II\): protocol of a pilot cluster randomised controlled trial.](#)

[Siddiqi K](#), [Huque R](#), [Jackson C](#), [Parrott S](#), [Dogar O](#), [Shah S](#), [Thomson H](#), [Sheikh A](#).

Abstract

INTRODUCTION:

Exposure to secondhand smoke (SHS) increases children's risk of acquiring chest and ear infections, tuberculosis, meningitis and asthma. Smoking bans in public places (where implemented) have significantly reduced adults' exposure to SHS. However, for children, homes remain the most likely place for them to be exposed to SHS. Additional measures are therefore

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required to protect children from SHS. **In a feasibility study in Dhaka, Bangladesh, we have shown that a school-based smoke-free intervention (SFI) was successful in encouraging children to negotiate and implement smoking restrictions in homes.** We will now conduct a pilot trial to inform plans to undertake a cluster randomised controlled trial(RCT) investigating the effectiveness and cost-effectiveness of SFI in reducing children's exposure to SHS.

METHODS AND ANALYSIS:

We plan to recruit 12 primary schools in Dhaka, Bangladesh. From these schools, we will recruit approximately 360 schoolchildren in year 5 (10-12 years old), that is, 30 per school. SFI consists of six interactive educational activities aimed at increasing pupils' knowledge about SHS and related harms, motivating them to act, providing skills to negotiate with adults to persuade them not to smoke inside homes and helping families to 'sign-up' to a voluntary contract to make their homes smoke-free. Children in the control arm will receive the usual education. We will estimate: recruitment and attrition rates, acceptability, fidelity to SFI, effect size, intracluster correlation coefficient, cost of intervention and adverse events. Our primary outcome will consist of SHS exposure in children measured by salivary cotinine. Secondary outcomes will include respiratory symptoms, lung function tests, healthcare contacts, school attendance, smoking uptake, quality of life and academic performance.

ETHICS AND DISSEMINATION:

The trial has received ethics approval from the Research Governance Committee at the University of York. Findings will help us plan for the definitive trial.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26307620/>

[Public Health](#). 2015 Dec;129(12):1602-9. doi: 10.1016/j.puhe.2015.08.004. Epub 2015 Sep 9.

Is there any association between parental education and child mortality? A study in a rural area of Bangladesh.

[Akter T](#), [Hoque DM](#), [Chowdhury EK](#), [Rahman M](#), [Russell M](#), [Arifeen SE](#).

Abstract

OBJECTIVES:

To assess the association between parental education and under-five mortality, using the Integrated Management of Childhood Illness (IMCI) data from rural Bangladesh. It also investigated whether the association of parental education with under-five mortality had changed over time.

STUDY DESIGN:

This study was nested in the IMCI cluster randomized controlled trial.

METHODS:

Participants considered for the analysis were all children aged under five years from the baseline (1995-2000) and the final (2002-2007) IMCI household survey. The analysis sample included 39,875 and 38,544 live births from the baseline and the final survey respectively. The outcome variable was under-five mortality and the exposure variables were mother's and father's education. Data were analysed with logistic regression.

RESULTS:

In 2002-2007, the odds of the under-five mortality were 38% lower for the children with mother having secondary education, compared to the children with uneducated mother. For similar educational differences for fathers, at the same time period, the odds of the

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under-five mortality were 16% lower. The association of mother's education with under-five mortality was significantly stronger in 2002-2007 compared to 1995-2000.

CONCLUSIONS:

Mother's education appears to have a strong and significant association with under-five mortality, compared to father's education. The association of mother's education with under-five mortality appears to have increased over time. Our findings indicate that investing on girls' education is a good strategy to combat infant mortality in developing countries.

Skin and hair disease

[N Engl J Med.](#) 2015 Dec 10;373(24):2305-13. doi: 10.1056/NEJMoa1500987.

Mass Drug Administration for Scabies Control in a Population with Endemic Disease

[Romani L¹](#), [Whitfeld MJ](#), [Koroivueta J](#), [Kama M](#), [Wand H](#), [Tikoduadua L](#), [Tuicakau M](#), [Koroi A](#), [Andrews R](#), [Kaldor JM](#), [Steer AC](#).

Abstract

BACKGROUND:

Scabies is an under-recognized cause of illness in many developing countries. It is associated with impetigo, which can lead to serious systemic complications. We conducted a trial of mass drug administration for scabies control in Fiji.

METHODS:

We randomly assigned three island communities to one of three different interventions for scabies control: standard care involving the administration of permethrin to affected persons and their contacts (standard-care group), mass administration of permethrin (permethrin group), or mass administration of ivermectin (ivermectin group). The primary outcome was the change in the prevalence of scabies and of impetigo from baseline to 12 months.

RESULTS:

A total of **2051 participants were enrolled; 803 were in the standard-care group, 532 in the permethrin group, and 716 in the ivermectin group.** From baseline to 12 months, the prevalence of scabies declined significantly in all groups, with the greatest reduction seen in the ivermectin group. **The prevalence declined from 36.6% to 18.8% in the standard-care group (relative reduction in prevalence, 49%; 95% confidence interval [CI], 37 to 60), from 41.7% to 15.8% in the permethrin group (relative reduction, 62%; 95% CI, 49 to 75), and from 32.1% to 1.9% in the ivermectin group (relative reduction, 94%; 95% CI, 83 to 100).** The prevalence of impetigo also declined in all groups, with the greatest reduction seen in the ivermectin group. The prevalence declined from 21.4% to 14.6% in the standard-care group (relative reduction, 32%; 95% CI, 14 to 50), from 24.6% to 11.4% in the permethrin group (relative reduction, 54%; 95% CI, 35 to 73), and from 24.6% to 8.0% in the ivermectin group (relative reduction, 67%; 95% CI, 52 to 83). Adverse events were mild and were reported more frequently in the ivermectin group than in the permethrin group (15.6% vs. 6.8%).

CONCLUSIONS:

Mass drug administration, particularly the administration of ivermectin, was efficacious for the control of scabies and impetigo.

Surgical problems

[J Acquir Immune Defic Syndr.](#) 2015 Aug 15;69(5):560-6. doi: 10.1097/QAI.0000000000000699.

Estimating the Cost of Early Infant Male Circumcision in Zimbabwe: Results From a Randomized Noninferiority Trial of AccuCirc Device Versus Mogen Clamp.

[Mangenah C¹](#), [Mavhu W](#), [Hatzold K](#), [Biddle AK](#), [Madidi N](#), [Ncube G](#), [Mugurungi O](#), [Ticklay I](#), [Cowan FM](#), [Thirumurthy H](#).

Abstract

BACKGROUND:

Safe and cost-effective programs for implementing early infant male circumcision (EIMC) in Africa need to be piloted. We present results on a relative cost analysis within a randomized non-inferiority trial of EIMC comparing the AccuCirc device with Mogen clamp in Zimbabwe.

METHODS:

Between January and June 2013, **male infants who met inclusion criteria were randomized to EIMC through either AccuCirc or Mogen clamp conducted by a doctor**, using a 2:1 allocation ratio. We evaluated the overall unit cost plus the key cost drivers of EIMC using both AccuCirc and Mogen clamp. Direct costs included consumable and nonconsumable supplies, device, personnel, associated staff training, and environmental costs. Indirect costs comprised capital and support personnel costs. In 1-way sensitivity analyses, we assessed potential changes in unit costs due to variations in main parameters, one at a time, holding all other values constant.

RESULTS:

The unit costs of EIMC using AccuCirc and Mogen clamp were \$49.53 and \$55.93, respectively. Key cost drivers were consumable supplies, capacity utilization, personnel costs, and device price. Unit prices are likely to be lowest at full capacity utilization and increase as capacity utilization decreases. Unit prices also fall with lower personnel salaries and increase with higher device prices.

CONCLUSIONS:

EIMC has a lower unit cost when using AccuCirc compared with Mogen clamp. To minimize unit costs, countries planning to scale-up EIMC using AccuCirc need to control costs of consumables and personnel. There is also need to negotiate a reasonable device price and maximize capacity utilization.

<http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26017658/>

[Int J Pediatr Otorhinolaryngol.](#) 2015 Sep;79(9):1556-60. doi: 10.1016/j.ijporl.2015.07.014. Epub 2015 Jul 20.

A comparison of two myringoplasty techniques in Nepalese children: a prospective randomized trial.

[Tripathi P](#), [Guragain RP](#), [Bhusal CL](#), [Karna SL](#), [Borgstein J](#).

Abstract

BACKGROUND:

In children, the success of myringoplasty with temporalis fascia is lower compared to adults and cartilage as an alternative graft material has shown higher success rate.

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OBJECTIVE:

To compare results of myringoplasty using tragal cartilage palisades with the use of temporalis fascia in children with large tympanic membrane perforations.

MATERIALS AND METHODS:

This is a prospective and randomized study conducted in children of age 6-14 years with large tympanic membrane perforation of more than two quadrants. Status of graft at or around 6 weeks after surgery was used as morphological outcome measure. Pre- and postoperative audiograms were compared to evaluate audiological outcome in two groups.

RESULTS:

Forty seven out of 55 patients completed follow-up. The graft uptake rate in the cartilage palisades and temporalis fascia myringoplasty group was 91.3% (21/23) and 83.33% (20/24), respectively; the difference was not statistically significant ($P=0.666$). The mean preoperative air-bone gaps (ABG) in cartilage palisades and temporalis fascia group were 36.2 ± 8.9 dB and 33.8 ± 7.5 dB, the difference was not statistically significant ($P=0.412$). Similarly, the postoperative ABG in cartilage palisades and temporalis fascia group were 25.1 ± 12.2 dB and 17.2 ± 9.2 dB, respectively, the difference was statistically significant ($P=0.040$). The gap closure was 11.0dB in palisades group and 16.8dB in fascia group, but it was not significant ($P=0.133$).

CONCLUSION:

In our study of pediatric myringoplasty, the morphological and functional outcomes in both cartilage palisades and temporalis fascia groups were comparable.

[J Pediatr Orthop](#). 2015 Oct-Nov;35(7):672-6. doi: 10.1097/BPO.0000000000000360.

Is Prone Position Ideal for Manipulation and Pinning of Displaced Pediatric Extension-type Supracondylar Fractures of Humerus?

A Randomized Control Trial.

[Venkatadass K](#), [Balachandar G](#), [Rajasekaran S](#).

Abstract

BACKGROUND:

Closed reduction and percutaneous pin fixation is the standard of care for displaced supracondylar fractures of humerus in children. Although it is routinely performed in supine position, some authors recommend prone position to be advantageous as it aids in gravity reduction and avoids elbow hyperflexion. This study was conducted to compare the ease of manipulation and pinning, clinical, and radiologic outcomes in supine versus prone position.

METHODS:

Fifty-two children with acute, grade III supracondylar humerus fractures without vascular injury were included in the study. They were grouped into prone ($n=26$) and supine ($n=26$) based on computer-generated block randomization. The duration of procedure, number of radiation exposures, attempts at closed reduction, and attempts at placing the pins were analyzed. Functional and radiologic outcomes were assessed for a minimum follow-up of 1 year.

RESULTS:

There was no significant difference between the 2 groups in the duration of procedure ($P=0.422$), number of radiation exposure ($P=0.470$), attempts at closed reduction ($P=0.904$), and attempts for pinning ($P=0.745$) and the final clinical and radiologic outcomes. One patient in prone group had cubitus varus of 8 degrees. Functionally, 2 in the supine group and 3 in prone group had poor outcomes.

CONCLUSIONS:

There is no significant difference in the ease of reduction and pinning between supine and prone positions. Grossly displaced fractures with skin puckering are difficult to manipulate in prone

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position. Supine position is ideal for closed reduction and pinning of all patterns of type III supracondylar fractures.

[Plast Reconstr Surg.](#) 2015 Jul;136(1):59e-66e. doi: 10.1097/PRS.0000000000001324.

Role of Postoperative Antimicrobials in Cleft Palate Surgery: Prospective, Double-Blind, Randomized, Placebo-Controlled Clinical Study in India.

[Aznar ML](#), [Schönmeyr B](#), [Echaniz G](#), [Nebeker L](#), [Wendby L](#), [Campbell A](#).

Abstract

BACKGROUND:

The purpose of this study was to determine whether administration of postoperative antibiotics affects the incidence of complications after primary cleft palate repair in a developing area.

METHODS:

This study was a prospective, double-blind, randomized, placebo-controlled trial composed of 518 consecutive patients who underwent primary cleft palate repair at a single institution. Patients were aged 1 to 43 years at the time of surgery (median, 9 years). The patients were divided randomly into two groups. **One group received a 5-day regimen of oral amoxicillin (50 mg/kg/day) postoperatively and the other group received placebo medication.** Both groups received a single dose of cefuroxime (30 mg/kg) before incision. Patients and providers were blinded to the randomization. Patients were followed postoperatively for early complications (infection and wound breakdown) and for late complications (palatal fistulas).

RESULTS:

The incidence of early complications was 13.8 percent among the patients in the placebo group and 8.7 percent among the patients in the antibiotic group ($p = 0.175$). Fistulas were noted in 17.1 percent in the placebo group and in 10.7 percent in the antibiotic group ($p = 0.085$). Logistic regression analysis identified visiting surgeons as the only covariate related to early complications (OR, 3.71; $p < 0.001$). However, the use of placebo (OR, 2.09; $p = 0.037$), female sex (OR, 2.04; $p = 0.047$), and Veau III and IV (OR, 3.31; $p = 0.004$) were observed as factors associated with the incidence of fistulas.

