RANDOMISED TRIALS IN CHILD HEALTH IN DEVELOPING COUNTRIES

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Please send suggestions about this booklet to:

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SEARCH STRATEGY

Pubmed Advanced strategy, search: ((Developing countries; Developing country; Countries, developing; Developed countries; Country, developing; Countries, developed; Developed country; Country, developed; Nations, developing; Developing nations OR India OR Africa OR Asia OR South America OR Papua New Guinea OR Asia-Pacific) and (Child*)) AND (randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract])) publication date between July 1st 2012 and June 30th 2013.

Introduction

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

The method of searching for studies to include uses PubMed, a search engine that is freely available and widely used in most countries throughout the world. The search strategy has been chosen to try to capture as many relevant studies as possible, although it is possible that some are missed. If you know of a relevant RCT 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 appropriately 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 211 studies were identified. These came from all regions of the world, mostly from developing country researchers. Several trials from 2012-13 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. More importantly, through HINARI (http://www.who.int/hinari/en/) a program set up by WHO in collaboration with major publishers, the full-text versions of over 11,000 journal titles and 18,0000 e-books are now 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. Previous editions (2002-2011) are available at: www.ichrc.org

Three trials reported significant reductions in mortality (marked with *** in the booklet), **among these:**

- In a 5-year study recording the outcomes of over 26,000 births in Malawi, the introduction of community volunteer peer counselor education and women's groups lead to reductions in neonatal and maternal mortality rates, after adjustment for confounding.

- In a meta-analysis of chlorhexidine for umbilical cord care in community care settings, 3 trials reported data on all-cause mortality that comprised 1325 deaths in 54,624 participants. The combined results showed a reduction in neonatal mortality of 23% with chlorhexidine use in community settings.

- In Pakistan, in the community treatment of neonates with suspected serious bacterial infections, the use of once-daily intramuscular procaine penicillin & gentamicin significantly reduced deaths compared to use of oral cotrimoxazole and daily IM gentamicin.

- See **DEVTA trial** (below)

Other important results in 2012-13

- A meta-analysis of trials of rotavirus vaccines showed that among infants in countries with high-mortality rates, RV1 (Rotarix) probably prevents 63% of severe rotavirus diarrhoea cases (RR 0.37, 95% CI 0.18 to 0.75; 5414 participants), and, based on one trial in Malawi and South Africa, 34% of severe all-cause diarrhoea cases (RR 0.66, 95% CI 0.44 to 0.98; 4939 participants). Vaccine efficacy was marginally lower in infants in high mortality rates for RV5 (Rotateq), and lower in older children (about 57% and 42% respectively). There was no measurable effect on mortality in 181,000 participants in 34 trials, however the studies were not powered to detect this.

- A meta-analysis of trials of zinc for the treatment of diarrhoea found perhaps more modest results than might be anticipated. In children aged greater than six months with acute diarrhoea, zinc supplementation may shorten the duration of diarrhoea by around 10 hours, and probably reduces the number of children whose diarrhoea persists until day seven. In children with signs of moderate malnutrition the effect is greater, reducing the duration of diarrhoea by around 27 hours.

- In Thailand, zinc supplementation was achieved in school children by fortifying rice, a possible mechanism for population supplementation.

- Among Mongolian children with vitamin D deficiency, vitamin D supplementation significantly reduced the risk of ARIs in winter. Compared with controls, children receiving vitamin D reported significantly fewer ARIs during the study period (mean: 0.80 vs. 0.45; P = .047), with a rate ratio of 0.52 (95% confidence interval: 0.31-0.89).

- Pregnant women in urban Zanzibar were more likely to have delivery by a skilled birth attendant (60% vs. 47%) when they were provided with SMS appointment reminders, health education text messages and vouchers to call their primary care practitioner or referral hospital in obstetric emergencies. There was no improvement in SBA access for rural women who received the same intervention.

- In rural China, mental development of 2-year old children born to mothers with iron deficiency was preserved by iron supplementation in pregnancy, even if the mother's iron deficiency was not fully corrected.

- A meta-analysis of trials for the treatment of giardiasis based on studies in India, Mexico, Peru, Iran, Cuba, and Turkey, compared albendazole (400 mg once daily for five to 10 days) with metronidazole (250 mg to 500 mg three times daily for five to 10 days), showing that cure rates were similar, and there were less side effects with a simpler regimen of albendazole.

- South African infants with HIV who were started on early ART (age less than 3 months) had significantly better locomotor and general development at 11 months compared to infants on deferred ART.

- In Ghana, household use of plastic bioSand filters reduced diarrheal disease rates by 60%, lead to 97% reduction in E. coli, and major improvement in water turbidity, and in Zambia water filters improved water quality and reduced rates of diarrhoea among families living with HIV.

- Among school children in India, a multi micronutrient-fortified drink taken daily reduced the prevalence of iron deficiency, iron deficiency anaemia, vitamin C and vitamin B (12) deficiency and improved micronutrient status.

- Obese South African children with iron deficiency have reduced absorption of iron.

- Vitamin D3 may help to preserve insulin secretion in children with new-onset diabetes, based on a trial in Brazil.

- School attendance was an outcome of several RCTs in 2013: in Zimbabwe, conditional and unconditional cash transfers to the poorest families increased school attendance, in Mali praziquantel and iron treatment improved children's school attendance among those suffering from Schistosomiasis, and among adolescent school girls in Ghana providing sanitary pads with education significantly improved school attendance.

- In villages in rural China, information on home-prepared recipes, food preparation and hygiene through group training of families, counselling and home visit, delivered through local health services improved weight and linear growth at 18 months of age.

- In separate trials in Mozambique and Uganda introduction of orange sweet potato to rural communities was an effective way to improve vitamin A intake in mothers and children.

- Among Indian children with acute seizures lasting more than 10 minutes, intranasal midazolam was as effective in stopping seizures as IV diazepam; midazolam could be given more rapidly than diazepam, although once given the onset of effect was slower.

- In Uganda the first phase-I infant trial of an HIV vaccine (ALVAC-HIV vCP1521) was carried out. Watch this space!

- Two studies from India and one from Ethiopia showed that locally produced ready-to-use therapeutic feeds improved weight gain in severely malnourished children compared to F100 milk feeds or standard supplemental feeding. In Malawi children with moderate malnutrition had more sustained weight gain with soy-whey RUTF than with corn-soy blend plus milk and oil, but nearly one-third of children with moderate malnutrition relapsed with moderate or severe malnutrition and 4% died during the 12 month follow-up.

- Giving multiple micronutrient supplements to pregnant women in Indonesia who were undernourished or anemic improved the motor and cognitive abilities of their children up to 3.5 years later.

- A single dose of Vitamin D in the second trimester of pregnancy (or one in the second and another in the third) to women in India increased birth weight, length and head circumference, and these gains remained at 9 months of age.

- Two trials of the tetravalent Dengue vaccine (CYD-TDV) in Peru and Singapore showed encouraging seroconversion rates, a 10-20-fold increase in serum neutralizing antibodies to the 4 Dengue serotypes in 66-94% of children 2-11 years of age.

- In underweight Filipino children, extraction of severely decayed primary teeth resulted in increased weight gain. Ouch!

There were some important negative trials:

- In the DEVTA trial, the largest RCT ever undertaken, involving 2 million pre-school children in India the mortality reduction from vitamin A was only 4% with confidence internals from an 11% reduction to a 3% increase. However the authors combined this mega-trial with a meta-analysis of all other vitamin A trials, concluding that vitamin A leads to a mortality reduction of 11%. The DEVTA trial is very important, suggesting that there may have been over-estimates of child mortality reductions from single interventions such as vitamin A. However looking back on earlier balanced estimates rom the Lancet Child Survival Series of 2003 a similar estimate (2% overall mortality reduction from vitamin A) was found.

- In a large multi-country trial of macronutrient complimentary feeding, giving either meat or micronutrient fortified cereal from 6 months of age did not lead to differences in linear growth. About one-third of infants at 6 months were stunted, and this increased to nearly half at 18 months of age. Maternal education and the length for age at 6 months were the strongest determinant of linear growth, emphasising the pre- and post-natal growth.

- In Gambia, calcium supplementation of boys in late childhood advanced the age of peak height velocity but resulted in 3.5 cm shorter adult stature. Where low calcium intakes and delayed puberty is common, calcium supplements may lead to early cessation of bone growth.

- Pros and cons of lopinavir/ritonavir-based ART. South African children with HIV who had perinatal exposure to nevirapine as part of HIV transmission prevention, and later viral suppression with ritonavir-boosted lopinavir, were more likely to have virological failure over 6 months if switched to a nevirapine-based ART, despite early improvements in CD4 count and growth. In another study, HIV-infected South African children receiving lopinavir/ritonavir-based regimens had less favourable changes in lipid profile and triglycerides, compared with those switched to nevirapine-based regimens. In Ugandan children treated with lopinavir/ritonavir-based ART, recurrences of malaria were less common than for those on non-nucleoside reverse transcriptase inhibitors, after treatment for malaria with artemether-lumefantrine.

- Among Pakistani children, the Typhoid Vi capsular polysaccharide vaccine was ineffective in protecting children less than 2 years of age from typhoid, but provided some protection in school aged children, although antibody levels may decline 2 years following vaccination

It is important to understand the context in which benefit (or harm) occurs in a trial. This context may 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 reported incompletely), and is one reason why there is a need for more large-scale implementation trials – not necessarily randomised - that provide insight into local context.

In the last 11 years there have been 1553 trials summarised in the various editions of this booklet. The public health benefits that have come from the huge number of 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. While malaria rates are falling, the same reductions 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.

This year there are an increasing number of publications of RCT protocols, indeed whole journals which publish only trial protocols, published prior to a study getting underway. This and the increasing number of on-line journals is one reason for the marked increase in annual publications in the last 11 years. 2013 is the first year when there was not an overall increase in the number of studies.

In 2012-13, for the first time in a decade there were more studies of mental health issues: among adolescents with HIV, war-affected youths in Uganda and Gaza, and orphans in Kenya, and more studies addressing maternal depression.

In 2012-13 also the impact of economic transition, Western morbidities and high-technology research was more evident, with clinical trials this year from India and China on issues related to non-communicable diseases, including obesity, diabetes, congenital heart disease, allergy, and modifying risk factors in childhood for adult cardiovascular disease.

More support is needed for developing public health research capacity in the poorest countries. The flourishing research output from China, India and other transitional countries is a welcome trend, but may mean that the health issues in the poorest nations with the highest child mortality burdens are over-shadowed, despite the overall increase in the number of trials. Ongoing eforts to reduce inequity in child health are especially important beyond 2015, and this will be served by appropriate research.

Trevor Duke
July 2013

Acknowledgement
Thanks to Eleanor Neal, for invaluable editorial assistance, and to AusAID for support to this work as part of the Knowledge Hubs for Health Initiative.

Acute respiratory infection

(See also Zinc, Pneumococcal vaccine, Hygiene and environmental health)

Treatment of severe pneumonia

Efficacy of zinc given as an adjunct in the treatment of severe and very severe pneumonia in hospitalized children 2-24 mo of age: a randomized, double-blind, placebo-controlled trial.

Wadhwa N, Chandran A, Aneja S, Lodha R, Kabra SK, Chaturvedi MK, Sodhi J, Fitzwater SP, Chandra J, Rath B, Kainth US, Saini S, Black RE, Santosham M, Bhatnagar S.

Am J Clin Nutr. 2013 Jun; 97(6): 1387-94. doi: 10.3945/ajcn.112.052951. Epub 2013 May 1

Source
Centre for Diarrheal Diseases and Nutrition Research, Department of Pediatrics and the Center for American Indian Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

Abstract
BACKGROUND:
Pneumonia is a leading cause of death; in India, an estimated 370,000 children die of pneumonia each year. Zinc has multiple influences on the immune response to infections. Zinc supplementation has been shown to prevent diarrhea and pneumonia in children. However, zinc's therapeutic effect on respiratory infections is less clear.

OBJECTIVE:
We evaluated the role of zinc as an adjunct to antibiotics in the treatment of children hospitalized for severe or very severe pneumonia.

DESIGN:
In this randomized, double blind, placebo-controlled trial, we enrolled 550 children aged 2-24 mo with severe or very severe pneumonia. Within each hospital and pneumonia-severity stratum, children were randomly assigned to receive zinc (20 mg elemental zinc/d) or a placebo in addition to antibiotics and supportive care.

RESULTS:
The time to recovery from severe or very severe pneumonia was similar in both groups (HR: 0.98; 95% CI: 0.82, 1.17). In the stratified analysis, zinc was shown to be efficacious in reducing the time to recovery in children with very severe pneumonia (HR: 1.52; 95% CI: 1.03, 2.23); however, the effect was no longer statistically significant after adjustment for differences in severely underweight children in the 2 groups.

CONCLUSIONS:
This study showed no overall benefit of the addition of zinc to antibiotics in reducing the time to recovery from pneumonia but showed a possible benefit of zinc supplementation in a subgroup of children with very severe pneumonia. Additional research is needed in specific subgroups

such as children with very severe pneumonia. This trial was registered at http://www.controlled-trials.com as ISRCTN48954234

Role of zinc in severe pneumonia: a randomized double bind placebo controlled study.

Shah GS, Dutta AK, Shah D, Mishra OP.

Ital J Pediatr. 2012 Aug 2;38:36. doi: 10.1186/1824-7288-38-36.

Source
Department of Pediatrics, BP Koirala Institute of Health Sciences, Dharan, Nepal. gaurishankarshah@live.com

Abstract
BACKGROUND:
Pneumonia is a leading cause of morbidity and mortality in children.

OBJECTIVE:
The aim of study was to evaluate the efficacy of Zinc supplementation in treatment of severe pneumonia in hospitalized children.

DESIGN/METHODS:
A double blind randomized, placebo- controlled clinical trial conducted at a tertiary care centre of a teaching hospital. Children with diagnosis of severe pneumonia were randomly assigned to receive supplementation with either elemental zinc or placebo by mouth at the time of enrolment. From day 2, they received 10 mg of their assigned treatment by mouth twice a day for 7 days along with standard antimicrobial therapy.

RESULTS:
The baseline characteristics like age, sex, weight, weight Z score, height, height Z score, weight for height Z score and hemoglobin were comparable in both study groups. The respiratory rate, chest indrawing, cyanosis, stridor, nasal flaring, wheeze and fever in both groups recorded at enrolment and parameters did not differ significantly between the two groups. The outcome measures like time taken for resolution of severe pneumonia, pneumonia, duration of hospital stay, nil per oral, intravenous fluid, oxygen use, treatment requiring 2nd line of drug and 3rd line drug were evaluated and found to be same.

CONCLUSION:
The present study did not show a statistically significant reduction in duration of severe pneumonia, or reduction in hospital stay for children given daily zinc supplementation along with standard antimicrobial therapy. Therefore, zinc supplementation given during the acute episode does not help in short term clinical recovery from severe pneumonia.

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Vitamin D and pneumonia

Randomized trial of vitamin D supplementation and risk of acute respiratory infection in Mongolia.

Camargo CA Jr, Ganmaa D, Frazier AL, Kirchberg FF, Stuart JJ, Kleinman K, Sumberzul N, Rich-Edwards JW.

Pediatrics. 2012 Sep;130(3):e561-7. doi: 10.1542/peds.2011-3029. Epub 2012 Aug 20.

Source
Massachusetts General Hospital, Boston, Massachusetts 02114, USA. ccamargo@partners.org

Abstract
OBJECTIVE:
Observational studies suggest that serum levels of 25-hydroxy-vitamin D (25[OH]D) are inversely associated with acute respiratory infections (ARIs). We hypothesized that vitamin D supplementation of children with vitamin D deficiency would lower the risk of ARIs.

METHODS:
By using cluster randomization, classrooms of 744 Mongolian schoolchildren were randomly assigned to different treatments in winter (January-March). This analysis focused on a subset of 247 children who were assigned to daily ingestion of unfortified regular milk (control; n = 104) or milk fortified with 300 IU of vitamin D(3) (n = 143). This comparison was double-blinded. The primary outcome was the number of parent-reported ARIs over the past 3 months.

RESULTS:
At baseline, the median serum 25(OH)D level was 7 ng/mL (interquartile range: 5-10 ng/mL). At the end of the trial, follow-up was 99% (n = 244), and the median 25(OH)D levels of children in the control versus vitamin D groups was significantly different (7 vs. 19 ng/mL; P < .001). **Compared with controls, children receiving vitamin D reported significantly fewer ARIs during the study period (mean: 0.80 vs. 0.45; P = .047), with a rate ratio of 0.52 (95% confidence interval: 0.31-0.89).** Adjusting for age, gender, and history of wheezing, vitamin D continued to halve the risk of ARI (rate ratio: 0.50 [95% confidence interval: 0.28-0.88]). Similar results were found among children either below or above the median 25(OH)D level at baseline (rate ratio: 0.41 vs. 0.57; P(interaction) = .27).

CONCLUSIONS:
Vitamin D supplementation significantly reduced the risk of ARIs in winter among Mongolian children with vitamin D deficiency.

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Bronchiolitis

Hypertonic (3%) Saline for Acute Viral Bronchiolitis: A Randomized Trial.

Sharma BS, Gupta MK, Rafik SP.

Indian Pediatr. 2012 Dec 5. pii: S097475591200360. [Epub ahead of print]

Source
Department of Pediatrics, SPMCHI, SMS Medical College, Jaipur, Rajasthan. Correspondence to: Dr Bhagwan Sahai Sharma, B-2, New Hira Bagh Flats, Near Nurse's Hostel, SMS Hospital Campus, Jaipur, Rajasthan 302 004, India. drbssharma@gmail.com.

Abstract
OBJECTIVE:
To compare the length of hospital stay (primary) and improvement in clinical severity scores (secondary) among children with bronchiolitis nebulized with 3% hypertonic saline or 0.9% saline.

DESIGN:
Randomized double blind controlled trial. Setting: Tertiary care teaching hospital PATIENTS: Hospitalized children (1-24 months) with acute bronchiolitis of moderate severity. Intervention: Nebulization of 4 ml of 3 % hypertonic saline or 4 ml of 0.9% saline along with 2.5 mg salbutamol at 4 hourly intervals till the patient was ready for discharge.

RESULTS:
Baseline characteristics were similar in two groups. [Mean age, months, 4.93±4.31 hypertonic saline group, 4.18±4.24 normal saline group, mean duration of symptoms at admission, days 3.6±2.87 hypertonic saline group, 3.8±2.34 normal saline group, and baseline O2 saturation % 94.43±2.77 hypertonic saline group and 95.23±2.45 normal saline group]. Median clinical severity score at admission was 6 (IQR-1) in both the groups. Clinical severity scores monitored afterwards 12 hourly till discharge (132 hours) did not show statistically significant differences in 3% and 0.9% saline groups. Mean length of hospital stay (time to reach predefined clinical severity score<3) was 63.93%22.43 hours in 3% saline group and 63.51±21.27hours in 0.9% saline group (P=0. 878). No adverse events were reported by the parents, caregivers or treating medical attendants in both groups.

CONCLUSION:
Nebulized 3% saline is not superior to 0.9% saline in infants with clinically diagnosed acute bronchiolitis.

Nebulized hypertonic-saline vs. epinephrine for bronchiolitis; proof of concept study of cumulative sum (CUSUM) analysis.

Gupta N, Puliyel A, Manchanda A, Puliyel J.

Indian Pediatr. 2012 Jul;49(7):543-7. Epub 2010 Oct 30.

Source
Department of Pediatrics and Neonatology, St Stephens Hospital, Delhi, India. drneeraj79@yahoo.co.in

Abstract
OBJECTIVE:
To apply cumulative sum (CUSUM) to monitor a drug trial of nebulized hypertonic-saline in bronchiolitis. To test if monitoring with CUSUM control lines is practical and useful as a prompt to stop the drug trial early, if the study drug performs significantly worse than the comparator drug.

DESIGN:
Prospective, open label, controlled trial using standard therapy (epinephrine) and study drug (hypertonic-saline) sequentially in two groups of patients.

SETTING:
Hospital offering tertiary-level pediatric care.

PATIENTS:
Children, 2 months to 2 years, with first episode of bronchiolitis, excluding those with cardiac disease, immunodeficiency and critical illness at presentation.

INTERVENTIONS:
Nebulized epinephrine in first half of the bronchiolitis season (n = 35) and hypertonic saline subsequently (n = 29). Continuous monitoring of response to hypertonic-saline using CUSUM control charts developed with epinephrine-response data. Main outcome measures: Clinical score, tachycardia and total duration of hospital stay.

RESULTS:
In the epinephrine group, the maximum CUSUM was +2.25 (SD 1.34) and minimum CUSUM was -2.26 (SD 1.34). CUSUM score with hypertonic saline group stayed above the zero line throughout the study. There was no statistical difference in the post-treatment clinical score at 24 hours between the treatment groups {Mean (SD) 3.516 (2.816): 3.552 (2.686); 95% CI: -1.416 to 1.356}, heart rate {Mean (SD) 136 (44): 137(12); 95% CI: -17.849 to 15.849) or duration of hospital stay (Mean (SD) 96.029 (111.41): 82.914 (65.940); 95% CI: -33.888 to 60.128}.

CONCLUSIONS:
The software we developed allows for drawing of control lines to monitor study drug performance. Hypertonic saline performed as well or better than nebulized epinephrine in bronchiolitis.

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Simple cough

To Compare the Effect of Dextromethorphan, Promethazine and Placebo on Nocturnal Cough in Children Aged 1-12 y with Upper Respiratory Infections: A Randomized Controlled Trial.

Bhattacharya M, Joshi N, Yadav S.

Indian J Pediatr. 2013 Apr 17. [Epub ahead of print]

Source
Department of Pediatrics, Maulana Azad Medical College & Lok Nayak Hospital, New Delhi, 110002, India, drmalvika_b@rediffmail.com.

Abstract
OBJECTIVES:
To evaluate whether promethazine and dextromethorphan reduce nocturnal cough and improve sleep quality in children aged 1-12 y with upper respiratory tract infection (URI).

METHODS:
This randomised double-blinded placebo-controlled trial was conducted in Pediatric outpatient department of Lok Nayak Hospital, Delhi. After randomization into promethazine, dextromethorphan and placebo groups, parental assessment of 120 children with URI for nocturnal cough severity (child), post-tussive vomiting (child) and sleep quality (child and parent) on the night before enrolment and after 3 d of assigned medication was measured using an internally validated indigenously prepared ordinal scale.

RESULTS:
Entire cohort improved in all the study parameters after 3 d. However, no superior benefit was noted when individual parameters were compared in the promethazine and dextromethorphan groups with the placebo group. Adverse effects were more frequent in the dextromethorphan and promethazine groups although the difference was not statistically significant.

CONCLUSIONS:
Nocturnal cough in URI is self-resolving and dextromethorphan and promethazine prescribed for the same are not superior to placebo.

Randomized controlled trial of probiotics to reduce common cold in schoolchildren.

Rerksuppaphol S, Rerksuppaphol L.

Pediatr Int. 2012 Oct;54(5):682-7. doi: 10.1111/j.1442-200X.2012.03647.x. Epub 2012 Jul 10.

Source
Department of Pediatrics, Srinakharinwirot University, NakornNayok, Thailand.
sanguansak_r@hotmail.com

Abstract
BACKGROUND:
The common cold is responsible for the largest proportion of school and work absenteeism and causes a huge economic burden. None of the current interventions is greatly effective for prevention. Our aim was to assess the efficacy of a two-strain combination probiotic for prevention of common cold symptoms in healthy schoolchildren.

METHODS:
A double-blind randomized controlled trial was performed during the winter season in a public school of central Thailand. Children, aged 8-13 years, were randomized to receive either a two-strain combination probiotic (Lactobacillus acidophilus and Bifidobacterium bifidum) or placebo given twice a day for 3 months. The primary outcome was any symptom of cold during the 3-month study period while vomiting, diarrhea, use of antibiotics, school absence due to any cause, school absence due to cold and duration of all symptoms were secondary outcomes.

RESULTS:
Of the 40 children in each group, 31 (77%) in the probiotic group, compared to 38 (95%) in the placebo group (P= 0.048), developed at least one symptom of cold. Children in the probiotics group had significantly lower risk of fever, cough, rhinorrhea, school absence, and school absence related to common cold compared to children in the placebo group. There was no impact on diarrhea and vomiting.

CONCLUSION:
A two-strain probiotic combination given twice a day for 3 months was able to reduce the symptoms of the common cold and school absenteeism in schoolchildren.

Zinc combined with vitamin A reduces upper respiratory tract infection morbidity in a randomised trial in preschool children in Indonesia.

Kartasurya MI, Ahmed F, Subagio HW, Rahfiludin MZ, Marks GC.

Br J Nutr. 2012 Dec 28;108(12):2251-60. doi: 10.1017/S0007114512000499. Epub 2012 Mar 14.

Source
Public Health Faculty, Diponegoro University, Semarang, Indonesia. m_kartasurya@yahoo.com

Abstract
Zn supplementation has shown inconsistent effects on respiratory morbidity in young children in developing countries. Few studies have focused on upper respiratory tract infection (URTI), a frequent cause of morbidity in this group, and potential benefit from Zn supplementation or factors that influence its efficacy. We investigated the effects of Zn supplementation on URTI before and after vitamin A supplementation. This randomised double-blinded controlled Zn supplementation study was conducted on 826 children aged 2-5 years. Placebo or Zn (10 mg/d) was given in syrup daily for 4 months, with 200 000 IU vitamin A (60 mg retinol) given to all children at 2 months. Health workers visited children every 3 d for compliance and morbidity

information. We found that 84 % of children experienced URTI during the study. Zn supplementation reduced the percentage of days with URTI (12 % reduction; P = 0·09), with greater impact following vitamin A supplementation (20 % reduction; P = 0·01). Vitamin A supplementation was associated with a decreased number but an increased duration of URTI episodes. We conclude that Zn combined with vitamin A supplementation significantly reduced the percentage of days with URTI in a population of preschool Indonesian children with marginal nutritional status. The results suggest that vitamin A status modifies the efficacy of Zn supplementation on URTI.

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Adolescent health

(See also Vaccines - HPV vaccine)

Sanitary pad interventions for girls' education in Ghana: a pilot study.

Montgomery P, Ryus CR, Dolan CS, Dopson S, Scott LM.

PLoS One. 2012;7(10):e48274. doi: 10.1371/journal.pone.0048274. Epub 2012 Oct 31.

Source
Centre for Evidence Based Intervention, University of Oxford, Oxford, Oxfordshire, United Kingdom. paul.montgomery@spi.ox.ac.uk

Abstract
BACKGROUND:
Increased education of girls in developing contexts is associated with a number of important positive health, social, and economic outcomes for a community. The event of menarche tends to coincide with girls' transitions from primary to secondary education and may constitute a barrier for continued school attendance and performance. Following the MRC Framework for Complex Interventions, a pilot controlled study was conducted in Ghana to assess the role of sanitary pads in girls' education.

METHODS:
A sample of 120 schoolgirls between the ages of 12 and 18 from four villages in Ghana participated in a non-randomized trial of sanitary pad provision with education. **The trial had three levels of treatment: provision of pads with puberty education; puberty education alone; or control (no pads or education). The primary outcome was school attendance.**

RESULTS:
After 3 months, providing pads with education significantly improved attendance among participants, (lambda 0.824, F=3.760, p<.001). After 5 months, puberty education alone improved attendance to a similar level (M=91.26, SD=7.82) as sites where pads were provided with puberty education (Rural M=89.74, SD=9.34; Periurban M=90.54, SD=17.37), all of which were higher than control (M=84.48, SD=12.39). The total improvement through pads with education intervention after 5 months was a 9% increase in attendance. After 3 months, providing pads with education significantly improved attendance among participants. The changes in attendance at the end of the trial, after 5 months, were found to be significant by site over time. With puberty education alone resulting in a similar attendance level.

CONCLUSION:
This pilot study demonstrated promising results of a low-cost, rapid-return intervention for girls' education in a developing context. Given the considerable development needs of poorer countries and the potential of young women there, these results suggest that a large-scale cluster randomized trial is warranted.

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Comment
School attendance was an outcome of several RCTs in 2013. As well as this trial above among adolescent school girls in Ghana showing that providing sanitary pads with education significantly improved school attendance, in Zimbabwe, conditional and unconditional cash transfers to the poorest families increased school attendance, and in Mali praziquantel and iron treatment improved children's school attendance among those suffering from Schistosomiasis.

Process and outcome evaluation of a community intervention for orphan adolescents in western Kenya.

Hallfors DD, Cho H, Mbai I, Milimo B, Itindi J.

J Community Health. 2012 Oct;37(5):1101-9. doi: 10.1007/s10900-012-9548-x.

Source
Pacific Institute for Research and Evaluation, 1516 E. Franklin St., Suite 200, Chapel Hill, NC 27154, USA. Hallfors@pire.org

Abstract
We conducted a 2-year pilot randomized controlled trial (N = 105) in a high HIV-prevalence area in rural western Kenya to test whether providing young orphan adolescents with uniforms, school fees, and community visitors improves school retention and reduces HIV risk factors. The trial was a community intervention, limited to one community. In this paper, we examined intervention implementation and its association with outcomes using longitudinal data. We used both quantitative and qualitative methods to evaluate the community-based model for orphan HIV prevention, with recommendations for future studies. Despite promising effects after 1 year, GEE analyses showed null effects after 2 years. Volunteer community visitors, a key element of the intervention, showed little of the expected effect although qualitative reports documented active assistance to prevent orphans' school absence. For future research, we recommend capturing the transition to high school, a larger sample size, and biomarker data to add strength to the research design. We also recommend a school-based intervention approach to improve implementation and reduce infrastructure costs. Finally, we recommend evaluating nurses as agents for improving school attendance and preventing dropout because of their unique ability to address critical bio-psychosocial problems.

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Moderators of treatment effectiveness for war-affected youth with depression in northern Uganda.

Betancourt TS, Newnham EA, Brennan RT, Verdeli H, Borisova I, Neugebauer R, Bass J, Bolton P.

J Adolesc Health. 2012 Dec;51(6):544-50. doi: 10.1016/j.jadohealth.2012.02.010. Epub 2012 Apr 5.

Source
Department of Global Health and Population, Harvard School of Public Health, Boston, Massachusetts 02115, USA. Theresa_Betancourt@harvard.edu

Abstract
PURPOSE:
As we build the evidence base of interventions for depression among war-affected youth, it is critical to understand factors moderating treatment outcomes. The current study investigated how gender and history of abduction by Lord's Resistance Army rebels moderated treatment outcomes for war-affected youth.

METHODS:
The study-a three-armed, randomized, controlled trial-was conducted with internally displaced war-affected adolescents in northern Uganda. Participants with significant depression symptoms (N = 304; 57% female; 14-17 years of age) were randomly assigned to an interpersonal psychotherapy group (IPT-G), a creative play/recreation group, or a wait-list control condition. Secondary analyses were conducted on data from this randomized controlled trial.

RESULTS:
A history of abduction by Lord's Resistance Army rebels was reported by 42% of the sample. Gender and abduction history interacted to moderate the effectiveness of IPT-G for the treatment of depression. In the IPT-G intervention arm, treatment effectiveness was greatest among female subjects without an abduction history, with effect size = 1.06. IPT-G was effective for the treatment of depression for both male and female subjects with a history of abduction (effect size = .92 and .50, respectively). Male subjects with no abduction history in IPT-G showed no significant improvement compared with those in the control conditions.

CONCLUSIONS:
Abduction history and gender are potentially important moderators of treatment effects, suggesting that these factors need to be considered when providing interventions for war-affected youth. IPT-G may be an effective intervention for female subjects without an abduction history, as well as for both male and female former child soldiers, but less so for male subjects without an abduction history.

A teacher-delivered intervention for adolescents exposed to ongoing and intense traumatic war-related stress: a quasi-randomized controlled study.

Berger R, Gelkopf M, Heineberg Y.

J Adolesc Health. 2012 Nov;51(5):453-61. doi: 10.1016/j.jadohealth.2012.02.011. Epub 2012 Apr 14.

Source
Department of Emergency Medicine, Ben Gurion University of Negev, Beer-Sheba, Israel.

Abstract
PURPOSE:
For the past 8 years, the residents of Sderot-a town in southern Israel-have been exposed to ongoing and intense war-related threat due to daily rocket attacks and mortar shelling from the adjacent Gaza region. This study first evaluates the prevalence of posttraumatic symptomatology in a sample of seventh- and eighth-grade students, and then assesses the efficacy of a universal teacher-delivered skill-oriented and present-focused intervention in preventing and reducing adolescents' posttraumatic stress-related symptoms.

METHOD:
In a quasi-randomized controlled trial, 154 seventh- and eighth-grade students with significant levels of war-related exposure were assigned to participate in either a manualized active 16-session intervention (Extended Enhancing Resiliency Amongst Students Experiencing Stress, ERASE-Stress) or a waiting-list control group. They were assessed using self-report measures before and after the intervention on posttraumatic stress-related symptoms, somatic complaints, functional impairment, and anxiety.

RESULTS:
At baseline, 43.5% were found to have a likely diagnosis of posttraumatic stress disorder. A month after the intervention ended, students in the active intervention showed statistically significant reduction on all outcome measures compared with those in the waiting-list control group.

CONCLUSIONS:
Extended ERASE-Stress-a universal teacher-delivered skill-oriented program not targeting traumatic memories and involving trained and supervised homeroom teachers-may help students suffering from significant war-related posttraumatic symptoms reduce their level of symptomatology and can serve as an important and effective component of a community mental health policy for communities affected by chronic trauma, such as war and terrorism.

Enhancing adolescent self-efficacy and collective efficacy through public engagement around HIV/AIDS competence: a multilevel, cluster randomized-controlled trial.

Carlson M, Brennan RT, Earls F.

Soc Sci Med. 2012 Sep;75(6):1078-87. doi: 10.1016/j.socscimed.2012.04.035. Epub 2012 May 24.

Source
Department of Psychiatry, Harvard Medical School, Children's Hospital-Boston, Boston, MA, USA.

Abstract
The potential capacity of children to confront the HIV/AIDS pandemic is rarely considered. Interventions to address the impact of the pandemic on children and adolescents commonly target only their vulnerabilities. We evaluated the Young Citizens Program, an adolescent-centered health promotion curriculum designed to increase self- and collective efficacy through public education and community mobilization across a municipality in the Kilimanjaro Region

of Tanzania. The theoretical framework for the program integrates aspects of human capability, communicative action, social ecology, and social cognition. The design consists of a cluster randomized-controlled trial (CRCT). Fifteen pairs of matched geopolitically defined neighborhoods of roughly 2000-4000 residents were randomly allocated to treatment and control arms. Within each neighborhood cluster, 24 randomly selected adolescents, ages 9-14, deliberated on topics of social ecology, citizenship, community health, and HIV/AIDS competence. Building on their acquired understanding and confidence, they dramatized the scientific basis and social context of HIV infection, testing, and treatment in their communities over a 28-week period. The curriculum comprised 5 modules: Group Formation, Understanding our Community, Health and our Community, Making Assessments and Taking Action in our Community and Inter-Acting in our Community. Adolescent participants and adult residents representative of their neighborhoods were surveyed before and after the intervention; data were analyzed using multilevel modelling. In treatment neighborhoods, adolescents increased their deliberative and communicative efficacy and adults showed higher collective efficacy for children. Following the CRCT assessments, the control group received the same curriculum. In the Kilimanjaro Region, the Young Citizens Program is becoming recognized as a structural, health promotion approach through which adolescent self-efficacy and child collective efficacy are generated in the context of civil society and local government.

Effect of prenatal counselling on compliance and outcomes of teenage pregnancy.

Mersal FA, Esmat OM, Khalil GM.

East Mediterr Health J. 2013 Jan;19(1):10-7.

Source
Department of Community Health Nursing, Faculty of Nursing, Ain-Shams University, Cairo, Egypt. khomarkh@yahoo.com

Abstract
To evaluate the effect of prenatal counselling on compliance for health promotion and pregnancy outcomes we conducted an experimental randomized control study on a sample of 86 teenage pregnant women attending the maternal and child health centre in Elkhosos village, Egypt. Data were collected pre-counselling, post-counselling and after delivery. At the post test, women in the study (counselling) group showed statistically significantly greater knowledge and compliance of health promotion ($P < 0.001$) than women in the control group. In the study group, 90.7% were full term at labour compared with 41.9% in the control group; 88.4% of the women in the study group had normal vaginal delivery compared with 76.7% of those in the control group. The health condition in 90.7% of the study group neonates was classified as good compared with only 46.5% in the control group. Only 9.3% of the study group babies had low birth weight compared with 32.6% of the control group babies ($P = 0.008$).

Association of breakfast intake with obesity, dietary and physical activity behavior among urban school-aged adolescents in Delhi, India: results of a cross-sectional study.

Randomised trials in child health in developing countries 2012-13

Arora M, Nazar GP, Gupta VK, Perry CL, Reddy KS, Stigler MH.

BMC Public Health. 2012 Oct 17;12:881. doi: 10.1186/1471-2458-12-881.

Source

Health Related Information Dissemination Amongst Youth, Safdarjung Development Area, New Delhi 110016, India. monika@hriday-shan.org

Abstract

BACKGROUND:
In developed countries, regular breakfast consumption is inversely associated with excess weight and directly associated with better dietary and improved physical activity behaviors. Our objective was to describe the frequency of breakfast consumption among school-going adolescents in Delhi and evaluate its association with overweight and obesity as well as other dietary, physical activity, and sedentary behaviors.

METHODS:
Design: Cross-sectional study. Setting: Eight schools (Private and Government) of Delhi in the year 2006. Participants: 1814 students from 8th and 10th grades; response rate was 87.2%; 55% were 8th graders, 60% were boys and 52% attended Private schools. Main outcome measures: Body mass index, self-reported breakfast consumption, diet, and physical activity related behaviors, and psychosocial factors. Data analysis: Mixed effects regression models were employed, adjusting for age, gender, grade level and school type (SES).

RESULTS:
Significantly more Government school (lower SES) students consumed breakfast daily as compared to Private school (higher SES) students (73.8% vs. 66.3%; $p<0.01$). More 8th graders consumed breakfast daily vs. 10th graders (72.3% vs. 67.0%; $p<0.05$). A dose-response relationship was observed such that overall prevalence of overweight and obesity among adolescents who consumed breakfast daily (14.6%) was significantly lower vs. those who only sometimes (15.2%) or never (22.9%) consumed breakfast ($p<0.05$ for trend). This relationship was statistically significant for boys (15.4 % vs. 16.5% vs. 26.0; $p<0.05$ for trend) but not for girls. Intake of dairy products, fruits, and vegetables was 5.5 (95% CI 2.4-12.5), 1.7 (95% CI 1.1-2.5) and 2.2 (95% CI 1.3-3.5) times higher among those who consumed breakfast daily vs. those who never consumed breakfast. Breakfast consumption was associated with greater physical activity vs. those who never consumed breakfast. Positive values and beliefs about healthy eating; body image satisfaction; and positive peer and parental influence were positively associated with daily breakfast consumption, while depression was negatively associated.

CONCLUSION:
Daily breakfast consumption is associated with less overweight and obesity and with healthier dietary- and physical activity-related behaviors among urban Indian students. Although prospective studies should confirm the present results, intervention programs to prevent or treat childhood obesity in India should consider emphasizing regular breakfast consumption.

Anaemia and iron deficiency

(See also Micronutrients and food fortification)

Effect of iron supplementation on development of iron deficiency anemia in breastfed infants.

Gokcay G, Ozden T, Karakas Z, Karabayir N, Yildiz I, Abali S, Sahip Y.

J Trop Pediatr. 2012 Dec;58(6):481-5. doi: 10.1093/tropej/fms028. Epub 2012 Jun 28.

Source
Institute of Child Health, Istanbul University, Istanbul, Turkey. gokcay@superonline.com

Abstract
This trial aimed to investigate the effect of iron supplementation on the development of iron deficiency anemia. The study encompassed 6-month-old infants who had been exclusively breastfed in the first 4 months of life. Infants in the supplemented group were given 1 mg kg(-1)day(-1) ferrous sulfate for 6 months starting at 6 months of age. Blood samples were taken at age 12 months. A 3-day-diet was evaluated at 1 year of age. Data of 51 infants in the supplemented and 54 infants in the control group were analyzed. **Mean hemoglobin values were similar in the two groups at the age of 12 months.** Mean ferritin level of the supplemented group was significantly higher than that of the control. There was a significant positive correlation between dietary iron intake and hemoglobin levels. **Nutrition might be more important than iron supplementation in preventing iron deficiency anemia during infancy**.

Use of iron-fortified rice reduces anemia in infants.

Nogueira Arcanjo FP, Santos PR, Arcanjo CP, Amancio OM, Braga JA.

J Trop Pediatr. 2012 Dec;58(6):475-80. doi: 10.1093/tropej/fms021. Epub 2012 May 29.

Source
Federal University of Ceara, Sobral Unit, Brazil. placidoarcanjo@yahoo.com.br

Abstract
Food fortification is advocated to tackle iron deficiency in anemic populations. Our objective was to evaluate the impact of iron-fortified rice (Ultrarice(®)) weekly on hemoglobin and anemia levels compared with standard rice (control). This cluster-randomized study deals with infants (10-23 months) from two public child day care centers in Brazil, n = 216, in an 18 week intervention. The intervention group received individual portions of fortified rice (50 g) provided 56.4 mg elemental/Fe. For intervention center: baseline mean hemoglobin was 11.44 ± 1.07 g/dl, and after intervention 11.67 ± 0.96 g/dl, p < 0.029; for control: baseline mean hemoglobin value was 11.35 ± 4.01 g/dl, and after intervention 11.36 ± 2.10 g/dl, p = 0.986. Anemia prevalence for intervention center was 31.25% at baseline, and 18.75% at end of study, p = 0.045; for control 43.50% were anemic at baseline, and 37.1% at the end of study, p = 0.22.

Number Needed to Treat was 7. **Iron-fortified rice was effective in increasing hemoglobin levels and reducing anemia in infants.**

Milk-based cornstarch porridge fortified with iron is effective in reducing anemia: a randomized, double-blind, placebo-controlled trial.

Arcanjo FP, Arcanjo CC, Arcanjo FC, Campos Lde A, Amancio OM, Braga JA.

J Trop Pediatr. 2012 Oct;58(5):370-4. doi: 10.1093/tropej/fms003. Epub 2012 Feb 16.

Source
Federal University of Ceara, Sobral Unit, Av. Comandante Maurocélio Rocha Ponte, 100 - Derby, 62.042-280 - Sobral - CE, Brazil. placidoarcanjo@terra.com.br

Abstract
This study evaluates the impact of a milk-based cornstarch porridge fortified with iron, in 4-year olds, compared with control on hemoglobin levels and anemia prevalence. This trial was a cluster-randomized, double-blind one, and used milk-based cornstarch porridge fortified with 10 mg elemental iron (FeSO(4)), daily, during 14 weeks, compared with control. The study population comprised 4-year-old preschoolers (n = 131). Mean hemoglobin values at baseline were found to be 10.6 ± 0.61 g dl(-1) for intervention group, and after intervention 11.5 ± 0.80 g/dl, $p < 0.0001$. For control, mean hemoglobin values at baseline were 10.9 ± 0.53 g/dl, and after intervention 11.2 ± 0.73, $p < 0.0001$. The increase in mean hemoglobin was much greater in the intervention than in the control group, 0.86-0.26 g dl(-1), respectively ($p < 0.0001$). Anemia prevalence reduced from 75% to 20%, $p < 0.0001$, in the intervention group, with no reduction in the control group. Number needed for treatment was four. **This study showed that milk-based cornstarch porridge fortified with ferrous sulfate increased hemoglobin levels and reduced anemia prevalence in 4-year-old preschoolers.**

Effects of iron and n-3 fatty acid supplementation, alone and in combination, on cognition in school children: a randomized, double-blind, placebo-controlled intervention in South Africa.

Baumgartner J, Smuts CM, Malan L, Kvalsvig J, van Stuijvenberg ME, Hurrell RF, Zimmermann MB.

Am J Clin Nutr. 2012 Dec;96(6):1327-38. doi: 10.3945/ajcn.112.041004. Epub 2012 Oct 24.

Source
Laboratory of Human Nutrition, Institute of Food, Nutrition and Health, Swiss Federal Institute of Technology Zürich, Switzerland. jeannine.baumgartner@gmail.com

Abstract
BACKGROUND:
Little is known about the combined effects of iron and n-3 (omega-3) fatty acid (FA) supplementation on cognitive performance. The provision of either DHA/EPA or iron alone in

rats with combined iron and n-3 FA deficiency has been reported to exacerbate cognitive deficits associated with deficiency.

OBJECTIVE:
We investigated the effects of iron and DHA/EPA supplementation, alone and in combination, in children with poor iron and n-3 FA status.

DESIGN:
In a 2-by-2 factorial trial, children with iron deficiency (ID) (n = 321; aged 6-11 y) were allocated to receive 1) iron (50 mg) plus DHA/EPA (420/80 mg), 2) iron plus placebo, 3) placebo plus a mixture of DHA and EPA (DHA/EPA), or 4) placebo plus placebo as oral supplements (4/wk) for 8.5 mo. Cognition was assessed at baseline and endpoint by using the Hopkins Verbal Learning Test (HVLT) and subscales of the Kaufman Assessment Battery for Children.

RESULTS:
Both iron and DHA/EPA significantly increased weight-for-age z scores. Iron increased the number of words recalled at HVLT recall 2 (intervention effect: 0.90; 95% CI: 0.18, 1.62), and in anemic children, iron increased scores in the Atlantis Delayed test (1.51; 95% CI: 0.03, 2.99) and HVLT recall 2 (2.02; 95% CI: 0.55, 3.49). DHA/EPA showed no benefit in any of the cognitive tests but decreased Atlantis test scores (-2.48; 95% CI: -3.99, -0.96) in children who were anemic at baseline and decreased Atlantis delayed scores (-0.9; 95% CI: -1.45, -0.36) in girls with ID, whereas boys tended to perform better.

CONCLUSIONS:
In children with poor iron and n-3 FA status, iron supplementation improved verbal and nonverbal learning and memory, particularly in children with anemia. In contrast, DHA/EPA supplementation had no benefits on cognition and impaired working memory in anemic children and long-term memory and retrieval in girls with ID.

Effectiveness of provider incentives for anaemia reduction in rural China: a cluster randomised trial.

Miller G, Luo R, Zhang L, Sylvia S, Shi Y, Foo P, Zhao Q, Martorell R, Medina A, Rozelle S.

BMJ. 2012 Jul 27;345:e4809. doi: 10.1136/bmj.e4809.

Source
Center for Health Policy/Center for Primary Care and Outcomes Research, Stanford Medical School, Stanford University, Stanford, CA 94305, USA. ngmiller@stanford.edu

Abstract
OBJECTIVES:
To test the impact of provider performance pay for anaemia reduction in rural China.

DESIGN:
A cluster randomised trial of information, subsidies, and incentives for school principals to reduce anaemia among their students. Enumerators and study participants were not informed of study arm assignment.

SETTING:
72 randomly selected rural primary schools across northwest China.

PARTICIPANTS:
3553 fourth and fifth grade students aged 9-11 years. All fourth and fifth grade students in sample schools participated in the study.

INTERVENTIONS:
Sample schools were randomly assigned to a control group, with no intervention, or one of three treatment arms: (a) an information arm, in which principals received information about anaemia; (b) a subsidy arm, in which principals received information and unconditional subsidies; and (c) an incentive arm, in which principals received information, subsidies, and financial incentives for reducing anaemia among students. Twenty seven schools were assigned to the control arm (1816 students at baseline, 1623 at end point), 15 were assigned to the information arm (659 students at baseline, 596 at end point), 15 to the subsidy arm (726 students at baseline, 667 at end point), and 15 to the incentive arm (743 students at baseline, 667 at end point).

MAIN OUTCOME MEASURES:
Student haemoglobin concentrations.

RESULTS:
Mean student haemoglobin concentration rose by 1.5 g/L (95% CI -1.1 to 4.1) in information schools, 0.8 g/L (-1.8 to 3.3) in subsidy schools, and 2.4 g/L (0 to 4.9) in incentive schools compared with the control group. This increase in haemoglobin corresponded to a reduction in prevalence of anaemia (Hb <115 g/L) of 24% in incentive schools. Interactions with pre-existing incentives for principals to achieve good academic performance led to substantially larger gains in the information and incentive arms: when combined with incentives for good academic performance, associated effects on student haemoglobin concentration were 9.8 g/L (4.1 to 15.5) larger in information schools and 8.6 g/L (2.1 to 15.1) larger in incentive schools.

CONCLUSIONS:
Financial incentives for health improvement were modestly effective. Understanding interactions with other motives and pre-existing incentives is critical.

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Iron status, malaria parasite loads and food policies: evidence from sub-Saharan Africa.

Bhargava A.

Econ Hum Biol. 2013 Jan;11(1):108-12. doi: 10.1016/j.ehb.2012.02.004. Epub 2012 Apr 30.

Source
University of Maryland School of Public Policy, College Park, MD 20742-1821, USA. Bhargava@umd.edu

Abstract
This brief article investigates the consequences of improving children's iron status for malaria parasite loads by analyzing data from Cote d'Ivoire, Zambia, and Tanzania; the treatment of iron

deficiencies has been argued to flare up malaria in under-nourished populations. **The data from a randomized controlled trial in Cote d'Ivoire showed statistically insignificant effects of the consumption of iron-fortified biscuits on children's malaria parasite loads.** Second, nutrient intakes data from Zambia showed insignificant correlations and associations between children's iron and folate intakes and malaria parasite loads. Third, malaria parasite loads did not change significantly for Tanzanian children receiving anthelmintic treatment; malaria loads were lower for older children and for those using bed nets. Overall, the evidence from sub-Saharan African countries suggests that small improvements in iron status achieved via suitable food policies are unlikely to have detrimental effects for children's malaria parasite loads.

A clinical study on Pandu Roga, iron deficiency anemia, with Trikatrayadi Lauha suspension in children.

Kumar A, Garai AK.

J Ayurveda Integr Med. 2012 Oct;3(4):215-22. doi: 10.4103/0975-9476.104446.

Source

Post Graduate Department of Bal Roga (Ayurvedic Paediatrics), National Institute of Ayurveda, Jaipur, Rajasthan, India.

Abstract

CONTEXT:
Nutritional iron deficiency is the most common cause of anemia in India. The nearest correlation of iron deficiency anemia (IDA) can be made with Pandu Roga in Ayurveda. As the IDA is a very common prevalent disease in the society and the side effects of oral allopathic iron preparations are very common, therefore to get a better alternative, an Ayurvedic herbomineral medicine, the Trikatrayadi Lauha, was subjected to a clinical trial in children suffering from IDA.

AIM:
Evaluation of safety and efficacy of the compound Trikatrayadi Lauha suspension in children with IDA.

SETTINGS AND DESIGN:
Randomized, double-blind placebo-controlled clinical study.

MATERIALS AND METHODS:
The study was conducted on 123 children of IDA for a period of 10 weeks. Clinical features and hematological parameters were documented before, during and after treatment.

STATISTICAL ANALYSIS USED:
Observations of the study were analyzed and findings were evaluated by using statistical methods (Student's t test)

RESULTS:
The present study shows that the trial drug Trikatrayadi Lauha suspension is effective to improve clinical features and hematological parameters significantly. The medicine is effective to increase the hemoglobin level 1.94 g/dL (8.52 -10.46 g/dL, $P < 0.001$) in 5 weeks and

3.33g/dL (8.52 -11.85g/dL, P < 0.001) in 10 weeks. No adverse effect of the trial drug was observed during the study.

CONCLUSIONS:
The results suggest that Trikatrayadi Lauha is significantly effective in the management of IDA in children.

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Comment
Trikatrayadi Lauha is a complex herbal mixture containing 12 ingredients, two of which are ferrosoferric oxide.

Iron fortification of whole wheat flour reduces iron deficiency and iron deficiency anemia and increases body iron stores in Indian school-aged children.

Muthayya S, Thankachan P, Hirve S, Amalrajan V, Thomas T, Lubree H, Agarwal D, Srinivasan K, Hurrell RF, Yajnik CS, Kurpad AV.

J Nutr. 2012 Nov;142(11):1997-2003. doi: 10.3945/jn.111.155135. Epub 2012 Sep 26.

Source
Division of Nutrition, St. John's Research Institute, St. John's National Academy of Health Sciences, Bangalore, India. sumi.muthayya@gmail.com

Abstract
Wheat is the primary staple food for nearly one-third of the world's population. NaFeEDTA is the only iron (Fe) compound suitable for fortifying high extraction flours. We tested the hypothesis that NaFeEDTA-fortified, whole wheat flour reduces Fe deficiency (ID) and improves body Fe stores (BIS) and cognitive performance in Indian children. In a randomized, double-blind, controlled, school feeding trial, **6- to 15-y-old, Fe-depleted children (n = 401) were randomly assigned to either a daily wheat-based lunch meal fortified with 6 mg of Fe as NaFeEDTA or an otherwise identical unfortified control meal.** Hemoglobin (Hb) and Fe status were measured at baseline, 3.5 mo, and 7 mo. Cognitive performance was evaluated at baseline and 7 mo in children (n = 170) at one of the study sites. **After 7 mo, the prevalence of ID and ID anemia in the treatment group significantly decreased from 62 to 21% and 18 to 9%, respectively.** There was a time x treatment interaction for Hb, serum ferritin, transferrin receptor, zinc protoporphyrin, and BIS (all P < 0.0001). Changes in BIS differed between the groups; it increased in the treatment group (0.04 ± 0.04 mmol/kg body weight) and decreased in the control group (-0.02 ± 0.04 mmol/kg body weight) (P < 0.0001). In sensory tests, NaFeEDTA-fortified flour could not be differentiated from unfortified flour. There were no significant differences in cognitive performance tests between the groups. NaFeEDTA-fortified wheat flour markedly improved BIS and reduced ID in Fe-depleted children. It may be recommended for wider use in national school feeding programs.

Efficacy of a multi micronutrient-fortified drink in improving iron and micronutrient status among schoolchildren with low iron stores in India: a randomised, double-masked placebo-controlled trial.

Thankachan P, Selvam S, Surendran D, Chellan S, Pauline M, Abrams SA, Kurpad AV.

Eur J Clin Nutr. 2013 Jan;67(1):36-41. doi: 10.1038/ejcn.2012.188. Epub 2012 Dec 12.

Source
St John's National Academy of Health Sciences, Bangalore, India. praxmail@gmail.com

Abstract
BACKGROUND/OBJECTIVES:
A multiple micronutrient-fortified drink could be an effective strategy to combating micronutrient deficiencies in school going children. To assess the efficacy of a multiple micronutrient-fortified drink in reducing iron deficiency (ID), ID anemia (IDA), anemia and improving micronutrient status among schoolchildren with low iron stores. The study employed a school-based, randomized, double-blind, placebo-controlled design.

SUBJECTS/METHODS:
Schoolchildren with low serum ferritin (SF <20 µg/l) (n=246), aged 6-12 years were randomly assigned to receive either a multi-micronutrient fortified or an unfortified identical control drink. The drinks were provided 6 days/week for 8 weeks. Anthropometric and biochemical assessments were taken at baseline and endline.

RESULTS:
Study groups at baseline were comparable, and compliance to the intervention was similar. The overall prevalence of ID, IDA and anemia was 64%, 19% and 24%, respectively. **The prevalence of ID, IDA, vitamin C and vitamin B(12) deficiencies significantly reduced by 42%, 18%, 21% and 5%, respectively, in the intervention arm (P<0.01) as compared with the control arm at the end of the study.** Similarly, the concentration of hemoglobin, SF, vitamin A, vitamin B(12), vitamin C and body iron stores were significantly higher in the intervention arm in comparison to the control arm (P<0.001). Red cell folate levels also improved significantly in the intervention arm (P=0.04), however, serum zinc status did not change in either of the study arms. Children who had received the fortified drink had significantly lower odds of being ID (0.15; 95% confidence interval (CI): 0.09-0.27), IDA (0.14; 95% CI: 0.04-0.52), vitamin B(12) deficient (0.36; 95% CI: 0.18-0.73) and vitamin C deficient (0.24; 95% CI: 0.13-0.46), after adjusting for baseline age, gender and weight. conclusions: **The multi micronutrient-fortified drink was efficacious in reducing the prevalence of ID, IDA, vitamin C and vitamin B(12) deficiency and improved micronutrient status in schoolchildren.**

Whole cowpea meal fortified with NaFeEDTA reduces iron deficiency among Ghanaian school children in a malaria endemic area.

Abizari AR, Moretti D, Zimmermann MB, Armar-Klemesu M, Brouwer ID.

J Nutr. 2012 Oct;142(10):1836-42. Epub 2012 Aug 22.

Source
Department of Community Nutrition, School of Medicine and Health Sciences, University for Development Studies, Tamale, Ghana. abizaria@yahoo.com

Abstract
Cowpeas, like other legumes, contain high amounts of native iron but are rich in phytic acid (PA) and polyphenols (PP) that inhibit iron absorption. NaFeEDTA may overcome the combined inhibitory effect of PA and PP. Our objective was to test the efficacy of NaFeEDTA-fortified cowpea meal in improving iron status of school children in a malaria endemic area. We conducted a double-blind, controlled trial with 5- to 12-y-old school children from 2 rural communities in northern Ghana (n = 241). Eligible children were randomly assigned to 2 treatment groups to receive either cowpea meal fortified with 10 mg Fe/meal as NaFeEDTA, or an identical but non-fortified cowpea meal. Meals were provided 3 d/wk for a period of ~7 mo under strict supervision. Mass deworming and malaria antigenemia screening and treatment were carried out at baseline and 3.5 mo into the trial. Consumption of cowpea flour fortified with NaFeEDTA resulted in improvement of hemoglobin ($P < 0.05$), serum ferritin ($P < 0.001$), and body iron stores ($P < 0.001$) and reduction of transferrin receptor ($P < 0.001$) compared with non-fortified flour. Fortification resulted in a 30 and 47% reduction in the prevalence of iron deficiency (ID) and iron deficiency anemia (IDA) ($P < 0.05$), respectively. The results indicate that fortification of cowpea flour with NaFeEDTA overcomes the combined inhibitory effect of PA and PP and, when used for targeted school-based fortification of cowpea flour, is effective in reducing the prevalence of ID and IDA among school children in malaria endemic rural northern Ghana.

