

# Characteristics and Response to Treatment among Aboriginal People Receiving Heroin-assisted Treatment

Eugenia Oviedo-Joekes, PhD,<sup>1,2</sup> Daphne Guh, MSc,<sup>2</sup> David C. Marsh, MD,<sup>1-5</sup> Suzanne Brissette, MD,<sup>6</sup> Bohdan Nosyk, PhD,<sup>2</sup> Michael Krausz, PhD,<sup>2,3</sup> Aslam Anis, PhD,<sup>1,2</sup> Wayne M. Christian,<sup>7</sup> Patricia Spittal, PhD,<sup>1,2</sup> Martin T. Schechter, PhD<sup>1,2</sup>

## ABSTRACT

**Background:** Medically prescribed diacetylmorphine, the active ingredient of heroin, has been shown to be effective for the treatment of severe opioid addiction. However, there are no data regarding its effectiveness among Aboriginal heroin injectors.

**Methods:** The present analyses were performed using data from the NAOMI study (North American Opiate Maintenance Initiative), an open-label randomized controlled trial that compared the effectiveness of injectable diacetylmorphine (45.8%) and hydromorphone (10%) vs. oral methadone (44.2%) among long-term treatment-refractory opioid-dependent individuals. Rates of retention and response to treatment were analyzed among participants from the Vancouver site (n=192).

**Results:** Baseline profiles were similar among Aboriginal (n=60) and non-Aboriginal (n=132) participants except for higher HIV positive rates among Aboriginal people (23.3% vs. 8.3%). Among Aboriginal participants in the injection and methadone groups, retention rates at 12 months were 84.4% vs. 57.1% and response rates were 68.8% vs. 53.4%, respectively. Aboriginal and non-Aboriginal rates were not significantly different.

**Discussion:** Offering treatment assisted with medically prescribed diacetylmorphine or hydromorphone to long-term treatment-refractory opioid-dependent Aboriginal people could be an effective way to attract them into and retain them in treatment as well as dramatically reduce the risk of HIV infection.

**Key words:** Aboriginal, Canada; opioid-dependence; substitution treatment; diacetylmorphine, injectable; hydromorphone, injectable; methadone, oral

La traduction du résumé se trouve à la fin de l'article.

*Can J Public Health* 2010;101(3):210-12.

Opioid dependence, particularly with regard to heroin, is a chronic relapsing disease associated with elevated risks of morbidity and mortality when untreated.<sup>1-3</sup> Based on the current evidence, substitution treatment with opioid agonists – mainly methadone – is the most effective approach for attracting and retaining patients in treatment, but a subset of patients do not benefit. In Europe<sup>4,7</sup> and Canada,<sup>8</sup> medically prescribed diacetylmorphine, the active ingredient of heroin, has been shown to be an effective alternative for this subgroup of the most severely affected long-term opioid users.

There is a paucity of evidence in Canada examining the effectiveness of substitution treatment for Aboriginal people who are opioid-dependent. This is particularly concerning because of the extent to which Aboriginal people are over-represented among injection drug using populations<sup>9</sup> as well as their reported lower access to substitution treatment compared to non-Aboriginal people.<sup>10</sup> For example in Vancouver, 26.6% of the people attending the supervised injection facility self-identify as being an Aboriginal person (Métis, First Nations, Inuit, Status or non-Status Indian).<sup>10</sup> In the same cohort, 4.7% of Aboriginal participants reported the use of methadone compared to 12.9% of non-Aboriginal (the difference was statistically significant).

In a randomized clinical trial,<sup>8</sup> we compared the effectiveness of injectable diacetylmorphine or hydromorphone with optimized methadone maintenance treatment (MMT) in the treatment of long-term opioid-dependent individuals. In the present analysis,

we examine the response to heroin-assisted treatment (HAT) among Aboriginal people. To our knowledge, this is the first such analysis.