CONCLUSION:

The authors' results indicate that postoperative antibiotic prophylaxis can reduce the incidence of fistulas after primary cleft palate repair in a developing area.

Tuberculosis

(See also Vaccines: Tuberculosis vaccine)

[BMC Infect Dis.](#) 2015 Oct 22;15:438. doi: 10.1186/s12879-015-1201-8.

Effect of isoniazid preventive therapy on immune responses to mycobacterium tuberculosis: an open label randomised, controlled, exploratory study.

[Biraro IA](#), [Egesa M](#), [Kimuda S](#), [Smith SG](#), [Toulza F](#), [Levin J](#), [Joloba M](#), [Katamba A](#), [Cose S](#), [Dockrell HM](#), [Elliott AM](#).

Abstract

BACKGROUND:

Randomised trials in child health in developing countries 2015-16

With the renewed emphasis to implement isoniazid preventive therapy (IPT) in Sub-Saharan Africa, we investigated the effect of IPT on immunological profiles among household contacts with latent tuberculosis.

METHODS:

Household contacts of confirmed tuberculosis patients were tested for latent tuberculosis using the QuantiFERON®-TB Gold In-Tube (QFN) assay and tuberculin skin test (TST). HIV negative contacts aged above 5 years, positive to both QFN and TST, were randomly assigned to IPT and monthly visits or monthly visits only. QFN culture supernatants from enrolment and six months' follow-up were analysed for M.tb-specific Th1, Th2, Th17, and regulatory cytokines by Luminex assay, and for M.tb-specific IgG antibody concentrations by ELISA. Effects of IPT were assessed as the net cytokine and antibody production at the end of six months.

RESULTS:

Sixteen percent of contacts investigated (47/291) were randomised to IPT (n = 24) or no IPT (n = 23). After adjusting for baseline cytokine or antibody responses, and for presence of a BCG scar, **IPT (compared to no IPT) resulted in a relative decline in M.tb-specific production of IFN gamma (adjusted mean difference at the end of six months (bootstrap 95% confidence interval (CI), p-value) -1488.6 pg/ml ((-2682.5, -294.8), p = 0.01), and IL- 2 (-213.1 pg/ml (-419.2, -7.0), p = 0.04).** A similar decline was found in anti-CFP-10 antibody levels (adjusted geometric mean ratio (bootstrap 95% CI), p-value) 0.58 ((0.35, 0.98), p = 0.04). We found no effect on M.tb-specific Th2 or regulatory or Th17 cytokine responses, or on antibody concentrations to PPD and ESAT-6.

CONCLUSIONS:

IPT led to a decrease in Th1 cytokine production, and also in the anti CFP-10 antibody concentration. This could be secondary to a reduction in mycobacterial burden or as a possible direct effect of isoniazid induced T cell apoptosis, and may have implications for protective immunity following IPT in tuberculosis-endemic countries.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2649398/>

J Antimicrob Chemother. 2015 Sep;70(9):2648-51. doi: 10.1093/jac/dkv158. Epub 2015 Jul 3.

Lack of cross-toxicity between isoniazid and ethionamide in severe cutaneous adverse drug reactions: a series of 25 consecutive confirmed cases.

Lehloanya RJ, Muloiwa R, Dlamini S, Gantsho N, Todd G, Dheda K.

Abstract

BACKGROUND:

Isoniazid and ethionamide are important first- and second-line anti-TB drugs (FLDs and SLDs), respectively. Ethionamide is a structural analogue of isoniazid and the two drugs share other similarities, including their metabolism, therapeutic targets, hepato-toxicity patterns and drug resistance. As a result, there has always been concern about possible cross-reactivity between them.

METHODS:

Among 69 patients with drug rash with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) to FLDs, FLDs were stopped and SLDs added when the skin and laboratory parameters had settled. This was followed by sequential and additive rechallenge with FLDs. We report 25 consecutive cases that developed confirmed cutaneous adverse drug reactions (CADRs) to isoniazid or ethionamide used as FLD and SLD, respectively.

RESULTS:

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Sixty-nine participants who developed CADRs on FLDs were enrolled in the study. **Twenty developed a rechallenge reaction to isoniazid and five reacted to ethionamide.** Four of the 20 isoniazid cases were patch test positive, 3/20 were skin prick test positive and 13/20 reacted to oral rechallenge. All seven cases that were patch and skin prick test positive were associated with systemic reactions. Twenty of the 25 cases had DRESS and 5 had SJS/TEN. Twenty-three of the 25 cases with rechallenge reactions were HIV infected. Importantly, **none of the cases that reacted to ethionamide during the rechallenge reacted to isoniazid and none who subsequently reacted to isoniazid reacted to ethionamide.**

CONCLUSIONS:

Our findings strongly suggest that the risk of cross-reactivity of isoniazid and ethionamide in DRESS syndrome and SJS/TEN is low. These findings have implications for clinical management.

[Pediatr Infect Dis J.](#) 2016 Jun;35(6):622-7. doi: 10.1097/INF.0000000000001115.

[The Effect of Deworming on Tests of Tuberculosis Infection in Children With Recent Tuberculosis Exposure: A Randomized Controlled Trial.](#)

[Van der Zalm MM](#), [van Soelen N](#), [Mandalakas AM](#), [Jacobsen M](#), [Detjen AK](#), [Marx FM](#), [Grewal HM](#), [Cotton MF](#), [Walzl G](#), [Hesseling AC](#).

Abstract

BACKGROUND:

Helminth infestations are associated with T-helper cell type 2 (Th2) immune responses, leading to suppression of Th1 responses required to control Mycobacterium tuberculosis infection. We hypothesized that deworming after documented M. tuberculosis exposure might improve Th1 immune responses.

METHODS:

This was a randomized controlled trial comparing the effect of early versus delayed (after 3 months) deworming on tuberculin skin testing (TST) and Quantiferon-Gold-in-tube responses among children from a setting with a known high burden of M. tuberculosis and helminth co-infection in Cape Town, South Africa. Children aged 6 to 15 years with documented M. tuberculosis exposure were enrolled. Ascaris lumbricoides status was measured by Ascaris-specific IgE and stool microscopy.

RESULTS:

A total of 250 children (mean age, 9.6 years) were enrolled; 11.9% (27/227) were Ascaris stool microscopy positive and 54.2% (135/249) were Ascaris stool and/or IgE positive (Ascaris status). In univariable analysis, deworming at enrollment was not associated with a negative TST at 3 months (odds ratio, 0.61; 95% confidence interval, 0.35-1.07; P = 0.08). In stratified analysis, children with a positive Ascaris status were more likely to be TST negative at 3 months if dewormed early (odds ratio, 0.49; 95% confidence interval, 0.23-1.04; P = 0.06). In multivariable analysis, deworming was not associated with TST status (adjusted odds ratios, 0.62; 95% confidence interval, 0.34-1.10; P = 0.10). There was no association between deworming and Quantiferon-Gold-in-tube status.

CONCLUSIONS:

Deworming in children with recent M. tuberculosis exposure is associated with a trend toward a negative TST result. Timing of deworming might influence interpretation of TST in settings with high burdens of tuberculosis and helminths.

[Cochrane Database Syst Rev](#). 2015 Sep 3;(9):CD007952. doi: 10.1002/14651858.CD007952.pub3.

Incentives and enablers to improve adherence in tuberculosis.

[Lutge EE](#), [Wiysonge CS](#), [Knight SE](#), [Sinclair D](#), [Volmink J](#).

Abstract

BACKGROUND:

Patient adherence to medications, particularly for conditions requiring prolonged treatment such as tuberculosis (TB), is frequently less than ideal and can result in poor treatment outcomes. Material incentives to reward good behaviour and enablers to remove economic barriers to accessing care are sometimes given in the form of cash, vouchers, or food to improve adherence.

OBJECTIVES:

To evaluate the effects of material incentives and enablers in patients undergoing diagnostic testing, or receiving prophylactic or curative therapy, for TB.

SEARCH METHODS:

We undertook a comprehensive search of the Cochrane Infectious Diseases Group Specialized Register; Cochrane Central Register of Controlled Trials (CENTRAL); MEDLINE; EMBASE; LILACS; Science Citation Index; and reference lists of relevant publications up to 5 June 2015.

SELECTION CRITERIA:

Randomized controlled trials of material incentives in patients being investigated for TB, or on treatment for latent or active TB.

DATA COLLECTION AND ANALYSIS:

At least two review authors independently screened and selected studies, extracted data, and assessed the risk of bias in the included trials. We compared the effects of interventions using risk ratios (RR), and presented RRs with 95% confidence intervals (CI). The quality of the evidence was assessed using GRADE.

MAIN RESULTS:

We identified 12 eligible trials. Ten were conducted in the USA: in adolescents (one trial), in injection drug or cocaine users (four trials), in homeless adults (three trials), and in prisoners (two trials). The remaining two trials, in general adult populations, were conducted in Timor-Leste and South Africa. Sustained incentive programmes. Only two trials have assessed whether material incentives and enablers can improve long-term adherence and completion of treatment for active TB, and neither demonstrated a clear benefit (RR 1.04, 95% CI 0.97 to 1.14; two trials, 4356 participants; low quality evidence). In one trial, the incentive, given as a daily hot meal, was not well received by the population due to the inconvenience of attending the clinic at midday, whilst in the other trial, nurses distributing the vouchers chose to "ration" their distribution among eligible patients, giving only to those whom they felt were most deprived. Three trials assessed the effects of material incentives and enablers on completion of TB prophylaxis with mixed results (low quality evidence). A large effect was seen with regular cash incentives given to drug users at each clinic visit in a setting with extremely low treatment completion in the control group (treatment completion 52.8% intervention versus 3.6% control; RR 14.53, 95% CI 3.64 to 57.98; one trial, 108 participants), but **no effects were seen in one trial assessing a cash incentive for recently released prisoners (373 participants), or another trial assessing material incentives offered by parents to teenagers (388 participants)**. Single once-only incentives. However in specific populations, such as recently released prisoners, drug users, and the homeless, trials show that material incentives probably do improve one-off clinic re-attendance for initiation or continuation of anti-TB prophylaxis (RR 1.58, 95% CI 1.27 to 1.96; three trials, 595 participants; moderate quality evidence), and may increase the return rate for reading of tuberculin skin test results (RR 2.16, 95% CI 1.41 to 3.29; two trials, 1371 participants; low quality evidence). Comparison of different types of incentives. Single trials in specific sub-populations suggest that an immediate cash incentive may be more

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effective than delaying the incentive until completion of treatment (RR 1.11, 95% CI 0.98 to 1.24; one trial, 300 participants; low quality evidence), cash incentives may be more effective than non-cash incentives (completion of TB prophylaxis: RR 1.26, 95% CI 1.02 to 1.56; one trial, 141 participants; low quality evidence; return for skin test reading: RR 1.13, 95% CI 1.07 to 1.19; one trial, 652 participants; low quality evidence); and higher cash incentives may be more effective than lower cash incentives (RR 1.08, 95% CI 1.01 to 1.16; one trial, 404 participants; low quality evidence).

AUTHORS' CONCLUSIONS:

Material incentives and enablers may have some positive short term effects on clinic attendance, particularly for marginal populations such as drug users, recently released prisoners, and the homeless, but **there is currently insufficient evidence to know if they can improve long term adherence to TB treatment.**

<http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26333525/>

Urinary tract infection

Urology

[J Pediatr Urol.](#) 2015 Dec;11(6):351.e1-6. doi: 10.1016/j.jpurol.2015.04.040. Epub 2015 Jul 29.

Transcutaneous posterior tibial nerve stimulation in pediatric overactive bladder: A preliminary report.

[Patidar N](#), [Mittal V](#), [Kumar M](#), [Sureka SK](#), [Arora S](#), [Ansari MS](#).

Abstract

BACKGROUND:

Non-neurogenic overactive bladder (OAB) is a common problem in children that may affect their quality of life. Various methods of neuromodulation have been reported to treat refractory lower urinary tract dysfunction. Since most of these techniques are invasive, they are less applicable in children.

OBJECTIVE:

To evaluate the efficacy of transcutaneous PTNS in treatment of OAB in children, in a randomized clinical setting.

STUDY DESIGN:

This study was single-blinded, prospective, sham controlled randomized trial. 40 children with non-neurogenic OAB refractory to behavioural and anticholinergic therapy were randomized either to test group or sham group. Neuromodulation was performed using two self-adhesive electrodes cephalad to medial malleolus. In test group the stimulation was given with voltage pulse intensity of 0 to 10 mA, pulse width of 200 μ s and frequency of 20 Hz. In sham group patch electrodes were applied to simulate the test group but no stimulation was given. In both groups, weekly session of 30 min was given for a period of 12 weeks. The OAB symptoms, severity of incontinence, number of voids daily (NV), average voided volume (AVV) and maximum voided volume (MVV) were evaluated before and after treatment.

