

B2. Project Description (not to exceed a total of 5 pages)

- detailed description of research project including objectives, background, literature review, proposed experiments, complete description of applicable methodologies, and a work plan showing individual tasks and responsibility for them
- statement describing the importance of the proposed project
- description of the collaborative arrangements between participating institutions defining general responsibilities and tasks assigned to each participating institution
- description of any planned workshops or symposia with clearly defined goals and expected outcomes
- explanation of why a China-Canada collaboration is necessary to realize the project goals (ie. what are the unique strengths and skills that the Chinese and Canadian collaborators bring to the project).

Excessive use of psychoactive substances is one of the main problems confronting health services in our society because of the numerous problems associated with their use and the subsequent costs involved. In Canada, these costs amount to more than 18.45 billion dollars yearly, approximately 2.7 % of the gross domestic product (Canadian Centre on Substance Abuse, 1997). Excessive drug use has multiple consequences: absenteeism and loss of productivity at work, road accidents, domestic violence and other family problems, spread of infectious diseases such as AIDS or hepatitis, crime, premature mortality, decreased levels of education, and loss of social and professional life. Opiates are among the drugs causing tremendous harm to individuals and to society (Brochu, Da Agra and Cousineau, 2002; Pernanen, Cousineau, Brochu and Sun, 2002). An American study (Tengs and al., 1995) clearly demonstrated that treatment of alcoholism and drug addiction is among the most profitable 500 interventions when considered in terms of years of life saved. They show that economic benefits from the prevention of excessive drug use would be 4 to 12 times the cost of the treatments themselves. It is important, however, that treatment methods be based on convincing data. Although several studies have investigated the relative effectiveness of drug addiction treatments, the factors that are most important in such treatments are still not completely understood due to a lack of empirical studies.

Since the 1960s, a variety of interventions have been aimed at reducing the harm caused by opiates (Dole, 1966). The main treatment intervention in Canada is the Methadone Maintenance Treatment (MMT), currently being provided to some 25,000 illicit opiate users nationwide (Ward, Hall, & Mattick, 1999; Ball & Ross, 1991; Fischer, 2000). Recent meta-analyses have provided quantitative support for the effectiveness of methadone maintenance treatment (Prendergast et al., 2002; Brewer et al., 1998; Marsch, 1998). However, heroin-addicted patients who are treated with the opiate-agonist methadone show less improvement when methadone treatment is not accompanied by psychosocial interventions (McLellan, 1993; Uchtenhagen et al., 1999). In addition, it has also become evident in Canada that MMT is limited in reach and effectiveness for the overall illicit opiate user population, both in encouraging abstinence and reducing harm (Fischer, Chin, Kuo, Kirst, & Vlahov, 2002); at this time, such treatment reaches only a minority of the estimated opiate user population in Canada (Strike et al., 2005).

In addition to MMT, other treatments have been implemented in many countries. In France, in 1999, more than 60,000 individuals were being treated with buprenorphine maintenance, which has proved to be more effective than methadone maintenance as the abstinence syndrome was less frequent, less intense, and of shorter duration (Auriacombe, 2000; Lert, 1998). Fingerhoo *et al.* (2001) found buprenorphine to be superior to clonidine in enabling opiate dependent patients to successfully complete an outpatient detoxification program. They note that 30-70% of their subjects abandoned methadone treatment within the first one or two years in treatment (Koester et al. 1999). A Swiss study has shown the overall effectiveness of the combination of heroin and methadone pharmacotherapy and psychosocial care, and a Dutch trial has provided data on the differential effectiveness of heroin vs. methadone in studies up to 2002 (Fischer et al., 2002). Based on the

effectiveness of previous studies, several countries have started scientific experiments on or have already established as part of their treatment system the prescription of heroin to treatment-resistant opiate addicts (Fischer et al., 2002b; Rehm et al., 2001; van den Brink et al., 2003; Stimson & Metrebian, 2003; EMCDDA, 2004). A clinical trial to explore the benefits of prescription of heroin (Project 'NAOMI') was begun in Canada at the end of 2004. The Canadian author of the present proposal is one of the investigators in NAOMI.