Overweight impairs efficacy of iron supplementation in iron-deficient South African children: a randomized controlled intervention.

Baumgartner J, Smuts CM, Aeberli I, Malan L, Tjalsma H, Zimmermann MB.

Int J Obes (Lond). 2013 Jan;37(1):24-30. doi: 10.1038/ijo.2012.145. Epub 2012 Sep 4.

Source
Centre of Exellence for Nutrition (CEN), North-West University, Potchefstroom, South Africa. jeannine.baumgartner@gmail.com

Abstract
BACKGROUND:
Many countries in the nutrition transition have high rates of iron deficiency (ID) and overweight (OW). ID is more common in OW children; this may be due to adiposity-related inflammation reducing iron absorption.

OBJECTIVE:
We investigated whether weight status predicts response to oral iron supplementation in ID South African children.

DESIGN:
A placebo-controlled trial of oral iron supplementation (50 mg, 4 × weeks for 8.5 months) was done in ID 6- to 11-year-old children (n=321); 28% were OW or obese. BMI-for-age z-scores (BAZ), hepcidin (in a sub-sample), hemoglobin, serum ferritin (SF), transferrin receptor (TfR), zinc protoporphyrin (ZnPP) and C-reactive protein (CRP) were measured; body iron was calculated from the SF to TfR ratio.

RESULTS:
At baseline, BAZ correlated with CRP (r=0.201, P<0.001) and CRP correlated with hepcidin (r=0.384, P<0.001). Normal weight children supplemented with iron had significantly lower TfR concentrations at endpoint than the OW children supplemented with iron and the children receiving placebo. **Higher BAZ predicted higher TfR (β=0.232, P<0.001) and lower body iron (β=-0.090, P=0.016) at endpoint, and increased the odds ratio (OR) for remaining ID at endpoint in both the iron and placebo groups (iron: OR 2.31, 95% CI: 1.13, 4.73; placebo: OR 1.78, 95% CI: 1.09, 2.91).** In the children supplemented with iron, baseline hepcidin and BAZ were significant predictors of endpoint TfR, with a trend towards a hepcidin × BAZ interaction (P=0.058).

CONCLUSION:
South African children with high BAZ have a two-fold higher risk of remaining ID after iron supplementation. This may be due to their higher hepcidin concentrations reducing iron absorption. Thus, the current surge in OW in rapidly developing countries may undercut efforts to control anemia in vulnerable groups

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Anaesthesia and intensive care

(See also Treatment of severe malaria)

Evaluation of efficacy of probiotics in prevention of candida colonization in a PICU-a randomized controlled trial.

Kumar S, Bansal A, Chakrabarti A, Singhi S.

Crit Care Med. 2013 Feb;41(2):565-72. doi: 10.1097/CCM.0b013e31826a409c.

Source
Department of Pediatrics, Advanced Pediatric Centre, Chandigarh, India.

Abstract
OBJECTIVE:
To evaluate the efficacy of probiotics in prevention of Candida colonization in a PICU.

DESIGN:
Prospective double blinded, randomized controlled trial.

SETTING:
PICU of a tertiary care teaching hospital in north India.

SUBJECTS:
One hundred fifty children (106 boys, 44 girls), 3 months to 12 yrs old, on broad spectrum antibiotics for at least 48 hrs were randomized using computer-generated random numbers to receive probiotic mix (EUGI) (n = 75) or placebo (n = 75).

INTERVENTION:
Patients received one sachet twice a day of either probiotics or placebo for 7 days. Probiotics contained Lactobacillus acidophillus, Lactobacillus rhamnosum, Bifidobacterium longum, Bifidobacterium bifidum, Saccharomyces boulardi, Saccharomyces thermophilus, fructo-oligosaccharides; and placebo-contained lactose packed in similar-looking sachets. Rectal swabs for fungal culture were taken at day 0, 7, and 14 of enrollment. **Primary outcome measure was prevalence of rectal colonization with Candida on day 14 postenrollment; secondary outcomes were growth of Candida in urine (candiduria) and blood (candidemia).** Patients were followed until completion of 14 days study period or death of patient.

RESULTS:
Demographic and clinical variables were comparable in two groups. Prevalence of Candida colonization on day 0 was similar (15 of 75) in both the groups. On day 7, 27.9% (19 of 68) patients in the probiotic group and 42.6% (29 of 68) patients in the placebo group were colonized (relative risk 0.65; 95% confidence interval 0.41-1.05; p = 0.07), whereas, **on day 14, colonization was observed in 31.3% (21 of 67) patients in the probiotic group and 50% (34 of 68) in the placebo group (relative risk 0.63; 95% confidence interval 0.41-0.96; p = 0.02).** Thus, the relative reduction in prevalence of Candida colonization on day 7 and 14 in the probiotic group was 34.5% and 37.2%, respectively. The increase in number of colonized patients from day 0 to 7 and day 0 to 14 was significant in the placebo group (p = 0.004 and

0.001, respectively) but not in the probiotic group (p = 0.30 and 0.19, respectively; McNemar test). **Candiduria was significantly less common in the probiotic group than in the placebo group (17.3% vs. 37.3%; relative risk 0.46; 95% confidence interval 0.26-0.82; p = 0.006). However, prevalence of candidemia did not differ significantly in two groups (1.6% in the probiotic group vs. 6.35% in placebo group; relative risk 0.46; 95% confidence interval 0.08-2.74; p = 0.39**).

CONCLUSIONS:
Supplementation with probiotics could be a potential strategy to reduce gastrointestinal Candida colonization and candiduria in critically ill children receiving broad spectrum antibiotics.

Comment
There was no comparison with nystatin, an oral non-absorbable antifungal agent. Avoiding broad-spectrum antibiotics where possible in critically ill children is another way to reduce candida infections.

Oral mucosal decontamination with chlorhexidine for the prevention of ventilator-associated pneumonia in children - a randomized, controlled trial.

Sebastian MR, Lodha R, Kapil A, Kabra SK.

Pediatr Crit Care Med. 2012 Sep;13(5):e305-10. doi: 10.1097/PCC.0b013e31824ea119.

Source
From the Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India.

Abstract
OBJECTIVE:
To study the efficacy of oral mucosal decontamination with chlorhexidine gel for the prevention of ventilator-associated pneumonia in children between 3 months and 15 yrs.

DESIGN:
Double blind randomized placebo controlled trial.

SETTING:
Pediatric intensive care unit of a tertiary care hospital in North India.

PATIENTS:
Eligible participants were patients aged 3 months to 15 yrs who required orotracheal or nasotracheal intubation and mechanical ventilation. Two hundred eighty-three children admitted to the pediatric intensive care unit between November 2007 and April 2009 were screened. Eighty-six patients fulfilled the study requirements.

INTERVENTION:

Either 1% chlorhexidine or placebo gel was applied on the buccal mucosa at 8-hr intervals for the entire duration of ventilation, subject to a maximum of 21 days. Patients were followed up for the development of ventilator-associated pneumonia, diagnosed using the Centers for Disease Control and Prevention criteria.

MAIN OUTCOME MEASURES:
Incidence of ventilator-associated pneumonia, duration of hospital stay, duration of intensive care unit stay, mortality, and characteristics of organisms isolated.

RESULTS:
Fourty-one children received 1% chlorhexidine, whereas 45 received placebo application. Patients of both groups were comparable with respect to baseline characteristics. **Incidence of ventilator-associated pneumonia was 39.6/1,000 ventilator days with 1% chlorhexidine and 38.1/1,000 ventilator days with placebo (relative risk 1.03, confidence interval 0.44-2.42, p = .46).** The duration of intensive care unit stay and hospital stay was a mean of 8.4 ± 5.8 vs. 9.6 ± 11.4 days (p = .58) and 16.1 ± 10.2 days vs. 15.1 ± 14.3 days (p = .19) with chlorhexidine and placebo, respectively. The mortality rates were similar in the two groups (p = .81). All but two isolates causing ventilator-associated pneumonia were gram-negative, with Acinetobacter species being the most common (14 of 26). No side effects of the applied gel were seen in either group.

CONCLUSION:
Oral mucosal application on 1% chlorhexidine gel did not prevent the development of ventilator-associated pneumonia in children 3 months to 15 yrs age.

Comparison of caudal analgesia between ropivacaine and ropivacaine with clonidine in children: A randomized controlled trial.

Laha A, Ghosh S, Das H.

Saudi J Anaesth. 2012 Jul;6(3):197-200. doi: 10.4103/1658-354X.101199.

Source
Department of Anaesthesiology, R. G. Kar Medical College, Kolkata, West Bengal, India.

Abstract
BACKGROUND:
Addition of clonidine to ropivacaine (0.2%) can potentially enhance analgesia without producing prolonged motor blockade. The aim of the present study was to compare the post-operative pain relieving quality of ropivacaine 0.2% and clonidine mixture to that of plain ropivacaine 0.2% following caudal administration in children.

METHODS:
In a prospective, double-blinded, randomized controlled trial, 30 ASA 1 pediatric patients undergoing infraumbilical surgery were randomly allocated to receive a caudal injection of either plain ropivacaine 0.2% (1 ml/kg) (group A) or a mixture of ropivacaine 0.2% (1 ml/kg) with clonidine 2 μg/kg (group B). Objective pain score and need for supplemental analgesics were compared during the 1(st) 24 hours postoperatively. Residual post-operative sedation and motor blockade were also assessed.

RESULTS:
Significantly prolonged duration of post-operative analgesia was observed in group B (P<0.0001). Heart rate and blood pressure were not different in 2 groups. Neither motor blockade nor post-operative sedation varied significantly between the groups.

CONCLUSION:
The combination of clonidine (2 μg/kg) and ropivacaine 0.2% was associated with an improved quality of post-operative analgesia compared to plain 0.2% ropivacaine. The improved analgesic quality of the clonidine-ropivacaine mixture was achieved without causing any significant degree of post-operative sedation or prolongation of motor blockade.

Sedative effects of oral midazolam, intravenous midazolam and oral diazepam.

Tyagi P, Dixit U, Tyagi S, Jain A.

J Clin Pediatr Dent. 2012 Summer;36(4):383-8.

Source
Department of Pedodontics and Preventive Dentistry, People's Dental Academy, Bhopal, Madhya Pradesh, India. drtyagip@gmail.com

Abstract
OBJECTIVES:
To evaluate and compare the behavioral changes and effect of sedative techniques in pediatric dental patients using Oral Midazolam, Intravenous Midazolam and Oral Diazepam as sedative agents.

MATERIALS AND METHODS:
Triple blind randomized control trial with 40 patients aged between 2-10 years, exhibiting definitely negative behavior was considered Patients were randomly assigned to one of the four treatment groups. Group I received midazolam 0.5 mg/kg orally, Group II received 0.5 mg/kg diazepam orally, Group III received 0.06 mg/kg midazolam intravenously and Group IV received oral placebo. Behavioral changes (sleep, crying, movement, and overall behavior) and effect of sedative techniques on pediatric patients were assessed.

RESULTS:
All the patients in group 3 were significantly better in post administrative behavior viz. sleep, crying and movement. Over all behavior scores for group 3 patients were significantly better than other three groups ($p < 0.001$). Positive behavior of patients in group 2 and 3 did not show significant difference but positive behavior in group 3 was significantly ($p < 0.05$) more than group 2. Placebo group showed the highest negative behavior.

CONCLUSION:
Sedative effects of oral midazolam and oral diazepam were comparable, where as intravenous midazolam produced more sedation. Anxiolysis was found to be more in both the midazolam groups than the diazepam group. Most number of positive changes were observed in midazolam groups as compared to diazepam group

Asthma and chronic lung disease

Environmental intervention for house dust mite control in childhood bronchial asthma.

El-Ghitany EM, Abd El-Salam MM.

Environ Health Prev Med. 2012 Sep;17(5):377-84.

Source
Tropical Health Department, High Institute of Public Health, Alexandria University, Egypt. ingy.elghitany@gmail.com

Abstract
OBJECTIVES:
This study was carried out to determine the effectiveness of physical and chemical environmental control measures for house dust mites (HDM) in controlling bronchial asthma in children.

METHODS:
A total of 160 asthmatic children who were sensitized to HDM underwent clinical and environmental assessment. The children were randomly allocated into one of four groups according to the intervention (chemical, physical, both chemical and physical, none) and the effectiveness of the intervention was assessed at 8 and 16 weeks.

RESULTS:
The group for which physical control measures were used showed significant improvement in all outcome measures, including mean differences of forced expiratory volume after 1 s (FEV1) and peak expiratory flow rate (PEFR), which were 2.05% and 4.65 l/min, respectively, at the 8-week follow-up evaluation. The percentage of severe asthma decreased from 45 to 22%. Similar results were obtained for the group with both chemical (tannic acid) and physical interventions ($p < 0.05$ for all measures). In the group where tannic acid was used as a chemical measure, the number of children with moderate and severe asthma decreased from 15 in each category to 11 and 7, respectively. In the control group, only the mean difference of PEFR (1.62 l/min) was significant after 16 weeks. Despite these promising findings, only the FEV1 was significantly different ($p = 0.014$) when the four groups were compared.

CONCLUSIONS:
Based on these results, we conclude that simple physical control measures have the potential to contribute to the control of asthma symptoms in asthmatic children sensitized to HDM allergen.

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Comparison of effects of 3 and 7% hypertonic saline nebulization on lung function in children with cystic fibrosis: a double-blind randomized, controlled trial.

Gupta S, Ahmed F, Lodha R, Gupta YK, Kabra SK.

J Trop Pediatr. 2012 Oct;58(5):375-81. doi: 10.1093/tropej/fms004. Epub 2012 Feb 28.

Source
Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India.

Abstract
BACKGROUND:
Beneficial effects of hypertonic saline on lung function in cystic fibrosis patients are well documented. However, the effects of various concentrations of hypertonic saline are not well studied. We, therefore, compared the effects of 3 and 7% hypertonic saline administered by nebulization on lung function in children with cystic fibrosis.

METHOD:
In a double-blind randomized controlled trial, **31 children with cystic fibrosis were randomized to receive either 3% saline or 7% saline nebulization twice daily for 28 days**. Spirometry was performed and functional status was measured on Day 14 and 28.
RESULTS:
Of 31 children enrolled in the study, 30 completed the 28 days follow up (15 in each group). **Percentage change in Forced Expiratory Volume during first second (FEV(1)) from baseline to Day 14 and on Day 28 was significantly higher in the group receiving 3% saline as compared with those receiving 7% saline inhalation.** There was some decrease in FEV(1) (percentage predicted) immediately after 7% saline inhalation unlike 3% saline. The functional status remained comparable between the two groups.

CONCLUSION:
The results suggest that 3% hypertonic saline nebulization was better than 7% saline inhalation. There is a need for studies with larger sample size and longer duration to confirm our results

Cardiovascular disease

Targeting preschool children to promote cardiovascular health: cluster randomized trial.

Céspedes J, Briceño G, Farkouh ME, Vedanthan R, Baxter J, Leal M, Boffetta P, Woodward M, Hunn M, Dennis R, Fuster V.

Am J Med. 2013 Jan;126(1):27-35.e3. doi: 10.1016/j.amjmed.2012.04.045. Epub 2012 Oct 9.

Source
Fundación Cardioinfantil Instituto de Cardiologia, Bogotá, Colombia.

Abstract
BACKGROUND:
School programs can be effective in modifying knowledge, attitudes, and habits relevant to long-term risk of chronic diseases associated with sedentary lifestyles. As part of a long-term research strategy, we conducted an educational intervention in preschool facilities to assess changes in preschoolers' knowledge, attitudes, and habits toward healthy eating and living an active lifestyle.

METHODS:
Using a cluster design, we randomly assigned 14 preschool facilities in Bogotá, Colombia to a 5-month educational and playful intervention (7 preschool facilities) or to usual curriculum (7 preschool facilities). A total of 1216 children aged 3-5 years, 928 parents, and 120 teachers participated. A structured survey was used at baseline, at the end of the study, and 12 months later to evaluate changes in knowledge, attitudes, and habits.

RESULTS:
Children in the intervention group showed a 10.9% increase in weighted score, compared with 5.3% in controls. The absolute adjusted difference was 3.90 units (95% confidence interval [CI], 1.64-6.16; P <.001). Among parents, the equivalent statistics were 8.9% and 3.1%, respectively (absolute difference 4.08 units; 95% CI, 2.03 to 6.12; P <.001), and among teachers, 9.4% and 2.5%, respectively (absolute difference 5.36 units; 95% CI, -0.29-11.01; P = .06). In the intervened cohort 1 year after the intervention, children still showed a significant increase in weighted score (absolute difference of 6.38 units; P <.001).

CONCLUSIONS:
A preschool-based intervention aimed at improving knowledge, attitudes, and habits related to healthy diet and active lifestyle is feasible, efficacious, and sustainable in very young children.

Community and Primary Health Services

(see also Environmental health)

Effects of unconditional and conditional cash transfers on child health and development in Zimbabwe: a cluster-randomised trial.

Robertson L, Mushati P, Eaton JW, Dumba L, Mavise G, Makoni J, Schumacher C, Crea T, Monasch R, Sherr L, Garnett GP, Nyamukapa C, Gregson S.

Lancet. 2013 Apr 13;381(9874):1283-92. doi: 10.1016/S0140-6736(12)62168-0. Epub 2013 Feb 27.

Source
Department of Infectious Disease Epidemiology, School of Public Health, Imperial College London, London, UK. l.robertson06@imperial.ac.uk

Abstract
BACKGROUND:
Cash-transfer programmes can improve the wellbeing of vulnerable children, but few studies have rigorously assessed their effectiveness in sub-Saharan Africa. We investigated the effects of unconditional cash transfers (UCTs) and conditional cash transfers (CCTs) on birth registration, vaccination uptake, and school attendance in children in Zimbabwe.

METHODS:
We did a matched, cluster-randomised controlled trial in ten sites in Manicaland, Zimbabwe. We divided each study site into three clusters. After a baseline survey between July, and September, 2009, clusters in each site were randomly assigned to UCT, CCT, or control, by drawing of lots from a hat. **Eligible households contained children younger than 18 years and satisfied at least one other criteria: head of household was younger than 18 years; household cared for at least one orphan younger than 18 years, a disabled person, or an individual who was chronically ill; or household was in poorest wealth quintile**. Between January, 2010, and January, 2011, households in UCT clusters collected payments every 2 months. Households in CCT clusters could receive the same amount but were monitored for compliance with several conditions related to child wellbeing. Eligible households in all clusters, including control clusters, had access to parenting skills classes and received maize seed and fertiliser in December, 2009, and August, 2010. Households and individuals delivering the intervention were not masked, but data analysts were. **The primary endpoints were proportion of children younger than 5 years with a birth certificate, proportion younger than 5 years with up-to-date vaccinations, and proportion aged 6-12 years attending school at least 80% of the time.** This trial is registered with ClinicalTrials.gov, number NCT00966849.

FINDINGS:
1199 eligible households were allocated to the control group, 1525 to the UCT group, and 1319 to the CCT group. Compared with control clusters, the proportion of children aged 0-4 years with birth certificates had increased by 1·5% (95% CI -7·1 to 10·1) in the UCT group and by 16·4% (7·8-25·0) in the CCT group by the end of the intervention period. The proportions of children aged 0-4 years with complete vaccination records was 3·1% (-3·8 to 9·9) greater in the UCT group and 1·8% (-5·0 to 8·7) greater in the CCT group than in the control group. **The proportions of children aged 6-12 years who attended school at least 80% of the time was 7·2% (0·8-13·7) higher in the UCT group and 7·6% (1·2-14·1) in the CCT group than in the control group.**

INTERPRETATION:
Our results support strategies to integrate cash transfers into social welfare programming in sub-Saharan Africa, but further evidence is needed for the comparative effectiveness of UCT and CCT programmes in this region.

FUNDING:
Wellcome Trust, the World Bank through the Partnership for Child Development, and the Programme of Support for the Zimbabwe National Action Plan for Orphans and Vulnerable Children.

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Developing the evidence-base for Safe Communities: a multi-level, partly randomised, controlled trial.

Seedat M, McClure R, Suffla S, van Niekerk A.

Int J Inj Contr Saf Promot. 2012;19(3):231-41. doi: 10.1080/17457300.2012.705303. Epub 2012 Aug 9.

Source
Institute for Social and Health Sciences, University of South Africa, Johannesburg, South Africa. Seedama@unisa.ac.za

Abstract
Safe Communities, representing a global activation of the public health logic, may be strengthened through theoretical, methodological, and empirical support. In the spirit of this Special Issue that aims to analyse the achievements and challenges inherent to Safe Communities, we offer our contribution in the form of a methodology of a multi-country child safety, peace and health promotion study. The study, situated within an African-centred initiative called Ukuphepha - an isiZulu word meaning demonstrating African safety - is underpinned by four theoretical claims that frame injury and violence prevention as a multi-disciplinary issue to be addressed through a suite of interventions to family and extended social systems. The interventions, sensitive to the priorities of each participating country, have been informed by the literature on effective interventions and the authors' joint experiences of community development. The study is designed as a population-based, multi-level, multi-intervention partly randomised controlled trial, and there are potentially 24 participant communities representing South Africa, Mozambique, Egypt, Zambia, Uganda, Bangladesh, Malaysia and Australia - over three commencement phases. Whereas process evaluation will focus on community engagement, impact evaluation will consider risk and protective factors, and outcome evaluation will examine the overall effectiveness of the interventions. Notwithstanding the many challenges, the study will provide insights into the methodology and mechanisms of ecologically-oriented interventions that locate injury and violence prevention as an activity arising from safety, peace and health promotion.

Community resource centres to improve the health of women and children in Mumbai slums: study protocol for a cluster randomized controlled trial.

Shah More N, Das S, Bapat U, Rajguru M, Alcock G, Joshi W, Pantvaidya S, Osrin D.

Trials. 2013 May 8;14(1):132. [Epub ahead of print]

Abstract
BACKGROUND: The trial addresses the general question of whether community resource centers run by a non-government organization improve the health of women and children in slums. The resource centers will be run the Society for Nutrition, Education and Health Action, and the trial will evaluate their effects on a series of public health indicators. Each resource center will be located in a vulnerable Mumbai slum area and will serve as a base for salaried community workers, supervised by officers and coordinators, to organize the collection and dissemination of health information, provision of services, home visits to identify and counsel families at risk, referral of individuals and families to appropriate services and support for their access, meetings of community members and providers, and events and campaigns on health issues.Methods/design: A cluster randomized controlled trial in which 20 urban slum areas with resource centers are compared with 20 control areas. Each cluster will contain approximately 600 households and randomized allocation will be in three blocked phases, of 12, 12 and 16 clusters. Any resident of an intervention cluster will be able to participate in the intervention, but the resource centers will target women and children, particularly women of reproductive age and children under 5.The outcomes will be assessed through a household census after 2 years of resource center operations. The primary outcomes are unmet need for family planning in women aged 15 to 49 years, proportion of children under 5 years of age not fully immunized for their ages, and proportion of children under 5 years of age with weight for height less than 2 standard deviations below the median for age and sex. Secondary outcomes describe adolescent pregnancies, home deliveries, receipt of conditional cash transfers for institutional delivery, other childhood anthropometric indices, use of public sector health and nutrition services, indices of infant and young child feeding, and consultation for violence against women and children.Trial registration: ISRCTN Register: ISRCTN56183183Clinical Trials Registry of India: CTRI/2012/09/003004.

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A health equity critique of social marketing: where interventions have impact but insufficient reach.

Langford R, Panter-Brick C.

Soc Sci Med. 2013 Apr;83:133-41. doi: 10.1016/j.socscimed.2013.01.036. Epub 2013 Feb 11.

Source
Department of Anthropology, Durham University, Dawson Building, South Road, Durham DH1 3LE, UK. Beki.langford@bristol.ac.uk

Abstract
Health interventions increasingly rely on formative qualitative research and social marketing techniques to effect behavioural change. Few studies, however, incorporate qualitative research into the process of program evaluation to understand both impact and reach: namely, to what

extent behaviour change interventions work, for whom, in what contexts, and why. We reflect on the success of a community-based hygiene intervention conducted in the slums of Kathmandu, Nepal, evaluating both maternal behaviour and infant health. We recruited all available mother-infant pairs (n = 88), and allocated them to control and intervention groups. Formative qualitative research on hand-washing practices included structured observations of 75 mothers, 3 focus groups, and 26 in-depth interviews. Our intervention was led by Community Motivators, intensively promoting hand-washing-with-soap at key junctures of food and faeces contamination. The 6-month evaluation period included hand-washing and morbidity rates, participant observation, systematic records of fortnightly community meetings, and follow-up interviews with 12 mothers. While quantitative measures demonstrated improvement in hand-washing rates and a 40% reduction in child diarrhoea, the qualitative data highlighted important equity issues in reaching the ultra-poor. We argue that a social marketing approach is inherently limited: focussing on individual agency, rather than structural conditions constraining behaviour, can unwittingly exacerbate health inequity. This contributes to a prevention paradox whereby those with the greatest need of a health intervention are least likely to benefit, finding hand-washing in the slums to be irrelevant or futile. Thus social marketing is best deployed within a range of interventions that address the structural as well as the behavioural and cognitive drivers of behaviour change. We conclude that critiques of social marketing have not paid sufficient attention to issues of health equity, and demonstrate how this can be addressed with qualitative data, embedded in both the formative and evaluative phases of a health intervention

Dengue

The impact of insecticide-treated school uniforms on dengue infections in school-aged children: study protocol for a randomised controlled trial in Thailand.

Wilder-Smith A, Byass P, Olanratmanee P, Maskhao P, Sringernyuang L, Logan JG, Lindsay SW, Banks S, Gubler D, Louis VR, Tozan Y, Kittayapong P.

Trials. 2012 Nov 15;13:212. doi: 10.1186/1745-6215-13-212.

Source
Centre for Global Health Research, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden.

Abstract
BACKGROUND:
There is an urgent need to protect children against dengue since this age group is particularly sensitive to the disease. Since dengue vectors are active mainly during the day, a potential target for control should be schools where children spend a considerable amount of their day. School uniforms are the cultural norm in most developing countries, worn throughout the day. We

hypothesise that insecticide-treated school uniforms will reduce the incidence of dengue infection in school-aged children. Our objective is to determine the impact of impregnated school uniforms on dengue incidence.

METHODS:
A randomised controlled trial will be conducted in eastern Thailand in a group of schools with approximately 2,000 students aged 7-18 years. Pre-fabricated school uniforms will be commercially treated to ensure consistent, high-quality insecticide impregnation with permethrin. A double-blind, randomised, crossover trial at the school level will cover two dengue transmission seasons.

DISCUSSION:
Practical issues and plans concerning intervention implementation, evaluation, analysing and interpreting the data, and possible policy implications arising from the trial are discussed.

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Development and mental health

(See also Maternal mental health, Anaemia and iron deficiency, Micronutrients and food fortification)

Efficacy of modified constraint induced movement therapy in improving upper limb function in children with hemiplegic cerebral palsy: A randomized controlled trial.

Choudhary A, Gulati S, Kabra M, Singh UP, Sankhyan N, Pandey RM, Kalra V.

Brain Dev. 2012 Dec 10. pii: S0387-7604(12)00277-X. doi: 10.1016/j.braindev.2012.11.001. [Epub ahead of print]

Source
Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110029, India.

Abstract
Purpose: The objective of this randomized single blind (outcome assessor) controlled trial was to evaluate the efficacy of 4weeks of modified constraint induced movement therapy (mCIMT) in improving upper limb function in 3-8years old children with hemiplegic cerebral palsy. Methods: Thirty-one children were randomly assigned to receive the mCIMT (N=16) with conventional therapy or conventional therapy alone (N=15). Children were evaluated three times (at enrollment, follow up at 4weeks and 12weeks). The primary outcome measure was difference in "change in mean total QUEST scores" at 4weeks of intervention between the intervention and the control arm. Results: After 4weeks of intervention, mCIMT group showed significant change in the affected upper limb in QUEST scores (10.7±5.2 vs 1.4±1.7, p<0.001) and time (s) to complete nine-hole-pegboard test compared with control group [60(0-130) vs 5(-12 to 30), p<0.001]. The improvement observed in upper limb function after 4weeks of intervention persisted 8weeks after discontinuation of intervention in mCIMT group. Conclusion: The modified constraint induced movement therapy appears to be effective in improving upper limb function in 3-8years old hemiplegic cerebral palsy children.

Occupational therapy home program for children with intellectual disabilities: a randomized, controlled trial.

Wuang YP, Ho GS, Su CY.

Res Dev Disabil. 2013 Jan;34(1):528-37. doi: 10.1016/j.ridd.2012.09.008. Epub 2012 Oct 18.

Source
Department of Occupational Therapy, Kaohsiung Medical University, Kaohsiung, Taiwan.

Abstract

This study aimed to investigate the effectiveness of a proposed occupational therapy home program (OTHP) for children with intellectual disabilities (ID). Children with ID were randomly and equally assigned to OTHP or to no OTHP groups. The primary outcome measures were Canadian Occupational Performance, Bruininks-Oseretsky Test of Motor Proficiency-Second Edition, and The Children's Assessment of Participation and Enjoyment scores at 10 and 20 weeks. The 20-week OTHP produced significant difference in fine motor function, activity participation, and parent satisfaction with performance, compared to those of no OTHP. Pediatricians can advise families to implement 20 weeks of OTHP with an average 15 min per session to facilitate functional changes of children with ID.

Effect of yoga on cognitive abilities in schoolchildren from a socioeconomically disadvantaged background: a randomized controlled study.

Chaya MS, Nagendra H, Selvam S, Kurpad A, Srinivasan K.

J Altern Complement Med. 2012 Dec;18(12):1161-7. doi: 10.1089/acm.2011.0579. Epub 2012 Aug 21.

Source
Swami Vivekananda Yoga Anusandhana Samasthana, Bangalore, India.

Abstract
OBJECTIVE:
The objective of this study was to assess the effect of yoga, compared to physical activity on the cognitive performance in 7-9 year-old schoolchildren from a socioeconomic disadvantaged background.

DESIGN:
Two hundred (200) schoolchildren from Bangalore, India, after baseline assessment of cognitive functioning were randomly allocated to either a yoga or a physical-activity group. Cognitive functions (attention and concentration, visuo-spatial abilities, verbal ability, and abstract thinking) were assessed using an Indian adaptation of the Wechsler Intelligence Scale for Children at baseline, after 3 months of intervention, and later at a 3-month follow-up.

RESULTS:
Of the 200 subjects, 193 were assessed at 3 months after the study, and then 180 were assessed at the 3-month follow-up. There were no significant differences in cognitive performance between the two study groups (yoga versus physical activity) at postintervention, after controlling for grade levels. Improvement in the mean scores of cognitive tests following intervention varied from 0.5 (Arithmetic) to 1.4 (Coding) for the yoga group and 0.7 (Arithmetic) to 1.6 (Vocabulary) in the physical-activity group.

CONCLUSIONS:
Yoga was as effective as physical activity in improving cognitive performance in 7-9 year old schoolchildren. Further studies are needed to examine the dose-response relationship between yoga and cognitive performance.

Efficacy of constraint-induced therapy on functional performance and health-related quality of life for children with cerebral palsy: a randomized controlled trial.

Hsin YJ, Chen FC, Lin KC, Kang LJ, Chen CL, Chen CY.

J Child Neurol. 2012 Aug;27(8):992-9. doi: 10.1177/0883073811431011. Epub 2012 Jan 12.

Source
Department of Physical Medicine and Rehabilitation, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, ROC.

Abstract
To better generalize training effects to the context of daily living, home-based constraint-induced therapy has been proposed. Therapeutic success of constraint-induced therapy is limited as to whether the improvements in functional performance can be transferred to quality of life. This randomized controlled trial aimed to investigate the efficacy of home-based constraint-induced therapy on functional performance and health-related quality of life. Twenty-two children with spastic unilateral cerebral palsy (6-8 years, 10 boys) were randomly assigned to receive constraint-induced therapy or traditional rehabilitation. Home-based constraint-induced therapy had immediate and maintaining effects on motor efficacy and functional performance and induced greater gains in health-related quality of life in the long run than in the short term. The home-based constraint-induced therapy protocol (relatively moderate intensity and shortened constraint time), which might balance the effectiveness and compliance of participants and caregivers, may be an effective alternative to conventional constraint-induced therapy.

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Supporting language and cognitive development of infants and young children living in children's homes in Turkey.

Berument SK, Sönmez D, Eyüpoğlu H.

Child Care Health Dev. 2012 Sep;38(5):743-52. doi: 10.1111/j.1365-2214.2011.01314.x. Epub 2011 Sep 27.

Source
Department of Psychology, Middle East Technical University, Ankara, Turkey. sibel@metu.edu.tr

Abstract
AIM:
The purpose of the present study was to improve language and cognitive development of infant and young children residing in institutional settings in Turkey.

METHOD:

In Study I, there were 12 children with a mean age of 35 months in the intervention group and 12 children with a mean age of 36 months in the control group.

RESULTS:
When both groups' pre-test post-test general development t scores and cognitive and language sub-domain developmental gaps were compared, neither the time nor the time by group interactions were significant. Nevertheless, both groups' developmental gap appeared to decline. In Study II, children were recruited from the same institution and randomly assigned to the intervention and control groups. Results indicated that infants and children who were in the intervention group showed a decline in the language and cognitive development gaps, whereas the control group children's developmental gaps were increased.

CONCLUSIONS:
It can be concluded that by increasing the quality of care in children's homes infants' and young children's development can be enhanced.
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Development of cognitive abilities of children infected with helminths through health education.

Lobato L, Miranda A, Faria IM, Bethony JM, Gazzinelli MF.

Rev Soc Bras Med Trop. 2012 Jul-Aug;45(4):514-9.

Source
Programa de Pós-Graduação em Enfermagem, Escola de Enfermagem, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brasil. lucaslobato87@gmail.com

Abstract
INTRODUCTION:
The aim of this study was to evaluate the effect of health education in learning and cognitive development of children infected, previously treated in an endemic area for helminthiasis.

METHODS:
It is a longitudinal, experimental, with random allocation of participants. The study included 87 children of both sexes enrolled in the school hall of Maranhão, State of Minas Gerais, Brazil, and divided into two groups: intervention and control. Initially the children were submitted to the parasitological fecal examination for infection diagnosis and, when positive, they were treated. For the data collection, a structured questionnaire and the psychological tests Raven, Wisc-III and DAP III were applied, before and after the educational intervention. For the group comparison, the Mann Whitney test was used, and established significance level of 5%.

RESULTS:
It was found that previously infected children who received the educational intervention, children showed higher performance than the control group in strutured questionnaire ($p<0.05$).

CONCLUSIONS:

It is acceptable to suppose the positive influence and the importance in the use of educational interventions in the cognitive recovery and learning of children previously treated with anthelmintics.
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A double-blind placebo controlled trial of Ginkgo biloba added to risperidone in patients with autistic disorders.

Hasanzadeh E, Mohammadi MR, Ghanizadeh A, Rezazadeh SA, Tabrizi M, Rezaei F, Akhondzadeh S.

Child Psychiatry Hum Dev. 2012 Oct;43(5):674-82. doi: 10.1007/s10578-012-0292-3.

Source
Psychiatric Research Center, Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, South Kargar Street, 13337 Tehran, Iran.

Abstract
Ginkgo biloba has been reported to affect the neurotransmitter system and to have antioxidant properties that could impact the pathogenesis of Autism Spectrum Disorder. Based on these studies, we decided to assess the effectiveness of Ginkgo biloba extract (Ginko T.D., Tolidaru, Iran) as an adjunctive agent to risperidone in the treatment of autism. Forty-seven outpatients with a DSM-IV-TR diagnosis of autism ages between 4 and 12 years were assigned to this double blinded clinical trial and were randomly divided into two groups. One group received risperidone plus Ginko T.D and the other received risperidone plus placebo. The dose of risperidone was 1-3 mg/day and the dose of Ginko T.D. was 80 mg/day for patients under 30 kg and 120 mg/day for patients above 30 kg. Patients were assessed using Aberrant Behavior Checklist-Community (ABC-C) rating scale and the side effect check list every 2 weeks until the endpoint. None of the 5 subscales of ABC-C rating scale showed significant differences between the two groups. Incidents of side effects were not significantly different between the two groups. Adding Ginkgo biloba to risperidone did not affect the treatment outcome of ADs. Nevertheless, further observations are needed to confirm this result.

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Diabetes

Effect of cholecalciferol as adjunctive therapy with insulin on protective immunologic profile and decline of residual β-cell function in new-onset type 1 diabetes mellitus.

Gabbay MA, Sato MN, Finazzo C, Duarte AJ, Dib SA.

Arch Pediatr Adolesc Med. 2012 Jul 1;166(7):601-7. doi: 10.1001/archpediatrics.2012.164.

Source
Diabetes Center of Endocrinology Division, Department ofMedicine, São Paulo Federal University, São Paulo, SP, Brazil. monicagabbay@gmail.com

Abstract
OBJECTIVE:
To evaluate the effect of vitamin D3 on cytokine levels, regulatory T cells, and residual β-cell function decline when cholecalciferol (vitamin D3 administered therapeutically) is given as adjunctive therapy with insulin in new-onset type 1 diabetes mellitus (T1DM).

DESIGN AND SETTING:
An 18-month (March 10, 2006, to October 28, 2010) randomized, double-blind, placebo-controlled trial was conducted at the Diabetes Center of São Paulo Federal University, São Paulo, Brazil.

PARTICIPANTS:
Thirty-eight patients with new-onset T1DM with fasting serum C-peptide levels greater than or equal to 0.6 ng/mL were randomly assigned to receive daily oral therapy of cholecalciferol, 2000 IU, or placebo.

MAIN OUTCOME MEASURE:
Levels of proinflammatory and anti-inflammatory cytokines, chemokines, regulatory T cells, hemoglobin A1c, and C-peptide; body mass index; and insulin daily dose.

RESULTS:
Mean (SD) chemokine ligand 2 (monocyte chemoattractant protein 1) levels were significantly higher (184.6 [101.1] vs 121.4 [55.8] pg/mL) at 12 months, as well as the increase in regulatory T-cell percentage (4.55% [1.5%] vs 3.34% [1.8%]) with cholecalciferol vs placebo. The cumulative incidence of progression to undetectable (≤0.1 ng/mL) fasting C-peptide reached 18.7% in the cholecalciferol group and 62.5% in the placebo group; stimulated C-peptide reached 6.2% in the cholecalciferol group and 37.5% in the placebo group at 18 months. Body mass index, hemoglobin A1c level, and insulin requirements were similar between the 2 groups.

CONCLUSIONS:
Cholecalciferol used as adjunctive therapy with insulin is safe and associated with a protective immunologic effect and slow decline of residual β-cell function in patients with new-onset T1DM. Cholecalciferol may be an interesting adjuvant in T1DM prevention trials.

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Diarrhoea

(See also Zinc, Vaccines and immunization - Rotavirus vaccine, Environmental health, hand-washing and sanitation)

Ringers lactate vs Normal saline for children with acute diarrhea and severe dehydration- a double blind randomized controlled trial.

Mahajan V, Sajan SS, Sharma A, Kaur J.

Indian Pediatr. 2012 Dec;49(12):963-8. Epub 2012 Mar 30.

Source
Department of Pediatrics, Government Medical College and Hospital,Chandigarh, India. vidushimahajan2003@yahoo.co.in

Abstract
OBJECTIVE:
WHO recommends Ringers lactate (RL) and Normal Saline (NS) for rapid intravenous rehydration in childhood diarrhea and severe dehydration. We compared these two fluids for improvement in pH over baseline during rapid intravenous rehydration in children with acute diarrhea.

DESIGN:
Double-blind randomized controlled trial

SETTING:
Pediatric emergency facilities at a tertiary-care referral hospital.

INTERVENTION:
Children with acute diarrhea and severe dehydration received either RL (RL-group) or NS (NS-group), 100 mL/kg over three or six hours. Children were reassessed after three or six hours. Rapid rehydration was repeated if severe dehydration persisted. Blood gas was done at baseline and repeated after signs of severe dehydration disappeared.
OUTCOME MEASURES:
Primary outcome was change in pH from baseline. Secondary outcomes included changes in serum electrolytes, bicarbonate levels, and base-deficit from baseline; mortality, duration of hospital stay, and fluids requirement.

RESULTS:
Twenty two children, 11 each were randomized to the two study groups. At primary end point (disappearance of signs of severe dehydration), the improvement in pH from baseline was not significant in RL-group [from 7.17 (0.11) to 7.28 (0.09)] as compared to NS-group [7.09 (0.11) to 7.21 (0.09)], P=0.17 (after adjusting for baseline serum Na/ Cl). Among this limited sample size, children in RL group required less fluids [median 310 vs 530 mL/kg, P=0.01] and had shorter median hospital stay [38 vs 51 hours, P=0.03].

CONCLUSIONS:
There was no difference in improvement in pH over baseline between RL and NS among children with acute diarrhea and severe dehydration.

Drugs for treating giardiasis.

Granados CE, Reveiz L, Uribe LG, Criollo CP.

Cochrane Database Syst Rev. 2012 Dec 12; 12:CD007787. doi: 10.1002/14651858.CD007787.pub2.

Source
Facultad de Medicina, Universidad Nacional de Colombia, Bogota D.C., Colombia.cegranadosg@unal.edu.co. caregra@gmail.com.

Abstract
BACKGROUND:
Giardiasis infection may be asymptomatic, or can cause diarrhoea (sometimes severe), weight loss, malabsorption, and, in children, failure to thrive. It is usually treated with metronidazole given three times daily for five to 10 days.

OBJECTIVES:
To evaluate the relative effectiveness of alternative antibiotic regimens for treating adults or children with symptomatic giardiasis.

SEARCH METHODS:
We searched the Cochrane Infectious Disease Group Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 6 2012); MEDLINE, EMBASE, LILACS and the International Clinical Trials Registry Platform Search Portal (3 July 2012).

SELECTION CRITERIA:
We included randomized controlled trials (RCT) comparing metronidazole administered for five to 10 days with any of the following drugs: metronidazole (single dose), tinidazole, albendazole, mebendazole, and nitazoxanide. The primary outcomes were parasitological and clinical cure.

DATA COLLECTION AND ANALYSIS:
Two authors independently assessed studies for inclusion, performed the risk of bias assessment, and extracted data. We summarized data using risk ratios and mean differences and we presented the results in forest plots and performed meta-analyses where possible. We assessed heterogeneity using the Chi(2) test, I(2) statistic and visual inspection; and we explored this by using subgroup analyses.We assessed the quality of evidence by using the GRADE approach.

MAIN RESULTS:
We included 19 trials, involving 1817 participants, of which 1441 were children. Studies were generally small, with poor methods reporting. . Most reported parasitological outcomes rather than clinical improvement.Ten trials, from India, Mexico, Peru, Iran, Cuba, and Turkey, compared albendazole (400 mg once daily for five to 10 days) with metronidazole (250 mg to 500 mg three times daily for five to 10 days). This once-daily regimen of albendazole is probably equivalent to metronidazole at achieving parasitological cure (RR 0.99, 95% CI 0.95 to 1.03; 932 participants, 10 trials; moderate quality evidence), and improving symptoms (RR 0.98, 95% confidence interval (CI) 0.93 to 1.04; 483 participants, five trials; moderate quality evidence), but the duration of follow-up was short (two to three weeks). Albendazole probably has fewer side effects than metronidazole (gastrointestinal side effects: RR 0.29, 95% CI 0.13 to 0.63; 717 participants, eight trials; moderate quality evidence; neurological side effects: RR 0.34, 95% CI 0.18 to 0.64; 453 participants, five trials; low quality evidence).Five trials from

Turkey, Spain and the UK compared mebendazole (200 mg three times daily for five to 10 days) with metronidazole (5 mg/kg (or 250 mg) three times daily for five to 10 days). These trials were small in size, and at high risk of bias. Consequently, reliable conclusions on the relative effectiveness cannot be made (very low quality evidence).Five further trials, from Iran, Spain and Peru, have evaluated shortened regimens of tinidazole (single dose; 179 participants, three trials), metronidazole (single dose; 55 participants, one trial), and nitazoxanide (three days; 55 participants, one trial). Again, these trials were at high risk of bias and too small to reliably detect or exclude important differences (very low quality evidence).

AUTHORS' CONCLUSIONS:
Albendazole may be of similar effectiveness to metronidazole, may have fewer side effects, and has the advantage of a simplified regimen. Large, high quality trials, assessing clinical outcomes (such as diarrhoea) will help assess further alternatives.

Clinical, epidemiological, and spatial characteristics of Vibrio parahaemolyticus diarrhea and cholera in the urban slums of Kolkata, India.

Kanungo S, Sur D, Ali M, You YA, Pal D, Manna B, Niyogi SK, Sarkar B, Bhattacharya SK, Clemens JD, Nair GB.

BMC Public Health. 2012 Sep 28;12:830. doi: 10.1186/1471-2458-12-830.

Source
National Institute of Cholera and Enteric Diseases, Kolkata, India.

Abstract
BACKGROUND:
There is not much information on the differences in clinical, epidemiological and spatial characteristics of diarrhea due to V. cholerae and V. parahaemolyticus from non-coastal areas. We investigated the differences in clinical, epidemiological and spatial characteristics of the two Vibrio species in the urban slums of Kolkata, India.

METHODS:
The data of a cluster randomized cholera vaccine trial were used. We restricted the analysis to clusters assigned to placebo. Survival analysis of the time to the first episode was used to analyze risk factors for V. parahaemolyticus diarrhea or cholera. A spatial scan test was used to identify high risk areas for cholera and for V. parahaemolyticus diarrhea.

RESULTS:
In total, 54,519 people from the placebo clusters were assembled. The incidence of cholera (1.30/1000/year) was significantly higher than that of V. parahaemolyticus diarrhea (0.63/1000/year). Cholera incidence was inversely related to age, whereas the risk of V. parahaemolyticus diarrhea was age-independent. The seasonality of diarrhea due to the two Vibrio species was similar. Cholera was distinguished by a higher frequency of severe dehydration, and V. parahaemolyticus diarrhea was by abdominal pain. Hindus and those who live in household not using boiled or treated water were more likely to have V. parahaemolyticus diarrhea. Young age, low socioeconomic status, and living closer to a project

healthcare facility were associated with an increased risk for cholera. The high risk area for cholera differed from the high risk area for V. parahaemolyticus diarrhea.
CONCLUSION:
We report coexistence of the two vibrios in the slums of Kolkata. The two etiologies of diarrhea had a similar seasonality but had distinguishing clinical features. The risk factors and the high risk areas for the two diseases differ from one another suggesting different modes of transmission of these two pathogens.

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Vibrio cholerae/mimicus in fecal microbiota of healthy children in a cholera endemic urban slum setting in Kolkata, India.

Nair GB, Ramamurthy T, Sur D, Kurakawa T, Takahashi T, Nomoto K, Takeda Y.

Microbiol Immunol. 2012 Nov;56(11):789-91. doi: 10.1111/j.1348-0421.2012.00497.x.

Source
National Institute of Cholera and Enteric Diseases, Yaho, Kunitachi, Tokyo, 186-8650, Japan.

Abstract
During a double-blind, randomized, placebo-controlled probiotic trial among 3758 children residing in an urban slum in Kolkata, India, Vibrio cholerae/mimicus was detected in fecal microbiota of healthy children. The importance of this finding in the local, regional and global transmission of cholera is discussed.

Water purification

(See also Hygiene and environmental health)

Evaluation of the impact of the plastic BioSand filter on health and drinking water quality in rural Tamale, Ghana.

Stauber CE, Kominek B, Liang KR, Osman MK, Sobsey MD.

Int J Environ Res Public Health. 2012 Oct 24;9(11):3806-23. doi: 10.3390/ijerph9113806.

Source
Institute of Public Health, Georgia State University, P.O. Box 3995, Atlanta, GA 30302, USA. cstauber@gsu.edu

Abstract
A randomized controlled trial of the plastic BioSand filter (BSF) was performed in rural communities in Tamale (Ghana) to assess reductions in diarrheal disease and improvements in household drinking water quality. Few studies of household water filters have been performed in this region, where high drinking water turbidity can be a challenge for other household water treatment technologies. During the study, the **longitudinal prevalence ratio for diarrhea**

comparing households that received the plastic BSF to households that did not receive it was 0.40 (95% confidence interval: 0.05, 0.80), suggesting an overall diarrheal disease reduction of 60%. The **plastic BSF achieved a geometric mean reduction of 97% and 67% for E. coli and turbidity, respectively**. These results suggest the plastic BSF significantly improved drinking water quality and reduced diarrheal disease during the short trial in rural Tamale, Ghana. The results are similar to other trials of household drinking water treatment technologies.

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Assessing water filtration and safe storage in households with young children of HIV-positive mothers: a randomized, controlled trial in Zambia.

Peletz R, Simunyama M, Sarenje K, Baisley K, Filteau S, Kelly P, Clasen T.

PLoS One. 2012;7(10):e46548. doi: 10.1371/journal.pone.0046548. Epub 2012 Oct 17.

Source
London School of Hygiene and Tropical Medicine, London, United Kingdom. Rachel.Peletz@lshtm.ac.u

Abstract
BACKGROUND:
Unsafe drinking water presents a particular threat to people living with HIV/AIDS (PLHIV) due to the increased risk of opportunistic infections, diarrhea-associated malabsorption of essential nutrients, and increased exposure to untreated water for children of HIV-positive mothers who use replacement feeding to reduce the risk of HIV transmission. This population may particularly benefit from an intervention to improve water quality in the home.

METHODS AND FINDINGS:
We conducted a 12-month randomized, controlled field trial in Zambia among 120 households with children <2 years (100 with HIV-positive mothers and 20 with HIV-negative mothers to reduce stigma of participation) to assess a high-performance water filter and jerry cans for safe storage. Households were followed up monthly to assess use, drinking water quality (thermotolerant coliforms (TTC), an indicator of fecal contamination) and reported diarrhea (7-day recall) among children <2 years and all members of the household. Because previous attempts to blind the filter have been unsuccessful, we also assessed weight-for-age Z-scores (WAZ) as an objective measure of diarrhea impact. Filter use was high, with 96% (596/620) of household visits meeting the criteria for users. The quality of water stored in intervention households was significantly better than in control households (3 vs. 181 TTC/100 mL, respectively, p<0.001). The intervention was associated with reductions in the longitudinal prevalence of reported diarrhea of 53% among children <2 years (LPR=0.47, 95% CI: 0.30-0.73, p=0.001) and 54% among all household members (LPR=0.46, 95% CI: 0.30-0.70, p<0.001). While reduced WAZ was associated with reported diarrhea (-0.26; 95% CI: -0.37 to -0.14, p<0.001), there was no difference in WAZ between intervention and control groups.
CONCLUSION:

In this population living with HIV/AIDS, a water filter combined with safe storage was used correctly and consistently, was highly effective in improving drinking water quality, and was protective against diarrhea.

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Endocrine disorders, vitamin D and bone health

Management of nutritional rickets in Indian children: a randomized controlled trial.

Aggarwal V, Seth A, Marwaha RK, Sharma B, Sonkar P, Singh S, Aneja S.

J Trop Pediatr. 2013 Apr;59(2):127-33. doi: 10.1093/tropej/fms058. Epub 2012 Oct 26.

Source
Department of Pediatrics, Kalawati Saran Children's Hospital and Lady Hardinge Medical College, New Delhi, India.

Abstract
INTRODUCTION:
Rickets is usually attributed to vitamin D deficiency. However, recent studies have implicated dietary calcium deficiency in its etiology. Information on relative efficacy of calcium, vitamin D or both together in healing of rickets is limited.

OBJECTIVE:
To study effect of treatment with calcium, vitamin D or a combination of these two on healing of nutritional rickets in young children.

DESIGN:
Randomized controlled trial.

METHODS:
Sixty-seven cases of nutritional rickets in the age group of 6 months to 5 years were randomly allocated to receive vitamin D (600 000 IU single intramuscular dose), calcium (75 mg/kg/day elemental calcium orally) or a combination of the above two for a period of 12 weeks. The demographic parameters, nutritional status, dietary calcium and phytate intake were assessed for all. Radiographs (wrist and knee) and biochemical parameters (serum calcium, inorganic phosphate, alkaline phosphatase, 25-hydroxycholecalciferol and parathyroid hormone) were evaluated at baseline, 6 and 12 weeks for evidence of healing.

RESULTS:
Mean dietary intake of calcium in all cases was low (204 ± 129 mg/day). Mean serum 25-hydroxycholecalciferol D level was 15.9 ± 12.4 ng/ml, and 82.1% of patients had serum vitamin D levels <20 ng/ml, indicative of vitamin D deficiency. After 6 and 12 weeks of treatment, radiological and biochemical evidence of healing rickets was observed in all treatment groups, albeit to a variable extent. The combined end point of normal serum alkaline phosphatase and complete radiological healing at 12 weeks was observed in 50% subjects on combination therapy as compared with 15.7% subjects on vitamin D alone and 11.7% on calcium alone.

CONCLUSIONS:
Children with rickets had a low serum vitamin D level and a low dietary calcium intake. The best therapeutic response was seen with a combination of vitamin D and calcium than either of them given alone. Trial registration number: CTRI/2010/091/000448.

School-based calcium-vitamin D with micronutrient supplementation enhances bone mass in underprivileged Indian premenarchal girls.

Khadilkar A, Kadam N, Chiplonkar S, Fischer PR, Khadilkar V.

Bone. 2012 Jul;51(1):1-7. doi: 10.1016/j.bone.2012.03.029. Epub 2012 Apr 4.

Source
Hirabai Cowasji Jehangir Medical Research Institute, Pune, India. anuradhavkhadilkar@gmail.com

Abstract
Low adult bone mass is linked to osteoporosis and fractures and is dependent on the extent of childhood and adolescent bone mineralization. The aim of the study was to investigate the effect of 1-year supplementation of calcium, multivitamin with zinc along with vitamin-D on bone mass accrual of school-going premenarchal girls from low income groups in Pune, India. Double-blind, matched-pair, cluster, randomization study was carried out in 214 premenarchal girls (8-12 years) from 2 schools in Pune, India. The two schools together formed 3 classes with 3 clusters each of age-matched girls of which one cluster was allocated to either one of the intervention groups (Ca-group:500 mg/d calcium, Ca+MZ-group:500 mg/d calcium+multivitamin tablet containing 15 mg/d zinc) or control group (C-group: multivitamin tablet without any minerals); all subjects received vitamin-D supplementation. Anthropometry, biochemical parameters, total body bone mineral content (TBBMC) and bone mineral density (TBBMD) (Dual energy X-ray absorptiometry) were assessed at baseline and endline. Post supplementation, mean percent increase in TBBMC was significantly higher in Ca-group (22.3%) and Ca+MZ-group (20.8%) compared to C-group (17.6%) ($p<0.05$) with no significant differences observed between Ca+MZ and Ca groups ($p>0.1$). Improvement in TBBMC-for-age Z-scores was higher in the two calcium supplemented groups (13.6%-22%) compared to the C-group (no improvement). Calcium supplementation, with or without multivitamins and zinc, showed a promising improvement in bone health especially with regards to improvement in bone related Z-scores in our population of underprivileged premenarchal girls.

Enhanced effect of zinc and calcium supplementation on bone status in growth hormone-deficient children treated with growth hormone: a pilot randomized controlled trial.

Ekbote V, Khadilkar A, Chiplonkar S, Mughal Z, Khadilkar V.

Endocrine. 2013 Jun;43(3):686-95. doi: 10.1007/s12020-012-9847-0. Epub 2012 Dec 9.

Source
Hirabai Cowasji Jehangir Medical Research Institute, Jehangir Hospital, Pune, India.

Abstract
Reduced bone mineral content in growth hormone-deficient children (GHD) has been reported. Calcium, zinc, and vitamin D play an important role in bone formation. Hence, the aim of this pilot randomized controlled study was to evaluate the effect of calcium, vitamin D, and zinc supplementation in prepubertal GHD children treated with GH on bone health parameters. After

1 year of treatment with GH (20 mg/m(2)/week), 31 GHD (mean age 8.7 ± 2.8 years, 18 boys) prepubertal children were randomised to receive calcium (500 mg/day) and vitamin D (60,000 IU/3 months) [Group A] or a similar supplement of calcium, vitamin D, and zinc (as per Indian Recommended Allowance) [Group B] along with GH therapy for the next 12 months. The two groups were similar in anthropometric and body composition parameters at baseline ($p > 0.1$). After 1 year of GH therapy, height-adjusted % gain was similar in both groups, 48 % in bone mineral content (BMC) and 45 % in bone area (BA). Height-adjusted % increase in BMC was significantly ($p < 0.05$) higher in the second year than in the first in both the groups. This % increase in BMC and BA was greater in Group B (51 and 36 % respectively) than in Group A (49 and 34 %), although marginally ($p < 0.05$). Supplementation of calcium and vitamin D along with GH therapy in GHD Indian children has the potential for enhancing bone mass accrual; this effect was further enhanced through the addition of zinc supplement.

Change of urinary fluoride and bone metabolism indicators in the endemic fluorosis areas of southern China after supplying low fluoride public water.

Chen S, Li B, Lin S, Huang Y, Zhao X, Zhang M, Xia Y, Fang X, Wang J, Hwang SA, Yu S.

BMC Public Health. 2013 Feb 20;13:156. doi: 10.1186/1471-2458-13-156.

Source
Department of Epidemiology, School of Public Health and Tropical Medicine, Southern Medical University, 1813 Guangzhou Dadao North, Guangzhou, Guangdong 510515, People's Republic of China. chshaox@mail.sysu.edu.cn

Abstract
BACKGROUND:
Few studies have evaluated health impacts, especially biomarker changes, following implementation of a new environmental policy. This study examined changes in water fluoride, urinary fluoride (UF), and bone metabolism indicators in children after supplying low fluoride public water in endemic fluorosis areas of Southern China. We also assessed the relationship between UF and serum osteocalcin (BGP), calcitonin (CT), alkaline phosphatase (ALP), and bone mineral density to identify the most sensitive bone metabolism indicators related to fluoride exposure.

