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# The economic burden of neuropathic pain in Canada

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The management of neuropathic pain (NeP) is a major healthcare consideration from a treatment perspective. The objective of this research was to quantify the economic burden of NeP in Canada. A cross-sectional observational study was conducted at primary care sites across three Canadian provinces among patients suffering from NeP associated with diabetic peripheral neuropathy, post-herpetic neuralgia, cervical radiculopathy and post-operative neuropathy. Economic burden of illness data were collected through an investigator chart review and patient self-administered

questionnaires to capture NeP resource utilisation and productivity losses. Primary care physicians enrolled 126 patients with a mean age of 58.7 years (standard deviation (SD) 13.5 years). The 3-month direct costs of NeP were estimated at \$1,137 (SD \$1,346) in 2003, of which 77% was attributable to NeP prescriptions, over-the-counter medications and visits to other healthcare providers. Indirect costs were estimated at \$1,430 (SD \$2,027). NeP represents a significant economic burden to the Canadian healthcare system.

**Key words:** cost of illness, neuropathic pain, Canada, healthcare resource utilisation

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## Introduction

The International Association for the Study of Pain defines neuropathic pain (NeP) as pain 'initiated or caused by a primary lesion or dysfunction in the nervous system'<sup>1</sup>. In addition to potentially lasting many years, the pain related to neuropathy is associated with poor sleep quality, anxiety and depression, referred to as the 'TRIAD of pain'<sup>2,3</sup>. Although Canadian statistics on the prevalence of NeP do not currently exist, the prevalence rate of NeP in the UK has been reported at 1% of the population<sup>4</sup>. Diabetic peripheral neuropathy (DPN) and post-herpetic neuralgia (PHN) are the two NeP conditions that have been most frequently studied. DPN is a significant complication of diabetes, affecting between 10% and 35% of diabetic patients<sup>5-8</sup>, although the incidence rises with age. PHN is the most common complication of herpes zoster, with approximately 15% of the population suffering from herpes zoster infection affected by PHN 1 month after the onset of the characteristic rash<sup>9,10</sup>.

The management of chronic pain, including NeP, is a major healthcare consideration. Treatment of NeP involves the use of a variety of drug therapies (opioids, antidepressants, anticonvulsants, local anaesthetics, topical capsaicin, steroids) as well as visits to physicians, other healthcare professionals and outpatient hospital departments. The costs associated with NeP are not well documented in the literature. However, recent studies suggest that the cost of NeP is considerable. For example, in a retrospective analysis of a large US health insurance population (n = 3

million), 55,686 of whom suffered from peripheral neuropathic disorders (PNDs), results indicated that healthcare expenses in the year 2000 were three-fold higher for PND patients (US\$17,355) than for non-PND patients (US\$5,715)<sup>11</sup>. Similar results were observed in a study using the Régie de l'Assurance Maladie du Québec (RAMQ) database that identified 4,912 patients with a PND diagnosis in 2002<sup>12,13</sup>. From a Quebec health ministry perspective, the 2002 costs of healthcare resources were 2.25-fold higher in the PND group (\$4,163) than in the non-PND group (\$1,846)<sup>12,13</sup>. The difference in the magnitude of the costs of PNDs between the US and Canada is mainly due to differences in the costs associated with hospitalisation (\$9,329 vs. \$1,803, respectively) and outpatient care (\$6,859 vs. \$1,009, respectively).

Whilst administrative databases are important tools for generating data to help answer policy and clinical questions, they do not target the impact of a condition on health-related quality of life, productivity loss and patients' out-of-pocket expenditures. To gain a better understanding of the humanistic and economic burden of NeP in Canada, an observational study was conducted to collect information on health-related quality of life (e.g. pain, general health, sleep, anxiety, depression, quality of life), resource use, loss of productivity due to NeP and impact on lifestyle. Medical and indirect costs are the focus of the current paper.