Therapeutic communities constitute one of the most intensive forms of long-term psychologically oriented treatment available to addicts (time in residence usually ranges from 9 to 12 months). Community activities are generally very structured. A "code of regulations" delineates banned behaviors and penalties and a system of privileges allows the participants to earn certain advantages that can be lost if rules are broken. Emphasis is put on community and personal responsibilities, as well as on the transformation of former behaviors and values. Participants with 'seniority' serve as models for newcomers. The group plays an important part in encouraging participation. Positive behavior is supported by the community while negative attitudes lead to confrontations with the group until they are modified. Numerous studies have shown that participation in therapeutic communities leads to benefits such as reduction in cocaine, heroin, and alcohol use, decreased criminal activity, increased job rates, and reduction of depressive symptoms (NIDA, 2002). Several studies suggest a link between the duration of treatment and its success (Dekel, Benbenishty and Amram, 2004; De Leon, 1984; Hubbard and al., 1984, 1989; Kooyman, 1993; Simpson and al., 1997; Simpson and Sells, 1982; Swartz, Lurigio and Slomka, 1996). A large number of studies evaluating community therapy programs showed that they were effective even with a very difficult clientele (prisoners) and in difficult therapeutic settings (detention centers) (Brochu and Schneeberger, 2001). However, very few studies looked at the effect of the program in relation to the client's reason for admittance, persistence in treatment, and progress while in treatment.

Empirical studies have shown that non-compliance and high drop-out rates constitute major problems for treatment programs. Studies in North America note that failure to comply with treatment regimens is one of the greatest obstacles to improving the effectiveness of drug abuse treatment (Landry, Guyon and Brochu, 2001). Often less than 25% of drug addict patients complete their treatment (Laflamme-Cusson and Moisan, 1993; Lewis and Ross, 1994). One exception is Methadone Maintenance Treatment, which generally shows lower attrition rates than all other treatment modalities (except heroin prescription) (Fischer et al., 2005), although even in these programs not every patient completes treatment. It is universally accepted in North America that programs aimed at motivating drug addicts to deal with their addiction are often inadequate. Since the 1960s, many intervention models have been considered. Motivational interviewing and different types of behavioral reinforcement have been used in drug abuse treatment strategies in order to create a therapeutic alliance between the patient and the therapist and improve poor treatment attendance (Anglin and Hser, 1990; Brooner et al. 2004; Kidorf & Stitzer, 1999; Lipton, 1994).

In Canada, it is widely accepted that psychological components constitute the stepping stones of every effective drug treatment. Their relevance is underlined by the fact that personal beliefs are influential determinants of behaviour, effecting motivation and thereby influencing treatment (Crowell and Anderson, 2004). Nonetheless, even those who have total confidence in psychological and behavioural approaches often regret the lack of an effective pharmacologic agent in drug dependence treatment.

In China, the need for drug dependence treatments became increasingly apparent in the 1980s. Current treatments for opiate dependence are largely based on the bio-social approach, including MMT and some interventions derived from traditional Chinese medicine. A few psychological interventions to treat drug dependence have also been used in rehabilitation centers (Fang, 2006).

The MMT was introduced in 2004 in Beijing, Yunnan, Sichuan, Guizhou, Zhejiang, and Guanxi provinces of China. The WHO collaborative study on Substitution Therapy for Opioid Dependence and

HIV/AIDS, sponsored and funded by the World Health Organization, was implemented in 2004 in China. The WHO study is a multi-site process and outcome evaluation of opioid dependence treatment programs and related HIV/AIDS treatment and prevention approaches in Asia and Eastern Europe, including China, Indonesia, Thailand, Lithuania, and Poland. In China, the National Institute on Drug Dependence (NIDD) is the leading institute in this project and has completed the evaluation of 100 subjects in Beijing. A randomized control clinical trial led by NIDD has been set up to examine the Methadone Maintenance Treatment used in conjunction with traditional Chinese medicine. In previous studies, it has been shown that traditional Chinese medicine can decrease withdrawal signs in opiate-addicted patients and thereby aid in recovery from the acute withdrawal symptoms that accompany abstinence after chronic heroin use. There is also evidence that some traditional Chinese medicine is effective in controlling protracted withdrawal symptoms. The administration of methadone in combination with Chinese medicine is also currently being used in China.

