

The Canadian STOP-PAIN Project

The Burden of Chronic Pain—Does Sex Really Matter?

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Objectives: The Canadian STOP-PAIN Project assessed the human and economic burden of chronic pain (CP) in individuals on waitlists of Canadian multidisciplinary pain treatment facilities. This article focuses on sex differences. Objectives were to (1) determine the pain characteristics and related biopsychosocial factors that best differentiated women and men with CP; and (2) examine whether public and private costs associated with CP differed according to sex.

Materials and Methods: Sample consisted of 441 women and 287 men who were evaluated using self-administered questionnaires and a structured interview protocol. A subsample (233 women and 137 men) recorded all pain-related expenditures in a comprehensive diary over 3 months.

Results: Results revealed that the burden of illness associated with CP was comparable in both sexes for average and worst pain intensity, pain impact on daily living, quality of life, and psychological well-being. The same was true for pain-related costs. The results of a hierarchical logistic regression analysis, in which sex was treated as the dependent variable, showed that factors that differentiated men and women were: work status, certain circumstances surrounding pain onset, present pain intensity, intake of particular types of pain medication, use of certain pain management strategies, pain beliefs, and utilization of particular health care resources.

Discussion: This study suggests that women and men who are referred to multidisciplinary pain treatment facilities do not differ significantly in terms of their pain-related experience. However, the aspects that differ may warrant further clinical attention when assessing and managing pain.

Key Words: chronic pain, sex, economic costs, biopsychosocial factors

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Before 1990, women were commonly excluded from pre-clinical and clinical studies because of their biological complexity (eg, reproductive cycle). Afterwards, the National Institutes of Health introduced a policy that required researchers to include women in medical and behavioral studies.¹ This resulted in growing interest from the scientific community and governmental organizations for more comprehensive research to explore sex and gender differences, leading to increased funding in the field. By the mid-1990s, Unruh² and Berkley³ reviewed the literature on gender and gender differences in pain perception. Their major conclusion was that chronic pain (CP) was more prevalent among women than men. The former group was also at a greater risk of experiencing a variety of recurrent pain, in multiple body regions. These authors also suggested that female patients tend to report greater pain severity and are more often disabled and psychologically affected by their pain.^{2,3} In a more recent critical review, Fillingim et al⁴ reached similar conclusions.

With the exception of a few studies,^{5–8} the most recent population-based studies showed that CP is a more prevalent condition in women worldwide.^{9–34} Similar results were found in primary care settings^{35–38} and multidisciplinary pain treatment facilities (MPTFs).^{39–51} Patients referred to

these types of facilities were found to be predominantly women, and they presented pain in a higher number of body regions than men.

Several studies^{40,41,47–50,52–54} have documented other sex and gender differences in the overall experience of CP (eg, severity, physical and psychological impact, pain management strategies, use of health care resources). There is also an abundant literature of studies aimed at understanding the interrelationships between sex and gender and pain-related variables. For example, multivariate regression models have been used to analyze the relative influence of sex and other demographic (eg, education), psychological (eg, depression), or cognitive factors (eg, catastrophizing thoughts) on the pain experience (eg, pain severity). However, a good number of these reports are based on relatively small sample sizes and/or examined a limited number of potential influencing factors. It is also interesting to point out that earlier studies have always used an analytic approach in which sex is viewed as a predictor—that is, an independent variable among others. None of the studies we reviewed treated this factor as the dependent measure to explore which component(s) of the pain experience and which related psychosocial factors contributed the most to differentiate women and men with CP. The Canadian STOP-PAIN Project assessed the human and economic burden of CP in a large number of patients on waitlists of MPTFs. The results were published in 2 earlier papers.^{55,56} The present article focuses on sex issues. The first objective was to examine the clinical pain characteristics and related biopsychosocial factors that best differentiate women and men with CP. The second objective was to investigate whether public and private economic expenditures associated with CP differed according to sex.

MATERIALS AND METHODS

Design Overview

A cross-sectional, multicentre design combined with a 3-month prospective follow-up in a subgroup of patients was carried out in a cohort of women and men with CP. Potential participants were recruited from waiting lists of 8 large university-affiliated MPTFs established in 7 provinces across Canada. Data were collected with a multidimensional self-administered questionnaire coupled to a structured interview protocol. A subsample of patients completed a self-administered costing tool for a 3-month period to assess and compare pain-related expenditures in women and men.