## METHODS

Data from an open-label randomized controlled trial conducted between March 2005 and July 2008 in Vancouver and Montreal,

### Author Affiliations

1. School of Population and Public Health, University of British Columbia, Vancouver, BC
2. Centre for Health Evaluation & Outcome Sciences, Providence Health Care, Vancouver, BC
3. Department of Psychiatry, University of British Columbia, Vancouver, BC
4. Vancouver Coastal Health & Providence Health Care, Vancouver, BC
5. Centre for Addiction Research BC, University of Victoria, Victoria, BC
6. Centre Hospitalier de l'Université de Montréal, Montréal, QC
7. Chief, Splots'in/Secwepemc Nation, Enderby, BC

**Correspondence:** Eugenia Oviedo-Joekes, St. Paul's Hospital, 620-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Tel: 604-682-2344, ext. 62973, Fax: 604-806-8210, E-mail: eugenia@mail.cheos.ubc.ca

**Acknowledgements:** The NAOMI trial was funded through an operating grant from the Canadian Institutes of Health Research with additional support from the Canada Foundation for Innovation, the Canada Research Chairs Program, the University of British Columbia, Providence Health Care, the University of Montreal, Centre de Recherche et Aide aux Narcomanes, the Government of Quebec, Vancouver Coastal Health Authority and the BC Centre for Disease Control. The authors acknowledge the dedication of N. Laliberté, C. Gartry, K. Sayers, P-A Guevremont, P. Schneeberger, J. Chettiar, K. Lock, J. Lawlor, P. Pelletier, S. Maynard, M-I. Turgeon, G. Brunelle, A. Chan, S. MacDonald, T. Corneil, J. Geller, S. Jutha, S. Chai, M. Piacsezna, S. Sizto, the many remaining staff and members of the DSMB (A. Marlatt, N. El-Guebaly, J. Raboud, D. Roy). The authors also recognize the many US and Canadian (J. Rehm, B. Fischer) scientists who contributed to the early design discussions but ultimately were unable to participate in the trial. Most importantly, the authors acknowledge and thank the NAOMI trial participants.

**Funding:** The study is funded by the Canadian Institutes of Health Research (CIHR).

**Conflict of Interest:** None to declare.

**Table 1.** Aboriginal and Non-Aboriginal Participants' Profile Comparisons at Baseline

	Aboriginal (n=60)	Non-Aboriginal (n=132)	p-value
<b>Socio-demographic</b>			
Age – years	41.38±8.30	40.70±8.13	0.598
Male – n (%)	31 (51.7)	87 (65.9)	0.060
School education – years	10.33±1.81	10.74±2.17	0.175
Precarious housing – n (%)	49 (81.7)	121 (91.7)	0.044
Sexually or physically abused in life – n (%)	26 (43.3)	61 (46.2)	0.710
Money from illegal activities prior month – n (%)	47 (78.3)	94 (71.2)	0.300
<b>Health</b>			
Overdoses in the past	3.02±3.33	3.77±7.31	0.331
Ever attempted suicide – n (%)	18 (30.0)	38 (28.8)	0.864
Hepatitis C positive – n (%)	52 (86.7)	104 (78.8)	0.195
HIV positive – n (%)	14 (23.3)	11 (8.3)	0.004
Previous drug treatments	10.17±11.11	11.44±11.81	0.472
Previous MMT	2.88±1.56	3.12±1.79	0.352
<b>Past drug use (years)</b>			
Injecting drugs	17.38±9.24	17.42±10.58	0.978
Heroin regular use in life	13.50±7.74	14.41±8.52	0.467
Illicit opioids regular use in life	5.67±7.23	6.02±8.44	0.765
Cocaine regular use in life	12.10±7.60	12.58±8.02	0.689
Cannabis regular use in life	11.65±12.48	13.02±11.73	0.476
<b>Current drug use (days)</b>			
Heroin use prior month	28.08±4.71	26.81±7.08	0.143
Illicit opioids use prior month	9.43±11.78	10.50±11.48	0.559
Cocaine use prior month	18.98±12.35	18.57±11.83	0.827
Cannabis use prior month	6.33±10.25	6.19±10.80	0.929

