

Creating and Measuring Integrated Solutions for Healthy Birth, Growth, and Development: a new Grand Challenge

Summary

The Bill & Melinda Gates Foundation is launching a new Grand Challenge: *Creating and Measuring Integrated Solutions for Healthy Birth, Growth, and Development*. This challenge focuses on new measurement tools and new combinations of approaches to ensure all children thrive – that they not only survive, but also have the chance to live healthy productive lives.

This challenge joins the *All Children Thriving* platform, which links Grand Challenges programs targeting healthy birth, growth, and development, including the global programs [Saving Brains](#) and [Saving Lives at Birth](#) and programs launched through Grand Challenges Brazil and Grand Challenges India. The platform supports the expansion of a global network of investigators working on similar issues; fostering linkages between the individual programs; building on existing databases, biorepositories, and clinical trial sites; and increasing opportunities for exchanging ideas and lessons learned.

Funding for this request for proposals

Who we will fund

- **Investigators in low-income and middle-income countries** (see [World Bank - Low Income Countries](#) for definitions). Subject to the eligibility requirements in the Rules & Guidelines and with the exceptions listed below, investigators in low- and middle-income countries are invited (in connection with the organization with which they are affiliated) to apply through the Bill & Melinda Gates Foundation's application portal. We reserve the right to determine eligibility for this call based on these characteristics. Grants will go to investigators in low- and middle-income countries, but we encourage partnerships with investigators in other countries, especially where the opportunity exists to build on existing collaborations.
- **Exceptions:**
 - **Brazilian investigators** are asked to apply through *Grand Challenges Brazil: All Children Thriving*.
 - **Indian investigators** are asked to apply through *Grand Challenges India: All Children Thriving*.
 - **South African investigators** are asked to apply through *Grand Challenges South Africa: All Children Thriving* via South Africa's Strategic Health Innovation Partnership (SHIP).

Funding levels

The request for proposals for *Creating and Measuring Integrated Solutions for Healthy Birth, Growth, and Development* will fund **seed grants at up to USD \$500,000 for two years** and **full grants at up to USD \$2.5 million for four years**. We expect that projects funded at either level with promising results will have the opportunity to apply for additional funding to build on initial success. How many seed grants and how many full grants will be funded depends on the response to the request for proposals. In

all cases, individual project budgets should be representative of the scope and magnitude of the proposed studies and carefully designed to get the best possible value out of the award.

Creating and Measuring Integrated Solutions for Healthy Birth, Growth, and Development

Background

Globally, over 6 million children under the age of five die each year, and approximately 165 million (26%) of the world's children have stunted growth jeopardizing subsequent physical as well as cognitive development. Much remains unknown about the root causes of unhealthy birth, growth, and development. Current evidence suggests that the causes – whether based on malnutrition, infectious disease, social or other factors – are interwoven, and that addressing them one at a time can solve only a small fraction of the problem. Furthermore, stunted growth and development can reduce human productivity and perpetuate poverty.

Program goal

We need to know how and when to most effectively intervene to ensure all children thrive – that they not only survive, but also have the chance to live healthy productive lives. The ultimate goal of this challenge is to determine what packages of interventions should be delivered to which group of individuals at what point in their life cycle to reduce the burden of fetal growth impairment and preterm birth, stunted postnatal growth, and impaired cognitive development.

Program objectives

We are looking for projects that – by piloting new approaches – will determine:

- 1)** What combinations of interventions are most effective for prevention and treatment of unhealthy birth, growth, and development;
- 2)** When in the human lifecycle they are most effectively applied; and
- 3)** How they are most effectively and practically integrated into a continuum of care, encompassing preconception, conception to birth, birth to two years, childhood, adolescence, and adulthood.

Interventions of interest include – but are not limited to – those focused on preconception and maternal nutrition (e.g., adequate micronutrient intake); exclusive breastfeeding to 6 months of age; complementary feeding from 6 to 24 months of age; food security and dietary diversity (e.g., accommodating seasonality); farm productivity and women farmers' income generation; infection control (e.g., vaccines, drugs, clean water access, sanitation, food hygiene, hand washing); reduced toxin exposure (e.g., indoor air pollution, aflatoxin, pesticides); reducing the burden of unhealthy pregnancy, including fetal growth delays (e.g., maternal stress, preeclampsia, gestational diabetes); reducing the burden of preterm birth; birth assistance; fostering newborn care (e.g., immediate initiation of breastfeeding, kangaroo care); family planning and birth spacing; infant nurturing and early child stimulation; addressing violence and abuse; and addressing the role of socioeconomic status and gender norms.