Participants and Procedure

Before the start of the study, ethical approval was obtained from the Research Ethics Board (REB) of all participating sites (Montreal Heart Institute REB being the leading institution). A total of 3343 CP patients were sent an invitation letter by the medical director of each MPTF to participate in the study. Forty percent of them (1351/3343) consented to be contacted by a research nurse, 191 could not be reached, 422 did not meet the eligibility criteria, and 10 did not complete the structured interview. Respondents were considered for participation only if they fulfilled the following criteria: (1) capable of providing informed consent; (2) 18 years or older; (3) pain (not cancer related) for at least 6 months, and without a condition requiring immediate evaluation and treatment; and (4) able to complete questionnaires in French or in English. The final study sample consisted of

728 patients (441 women and 287 men) (corrected response rate: 24.9%) (The denominator of the corrected response rate was calculated by subtracting the number of excluded participants from the total number of patients invited to participate [3343–422 = 2921]). A full description of patient distribution per MPTF site as well as a flow diagram of response rate is provided in another study.⁵⁵

A subgroup of 512 patients was randomly selected from the initial sample (70%) to complete the Ambulatory Home Care Record (AHCR)⁵⁷ on a daily basis over a 3-month period to measure their public and private pain-related expenditures. A research nurse contacted each patient on a monthly basis and conducted a telephone interview to review the costs they recorded on the AHCR and to minimize any missing data.

Measures

The choice of questionnaires and assessment tools used in the present study was based on (1) the recommendations of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials^{58,59}; (2) the quality of their psychometric properties (eg, validity, reliability); (3) the availability of French and English versions; and (4) the required time for completion.

Self-Administered Questionnaires

Sociodemographic Variables: Sociodemographic data included sex, age, education level, marital status, and current work status.

Pain Characteristics: Women and men were asked about the duration of their pain (years or months) and its present pain intensity, along with average and worst pain intensity in the past 7 days, rated on a standard numeric rating scale (NRS) (0 = no pain to 10 = worst possible pain).⁶⁰

Physical Factors: Pain impact on various aspects of daily living was assessed with the interference items of the modified Brief Pain Inventory using a 0 to 10 scale (0 = does not interfere, 10 = completely interferes).^{61,62} Sleep problems were investigated using 4 items of the Chronic Pain Sleep Inventory (4-point Likert scale: 1 = almost never, 4 = almost always).⁶³ Physical health-related quality of life was assessed by using the SF36 Health Survey version 2,⁶⁴ using the Physical Summary Scale, which comprises items concerning functioning and ability to perform physical activities.

Psychological Factors: The Beck Depression Inventory (BDI-1)⁶⁵ was used to measure depression levels as well as suicidal ideation (Q#9 of the BDI). Anxiety and anger levels were measured with a 0 to 10 NRS (0 = not at all, 10 = extremely). Perceived mental quality of life was assessed using the Mental Summary Scale of the SF36 Health Survey version 2, which provides a global score composed of overall vitality, psychological distress, well-being, and social functioning.

Cognitive Factors: Women and men were asked to complete the short version of the Survey of Pain Attitudes (SOPA-SF),^{60,66} which consists of 14 items (5-point Likert scale: 0 = this is very untrue for me, 5 = this is very true for me), and assesses 7 dimensions associated with the patients' attitudes and beliefs about their pain. They also filled out the Pain Catastrophizing Scale,⁶⁷ which is a 13-item questionnaire (4-point Likert scale: 0 = not at all, 4 = all the time) which includes 3 subscales on rumination, exaggeration, and helplessness.

Structured Interview

During the telephone or face-to-face interview with the research nurses, patients were asked about the (1) circumstances surrounding the onset of their pain; (2) their family pain history, which was defined as having one or more first-degree or second-degree family members affected by CP; (3) current medication used for pain; (4) current non-pharmacological pain-alleviating strategies and techniques (including the use of alcohol and illicit drugs); and (5) type of health care professionals consulted since pain onset.