METHODS:
Four fluorosis-endemic villages (intervention villages) in Guangdong, China were randomly selected to receive low-fluoride water. One non-endemic fluorosis village with similar socio-economic status, living conditions, and health care access, was selected as the control group. 120 children aged 6-12 years old were randomly chosen from local schools in each village for the study. Water and urinary fluoride content as well as serum BGP, CT, ALP and bone mineral density were measured by the standard methods and compared between the children residing in the intervention villages and the control village. Benchmark dose (BMD) and benchmark dose lower limit (BMDL) were calculated for each bone damage indicator.

RESULTS:
Our study found that after water source change, fluoride concentrations in drinking water in all intervention villages (A-D) were significantly reduced to 0.11 mg/l, similar to that in the control

village (E). Except for Village A where water change has only been taken place for 6 years, urinary fluoride concentrations in children of the intervention villages were lower or comparable to those in the control village after 10 years of supplying new public water. The values of almost all bone indicators in children living in Villages B-D and ALP in Village A were either lower or similar to those in the control village after the intervention. CT and BGP are sensitive bone metabolism indicators related to UF. While assessing the temporal trend of different abnormal bone indicators after the intervention, bone mineral density showed the most stable and the lowest abnormal rates over time.

CONCLUSIONS:
Our results suggest that supplying low fluoride public water in Southern China is successful as measured by the reduction of fluoride in water and urine, and changes in various bone indicators to normal levels. A comparison of four bone indicators showed CT and BGP to be the most sensitive indicators.

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The effect of prepubertal calcium carbonate supplementation on the age of peak height velocity in Gambian adolescents.

Prentice A, Dibba B, Sawo Y, Cole TJ.

Am J Clin Nutr. 2012 Nov;96(5):1042-50. doi: 10.3945/ajcn.112.037481. Epub 2012 Sep 18.

Source
Medical Research Council Human Nutrition Research, Cambridge, United Kingdom. ann.prentice@mrc-hnr.cam.ac.uk

Abstract
BACKGROUND:
Limited evidence suggests that calcium intake before puberty influences adolescent height growth and the timing of puberty. Such an effect might be particularly marked in populations in whom low calcium intake, stunting, and delayed puberty are common.

OBJECTIVE:
The objective was to test whether 12 mo of calcium supplementation at age 8-12 y to increase intakes toward international recommendations had long-term effects on adolescent growth and pubertal development in rural Gambian children.

DESIGN:
This was a longitudinal study of 160 Gambian boys (n = 80) and girls (n = 80) who had participated in a 12-mo, randomized, double-blind, placebo-controlled, calcium carbonate supplementation trial (1000 mg Ca/d, 5 d/wk) at age 8-12 y. Anthropometric measures were made every 1-2 y until age 21-25 y; pubertal status and menarche data were collected. Repeated-measures ANCOVA and Superimposition by Translation and Rotation Method (SITAR) growth models were used to assess the effects of treatment.

RESULTS:

In boys, midadolescent height growth was advanced in the calcium group, which resulted in greater stature at a mean age of 15.5 y (mean ± SEM: 2.0 ± 0.8 cm; P = 0.01) and an earlier age of peak height velocity by 7.4 ± 2.9 mo. Subsequently, the calcium group stopped growing earlier (P = 0.02) and was 3.5 ± 1.1 cm shorter (P = 0.002) at a mean age of 23.5 y. Weight and midupper arm circumference paralleled height. No significant effects were observed in girls, but a sex-by-supplement interaction on height growth could not be confirmed.

CONCLUSION:
Calcium supplementation of boys in late childhood advanced the age of peak height velocity and resulted in shorter adult stature in a population in whom low calcium intakes and delayed puberty are common. This trial was registered at isrctn.org as ISRCTN28836000.

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Epilepsy and acute seizures

A randomized controlled trial of intranasal-midazolam versus intravenous-diazepam for acute childhood seizures.

Thakker A, Shanbag P.

J Neurol. 2013 Feb;260(2):470-4. doi: 10.1007/s00415-012-6659-3. Epub 2012 Sep 16.

Source
Division of Child Neurology and Epilepsy, Department of Pediatrics, Lokmanya Tilak Municipal Medical College and General Hospital, B2-504, Gold Coin CHS, Tardeo Road, Sion, Mumbai 400 034, India. arpitathakker@gmail.com

Abstract
The objective of this study is to compare the safety and efficacy of midazolam given intranasally with diazepam given intravenously in the treatment of acute childhood seizures. A randomized controlled study was conducted in a pediatric emergency department in a tertiary general hospital. **Fifty children aged from 1 month to 12 years presenting with acute seizures of at least 10 min duration were enrolled during a 12 month period. Intranasal midazolam (0.2 mg/kg) and intravenous diazepam (0.3 mg/kg) were administered**. The main outcome measures were interval between arrival at hospital and starting treatment and interval between arrival at hospital and cessation of seizures. Intranasal midazolam and intravenous diazepam were equally effective. **Overall 18 of 27 seizures were controlled with midazolam and 15 of 23 with diazepam.** The mean interval between arrival at hospital and starting treatment was significantly shorter in the midazolam group [3.37 min (SD 2.46)] as compared to the diazepam group [14.13 min (SD 3.39)]. **The mean interval between cessation of seizures and arrival at hospital was significantly shorter in the midazolam group [6.67 min (SD 3.12)] as compared to the diazepam group [17.18 min (SD 5.09)]. The mean interval between control of seizures and administration of the drug was shorter in the diazepam group [2.67 min (SD 2.31)] as compared to the midazolam group [3.01 min (SD 2.79)].** No significant side effects were observed in either group. Seizures were controlled more quickly with intravenous diazepam than with intranasal midazolam. Midazolam was as safe and effective as diazepam. The overall interval between arrival at hospital and cessation of seizures was shorter with intranasal midazolam than with intravenous diazepam. The intranasal route can be possibly used not only in medical centres, but with appropriate instruction by the parents of children with acute seizures at home.

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Use of the modified Atkins diet for treatment of refractory childhood epilepsy: a randomized controlled trial.

Sharma S, Sankhyan N, Gulati S, Agarwala A.

Epilepsia. 2013 Mar;54(3):481-6. doi: 10.1111/epi.12069. Epub 2013 Jan 7.

Source
Division of Pediatric Neurology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India.

Abstract
PURPOSE:
The aim of this study was to evaluate the efficacy of the modified Atkins diet in a randomized controlled trial in children with refractory epilepsy.

METHODS:
Children aged 2-14 years who had daily seizures despite the appropriate use of at least three anticonvulsant drugs were enrolled. Children were randomized to receive either the modified Atkins diet or no dietary intervention for a period of 3 months. The ongoing anticonvulsant medications were continued unchanged in both the groups. Seizure control at 3 months was the primary end point. Analysis was intention to treat. Adverse effects of the diet were assessed by parental reports (ClinicalTrials.gov Identifier: NCT00836836).

KEY FINDINGS:
Among a total of 102 children, 50 were in the diet group and 52 in the control group. Four children discontinued the diet before the study end point, and three children in the control group were lost to follow-up. The mean seizure frequency at 3 months, expressed as a percentage of the baseline, was significantly less in the diet group: 59 ± 54 (95% confidence interval [CI] 44-74.5) versus 95.5 ± 48 (95% CI 82-109), p = 0.003. The proportion of children with >90% seizure reduction (30% vs. 7.7%, p = 0.005) and >50% seizure reduction was significantly higher in the diet group (52% vs. 11.5%, p < 0.001). Constipation was the most common adverse effect among children on the diet (23, 46%).
SIGNIFICANCE:
The modified Atkins diet was found to be effective and well tolerated in children with drug-refractory epilepsy.

Hygiene and Environmental Health

Sustained improvements in handwashing indicators more than 5 years after a cluster-randomised, community-based trial of handwashing promotion in Karachi, Pakistan.

Bowen A, Agboatwalla M, Ayers T, Tobery T, Tariq M, Luby SP.

Trop Med Int Health. 2013 Mar;18(3):259-67. doi: 10.1111/tmi.12046. Epub 2013 Jan 7.

Source
Centers for Disease Control and Prevention, Atlanta, GA, USA. abowen@cdc.gov

Abstract
OBJECTIVE:
To evaluate handwashing behaviour 5 years after a handwashing intervention in Karachi, Pakistan.

METHODS:
In 2003, we randomised neighbourhoods to control, handwashing promotion, or handwashing promotion and water treatment. Intervention households were given soap +/- water treatment product and weekly handwashing education for 9 months. In 2009, we re-enrolled 461 households from the three study groups: control (160), handwashing (141), and handwashing + water treatment (160) and assessed hygiene-related outcomes, accounting for clustering.

RESULTS:
Intervention households were 3.4 times more likely than controls to have soap at their handwashing stations during the study visit [293/301 (97%) vs. 45/159 (28%), P < 0.0001]. While nearly all households reported handwashing after toileting, intervention households more commonly reported handwashing before cooking [relative risk (RR) 1.2 (95% confidence interval (CI) 1.0-1.4)] and before meals [RR 1.7 (95% CI, 1.3-2.1)]. Control households cited a mean of 3.87 occasions for washing hands; handwashing households, 4.74 occasions; and handwashing + water treatment households, 4.78 occasions (P < 0.0001). Households reported purchasing a mean of 0.65 (control), 0.91 (handwashing) and 1.1 (handwashing + water treatment) bars of soap/person/month (P < 0.0001).

CONCLUSIONS:
Five years after receiving handwashing promotion, intervention households were more likely to have soap at the household handwashing station, know key times to wash hands and report purchasing more soap than controls, suggesting habituation of improved handwashing practices in this population. Intensive handwashing promotion may be an effective strategy for habituating hygiene behaviours and improving health.

Association between intensive handwashing promotion and child development in Karachi, Pakistan: a cluster randomized controlled trial.

Bowen A, Agboatwalla M, Luby S, Tobery T, Ayers T, Hoekstra RM.

Arch Pediatr Adolesc Med. 2012 Nov;166(11):1037-44. doi: 10.1001/archpediatrics.2012.1181

Source
Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA. abowen@cdc.gov

Abstract
OBJECTIVE:
To evaluate associations between handwashing promotion and child growth and development.

DESIGN:
Cluster randomized controlled trial.

SETTING:
Informal settlements in Karachi, Pakistan.

PARTICIPANTS:
A total of 461 children who were enrolled in a trial of household-level handwashing promotion in 2003 and were younger than 8 years at reassessment in 2009.

INTERVENTIONS:
In 2003, neighborhoods were randomized to control (n = 9), handwashing promotion (n = 9), or handwashing promotion and drinking water treatment (n = 10); intervention households received free soap and weekly handwashing promotion for 9 months.

MAIN OUTCOME MEASURES:
Anthropometrics and developmental quotients measured with the Battelle Developmental Inventory II at 5 to 7 years of age.

RESULTS:
Overall, 24.9% (95% CI, 20.0%-30.6%) and 22.1% (95% CI, 18.0%-26.8%) of children had z scores that were more than 2 SDs below the expected z scores for height and body mass index for age, respectively; anthropometrics did not differ significantly across study groups. Global developmental quotients averaged 104.4 (95% CI, 101.9-107.0) among intervention children and 98.3 (95% CI, 93.1-103.4) among control children (P = .04). Differences of similar magnitude were measured across adaptive, personal-social, communication, cognitive, and motor domains.

CONCLUSIONS:
Although growth was similar across groups, **children randomized to the handwashing promotion during their first 30 months of age attained global developmental quotients 0.4 SDs greater than those of control children at 5 to 7 years of age**. These gains are comparable to those of at-risk children enrolled in publicly funded preschools in the United States and suggest that handwashing promotion could improve child well-being and societal productivity.

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Effect of intensive hand washing education on hand washing behaviors in thai households with an influenza-positive child in urban Thailand.

Kaewchana S, Simmerman M, Somrongthong R, Suntarattiwong P, Lertmaharit S, Chotipitayasunondh T.

Asia Pac J Public Health. 2012 Jul;24(4):577-85. doi: 10.1177/1010539510393728. Epub 2011 Feb 28.

Source
Chulalongkorn University, Bangkok, Thailand. suchadak@tuc.or.th

Abstract
This study assessed the effect of intensive education on self-reported frequency of hand washing (FHW), measured quality of hand washing (QHW), and measured scores of knowledge, attitude, and practice (KAP) after 7 days and 90 days home-based intensive education of participants (aged >7 years) in households with a influenza-positive child. The authors provided intensive hand washing education using interactive participation including individual training, self-monitoring diary, provision of soap, and so on. There were significant improvements on FHW and QHW on day 7, control group (n(1) = 135) reported 3.9 hand washing episodes/day, whereas the intervention group (n(2) = 140) reported 5.7 episodes/day; control group (n(1) = 164) obtained a 3.2 measured quality score, whereas the intervention group (n(2) = 166) obtained a score of 6.4. Pre-education and 90 days post-education, FHW significantly improved by 2 episodes/day and QHW increased by 3 scores/episode. Knowledge of influenza and hand washing following coughing/sneezing showed significant improvement, but attitude modification toward severity of influenza requires a more intensified and longer intervention.

Impact of a school-based hygiene promotion and sanitation intervention on pupil hand contamination in Western Kenya: a cluster randomized trial.

Greene LE, Freeman MC, Akoko D, Saboori S, Moe C, Rheingans R.

Am J Trop Med Hyg. 2012 Sep;87(3):385-93. doi: 10.4269/ajtmh.2012.11-0633. Epub 2012 Jul 16.

Source
Center for Global Safe Water, Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA 30322, USA. lgreen4@emory.edu

Abstract
Handwashing with soap effectively reduces exposure to diarrhea-causing pathogens. Interventions to improve hygiene and sanitation conditions in schools within low-income countries have gained increased attention; however, their impact on schoolchildren's exposure to fecal pathogens has not been established. Our trial examined whether a school-based water, sanitation, and hygiene intervention reduced Escherichia coli contamination on pupils' hands in western Kenya. A hygiene promotion and water treatment intervention did not reduce risk of E. coli presence (relative risk [RR] = 0.92, 95% confidence interval [CI] = 0.54-1.56); the addition

of new latrines to intervention schools significantly increased risk among girls (RR = 2.63, 95% CI = 1.29-5.34), with a non-significant increase among boys (RR = 1.36, 95% CI = 0.74-2.49). Efforts to increase usage of school latrines by constructing new facilities may pose a risk to children in the absence of sufficient hygiene behavior change, daily provision of soap and water, and anal cleansing materials.

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Interim evaluation of a large scale sanitation, hygiene and water improvement programme on childhood diarrhea and respiratory disease in rural Bangladesh.

Huda TM, Unicomb L, Johnston RB, Halder AK, Yushuf Sharker MA, Luby SP.

Soc Sci Med. 2012 Aug;75(4):604-11. doi: 10.1016/j.socscimed.2011.10.042. Epub 2011 Dec 13.

Source
International Centre for Diarrheal Diseases Research, Bangladesh. tariquehuda@yahoo.com

Abstract
Started in 2007, the Sanitation Hygiene Education and Water Supply in Bangladesh (SHEWA-B) project aims to improve the hygiene, sanitation and water supply for 20 million people in Bangladesh, and thus reduce disease among this population. This paper assesses the effectiveness of SHEWA-B on changing behaviors and reducing diarrhea and respiratory illness among children < 5 years of age. We assessed behaviors at baseline in 2007 and after 6 months and 18 months by conducting structured observation of handwashing behavior in 500 intervention and 500 control households. In addition we conducted spot checks of water and sanitation facilities in 850 intervention and 850 control households. We also collected monthly data on diarrhea and respiratory illness from 500 intervention and 500 control households from October 2007 to September 2009. Participants washed their hands with soap < 3% of the time around food related events in both intervention and control households at baseline and after 18 months. Washing both hands with soap or ash after cleaning a child's anus increased from 22% to 36%, and no access to a latrine decreased from 10% to 6.8% from baseline to 18 months. The prevalence of diarrhea and respiratory illness, among children <5 years of age were similar in intervention and control communities throughout the study. This large scale sanitation, hygiene and water improvement programme resulted in improvements in a few of its targeted behaviors, but these modest behavior changes have not yet resulted in a measurable reduction in childhood diarrhea and respiratory illness.

Appropriate time-interval application of alcohol hand gel on reducing influenza-like illness among preschool children: a randomized, controlled trial.

Randomised trials in child health in developing countries 2012-13

Pandejpong D, Danchaivijitr S, Vanprapa N, Pandejpong T, Cook EF.

Am J Infect Control. 2012 Aug;40(6):507-11. doi: 10.1016/j.ajic.2011.08.020. Epub 2012 Jan 20.

Source
Department of Medicine, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand. sidpd@mahidol.ac.th

Abstract
BACKGROUND:
We studied the efficacy of different time-interval applications of alcohol hand gel as a strategy for the prevention of influenza-like illness (ILI) in preschool-age children.

METHODS:
We performed a classroom-based cluster randomization at a kindergarten school in Bangkok, Thailand. A total of 1437 children were placed into 3 test groups, based on the frequency of alcohol hand gel use for hand hygiene: only before lunch (q lunch), every 120 minutes (q 120), and every 60 minutes (q 60). The primary outcome was a change in the school absenteeism rate caused by ILI.

RESULTS:
The rates of absenteeism from confirmed ILI (sick days/present days) were 0.026 in the q lunch group, 0.025 in the q 120 group, and 0.017 in the q 60 group. Significant reductions in absenteeism rates were seen when comparing the q 60 group with the q 120 group (rate difference, 0.009; 95% confidence interval [CI], -0.002 to 0.015; P = .008) and comparing the q 60 group with the q lunch group (rate difference, 0.0096; 95% CI, 0.004-0.016; P = .002). No such differences were detected between the q 120 and q lunch groups (rate difference, 0.001; 95% CI, 0.005-0.007; P = .743).

CONCLUSIONS:
The compulsory hourly use of alcohol gel as classroom hand disinfection could significantly reduce the rate of absenteeism from ILI in preschool-age children.

Health worker education and training

The impact of training non-physician clinicians in Malawi on maternal and perinatal mortality: a cluster randomised controlled evaluation of the enhancing training and appropriate technologies for mothers and babies in Africa (ETATMBA) project.

Ellard D, Simkiss D, Quenby S, Davies D, Kandala NB, Kamwendo F, Mhango C, O'Hare JP.

BMC Pregnancy Childbirth. 2012 Oct 25;12:116. doi: 10.1186/1471-2393-12-116.

Source
Warwick Clinical Trials Unit, Division of Health Sciences, Warwick Medical School, The University of Warwick, Coventry CV4 7AL, UK. d.r.ellard@warwick.ac.uk

Abstract
BACKGROUND:
Maternal mortality in much of sub-Saharan Africa is very high whereas there has been a steady decline in over the past 60 years in Europe. Perinatal mortality is 12 times higher than maternal mortality accounting for about 7 million neonatal deaths; many of these in sub-Saharan countries. Many of these deaths are preventable. Countries, like Malawi, do not have the resources nor highly trained medical specialists using complex technologies within their healthcare system. Much of the burden falls on healthcare staff other than doctors including non-physician clinicians (NPCs) such as clinical officers, midwives and community health-workers. The aim of this trial is to evaluate a project which is training NPCs as advanced leaders by providing them with skills and knowledge in advanced neonatal and obstetric care. Training that will hopefully be cascaded to their colleagues (other NPCs, midwives, nurses).

METHODS/DESIGN:
This is a cluster randomised controlled trial with the unit of randomisation being the 14 districts of central and northern Malawi (one large district was divided into two giving an overall total of 15). Eight districts will be randomly allocated the intervention. Within these eight districts 50 NPCs will be selected and will be enrolled on the training programme (the intervention). Primary outcome will be maternal and perinatal (defined as until discharge from health facility) mortality. Data will be harvested from all facilities in both intervention and control districts for the lifetime of the project (3-4 years) and comparisons made. In addition a process evaluation using both quantitative and qualitative (e.g. interviews) will be undertaken to evaluate the intervention implementation.

DISCUSSION:
Education and training of NPCs is a key to improving healthcare for mothers and babies in countries like Malawi. Some of the challenges faced are discussed as are the potential limitations. It is hoped that the findings from this trial will lead to a sustainable improvement in healthcare and workforce development and training.

A model for the adoption of ICT by health workers in Africa.

Jimoh L, Pate MA, Lin L, Schulman KA.

Int J Med Inform. 2012 Nov;81(11):773-81. doi: 10.1016/j.ijmedinf.2012.08.005. Epub 2012 Sep 15.

Source
Duke University School of Medicine, Durham, NC, USA.

Abstract
PURPOSE:
To investigate the potential of information and communication technology (ICT) adoption among maternal and child health workers in rural Nigeria.

METHODS:
A prospective, quantitative survey design was used to collect data from quasi-randomly selected clusters of 25 rural health facilities in 5 of the 36 states in Nigeria over a 2-month period from June to July 2010. A total of 200 maternal and child health workers were included in the survey, and the data were analyzed using a modified theory of acceptance model (TAM).

RESULTS:
There was no significant difference between ICT knowledge and attitude scores across states. There were significant differences in perceived ease of use (P<.001) and perceived usefulness scores (P=.001) across states. Midwives reported higher scores on all the constructs but a lower score on endemic barriers (which is a more positive outcome). However, the differences were only statistically significant for perceived usefulness (P=.05) and endemic barriers (P<.001). Regression analysis revealed that there was no interaction between worker group and age. Older workers were likely to have lower scores on knowledge and attitude but higher scores on perceived ease of use and perceived usefulness. Lastly, we found that worker preference for ICT application in health varied across worker groups and conflicted with government/employer priorities.

CONCLUSIONS:
Although the objective of this study was exploratory, the results provide insight into the intricacies involved in the deployment of ICT in low-resource settings. Use of an expanded TAM should be considered as a mandatory part of any pre-implementation study of ICT among health workers in sub-Saharan Africa.

Hepatitis and liver disease

Primary prophylaxis of overt hepatic encephalopathy in patients with cirrhosis: an open labeled randomized controlled trial of lactulose versus no lactulose.

Sharma P, Sharma BC, Agrawal A, Sarin SK.

J Gastroenterol Hepatol. 2012 Aug;27(8):1329-35. doi: 10.1111/j.1440-1746.2012.07186.x.

Source
Department of Gastroenterology, G B Pant Hospital, New Delhi, India.

Abstract
BACKGROUND AND AIM:
Development of overt hepatic encephalopathy (HE) is associated with poor prognosis in patients with cirrhosis. Lactulose is used for the treatment of HE. There is no study on the prevention of overt HE using lactulose in patients who never had HE earlier.

METHODS:
Consecutive cirrhotic patients who never had an episode of overt HE were randomized to receive lactulose (Gp-L) or no lactulose (Gp-NL). All patients were assessed by psychometry (number connection test [NCT-A and B], figure connection test if illiterate [FCT-A and B], digit symbol test [DST], serial dot test [SDT], line tracing test [LTT]) and critical flicker frequency test (CFF) at inclusion and after 3 months. These patients were followed every month for 12 months for development of overt HE.

RESULTS:
Of 250 patients screened, 120 (48%) meeting the inclusion criteria were randomized to Gp-L (n = 60) and Gp-NL (n = 60). Twenty (19%) of 105 patients followed for 12 months developed an episode of overt HE. **Six (11%) of 55 in the lactulose (Gp-L) group and 14 (28%) of 50 in the Gp-NL (P = 0.02) developed overt HE.** Ten (20%) of 50 patients in Gp-NL and five (9%) of 55 patients in the Gp-L group died, P = 0.16. Number of patients with minimal hepatic encephalopathy (MHE) were comparable in two groups at baseline (Gp-L vs Gp-NL, 32:36, P = 0.29). Lactulose improved MHE in 66% of patients in Gp-L. Taking a cutoff < 38 Hz sensitivity and specificity of CFF in predicting HE were 52% and 77% at baseline and 52% and 82% at 3 months of treatment. On multivariate analysis, Child's score and presence of MHE at baseline were significantly associated with development of overt HE.

CONCLUSIONS:
Lactulose is effective for primary prevention of overt hepatic encephalopathy in patients with cirrhosis.

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HIV / AIDS

Computer-generated reminders and quality of pediatric HIV care in a resource-limited setting.

Were MC, Nyandiko WM, Huang KT, Slaven JE, Shen C, Tierney WM, Vreeman RC.

Pediatrics. 2013 Mar;131(3):e789-96. doi: 10.1542/peds.2012-2072. Epub 2013 Feb 25.

Source
Department of Medicine, Indiana University School of Medicine, Indianapolis, IN 46254, USA. mwere@iupui.edu

Abstract
OBJECTIVES:
To evaluate the impact of clinician-targeted computer-generated reminders on compliance with HIV care guidelines in a resource-limited setting.

METHODS:
We conducted this randomized, controlled trial in an HIV referral clinic in Kenya caring for HIV-infected and HIV-exposed children (<14 years of age). For children randomly assigned to the intervention group, printed patient summaries containing computer-generated patient-specific reminders for overdue care recommendations were provided to the clinician at the time of the child's clinic visit. For children in the control group, clinicians received the summaries, but no computer-generated reminders. We compared differences between the intervention and control groups in completion of overdue tasks, including HIV testing, laboratory monitoring, initiating antiretroviral therapy, and making referrals.

RESULTS:
During the 5-month study period, 1611 patients (49% female, 70% HIV-infected) were eligible to receive at least 1 computer-generated reminder (ie, had an overdue clinical task). We observed a fourfold increase in the completion of overdue clinical tasks when reminders were availed to providers over the course of the study (68% intervention vs 18% control, P < .001). Orders also occurred earlier for the intervention group (77 days, SD 2.4 days) compared with the control group (104 days, SD 1.2 days) (P < .001). Response rates to reminders varied significantly by type of reminder and between clinicians.

CONCLUSIONS:
Clinician-targeted, computer-generated clinical reminders are associated with a significant increase in completion of overdue clinical tasks for HIV-infected and exposed children in a resource-limited setting.

Ante-retroviral therapy (ART)

Comment
Studies in 2012-13 demonstrate the pros and cons of lopinavir/ritonavir-based ART. South African children with HIV who had perinatal exposure to nevirapine as part of HIV

transmission prevention, and later viral suppression with ritonavir-boosted lopinavir, were more likely to have virological failure over 6 months if switched to a nevirapine-based ART, despite early improvements in CD4 count and growth. In another study, HIV-infected South African children receiving lopinavir/ritonavir-based regimens had less favourable changes in lipid profile and triglycerides, compared to those switched to nevirapine-based regimens. Among Ugandan children treated with lopinavir/ritonavir-based ART, recurrences of malaria were less common than for those on non-nucleoside reverse transcriptase inhibitors, after treatment for malaria with artemether-lumefantrine.

Early versus deferred antiretroviral therapy for children older than 1 year infected with HIV (PREDICT): a multicentre, randomised, open-label trial.

Puthanakit T, Saphonn V, Ananworanich J, Kosalaraksa P, Hansudewechakul R, Vibol U, Kerr SJ, Kanjanavanit S, Ngampiyaskul C, Wongsawat J, Luesomboon W, Ngo-Giang-Huong N, Chettra K, Cheunyam T, Suwarnlerk T, Ubolyam S, Shearer WT, Paul R, Mofenson LM, Fox L, Law MG, Cooper DA, Phanuphak P, Vun MC, Ruxrungtham K; PREDICT Study Group.

Lancet Infect Dis. 2012 Dec;12(12):933-41. doi: 10.1016/S1473-3099(12)70242-6. Epub 2012 Oct 9.

Source

HIV Netherlands Australia Thailand Research Collaboration, Bangkok, Thailand.

Abstract

BACKGROUND:

The optimum time to start antiretroviral therapy for children diagnosed with HIV infection after 1 year of age is unknown. We assessed whether antiretroviral therapy could be deferred until CD4 percentages declined to less than 15% without affecting AIDS-free survival.

METHODS:

In our multicentre, randomised, open-label trial at nine research sites in Thailand and Cambodia, we enrolled children aged 1-12 years who were infected with HIV and had CD4 percentages of 15-24%. **Participants were randomly assigned (1:1) by a minimisation scheme to start antiretroviral therapy at study entry (early treatment group) or antiretroviral therapy to start when CD4 percentages declined to less than 15% (deferred treatment group**). The primary endpoint was AIDS-free survival (based on US Centers for Disease Control and Prevention category C events) at week 144, assessed with the Kaplan-Meier analysis and the log-rank approach. This study is registered with ClinicalTrials.gov, number NCT00234091.

FINDINGS:

Between March 28, 2006, and Sept 10, 2008, we enrolled 300 Thai and Cambodian children infected with HIV, with a median age of 6·4 years (IQR 3·9-8·4). **150 children were randomly allocated early antiretroviral therapy (one participant was excluded from analyses after withdrawing before week 0) and 150 children were randomly allocated deferred antiretroviral therapy.** Median baseline CD4 percentage was 19% (16-22%). 69 children (46%) in the deferred treatment group started antiretroviral therapy during the study. **AIDS-free survival at week 144 in the deferred treatment group was 98·7% (95% CI 94·7-99·7; 148**

of 150 patients) compared with 97·9% (93·7-99·3; 146 of 149 patients) in the early treatment group (p=0·6).

INTERPRETATION:
AIDS-free survival in both treatment groups was high. This low event rate meant that our study was underpowered to detect differences between treatment start times and thus additional follow-up of study participants or future studies are needed to answer this clinical question.

Early antiretroviral therapy improves neurodevelopmental outcomes in infants.

Laughton B, Cornell M, Grove D, Kidd M, Springer PE, Dobbels E, van Rensburg AJ, Violari A, Babiker AG, Madhi SA, Jean-Philippe P, Gibb DM, Cotton MF.

AIDS. 2012 Aug 24;26(13):1685-90.

Source
Children's Infectious Diseases Clinical Research Unit, Department of Paediatrics and Child Health, Stellenbosch University and Tygerberg Children's Hospital, Cape Town, South Africa. BL2@sun.ac.za

Abstract
OBJECTIVES:
To evaluate the effect of early versus deferred antiretroviral therapy (ART) on the neurodevelopment of infants from Cape Town participating in the Children with HIV Early Antiretroviral Therapy (CHER) trial.

DESIGN:
HIV-infected infants were randomized to early (<3 months) or deferred ART. HIV-uninfected infants (HIV-exposed and HIV-unexposed) provide background data.

METHODS:
Neurological examination and Griffiths Mental Development Scales (GMDS) were administered between 10-16 months of age by testers blind to HIV status and randomized allocation. Mean quotients were compared using paired Student's t-tests.

RESULTS:
Sixty-four infants on early ART and 26 on deferred ART (of potential 77 and 38 respectively on CHER trial) were assessed at median age 11 months (range 10-16). **On the GMDS, all scores were lower in the deferred arm and the General Griffiths and Locomotor Scores were significantly lower: mean (SD)=100.1 (13.8) vs. 106.3 (10.6) P=0.02; and 88.9 (16.3) vs. 97.7 (12.5), P<0.01, respectively.** Children with HIV who received early ART performed as well as children without HIV except on the Locomotor subscale. Both infected and uninfected mean GMDS scores were within the average range.

CONCLUSION:
Infants initiated on early ART have significantly better Locomotor and general scores on the GMDS at median age 11 months compared to infants on deferred ART, despite careful monitoring and ready access to ART in the latter.

Switching children previously exposed to nevirapine to nevirapine-based treatment after initial suppression with a protease-inhibitor-based regimen: long-term follow-up of a randomised, open-label trial.

Kuhn L, Coovadia A, Strehlau R, Martens L, Hu CC, Meyers T, Sherman G, Hunt G, Persaud D, Morris L, Tsai WY, Abrams EJ.

Lancet Infect Dis. 2012 Jul;12(7):521-30. doi: 10.1016/S1473-3099(12)70051-8. Epub 2012 Mar 16.

Source
Gertrude H Sergievsky Center, College of Physicians and Surgeons, and Department of Epidemiology, Columbia University, New York, NY 10032, USA. lk24@columbia.edu

Abstract
BACKGROUND:
Protease-inhibitor-based treatment is recommended as first-line for infants infected with HIV who have been previously exposed to nevirapine prophylaxis. However, long-term use poses adherence challenges, is associated with metabolic toxic effects, restricts second-line options, and is costly. We present the long-term outcomes of switching nevirapine-exposed children to nevirapine-based treatment after effective suppression of virus replication with a protease-inhibitor-based regimen.

METHODS:
We did a randomised trial to compare long-term viral suppression with nevirapine-based versus protease-inhibitor-based (ritonavir-boosted lopinavir) treatment in children who had achieved suppression with protease-inhibitor-based treatment. Randomisation (1:1) was by cohort blocks of variable size between eight and 12. Eligible children were younger than 24 months who were previously exposed to nevirapine for prevention of mother-to-child transmission, and achieved virological suppression of less than 400 copies per mL when treated with the regimen based on ritonavir-boosted lopinavir in Johannesburg, South Africa. We gave all drugs as liquids and adjusted doses at each visit in accordance with growth. We continued follow-up for a minimum of 90 weeks and maximum of 232 weeks after randomisation. We quantified HIV RNA every 3 months. Our primary endpoint was any viraemia greater than 50 copies per mL. Our analysis was by modified intention to treat. This study is registered with ClinicalTrials.gov, number NCT00117728.

FINDINGS:
We followed up the children for a median of 156 weeks and there were three deaths in each group. **Children in the switch group (Kaplan-Meier probability 0·595) were less likely to experience non-suppression greater than 50 copies per mL than in the control group (0·687; p=0·01) and had better CD4 and growth responses initially after switching** (52 children in the switch group vs 66 control group met this endpoint). By 156 weeks after randomisation, more children had virological failure--which we defined as confirmed viraemia of more than 1000 copies per mL--in the switch group (22 children) than in the control group (ten children; p=0·009). **We detected all 22 failures in the switch group by 52 weeks compared with five in the control group.** Virological failure was related to non-adherence and pretreatment drug resistance. In children without pretreatment drug resistance, we did not identify a significant difference in virological failure between the switch (Kaplan-Meier probability 0·140) and control (0·095) groups (p=0·34; seven failures in the switch group vs five

in the control group). Children in the switch group were significantly more likely to develop grade 1-3 alanine aminotransferase abnormalities over the duration of follow-up.
INTERPRETATION:
Viral-load testing through 52 weeks can identify all children likely to fail this protease-inhibitor-switch strategy. Switching children once suppressed to a nevirapine-based regimen might be a valuable treatment option if adequate viral-load monitoring can be done.

Comment
Although there were short term gains in terms of CD4 counts and growth after swiching to nevirapine, children who had perinatal exposure to nevirapine as part of transmission prevention, and later viral suppression with ritonavir-boosted lopinavir, were more likely to have medium-term virological failure if switched to a nevirapine-based ART. So it is arguable that switching to this regimen is a "valuable treatment option".

Metabolic abnormalities and body composition of HIV-infected children on Lopinavir or Nevirapine-based antiretroviral therapy.

Arpadi S, Shiau S, Strehlau R, Martens L, Patel F, Coovadia A, Abrams EJ, Kuhn L.

Arch Dis Child. 2013 Apr;98(4):258-64. doi: 10.1136/archdischild-2012-302633. Epub 2012 Dec 5.

Source
Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Columbia University Medical Center, 630 W. 168th Street, New York, NY 10032, USA. sma2@columbia.edu

Abstract
BACKGROUND:
Few studies have assessed metabolic and body composition alterations in perinatally HIV-infected African children on antiretroviral therapy (ART). We compared metabolic profiles and regional fat of children on ritonavir-boosted lopinavir (lopinavir/ritonavir), lamivudine and stavudine to those switched to nevirapine, lamivudine and stavudine.

METHODS:
This study evaluated metabolic and body composition outcomes in 156 HIV-infected children completing a randomised trial that assessed the continued use of lopinavir/ritonavir-based ART or switch to nevirapine-based ART in Johannesburg, South Africa (2005-2010). Fasting total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides total and regional body fat (BF) were measured. A clinical assessment for lipodystrophy (LD) was conducted.

RESULTS:
156 children (mean age 5.1±0.8 years, mean duration of treatment 4.2±0.7 years, mean time since randomisation 3.4±0.7 years) were enrolled. 85 were randomised to the lopinavir/ritonavir group and 71 to the nevirapine group. The lopinavir/ritonavir group had lower mean HDL (1.3±0.4 vs 1.5±0.4 mmol/l, $p<0.001$) and higher mean TC (4.4±1.0 vs 4.1±0.8 mmol/l, $p=0.097$), LDL (2.6±0.9 vs 2.3±0.7 mmol/l, $p=0.018$) and triglycerides (1.1±0.4 vs 0.8±0.3

mmol/l, p<0.001). The lopinavir/ritonavir group had more total BF by mean skinfold sum (43±11.1 vs 39±10.1 mm, p=0.031) and BF% by bioelectrical impedance analysis (17.0±7.0 vs 14.1±8.0%, p=0.022). Thirteen (8.4%) met criteria for LD.

CONCLUSIONS:
Unfavourable alterations in lipid profile and triglycerides, and differences in fat are detectable in young HIV-infected South African children receiving lopinavir/ritonavir-based regimens versus those switched to nevirapine-based regimens. Interventions to mitigate these alterations are warranted to reduce long-term cardiovascular disease risk.

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Lipid profiles in young HIV-infected children initiating and changing antiretroviral therapy.

Strehlau R, Coovadia A, Abrams EJ, Martens L, Arpadi S, Meyers T, Kuhn L.

J Acquir Immune Defic Syndr. 2012 Aug 1;60(4):369-76. doi: 10.1097/QAI.0b013e318243760b.

Source
Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, University of the Witwatersrand, Johannesburg, South Africa.

Abstract
BACKGROUND:
Both HIV infection and antiretroviral therapy are associated with dyslipidemias in adults, but there are fewer data on outcomes in young children. Here we examined lipid profile changes in a cohort of young children before and after suppression on an initial ritonavir-boosted lopinavir (LPV/r)-based regimen and after switch to a nevirapine (NVP)-based regimen.

METHODS:
One hundred ninety-five HIV-infected children who initiated LPV/r-based therapy when <24 months of age at 1 site in Johannesburg, South Africa, and who achieved viral suppression (<400 copies/mL sustained for ≥ 3 months) were randomized to either continue on the LPV/r-based regimen (n = 99) or to switch to a NVP-based regimen (n = 96). Nonfasting concentrations of total cholesterol (TC), low-density lipoprotein, high-density lipoprotein (HDL), and triglycerides (TG) were measured pretreatment, at randomization when suppressed, and at 9, 20, and 31 months postrandomization.

RESULTS:
Median age at treatment initiation was 9 months, and the initial regimen was maintained for an average of 9 months before randomization. TC, low-density lipoprotein, and HDL increased from pretreatment to randomization (P < 0.0001) and TC/HDL ratio and TG decreased (P < 0.0001). After switching to NVP, HDL was significantly higher (P < 0.02) and TC/HDL and TG significantly lower (P < 0.0001) through 31 months postswitch relative to remaining on the LPV/r-based regimen.

CONCLUSION:

Initiating antiretroviral therapy was associated with changes to a more favorable lipid profile in young children. **Switching from a LPV/r-based regimen to a NVP-based regimen accentuated and continued these improvements.** Investigation of safe and effective methods for managing dyslipidemias in children of different ages in resource-limited settings is warranted.

Adherence to antiretroviral therapy and acceptability of planned treatment interruptions in HIV-infected children.

Harrison L, Ananworanich J, Hamadache D, Compagnucci A, Penazzato M, Bunupuradah T, Mazza A, Ramos JT, Flynn J, Rampon O, Mellado Pena MJ, Floret D, Marczynska M, Puga A, Forcat S, Riault Y, Lallemant M, Castro H, Gibb DM, Giaquinto C; Paediatric European Network for Treatment of AIDS (PENTA) 11 Trial Team.

AIDS Behav. 2013 Jan;17(1):193-202. doi: 10.1007/s10461-012-0197-y.

Source
Medical Research Council Clinical Trials Unit, Aviation House, 125 Kingsway, London, WC2B 6NH, UK.

Abstract
There have been no paediatric randomised trials describing the effect of planned treatment interruptions (PTIs) of antiretroviral therapy (ART) on adherence, or evaluating acceptability of such a strategy. In PENTA 11, HIV-infected children were randomised to CD4-guided PTIs (n = 53) or continuous therapy (CT, n = 56). Carers, and children if appropriate, completed questionnaires on adherence to ART and acceptability of PTIs. There was no difference in reported adherence on ART between CT and PTI groups; non-adherence (reporting missed doses over the last 3 days or marking <100 % adherence since the last clinical visit on a visual analogue scale) was 18 % (20/111) and 14 % (12/83) on carer questionnaires in the CT and PTI groups respectively (odds ratios, OR (95 % CI) = 1.04 (0.20, 5.41), $\chi(2)$ (1) = 0.003, p = 0.96). Carers in Europe/USA reported non-adherence more often (31/121, 26 %) than in Thailand (1/73, 1 %; OR (95 % CI) = 54.65 (3.68, 810.55), $\chi(2)$ (1) = 8.45, p = 0.004). The majority of families indicated they were happy to have further PTIs (carer: 23/36, 64 %; children: 8/13, 62 %), however many reported more clinic visits during PTI were a problem (carer: 15/36, 42 %; children: 6/12, 50 %).

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Antiretroviral agents and prevention of malaria in HIV-infected Ugandan children.

Achan J, Kakuru A, Ikilezi G, Ruel T, Clark TD, Nsanzabana C, Charlebois E, Aweeka F, Dorsey G, Rosenthal PJ, Havlir D, Kamya MR.

N Engl J Med. 2012 Nov 29;367(22):2110-8. doi: 10.1056/NEJMoa1200501.

Source

Department of Pediatrics and Child Health, Makerere University College of Health Sciences, Kampala, Uganda. achanj@yahoo.co.uk

Abstract
BACKGROUND:
Human immunodeficiency virus (HIV) protease inhibitors show activity against Plasmodium falciparum in vitro. We hypothesized that the incidence of malaria in HIV-infected children would be lower among children receiving lopinavir-ritonavir-based antiretroviral therapy (ART) than among those receiving nonnucleoside reverse-transcriptase inhibitor (NNRTI)-based ART.

METHODS:
We conducted an open-label trial in which HIV-infected **children 2 months to 5 years of age who were eligible for ART or were currently receiving NNRTI-based ART were randomly assigned to either lopinavir-ritonavir-based ART or NNRTI-based ART and were followed for 6 months to 2 years.** Cases of uncomplicated malaria were treated with artemether-lumefantrine. The primary end point was the incidence of malaria.

RESULTS:
We enrolled 176 children, of whom 170 received the study regimen: 86 received NNRTI-based ART, and 84 lopinavir-ritonavir-based ART. **The incidence of malaria was lower among children receiving the lopinavir-ritonavir-based regimen than among those receiving the NNRTI-based regimen (1.32 vs. 2.25 episodes per person-year; incidence-rate ratio, 0.59; 95% confidence interval [CI], 0.36 to 0.97; P=0.04),** as was the risk of a recurrence of malaria after treatment with artemether-lumefantrine (28.1% vs. 54.2%; hazard ratio, 0.41; 95% CI, 0.22 to 0.76; P=0.004). The median lumefantrine level on day 7 after treatment for malaria was significantly higher in the lopinavir-ritonavir group than in the NNRTI group. **In the lopinavir-ritonavir group, lumefantrine levels exceeding 300 ng per milliliter on day 7 were associated with a reduction of more than 85% in the 63-day risk of recurrent malaria.** A greater number of serious adverse events occurred in the lopinavir-ritonavir group than in the NNRTI group (5.6% vs. 2.3%, P=0.16). Pruritus occurred significantly more frequently in the lopinavir-ritonavir group, and elevated alanine aminotransferase levels significantly more frequently in the NNRTI group.

CONCLUSIONS:
Lopinavir-ritonavir-based ART as compared with NNRTI-based ART reduced the incidence of malaria by 41%, with the lower incidence attributable largely to a significant reduction in the recurrence of malaria after treatment with artemether-lumefantrine. Lopinavir-ritonavir-based ART was accompanied by an increase in serious adverse events. (Funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development; ClinicalTrials.gov number, NCT00978068.).

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Prevalence of asymptomatic parasitemia and gametocytemia among HIV-infected Ugandan children randomized to receive different antiretroviral therapies.

Ikilezi G, Achan J, Kakuru A, Ruel T, Charlebois E, Clark TD, Rosenthal PJ, Havlir D, Kamya MR, Dorsey G.

Am J Trop Med Hyg. 2013 Apr;88(4):744-6. doi: 10.4269/ajtmh.12-0658. Epub 2013 Jan 28.

Source
Infectious Diseases Research Collaboration, Kampala, Uganda. gloria2k2@yahoo.co.uk

Abstract
In a recent randomized controlled trial, the use of protease inhibitor (PI)-based antiretroviral therapy (ART) was associated with a significantly lower incidence of malaria compared with non-nucleoside reverse transcriptase inhibitor-based ART in a cohort of human immunodeficiency virus-infected Ugandan children living in an area of high malaria transmission intensity. In this report, we compared the prevalence of asymptomatic parasitemia and gametocytemia using data from the same cohort. The prevalence of asymptomatic parasitemia did not differ between the two ART treatment arms. The PI-based arm was associated with a lower risk of gametocytemia at the time of diagnosis of malaria (6.6% versus 14.5%, P = 0.03) and during the 28 days after malaria diagnosis (3.4% versus 6.5%, P = 0.04). Thus, in addition to decreasing the incidence of malaria, the use of PI-based ART may lower transmission, as a result of a decrease in gametocytemia, in areas of high malaria transmission intensity.

Management of HIV-related conditions

Behavior and psychological functioning of young children of HIV-positive mothers in South Africa.

Sipsma H, Eloff I, Makin J, Finestone M, Ebersohn L, Visser MJ, Sikkema KJ, Allen CA, Ferreira R, Forsyth B.

AIDS Care. 2013;25(6):721-5. doi: 10.1080/09540121.2013.779627. Epub 2013 Mar 21.

Source
a Department of Health Policy and Administration , Yale School of Public Health , New Haven , CT , USA.

Abstract
Adults with HIV are living longer due to earlier diagnosis and increased access to antiretroviral medications. Therefore, fewer young children are being orphaned and instead, are being cared for by parents who know they are HIV positive, although they may be asymptomatic. Presently, it is unclear whether the psychological functioning of these young children is likely to be affected or, alternatively, whether it is only when a mother is ill, that children suffer adverse effects. We, thus, aimed to compare the behavior and psychological functioning of young children (aged 6-10 years) of HIV-positive and HIV-negative mothers. We also aimed to examine the association between HIV status disclosure and child outcomes. This study uses cross-sectional data from the baseline assessment of a randomized controlled trial conducted in Tshwane, South Africa. Participants (n=509) and their children were recruited from area health clinics. Among the 395 mothers with HIV, 42% reported symptoms of HIV disease. Multivariate linear regression models suggested that after adjusting for socio-demographic characteristics, children of HIV-positive mothers had significantly greater externalizing

behaviors than children of HIV-negative mothers. Importantly, children whose mothers were symptomatic had greater internalizing and externalizing behaviors compared with children of HIV-negative mothers, but this was not true for children of asymptomatic mothers. Additionally, among children of HIV-positive mothers, those who had been told their mothers were sick compared with children who had been told nothing had less internalizing and externalizing behaviors and improved daily living skills. This study, therefore, provides evidence that maternal HIV disease can affect the behaviors of young children in South Africa but, importantly, only when the mothers are symptomatic from their disease. Furthermore, results suggest that disclosure of maternal illness but not HIV status was associated with improved behavior and psychological functioning among young children.

Correlation of selenium and zinc levels to antiretroviral treatment outcomes in Thai HIV-infected children without severe HIV symptoms.

Bunupuradah T, Ubolyam S, Hansudewechakul R, Kosalaraksa P, Ngampiyaskul C, Kanjanavanit S, Wongsawat J, Luesomboon W, Pinyakorn S, Kerr S, Ananworanich J, Chomtho S, van der Lugt J, Luplertlop N, Ruxrungtham K, Puthanakit T; PREDICT study group.

Eur J Clin Nutr. 2012 Aug;66(8):900-5. doi: 10.1038/ejcn.2012.57. Epub 2012 Jun 20.

Source
HIV Netherlands Australia Thailand Research Collaboration, Thai Red Cross AIDS Research Center, Bangkok, Thailand. torsak.b@hivnat.org

Abstract
BACKGROUND/OBJECTIVES:
Deficiencies in antioxidants contribute to immune dysregulation and viral replication. To evaluate the correlation of selenium (Se) and zinc (Zn) levels on the treatment outcomes in HIV-infected children.

SUBJECTS/METHODS:
HIV-infected Thai children 1-12 years old, CD4 15-24%, without severe HIV symptoms were included. Se and Zn levels were measured by graphite furnace atomic absorption spectrometry at baseline and 48 weeks. Deficiency cutoffs were Se <0.1 μmol/l and Zn <9.9 μmol/l. Serum ferritin and C-reactive protein (CRP) were measured every 24 weeks. No micronutrient supplement was prescribed.

RESULTS:
In all, 141 children (38.3% male) with a median (interquartile range (IQR)) age of 7.3 (4.2-9.0) years were enrolled. Median baseline CD4% was 20%, HIV-RNA was 4.6 log(10)copies/ml. At baseline, median (IQR) Se and Zn levels were 0.9 (0.7-1.0) μmol/l and 5.9 (4.8-6.9) μmol/l, respectively. None had Se deficiency while all had Zn deficiency. Over 48 weeks, 97 initiated antiretroviral therapy (ART) and 81% achieved HIV-RNA <50 copies/ml with 11% median CD4 gain. The mean change of Se was 0.06 μmol/l (P=0.003) and Zn was 0.42 μmol/l (P=0.003), respectively. By multivariate analysis in children who received ART, predictors for greater increase of CD4% from baseline were lower baseline CD4% (P<0.01) and higher baseline Zn level (P=0.02). The predictors for greater decrease of HIV-RNA from baseline were higher baseline HIV-RNA and higher ferritin (both P<0.01). No association of CRP with the changes from baseline of CD4% or HIV-RNA was found.

CONCLUSION:
In HIV-infected Thai children without severe immune deficiency who commenced ART, no correlation between Se and ART treatment outcomes was found. Higher pre-ART Zn levels were associated with significant increases in CD4% at 48 weeks.

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Prevention of parent to child transmission

The study of HIV and antenatal care integration in pregnancy in Kenya: design, methods, and baseline results of a cluster-randomized controlled trial.

Turan JM, Steinfeld RL, Onono M, Bukusi EA, Woods M, Shade SB, Washington S, Marima R, Penner J, Ackers ML, Mbori-Ngacha D, Cohen CR.

PLoS One. 2012;7(9):e44181. doi: 10.1371/journal.pone.0044181 Epub 2012 Sep 6.

Source
Department of Health Care Organization and Policy, University of Alabama at Birmingham, Birmingham, Alabama, United States of America. jmturan@uab.edu

Abstract
BACKGROUND:
Despite strong evidence for the effectiveness of anti-retroviral therapy for improving the health of women living with HIV and for the prevention of mother-to-child transmission (PMTCT), HIV persists as a major maternal and child health problem in sub-Saharan Africa. In most settings antenatal care (ANC) services and HIV treatment services are offered in separate clinics. Integrating these services may result in better uptake of services, reduction of the time to treatment initiation, better adherence, and reduction of stigma.

METHODOLOGY/PRINCIPAL FINDINGS:
A prospective cluster randomized controlled trial design was used to evaluate the effects of integrating HIV treatment into ANC clinics at government health facilities in rural Kenya. **Twelve facilities were randomized to provide either fully integrated services (ANC, PMTCT, and HIV treatment services all delivered in the ANC clinic) or non-integrated services (ANC clinics provided ANC and basic PMTCT services and referred clients to a separate HIV clinic for HIV treatment).** During June 2009- March 2011, 1,172 HIV-positive pregnant women were enrolled in the study. The main study outcomes are rates of maternal enrollment in HIV care and treatment, infant HIV testing uptake, and HIV-free infant survival. Baseline results revealed that the intervention and control cohorts were similar with respect to socio-demographics, male partner HIV testing, sero-discordance of the couple, obstetric history, baseline CD4 count, and WHO Stage. Challenges faced while conducting this trial at low-resource rural health facilities included frequent staff turnover, stock-outs of essential supplies, transportation challenges, and changes in national guidelines.

CONCLUSIONS/SIGNIFICANCE:

This is the first randomized trial of ANC and HIV service integration to be conducted in rural Africa. It is expected that the study will provide critical evidence regarding the implementation and effectiveness of this service delivery strategy, with important implications for programs striving to eliminate vertical transmission of HIV and improve maternal health.

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Reducing the risk of HIV infection during pregnancy among South African women: A randomized controlled trial.

Jones DL, Peltzer K, Villar-Loubet O, Shikwane E, Cook R, Vamos S, Weiss SM.

AIDS Care. 2013 Jun;25(6):702-9. doi: 10.1080/09540121.2013.772280. Epub 2013 Feb 25.

Source
a Psychiatry and Behavioral Sciences , University of Miami Miller School of Medicine , Miami, FL , USA.

Abstract
Mpumalanga Province, South Africa has one of the highest HIV/AIDS diagnosis rates among pregnant women (~29.4%). This study sought to enhance male involvement in pregnancy to increase HIV disclosure, sexual communication, HIV knowledge and reduce unprotected sex. Participants attending Antenatal Clinics (ANC) completed HIV counseling and testing and were enrolled with male partners (n=239 couples, 478 individuals). Twelve ANCs were randomly assigned to provide a prevention of mother-to-child transmission (PMTCT) intervention or the standard of care, health education sessions plus PMTCT. Participants were assessed at baseline and post-intervention (approximately 6-8 weeks post-baseline) on demographics, sexual behavior, HIV-related knowledge, and conflict resolution strategies. Experimental participants increased HIV knowledge, use of negotiation, and decreased intimate partner violence. Additionally, they were more likely to have increased condom use from baseline to post-intervention (OR=5.1, 95% CI=[2.0, 13.3]). Seroconversions in the control condition exceeded experimental (6 vs. 0). HIV serostatus disclosure to partner did not increase over time for men or women within the experimental or control condition. Male involvement in pregnancy may be an important strategy to reduce sexual risk behavior and HIV transmission. Results support the utility of group interventions to enhance communication and HIV knowledge among pregnant couples.

Infant feeding practices were not associated with breast milk HIV-1 RNA levels in a randomized clinical trial in Botswana.

Rossenkhan R, Novitsky V, Sebunya TK, Leidner J, Hagan JE, Moyo S, Smeaton L, Lockman S, Musonda R, Ndung'u T, Gaseitsiwe S, Thior I, Mmalane M, Makhema J, Essex M, Shapiro R.

AIDS Behav. 2012 Jul;16(5):1260-4. doi: 10.1007/s10461-011-0035-7.

Source
Botswana-Harvard AIDS Institute, Gaborone, Botswana.

Abstract
Exclusive breastfeeding has been associated with a reduced risk of late vertical HIV transmission as compared to an infant diet composed of breast milk mixed with supplemental foods or liquids. Hypothesized mechanisms include increased infectivity of breast milk from mothers who practice mixed breastfeeding (MBF), or mechanisms such as increased gastrointestinal permeability in the infant caused by mixed feeding. It has been proposed that MBF may result in subclinical mastitis and higher breast milk HIV titers. However, little is known about the relationship between feeding strategy and breast milk viral load. We measured the HIV-1 concentration in breast milk in a sub-cohort of women enrolled in a mother-to-child HIV transmission prevention trial (the "Mashi" study). We report no observed relationship between MBF and measured breast milk viral RNA load. Our findings suggest that the increased transmission risk associated with higher breast milk HIV-1 RNA during MBF is unlikely.

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HIV vaccine

Feasibility and safety of ALVAC-HIV vCP1521 vaccine in HIV-exposed infants in Uganda: results from the first HIV vaccine trial in infants in Africa.

Kintu K, Andrew P, Musoke P, Richardson P, Asiimwe-Kateera B, Nakyanzi T, Wang L, Fowler MG, Emel L, Ou SS, Baglyos L, Gurunathan S, Zwerski S, Jackson JB, Guay L.

J Acquir Immune Defic Syndr. 2013 May 1;63(1):1-8. doi: 10.1097/QAI.0b013e31827f1c2d

Source
Makerere University-Johns Hopkins University Research Collaboration, Kampala, Uganda. kkintu@mujhu.org

Abstract
BACKGROUND:
The development of a safe and effective vaccine against HIV type 1 for the prevention of mother-to-child transmission of HIV would significantly advance the goal of eliminating HIV infection in children. Safety and feasibility results from phase 1, randomized, double-blind, placebo-controlled trial of ALVAC-HIV vCP1521 in infants born to HIV type 1-infected women in Uganda are reported.

METHODS:
HIV-exposed infants were enrolled at birth and randomized (4:1) to receive vaccine or saline placebo intramuscular injections at birth, 4, 8, and 12 weeks of age. Vaccine reactogenicity was assessed at vaccination and days 1 and 2 postvaccination. Infants were followed until 24 months of age. HIV infection status was determined by HIV DNA polymerase chain reaction.

RESULTS:

From October 2006 to May 2007, 60 infants (48 vaccine and 12 placebo) were enrolled with 98% retention at 24 months. One infant was withdrawn, but there were no missed visits or vaccinations among the 59 infants retained. Immune responses elicited by diphtheria, polio, hepatitis B, haemophilus influenzae type B, and measles vaccination were similar in the 2 arms. The vaccine was well tolerated with no severe or life-threatening reactogenicity events. Adverse events were equally distributed across both study arms. Four infants were diagnosed as HIV infected [3 at birth (2 vaccine and 1 placebo) and 1 in vaccine arm at 2 weeks of age].