± Standard Deviation

Canada, involving 251 participants were used. This study has been described in full detail elsewhere.<sup>8,11,12</sup> Briefly, patients were randomly assigned to receive oral methadone (n=111), injectable diacetylmorphine (n=115) or injectable hydromorphone (n=25) for a period of 12 months. The injectable drugs were provided in double-blind fashion. Treatments were provided following Canadian Best Practices guidelines.<sup>13</sup>

Analyses were performed only for the Vancouver site (n=192), since no Aboriginal participants were recruited at the Montreal site. Primary outcomes among Aboriginal and non-Aboriginal participants were a) retention in addiction treatment at 12 months, and b) response to treatment based on the European Addiction Severity Index.<sup>14</sup> Rate ratios and 95% confidence intervals were calculated, and analyses were on an intention-to-treat basis. Participants with missing values (only 5%) were considered not retained and non-responders.

**RESULTS**

Of the 192 participants at the Vancouver site, 60 (31.3%) self-identified as Aboriginal. Baseline profiles showed no differences between Aboriginal (n=60) and non-Aboriginal (n=132) people in the majority of baseline variables evaluated. However, Aboriginal people reported better housing and higher HIV infection rates compared to non-Aboriginal individuals.

After excluding each participant's initial 90 days of dose adjustment, the average daily dosage of diacetylmorphine and hydromorphone received by Aboriginal participants was 419.4 mg and 155.5 mg, respectively, compared to 414.4 mg and 221.3 mg, respectively, among non-Aboriginal participants, when prescribed alone. Aboriginal and non-Aboriginal participants who were prescribed MMT alone received mean daily doses of 92.5 mg and 97.3 mg, respectively.

Among Aboriginal participants in the injection and methadone groups, retention rates at 12 months were 84.4% vs. 57.1% (statistically significant) and response rates were 68.8% vs. 53.4%, respectively. Among non-Aboriginal participants, retention in injection compared to methadone was 90.7% vs. 50.9% and response was

66.7% vs. 43.9% (both significant). Aboriginal and non-Aboriginal rates were not significantly different.

**DISCUSSION**

The aim of this study was to evaluate the profile and response of Aboriginal participants in the NAOMI study. Among this group, treatment with injectable diacetylmorphine or hydromorphone was more effective than optimized MMT. In addition, there were no differences between Aboriginal and non-Aboriginal people in their baseline profile (except with respect to HIV prevalence) nor in their response to treatment. Moreover, Aboriginal people showed MMT retention rates higher than population-based rates in BC.<sup>15</sup>

Aboriginal people are over-represented among those who are severely affected by heroin addiction. The evidence of HAT effectiveness among Aboriginal participants in this study has important implications related to a) their reported lower access to substitution treatment compared to non-Aboriginal people<sup>10</sup> and b) their higher vulnerability for HIV infection,<sup>16</sup> consistent with their higher HIV rates in this study. Access and retention in substitution treatment is associated with a reduction in drug-related HIV-transmission risk behaviour.<sup>17</sup> Therefore, the higher retention rate in the HAT group is a key factor considering the high rates of HIV among Aboriginal people injecting drugs when compared to non-Aboriginal injecting drug users.

Offering medically prescribed diacetylmorphine or hydromorphone to Aboriginal people with severe long-term opioid dependence could be an effective means of attracting and retaining them in treatment, reducing the risk of HIV infection, and facilitating the provision of antiretroviral treatment for those already infected.

