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Study to Assess Long-term Opioid Maintenance Effectiveness

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**What is the SALOME clinical trial?**

A1. The Study to Assess Longer-term Opioid Medication Effectiveness is a clinical trial that will test whether diacetylmorphine, the active ingredient of heroin, is as good as hydromorphone (Dilaudid®), a licensed medication, in benefiting people suffering from chronic opioid addiction who are not benefiting sufficiently from other treatments. Also, this study will test if those effectively treated with these 2 injectable medications can be successfully switched and retained to the oral formulations of the medications.

**What is the NAOMI clinical trial?**

The North American Opiate Medication Initiative (NAOMI) was a randomized trial aimed at testing whether medically prescribed diacetylmorphine, the active ingredient in heroin, was more efficient than methadone therapy for individuals with chronic opioid dependence who were not benefiting from other conventional treatments. The results show that patients treated with injectable diacetylmorphine were more likely to stay in treatment and more likely to reduce their use of illegal drugs and other illegal activities than patients treated with oral methadone.

**If the NAOMI trial was a success, why the treatment did not continue?**

The NAOMI investigators requested permission to prescribe diacetylmorphine under compassionate use through Health Canada's Special Access Program. However, the requests were denied. Also, the funding for both clinics (Vancouver and Montreal) was part of a CIHR grant that ended with the study period. Canada is the only country where diacetylmorphine has been tested for addiction treatment and has been denied compassionate use.

**How are SALOME and NAOMI trials related?**

In the NAOMI study, a small group of patients received hydromorphone (Dilaudid®) instead of diacetylmorphine in a double-blind basis (nor the patients or staff knew which drug they were receiving), for the purpose of validation of self-reported use of street heroin in urine toxicological tests. An unexpected finding was that injection patients could not accurately discriminate whether they were receiving diacetylmorphine or hydromorphone. We also observed similar results and benefits with

both these drugs although the small number of participants receiving hydromorphone does not permit us to draw any definite and scientifically valid conclusions as to the efficacy of hydromorphone as a treatment option. Should hydromorphone be proven to be as good as diacetylmorphine, the benefits of this form of injectable treatment may be achievable without the emotional and regulatory barriers often presented by heroin maintenance. Therefore, the NAOMI investigators designed a study to test this hypothesis, as a next step of the NAOMI study.

**Why is this study being funded?**

SALOME addresses critical social and ethical concerns dealing with addiction. Opioid-dependent people are in need of treatment options to avoid marginalization from the health care system. This study aims to answer questions that could lead to improvements in the health of persons with chronic addictions and identify new ways of reintegrating this population into society.

**When and where is this trial being conducted?**

The trial is expected to begin in the fall of 2009 in Vancouver and Montreal. These cities have the largest heroin-dependent populations in Canada.

**What are the benefits of this project to Canadians and the drug dependent population?**

Opioid addiction, mostly manifested as heroin addiction, creates tremendous social and health costs. These include crime, diseases such as HIV and Hepatitis C and unemployment. The leaders of the trial believe that prescribed diacetylmorphine and hydromorphone could save Canadians an enormous amount of money and untold suffering. Similar studies conducted in Europe and Canada among people with chronic addictions have reported improved health status, decreased use of illicit drugs, significant reductions in criminal activity and increased employment.

**Why is CIHR investing $1 million to help persons with opioid addiction when there are Canadians waiting in line-ups for cancer treatments?**

CIHR is supporting this research project because it is the major federal agency responsible for funding health research in Canada. Its mandate is to improve the health of Canadians, including vulnerable populations. It is an excellent example of CIHR's investment in solving the health challenges of those in need and it reflects CIHR's goal of broadening our horizon of scientific knowledge and transferring that knowledge to improved health for all Canadians. CIHR believes this research project will provide valuable information for the treatment of heroin addiction.

The SALOME protocol was reviewed by a peer review by independent researchers who score and select protocols based on the pertinence of the research and the scientific quality of the protocol. The SALOME protocol received excellent scores and was also reviewed and approved by the Ethics Committees of the participating institutions

**How many persons with heroin addiction are there in Canada? Will this project involve all of them?**

There are some 60,000 to 90,000 persons affected by opiate addiction in Canada. This study will enrol the most chronically drug-dependent members of this population in Vancouver and Montreal—those who are not benefiting from other treatments, such as methadone therapy and abstinence-based programs, and continue injecting street heroin.

**How much does addiction cost to Canadian society?**

Addiction costs Canadian taxpayers hundreds of millions of dollars per year. Illicit drug use costs approximately 8.2 billion dollars. A recent “cost of illness” analysis estimated over $45,000 per year in societal costs per person who has an addiction.