RESULTS:

On assessment of subjective improvement of OAB symptoms, 66.66% patients reported cure and 23.81% patients reported significant improvement of symptoms in test group whereas in sham group only 6.25% patients reported significant improvement. In test group 71.42% patients reported complete improvement in incontinence whereas in sham group only 12.5%

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patient reported complete improvement. The AVV, MVV and NV improved significantly in test group ($p < 0.001$) as compared to sham group (Table).

DISCUSSION:

The present study is unique as none of the earlier studies in children were sham controlled. It is also first PTNS study in which patch electrodes were used; therefore it is completely noninvasive. This technique provides better patient acceptability and compliance. This study proved that, there is a definite effect of PTNS as compared to placebo because when patients from sham group were treated actively, they responded well. The present study has few limitations as it has relatively short follow-up period of 12 weeks. Relapse of OAB symptoms and maintenance schedule of PTNS need to be assessed further.

CONCLUSION:

Transcutaneous PTNS is superior to placebo in treatment of non-neurogenic overactive bladder in children. In view of its effectiveness and acceptability we believe that transcutaneous PTNS should be part of pediatric urology armamentarium for treatment of OAB.

Vaccines and immunization

(see also deworming)

[BMJ Open](#). 2015 Sep 18;5(9):e007972. doi: 10.1136/bmjopen-2015-007972.

[Interventions to increase immunisation coverage among children 12-23 months of age in India through participatory learning and community engagement: pilot study for a cluster randomised trial.](#)

[Johri M](#), [Chandra D](#), [Koné GK](#), [Dudeja S](#), [Sylvestre MP](#), [Sharma JK](#), [Pahwa S](#).

Abstract

OBJECTIVE:

With the aim of conducting a future cluster randomised trial to assess intervention impact on child vaccination coverage, we designed a pilot study to assess feasibility and aid in refining methods for the larger study.

TRIAL DESIGN:

Cluster-randomised design with a 1:1 allocation ratio.

METHODS:

Clusters were 12 villages in rural Uttar Pradesh. All women residing in a selected village who were mothers of a child 0-23 months of age were eligible; participants were chosen at random. Over 4 months, intervention group (IG) villages received: (1) home visits by volunteers; (2) community mobilisation events to promote immunisation. Control group (CG) villages received community mobilisation to promote nutrition. A toll-free number for immunisation was offered to all IG and CG village residents. Primary outcomes were ex-ante criteria for feasibility of the main study related to processes for recruitment and randomisation (50% of villages would agree to participate and accept randomisation; 30 women could be recruited in 70% of villages), and retention of participants (50% of women retained from baseline to endline). Clusters were assigned to IG or CG using a computer-generated randomisation schedule. Neither participants nor those delivering interventions were blinded, but those assessing outcomes were blinded to group assignment.

RESULTS:

All villages contacted agreed to participate and accepted randomisation. 36 women were recruited per village; 432 participants were randomised (IG n=216; CG n=216). No clusters

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were lost to follow-up. The main analysis included 86% (373/432) of participants, 90% (195/216) from the IG and 82% (178/216) from the CG.

CONCLUSIONS:

Criteria related to feasibility were satisfied, giving us confidence that we can successfully conduct a larger cluster randomised trial. Methodological lessons will inform design of the main study.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26384721/>

[Ital J Pediatr.](#) 2015 Aug 21;41:61. doi: 10.1186/s13052-015-0168-9.

[The effect of the facilitated tucking position in reducing vaccination-induced pain in newborns.](#)

[Kucukoglu S](#), [Kurt S](#), [Aytekin A](#).

Abstract

BACKGROUND:

This study was conducted to evaluate the pain perceptions of newborns during the hepatitis B (HBV) vaccinations performed in the facilitated tucking position and the classical holding position, respectively.

METHODS:

The randomized controlled experimental study was conducted between 1 September 2014 and 30 December 2014 at the neonatal intensive care unit of a Turkish university hospital. **One group of infants was held in the facilitated tucking position (the treatment group; n = 30) during HBV vaccination; infants in the other group were held in the classical holding position (the control group; n = 30) during HBV vaccination.** The Neonatal Infant Pain Scale (NIPS) scores of the infants in the treatment and control groups were compared during procedure. Also, the infants' physiological parameters were compared before, during, and after the procedure. Descriptive statistics, a chi-square test, and an independent samples t-test were used to assess the data.

RESULTS:

The mean pain scores of infants vaccinated in the facilitated tucking position (2.83 ± 1.18) were significantly statistically lower than the scores of infants vaccinated in the classical holding position (6.47 ± 1.07) ($p < 0.05$).

CONCLUSIONS:

The pain perceptions of newborns held in the facilitated tucking position during HBV vaccination were lower. The facilitated tucking position, a non-pharmacological method, is recommended as an effective and useful method for reducing pain during the procedure.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26293573/>

Comment

“Facilitated tucking” is simply flexion of the knee in a comfortable, supported position with the baby lying on the side.



BCG vaccine

[Indian J Tuberc.](#) 2015 Oct;62(4):226-9. doi: 10.1016/j.ijtb.2015.08.002. Epub 2016 Jan 23.

[Does effect of BCG vaccine decrease with time since vaccination and increase tuberculin skin test reaction?](#)

[Subramani R](#), [Datta M](#), [Swaminathan S](#).

Abstract

The protective efficacy of BCG was studied for over 15 years, from 1968, in South India. A secondary analysis of data was performed to investigate the relationship between Bacille Calmette-Guérin (BCG) and tuberculosis (TB) disease and between BCG and positive tuberculin skin test for different time periods among children aged less than 10 years. A randomized controlled trial was conducted, where **281,161 persons were allocated to receive BCG 0.1mg, BCG 0.01mg or placebo. Tuberculin skin test was performed at baseline and at 4 years after BCG vaccination.** Surveys were conducted every 2.5 years to detect all new cases of culture-positive/smear-positive TB occurring in the community over a 15-year period. Relative risk (RR) was obtained from the ratio of incidence among the vaccinated and the placebo groups. **Among those children vaccinated with 0.1mg of BCG, the RR for TB was 0.56 (95% CI: 0.32-0.87, P=0.01) at 12.5 years but increased to 0.73 later.** Similar pattern was seen with 0.01mg. The increase in the number of skin test positives with 0.1mg of BCG was 57.8%, 49.4% and 34% for cut-off points at $\geq 10\text{mm}$, $\geq 12\text{mm}$ and $\geq 15\text{mm}$, respectively. The study suggests that the effect of BCG may decrease since vaccination and the tuberculin positive was higher at post-vaccination test period due to BCG.

Comment

The standard dose of BCG is 0.1mg. The original study clearly showed that a 10-fold dilution is much less effective. This study was commenced in 1968, but could not be justified now.

[Vaccine.](#) 2015 Sep 8;33(37):4719-26. doi: 10.1016/j.vaccine.2015.03.074. Epub 2015 Apr 7.

[A randomized clinical trial in adults and newborns in South Africa to compare the safety and immunogenicity of bacille Calmette-Guérin \(BCG\)](#)

vaccine administration via a disposable-syringe jet injector to conventional technique with needle and syringe.

[Geldenhuys HD](#), [Mearns H](#), [Foster J](#), [Saxon E](#), [Kagina B](#), [Saganic L](#), [Jarrahian C](#), [Tameris MD](#), [Dintwe OB](#), [Van Rooyen M](#), [Luabeya KK](#), [Hussey G](#), [Scriba TJ](#), [Hatherill M](#), [Zehring D](#).

Abstract

INTRODUCTION:

Intradermal bacille Calmette-Guérin (BCG) vaccination by needle-free, disposable-syringe jet injectors (DSJI) is an alternative to the Mantoux method using needle and syringe (NS). We compared the safety and immunogenicity of BCG administration via the DSJI and NS techniques in adults and newborn infants at the South African Tuberculosis Vaccine Initiative (SATVI) research site in South Africa.

METHOD:

Thirty adults and 66 newborn infants were randomized 1:1 to receive intradermal BCG vaccine (0.1 mL in adults; 0.05 mL in infants) via DSJI or NS. Wheal diameter (mm) and skin fluid deposition at the site of injection (SOI) were measured immediately post-vaccination. Adverse events and SOI reactivity data were collected 30 min and 1, 2, 4, and 12 weeks after vaccination for adults and at 30 min and 4, 10, and 14 weeks for infants. Blood was collected in infants at 10 and 14 weeks to assess BCG-specific T-cell immune responses.

RESULTS:

More infant BCG vaccinations by DSJI deposited >5 µL fluid on the skin surface, compared to NS (49% versus 9%, $p=0.001$). However, all 12 infant vaccinations that did not produce any SOI wheal occurred in the NS group (36%, $p<0.001$). Median wheal diameter, in participants for which an SOI wheal formed, did not differ significantly between groups in infants (combined 3.0mm IQR 2.0 to 4.0, $p=0.59$) or in adults (combined 9.0mm IQR 7.0 to 10.0, $p=0.13$). Adverse events were similar between study arms. Proportion of participants with BCG scars after three months did not differ in adults (combined 97%, $p=0.67$) or infants (combined 62%, $p=0.13$). Frequencies of BCG-specific clusters of differentiation 4 (CD4) and clusters of differentiation 8 (CD8) T-cells co-expressing IFN- γ , TNF- α , IL-2, and/or IL-17 were not different in the DSJI and NS groups.

CONCLUSION:

BCG vaccination of newborn infants via DSJI was more likely to deliver an appropriate intradermal wheal at the SOI as compared to NS, despite leaving more fluid on the surface of the skin. Safety, reactivity, and antigen-specific T-cell immune responses did not differ between DSJI and NS techniques.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC25862299/>

[Trop Med Int Health](#). 2015 Dec;20(12):1733-44. doi: 10.1111/tmi.12614. Epub 2015 Oct 22.

Tuberculin reaction and BCG scar: association with infant mortality.

[Timmermann CA](#), [Biering-Sørensen S](#), [Aaby P](#), [Fisker AB](#), [Monteiro I](#), [Rodrigues A](#), [Benn CS](#), [Ravn H](#).

Abstract

OBJECTIVE:

To test the hypothesis that having a scar and a positive tuberculin skin test (TST) response after vaccination with Bacille Calmette-Guérin (BCG) is associated with reduced infant mortality.

METHODS:

We studied cohorts of 2709 normal-birthweight (NBW) and 1102 low-birthweight (LBW) infants in Guinea-Bissau. Children were enrolled in randomised trials between year 2002 and

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2008 and received BCG vaccination at birth. BCG scars and TST responses were assessed at 2 and 6 months of age. The infants were followed for mortality to 12 months of age, and survival was analysed using Cox regression.

RESULTS:

At age 2 months, 88% of NBW children and 91% of LBW children had a BCG scar, and 36% and 17% had a TST response, respectively. The LBW infants had nearly twofold higher mortality (4.5%) than the NBW infants (2.8%) between 2 and 12 months of age. In the LBW cohort, the adjusted mortality rate ratio (MRR) comparing children with a BCG scar with those without was 0.42 (95% CI = 0.19; 0.93). There was a similar tendency for TST positivity: MRR = 0.47 (95% CI = 0.14; 1.54). For LBW children who had both a positive TST reaction and a scar, the MRR was 0.22 (95% CI = 0.05; 0.87). For NBW children, a scar and a positive TST were associated with 20% reductions in mortality, which did not reach statistical significance.

CONCLUSION:

We confirmed previous observations that **having a scar and a TST response after BCG vaccination is associated with lower mortality risk**. The possibility of revaccinating scar-negative children should be considered.

[Vaccine](#). 2015 Sep 11;33(38):4782-9. doi: 10.1016/j.vaccine.2015.07.096. Epub 2015 Aug 7.

[Delayed BCG vaccination results in minimal alterations in T cell immunogenicity of acellular pertussis and tetanus immunizations in HIV-exposed infants.](#)

[Blakney AK](#), [Tchakoute CT](#), [Hesseling AC](#), [Kidzeru EB](#), [Jones CE](#), [Passmore JA](#), [Sodora DL](#), [Gray CM](#), [Jaspan HB](#).

Abstract

BACKGROUND:

Bacille Calmette-Guerin (BCG) is effective in preventing disseminated tuberculosis (TB) in children but may also have non-specific benefits, and is thought to improve immunity to unrelated antigens through trained innate immunity. In HIV-infected infants, there is a risk of BCG-associated adverse events. We aimed to explore whether delaying BCG vaccination by 8 weeks, in utero or perinatal HIV infection is excluded, affected T-cell responses to *B. pertussis* (BP) and tetanus toxoid (TT), in HIV-exposed, uninfected infants.

METHODS:

Infants were randomized to receive BCG vaccination at birth or 8 weeks of age. At 8 and 14 weeks, T cell proliferation and intracellular cytokine (IL-2, IL-13, IL-17, and IFN- γ) expression was analyzed in response to BP, TT and Staphylococcal enterotoxin B (SEB) antigens.

RESULTS:

Delaying BCG vaccination did not alter T-cell proliferation to BP or TT antigens. Infants immunized with BCG at birth had higher CD4+ T cell proliferation to SEB at 14 weeks of age (p=0.018). Birth-vaccinated infants had increased CD8+ IL-2 expression in response to BP, but not TT or SEB, at 8 weeks. Infants vaccinated with BCG at 8 weeks had significantly lower IL-13 expression by BP-specific CD4+ and CD8+ T cells at 14 weeks (p=0.032 and p=0.0035, respectively). There were no observed differences in multifunctional cytokine response to TT, BP or SEB between infants vaccinated with BCG at birth versus 8 weeks of age.