## Patients and methods

### Study design and population

A cross-sectional observational study was conducted at primary care sites across three

provinces (Alberta, Ontario and Quebec) among patients with DPN, PHN, cervical radiculopathy (CR) and post-operative neuropathy (PON). The study received ethical approval from the College of Physicians and Surgeons of Alberta for conduct of the study in Alberta, and the Institutional Review Board Services for conduct of the study in Quebec and Ontario. The study was conducted in accordance with the Declaration of Helsinki as adopted by the 48th General Assembly, Somerset West, Republic of South Africa, October 1996.

Patients were invited to participate in the study if they were 18 years of age or older and had been treated by the same primary care physician for at least 3 months for:

- (1) DPN associated with diabetic distal symmetrical sensory polyneuropathy;
- (2) PHN: pain in the distribution of the spinal nerve dermatome or sensory cranial nerve present for at least 3 months following crusting of skin lesions associated with an acute outbreak of herpes zoster;
- (3) CR: chronic neck pain associated with cervical nerve irritation or pinching with radiation to the shoulder, arm or hand; or (4) PON: pain developed after open thoracotomy, mastectomy or inguinal hernia surgeries. In addition, the PON must have included at least one of the following symptoms: hypoesthesia, hyperesthesia, allodynia or hyperalgesia; and the pain must have been different from that experienced pre-operatively.

Patients were excluded if they were enrolled or had been enrolled in a clinical trial within 30 days of the study start or if they could not follow the study protocol. All enrolled patients

reviewed, signed and dated an informed consent form before participating in the study.

## Data collection

To estimate the economic burden of NeP, primary data were collected from investigator and patient self-administered questionnaires. The investigator questionnaire included questions on the medical history of the patients (e.g. duration of NeP, co-morbidities) and a 3-month retrospective chart review that captured medical resources used to treat NeP and its related complications. The patient questionnaire included sociodemographic questions, other health resources used that were not captured in the physician questionnaire (e.g. over-the-counter (OTC) medications, massage therapy) and questions estimating the impact of NeP on lifestyle and work productivity. At the end of the questionnaire, patients were invited to indicate what proportion of their income they would be prepared to pay to completely alleviate their NeP.

## Healthcare resources

The 3-month healthcare resource utilisation items recorded in the physician questionnaire included: (1) duration of therapy; (2) number of NeP-related physician visits (i.e. to general practitioners and specialists); (3) NeP-related diagnostic tests or procedures; (4) NeP-related inpatient services; (5) NeP-related emergency room visits; and (6) class of prescribed pain-related medications, e.g. opioids (i.e. short- and long-acting opioids), non-steroidal anti-inflammatory drugs (NSAIDs) (including selective COX-2 inhibitors), antiepileptic agents (e.g. gabapentin, carbamazepine) and

antidepressants (i.e. tricyclic antidepressants (TCAs), selective serotonin re-uptake inhibitors and selective noradrenaline re-uptake inhibitors). Physicians were also asked whether or not the patient was waiting to see or currently seeing one or more pain management specialists.

Patients also reported on the healthcare resource utilisation not necessarily known by their treating physicians (i.e. other healthcare provider visits within the past 3 months, such as to a massage therapist) and health products or supplies purchased in the past month. Patients recorded their use of OTC pain medications in the 7 days before the study (i.e. acetaminophen, ibuprofen, acetylsalicylic acid (aspirin)).

### **Lifestyle and productivity**

To understand better the impact of NeP on work and life in general, the following questions were included in the patient questionnaire: (1) problems experienced with work or other usual daily activities due to NeP in the following areas: time lost from work or other activities, accomplished less than desired, limited in type of work or activities, and difficulty performing work or other activities; and (2) amount of time that NeP interfered with social activities.

To calculate the loss of productivity, patients reported time lost from unpaid work days (both full and partial days) over the previous month owing to NeP (e.g. housework, care of children and seniors, volunteer work, seeking medical care for NeP). Employed patients at the time of the study also reported time lost from paid employment over the previous month owing to NeP.

### **Cost calculation**

Various sources were used to determine the 3-month costs associated with the management of NeP. Unit prices for services of physicians and other health professionals were obtained from the 2003 Ontario Schedule of Benefits. The unit prices for hospital services were obtained from the Ontario Case Costing Initiative, which provides fully allocated costs.

