

Why we object to NAOMI

Heroin maintenance in Canada

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Heroin maintenance is a controversial treatment for addicts who have not had success with methadone treatment. A Swiss cohort study¹ and a controlled trial in the Netherlands² demonstrated that heroin injection programs improved health and social outcomes. The North American Opiate Medication Initiative (NAOMI) will attempt to replicate these findings in Canada.

Similar in design to the Dutch trial,² NAOMI will recruit 470 heroin addicts in Vancouver, BC; Montreal, Que; and Toronto, Ont. The control group will receive methadone; the intervention group will receive methadone and medically prescribed heroin, injected under supervision 2 to 3 times daily for 1 year. The heroin doses will then be tapered, and participants will be offered standard treatment; both groups will be followed up for an additional year.

Investigators making the case for NAOMI point out that heroin addiction is associated with high morbidity, mortality, and social and health costs. Only 15% to 20% of the estimated 60 000 to 90 000 opioid addicts in Canada are currently in treatment,³ and methadone has a treatment-retention rate of only 60%. For those who have failed a trial of methadone, heroin maintenance is preferable to the criminal activities required to purchase street heroin.

Untreated heroin addiction is a serious public health problem. We believe, however, that NAOMI, as currently designed, fails on public health and scientific grounds and might divert resources and attention away from more cost-effective treatments.

We have 5 objections to NAOMI. First is the cost and the effects on the lives of patients in recovery. Heroin maintenance is estimated to cost \$22 000 per patient yearly, compared with \$5000 to \$6000 for community-based methadone treatment.⁴ Specially constructed injection rooms are required, and nurses and security guards must be on site at all times. Pharmaceutical heroin must be imported from Europe and transported by armed guard. Because the effects of heroin last only 4 to 6 hours, patients must visit the injection site 2 or 3 times daily, making it difficult for them to engage in productive activity. Heroin maintenance likely will be limited to specialized treatment centres in Canada's largest cities, tying patients to specific locations.

We are also concerned about patient safety. Subjects will inject heroin at a dose that might be higher than their street-heroin dose in combination with methadone (itself a potent opioid with a high risk of overdose). In one

study,⁵ almost half the patients experienced respiratory depression, greatly reduced oxygen saturation, and paroxysmal electroencephalogram patterns after receiving their usual heroin maintenance dose.⁵⁻⁷ Previous studies found no excess mortality or hospitalization due to overdose, but these studies were small and short-term. While NAOMI has protocols to treat overdose on site, it is also important to detect, monitor, and prevent off-site hypoxia, which could have long-term neurologic consequences. Autopsy shows evidence that heroin users have hypoxic and ischemic brain damage,⁸ and neuropsychologic testing shows evidence of cognitive impairment.⁹ Heroin in combination with methadone requires the same vigilance as any other new and potent medication.

We are also concerned that NAOMI is not justified from a public health perspective. Although expensive and potentially unsafe, heroin maintenance might be justified if large numbers of opioid addicts failed methadone treatment and heroin maintenance were their only option. Yet, despite its extremely loose eligibility criteria, NAOMI has recruited only 85 participants in the past year,¹⁰ and the Toronto site closed because of difficulty recruiting subjects in the pilot phase.

The investigators appear to have greatly overestimated the size of their study population and the public health need for this trial. The evidence strongly suggests that treatment access, not treatment resistance, is the main barrier to methadone treatment. Many, perhaps most, of the illicit opioid users in Canada are injecting prescription opioids¹¹ and would not be eligible for heroin maintenance. Some provinces have a very limited number of methadone providers, and many cities do not have any physicians who prescribe methadone. Buprenorphine, an effective alternative to methadone, is not even available in Canada. In France, where buprenorphine has been available for 10 years, 50% of heroin users are in treatment.¹²

Fourth, NAOMI is similar in design to the Dutch trial.² Heroin users were eligible for the Dutch trial if they continued to use heroin while using 60 mg of methadone for several weeks.¹³ This dose is barely within the therapeutic range of 50 to 120 mg, and many patients require months of counseling and dosage titration before they discontinue their drug use. The initiative could end up targeting patients who have received inadequate methadone treatment, rather than those who are truly resistant to treatment.

Several effective strategies have been developed to improve treatment retention in methadone programs, including behavioural interventions with drop-outs,¹⁴ optimal methadone dosing,¹⁵⁻¹⁷ provision of counseling and social services,¹⁸ flexible clinic policies,¹⁹ and buprenorphine or other oral opioids (such as morphine or hydromorphone) for patients who cannot tolerate methadone. Heroin maintenance is the least cost-effective, safe, or practical of the various approaches to improving treatment retention. Further, recent analyses suggest that retention rates for methadone programs are higher than 60%,²⁰ and drop-outs often re-enter methadone treatment.^{17,21}

Finally, NAOMI, as currently designed, is a poor test of its primary hypothesis. The intervention group in the Dutch trial² received a very high mean daily opioid dose (65 mg of methadone and 500 mg of intravenous heroin) while the control group continued to receive a suboptimal methadone dose (75 mg). This design bias seriously weakens the validity of the trial and the various secondary analyses that have arisen from it.^{4,22} The standard of care for methadone programs in Ontario is to increase doses gradually until patients stop using heroin.²³ The mean daily dose of the methadone program at the Centre for Addiction and Mental Health is 92 mg.²⁴ Patients who continue to use heroin are typically using doses well above 100 mg. To avoid this bias, NAOMI should employ explicit evidence-based methadone-dosing protocols. The methadone-only group should have a separate team of physicians with experience providing methadone treatment and therapists who are committed to helping patients achieve abstinence.

Funded for \$8 million by the Canadian Institutes of Health Research, NAOMI is one of the most expensive controlled trials ever conducted in Canada. In contrast, the Australian National Evaluation of Pharmacotherapies for Opioid Dependence, funded for \$7 million, has conducted 13 clinical trials involving more than 1400 subjects, including several randomized controlled trials on opioid-agonist therapy.²⁵ Already, NAOMI has attracted enormous media attention and calls for permanent heroin maintenance programs. We have asked NAOMI investigators, funding bodies, and ethics committees to review the study protocol in light of our scientific and safety concerns, which were not fully recognized when NAOMI underwent scientific and ethical review in 1999. We are concerned that NAOMI's limitations will be ignored and the implementation of heroin maintenance programs will sidetrack evidence-based treatment initiatives.

Canada is one of the few countries in the world where most opiate addicts receive treatment from community-based family physicians. Yet physicians are offered limited training and many family physicians work in isolation with little support. Meanwhile, prescription opioid use, misuse, and addiction are growing in Canada. We urge clinicians, researchers, and policy-makers to keep heroin maintenance in perspective and to focus on the most urgent priorities: greater access to methadone and

buprenorphine treatment for all regions in Canada, comprehensive physician training, access to therapists and essential social services, appropriate incentives for physicians to work with addicted patients, and greater integration of addiction treatment with the health care system. ❖

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