Cholera vaccine

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[N Engl J Med](#). 2016 May 5;374(18):1723-32. doi: 10.1056/NEJMoa1510330.

Efficacy of a Single-Dose, Inactivated Oral Cholera Vaccine in Bangladesh.

[Qadri F](#), [Wierzba TF](#), [Ali M](#), [Chowdhury F](#), [Khan AI](#), [Saha A](#), [Khan IA](#), [Asaduzzaman M](#), [Akter A](#), [Khan A](#), [Begum YA](#), [Bhuiyan TR](#), [Khanam F](#), [Chowdhury MI](#), [Islam T](#), [Chowdhury AI](#), [Rahman A](#), [Siddique SA](#), [You YA](#), [Kim DR](#), [Siddik AU](#), [Saha NC](#), [Kabir A](#), [Cravioto A](#), [Desai SN](#), [Singh AP](#), [Clemens JD](#).

Abstract

BACKGROUND:

A single-dose regimen of the current killed oral cholera vaccines that have been prequalified by the World Health Organization would make them more attractive for use against endemic and epidemic cholera. We conducted an efficacy trial of a single dose of the killed oral cholera vaccine Shanchol, which is currently given in a two-dose schedule, in an urban area in which cholera is highly endemic.

METHODS:

Non-pregnant residents of Dhaka, Bangladesh, who were **1 year of age or older were randomly assigned to receive a single dose of oral cholera vaccine or oral placebo**. The primary outcome was vaccine protective efficacy against culture-confirmed cholera occurring 7 to 180 days after dosing. Prespecified secondary outcomes included protective efficacy against severely dehydrating culture-confirmed cholera during the same interval, against cholera and severe cholera occurring 7 to 90 versus 91 to 180 days after dosing, and against cholera and severe cholera according to age at baseline.

RESULTS:

A total of 101 episodes of cholera, 37 associated with severe dehydration, were detected among the 204,700 persons who received one dose of vaccine or placebo. **The vaccine protective efficacy was 40% (95% confidence interval [CI], 11 to 60%; 0.37 cases per 1000 vaccine recipients vs. 0.62 cases per 1000 placebo recipients) against all cholera episodes, 63% (95% CI, 24 to 82%; 0.10 vs. 0.26 cases per 1000 recipients) against severely dehydrating cholera episodes, and 63% (95% CI, -39 to 90%), 56% (95% CI, 16 to 77%), and 16% (95% CI, -49% to 53%) against all cholera episodes among persons vaccinated at the age of 5 to 14 years, 15 or more years, and 1 to 4 years, respectively**, although the differences according to age were not significant (P=0.25). Adverse events occurred at similar frequencies in the two groups.

CONCLUSIONS:

A single dose of the oral cholera vaccine was efficacious in older children (≥ 5 years of age) and in adults in a setting with a high level of cholera endemicity.

[Lancet](#). 2015 Oct 3;386(10001):1362-71. doi: 10.1016/S0140-6736(15)61140-0. Epub 2015 Jul 9.

Feasibility and effectiveness of oral cholera vaccine in an urban endemic setting in Bangladesh: a cluster randomised open-label trial.

[Qadri F](#), [Ali M](#), [Chowdhury F](#), [Khan AI](#), [Saha A](#), [Khan IA](#), [Begum YA](#), [Bhuiyan TR](#), [Chowdhury MI](#), [Uddin MJ](#), [Khan JA](#), [Chowdhury AI](#), [Rahman A](#), [Siddique SA](#), [Asaduzzaman M](#), [Akter A](#), [Khan A](#), [Ae You Y](#), [Siddik AU](#), [Saha NC](#), [Kabir A](#), [Riaz BK](#), [Biswas SK](#), [Begum F](#), [Unicomb L](#), [Luby SP](#), [Cravioto A](#), [Clemens JD](#).

Abstract

BACKGROUND:

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Cholera is endemic in Bangladesh with epidemics occurring each year. The decision to use a cheap oral killed whole-cell cholera vaccine to control the disease depends on the feasibility and effectiveness of vaccination when delivered in a public health setting. We therefore assessed the feasibility and protective effect of delivering such a vaccine through routine government services in urban Bangladesh and evaluated the benefit of adding behavioural interventions to encourage safe drinking water and hand washing to vaccination in this setting.

METHODS:

We did this cluster-randomised open-label trial in Dhaka, Bangladesh. We randomly assigned 90 clusters (1:1:1) to vaccination only, vaccination and behavioural change, or no intervention. The primary outcome was overall protective effectiveness, assessed as the risk of severely dehydrating cholera during 2 years after vaccination for all individuals present at time of the second dose. This study is registered with ClinicalTrials.gov, number [NCT01339845](https://clinicaltrials.gov/ct2/show/study/NCT01339845).

FINDINGS:

Of 268,896 people present at baseline, we analysed 267,270: 94,675 assigned to vaccination only, 92,539 assigned to vaccination and behavioural change, and 80,056 assigned to non-intervention. Vaccine coverage was 65% in the vaccination only group and 66% in the vaccination and behavioural change group. Overall protective effectiveness was 37% (95% CI lower bound 18%; $p=0.002$) in the vaccination group and 45% (95% CI lower bound 24%; $p=0.001$) in the vaccination and behavioural change group. We recorded no vaccine-related serious adverse events.

INTERPRETATION:

Our findings provide the first indication of the effect of delivering an oral killed whole-cell cholera vaccine to poor urban populations with endemic cholera using routine government services and will help policy makers to formulate vaccination strategies to reduce the burden of severely dehydrating cholera in such populations.

[Am J Trop Med Hyg.](https://doi.org/10.4269/ajtmh.14-0683) 2015 Sep;93(3):527-33. doi: 10.4269/ajtmh.14-0683. Epub 2015 Jun 15.

[A Randomized, Placebo-Controlled Trial Evaluating Safety and Immunogenicity of the Killed, Bivalent, Whole-Cell Oral Cholera Vaccine in Ethiopia.](#)

[Desai SN](#), [Akalu Z](#), [Teshome S](#), [Teferi M](#), [Yamuah L](#), [Kim DR](#), [Yang JS](#), [Hussein J](#), [Park JY](#), [Jang MS](#), [Mesganaw C](#), [Taye H](#), [Beyene D](#), [Bedru A](#), [Singh AP](#), [Wierzba TF](#), [Aseffa A](#).

Abstract

Killed whole-cell oral cholera vaccine (OCV) has been a key component of a comprehensive package including water and sanitation measures for recent cholera epidemics. The vaccine, given in a two-dose regimen, has been evaluated in a large number of human volunteers in India, Vietnam, and Bangladesh, where it has demonstrated safety, immunogenicity, and clinical efficacy. We conducted a double-blind randomized placebo-controlled trial in Ethiopia, where we evaluated the safety and immunogenicity of the vaccine in 216 healthy adults and children. OCV was found to be safe and elicited a robust immunological response against *Vibrio cholerae* O1, with 81% adults and 77% children demonstrating seroconversion 14 days after the second dose of vaccine. This is the first study to evaluate safety and immunogenicity of the vaccine in a population outside Asia using a placebo-controlled, double-blind, randomized study design.

<http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26078323/>

Dengue vaccine

Enterovirus 71 vaccine

[BMC Med.](#) 2015 Sep 17;13:226. doi: 10.1186/s12916-015-0448-7.

[Immunity and clinical efficacy of an inactivated enterovirus 71 vaccine in healthy Chinese children: a report of further observations.](#)

[Liu L](#), [Mo Z](#), [Liang Z](#), [Zhang Y](#), [Li R](#), [Ong KC](#), [Wong KT](#), [Yang E](#), [Che Y](#), [Wang J](#), [Dong C](#), [Feng M](#), [Pu J](#), [Wang L](#), [Liao Y](#), [Jiang L](#), [Tan SH](#), [David P](#), [Huang T](#), [Zhou Z](#), [Wang X](#), [Xia J](#), [Guo L](#), [Wang L](#), [Xie Z](#), [Cui W](#), [Mao Q](#), [Liang Y](#), [Zhao H](#), [Na R](#), [Cui P](#), [Shi H](#), [Wang J](#), [Li Q](#).

Abstract

BACKGROUND:

To investigate the long-term effects on immunity of an inactivated enterovirus 71 (EV71) vaccine and its protective efficacy.

METHODS:

A sub-cohort of 1,100 volunteers from Guangxi Province in China was eligible for enrolment and randomly administered either the EV71 vaccine or a placebo on days 0 and 28 in a phase III clinical trial and then observed for the following 2 years with approval by an independent ethics committee of Guangxi Zhuang Autonomous Region, China. Serum samples from the 350 participants who provided a full series of blood samples (at all the sampling points) within the 2-year period were collected. Vaccine-induced immune effects, including the neutralizing antibody titres and cross-protection against different genotypes of EV71, were examined. This study also evaluated the protective efficacy of this vaccine based upon clinical diagnosis.

RESULTS:

This sub-cohort showed a >60% drop-out rate over 2 years. **The seroconversion rates among the 161 immunized subjects remained >95% at the end of study.** The geometric mean titres of neutralizing antibodies (anti-genotype C4) 360 days after vaccination in 350 subjects were 81.0 (subjects aged 6-11 months), 98.4 (12-23 months), 95.0 (24-35 months), and 81.8 (36-71 months). These titres subsequently increased to 423.1, 659.0, 545.0, and 321.9, respectively, at 540 days post-immunization (d.p.i.), and similar levels were maintained at 720 d.p.i. Higher IFN- γ /IL-4-specific responses to the C4 genotype of EV71 and cross-neutralization reactivity against major EV71 genotype strains were observed in the vaccine group compared to those in the placebo group. Five EV71-infected subjects were observed in the placebo-treated control group and none in the vaccine-immunized group in per-protocol analysis.

CONCLUSION:

These results are consistent with the induction of dynamic immune responses and protective efficacy of the vaccine against most circulating EV71 strains.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26381232/>

HIV vaccine

HPV vaccine

[Lancet Oncol.](#) 2016 Jan;17(1):67-77. doi: 10.1016/S1470-2045(15)00414-3. Epub 2015 Dec 2.

Immunogenicity and HPV infection after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre prospective cohort study.

[Sankaranarayanan R](#), [Prabhu PR](#), [Pawlita M](#), [Gheit T](#), [Bhatla N](#), [Muwonge R](#), [Nene BM](#), [Esmay PO](#), [Joshi S](#), [Poli UR](#), [Jivarajani P](#), [Verma Y](#), [Zomawia E](#), [Siddiqi M](#), [Shastri SS](#), [Jayant K](#), [Malvi SG](#), [Lucas E](#), [Michel A](#), [Butt J](#), [Vijayamma JM](#), [Sankaran S](#), [Kannan TP](#), [Varghese R](#), [Divate U](#), [Thomas S](#), [Joshi G](#), [Willhauck-Fleckenstein M](#), [Waterboer T](#), [Müller M](#), [Sehr P](#), [Hingmire S](#), [Kriplani A](#), [Mishra G](#), [Pimple S](#), [Jadhav R](#), [Sauvagat C](#), [Tommasino M](#), [Pillai MR](#); [Indian HPV Vaccine Study Group](#).

Abstract

BACKGROUND:

An increase in worldwide HPV vaccination could be facilitated if fewer than three doses of vaccine are as effective as three doses. We originally aimed to compare the immunogenicity and frequency of persistent infection and cervical precancerous lesions caused by vaccine-targeted HPV after vaccination with two doses of quadrivalent vaccine on days 1 and 180 or later, with three doses on days 1, 60, and 180 or later, in a cluster-randomised trial. Suspension of the recruitment and vaccination due to events unrelated to our study meant that some enrolled girls could not be vaccinated and some vaccinated girls received fewer than the planned number of vaccinations by default. As a result, we re-analysed our data as an observational cohort study.

METHODS:

Our study was designed to be done in nine locations (188 clusters) in India. Participants were unmarried girls aged 10-18 years vaccinated in four cohorts: girls who received three doses of vaccine on days 1, 60, and 180 or later, two doses on days 1 and 180 or later, two doses on days 1 and 60 by default, and one dose by default. The primary outcomes were immunogenicity in terms of L1 genotype-specific binding antibody titres, neutralising antibody titres, and antibody avidity after vaccination for the vaccine-targeted HPV types 16, 18, 6, and 11 and incident and persistent infections with these HPVs. Analysis was per actual number of vaccine doses received. This study is registered with ISRCTN, number ISRCTN98283094; and with ClinicalTrials.gov, number [NCT00923702](#).