For prescription medications, a best available price was applied to each item from the Ontario Drug Benefit Formulary or from wholesale pharmacy catalogue sources. For each class of pain-related medication, typical medication(s), dosage(s) and form(s) were identified (e.g. amitriptyline 150 mg for TCAs) using the RAMQ database and validated by clinical expert opinion in order to calculate prices for 3 months. A mark-up of 10% and a dispensing fee (i.e. \$6.47) were added to the total cost for each prescription medication. To calculate the 3-month cost of OTC medications per patient, information was provided by patients on the specific brand, dosage and average number of pills per day. The consumption cost of pain-related OTC medications over 1 week was extrapolated to a 3-month period. Unit prices were obtained from pharmacy wholesalers' catalogues and mark-ups of 40% were applied. If the information was not available from catalogues, retail sources were used to obtain a typical cost.

Indirect costs due to days missed from paid work were calculated using the 2003 Canadian average hourly wage from Statistics Canada. The 2003 minimum wage was used to value

the number of unpaid days lost. The recall period for time lost was 1 month and the number of days per month lost was multiplied by three to represent a 3-month period.

For each patient, healthcare resources used and days lost due to NeP were calculated by applying the corresponding unit prices. Individual costs were summed before deriving an average 3-month cost per patient. All costs were expressed in 2003 Canadian dollars. When 2003 prices were not available, the consumer price index for health and personal care was used to adjust costs. Since more than two-thirds of the participants were from Ontario, unit prices were from Ontario regardless of the province in which patients were enrolled and treated.

### Statistical analyses

Statistical comparisons were made between patients with different pain severity levels to investigate the association between pain severity and cost. Severity of pain was defined by the patient's answers to Question 3 (i.e. average pain) of the modified Brief Pain Inventory instrument<sup>14</sup>, which was self-administered in this study to measure pain intensity. On a scale from 0–10, mild average pain was defined by a score of 0–3, moderate pain by a score of 4–6 and severe pain by a score of  $\geq 7$ .

Statistical analyses involved univariate (analysis of variance) and multivariate (ordinary least squares (OLS)) techniques to investigate the impact of different pain severity levels on costs. Post-hoc comparison of means was performed using Tukey's method for multiple comparisons. To address

potential differences among patients owing to the observational nature of this study, OLS regressions were conducted to account for differences between patients in gender, age, duration of NeP, pain severity level, number of concomitant diseases and number of classes of medication. Statistical analyses were performed with SAS version 8.1 using PROC GLM for the univariate analyses and PROC REG for the OLS regressions.

## Results

### Patient characteristics

Nineteen primary care physicians enrolled 126 patients in the study. More than two-thirds (69%) of the patients and physicians were from Ontario, 19% from Quebec and 12% from Alberta. Fifty-seven (45.2%) patients were treated for CR, 49 (38.9%) for DPN, 13 (10.3%) for PHN and 7 (5.6%) for PON. Twenty-one (16.7%) patients reported mild pain, 64 (50.8%) reported moderate pain and 41 (32.5%) reported severe pain.

The mean age of the patients was 58.7 years (standard deviation (SD) 13.5 years) and 53.2% of the population were male. The mean duration of NeP was 6.6 years (SD 6.6 years) and the physician assessment indicated that almost two-thirds of the population (61.1%) had three or more co-morbid conditions. In terms of sociodemographics, one-quarter (24.6%) of the patients were employed or self-employed at the time of the study. Almost one out of four patients was on short- (4.8%) or long-term (19.1%) disability. A substantial proportion (41.3%) of NeP patients had an annual income of less than \$20,000. Sociodemographics for

Table 1. Sociodemographic characteristics of the study participants

	Total (n =126)	Mild pain (n =21)	Moderate pain (n =64)	Severe pain (n =41)
Age (years)	58.7 (sd 13.5)	64.1 (sd 13.9)	56.8 (sd 12.6)	58.9 (sd 14.2)
Male gender (%)	53.2	52.4	57.8	46.3
Duration of NeP (years)	6.6 (sd 6.6)	5.4 (sd 6.2)	6.7 (sd 6.8)	7.2 (sd 6.7)
Employment status				
Employed or self- employed (%)	24.6	33.3	23.4	22.0
Retired (%)	48.4	61.9	46.9	43.9
Short-term disability (%)	4.8	4.8	4.7	4.9
Long-term disability (%)	19.1	0.0	20.3	26.8
Other	3.1	0.0	4.7	2.4

the total patient population according to their levels of pain severity are presented in Table 1.