Pain-related Expenditures Diary

Pain-related costs were measured with the AHCR,⁵⁷ an instrument that comprehensively assesses public—that is, consultations with health care providers, laboratory and diagnostic tests, medications covered by government-sponsored drug programs—and private expenditures. Private costs included (1) out-of-pocket expenses incurred by the patients and their family members—that is, expenditures for consultations with health care professionals not covered by provincial health government, household help, medications, and travel expenses; (2) time costs—that is, monetary value assigned to the time patients and their family care givers dedicated to receiving and providing care; and (3) third party insurance—that is, payments insurance companies made for health care services. Further details about the AHCR are provided in another STOP-PAIN article⁵⁶ and other studies.^{57,68–70}

Statistical Analysis

Before analysis, the distributions of all the measures were examined separately. Some sociodemographic variables were dichotomized to ensure a sufficient number of patients per category. Using the same rationale, the measures under the domain “health behaviors and pain management strategies” were or have been dichotomized as currently “used” or “not used” (yes vs. no). In a first set of analyses, means and frequencies were computed, and independent *t* test or χ^2 tests were performed to compare female and male patients on the following measures: (1) sociodemographic factors; (2) pain characteristics; (3) health behaviors and pain management strategies; (4) physical factors; (5) psychological factors; (6) cognitive factors; and (7) health care utilization. Effect sizes of the observed differences were estimated using Cohen *d* for continuous variables, and Φ coefficients for categorical variables.^{71,72}

To determine which components of the pain experience and related biopsychosocial factors were significantly associated with sex and best differentiated women from men, all the variables that were statistically significant ($P < 0.05$) in the univariate analyses were entered into an exploratory hierarchical logistic regression analysis (HLRA) model in which sex was treated as the dependent measure. Variables that were nonsignificant ($P > 0.05$) in each block were removed from the model at every step using a process of backward elimination. The HLRA included a total of 5 steps corresponding to 5 different domains of independent variables that were entered in an order corresponding to a conceptual framework describing the hierarchical interrelationships between the variables under study.⁷³ In line with the strategy advocated by Victora et al⁷³ for epidemiologic analyses, we based our decision regarding entry order on several reasons having to do with the clinical significance and relevance of the examined factors, their theoretical hierarchical importance,

as well as the intent to identify their unique contribution after having adjusted for other influencing variables. More specifically, entry order of the different blocks of factors was chosen on the basis of (1) how they are considered to be proximate or distal determinants of predicting sex in CP patients; (2) how they are temporally and sequentially related; and (3) supporting evidence derived from the existing literature on biopsychosocial factors involved in pain-related sex differences. The first set of variables included into the HLRA was the sociodemographic one, with the rationale that sex differences in other domains would not be attributable to these variables (eg, education level). Characteristics of the pain experience in terms of duration, intensity, etc., were entered in the second step while the variables included in the domain “health behaviors and pain management strategies” were entered in the third step, as these 2 sets of variables may influence the association between sex and the other domains not already entered in the model (eg, pain interference, emotional well-being). The fourth block included the physical, psychological, and cognitive factors, and these variables were entered all at once in the model to assess whether they added predictive value over and above the previously entered ones (eg, pain intensity). Variables grouped in the health care utilization domain were entered last to ensure that the findings were not attributable to the patients’ general physical or psychological condition, or other variables already entered in the model.

Regarding the economic analysis, a detailed description of the calculation of the economic costs of CP is provided in an earlier paper.⁵⁶ Pain-related costs of care were expressed in Canadian dollars, and were grouped into 5 categories: (1) public expenditures; (2) private expenditures which were subdivided into (a) out-of-pocket, (b) third party insurance, and (c) time costs; and (3) overall total costs. An extremely low case (cost: \$0.62) in the total public expenditures category was identified as an outlier and deleted from the analysis. As the distributions of the categories of costs were positively skewed, a logarithmic transformation (using the log to the base 10) was carried out on the data, and sex comparisons were performed using independent *t* tests.