FINDINGS:

Vaccination of eligible girls was initiated on Sept 1, 2009, and continued until April 8, 2010. Of 21 258 eligible girls identified at 188 clusters, 17 729 girls were recruited from 178 clusters before suspension. 4348 (25%) girls received three doses, 4979 (28%) received two doses on days 1 and 180 or later, 3452 (19%) received two doses at days 1 and 60, and 4950 (28%) received one dose. **Immune response in the two-dose HPV vaccine group was non-inferior to the three-dose group** (median fluorescence intensity ratio for HPV 16 1.12 [95% CI 1.02-1.23] and for HPV 18 1.04 [0.92-1.19]) at 7 months, but was inferior in the two-dose default (0.33 [0.29-0.38] for HPV 16 and 0.51 [0.43-0.59] for HPV 18) and one-dose default (0.09 [0.08-0.11] for HPV 16 and 0.12 [0.10-0.14] for HPV 18) groups at 18 months. **The geometric mean avidity indices after fewer than three doses by design or default were non-inferior to those after three doses of vaccine. Fewer than three doses by design and default induced detectable concentrations of neutralising antibodies to all four vaccine-targeted HPV types, but at much lower concentration after one dose.** Cervical samples from 2649 participants were tested and the frequency of incident HPV 16, 18, 6, and 11 infections was similar irrespective of the number of vaccine doses received. The testing of at least two samples from 838 participants showed that there was no persistent HPV 16 or 18 infections in any study group at a median follow-up of 4.7 years (IQR 4.2-5.1).

INTERPRETATION:

Despite the limitations imposed by the suspension of the HPV vaccination, our findings lend support to the **WHO recommendation of two doses, at least 6 months apart, for routine**

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vaccination of young girls. The short-term protection afforded by one dose of HPV vaccine against persistent infection with HPV 16, 18, 6, and 11 is similar to that afforded by two or three doses of vaccine and merits further assessment.

[http://linkinghub.elsevier.com/retrieve/pii/S1470-2045\(15\)00414-3](http://linkinghub.elsevier.com/retrieve/pii/S1470-2045(15)00414-3)

[Pediatrics](#). 2015 Jul;136(1):e28-39. doi: 10.1542/peds.2014-3745.

Immunogenicity and Safety of a 9-Valent HPV Vaccine.

[Van Damme P](#), [Olsson SE](#), [Block S](#), [Castellsague X](#), [Gray GE](#), [Herrera T](#), [Huang LM](#), [Kim DS](#), [Pitisuttithum P](#), [Chen J](#), [Christiano S](#), [Maansson R](#), [Moeller E](#), [Sun X](#), [Vuocolo S](#), [Luxembourg A](#).

Abstract

OBJECTIVES:

Prophylactic vaccination of young women aged 16 to 26 years with the 9-valent (6/11/16/18/31/33/45/52/58) human papillomavirus (HPV) virus-like particle (9vHPV) vaccine prevents infection and disease. We conducted a noninferiority immunogenicity study to bridge the findings in young women to girls and boys aged 9 to 15 years.

METHODS:

Subjects (N = 3066) received a 3-dose regimen of 9vHPV vaccine administered at day 1, month 2, and month 6. Anti-HPV serologic assays were performed at day 1 and month 7.

Noninferiority required that the lower bound of 2-sided 95% confidence intervals of geometric mean titer ratios (boys:young women or girls:young women) be >0.67 for each HPV type.

Systemic and injection-site adverse experiences (AEs) and serious AEs were monitored.

RESULTS:

At 4 weeks after dose 3, >99% of girls, boys, and young women seroconverted for each vaccine HPV type. Increases in geometric mean titers to HPV types 6/11/16/18/31/33/45/52/58 were elicited in all vaccine groups. Responses in girls and boys were noninferior to those of young women. Persistence of anti-HPV responses was demonstrated through 2.5 years after dose 3. Administration of the 9vHPV vaccine was generally well tolerated. A lower proportion of girls (81.9%) and boys (72.8%) than young women (85.4%) reported injection-site AEs, most of which were mild to moderate in intensity.

CONCLUSIONS:

These data support bridging the efficacy findings with 9vHPV vaccine in young women 16 to 26 years of age to girls and boys 9 to 15 years of age and implementing gender-neutral HPV vaccination programs in preadolescents and adolescents.

<http://pediatrics.aappublications.org/cgi/pmidlookup?view=long&pmid=26101366>

Influenza vaccine

[Pediatr Infect Dis J](#). 2015 Jul;34(7):774-82. doi: 10.1097/INF.0000000000000709.

Immunogenicity and Safety of a Trivalent Inactivated Influenza Vaccine in Children 6 Months to 17 Years of Age, Previously Vaccinated with an AS03-Adjuvanted A(H1N1)Pdm09 Vaccine: Two Open-label, Randomized Trials.

[Vesikari T](#), [Richardus JH](#), [Berglund J](#), [Korhonen T](#), [Flodmark CE](#), [Lindstrand A](#), [Silfverdal SA](#), [Bambure V](#), [Caplanusi A](#), [Dieussaert I](#), [Roy-Ghanta S](#), [Vaughn DW](#).

Abstract

BACKGROUND:

During the influenza pandemic 2009-2010, an AS03-adjuvanted A(H1N1)pdm09 vaccine was used extensively in children 6 months of age and older, and during the 2010-2011 influenza season, the A(H1N1)pdm09 strain was included in the seasonal trivalent inactivated influenza vaccine (TIV) without adjuvant. We evaluated the immunogenicity and safety of TIV in children previously vaccinated with the AS03-adjuvanted A(H1N1)pdm09 vaccine.

METHODS:

Healthy children were randomized (1:1) to receive TIV or a control vaccine. Children were aged 6 months to 9 years (n = 154) and adolescents 10-17 years (n = 77) when they received AS03-adjuvanted A(H1N1)pdm09 vaccine at least 6 months before study enrolment.

Hemagglutination inhibition (HI) and neutralizing antibody responses against the A(H1N1)pdm09 strain were evaluated before (day 0) and at day 28 and month 6 after study vaccination. Reactogenicity was assessed during the 7 day postvaccination period, and safety was assessed for 6 months.

RESULTS:

At day 0, >93.9% of all children had HI titers $\geq 1:40$ for the A(H1N1)pdm09 strain, which increased to 100% at both day 28 and month 6 in the TIV group. Between days 0 and 28, HI antibody geometric mean titers against A(H1N1)pdm09 increased by 9-fold and 4-fold in children 6 months to 9 years of age and 10-17 years of age, respectively.

CONCLUSION:

AS03-adjuvanted A(H1N1)pdm09 vaccine-induced robust immune responses in children that persisted into the next season, yet were still boosted by TIV containing A(H1N1)pdm09. The reactogenicity and safety profile of TIV did not appear compromised by prior receipt of AS03-adjuvanted A(H1N1)pdm09 vaccine.

Japanese encephalitis virus vaccine

[J Infect Dis.](#) 2015 Sep 1;212(5):715-25. doi: 10.1093/infdis/jiv023. Epub 2015 Jan 18.

[A Japanese Encephalitis Vaccine From India Induces Durable and Cross-protective Immunity Against Temporally and Spatially Wide-ranging Global Field Strains.](#)

[Singh A](#), [Mitra M](#), [Sampath G](#), [Venugopal P](#), [Rao JV](#), [Krishnamurthy B](#), [Gupta MK](#), [Sri Krishna S](#), [Sudhakar B](#), [Rao NB](#), [Kaushik Y](#), [Gopinathan K](#), [Hegde NR](#), [Gore MM](#), [Krishna Mohan V](#), [Ella KM](#).

Abstract

BACKGROUND:

Japanese encephalitis (JE) is a vaccine-preventable acute disease. We report the results of a phase 2/3 trial of JENVAC, a Vero cell-derived vaccine developed using an Indian strain of JE virus (JEV).

METHODS:

JENVAC was administered in 2 doses 28 days apart, and immunogenicity was compared to that from a single dose of SA-14-14-2, the only approved JE vaccine and regimen at the time in India.

RESULTS:

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After both the doses, seroconversion and seroprotection were >90% for JENVAC. For SA-14-14-2, seroconversion and seroprotection were 57.69% and 77.56%, respectively, on day 28 and 39.74% and 60.26%, respectively, on day 56. The geometric mean titers at day 28 and day 56 were 145.04 and 460.53, respectively, for JENVAC and 38.56 and 25.29, respectively, for SA-14-14-2. With a single dose of JENVAC, seroprotection titers lasted at least 12 months in >80% of the subjects. Following receipt of 2 doses, 61.17% of subjects retained seroprotection titers at 24 months, and immunogenicity criteria were higher than that for SA-14-14-2 at 12, 18, and 24 months each. Sera from JENVAC subjects neutralized JEV genotypes I, II, III, and IV equally well. Adverse events were not significantly different between the 2 vaccines.

CONCLUSIONS:

JENVAC elicits long-lasting, broadly protective immunity.

Malaria vaccine

[N Engl J Med](#). 2015 Nov 19;373(21):2025-37. doi: 10.1056/NEJMoa1505819. Epub 2015 Oct 21.

Genetic Diversity and Protective Efficacy of the RTS,S/AS01 Malaria Vaccine.

[Neafsey DE](#), [Juraska M](#), [Bedford T](#), [Benkeser D](#), [Valim C](#), [Griggs A](#), [Lievens M](#), [Abdulla S](#), [Adjei S](#), [Agbenyega T](#), [Agnandji ST](#), [Aide P](#), [Anderson S](#), [Ansong D](#), [Aponte JJ](#), [Asante KP](#), [Bejon P](#), [Birkett AJ](#), [Bruls M](#), [Connolly KM](#), [D'Alessandro U](#), [Dobaño C](#), [Gesase S](#), [Greenwood B](#), [Grimsby J](#), [Tinto H](#), [Hamel MJ](#), [Hoffman I](#), [Kamthunzi P](#), [Kariuki S](#), [Kremsner PG](#), [Leach A](#), [Lell B](#), [Lennon NJ](#), [Lusingu J](#), [Marsh K](#), [Martinson F](#), [Molel JT](#), [Moss EL](#), [Njuguna P](#), [Ockenhouse CF](#), [Ogutu BR](#), [Otieno W](#), [Otieno L](#), [Otieno K](#), [Owusu-Agyei S](#), [Park DJ](#), [Pellé K](#), [Robbins D](#), [Russ C](#), [Ryan EM](#), [Sacarlal J](#), [Sogoloff B](#), [Sorgho H](#), [Tanner M](#), [Theander T](#), [Valea I](#), [Volkman SK](#), [Yu Q](#), [Lapierre D](#), [Birren BW](#), [Gilbert PB](#), [Wirth DF](#).

Abstract

BACKGROUND:

The RTS,S/AS01 vaccine targets the circumsporozoite protein of *Plasmodium falciparum* and has partial protective efficacy against clinical and severe malaria disease in infants and children. We investigated whether the vaccine efficacy was specific to certain parasite genotypes at the circumsporozoite protein locus.

METHODS:

We used polymerase chain reaction-based next-generation sequencing of DNA extracted from samples from 4985 participants to survey circumsporozoite protein polymorphisms. We evaluated the effect that polymorphic positions and haplotypic regions within the circumsporozoite protein had on vaccine efficacy against first episodes of clinical malaria within 1 year after vaccination.

RESULTS:

In the per-protocol group of 4577 RTS,S/AS01-vaccinated participants and 2335 control-vaccinated participants who were 5 to 17 months of age, the 1-year cumulative vaccine efficacy was 50.3% (95% confidence interval [CI], 34.6 to 62.3) against clinical malaria in which parasites matched the vaccine in the entire circumsporozoite protein C-terminal (139 infections), as compared with 33.4% (95% CI, 29.3 to 37.2) against mismatched malaria (1951 infections) (P=0.04 for differential vaccine efficacy). The vaccine efficacy based on the hazard ratio was 62.7% (95% CI, 51.6 to 71.3) against matched infections versus

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54.2% (95% CI, 49.9 to 58.1) against mismatched infections (P=0.06). In the group of infants 6 to 12 weeks of age, there was no evidence of differential allele-specific vaccine efficacy.

CONCLUSIONS:

These results suggest that among children 5 to 17 months of age, the RTS,S vaccine has greater activity against malaria parasites with the matched circumsporozoite protein allele than against mismatched malaria. The overall vaccine efficacy in this age category will depend on the proportion of matched alleles in the local parasite population; in this trial, less than 10% of parasites had matched alleles. (Funded by the National Institutes of Health and others.).

http://www.nejm.org/doi/abs/10.1056/NEJMoa1505819?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dwww.ncbi.nlm.nih.gov

[Lancet Infect Dis.](#) 2015 Dec;15(12):1450-8. doi: 10.1016/S1473-3099(15)00239-X. Epub 2015 Sep 2.

[Immunogenicity of the RTS,S/AS01 malaria vaccine and implications for duration of vaccine efficacy: secondary analysis of data from a phase 3 randomised controlled trial.](#)

[White MT](#), [Verity R](#), [Griffin JT](#), [Asante KP](#), [Owusu-Agyei S](#), [Greenwood B](#), [Drakeley C](#), [Gesase S](#), [Lusingu J](#), [Ansong D](#), [Adjei S](#), [Agbenyega T](#), [Ogutu B](#), [Otieno L](#), [Otieno W](#), [Agnandji ST](#), [Lell B](#), [Kremsner P](#), [Hoffman I](#), [Martinson F](#), [Kamthunzu P](#), [Tinto H](#), [Valea I](#), [Sorgho H](#), [Oneko M](#), [Otieno K](#), [Hamel MJ](#), [Salim N](#), [Mtoro A](#), [Abdulla S](#), [Aide P](#), [Sacarlal J](#), [Aponte JJ](#), [Njuguna P](#), [Marsh K](#), [Bejon P](#), [Riley EM](#), [Ghani AC](#).

