Building Psychiatric Clinical Research Capacity in Low and Middle Income Countries: the Cuban-Canadian Partnership Project

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ABSTRACT

Clinical trials research is expanding in low and middle income countries. The capacity to conduct this research should be built using local organizations responsible to local authorities and consistent with international standards of practice. Furthermore, enhancing health research capacity can lead to improvements in care and health human resource competency development. This paper describes the creation, and application of a novel psychopharmacologic clinical research development project conducted in partnership between Cuban and Canadian institutions that illustrates these issues in the domain of mental health.

Key words: clinical trials, capacity building; low and middle income countries; training; mental health

Introduction

Neuropsychiatric disorders are common, often chronic illnesses with substantial morbidity, increased rates of mortality and long-term negative economic impacts that make up approximately 14 percent of the global burden of disease. Six of the top ten diseases that result in the most years lived with disability are psychiatric disorders (WHO, 2001; DCPP, 2008; Mathers, 2006).

Effective pharmacologic treatments for these disorders are becoming widely available and new products are being developed and studied in jurisdictions that have the capacity to conduct basic and clinical research. Historically, psychopharmacologic research capacity has been located primarily in high-income countries but more recently both basic and clinical studies are being conducted in low or middle-income countries (Patel, 2007). These activities have the potential to increase availability of pharmaceutical treatments and to enhance economic development through commercialization of pharmaceutical products.

Many jurisdictions previously uninvolved in clinical psychopharmacology research are developing these capabilities and participating in the arena of global pharmaceutical research. It is necessary that these developments adhere to international, national and regional standards, such as the GCP guidelines (CIOMS, 2002; Saldon et. al. 2005; ICDRA, 2004; NCB, 2005). In some locations, the capacity to conduct

psychopharmacologic clinical trials is limited and these jurisdictions may need to utilize external support, advice and assistance in order to develop their capacity to meet international expectations for scientific quality and ethical adherence (Pena-Icart, 2002, Perery, 2009).

Furthermore, the scientific rigour of psychopharmacologic research may be a useful foundation from which to provide up-to-date, evidence-based clinical care. The participation of health providers in clinical research enhances their diagnostic, measurement, outcomes evaluation and ethical care capacities. This then can translate into improved patient care. Canadian research has shown that teaching primary care physicians clinical research methods leads to improved care and better outcomes when compared to usual teaching approaches (Kutcher et. al., 2002). Since a health sector priority for Cuba also included enhancing primary care services, this project was able to address multiple health and economic sector priorities simultaneously: improving clinical research capability; enhancing primary mental health care delivery; and, enhancing economic development through health-sector-related commercialization.

Cuba has identified the development of pharmaceutical research as part of its national health strategy. This included both basic and clinical research (Ministry of Public Health of Cuba, 2004). This was also consistent with the creation of health sector commercialization as part of Cuban economic development.

The Department of Psychiatry at Dalhousie University had developed an extensive psychiatric clinical trials program and has achieved national and international recognition for its work. Ongoing collaboration between the Department, the Faculty of Medicine, and the Provincial Government of Nova Scotia (Canada) resulted in an invitation issued by the Provincial Government to participate in a trade/health mission to Cuba. During this mission, a representative from the Department (SK) made contact with a representative from the National Coordinating Center of Clinical Trials of Cuba (CENCEC) – (MAP) and an agreement to explore the development of a clinical trials training project was signed by Ministers of the Governments of Cuba and Nova Scotia.

As a result the Cuba-Canada collaboration "Psychopharmacological Training and Research Capacity Building in Cuba Project" was developed collaboratively by the Department and CENCEC, funded through a competitive granting process directed by the Canadian International Development Agency (CIDA), administered through the Association of Universities and Colleges of Canada University Partnerships in Cooperation and Development Tier II initiative and implemented. This paper describes the process and activities of that project and how that project demonstrates innovation in clinical research development and the application of clinical research training to enhance clinical care.

Project Progress and Outcomes:

Project directors SK and MAP obtained support for the project from appropriate organizations in Cuba and created a project development and implementation team involving experts from both organizations. An advisory committee consisting of mental health experts in Cuba and Nova Scotia was formed. Clinical trials training materials created by the Canadian group were culturally contextualized by the Cuban partners and the subsequent training program was then delivered by the Canadian team to a selected group of CENCEC employees and Cuban psychiatrists who then became the Cuban training team. The program included intensive training in data collection; psychiatric diagnosis, psychiatric disorders, outcome tool assessments; adverse events monitoring; case report forms; ethical issues in psychiatric research and research consent procedures; good clinical practice (GCP) procedures; and clinical trials monitoring. Knowledge acquisition for the group was evaluated using pre- and post-tests where results demonstrated significant improvements in knowledge in all domains identified above. Upon successful completion of the training program the Cuban team then conducted further training sessions with Cuban health providers, first with the assistance of Canadian team members and then independently. Subsequent to the training, a clinical research trial was designed by the development team for independent application in Cuba.

