

REQUEST FOR PROPOSALS

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Saving Brains

Determine the economic impact of poverty-related risk factors for cognitive development and human capital

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Executive Summary

Grand Challenges Canada is requesting proposals for economic modeling relevant to its Saving Brains initiative. The ultimate aim of the Saving Brains initiative is to identify and develop effective and efficient means to promote cognitive development in the first thousand days of development – between conception and two years of age – and thereby help children reach their full potential.

Over 200 million children fail to reach their full cognitive developmental potential. Poverty is both a cause and a result of this failure. This creates a vicious cycle whereby malnutrition, infection, poor management of pregnancy and birth complications, and a lack of cognitive stimulation and nurturing before two years of age have long-lasting effects on cognitive development that decrease productivity in adulthood. Alongside efforts to strengthen health systems and tackle the broader determinants of poor health, preventing exposure to, and effect of, these risk factors in the first thousand days has the potential to increase the productive wealth embodied in the intellectual, social and physical capability of the individual, which is key to the development of individuals, communities, and societies.

This Request for Proposals seeks investigators to participate in a consortium to estimate the global economic impact of cognitive underdevelopment as a result of these poverty-related risk factors: malnutrition, infection, poor management of pregnancy and birth complications, and a lack of cognitive stimulation and nurturing. The consortium will include investigators with primary affiliations to organizations based in low- or middle-income countries. A consortium manager is also being sought through this call.

This Request for Proposals commits up to 2M CAD to be awarded over 15 months.

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1. Introduction

Over 200 million children are not able to fulfill their developmental potential. This impaired development is often measured in terms of small body size: fetal, newborn and child growth restriction accounts for one-fifth of the global disability-adjusted life years in children less than 5 years of age.

A less visible effect of impaired development—but perhaps with the most significant economic impact—is the reduction of cognitive abilities and associated social capacities. Physically stunted children also have stunted brain development and stunted potential. A child with reduced growth by two years of age is at increased risk for cognitive and educational deficits, translating into less time spent in school, and less learned per school year. Since the risk factors to healthy development are more prevalent in impoverished areas, this can serve to lock individuals into poverty. It is estimated that the cognitive and educational deficits accumulated by stunted children living in poverty result in greater than a 20% loss in annual income in adulthood¹.

The most robustly associated poverty-related risk factors to cognitive development in developing countries are malnutrition, infection, poor management of pregnancy and birth complications, and a lack of cognitive stimulation and nurturing during childhood development. At the same time, the mechanisms by which these interconnected factors limit cognitive development, and their relative contribution to the global burden of cognitive deficits are poorly understood.

Grand Challenges Canada has launched the Saving Brains initiative to promote the fulfillment of human capital potential by focusing on interventions in the first thousand days – between conception and two years of age. **Human capital** is defined as the productive wealth embodied in the intellectual, social and physical capability of the individual, and is key to the development of individuals, communities, and whole societies. It reflects the cognitive abilities, social functioning (e.g., behaviour and psychological functioning), physical capacity and health status that allow an individual to be a productive member of society.

The key role of governments and international agencies in providing strong policy and health care environments that nurture early child development was emphasized in a report by the Knowledge Network for Early Childhood Development of the WHO Commission on the Social Determinants of Health.² In parallel to strengthening of health and education systems and tackling broader determinants of poor health, early childhood development is fostered by adequate nutrition, prevention and treatment of infection, safe birthing practices, and nurturing and stimulation. These interventions administered in the first thousand days have the potential to lead to dramatic

¹ Grantham-McGregor et al. Developmental potential in the first 5 years for children in developing countries. *Lancet*, 2007 **36**:60-70.

² Irwin LG, Siddiqi A, Hertzman C. Early child development: a powerful equalizer—final report of the early child development knowledge network of the Commission on Social Determinants of Health. Geneva: World Health Organization, 2007. <http://whqlibdoc.who.int/hq/2007/a91213.pdf>. (accessed Dec 19, 2010).

improvements in health and productivity in adulthood. The Saving Brains initiative has significant transformational potential to unlock the potential of individuals and communities and, over a generation, help to break the cycle of poverty that has entrapped so many developing countries.