CONCLUSION:
The ALVAC-HIV vCP1521 vaccination was feasible and safe in infants born to HIV-infected women in Uganda. The conduct of high-quality infant HIV vaccine trials is achievable in Africa

Helminth and other gastrointestinal disorders

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

Deworming

(see also Vitamin A)

Population deworming every 6 months with albendazole in 1 million pre-school children in north India: DEVTA, a cluster-randomised trial.

Awasthi S, Peto R, Read S, Richards SM, Pande V, Bundy D; DEVTA (Deworming and Enhanced Vitamin A) team.

*** Lancet. 2013 Apr 27;381(9876):1478-86. doi: 10.1016/S0140-6736(12)62126-6. Epub 2013 Mar 14.

Source
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Abstract
BACKGROUND:
In north India many pre-school children are underweight, many have intestinal worms, and 2-3% die at ages 1·0-6·0 years. We used the state-wide Integrated Child Development Service (ICDS) infrastructure to help to assess any effects of regular deworming on mortality.

METHODS:
Participants in this cluster-randomised study were children in catchment areas of 8338 ICDS-staffed village child-care centres (under-5 population 1 million) in 72 administrative blocks. **Groups of four neighbouring blocks were cluster-randomly allocated in Oxford between 6-monthly vitamin A (retinol capsule of 200,000 IU retinyl acetate in oil, to be cut and dripped into the child's mouth every 6 months), albendazole (400 mg tablet every 6 months), both, or neither (open control).** Analyses of albendazole effects are by block (36 vs 36 clusters). The study spanned 5 calendar years, with 11 6-monthly mass-treatment days for all children then aged 6-72 months. Annually, one centre per block was randomly selected and visited by a study team 1-5 months after any trial deworming to sample faeces (for presence of worm eggs, reliably assessed only after mid-study), weigh children, and interview caregivers. Separately, all 8338 centres were visited every 6 months to monitor pre-school deaths (100,000 visits, 25,000 deaths at age 1·0-6·0 years [the primary outcome]). This trial is registered at ClinicalTrials.gov, NCT00222547.

FINDINGS:
Estimated compliance with 6-monthly albendazole was 86%. Among 2589 versus 2576 children surveyed during the second half of the study, nematode egg prevalence was 16% versus 36%, and most infection was light. After at least 2 years of treatment, weight at ages 3·0-6·0 years (standardised to age 4·0 years, 50% male) was 12·72 kg albendazole versus 12·68 kg control (difference 0·04 kg, 95% CI -0·14 to 0·21, p=0·66). Comparing the 36 albendazole-allocated versus 36 control blocks in analyses of the primary outcome, deaths per child-care centre at ages 1·0-6·0 years during the 5-year study were 3·00 (SE 0·07) albendazole versus 3·16 (SE 0·09) control, difference 0·16 (SE 0·11, mortality ratio 0·95, 95% CI 0·89 to 1·02, p=0·16),

suggesting absolute risks of dying between ages 1·0 and 6·0 years of roughly 2·5% albendazole versus 2·6% control. No specific cause of death was significantly affected.

INTERPRETATION:
Existing ICDS village staff can be organised to deliver simple pre-school interventions sustainably for many years at low cost, but **regular deworming had little effect on mortality in this lightly infected pre-school population.**

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Comment
This was the largest RCT ever undertaken, involving 2 million pre-school children in India. The results have surprised many, given that the mortality reduction from vitamin A was only 4% with confidence internals from an 11% reduction to a 3% increase, and deworming had no effect on mortality, and surprisingly no effect on growth. This trial has been controversial, not because the results are questionable, the trial was very well conducted and analysed. What it suggests is that estimates of effect of single interventions, (such as the previously estimated 25% reduction in mortality from vitamin A) are often exaggerated. True mortality reductions are more likely to occur when there is health services development and comprehensive approaches to poverty reduction, healthy lifestyles and disease prevention. We have put much store in the role of vitamins and single interventions as magic bullets in reducing child deaths, and it is time to reconsider trhat true development is not as simple as it has been made out to be by much of the global health community.

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.

Cochrane Database Syst Rev. 2012 Nov 14;11:CD000371. doi: 10.1002/14651858.CD000371.pub5.

Source
International Health Group, Liverpool School of Tropical Medicine, Liverpool, UK. David.Taylor-Robinson@liverpool.ac.uk
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. The WHO state this will improve nutritional status, haemoglobin, and cognition and thus will improve health, intellect, and school attendance. Consequently, it is claimed that school performance will improve, child mortality will decline, and economic productivity will increase. Given the important health and societal benefits attributed to this intervention, we sought to determine whether they are based on reliable evidence.

OBJECTIVES:

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

SEARCH METHODS:
In February 2012, we searched the Cochrane Infectious Diseases Group Specialized Register, MEDLINE, EMBASE, LILACS, mRCT, and reference lists, and registers of ongoing and completed trials.

SELECTION CRITERIA:
We selected randomized controlled trials (RCTs) and quasi-RCTs comparing deworming drugs for geohelminth worms with placebo or no treatment in children aged 16 years or less, reporting on weight, haemoglobin, and formal test of intellectual development. In cluster-RCTs treating communities or schools, we also sought data on school attendance, school performance, and mortality. We included trials that included health education with deworming.

DATA COLLECTION AND ANALYSIS:
At least two authors independently assessed the trials, evaluated risk of bias, and extracted data. Continuous data were analysed using the mean difference (MD) with 95% confidence intervals (CI). Where data were missing, we contacted trial authors. We used GRADE to assess evidence quality, and this is reflected in the wording we used: high quality ("deworming improves...."); moderate quality ("deworming probably improves..."); low quality ("deworming may improve...."); and very low quality ("we don't know if deworming improves....").

MAIN RESULTS:
We identified 42 trials, including eight cluster trials, that met the inclusion criteria. Excluding one trial where data are awaited, the 41 trials include 65,168 participants.Screening then treatingFor children known to be infected with worms (by screening), a single dose of deworming drugs may increase weight (0.58 kg, 95% CI 0.40 to 0.76, three trials, 139 participants; low quality evidence) and may increase haemoglobin (0.37 g/dL, 95% CI 0.1 to 0.64, two trials, 108 participants; low quality evidence), but we do not know if there is an effect on cognitive functioning (two trials, very low quality evidence).Single dose deworming for all childrenIn trials treating all children, a single dose of deworming drugs gave mixed effects on weight, with no effects evident in seven trials, but large effects in two (nine trials, 3058 participants, very low quality evidence). The two trials with a positive effect were from the same very high prevalence setting and may not be easily generalised elsewhere. Single dose deworming probably made little or no effect on haemoglobin (mean difference (MD) 0.06 g/dL, 95% CI -0.06 to 0.17, three trials, 1005 participants; moderate evidence), and may have little or no effect on cognition (two trials, low quality evidence).Mulitple dose deworming for all childrenOver the first year of follow up, multiple doses of deworming drugs given to all children may have little or no effect on weight (MD 0.06 kg, 95% CI -0.17 to 0.30; seven trials, 2460 participants; low quality evidence); haemoglobin, (mean 0.01 g/dL lower; 95% CI 0.14 lower to 0.13 higher; four trials, 807 participants; low quality evidence); cognition (three trials, 30,571 participants, low quality evidence); or school attendance (4% higher attendance; 95% CI -6 to 14; two trials, 30,243 participants; low quality evidence);For time periods beyond a year, there were five trials with weight measures. One cluster-RCT of 3712 children in a low prevalence area showed a large effect (average gain of 0.98 kg), whilst the other four trials did not show an effect, including a cluster-RCT of 27,995 children in a moderate prevalence area (five trials, 37,306 participants; low quality evidence). For height, we are uncertain whether there is an effect of deworming (-0.26 cm; 95% CI -0.84 to 0.31, three trials, 6652 participants; very low

quality evidence). Deworming may have little or no effect on haemoglobin (0.00 g/dL, 95%CI -0.08 to 0.08, two trials, 1365 participants, low quality evidence); cognition (two trials, 3720 participants; moderate quality evidence). For school attendance, we are uncertain if there is an effect (mean attendance 5% higher, 95% CI -0.5 to 10.5, approximately 20,000 participants, very low quality evidence).Stratified analysis to seek subgroup effects into low, medium and high helminth endemicity areas did not demonstrate any pattern of effect. In a sensitivity analysis that only included trials with adequate allocation concealment, we detected no significant effects for any primary outcomes.One million children were randomized in a deworming trial from India with mortality as the primary outcome. This was completed in 2005 but the authors have not published the results.

AUTHORS' CONCLUSIONS:
Screening children for intestinal helminths and then treating infected children appears promising, but the evidence base is small. Routine deworming drugs given to school children has been more extensively investigated, and has not shown benefit on weight in most studies, except for substantial weight changes in three trials conducted 15 years ago or more. Two of these trials were carried out in the same high prevalence setting. For haemoglobin and cognition, community deworming seems to have little or no effect, and the evidence in relation to school attendance, and school performance is generally poor, with no obvious or consistent effect. **Our interpretation of this data is that it is probably misleading to justify contemporary deworming programmes based on evidence of consistent benefit on nutrition, haemoglobin, school attendance or school performance as there is simply insufficient reliable information to know whether this is so**.

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Current status of the efficacy and effectiveness of albendazole and mebendazole for the treatment of Ascaris lumbricoides in North-Western Indonesia.

Lubis IN, Pasaribu S, Lubis CP.

Asian Pac J Trop Med. 2012 Aug;5(8):605-9. doi: 10.1016/S1995-7645(12)60125-4.

Source
Department of Paediatrics, School of Medicine, University of North Sumatera, Medan, Indonesia. inkelubis@yahoo.com

Abstract
OBJECTIVE:
To investigate the efficacy and effectiveness of albendazole and mebendazole in the treatment of Ascaris lumbricoides (A. lumbricoides) in the North-Western Indonesia.

METHODS:
229 primary school children who were positive for A. lumbricoides in their stool were recruited in the study. 123 children received single-dose of 400 mg albendazole and 106 children received single-dose 500 mg of mebendazole. After 1 week, their stools were examined for the cure rate (CR) and egg reduction rate (ERR). Egg culture was also performed and observation was made on week-1, -3, -4.

RESULTS:
have shown a non-significant difference in CR 96.7%vs. 100% and ERR of 99.3%vs. 100.0% for albendazole and mebendazole groups respectively (P>0.05). In-vitro egg culture has shown trends of decrease in the percentage of the unfertilized eggs and in ≥ 2 cell eggs in both treatment groups (P<0.05). The embryonated eggs from the albendazole groups has shown an increase from 7.3% on week-1 to 13.8% on week-4, whilst the mebendazole group has shown a constant increase during the whole 4 weeks of culture from 7.5% to 28.3% (P<0.01).

CONCLUSIONS:
No evidence of drug resistance is noted so far from the area of North-Western part of Indonesia. In addition, although both drugs showed incomplete ovicidal effects, single-dose albendazole is better than mebendazole in sterilizing A. lumbricoides eggs.

Effect of deworming vs Iron-Folic acid supplementation plus deworming on growth, hemoglobin level, and physical work capacity of schoolchildren.

Bhoite RM, Iyer UM.

Indian Pediatr. 2012 Aug;49(8):659-61.

Source
Department of Foods and Nutrition, Faculty of Family and Community Sciences, The Maharaja Sayajirao University of Baroda, Vadodara, Gujarat, India.

Abstract
The effect of deworming vs deworming and weekly Iron-Folic acid (IFA) on growth, hemoglobin level, and physical work capacity of children was studied. Children from three rural schools studying from 4th to 7th standard were selected. One set of school children were given deworming tablet (400 mg albendezole) once in six months while the second school children received deworming tablet along with weekly dose of Iron Folic acid Tablet (60 mg of elemental iron and 0.5 mg folic acid). Anthropometric measurements, hemoglobin, and physical work capacity was estimated. No significant change was noticed in the prevalence of malnutrition or physical work capacity of the children. As compared to only deworming, IFA + Deworming showed 17.3% increase in the hemoglobin levels (P<0.001). Thus weekly IFA along with deworming has shown beneficial effect on the hemoglobin levels of the children.

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Health-education package to prevent worm infections in Chinese schoolchildren.

Bieri FA, Gray DJ, Williams GM, Raso G, Li YS, Yuan L, He Y, Li RS, Guo FY, Li SM, McManus DP.

N Engl J Med. 2013 Apr 25;368(17):1603-12. doi: 10.1056/NEJMoa1204885.

Source
Queensland Institute of Medical Research, Herston, Australia.

Abstract
BACKGROUND:
Soil-transmitted helminths are among the most prevalent sources of human infections globally. We determined the effect of an educational package at rural schools in Linxiang City District, Hunan province, China, where these worms are prevalent. The intervention aimed to increase knowledge about soil-transmitted helminths, induce behavioral change, and reduce the rate of infection.

METHODS:
We conducted a single-blind, unmatched, cluster-randomized intervention trial involving 1718 children, 9 to 10 years of age, in 38 schools over the course of 1 school year. Schools were randomly assigned to the health-education package, which included a cartoon video, or to a control package, which involved only the display of a health-education poster. Infection rates, knowledge about soil-transmitted helminths (as assessed with the use of a questionnaire), and hand-washing behavior were assessed before and after the intervention. Albendazole was administered in all the participants at baseline and in all the children who were found to be positive for infection with soil-transmitted helminths at the follow-up assessment at the end of the school year.

RESULTS:
At the follow-up assessment, the mean score for the knowledge of helminths, calculated as a percentage of a total of 43 points on a questionnaire, was 90% higher in the intervention group than in the control group (63.3 vs. 33.4, P<0.001), the percentage of children who washed their hands after using the toilet was nearly twice as high in the intervention group (98.9%, vs. 54.2% in the control group; P<0.001), and the incidence of infection with soil-transmitted helminths was 50% lower in the intervention group than in the control group (4.1% vs. 8.4%, P<0.001). No adverse events were observed immediately (within 15 minutes) after albendazole treatment.

CONCLUSIONS:
The health-education package increased students' knowledge about soil-transmitted helminths and led to a change in behavior and a reduced incidence of infection within 1 school year. (Funded by UBS Optimus Foundation, Zurich, Switzerland; Australian New Zealand Clinical Trials Registry number, ACTRN12610000048088.).

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Impact of anthelminthic treatment in pregnancy and childhood on immunisations, infections and eczema in childhood: a randomised controlled trial.

Ndibazza J, Mpairwe H, Webb EL, Mawa PA, Nampijja M, Muhangi L, Kihembo M, Lule SA, Rutebarika D, Apule B, Akello F, Akurut H, Oduru G, Naniima P, Kizito D, Kizza M, Kizindo R, Tweyongere R, Alcock KJ, Muwanga M, Elliott AM.

PLoS One. 2012;7(12):e50325. doi: 10.1371/journal.pone.0050325. Epub 2012 Dec 7.

Source
Medical Research Council/Uganda Virus Research Institute Uganda Research Unit on AIDS, Entebbe, Uganda.

Abstract
BACKGROUND:
Helminth infections may modulate immune responses to unrelated pathogens and allergens; these effects may commence prenatally. We addressed the hypothesis that anthelminthic treatment in pregnancy and early childhood would improve responses to immunisation and modulate disease incidence in early childhood with both beneficial and detrimental effects.

METHODS AND FINDINGS:
A randomised, double-blind, placebo-controlled trial was conducted in Entebbe, Uganda [ISRCTN32849447]. In three independent randomisations, 2507 pregnant women were allocated to receive single-dose albendazole or placebo, and praziquantel or placebo; 2016 of their offspring were randomised to receive quarterly single-dose albendazole or placebo from age 15 months to 5 years. Primary outcomes were post-immunisation recall responses to BCG and tetanus antigens, and incidence of malaria, diarrhoea, and pneumonia; incidence of eczema was an important secondary outcome. Analysis was by intention-to-treat. Of 2345 live births, 1622 (69%) children remained in follow-up at age 5 years. 68% of mothers at enrolment, and 11% of five-year-olds, had helminth infections. Maternal hookworm and Schistosoma mansoni were effectively treated by albendazole and praziquantel, respectively; and childhood hookworm and Ascaris by quarterly albendazole. Incidence rates of malaria, diarrhoea, pneumonia, and eczema were 34, 65, 10 and 5 per 100 py, respectively. Albendazole during pregnancy caused an increased rate of eczema in the children (HR 1.58 (95% CI 1.15-2.17), p=0.005). Quarterly albendazole during childhood was associated with reduced incidence of clinical malaria (HR 0.85 (95% CI 0.73-0.98), p=0.03). There were no consistent effects of the interventions on any other outcome.

CONCLUSIONS:
Routine use of albendazole in pregnancy may not always be beneficial, even in tropical developing countries. By contrast, regular albendazole treatment in preschool children may have an additional benefit for malaria control where helminths and malaria are co-endemic. Given the low helminth prevalence in our children, the effect of albendazole on malaria is likely to be direct.

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Generalized urticaria induced by the Na-ASP-2 hookworm vaccine: implications for the development of vaccines against helminths.

Diemert DJ, Pinto AG, Freire J, Jariwala A, Santiago H, Hamilton RG, Periago MV, Loukas A, Tribolet L, Mulvenna J, Correa-Oliveira R, Hotez PJ, Bethony JM.

J Allergy Clin Immunol. 2012 Jul;130(1):169-76.e6. doi: 10.1016/j.jaci.2012.04.027. Epub 2012 May 26.

Source
Albert B. Sabin Vaccine Institute, Washington, DC 20037, USA. david.diemert@sabin.org

Abstract
BACKGROUND:
Necator americanus Ancylostoma-secreted protein 2 (Na-ASP-2) is secreted by infective hookworm larvae on entry into human hosts. Vaccination of laboratory animals with recombinant Na-ASP-2 provides significant protection against challenge infections. In endemic areas antibodies to Na-ASP-2 are associated with reduced risk of heavy N americanus infections.

OBJECTIVE:
To assess the safety and immunogenicity of recombinant Na-ASP-2 adjuvanted with Alhydrogel in healthy Brazilian adults previously infected with N americanus.

METHODS:
Participants were randomized to receive Na-ASP-2 or hepatitis B vaccine. Major IgG and IgE epitopes of the Na-ASP-2 molecule were mapped by using sera from these same subjects. Seroepidemiologic studies in adults and children residing in hookworm-endemic areas were conducted to assess the prevalence of IgE responses to Na-ASP-2.

RESULTS:
Vaccination with a single dose of Na-ASP-2 resulted in generalized urticarial reactions in several volunteers. These reactions were associated with pre-existing Na-ASP-2-specific IgE likely induced by previous hookworm infection. Surveys revealed that a significant proportion of the population in hookworm-endemic areas had increased levels of IgE to Na-ASP-2. Epitope mapping demonstrated sites on the Na-ASP-2 molecule that are uniquely or jointly recognized by IgG and IgE antibodies.

CONCLUSION:
Infection with N americanus induces increased levels of total and specific IgE to Na-ASP-2 that result in generalized urticaria on vaccination with recombinant Na-ASP-2. These data advance knowledge of vaccine development for helminths given their propensity to induce strong T(H)2 responses. Study data highlight the important differences between the immune responses to natural helminth infection and to vaccination with a recombinant helminth antigen.

Helicobacter pylori

Eradication of Helicobacter pylori in children in Vietnam in relation to antibiotic resistance.

Nguyen TV, Bengtsson C, Yin L, Nguyen GK, Hoang TT, Phung DC, Sörberg M, Granström M.

Helicobacter. 2012 Aug;17(4):319-25. doi: 10.1111/j.1523-5378.2012.00950.x. Epub 2012 Apr 20.

Source
Department of Pediatrics, Hanoi Medical University and National Hospital of Pediatrics, Hanoi, Vietnam.

Abstract
BACKGROUND:
Low Helicobacter pylori eradication rates are common in pediatric trials especially in developing countries. The aim of the study was to investigate the role of antibiotic resistance, drug dosage, and administration frequency on treatment outcome for children in Vietnam.

MATERIALS AND METHODS:
Antibiotics resistance of H. pylori was analyzed by the Etest in 222 pretreatment isolates from children 3-15 years of age who were originally recruited in a randomized trial with two treatment regiments: lansoprazole with amoxicillin and either clarithromycin (LAC) or metronidazole (LAM) in two weight groups with once- or twice-daily administration. The study design was an observational study embedded in a randomized trial.

RESULTS:
The overall resistance to clarithromycin, metronidazole, and amoxicillin was 50.9%, 65.3%, and 0.5%, respectively. In LAC, eradication was linked to the strains being susceptible to clarithromycin (78.2% vs 29.3%, p = .0001). Twice-daily dosage of proton-pump inhibitor (PPI) and clarithromycin was more effective for eradication than once-daily dosage for resistant strains (50.0% vs 14.7%, p = .004) and tended to be so also for sensitive strains (87.5% vs 65.2%, p = .051). Exact antibiotic dose per body weight resulted in more eradication for resistant strains (45.3% vs 8.0%, p = .006). These differences were less pronounced for the LAM regimen, with twice-daily PPI versus once daily for resistant strains resulting in 69.2% and 50.0% eradication (p = .096), respectively.

CONCLUSIONS:
Helicobacter pylori clarithromycin resistance was unexpectedly high in young children in Vietnam. Clarithromycin resistance was an important cause for eradication treatment failure. Twice-daily administration and exact antibiotic dosing resulted in more eradicated infections when the strains were antibiotic resistant, which has implications for the study design in pediatric H. pylori eradication trials.

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Survey of anaemia and Helicobacter pylori infection in adolescent girls in Suihua, China and enhancement of iron intervention effects by H. pylori eradication.

Xia W, Zhang X, Wang J, Sun C, Wu L.

Br J Nutr. 2012 Jul;108(2):357-62. doi: 10.1017/S0007114511005666. Epub 2011 Oct 18.

Source

Department of Children Health and Hygiene, School of Public Health, Harbin Medical University, Harbin, Heilongjiang Province, People's Republic of China.

Abstract
In the present study, we investigated the prevalence of anaemia and Fe deficiency anaemia (IDA) and explored the relationship between Helicobacter pylori infection and IDA in adolescent girls. A total of 1037 adolescent girls from Suihua, China were enrolled. Hb, serum ferritin (SF), serum transferrin receptor (sTfR) and serum IgG antibodies to H. pylori were measured. Participants with IDA and co-existing H. pylori infection (n 80) who had an intake of >25 mg/d of Fe were assigned randomly to the intervention and control groups. **Patients in the intervention group were administered a 12-week course of oral EDTA-Na-Fe (60 mg Fe/dose, three times a week) and a 2-week course of colloidal bismuth subcitrate, amoxicillin and metronidazole.** Subjects in the control group were administered EDTA-Na-Fe alone. Hb, SF and sTfR were reassessed 3 months after the 12-week regimen ended. Prevalence of anaemia, Fe deficiency (defined as SF < 12·0 μg/l), IDA and H. pylori infection in the population of 1037 was 19.5, 40.4, 17.1 and 31.2 %, respectively. The prevalence of H. pylori infection in the IDA group was 46.9 %, while the non-anaemic group had 28.1 % prevalence. A significant increase in Hb and SF and a decrease in sTfR value were found in the intervention group and the H. pylori-negative group. Findings suggest that IDA is still one of the prominent problems in adolescent girls. There is an association between H. pylori infection and IDA. **Treatment of H. pylori infection is associated with a more rapid response to oral Fe therapy.**

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Schistosomiasis

Performance and safety of praziquantel for treatment of intestinal schistosomiasis in infants and preschool children.

Sousa-Figueiredo JC, Betson M, Atuhaire A, Arinaitwe M, Navaratnam AM, Kabatereine NB, Bickle Q, Stothard JR.

PLoS Negl Trop Dis. 2012;6(10):e1864. doi: 10.1371/journal.pntd.0001864. Epub 2012 Oct 18.

Source
Disease Control Strategy Group, Liverpool School of Tropical Medicine, Liverpool, United Kingdom.

Abstract
BACKGROUND:
In 2012 the WHO formally recognised that infants and preschool children are at significant risk of schistosomiasis and qualify for treatment with praziquantel (PZQ). Targeted surveys determining both the performance and safety of this drug are now needed in endemic areas. We have formally assessed parasitological cure and putative side-effects in a prospective cohort of

Schistosoma mansoni-infected children (aged 5 months-7 years old) in lakeshore settings of Uganda.

METHODOLOGY/PRINCIPAL FINDINGS:
From a total of 369 children found to be egg-patent for intestinal schistosomiasis, 305 were followed-up three to four weeks after PZQ treatment and infection status re-assessed. Separately, a previously tested side-effect questionnaire was employed before and 24 hours after PZQ treatment to assess incidence and amelioration of symptoms in young children and their mothers. While the overall observed parasitological cure was 56.4%, a significant difference was found between a sub-set of children who had a history of multiple PZQ treatments (between one and four in an 18 month period), where cure rate was 41.7%, and those who had never received treatment (cure rate was 77·6%). PZQ proved to be safe, with only mild reported side effects which cleared within a month after treatment. Prevalence of reported symptoms was significantly lower in children than in mothers, and fewer side-effects were reported upon subsequent rounds of PZQ treatment.

CONCLUSION/SIGNIFICANCE:
Our findings show that PZQ treatment of young children resulted in satisfactory cure rates, and marked reduction in egg-output, with only mild and transient reported side-effects. However, the cure rate is clearly lower in younger children and those with history of previous treatment. Cure rate, but not egg reduction rate, was also lower in children with heavier pre-intervention infection intensity. With chemotherapy now recommended as a long-term strategy for disease control in young children, research into optimising the periodicity of targeted treatment strategies is now crucial.

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Efficacy of praziquantel against Schistosoma mekongi and Opisthorchis viverrini: a randomized, single-blinded dose-comparison trial.

Lovis L, Mak TK, Phongluxa K, Ayé Soukhathammavong P, Vonghachack Y, Keiser J, Vounatsou P, Tanner M, Hatz C, Utzinger J, Odermatt P, Akkhavong K.

PLoS Negl Trop Dis. 2012;6(7):e1726. doi: 10.1371/journal.pntd.0001726. Epub 2012 Jul 24.

Source
Laboratory of Parasitology, University of Neuchâtel, Neuchâtel, Switzerland.

Abstract
BACKGROUND:
Schistosomiasis and opisthorchiasis are of public health importance in Southeast Asia. Praziquantel (PZQ) is the drug of choice for morbidity control but few dose comparisons have been made.

METHODOLOGY:
Ninety-three schoolchildren were enrolled in an area of Lao PDR where Schistosoma mekongi and Opisthorchis viverrini coexist for a PZQ dose-comparison trial. Prevalence and intensity of infections were determined by a rigorous diagnostic effort (3 stool specimens, each examined with triplicate Kato-Katz) before and 28-30 days after treatment. Ninety children with full

baseline data were randomized to receive PZQ: the 40 mg/kg standard single dose (n=45) or a 75 mg/kg total dose (50 mg/kg+25 mg/kg, 4 hours apart; n=45). Adverse events were assessed at 3 and 24 hours posttreatment.

PRINCIPAL FINDINGS:
Baseline infection prevalence of S. mekongi and O. viverrini were 87.8% and 98.9%, respectively. S. mekongi cure rates were 75.0% (95% confidence interval (CI): 56.6-88.5%) and 80.8% (95% CI: 60.6-93.4%) for 40 mg/kg and 75 mg/kg PZQ, respectively (P=0.60). O. viverrini cure rates were significantly different at 71.4% (95% CI: 53.4-84.4%) and 96.6% (95% CI: not defined), respectively (P=0.009). Egg reduction rates (ERRs) against O. viverrini were very high for both doses (>99%), but slightly lower for S. mekongi at 40 mg/kg (96.4% vs. 98.1%) and not influenced by increasing diagnostic effort. O. viverrini cure rates would have been overestimated and no statistical difference between doses found if efficacy was based on a minimum sampling effort (single Kato-Katz before and after treatment). Adverse events were common (96%), mainly mild with no significant differences between the two treatment groups.

CONCLUSIONS/SIGNIFICANCE:
Cure rate from the 75 mg/kg PZQ dose was more efficacious than 40 mg/kg against O. viverrini but not against S. mekongi infections, while ERRs were similar for both doses.

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Efficacy of praziquantel syrup versus crushed praziquantel tablets in the treatment of intestinal schistosomiasis in Ugandan preschool children, with observation on compliance and safety.

Navaratnam AM, Sousa-Figueiredo JC, Stothard JR, Kabatereine NB, Fenwick A, Mutumba-Nakalembe MJ.

Trans R Soc Trop Med Hyg. 2012 Jul;106(7):400-7. doi: 10.1016/j.trstmh.2012.03.013. Epub 2012 May 30.

Source
Department of Infectious Disease Epidemiology, Imperial College London, London W2 1PG, UK. amnavaratnam@gmail.com

Abstract
Preschool children (aged ≤5 years) have so far been overlooked by mass treatment campaigns targeting schistosomiasis, even though praziquantel (PZQ) has been shown to be well tolerated and effective within this age group. The WHO provided the Ugandan Ministry of Health with a syrup formulation of PZQ with the aim of assessing its safety and efficacy in comparison with crushed PZQ tablets for the treatment of intestinal schistosomiasis in preschool children. This study included 1144 preschool children randomly assigned to two treatment arms (PZQ syrup or crushed PZQ tablet) regardless of infection status for direct comparison. Diagnosis of intestinal schistosomiasis was assessed using single stool sample, double Kato-Katz smear examinations. Parasitological cure was assessed 3 weeks after treatment. **The observed cure rate was 80.9% for the PZQ syrup arm and 81.7% for the crushed PZQ tablet arm, with egg reduction rates of 86.1% and 89.0%, respectively.** Pre-treatment infection intensity was observed to influence cure rates significantly, with cure rates of 88.6% for light infections, 74.5% for

moderate infections and 67.4% for heavy infections. No significant difference was found in non-compliance between the PZQ syrup (11.1%) and crushed PZQ tablet (14.7%) arms. PZQ syrup and crushed PZQ tablets have very similar efficacies in the treatment of intestinal schistosomiasis in preschool children.

Coeliac disease

Effect of addition of short course of prednisolone to gluten-free diet on mucosal epithelial cell regeneration and apoptosis in celiac disease: a pilot randomized controlled trial.

Shalimar, Das P, Sreenivas V, Datta Gupta S, Panda SK, Makharia GK.

Dig Dis Sci. 2012 Dec;57(12):3116-25. doi: 10.1007/s10620-012-2294-1. Epub 2012 Jun 30.

Source
Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, 110029, India.

Abstract
BACKGROUND:
Identification of adjuvant treatment is necessary for rapid and effective treatment in patients with celiac disease. In a pilot randomized controlled trial, the effect of prednisolone on enterocyte apoptosis and regeneration in celiac disease was investigated.

PATIENTS AND METHODS:
Thirty-three treatment-naïve patients with celiac disease were randomized to either gluten-free diet (GFD, n = 17) or GFD + prednisolone (1 mg/kg for 4 weeks, n = 16). Duodenal biopsies were taken at baseline and at 4 and 8 weeks posttreatment. Six patients with functional dyspepsia were recruited as controls. All these biopsies were stained for markers of intrinsic apoptotic pathway (AIF, H2AX, p53), common apoptotic pathway (CC3, M30), apoptotic inhibitors (XIAP, Bcl2), and epithelial proliferation (Ki-67). Apoptotic (AI) and proliferation indices (PI) were compared.

RESULTS:
At baseline duodenal biopsies, the end apoptotic products H2AX and M30 were significantly increased. In comparison with those treated with GFD alone, after 4 weeks of GFD + prednisolone treatment, some markers of both intrinsic and common apoptotic pathways showed rapid decline. After prednisolone withdrawal, there was overexpression of H2AX, CC3, and p53 in the latter group. In comparison with those treated with only GFD, patients treated with prednisolone showed suppression of mucosal PI, which started rising again after withdrawal of prednisolone.

CONCLUSIONS:
Apoptosis takes place in mucosal epithelium in celiac disease. Addition of short course of prednisolone suppresses apoptosis rapidly. However, it also suppresses epithelial regeneration; hence, if used, it should be withdrawn after an initial short course.

Kidney disease

Randomized Controlled Trial of Enalapril on Decline in Glomerular Filtration Rate and Proteinuria in Children with Chronic Kidney Disease.

Hari P, Sahu J, Sinha A, Pandey RM, Bal CS, Bagga A.

Indian Pediatr. 2013 Mar 5. pii: S097475591300036. [Epub ahead of print]

Source
Departments of Pediatrics, *Biostatistics and #Nuclear Medicine, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India. Correspondence to: Dr Pankaj Hari, Additional Professor, Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110 029, India. pankajhari@hotmail.com.

Abstract
OBJECTIVE:
To evaluate the efficacy of enalapril with no enalapril treatment on decline in glomerular filtration rate and reduction in proteinuria in children with chronic kidney disease (CKD).

Design:
Open label, randomized controlled trial.

Setting:
Pediatric nephrology clinic at a tertiary care referral hospital.

INTERVENTION:
Children with GFR between 15-60 mL/min/1.73 m2 were randomized to receive either enalapril at 0.4 mg/kg /day or no enalapril for 1 year.

OUTCOME MEASURES:
Primary outcomes: Change in GFR using 99mTc-DTPA and urine protein to creatinine ratio. Secondary outcomes included occurrence of composite outcome (30% decline in GFR or end stage renal disease) and systolic and diastolic blood pressure SDS during the study period.

RESULTS:
41 children were randomized into two groups; 20 received enalapril while 21 did not receive enalapril. **During 1 year, GFR decline was not different in enalapril and non enalapril groups(regression coefficient 0.40, 95% CI -4.29 to 5.09, P=0.86).** The mean proteinuria reduction was 65% in the enalapril group, significantly higher than in non-enalapril group; the difference remained significant after adjustment for blood pressure (regression coefficient 198.5, CI 97.5, 299.3; P<0.001). Three (17.6%) patients in enalapril and 7 (36.8%) in non-enalapril group attained the composite outcome. On subgroup analysis, in proteinuric children occurrence of composite outcome was significantly lower with enalapril treatment after adjustment for proteinuria and blood pressure.

CONCLUSIONS:

Enalapril is effective in reducing proteinuria in children with CKD and might be renoprotective in proteinuric CKD

Treatment with tacrolimus and prednisolone is preferable to intravenous cyclophosphamide as the initial therapy for children with steroid-resistant nephrotic syndrome.

Gulati A, Sinha A, Gupta A, Kanitkar M, Sreenivas V, Sharma J, Mantan M, Agarwal I, Dinda AK, Hari P, Bagga A.

Kidney Int. 2012 Nov;82(10):1130-5. doi: 10.1038/ki.2012.238. Epub 2012 Jul 4.

Source
Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India.

Abstract
There are limited data on the relative efficacy and safety of calcineurin inhibitors and alkylating agents for idiopathic steroid-resistant nephrotic syndrome in children. To clarify this, we compared tacrolimus and intravenous cyclophosphamide therapy in a multicenter, randomized, controlled trial of 131 consecutive pediatric patients with minimal change disease, focal segmental glomerulosclerosis, or mesangioproliferative glomerulonephritis, stratified for initial or late steroid resistance. Patients were randomized to receive tacrolimus for 12 months or 6-monthly infusions of intravenous cyclophosphamide with both arms receiving equal amounts of alternate-day prednisolone. The primary outcome of complete or partial remission at 6 months, based on spot urine protein to creatinine ratios, was significantly higher in children receiving tacrolimus compared to cyclophosphamide (hazard ratio 2.64). **Complete remission was significantly higher with tacrolimus (52.4%) than with cyclophosphamide (14.8%).** The secondary outcome of sustained remission or steroid-sensitive relapse of nephrotic syndrome at 12 months was significantly higher with tacrolimus than cyclophosphamide. Treatment withdrawal was higher with cyclophosphamide, chiefly due to systemic infections. Compared to cyclophosphamide, 3 patients required treatment with tacrolimus to achieve 1 additional remission. Thus, tacrolimus and prednisolone are effective, safe, and preferable to cyclophosphamide as the initial therapy for patients with steroid-resistant nephrotic syndrome.

Malaria

(See also Thalassaemia)

Malaria vaccines

A phase 3 trial of RTS,S/AS01 malaria vaccine in African infants.

RTS,S Clinical Trials Partnership, Agnandji ST, Lell B, Fernandes JF, Abossolo BP, Methogo BG, Kabwende AL, Adegnika AA, Mordmüller B, Issifou S, Kremsner PG, Sacarlal J, Aide P, Lanaspa M, Aponte JJ, Machevo S, Acacio S, Bulo H, Sigauque B, Macete E, Alonso P, Abdulla S, Salim N, Minja R, Mpina M, Ahmed S, Ali AM, Mtoro AT, Hamad AS, Mutani P, Tanner M, Tinto H, D'Alessandro U, Sorgho H, Valea I, Bihoun B, Guiraud I, Kaboré B, Sombié O, Guiguemdé RT, Ouédraogo JB, Hamel MJ, Kariuki S, Oneko M, Odero C, Otieno K, Awino N, McMorrow M, Muturi-Kioi V, Laserson KF, Slutsker L, Otieno W, Otieno L, Otsyula N, Gondi S, Otieno A, Owira V, Oguk E, Odongo G, Woods JB, Ogutu B, Njuguna P, Chilengi R, Akoo P, Kerubo C, Maingi C, Lang T, Olotu A, Bejon P, Marsh K, Mwambingu G, Owusu-Agyei S, Asante KP, Osei-Kwakye K, Boahen O, Dosoo D, Asante I, Adjei G, Kwara E, Chandramohan D, Greenwood B, Lusingu J, Gesase S, Malabeja A, Abdul O, Mahende C, Liheluka E, Malle L, Lemnge M, Theander TG, Drakeley C, Ansong D, Agbenyega T, Adjei S, Boateng HO, Rettig T, Bawa J, Sylverken J, Sambian D, Sarfo A, Agyekum A, Martinson F, Hoffman I, Mvalo T, Kamthunzi P, Nkomo R, Tembo T, Tegha G, Tsidya M, Kilembe J, Chawinga C, Ballou WR, Cohen J, Guerra Y, Jongert E, Lapierre D, Leach A, Lievens M, Ofori-Anyinam O, Olivier A, Vekemans J, Carter T, Kaslow D, Leboulleux D, Loucq C, Radford A, Savarese B, Schellenberg D, Sillman M, Vansadia P.

N Engl J Med. 2012 Dec 13;367(24):2284-95. doi: 10.1056/NEJMoa1208394. Epub 2012 Nov 9.

Source

Albert Schweitzer Hospital, Lambaréné, Gabon.

Abstract

BACKGROUND:

The candidate malaria vaccine RTS,S/AS01 reduced episodes of both clinical and severe malaria in children 5 to 17 months of age by approximately 50% in an ongoing phase 3 trial. We studied infants 6 to 12 weeks of age recruited for the same trial.

METHODS:

We administered RTS,S/AS01 or a comparator vaccine to 6537 infants who were 6 to 12 weeks of age at the time of the first vaccination in conjunction with Expanded Program on Immunization (EPI) vaccines in a three-dose monthly schedule. Vaccine efficacy against the first or only episode of clinical malaria during the 12 months after vaccination, a coprimary end point, was analyzed with the use of Cox regression. Vaccine efficacy against all malaria episodes, vaccine efficacy against severe malaria, safety, and immunogenicity were also assessed.

RESULTS:

The incidence of the first or only episode of clinical malaria in the intention-to-treat population during the 14 months after the first dose of vaccine was 0.31 per person-year in the RTS,S/AS01

group and 0.40 per person-year in the control group, for a vaccine efficacy of 30.1% (95% confidence interval [CI], 23.6 to 36.1). Vaccine efficacy in the per-protocol population was 31.3% (97.5% CI, 23.6 to 38.3). Vaccine efficacy against severe malaria was 26.0% (95% CI, -7.4 to 48.6) in the intention-to-treat population and 36.6% (95% CI, 4.6 to 57.7) in the per-protocol population. Serious adverse events occurred with a similar frequency in the two study groups. One month after administration of the third dose of RTS,S/AS01, 99.7% of children were positive for anti-circumsporozoite antibodies, with a geometric mean titer of 209 EU per milliliter (95% CI, 197 to 222).

CONCLUSIONS:
The RTS,S/AS01 vaccine coadministered with EPI vaccines provided modest protection against both clinical and severe malaria in young infants. (Funded by GlaxoSmithKline Biologicals and the PATH Malaria Vaccine Initiative; RTS,S ClinicalTrials.gov number, NCT00866619.).

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Insecticide-treated bed nets

(See also Dengue)

A quasi-experimental evaluation of an interpersonal communication intervention to increase insecticide-treated net use among children in Zambia.

Keating J, Hutchinson P, Miller JM, Bennett A, Larsen DA, Hamainza B, Changufu C, Shiliya N, Eisele TP.

Malar J. 2012 Sep 7;11:313.

Source
Department of Global Health Systems and Development, Tulane University School of Public Health and Tropical Medicine, 1440 Canal Street, Suite 2200, New Orleans, LA 70112, USA. keating@tulane.edu

Abstract
BACKGROUND:
This paper presents results from an **evaluation of the effect of a community health worker (CHW) -based, interpersonal communication campaign (IPC) for increasing insecticide-treated mosquito net (ITN) use among children in Luangwa District, Zambia**, an area with near universal coverage of ITNs and moderate to low malaria parasite prevalence.

METHODS:
A quasi-experimental community randomized control trial was conducted from 2008 to 2010. CHWs were the unit of randomization. Cross-sectional data were collected from houses in both 2008 and 2010 using simple random sampling of a complete household enumeration of the district. A difference-in -differences approach was used to analyse the data.

RESULTS:
ITN use among children <5 years old in households with ≥1 ITN increased overall from 54% in 2008 to 81% in 2010 ($\chi(2) = 96.3$, $p < 0.01$); however, there was no difference in increase between the treatment and control arms in 2010 ($p > 0.05$). ITN use also increased among children five to 14 years old from 37% in 2008 to 68% in 2010. **There was no indication that the CHW-based intervention activities had a significant effect on increasing ITN use in this context, over and above what is already being done to disseminate information on the importance of using an ITN to prevent malaria infection.**

DISCUSSION:
ITN use increased dramatically in the district between 2008 and 2010. It is likely that IPC activities in general may have contributed to the observed increase in ITN use, as the increased observed in this study was far higher than the increase observed between 2008 and 2010 malaria indicator survey (MIS) estimates. Contamination across control communities, coupled with linear settlement patterns and subsequent behavioural norms related to communication in the area, likely contributed to the observed increase in net use and null effect in this study.
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Insecticide-treated plastic sheeting for emergency malaria prevention and shelter among displaced populations: an observational cohort study in a refugee setting in Sierra Leone.

Burns M, Rowland M, N'guessan R, Carneiro I, Beeche A, Ruiz SS, Kamara S, Takken W, Carnevale P, Allan R.

Am J Trop Med Hyg. 2012 Aug;87(2):242-50. doi: 10.4269/ajtmh.2012.11-0744.

Source
Wageningen University, Wageningen, The Netherlands. matt.r.burns75@gmail.com

Abstract
A double-blind phase III malaria prevention trial was conducted in two refugee camps using pre-manufactured insecticide-treated plastic sheeting (ITPS) or untreated polyethylene sheeting (UPS) randomly deployed to defined sectors of each camp. In Largo camp the ITPS or UPS was attached to inner walls and ceilings of shelters, whereas in Tobanda the ITPS or UPS was used to line only the ceiling and roof. In Largo the Plasmodium falciparum incidence rate in children up to 3 years of age who were cleared of parasites and monitored for 8 months was 163/100 person-years under UPS and 63 under ITPS (adjusted odds ratio [AOR] = 0.40, 95% confidence interval [CI] = 0.33-0.47). In Tobanda incidence was 157/100 person-years under UPS and 134 under ITPS (AOR = 0.85, 95% CI = 0.75-0.95). Protective efficacy was 61% under fully lined ITPS and 15% under roof lined ITPS. Anemia rates improved under ITPS in both camps. This novel tool proved to be a convenient, safe, and long-lasting method of malaria control when used as a full shelter lining in an emergency setting.

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ITN protection, MSP1 antibody levels and malaria episodes in young children of rural Burkina Faso.

Kynast-Wolf G, Wakilzadeh W, Coulibaly B, Schnitzler P, Traoré C, Becher H, Müller O.

Acta Trop. 2012 Aug;123(2):117-22. doi: 10.1016/j.actatropica.2012.04.010. Epub 2012 Apr 28.

Source
Institute of Public Health, Ruprecht-Karls-University Heidelberg, Germany. gisela.kynast-wolf@urz.uni-heidelberg.de

Abstract
Malaria blood-stage vaccines are in an early phase of clinical development with MSP1 being a major antigen candidate. There are limited data on the protective efficacy of antibodies against subunits of MSP1 in the malaria endemic areas of sub-Saharan Africa. This prospective cohort study was nested into a large insecticide-treated mosquito net (ITN) trial during which neonates were individually randomised to ITN protection from birth vs. protection from month six onwards in rural Burkina Faso. A sub sample of 120 children from three villages was followed for 10 months with six measurements of MSP1(42) antibodies (ELISA based on recombinant 42kDa fragment) and daily assessment of malaria episodes. Time to the next malaria episode was determined in relation to MSP1(42) antibody titres. MSP1(42) antibody titres were dependent on age, season, ITN-group, number of previous malaria episodes and parasitaemia. There were no significant differences in time until the next malaria episode in children with low compared to children with high MSP1(42) antibody titres at any point in time (101 vs. 97 days in May, p=0.6; 58 vs. 84 days in September, p=0.3; 144 vs. 161 days in March, p=0.5). The findings of this study support the short-lived nature of the humoral immune response in infants of malaria endemic areas. The study provides no evidence for antibodies against a subunit of MSP1 being protective against new malaria episodes in infants.

Other preventative interventions

Combination of malaria vector control interventions in pyrethroid resistance area in Benin: a cluster randomised controlled trial.

Corbel V, Akogbeto M, Damien GB, Djenontin A, Chandre F, Rogier C, Moiroux N, Chabi J, Banganna B, Padonou GG, Henry MC.

Lancet Infect Dis. 2012 Aug;12(8):617-26. doi: 10.1016/S1473-3099(12)70081-6. Epub 2012 Jun 7.

Source
Institut de Recherche pour lDéveloppement, Maladies Infectieuses et Vecteurs, Ecologie, Génétique, Evolution et Contrôle (IRD 224-CNRS 5290 UM1-UM2), Cotonou, Benin, and Montpellier, France. vincent.corbel@ird.fr

Abstract
BACKGROUND:

Malaria control efforts and elimination in Africa are being challenged by the development of resistance of parasites to antimalarial drugs and vectors to insecticides. **We investigated whether the combination of long-lasting insecticidal mosquito nets (LLINs) with indoor residual spraying (IRS) or carbamate-treated plastic sheeting (CTPS) conferred enhanced protection against malaria and better management of pyrethroid-resistance in vectors than did LLINs alone.**

METHODS:
We did a cluster randomised controlled trial in 28 villages in southern Benin, west Africa. Inclusion criteria of the villages were moderate level of pyrethroid resistance in malaria vectors and minimum distance between villages of 2 km. We assessed four malaria vector control interventions: LLIN targeted coverage to pregnant women and children younger than 6 years (TLLIN, reference group), LLIN universal coverage of all sleeping units (ULLIN), TLLIN plus full coverage of carbamate-IRS applied every 8 months (TLLIN+IRS), and ULLIN plus full coverage of CTPS lined up to the upper part of the household walls (ULLIN+CTPS). The interventions were allocated to villages by a block randomisation on the basis of preliminary surveys and children of each village were randomly selected to participate with computer-generated numbers. The primary endpoint was the incidence density rate of Plasmodium falciparum clinical malaria in children younger than 6 years as was analysed by Poisson regression taking into account the effect of age and the sampling design with a generalised estimating equation approach. Clinical and parasitological information were obtained by active case detection of malaria episodes during 12 periods of 6 consecutive days scheduled at six weekly intervals and by cross-sectional surveys of asymptomatic plasmodial infections. Children or study investigators were not masked to study group. This study is registered with Current Controlled Trials, number ISRCTN07404145.

FINDINGS:
Of 58 villages assessed, 28 were randomly assigned to intervention groups. 413-429 children were followed up in each intervention group for 18 months. The clinical incidence density of malaria was not reduced in the children from the ULLIN group (incidence density rate 0·95, 95% CI 0·67-1·36, p=0·79), nor in those from the TLLIN+IRS group (1·32, 0·90-1·93, p=0·15) or from the ULLIN+CTPS group (1·05, 0·75-1·48, p=0·77) compared with the reference group (TLLIN). The same trend was observed with the prevalence and parasite density of asymptomatic infections (non significant regression coefficients).

INTERPRETATION:
No significant benefit for reducing malaria morbidity, infection, and transmission was reported when combining LLIN+IRS or LLIN+CTPS compared with a background of LLIN coverage. These findings are important for national malaria control programmes and should help the design of more cost-effective strategies for malaria control and elimination.

FUNDING:
Ministère Français des Affaires Etrangères et Européennes (FSP project 2006-22), Institut de Recherche pour le Développement, President's Malaria Initiative (PMI) of US Governement.

Rapid diagnostic tests and malaria diagnosis

Effects of malaria volunteer training on coverage and timeliness of diagnosis: a cluster randomized controlled trial in Myanmar.

Ohnmar, Tun-Min, San-Shwe, Than-Win, Chongsuvivatwong V.

Malar J. 2012 Sep 4;11:309. doi: 10.1186/1475-2875-11-309.

Source
Department of Medical Research (Lower Myanmar), Yangon, Myanmar.
ohnmar.hlabaw@gmail.com

Abstract
BACKGROUND:
The use of community volunteers is expected to improve access to accurate diagnosis and timely treatment of malaria, using rapid diagnostic test (RDT) and artemisinin-based combination therapy (ACT). However, empirical data from the field are still limited. **The aim of this study was to assess whether training village volunteers on the use of Paracheck-Pf® RDT and ACT (artemether-lumefantrine (AL)) for Plasmodium falciparum and presumptive treatment with chloroquine for Plasmodium vivax had an effect on the coverage of timely diagnosis and treatment and on mortality in malaria-endemic villages without health staff in Myanmar.**

METHODS:
The study was designed as a cluster randomized controlled trial with a cross-sectional survey at baseline, a monthly visit for six months following the intervention (village volunteers trained and equipped with Paracheck-Pf®) and an endline survey at six months follow-up. Survey data were supplemented by the analysis of logbooks and field-based verbal autopsies. Villages with midwives (MW) in post were used as a third comparison group in the endline survey. Intention-to-treat analysis was used.

RESULTS:
Of 38 villages selected, 21 were randomly assigned to the intervention (two villages failed to participate) and 17 to the comparison group. The two groups had comparable baseline statistics. The blood tests provided by volunteers every month declined over time from 279 tests to 41 but not in MW group in 18 villages (from 326 to 180). **In the endline survey, among interviewed subjects (268 intervention, 287 in comparison, 313 in MW), the coverage of RDT was low in all groups** (14.9%, SE 2.4% in intervention; 5.7%, SE 1.7% in comparison; 21.4%, SE 2.6% in MW) although the intervention (OR 3.2, 95% CI 1.5-6.7) and MW (OR 5.4, 95% CI 2.6-11.0) were more likely to receive a blood test. Mean (SE) of blood tests after onset of fever in days was delayed (intervention 3.6 (0.3); comparison 4.8 (1.3); MW 3.2 (0.4)). Malaria mortality rates per 100,000 populations in a year were not significantly different (intervention 130 SE 37; comparison 119 SE 34; MW 50 SE 18). None of the dead cases had consulted volunteers.

CONCLUSIONS:
The results show that implementing volunteer programmes to improve the coverage of accurate and timely diagnosis with RDT and early treatment may be beneficial but the timeliness of detection and sustainability must be improved.

Treatment of uncomplicated malaria

Home- or community-based programmes for treating malaria.

Okwundu CI, Nagpal S, Musekiwa A, Sinclair D.

Cochrane Database Syst Rev. 2013 May 31;5:CD009527. doi: 10.1002/14651858.CD009527.pub2.

Source
Centre for Evidence-based Health Care, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, South Africa.

Abstract
BACKGROUND:
Malaria is an important cause of morbidity and mortality, in particular among children and pregnant women in sub-Saharan Africa. Prompt access to diagnosis and treatment with effective antimalarial drugs is a central component of the World Health Organization's (WHO) strategy for malaria control. Home- or community-based programmes for managing malaria are one strategy that has been proposed to overcome the geographical barrier to malaria treatment.

OBJECTIVES:
To evaluate home- and community-based management strategies for treating malaria.
SEARCH METHODS:
We searched the Cochrane Central Register of Controlled Trials published in The Cochrane Library; MEDLINE; EMBASE; Science Citation Index; PsycINFO/LIT; CINAHL; WHO clinical trial registry platform; and the metaRegister of Controlled Trials up to September 2012.

SELECTION CRITERIA:
Randomized controlled trials (RCTs) and non-RCTs that evaluated the effects of a home- or community-based programme for treating malaria in a malaria endemic setting.

DATA COLLECTION AND ANALYSIS:
Two authors independently screened and selected studies, extracted data, and assessed the risk of bias. Where possible the effects of interventions are compared using risk ratios (RR), and presented with 95% confidence intervals (CI). The quality of the evidence was assessed using the GRADE approach.

MAIN RESULTS:
We identified 10 trials that met the inclusion criteria. The interventions involved brief training of basic-level health workers or mothers, and most provided the antimalarial for free or at a highly subsidized cost. In eight of the studies, fevers were treated presumptively without parasitological confirmation with microscopy or a rapid diagnostic test (RDT). Two studies trained community health workers to use RDTs as a component of community management of fever. Home- or community-based strategies probably increase the number of people with fever who receive an appropriate antimalarial within 24 hours (RR 2.27, 95% CI 1.79 to 2.88 in one trial; RR 9.79, 95% CI 6.87 to 13.95 in a second trial; 3099 participants, moderate quality evidence). They may also reduce all-cause mortality, but to date this has only been demonstrated in rural Ethiopia (RR 0.58, 95% CI 0.44 to 0.77, one trial, 13,677 participants, moderate quality evidence).Hospital admissions in children were reported in one small trial from urban Uganda,

with no effect detected (437 participants, very low quality evidence). No studies reported on severe malaria. For parasitaemia prevalence, the study from urban Uganda demonstrated a reduction in community parasite prevalence (RR 0.22, 95% CI 0.08 to 0.64, 365 participants), but a second study in rural Burkina Faso did not (1006 participants). Home- or community-based programmes may have little or no effect on the prevalence of anaemia (three trials, 3612 participants, low quality evidence). None of the included studies reported on adverse effects of using home- or community-based programmes for treating malaria.In two studies which trained community health workers to only prescribe antimalarials after a positive RDT, prescriptions of antimalarials were reduced compared to the control group where community health workers used clinical diagnosis (RR 0.39, 95% CI 0.18 to 0.84, two trials, 5944 participants, moderate quality evidence). In these two studies, mortality and hospitalizations remained very low in both groups despite the lower use of antimalarials (two trials, 5977 participants, low quality evidence).

AUTHORS' CONCLUSIONS:
Home- or community-based interventions which provide antimalarial drugs free of charge probably improve prompt access to antimalarials, and there is moderate quality evidence from rural Ethiopia that they may impact on childhood mortality when implemented in appropriate settings. **Programmes which treat all fevers presumptively with antimalarials lead to overuse antimalarials, and potentially undertreat other causes of fever such as pneumonia.** Incorporating RDT diagnosis into home- or community-based programmes for malaria may help to reduce this overuse of antimalarials, and has been shown to be safe under trial conditions.

Is home management of fevers a cost-effective way of reducing under-five mortality in Africa? The case of a rural Ghanaian District.

Nonvignon J, Chinbuah MA, Gyapong M, Abbey M, Awini E, Gyapong JO, Aikins M.

Trop Med Int Health. 2012 Aug;17(8):951-7. doi: 10.1111/j.1365-3156.2012.03018.x. Epub 2012 May 30.

Source
School of Public Health, College of Health Sciences, University of Ghana, Legon, Accra, Ghana.

Abstract
OBJECTIVE:
To assess the cost-effectiveness of two strategies of home management of under-five fevers in Ghana - treatment using antimalarials only (artesunate-amodiaquine - AAQ) and combined treatment using antimalarials and antibiotics (artesunate-amodiaquine plus amoxicillin - AAQ + AMX).

METHODS:
We assessed the costs and cost-effectiveness of AAQ and AAQ + AMX compared with a control receiving standard care. Data were collected as part of a cluster randomised controlled trial with a step-wedged design. Approximately, 12,000 children aged 2-59 months in Dangme West District in southern Ghana were covered. Community health workers delivered the interventions. Costs were analysed from societal perspective, using anaemia cases averted,

under-five deaths averted and disability-adjusted life years (DALYs) averted as effectiveness measures.

RESULTS:
Total economic costs for the interventions were US$ 204,394.72 (AAQ) and US$ 260,931.49 (AAQ + AMX). Recurrent costs constituted 89% and 90% of the total direct costs of AAQ and AAQ + AMX, respectively. Deaths averted were 79.1 (AAQ) and 79.9 (AAQ + AMX), with DALYs averted being 2264.79 (AAQ) and 2284.57 (AAQ + AMX). The results show that cost per anaemia case averted were US$ 150.18 (AAQ) and US$ 227.49 (AAQ + AMX) and cost per death averted was US$ 2585.58 for AAQ and US$ 3272.20 for AAQ + AMX. Cost per DALY averted were US$ 90.25 (AAQ) and US$ 114.21 (AAQ + AMX).

CONCLUSION:
Both AAQ and AAQ + AMX approaches were cost-effective, each averting one DALY at less than the standard US$ 150 threshold recommended by the World Health Organisation. However, AAQ was more cost-effective. Home management of under-five fevers in rural settings is cost-effective in reducing under-five mortality.

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Repeated artemisinin-based combination therapies in a malaria hyperendemic area of Mali: efficacy, safety, and public health impact.