## Resource use

### Medications

As reported by participating physicians, the mean number of classes of pain-related medications used over the last 3 months was 2.3 (sd 1.6) for all patients. More specifically, during this time 85.7% of patients had been prescribed a pharmacotherapy of one of the following classes: opioids (i.e. short- and long-acting opioids), NSAIDs (including selective COX-2 inhibitors), antiepileptic agents and antidepressants (i.e. TCAs, selective serotonin re-uptake inhibitors and selective noradrenaline re-uptake inhibitors). Almost one-half (45.3%) of the patients had been prescribed two or more classes of these pain-related medications. Of the 14.3% who were not prescribed any of these pain-related

prescription medications, most were patients with mild pain (Table 2).

Among patients who received at least one pain-related prescription medication, opioids (41.5%), antidepressants (37.5%) and NSAIDs (32.7%) were the most commonly prescribed. Antiepileptic agents were prescribed in 24.5% of patients, the majority of patients being prescribed gabapentin. One-quarter of the patients received adjunctive medications (e.g. anxiolytics, sedative hypnotics).

In addition, almost two out of three patients (60.3%) had taken an OTC for their NeP over the 7-day period prior to the study. Acetaminophen was the most frequently bought OTC, followed by acetylsalicylic acid (aspirin) and ibuprofen. More than 10% of patients purchased health products (15.9%) or used natural herbal products (11.9%). Table

Table 2. Three-month prescribed and non-prescribed neuropathic pain treatments

	Total	Mild pain	Moderate pain	Severe pain
<b>Number of classes of prescription medications prescribed over the last 3 months (all patients)</b>	<b>(n = 126)</b>	<b>(n = 21)</b>	<b>(n = 64)</b>	<b>(n = 41)</b>
0	14.3%	23.8%	12.5%	12.2%
1	40.5%	38.1%	51.6%	24.4%
2	26.2%	33.3%	18.8%	34.2%
≥3	19.1%	4.8%	17.2%	29.3%
<b>Class of medications prescribed over the last 3 months (among users)</b>	<b>(n = 108)</b>	<b>(n = 16)</b>	<b>(n = 56)</b>	<b>(n = 36)</b>
Opioids (long- and short-acting)	41.5%	29.0%	35.5%	57.9%
NSAIDs (including selective COX-2 inhibitors)	32.7%	18.1%	39.6%	29.9%
Antiepileptic agents	24.5%	7.2%	21.9%	38.5%
Antidepressant (TCAs, SSRIs, SNRIs)	37.5%	29.0%	38.3%	40.7%
Topical analgesics	4.1%	0.0%	5.5%	4.3%
Adjunctive medications (sedative hypnotics, muscle relaxants, anxiolytics)	24.5%	7.2%	30.6%	38.5%
<b>OTC drugs bought in the last 7 days (among users)</b>	<b>(n = 76)</b>	<b>(n = 10)</b>	<b>(n = 42)</b>	<b>(n = 24)</b>
Paracetamol/acetaminophen	7.7%	0.0%	12.3%	5.7%
Ibuprofen	7.7%	6.8%	10.2%	4.3%
Naproxen sodium	1.0%	0.0%	2.0%	0.0%
Aspirin	9.1%	6.8%	11.3%	7.1%
Acetaminophen	25.4%	15.9%	26.6%	28.6%
Health products or supplies purchased for pain over the last month (all patients)	15.9%	9.5%	18.8%	4.6%
Natural or herbal products used for pain over the last month (all patients)	11.9%	14.3%	10.9%	12.2%

2 presents this information for all patients according to their level of pain severity.