**Could prescribed diacetylmorphine and hydromorphone therapy reduce these costs?**

The NAOMI study with diacetylmorphine, as well as the European trials, reported improved health status, decreased use of illicit drugs, lower criminal activity and increased employment among individuals under diacetylmorphine maintenance treatment. These same studies showed that, overall, prescribed diacetylmorphine treatment saved much more money than it costs.

**How will the SALOME trial ensure that only those who need it (severely affected, long-term opioid users) will participate?**

Stringent controls have been placed on the screening of participants to ensure that only those who fall within the “chronic” category are selected. The SALOME study has defined "chronic" as persons with a history of at least five years of documented drug addiction. As well, participants must have been using heroin frequently for at least one year immediately prior to entry into the study.

**Where will the heroin come from and where will it be kept in a safe location throughout the study?**

It is pharmaceutical-grade heroin manufactured by a pharmaceutical company outside Canada. It will be purchased and imported with permission of the Government of Canada. It will be kept in a safe location.

**Is it legal to provide heroin to persons with an addiction?**

There is a legal mechanism in Canada for making heroin available for federally approved scientific studies.

**What safety measures are in place to ensure the heroin is not stolen?**

There are clear safety procedures incorporated into the study to ensure protection of staff, participants and the general public. The heroin will be dispensed to individuals and must be used under the observation of trained health care professionals in the high-security medical clinics developed for the trial. Strict security provisions will prevent the theft of the drug or removal of any of the drug from the medical clinics.

**How is the trial addressing the concerns of the Canadian public about the study?**

In the last years, during NAOMI, Advisory Boards have been established in Vancouver and Montreal, the cities participating in the trial. The same steps were taken for SALOME. The Advisory Boards meet regularly and include representatives from provincial medical colleges, government, law enforcement, community groups, addiction medicine, and the opioid-dependent population.

SALOME has also invited representatives of the business and residential neighbours of the Vancouver site to participate in its Neighbourhood Advisory Committee. In Montreal, these representatives are already members of the Advisory Committee

**Does SALOME aim to promote legalization of heroin?**

The NAOMI study showed that medically prescribed diacetylmorphine is effective in the treatment of long-term, chronic opioid users with severe health and psychosocial problems associated to the drug use. The next step would be to license diacetylmorphine for addiction treatment. License it is not legalization. Licence will allow the use of diacetylmorphine, under restricted conditions, for the treatment of this severely affected population. The SALOME clinical trial seeks rigorous scientific evidence as to the usefulness of hydromorphone in the treatment of a limited number of people with chronic addictions for whom there are currently no effective treatments in Canada.

**By giving heroin to people, won't you create more people who will have a heroin addiction?**

The participants in the study already have had a dependence to heroin for many years and are not benefiting sufficiently from other forms of treatment such as methadone therapy and abstinence programs. The study is intended to find alternative treatment methods that might benefit people who have serious chronic opioid dependence and drug related problems and comorbidities (for example, mental problems, HIV).

**How can public funds be used for the purchase of heroin to be given away to people who have a heroin addiction?**

Health Canada has recognized the high social and health costs associated with untreated opioid addiction. CIHR has endorsed, in principle, research that will help expand the evidence base and the range of available treatments, prevention and harm reduction models.

**Wouldn't it be better to spend money on preventing people from using heroin in the first place?**

The federal government is funding a range of studies on the prevention of addiction that includes developing innovative prevention and educational programs, in particular for youth. The participants in the SALOME clinical trial will, however, be people who have already developed an addiction to heroin and aren't benefiting from other forms of treatment.

Prevention is key and has been proven to reduce the number of youngsters initiating in drug use. However, preventive measures are not always successful, especially among the most vulnerable populations. This means there will be always a group, the most vulnerable, that will engage in drug use and will suffer marginalization and serious health consequences. The health and social care system needs to be prepared to offer assistance to the most vulnerable groups.

**Is the intent for people who receive injection therapy and benefit from it to remain on government supplied heroin for the rest of their lives?**

Opioid addiction is a chronic relapsing disease. As any other chronic condition, treatment is needed for life. The relapsing nature of this condition means people go through different stages in their drug dependence along their life: abstinence, recovery, substitution treatment, etc. The stage and its length strongly depend on their individual circumstances, the social context and the available services in the community. Data from long-term studies with diacetylmorphine in Europe shows some patients remain on this treatment for years, but also many of them transition from injection to oral substitution and also to abstinence. They also suggest that providing people with prescription heroin in a controlled and supervised manner removes the need for them to commit crimes to obtain their drugs. It also introduces participants to an environment where they can get vital support: counselling, the help of social workers and housing officers, employment training and so on. This has allowed many opioid-dependent Europeans to live more productive lives and lessen the social and health costs associated with addiction.