In order to provide focus on the most impactful scientific and policy solutions, Grand Challenges Canada has committed 10M CAD for studies that will assess the long-term effect of interventions administered in the first thousand days by re-enrolling and assessing the human capital of participants from completed randomized controlled trials of interventions against major risk factors to cognitive development (see *Saving Brains: Identify early life interventions that promote fulfillment of human capital - May 2011 Request for Proposals*). Since the economic impact of cognitive deficits and limited human capital as a result of major poverty-related risk factors has not been well defined, and could serve to motivate the actions of governments, international agencies and innovators, this Request for Proposals has now been developed to complement the re-enrollment studies.

This is a Request for Proposals for economic modeling of the impact of wasted human capital as a result of the four poverty-related risk factors to cognitive development present in the first thousand days. Eligible investigators are invited to register intent to participate in an interdisciplinary consortium that will calculate the economic consequences of childhood malnutrition, infection, poor pregnancy and birth outcomes, and a lack of cognitive stimulation and nurturing decreasing adult productivity. This is part of the Focus Phase of the Saving Brains initiative.

1.1 GRAND CHALLENGES CANADA

In the 2008 Federal Budget, the Government of Canada announced the creation of the Development Innovation Fund to:

...
“support the best minds in the world as they search for breakthroughs in global health and other areas that have the potential to bring about enduring changes in the lives of millions of people in poor countries.”

“For example, new vaccines and cures could save millions of lives lost to tropical diseases. Higher-yield, drought-resistant crops could prevent future famines. And lower-emission energy sources could power industrial development and job creation with a minimal carbon footprint.”

Grand Challenges Canada, a Canadian not-for-profit organization, is the vehicle to deliver the Development Innovation Fund, in a consortium with the International Development Research Centre (a Canadian Crown corporation); and the Canadian Institutes of Health Research (a Government of Canada agency). Grand Challenges Canada is hosted by the McLaughlin-Rotman Centre for Global Health (University Health Network and University of Toronto).

The **vision** of Grand Challenges Canada is to develop a consortium of world-leading Canadian and international scientists, research organizations, and leaders from the business sector, to develop breakthrough solutions to global challenges and ensure that these solutions are available to those who need them the most.

Grand Challenges Canada's **mission** is to identify global grand challenges, fund a global community of researchers and related institutions on a competitive basis to address them and support the implementation/commercialization of the solutions that emerge.

Grand Challenges Canada's core **values** include: scientific excellence, collaboration and partnership, and accountability for results.

Grand Challenges Canada is funded by Canada's international development assistance envelope. Canada is the first country to take a grand challenges approach to global health innovation through foreign aid.

1.2 'SAVING BRAINS' INITIATIVE GOAL AND KEY OBJECTIVES

The overall goal of the Saving Brains initiative is to develop solutions targeted at the first thousand days of development that have positive long-term effects on cognitive development and human capital. To achieve this goal, the initiative sets out the following **key objectives**:

1. To provide evidence for the relative effect size on human capital of interventions in the first thousand days that are relevant to low- and middle-income countries. These interventions will address risk factors for cognitive development such as malnutrition, infection, poor pregnancy or birth outcomes, and lack of cognitive stimulation. This objective will be addressed through studies solicited in the Request for Proposals announced on May 31, 2011. The competition has closed, and we are currently evaluating proposals.
2. To estimate the economic impact of limited cognitive development resulting from exposure to major risk factors in the first thousand days in low- and middle-income countries. This is the focus of the current Request for Proposals.
3. To define a standard set of common outcomes metrics of human capital to enable comparison of effect size across studies. This will be done in conjunction with the studies funded under Key Objective 1.
4. To develop innovative, sustainable and scaleable ways to deliver solutions that effectively promote human capital formation. It is expected that sustainable implementation of the interventions will require innovative social or business models that function within the context of strengthening health systems and improving socio-economic determinants of poor health. This will be the focus of a later Request for Proposals.

The first phase of the initiative, the **Focus Phase**, is designed to address Key Objectives 1, 2 and 3. This Request for Proposals is focused exclusively on funding economic modeling studies that will address Key Objective 2. We intend to solicit innovative methods to scale-up priority early life interventions that increase human capital (Key Objective 3) in a second phase, the **Solution Phase**. Each Request for Proposals is open to all investigators, regardless of their participation in prior phases of the initiative.

2. Approach

2.1 PROGRAM GOAL

The goal of this Request for Proposals is to fund a consortium of investigators to estimate the economic impact of poverty-related risk factors for cognitive development and human capital formation. A consortium manager is also sought under this Request for Proposals; it is expected that this role will be filled by one of the funded investigators.