Laboratory and infrastructure analysis was conducted by the Canadian partners at the preliminary sites chosen to conduct the initial study. As a result of this analysis, two sites (one in Havana and one in Cienfuegos) where deemed to have the necessary capacities needed to support the project and were selected to participate in the study. All of the research staff associated with these sites received the training described above. Primary investigators (PI) at each site were identified and received additional training in clinical research project management and data collection. A study monitoring group consisting of CENCEC employees independent of site investigators was established and trained in the principles and practice of study monitoring.

A study data base was established, study documents were developed (including case report forms) and an analysis plan determined. Additional training on statistical procedures was provided to CENCEC employees responsible for data analysis. Ethical submissions were developed and submitted to the appropriate ethics review boards.

Six Cuban participants became the CENCEC-based training team. In addition to this group, sixty eight other research and mental health professionals in Cuba were trained by the Dalhousie team. The senior psychiatrist involved with the project also underwent a three months clinical upgrading experience in the Dalhousie University Department of Psychiatry, Halifax,

Fourteen learners selected by CENCEC also received additional training in Canada on a variety of topics pertinent to clinical trial research, psychiatric care, data management, statistics and English language. In addition, three Canadian team members each received Spanish language training.

All individuals trained completed pre- and post-testing of pertinent knowledge addressed in the training sessions. Taken as a group, there was a statistically significant increase in knowledge demonstrated by the pre- and post-test score analysis (P<0.001).

Knowledge assessment before and after the delivery of the training program:

Subject	N	Pretest value mean± SD	Posttest value mean± SD	Mean paired difference (IC 95%), p Value.
• Clinical Trials	39	16,4 ± 4,1	20,0 ± 3,4	-3.6 (-4.6; -2.6), p< 0.001
• ICH-GCP	38	17,5 ± 3,5	21,8 ± 2,3	-4.3 (-5.1; -3.4), p< 0.001
• Depression	37	11,7± 2,6	13,5 ± 1,4	-1.9 (-2.6; -1.2), p< 0.001
• Anxiety	37	17,0 ± 5,1	22,3 ± 3,0	-5.3 (-6.7; -4.0), p< 0.001
• Schizophrenia	16	12,1 ± 3,7	15,5 ± 0,8	-3.4 (-5.1; -1.7), p< 0.001

Seven potential research sites were identified by CENCEC. Site infrastructure analysis was conducted on each site by the Dalhousie and CENCEC teams. Of the seven potential sites identified, two met criteria for use. Sites selected were Gustavo Aldereguía Hospital in Cienfuegos and the Guanabacoa Community Mental Health Center in Havana.

The academic clinical trial:

An academic, multi-center, randomized, double blind placebo-controlled clinical trial was performed in the two selected clinical sites by Cuban investigators trained in the program. The purpose was twofold: first, to conduct a scientifically rigorous clinical trial that would advance the treatment of depression in Cuba; second, to demonstrate under conditions of external audit, that the CENCEC partners had established the capability to conduct a psychiatric clinical trial to international standards.

The trial was independently monitored by the Quality Assurance Unit of CENCEC and upon completion was independently evaluated by external, independent experts. An additional independent review of the project was conducted by CIDA. All evaluations were positive and the trial was found to meet international standards in CGP and protocol adherence.

Finally, another independent audit of one of the two sites was conducted by auditors from CECMED (Centro Nacional para el Control Estatal de la Calidad de los Medicamentos), the national regulatory agency in Cuba. This audit did not identify any substantial concerns in the conduct or outputs of the trial.

Post-trial focus groups conducted by the Dalhousie team with study site participants identified a number of clinical care benefits that were extended from the trial experience to clinical care practices used by clinicians who were involved in the trial. These will be described more fully in an upcoming publication and included but were not limited to: improved diagnosis and outcome measurement of depression; improved consent to treatment procedures for patients; improved psycho education about depression for patients, families and the local community; and, improved satisfaction with care from patients, families and providers.

Discussion and Conclusion:

This description of the Psycho-Pharmacological Training and research Capacity project illustrates how capacity to design, develop, deliver and evaluate clinical trials research in psychiatric disorders was developed in a low-middle income country suffering from substantial economic constraints and how the capacity to develop and conduct clinical research was established. Furthermore, it demonstrates how clinical care can be improved in a low income country without substantial infusion of new clinical resources by providing training in clinical research methodology to usual health care providers.

