Abstract from Current Literatures

Live, Attenuated, Tetravalent Butantan–Dengue Vaccine in Children and Adults

Kallás EG, Cintra MA, Moreira JA, Patiño EG, Braga PE, Tenório JC, Infante V, Palacios R, de Lacerda MV, Batista Pereira D, da Fonseca AJ. Live, attenuated, tetravalent Butantan–dengue vaccine in children and adults. New England Journal of Medicine. 2024 Feb 1;390(5):397-408.

Background: Butantan–Dengue Vaccine (Butantan-DV) is an investigational, single-dose, live, attenuated, tetravalent vaccine against dengue disease, but data on its overall efficacy are needed.

Methods: In an ongoing phase 3, double-blind trial in Brazil, we randomly assigned participants to receive Butantan-DV or placebo, with stratification according to age (2 to 6 years, 7 to 17 years, and 18 to 59 years); 5 years of follow-up is planned. The objectives of the trial were to evaluate overall vaccine efficacy against symptomatic, virologically confirmed dengue of any serotype occurring more than 28 days after vaccination (the primary efficacy end point), regardless of serostatus at baseline, and to describe safety up to day 21 (the primary safety end point). Here, vaccine efficacy was assessed on the basis of 2 years of follow-up for each participant, and safety as solicited vaccine-related adverse events reported up to day 21 after injection. Key secondary objectives were to assess vaccine efficacy among participants according to dengue serostatus at baseline and according to the dengue viral serotype; efficacy according to age was also assessed.

Results: Over a 3-year enrollment period, 16,235 participants received either Butantan-DV (10,259 participants) or placebo (5976 participants). The overall 2-year vaccine efficacy was 79.6% (95% confidence interval [CI], 70.0 to 86.3) — 73.6% (95% CI, 57.6 to 83.7) among participants with no evidence of previous dengue exposure and 89.2% (95% CI, 77.6 to 95.6) among those with a history of exposure. Vaccine efficacy was 80.1% (95% CI, 66.0 to 88.4) among participants 2 to 6 years of age, 77.8% (95% CI, 55.6 to 89.6) among those 7 to 17 years of age, and 90.0% (95% CI, 68.2 to 97.5) among those 18 to 59 years of age. Efficacy against DENV-1 was 89.5% (95% CI, 78.7 to 95.0) and against DENV-2 was 69.6% (95% CI, 50.8 to 81.5). DENV-3 and DENV-4 were not detected during the follow-up period. Solicited systemic vaccine- or placebo-related adverse events within 21 days after injection were more common with Butantan-DV than with placebo (58.3% of participants, vs. 45.6%).

Conclusions: A single dose of Butantan-DV prevented symptomatic DENV-1 and DENV-2, regardless of dengue serostatus at baseline, through 2 years of follow-up. (Funded by Instituto Butantan and others; DEN-03-IB ClinicalTrials.gov number, NCT02406729, and WHO ICTRP number, U1111-1168-8679.)

Effects of Cooking with Liquefied Petroleum Gas or Biomass on Stunting in Infants

Checkley W, Thompson LM, Sinharoy SS, Hossen S, Moulton LH, Chang HH, Waller L, Steenland K, Rosa G, Mukeshimana A, Ndagijimana F. Effects of cooking with liquefied petroleum gas or biomass on stunting in infants. New England Journal of Medicine. 2024 Jan 4;390(1):44-54.

Background: Household air pollution is associated with stunted growth in infants. Whether the replacement of biomass fuel (e.g., wood, dung, or agricultural crop waste) with liquefied petroleum gas (LPG) for cooking can reduce the risk of stunting is unknown.

Methods: We conducted a randomized trial involving 3200 pregnant women 18 to 34 years of age in four low- and middle-income countries. Women at 9 to less than 20 weeks' gestation were randomly assigned to use a free LPG cookstove with continuous free fuel delivery for 18 months (intervention group) or to continue using a biomass cookstove (control group). The length of each infant was measured at 12 months of age, and personal exposures to fine particulate matter (particles with an aerodynamic diameter of $\leq$2.5 μm) were monitored starting at pregnancy and continuing until the infants were 1 year of age. The primary outcome for which data are presented in the current report — stunting (defined as a length-for-age z score that was more than two standard deviations below the median of a growth standard) at 12 months

of age - was one of four primary outcomes of the trial. Intention-to-treat analyses were performed to estimate the relative risk of stunting.

Results: Adherence to the intervention was high, and the intervention resulted in lower prenatal and postnatal 24-hour personal exposures to fine particulate matter than the control (mean prenatal exposure, 35.0 ìg per cubic meter vs. 103.3 μg per cubic meter; mean postnatal exposure, 37.9 μg per cubic meter vs. 109.2 μg per cubic meter). Among 3061 live births, 1171 (76.2%) of the 1536 infants born to women in the intervention group and 1186 (77.8%) of the 1525 infants born to women in the control group had a valid length measurement at 12 months of age. Stunting occurred in 321 of the 1171 infants included in the analysis (27.4%) of the infants born to women in the intervention group and in 299 of the 1186 infants included in the analysis (25.2%) of those born to women in the control group (relative risk, 1.10; 98.75% confidence interval, 0.94 to 1.29; P=0.12).

Conclusions: An intervention strategy starting in pregnancy and aimed at mitigating household air pollution by replacing biomass fuel with LPG for cooking did not reduce the risk of stunting in infants. (Funded by the National Institutes of Health and the Bill and Melinda Gates Foundation; HAPIN ClinicalTrials.gov number, NCT02944682.)