Sagara I, Fofana B, Gaudart J, Sidibe B, Togo A, Toure S, Sanogo K, Dembele D, Dicko A, Giorgi R, Doumbo OK, Djimde AA.

Am J Trop Med Hyg. 2012 Jul;87(1):50-6. doi: 10.4269/ajtmh.2012.11-0649.

Source
Malaria Research and Training Center, Department of Epidemiology of Parasitic Diseases, Faculty of Medicine, Pharmacy and Odonto-Stomatology, University of Bamako, Bamako, Mali. isagara@icermali.org

Abstract
Artemisinin-based combination therapies (ACTs) are the first-line treatment of uncomplicated malaria. The public health benefit and safety of repeated administration of a given ACT are poorly studied. We conducted a randomized trial comparing artemether-lumefantrine, artesunate plus amodiaquine (AS+AQ) and artesunate plus sulfadoxine-pyrimethamine (AS+SP) in patients 6 months of age and older with uncomplicated malaria in Mali from July 2005 to July 2007. The patient received the same initial treatment of each subsequent uncomplicated malaria episode except for treatment failures where quinine was used. Overall, 780 patients were included. **Patients in the AS+AQ and AS+SP arms had significantly less risk of having malaria episodes; risk ratio (RR) = 0.84 (P = 0.002) and RR = 0.80 (P = 0.001), respectively**. The treatment efficacy was similar and above 95% in all arms. Although all drugs were highly efficacious and well tolerated, AS+AQ and AS+SP were associated with less episodes of malaria.

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Current status of artemisinin-resistant falciparum malaria in South Asia: a randomized controlled artesunate monotherapy trial in Bangladesh.

Starzengruber P, Swoboda P, Fuehrer HP, Khan WA, Hofecker V, Siedl A, Fally M, Graf O, Teja-Isavadharm P, Haque R, Ringwald P, Noedl H.

PLoS One. 2012;7(12):e52236. doi: 10.1371/journal.pone.0052236. Epub 2012 Dec 18.

Source
Institute of Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Vienna, Austria.

Abstract
OBJECTIVE:
Recent reports indicate that first cases of genuine artemisinin resistance have already emerged along the Thai-Cambodian border. The main objective of this trial was to track the potential emergence of artemisinin resistance in Bangladesh, which in terms of drug resistance forms a gateway to the Indian subcontinent.

METHODS:
We conducted an open-label, randomized, controlled 42-day clinical trial in Southeastern Bangladesh to investigate the potential spread of clinical artemisinin resistance from Southeast Asia. A total of 126 uncomplicated falciparum malaria patients were randomized to one of 3 treatment arms (artesunate monotherapy with 2 or 4 mg/kg/day once daily or quinine plus doxycycline TID for 7 days). Only cases fulfilling a stringent set of criteria were considered as being artemisinin-resistant.

FINDINGS:
The 28-day and 42-day cure rates in the artesunate monotherapy (2 and 4 mg/kg) and quinine/doxycyline arms were 97.8% (95% confidence interval, CI: 87.8-99.8%), 100% (95% CI: 91.1-100%), and 100% (95% CI: 83.4-100%), respectively. One case of re-infection was seen in the artesunate high dose arm, and a single case of recrudescence was observed in the low dose group on day 26. No differences in median parasite and fever clearance times were found between the 2 artesunate arms (29.8 h and 17.9 h vs. 29.5 h and 19.1 h). Not a single case fulfilled our criteria of artemisinin resistance. Parasite clearance times were considerably shorter and ex vivo results indicate significantly higher susceptibility (50% inhibitory concentration for dihydroartemisinin was 1.10 nM; 95% CI: 0.95-1.28 nM) to artemisinins as compared to SE-Asia.

CONCLUSION:
There is currently no indication that artemisinin resistance has reached Bangladesh. However, the fact that resistance has recently been reported from nearby Myanmar indicates an urgent need for close monitoring of artemisinin resistance in the region.

In vivo susceptibility of Plasmodium falciparum to artesunate in Binh Phuoc Province, Vietnam.

Tran TH, Nguyen TT, Nguyen HP, Boni MF, Ngo VT, Nguyen TN, Le HT, Cao QT, Pham VT, Phung DT, Le TL, Le TD, Merson L, Dolecek C, Stepniewska K, Ringwald P, White NJ, Farrar J, Wolbers M.

Malar J. 2012 Oct 26;11:355. doi: 10.1186/1475-2875-11-355.

Source
Wellcome Trust Major Overseas Programme (MOP), Oxford University Clinical Research Unit **(OUCRU), Ho Chi Minh City, Vietnam. hientt@oucru.org**

Abstract
BACKGROUND:
By 2009, there were worrying signs from western Cambodia that parasitological responses to artesunate-containing treatment regimens for uncomplicated Plasmodium falciparum malaria were slower than elsewhere which suggested the emergence of artemisinin resistance. Vietnam shares a long land border with Cambodia with a large number of migrants crossing it on a daily basis. Therefore, there is an urgent need to investigate whether there is any evidence of a change in the parasitological response to the artemisinin derivatives in Vietnam.

METHODS:
From August 2010 to May 2011, a randomized controlled clinical trial in uncomplicated falciparum malaria was conducted to compare two doses of artesunate (AS) (2mg/kg/day versus 4 mg/kg/day for three days) followed by dihydroartemisinin-piperaquine (DHA-PPQ) and a control arm of DHA-PPQ. The goal was characterization of the current efficacy of artesunate in southern Vietnam. The primary endpoint of this study was the parasite clearance half-life; secondary endpoints included the parasite reduction ratios at 24 and 48 hours and the parasite clearance time.

RESULTS:
166 patients were recruited into the study. The median parasite clearance half-lives were 3.54 (AS 2mg/kg), 2.72 (AS 4mg/kg), and 2.98 hours (DHA-PPQ) (p=0.19). The median parasite-reduction ratio at 24 hours was 48 in the AS 2mg/kg group compared with 212 and 113 in the other two groups, respectively (p=0.02). The proportions of patients with a parasite clearance time of >72 hours for AS 2mg/kg, AS 4mg/kg and DHA-PPQ were 27%, 27%, and 22%, respectively. Early treatment failure occurred in two (4%) and late clinical failure occurred in one (2%) of the 55 patients in the AS 2mg/kg group, as compared with none in the other two study arms. The PCR-corrected adequate clinical and parasitological response (APCR) rates in the three groups were 94%, 100%, and 100% (p=0.04).

CONCLUSIONS:
This study demonstrated faster P. falciparum parasite clearance in southern Vietnam than in western Cambodia but slower clearance in comparison with historical data from Vietnam. Further studies to determine whether this represents the emergence of artemisinin resistance in this area are needed. Currently, the therapeutic response to DHA-PPQ remains satisfactory in southern Vietnam.

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A randomized clinical trial comparing the effectiveness and tolerability of artemisinine-naphthoquine (Arco®) and artemether-lumefantrine (Coartem®) in the treatment of uncomplicated malaria in Benin

Kinde-Gazard D, Ogouyèmi-Hounto A, Capo-Chichi L, Gbaguidi J, Massougbodji A.

Bull Soc Pathol Exot. 2012 Aug;105(3):208-14. doi: 10.1007/s13149-012-0211-7. Epub 2012 Feb 11.

Abstract
The Ministry of Health recommended in Benin, since 2004, artemisinin-based combination, artemether-lumtefantrine (Coartem®), therapy for the treatment of uncomplicated malaria. To resolve the difficulties related to observance, we are interested in a new combination, artemisinin-naphthoquine (Arco®). A study was conducted to assess and compare the efficacy and tolerability of the fixed combination artemisinin (125 mg)-naphthoquine (50 mg), a single-dose drug, administered one day versus artemether (20 mg)-lumefantrine (120 mg).**The clinical assessment was a single-blinded, two-arm, randomized trial comparing Arco® combination as a single-dose regimen and three-day regimen of Coartem® for the treatment of uncomplicated falciparum malaria, from july to october 2008 and may to september 2009, with 28 days of follow-up in children.** PCR genotyping was used to classify re-infection or recrudescence. The primary outcome measures for efficacy were cure rates on days 3, 7, 14, 21 and 28. Secondary outcomes included parasite clearance time and fever clearance time. The main outcome measures for safety were incidences of post-treatment clinical and laboratory adverse events. A total of 174 patients (84 in Arco® group and 90 in Coartem® group) were evaluated for clinical and parasitological outcomes. **The cure rate was 98.8% for Arco® and 100% for Coartem® on day 28, with no statistically significant difference. Fever clearance was obtained within 24 hours in both groups. The parasite clearance is obtained at 48 hours in Arco® group and at 60 hours in Coartem® group.** Both treatments were well tolerated without major side effects. This study therefore concluded that the combination of artemisinin-naphthoquine is as effective and well tolerated as the combination artemether-lumefantrine in the treatment of uncomplicated malaria in Benin children. This medication administered in single dose is therapy of choice to reduce compliance problems during malaria treatment and also to facilitate community-based care of malaria.

Glucose-6-phosphate dehydrogenase deficiency, chlorproguanil-dapsone with artesunate and post-treatment haemolysis in African children treated for uncomplicated malaria.

Van Malderen C, Van Geertruyden JP, Machevo S, González R, Bassat Q, Talisuna A, Yeka A, Nabasumba C, Piola P, Daniel A, Turyakira E, Forret P, Van Overmeir C, van Loen H, Robert A, D' Alessandro U.

Malar J. 2012 Jul 10;11:139. doi: 10.1186/1475-2875-11-139.

Source
Faculté de pharmacie et des sciences biomédicales, Université catholique de Louvain, Brussels, Belgium. carine.vanmalderen@uclouvain.be

Abstract
BACKGROUND:
Malaria is a leading cause of mortality, particularly in sub-Saharan African children. Prompt and efficacious treatment is important as patients may progress within a few hours to severe and possibly fatal disease. **Chlorproguanil-dapsone-artesunate (CDA) was a promising artemisinin-based combination therapy (ACT), but its development was prematurely stopped because of safety concerns secondary to its associated risk of haemolytic anaemia in glucose-6-phosphate dehydrogenase (G6PD)-deficient individuals.** The objective of the study was to assess whether CDA treatment and G6PD deficiency are risk factors for a post-treatment haemoglobin drop in African children<5 years of age with uncomplicated malaria.

METHODS:
This case-control study was performed in the context of a larger multicentre randomized clinical trial comparing safety and efficacy of four different ACT in children with uncomplicated malaria. Children, who after treatment experienced a haemoglobin drop≥2 g/dl (cases) within the first four days (days 0, 1, 2, and 3), were compared with those without an Hb drop (controls). Cases and controls were matched for study site, sex, age and baseline haemoglobin measurements. Data were analysed using a conditional logistic regression model.

RESULTS:
G6PD deficiency prevalence, homo- or hemizygous, was 8.5% (10/117) in cases and 6.8% (16/234) in controls (p=0.56). The risk of a Hb drop≥2 g/dl was not associated with either G6PD deficiency (adjusted odds ratio (AOR): 0.81; p=0.76) or CDA treatment (AOR: 1.28; p=0.37) alone. However, patients having both risk factors tended to have higher odds (AOR: 11.13; p=0.25) of experiencing a Hb drop≥2 g/dl within the first four days after treatment, however this finding was not statistically significant, mainly because G6PD deficient patients treated with CDA were very few. In non-G6PD deficient individuals, the proportion of cases was similar between treatment groups while in G6PD-deficient individuals, haemolytic anaemia occurred more frequently in children treated with CDA (56%) than in those treated with other ACT (29%), though the difference was not significant (p=0.49).

CONCLUSION:
The use of CDA for treating uncomplicated malaria may increase the risk of haemolytic anaemia in G6PD-deficient children.

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Multicentre study evaluating the non-inferiority of the new paediatric formulation of artesunate/amodiaquine versus artemether/lumefantrine for the management of uncomplicated Plasmodium falciparum malaria in children in Cameroon, Ivory Coast and Senegal.

Faye B, Kuété T, Kiki-Barro CP, Tine RC, Nkoa T, Ndiaye JL, Kakpo CA, Sylla K, El Menan H, Gaye O, Faye O, Same-Ekobo A, Moussa K.

Malar J. 2012 Dec 27;11:433. doi: 10.1186/1475-2875-11-433.

Source
Service de Parasitologie-Mycologie, Faculté de Médecine, Université Cheikh Anta Diop, Dakar Fann, Dakar, BP 5005, Sénégal. bfaye67@yahoo.fr

Abstract
BACKGROUND:
This multicentre study was carried out in Cameroon, Ivory Coast and Senegal to evaluate the non-inferiority of the new paediatric formulation of artesunate/amodiaquine (AS+AQ)(Camoquin-Plus Paediatric®) in suspension form versus artemether/lumefantrine (AL)(Coartem®) in the management of African children with uncomplicated falciparum malaria.

METHODS:
It was an open randomized trial including children aged between 7 months and 7 years. The endpoints were Adequate Clinical and Parasitological Response (ACPR) at day 28, the clinical and biological tolerability. Statistical analyses were done in Intention To Treat (ITT) and in Per protocol (PP).

RESULTS:
At the end of the study 481 patients were enrolled in the three countries (249 in the AS+AQ arm and 232 in the AL arm). ACRP in ITT after PCR correction did not show any statistical difference between the two groups with 97.6% for AS+AQ versus 94.8% for AL. In the PP analysis, the corrected ACRP were respectively 98.7% and 96.9% for the two regimens. The clinical tolerance was good without significant difference. Anaemia was significantly higher at D7 in the two groups compared to D0.

CONCLUSION:
This study demonstrates the non-inferiority of AS+AQ versus AL, its efficacy and tolerance in the management of uncomplicated Plasmodium falciparum malaria in African children.

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The effects of ACT treatment and TS prophylaxis on Plasmodium falciparum gametocytemia in a cohort of young Ugandan children.

Kakuru A, Jagannathan P, Arinaitwe E, Wanzira H, Muhindo M, Bigira V, Osilo E, Homsy J, Kamya MR, Tappero JW, Dorsey G.

Am J Trop Med Hyg. 2013 Apr;88(4):736-43. doi: 10.4269/ajtmh.12-0654. Epub 2013 Feb 4

Source
Infectious Diseases Research Collaboration, Kampala, Uganda. abelkakuru@gmail.com

Abstract
Artemisinin-based combination therapies (ACTs) and trimethoprim-sulfamethoxazole (TS) prophylaxis are important tools for malaria control, but there are concerns about their effect on gametocytes, the stage of the parasite responsible for transmission. We conducted a longitudinal clinical trial in a cohort of HIV-infected and uninfected children living in an area of high

malaria transmission intensity in Uganda. Study participants were randomized to artemether-lumefantrine (AL) or dihydroartemisinin-piperaquine (DP) for all treatments of uncomplicated malaria (N = 4,380) as well as TS prophylaxis for different durations. The risks of gametocytemia detected by microscopy in the 28 days after antimalarial therapy were compared using multivariate analyses. The risk of gametocyte detection was significantly higher in patients treated with DP compared with AL (adjusted relative risk = 1.85, P < 0.001) and among children prescribed TS prophylaxis (adjusted relative risk = 1.76, P < 0.001). The risk of gametocytemia and its potential for increasing transmission should be considered when evaluating different ACTs and TS prophylaxis for malaria control.

Treatment of severe or complicated malaria

The effect of blood storage age on treatment of lactic acidosis by transfusion in children with severe malarial anaemia: a pilot, randomized, controlled trial.

Dhabangi A, Mworozi E, Lubega IR, Cserti-Gazdewich CM, Maganda A, Dzik WH.

Malar J. 2013 Feb 6;12:55. doi: 10.1186/1475-2875-12-55.

Source
Child Health and Development Centre, Makerere University, Kampala, Uganda. adhabangi@gmail.com

Abstract
BACKGROUND:
Severe malarial anaemia requiring blood transfusion is a life-threatening condition affecting millions of children in sub-Saharan Africa. Up to 40% of children with severe malarial anaemia have associated lactic acidosis. Lactic acidosis in these children is strongly associated with fatal outcomes and is corrected by blood transfusion. However, it is not known whether the storage age of blood for transfusion affects resolution of lactic acidosis. The objective of this pilot study was to evaluate the effect of blood storage age on resolution of lactic acidosis in children with severe malarial anaemia and demonstrate feasibility of conducting a large trial.

METHODS:
Children aged six to 59 months admitted to Acute Care Unit of Mulago Hospital (Kampala, Uganda) with severe malarial anaemia (haemoglobin ≤ 5 g/dL) and lactic acidosis (blood lactate ≥5 mmol/L), were randomly assigned to receive either blood of short storage age (one to 10 days) or long storage age (21-35 days) by gravity infusion. Seventy-four patients were enrolled and randomized to two equal-sized study arms. Physiological measurements, including blood lactate, oxygen saturation, haemoglobin, and vital signs, were taken at baseline, during and after transfusion. The primary outcome variable was the proportion of children whose lactic acidosis resolved by four hours after transfusion.

RESULTS:

Thirty-four of 37 (92%) of the children in the short storage treatment arm compared to 30/37 (81%) in the long storage arm achieved a blood lactate <5 mmol/L by four hours post transfusion (p value = 0.308). The mean time to lactic acidosis resolution was 2.65 hours (95% CI; 2.25-3.05) in the short storage arm, compared to 3.35 hours (95% CI; 2.60-4.10) in the long storage arm (p value = 0.264).

CONCLUSION:
Pilot data suggest that among children with severe malarial anaemia and lactic acidosis transfused with packed red blood cells, the storage age of blood does not affect resolution of lactic acidosis. The results support a larger and well-powered study that is under way.

TRIAL REGISTRATION:

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Treatment of vivax malaria

Relapses contribute significantly to the risk of Plasmodium vivax infection and disease in Papua New Guinean children 1-5 years of age.

Betuela I, Rosanas-Urgell A, Kiniboro B, Stanisic DI, Samol L, de Lazzari E, Del Portillo HA, Siba P, Alonso PL, Bassat Q, Mueller I.

J Infect Dis. 2012 Dec 1;206(11):1771-80. doi: 10.1093/infdis/jis580. Epub 2012 Sep 10.

Source
Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea.

Abstract
BACKGROUND:
Plasmodium vivax forms long-lasting hypnozoites in the liver. How much they contribute to the burden of P. vivax malaria in children living in highly endemic areas is unknown.

METHODS:
In this study, **433 Papua New Guinean children aged 1-5 years were Randomized to receive artesunate (7 days) plus primaquine (14 days), artesunate alone or no treatment and followed up actively for recurrent Plasmodium infections and disease for 40 weeks.**

RESULTS:
Treatment with artesunate-primaquine reduced the risk of P. vivax episodes by 28% (P = .042) and 33% (P = .015) compared with the artesunate and control arms, respectively. A significant reduction was observed only in the first 3 months of follow-up (artesunate-primaquine vs control, -58% [P = .004]; artesunate-primaquine vs artesunate, -49% [P = .031]) with little difference thereafter. Primaquine treatment also reduced the risk of quantitative real-time polymerase chain reaction- and light microscopy-positive P. vivax reinfections by 44% (P < .001) and 67% (P < .001), respectively. Whereas primaquine treatment did not change the risk

of reinfection with Plasmodium falciparum, fewer P. falciparum clinical episodes were observed in the artesunate-primaquine arm.

CONCLUSIONS:
Hypnozoites are an important source of P. vivax infection and contribute substantially to the high burden of P. vivax disease observed in young Papua New Guinean children. **Even in highly endemic areas with a high risk of reinfection, antihypnozoite treatment should be given to all cases with parasitologically confirmed P. vivax infections.**

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Comment
All children in this trial were tested for G6PD deficiency before enrolment. Primaquine only reduced the incidence of low-density P. vivax infections, not high-intensity infections.

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)

Effectiveness of Indigenous Ready-to-Use Therapeutic Food in Community-based Management of Uncomplicated Severe Acute Malnutrition: a Randomized Controlled Trial from India.

Shewade HD, Patro BK, Bharti B, Soundappan K, Kaur A, Taneja N.

J Trop Pediatr. 2013 Jun 10. [Epub ahead of print]

Source
Department of Community Medicine, School of Public Health, PGIMER, Chandigarh 160012. India.

Abstract
A randomized controlled trial was conducted in Chandigarh, India (2011), to determine the effectiveness of indigenous ready-to-use therapeutic food (RUTF) in community-based management of uncomplicated severe acute malnutrition (SAM). Intervention was through outpatient therapeutic program site (OTP). Study and control group children (6 months-5 years) were followed up weekly for 12 weeks, in OTP and at home. All children received supplementary nutrition through anganwadis under integrated child development scheme. **Study children, in addition, received therapeutic dose of RUTF in OTP. Primary outcome, 115% of baseline weight, was attained in 6 of 13 (46.2%) and 1 of 13 (7.7%) children among study and control group, respectively [odds ratio: 10.28, 95% confidence interval (CI): 1.02-103.95].** Compared with control group, addition of RUTF in study group resulted in average additional increase in weight by 13 g/kg of baseline weight/week/child (95% CI: 2-23). Indigenous RUTF was effective in community-based management of uncomplicated SAM.

KEYWORDS:
community-based management, ready-to-use therapeutic food (RUTF), severe acute malnutrition (SAM)

Locally-Prepared Ready-to-Use Therapeutic Food for Children with Severe Acute Malnutrition: A Controlled Trial.

Thakur GS, Singh HP, Patel C.

Indian Pediatr. 2013 Mar 8;50(3):295-9. Epub 2012 Oct 5.

Source
Department of Pediatrics, Gandhi Memorial Hospital and SS Medical College, Rewa, MP, India. Correspondence to: Dr Govindsingh P Thakur, Kochar ward, Hinganghat, Wardha, Maharashtra, 442301, India. gowin1234@gmail.com.
Abstract

OBJECTIVE:
To compare the efficacy of locally-prepared ready-to-use therapeutic food (LRUTF) and locally-prepared F100 diet in promoting weight-gain in children with severe acute malnutrition during rehabilitation phase in hospital.

STUDY DESIGN:
Non-randomized Controlled trial.

SETTING:
Pediatric ward of tertiary care public hospital in Central India.
STUDY PERIOD:
1 October, 2009 to 30th May, 2010.
SUBJECTS:
Children aged 6 to 60 months, diagnosed as severe acute malnutrition and hospitalized during study period.

INTERVENTION:
Random group allocation followed for selection of intervention and control cohorts. The control cohort enrolled during October 1, 2009 to January 31, 2010 received F100 while the intervention cohort enrolled during 1 February to 15 May 2010 received LRUTF. Subjects receiving either of the two therapeutic foods were temporally separated to minimize the spillover effect. The study subjects and the technician delegated for measuring weight was blinded for type of intervention. PRIMARY OUTCOME VARIABLE: Rate of weight-gain/kg/day. RESUltS: There were 49 subjects in each group. Both groups were comparable. **Rate of weight-gain was found to be (9.59±3.39 g/kg/d) in LRUTF group and (5.41±1.05 g/kg/d) in locally prepared F100 group.** Significant difference in rate of weight gain was observed in LRUTF group (P<0.0001; 95% CI 3.17-5.19). No serious adverse effect was observed with use of LRUTF.

CONCLUSION:
LRUTF promotes more rapid weight-gain when compared with F100 in patients with severe acute malnutrition during rehabilitation phase

Treatment of moderate acute malnutrition with ready-to-use supplementary food results in higher overall recovery rates compared with a corn-soya blend in children in southern Ethiopia: an operations research trial.

Karakochuk C, van den Briel T, Stephens D, Zlotkin S.

Am J Clin Nutr. 2012 Oct;96(4):911-6. Epub 2012 Sep 5.

Source
Department of Nutritional Sciences and the Dalla Lana School of Public Health, University of Toronto, Toronto, Canada.

Abstract
BACKGROUND:

Randomised trials in child health in developing countries 2012-13

Moderate and severe acute malnutrition affects 13% of children <5 y of age worldwide. Severe acute malnutrition affects fewer children but is associated with higher rates of mortality and morbidity. Supplementary feeding programs aim to treat moderate acute malnutrition and prevent the deterioration to severe acute malnutrition.

OBJECTIVE:
The aim was to compare recovery rates of children with moderate acute malnutrition in supplementary feeding programs by using the newly recommended ration of ready-to-use supplementary food (RUSF) and the more conventional ration of corn-soya blend (CSB) in Ethiopia.

DESIGN:
A total of 1125 children aged 6-60 mo with moderate acute malnutrition received 16 wk of CSB or RUSF. Children were randomly assigned to receive one or the other food. The daily rations were purposely based on the conventional treatment rations distributed at the time of the study in Ethiopia: 300 g CSB and 32 g vegetable oil in the control group (1413 kcal) and 92 g RUSF in the intervention group (500 kcal). The higher ration size of CSB was provided because of expected food sharing.

RESULTS:
The HR for children in the CSB group was 0.85 (95% CI: 0.73, 0.99), which indicated that they had 15% lower recovery (P = 0.039). Recovery rates of children at the end of the 16-wk treatment period trended higher in the RUSF group (73%) than in the CSB group (67%) (P = 0.056).

CONCLUSION:
In comparison with CSB, **the treatment of moderate acute malnutrition with RUSF resulted in higher recovery rates in children, despite the large ration size and higher energy content of the conventional CSB ration.**

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Comment
There were several trials of locally produced Ready to Use Therapeutic Foods this year. For more information on RUTF click here.
A typical recipe for RUTF (from the above technical paper) is:
Full fat milk powder 30%
Sugar 28%
Vegetable oil 15% (soy oil, cottonseed oil, rapeseed oil and corn oil. Rapeseed oil and soybean oil provide a good balance of essential fatty acids)
Peanut butter 25% (or peanuts that have been roasted and ground)
Mineral multi-vitamin mixture 1.6%

Children successfully treated for moderate acute malnutrition remain at risk for malnutrition and death in the subsequent year after recovery.

Chang CY, Trehan I, Wang RJ, Thakwalakwa C, Maleta K, Deitchler M, Manary MJ.

J Nutr. 2013 Feb;143(2):215-20. doi: 10.3945/jn.112.168047. Epub 2012 Dec 19.

Source
Department of Pediatrics, Washington University, St. Louis, MO, USA.

Abstract
Moderate acute malnutrition (MAM) affects 11% of children <5 y old worldwide and increases their risk for morbidity and mortality. It is assumed that successful treatment of MAM reduces these risks. **A total of 1967 children aged 6-59 mo successfully treated for MAM in rural Malawi following randomized treatment with corn-soy blend plus milk and oil (CSB++), soy ready-to-use supplementary food (RUSF), or soy/whey RUSF were followed for 12 mo. The initial supplementary food was given until the child reached a weight-for-height Z-score (WHZ) >-2.** The median duration of feeding was 2 wk, with a maximum of 12 wk. The hypothesis tested was that children treated with either RUSF would be more likely to remain well-nourished than those treated with CSB++. The primary outcome, remaining well-nourished, was defined as mid-upper arm circumference ≥12.5 cm or WHZ ≥-2 for the entire duration of follow-up. During the 12-mo follow-up period, **only 1230 (63%) children remained well-nourished, 334 (17%) relapsed to MAM, 190 (10%) developed severe acute malnutrition, 74 (4%) died, and 139 (7%) were lost to follow-up.** Children who were treated with soy/whey RUSF were more likely to remain well-nourished (67%) than those treated with CSB++ (62%) or soy RUSF (59%) (P = 0.01). A seasonal pattern of food insecurity and adverse clinical outcomes was observed. This study demonstrates that children successfully treated for MAM with soy/whey RUSF are more likely to remain well-nourished; however, all children successfully treated for MAM remain vulnerable.

Randomized controlled trial of meat compared with multimicronutrient-fortified cereal in infants and toddlers with high stunting rates in diverse settings.

Krebs NF, Mazariegos M, Chomba E, Sami N, Pasha O, Tshefu A, Carlo WA, Goldenberg RL, Bose CL, Wright LL, Koso-Thomas M, Goco N, Kindem M, McClure EM, Westcott J, Garces A, Lokangaka A, Manasyan A, Imenda E, Hartwell TD, Hambidge KM.

Am J Clin Nutr. 2012 Oct;96(4):840-7. Epub 2012 Sep 5.

Source
Department of Pediatrics, Section of Nutrition, University of Colorado Denver, Aurora, CO 80045, USA. nancy.krebs@ucdenver.edu

Abstract
BACKGROUND:

Improved complementary feeding is cited as a critical factor for reducing stunting. Consumption of meats has been advocated, but its efficacy in low-resource settings has not been tested.

OBJECTIVE:
The objective was to **test the hypothesis that daily intake of 30 to 45 g meat from 6 to 18 mo of age would result in greater linear growth velocity and improved micronutrient status in comparison with an equicaloric multimicronutrient-fortified cereal.**

DESIGN:
This was a cluster randomized efficacy trial conducted in the Democratic Republic of Congo, Zambia, Guatemala, and Pakistan. Individual daily portions of study foods and education messages to enhance complementary feeding were delivered to participants. Blood tests were obtained at trial completion.

RESULTS:
A total of 532 (86.1%) and 530 (85.8%) participants from the meat and cereal arms, respectively, completed the study. **Linear growth velocity did not differ between treatment groups: 1.00 (95% CI: 0.99, 1.02) and 1.02 (95% CI: 1.00, 1.04) cm/mo for the meat and cereal groups, respectively (P = 0.39).** From baseline to 18 mo, stunting [length-for-age z score (LAZ) <-2.0] rates increased from ~33% to nearly 50%. Years of maternal education and maternal height were positively associated with linear growth velocity (P = 0.0006 and 0.003, respectively); LAZ at 6 mo was negatively associated (P < 0.0001). Anemia rates did not differ by group; iron deficiency was significantly lower in the cereal group.

CONCLUSION:
The high rate of stunting at baseline and the lack of effect of either the meat or multiple micronutrient-fortified cereal intervention to reverse its progression argue for multifaceted interventions beginning in the pre- and early postnatal periods.

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Effects of psychosocial stimulation on improving home environment and child-rearing practices: results from a community-based trial among severely malnourished children in Bangladesh.

Nahar B, Hossain MI, Hamadani JD, Ahmed T, Grantham-McGregor S, Persson LA.

BMC Public Health. 2012 Aug 7;12:622. doi: 10.1186/1471-2458-12-622.

Source
International Maternal and Child Health (IMCH), Department of Women's and Children's Health, Uppsala University, Akademiska sjukhuset, SE-751 85, Uppsala, Sweden. baitun.nahar@kbh.uu.se

Abstract
BACKGROUND: Parenting programmes are effective in enhancing parenting practices and child development. This study evaluated the effects of a intervention with psychosocial

stimulation (PS) on the quality of the home environment and mothers' child-rearing practices in a community-based trial with severely malnourished Bangladeshi children.

METHOD: Severely underweight children (n = 507), 6–24 months of age, were randomly assigned to five groups: PS; food supplementation (FS); PS + FS; clinic-control (CC); and, hospital-control (CH). PS included fortnightly follow-up visits for six months at community clinics where a play leader demonstrated play activities and gave education on child development and child rearing practices. FS comprised cereal-based supplements (150–300 kcal/day) for three months. All groups received medical care, micronutrient supplements and growth monitoring. Mothers were given the Home Observation for Measurement of the Environment (HOME) inventory and a questionnaire on parenting at baseline and after six months to assess the outcome.

RESULTS: 322 children completed the study. After six months of intervention the PS + FS and PS groups benefitted in the total HOME score (depending on the comparison group, effect sizes varied from 0.66 to 0.33 SD) The PS + FS and PS groups also benefitted in two HOME subscales: maternal involvement (effect sizes: 0.8 to 0.55 SD) and play materials, (effect sizes: 0.46 to 0.6 SD), and child-rearing practices scores (effect size: 1.5 to 1.1 SD). The PS + FS group benefitted 4.0 points in total HOME score compared with CH, 4.8 points compared with CC and 4.5 points compared with FS ($p < 0.001$ for all). The PS group benefitted 2.4 points compared with CH ($p = 0.035$), 3.3 points compared with CC ($p = 0.004$), and 2.9 points compared with FS ($p = 0.006$). Child-rearing practice scores of the PS + FS group improved 7.7, 6.4 and 6.6 points and the PS group improved 8.5, 7.2 and 7.4 points more than CH, CC and FS, respectively ($p < 0.001$ for all).

CONCLUSIONS: Child-rearing practices of mothers of severely malnourished children and the quality of their home environment can be improved through community-based psychosocial stimulation with or without food supplementation. This may be of importance to promote child development.

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Maternal health

Antenatal corticosteroids trial in preterm births to increase neonatal survival in developing countries: study protocol.

Althabe F, Belizán JM, Mazzoni A, Berrueta M, Hemingway-Foday J, Koso-Thomas M, McClure E, Chomba E, Garces A, Goudar S, Kodkany B, Saleem S, Pasha O, Patel A, Esamai F, Carlo WA, Krebs NF, Derman RJ, Goldenberg RL, Hibberd P, Liechty EA, Wright LL, Bergel EF, Jobe AH, Buekens P.

Reprod Health. 2012 Sep 19;9:22. doi: 10.1186/1742-4755-9-22.

Source

Institute for Clinical Effectiveness and Health Policy (IECS), Dr. Emilio Ravignani 2024, Buenos Aires, C1414CPV, Argentina.

Abstract

BACKGROUND:
Preterm birth is a major cause of neonatal mortality, responsible for 28% of neonatal deaths overall. The administration of antenatal corticosteroids to women at high risk of preterm birth is a powerful perinatal intervention to reduce neonatal mortality in resource rich environments. The effect of antenatal steroids to reduce mortality and morbidity among preterm infants in hospital settings in developed countries with high utilization is well established, yet they are not routinely used in developing countries. The impact of increasing antenatal steroid use in hospital or community settings with low utilization rates and high infant mortality among premature infants due to lack of specialized services has not been well researched. There is currently no clear evidence about the safety of antenatal corticosteroid use for community-level births.

METHODS:
We hypothesize that a multi country, two-arm, parallel cluster randomized controlled trial to evaluate whether a multifaceted intervention to increase the use of antenatal corticosteroids, including components to improve the identification of pregnancies at high risk of preterm birth and providing and facilitating the appropriate use of steroids, will reduce neonatal mortality at 28 days of life in preterm newborns, compared with the standard delivery of care in selected populations of six countries. 102 clusters in Argentina, Guatemala, Kenya, India, Pakistan, and Zambia will be randomized, and around 60,000 women and newborns will be enrolled. Kits containing vials of dexamethasone, syringes, gloves, and instructions for administration will be distributed. Improving the identification of women at high risk of preterm birth will be done by (1) diffusing recommendations for antenatal corticosteroids use to health providers, (2) training health providers on identification of women at high risk of preterm birth, (3) providing reminders to health providers on the use of the kits, and (4) using a color-coded tape to measure uterine height to estimate gestational age in women with unknown gestational age. In both intervention and control clusters, health providers will be trained in essential newborn care for low birth weight babies. The primary outcome is neonatal mortality at 28 days of life in preterm infants.

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Making birthing safe for Pakistan women: a cluster randomized trial.

Khan MA, Mirza S, Ahmed M, Rasheed A, Khan A, Walley J, Nisar N.

BMC Pregnancy Childbirth. 2012 Jul 15;12:67.

Source
Association for Social Development, Islamabad, Pakistan.

Abstract
BACKGROUND:
Two out of three neonatal deaths occur in just 10 countries and Pakistan stands third among them. Maternal mortality is also high with most deaths occurring during labor, birth, and first few hours after birth. Enhanced access and utilization of skilled delivery and emergency obstetric care is the demonstrated strategy in reducing maternal and neonatal mortality. This trial aims to compare reduction in neonate mortality and utilization of available safe birthing and Emergency Obstetric and Neonatal Care services among pregnant mothers receiving 'structured birth planning', and/or 'transport facilitation' compared to routine care.

METHODS:
A pragmatic cluster randomized trial, with qualitative and economic studies, will be conducted in Jhang, Chiniot and Khanewal districts of Punjab, Pakistan, from February 2011 to May 2013. At least 29,295 pregnancies will be registered in the three arms, seven clusters per arm; 1) structured birth planning and travel facilitation, 2) structured birth planning, and 3) control arm. Trial will be conducted through the Lady Health Worker program. Main outcomes are difference in neonatal mortality and service utilization; maternal mortality being the secondary outcome. Cluster level analysis will be done according to intention-to-treat.

DISCUSSION:
A nationwide network of about 100,000 lady health workers is already involved in antenatal and postnatal care of pregnant women. They also act as "gatekeepers" for the child birthing services. This gate keeping role mainly includes counseling and referral for skill birth attendance and travel arrangements for emergency obstetric care (if required). The review of current arrangements and practices show that the care delivery process needs enhancement to include adequate information provision as well as informed "decision" making and planned "action" by the pregnant women. The proposed three-year research is to develop, through national technical working group process, and then test a set of arrangements for achieving the enhanced utilization of safe birthing services.

Effect of educational software on self-efficacy of pregnant women to cope with labor: a randomized controlled trial.

Vasegh Rahimparvar SF, Hamzehkhani M, Geranmayeh M, Rahimi R.

Arch Gynecol Obstet. 2012 Jul;286(1):63-70. doi: 10.1007/s00404-012-2243-4. Epub 2012 Feb 19.

Source
Department of Midwifery, Tehran University of Medical Sciences, Tehran, Iran. vaseghrh@tums.ac.ir

Abstract
AIM:
The aim of this study was to determine the effect of educational software on self-efficacy of Iranian pregnant women to cope with labor.

METHODS:
This study was a randomized controlled trial which was carried out on 150 Iranian nulliparous pregnant women randomly assigned to two groups of 75 women each. **The control group routinely did not receive any kind of childbirth education and the intervention group only received the childbirth educational software for 6-8 weeks.** In order to determine self-efficacy, the **Childbirth Self Efficacy Questionnaire (CBSEI) was used which measures the outcome expectancy and the self-efficacy expectancy of the first and second stages of labor separately**. This questionnaire was completed at 28-32-week gestation as a pre-test and at 36-38 weeks as a post-test by the participants. Data were analyzed using Chi-square, Mann-Whitney U and Wilcoxon tests.

RESULTS:
After the intervention, the median and mean of CBSEI scores for the intervention and the control groups were 607, 604/20 ± 16/630 and 394, 392/51 ± 16/758, respectively. There was a statistical difference between the two groups (p = 0.001). Also, statistically significant differences existed in the median of outcome expectancy and self-efficacy expectancy after intervention in both stages of labor between the two groups (p = 0.001).

CONCLUSIONS:
The educational software program significantly increased self-efficacy of Iranian pregnant women to cope with labor. Despite lack of educational childbirth classes in Iran, the use of this method is recommended. However, to find whether this technique can be substituted for the educational classes, further studies are needed.

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Intramuscular versus intravenous anti-D for preventing Rhesus alloimmunization during pregnancy.

Okwundu CI, Afolabi BB.

Cochrane Database Syst Rev. 2013 Jan 31;1:CD007885. doi: 10.1002/14651858.CD007885.pub2.

Source
Centre for Evidence-Based Health Care, Faculty of Health Sciences, Stellenbosch University, Tygerberg, South Africa. ciokwundu@sun.ac.za.

Abstract
BACKGROUND:
Antibodies to the red cell Rhesus D (RhD) antigen can be produced during pregnancy in a RhD-negative mother carrying a RhD-positive fetus, in particular following feto-maternal haemorrhage at birth or following any procedure that may cause feto-maternal haemorrhage. While the first baby is usually not harmed, these antibodies may cause haemolytic disease of the fetus/newborn (HDFN) in subsequent RhD-positive babies. RhD incompatibility is a major cause of HDFN.To reduce the risk of HDFN, anti-D is given to RhD-negative mothers at 28 or 30 weeks of pregnancy and within 72 hours of potential maternal exposure to fetal red cells. Anit-D is currently available in both intramuscular (IM) and intravenous (IV) preparations.

OBJECTIVES:
To compare the efficacy and effectiveness of IM versus IV anti-D IgG in preventing RhD alloimmunization in RhD-negative pregnant women.
SEARCH METHODS:
We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 September 2012).

SELECTION CRITERIA:
Randomized controlled trials, quasi-randomized trials and cluster-randomized trials comparing IM and IV anti-D for preventing RhD alloimmunization in RhD-negative pregnant women.

DATA COLLECTION AND ANALYSIS:
Two review authors independently assessed trials for inclusion and assessed trial quality. Two review authors extracted data. Data were checked for consistency by both authors.

MAIN RESULTS:
Two studies involving 447 (with sample sizes 14 and 432) RhD negative women were included. The studies compared IM and IV administration of anti-D prophylaxis. In both studies the women received a 1500 IU (300 microgram) dose of Rhophylac during week 28 of gestation. There was no incidence of RhD alloimmunization in either of the studies, as the sample size was insufficient for meaningful comparison of this uncommon outcome. One of the studies found that the mean anti-D IgG concentrations after IV and IM administration differed up to seven days (36.1 (2.6) ng/mL IV; 19.8 (8.7) ng/mL IM on day seven). However, from two to three weeks post-administration, the concentrations were similar for both routes of administration. None of the women involved in the studies developed antibodies against the RhD antigen.

AUTHORS' CONCLUSIONS:
It appears that **IM and IV administration of anti-D are equally effective**. The number of included studies and the number of participants are not enough to assess whether there are any differences. Anti-D can be administered by IM or IV injection. The choice of IM or IV route of administration will depend on the available preparations, the dose to be administered and also on the patients' preferences. This review found insufficient information upon which to guide practice due to the limited number of included studies, small sample sizes and methodological limitations

Mobile phones as a health communication tool to improve skilled attendance at delivery in Zanzibar: a cluster-randomised controlled trial.

Lund S, Hemed M, Nielsen BB, Said A, Said K, Makungu MH, Rasch V.

BJOG. 2012 Sep;119(10):1256-64. doi: 10.1111/j.1471-0528.2012.03413.x. Epub 2012 Jul 17.

Source
Department of International Health, Immunology and Microbiology, University of Copenhagen, Copenhagen, Denmark. stine_lund@dadlnet.dk

Abstract
OBJECTIVE:
To examine the association between a mobile phone intervention and skilled delivery attendance in a resource-limited setting.

DESIGN:
Pragmatic cluster-randomised controlled trial with primary healthcare facilities as the unit of randomisation.

SETTING:
Primary healthcare facilities in Zanzibar.

POPULATION:
Two thousand, five hundred and fifty pregnant women (1311 interventions and 1239 controls) who attended antenatal care at one of the selected primary healthcare facilities were included at their first antenatal care visit and followed until 42 days after delivery. All pregnant women were eligible for study participation.

METHODS:
Twenty-four primary healthcare facilities in six districts in Zanzibar were allocated by simple randomisation to either mobile phone intervention (n = 12) or standard care (n = 12). The intervention consisted of a short messaging service (SMS) and mobile phone voucher component.

MAIN OUTCOME MEASURES:
Skilled delivery attendance.

RESULTS:

The mobile phone intervention was associated with an increase in skilled delivery attendance: 60% of the women in the intervention group versus 47% in the control group delivered with skilled attendance. The intervention produced a significant increase in skilled delivery attendance amongst urban women (odds ratio, 5.73; 95% confidence interval, 1.51-21.81), but did not reach rural women.

CONCLUSIONS:
The mobile phone intervention significantly increased skilled delivery attendance amongst women of urban residence. **Mobile phone solutions may contribute to the saving of lives of women and their newborns and the achievement of Millennium Development Goals 4 and 5, and should be considered by maternal and child health policy makers in developing countries.**

Comment
This is an important study, suggesting great potential for improving maternal health outcomes using mobile phones. The mobile phone intervention was an automated short messaging service (SMS) system providing mothers with registered phone numbers with health education and appointment reminder texts, and a mobile phone voucher system for two-way communication with their primary healthcare providers or referral hospital in the case of obstetric emergencies.

Maternal nutrition and micronutrient supplementation

(See also HIV - Prevention of parent to child transmission, Cardiovascular disease)

A randomized trial to investigate the effects of pre-natal and infant nutritional supplementation on infant immune development in rural Gambia: the ENID trial: Early Nutrition and Immune Development.

Moore SE, Fulford AJ, Darboe MK, Jobarteh ML, Jarjou LM, Prentice AM.

BMC Pregnancy Childbirth. 2012 Oct 11;12:107. doi: 10.1186/1471-2393-12-107.

Source
MRC Keneba, MRC Unit The Gambia, PO Box 273, Banjul, The Gambia. smoore@mrc.gm

Abstract
BACKGROUND:
Recent observational research indicates that immune development may be programmed by nutritional exposures early in life. Such findings require replication from trials specifically designed to assess the impact of nutritional intervention during pregnancy on infant immune development. The current trial seeks to establish: (a) which combination of protein-energy (PE) and multiple-micronutrient (MMN) supplements would be most effective; and (b) the most critical periods for intervention in pregnancy and infancy, for optimal immune development in infancy.

METHODS/DESIGN:
The ENID Trial is a 2 x 2 x 2 factorial randomized, partially blind trial to assess whether nutritional supplementation to pregnant women (from < 20 weeks gestation to term) and their infants (from 6 to 12 months of age) can enhance infant immune development. Eligible pregnant women from the West Kiang region of The Gambia (pregnancy dated by ultrasound examination) are randomized on entry to 4 intervention groups (Iron-folate (FeFol = standard care), multiple micronutrients (MMN), protein-energy (PE), PE + MMN). Women are visited at home weekly for supplement administration and morbidity assessment and seen at MRC Keneba at 20 and 30 weeks gestation for a detailed antenatal examination, including ultrasound. At delivery, cord blood and placental samples are collected, with detailed infant anthropometry collected within 72 hours. Infants are visited weekly thereafter for a morbidity questionnaire. From 6 to 12 months of age, infants are further randomized to a lipid-based nutritional supplement, with or without additional MMN. The primary outcome measures of this study are thymic development during infancy, and antibody response to vaccination. Measures of cellular markers of immunity will be made in a selected sub-cohort. Subsidiary studies to the main trial will additionally assess the impact of supplementation on infant growth and development to 24 months of age.

DISCUSSION:
The proposed trial is designed to test whether nutritional repletion can enhance early immune development and, if so, to help determine the most efficacious form of nutritional support. Where there is evidence of benefit from a specific intervention/combination of interventions, future research should focus on refining the supplements to achieve the optimal, most cost-effective balance of interventions for improved health outcomes.

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Patterns of body composition among HIV-infected, pregnant Malawians and the effects of famine season.

Ramlal RT, Tembo M, Soko A, Chigwenembe M, Tohill BC, Kayira D, King CC, Chasela C, Jamieson D, van der Horst C, Bentley ME, Adair LS; BAN Study Team.

Matern Child Health J. 2013 Feb;17(2):265-73. doi: 10.1007/s10995-012-0970-6.

Source
University of North Carolina, Chapel Hill, NC, USA. roshan.m.thomas@gmail.com

Abstract
We describe change in weight, midupper arm circumference (MUAC), arm muscle area (AMA) and arm fat area (AFA) in 1130 pregnant HIV-infected women with CD4 counts > 200 as part of the BAN Study (www.thebanstudy.org), **a randomized, controlled clinical trial to evaluate antiretroviral and nutrition interventions to reduce mother-to-child transmission of HIV during breast feeding.** In a longitudinal analysis, we found a linear increase in weight with a mean rate of weight gain of 0.27 kgs/week, from baseline (12 to 30 weeks gestation) until the last follow-up visit (32-38 weeks). Analysis of weight gain showed that 17.1% of the intervals between visits resulted in a weight loss. In unadjusted models, MUAC and AMA increased and AFA declined during late pregnancy. Based on multivariable regression analysis, exposure to the famine season resulted in larger losses in AMA [-0.08, 95% CI -0.14, -0.02; p = 0.01] while AFA losses occurred irrespective of season [-0.55, 95%: -0.95, -0.14, p = 0.01]. CD4 was associated with AFA [0.21, 95% CI 0.01, 0.41, p = .04]. Age was positively associated with MUAC and AMA. Wealth was positively associated with MUAC, AFA, and weight. While patterns of anthropometric measures among HIV-infected, pregnant women were found to be similar to those reported for uninfected women in sub-Saharan Africa, effects of the famine season among undernourished, Malawian women are of concern. Strategies to optimize nutrition during pregnancy for these women appear warranted.

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Maternal multiple micronutrient supplements and child cognition: a randomized trial in Indonesia.

Prado EL, Alcock KJ, Muadz H, Ullman MT, Shankar AH; SUMMIT Study Group.

Pediatrics. 2012 Sep;130(3):e536-46. Epub 2012 Aug 20.

Source
SUMMIT Institute of Development, Mataram, Indonesia. elprado@ucdavis.edu

Abstract

OBJECTIVES:
We investigated the relative benefit of maternal multiple micronutrient (MMN) supplementation during pregnancy and until 3 months postpartum compared with iron/folic acid supplementation on child development at preschool age (42 months).

METHODS:
We assessed 487 children of mothers who participated in the Supplementation with Multiple Micronutrients Intervention Trial, a cluster-randomized trial in Indonesia, on tests adapted and validated in the local context measuring motor, language, visual attention/spatial, executive, and socioemotional abilities. Analysis was according to intention to treat.

RESULTS:
In children of undernourished mothers (mid-upper arm circumference <23.5 cm), a significant benefit of MMNs was observed on motor ability (B = 0.39 [95% confidence interval (CI): 0.08-0.70]; P = .015) and visual attention/spatial ability (B = 0.37 [95% CI: 0.11-0.62]; P = .004). In children of anemic mothers (hemoglobin concentration <110 g/L), a significant benefit of MMNs on visual attention/spatial ability (B = 0.24 [95% CI: 0.02-0.46]; P = .030) was also observed. No robust effects of maternal MMN supplementation were found in any developmental domain over all children.

CONCLUSIONS:
When pregnant women are undernourished or anemic, provision of MMN supplements can improve the motor and cognitive abilities of their children up to 3.5 years later, particularly for both motor function and visual attention/spatial ability. Maternal MMN but not iron/folic acid supplementation protected children from the detrimental effects of maternal undernutrition on child motor and cognitive development.

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Micronutrient supplementation and pregnancy outcomes: double-blind randomized controlled trial in China.

Liu JM, Mei Z, Ye R, Serdula MK, Ren A, Cogswell ME.

JAMA Intern Med. 2013 Feb 25;173(4):276-82. doi: 10.1001/jamainternmed.2013.1632.

Source
Institute of Reproductive and Child Health/Ministry of Health Key Laboratory of Reproductive Health and Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, Beijing, China. liujm@pku.edu.cn

Abstract
BACKGROUND:
Beyond perinatal folic acid supplementation, the need for additional prenatal prophylaxis of iron with or without other micronutrients remains unclear. We aim to investigate the maternal and infant health effects of iron plus folic acid and multiple micronutrient supplements vs folic acid alone when provided to pregnant women with no or mild anemia.

METHODS:

In this randomized double-blind controlled trial, 18,775 nulliparous pregnant women with mild or no anemia were enrolled from 5 counties of northern China from May 2006 through April 2009. Women were randomly assigned to daily folic acid (400 μg) (control), folic acid-iron (30 mg), or folic acid, iron, and 13 additional vitamins and minerals provided before 20 weeks gestation to delivery. Primary outcome was perinatal mortality. Secondary outcomes included neonatal and infant mortality, preterm delivery, birth weight, birth length, gestational duration, and maternal hemoglobin concentration and anemia.

RESULTS:
A total of 92.7% of women consumed 80% to 100% of supplements as instructed. On average, women consumed 177 supplements. **Compared with daily prenatal folic acid, supplementation with iron-folic acid with or without other micronutrients did not affect the rate of perinatal mortality (8.8, 8.7, and 8.3, respectively) per 1000 births, and relative risks (RRs) were 1.00 (95% CI, 0.68-1.46; P = .99) and 0.94 (95% CI, 0.64-1.39; P = .76), respectively.** Risk of other adverse maternal and infant outcomes also did not differ, except that RRs for third-trimester maternal anemia were 0.72 (95% CI, 0.63-0.83; P < .001) and 0.71 (95% CI, 0.62-0.82; P < .001), respectively.

CONCLUSION:
Prenatal iron-folic acid and other micronutrient supplements provided to Chinese women with no or mild anemia prevented later pregnancy anemia beyond any benefit conferred by folic acid alone but did not affect perinatal mortality or other infant outcomes.

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Effect of vitamin D supplementation during pregnancy on neonatal mineral homeostasis and anthropometry of the newborn and infant.

Kalra P, Das V, Agarwal A, Kumar M, Ramesh V, Bhatia E, Gupta S, Singh S, Saxena P, Bhatia V.

Br J Nutr. 2012 Sep 28;108(6):1052-8. doi: 10.1017/S0007114511006246. Epub 2012 Jan 3.

Source
Department of Endocrinology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226 014, India.

Abstract
Hypovitaminosis D is common in India. In the present prospective partially randomised study of vitamin D (D_3) supplementation during pregnancy, **subjects were randomised in the second trimester to receive either one oral dose of 1500 μg vitamin D_3 (group 1, n 48) or two doses of 3000 μg vitamin D_3 each in the second and third trimesters (group 2, n 49).** Maternal 25-hydroxyvitamin D (25(OH)D) at term, cord blood (CB) alkaline phosphatase (ALP), neonatal serum Ca and anthropometry were measured in these subjects and in forty-three non-supplemented mother-infant pairs (usual care). Median maternal 25(OH)D at term was higher in group 2 (58·7, interquartile range (IQR) 38·4-89·4 nmol/l) v. group 1 (26·2, IQR 17·7-57·7 nmol/l) and usual-care group (39·2, IQR 21·2-73·4 nmol/l) (P = 0·000). CB ALP was increased (>8.02 μkat/l or >480 IU/l) in 66·7 % of the usual-care group v. 41·9 % of group 1 and 38·9 % of group 2 (P = 0·03). Neonatal Ca and CB 25(OH)D did not differ significantly in the three

groups. **Birth weight, length and head circumference were greater and the anterior fontanelle was smaller in groups 1 and 2 (3·08 and 3·03 kg, 50·3 and 50·1 cm, 34·5 and 34·4 cm, 2·6 and 2·5 cm, respectively) v. usual care (2·77 kg, 49·4, 33·6, 3·3 cm; P = 0·000 for length, head circumference and fontanelle and P = 0·003 for weight).** These differences were still evident at 9 months. We conclude that both 1500 μg and two doses of 3000 μg vitamin D_3 had a beneficial effect on infant anthropometry, the larger dose also improving CB ALP and maternal 25(OH)D.

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Nutritional Factors Associated with Antenatal Depressive Symptoms in the Early Stage of Pregnancy Among Urban South Indian Women.

Lukose A, Ramthal A, Thomas T, Bosch R, Kurpad AV, Duggan C, Srinivasan K.

Matern Child Health J. 2013 Feb 26. [Epub ahead of print]

Source
Division of Nutrition, Mother and Child Unit, St. John's Research Institute, Sarjapur Road, Bangalore, 560034, India.

Abstract
Many women of reproductive age from developing countries have poor nutritional status, and the prevalence of depression during pregnancy is high. The objective of the present study was to assess the prevalence of antenatal depressive symptoms in early pregnancy, and to identify the demographic and nutritional factors associated with these symptoms in a sample of urban South Indian pregnant women. **This cross-sectional study was the baseline assessment of a prospective randomized controlled trial of vitamin B(12) supplementation in urban pregnant south Indian women between the ages of 18 and 40 years** (www.clinicaltrials.gov : NCT00641862). 365 women in their first trimester of pregnancy were screened for depressive symptoms at an urban clinic in Karnataka, South India, using the Kessler Psychological Distress Scale (K-10). Nutritional, clinical and biochemical factors were also assessed. Mean (SD) age of the cohort was 22.6 (3.7) years and mean (SD) BMI was 20.4 (3.3) kg/m(2). 121 (33 %) of the women in the 1st trimester had symptoms consistent with depression (K-10 score >6). In multivariate log binomial regression analysis, presence of antenatal depressive symptoms in the first trimester were positively associated with vomiting, prevalence ratio (PR) = 1.54 (95 % CI 1.10, 2.16) and negatively with anemia, PR = 0.67 (95 % CI 0.47, 0.96). Nutrient intakes, serum vitamin B(12), methylmalonic acid, homocysteine and red cell folate levels were not associated with measures of depression. **Antenatal depressive symptoms in early pregnancy are highly prevalent in urban Indian women and are more common in women with vomiting and without anemia. In this cross-sectional data, blood concentrations of vitamin B(12) and folate were not associated with depressive symptoms.** The relationship between nutritional status and depressive symptoms may require larger and longitudinal studies

Effect of iron deficiency anemia in pregnancy on child mental development in rural China.

Chang S, Zeng L, Brouwer ID, Kok FJ, Yan H.

Pediatrics. 2013 Mar;131(3):e755-63. doi: 10.1542/peds.2011-3513. Epub 2013 Feb 11.

Source
United Nations Children's Fund Office for China, Beijing, China.

Abstract
OBJECTIVE:
To determine the impact of iron deficiency anemia (IDA) in pregnancy on young child development.

METHODS:
A 2-year follow-up of 850 children born to women who participated in a double-blind cluster randomized controlled trial of prenatal micronutrient supplementation in western rural China. These women were randomly assigned to receive either daily folic acid, iron/folic acid (60 mg iron), or multiple micronutrients (with 30 mg iron) during pregnancy. Children were categorized into the prenatal-IDA and prenatal-non-IDA groups based on the mother's hemoglobin in the third trimester. Each group contained 3 subgroups based on mother's treatment: folic acid, iron/folic acid, and multiple micronutrients. Bayley scales of infant development were administered to the children to assess their development at 3, 6, 12, 18, and 24 months of age.

RESULTS:
Compared with the prenatal-non-IDA group, the prenatal-IDA group showed a significantly lower mental development index at 12, 18, and 24 months of age. The adjusted mean difference was 5.8 (95% confidence interval [CI], 1.1-10.5), 5.1 (95% CI, 1.2-9.0), and 5.3 (95% CI, 0.9-9.7), respectively. **Further analysis showed that the mental development indexes in the prenatal-IDA group and prenatal-non-IDA group were similar with supplementation of iron/folic acid but were significantly lower in the prenatal-IDA group with supplementation of folic acid or multiple micronutrients.**

CONCLUSIONS:
Prenatal IDA in the third trimester is associated with mental development of the child. However, prenatal supplementation with sufficient iron protects child development even when the woman's IDA was not properly corrected in pregnancy

Women's groups

Effect of women's groups and volunteer peer counselling on rates of mortality, morbidity, and health behaviours in mothers and children in rural Malawi (MaiMwana): a factorial, cluster-randomised controlled trial.