Comparisons Between Men and Women Suffering from CP

Results from the first set of univariate analyses are summarized in Table 1. Both groups were similar in terms of their sociodemographic profile except for work status (see section A in Table 1); the proportion of patients who were unemployed or on disability (permanent or temporary) was significantly higher in men than women ($\chi^2 = 12.81$, $P < 0.000$). Pain duration was comparable in the 2 groups (section B, Table 1) but circumstances surrounding their pain onset varied significantly ($\chi^2 = 23.33$, $P < 0.001$). Similarly, concerning family history of CP, a higher proportion of women reported a positive history than men ($\chi^2 = 5.28$, $P < 0.02$). Average and worst pain intensity reported in the 7 days preceding data collection was similar in patients of both the sexes. A statistically significant group difference ($P = 0.03$) emerged in the present pain intensity rating but the size of this difference on the 0 to 10 NRS was quite small (women: mean [SD] = 6.3 ± 2.3, men = 5.9 ± 2.4; effect size [*d*] = 0.17).

In terms of health behaviors and pain management strategies (section C, Table 1), more men were current

TABLE 1. Comparisons Between Women and Men on Waiting Lists of Multidisciplinary Pain Treatment Facilities

Variables	N	Women	Men	P	ES
<i>Sociodemographic variables</i>					
Age (mean [SD])	728	51.0 (13.3)	50.6 (11.4)	0.66	0.03
Marital status (%)—married/common law*	728	62.6	66.2	0.32	0.04
Education level (%)—university/college/technical†	726	55.2	51.4	0.31	0.04
Work status (%)—unemployed/on disability‡	726	36.6	50.0	0.000*§	0.13
<i>Pain characteristics</i>					
Pain duration (y; mean [SD])	728	8.7 (8.8)	9.1 (9.7)	0.53	−0.04
Family history of CP (% of yes)	725	48.4	39.7	0.02*	0.09
Circumstances surrounding pain onset	728			0.000*	0.18
Accident/trauma (%)		35.4	51.6		
Illness (%)		8.6	10.1		
Surgery (%)		20.9	13.2		
No precise event (%)		29.9	20.2		
Other (%)		5.2	4.9		
Pain intensity (NRS) (mean [SD])					
Present pain	728	6.3 (2.3)	5.9 (2.4)	0.03*	0.17
Average pain in the past 7 d	725	6.9 (2.0)	6.7 (1.9)	0.12	0.10
Worst pain in the past 7 d	725	8.6 (1.6)	8.4 (1.6)	0.11	0.13
<i>Health behaviors and pain management strategies</i>					
Consumption habits (% of yes)					
Tobacco	726	34.9	42.2	0.05*	0.07
Alcohol to manage pain	728	20.9	32.4	0.000*	0.13
Illicit drugs to manage pain	725	24.1	32.3	0.02*	0.09
Medication or products currently used to relieve pain (% of yes)					
NSAIDs—coxibs	722	24.0	22.5	0.66	0.02
Short-acting opioids	725	43.9	56.1	0.07	0.07
Long-acting opioids	720	20.1	28.3	0.01*	0.09
Antidepressants	724	45.1	34.4	0.004*	0.11
Anticonvulsants	716	21.6	12.1	0.001*	0.12
Muscle relaxants	716	21.6	12.1	0.001*	0.12
Natural products	725	9.2	4.0	0.05*	0.07
Cannabis	726	8.6	17.5	0.000*	0.13
Strategies currently used to alleviate pain (% of yes)					
Implantable nerve stimulator	724	3.4	3.2	0.85	0.01
Injections/blocks	726	6.6	4.5	0.25	0.04
Relaxation	726	47.0	44.4	0.49	0.03
Imagery	726	23.9	16.4	0.02*	0.09
Hypnosis	726	2.5	0.7	0.07	0.07
Distraction	726	62.0	58.0	0.28	0.04
Biofeedback	726	2.5	2.1	0.73	0.01
Massage	724	28.5	25.2	0.32	0.03
Electrostimulation transcutaneous electrical nerve stimulation	725	13.2	14.7	0.57	0.02
Acupuncture	727	8.8	2.4	0.001*	0.13
Ice	726	37.5	29.7	0.03*	0.08
Heat	727	59.2	51.4	0.04*	0.08
Hydrotherapy/hot bath	726	54.8	45.8	0.02*	0.08
Exercise	722	50.3	46.3	0.29	0.04
Activity pacing	725	54.3	47.0	0.05*	0.07
<i>Physical factors</i>					
Physical summary score of SF-36v2 (mean [SD])	725	29.8 (8.2)	29.9 (8.6)	0.77	−0.01
Pain interference items of the Modified Brief Pain Inventory (mean [SD])					
General activity	725	7.3 (2.3)	7.0 (2.3)	0.09	0.13
Mood	726	6.7 (2.7)	6.5 (2.7)	0.30	0.07
Walking ability	727	6.3 (3.1)	6.2 (3.0)	0.69	0.03
Relations with others	727	5.7 (3.2)	5.6 (3.0)	0.91	0.03
Sleep	727	7.0 (2.9)	7.1 (2.7)	0.63	−0.03
Normal work	726	7.6 (2.3)	7.4 (2.5)	0.29	0.08
Enjoyment of life	727	7.2 (2.8)	7.3 (2.6)	0.62	−0.04
Recreational activities	726	7.8 (2.6)	7.8 (2.5)	0.65	0.00
Social activities	726	7.0 (2.9)	7.0 (2.8)	0.98	0.00
Self-care	725	4.6 (3.2)	4.4 (3.1)	0.52	0.06
Chronic Pain Sleep Inventory: “How often did you” (mean [SD])					
Have trouble falling asleep because of pain?	721	3.0 (1.0)	3.0 (1.0)	0.53	0.00