Development and validation of a predictive model for seizure recurrence following discontinuation of antiseizure medication in children with epilepsy: a systematic review and meta-analysis, and prospective cohort study

Dai K, Tang D, Bao L, Li S, Chen N, Ye W, Song A, Liao S, Li T. Development and validation of a predictive model for seizure recurrence following discontinuation of antiseizure medication in children with epilepsy: a systematic review and meta-analysis, and prospective cohort study. eClinicalMedicine. 2025 Apr 1;82:103154.

Background: Seizure relapse in pediatric patients with epilepsy after antiseizure medication (ASM) withdrawal is a critical concern, yet the risk factors are not fully understood. Identifying these factors is essential for personalized treatment planning.

Methods: In this systematic review and meta-analysis, and prospective cohort study, we conducted a meta-analysis of cohort studies to derive a predictive model for seizure recurrence post-ASM discontinuation, then validated it in a prospective cohort study. The derivation cohort was derived from a systematic, search of PubMed, Web of Science, Embase, and Cochrane Library (from inception to May 1,2024) for English-language cohort studies on risk factors for seizure recurrence after ASM withdrawal in pediatric epilepsy, focusing on children initiating ASM tapering with documented relapse, while excluding case reports, and non-pharmacological interventions. Risk factors were selected and weighted according to the statistical significance of pooled relative risks (RRs), with â coefficients derived from log-transformed RRs to establish weighted scores in the predictive model. The validation cohort included children with epilepsy enrolled between February 16, 2015 and November 15, 2024, from two Chinese hospitals. Inclusion criteria comprised first-time ASM withdrawal candidates aged <18 years with ≥24-month follow-up, while exclusion criteria focused on incomplete data, protocol deviations, and non-pharmacological interventions. This study is registered at https://www.medicalresearch.org.cn/ (MR-50-24-042059).

Findings: A total of 26 cohort studies were identified from the systematic review and included in the meta-analysis. The derivation cohort included 4080 children with epilepsy, of whom 959 (23.50%) experienced seizure recurrence. The predictive model identified nine significant risk factors: intellectual disability, abnormal neurological examination or motor deficit, history of febrile seizures, only focal onset seizures, overall number of ASM used, duration of epilepsy ≥3 years, abnormal electroencephalogram (EEG) at the start of ASM tapering, abnormal EEG after ASM taperin1.g, and age at first seizure ≥10 years. β coefficients were derived from the logarithm of pooled relative risks for each factor and converted into weighted scores, yielding a maximum total risk score of 17. The validation cohort comprised 341 patients with a median follow-up duration of 2.84 (0.27–9.75) years, and 122 (35.8%) out of them had seizure relapses. The model demonstrated robust performance in the validation cohort, with an AUC of 0.85 (95% CI: 0.81–0.91), sensitivity of 0.74 (95% CI: 0.68–0.80), and specificity of 0.82 (95% CI: 0.75–0.89).

Interpretation: Our evidence-based predictive model offers a robust tool for estimating the risk of seizure recurrence in pediatric patients with epilepsy after ASM withdrawal, aiding clinicians in personalized treatment decisions. While this tool enhances personalized treatment decisions in epilepsy management, its predictive thresholds require external validation across diverse clinical settings and populations to ensure broad clinical applicability.

Pathways through which water, sanitation, hygiene, and nutrition interventions reduce antibiotic use in young children: a mediation analysis of a cohort nested within a cluster-randomized trial

Nguyen AT, Heitmann GB, Mertens A, Ashraf S, Rahman MZ, Ali S, Rahman M, Arnold BF, Grembi JA, Lin A, Ercumen A. Pathways through which water, sanitation, hygiene, and nutrition interventions reduce antibiotic use in young children: a mediation analysis of a cohort nested within a cluster-randomized trial. eClinicalMedicine. 2025 Apr 1;82.

Background: Low-cost, household-level water, sanitation, and hygiene (WASH) and nutrition interventions can reduce pediatric antibiotic use, but the mechanism through which interventions reduce antibiotic use has not been investigated.

Methods: We conducted a causal mediation analysis using data collected between September 2013 and October 2015 from a cohort nested within the WASH Benefits Bangladesh cluster-randomized trial (NCT01590095). Among a subsample of children within the WASH, nutrition, nutrition + WASH, and control arms (N = 1409 children; 267 clusters), we recorded caregiver-reported antibiotic use at ages 14 and 28 months and collected stool at age 14 months. Our primary outcome was any caregiver-reported antibiotic use by index children within the past 30 or 90 days measured at age 14 and 28 months. Mediators included caregiver-reported child diarrhea, acute respiratory infection (ARI), and fever; and enteric pathogen carriage in stool measured by qPCR. Both intervention-mediator and mediator-outcome models were controlled for mediator-outcome confounders.

Findings: The receipt of any WASH or nutrition intervention reduced caregiver-reported antibiotic use through all pathways in the past month by 5.5 percentage points (95% CI 1.2, 9.9), from 49.5% (95% CI 45.9%, 53.0%) in the control group to 45.0% (95% CI 42.7%, 47.2%) in the pooled intervention group. When separating this effect into different pathways, we found that interventions reduced antibiotic use by 0.6 percentage points (95% CI 0.1, 1.3) through reduced diarrhea, 0.7 percentage points (95% CI 0.1, 1.5) through reduced ARI with fever, and 1.5 percentage points (95% CI 0.4, 3.0) through reduced prevalence of enteric viruses. Interventions reduced antibiotic use through any of these measured mediators by 2.1 percentage points (95% CI ”0.3, 4.5).

Interpretation: WASH and nutrition interventions reduced pediatric antibiotic use through the prevention of enteric and respiratory infections in a rural, low-income population. Given that many of these infections are caused by viruses or parasites, WASH and nutrition interventions may help reduce inappropriate antibiotic use in similar settings.