2.2 PROGRAM SCOPE

This Request for Proposals aims to fund a quantitative estimation of the economic consequences of major poverty-related risk factors to cognitive development that can be defended on epidemiologic and economic grounds. The identification and measurement of the consequences of limited cognitive development underlying the valuation will also be important outcomes of this program.

We are specifically interested in the consequences of the following four major risk factors to cognitive development in the first thousand days:

1. Malnutrition, including macronutrient deficiencies (protein, lipids), micronutrient deficiencies (iron, iodine, vitamin A, zinc), and suboptimal breastfeeding practices.
2. Infection, including HIV, malaria, tuberculosis, and those causing diarrheal diseases, pneumonia, neglected tropical diseases, and vaccine preventable diseases.
3. Poor management of pregnancy and birth complications, including preeclampsia, birth asphyxia, preterm delivery and low birth weight.
4. Lack of cognitive stimulation and nurturing, including when driven by maternal depression.

It is expected that the model will use realistic assumptions and be populated with the most recent and defensible data appropriate to estimate worldwide economic impact.

Applicants are expected to leverage and build upon existing analyses and studies in developing and populating this model.

We also seek estimates of the impact of substantially reducing each risk factor.

Further, the consortium will provide input on appropriate health and economic metrics to track in the re-enrollment studies funded through the program (see [*Saving Brains: Identify early life interventions that promote fulfillment of human capital-May 2011 Request for Proposals*](#)) to enable increased accuracy of the estimates.

To ensure that the output of this work is presented in a format that is accessible to a broader policy audience and can be used to explore the impact of introducing interventions or policies, the consortium funded under this program is expected to engage potential end-users from the outset and throughout the process. Potential end-users may include country-level ministries of health and finance, advocacy groups and

other policy decision-makers, and scientists and other innovators focused on solutions to promote cognitive development and human capital formation.

2.3 SIZE AND LENGTH OF GRANTS

The total fund available to support this work is 2M CAD. To enable the success of the project, we will fund a consortium composed of 3-6 investigators or teams of investigators focused on specific risk factors. It is expected that one of these investigators will manage the consortium. Upon review, successful investigators will be funded for up to 3 months to collectively develop a consortium concept plan, which will detail the consortium's scope of work, technical approach and operation plan, and will form the basis of the grant agreement between the consortium and Grand Challenges Canada. It is expected that the consortium will complete its work within 12 months of signing the grant agreement with Grand Challenges Canada. The level of funding requested should be sufficient to assure completion of the goals in the stated time frame.

3. Activities & Deliverables

The *Initial Deliverable* is a concept plan that details how the consortium will operate and the approach it will take to develop the final deliverables.

The *Final Deliverables* for this grant are:

- The identification and measurement of the most impactful of the major poverty-related risk factors for cognitive development and human capital formation in low- and middle-income countries;
- An estimation of the economic impact of the most impactful risk factors for cognitive development and human capital formation;
- An estimation of the economic benefit of reducing or eliminating the most impactful factors; and
- A user-friendly populated economic model that can be used to derive the estimations of these scenarios.

The *Interim Deliverables* listed below will help to demonstrate project progress and success by the consortium:

- Quarterly video/teleconferences and/or in-person meetings with the Grand Challenges Canada Program Officer to report on progress and work through challenges.
- A written progress report at project mid-point to evaluate progress against project milestones. Instructions for the reports will be provided to grant recipients.
- Dissemination of knowledge through publications in peer-reviewed literature, conferences, social media, etc.

The investigators funded under this Request for Proposals will be expected to:

- Work as a consortium with other investigators funded under this initiative.
- Advise on the health and economic metrics to include in the follow-up studies funded under the *Saving Brains: Identify early life interventions that promote fulfillment of human capital-May 2011* Request for Proposals.
- Participate in a community of innovators that will meet up to twice yearly.
- Commit to Grand Challenges Canada's Global Access and Ethics policies (see www.grandchallenges.ca).
- Engage end-users from the outset and throughout the project.

The consortium manager is also expected to:

- Have the individual capacity and organizational support required to coordinate the operations of the consortium members.
- Be the primary point of contact with Grand Challenges Canada for program and grants administrative purposes.

4. Rules and Guidelines

Grand Challenges Canada staff will be involved in shaping the work over time.

4.1 ELIGIBILITY CRITERIA

1. Applicants must be affiliated with an organization capable of supporting the proposed activities and administering grants. Eligible organizations can be not-for-profit, for-profit, or other recognized institutions that can successfully execute the proposed activities.
2. Principal investigators/innovators must be primarily affiliated with an institution or organization in a low-, lower-middle-, or upper-middle-income country; or must collaborate with an investigator primarily affiliated an institution or organization in a low-, lower-middle-, or upper-middle-income country.