Lewycka S, Mwansambo C, Rosato M, Kazembe P, Phiri T, Mganga A, Chapota H, Malamba F, Kainja E, Newell ML, Greco G, Pulkki-Brännström AM, Skordis-Worrall J, Vergnano S, Osrin D, Costello A.

*** Lancet. 2013 May 18;381(9879):1721-35. doi: 10.1016/S0140-6736(12)61959-X.

Source
Institute for Global Health, University College London, London, UK.

Abstract
BACKGROUND:
Women's groups and health education by peer counsellors can improve the health of mothers and children. We assessed their effects on mortality and breastfeeding rates in rural Malawi.

METHODS:
We did a 2×2 factorial, cluster-randomised trial in 185,888 people in Mchinji district. 48 equal-sized clusters were randomly allocated to four groups with a computer-generated number sequence. 24 facilitators guided groups through a community action cycle to tackle maternal and child health problems. 72 trained volunteer peer counsellors made home visits at five timepoints during pregnancy and after birth to support breastfeeding and infant care. Primary outcomes for the women's group intervention were maternal, perinatal, neonatal, and infant mortality rates (MMR, PMR, NMR, and IMR, respectively); and for the peer counselling were IMR and exclusive breastfeeding (EBF) rates. Analysis was by intention to treat. The trial is registered as ISRCTN06477126.

FINDINGS:
We monitored outcomes of 26,262 births between 2005 and 2009. In a factorial model adjusted only for clustering and the volunteer peer counselling intervention, in women's group areas, for years 2 and 3, we noted non-significant decreases in NMR (odds ratio 0.93, 0.64-1.35) and MMR (0.54, 0.28-1.04). After adjustment for parity, socioeconomic quintile, and baseline measures, effects were larger for NMR (0.85, 0.59-1.22) and MMR (0.48, 0.26-0.91). Because of the interaction between the two interventions, a stratified analysis was done. For women's groups, in adjusted analyses, MMR fell by 74% (0.26, 0.10-0.70), and NMR by 41% (0.59, 0.40-0.86) in areas with no peer counsellors, but there was no effect in areas with counsellors (1.09, 0.40-2.98, and 1.38, 0.75-2.54). Factorial analysis for the peer counselling intervention for years 1-3 showed a fall in IMR of 18% (0.82, 0.67-1.00) and an improvement in EBF rates (2.42, 1.48-3.96). The results of the stratified, adjusted analysis showed a 36% reduction in IMR (0.64, 0.48-0.85) but no effect on EBF (1.18, 0.63-2.25) in areas without women's groups, and in areas with women's groups there was no effect on IMR (1.05, 0.82-1.36) and an increase in EBF (5.02, 2.67-9.44). The cost of women's groups was US$114 per year of life lost (YLL) averted and that of peer counsellors was $33 per YLL averted, using stratified data from single intervention comparisons.

INTERPRETATION:
Community mobilisation through women's groups and volunteer peer counsellor health education are methods to improve maternal and child health outcomes in poor rural populations in Africa.

Neonatal care

Umbilical cord antiseptics for preventing sepsis and death among newborns.

Imdad A, Bautista RM, Senen KA, Uy ME, Mantaring Iii JB, Bhutta ZA.

*** Cochrane Database Syst Rev. 2013 May 31;5:CD008635. doi: 10.1002/14651858.CD008635.pub2.

Source
Department of Pediatrics, SUNY Upstate Medical University, Syracuse, New York, USA, 13202.

Abstract
BACKGROUND:
The umbilical cord is a structure made of blood vessels and connective tissue that connects the baby and placenta in utero. The umbilical cord is cut after birth, which separates the mother and her baby both physically and symbolically. Omphalitis is defined as infection of the umbilical cord stump. Tracking of bacteria along the umbilical vessels may lead to septicaemia that can result in neonatal morbidity and mortality, especially in developing countries.

OBJECTIVES:
To determine the effect of application of antimicrobials on newborn's umbilical cord versus routine care for prevention of morbidity and mortality in hospital and community settings.

SEARCH METHODS:
We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (1 October 2012). In addition, we also searched LILACS (1982 to 11 October 2012) and HERDIN NeON (October 2012)

SELECTION CRITERIA:
We included randomized, cluster-randomized and quasi-randomized controlled trials of topical cord care compared with no topical care, and comparisons between different forms of care.

DATA COLLECTION AND ANALYSIS:
Two review authors independently assessed trials for inclusion, trial quality and subsequently extracted data. Data were checked for accuracy.

MAIN RESULTS:
The search identified 77 trials. We included 34 trials in the review involving 69,338 babies, five studies are awaiting classification and there are two ongoing community trials. Included studies were conducted in both developed and developing countries. Among the 34 included trials, three were large, cluster-randomized trials conducted in community settings in developing countries and 31 studies were conducted in hospital settings mostly in developed countries. Data for community and hospital studies were analyzed separately. The three trials conducted in community settings contributed 78% of the total number of children included in this review. Of the trials conducted in hospital settings, the majority had small sample sizes. There were 22 different interventions studied across the included trials and the most commonly studied

antiseptics were 70% alcohol, triple dye and chlorhexidine.**Only one antiseptic, chlorhexidine was studied in community settings for umbilical cord care. Three community trials reported data on all-cause mortality that comprised 1325 deaths in 54,624 participants and combined results showed a reduction of 23% (average risk ratio (RR) 0.77, 95% confidence interval (CI) 0.63 to 0.94, random-effects, T^2 = 0.02, I^2 = 50%) in the chlorhexidine group compared with control.** The reduction in omphalitis ranged from 27% to 56% depending on the severity of infection. Cord separation time was increased by 1.7 days in the chlorhexidine group compared with dry cord care (mean difference (MD) 1.75 days, 95% CI 0.44 to 3.05, random-effects, T^2 = 0.88, I^2 = 100%). Washing of umbilical cord with soap and water was not advantageous compared with dry cord care in community settings.Among studies conducted in hospital settings, no study reported data for mortality or tetanus. No antiseptic was advantageous to reduce the incidence of omphalitis compared with dry cord care in hospital settings. Topical triple dye application reduced bacterial colonization with Staphylococcus aureus compared with dry cord care (average RR 0.15, 95% CI 0.10 to 0.22, four studies, n = 1319, random-effects, T^2 = 0.04, I^2 = 24%) or alcohol application (average RR 0.45, 95% CI 0.25 to 0.80, two studies, n = 487, random-effects, T^2 = 0.00, I^2 = 0%). There was no advantage of application of alcohol and triple dye for reduction of colonization with streptococcus. Topical alcohol application was advantageous in reduction of colonization with Enterococcus coli compared with dry cord care (average RR 0.73, 95% CI 0.58 to 0.92, two studies, n = 432, random-effects, T^2 = 0.00, I^2 = 0%) and in a separate analysis, triple dye increased the risk of colonization compared with alcohol (RR 3.44, 95% CI 2.10 to 5.64, one study, n = 373). Cord separation time was significantly increased with topical application of alcohol (MD 1.76 days, 95% CI 0.03 to 3.48, nine studies, n = 2921, random-effects, T^2 = 6.54, I^2 = 97%) and triple dye (MD 4.10 days, 95% CI 3.07 to 5.13, one study, n = 372) compared with dry cord care in hospital settings. The number of studies was insufficient to make any inference about the efficacy of other antiseptics.

AUTHORS' CONCLUSIONS:
There is significant evidence to suggest that topical application of chlorhexidine to umbilical cord reduces neonatal mortality and omphalitis in community and primary care settings in developing countries. It may increase cord separation time however, there is no evidence that it increases risk of subsequent morbidity or infection.There is insufficient evidence to support the application of an antiseptic to umbilical cord in hospital settings compared with dry cord care in developed countries.

Community-based treatment of serious bacterial infections in newborns and young infants: a randomized controlled trial assessing three antibiotic regimens.

Zaidi AK, Tikmani SS, Warraich HJ, Darmstadt GL, Bhutta ZA, Sultana S, Thaver D.

*** Pediatr Infect Dis J. 2012 Jul;31(7):667-72. doi: 10.1097/INF.0b013e318256f86c.

Source
Department of Pediatrics and Child Health, Aga Khan University, Karachi, Pakistan. anita.zaidi@aku.edu

Abstract
BACKGROUND:

Sepsis in the neonatal period is a major cause of child mortality in low-income countries. Hospitalization and parenteral penicillin/ampicillin and gentamicin therapy are recommended for management. Many families, however, are unable to access hospital care, and most home-delivered newborns who develop sepsis die without receiving antibiotic therapy. Appropriate community-based therapy in such situations is undefined. We compared failure rates of 3 clinic-based antibiotic regimens in 0- to 59-day-old infants with possible serious bacterial infection whose families refused hospitalization in Karachi communities with high neonatal mortality rates>45/1000 live births.

METHODS:
Eligible infants were randomly assigned to 7 days of: (1) procaine penicillin [50,000 units/kg once daily (OD) by intramuscular injection (IM)] and gentamicin (5 mg/kg OD IM) reference arm, (2) ceftriaxone (50 mg/kg OD IM), or (3) oral trimethoprim-sulfamethoxazole (TMP-SMX) at 10 mg/kg/day divided twice daily and gentamicin IM OD. Primary outcome was treatment failure, defined as death, deterioration in clinical condition during therapy or no improvement after 2 days.

RESULTS:
Possible serious bacterial infection was diagnosed in 704 infants, among 5766 screened. **Among 434 (61.6%) randomized to clinic-based therapy, there were 13 of 145 failures with penicillin-gentamicin, 22 of 145 with ceftriaxone and 26 of 143 with TMP-SMX-gentamicin.** Treatment failure was significantly higher with TMP-SMX-gentamicin compared with penicillin-gentamicin [relative risk 2.03, 95% confidence interval: 1.09-3.79] by intention-to-treat analysis. Differences were not significant in the ceftriaxone versus penicillin-gentamicin comparison [relative risk 1.69, 95% confidence interval 0.89-3.23). By 14 days, there were 2 deaths in the penicillin-gentamicin group, 3 in the ceftriaxone group and 11 in the TMP-SMX-gentamicin group [relative risk 5.58, 95% confidence interval: 1.26-24.72 (group 3 versus 1)].

CONCLUSION:
When hospitalization of sick infants is unfeasible, outpatient therapy with injectable antibiotics is an effective option. **Procaine penicillin-gentamicin was superior to TMP-SMX-gentamicin. Ceftriaxone is a more expensive option, and may be less effective, although this requires further research.**

Comment
A recent meta-analysis (Downie L, et al.) showed that community-acquired neonatal sepsis due to antibiotic resistant bacteria is an emerging and substantial problem, and the currently recommended first-line or second-line antibiotics often do not provide adequate cover. The commonest causes of neonatal bacteramia are: Staphylococcus aureus, Escherichia coli *and* Klebsiella *spp., and in older infants,* S aureus, Streptococcus pneumoniae, Klebsiella *and* E coli, *and non-typhoidal* Salmonella. *Among community-acquired neonatal bacteraemia, resistance or reduced susceptibility to the combination of penicillin and gentamicin and to third-generation cephalosporins occurs in more than 40% of cases. Among community acquired bacteraemia in infants 1–12 months, resistance or reduced susceptibility to the combination of penicillin and gentamicin and to third-generation cephalosporins occurs in more than 35% of cases. With the reduction in price and more widespread availability in many developing countries, third-generation cephalosporins are now used as first-line treatment for severe sepsis. However, third-generation cephalosporins were not more effective against common bloodstream bacterial pathogens than the combination of penicillin and gentamicin, and overuse may be increasing antibiotic resistance in some bacteria. Daily procaine penicillin remains a good option for outpatient management of many serious infections.*

Impact of community-based behaviour-change management on perceived neonatal morbidity: a cluster-randomized controlled trial in Shivgarh, Uttar Pradesh, India.

Willis JR, Kumar V, Mohanty S, Singh V, Kumar A, Singh JV, Misra RP, Awasthi S, Singh P, Gupta A, Baqui AH, Santosham M, Darmstadt GL; Saksham Study Group.

J Trop Pediatr. 2012 Aug;58(4):286-91. Epub 2011 Dec 6.

Source

International Center for Advancing Neonatal Health, Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD 21205, USA.

Abstract

In the context of high neonatal mortality rate (NMR) in developing country settings, a promising strategy for enhancing newborn health is promotion of preventive newborn care practices. We measured the effect of a behaviour-change intervention on perceived neonatal illnesses in rural Uttar Pradesh, India. The study was nested in a cluster-randomized controlled trial of the impact of a package of essential newborn care on NMR. We prospectively enrolled 802 mothers and administered a questionnaire on perceived neonatal morbidities. Regression analysis showed that newborns in the intervention clusters had significantly lower risk of perceived diarrhoea [adjusted relative risk (aRR) 0.67, 95% confidence interval (CI) 0.49-0.90] and skin-related complications [aRR 0.67, 95% CI 0.45-1.00] compared to newborns in the comparison area. Assuming incidence of perceived illnesses is a proxy for actual morbidity rates, we conclude that promotion of preventive care practices through behaviour-change interventions was effective in reducing neonatal morbidities.

Randomized trial of early developmental intervention on outcomes in children after birth asphyxia in developing countries.

Carlo WA, Goudar SS, Pasha O, Chomba E, Wallander JL, Biasini FJ, McClure EM, Thorsten V, Chakraborty H, Wallace D, Shearer DL, Wright LL; Brain Research to Ameliorate Impaired Neurodevelopment-Home-Based Intervention Trial Committee and the National Institute of Child Health and Human Development Global Network for Women's and Children's Health Research Investigators.

Collaborators (26)

Bellad RM, Dhaded SM, Mahantshetti NS, Kodkany BS, Pasha O, Abbasi Z, Chomba E, Carlo WA, Biasini FJ, Chakraborty H, McClure EM, Wallace D, Thorsten V, Derman RJ, Goldenberg RL, Shearer D, Wallander J, Wright LL, Goudar S, Kodkany BS, Goldenberg R, Pasha O, McClure B, Wallace D, Thorsten V, Goudar SS.
J Pediatr. 2013 Apr;162(4):705-712.e3. doi: 10.1016/j.jpeds.2012.09.052. Epub 2012 Nov 16.

Source

University of Alabama at Birmingham, Birmingham, AL; Center for Infectious Disease Research in Zambia, Lusaka, Zambia. wcarlo@peds.uab.edu

Abstract
OBJECTIVE:
To determine if early developmental intervention (EDI) improves developmental abilities in resuscitated children.

STUDY DESIGN:
This was a parallel group, **randomized controlled trial of infants unresponsive to stimulation who received bag and mask ventilation as part of their resuscitation at birth and infants who did not require any resuscitation born in rural communities in India, Pakistan, and Zambia. Intervention infants received a parent-implemented EDI delivered with home visits by parent trainers every other week for 3 years starting the first month after birth.** Parents in both intervention and control groups received health and safety counseling during home visits on the same schedule. The main outcome measure was the Mental Development Index (MDI) of the Bayley Scales of Infant Development, 2nd edition, assessed at 36 months by evaluators unaware of treatment group and resuscitation history.

RESULTS:
MDI was higher in the EDI (102.6 ± 9.8) compared with the control resuscitated children (98.0 ± 14.6, 1-sided P = .0202), but there was no difference between groups in the nonresuscitated children (100.1 ± 10.7 vs 97.7 ± 10.4, P = .1392). The Psychomotor Development Index was higher in the EDI group for both the resuscitated (P = .0430) and nonresuscitated children (P = .0164).

CONCLUSIONS:
This trial of home-based, parent provided EDI in children resuscitated at birth provides evidence of treatment benefits on cognitive and psychomotor outcomes. MDI and Psychomotor Development Index scores of both nonresuscitated and resuscitated infants were within normal range, independent of early intervention.

Implementing a simplified neonatal resuscitation protocol-helping babies breathe at birth (HBB) - at a tertiary level hospital in Nepal for an increased perinatal survival.

Ashish KC, Målqvist M, Wrammert J, Verma S, Aryal DR, Clark R, Naresh PK, Vitrakoti R, Baral K, Ewald U.

BMC Pediatr. 2012 Oct 5;12:159. doi: 10.1186/1471-2431-12-159.

Source
International Maternal and Child Health, Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden. ashish.k.c@kbh.uu.se

Abstract
BACKGROUND:
Reducing neonatal death has been an emerging challenge in low and middle income countries in the past decade. The development of the low cost interventions and their effective delivery are needed to reduce deaths from birth asphyxia. This study will assess the impact of a simplified neonatal resuscitation protocol provided by Helping Babies Breathe (HBB) at a tertiary hospital in Nepal. Perinatal outcomes and performance of skilled birth attendants on management of intrapartum-related neonatal hypoxia will be the main measurements.

METHODS/DESIGN:
The study will be carried out at a tertiary level maternity hospital in Nepal. A prospective cohort-study will include a six-month baseline a six month intervention period and a three-month post intervention period. A quality improvement process cycle will introduce the neonatal resuscitation protocol. A surveillance system, including CCD cameras and pulse oximeters, will be set up to evaluate the intervention.

DISCUSSION:
Along with a technique to improve health workers performance on the protocol, the study will generate evidence on the research gap on the effectiveness of the simplified neonatal resuscitation protocol on intrapartum outcome and early neonatal survival. This will generate a global interest and inform policymaking in relation to delivery care in all income settings.

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)

Micronutients and food fortification

(See also School health, Zinc)

Multi-micronutrient-fortified biscuits decreased the prevalence of anaemia and improved iron status, whereas weekly iron supplementation only improved iron status in Vietnamese school children.

Hieu NT, Sandalinas F, de Sesmaisons A, Laillou A, Tam NP, Khan NC, Bruyeron O, Wieringa FT, Berger J.

Br J Nutr. 2012 Oct 28;108(8):1419-27. doi: 10.1017/S0007114511006945. Epub 2012 Jan 16.

Source
Groupe de Recherche et d'Echanges Technologiques, 45 bis avenue de la Belle Gabrielle, 94736 Nogent-sur-Marne, France.

Abstract
In Vietnam, nutrition interventions do not target school children despite a high prevalence of micronutrient deficiencies. The present randomised, placebo-controlled study **evaluated the impact of providing school children (n 403) with daily multiple micronutrient-fortified biscuits (FB) or a weekly Fe supplement (SUP) on anaemia and Fe deficiency.** Micronutrient status was assessed by concentrations of Hb, and plasma ferritin (PF), transferrin receptor (TfR), Zn and retinol. **After 6 months of intervention, children receiving FB or SUP had a significantly better Fe status when compared with the control children (C), indicated by higher PF (FB: geometric mean 36·9 (95% CI 28·0, 55·4) μg/l; SUP: geometric mean 46·0 (95% CI 33·0, 71·7) μg/l; C: geometric mean 34·4 (95% CI 15·2, 51·2) μg/l; P < 0·001) and lower TfR concentrations (FB: geometric mean 5·7 (95% CI 4·8, 6·52) mg/l; SUP: geometric mean 5·5 (95% CI 4·9, 6·2) mg/l; C: geometric mean 5·9 (95% CI 5·1, 7·1) mg/l; P = 0·007).** Consequently, body Fe was higher in children receiving FB (mean 5·6 (sd 2·2) mg/kg body weight) and SUP (mean 6·1 (sd 2·5) mg/kg body weight) compared with the C group (mean 4·2 (sd 3·3) mg/kg body weight, P < 0·001). **However, anaemia prevalence was significantly lower only in the FB group (1·0%) compared with the C group (10·4%, P = 0·006), with the SUP group being intermediate (7·4%).** Children receiving FB had better weight-for-height Z-scores after the intervention than children receiving the SUP (P = 0·009). Vitamin A deficiency at baseline modified the intervention effect, with higher Hb concentrations in vitamin A-deficient children receiving FB but not in those receiving the SUP. **This indicates that vitamin A deficiency is implicated in the high prevalence of anaemia in Vietnamese school children, and that interventions should take other deficiencies besides Fe into account to improve Hb concentrations. Provision of biscuits fortified with multiple micronutrients is effective in reducing anaemia prevalence in school children.**

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Effect of long-term intermittent supplementation with multiple micronutrients compared with iron-and-folic acid supplementation on Hb and micronutrient status of non-anaemic adolescent schoolgirls in rural Bangladesh.

Ahmed F, Khan MR, Akhtaruzzaman M, Karim R, Williams G, Banu CP, Nahar B, Darnton-Hill I.

Br J Nutr. 2012 Oct 28;108(8):1484-93. doi: 10.1017/S0007114511006908. Epub 2012 Jan 16.

Source
Department of Family Sciences, College for Women, Kuwait University, Safat 13060, Kuwait. farukahmed116@gmail.com

Abstract
The present study examined **whether long-term supplementation with once- and twice-weekly multiple micronutrients (MMN-1 and MMN-2) can improve Hb and micronutrient status more than twice-weekly Fe-folic acid (IFA-2) supplementation in non-anaemic adolescent girls in Bangladesh.** An equal number of 324 rural schoolgirls aged 11-17 years were given MMN-1 or MMN-2 or IFA-2 supplements for 52 weeks in a randomised, double-blind trial. Blood samples were collected at baseline, and at 26 and 52 weeks of supplementation. **The girls receiving IFA-2 supplements were more likely to be anaemic than the girls receiving MMN-2 supplements for 26 weeks (OR 5·1, 95% CI 1·3, 19·5; P = 0·018).** All three supplements reduced Fe deficiency effectively. Both the MMN-1 and MMN-2 groups showed significantly greater improvements in vitamins A, B(2) and C status than the girls in the IFA-2 group, as might be expected. **Receiving a MMN-1 supplement was found to be less effective than MMN-2 supplement in improving Fe, vitamins A, B(2) and folic acid status.** Receiving micronutrient supplements beyond 26 weeks showed little additional benefit in improving micronutrient status. In conclusion, given twice-weekly for 26 weeks, MMN supplements can improve micronutrient status effectively with no significant increase in Hb concentration compared with IFA supplements in non-anaemic Bangladeshi adolescent girls. However, it significantly reduces the risk of anaemia. Before any recommendations can be made, further research, including into cost-effectiveness, is needed to see whether MMN supplementation has any additional longer-term health benefits over that of IFA supplementation in this population.

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Multiple micronutrient supplementation in Tanzanian infants born to HIV-infected mothers: a randomized, double-blind, placebo-controlled clinical trial.

Duggan C, Manji KP, Kupka R, Bosch RJ, Aboud S, Kisenge R, Okuma J, Fawzi WW.

Am J Clin Nutr. 2012 Dec;96(6):1437-46. doi: 10.3945/ajcn.112.044263. Epub 2012 Nov 7.

Source

Department of Nutrition, Harvard School of Public Health, Boston, MA, USA. christopher.duggan@childrens.harvard.edu

Abstract
BACKGROUND:
Multiple micronutrients (vitamin B complex and vitamins C and E) were effective at reducing infectious disease morbidity, HIV disease progression, and poor pregnancy outcomes in HIV-infected women.

OBJECTIVE:
The objective was to evaluate whether direct supplementation of these micronutrients to HIV-exposed infants reduces mortality and morbidity.

DESIGN:
Infants born to HIV-infected women from Dar es Salaam, Tanzania, were randomly assigned to receive daily oral supplementation of multiple multivitamins (vitamin B complex and vitamins C and E) or placebo from age 6 wk for 24 mo. All-cause mortality, hospitalizations, and unscheduled clinic visits were recorded. Morbidities were recorded during monthly follow-up visits. All mothers received multiple micronutrients throughout the study.

RESULTS:
A total of 1193 infants were randomly assigned to receive micronutrients and 1194 to receive placebo. **There were 138 child deaths in the multivitamin group and 124 deaths in the placebo group (HR: 1.13; 95% CI: 0.88, 1.44; P = 0.33). Hospitalizations (RR: 0.83; 95% CI: 0.62, 1.13; P = 0.23), unscheduled clinic visits (RR: 0.97; 95% CI: 0.85, 1.10; P = 0.59), and maternal reports of diarrhea (RR: 0.97; 0.87, 1.10; P = 0.64) were not significantly different between the 2 groups.** Fever (P = 0.02) and vomiting (P = 0.007) were significantly lower in the multivitamin group. Among 429 children whose mothers received antiretroviral (ARV) therapy, multivitamin use had no effect on mortality but was associated with a significant reduction in hospitalizations (P = 0.035), episodes of fever (P = 0.005), and episodes of fever and cough (P = 0.019).

CONCLUSIONS:
In the setting of maternal micronutrient supplementation, supplementation of HIV-exposed infants with vitamin B and vitamins C and E does not reduce mortality. Studies of nutrition supplementation in ARV-exposed infants may be warranted.

Extruded rice grains fortified with zinc, iron, and vitamin A increase zinc status of Thai school children when incorporated into a school lunch program.

Pinkaew S, Winichagoon P, Hurrell RF, Wegmuller R.

J Nutr. 2013 Mar;143(3):362-8. doi: 10.3945/jn.112.166058. Epub 2013 Jan 9.

Source
Laboratory for Human Nutrition, Institute of Food, Nutrition and Health, ETH Zurich, Zurich, Switzerland.

Abstract
Iron (Fe), zinc (Zn), and vitamin A (VA) deficiencies are common among children in developing countries and often occur in the same individual. Rice is widely consumed in the developing countries of Asia and the low phytate in polished rice makes it ideal for Zn and Fe fortification. Triple-fortified rice grains with Zn, Fe, and VA were produced using hot extrusion technology. **The main objective of the present study was to determine the impact of triple-fortified extruded rice on Zn status in school children in Southern Thailand.** Although serum zinc was the main outcome indicator, Fe and VA status were also assessed. **School children with low serum zinc (n = 203) were randomized to receive either triple-fortified rice (n = 101) or natural control rice (n = 102) as a component of school lunch meals for 5 mo.** Serum Zn, hemoglobin, serum ferritin, serum retinol, and C-reactive protein were measured at baseline and at the end of the study. **After the intervention, serum Zn increased (P < 0.05) in both the fortification (11.3 ± 1.3 μmol/L) and control (10.6 ± 1.4 μmol/L) groups, most likely due to the proper implementation of the school lunch and school milk programs, with the increase greater in the group receiving the triple-fortified rice (P < 0.05).** Because the children were not Fe or VA deficient at baseline, there was no change in Fe or VA status. We conclude that Zn fortification of extruded rice grains is efficacious and can be used to improve Zn status in school children.

Maize porridge enriched with a micronutrient powder containing low-dose iron as NaFeEDTA but not amaranth grain flour reduces anemia and iron deficiency in Kenyan preschool children.

Macharia-Mutie CW, Moretti D, Van den Briel N, Omusundi AM, Mwangi AM, Kok FJ, Zimmermann MB, Brouwer ID.

J Nutr. 2012 Sep;142(9):1756-63. doi: 10.3945/jn.112.157578. Epub 2012 Jul 18.

Source
Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands. catemutie@yahoo.com

Abstract
Few studies have evaluated the impact of fortification with iron-rich foods such as amaranth grain and multi-micronutrient powder (MNP) containing low doses of highly bioavailable iron to control iron deficiency anemia (IDA) in children. **We assessed the efficacy of maize porridge enriched with amaranth grain or MNP to reduce IDA in Kenyan preschool children**. In a 16-wk intervention trial, children (n = 279; 12-59 mo) were randomly assigned to: unrefined maize porridge (control; 4.1 mg of iron/meal; phytate:iron molar ratio 5:1); unrefined maize (30%) and amaranth grain (70%) porridge (amaranth group; 23 mg of iron/meal; phytate:iron molar ratio 3:1); or unrefined maize porridge with MNP (MNP group; 6.6 mg iron/meal; phytate:iron molar ratio 2.6:1; 2.5 mg iron as NaFeEDTA). Primary outcomes were anemia and iron status with treatment effects estimated relative to control. At baseline, 38% were anemic and 30% iron deficient. **Consumption of MNP reduced the prevalence of anemia [-46% (95% CI: -67, -12)], iron deficiency [-70% (95% CI: -89, -16)], and IDA [-75% (95% CI: -92, -20)]. The soluble transferrin receptor [-10% (95% CI: -16, -4)] concentration was lower, whereas the hemoglobin (Hb) [2.7 g/L (95% CI: 0.4, 5.1)] and plasma ferritin [40% (95% CI: 10, 95)] concentrations increased in the MNP group.** There was no significant change in Hb or iron status in the amaranth group. Consumption of maize

porridge fortified with low-dose, highly bioavailable iron MNP can reduce the prevalence of IDA in preschool children. In contrast, fortification with amaranth grain did not improve iron status despite a large increase in iron intake, likely due to high ratio of phytic acid:iron in the meal.

Effect on school attendance and performance of iron and multiple micronutrients as adjunct to drug treatment of Schistosoma-infected anemic schoolchildren.

Ayoya MA, Spiekermann-Brouwer GM, Traoré AK, Garza C.

Food Nutr Bull. 2012 Dec;33(4):235-41.

Source
UNICEF Country Office, 125 Rue Faubert, Petionville, Port-au-Prince, Haiti. mayoya@unicef.org

Abstract
BACKGROUND:
Relationships among Schistosoma haematobium, anemia, and iron deficiency have been documented, and all have been found to be associated with a decline in school attendance and lower performance.

OBJECTIVE:
To assess the effect of single or combined iron and multiple micronutrients and/or praziquantel on school attendance and achievement in randomly selected 7- to 12-year-old anemic children with documented S. haematobium infection (n = 406) in Mali over a 3-month period.

METHODS:
Schistosomiasis infection was diagnosed by the presence of schistosome eggs in the urine. Venous blood samples (5 mL) were drawn from an antecubital vein for hemoglobin assessment. **Children were randomly assigned to one of four treatment groups: praziquantel alone, praziquantel + iron, praziquantel + multiple micronutrients, and praziquantel + multiple micronutrients + iron.** School attendance was defined by the number of days the child was absent from class. Achievement was defined by the child's overall school grades.

RESULTS:
Changes within treatment groups from baseline to the end of study were found for attendance ($p < .001$) but not for achievement ($p > .05$). Significant supplement treatments by age group interactions were found in 7- to 9-year-old children for attendance. **Further exploration of treatment effects in this age group showed that only iron treatment's main effect was significant on attendance ($p = .049$) and was of borderline significance on school grades ($p = .08$).**

CONCLUSIONS:
Combined praziquantel and iron treatment improved children's school attendance and performance better than praziquantel alone, particularly among younger children.

Effect of wheat flour fortified with sodium iron EDTA on urinary zinc excretion in school-aged children.

Amalrajan V, Thankachan P, Selvam S, Kurpad A.

Food Nutr Bull. 2012 Sep;33(3):177-9.

Source
Division of Nutrition, St. John's Research Institute, St. John's National Academy of Health Sciences, Bangalore 560034, India.

Abstract
BACKGROUND:
Foods fortified with sodium iron ethylenediaminetetraacetate (NaFeEDTA) have been shown to improve iron status in children, but little is known about the effect of this salt on urinary zinc excretion, particularly in children. This is particularly relevant, since zinc deficiency is known to limit growth and development in young children.

OBJECTIVE:
To determine the effect of NaFeEDTA-fortified wheat flour on urinary zinc excretion.

METHODS:
This study was a part of a randomized, controlled trial that was carried out among 6- to 13-year-old iron-depleted schoolchildren (n = 179) who had received either a NaFeEDTA-fortified wheat meal (iron group) or an identical control meal without added iron (control group) for a period of 7 months. Urinary zinc concentration was assessed at the end of the intervention period by spot urine samples.

RESULTS:
Iron status in the iron group was significantly improved according to measurements of hemoglobin and serum ferritin ($p < .001$). However, there was no significant difference in urinary zinc excretion between the iron group (median, 38.4 microg/dL; 25th-75th percentiles, 18.2-67.1 microg/dL) and the control group (median, 33.1 microg/dL; 25th-75th percentiles, 12.4-54.2 microg/dL).

CONCLUSIONS:
Iron fortification of foods with NaFeEDTA does not affect urinary zinc excretion in children.

Breastfeeding and Complementary feeding

Does warming the breasts affect the amount of breastmilk production?

Yiğit F, Çiğdem Z, Temizsoy E, Cingi ME, Korel Ö, Yıldırım E, Ovalı F.

Breastfeed Med. 2012 Dec;7(6):487-8. doi: 10.1089/bfm.2011.0142. Epub 2012 Mar 16.

Source
School of Nursing, Maltepe University, Üsküdar, Istanbul, Turkey.

Abstract
BACKGROUND AND OBJECTIVE:
Increasing the amount of breastmilk is vital for both the nursing mother and child. Warming up breasts before using electrical pumps to pump out breastmilk may help to increase the amount of breastmilk, especially in the mothers of babies who are being nursed in the neonatal intensive care unit.

SUBJECTS AND METHODS:
Thirty-nine mothers whose babies had been admitted to the neonatal intensive care unit were analyzed. **A breast compress that was warmed up in a microwave oven for 1 minute at 180 W was applied to one of the breasts for 20 minutes, and both breasts were sucked by an electrical breast pump for 15 minutes**. The amount of breastmilk after each procedure was recorded.

RESULTS:
The amount of breastmilk that was obtained from warmed breasts was significantly higher than that obtained from nonwarmed breasts (maximum, 47.02 ± 23.01 mL vs. 33.15 ± 19.98 mL) (p=0.000).

CONCLUSION:
Warming up breasts by a breast compress is easy and affordable, and this procedure increases the amount of breastmilk, thus facilitating infant nutrition and recovery especially in the neonatal intensive care unit.

The effect of training administered to working mothers on maternal anxiety levels and breastfeeding habits.

Çiftçi EK, Arikan D.

J Clin Nurs. 2012 Aug;21(15-16):2170-8. doi: 10.1111/j.1365-2702.2011.03957.x. Epub 2011 Dec 9.

Source
Department of Child Health Nursing, School of Nursing, Harran University, Şanlıurfa, Turkey.

Abstract
AIM AND OBJECTIVE:
This study was conducted to determine the effect of training administered to working mothers and its duration on maternal anxiety levels and breastfeeding habits.
BACKGROUND:
Within the scope of Health for All in the 21st Century project, a goal was set to increase the rate of infants fed exclusively by breastfeeding during the first six months of life to 80% by the year 2015.

DESIGN:
A randomised design with repeated measures.

METHODS:

During collection of pretest data, a Personal Information Form, a Questionnaire Form and a State Trait Anxiety Inventory were administered to the mothers in the experimental and control groups. Five home visits were conducted starting two weeks before the date when mothers returned to work and ending when the infants became six months old. Breastfeeding techniques were taught to these mothers. Data were subjected to Proc MEAN, FREQ, anova and GENMOD procedures.

RESULTS:
The rate of natural feeding (breastfeeding exclusively) among trained mothers was greater than untrained mothers. The frequency of breastfeeding affects maternal anxiety levels; the anxiety level of mothers decreased with increasing frequency of breastfeeding.
CONCLUSION:
Educating working mothers about breastfeeding reduces their anxiety levels and influences positively their breastfeeding habits.

RELEVANCE TO CLINICAL PRACTICE:
With the support of health-care staff to increase awareness and knowledge on the value and sufficiency of breast milk, the rate and period of natural feeding increased significantly among working mothers.

Mother's perceptions and experiences of infant feeding within a community-based peer counselling intervention in South Africa.

Nor B, Ahlberg BM, Doherty T, Zembe Y, Jackson D, Ekström EC; PROMISE-EBF Study Group.

Matern Child Nutr. 2012 Oct;8(4):448-58. doi: 10.1111/j.1740-8709.2011.00332.x. Epub 2011 Jul 8.

Source
Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden.
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Abstract
Exclusive breastfeeding (EBF) has the potential to significantly reduce infant mortality, but is frequently not practiced in low-income settings where infants are vulnerable to malnutrition and infections including human immunodeficiency virus (HIV). **This study explores mothers' experiences of infant feeding after receiving peer counselling promoting exclusive breast or formula feeding.** This qualitative study was embedded in a cluster randomized peer counselling intervention trial in South Africa that aimed to evaluate the effect of peer counselling on EBF. Participants were selected from the three districts that were part of the trial reflecting different socio-economic conditions, rural-urban locations and HIV prevalence rates. Seventeen HIV-positive and -negative mothers allocated to intervention clusters were recruited. **Despite perceived health and economic benefits of breastfeeding, several barriers to EBF remained, which contributed to a preference for mixed feeding. The understanding of the promotional message of 'exclusive' feeding was limited to 'not mixing two milks': breast or formula and did not address early introduction of foods and other liquids.** Further, a crying infant or an infant who did not sleep at night were given as strong reasons for introducing semi-solid foods as early as 1 month. In addition, the need to adhere to the cultural practice of

'cleansing' and the knowledge that this practice is not compatible with EBF appeared to promote the decision to formula feed in HIV-positive mothers. Efforts to reduce barriers to EBF need to be intensified and further take into account the strong cultural beliefs that promote mixed feeding.

Cluster-randomized trial on complementary and responsive feeding education to caregivers found improved dietary intake, growth and development among rural Indian toddlers.

Vazir S, Engle P, Balakrishna N, Griffiths PL, Johnson SL, Creed-Kanashiro H, Fernandez Rao S, Shroff MR, Bentley ME.

Matern Child Nutr. 2013 Jan;9(1):99-117. doi: 10.1111/j.1740-8709.2012.00413.x. Epub 2012 May 24.

Source
Behavioral Sciences Unit of Field Studies, National Institute of Nutrition (ICMR), Hyderabad, India. s_vazir@hotmail.com

Abstract
Inadequate feeding and care may contribute to high rates of stunting and underweight among children in rural families in India. **This cluster-randomized trial tested the hypothesis that teaching caregivers appropriate complementary feeding and strategies for how to feed and play responsively through home-visits would increase children's dietary intake, growth and development compared with home-visit-complementary feeding education alone or routine care.** Sixty villages in Andhra Pradesh were randomized into three groups of 20 villages with 200 mother-infant dyads in each group. The control group (CG) received routine Integrated Child Development Services (ICDS); the complementary feeding group (CFG) received the ICDS plus the World Health Organization recommendations on breastfeeding and complementary foods; and the responsive complementary feeding and play group (RCF&PG) received the same intervention as the CFG plus skills for responsive feeding and psychosocial stimulation. Both intervention groups received bi-weekly visits by trained village women. The groups did not differ at 3 months on socioeconomic status, maternal and child nutritional indices, and maternal depression. After controlling for potential confounding factors using the mixed models approach, the 12-month intervention to the CFG and RCF&PG significantly ($P < 0.05$) increased median intakes of energy, protein, Vitamin A, calcium (CFG), iron and zinc, reduced stunting [0.19, confidence interval (CI): 0.0-0.4] in the CFG (but not RCF&PG) and increased ($P < 0.01$) Bayley Mental Development scores (mean = 3.1, CI: 0.8-5.3) in the RCF&PG (but not CFG) compared with CG. **Community-based educational interventions can improve dietary intake, length (CFG) and mental development (RCF&PG) for children under 2 years in food-secure rural Indian families.**

Infant feeding modes and determinants among HIV-1-infected African Women in the Kesho Bora Study.

Bork K, Cames C, Cournil A, Musyoka F, Ayassou K, Naidu K, Mepham S, Gichuhi C, Read JS, Gaillard P, de Vincenzi I; Kesho Bora Study Group.

J Acquir Immune Defic Syndr. 2013 Jan 1;62(1):109-18. doi: 10.1097/QAI.0b013e318277005e.

Source
Institut de Recherche pour le Développement (IRD), UMI233 IRD/UM1, Montpellier, France. kirsten.bork@ird.fr

Abstract
To assess breastfeeding modes and determinants in a prevention of mother-to-child transmission study.

DESIGN:
HIV-1-infected pregnant women from 5 sites in Burkina Faso, Kenya, and South Africa were enrolled in the study that comprised 2 prospective cohorts and 1 randomized controlled trial. Women were counseled to either breastfeed exclusively up to 6 months or formula feed from birth.

METHODS:
Determinants of breastfeeding initiation and continuation by 3 months postpartum were investigated using multiple logistic regression analysis. Neonatal morbidity was defined as mother-reported fever, diarrhea, or vomiting during the first month of life.

RESULTS:
Among 1028, 781 women (76%) initiated breastfeeding and 565 of 995 (56%) were still breastfeeding at 3 months postpartum (30% exclusively, 18% predominantly, and 8% partially). Study site (Durban, Mombasa, and Nairobi compared with Bobo-Dioulasso), CD4 cell count (<200 cells/mm), secondary schooling (compared with none), and emergency cesarean delivery (compared with vaginal delivery) were independently associated with a lower probability of ever breastfeeding. The odds of still breastfeeding by 3 months postpartum (among those breastfeeding by 1 month) were lower in Mombasa, Nairobi, and Somkhele (compared with Bobo-Dioulasso) and among infants with neonatal morbidity [0.60 (0.37-0.976)]. The odds of exclusive breastfeeding (EBF) by 3 months (if EBF by 1 month) were lower in Mombasa and Nairobi, in ill neonates [0.54 (0.31-0.93)] and boys [0.51 (0.34-0.77)].

CONCLUSIONS:
EBF was of short duration, particularly for boys. The importance of neonatal morbidity for breastfeeding cessation requires further investigation. Infant feeding counseling might need adaptation to better support mothers of boys and ill neonates.

Scaling up of breastfeeding promotion programs in low- and middle-income countries: the "breastfeeding gear" model.

Pérez-Escamilla R, Curry L, Minhas D, Taylor L, Bradley E.

Adv Nutr. 2012 Nov 1;3(6):790-800. doi: 10.3945/an.112.002873.

Source
Yale School of Public Health and Yale Global Health Leadership Institute, New Haven, CT, USA. rafael.perez-escamilla@yale.edu

Abstract
Breastfeeding (BF) promotion is one of the most cost-effective interventions to advance mother-child health. Evidence-based frameworks and models to promote the effective scale up and sustainability of BF programs are still lacking. A systematic review of peer-reviewed and gray literature reports was conducted to identify key barriers and facilitators for scale up of BF programs in low- and middle-income countries. The review identified BF programs located in 28 countries in Africa, Latin America and the Caribbean, and Asia. Study designs included case studies, qualitative studies, and observational quantitative studies. Only 1 randomized, controlled trial was identified. A total of 22 enabling factors and 15 barriers were mapped into a scale-up framework termed "AIDED" that was used to build the parsimonious breastfeeding gear model (BFGM). Analogous to a well-oiled engine, the BFGM indicates the need for several key "gears" to be working in synchrony and coordination. Evidence-based advocacy is needed to generate the necessary political will to enact legislation and policies to protect, promote, and support BF at the hospital and community levels. This political-policy axis in turn drives the resources needed to support workforce development, program delivery, and promotion. Research and evaluation are needed to sustain the decentralized program coordination "gear" required for goal setting and system feedback. The BFGM helps explain the different levels of performance in national BF outcomes in Mexico and Brazil. Empirical research is recommended to further test the usefulness of the AIDED framework and BFGM for global scaling up of BF programs.

Effectiveness of an educational intervention to improve child feeding practices and growth in rural China: updated results at 18 months of age.

Zhang J, Shi L, Chen DF, Wang J, Wang Y.

Matern Child Nutr. 2013 Jan;9(1):118-29. doi: 10.1111/j.1740-8709.2012.00447.x. Epub 2012 Oct 1.

Source
Department of Child, Adolescent and Women's Health, School of Public Health, Peking University Health Science Center, Beijing, China.

Abstract
Inappropriate complementary feeding practices have led to, in part, significant disparities in growth and nutritional status between rural and urban children in China. **A cluster-randomised, controlled trial was implemented in Laishui, China to assess the effectiveness of an educational intervention on caregivers' feeding practices and children's growth.** Eight townships were randomly assigned to the intervention or control. Five hundred ninety-nine healthy infants were enrolled at 2-4 months old, and were followed up at ages 6, 9, 12, 15 and 18 months. **The intervention group received information on enhanced home-prepared recipes and food preparation and hygiene through group training, counselling and home visit.** Key outcomes were children's physical growth, caregivers' knowledge and behaviours on complementary feeding, and the infant and child feeding index (ICFI). Analysis was by intention to treat. The intervention group achieved better knowledge and practices related to complementary feeding, and significantly higher ICFI scores at each follow-up point. **Children**

in the intervention group achieved higher z-scores for weight-for-age (WAZ) and weight-for-height (WHZ) than the control (0.18 vs. 0.01 and 0.49 vs. 0.19, respectively) at 18 months old, and were less likely to have stunted growth (odds ratio = 0.71, 95% confidence interval: 0.53-0.94). Mixed model showed that the intervention group achieved significantly better linear growth over time, including WAZ (P = 0.016), WHZ (P = 0.030) and HAZ (P = 0.078). These results indicated that an educational intervention delivered through local health services can enhance caregivers' knowledge and practices of complementary feeding and ultimately improve children's growth.

Comment
This is an important study, showing that educational interventions when delivered through local health services can be successful in improving feeding practices and nutritional outcomes.

A six-month intervention with two different types of micronutrient-fortified complementary foods had distinct short- and long-term effects on linear and ponderal growth of Vietnamese infants.

Pham VP, Nguyen VH, Salvignol B, Treche S, Wieringa FT, Dijkhuizen MA, Nguyen CK, Pham DT, Schwartz H, Berger J.

J Nutr. 2012 Sep;142(9):1735-40. doi: 10.3945/jn.111.154211. Epub 2012 Jul 18.

Source
Hanoi Medical University, Hanoi, Vietnam.

Abstract
Traditional complementary foods (CF) with a low nutrient density have been implicated in growth faltering, stunting, and other adverse outcomes in children. The efficacy of 2 types of locally produced, micronutrient-fortified CF to prevent stunting of infants living in rural Vietnam was evaluated. In a village-randomized controlled study, 426 infants, 5 mo of age, received for 6 mo a fortified CF, either as an instant flour (FF) or a food complement (FC) in village canteens, or traditional CF at home (C). After 6 mo of intervention, weight, length, length-for-age Z-score (LAZ) and weight-for-age Z-score were greater in the 2 intervention groups compared with the C group, with an estimated effect of +0.22 LAZ for the FF group and +0.21 LAZ for the FC group. At the last follow-up, 18 mo after the intervention, there was no significant difference in height-for-age Z-score (HAZ) between the groups, even though the HAZ in the FF group was 0.17 greater than that in the C group (P = 0.18). In contrast, the weight-for-height Z-score and BMI Z-score, indices of ponderal growth, were greater in the FF group (-0.49 and -0.26, respectively) than in the FC group (-0.73 and -0.49, respectively), with Z-scores in the C group intermediate and not significantly different from the others. This study shows that regular provision of locally produced CF fortified with micronutrients partly stopped growth faltering in Vietnamese infants, with differential effects on long-term length and ponderal growth. Providing only micronutrients instead of a complete array of nutrients might result in only short-term length growth benefits.

Macronutrient nutrition interventions

(See also Vitamin A)

Meat supplementation increases arm muscle area in Kenyan schoolchildren.

Neumann CG, Jiang L, Weiss RE, Grillenberger M, Gewa CA, Siekmann JH, Murphy SP, Bwibo NO.

Br J Nutr. 2013 Apr 14;109(7):1230-40. doi: 10.1017/S0007114512003121. Epub 2012 Aug 2.

Source
Fielding School of Public Health, University of California at Los Angeles, Los Angeles, CA, USA. cneumann@ucla.edu

Abstract
The present study examines the effect of animal-source-food (ASF) intake on arm muscle area growth as part of a larger study examining causal links between ASF intake, growth rate, physical activity, cognitive function and micronutrient status in Kenyan schoolchildren. This **randomised, controlled feeding intervention study was designed with three isoenergetic feeding interventions of meat, milk, and plain traditional vegetable stew (githeri), and a control group receiving no snack.** A total of twelve elementary schools were randomly assigned to interventions, with three schools per group, and two cohorts of 518 and 392 schoolchildren were enrolled 1 year apart. Children in each cohort were given feedings at school and studied for three school terms per year over 2 years, a total of 9 months per year: cohort I from 1998 to 2000 and cohort II from 1999 to 2001. Food intake was assessed by 24 h recall every 1-2 months and biochemical analysis for micronutrient status conducted annually (in cohort I only). Anthropometric measurements included height, weight, triceps skinfold (TSF) and mid-upper-arm circumference (MUAC). Mid-upper-arm muscle area (MAMA) and mid-upper-arm fat area (MAFA) were calculated. The two cohorts were combined for analyses. The meat group showed the steepest rates of gain in MUAC and MAMA over time, and the milk group showed the next largest significant MUAC and MAMA gain compared with the plain githeri and control groups ($P< 0.05$). The meat group showed the least increase in TSF and MAFA of all groups. These findings have implications for increasing micronutrient intake and lean body mass in primary schoolchildren consuming vegetarian diets.

Oncology

(see also HIV – management of HIV related conditions)

Impact of exercise on lower activity levels in children with acute lymphoblastic leukemia: a randomized controlled trial from Turkey.

Tanir MK, Kuguoglu S.

Rehabil Nurs. 2013 Jan-Feb;38(1):48-59. doi: 10.1002/rnj.58. Epub 2012 Oct 18.

Source
Zonguldak Karaelmas University, Zonguldak School of Nursing, Department of Pediatric Nursing, Zonguldak, Turkey. meltemkurtuncu@yahoo.com

Abstract
This randomized, controlled experimental study was carried out to determine the effects of an exercise program on both physical parameters and the quality of life of children with acute lymphoblastic leukemia (ALL). A total of 41 children with ALL (20 trial and 21 control cases) at two university hospitals were accepted into the study. Due to the demise of one of the children in the trial group, the study was completed with 19 trial and 21 control patients, a total of 40 children and their parents. Regular and systematic exercise regimens implemented by children with ALL have resulted in improved testing results, enhanced physical performance, and better laboratory results compared with a control group and to children's scores before the initiation of such a program.

Ophthalmology

Trachoma

(See also Hygiene)

Can we stop mass drug administration prior to 3 annual rounds in communities with low prevalence of trachoma?: PRET Ziada trial results.

Yohannan J, Munoz B, Mkocha H, Gaydos CA, Bailey R, Lietman TA, Quinn T, West SK.

JAMA Ophthalmol. 2013 Apr;131(4):431-6. doi: 10.1001/jamaophthalmol.2013.2356.

Source
Dana Center for Preventive Ophthalmology, USA.

Abstract
IMPORTANCE:
The World Health Organization recommends at least 3 annual mass drug administrations (MDAs) of azithromycin in places where the prevalence of follicular trachoma (FT) is greater than 10%. However, stopping MDA prior to 3 rounds, if monitoring indicates an absence of infection with Chlamydia trachomatis even if FT persists, may be more cost-effective.

OBJECTIVE:
To determine the prevalence of infection in communities randomized to **3 rounds of annual MDAs with azithromycin compared with communities randomized to a stopping rule, where MDA could cease if the infection rate was low.** DESIGN A 1:1 community randomized trial comparing usual care with a cessation rule. The Partnership for the Rapid Elimination of Trachoma-Ziada Trial was conducted from February 1, 2010, through September 1, 2011.

SETTING:
Sixteen communities in Tanzania with trachoma prevalence rates between 10% and 20%.

PARTICIPANTS:
A total of 100 children aged 5 years or younger randomly drawn from each community. Children had to reside in an eligible community, have no ocular condition that prevented trachoma grading or ocular specimen collection, and have a guardian who could provide consent for participation.

INTERVENTIONS:
Cessation of MDA with azithromycin if the community had no infection in their sample at 6 months or 18 months.

MAIN OUTCOME MEASURE:
The prevalence of C trachomatis at 18 months.

RESULTS:

None of the intervention communities met criteria to stop MDA based on the 6-month or 18-month survey; all, as well as the usual care communities, were scheduled for a third MDA round. There was no difference in infection (2.9% vs 4.7%; P = .25) between the usual care and cessation rule communities at 18 months.

CONCLUSIONS AND RELEVANCE:
In this setting, communities with low (10%-20%) initial prevalence of active trachoma did not have MDA stopped before 3 annual rounds on the basis of monitoring for infection. Infection with C trachomatis in communities with average trachoma rates at 12% to 13% cannot be eliminated before 3 rounds of MDA with azithromycin.

The easiest children to reach are most likely to be infected with ocular Chlamydia trachomatis in trachoma endemic areas of Niger.

Amza A, Kadri B, Nassirou B, Yu SN, Stoller NE, Bhosai SJ, Zhou Z, McCulloch CE, West SK, Bailey RL, Keenan JD, Lietman TM, Gaynor BD.

PLoS Negl Trop Dis. 2013;7(1):e1983. doi: 10.1371/journal.pntd.0001983. Epub 2013 Jan 10.

Source
Programme National de Lutte Contre la Cecité, Niamey, Niger.

Abstract
BACKGROUND:
Control programs for trachoma use mass antibiotic distributions to treat ocular Chlamydia trachomatis in an effort to eliminate this disease worldwide. To determine whether children infected with ocular Chlamydia are more likely to present later for examination than those who are uninfected, we compare the order of presentation for examination of children 0-5 years, and the presence of ocular Chlamydia by PCR in 4 villages in Niger where trachoma is endemic.

METHODS:
We conducted a cluster-randomized, controlled trial where 48 randomly selected villages in Niger are divided into 4 study arms of different mass treatment strategies. In a substudy of the main trial, we randomly selected 1 village from each of the 4 study arms (4 total villages) and we evaluated the odds of ocular Chlamydia versus the rank order of presentation for examination and laboratory assessment before treatment was offered.

FINDINGS:
We found the odds of harboring ocular Chlamydia dropped by more than 70% from the first child examined to the last child examined (OR 0.27, 95% CI 0.13-0.59, P=0.001) in the 4 randomly selected villages. We found the odds of active trachoma dropped by 80% from the first child examined to the last child examined (OR 0.20, 95% CI 0.10-0.4, P<0.0001) in the 48 villages in the main trial.

INTERPRETATION:
This study demonstrates that even if the WHO recommended 80% treatment coverage is not reached in certain settings, children 0-5 years with the greatest probability of ocular Chlamydia have higher odds of receiving attention because they are the first to present.

These results suggest there may be diminishing returns when using scarce resources to track down the last few children in a mass treatment program.

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Comment
This is an important study, which shows that symptomatic children with ocular Chlamydia are most likely to be brought to receive antibiotics as part of mass drug administration. This is an encouraging counter-point to the theory that children most affected (with a particular disease) are likely to be living more remotely, or their parents more likely to have poor care seeking behaviour, so less likely to be treated. The study suggests that families are motivated to seek care when it is provided, and that they link the symptoms with the program. Whether this applies to other disease interventions and programs is not clear, but it is encouraging.

A cluster-randomized controlled trial evaluating the effects of mass azithromycin treatment on growth and nutrition in Niger.

Amza A, Kadri B, Nassirou B, Stoller NE, Yu SN, Zhou Z, West SK, Mabey DC, Bailey RL, Keenan JD, Porco TC, Lietman TM, Gaynor BD.

Am J Trop Med Hyg. 2013 Jan;88(1):138-43. doi: 10.4269/ajtmh.2012.12-0284. Epub 2012 Dec 3.

Source
Université Abdou Moumouni de Niamey, Programme National de Lutte Contre la Cécité, Niamey, Niger. dr.amzaabdou@gmail.com

Abstract
Antimicrobials are used primarily to treat infectious disease, but they have other effects. Here, we assess anthropometry measurements in children 6-60 months in 24 communities randomized to one or two mass azithromycin distributions over a 1-year period in Niger. We compared the prevalence of wasting, low mid-upper arm circumference, stunting, and underweight in communities in the two treatment arms. **We were unable to prove that there was a difference in the prevalence of wasting in the 12 communities that received one mass azithromycin distribution versus the 12 communities that received two mass azithromycin distributions (odds ratio = 0.75, 95% confidence interval = 0.46-1.23).** Likewise, we were unable to detect a difference in the two treatment arms for low mid-upper arm circumference, stunting, and underweight. There may not be an association between antibiotic use and improved growth in humans, or this trial was not powerful enough to detect an association if it exists.

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Oral health / dentistry

(See Health education)

Caries risk management: effect on caries incidence in a sample of Lebanese preschool children.

Chedid NR, Bourgeois D, Kaloustian H, Pilipili C, Baba NZ.

Odontostomatol Trop. 2012 Sep;35(139):26-40.

Source
Dpt Pediatric and Community Dentistry, Fac. Médecine dentaire, Univ. Saint-Joseph, Beirut, Lebanon.

Abstract
OBJECTIVES:
This clinical prospective study describes how caries preventive measures applied according to caries risk affect new caries incidence in a group of preschoolers, as compared to a group where standardized caries prevention is applied, regardless of risk.

METHOD AND MATERIALS:
Healthy children, aged four years or less, recruited at the Faculté de Médecine Dentaire, Université Saint-Joseph, Beirut, Lebanon were assigned, after parental consent, to an experimental or a control group. Caries risk was determined based on a parental questionnaire, salivary levels of Steptococcus mutans (Sm) and Lactobacillus (Lb), salivary buffer capacity, plaque levels and carious lesions prevalence, then subjects were classified into four caries risk categories. **In the experimental group, preventive measures designed for each risk category were applied periodically, whereas control subjects received only standardized preventive measures at regular intervals.** All subjects were reevaluated for Sm, Lb, salivary buffer capacity, plaque and new carious lesions after 24 months.

RESULTS:
Statistically significant reductions in salivary Sm (p=0.001) and Lb (p=0.003) levels, plaque scores (p=0) and caries incidence (p=0.003) were observed in the experimental group. In the control group, no significant differences were observed between initial and final Sm (p=0.18) and Lb (p=0.109) levels or plaque scores (p=0.255), and caries incidence was not significantly reduced (p=0.584).