Healthcare providers and diagnostic tests  
Table 3 reports resource use in NeP patients according to the level of pain severity. The mean number of physician visits was 2.2 (SD 1.9) in the 3 months before participating in the study, which did not vary significantly as a function of pain severity. One out of four (25.4%) patients visited other healthcare

professionals, most frequently physical therapists (9.5%) and massage therapists (8.7%). During the same period, one out of four patients (27.8%) visited a specialist for their NeP. Specialists most often consulted were neurologists (6.3%), rheumatologists (4.0%) and pain management specialists (3.2%). One out of six patients (16.7%) was waiting to be evaluated by a pain specialist.

Approximately one-third (34.9%) of patients



Table 3. Three-month resource use

	Total (n = 126)	Mild pain (n = 21)	Moderate pain (n = 64)	Severe pain (n = 41)
Number of primary care office visits	2.2 (SD 1.9)	2.1 (SD 2.4)	2.2 (SD 1.7)	2.2 (SD 2.0)
Number of physician phone calls	0.3 (SD 0.7)	0.1 (SD 0.5)	0.1 (SD 0.5)	0.5 (SD 1.0)
<b>Number of patients visiting specialists</b>				
No specialists	72.2%	71.4%	67.2%	80.5%
One specialist	21.4%	19.1%	26.6%	14.6%
Two or more specialists	6.4%	9.5%	6.3%	4.9%
<b>Number of patients undergoing diagnostic tests</b>				
No tests	65.1%	61.9%	62.5%	70.7%
One test	17.5%	19.0%	20.3%	12.2%
Two tests	8.7%	4.8%	7.8%	12.2%
Three or more tests	8.7%	14.3%	9.4%	4.9%
Number of emergency room visits	0.0 (SD 0.2)	0.1 (SD 0.3)	0.0 (SD 0.2)	0.0 (SD 0.0)
<b>Number of patients visiting other healthcare professionals</b>				
No visits	74.6%	85.7%	64.1%	85.4%
One visit	19.1%	9.5%	26.6%	12.2%
Two visits	3.2%	0.0%	6.3%	0.0%
Three or more visits	3.2%	4.8%	3.1%	2.4%

SD, standard deviation.

had undergone at least one diagnostic test over the previous 3 months. The most frequent diagnostic tests were blood tests (25.4% of all patients), radiography (15.1%), nerve conduction studies (6.3%) and computed tomography scans (4.8%). There were no important differences in resource utilisation among the pain severity categories.

### Lifestyle and productivity

The majority of patients reported being limited by NeP. As shown in Table 4 under the category 'Lifestyle', two-thirds of patients (65.9%) cut down time spent on work or other activities and

almost three-quarters (72.2%) reported having difficulty performing at work and in other activities. The greater the pain severity, the greater the level of impairment. In answer to the question regarding what percentage of their income they would be prepared to pay to alleviate their NeP completely, the median response was 20.0% for all patients (mild and moderate pain, 10.0%; severe pain, 60.0%).

Patients who were employed missed a mean of 2.6 (SD 6.4) full work days and 1.8 (SD 3.4) partial work days over the month preceding the study (Table 4 under '1-month time lost'). An average of 4.7 (SD 7.8)

