World Health Organization

The WHO PROPS Trial
(PRObiotics in Preterm and Small for gestational age infants)

Date 10th February 2025

Contact Dr. Karen Edmond, Scientist, Newborn and Child Health and Development Unit, World Health Organization, is leading all pretrial and trial activities. Contact details: Karen Edmond, edmondk@who.int, phone +41 22 791 21 11

Title The WHO PROPS Trial (PRObiotics in Preterm and Small for gestational age infants)

Details Aims and objectives of the trial: The overall aim of this trial is to assess the effect of probiotic supplementation on mortality, morbidity, and growth in preterm or term small for gestational age (SGA) infants in the first six months of life in South Asia and Sub-Saharan Africa. For preterm infants, the primary objective is to assess the effectiveness of probiotic supplementation on mortality from enrolment to six months of age. For term SGA infants the primary objective is to assess the effectiveness of probiotic supplementation on underweight-free survival from enrolment to six months of age. Secondary objectives are: to assess effect on morbidities (sepsis, necrotising enterocolitis, severe diarrhoea and growth [wasting and underweight]) from enrolment to six months of age; to determine safety outcomes (serious adverse events [SAEs] and probiotic sepsis from enrolment to six months of age; and to understand faecal colonisation of probiotic organisms from enrolment to six months of age.

Design. Double-blind, individually-randomised, placebo-controlled, parallel-group clinical trial.

Intervention and placebo administration: The intervention will be the strains *Bifidobacterium longum subsp. Infantis* DSM33361 (*B. Infantis*) and *Lactobacillus rhamnosus* GG DSM33156 (*L. rhamnosus GG*). The doses will be 0.35 billion colony forming units (CFU) *B. infantis* and 1 billion CFU *L. rhamnosus* GG once daily for 28 days. The strains will be mixed with maltodextrin powder. The placebo will be maltodextrin powder alone without the probiotic organisms. The supplements will be given daily by the family to the baby, directly observed by research staff during home visits.

Study setting and recruitment: The study is being conducted in five sites in five countries; Bangladesh, Ethiopia, Kenya, Nigeria and Pakistan, which were selected after an open call for expressions of interest. Study recruitment will be at hospitals in the study sites. Infants will be enrolled at within two days of birth, and supplementation will commence at that time. Infants will be followed up monthly at home during home visits from research staff. A total of 14,000 infants will be enrolled across the five participating sites.

Programmatic implications Numerous small trials conducted in the last ten years have reported that probiotics can improve short- and long-term mortality, necrotising enterocolitis, sepsis, growth and neurodevelopment in preterm and term SGA infants. In 2022, a World Health Organization (WHO) guideline development group (GDG) reviewed the evidence for the impact of probiotics in preterm and term SGA infants and their final guidelines included a conditional recommendation for the use of probiotics for human milk fed infants < 32 weeks gestation or < 1.5kg at birth. However, the evidence of effect on all critical outcomes (mortality, necrotising enterocolitis, sepsis and growth) was graded as low quality due to heterogeneity, risk of bias, indirectness and imprecision. In addition the GDG was not able to make a recommendation on type (i.e. genera, species or strain), formulation (e.g. powder or drops), dose, timing or duration of probiotic administration as there was insufficient evidence.

WHO and other organisations have recommended that further large high-quality trials are implemented to provide evidence of sufficient quality and applicability to inform policy and practice. The WHO GDG recommended that rigorous new research was needed to improve certainty of evidence on critical outcomes and also to understand optimal strains, dosing and duration of probopic supplementation and related impact.

For further information please contact | **Karen Edmond** **edmondk@who.int**

Timeline	Infants will be enrolled over a period of 18 months and followed up until they reach six months of age.
Geographic location	Bangladesh, Ethiopia, Kenya, Nigeria, Pakistan
Principal investigators	Ethiopia - Mahlet Abayneh Gizaw, St Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia Nigeria - Adejumoke Idowu Ayede, College of Medicine, University of Ibadan and University College Hospital, Ibadan, Nigeria Bangladesh - Mohammod Shahidullah, Projahnmo Research Foundation, Dhaka, Bangladesh Kenya - Benson Singa, Kenya Medical Research Institute, Nairobi, Kenya Pakistan - Fyezah Jehan, Aga Khan University, Karachi, Pakistan
Main external funders	Bill and Melinda Gates Foundation
Coordinator / sponsor	The trial is coordinated and sponsored by the World Health Organization (WHO) Newborn and Child Health and Development Unit (NBC)
Additional documents	Clinical trial registry. ISRCTN.Website. Also available on request. Trial protocol. WHO Ethical Review Committee. Also available on request. Statistical analysis plan. WHO PROPS-TCU. Also available on request

For further information please contact
Karen Edmond
edmondk@who.int