What we are looking for

To reach these objectives, we are looking for projects that propose innovation in the following areas:

- **Measurement tools:** Pilot tests of new measurement tools, such as those based on a new technology or new biomarkers of linear growth, cognitive function, or gestational age, including rapid response indicators of intervention success or failure
- **Intervention packages:** Tests of new interventions – especially combinations of interventions – that 1) develop a new human cohort with unique advantages over existing cohorts, such as the potential for developing a unique biorepository; or 2) add an activity, such as a prospective pilot trial of an intervention or new measurement tool, to ongoing work with a human cohort, including at sites of intervention trials and sites for public health surveillance
- **Analytical tools:** Pilot tests of new analytical tools that use existing biorepositories or existing health and development databases for retrospective analysis

We will give highest priority to those projects that:

- Build on ongoing work in some way, especially by building on clinical trial sites where the sustained availability of descriptive data has had demonstrable success in helping design interventions, stratifying populations by risk factor, and enabling an understanding of the community that includes barriers and constraints to delivery of interventions and to implementation of government programs
- Incorporate multiple of the areas of innovation listed above, e.g., testing multiple interventions, especially sets of interventions targeting combinations of outcomes spanning healthy birth, growth, and development; combining a new measurement tool with a new intervention; or combining retrospective analysis of a database with the design and piloting of a new intervention
- Clearly incorporate measures of success reasonable for the timespan of the grant, such as a series of measurements to monitor trends or an early measurement useful to predict success at the end of the grant period
- Have a project plan whereby after two years – the end of the seed grant period and the halfway point for the full grant period – grantees will be in a position to participate in initial collaborative meetings to explore how the results from their project could inform the design of more extensive intervention packages for testing in single large cohorts
- Could contribute to a portfolio of funded projects that addresses a country's regional diversity and the need to provide health equity for diverse vulnerable populations
- Explain how proposed interventions will be tested in communities so that they have the highest likelihood of being relevant for implementation more broadly in the country's public health system

Examples of types of projects for each of the two categories of grants:

- **Seed grants:** Funded at up to \$500,000 USD per two-year project, these awards do not require extensive preliminary data and are meant to provide an opportunity to test particularly bold ideas, including applying approaches from outside the field of maternal and child health. New

approaches could be piloted as additions to ongoing projects already funded under existing Grand Challenges programs launched by the Gates Foundation or its partners, including [Saving Brains](#), [Saving Lives at Birth](#), [Stars in Global health](#), and [Grand Challenges Explorations](#).

- **Full grants:** Funded at up to \$2.5 million USD per four-year project, these awards do require substantial preliminary data and are meant to provide an opportunity to develop, refine, and rigorously test combinations of activities, including sets of interventions for which some or all have previously shown promise in controlled or limited settings.

Examples of what we are looking for

- Approaches to clinical trial design that allow testing combinations of interventions and relatively rapidly determining which subsets of interventions are yielding impact
- Approaches that help determine how to effectively and efficiently deliver all necessary interventions together as a package to promote children thriving and health equity
- Approaches that reveal the interplay of biological pathways associated with stress, inflammation, and nutrition, and how such pathways might be targeted to simultaneously prevent multiple pathologies, such as intrauterine growth retardation and preterm birth, stunted postnatal growth, and impaired cognitive development
- Approaches that specifically combine interventions focused on improving child survival with those focused on improving healthy child development, including cognitive function
- Approaches, tools, and biomarkers for stratifying populations to determine who would benefit from a preventive intervention package, and who is at higher risk and warrants a therapeutic intervention package, including determining what is the optimal duration of treatment to prevent relapse
- Approaches, tools, and biomarkers for stratifying populations to reduce the risk of interventions causing unintended harm (e.g., metabolic disease, including obesity)
- Approaches for 1) rapid measurement of physical growth velocity and body composition; 2) measuring brain function and development, with a focus on tests that are simple, reliable, non-invasive, objective, universally applicable, and include those appropriate for fetal life, newborns, or early infancy; 3) measuring gestational age, with a focus on tests that are simple, reliable, non-invasive, universally applicable, and include those that can be applied to pregnant women or to the newborn or infant; 4) predicting or identifying metabolic complications or diseases in pregnancy that affect birth or postnatal outcomes; 5) measuring individual food intake, including validated and simple markers to assess exclusive breastfeeding practices; 6) developing integrated markers of systemic inflammation; and 7) developing combinations of tests – either new or preexisting tests – that when evaluated in combination provide better predictors of the outcomes of interest than any single test
- Approaches that specifically address the roles of women as perceived by society – from adolescence to motherhood – creating new or better opportunities to improve children’s health and development (e.g., new uses of women’s self-help groups)