Table 4. Lifestyle and 1-month time lost

	Total (n = 126)	Mild pain (n = 21)	Moderate pain (n = 64)	Severe pain (n = 41)
<b>Lifestyle</b>				
Cut down time spent on work or other activities (% Yes)	65.9	42.9	67.2	75.6
Accomplished less than would have liked (% Yes)	76.2	61.9	76.6	82.9
Limited in kind of work or other activities (% Yes)	69.8	47.6	68.8	82.9
Difficulty performing work or other activities (% Yes)	72.2	42.9	78.1	78.1
<b>1-Month time lost</b>				
<b>Employed full- or part-time</b>	<i>Total</i> (n = 31)	<i>Mild</i> <i>pain (n = 6)</i>	<i>Moderate</i> <i>pain (n = 18)</i>	<i>Severe</i> <i>pain (n = 7)</i>
Missed full work day	2.6 (SD 6.4)	0.0 (SD 0.0)	1.4 (SD 1.9)	7.6 (SD 12.7)
Missed partial work day	1.8 (SD 3.4)	1.4 (SD 1.7)	2.0 (SD 4.0)	1.8 (SD 2.9)
Missed full unpaid work day	4.7 (SD 7.8)	2.3 (SD 4.0)	3.1 (SD 5.7)	9.3 (SD 11.6)
Missed partial unpaid work day	3.6 (SD 4.0)	4.2 (SD 3.6)	3.4 (SD 4.4)	3.3 (SD 4.2)
<b>On short- or long-term disability</b>	<i>Total</i> (n = 33)	<i>Mild</i> <i>pain (n = 1)</i>	<i>Moderate</i> <i>pain (n = 19)</i>	<i>Severe</i> <i>pain (n = 13)</i>
Missed full unpaid work day	12.5 (SD 11.1)	0	11.2 (SD 11.4)	14.8 (SD 10.8)
Missed partial unpaid work day	13.3 (SD 11.4)	28.0	12.5 (SD 11.4)	13.0 (SD 11.6)
<b>Not working in paid employment</b>	<i>Total</i> (n = 64)	<i>Mild</i> <i>pain (n = 14)</i>	<i>Moderate</i> <i>pain (n = 29)</i>	<i>Severe</i> <i>pain (n = 21)</i>
Missed full unpaid work day	6.8 (SD 10.4)	0.0 (SD 0.0)	6.9 (SD 10.0)	10.6 (SD 12.2)
Missed partial unpaid work day	7.9 (SD 10.2)	0.6 (SD 1.8)	8.1 (SD 9.2)	12.1 (SD 12.3)
Median willingness to pay to alleviate NeP (% of income)	20.0	10.0	10.0	60.0

SD, standard deviation; NeP, neuropathic pain.

missed full unpaid work days owing to NeP was observed (e.g. housework, volunteer work) over the last 4 weeks. Table 4 shows that time lost from paid and unpaid work days generally increased with the level of pain for NeP patients who were: (1) employed (patients indicating that they were currently employed full-time, part-time or self-employed); (2) on sick leave (i.e. long- or short-term disability); and (3) retired (not employed or on leave). Because two respondents reported both being

employed and on disability, their information was included in both categories.

Table 5. Average 3-month cost per neuropathic pain patient in 2003 Canadian dollars (\$)

	Total (n = 126)	Mild pain (n = 21)	Moderate pain (n = 64)	Severe pain (n = 41)
Physicians	62 (SD 55)	59 (SD 68)	60 (SD 47)	68 (SD 60)
Specialists	46 (SD 98)	43 (SD 88)	55 (SD 111)	35 (SD 80)
Other healthcare providers	270 (SD 1,048)	101 (SD 369)	465 (SD 1,422)	53 (SD 232)
Emergency room visits	8 (SD 43)	23 (SD 74)	8 (SD 43)	0 (SD 0)
Diagnostic tests	111 (SD 300)	186 (SD 441)	95 (SD 276)	98 (SD 247)
Surgical procedures	2 (SD 13)	0 (SD 0)	2 (SD 13)	2 (SD 16)
Prescription medications	362 (SD 520)	140 (SD 228)	401 (SD 621)	415 (SD 428)
OTC medications	239 (SD 274)	138 (SD 207)	262 (SD 295)	257 (SD 262)
Healthcare products	29 (SD 120)	20 (SD 72)	44 (SD 161)	10 (SD 25)
Natural or herbal products	7 (SD 27)	7 (SD 24)	9 (SD 33)	5 (SD 15)
<b>Total direct costs</b>	<b>1,137 (SD 1,346)</b>	<b>716 (SD 861)</b>	<b>1,400 (SD 1,723)</b>	<b>942 (SD 611)</b>
Time loss: paid work	273 (SD 1,122)	82 (SD 247)	260 (SD 833)	391 (SD 1,666)
Time loss: unpaid work	1,157 (SD 1,529)	248 (SD 582)	1,171 (SD 1,492)	1,600 (SD 1,731)
<b>Total indirect costs</b>	<b>1,430 (SD 2,027)</b>	<b>330 (SD 654)</b>	<b>1,432 (SD 1,672)</b>	<b>1,991 (SD 2,695)</b>
<b>Total costs</b>	<b>2,567 (SD 2,711)</b>	<b>1,047 (SD 1,404)</b>	<b>2,831 (SD 2,860)</b>	<b>2,933 (SD 2,764)</b>

OTC, over-the-counter; SD, standard deviation.