Abstract

BACKGROUND:

The RTS,S/AS01 malaria vaccine targets the circumsporozoite protein, inducing antibodies associated with the prevention of *Plasmodium falciparum* infection. We assessed the association between anti-circumsporozoite antibody titres and the magnitude and duration of vaccine efficacy using data from a phase 3 trial done between 2009 and 2014.

METHODS:

Using data from 8922 African children aged 5-17 months and 6537 African infants aged 6-12 weeks at first vaccination, we analysed the determinants of immunogenicity after RTS,S/AS01 vaccination with or without a booster dose. We assessed the association between the incidence of clinical malaria and anti-circumsporozoite antibody titres using a model of anti-circumsporozoite antibody dynamics and the natural acquisition of protective immunity over time.

FINDINGS:

RTS,S/AS01-induced anti-circumsporozoite antibody titres were greater in children aged 5-17 months than in those aged 6-12 weeks. Pre-vaccination anti-circumsporozoite titres were associated with lower immunogenicity in children aged 6-12 weeks and higher immunogenicity in those aged 5-17 months. The immunogenicity of the booster dose was strongly associated with immunogenicity after primary vaccination. Anti-circumsporozoite titres wane according to a biphasic exponential distribution. In participants aged 5-17 months, the half-life of the short-lived component of the antibody response was 45 days (95% credible interval 42-48) and that of the long-lived component was 591 days (557-632). After primary vaccination 12% (11-13) of the response was estimated to be long-lived, rising to 30% (28-32%) after a booster dose. An anti-circumsporozoite antibody titre of 121 EU/mL (98-153) was estimated to prevent 50% of infections. Waning anti-circumsporozoite antibody titres predict the duration of efficacy against

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clinical malaria across different age categories and transmission intensities, and efficacy wanes more rapidly at higher transmission intensity.

INTERPRETATION:

Anti-circumsporozoite antibody titres are a surrogate of protection for the magnitude and duration of RTS,S/AS01 efficacy, with or without a booster dose, providing a valuable surrogate of effectiveness for new RTS,S formulations in the age groups considered.

[http://linkinghub.elsevier.com/retrieve/pii/S1473-3099\(15\)00239-X](http://linkinghub.elsevier.com/retrieve/pii/S1473-3099(15)00239-X)

[Lancet](#). 2015 Jul 4;386(9988):31-45. doi: 10.1016/S0140-6736(15)60721-8. Epub 2015 Apr 23.

[Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial.](#)

[RTS,S Clinical Trials Partnership.](#)

Abstract

BACKGROUND:

The efficacy and safety of the RTS,S/AS01 candidate malaria vaccine during 18 months of follow-up have been published previously. Herein, we report the final results from the same trial, including the efficacy of a booster dose.

METHODS:

From March 27, 2009, until Jan 31, 2011, children (age 5-17 months) and young infants (age 6-12 weeks) were enrolled at 11 centres in seven countries in sub-Saharan Africa. Participants were randomly assigned (1:1:1) at first vaccination by block randomisation with minimisation by centre to receive **three doses of RTS,S/AS01 at months 0, 1, and 2 and a booster dose at month 20 (R3R group); three doses of RTS,S/AS01 and a dose of comparator vaccine at month 20 (R3C group);** or a comparator vaccine at months 0, 1, 2, and 20 (C3C [control group]). Participants were followed up until Jan 31, 2014. Cases of clinical and severe malaria were captured through passive case detection. Serious adverse events (SAEs) were recorded. Analyses were by modified intention to treat and per protocol. The coprimary endpoints were the occurrence of malaria over 12 months after dose 3 in each age category. In this final analysis, we present data for the efficacy of the booster on the occurrence of malaria. Vaccine efficacy (VE) against clinical malaria was analysed by negative binomial regression and against severe malaria by relative risk reduction. This trial is registered with ClinicalTrials.gov, number [NCT00866619](#).

FINDINGS:

8922 children and 6537 young infants were included in the modified intention-to-treat analyses. Children were followed up for a median of 48 months (IQR 39-50) and young infants for 38 months (34-41) after dose 1. From month 0 until study end, compared with 9585 episodes of clinical malaria that met the primary case definition in children in the C3C group, **6616 episodes occurred in the R3R group (VE 36.3%, 95% CI 31.8-40.5) and 7396 occurred in the R3C group (28.3%, 23.3-32.9)**; compared with 171 children who experienced at least one episode of severe malaria in the C3C group, 116 children experienced at least one episode of severe malaria in the R3R group (32.2%, 13.7 to 46.9) and 169 in the R3C group (1.1%, -23.0 to 20.5). In young infants, compared with 6170 episodes of clinical malaria that met the primary case definition in the C3C group, 4993 episodes occurred in the R3R group (VE 25.9%, 95% CI 19.9-31.5) and 5444 occurred in the R3C group (18.3%, 11.7-24.4); and compared with 116 infants who experienced at least one episode of severe malaria in the C3C group, 96 infants experienced at least one episode of severe malaria in the R3R group (17.3%, 95% CI -9.4 to 37.5) and 104 in the R3C group (10.3%, -17.9 to 31.8). In children, 1774 cases of clinical

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malaria were averted per 1000 children (95% CI 1387-2186) in the R3R group and 1363 per 1000 children (995-1797) in the R3C group. **The numbers of cases averted per 1000 young infants were 983 (95% CI 592-1337) in the R3R group and 558 (158-926) in the R3C group.** The frequency of SAEs overall was balanced between groups. However, meningitis was reported as a SAE in 22 children: 11 in the R3R group, ten in the R3C group, and one in the C3C group. The incidence of generalised convulsive seizures within 7 days of RTS,S/AS01 booster was 2.2 per 1000 doses in young infants and 2.5 per 1000 doses in children.

INTERPRETATION:

RTS,S/AS01 prevented a substantial number of cases of clinical malaria over a 3-4 year period in young infants and children when administered with or without a booster dose. Efficacy was enhanced by the administration of a booster dose in both age categories. Thus, the vaccine has the potential to make a substantial contribution to malaria control when used in combination with other effective control measures, especially in areas of high transmission.

Measles vaccine

Meningococcal vaccine

Pneumococcal vaccine

Polio vaccine

[Lancet Infect Dis.](#) 2015 Nov;15(11):1273-82. doi: 10.1016/S1473-3099(15)00219-4. Epub 2015 Aug 26.

Inactivated poliovirus vaccine given alone or in a sequential schedule with bivalent oral poliovirus vaccine in Chilean infants: a randomised, controlled, open-label, phase 4, non-inferiority study.

[O'Ryan M](#), [Bandyopadhyay AS](#), [Villena R](#), [Espinoza M](#), [Novoa J](#), [Weldon WC](#), [Oberste MS](#), [Self S](#), [Borate BR](#), [Asturias EJ](#), [Clemens R](#), [Orenstein W](#), [Jimeno J](#), [Rüttimann R](#), [Costa Clemens SA](#); [Chilean IPV/bOPV study group](#).

Abstract

BACKGROUND:

Bivalent oral poliovirus vaccine (bOPV; types 1 and 3) is expected to replace trivalent OPV (tOPV) globally by April, 2016, preceded by the introduction of at least one dose of inactivated poliovirus vaccine (IPV) in routine immunisation programmes to eliminate vaccine-associated or vaccine-derived poliomyelitis from serotype 2 poliovirus. Because data are needed on sequential IPV-bOPV schedules, we assessed the immunogenicity of two different IPV-bOPV schedules compared with an all-IPV schedule in infants.

METHODS:

We did a randomised, controlled, open-label, non-inferiority trial with healthy, full-term (>2.5 kg birthweight) infants aged 8 weeks (\pm 7 days) at six well-child clinics in Santiago, Chile. We used supplied lists to randomly assign infants (1:1:1) to receive **three polio vaccinations (IPV**

by injection or bOPV as oral drops) at age 8, 16, and 24 weeks in one of three sequential schedules: IPV-bOPV-bOPV, IPV-IPV-bOPV, or IPV-IPV-IPV. We did the randomisation with blocks of 12 stratified by study site. All analyses were done in a masked manner. **Co-primary outcomes were non-inferiority of the bOPV-containing schedules compared with the all-IPV schedule for seroconversion** (within a 10% margin) and antibody titres (within two-thirds log₂ titres) to poliovirus serotypes 1 and 3 at age 28 weeks, analysed in the per-protocol population. Secondary outcomes were seroconversion and titres to serotype 2 and faecal shedding for 4 weeks after a monovalent OPV type 2 challenge at age 28 weeks. Safety analyses were done in the intention-to-treat population. This trial is registered with ClinicalTrials.gov, number [NCT01841671](https://clinicaltrials.gov/ct2/show/study/NCT01841671), and is closed to new participants.

FINDINGS:

Between April 25 and August 1, 2013, we assigned 570 infants to treatment: 190 to IPV-bOPV-bOPV, 192 to IPV-IPV-bOPV, and 188 to IPV-IPV-IPV. 564 (99%) were vaccinated and included in the intention-to-treat cohort, and 537 (94%) in the per-protocol analyses. In the IPV-bOPV-bOPV, IPV-IPV-bOPV, and IPV-IPV-IPV groups, respectively, the proportions of children with seroconversion to type 1 poliovirus were 166 (98·8%) of 168, 95% CI 95·8-99·7; 178 (100%), 97·9-100·0; and 175 (100%), 97·9-100·0. Proportions with seroconversion to type 3 poliovirus were 163 (98·2%) of 166, 94·8-99·4; 177 (100%), 97·9-100·0, and 172 (98·9%) of 174, 95·9-99·7. **Non-inferiority was thus shown for the bOPV-containing schedules compared with the all-IPV schedule, with no significant differences between groups.** In the IPV-bOPV-bOPV, IPV-IPV-bOPV, and IPV-IPV-IPV groups, respectively, the proportions of children with seroprotective antibody titres to type 1 poliovirus were 168 (98·8%) of 170, 95% CI 95·8-99·7; 181 (100%), 97·9-100·0; and 177 (100%), 97·9-100·0. Proportions to type 3 poliovirus were 166 (98·2%) of 169, 94·9-99·4; 180 (100%), 97·9-100·0; and 174 (98·9%) of 176, 96·0-99·7. Non-inferiority comparisons could not be done for this outcome because median titres for the groups receiving OPV were greater than the assay's upper limit of detection (log₂ titres >10·5). The proportions of children seroconverting to type 2 poliovirus in the IPV-bOPV-bOPV, IPV-IPV-bOPV, and IPV-IPV-IPV groups, respectively, were 130 (77·4%) of 168, 95% CI 70·5-83·0; 169 (96·0%) of 176, 92·0-98·0; and 175 (100%), 97·8-100. IPV-bOPV schedules resulted in almost a 0·3 log reduction of type 2 faecal shedding compared with the IPV-only schedule. No participants died during the trial; 81 serious adverse events were reported, of which one was thought to be possibly vaccine-related (intestinal intussusception).

INTERPRETATION:

Seroconversion rates against polioviruses types 1 and 3 were non-inferior in sequential schedules containing IPV and bOPV, compared with an all-IPV schedule, and proportions of infants with protective antibodies were high after all three schedules. One or two doses of bOPV after IPV boosted intestinal immunity for poliovirus type 2, suggesting possible cross protection. Additionally, there was evidence of humoral priming for type 2 from one dose of IPV. Our findings could give policy makers flexibility when choosing a vaccination schedule, especially when trying to eliminate vaccine-associated and vaccine-derived poliomyelitis.

[Lancet Infect Dis](https://doi.org/10.1016/S1473-3099(15)00093-6). 2015 Aug;15(8):889-97. doi: 10.1016/S1473-3099(15)00093-6. Epub 2015 Jun 17.

[Monovalent type-1 oral poliovirus vaccine given at short intervals in Pakistan: a randomised controlled, four-arm, open-label, non-inferiority trial.](#)

[Mir F](#)¹, [Quadri F](#)¹, [Mach O](#)², [Ahmed I](#)¹, [Bhatti Z](#)¹, [Khan A](#)¹, [Rehman NU](#)¹, [Durry E](#)³, [Salama M](#)², [Oberste SM](#)⁴, [Weldon WC](#)⁴, [Sutter RW](#)², [Zaidi AK](#)⁵.

Abstract

BACKGROUND:

Supplementary immunisation activities with oral poliovirus vaccines (OPVs) are usually separated by 4 week intervals; however, shorter intervals have been used in security-compromised areas and for rapid outbreak responses. **We assessed the immunogenicity of monovalent type-1 oral poliovirus vaccine (mOPV1) given at shorter than usual intervals** in Karachi, Pakistan.