CONCLUSION:
The present study's results suggest that caries preventive measures applied according to caries risk may reduce caries risk factors and new caries incidence in preschool-aged children. These findings deserve further investigation to benefit early childhood caries prevention on a larger scale.

Effect of a school-based oral health-education program on Iranian children: results from a group randomized trial.

Yekaninejad MS, Eshraghian MR, Nourijelyani K, Mohammad K, Foroushani AR, Zayeri F, Pakpour AH, Moscowchi A, Tarashi M.

Eur J Oral Sci. 2012 Oct;120(5):429-37. doi: 10.1111/j.1600-0722.2012.00993.x. Epub 2012 Aug 24.

Source
Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.

Abstract
Parents and school staff play important roles in promoting children's oral health. Our study goals were to investigate whether an intervention targeting parents and school staff can improve the oral-health behavior and oral-health status of schoolchildren. Three-hundred and ninety-two schoolchildren in six schools in Tehran participated in a group randomized trial from September 2010 to March 2011. Schools were randomly allocated into three groups: comprehensive, student, and control. **Intervention in the comprehensive group consisted of strategies to encourage children, their parents, and school staff to increase the frequency of toothbrushing and flossing. In the student group, the intervention targeted only children. The control group received no intervention.** The primary outcome was change in oral-health behaviors (brushing and flossing), while the secondary outcomes were changes in oral hygiene and Community Periodontal indices and in Health Belief Model components. Multilevel modeling was employed for data analyses. **Students who were in the comprehensive intervention group brushed and flossed significantly more frequently compared with those in the student intervention group.** Although students' gingival health improved significantly in the comprehensive intervention group, such significant improvement was not seen in the student group. In conclusion, promising results are seen when the oral-health education targets both school and home settings.

Gingivitis and plaque scores of 8- to 11-year-old Burmese children following participation in a 2-year school-based toothbrushing programme.

Rosema NA, van Palenstein Helderman WH, Van der Weijden GA.

Int J Dent Hyg. 2012 Aug;10(3):163-8. doi: 10.1111/j.1601-5037.2012.00553.x. Epub 2012 Apr 30.

Source
Department of Periodontology, Academic Centre for Dentistry, Amsterdam (ACTA), University of Amsterdam and VU University, Amsterdam, The Netherlands. n.rosema@acta.nl

Abstract
AIM:

The present study assessed whether gingivitis and plaque scores of 8- to 11-year-old school children who participated in a SBTB programme for 2 years were lower than those of children who did not participate in the programme.

MATERIAL AND METHODS:
The present study was performed using an examiner-blind, parallel group design and was performed in Burma (Myanmar) in 2006. Three of the five schools where daily SBTB programmes took place after lunch and which were performed under teacher supervision were randomly selected; three non-participating schools (non-SBTB) from the same area were assigned as controls. Twenty-five children per school were examined for gingivitis (bleeding on marginal probing) and plaque (Quigley & Hein).

RESULTS:
In total, 150 8- to 11-year-old children participated, with 75 children in either group. The test group (SBTB) exhibited an overall mean bleeding score of 0.76. For the control group (non-SBTB), this score was 0.83. With respect to the overall mean plaque scores, the test group exhibited a score of 2.93, whereas the control group exhibited a score of 2.91. No statistically significant differences between the test and the control group were observed.

CONCLUSION:
The present study did not reveal a statistically significant effect of daily SBTB programmes in 8- to 11-year-old school children with respect to gingivitis and plaque scores.

Comment
SBTB = "School-based Tooth Brushing" program!

Effect of CPP-ACP paste on dental caries in primary teeth: a randomized trial.

Sitthisettapong T, Phantumvanit P, Huebner C, Derouen T.

J Dent Res. 2012 Sep;91(9):847-52. doi: 10.1177/0022034512454296. Epub 2012 Jul 17.

Source
Faculty of Dentistry, Thammasat University, Rangsit Campus, Patumthani, Thailand.

Abstract
This clinical trial tested the effect of daily application of 10% w/v calcium phosphopeptide-amorphous calcium phosphate (CPP-ACP) paste for 1 yr when added to regular toothbrushing with fluoridated toothpaste to prevent dental caries in pre-school children. High-caries-risk children aged 2½ to 3½ yrs in a suburban area of central Thailand were assigned to receive either CPP-ACP (n = 150) or a placebo control (n = 146) in addition to fluoridated toothpaste. The International Caries Detection and Assessment System (ICDAS) was recorded at baseline, 6 mos, and 1 yr. At 1 yr, a significant increase in mean numbers of enamel and dentin caries lesions, as well as dmfs, was found in both groups ($p < 0.001$). No significant difference was observed between groups on these 3 outcome measures ($p = 0.23$, 0.84, and 0.91, respectively). The odds of enamel caries lesion transitions to a state of regression or stability, compared with

progression from baseline, was also not different between groups [OR = 1.00, 95% CI (0.86, 1.17)]. This trial found that daily application of 10% w/v CPP-ACP paste on school days for 1 yr, when added to regular toothbrushing with a fluoride toothpaste, had no significant added effect in preventing caries in the primary dentition of these pre-school children (ClinicalTrials.gov number CT01 604109).

Evaluating the effect of probiotic containing milk on salivary mutans streptococci levels.

Juneja A, Kakade A.

J Clin Pediatr Dent. 2012 Fall;37(1):9-14.

Source
Department of Pediatric and Preventive Dentistry, Jamia Millia Islamia, New Delhi, India. akajuneja@yahoo.com

Abstract
PURPOSE:
To evaluate the changes in mutans streptococci counts in saliva after short term probiotic intervention and its delayed effects on salivary mutans streptococci count.

METHODS:
40 children in the age group of 12-15 years with medium to high caries activity were randomly divided into Group I Control (plain milk group) and Group II Experimental (probiotic supplemented milk group). Duration of the study was 9 weeks; which was evenly divided into three phases: baseline, intervention and post-treatment period; each phase consisting of three weeks. After baseline period of 3 weeks, children in group I were given plain milk and in group II milk containing probiotic Lactobacillus rhamnosus hct 70 for 3 weeks; followed by a 3 weeks follow up period. After every phase saliva samples were collected to estimate salivary mutans streptococci counts.

RESULTS:
The difference in the post follow up mutans streptococci count of group I and group II, was highly significant with p value < 0.001. In the control group, the difference in the mean salivary baseline, post treatment and post follow up mutans streptococci counts was not statistically significant (p > 0.001). **In the experimental probiotic group, the difference in mean salivary baseline, post treatment and post follow up mutans streptococci counts was statistically highly significant (p = 0.000, p < 0.001).**

CONCLUSIONS:
Statistically significant reduction in salivary mutans streptococci counts immediately after consumption of probiotic Lactobacillus rhamnosus hct 70 containing milk suggest a beneficial effect of probiotic Lactobacillus rhamnosus hct 70 in the prevention of dental caries

Caries preventive efficacy of silver diammine fluoride (SDF) and ART sealants in a school-based daily fluoride toothbrushing program in the Philippines.

Monse B, Heinrich-Weltzien R, Mulder J, Holmgren C, van Palenstein Helderman WH.

BMC Oral Health. 2012 Nov 21;12:52. doi: 10.1186/1472-6831-12-52.

Source
Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH, GIZ Office Manila, PDCP Bank Centre, V,A, Rufino cor, L,P, Leviste Str, Makati City, Metro Manila, Philippines. bella.monse@giz.de

Abstract
BACKGROUND:
Occlusal surfaces of erupting and newly erupted permanent molars are particularly susceptible to caries.The objective of the study was to assess and compare the effect of a single application of 38% SDF with ART sealants and no treatment in preventing dentinal (D3) caries lesions on occlusal surfaces of permanent first molars of school children who participated in a daily school-based toothbrushing program with fluoride toothpaste.

METHODS:
The prospective community clinical trial in the Philippines was conducted over a period of 18 months and included 704 six- to eight-year-old school children in eight public elementary schools with a daily school-based fluoride toothpaste brushing program. Children were randomly assigned for SDF application or ART sealant treatment. Children from two of the eight schools did not receive SDF or ART sealant treatment and served as controls. SDF or ART sealant treatment was applied on sound occlusal surfaces of permanent first molars. Surfaces that were originally defined as sound at baseline but which changed to dentinal (D3) caries lesions were defined as surfaces with new caries (caries increment). Non-compliance to the daily toothbrushing program in three schools offered the opportunity to analyze the caries preventive effect of SDF and sealants separately in fluoride toothpaste brushing and in non-toothbrushing children.

RESULTS:
In the brushing group, caries increment in the SDF treatment group was comparable with the non-treatment group but caries increment in the sealant group was lower than in the non-treatment group with a statistically significant lower hazard ratio of 0.12 (0.02-0.61). In the non-brushing group, caries increment in the SDF treatment group and the sealant group was lower than the non-treatment group but the hazard ratio was only statistically significant for the sealant group (HR 0.33; 0.20-0.54). Caries increment was lower in toothbrushing children than in non-toothbrushing children. Hazard ratios reached statistical significance for the non-treated children (HR 0.43; 0.21-0.87) and the sealant-treated children (HR 0.15; 0.03-0.072).

CONCLUSIONS:
A one-time application of 38% SDF on the occlusal surfaces of permanent first molars of six- to eight-year-old children is not an effective method to prevent dentinal (D3) caries lesions. ART sealants significantly reduced the onset of caries over a period of 18 months.

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Anxiety in children during occlusal ART restorations in primary molars placed in school environment and hospital dental setup.

Roshan NM, Sakeenabi B.

Clin Pediatr Dent. 2012 Summer;36(4):349-52.

Source
Department of Pedodontics and Preventive Dentistry, College of Dental Sciences, Davangere, Karnataka, India. drroshannm@yahoo.co.in

Abstract
OBJECTIVE:
To evaluate the anxiety in children during occlusal atraumatic restorative treatment (ART) in the primary molars of children; and compare the anxiety for ART procedure performed in school environment and in hospital dental setup.

STUDY DESIGN:
A randomized controlled trial where one dentist placed 120 ART restorations in 60 five- to seven year-olds who had bilateral matched pairs of occlusal carious primary molars. A split-mouth design was used to place restorations in school and in hospital dental setup, which were assigned randomly to contralateral sides. Anxiety was evaluated by Modified Venhem score and the heart rate of the children at five fixed moments during dental treatment.

RESULTS:
At the entrance of the children into the treatment room, statistically significant difference between treatment in school environment and treatment in hospital dental setup for venham score and heart rate could be found ($P = 0.023$ and $P = 0.037$ respectively). At the start of the treatment procedure higher venham score and heart rate was observed in children treated in hospital dental setup in comparison with the children treated in school environment, finding was statistically significant ($P = 0.011$ and $P = 0.029$ respectively). During all other three points of treatment, the Venham scores of the children treated in school were lower than those of the children treated in hospital dental setup but statistically not significant ($P > 0.05$). Positive co-relation between Venham scores and Heart rate was established. No statistically significant relation could be established between boys and girls.

CONCLUSIONS:
Overall anxiety in children for ART treatment was found to be less and the procedure was well accepted irrespective of environment where treatment was performed Hospital dental setup by itself made children anxious during entrance and starting of the treatment when compared to children treated in school environment.

The effects of extraction of pulpally involved primary teeth on weight, height and BMI in underweight Filipino children. A cluster randomized clinical trial.

Monse B, Duijster D, Sheiham A, Grijalva-Eternod CS, van Palenstein Helderman W, Hobdell MH.

BMC Public Health. 2012 Aug 31;12:725. doi: 10.1186/1471-2458-12-725

Source
Department of Preventive Dentistry, Academic Centre for Dentistry Amsterdam, Gustav Mahlerlaan 3004, Amsterdam, 1081LA, The Netherlands.

Abstract
BACKGROUND:
Severe dental caries and the treatment thereof are reported to affect growth and well-being of young children. The objective of this study was to assess the effects of extraction of severely decayed pulpally involved primary teeth on weight and height in underweight preschool Filipino children.

METHODS:
Underweight preschool Filipino children with severe dental decay had their pulpally involved primary teeth extracted during a stepped wedge cluster randomized clinical trial. Day care centers were randomly divided into two groups; children from Group A day care centers received treatment as soon as practical, whereas children from Group B day care centers were treated four months after Group A. Clinical oral examinations using WHO criteria and the pufa-index were carried out. Anthropometric measurements were done on both groups immediately before treatment of Group A and at follow-up four months later. Height and weight z-scores were calculated using 2006 and 2007 WHO Growth Standards. Multilevel analysis was used to assess the effect of dental extractions on changes in anthropometric measurements after dental treatment.

RESULTS:
Data on 164 children (85 in Group A and 79 in Group B), mean age 59.9 months, were analyzed. Both groups gained weight and height during the trial period. Children in Group A significantly increased their BMI ($p < 0.001$), and their weight-for-age ($p < 0.01$) and BMI-for-age z-scores ($p < 0.001$) after dental treatment, whereas untreated children in Group B did not. Children in Group A had significantly more weight gain ($p < 0.01$) compared to untreated children in Group B. However, children in Group A had an inverse change in height gain ($p < 0.001$). Adjustment for the time interval between the two visits had little effect on the results.

CONCLUSIONS:
The extraction of severely decayed primary teeth resulted in significant weight gain in underweight Filipino children. Untreated dental decay should be considered an important co-factor affecting child growth and should be considered when planning for interventions to improve child growth.

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Research methods

Smartphone versus pen-and-paper data collection of infant feeding practices in rural China.

Zhang S, Wu Q, van Velthoven MH, Chen L, Car J, Rudan I, Zhang Y, Li Y, Scherpbier RW.

J Med Internet Res. 2012 Sep 18;14(5):e119.

Source
Department of Integrated Early Childhood Development, Capital Institute of Pediatrics, Beijing, China.

Abstract
BACKGROUND:
Maternal, Newborn, and Child Health (MNCH) household survey data are collected mainly with pen-and-paper. Smartphone data collection may have advantages over pen-and-paper, but little evidence exists on how they compare.

OBJECTIVE:
To compare smartphone data collection versus the use of pen-and-paper for infant feeding practices of the MNCH household survey. We compared the two data collection methods for differences in data quality (data recording, data entry, open-ended answers, and interrater reliability), time consumption, costs, interviewers' perceptions, and problems encountered.

METHODS:
We recruited mothers of infants aged 0 to 23 months in four village clinics in Zhaozhou Township, Zhao County, Hebei Province, China. We randomly assigned mothers to a smartphone or a pen-and-paper questionnaire group. A pair of interviewers simultaneously questioned mothers on infant feeding practices, each using the same method (either smartphone or pen-and-paper).

RESULTS:
We enrolled 120 mothers, and all completed the study. Data recording errors were prevented in the smartphone questionnaire. In the 120 pen-and-paper questionnaires (60 mothers), we found 192 data recording errors in 55 questionnaires. There was no significant difference in recording variation between the groups for the questionnaire pairs (P = .32) or variables (P = .45). The smartphone questionnaires were automatically uploaded and no data entry errors occurred. We found that even after double data entry of the pen-and-paper questionnaires, 65.0% (78/120) of the questionnaires did not match and needed to be checked. The mean duration of an interview was 10.22 (SD 2.17) minutes for the smartphone method and 10.83 (SD 2.94) minutes for the pen-and-paper method, which was not significantly different between the methods (P = .19). The mean costs per questionnaire were higher for the smartphone questionnaire (¥143, equal to US $23 at the exchange rate on April 24, 2012) than for the pen-and-paper questionnaire (¥83, equal to US $13). The smartphone method was acceptable to interviewers, and after a pilot test we encountered only minor problems (eg, the system halted for a few seconds or it shut off), which did not result in data loss.

CONCLUSIONS:

This is the first study showing that smartphones can be successfully used for household data collection on infant feeding in rural China. Using smartphones for data collection, compared with pen-and-paper, eliminated data recording and entry errors, had similar interrater reliability, and took an equal amount of time per interview. While the costs for the smartphone method were higher than the pen-and-paper method in our small-scale survey, the costs for both methods would be similar for a large-scale survey. Smartphone data collection should be further evaluated for other surveys and on a larger scale to deliver maximum benefits in China and elsewhere.

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School health

(See Nutrition, Ophthalmology, Adolescent health, Anaemia and iron deficiency)

Skin disease

Comparative efficacy and safety of topical permethrin, topical ivermectin, and oral ivermectin in patients of uncomplicated scabies.

Chhaiya SB, Patel VJ, Dave JN, Mehta DS, Shah HA.

Indian J Dermatol Venereol Leprol. 2012 Sep-Oct;78(5):605-10. doi: 10.4103/0378-6323.100571.

Source
Department of Pharmacology, C. U. Shah Medical College, Surendranagar, Gujarat, India.

Abstract
BACKGROUND:
Ivermectin has opened a new era in the management of scabies as orally effective drug. However, topical route has been little explored for ivermectin.

AIMS:
To compare the efficacy and safety of topical permethrin, oral ivermectin, and topical ivermectin in the treatment of uncomplicated scabies.

METHODS:
This was an open-label, randomized, comparative, parallel clinical trial conducted in 315 patients, randomly allocated to 3 groups. First group received permethrin 5% cream as single application, second group received tablet ivermectin 200 mcg/kg as single dose, and third group received ivermectin 1% lotion as single application. All the patients received anti-histaminic for pruritus. The patients were followed up at intervals of 1, 2, 3, and 4 weeks. If there were no signs of cure, the same intervention was repeated at each follow up. Primary efficacy variable was clinical cure of lesions. Statistical analysis was done by chi square test and one way ANOVA test using SPSS version 12.

RESULTS:
At the end of first week, cure rate was 74.8% in permethrin group, 30% in oral ivermectin group, and 69.3% in topical ivermectin group ($P < 0.05$). **At the end of second week, cure rate was 99% in permethrin group, 63% in oral ivermectin group, and 100% in topical ivermectin group ($P < 0.05$).** At the end of third week, 100% cure rate was observed in permethrin and topical ivermectin group while 99% in oral ivermectin group ($P = 0.367$). No serious adverse events were observed.

CONCLUSIONS:
Permethrin and topical ivermectin were equally effective against scabies while oral ivermectin was significantly less effective up to 2 weeks. Topical ivermectin can be used as an alternative to permethrin.

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Clinical efficacy and safety of a pharmacopial polyherbal Unani formulation in pityriasis versicolor: a comparative randomized single-blind study.

Lone AH, Ahmad T, Anwar M, Sofi G.

J Altern Complement Med. 2012 Oct;18(10):978-82. doi: 10.1089/acm.2011.0520. Epub 2012 Aug 7.

Source
Department of Medicine and Dermatology, National Institute of Unani Medicine (NIUM), Bangalore, India. drazadnium@rediffmail.com

Abstract
BACKGROUND:
Pityriasis versicolor (PV) is a common superficial fungal infection of skin caused by the fungus, Malassezia furfur. It can occur at any age but occurs mainly during adolescence and typically presents with hypopigmented or hyperpigmented scaling plaques, generally on the trunk and upper arms. It often poses a therapeutic challenge. In the Unani system of medicine, many herbal drugs are used empirically for its treatment.

OBJECTIVES:
The objective of this study was to evaluate safety and efficacy of a topical Polyherbal Unani formulation in the management of PV on scientific parameters.
DESIGN:
This was a randomized, single-blind, standard controlled study.

LOCATION:
This study was performed in the Dermatology Outpatient Department, National Institute of Unani Medicine, Bangalore, India.

SUBJECTS AND INTERVENTIONS:
Forty-six (46) patients with PV were included in the study after taking informed consents and were randomly allocated to test and control groups. **In the test group, a polyherbal formulation was advised for topical application while in the control group, sodium thiosulphate lotion (20%) was advised locally for a duration of 1 month.** The assessment of the severity of PV and efficacy of treatment in both groups was carried out using the Total Sign and Symptom Score (TSSS) scale. Data were analyzed with the Instat Graph pad.

RESULTS:
The mean±standard error of the mean (SEM) scores of TSSS in the test group were 7.7±1.174 and 0.9±0.7881 before and after treatment, respectively, while it was 6.9±0.8756 and 1.2±0.7888 in the control group before and after treatment, respectively. Mean±SEM of TSSS of both groups was found to be significantly lowered ($p<0.001$) after treatment when compared with mean±SEM of TSSS before treatment. However, the polyherbal formulation showed precedence over the standard drug by exhibiting comparatively quicker response. Furthermore, no unpleasant side-effects were observed in the test group during and after the study.

CONCLUSIONS:

This study concluded that polyherbal Unani formulation is safe, effective, and superior to standard drug in the treatment of PV.

Comparison between autologous noncultured epidermal cell suspension and suction blister epidermal grafting in stable vitiligo: a randomized study.

Budania A, Parsad D, Kanwar AJ, Dogra S.

Br J Dermatol. 2012 Dec;167(6):1295-301. doi: 10.1111/bjd.12007.

Source
Department of Dermatology, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India.

Abstract
BACKGROUND:
Vitiligo is an acquired disorder of pigmentation due to loss of epidermal melanocytes. Autologous noncultured epidermal cell suspension (NCES; a cellular grafting technique) and suction blister epidermal grafting (SBEG; a tissue grafting technique) are important established surgical modalities for the treatment of stable vitiligo.

OBJECTIVES:
To compare the two techniques, NCES and SBEG, for producing repigmentation in patients with stable vitiligo.

METHODS:
We randomized 41 patients with 54 stable vitiligo lesions into two groups. Patients in group 1 were treated with NCES, and those in group 2 with SBEG. They were evaluated 16 weeks postsurgery for the extent of repigmentation, colour match, change in Dermatology Life Quality Index (DLQI) score and patient satisfaction.

RESULTS:
The extent of repigmentation was excellent (showing 90-100% repigmentation) in 71% of lesions in the NCES group and 27% of lesions in the SBEG group (P = 0·002). Repigmentation ≥ 75% (good repigmentation) was observed in 89% of lesions in the NCES group and 85% of lesions in the SBEG group (P = 0·61). There was a significant decline in DLQI score in both the groups; the mean decline among groups differed significantly (P = 0·045). No significant difference was seen in colour match and pattern of repigmentation. Adverse effects were minimal.

CONCLUSIONS:
NCES is significantly better than SBEG and should be the preferred treatment for patients with stable vitiligo. To best of our knowledge, this is the first study directly comparing these two techniques

Researching accessible and affordable treatment for common dermatological problems in developing countries. An Ethiopian experience.

Shimelis ND, Asticcioli S, Baraldo M, Tirillini B, Lulekal E, Murgia V.

Int J Dermatol. 2012 Jul;51(7):790-5. doi: 10.1111/j.1365-4632.2011.05235.x.

Source
All African Leprosy and Dermatology Education and Training Center, Addis Ababa University, Addis Ababa, Ethiopia.

Abstract
BACKGROUND:
Skin diseases are very common in rural and urban areas of Ethiopia, and traditional preparations of plant origin might represent the only alternative to synthetic drugs. Improving knowledge of traditional medicines and assessing their safety and effectiveness is necessary.

METHODS:
We conducted a two-arm, randomized, double-blind, placebo-controlled trial assessing the efficacy of some cosmetic herbal preparations for common dermatologic problems: a 3% thyme essential oil antifungal cream and a 10% chamomile extract cream for eczema-like lesions.

RESULTS:
Ten subjects (66.5%) treated with the 3% thyme active cream were completely healed vs. four subjects (28.5%) from the placebo group (P=0.040). A large number of subjects treated with the chamomile cream were healed or improved, but no significant differences were found between active cream and placebo. A high rate of treatment acceptance was registered in both groups, no adverse effects were reported.

CONCLUSIONS:
A 3% thyme essential oil cream could represent a cheap and easily available opportunity to treat and heal mild to moderate cases of fungal infections; a common emollient cream could be a very effective intervention when treating mild to moderate cases of pityriasis alba and eczema-like lesions. Further research is needed.

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Surgical problems

Untreated surgical conditions in Sierra Leone: a cluster randomised, cross-sectional, countrywide survey.

Groen RS, Samai M, Stewart KA, Cassidy LD, Kamara TB, Yambasu SE, Kingham TP, Kushner AL.

Lancet. 2012 Sep 22;380(9847):1082-7. doi: 10.1016/S0140-6736(12)61081-2. Epub 2012 Aug 14.

Source
Surgeons OverSeas, New York, NY 10003, USA. rsgroen@hotmail.com

Abstract
BACKGROUND:
Surgical care is increasingly recognised as an important part of global health yet data for the burden of surgical disease are scarce. The Surgeons OverSeas Assessment of Surgical Need (SOSAS) was developed to measure the prevalence of surgical conditions and surgically treatable deaths in low-income and middle-income countries. We administered this survey countrywide in Sierra Leone, which ranks 180 of the 187 nations on the UN Development Index.

METHODS:
The study was done between Jan 9 and Feb 3, 2012. 75 of 9671 enumeration areas, the smallest administrative units in Sierra Leone, were randomly selected for the study clusters, with a probability proportional to the population size. In each cluster 25 households were randomly selected to take part in the survey. Data were collected via handheld tablets by trained local medical and nursing students. A household representative was interviewed to establish the number of household members (defined as those who ate from the same pot and slept in the same structure the night before the interview), identify deaths in the household during the previous year, and establish whether any of the deceased household members had a condition needing surgery in the week before death. Two randomly selected household members underwent a head-to-toe verbal examination and need for surgical care was recorded on the basis of the response to whether they had a condition that they believed needed surgical assessment or care.

FINDINGS:
Of the 1875 targeted households, data were analysed for 1843 (98%). 896 of 3645 (25%; 95% CI 22·9-26·2) respondents reported a surgical condition needing attention and 179 of 709 (25%; 95% CI 22·5-27·9) deaths of household members in the previous year might have been averted by timely surgical care.

INTERPRETATION:
Our results show a large unmet need for surgical consultations in Sierra Leone and provide a baseline against which future surgical programmes can be measured. Additional surveys in other low-income and middle-income countries are needed to document and confirm what seems to be a neglected component of global health.

Parental evaluation of postoperative outcome of circumcision with Plastibell or conventional dissection by dorsal slit technique: A randomized controlled trial.

Nagdeve NG, Naik H, Bhingare PD, Morey SM.

J Pediatr Urol. 2012 Nov 1. pii: S1477-5131(12)00210-0. doi: 10.1016/j.jpurol.2012.08.001. [Epub ahead of print]

Source
Pediatric Surgery Unit, Department of Surgery, Government Medical College, Nagpur, India. Electronic address: nileshngn74@yahoomail.co.in.

Abstract
AIM:
To evaluate and compare parental satisfaction after Plastibell and conventional dissection circumcision.

METHODS:
198 children were randomly and equally allocated to two groups (PD: Plastibell and CDS: dissection) for circumcision. Follow-up was done at 7th, 15th and 90th day after surgery. Written questionnaires were given to parents at the time of discharge to complete and return at the 15th and 90th day follow-up visits.

RESULTS:
Both groups were balanced with respect to various demographic factors, indications for surgery and Kayaba's classification of the prepuce. Surgical duration was significantly shorter for the PD as compared to the CDS group (5.91 ± 1.74 min vs. 23.52 ± 5.94 min; $p < 0.0001$ H.S.). Swelling, dysuria and infection were the prominent problems reported in both groups in the first 7 days. The Plastibell separated earlier in younger children ($p < 0.0001$). Postoperatively, children in the PD group required 2.79 fold more analgesic than those in the CDS group. 97.9% of parents in the PD group and 80.2% of parents in the CDS group claimed satisfactory aesthetic results. The PD group parents were statistically significantly more concerned about swelling.

CONCLUSIONS:
Plastibell use has comparable outcomes to the conventional dissection technique for paediatric circumcision and has an obvious advantage of shorter surgical duration. However, it is less comfortable in the postoperative period due to swelling, and requires greater use of analgesics.

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Surgical outcome in children undergoing hypospadias repair under caudal epidural vs penile block.

Kundra P, Yuvaraj K, Agrawal K, Krishnappa S, Kumar LT.

Paediatr Anaesth. 2012 Jul;22(7):707-12. doi: 10.1111/j.1460-9592.2011.03702.x. Epub 2011 Sep 29.

Source
Department of Anaesthesiology & Critical Care, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India. p_kundra@hotmail.com

Abstract
AIM AND OBJECTIVE:
To evaluate the effect of penile block vs caudal epidural on the quality of analgesia and surgical outcome following hypospadias repair.

BACKGROUND:
Intraoperative penile engorgement because of caudal epidural may result in tension on surgical sutures and alter surgical outcome.

METHODS:
Fifty-four ASA I and II children were randomly allocated to group P (penile block, 0.25% bupivacaine, 0.5 mg·kg(-1) ; n = 27) and group C (caudal epidural, 0.25% bupivacaine, 0.5 ml·kg(-1) ; n = 27), respectively. Quality of analgesia was assessed by visual analog scale (VAS) score recorded at 0, 0.5, 3, 6, 12, 24 h, and once a day for the next 4 days. Duration of analgesia was calculated from the institution of block to the first analgesic demand by child or VAS > 5. Total morphine consumption in the first 48 h and oral paracetamol consumption till 5th day were recorded. Children were regularly followed up in their respective outpatient clinic for early or late complications.

RESULTS:
In group P, lower mean VAS scores were seen from 0.5 h after surgery till day 3 and analgesia lasted for significantly longer duration (82 min) when compared with caudal epidural, P < 0.001. Incidence of urethral fistula formation after primary hypospadias repair was 19.2%, and all had received caudal epidural. An increase of 27% in penile volume from baseline value was observed 10 min after caudal epidural placement, P < 0.05.

CONCLUSION:
Penile block provided better analgesia when compared with caudal epidural in children undergoing primary hypospadias repair. Postoperative urethral fistula formation was more likely in children who received caudal epidural.

Effects of conjugated linoleic acid and high oleic acid safflower oil in the treatment of children with HPV-induced laryngeal papillomatosis: a randomized, double-blinded and crossover preliminary study.

Louw L.

Lipids Health Dis. 2012 Oct 12;11:136. doi: 10.1186/1476-511X-11-136.

Source
Department Otorhinolaryngology, Faculty of Health Sciences, University of the Free State, Box 339G42, Bloemfontein 9300, South Africa. gnanll@ufs.ac.za

Abstract

BACKGROUND:

Surgery is the mainstay therapy for HPV-induced laryngeal papillomatosis (LP) and adjuvant therapies are palliative at best. **Research revealed that conjugated-linoleic acid (CLA) may improve the outcome of virally-induced diseases. The effects of Clarinol™ G-80 (CLA) and high oleic safflower oil (HOSF) on children with LP (concomitant with surgery) were evaluated**.

DESIGN:

A randomized, double-blinded, crossover and reference-oil controlled trial was conducted at a South African medical university. Study components included clinical, HPV type/load and lymphocyte/cytokine analyses, according to routine laboratory methods.

PARTICIPANTS:

Overall: ten children enrolled; eight completed the trial; five remained randomized; seven received CLA first; all treatments remained double-blinded.

INTERVENTION:

Children (4 to 12 years) received 2.5 ml p/d CLA (8 weeks) and 2.5 ml p/d HOSF (8 weeks) with a washout period (6 weeks) in-between. The one-year trial included a post-treatment period (30 weeks) and afterwards was a one-year follow-up period.

MAIN OUTCOME MEASURES:

Changes in numbers of surgical procedures for improved disease outcome, total/anatomical scores (staging system) for papillomatosis prevention/viral inhibition, and lymphocyte/cytokine counts for immune responses between baselines and each treatment/end of trial were measured.

FINDINGS:

After each treatment all the children were in remission (no surgical procedures); after the trial two had recurrence (surgical procedures in post-treatment period); after the follow-up period three had recurrence (several surgical procedures) and five recovered (four had no surgical procedures). Effects of CLA (and HOSF to a lesser extent) were restricted to mildly/moderately aggressive papillomatosis. Children with low total scores (seven/less) and reduced infections (three/less laryngeal sub-sites) recovered after the trial. No harmful effects were observed. The number of surgical procedures during the trial (n6/available records) was significantly lower [(p 0.03) (95% CI 1.1; 0)]. Changes in scores between baselines and CLA treatments (n8) were significantly lower: total scores [(p 0.02) (95% CI -30.00; 0.00)]; anatomical scores [(p 0.008) (95% CI -33.00: -2.00)]. Immune enhancement could not be demonstrated.

CONCLUSIONS:

These preliminary case and group findings pave the way for further research on the therapeutic potential of adjuvant CLA in the treatment of HPV-induced LP.

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Thalassemia

Deferiprone (GPO-L-ONE(®)) monotherapy reduces iron overload in transfusion-dependent thalassemias: 1-year results from a multicenter prospective, single arm, open label, dose escalating phase III pediatric study (GPO-L-ONE; A001) from Thailand.

Viprakasit V, Nuchprayoon I, Chuansumrit A, Torcharus K, Pongtanakul B, Laothamatas J, Srichairatanakool S, Pooliam J, Supajitkasem S, Suriyaphol P, Tanphaichitr VS, Tuchinda S.

Am J Hematol. 2013 Apr;88(4):251-60. doi: 10.1002/ajh.23386. Epub 2013 Mar 5.

Source
Hematology/Oncology Division, Department of Pediatrics and Thalassemia Center, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. vip.vip@mahidol.ac.th

Abstract
Accessibility to iron chelators including deferoxamine and deferasirox remains obscured in many developing countries. **To provide an alternative, the government pharmaceutical organization of Thailand (GPO) manufactured deferiprone which has similar bioequivalent to the standard product.** Seventy-three pediatric patients with severe β thalassemias, age range 3.2-19 years, were recruited to a 1-year multicenter prospective, single arm, open label, dose escalating Phase III study of deferiprone to determine its clinical efficacy and safety. Sixty-four patients (87.6%) completed the study with good compliance (>94%). Average deferiprone dose was 79.1±4.3 mg/kg/day. Overall, mean serum ferritin (SF) levels at 1 year were not significantly changed from baseline. However, 45% of patients (response group) had SF reduced >15% from baseline at 1 year with a median reduction of 1,065 ng ml(-1) . Baseline SF was the major factor that predicts clinical efficacy; patients with baseline SF>3,500 ng ml(-1) had the most significant fall of SF at 1 year. A subgroup analysis by MRI-T2* confirmed that the response group had higher baseline liver iron and deferiprone could significantly reduce liver iron overload and normalize levels of ALT at 1 year. Although, gastrointestinal irritation (20.5%) was the most common drug-related adverse events (AEs) followed by transaminitis (16.4%) and neutropenia (6.8%), all patients were well tolerated. There was no mortality and agranulocytosis found in this trial. **Monotherapy of deferiprone with appropriate dose adjustment and monitoring for adverse events appeared to be an effective chelation therapy in some patients with good compliance and acceptable safety profiles.**

Lack of associations of α(+)-thalassemia with the risk of Plasmodium falciparum and Plasmodium vivax infection and disease in a cohort of children aged 3-21 months from Papua New Guinea.

Rosanas-Urgell A, Senn N, Rarau P, Aponte JJ, Reeder JC, Siba PM, Michon P, Mueller I.

Int J Parasitol. 2012 Nov;42(12):1107-13. doi: 10.1016/j.ijpara.2012.10.001. Epub 2012 Oct 17.

Source
Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea.

Abstract
Despite consistent evidence of a protective effect of α(+)-thalassemia against severe Plasmodium falciparum disease, the mechanisms underlying this protection remain unknown. An increase in risk of Plasmodium vivax malaria in early childhood resulting in a cross-species protection against severe P. falciparum malaria has been proposed as a possible mechanism in Melanesian children. The association of α(+)-thalassemia genotypes with a risk of P. falciparum and P. vivax infection and uncomplicated illness was reassessed in a cohort of 1,112 Papua New Guinean children, followed from 3 to 21 months of age. Three hundred and eighty-nine (35.0%) children were homozygous for α(+)-thalassemia (-α/-α), 506 (45.5%) heterozygous (αα/-α) and 217 (19.5%) homozygous for the wild-type allele. **No significant differences in the incidence of P. falciparum (Pf) or P. vivax (Pv) malaria were observed between α(+)-thalassemia homozygote (Pf: incidence rate ratio (IRR)=1.13, CI(95) (0.82, 1.56), P=0.45, Pv: IRR=1.15, CI(95) (0.88, 1.50), P=0.31), heterozygote (Pf: IRR=0.98, CI(95) (0.71, 1.34), P=0.93, Pv: IRR=1.14, CI(95) (0.88, 1.48), P=0.33) and wild-type children.** The prevalence of infection with either species did not differ between α(+)-thalassemia genotypes, although densities of P. vivax (but not of P. falciparum) infections were significantly higher in α(+)-thalassemia homozygote and heterozygote children. An excessive risk of moderate-to-severe anemia (Hb<8 g/dl) was observed in α(+)-thalassemia homozygote children (IRR=1.54, CI(95) (1.12, 2.11), P=0.008). **This study therefore failed to confirm an increased risk of P. vivax or P. falciparum malaria in very young, α(+)-thalassemic children without significant levels of acquired immunity.** This confirms the lack of protection by α(+)-thalassemia against uncomplicated P. falciparum and challenges the hypothesis of immunological cross-protection between P. falciparum and P. vivax as a mechanism underlying α(+)-thalassemia protection against severe P. falciparum disease in Melanesian children

Tuberculosis

Safety of long-term isoniazid preventive therapy in children with HIV: a comparison of two dosing schedules.

le Roux SM, Cotton MF, Myer L, le Roux DM, Schaaf HS, Lombard CJ, Zar HJ.

Int J Tuberc Lung Dis. 2013 Jan;17(1):26-31. doi: 10.5588/ijtld.11.0820. Epub 2012 Nov 8.

Source
Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa. stanzi.leroux@gmail.com

Abstract
SETTING:
Two paediatric hospitals in Cape Town, South Africa.

OBJECTIVE:
To investigate the incidence of and risk factors for severe liver injury in human immunodeficiency virus (HIV) infected children receiving long-term isoniazid preventive therapy (IPT).

DESIGN:
Randomised trial of **IPT or placebo given daily or thrice weekly to HIV-infected children aged ≥8 weeks; placebo was discontinued early.** Alanine transaminase (ALT) was measured at baseline, 6-monthly and during illness: an increase of ≥10 times the upper limit of normal defined severe liver injury.

RESULTS:
Of 324 children enrolled, 297 (91.6%) received IPT (559.1 person-years [py]). Baseline median age was 23 months (interquartile range [IQR] 9.5-48.6) and median CD4%, 20% (IQR 13.6-26.9). **A total of 207 (63.9%) children received combination antiretroviral therapy: 19 developed severe liver injury, 16 while receiving IPT.** Among these there were 8 cases of viral hepatitis (5 with hepatitis A), 2 antiretroviral-induced liver injuries and 1 case of abdominal tuberculosis. IPT-related severe liver injury occurred in 1.7% (5/297, 0.78/100 py). No child developed hepatic failure; one died of an unrelated cause. All surviving children subsequently tolerated IPT.

CONCLUSIONS:
This study suggests that long-term IPT has a low toxicity risk in HIV-infected children. In the absence of chronic viral hepatitis, IPT can be safely re-introduced following recovery from liver injury.

Vitamin D, tuberculin skin test conversion, and latent tuberculosis in Mongolian school-age children: a randomized, double-blind, placebo-controlled feasibility trial.

Ganmaa D, Giovannucci E, Bloom BR, Fawzi W, Burr W, Batbaatar D, Sumberzul N, Holick MF, Willett WC.

Am J Clin Nutr. 2012 Aug;96(2):391-6. doi: 10.3945/ajcn.112.034967. Epub 2012 Jul 3.

Source
Department of Nutrition, Harvard School of Public Health, Boston, MA, USA. gdavaasa@hsph.harvard.edu

Abstract
BACKGROUND:
By modulating immune function, vitamin D might increase innate immunity and inhibit the growth of initial bacterial invasion and protect against tuberculosis infection.

OBJECTIVE:
We examined the effect of vitamin D supplementation on tuberculin skin test (TST) conversion.

DESIGN:
A double-blind, placebo-controlled study was conducted in 120 Mongol schoolchildren. We estimated the prevalence of latent tuberculosis infection at baseline and examined the effect of vitamin D (800 IU/d) on serum concentrations of 25-hydroxyvitamin D [25(OH)D] and TST conversion.

RESULTS:
At baseline, the mean (±SD) 25(OH)D concentration was 7 ± 4 ng/mL, and all concentrations were <20 ng/mL. **Vitamin D supplementation increased serum 25(OH)D by a mean of 12.7 ng/mL compared with placebo (P < 0.0001).** At baseline, 16 children in the vitamin D group and 18 in the placebo group were TST positive (P = 0.7). **Over 6 mo, TSTs converted to positive in 5 (11%) children receiving vitamin D compared with 11 (27%) receiving placebo (RR: 0.41; 95% CI: 0.16, 1.09; P = 0.06).** Only one TST conversion occurred among those whose serum 25(OH)D concentration increased to >20 ng/mL, whereas 8 TST conversions occurred in those whose final 25(OH)D concentration remained <10 ng/mL (P = 0.05). **The mean increase in stature was 2.9 ± 1.6 cm in the vitamin D group and 2.0 ± 1.7 cm in the placebo group (95% CI: 2.16, 2.81; P < 0.003).**

CONCLUSIONS:
Vitamin D supplementation for 6 mo had significant favorable effects on serum 25(OH)D concentrations and on growth in stature. A trend was seen toward fewer TST conversions in the vitamin D group. This trial was registered at clinicaltrials.gov as NCT01244204.

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Vaccines and immunization

(See also Helminth infections)

BCG vaccine

(See also Tuberculosis)

No effect of oral polio vaccine administered at birth on mortality and immune response to BCG. A natural experiment.

Lund N, Andersen A, Monteiro I, Aaby P, Benn CS.

Vaccine. 2012 Oct 19;30(47):6694-9. doi: 10.1016/j.vaccine.2012.08.055. Epub 2012 Sep 6.

Source
Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark. najaaraq@dadlnet.dk

Abstract
BACKGROUND:
WHO recommends oral polio vaccine at birth (OPV0) in polio endemic countries. During a period without OPV in Guinea-Bissau in 2004, we observed that not receiving OPV0 was associated with significantly decreased mortality in boys and better immune response to BCG vaccination. In 2007, whilst conducting a trial of BCG and vitamin A supplementation (VAS) at birth to low birthweight (LBW) children, OPV was again lacking for a short period. We used this natural experiment to test the previous observations.

METHODS:
In the trial LBW infants were randomised to early or delayed BCG and VAS or placebo at birth. We noted whether the children received OPV0 or not. We compared children who received No OPV0 with those who received OPV0 in the 2 months before and the 2 months after the period without OPV. Mortality was compared in Cox regression models providing adjusted hazard ratios (aHR); the immune response to BCG was assessed in Poisson models providing adjusted prevalence ratios (aPR).

RESULTS:
Ninety-nine children received No OPV0 and were compared with 243 children who received OPV0. **No OPV0 was associated with insignificantly higher mortality during the first year of life, the aHR being 1.83 (95% CI: 0.93-3.61).** The effect was similar in boys and girls. Overall, there was no significant association between No OPV0 and having a positive PPD response (aPR=1.33 (0.64-2.78)) or a scar (aPR=1.02 (0.93-1.11)) after BCG vaccination, though No OPV0 boys were more likely to develop a scar (aPR: 1.10 (1.01-1.20)).
CONCLUSIONS:
The findings did not support our previous observation that not receiving OPV0 was associated with reduced mortality in boys. The findings weakly supported that OPV0 leads to a dampened response to simultaneously administered BCG vaccine in boys

Diphtheria-Tetanus-Pertussus vaccine

Diphtheria-tetanus-pertussis vaccination administered after measles vaccine: increased female mortality?

Benn CS, Aaby P.

Pediatr Infect Dis J. 2012 Oct;31(10):1095-7. doi: 10.1097/INF.0b013e318263135e.

Source
Bandim Health Project, Research Center for Vitamins and Vaccines, Statens Serum Institut, Copenhagen S, Denmark. cb@ssi.dk

Abstract
In low-income countries, children should receive 3 doses of diphtheria-tetanus-pertussis vaccine (DTP) at 6, 10 and 14 weeks of age, and measles vaccine at 9 months of age. However, there is often a delay in administering the vaccines, and DTP is often given after measles vaccine. Previous observations suggest that this practice is associated with increased mortality for female, but not for male children. Within a vitamin A trial in Guinea-Bissau, vaccination status was registered at the time of measles vaccination at 9 months; 141 (31%) of 455 children were missing 1 or more DTP vaccines and were likely to receive them afterward. We examined whether missing DTP vaccine at this time point was associated with sex-differential effects on mortality. In female children, missing DTP was associated with 3.55 (95% confidence interval: 1.23-10.26) times higher risk of dying before 36 months of age, whereas it made no difference in male children (0.97 [0.34-2.80]). The result supports that receiving DTP after measles vaccine affects female children negatively.

Comment
This study adds to many observations by the same group over 2 decades. Confounding could have played a role in the results of this non-randomised trial. For example, children with incomplete DTP vaccination could have been delayed in receiving their routine vaccinations because the child had been sick, or the family had poor care seeking behaviour, putting them at higher risk of death. The authors note that although both boys and girls with incomplete DTP vaccinations had lower nutritional status at enrollment than those who were fully vaccinated, this is unlilely to explain the observed large difference in mortality in female children, nor would it explain why there was no effect in male children. The order that vaccines are given seems to have an effect on high mortality populations, independent of the disease they are designed to protect against.

Dengue vaccine

Immunogenicity and safety of recombinant tetravalent dengue vaccine (CYD-TDV) in individuals aged 2-45 y: Phase II randomized controlled trial in Singapore.

Leo YS, Wilder-Smith A, Archuleta S, Shek LP, Chong CY, Leong HN, Low CY, Oh ML, Bouckenooghe A, Wartel TA, Crevat D.

Hum Vaccin Immunother. 2012 Sep;8(9):1259-71. doi: 10.4161/hv.21224. Epub 2012 Aug 16.

Source
Tan Tock Seng Hospital; Singapore.

Abstract
This was a multicenter, blinded, Phase II study (NCT00880893) conducted in Singapore. **The primary objectives were to evaluate the safety of a tetravalent dengue vaccine (TDV) comprising four recombinant, live, attenuated viruses (CYD-TDV) and the dengue virus serotype-specific antibody responses before and 28 d after each vaccination**. Participants were randomized 3:1 to receive three doses of CYD-TDV or a control vaccine at 0, 6 and 12 mo. Control vaccine was placebo for the first dose (all ages) and for subsequent doses, licensed hepatitis-A for children (aged 2-11 y) or influenza vaccine for adolescents (12-17 y) and adults (18-45 y). Between April and October 2009, 317 children, 187 adolescents and 696 adults were enrolled**. In all age groups, reactogenicity was higher after the first injection of CYD-TDV than after placebo control. Reactogenicity after subsequent CYD-TDV doses was no higher than after the first dose, and tended to be lower or similar to that seen after active control vaccination.** Seropositivity rates and geometric mean neutralizing antibody titers (GMTs; 1/dil) against all four dengue virus serotypes increased in all age groups after each of the three CYD-TDV doses. Post-dose 3, 66.5% of all participants were seropositive to all four serotypes, and 87.2% were seropositive to ≥ 3 serotypes; GMTs for all participants ranged from 43.0 against dengue virus serotype 1 to 100 against dengue virus serotype 4. GMTs were higher in children than in adolescents**. These results support the continued development of CYD-TDV for the prevention of dengue disease.**

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Immunogenicity and safety of tetravalent dengue vaccine in 2-11 year-olds previously vaccinated against yellow fever: randomized, controlled, phase II study in Piura, Peru.

Lanata CF, Andrade T, Gil AI, Terrones C, Valladolid O, Zambrano B, Saville M, Crevat D.

Vaccine. 2012 Sep 7;30(41):5935-41. doi: 10.1016/j.vaccine.2012.07.043. Epub 2012 Jul 31

Source
Instituto de Investigacion Nutricional, Av. La Molina 1885, La Molina Lima-12, Peru.

Abstract

In a randomized, placebo-controlled, monocenter, observer blinded study conducted in an area where dengue is endemic, we assessed the safety and immunogenicity of a recombinant, live, attenuated, tetravalent dengue vaccine candidate (CYD-TDV) in 2-11 year-olds with varying levels of pre-existing yellow-fever immunity due to vaccination 1-7 years previously. **199 children received 3 injections of CYD-TDV (months 0, 6 and 12) and 99 received placebo (months 0 and 6) or pneumococcal polysaccharide vaccine (month 12).** One month after the third dengue vaccination, serotype specific neutralizing antibody GMTs were in the range of 178-190 (1/dil) (versus 16.7-38.1 in the control group), a 10-20 fold-increase from baseline, and 94% of vaccines were seropositive to all four serotypes (versus 39% in the control group). There were no vaccine-related SAEs. The observed reactogenicity profile was consistent with phase I studies, with severity grade 1-2 injection site pain, headache, malaise and fever most frequently reported and no increase after subsequent vaccinations. Virologically confirmed dengue cases were seen after completion of the 3 doses: 1 in the CYD-TDV group (N=199), and 3 in the control group (N=99). **A 3-dose regimen of CYD-TDV had a good safety profile in 2-11 year olds with a history of YF vaccination and elicited robust antibody responses that were balanced against the four serotypes**

HPV vaccine

Human papillomavirus vaccination in Tanzanian schoolgirls: cluster-randomized trial comparing 2 vaccine-delivery strategies.

Watson-Jones D, Baisley K, Ponsiano R, Lemme F, Remes P, Ross D, Kapiga S, Mayaud P, de Sanjosé S, Wight D, Changalucha J, Hayes R.

J Infect Dis. 2012 Sep 1;206(5):678-86. doi: 10.1093/infdis/jis407. Epub 2012 Jun 18.

Source
London School of Hygiene and Tropical Medicine, London, UK. deborah.watson-jones@lshtm.ac.uk

Abstract
BACKGROUND:
We compared vaccine coverage achieved by 2 different delivery strategies for the quadrivalent human papillomavirus (HPV) vaccine in Tanzanian schoolgirls.

METHODS:
In a cluster-randomized trial of HPV vaccination conducted in Tanzania, 134 primary schools were randomly assigned to class-based (girls enrolled in primary school grade [class] 6) or age-based (girls born in 1998; 67 schools per arm) vaccine delivery. The primary outcome was coverage by dose.

RESULTS:
There were 3352 and 2180 eligible girls in schools randomized to class-based and age-based delivery, respectively. HPV vaccine coverage was 84.7% for dose 1, 81.4% for dose 2, and 76.1% for dose 3. For each dose, coverage was higher in class-based schools than in age-based schools (dose 1: 86.4% vs 82.0% [P = .30]; dose 2: 83.8% vs 77.8% [P = .05]; and dose 3: 78.7% vs 72.1% [P = .04]). Vaccine-related adverse events were rare. Reasons for

not vaccinating included absenteeism (6.3%) and parent refusal (6.7%). School absenteeism rates prior to vaccination ranged from 8.1% to 23.5%.

CONCLUSIONS:
HPV vaccine can be delivered with high coverage in schools in sub-Saharan Africa. Compared with age-based vaccination, class-based vaccination located more eligible pupils and achieved higher coverage. HPV vaccination did not increase absenteeism rates in selected schools. Innovative strategies will be needed to reach out-of-school girls.

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Reasons for receiving or not receiving HPV vaccination in primary schoolgirls in Tanzania: a case control study.

Watson-Jones D, Tomlin K, Remes P, Baisley K, Ponsiano R, Soteli S, de Sanjosé S, Changalucha J, Kapiga S, Hayes RJ.

PLoS One. 2012;7(10):e45231. doi: 10.1371/journal.pone.0045231. Epub 2012 Oct 24.

Source
London School of Hygiene and Tropical Medicine, London, United Kingdom. Deborah.Watson-Jones@lshtm.ac.uk

Abstract
BACKGROUND:
There are few data on factors influencing human papillomavirus (HPV) vaccination uptake in sub-Saharan Africa. We examined the characteristics of receivers and non-receivers of HPV vaccination in Tanzania and identified reasons for not receiving the vaccine.

METHODS:
We conducted a case control study of HPV vaccine receivers and non-receivers within a phase IV cluster-randomised trial of HPV vaccination in 134 primary schools in Tanzania. Girls who failed to receive vaccine (pupil cases) and their parents/guardians (adult cases) and girls who received dose 1 (pupil controls) of the quadrivalent vaccine (Gardasil™) and their parents/guardians (adult controls) were enrolled from 39 schools in a 1:1 ratio and interviewed about cervical cancer, HPV vaccine knowledge and reasons why they might have received or not received the vaccine. Conditional logistic regression was used to determine factors independently associated with not receiving HPV vaccine.

RESULTS:
We interviewed 159 pupil/adult cases and 245 pupil/adult controls. **Adult-factors independently associated with a daughter being a case were older age, owning fewer household items, not attending a school meeting about HPV vaccine, and not knowing anyone with cancer. Pupil-factors for being a case included having a non-positive opinion about the school de-worming programme, poor knowledge about the location of the cervix, and not knowing that a vaccine could prevent cervical cancer. Reasons for actively refusing vaccination included concerns about side effects and infertility.** Most adult and pupil cases reported that they would accept the HPV vaccine if it were offered again (97% and 93% respectively).

CONCLUSIONS:
Sensitisation messages, especially targeted at older and poorer parents, knowledge retention and parent meetings are critical for vaccine acceptance in Tanzania. Vaccine side effects and fertility concerns should be addressed prior to a national vaccination program. Parents and pupils who initially decline vaccination should be given an opportunity to reconsider their decision.

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Influenza vaccine

Design and initiation of a study to assess the direct and indirect effects of influenza vaccine given to children in rural India.

Sullender W, Fowler K, Krishnan A, Gupta V, Moulton LH, Lafond K, Widdowson MA, Lal RB, Broor S.

Vaccine. 2012 Jul 27;30(35):5235-9. doi: 10.1016/j.vaccine.2012.06.002. Epub 2012 Jun 16

Source
University of Alabama Birmingham, Birmingham, AL, USA. wsull@me.com

Abstract
The burden of disease due to influenza is not well characterized for children in developing countries and the effectiveness of available influenza vaccines in lower resource settings has not been established. **We initiated a prospective, longitudinal, phase IV, household-randomized, controlled, observer-blinded three year study (2009-2011) in a rural community of India to measure the total and indirect household protective effects of immunizing children ages 6 months through 10 years with seasonal inactivated trivalent influenza vaccine (TIV) or a control vaccine (n=3697).** Active weekly surveillance was conducted year round with home visits for identification of febrile acute respiratory illness (FARI) conducted for all vaccine recipients and household members (n=18,220). Nasal and throat swabs were collected from each FARI episode for influenza detection by real-time reverse transcription polymerase chain reaction. The primary outcome was reduction in laboratory confirmed influenza infections in the influenza vaccine versus control vaccine group, with secondary outcome assessing indirect effects among the entire study population. This report describes the study site, cluster study design, choice of study and control vaccines, and the initial enrollment in the study.

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Safety and immunogenicity of an adjuvanted whole virion, inactivated A (H1N1) 2009 influenza vaccine in young and elderly adults, and children.

Kulkarni PS, Manjunath K, Agarkhedkar S; Group of SII IIV Studies.

Vaccine. 2012 Dec 17;31(1):20-2. doi: 10.1016/j.vaccine.2012.10.081. Epub 2012 Nov 4.

Source
Serum Institute of India Ltd., Pune, India. drpsk@seruminstitute.com

Abstract
An alum adjuvanted whole virion inactivated vaccine against the A (H1N1) 2009 pandemic virus was developed in India. Two double-blind, randomized studies were conducted. Fifty adults (18-50 years) were enrolled in the Phase I study, **whereas the Phase II/III study consisted of 330 adults (≥18 years) and children ≥3 years.** Safety (both studies) and immunogenicity (Phase II/III study) by hemagglutination inhibition (HI) antibody titers, of 10 μg or 15 μg of hemagglutinin (HA) antigen were compared. In the Phase I study, mostly mild and transient injection site and systemic reactions were reported. Similar events were seen in the Phase II/III study. The overall seroprotection was 96% and 89% with 10 and 15 μg doses, respectively, while the seroconversion was 92% and 88%. **The new Indian-made pandemic H1N1 vaccine is safe and immunogenic in adults and children above 3 years of age**.

Comparison of immunogenicity and reactogenicity of split versus subunit influenza vaccine in Korean children aged 6-35 months.

Kim YK, Eun BW, Kim NH, Kang EK, Lee BS, Kim DH, Lim JS.

Scand J Infect Dis. 2013 Jun;45(6):460-8. doi: 10.3109/00365548.2012.755267. Epub 2013 Jan 7.

Source
From the Department of Pediatrics, Korea University College of Medicine , Seoul.

Abstract
Abstract Background: Studies comparing the immunogenicity and reactogenicity of trivalent inactivated subunit (SU) and split (SPL) vaccines in children in Asia are limited. In 2008, we assessed the safety and immunogenicity of SU and SPL influenza vaccines in Korean children aged 6-35 months. Methods: **We studied 2 non-randomized cohorts of children who received either SU or SPL vaccine in an open-label non-stratified controlled trial at 6 hospitals in Korea.** We measured antibody titers with a hemagglutination-inhibition assay at baseline and 30 days after the first or second flu shot. The primary goal was the determination of vaccine immunogenicity according to the European Union Committee of Human Medicinal Products licensing criteria. Results: **Out of a total of 106 participants aged 6-35 months, 47 received the SPL vaccine and 59 the SU vaccine.** After vaccination, 41 (87.2%), 40 (85.1%), and 33 (70.2%) of the 47 subjects in the SPL group had titers ≥ 1:40 against H1N1, H3N2, and B, respectively. In the SU group, 42 (71.2%), 34 (57.6%), and 22 (37.3%) of 59 subjects had titers ≥ 1:40 against H1N1, H3N2, and B, respectively. The post-vaccination geometric mean titers of H1N1, H3N2, and B (SPL vs SU) were 119.1, 99.8, and 61.4 vs 75.4, 51.2, and 24.1, respectively. There were no serious vaccine-related adverse events. There were no differences between the SPL and SU vaccines with respect to adverse events. Conclusions: **The**

immunogenicity of the SPL vaccine appears to be better than that of the SU vaccine in children aged 6-35 months in Korea.