(Continued)

TABLE 1. (continued)

Variables	N	Women	Men	P	ES
Need medication to fall asleep?	722	2.9 (1.2)	2.8 (1.2)	0.30	0.08
Be awakened by pain during the night?	723	2.9 (1.0)	2.9 (1.0)	0.69	0.00
Be awakened by pain in the morning?	721	3.0 (1.0)	2.9 (1.0)	0.28	0.10
Have trouble staying awake during the day?	722	2.3 (1.0)	2.4 (0.9)	0.98	-0.11
<i>Psychological factors (mean [SD])</i>					
Mental summary score of SF-36v2	725	37.6 (14.2)	38.3 (13.4)	0.50	-0.05
Beck Depression Inventory (BDI)	723	19.2 (10.3)	18.1 (9.9)	0.15	0.11
Suicidal ideation (Q.#9—BDI)	725	0.4 (0.6)	0.4 (0.6)	0.43	0.00
Anxiety (NRS)	726	5.2 (3.0)	5.0 (2.9)	0.44	0.07
Anger (NRS)	726	4.3 (3.2)	4.2 (3.1)	0.71	0.03
<i>Cognitive factors</i>					
Pain Catastrophizing Scale (mean [SD])					
Rumination	725	10.3 (4.3)	10.5 (4.2)	0.47	-0.05
Magnification	725	5.5 (3.3)	5.6 (3.2)	0.65	-0.03
Helplessness	727	14.4 (6.0)	13.7 (6.0)	0.14	0.12
Survey of Pain Attitudes (mean [SD])					
Pain control	723	1.6 (1.1)	1.6 (1.1)	0.88	0.00
Disability	725	2.6 (1.2)	2.8 (1.2)	0.03*	-0.17
Harm	728	2.6 (1.0)	2.7 (1.0)	0.39	-0.10
Emotional	726	2.5 (1.2)	2.4 (1.2)	0.20	0.08
Medication	728	3.3 (0.9)	3.3 (0.9)	0.73	0.00
Solicitude	728	2.1 (1.2)	1.9 (1.2)	0.01*	0.17
Medical cure	727	1.8 (1.2)	1.8 (1.2)	0.42	0.00
<i>Health care utilization</i>					
No. health care professionals consulted since pain onset					
Medical disciplines	723	3.9 (2.0)	3.8 (1.8)	0.21	0.05
Physical disciplines	728	2.0 (1.2)	1.9 (1.2)	0.32	0.08
Counseling disciplines	728	0.7 (0.9)	0.8 (0.9)	0.14	-0.11
Alternative medicine disciplines	727	0.9 (1.1)	0.7 (1.0)	0.01*	0.19

*Statistically significant difference between F and M ($P \leq 0.05$).

†Education level was recorded into 2 categories: university/college/technique versus elementary school/high school.

‡Marital status was recorded into 2 categories: married/common law versus single/separated/divorced/widowed.