The intent of the SALOME project is to determine whether some participants become healthier and reduce their illicit drug use or are able to switch to other forms of treatment. SALOME also intends to test if after stabilizing patients on injectable medications they can transition to oral formulations, without loosing effectiveness.

**How will the SALOME project be conducted?**

The project will be conducted in five phases: Recruitment, Screening, Study Period, Transition Period and Research follow-up.

**Phase 1: Recruitment**

Potential volunteer participants will be recruited in Vancouver and Montreal from service agencies, volunteer lists, needle exchange programs and other sources.

**Phase 2: Screening**

Participants will undergo a screening process to determine if they match the research team's definition of suffering a "chronic, long-term" opioid addiction. Their past treatment and drug dependence will be documented and they will be required to give informed consent for their participation. This phase is expected to take three weeks.

**Phase 3: Treatment Period**

SALOME involves two-stages, six months each. In Stage I half of the 322 participants will be randomized to receive injectable diacetylmorphine, and the other half will receive injectable hydromorphone. Study medications will be provided on a double-blind basis with only study pharmacists aware of the treatment received. In Stage II all volunteers retained in injection treatment at the end of Stage I will be eligible to enter Stage II. Half the participants will then be randomized to continue injection treatment exactly as in Stage I while the other half will switch to the oral equivalent of the same medication (diacetylmorphine or hydromorphone). The oral formulations will also be provided on a double-blind basis.

Treatment session: After a 5 minutes assessment (for safety), participants will receive their medication. After injection or ingestion of the medications, participants will be observed for 15 minutes until attending medical personnel determine that it is safe for them to leave. The administration of prescriptions will be overseen for both groups by addiction medicine specialists.

Throughout the treatment period, social workers will be assigned to both groups to assist them with reaching other addiction services and community resources such as housing and job training services.

At any time, participants may choose to switch to methadone treatment, to drug-free programs, to detox programs or any other option available.

**Phase 4: Transition Period**

In this three-month phase, participants are transitioned to other programs, such as methadone therapy, drug-free programs, or detox programs.

**Phase 5: Research Follow-Up**

During the treatment period, the research team will also see each participant regularly at a separate research clinic. Volunteers will fill in questionnaires about their status (Addiction Severity Index, use of illicit drugs during the study period, criminal activity, health status), to provide data for a more accurate picture of the daily lives of people with addiction.

The research team will track them for their outcomes, independent of the treatment program, throughout their treatment and for six months after the transition period.

To avoid biases in the study, participants will be monitored by the research team even if they choose to leave treatment.

**Won't the SALOME study add to public nuisance problems in the cities where it is conducted?**

There were neither security problems nor any evidence whatsoever of neighbourhood disruption in either city during the NAOMI trial. There was a dedicated line for complaints in regards to disruptions caused by study clinic, and it never received a single call. An independent study (NAOMI-Impact) also indicated there were no problems encountered in the neighbourhoods where the NAOMI clinics were situated

Experience from other countries also indicates that this is not a major concern. For example, in Switzerland the heroin program was supported by majorities as high as over 70 per cent in three national referenda.

**How is this project different from a supervised injection site?**

SALOME is a rigorously controlled, scientific study that offers treatment to opioid dependent people, testing innovative options. Physicians who specialize in addictions management will supervise participants and record data. Participants will receive pharmacological (prescribed diacetylmorphine, hydromorphone, concomitant medications), medical, as well as psychosocial treatment, in order to stabilize them and reduce the harm associated to their drug dependence.

The Vancouver supervised injection site, Insite, is a clean, safe environment where users can inject their own drugs under the supervision of clinical staff. Vancouver Coastal Health operates Insite under a constitutional exception to the Controlled Drugs and Substances Act and provides on-site clinical expertise. VCH has partnered with the BC Centre for Excellence in HIV/AIDS to evaluate Insite over the term of the pilot project to evaluate its impact on public health outcomes in terms of, for example, the transmission of blood borne infections.

Many NAOMI participants were and are users of the Vancouver supervised injection site. We expect also the same for SALOME.

**Who is the SALOME research team?**

The study will be headed by Dr. Michael Krausz and Dr. Eugenia Oviedo-Joekes. The other principal investigators include Dr. Martin T. Schechter, Dr. David C. Marsh, Dr. Aslam H. Anis, Bohdan Nosyk and Dr. Christian Schultz of the University of British Columbia; and Dr. Suzanne Brissette and Dr. Julie Bruneau of the Service de médecine des toxicomanies du Centre Hospitalier de l'Université de Montréal .

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