METHODS:

This was a multicentre, randomised, controlled, four-arm, open-label, non-inferiority trial done at five primary health-care centres in low-income communities in and around Karachi, Pakistan. Eligible participants were healthy newborn babies with a birthweight of at least 2.5 kg, for whom informed consent was provided by their parent or guardian, and lived less than 30 km from the study clinic. After receiving a birth dose of trivalent OPV, we enrolled and randomly assigned newborn babies (1:1:1:1) to receive two doses of mOPV1 with an interval of 1 week (mOPV1-1 week), 2 weeks (mOPV1-2 weeks), or 4 weeks (mOPV1-4 weeks) between doses, or two doses of bivalent OPV (bOPV) with an interval of 4 weeks between doses (bOPV-4 weeks). We gave the first study dose of OPV at age 6 weeks. We did the randomisation with a centrally generated, computerised allocation sequence with blocks of 16; participants' families and study physicians could not feasibly be masked to the allocations. Trial participants were excluded from local supplementary immunisation activities during the study period. The primary outcome was non-inferiority (within a 20% margin) between groups in seroconversion to type-1 poliovirus. The primary and safety analyses were done in the per-protocol population of infants who received all three doses of vaccine. This trial is registered with ClinicalTrials.gov, number [NCT01586572](https://clinicaltrials.gov/ct2/show/study/NCT01586572), and is closed to new participants.

FINDINGS:

Between March 1, 2012, and May 31, 2013, we enrolled 1009 newborn babies, and randomly assigned 829 (82%) to treatment. 554 (67%) of the 829 babies were included in the per-protocol analysis. Proportions of seroconversion to type-1 poliovirus were 107/135 (79%, 95% CI 72.4-86.1) with mOPV1-1 week, 108/135 (80%, 73.2-86.8) with mOPV1-2 weeks, 129/148 (87%, 80.9-92.0) with mOPV1-4 weeks, and 107/136 (79%, 71.8-85.6) with bOPV-4 weeks. **Non-inferiority was shown between groups and no significant differences were noted.** Ten participants died during the trial. Seven of these deaths occurred during the lead-in period before randomisation (two from diarrhoea, five from unknown causes). Three infants died from sepsis after random assignment. No deaths were attributed to the procedures or vaccines. Additionally, we noted no events of vaccine-associated paralysis.

INTERPRETATION:

We identified no significant differences in responses to mOPV1 given with shorter intervals between doses than with the standard 4 week intervals. The short-interval strategy could be particularly beneficial when temporary windows of opportunity for safe access can be granted in areas of conflict--eg, during cease-fire periods. In such situations, we recommend shortening the interval between OPV doses to 7 days.

Rotavirus vaccine

Salmonella typhi vaccine

[Clin Infect Dis.](https://doi.org/10.1093/cid/civ295) 2015 Aug 1;61(3):393-402. doi: 10.1093/cid/civ295. Epub 2015 Apr 13.

Safety and immunogenicity of a Vi polysaccharide-tetanus toxoid conjugate vaccine (Typbar-TCV) in healthy infants, children, and adults in typhoid endemic areas: a multicenter, 2-cohort, open-label, double-blind, randomized controlled phase 3 study.

[Mohan VK](#), [Varanasi V](#), [Singh A](#), [Pasetti MF](#), [Levine MM](#), [Venkatesan R](#), [Ella KM](#).

Abstract

BACKGROUND:

Enteric fever caused by Salmonella Typhi remains a major public health problem in developing countries. Typbar-TCV is a single-dose typhoid Vi polysaccharide-tetanus toxoid conjugate vaccine for persons ≥ 6 months of age.

METHODS:

Six hundred fifty-four healthy subjects aged 2-45 years enrolled in a double-blind, randomized controlled trial (RCT) received a single dose of Typbar-TCV or comparator "Vi polysaccharide" (Typbar), and 327 healthy subjects aged 6-23 months received a single dose of Typbar-TCV in an open-label trial (OLT); both received single- or multidose presentations from different lots. After 2 years, subsets in each group received a booster dose. The primary objective included analysis of geometric mean titer (GMTs) and 4-fold rise of anti-Vi serum immunoglobulin G (IgG) enzyme-linked immunosorbent assay titers over baseline (seroconversion [SCN]) 42 days after immunization.

RESULTS:

Typbar-TCV recipients in the RCT attained higher anti-Vi IgG GMTs 42 days after immunization (SCN, 97%; GMT, 1293 [95% confidence interval {CI}, 1153-1449]) than recipients of Typbar (SCN, 93%; GMT, 411 [95% CI, 359-471]) ($P < .001$). Typbar-TCV was highly immunogenic in the OLT (SCN, 98%; GMT, 1937 [95% CI, 1785-2103]). Two years after vaccination, anti-Vi titers remained higher in Typbar-TCV subjects (GMT, 82 [95% CI, 73-92]); and exhibited higher avidity (geometric mean avidity index [GMAI], 60%) than in Typbar recipients (GMT, 46 [95% CI, 40-53]; GMAI 46%) in the RCT ($P < .001$). OLT Typbar-TCV recipients achieved GMT of 48 (95% CI, 42-55) and GMAI of 57%. Typbar-TCV induced multiple IgG subclasses and strong booster responses in all ages. No serious vaccine-attributable adverse events were observed.

CONCLUSIONS:

Single-dose Typbar-TCV is well tolerated and induces robust and long-lasting serum anti-Vi IgG across age groups.

Tuberculosis vaccine

Safety and immunogenicity of candidate vaccine M72/AS01E in adolescents in a TB endemic setting.

[Penn-Nicholson A](#), [Geldenhuys H](#), [Burny W](#), [van der Most R](#), [Day CL](#), [Jongert E](#), [Moris P](#), [Hatherill M](#), [Ofori-Anyinam O](#), [Hanekom W](#); [Vaccine Study Team](#), [Bollaerts A](#), [Demoitie MA](#), [Kany Luabeya AK](#), [De Ruymaeker E](#), [Tameris M](#), [Lapierre D](#), [Scriba TJ](#).

Abstract

BACKGROUND:

Vaccination that prevents tuberculosis (TB) disease, particularly in adolescents, would have the greatest impact on the global TB epidemic. Safety, reactogenicity and immunogenicity of the

Randomised trials in child health in developing countries 2015-16

vaccine candidate M72/AS01E was evaluated in healthy, HIV-negative adolescents in a TB endemic region, regardless of Mycobacterium tuberculosis (M.tb) infection status.

METHODS:

In a phase II, double-blind randomized, controlled study ([NCT00950612](https://clinicaltrials.gov/ct2/show/study/NCT00950612)), two doses of M72/AS01E or placebo were administered intramuscularly, one month apart. Participants were followed-up post-vaccination, for 6 months. M72-specific immunogenicity was evaluated by intracellular cytokine staining analysis of T cells and NK cells by flow cytometry.

RESULTS:

No serious adverse events were recorded. **M72/AS01E induced robust T cell and antibody responses, including antigen-dependent NK cell IFN- γ production. CD4 and CD8 T cell responses were sustained at 6 months post vaccination.** Irrespective of M.tb infection status, vaccination induced a high frequency of M72-specific CD4 T cells expressing multiple combinations of Th1 cytokines, and low level IL-17. We observed rapid boosting of immune responses in M.tb-infected participants, suggesting natural infection acts as a prime to vaccination.

CONCLUSIONS:

The clinically acceptable safety and immunogenicity profile of M72/AS01E in adolescents living in an area with high TB burden support the move to efficacy trials.

[http://linkinghub.elsevier.com/retrieve/pii/S0264-410X\(15\)00761-6](http://linkinghub.elsevier.com/retrieve/pii/S0264-410X(15)00761-6)

[Vaccine](#). 2015 Jul 9;33(30):3592-9. doi: 10.1016/j.vaccine.2015.05.036. Epub 2015 Jun 3.

The tuberculosis vaccine H4:IC31 is safe and induces a persistent polyfunctional CD4 T cell response in South African adults: A randomized controlled trial.

[Geldenhuys H](#), [Mearns H](#), [Miles DJ](#), [Tameris M](#), [Hokey D](#), [Shi Z](#), [Bennett S](#), [Andersen P](#), [Kromann I](#), [Hoff ST](#), [Hanekom WA](#), [Mahomed H](#), [Hatherill M](#), [Scriba TJ](#); [H4:IC31 Trial Study Group](#), [van Rooyen M](#), [Bruce McClain J](#), [Ryall R](#), [de Bruyn G](#); [H4:IC31 Trial Study Groupa](#).

Abstract

BACKGROUND:

New, more effective vaccines to prevent tuberculosis (TB) disease are needed urgently. H4:IC31 is an investigational vaccine that contains a fusion protein of the immunodominant antigens TB10.4 and Ag85B, formulated in IC31 adjuvant. We assessed the safety and immunogenicity of H4:IC31 in South African adults from a TB endemic setting.

METHODS:

In this double blind, placebo controlled, phase I trial, Mycobacterium tuberculosis-uninfected, HIV-uninfected, healthy adults with a history of childhood BCG vaccination were randomly allocated to two intramuscular vaccinations with 5, 15, 50 or 150 μ g H4 formulated in 500nmol IC31, two months apart. Vaccinees were followed for six months to assess safety; immunogenicity was measured by ELISpot and intracellular cytokine staining assays.

RESULTS:

Thirty-two participants received H4:IC31 and 8 received placebo. Injection site adverse events were common but mild; mild fatigue was the most common systemic adverse event. Frequencies of adverse events did not differ between dosage groups. Detectable antigen-specific CD4 T cell responses were induced by all doses of H4:IC31, but doses below 50 μ g induced the highest frequencies of CD4 T cells, comprised predominantly of IFN- γ (+)TNF- α (+)IL-2(+) or TNF- α (+)IL-2(+) cells. These memory responses persisted up to the end of follow up, on study day 182.

CONCLUSIONS:

H4:IC31 demonstrated an acceptable safety profile and was immunogenic in South African adults. In this trial, the 15 µg dose appeared to induce the most optimal immune response.

Typhoid vaccine

Varicella vaccine

Vitamin A

(See also: Maternal health - nutrition and micronutrient supplementation; HIV - prevention of mother to child transmission; Helminths)

[Allergy](#). 2015 Aug;70(8):985-94. doi: 10.1111/all.12641. Epub 2015 May 18.

[Neonatal vitamin A supplementation associated with increased atopy in girls.](#)

[Aage S](#), [Kiralý N](#), [Da Costa K](#), [Byberg S](#), [Bjerregaard-Andersen M](#), [Fisker AB](#), [Aaby P](#), [Benn CS](#).

Abstract

BACKGROUND:

Neonatal vitamin A supplementation (NVAS) is currently being considered as policy in countries at risk of deficiency. A previous study suggested that NVAS may be associated with increased atopy. We examined the effect of NVAS on atopy by conducting long-term follow-up of a previous randomized controlled trial in Guinea-Bissau.

METHODS:

In 2002-2004, we randomized 4345 normal birthweight neonates to NVAS (50 000 IU retinyl palmitate) or placebo together with their Bacillus Calmette-Guérin vaccination. In 2013, we visited the 1692 (39%) children now aged 8-10 years who were still living in the study area, and 1478 (87%) were found at home. Provided consent, a skin prick test was performed, and history of allergic symptoms was recorded. Associations of NVAS and atopy (defined as skin prick test reaction of ≥ 3 mm) were analysed using binomial regression.

RESULTS:

Of the 1430 children with a valid skin prick test, 228 (16%) were positive (more boys (20%) than girls (12%), P-value < 0.0001). NVAS did not increase the overall risk of atopy (RR 1.10 [95% CI 0.87-1.40]). However, NVAS was associated with significantly increased risk among females (RR 1.78 [1.17-2.72]) but not among males (0.86 [0.64-1.15], P-value for interaction between NVAS and gender = 0.005). Furthermore, NVAS was associated with increased risk of wheezing among females (RR 1.80 [1.03-3.17], but not among males, P-value for interaction = 0.05).

CONCLUSION:

The study corroborated previous observations; NVAS was associated with increased risk of atopy and wheezing, in this study only among females. Further studies on NVAS and atopy are warranted.

Comment

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There were several large trials of neonatal vitamin A supplementation reported on in 2014-15, finding minimal or no effect on mortality, so is not recommended by WHO.

[Am J Clin Nutr.](#) 2015 Aug;102(2):497-504. doi: 10.3945/ajcn.115.112383. Epub 2015 Jul 15.

High provitamin A carotenoid serum concentrations, elevated retinyl esters, and saturated retinol-binding protein in Zambian preschool children are consistent with the presence of high liver vitamin A stores.

[Mondloch S](#), [Gannon BM](#), [Davis CR](#), [Chileshe J](#), [Kaliwile C](#), [Masi C](#), [Rios-Avila L](#), [Gregory JF 3rd](#), [Tanumihardjo SA](#).

Abstract

BACKGROUND:

Biomarkers of micronutrient status are needed to best define deficiencies and excesses of essential nutrients.

OBJECTIVE:

We evaluated several supporting biomarkers of vitamin A status in Zambian children to determine whether any of the biomarkers were consistent with high liver retinol stores determined by using retinol isotope dilution (RID).

DESIGN:

A randomized, placebo-controlled, biofortified maize efficacy trial was conducted in 140 rural Zambian children from 4 villages. A series of biomarkers were investigated to better define the vitamin A status of these children. In addition to the assessment of total-body retinol stores (TBSs) by using RID, tests included analyses of serum carotenoids, retinyl esters, and pyridoxal-5'-phosphate (PLP) by using high-pressure liquid chromatography, retinol-binding protein by using ELISA, and alanine aminotransferase (ALT) activity by using a colorimetric assay.