**REFERENCES**

- Gibson DR, Brand R, Anderson K, Kahn JG, Perales D, Guydish J. Two- to six-fold decreased odds of HIV risk behavior associated with use of syringe exchange. *J Acquir Immune Defic Syndr* 2002;31:237-42.
- Termorshuizen F, Krol A, Prins M, van Ameijden EJ. Long-term outcome of chronic drug use: The Amsterdam Cohort Study among Drug Users. *Am J Epidemiol* 2005;161:271-79.
- Brugal MT, Domingo-Salvany A, Puig R, Barrio G, García de Olalla P, de la Fuente L. Evaluating the impact of methadone maintenance programmes on

**Table 2.** Retention and Response in Treatment by Treatment Group and Ethnicity at 12 Months

	HAT		MMT	
	Aboriginal (n=32)	Non-Aboriginal (n=75)	Aboriginal (n=28)	Non-Aboriginal (n=57)
a) Retention in addiction treatment – n (%)				
NAOMI HAT – n (%)	27 (84.4)	68 (90.7)	16 (57.1)	29 (50.9)
NAOMI MMT – n (%)	3 (11.1)	12 (17.6)	12 (75.0)	22 (75.9)
Other MMT – n (%)	2 (7.4)	1 (1.5)	3 (18.8)	7 (24.1)
Other treatments – n (%)	–	1 (1.5)	–	–
Abstinence – n (%)	–	1 (1.5)	1 (6.3)	–
Aboriginal vs. Non-Aboriginal*	0.93 (0.79, 1.10) (p=0.35)		1.12 (0.75, 1.69) (p=0.59)	
HAT vs. MMT*				
Aboriginal		1.48 (1.04, 2.10) (p=0.02)		
Non-Aboriginal		1.78 (1.37, 2.32) (p<0.001)		
b) Clinical response – n (%)				
Drug response alone	22 (68.8)	50 (66.7)	15 (53.4)	25 (43.9)
Legal response alone	7 (31.8)	15 (30.0)	2 (13.3)	8 (32.0)
Both drug and legal response	2 (9.1)	1 (2.0)	1 (6.7)	4 (16.0)
Both drug and legal response	13 (59.1)	34 (68.0)	12 (80.0)	13 (52.0)
Aboriginal vs. Non-Aboriginal*	1.03 (0.78, 1.37) (p=0.83)		1.22 (0.78, 1.92) (p=0.40)	
HAT vs. MMT*				
Aboriginal		1.28 (0.85, 1.95) (p=0.23)		
Non-Aboriginal		1.52 (1.09, 2.12) (p=0.009)		

HAT= Heroin/Hydromorphone-assisted treatment, injectable; MMT= methadone maintenance treatment.

a) Retention in treatment: treatment status at 12 months; Other MMT refers to patients being prescribed methadone but not by the trial doctors

b) Clinical response at 12 months: response to treatment based on the European Addiction Severity Index.

\* Relative risk (95% confidence interval).

mortality due to overdose and AIDS in a cohort of heroin users in Spain. *Addiction* 2005;100:981-89.