4.2 APPLICATION INSTRUCTIONS

Application guidelines are posted on the Grand Challenges Canada website (grandchallenges.ca). Applicants should submit completed Letters of Intent to savingbrains@grandchallenges.ca.

Applicant organizations must fully meet the eligibility criteria and make certain that they are fully capable of complying with all the requirements and terms of award, including Grand Challenges Canada policies.

In a Letter of Intent, applicants must clearly state a willingness to work within a consortium and what will be contributed to this consortium project while addressing the evaluation criteria (Section 4.5). The Letter of Intent is expected to include:

- Significance of the risk factor or conditions of focus to cognitive development, both in terms of effect size and prevalence
- Focused review of literature relevant to the proposed work
- Novelty of the proposed work within the context of the reviewed literature
- Approach to model generation, including approaches to manage uncertainty, double counting, risk factor interactions and discounting
- Approach to data acquisition, including the suitability of proposed data for meeting the goals of the work
- Approach to end-user engagement, including letters of support from potential end-users
- Investigator expertise and organizational capacity
- High-level budget

Applicants should indicate the specific risk factor(s) they are best suited to address as part of a consortium. Applicants may address one or multiple risk factors, or a subset of conditions under a risk factor.

Applicants interested and capable of managing the consortium must indicate this in their application.

Please note that Grand Challenges Canada will not provide individual critiques or feedback on why an application was not selected.

Successful applicants will be assembled at a planning meeting to set the framework for the technical approach for the work and a plan of operation. The consortium will be responsible for submitting a concept plan, which, upon successful review, will form the basis of grant negotiations with Grand Challenges Canada.

4.3 REVIEW PROCESS

The Canadian Institutes of Health Research is responsible for conducting the peer review of proposals. A review committee of external reviewers including experts from low- and middle-income countries will advise on the merit of letters of intent and full proposal(s) based on the evaluation criteria (see Section 4.5). Final selection decisions will be made by the Board of Directors of Grand Challenges Canada.

4.4 APPLICATION SCHEDULE

Key Deadlines	Event
December 12, 2011	Application deadline for Letters of Intent at 11:59 pm ET
March 2012	Notice of peer review committee decision and invitation for successful applicants to participate in consortium
June 2012	Deadline for consortium concept plan

4.5 EVALUATION CRITERIA

1. Significance

The proposed work is novel and innovative and focused on risk factor(s) that significantly contributes to the global burden of limited cognitive development. The applicant summarized the relevant literature and set the proposed work in context among existing estimates and underlying studies. The significance of focusing on the proposed risk factor(s) is explained and justifiable. A conceptual framework illustrating the path(s) through which the factor(s) of focus impacts upon cognitive development is presented. The proposed work has an appropriate geographical focus (ie, low-income, low-resource areas).

2. Methodological Approach

The proposed approach to model construction is based on sound scientific analysis and technical rigour, and is based on realistic assumptions. The applicant describes suitable approaches to model validation and sensitivity to assumptions. The applicant clearly describes rational approaches to managing

issues that could undermine the validity of the model, including uncertainty, double counting and risk factor interactions. The manner by which potential end-users will be engaged is defined, and proof of their support is demonstrated.

3. Data Acquisition

The appropriate data for deriving a realistic and defensible estimate is accessible.

4. Investigator Expertise and Organizational Capability

The principal investigator, co-investigators and research team are appropriately trained, experienced and suited to carry out the proposed work. The applicant organization is financially viable and capable of supporting the proposed activities and administering grants.

5. Willingness to Collaborate

The applicant states a willingness to work within a consortium. The applicant confirms that, if successful at the Letter of Intent stage, the applicant will participate in consortium activities, including the development of the consortium concept plan with other successful applicants. Funding will be contingent upon demonstration of collaboration within the consortium

6. Best Value of Effort

The scope of the proposed work and funds requested are reasonable and commensurate with the proposed study goals. Previous non-public or proprietary analyses related to this problem are contributed to the effort.