Sums may not add up owing to rounding.

### Three-month costs

Table 5 presents the 3-month costs for the management of NeP patients. The average total costs were \$2,567 (SD \$2,711), 55.7% of which were indirect costs related to time lost from paid and unpaid work days (\$1,430, SD \$2,027). Prescription medications accounted for 31.8% of the 3-month average direct medical costs, which were estimated at \$1,137 (SD \$1,346). Other healthcare providers (e.g. massage therapists) as well as OTC and healthcare/natural products each represented 24% of the total direct medical costs.

The total 3-month costs associated with mild, moderate and severe pain were \$1,047 (SD \$1,404), \$2,831 (SD \$2,860) and \$2,933 (SD \$2,764), respectively. The differences in the total costs observed between mild and

moderate pain and between mild and severe pain were significantly different according to Tukey's studentised test and OLS regression (not presented) ( $p < 0.05$  in both univariate and multivariate analyses).

## Discussion

Our study results suggest that the cost of NeP management in Canada is substantial. Patients consumed a variety of medical resources (e.g. physician and other healthcare provider visits, laboratory and diagnostic tests, prescribed and non-prescribed medicines) for the treatment of NeP, which translates into substantial costs to society estimated at \$2,567 (SD \$2,711) per patient per 3-month period. Pain interfered substantially with usual daily activities (e.g. 72.2% reported difficulty performing work or

other activities), work (e.g. 2.6 full days of work missed over 1 month among employed patients) and ability to perform household activities or volunteer work (e.g. 4.7 full unpaid work days missed over the last month).

Caution should be used in this interpretation of the results of the study owing to the relatively small number of patients, especially when the sample is divided in subgroups (e.g. employed) or analysed by pain severity levels. Also, patients were recruited for the study by their general physicians; therefore they were actively seeking care and may not be representative of the Canadian NeP population. In addition, only patients with DPN, PHN, CR and PON were included in our study, which may not represent the whole spectrum of NeP. Because this study was conducted in three Canadian provinces, caution should be used when extrapolating these results to other provinces owing to potential differences in access to services and medical care. Furthermore, it is difficult to assess the potential selection bias of this study since no information was collected on those patients who were not invited to participate or who were invited but declined. Finally, whilst physicians and patients were instructed to report only resources used or work/activity lost for which NeP was the primary reason, there is a possibility that they may also be related to other conditions.

However, our findings are comparable with other studies in terms of description of pain, impact of NeP on lifestyle and productivity, and medication use. In a recent European study conducted among NeP patients, 602 NeP patients (mean age 63 years) were

recruited in primary care sites in six European countries by 125 community-based physician practices<sup>15</sup>. Almost 80% of these European patients reported moderate (54%) and severe (25%) pain, which is similar to the results of our study (i.e. moderate 51% and severe 33%).

Among the 104 patients who were working at the time of the study (17.3% of total sample compared with 24.6% in our patients), the average number of days missed from work during the last 4 weeks was 5.5 (sd: 9.8). In comparison, the full and partial work days missed observed in our study were 2.6 (sd 6.4) and 1.8 (sd 3.4) over the last month, respectively. The impact of NeP on ability to work owing to pain was also observed in Sweden<sup>2</sup> for 126 peripheral NeP patients treated in two hospitals between January 1991 and May 1997. Among 104 participating patients below the age of 65 years, 43 (41.3%) received sickness pension and 22 (21.2%) worked part time as a consequence of their NeP condition.

Surprisingly, a high proportion of patients were prescribed opioids and NSAIDs in our study. This was also observed by Berger et al<sup>11</sup> in a study using a large US administrative database, in which 55,686 patients with PNDs were identified. In this study, 53.2% of the patients were treated with short-acting opioids and 39.7% with NSAIDs/salicylates/COX-2 inhibitors. In comparison, only 11.1% and 11.3% were prescribed antiepileptics or antidepressants, respectively.