§Current work status was recorded into 2 categories: unemployed/being on disability (temporary or permanent) versus being full-time or part-time employed, homemaker, student, or retired.

||ES: (1) Cohen d was calculated for mean group differences on categorical variables; $d \pm 0.20$ = small ES, $d \pm 0.50$ = moderate ES, and $d \pm 0.80$ = large ES; (2) Φ was calculated for group differences on categorical variables where $\Phi \pm 0.10$ = small ES, $\Phi \pm 0.30$ = moderate ES, and $\Phi \pm 0.50$ = large ES.

CP indicates chronic pain; ES, effect size; NRS, numerical rating scale.

smokers ($\chi^2 = 3.95$, $P = 0.05$), and they made a greater use of alcohol ($\chi^2 = 12.22$, $P < 0.000$), illegal drugs ($\chi^2 = 5.84$, $P = 0.02$), and cannabis ($\chi^2 = 12.73$, $P < 0.000$) to manage their pain compared with their female counterparts. With regard to pain medication, long-lasting opioids were prescribed significantly more frequently in men than in women ($\chi^2 = 6.35$, $P = 0.01$), whereas female patients were more often given antidepressants ($\chi^2 = 8.21$, $P = 0.004$), anti-convulsants ($\chi^2 = 10.52$, $P = 0.001$), and muscle relaxants ($\chi^2 = 10.52$, $P = 0.001$). A significantly higher proportion of women than men reported taking natural products to alleviate their pain ($\chi^2 = 3.96$, $P = 0.05$) and making use of certain types of active strategies such as pain imagery techniques ($\chi^2 = 5.78$, $P = 0.02$) and pacing activities ($\chi^2 = 3.69$, $P = 0.05$). Physical therapy techniques including the application of ice ($\chi^2 = 4.65$, $P = 0.03$) and heat ($\chi^2 = 4.27$, $P = 0.04$), hydrotherapy or hot bath ($\chi^2 = 5.80$, $P = 0.02$), and acupuncture ($\chi^2 = 11.97$, $P = 0.001$) were also significantly more employed by women. Other types of pain management strategies were equally used by men and women.

Health-related quality-of-life measures revealed no significant difference between women and men, their scores being comparable on the Physical and Mental Summary

Subscales of SF12-v2. The extent to which CP interfered with various aspects of daily living did not differ significantly according to sex. The same was true for pain-related sleep problems (section D, Table 1). Patients' depression levels, suicidal ideation, and anxiety and anger scores were also comparable in both the sexes (section E, Table 1).

Group comparisons on cognitive factors such as the tendency to catastrophize in the face of pain revealed no significant sex difference on any of the pain catastrophizing scale subscales (section F, Table 1). Patients' pain attitudes as measured by the different subscales of the SOPA were also comparable in men and women except for the former group who tended to believe that they were more disabled by their pain ($t_{723} = -2.22$, $P = 0.03$); whereas women thought that others, especially family members, should be more solicitous in response to their pain experience ($t_{726} = 2.50$, $P = 0.01$).

With regard to the last domain of variables having to do with the number of health care professionals consulted since pain onset (section G, Table 1), no significant difference was found between female and male patients, and this was true irrespective of the type of health care discipline—that is, medical, physical, or counseling. A statistically significant difference emerged in the mean number of consultations made by women in alternative medicine

($t_{725} = 2.62, P = 0.01$) but it is important to take into account that the mean value is very low in both the groups and the difference is only of the order of 0.2 professionals (women: mean [SD] = 0.9 [1.1], men = 0.7 [1.0]; effect size [d] = 0.19). It is worth noting that none of the other significant sex differences reported above were associated with moderate or large magnitude effect sizes, all their d values varying between 0.09 and 0.18 (Table 1).

Identification of Factors that Best Differentiate Women and Men With CP

Table 2 shows the results of the HLRA used to identify the factors that significantly and independently differentiated women and men with CP. In the sociodemographic domain, work status was a significant predictor, men being more likely to be unemployed or on disability than their female counterparts (odds ratio [OR] = 1.82, $P < 0.0001$). Relative to women, men were twice as likely to have CP because of an accident/trauma than to surgery (OR = $1 \div 0.43 = 2.32, P < 0.000$), whereas more women were unable to associate their pain onset to a precise event (OR = 0.45, $P < 0.000$). The results also showed that higher present pain intensity ratings were more likely to be reported by women than men (OR = 0.89, $P < 0.001$), however, this did not apply to their ratings of average and worst pain in the past 7 days.