The therapeutic effects of a variety of traditional Chinese Medicines could be subtly different because of their various compositions. For instance, some could be more effective in controlling rhinorrhea, lacrymation and sweating; some would prove to be more effective in relieving pain, while others could be more effective in controlling nausea and vomiting or treating insomnia problems, all of these different aspects being related to opiate detoxification (Cui et al., 2004; Huang et al., 2001, Li, Li and Wu, 2005, Liu et al., 2001; Wu et al., 2004; Xu et al., 2003). Currently, the State Food and Drug Administration of China have issued approval for 10 Chinese medicine treatments to be added to clinical practice for acute opiate detoxification (Liang et al, 2003; Li S.C. et al, 2005; Li L. J. et al, 2003). The efficacy of Chinese medicine in controlling opiate withdrawal symptoms can either be summarized as: 1) less effective than narcotic detoxification agents, 2) similarly or even more effective than non-narcotic detoxification agents (e.g. clonidine, lofexidine hydrochloride), 3) moderately effective but limited in that it has limitations when treating patients with severe drug addiction. (Li Z.H. et al. 2005; Wang et al., 2003).

Auricular acupuncture has become one of the most widely used alternative treatments for cocaine and heroin addicts. Acupuncture has been used in China for more than 2500 years and is used to treat a variety of pathologies. Supporters of acupuncture postulate the existence of meridians that are connected with specific physical parts. Stimulation of a precise point provides therapy to the organ with which it is connected. Acupuncture can be used during all three stages of treatment of addiction: detoxification, rehabilitation, and relapse prevention (Margolin et al., 1999, 2002; Wells, 1995). A study by Moner (1996) revealed that the use of acupuncture with addicts helped reduce the psychological symptoms caused by abstinence. However in North America this form of treatment has a high drop-out rate and is less effective when used alone. Moner concludes that the addition of a psychotherapeutic aspect to treatment might increase the rate of success.

When major programs for drug addiction in China and Canada are compared, it is clear that Canada has emphasized the psychological model while China has focused on the biological model. This can be explained by the greater development of psychology in Canada, reflected in the number of active psychology institutions across the country. In China, the importance of traditional Chinese medicine, illustrated by the presence of more than fifty university programs on various areas, can be linked to the dominance of the biological model in treatment. Using these two approaches, an integrative bio-psycho-social intervention concept, in which a Chinese socio-biological model and a Canadian socio-psychological model are integrated, will allow us to provide evidence-based recommendations for the most effective opioid dependence treatment programs. Such a comparative study provides a unique opportunity to understand why some treatments are effective, thus allowing both evaluation and integration of the models under consideration.

Benefits and Scope of the Project

The study will be undertaken at study sites in both countries. Determining the complementary aspects of the two different approaches to treating opioid addiction will allow us to evaluate the

benefits of various aspects of both theory and practice in order to provide a more effective intervention model. Such a model should be able to take into consideration differences between clients, whether social, cultural, or geographic.

Goals

- 1) to collect, review, and analyze experiences and data from sites in the two countries in which opioid treatment programs have been implemented and to compare the Canadian socio-psychological approach to intervention with the Chinese socio-biological approach;
- 2) to document similarities and differences, with relation to both individual improvement and community impact, of the approaches used in Canada and in China and to analyze the reasons for these similarities and differences;
- 3) to develop and disseminate, on the basis of this study's findings, recommendations for the best practices to be used in future treatment of opioid addiction.

Specific Objectives and Methods

Objective 1: To collect, review, and analyze experiences and data from sites in the two countries in which opioid dependence treatment programs have been implemented and to compare the Canadian psycho-social approach to intervention with the Chinese bio-social approach

Rationale: To provide a concise, unbiased, and systematic analysis regarding the effectiveness of addiction treatment programs in the two countries, some meta-analysis appears necessary.

Methods: Our project will do critical reviews and meta-analysis of the impact data on opioid treatment found in the scientific and 'grey' literature of the two countries from the 1990s to the present. Studies to be included in the review, and in the meta-analysis, will be selected through a systematic consultation of the PubMed, Medline, Current Contents, and PsycInfo databases in Canada and CNKI, CALIS and Wanfang databases in China and via Peking University TELNET, Chinese University of Hongkong TELNET, and National Taiwan University TELNET for Chinese literature using related key words such as 'opioid dependence', 'heroin dependence', 'methadone maintenance', 'heroin prescription', 'buprenorphine maintenance', 'therapeutic community', 'acupuncture', 'treatment impact', and 'treatment effectiveness' in English and in Chinese. Reference lists of all relevant studies will be scrutinized in order to find additional references. Researchers specialized in the field or having published studies on the impact of opioid dependence treatment in the last five years will be contacted by letter or e-mail in order to get their last publications. Work in English, French, and Chinese will be considered. Data entry and statistical analysis will be performed with the use of common software for meta-analysis such as Review Manager software (RevMan 4.2, Cochrane Collaboration, Oxford, United Kingdom) or Comprehensive Meta-Analysis software package (Borenstein and Borenstein, 1999) in the two countries (Rosenthal, 1984; Hunter & Schmidt, 1990).