4.6 ALLOWABLE COSTS

Grant funds may be used for the following cost categories:

1. Personnel: *Please note that salary support is an allowable cost.*
2. Travel
3. Consultants
4. Direct Supplies
5. Equipment: *Please note that partial or full support for equipment may be requested. Funding for infrastructure will be limited.*
6. Other Research Costs
7. Sub-grants/Sub-contracts
8. Indirect costs: *Please note that Grand Challenges Canada will provide a limited amount of indirect costs based on the nature of the applicant organization, to a maximum of 13% of direct costs of the Grantee's administered grant value (1-7 outlined above).*

Please note that proposals with thoughtful and efficient use of resources will be preferred over proposals representing comparable efforts that do not have the same value for the investment.

4.7 PRIVACY NOTICE

To help us in the evaluation and analysis of projects, all proposals, documents, communications, and associated materials submitted to Grand Challenges Canada (collectively, “Submission Materials”) will become the property of Grand Challenges Canada and will be shared with other members of the Grand Challenges Canada consortium (the International Development Research Centre and Canadian Institutes of Health Research). We will report publicly on the number of Letters of Intent received and the countries from which they originated. The proposals will be subject to confidential external review by independent subject matter experts and potential co-funders, in addition to analysis by our staff. Please carefully consider the information included in the Submission Materials. If you have any doubts about the wisdom of disclosure of confidential or proprietary information, we recommend you consult with your legal counsel and take any steps you deem necessary to protect your intellectual property. You may wish to consider whether such information is critical for evaluating the submission, and whether more general, non-confidential information may be adequate as an alternative for these purposes.

We respect confidential information we receive. Nonetheless, notwithstanding your characterization of any information as being confidential, we may publicly disclose all information contained in Submission Materials to the extent as may be required by law and as is necessary for potential co-funders and external reviewers, such as government entities, to evaluate them and the manner and scope of potential funding consistent with appropriate regulations and their internal guidelines and policies.

4.8 WARRANTY

By providing any Submission Materials, the sender warrants Grand Challenges Canada that they have the right to provide the information submitted. Applicants with questions concerning the contents of their Submission Materials may contact Grand Challenges Canada by email at savingbrains@grandchallenges.ca.

4.9 INTELLECTUAL PROPERTY

The output of this program may lead to innovative tools and/or products to help meet urgent global health needs. Intellectual property rights and the management of intellectual property rights are likely to play an important role in achieving the goals of this program. Grand Challenges Canada’s Global Access Strategy will guide our approach to intellectual property and we urge all applicants, to consider their willingness to comply with the Grand Challenges Canada Global Access Strategy, the guiding principles of which are as follows:

1. Breakthrough solutions to global challenges are made accessible to those in need, particularly in the developing world. Accessibility relates to both price and availability.
2. Knowledge gained through discovery is broadly, and as promptly as possible, distributed between related projects and to the global scientific community.

3. Commercialization of resulting outputs is encouraged, as long as the first two principles are achieved.

Grantees will be required to formally agree to a Global Access Agreement with Grand Challenges Canada in line with the Guiding Principles. For further information, please refer to Grand Challenges Canada's Global Access Policy at <http://www.grandchallenges.ca/grand-challenges/maternal-neonatal-and-child-health/saving-brains-program-information/>.

5. Research Assurances

It is the policy of Grand Challenges Canada that research involving human subjects, research with animals, and research subject to additional regulatory requirements must be conducted in accordance with the highest internationally recognized ethical standards. In order to receive funds from Grand Challenges Canada, initially and throughout the course of a research project, researchers must affirm and document compliance with the guiding ethical principles and standards outlined below.

1. Research involving human participants must be conducted in a manner that demonstrates, protects and preserves respect for persons, concern for the welfare of individuals, families and communities, and justice.³
2. Research involving animals must be conducted in a manner that ensures their humane care and treatment.
3. Certain research endeavors, including but not limited to research with recombinant DNA, biohazards, and genetically modified organisms, may be subject to enhanced regulation and oversight.

While not necessary for the Letter of Intent, and as applicable to the individual project, Grand Challenges Canada will require that for each venue in which any part of the project is conducted (either by your organization or a subgrantee or subcontractor) all legal and regulatory approvals for the activities being conducted will be obtained in advance of commencing the regulated activity. We will further require you to agree that no funds will be expended to enroll human subjects until the necessary regulatory and ethical bodies' approvals are obtained. For further details, please see the Grand Challenges Canada Ethics policy at <http://www.grandchallenges.ca/grand-challenges/maternal-neonatal-and-child-health/saving-brains-program-information/>.

³ Modified from the core principles articulated in TCPS 2 (<http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/chapter1-chapitre1/#toc01-1b>).