Introducing INSPIRE: An Implementation Research Collaboration Between the Department of Foreign Affairs, Trade and Development Canada and the World Health Organization

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Abstract: The government of Canada, through the Department of Foreign Affairs, Trade and Development (DFATD) has supported global efforts to reduce the impact of the HIV pandemic. In 2012, WHO and DFATD launched an implementation research initiative to increase access to interventions that were known to be effective in the prevention of mother-to-child transmission of HIV and to learn how these could be successfully integrated with other essential services for mothers and children. In addition to facilitating the implementation research projects, DFATD and WHO promoted four approaches: (1) Country-specific implementation research prioritization exercises, (2) Ministry of Health involvement, (3) Country-led, innovative, high-quality research, and (4) Leveraging regional networks and learning opportunities. While no single aspect of INSPIRE is unique, the process endeavors to promote and support high-quality, rigorous, locally-led implementation research that will have a substantial impact on the health and survival of HIV-infected women and their children.

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BACKGROUND

The government of Canada, through the Department of Foreign Affairs, Trade and Development (DFATD) (including the former Canadian International Development Agency) has consistently supported global efforts to reduce the impact of the HIV pandemic. This includes past support to global initiatives such as the World Health Organization (WHO) “3 × 5” campaign to start 3 million HIV-infected people on lifelong antiretroviral treatment (ART) by 2005 and to the Global Fund to Fight AIDS, Tuberculosis and Malaria, since it was founded in 2002. Canada also supports other multilateral and bilateral programs in sub-Saharan Africa (SSA) and elsewhere.

As part of the Canadian HIV Vaccine Initiative, Canada is currently funding a range of activities with the aim of developing an affordable globally available HIV vaccine through large and small development grants. Although this innovative work holds much promise for the longer term, it is critical that efforts to prevent transmission continue to be strengthened.

In this spirit, in 2010, WHO and DFATD started discussing a new initiative to increase access to interventions that were known to be effective in the prevention of mother-to-child transmission of HIV (PMTCT) and how these could be successfully integrated with other essential services for mothers and children in SSA. This coincided with the release of revisions to the WHO HIV guidelines that extended the use of antiretroviral drugs (ARVs) to prevent HIV transmission through breastfeeding.1 Reflecting on the challenges to achieving high coverage of highly effective ARVs throughout the MTCT risk period and opportunities that the new recommendations offered, DFATD and WHO agreed to focus on how to overcome barriers to HIV service delivery through an iterative process of implementation and learning. A 5-year program was conceived to support high-quality implementation research in 3 high-burden countries in SSA that were facing different situations (Malawi, Nigeria, and Zimbabwe). The idea was to improve the access, quality, and uptake of PMTCT services by enhancing service delivery in health facilities and strengthening national program and health systems. Here we briefly describe what has characterized INSPIRE (INtegrating and Scaling up Pmtct though Implementation REsearch) and how it will contribute to the health and well-being of women and children in Africa.

WHAT HAS CHARACTERIZED INSPIRE

In addition to facilitating the implementation research projects and their findings, DFATD and WHO adopted 4 approaches that demonstrate their underlying
commitment to country ownership, capacity development, excellence, and innovation.

Country-Specific Implementation Research Prioritization Exercises

Using a process developed by the Child Health Nutrition Research Initiative (CHNRI), a 2-day consultation that brought together local researchers, district health staff, and senior national program managers was organized in each of the 3 countries. A systematic process was followed to identify challenges to PMTCT service delivery and then formulate research questions that responded to these challenges. Each research question was scored by all participants, using a set of specific criteria to rank the importance and feasibility of research questions. In each of the countries, the highest scoring questions were used as the basis of the request for research proposals. This process is described in detail in one of the accompanying articles in this supplement.

Ministry of Health Involvement

From the beginning of INSPIRE, it was recognized that the respective Ministries of Health (MOH) needed to be at the center of planning and the implementation research. In each of the countries, the MOH has led the research prioritization exercises, participated in the design of studies, and is part of the investigative team. Senior MOH staff have accompanied WHO technical staff and consultants on site visits to assess progress and ensure the integrity of the studies. The MOH and WHO country offices regularly convene meetings with the researchers and other partners to discuss how the studies might inform national programs. This has not only been important for the feasibility of the studies, but will facilitate inclusion of the lessons learned over the course of the research and consideration of findings at the end of the study period.

Achieving Country-Led, Innovative High-Quality Research

In many SSA countries, local researchers have often not had the chance to lead large implementation research projects. Ideas, protocols, and funds are commonly imported and local researchers, while certainly involved, are not always the driving force behind the work. In INSPIRE, the principal investigators are all local researchers, although collaboration with research groups inside and outside the countries has been encouraged. After the country research prioritization exercises and public invitation for letters of interest, a competitive peer-review process was followed to select the best of local proposals. The top 3 teams from each country were subsequently brought together for a 1-week proposal development workshop, at which WHO technical staff, epidemiologists, statisticians, and qualitative scientists provided detailed support and advice on study design, formative work, and data management. Teams returned home and submitted final proposals, which were externally reviewed and scored by international experts again. Six projects were selected for funding.