Despite a mean duration of pain of 6.6 years, we found that some patients were undergoing radiography and nerve conduction studies. Unfortunately, the use of

diagnostic/investigational tests was not cross-tabulated with the duration of NeP to determine whether these patients were patients with a more recent history of pain or whether there was a lag between onset of (neuropathic) pain and diagnosis of NeP. This is left for future research.

Because the majority of patients were from Ontario, pricing was done using Ontario unit costs and may therefore not account for provincial differences in unit costs. There were also a number of assumptions made to derive the 3-month costs of NeP. The cost of OTC medication was extrapolated from 1 week to 3 months. Similarly, in calculating indirect costs, the number of days lost due to NeP was reported over a 1-month period and extrapolated to a 3-month period, which may not be accurate. However, our estimate of the indirect costs associated with unpaid work is conservative because the minimum wage was used to value this time lost. If unpaid work had been valued at the average Canadian hourly rate, the indirect costs of this study would have been \$3,546 instead of \$1,430. Despite the limitations associated with this study, the results indicate that NeP represents an important economic burden in terms of direct and indirect costs. Whilst there are limitations to comparing different studies, our direct cost estimate is comparable with other Canadian cost figures. Extrapolation of the 3-month direct costs for our patient population to a 1-year period ( $\$1,137 \times 4 = \$4,548$ ) approximates the 1-year 2002 RAMQ (Quebec) costs estimated for patients with PNDs ( $\$4,163$ )<sup>12,13</sup>. This study, which was conducted using the RAMQ database, also reported that patients with PNDs consumed more direct

medical resources than those with non-PNDs.

Although no direct comparisons were made in the present study with other chronic pain conditions, our estimate of the direct costs of NeP extrapolated to 6 months (i.e.  $\$1,137 \times 2 = \$2,274$ ) approaches the Ontario costs reported for rheumatoid arthritis ( $\$2,575$ ) and osteoarthritis ( $\$1,976$ )<sup>16</sup>. Although the extrapolation to a 6-month period of the indirect costs observed in our study (i.e.  $\$1,430 \times 2 = \$2,860$ ) was slightly higher than the indirect costs associated with rheumatoid arthritis ( $\$2,098$ ), it was much higher than that reported for osteoarthritis ( $\$880$ ). It is important to note that in the Ontario study that estimated costs for rheumatoid arthritis and osteoarthritis, the authors used a methodology similar to ours to calculate indirect costs due to time lost doing chores, including paid help. However, in their calculation of indirect costs the authors used a value of \$10 per hour whereas we used the minimum wage (\$7.45).

In the analysis by pain severity levels, the average direct cost per patient was higher among patients with moderate pain. One explanation is related to the higher cost associated with visits to other healthcare providers among this moderate pain population (\$465 vs. \$53 for severe pain patients), which uses more nontraditional therapies than patients with severe pain (35.9% vs. 14.6%, respectively). Another explanation is that patients' and physicians' perception of pain severity may be different. As physicians are the main drivers of medical resource use, using the physicians' assessment of pain intensity instead of the patient self-administered m-BPI questionnaire to classify

pain severity, as in our study, may have yielded different results. Whether to consider the patient or the physician assessment of pain in economic evaluations of pain-related conditions is left for future research.

Nonetheless, our results indicate that the total cost of NeP management in Canada is substantial, with an average 3-month cost per patient estimated at \$2,567 (SD \$2,711). Indirect costs due to time lost from paid and unpaid work accounted for 56% of this total cost. The study also indicated that more than 20% of the direct costs related to the consumption of OTC medications were paid by patients. Furthermore, some resource uses, such as visits to other healthcare providers, are not fully reimbursed and represent a cost to the patient. Other results not presented in this paper indicate that NeP interferes with work, social activities, sleep and quality of life, and is associated with depression and anxiety. This study represents a first attempt at estimating the economic costs attributed to NeP in Canada. Future research is warranted to collect additional information and to improve the management of NeP in Canada.

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