This project was initiated through the activities of a Government-to-Government trade mission pertaining to health sector economic development and brought together institutions from both countries that would otherwise not have had the opportunity to meet and collaborate. The collaboration between Cuban and Canadian partners led to the creation and sustainability of a psychiatric clinical trials capacity in Cuba that can now be used to address pharmaceutical regulatory requirements for psychotropic medications in Cuba and elsewhere. The capacity for Cuba to address its health care needs was enhanced and the potential for improving the care of people suffering from mental disorders in Cuba was increased.

The success of this project may provide a model that can be used by other low to middle income countries to substantially enhance their clinical research capabilities, The application of this methodology to other countries in the Region of the Americas has already begun with CENCEC bringing their newly developed expertise in clinical trials research to Latin America. This approach differs substantially from much clinical research as it is usually conducted in low to middle income countries where large multinational corporations (pharmaceutical companies and contract research organizations) conduct research that results in little sustained clinical research capacity development and clinical research sustainability in the host country. Furthermore, this project has identified that the development and application of clinical research has a positive effect on improving clinical care simply through the type of training made available to health care providers. This approach to health resource development has not been adequately explored as a method of enhancing health care without substantial new investments in education and training.

A number of "lessons learned" from this project should be considered if replication is attempted elsewhere. These include but are not limited to:

1. A comprehensive approach – this must include the development of appropriate ethical guidelines, training and infrastructure.

2. The type of training and research conducted must take into account the capacity of the local laboratory infrastructure; and the local medical system to support the research; the ability of patients to participate, and the cultural context.

3. A collaborative process with clear goals, outcomes and objective, all partners, including the developing country partner must be involved in the process, from conceptualization, to implementation and evaluation.

4. A sustainability and capacity building model – in this case the train the trainers model was embedded in a national organization that has the responsibility for coordinating clinical trials across the country.

5. An independent evaluation framework – the evaluation of the project and of the clinical trials conducted as part of this project were both conducted by experts independent of the involved parties.

6. Appropriate project funding – although not described in the information provided above, it was necessary that funding be flexible enough to allow for the purchase and maintenance of needed equipment as well as for human resource capacity development.

Some of these findings are consistent with research and projects conducted elsewhere, and echo the sentiments of partners in developing countries. A recent series of courses in Genomics and Public Health Policy, conducted by the McLaughlin-Rotman Centre for Global Health, collected a series of recommendations from 232 developing world experts from 58 countries. Some of the highlights of the recommendations included the need to collaborate through regional, international and national networks; the importance of building capacity based on needs assessments and the adaption of successful models used elsewhere; the need to develop local capacity to address ethical, social and cultural issues; enhancing funding available; and, promoting the importance of biotechnology at the political level (Daar et. al., 2007).

We conclude that with the proper project development, operation, funding and oversight, the capacity to conduct clinical trials can be created in low and middle income countries. This capacity can then be used locally to both advance economic development and enhance the care for individuals suffering from mental disorders.

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Stan Kutcher MD is an internationally-renowned expert in the area of adolescent mental health and a national and international leader in mental health research, advocacy, training, policy, and health services innovation. Internationally he has worked with various governments, international organizations and through Canadian government agencies to address a variety of mental health issues. His current interests include translating mental health research into clinical care, patient and parent empowerment, health systems/health policy and optimization of mental health care/mental health clinical research through the training of community based health human resources in primary care. He is the author of more than 200 scientific papers and also author/co-author of a number of medical textbooks, has edited the Child and Adolescent Psychopharmacology News and has been a consultant to various organizations on issues pertaining to mental health treatments and program reviews in children, adolescents and adults alike.

Bianca Horner MD is a lecturer in the Department of Psychiatry at Dalhousie University and family physician. She was part of a team from Dalhousie University that worked with the Centro Nacional Coordinador de Ensayos Clínicos (CENCEC) in Cuba on the Psycho-pharmacological Training and Research Capacity Program, a project that concluded at the end of March 2009. The partners have been working together to develop the capacity of the Cuban partner to conduct clinical trials research through the joint development of a curriculum and training program and other capacity building activities in Halifax and Canada.

Maria Amparo Pascual MD is director and founder of National Coordinating Center for Clinical Trials (CENCEC) and Professor of Medical Science University of Havana. Prior to her current position, she worked at the Cuban Ministry of Public Health and the National Oncology Institute. She is member of the Working Group for GCP at PAHO/WHO since 2000. She is one of the authors of the Cuban GCP ICH-Harmonized Guidelines. Dr. Pascual is the Cuban Coordinator of the Project Psycho-pharmacological Training and Research Capacity in Cuba with Dalhousie University, Canada.

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