- Approaches that determine how to shift the emphasis to earlier prevention within the first 1,000 days of life, including determining the value of intervening in the first 100 days and preconception
- Approaches that yield actionable knowledge by characterizing populations for which there has been striking progress in children thriving

Examples of what we are NOT looking for

- Basic research that does not provide a clear path to development and testing of prevention and treatment strategies
- Studies that lead to solutions applicable to only a small fraction of the population (e.g., because of a focus on a specific disease or condition with limited incidence)
- Projects without the potential to expand in scale to provide solutions to a greater number or diversity of people
- Studies that propose interventions that detract from favorable family practices (e.g., studies that would lead to inappropriate early cessation of breast feeding, deter skin-to-skin care, or disrupt routine immunizations)
- Projects lacking metrics to determine success or failure and to allow decisions about the appropriateness of follow-on funding
- Solutions that are only slight improvements over existing approaches (e.g., replication of an approach in a new geography in the absence of added innovation)

Characteristics of successful proposals

How we evaluate proposals

We seek proposals that clearly demonstrate the attributes below:

- Potential to lead to prevention and treatment solutions with substantial **impact**
- **Innovation**, including creativity of the project’s approach and clear differentiation from existing approaches
- **Scientific and technical excellence**, including a clear and rigorous conceptual framework for research activities
- Unique project **resources**, including investigator and organization capabilities and potential for collaboration
- **Value** in terms of appropriateness of the budget and timeline relative to project complexity, risk, and potential impact

Collaboration

This request for proposals seeks to create a consortium of individually funded projects that will benefit from sharing information between projects. We expect that such sharing will help to ensure that the goals of the innovative approaches in individual projects are ultimately integrated with each other, thereby increasing the chances that the programs will be greater than the sum of their parts. Furthermore we expect that sharing experimental methods, data, and resources will ultimately improve the ability to compare and validate local research findings and to develop interventions and products

that can have impact at a greater scale. The specific terms of the collaborative activities will be negotiated prior to the grant award. Collaborative efforts include:

- **Cohort harmonization** - When collaborating with projects with existing cohorts or establishing new cohorts, investigators will be expected to participate, whenever possible, in cohort harmonization. Study sites will be expected to develop and follow standard operating procedures and quality control protocols for specimen collections and participate in the establishment of a minimum common set of data and specimens to be collected across the program.
- **Data sharing** - A data sharing plan will be developed that is equitable, ethical, and efficient. It will include a policy covering 1) sharing data for confidential and strictly internal use at the Gates Foundation, and 2) sharing data with the broader scientific community.

Grand Challenges

Definition

Grand Challenges is a family of initiatives fostering innovation to solve key problems in global health and development for those most in need. It seeks to establish a portfolio of projects with complementary approaches that encompass multiple types of innovation, including innovation in biological research, medical health technology and product development, service delivery, and behavior change. Grand Challenges initiatives therefore seek to:

- Engage diverse investigators, including those outside of the areas that might traditionally be associated with the initiative
- Encourage partnerships that bring together investigators from diverse organizations, including for-profit institutions, non-governmental organizations, academic and health research institutions, foundations, and civil society groups

History

Today, a variety of funding partners use “Grand Challenges” to accelerate research, creating an expanding network of funding and research partnerships spanning diverse topics. Below are some key examples highlighting how the Grand Challenges family has grown over time:

- In 2003, the Bill & Melinda Gates Foundation launched [Grand Challenges in Global Health](#), a US\$450-million research initiative that came to include multiple funding partners and, in 2007, it launched [Grand Challenges Explorations](#) (GCE), an accelerated program providing small, initial grants for exploratory research.
- In 2010, the Canadian government funded [Grand Challenges Canada](#) to support global health researchers in low- and middle-income countries and in Canada through multiple grant programs.
- In 2011, USAID launched [Grand Challenges for Development](#), an initiative that brought the Grand Challenges approach to diverse new areas, including agriculture and child reading, through multiple grant programs.

- In 2012, the Gates Foundation and the Brazilian government established [Grand Challenges Brazil](#), a partnership to fund researchers in Brazil through GCE and, to date, the grant program [Reducing the Burden of Preterm Birth](#).
- In 2013, the Gates Foundation and the Indian government launched [Grand Challenges India](#), a partnership to fund researchers in India through GCE and, to date, the grant programs [Achieving Healthy Growth through Agriculture and Nutrition](#) and [Reinvent the Toilet Challenge – India](#).