- van den Brink W, Hendriks VM, Blanken P, Koeter MW, van Zwieten BJ, van Ree JM. Medical prescription of heroin to treatment resistant heroin addicts: Two randomised controlled trials. *BMJ* 2003;327:310.
- Rehm J, Gschwend P, Steffen T, Gutzwiller F, Dobler-Mikola A, Uchtenhagen A. Feasibility, safety, and efficacy of injectable heroin prescription for refractory opioid addicts: A follow-up study. *Lancet* 2001;358:1417-23.
- March JC, Oviedo-Joekes E, Perea-Milla E, Carrasco F. Controlled trial of prescribed heroin in the treatment of opioid addiction. *J Subst Abuse Treat* 2006;31:203-11.
- Haasen C, Verthein U, Degkwitz P, Berger J, Krausz M, Naber D. Heroin-assisted treatment for opioid dependence: Randomised controlled trial. *Br J Psychiatry* 2007;191:55-62.
- Oviedo-Joekes E, Brissette S, Marsh DC, Lauzon P, Guh D, Anis A, et al. Diacetylmorphine versus methadone for the treatment of opioid addiction. *N Engl J Med* 2009;361:777-86.
- PHAC. HIV/AIDS Among Aboriginal Peoples in Canada: A continuing concern. *HIV/AIDS Epi Update*. Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, 2006.
- Kerr T, Marsh D, Li K, Montaner J, Wood E. Factors associated with methadone maintenance therapy use among a cohort of polysubstance using injection drug users in Vancouver. *Drug Alcohol Depend* 2005;80:329-35.
- Oviedo-Joekes E, Nosyk B, Marsh D, Guh D, Brissette S, Gartry C, et al. Scientific and political challenges in North America's first randomized controlled trial of heroin-assisted treatment for severe heroin addiction: Rationale and design of the NAOMI Study. *Clinical Trials* 2009;6:261-71.
- Oviedo-Joekes E, Nosyk B, Brissette S, Chettiar J, Schneeberger P, Marsh DC, et al. The North American Opiate Medication Initiative (NAOMI): Profile of Participants in North America's First Trial of Heroin-Assisted Treatment. *J Urban Health* 2008;85:812-25.
- Health Canada. Best practices in methadone maintenance treatment. Ottawa, ON: Minister of Public Works and Government Services Canada, 2002.
- Kokkevi A, Hartgers C. EuropASI: European adaptation of a multidimensional assessment instrument for drug and alcohol dependence. *Eur Addict Res* 1995;1:208-10.
- Nosyk B, MacNab YC, Sun H, Fischer B, Marsh DC, Schechter MT, et al. Proportional hazards frailty models for recurrent methadone maintenance treatment. *Am J Epidemiol* 2009;170:783-92.
- Craib KJ, Spittal PM, Wood E, Laliberte N, Hogg RS, Li K, et al. Risk factors for elevated HIV incidence among Aboriginal injection drug users in Vancouver. *CMAJ* 2003;168:19-24.
- Gowing L, Farrell M, Bornemann R, Ali R. Substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database Syst Rev* 2004;CD004145.

Received: November 3, 2009  
Accepted: January 23, 2010

## RÉSUMÉ

**Contexte :** Prescrite à des fins médicales, la diacétylmorphine, ingrédient actif de l'héroïne, a prouvé son efficacité dans le traitement de la dépendance sévère aux opiacés. Cependant, il n'existe pas de données sur son efficacité chez les héroïnomanes autochtones.

**Méthode :** Nos analyses ont été effectuées à l'aide des données de l'étude NAOMI (North American Opiate Maintenance Initiative), un essai ouvert randomisé et contrôlé qui compare l'efficacité de la diacétylmorphine injectable (45,8 %) et de l'hydromorphone (10 %) au traitement oral à la méthadone (44,2 %) chez les opiomanes réfractaires aux traitements prolongés. Nous avons analysé les taux de maintien et de réponse au traitement chez les participants de l'étude à Vancouver (n=192).

**Résultats :** Les profils de référence des participants autochtones (n=60) et non autochtones (n=132) étaient semblables, à l'exception du taux de séropositivité VIH, plus élevé chez les Autochtones (23,3 % c. 8,3 %). Parmi les participants autochtones des groupes du traitement par injection et du traitement à la méthadone, les taux de maintien après 12 mois étaient de 84,4 % et de 57,1 %, et les taux de réponse étaient de 68,8 % et de 53,4 %, respectivement. Les taux pour les Autochtones n'étaient pas significativement différents des taux pour les Non-Autochtones.

**Discussion :** Offrir aux opiomanes autochtones réfractaires aux traitements prolongés un traitement assisté par la diacétylmorphine prescrite à des fins médicales ou par l'hydromorphone pourrait être un moyen efficace de les attirer vers les centres de traitement et de réduire considérablement leurs risques de contracter des infections à VIH.

**Mots clés :** Autochtones, Canada; dépendance aux opiacés; thérapie de substitution; diacétylmorphine injectable; hydromorphone injectable; méthadone, voie orale