Objective 2: To document similarities and differences, with relation to both individual improvement and community impact, of the approaches used in Canada and in China and to analyze the reasons for these similarities and differences.

Rationale: Once we have determined which approaches effect opioid dependence, we will attempt to understand the nature of the effect and why it occurs.

Methods: To do this, a second review of the literature will be necessary to identify those works which best describe approaches that have been found successful. Once these have been identified, focus groups will be conducted in China and in Canada with experienced professionals in order to understand why these approaches are effective for the treatment of opioid dependency. A combined report of our findings will be written in China and in Canada and translated into English and Chinese. Finally, the most effective aspects of addiction treatment will be compared and a common report (China-Canada) will be written regarding the components of the most successful approaches. (In China, an innovative empirical study will be done on persistence rate of client in treatment comparing classical MMT approach to MMT enhanced with motivational interviewing component. This study will be done using separate budget see annex)

Objective 3: On the basis of the study findings, to develop and disseminate recommendations for methods to be used in future treatment of opioid addiction.

Rationale: Besides determining and assessing treatment approaches, it is an essential part of this project that the findings be translated into recommendations for future implementation of treatment programs. Given this, it is imperative that our findings and recommendations be effectively disseminated among those concerned with creating the relevant policies and programs as well as to professional audiences.

Methods: Once all of the project's data is collected and available, we propose to convene a two-day workshop in both countries at which our preliminary data and findings will be presented and discussed. The experts to be included in the work group will be selected in consultation with the national administration of treatment in China and the Canadian Center of Substance Abuse (CCSA) in Canada. Following the workshop, participants will spend five days visiting various sites in order to observe the clinical practices that our meta-analysis has identified as the most effective. Five experts from Canada will go to China for the workshop and the site observations and then, working with the project investigators, will formulate a core set of 'evidence-based' recommendations. The following month, five experts from China, plus the project investigators, will come to Canada and do the same. These two sets of recommendations will then be combined and included in a draft study report that will be sent to every participant for comments. A final report will then be written.

Applicant Institution and Investigators

In Canada, the principal applicant institution for this project is Research and Intervention on Substance Abuse – Quebec (RISQ), University of Montreal, Canada. The RISQ is a leader in basic, clinical, and social research related to addictions and is actively engaged in policy making at all levels of government. It is explicitly committed to 'harm reduction' principles. The International Center for Comparative Criminology of the University of Montreal will administer the project funds for the investigators in the study. Professor Serge Brochu, the co-director of RISQ, will administer and supervise this project. Dr. Fu Sun will serve as researcher on the project.

In China, the principal applicant institution is the National Institute on Drug Dependence (NIDD), the largest national centre on drug abuse, affiliated with Peking University. NIDD is a national institute engaging in basic, clinical, and social research on drug dependence in China, providing first-hand data for the policy making regarding national drug control, prevention, and treatment. Professor Lin Lu, the director of NIDD, will administer and supervise this project. Dr. Jie Shi will serve as researcher in this study.

The proposed study will be led and conducted by two co-principal investigators, each responsible for their local study site: Dr. Serge Brochu (Montreal) and Dr. Lin Lu. Dr. Brochu is scientific director of RISQ and professor of Criminology and Psychology at the University de Montreal, and former director of the Centre for Comparative Criminology; Both Dr. Brochu and Dr. Lu list the area of drug use as one of their main areas of research interest and expertise and are internationally known for their work in this area.

Collaborative arrangements between participating institutions

The two principal investigators (Brochu and Lu) will engage in close and effective collaboration and communication. Research data and information will be exchanged consistently within the study teams for data comparison purposes.

Knowledge Transfer and Dissemination

In addition to the focus groups and workshop to be organized in the two countries in collaboration with national treatment organizations as part of the project itself, the investigators will develop an international systematic dissemination plan for the research report and recommendations from the study. Furthermore, results will be disseminated via academic publications and peer-reviewed conference presentations.