HLRA results revealed that the use of certain pain management strategies contributed to differentiate women and men irrespective of their pain characteristics and work status. Men were two and a half times more likely than women to report using cannabis to alleviate their pain (OR = 2.56, $P < 0.000$). Alcohol also tended to be employed as a means of pain-relief by a greater proportion of men (OR = 1.80, $P = 0.002$). In contrast, techniques

such as imagery (OR = 0.56, $P = 0.008$), hydrotherapy/hot bath (OR = 0.62, $P = 0.005$), and acupuncture (OR = 0.30, $P = 0.008$) were more characteristic of patients of female sex. With regard to pain medication, women were more likely to be given antidepressants (OR = 0.63, $P = 0.009$) and anticonvulsants (and muscle relaxants) (OR = 0.48, $P = 0.003$) than their male counterparts. No other differential pattern emerged in the type of pain medications prescribed to women and men.

None of the pain-related physical and psychological factors qualified as a predictor of sex in the HLRA due to the lack of significant group differences at the univariate level (Table 1). Only one of the cognitive factors having to do with pain beliefs/attitudes reached statistical significance in the regression model. Results obtained on the pain solicitude subscale of the SOPA showed that thinking that others should be more solicitous toward their pain experience was more characteristic of female than male patients (OR = 0.82, $P = 0.006$). No other significant predictor of sex emerged on the SOPA. A last variable of the “health care utilization” domain was entered in the fifth step of the HLRA and contributed to significantly improve the prediction of sex over and above all the other already entered into the model. This result revealed a significant tendency of women to consult more health care professionals in alternative medicine for their CP than men (OR = 0.82, $P = 0.018$).

Statistically significant ORs obtained in the HLRA analysis were further examined in terms of effect size using the formula and interpretation proposed by Chinn⁷⁴ (Cohen $d = \ln(\text{OR})/1.81$) where small ($d = 0.25$), medium ($d = 0.50$), and large ($d = 0.80$) effect sizes correspond to OR values of 1.57, 2.47, and 4.25, respectively, and to 0.64, 0.40, and 0.24 for $\text{OR} < 1.00$. Except for the use of

TABLE 2. Results of the Hierarchical Logistic Regression Analysis Showing the Significant Predictors of Sex/Gender of Chronic Pain Patients

Variables	β	SE	OR* (95% CI)	Pseudo- R^2 (Cox and Snell)	P
Step 1: Sociodemographic variables				0.021	
Work status—unemployed/on disability vs. others	0.60	0.16	1.82 (1.34-2.48)		0.000
Step 2: Pain characteristics				0.062	
Circumstances surrounding pain onset					
Surgery vs. accident/trauma	-0.84	0.23	0.43 (0.28-0.68)		0.000
No precise event vs. accident/trauma	-0.79	0.21	0.45 (0.30-0.68)		0.000
Present pain intensity ‡	-0.11	0.04	0.89 (0.84-0.96)		0.001
Step 3: Health behaviors and pain management strategies				0.146	
Alcohol	0.59	0.19	1.80 (1.23-2.63)		0.002
Antidepressants	-0.46	0.18	0.63 (0.44-0.90)		0.009
Anticonvulsants†	-0.73	0.24	0.48 (0.30-0.78)		0.003
Cannabis	0.94	0.27	2.56 (1.52-4.33)		0.000
Imagery	-0.58	0.22	0.56 (0.36-0.86)		0.008
Acupuncture	-1.21	0.46	0.30 (0.12-0.73)		0.008
Hydrotherapy/hot bath	-0.48	0.17	0.62 (0.44-0.87)		0.005
Step 4: Physical, psychological, and cognitive factors				0.156	
Solicitude subscale of the SOPA‡	-0.20	0.07	0.82 (0.72-0.95)		0.006
Step 5: Health care utilization				0.163	
No. professionals consulted in alternative disciplines‡	-0.20	0.09	0.82 (0.69-0.97)		0.018

*The dependant variable in the model (sex) was coded as 1 for women and 2 for men. Therefore, for a given variable X an OR > 1 indicates that M were more likely to have the characteristic represented by X if X was binary or to have a higher mean value of X if X was continuous. Conversely, an OR < 1 has a similar interpretation, this time for women instead of men.