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Japanese encephalitis virus vaccine

Single-dose, live-attenuated Japanese encephalitis vaccine in children aged 12-18 months: randomized, controlled phase 3 immunogenicity and safety trial.

Feroldi E, Pancharoen C, Kosalaraksa P, Watanaveeradej V, Phirangkul K, Capeding MR, Boaz M, Gailhardou S, Bouckenooghe A.

Hum Vaccin Immunother. 2012 Jul;8(7):929-37. doi: 10.4161/hv.20071. Epub 2012 Jul 1.

Source
Sanofi Pasteur Clinical Development Department, Marcy l'Etoile, France. Emmanuel.feroldi@sanofipasteur.com

Abstract
This trial in 1200 JE-vaccination naïve children (age 12-18 mo) in Thailand and the Philippines aimed to demonstrate consistency of three successive industrial scale manufacturing lots of live attenuated Japanese encephalitis chimeric virus vaccine (JE-CV) and consistency between industrial scale manufacturing lots and a fourth, development lot. Children received JE-CV from one of three successive industrial scale lots produced in Thailand (n = 899), or from a fourth development lot produced in the USA (n = 199), or hepatitis A control vaccine (n = 102). Antibodies were assessed by 50% plaque reduction neutralization test (PRNT(50)) at screening and Day 28. Seroconversion rates (titer of < 10 at baseline and ≥ 10 on Day 28, or a four-fold rise from a baseline titer of ≥ 10) were determined per group. Lot-to-lot consistency of seroconversion rate and GMT was demonstrated between the 3 industrial scale lots, and between these lots and the US lot. Seroconversion rate on pooled data 28 d after JE-CV vaccination (Thai lots) was 95.0% [95% confidence interval (CI); 93.3-96.3]. The safety profile of JE-CV was favorable and comparable with hepatitis A vaccine. There were no serious adverse events related to vaccination. This study demonstrated the consistency of three successive industrial scale JE-CV vaccine lots, as well as consistency with a development lot. The study also demonstrated that a single dose of JE-CV is well tolerated and elicits a high protective immune response, seroconverting 95% of JE-naïve Asian children aged 12-18 mo.

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Measles vaccine

Effect of second dose of measles vaccine on measles antibody status: a randomized controlled trial.

Fazilli A, Mir AA, Shah RJ, Bhat IA, Fomda BA, Bhat MA.

Indian Pediatr. 2013 May 8;50(5):473-6. Epub 2012 Nov 5.

Source
Departments of Community Medicine, Microbiology and Pediatrics, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, J and K, India. Correspondence to: Dr Mushtaq Ahmad Bhat, Additional Professor Pediatrics, SKIMS, Srinagar, Kashmir, India. mbhat47@rediffmail.com.

Abstract
OBJECTIVE:
To evaluate the effect of the second dose of measles vaccine on measles antibody status during childhood.

SETTING:
Immunization centre of Under-five Clinic of the Department of Community Medicine at a tertiary-hospital.
STUDY DESIGN:
Randomized Controlled trial.
SUBJECTS:
Children from 6 years to 17 year old. 188 with simple obesity, and 431 with obesity and metabolic abnormalities. 274 age and gender-matched healthy children as controls.

METHODS:
Blood samples were collected from all subjects for baseline measles serology by heel puncture at 9-12 months of age. All subjects were given the first dose of measels vaccine. **At second visit (3-5 months later), after collecting the blood sample from all, half the children were randomized to receive the second dose of measles vaccine (study group), followed by collection of the third sample six weeks later in all the subjects.**

RESULTS:
A total of 78 children were enrolled and 30 children in each group could be analyzed. 11(36.6%) children in the study group and 13 (43.3%) children in the control group had protective levels of measles IgG at baseline. **Around 93.3% of children in the study group had protective measles antibody titers as against 50% in the control group at the end of the trial.** The Geometric Mean Titre (GMT) of measles IgG increased from 14.8 NTU/mL to 18.2 NTU/mL from baseline to six weeks following receipt of the second dose of the vaccine in the study group, as compared to a decrease from 16.8 NTU/mL to 12.8 NTU/mL in the control group.

CONCLUSION:
A second dose of measles vaccine boosts the measles antibody status in the study population as compared to those who receive only a single dose

Effect of multivitamin supplementation on measles vaccine response among HIV-exposed uninfected Tanzanian infants.

Sudfeld CR, Duggan C, Histed A, Manji KP, Meydani SN, Aboud S, Wang M, Giovannucci EL, Fawzi WW.

Clin Vaccine Immunol. 2013 May 29. [Epub ahead of print]

Source
Departments of Epidemiology.

Abstract
Immunization and nutritional interventions are mainstays of child health programs in sub-Saharan Africa, yet few published data on their interaction exist. **HIV-exposed infants (uninfected) enrolled in a randomized placebo-controlled trial of multivitamins (vitamin B-complex, C and E) conducted in Tanzania were sampled for assessment of measles IgG quantity and avidity at 15-18 months.** Infants were vaccinated between 8.5-12 months and all mothers received high dose multivitamins as standard of care. **Of 201 HIV-exposed infants enrolled, 138 (68.7%) were measles seropositive. There was no effect of infant multivitamin supplementation on measles seroconversion proportions, IgG concentrations, and IgG avidity (p>0.05).** The measles seroconversion proportion was greater for HIV-exposed infants vaccinated at 10-11 as compared to 8.5-10 months (p=0.032), and for infants whose mothers had a CD4 T-cell count <200 cells/μL as compared to >350 cells/μL (p=0.039). **Stunted infants had significantly decreased IgG quantity as compared to non-stunted infants (p=0.012).** As for measles avidity, HIV-exposed infants vaccinated at 10-11 months had increased antibody avidity (p=0.031). Maternal CD4 T-cell counts <200 cells/μL were associated with decreased avidity as compared to >350 cells/μL (p=0.047), as were lower infant height-for-age z-scores (p=0.016). **Supplementation with multivitamins containing B-complex, C, and E does not appear to improve measles vaccine response for HIV-exposed infants.** Studies are needed to better characterize the impact of maternal HIV disease severity on immune system development of HIV-exposed infants and the effect of malnutrition interventions on vaccine responses.

Meningococcal vaccine

Immunogenicity and safety of a new meningococcal A conjugate vaccine in Indian children aged 2-10 years: a phase II/III double-blind randomized controlled trial.

Hirve S, Bavdekar A, Pandit A, Juvekar S, Patil M, Preziosi MP, Tang Y, Marchetti E, Martellet L, Findlow H, Elie C, Parulekar V, Plikaytis B, Borrow R, Carlone G, Kulkarni PS, Goel A, Suresh K, Beri S, Kapre S, Jadhav S, Preaud JM, Viviani S, LaForce FM.

Vaccine. 2012 Oct 5;30(45):6456-60. doi: 10.1016/j.vaccine.2012.08.004. Epub 2012 Aug 13.

Source
King Edward Memorial Hospital Research Centre, Rasta Peth, Pune, India.

Abstract
This study compares the immunogenicity and safety of a single dose of a new meningococcal A conjugate vaccine (PsA-TT, MenAfriVac™, Serum Institute of India Ltd., Pune) against the meningococcal group A component of a licensed quadrivalent meningococcal polysaccharide vaccine (PsACWY, Mencevax ACWY(®), GSK, Belgium) 28 days after vaccination in Indian children. **This double-blind, randomized, controlled study included 340 Indian children aged 2-10 years** enrolled from August to October 2007; 169 children received a dose of PsA-TT while 171 children received a dose of PsACWY. **Intention-to-treat analysis showed that 95.2% of children in PsA-TT group had a ≥4-fold response in serum bactericidal titers (rSBA) 28 days post vaccination as compared to 78.2% in the PsACWY group.** A significantly higher rSBA GMT (11,209, 95%CI 9708-12,942) was noted in the PsA-TT group when compared to PsACWY group (2838, 95%CI 2368-3401). **Almost all children in both vaccine groups had a ≥4-fold response in group A-specific IgG concentration but the IgG GMC was significantly greater in the PsA-TT group** (89.1 µg/ml, 95%CI 75.5-105.0) when compared to the PsACWY group (15.3 µg/ml, 95%CI 12.3-19.2). Local and systemic reactions during the 4 days after immunization were similar for both vaccine groups except for tenderness (30.2% in PsA-TT group vs 12.3% in PsACWY group). None of the adverse events or serious adverse events was related to the study vaccines. **We conclude that MenAfriVac™ is well tolerated and significantly more immunogenic when compared to a licensed polysaccharide vaccine, in 2-to-10-year-old Indian children.**

Pneumococcal vaccine

Safety and immunogenicity of neonatal pneumococcal conjugate vaccination in Papua New Guinean children: a randomised controlled trial.

Pomat WS, van den Biggelaar AH, Phuanukoonnon S, Francis J, Jacoby P, Siba PM, Alpers MP, Reeder JC, Holt PG, Richmond PC, Lehmann D; Neonatal Pneumococcal Conjugate Vaccine Trial Study Team.

Collaborators (69)

Aemamero E, Akunaii M, Aole H, Bilam E, Dreyam M, Eza'e S, Francis J, Fufu N, Hasu E, Helivi L, Inapero G, Jack T, James S, Javati A, Keno H, Kirarock W, Ko'ezo I, Lai M, Lapiso A, Laumaea AM, Maraga S, Martin M, Michael A, Michaels M, Mope A, Namuigi P, Nivio B, Ove P, Opa C, Orami T, Paul N, Phuanukoonnon S, Poigeno G, Pomat WS, Reeder J, Saleu G, Sehuko R, Siba P, Siba V, Sie A, Sinke L, Totave J, Uro B, Vengiau G, Wawa'e L, Wayaki T, Yoannes M, Ande J, Apa J, Frank D, Pame W, Pomat N, Keasu P, Pikuri A, Pok H, Alpers KS, Devitt C, Holt PG, Jacoby P, Laing I, Lehmann D, Nadal-Sims M, van den Biggelaar A, Richmond PC, Chidlow G, Harnett J, Smith DW, Alpers MP, Leach AJ.

PLoS One. 2013;8(2):e56698. doi: 10.1371/journal.pone.0056698. Epub 2013 Feb 22.

Source
Papua New Guinean Institute of Medical Research, Goroka, Papua New Guinea.

Abstract
BACKGROUND:
Approximately 826,000 children, mostly young infants, die annually from invasive pneumococcal disease. A 6-10-14-week schedule of pneumococcal conjugate vaccine (PCV) is efficacious but neonatal PCV may provide earlier protection and better coverage. We conducted an open randomized controlled trial in Papua New Guinea to compare safety, immunogenicity and priming for memory of 7-valent PCV (PCV7) given in a 0-1-2-month (neonatal) schedule with that of the routine 1-2-3-month (infant) schedule.

METHODS:
We randomized **318 infants at birth to receive PCV7 in the neonatal or infant schedule or no PCV7.** All infants received 23-valent pneumococcal polysaccharide vaccine (PPV) at age 9 months. **Serotype-specific serum IgG for PCV7 (VT) serotypes and non-VT serotypes 2, 5 and 7F were measured at birth and 2, 3, 4, 9, 10 and 18 months of age.** Primary outcomes were geometric mean concentrations (GMCs) and proportions with concentration ≥ 0.35 μg/ml of VT serotype-specific pneumococcal IgG at age 2 months and one month post-PPV.

RESULTS:
We enrolled 101, 105 and 106 infants, respectively, into neonatal, infant and control groups. Despite high background levels of maternally derived antibody, both PCV7 groups had higher GMCs than controls at age 2 months for serotypes 4 ($p<0.001$) and 9V ($p<0.05$) and at age 3 months for all VTs except 6B. GMCs for serotypes 4, 9V, 18C and 19F were significantly higher ($p<0.001$) at age 2 months in the neonatal (one month post-dose2 PCV7) than in the infant group (one month post-dose1 PCV7). PPV induced significantly higher VT antibody responses in PCV7-primed than unprimed infants, with neonatal and infant groups equivalent. High VT and non-VT antibody concentrations generally persisted to age 18 months.

CONCLUSIONS:
PCV7 is well-tolerated and immunogenic in PNG neonates and young infants and induces immunologic memory to PPV booster at age 9 months with antibody levels maintained to age 18 months.

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Effect of age and vaccination with a pneumococcal conjugate vaccine on the density of pneumococcal nasopharyngeal carriage.

Roca A, Bottomley C, Hill PC, Bojang A, Egere U, Antonio M, Darboe O, Greenwood BM, Adegbola RA.

Clin Infect Dis. 2012 Sep;55(6):816-24. doi: 10.1093/cid/cis554. Epub 2012 Jun 14.

Source
Medical Research Council Unit, Gambia. aroca@mrc.gm
Abstract
BACKGROUND:

This study evaluated the impact of age and pneumococcal vaccination on the density of pneumococcal nasopharyngeal carriage.

METHODS:
A cluster-randomized trial was conducted in rural Gambia. **In 11 villages (the vaccine group), all residents received 7-valent pneumococcal conjugate vaccine (PCV-7), while in another 10 villages (the control group), only children <30 months old or born during the study period received PCV-7.** Cross-sectional surveys (CSSs) were conducted to collect nasopharyngeal swabs before vaccination (baseline CSS) and 4, 12, and 22 months after vaccination. Pneumococcal density was defined using a semiquantitative classification (range, 1-4) among colonized individuals. An age-trend analysis of density was conducted using data from the baseline CSS. Mean pneumococcal density was compared in CSSs conducted before and after vaccination.

RESULTS:
Mean bacterial density among colonized individuals in the baseline CSS was 2.57 for vaccine-type (VT) and non-vaccine-type (NVT) pneumococci; it decreased with age (P < .001 for VT and NVT). There was a decrease in the density of VT carriage following vaccination in individuals older than 5 years (from 2.44 to 1.88; P = .001) and in younger individuals (from 2.57 to 2.11; P = .070) in the vaccinated villages. **Similar decreases in density were observed with NVT within vaccinated and control villages. No significant differences were found between vaccinated and control villages in the postvaccination comparisons for either VT or NVT.**

CONCLUSIONS:
A high density of carriage among young subjects might partly explain why children are more efficient than adults in pneumococcal transmission. **PCV-7 vaccination lowered the density of VT and of NVT pneumococcal carriage in the before-after vaccination analysis.** Clinical Trials Registration: ISRCTN51695599.

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Comment
Pneumococcal conjugate vaccine may have a protective herd immunity effect by reduction in density of nasopharyngeal carriage and reduced transmission. What is surprising in this study is the observed decrease in non-vaccine strains after vaccination. This component of the study was a before-and-after comparison, making it possible that secular trends or other confounding influenced the results. This finding remains unexplained, and is counter-intuitive to other studies that indicate serotype replacement with non-vaccine serotypres is common (including the same research groups below, in neonates).

Indirect effect of 7-valent pneumococcal conjugate vaccine on pneumococcal carriage in newborns in rural Gambia: a randomised controlled trial.

Egere U, Townend J, Roca A, Akinsanya A, Bojang A, Nsekpong D, Greenwood B, Adegbola RA, Hill PC.

PLoS One. 2012;7(11):e49143. doi: 10.1371/journal.pone.0049143 Epub 2012 Nov 21.

Source
Medical Research Council Unit, Banjul, The Gambia. uegere@mrc.gm

Abstract
BACKGROUND:
Gambian infants frequently acquire Streptococcus pneumoniae soon after birth. We investigated the indirect effect of 7-valent pneumococcal conjugate vaccine (PCV-7) on pneumococcal acquisition in newborn Gambian babies.

METHODS:
Twenty-one villages were randomised to receive PCV-7 to all subjects (11 vaccinated villages) or to infants aged 2-30 months (10 control villages). Other control villagers received Meningococcal C conjugate vaccine. From 328 babies born during the trial, nasopharyngeal swabs were collected after birth, then weekly until 8 weeks of age when they received their first dose of PCV-7. Pneumococcal carriage and acquisition rates were compared between the study arms and with a baseline study.

RESULTS:
57.4% of 2245 swabs were positive for S. pneumoniae. Overall carriage was similar in both arms. In vaccinated villages fewer infants carried pneumococci of vaccine serotypes (VT) (16.9% [31/184] vs. 37.5% [54/144], p<0.001) and more carried pneumococci of non-vaccine serotypes (NVT) (80.9% [149/184] vs. 75.7% [109/144], p = 0.246). **Infants from vaccinated villages had a significantly lower acquisition rate of VT (HR 0.39 [0.26-0.58], p<0.001) and increased acquisition of NVT (HR 1.16 [0.87-1.56], p = 0.312).** VT carriage (51.6% vs. 37.5%, p = 031 in control and 46.1% vs. 16.8%, p<0.001 in vaccinated villages) and acquisition rates (HR 0.68 [0.50-0.92], p = 0.013 in control villages and HR 0.31 [0.19-0.50], p<.001 in vaccinated villages) were significantly lower in both study arms than in the baseline study. **NVT carriage (63.2% vs. 75.7%, p = 0.037 in control and 67.2% vs. 75.3%, p = 0.005 in vaccinated villages) and acquisition rates (HR 1.48 [1.06-2.06], p = 0.022) and (HR 1.52 [1.11-2.10], p = 0.010 respectively) were significantly higher.**

CONCLUSION:
PCV-7 significantly reduced carriage of VT pneumococci in unvaccinated infants. This indirect effect likely originated from both the child and adult vaccinated populations. **Increased carriage of NVT pneumococci needs ongoing monitoring.**

Immunogenicity and Safety of a 13-Valent Pneumococcal Conjugate Vaccine in Healthy Infants and Toddlers Given with Routine Vaccines in India.

Amdekar YK, Lalwani SK, Bavdekar A, Balasubramanian S, Chhatwal J, Bhat SR, Verghese VP, Tansey SP, Gadgil D, Jiang Q, Pride M, Emini EA, Gruber WC, Scott DA.

Pediatr Infect Dis J. 2012 Nov 28. [Epub ahead of print]

Source
From the *Consultant Pediatrician, Jaslok Hospital and Research Center, Mumbai, India; †Bharati Vidyapeeth University Medical College Pune, India; ‡Department of Pediatrics, K. E. M. Hospital Research Centre, Rasta Peth, Pune, India; §Kanchi Kamakoti CHILDS Trust Hospital and The CHILDS Trust Medical Research Foundation, Nungambakkam, Chennai, India; ¶Christian Medical College & Hospital, Ludhiana, Punjab, India; ‖Department of Pediatrics, St. Johns Medical College, Bangalore, India; **Department of Child Health, Christian Medical College, Vellore, India; ††Pfizer Inc, Maidenhead, United Kingdom; ‡‡Pfizer Pharmaceutical India Pvt. Ltd; §§Pfizer Inc, Collegeville, Pennsylvania; ¶¶Pfizer Inc, Pearl River, New York.

Abstract
BACKGROUND:: The childhood burden of disease due to Streptococcus pneumoniae is particularly high in India. **The immunogenicity and safety of 13-valent pneumococcal conjugate vaccine (PCV13) was compared with 7-valent pneumococcal conjugate vaccine (PCV7) in a randomized, active-controlled, double-blind trial conducted at 12 sites in India**. METHODS:: Healthy infants received PCV13 or PCV7 at 6, 10, and 14 weeks of age (infant series), and 12 months of age (toddler dose) along with routine pediatric vaccinations. Immunoglobulin G responses against the 13 pneumococcal serotypes were evaluated 1 month after the infant series and posttoddler dose. Pertussis and poliomyelitis immune responses were assessed 1 month after the infant series. Safety and tolerability were also assessed. RESULTS:: **The immunogenicity results for the 7 common serotypes and the concomitant vaccines (whole-cell pertussis and oral poliovirus) were similar for subjects receiving PCV13 and subjects receiving PCV7. Immune responses to the 6 additional serotypes were higher in the PCV13 group compared with the PCV7 group. PCV13 and PCV7 had similar safety and tolerability profiles.** CONCLUSIONS:: PCV13 has similar immunogenicity to PCV7 in response to the 7 common serotypes, and generally higher immunogenicity in response to the 6 additional serotypes. PCV13 may provide added protection against pneumococcal disease caused by the additional 6 serotypes, and does not interfere with immune responses to whole-cell pertussis and oral poliovirus vaccines. PCV13 has an acceptable safety profile in both infants and toddlers, comparable to that of PCV7.

Immunogenicity and safety of 10-valent pneumococcal non-typeable Haemophilus influenzae protein D-conjugate vaccine (PHiD-CV) co-administered with routine childhood vaccines in Taiwan.

Lin TY, Lu CY, Chang LY, Chiu CH, Huang YC, Bock HL, Tang H, François N, Moreira M, Schuerman L, Huang LM.

J Formos Med Assoc. 2012 Sep;111(9):495-503. doi: 10.1016/j.jfma.2011.07.014. Epub 2012 Mar 18.

Source
Chang Gung Children's Hospital, Chang Gung University College of Medicine, Taiwan.

Abstract
BACKGROUND/PURPOSE:

The immunogenicity and safety of the 10-valent pneumococcal nontypeable Haemophilus influenzae (H. Influenzae) protein D conjugate vaccine (PHiD-CV), co-administered with routine childhood vaccines, were assessed in Taiwanese infants.

METHODS:
In this open study, 230 healthy infants were primed with three doses of PHiD-CV (Synflorix) and diphtheria, tetanus, acellular pertussis, hepatitis B (HBV), inactivated poliomyelitis and Haemophilus influenzae type b (Hib) conjugate vaccine (DTPa-HBV-IPV/Hib vaccine) at 1.5, 3 and 6 months of age and two doses of oral human rotavirus vaccine at 1.5 and 3 months. Pneumococcal immune responses were assessed 1 month post-dose three, by 22F-inhibition ELISA and opsonophagocytic activity (OPA) assay. Local and general solicited/unsolicited symptoms and serious adverse events (SAEs) were recorded.

RESULTS:
At least 95.4% of participants had an antibody concentration ≥ 0.2 µg/mL against each vaccine serotype. At least 96.1% of participants had an OPA titer ≥ 8 against each vaccine serotype except 6B (87.3%). All infants, but one, were seropositive for antibodies against nontypeable H. influenzae protein D. Immune responses to the co-administered vaccines were good and in line with previous reports. PHiD-CV was well tolerated, with low (≤ 6.3%) incidences of grade 3 solicited local symptoms. The frequencies of general symptoms were in line with other pneumococcal conjugate vaccine studies. There were no systematic increases in incidences of solicited general or local symptoms with successive doses. There were no reports of grade 3 fever (rectal temperature > 40 °C) or SAEs considered to be causally related to vaccination.

CONCLUSION:
PHiD-CV co-administered with routine childhood vaccines within the first 6 months of life, was highly immunogenic, and well tolerated in Taiwanese infants.

Rotavirus vaccine

Vaccines for preventing rotavirus diarrhoea: vaccines in use.

Soares-Weiser K, Maclehose H, Bergman H, Ben-Aharon I, Nagpal S, Goldberg E, Pitan F, Cunliffe N.

Cochrane Database Syst Rev. 2012 Nov 14;11:CD008521. doi: 10.1002/14651858.CD008521.pub3.

Source
Enhance Reviews Ltd,Wantage, UK. karla@enhance-reviews.com

Abstract
BACKGROUND:
Rotavirus results in more diarrhoea-related deaths in children less than five years of age than any other single agent in countries with high childhood mortality. It is also a common cause of

diarrhoea-related hospital admissions in countries with low childhood mortality. Currently licensed rotavirus vaccines include a monovalent rotavirus vaccine (RV1; Rotarix, GlaxoSmithKline Biologicals) and a pentavalent rotavirus vaccine (RV5; RotaTeq, Merck & Co., Inc.). Lanzhou lamb rotavirus vaccine (LLR; Lanzhou Institute of Biomedical Products) is used in China only.

OBJECTIVES:
To evaluate rotavirus vaccines approved for use (RV1, RV5, and LLR) for preventing rotavirus diarrhoea.

SEARCH METHODS:
We searched MEDLINE (via PubMed) (1966 to May 2012), the Cochrane Infectious Diseases Group Specialized Register (10 May 2012), CENTRAL (published in The Cochrane Library 2012, Issue 5), EMBASE (1974 to 10 May 2012), LILACS (1982 to 10 May 2012), and BIOSIS (1926 to 10 May 2012). We also searched the ICTRP (10 May 2012), www.ClinicalTrials.gov (28 May 2012) and checked reference lists of identified studies.

SELECTION CRITERIA:
We selected randomized controlled trials (RCTs) in children comparing rotavirus vaccines approved for use with placebo, no intervention, or another vaccine.

DATA COLLECTION AND ANALYSIS:
Two authors independently assessed trial eligibility, extracted data, and assessed risk of bias. We combined dichotomous data using the risk ratio (RR) and 95% confidence intervals (CI). We stratified the analysis by child mortality, and used GRADE to evaluate evidence quality.

MAIN RESULTS:
Forty-one trials met the inclusion criteria and enrolled a total of 186,263 participants. Twenty-nine trials (101,671 participants) assessed RV1, and 12 trials (84,592 participants) evaluated RV5. We did not find any trials assessing LLR.RV1Children aged less than one year: In countries with low-mortality rates, RV1 prevents 86% of severe rotavirus diarrhoea cases (RR 0.14, 95% CI 0.07 to 0.26; 40,631 participants, six trials; high-quality evidence), and, based on one large multicentre trial in Latin America and Finland, probably prevents 40% of severe all-cause diarrhoea episodes (rate ratio 0.60, 95% CI 0.50 to 0.72; 17,867 participants, one trial; moderate-quality evidence). **In countries with high-mortality rates, RV1 probably prevents 63% of severe rotavirus diarrhoea cases (RR 0.37, 95% CI 0.18 to 0.75; 5414 participants, two trials; moderate-quality evidence), and, based on one trial in Malawi and South Africa, 34% of severe all-cause diarrhoea cases (RR 0.66, 95% CI 0.44 to 0.98; 4939 participants, one trial; moderate-quality evidence)**.Children aged up to two years: In countries with low-mortality rates, RV1 prevents 85% of severe rotavirus diarrhoea cases (RR 0.15, 95% CI 0.12 to 0.20; 32,854 participants, eight trials; high-quality evidence), and probably 37% of severe all-cause diarrhoea episodes (rate ratio 0.63, 95% CI 0.56 to 0.71; 39,091 participants, two trials; moderate-quality evidence). **In countries with high-mortality rates, based on one trial in Malawi and South Africa, RV1 probably prevents 42% of severe rotavirus diarrhoea cases (RR 0.58, 95% CI 0.42 to 0.79; 2764 participants, one trial; moderate-quality evidence), and 18% of severe all-cause diarrhoea cases (RR 0.82, 95% CI 0.71 to 0.95; 2764 participants, one trial; moderate-quality evidence)**.RV5Children aged less than one year: In countries with low-mortality rates, RV5 probably prevents 87% of severe rotavirus diarrhoea cases (RR 0.13, 95% CI 0.04 to 0.45; 2344 participants, three trials; moderate-quality evidence), and, based on one trial in Finland, may prevent 72% of severe all-cause diarrhoea cases (RR 0.28, 95% CI 0.16 to 0.48; 1029 participants, one trial; low-quality

evidence**). In countries with high-mortality rates, RV5 prevents 57% of severe rotavirus diarrhoea (RR 0.43, 95% CI 0.29 to 0.62; 5916 participants, two trials; high-quality evidence), but there was insufficient data to assess the effect on severe all-cause diarrhoea.**Children aged up to two years: Four studies provided data for severe rotavirus and all-cause diarrhoea in countries with low-mortality rates. Three trials reported on severe rotavirus diarrhoea cases and found that RV5 probably prevents 82% (RR 0.18, 95% CI 0.07 to 0.50; 3190 participants, three trials; moderate-quality evidence), and another trial in Finland reported on severe all-cause diarrhoea cases and found that RV5 may prevent 96% (RR 0.04, 95% CI 0.00 to 0.70; 1029 participants, one trial; low-quality evidence). In high-mortality countries, RV5 prevents 41% of severe rotavirus diarrhoea cases (RR 0.59, 95% CI 0.43 to 0.82; 5885 participants, two trials; high-quality evidence), and 15% of severe all-cause diarrhoea cases (RR 0.85, 95% CI 0.75 to 0.98; 5977 participants, two trials; high-quality evidence).**There was no evidence of a vaccine effect on mortality (181,009 participants, 34 trials; low-quality evidence), although the trials were not powered to detect an effect on this end point.**Serious adverse events were reported in 4565 out of 99,438 children vaccinated with RV1 and in 1884 out of 78,226 children vaccinated with RV5. Fifty-eight cases of intussusception were reported in 97,246 children after RV1 vaccination, and 34 cases in 81,459 children after RV5 vaccination. No significant difference was found between children receiving RV1 or RV5 and placebo in the number of serious adverse events, and intussusception in particular.

AUTHORS' CONCLUSIONS:
RV1 and RV5 prevent episodes of rotavirus diarrhoea. The vaccine efficacy is lower in high-mortality countries; however, due to the higher burden of disease, the absolute benefit is higher in these settings. No increased risk of serious adverse events including intussusception was detected, but post-introduction surveillance studies are required to detect rare events associated with vaccination.

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Human rotavirus vaccine Rotarix™ provides protection against diverse circulating rotavirus strains in African infants: a randomized controlled trial.

Steele AD, Neuzil KM, Cunliffe NA, Madhi SA, Bos P, Ngwira B, Witte D, Todd S, Louw C, Kirsten M, Aspinall S, Van Doorn LJ, Bouckenooghe A, Suryakiran PV, Han HH.

BMC Infect Dis. 2012 Sep 13;12:213. doi: 10.1186/1471-2334-12-213.

Source
Rotavirus Vaccine Program, PATH, 2201 Westlake Ave, Seattle, WA 98121, USA. duncan.steele@gatesfoundation.org

Abstract
BACKGROUND:
Rotaviruses are the most important cause of severe acute gastroenteritis worldwide in children <5 years of age. The human, G1P[8] rotavirus vaccine Rotarix™ significantly reduced severe rotavirus gastroenteritis episodes in a Phase III clinical trial conducted in infants in South Africa and Malawi. This paper examines rotavirus vaccine efficacy in preventing severe rotavirus

gastroenteritis, during infancy, caused by the various G and P rotavirus types encountered during the first rotavirus-season.

METHODS:
Healthy infants aged 5-10 weeks were enrolled and randomized into three groups to receive either two (10 and 14 weeks) or three doses of Rotarix™ (together forming the pooled Rotarix™ group) or three doses of placebo at a 6,10,14-week schedule. Weekly home visits were conducted to identify gastroenteritis episodes. Rotaviruses were detected by ELISA and genotyped by RT-PCR and nucleotide sequencing. The percentage of infants with severe rotavirus gastroenteritis caused by the circulating G and P types from 2 weeks post-last dose until one year of age and the corresponding vaccine efficacy was calculated with 95% CI.

RESULTS:
Overall, 4939 infants were vaccinated and 4417 (pooled Rotarix™ = 2974; placebo = 1443) were included in the per protocol efficacy cohort. G1 wild-type was detected in 23 (1.6%) severe rotavirus gastroenteritis episodes from the placebo group. This was followed in order of detection by G12 (15 [1%] in placebo) and G8 types (15 [1%] in placebo). **Vaccine efficacy against G1 wild-type, G12 and G8 types were 64.1% (95% CI: 29.9%; 82%), 51.5% (95% CI:-6.5%; 77.9%) and 64.4% (95% CI: 17.1%; 85.2%), respectively.** Genotype P[8] was the predominant circulating P type and was detected in 38 (2.6%) severe rotavirus gastroenteritis cases in placebo group. The remaining circulating P types comprised of P[4] (20 [1.4%] in placebo) and P[6] (13 [0.9%] in placebo). *Vaccine efficacy against P[8] was 59.1% (95% CI: 32.8%; 75.3%), P[4] was 70.9% (95% CI: 37.5%; 87.0%) and P[6] was 55.2% (95% CI: -6.5%; 81.3%)*

CONCLUSIONS:
Rotarix™ vaccine demonstrated efficacy against severe gastroenteritis caused by diverse circulating rotavirus types. These data add to a growing body of evidence supporting heterotypic protection provided by Rotarix™.

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Typhoid vaccine

Effectiveness of Vi capsular polysaccharide typhoid vaccine among children: a cluster randomized trial in Karachi, Pakistan.

Khan MI, Soofi SB, Ochiai RL, Habib MA, Sahito SM, Nizami SQ, Acosta CJ, Clemens JD, Bhutta ZA; DOMI Typhoid Karachi Vi Effectiveness Study Group.

Collaborators (12)

Khan MJ, Memon Z, Puri MK, Kim DR, Park JK, You Y, Ali M, Choi SY, Alam D, Hasan R, Zafar A, Donner A.

Vaccine. 2012 Aug 3;30(36):5389-95. doi: 10.1016/j.vaccine.2012.06.015. Epub 2012 Jun 18.

Source
International Vaccine Institute, Seoul, Republic of Korea.

Abstract
BACKGROUND:
Typhoid fever is endemic in Karachi, with an incidence among children ranging from 170 to 450 per 100,000 child-years. Vaccination strategies are important for prevention, and the Vi capsular polysaccharide (ViCPS) vaccine has been shown to be effective in reducing the burden of typhoid fever.

METHODS:
A cluster randomized trial was conducted in three low socioeconomic urban squatter settlements in Karachi, Pakistan between 2002 and 2007. Subsamples were followed up for assessment of immune response and adverse events after vaccination.

RESULTS:
The study participants were similar in a wide variety of socio-demographic and economic characteristics at baseline. **A total of 27,231 individuals of the total target population of 51,965 in 120 clusters either received a ViCPS vaccine (13,238 [52% coverage]) or the control Hepatitis A vaccine (13,993 [53%]). Typhoid fever was diagnosed in 30 ViCPS vaccine recipients and 49 Hepatitis A vaccine recipients with an adjusted total protective effectiveness of 31% (95%CI: -28%, 63%). The adjusted total vaccine protective effectiveness was -38% (95%CI: -192%, 35%) for children aged 2-5 years and 57% (95%CI: 6%, 81%) for children 5-16 years old.**

CONCLUSION:
The ViCPS vaccine did not confer statistically significant protection to children in the study areas, and there was a decline in antibody response 2 years post-vaccination. However, the ViCPS vaccine showed significant total protection in children 5-16 years of age, which is consistent with other studies of ViCPS vaccine conducted in India, Nepal, China and South Africa. These findings suggest that ViCPS vaccination of school-aged children will protect the children of urban, typhoid endemic areas against typhoid fever.

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Vitamin A

(See also Maternal health, nutrition and micronutrient supplementation, HIV prevention of mother to child transmission)

Vitamin A supplementation every 6 months with retinol in 1 million pre-school children in north India: DEVTA, a cluster-randomised trial.

Awasthi S, Peto R, Read S, Clark S, Pande V, Bundy D; DEVTA (Deworming and Enhanced Vitamin A) team.

Collaborators (74)

Ayyar L, Chandra A, Joshi VC, Narang N, Rehman H, Saxena N, Prakash N, Sharma A, Sharma M, Tripathi M, Upreti DK, Das R, Lal A, Rastogi T, Mani SS, Chitransh D, Pandey L, Tandon A, Bajpai D, Chandra U, Dwivedi A, Pant PK, Shukla V, Ahmad A, Ahmad H, Bahadur J, Chandra H, Chandra R, Chaturvedi A, Dwivedi S, Kumar A, Kumar D, Kumar M, Kumar N, Kumar R, Kumar S, Kumar S 1st, Kumar S 2nd, Pal C, Prasad M, Kumar R 1st, Kumar R 2nd, Rashid Z, Singh H, Shukla H, Shukla KB, Shukla SS, Shukla VB, Singh S, Singh S, Verma SS, Verma SS, Chandra R, Haq I, Kazi M, Kumar A, Kumar K, Kumar M, Kumar S, Lal B, Tiwari AK, Awasthi S, Maseeh A, Najeeb S, Neetu L, Parween S, Rai B, Rastogi T, Sharma A, Shukla R, Shukla S, Shukla L, Srivastava A, Srivastava VK.

Lancet. 2013 Apr 27;381(9876):1469-77. doi: 10.1016/S0140-6736(12)62125-4. Epub 2013 Mar 14.

Source
King George's Medical University, Lucknow, Uttar Pradesh, India.

Abstract
BACKGROUND:
In north India, vitamin A deficiency (retinol <0·70 μmol/L) is common in pre-school children and 2-3% die at ages 1·0-6·0 years. We aimed to assess whether periodic vitamin A supplementation could reduce this mortality.

METHODS:
Participants in this cluster-randomised trial were pre-school children in the defined catchment areas of 8338 state-staffed village child-care centres (under-5 population 1 million) in 72 administrative blocks. Groups of four neighbouring blocks (clusters) were cluster-randomly allocated in Oxford, UK, between 6-monthly vitamin A (retinol capsule of 200,000 IU retinyl acetate in oil, to be cut and dripped into the child's mouth every 6 months), albendazole (400 mg tablet every 6 months), both, or neither (open control). Analyses of retinol effects are by block (36 vs 36 clusters). The study spanned 5 calendar years, with 11 6-monthly mass-treatment days for all children then aged 6-72 months. Annually, one centre per block was randomly selected and visited by a study team 1-5 months after any trial vitamin A to sample blood (for retinol assay, technically reliable only after mid-study), examine eyes, and interview caregivers. Separately, all 8338 centres were visited every 6 months to monitor pre-school deaths (100,000 visits, 25,000 deaths at ages 1·0-6·0 years [the primary outcome]). This trial is registered at ClinicalTrials.gov, NCT00222547.

FINDINGS:
Estimated compliance with 6-monthly retinol supplements was 86%. Among 2581 versus 2584 children surveyed during the second half of the study, mean plasma retinol was one-sixth higher (0·72 [SE 0·01] vs 0·62 [0·01] μmol/L, increase 0·10 [SE 0·01] μmol/L) and the prevalence of severe deficiency was halved (retinol <0·35 μmol/L 6%vs 13%, decrease 7% [SE 1%]), as was that of Bitot's spots (1·4%vs 3·5%, decrease 2·1% [SE 0·7%]). Comparing the 36 retinol-allocated versus 36 control blocks in analyses of the primary outcome, deaths per child-care centre at ages 1·0-6·0 years during the 5-year study were 3·01 retinol versus 3·15 control (absolute reduction 0·14 [SE 0·11], mortality ratio 0·96, 95% CI 0·89-1·03, p=0·22), suggesting absolute risks of death between ages 1·0 and 6·0 years of approximately 2·5% retinol versus 2·6% control. No specific cause of death was significantly affected.

INTERPRETATION:
DEVTA contradicts the expectation from other trials that vitamin A supplementation would reduce child mortality by 20-30%, but cannot rule out some more modest effect. Meta-analysis of DEVTA plus eight previous randomised trials of supplementation (in various different populations) yielded a weighted average mortality reduction of 11% (95% CI 5-16, p=0·00015), reliably contradicting the hypothesis of no effect.

FUNDING:
UK Medical Research Council, USAID, World Bank (vitamin A donated by Roche).

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Comment

This was the largest RCT ever undertaken, involving 2 million pre-school children in India. The results have surprised many, given that the mortality reduction from vitamin A was only 4% with confidence internals from an 11% reduction to a 3% increase, and deworming had no effect on mortality, and surprisingly no effect on growth. This trial has been controversial, not because the results are questionable, the trial was very well conducted and analysed. What it suggests is that estimates of effect of single interventions, (such as the previously estimated 25% reduction in mortality from vitamin A) are often exaggerated. True mortality reductions are more likely to occur when there is health services development and comprehensive approaches to poverty reduction, healthy lifestyles and disease prevention. We have put much store in the role of vitamins and single interventions as magic bullets in reducing child deaths, and it is time to reconsider trhat true development is not as simple as it has been made out to be by much of the global health community. It is interesting to look back on the earlier estimates of mortality reduction that might be expected to occur from scaling up Vitamin A. These were published in the Lancet Child Survival Series in 2003, as part of an estimate of the proportional reduction in mortality that might be expected from 23 high-priority interventions. The estimate was 2%, very similar to the DEVTA trial.

A large-scale intervention to introduce orange sweet potato in rural Mozambique increases vitamin A intakes among children and women.

Hotz C, Loechl C, de Brauw A, Eozenou P, Gilligan D, Moursi M, Munhaua B, van Jaarsveld P, Carriquiry A, Meenakshi JV.

Br J Nutr. 2012 Jul 14;108(1):163-76. doi: 10.1017/S0007114511005174. Epub 2011 Oct 10.

Source
HarvestPlus, International Food Policy Research Institute, Washington, DC 20006, USA. christinehotz.to@gmail.com

Abstract
β-Carotene-rich orange sweet potato (OSP) has been shown to improve vitamin A status of infants and young children in controlled efficacy trials and in a small-scale effectiveness study with intensive exposure to project inputs. However, the potential of this important food crop to reduce the risk of vitamin A deficiency in deficient populations will depend on the ability to distribute OSP vines and promote its household production and consumption on a large scale. In rural Mozambique, we conducted a randomised, controlled **effectiveness study of a large-scale intervention to promote household-level OSP production and consumption using integrated agricultural, demand creation/behaviour change and marketing components.** The following two intervention models were compared: a low-intensity (1 year) and a high-intensity (nearly 3 years) training model. **The primary nutrition outcomes were OSP and vitamin A intakes by children 6-35 months and 3-5·5 years of age, and women**. The intervention resulted in significant net increases in OSP intakes (model 1: 46, 48 and 97 g/d) and vitamin A intakes (model 1: 263, 254 and 492 μg retinol activity equivalents/d) among the younger children, older children and women, respectively. **OSP accounted for 47-60 % of all sweet potato consumed and, among reference children, provided 80 % of total vitamin A intakes.** A similar magnitude of impact was observed for both models, suggesting that group-level trainings in nutrition and agriculture could be limited to the first project year without compromising impact. Introduction of OSP to rural, sweet potato-producing communities in Mozambique is an effective way to improve vitamin A intakes.

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Introduction of β-carotene-rich orange sweet potato in rural Uganda resulted in increased vitamin A intakes among children and women and improved vitamin A status among children.

Hotz C, Loechl C, Lubowa A, Tumwine JK, Ndeezi G, Nandutu Masawi A, Baingana R, Carriquiry A, de Brauw A, Meenakshi JV, Gilligan DO.

J Nutr. 2012 Oct;142(10):1871-80. Epub 2012 Aug 8.

Source
HarvestPlus, International Food Policy Research Institute, Washington DC, USA. christinehotz.to@gmail.org

Abstract
Vitamin A deficiency (VAD) persists in Uganda and the consumption of β-carotene-rich orange sweet potato (OSP) may help to alleviate it. **Two large-scale, 2-y intervention programs were implemented among Ugandan farmer households to promote the production and consumption of OSP.** The programs differed in their inputs during year 2, with one being more intensive (IP) and the other being reduced (RP). A randomized, controlled effectiveness study compared the impact of the IP and RP with a control on OSP and vitamin A intakes among children aged 6-35 mo (n = 265) and 3-5 y (n = 578), and women (n = 573), and IP compared with control on vitamin A status of 3- to 5-y-old children (n = 891) and women (n = 939) with serum retinol <1.05 μmol/L at baseline. The net OSP intake increased in both the IP and RP groups (P < 0.01), accounting for 44-60% of vitamin A intake at follow-up. The prevalence of inadequate vitamin A intake was reduced in the IP and RP groups compared with controls among children 6-35 mo of age (>30 percentage points) and women (>25 percentage points) (P < 0.01), with no differences between the IP and RP groups of children (P = 0.75) or women (P = 0.17). There was a 9.5 percentage point reduction in prevalence of serum retinol <1.05 μmol/L for children with complete data on confounding factors (n = 396; P < 0.05). At follow-up, vitamin A intake from OSP was positively associated with vitamin A status (P < 0.05). **Introduction of OSP to Ugandan farming households increased vitamin A intakes among children and women and was associated with improved vitamin A status among children.**

Vitamin D

(See Tuberculosis, and Endocrine disorders and bone health)

Zinc

(see also: Acute respiratory infection, Diarrhoea, Nutrition – micronutrients, Vitamin A, Cholera vaccine)

Oral zinc for treating diarrhoea in children.

Lazzerini M, Ronfani L.

Cochrane Database Syst Rev. 2013 Jan 31;1:CD005436. doi: 10.1002/14651858.CD005436.pub4.

Source
Unit for Health Services Research and International Health,WHO Collaborating Centre forMaternal and ChildHealth, Institute forMaternal and Child Health, Trieste, Italy. lazzerini@burlo.trieste.it.

Abstract
BACKGROUND:
In developing countries, diarrhoea causes around two million child deaths annually. Zinc supplementation during acute diarrhoea is currently recommended by the World Health Organization and UNICEF.

OBJECTIVES:
To evaluate oral zinc supplementation for treating children with acute or persistent diarrhoea.

SEARCH METHODS:
In February 2012, we searched the Cochrane Infectious Diseases Group Specialized Register, CENTRAL (The Cochrane Library 2011, Issue 11), MEDLINE, EMBASE, LILACS, CINAHL, mRCT, and reference lists. We also contacted researchers.

SELECTION CRITERIA:
Randomized controlled trials comparing oral zinc supplementation with placebo in children aged one month to five years with acute or persistent diarrhoea, including dysentery.

DATA COLLECTION AND ANALYSIS:
Both authors assessed trial eligibility and risk of bias, extracted and analysed data, and drafted the review. Diarrhoea duration and severity were the primary outcomes. We summarized dichotomous outcomes using risk ratios (RR) and continuous outcomes using mean differences (MD) with 95% confidence intervals (CI). Where appropriate, we combined data in meta-analyses (using the fixed- or random-effects model) and assessed heterogeneity.The quality of evidence has been assessed using the GRADE methods

MAIN RESULTS:
Twenty-four trials, enrolling 9128 children, met our inclusion criteria. The majority of the data is from Asia, from countries at high risk of zinc deficiency, and may not be applicable elsewhere. Acute diarrhoea. There is currently not enough evidence from well conducted randomized controlled trials to be able to say whether zinc supplementation during acute diarrhoea reduces death or hospitalization (very low quality evidence).**In children aged greater than six months with acute diarrhoea, zinc supplementation may shorten the duration of**

diarrhoea by around 10 hours (MD -10.44 hours, 95% CI -21.13 to 0.25; 2175 children, six trials, low quality evidence), and probably reduces the number of children whose diarrhoea persists until day seven (RR 0.73, 95% CI 0.61 to 0.88; 3865 children, six trials, moderate quality evidence). In children with signs of moderate malnutrition the effect appears greater, reducing the duration of diarrhoea by around 27 hours (MD -26.98 hours, 95% CI -14.62 to -39.34; 336 children, three trials, high quality evidence). Conversely, In children aged less than six months, the available evidence suggests zinc supplementation may have no effect on mean diarrhoea duration (MD 5.23 hours, 95% CI -4.00 to 14.45; 1334 children, two trials, low quality evidence), and may even increase the proportion of children whose diarrhoea persists until day seven (RR 1.24, 95% CI 0.99 to 1.54; 1074 children, one trial, moderate quality evidence).No trials reported serious adverse events, but zinc supplementation during acute diarrhoea causes vomiting in both age groups (RR 1.59, 95% 1.27 to 1.99; 5189 children, 10 trials, high quality evidence). Persistent diarrhoea. **In children with persistent diarrhoea, zinc supplementation probably shortens the duration of diarrhoea by around 16 hours (MD -15.84 hours, 95% CI -25.43 to -6.24; 529 children, five trials, moderate quality evidence).**

AUTHORS' CONCLUSIONS:
In areas where the prevalence of zinc deficiency or the prevalence of moderate malnutrition is high, zinc may be of benefit in children aged six months or more.The current evidence does not support the use of zinc supplementation in children below six months of age.

Effectiveness of zinc supplementation to full term normal infants: a community based double blind, randomized, controlled, clinical trial.

Radhakrishna KV, Hemalatha R, Geddam JJ, Kumar PA, Balakrishna N, Shatrugna V.

PLoS One. 2013 May 30;8(5):e61486. doi: 10.1371/journal.pone.0061486. Print 2013.

Source
National Institute of Nutrition (ICMR), Hyderabad, Andhra Pradesh, India.

Abstract
The study was aimed to **test whether zinc supplementation, if initiated early, can prevent stunting and promote optimum body composition in full term infants.** For this, full term pregnant women from low income urban community were enrolled and were followed-up for 24 months postpartum. Body mass index (BMI) was calculated from maternal weight and height that were collected one month after delivery. Infants' weight, and length, head, chest and mid upper arm circumferences and skin fold thicknesses at triceps, biceps and subscapular area were collected at baseline (before randomization) and once in three months up till 24 months**. Three hundred and twenty four infants were randomized and allocated to zinc (163) or placebo (161) groups respectively.** Supplementation of zinc was initiated from 4 months of age and continued till children attained 18 months. The control (placebo) group of children received riboflavin 0.5 mg/day, whereas the intervention (zinc) group received 5 mg zinc plus riboflavin 0.5 mg/day. When infants were 18 months old, dietary intakes (in 78 children) were calculated by 24 hour diet recall method and hemoglobin, zinc, copper and vitamin A were quantified in blood samples collected from 70 children. The results showed prevalence of undernutrition (body mass index <18.5) in 37% of the mothers. Mean±SD calorie consumption and zinc

intakes from diets in infants were 590±282.8 Kcal/day and 0.97±0.608 mg/day respectively. Multiple linear regression models demonstrated maternal weight as a strong predictor of infants' weight and length at 18 months of age. As expected, diarrhea duration impacted infants' linear growth and weight gain adversely. **Zinc supplementation for a mean period of 190 days, starting from 4 months up to 18 months of age, in full term normal infants, consuming an average energy of 590 Kcal/day, had significant effect on the skin fold thicknesses, but not on their linear growth.**

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Short-Course Prophylactic Zinc Supplementation for Diarrhea Morbidity in Infants of 6 to 11 Months.

Malik A, Taneja DK, Devasenapathy N, Rajeshwari K.

Pediatrics. 2013 Jun 3. [Epub ahead of print]

Source
Departments of Community Medicine, and.

Abstract
BACKGROUND:Zinc supplementation during diarrhea substantially reduces the incidence and severity of diarrhea. However, the effect of short-course zinc prophylaxis has been observed only in children >12 months of age. Because the incidence of diarrhea is comparatively high in children aged 6 to 11 months, we assessed the prophylactic effect of zinc on incidence and duration of diarrhea in this age group.METHODS:**In this randomized, double-blind, placebo-controlled trial, we enrolled infants aged 6 to 11 months from an urban resettlement colony in Delhi, India, between January 1, 2011, and January 15, 2012. We randomly assigned 272 infants to receive either 20 mg of zinc or a placebo suspension orally every day for 2 weeks.** The primary outcome was the incidence of diarrhea per child-year. All analyses were done by intention-to-treat.RESULTS:A total of 134 infants in the zinc and 124 in the placebo groups were assessed for the incidence of diarrhea. **There was a 39% reduction (crude incident rate ratio [IRR] 0.61, 95% confidence interval [CI] 0.53-0.71) in episodes of diarrhea, 39% (adjusted IRR 0.61, 95% CI 0.54-0.69) in the total number of days that a child suffered from diarrhea, and reduction of 36% in duration per episode of diarrhea (IRR 0.64, 95% CI 0.56-0.74) during the 5 months of follow-up.**CONCLUSIONS:Short-course prophylactic zinc supplementation for 2 weeks may reduce diarrhea morbidity in infants of 6 to 11 months for up to 5 months, in populations with high prevalence of wasting and stunting.

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Beneficial effects of zinc supplementation on head circumference of Nepalese infants and toddlers: a randomized controlled trial.

Surkan PJ, Shankar M, Katz J, Siegel EH, Leclerq SC, Khatry SK, Stoltzfus RJ, Tielsch JM.

Eur J Clin Nutr. 2012 Jul;66(7):836-42. doi: 10.1038/ejcn.2012.42. Epub 2012 May 9.

Source
Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA. psurkan@jhsph.edu

Abstract
BACKGROUND/OBJECTIVE:
To assess the effects of micronutrient supplementation on head circumference of rural Nepali infants and children.

SUBJECTS/METHODS:
We used a randomized controlled trial to assess the effects of micronutrient supplementation on head circumference in 569 rural Nepali infants and children aged 4-17 months. Children were randomized to: (1) zinc, (2) iron-folic acid, (3) zinc plus iron-folic acid or (4) a placebo group. Data on head circumference were collected during five visits at ~3 month intervals over the course of a year. We calculated change in head circumference in treatment groups receiving zinc and iron comparing the first and fifth visits as well as used generalized estimating equations (GEE) to take advantage of data from all points in time. Models were adjusted for covariates unbalanced in the randomization and for baseline head circumference.

RESULTS:
Estimating differences in head circumference between baseline and visit 5, **children in the zinc treatment group showed smaller decreases in head circumference z-score compared with placebo (adjusted β=0.13, 95% confidence interval (CI): 0.03 to 0.23).** Using GEE, zinc treatment was associated with 0.11 (95% CI: 0.05 to 0.17) decrease in the rate of decline in head circumference z-score across visits as compared with placebo. Iron-folic acid supplementation was not associated with head circumference z-scores when comparing visits 1 with 5 or including data across all visits in adjusted models.

CONCLUSION:
Our results suggest that zinc supplementation confers a beneficial effect on the rate of head growth in Nepali infants.

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Effect of preventive supplementation with zinc and other micronutrients on non-malarial morbidity in Tanzanian pre-school children: a randomized trial.

Veenemans J, Schouten LR, Ottenhof MJ, Mank TG, Uges DR, Mbugi EV, Demir AY, Kraaijenhagen RJ, Savelkoul HF, Verhoef H.

PLoS One. 2012;7(8):e41630. doi: 10.1371/journal.pone.0041630. Epub 2012 Aug 3.

Source
Cell Biology and Immunology Group, Wageningen University, Wageningen, The Netherlands.

Abstract
BACKGROUND:

The efficacy of preventive zinc supplementation against diarrhea and respiratory illness may depend on simultaneous supplementation with other micronutrients. We aimed to assess the effect of supplementation with zinc and multiple micronutrients on diarrhea and other causes of non-malarial morbidity.

METHODS AND FINDINGS:
Rural Tanzanian children (n=612) aged 6-60 months and with height-for-age z-score < -1.5 SD were randomized to daily supplementation with zinc (10 mg) alone, multi-nutrients without zinc, multi-nutrients with zinc, or placebo. Children were followed for an average of 45 weeks. During follow-up, we recorded morbidity episodes. We found no evidence that concurrent supplementation with multi-nutrients influenced the magnitude of the effect of zinc on rates of diarrhea, respiratory illness, fever without localizing signs, or other illness (guardian-reported illness with symptoms involving skin, ears, eyes and abscesses, but excluding trauma or burns). **Zinc supplementation reduced the hazard rate of diarrhea by 24% (4%-40%).** By contrast, multi-nutrients seemed to increase this rate (HR; 95% CI: 1.19; 0.94-1.50), particularly in children with asymptomatic Giardia infection at baseline (2.03; 1.24-3.32). Zinc also protected against episodes of fever without localizing signs (0.75; 0.57-0.96), but we found no evidence that it reduced the overall number of clinic visits.

CONCLUSIONS:
We found no evidence that the efficacy of zinc supplements in reducing diarrhea rates is enhanced by concurrent supplementation with other micronutrients. By reducing rates of fever without localizing signs, supplementation with zinc may reduce inappropriate drug use with anti-malarial medications and antibiotics.

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Zinc and copper supplementation are not cost-effective interventions in the treatment of acute diarrhea.

Patel AB, Badhoniya N, Dibley MJ.

J Clin Epidemiol. 2013 Jan;66(1):52-61. doi: 10.1016/j.jclinepi.2012.06.012.
Source
Lata Medical Research Foundation, 9/1 Vasant Nagar, Nagpur 440 022, India. dr_apatel@yahoo.com

Abstract
BACKGROUND:
Diarrhea is one of the principal causes of morbidity and mortality among children in the developing world. Cumulative costs of treating diarrhea would be high and would further increase if zinc was used as an adjunct to treatment of acute diarrhea.

OBJECTIVE:
To determine the impact of zinc supplementation on the mean predicted costs of treating acute diarrhea and the incremental cost-effectiveness (CE) as compared with placebo, from the provider's (government) and patient's perspective.

STUDY DESIGN AND SETTING:

In a randomized, double-blind, placebo-controlled clinical trial, 808 children aged 6-59 months with acute diarrhea were individually randomized to placebo (Pl), zinc (Zn) only, and zinc and copper (Zn + Cu) together with standard treatment of acute diarrhea. The actual resource utilization and cost data were collected for all participants. The incremental CE ratio and its 95% confidence interval (95% CI) were assessed.

RESULTS:
The relative CE for treating acute diarrhea was 1.5 (95% CI: 1.50, 1.52) times more when supplemented with zinc and 1.7 (95% CI: 1.69, 1.71) times more when supplemented with Zn + Cu with no additional beneficial effect.

CONCLUSION:
This study showed that zinc or zinc with copper supplementation were not cost-effective in the treatment of acute diarrhea in this study population.

Therapeutic zinc and copper supplementation in acute diarrhea does not influence short-term morbidity and growth: double-blind randomized controlled trial.

Patel AB, Dibley MJ, Mamtani M, Badhoniya N, Kulkarni H.

Pediatr Infect Dis J. 2013 Jan;32(1):91-3. doi: 10.1097/INF.0b013e31826fb32d.

Source
Lata Medical Research Foundation, Indira Gandhi Government Medical College, Nagpur, India.

Abstract
Our objective was to evaluate the effect of zinc and copper supplementation in acute diarrhea on morbidity and growth during 12 weeks of follow-up. In a double-blind randomized controlled clinical trial of 724 children aged 6-59 months, none of the 11 evaluated outcomes showed significant association with zinc or zinc and copper supplementation. **Thus, therapeutic zinc supplementation may not always yield short-term benefits.**