RESULTS:

Children (n = 133) were analyzed quantitatively for TBSs by using RID. TBSs, retinyl esters, some carotenoids, and PLP differed by village site. Serum carotenoids were elevated above most nonintervened reference values for children. α -Carotene, β -carotene, and lutein values were >95th percentile from children in the US NHANES III, and 13% of children had hypercarotenemia (defined as total carotenoid concentration >3.7 $\mu\text{mol/L}$). Although only 2% of children had serum retinyl esters >10% of total retinol plus retinyl esters, 16% of children had >5% as esters, which was consistent with high liver retinol stores. Ratios of serum retinol to retinol-binding protein did not deviate from 1.0, which indicated full saturation. ALT activity was low, which was likely due to underlying vitamin B-6 deficiency, which was confirmed by very low serum PLP concentrations.

CONCLUSIONS:

The finding of hypervitaminosis A in Zambian children was supported by high circulating concentrations of carotenoids and mildly elevated serum retinyl esters. ALT-activity assays may be compromised with co-existing vitamin B-6 deficiency. Nutrition education to improve intakes of whole grains and animal-source foods may enhance vitamin B-6 status in Zambians.

Vitamin D

[Trials.](#) 2015 Jul 14;16:300. doi: 10.1186/s13063-015-0825-8.

Maternal vitamin D supplementation during pregnancy and lactation to promote infant growth in Dhaka, Bangladesh (MDIG trial): study protocol for a randomized controlled trial.

Roth DE, Gernand AD, Morris SK, Pezzack B, Islam MM, Dimitris MC, Shanta SS, Zlotkin SH, Willan AR, Ahmed T, Shah PS, Murphy KE, Weksberg R, Choufani S, Shah R, Al Mahmud A.

Abstract

BACKGROUND:

Vitamin D regulates bone mineral metabolism and skeletal development. Some observational studies have suggested that prenatal vitamin D deficiency increases the risk of adverse pregnancy and/or birth outcomes; however, there is scant evidence from controlled trials, leading the World Health Organization to advise against routine vitamin D supplementation in pregnancy. Importantly, little is known about the effect of maternal vitamin D status on infant linear growth in communities in South Asia where stunting is highly prevalent and maternal-infant vitamin D status is commonly suboptimal.

METHODS/DESIGN:

The Maternal Vitamin D for Infant Growth study is a randomized, placebo-controlled, dose-ranging trial of maternal vitamin D supplementation during pregnancy and lactation in Dhaka, Bangladesh. The primary aims are to estimate (1) the effect of maternal prenatal oral vitamin D3 supplementation (4200 IU/wk, 16,800 IU/wk, or 28,000 IU/wk, administered as weekly doses) versus placebo on infant length at 1 year of age and (2) the effect of maternal postpartum oral vitamin D3 supplementation (28,000 IU/wk) versus placebo on length at 1 year of age among infants born to women who received vitamin D 28,000 IU/wk during pregnancy. Generally healthy pregnant women (n = 1300) in the second trimester (17-24 weeks of gestation) are randomized to one of five parallel arms: placebo 4200 IU/wk, 16,800 IU/wk, or 28,000 IU/wk in the prenatal period and placebo in the postpartum period or 28,000 IU/wk in the prenatal period and 28,000 IU/wk in the postpartum period. Household- and clinic-based follow-up of mother-infant pairs is conducted weekly by trained personnel until 26 weeks postpartum and every 3 months thereafter. The primary trial outcome measure is length for age z-score at 1 year of age. Anthropometric measurements, clinical information, and biological specimens collected at scheduled intervals will enable the assessment of a range of maternal, perinatal, and infant outcomes.

DISCUSSION:

The role of vitamin D in maternal and infant health remains unresolved. This trial is expected to contribute unique insights into the effects of improving maternal-infant vitamin D status in a low-income setting where stunting and adverse perinatal outcomes represent significant public health burdens.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC26169781/>

Zinc

(see also: Acute respiratory infection, Diarrhoea, Nutrition – micronutrients, Vitamin A, Cholera vaccine)

[J Nutr.](#) 2015 Sep;145(9):2153-60. doi: 10.3945/jn.115.212308. Epub 2015 Jul 22.

Daily Zinc but Not Multivitamin Supplementation Reduces Diarrhea and Upper Respiratory Infections in Tanzanian Infants: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial.

[McDonald CM](#), [Manji KP](#), [Kisenge R](#), [Aboud S](#), [Spiegelman D](#), [Fawzi WW](#), [Duggan CP](#).

Abstract

BACKGROUND:

Although various micronutrient regimens have been shown to prevent and treat common infectious diseases in children, the effects of daily multivitamin (MV) and/or zinc supplementation have not been widely evaluated in young African infants.

OBJECTIVE:

The objective was to determine whether daily supplementation of HIV-unexposed Tanzanian infants with MVs or zinc reduces the risk of infectious morbidity compared with placebo.

METHODS:

In a 2 × 2 factorial, double-blind, randomized controlled trial, 2400 infants who were 6 wk of age and born to HIV-negative mothers in a low-malaria setting were randomly assigned to receive daily oral supplementation of MVs (vitamin B complex and vitamins C and E), zinc, zinc + MVs, or placebo for 18 mo. Morbidity was assessed by study nurses at monthly visits and by physicians every 3 mo and/or when the child was acutely ill.

RESULTS:

No significant differences were found in the percentage of nurse visits during which diarrhea, cough, or any other symptom were reported throughout the previous month when receiving either zinc or MVs. However, physician diagnoses of all types of diarrhea (RR = 0.88; 95% CI: 0.81, 0.96; P = 0.003), dysentery (RR = 0.84; 95% CI: 0.74, 0.95; P = 0.006), and acute upper respiratory infection (RR = 0.92; 95% CI: 0.88, 0.97; P = 0.0005) were significantly lower for infants supplemented with zinc than for those who did not receive zinc. Among the 2360 infants for whom vital status was obtained, there was a nonsignificant increase in all-cause mortality among infants who received zinc (HR = 1.80; 95% CI: 0.98, 3.31; P = 0.06) compared with those who did not receive zinc. MVs did not alter the rates of any recorded physician diagnoses or mortality. Neither zinc nor MVs reduced hospitalizations or unscheduled outpatient visits.

CONCLUSIONS:

Daily zinc supplementation of Tanzanian infants beginning at the age of 6 wk may lower the burden of diarrhea and acute upper respiratory infections, but provision of MVs using the regimen in this trial did not confer additional benefit.

[J Nutr](#). 2016 Jan;146(1):114-23. doi: 10.3945/jn.115.216606. Epub 2015 Nov 25.

Rural Beninese Children Are at Risk of Zinc Deficiency According to Stunting Prevalence and Plasma Zinc Concentration but Not Dietary Zinc Intakes.

[Galetti V](#), [Mitchikpè CE](#), [Kujinga P](#), [Tossou F](#), [Hounhouigan DJ](#), [Zimmermann MB](#), [Moretti D](#).

Abstract

BACKGROUND:

Three commonly recommended indicators for risk assessment of population zinc deficiency are stunting rates among children aged <5 y, prevalence of inadequate dietary zinc intake, and prevalence of low plasma zinc (PZn). Data on zinc status in Benin are mainly drawn from stunting rates and data on PZn and dietary zinc intake are lacking.

OBJECTIVES:

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The aims of this study were 1) to assess the risk of zinc deficiency in preschool and school-age children from rural communities in northern Benin by means of the 3 indicators for population assessment, 2) to evaluate their level of agreement, and 3) to identify predictors of PZn and height-for-age z scores (HAZ).

METHODS:

We analyzed preintervention data collected during 2 efficacy trials and cross-sectionally assessed the risk of zinc deficiency in preschool (1-5 y, n = 326) and school-age children (5-10 y, n = 272) by 1) conducting a 3-d weighed food record survey, coupled with direct zinc and phytic acid analysis of consumed foodstuffs, and calculating usual dietary zinc intakes in a subsample of school-age children (n = 36); 2) analyzing PZn in all children (n = 598); and 3) measuring anthropometry indexes for assessment of stunting (HAZ <-2 SD) in all children (n = 594) and in <5-y-old children only (n = 273). We derived predictors of PZn and HAZ by using multivariate regression with mixed-effect models.

RESULTS:

Prevalence of inadequate intakes of zinc ranged from 11% to 80% depending on whether the estimated average requirements (EARs) by the International Zinc Nutrition Consultative Group or the EARs derived from the WHO's recommended nutrient intakes were used. Prevalence of low PZn adjusted for acute-phase protein status was 45.7%, with higher rates among preschoolers than school-age children (P = 0.002). The stunting rate in <5-y-old children was 51.3%. PZn was predicted by age, methodologic factors, and socioeconomic status, whereas HAZ was predicted by age, sex, hemoglobin, and socioeconomic status.

CONCLUSIONS:

The prevalence of <5-y stunting and the prevalence of low PZn indicate that the risk of zinc deficiency is elevated in this population. Risk estimates based on the prevalence of inadequacy of zinc intakes varied depending on the EARs used, and a consensus would facilitate nutrition survey evaluations.

[Am J Clin Nutr.](#) 2015 Nov;102(5):1238-48. doi: 10.3945/ajcn.115.117028. Epub 2015 Oct 14.

Efficacy of highly bioavailable zinc from fortified water: a randomized controlled trial in rural Beninese children.

[Galetti V](#), [Kujinga P](#), [Mitchikpè CE](#), [Zeder C](#), [Tay F](#), [Tossou F](#), [Hounhouigan JD](#), [Zimmermann MB](#), [Moretti D](#).

Abstract

BACKGROUND:

Zinc deficiency and contaminated water are major contributors to diarrhea in developing countries. Food fortification with zinc has not shown clear benefits, possibly because of low zinc absorption from inhibitory food matrices. **We used a novel point-of-use water ultrafiltration device configured with glass zinc plates to produce zinc-fortified, potable water.**

OBJECTIVE:

The objective was to determine zinc bioavailability from filtered water and the efficacy of zinc-fortified water in improving zinc status.

DESIGN:

In a crossover balanced study, we measured fractional zinc absorption (FAZ) from the zinc-fortified water in 18 healthy Swiss adults using zinc stable isotopes and compared it with zinc-fortified maize porridge. **We conducted a 20-wk double-blind randomized controlled trial (RCT) in 277 Beninese school children from rural settings who were randomly assigned to receive a daily portion of zinc-fortified filtered water delivering 2.8 mg Zn**

(Zn+filter), nonfortified filtered water (Filter), or nonfortified nonfiltered water (Pump) from the local improved supply, acting as the control group. The main outcome was plasma zinc concentration (PZn), and the 3 groups were compared by using mixed-effects models. Secondary outcomes were prevalence of zinc deficiency, diarrhea prevalence, and growth.

RESULTS:

Geometric mean (-SD, +SD) FAZ was 7-fold higher from fortified water (65.9%; 42.2, 102.4) than from fortified maize (9.1%; 6.0, 13.7; P < 0.001). In the RCT, a significant time-by-treatment effect on PZn (P = 0.026) and on zinc deficiency (P = 0.032) was found; PZn in the Zn+filter group was significantly higher than in the Filter (P = 0.006) and Pump (P = 0.025) groups. We detected no effect on diarrhea or growth, but our study did not have the duration and power to detect such effects.

CONCLUSIONS:

Consumption of filtered water fortified with a low dose of highly bioavailable zinc is an effective intervention in children from rural African settings. Large community-based trials are needed to assess the effectiveness of zinc-fortified filtered water on diarrhea and growth

[Acta Paediatr.](#) 2015 Aug;104(8):e367-71. doi: 10.1111/apa.12645. Epub 2014 Apr 29.

[Oral zinc supplements are ineffective for treating acute dehydrating diarrhoea in 5-12-year-olds.](#)

[Negi R](#), [Dewan P](#), [Shah D](#), [Das S](#), [Bhatnagar S](#), [Gupta P](#).

Abstract

AIM:

Many countries have guidelines recommending the use of oral zinc in acute dehydrating diarrhoea in children aged 2 months to 5 years of age, but no guidelines exist for older children. This study tested how effective existing recommendations are in children from 5 to 12 years of age.

METHODS:

Children hospitalised with acute dehydrating diarrhoea (n = 134) were randomised to receive 40 mg of oral zinc sulphate tablets or a placebo for 14 days. The primary outcome variable was the time taken for diarrhoea to stop. Secondary outcome variables included time taken for rehydration, duration of hospitalisation and recurrence of diarrhoea in the next 3 months.

RESULTS:

The median time for resolution of diarrhoea was 60 h in both groups. The zinc group was marginally better, but not statistically significant, for resolution (hazard ratio = 0.89, 95% CI 0.63-1.24), rehydration (hazard ratio = 0.93, 95% CI 0.66-1.32) and hospitalisation (hazard ratio = 0.94, 95% CI 0.67-1.34). The risk ratio of recurrence for zinc versus placebo (95% CI) was 0.65 [0.37-1.23] [p = 0.11].

CONCLUSION:

Daily zinc supplements (40 mg for 14 days) in children aged 5-12 years with acute dehydrating diarrhoea did not shorten the duration of diarrhoea or reduce subsequent episodes. Further adequately sized, community-based trials are needed.