Since then, WHO has convened annual investigator meetings, organized site visits by experts in implementation research, and facilitated the exchange of ideas and skills among the INSPIRE teams.

Leveraging Regional Networks and Learning Opportunities

INSPIRE has seen a number of collaborations evolve both within the 3 countries and also with researchers based in neighboring countries (but not all working on PMTCT). In 1 country (Malawi), researchers working on separate projects successfully applied together for an additional grant to add side-studies that are synergistic with both parent projects. In another country (Zimbabwe), a team with particular capacity in database management, shared these skills with a team that is located in a more rural part of the country. In yet another setting, a group with regional expertise (Ghana) provided training and ongoing assistance to strengthen an intervention (Nigeria), based on continuous quality improvement. Ideas as to how to improve the quality of routine data have been shared among all teams. In all countries, the INSPIRE teams were substantially involved with national adaptations of the 2013 WHO Consolidated ARV guidelines. The 6 teams also hosted a satellite session on design issues and challenges in PMTCT implementation research at the 20th International AIDS conference in Melbourne (July 2014).

INSPIRE IS TIMELY AND HAS ALREADY TAUGHT SEVERAL LESSONS

The early planning for INSPIRE not only coincided with the release of the revised 2010 WHO HIV guidelines for ARVs but also with the recognition that implementation research is critical, if universal coverage is to be achieved and such interventions are to benefit the most hard-to-reach communities. In the same year that DFATD was discussing INSPIRE with WHO, the Journal of Acquired Immune Deficiency Syndromes (JAIDS) started accepting manuscripts on Implementation and Operational Research, as a new focus of interest. Manuscripts that reflected the “translation of knowledge, practices, and technologies into clinical care of adult and pediatric patients with HIV/AIDS, and their evidence-based effectiveness in ‘real-world settings’ … would be … of particular interest.” In the same year, a background article for the first Global Symposium on Health Systems Research in Montreux, Switzerland, highlighted the lack of studies that tested different approaches for scaling up essential maternal and child services, including HIV-related interventions. Funders such as the Global Fund were also demanding more from their investments, and today, there is greater emphasis on the need to learn while implementing.

Although the teams have addressed many challenges specific to their projects and these are discussed in the accompanying articles, some cross-cutting issues are worth highlighting:

- Many implementation and operations research studies report simple observations without attempting more rigorous, comparative designs. All the INSPIRE projects started with randomized study designs—one study had to revert to comparative cohorts because “standard of care” interventions
were introduced by another funding program that prevented randomization. However, INSPIRE does demonstrate that comparative implementation research studies can be ethically designed and implemented, even in primary care and remote settings and, therefore, can offer a higher quality of evidence and program relevance than simple observations.

- All projects are examining interventions to improve retention-in-care of HIV-infected women and their children. Yet, there are no standard definitions of how to measure “retention-in-care.” The teams have, therefore, developed definitions that they will apply in their analyses. They will be able to see how predictive of more simple measures and indicators such as attendance at a single time point these are.
- All INSPIRE projects will use routine health system data to analyze their primary outcome measures. However, project teams have found significant problems with the completeness and accuracy of data found in registers and other clinic records. The teams have been able to raise awareness at local clinics and district health offices about the importance of good records and how they can be used to monitor and improve services. They have also developed a number of systems to improve data recording for study purposes.
- Three of the INSPIRE projects have included significant costing components and will look at the sustainability of interventions as outcome measures. The teams have built these measures into their primary prospective data collection systems, which will increase their reliability and value.
- INSPIRE has invested heavily to develop high-quality implementation research studies led by local investigators. Although the results of studies can be quantified in terms of significance and the ability to generalize about findings, it is difficult to similarly quantify the value of capacity development and local leadership.

**CONCLUSIONS**

DFATD and the WHO urge continued investment so that we can achieve the elimination of new pediatric HIV infections and promote the health and survival of HIV-infected women and HIV-exposed children. Optimizing the value of those investments will be critical, if we are to succeed, and will depend heavily on generating reliable evidence through systematic learning so that we can implement effective scaling-up interventions. INSPIRE is the embodiment of this approach to generate and apply knowledge for the purpose of improving the lives of mothers and children. Although final results and lessons are still pending, the vision behind INSPIRE is already proving to be justified as intermediate results are already emerging.

In the context of “Option B+” (lifelong ART for all HIV-infected pregnant and breastfeeding women) being adopted by more southern African countries, learning how to retain HIV-infected mothers and their children in care becomes more important than ever. The lifesaving clinical and prevention benefits of lifelong ART is contingent on mothers attending health services, adhering to their drug regimens, and remaining in care. INSPIRE is testing a number of innovative interventions in very different settings. The formative work and scale of the studies will inform the relevance of the findings for each national program and indicate how findings about an intervention in one country may apply elsewhere.

Although no single aspect of INSPIRE is unique, the process endeavors to promote and support high-quality, rigorous locally led implementation research that will have a substantial impact on the health and survival of HIV-infected women and their children. In addition, it is our hope that it will also develop a generation of researchers who are able to contribute to national research agendas in the future. It is eagerly anticipated that the total contribution of INSPIRE will be more than the sum of the individual parts.

**REFERENCES**