†Given that a perfect correlation was observed between the use of anticonvulsants and muscle relaxants, only the former was kept and entered into the regression model.

‡Continuous variable.

CI indicates confidence interval; OR, odds ratio; SE, standard error of β ; SOPA, Survey of Pain Attitude.

acupuncture, none of the significant predictors of sex had an OR value associated to a large effect size (Table 2). Most of the ORs for the other variables were associated with effect sizes of a small magnitude (eg, work status, present pain intensity, intake of alcohol and antidepressants, use of imagery and hydrotherapy/bath, SOPA solicitude subscale, number of health professionals consulted in alternative medicine); whereas variables such as the circumstances surrounding pain onset, intake of anticonvulsants, and use of cannabis had ORs of moderate effect size.

Comparisons Between the Pain-related Economic Costs in Women and Men

Seventy-two percent of the selected patients (370/512; women = 233, men = 137) completed the AHCR for at least 1 month. Others did not return the AHCR (125/512: 24.4%) or were excluded because they had their first appointment at the pain clinic (17/512: 3.3%). A total of 272 participants completed the AHCR for 3 months, 35 for 2 months, and 63 for 1 month. Table 3 shows the monthly pain-related costs for female and male patients by expenditure category. Wide variations were found in both the groups but most of their total expenditures were privately financed. Sex comparisons revealed no significant difference in total public or private expenditures. The same was true for their total overall expenses.

DISCUSSION

To our knowledge, this study is the first to explore the factors that best differentiate women and men with CP using sex as the dependent variable and a wide variety of biopsychosocial parameters. On the basis of a large sample size, this study is also the first to compare the human and economic burden of CP in female and male patients on waitlists of MPTFs across Canada. Our results did not reveal sex differences in the burden of illness associated with CP. The impairment experienced in women and men was comparable in terms of pain severity (average and worst), its impact on various aspects of daily living, quality of life, and psychological well-being.

These results can perhaps be explained by the fact that these patients had CP for many years (mean > 8 y), and were typically referred to tertiary pain care centers after all other health care resources had been exhausted, and after various treatments—including therapies in alternative medicine—had been tried. Considering the long waiting lists of MPTFs,^{75,76} it is not uncommon for these patients' condition to have considerably deteriorated both physically and psychologically.⁵⁵ It is therefore possible that both the

pain duration and severity have contributed to reduce or eliminate sex differences with regards to pain intensity, pain interference, psychological distress, and quality of life.

Our results contrast with some of the conclusions of literature reviews by Berkley,³ Fillingim et al,⁴ and Unruh² who suggest that women experience CP of greater severity, and are more physically and psychologically disabled than men. However, several studies conducted with the population of patients referred to MPTFs (before starting treatment) revealed results similar to ours, suggesting that women and men experienced comparable pain severity in terms of intensity^{39,41,49,50,52,53} and interference on daily living,^{39,41,49,50,77} as well as similar depression and anxiety levels.^{41,48,50,52,53,77} Other studies identified sex differences on some of the above parameters but their results went in either directions—that is, women > men^{45,49}; or women < men.⁴⁷ From a clinical perspective, the present results suggest that, with the exception of a few specific aspects (see below), men and women referred in MPTFs do not really require distinct treatment strategies as they appear to have a comparable profile in terms of their overall clinical condition. Our work also distinguishes itself by the use of a hierarchical logistic regression model based on an a priori conceptual framework which took into account how the factors are temporally and sequentially related and whether they can be viewed as proximate or distal determinants in the prediction of sex in patients with CP.

Results of our exploratory HLRA revealed some factors that contributed in differentiating males and females with pain. Work status, certain circumstances surrounding pain onset, present pain intensity, use of certain types of pain medication and pain management strategies, pain beliefs, and utilization of particular types of health care resources were significantly associated with a particular sex. For example, the use of alcohol or cannabis for alleviating pain was significantly more frequent in men than in women, and the “use of cannabis for alleviating pain” variable had an effect size of medium magnitude. These results are of clinical interest, as alcohol and cannabis consumption may require closer assessment in men and tailored clinical interventions might need to be considered. Reasons why men were significantly less inclined than women to use certain types of active pain management strategies such as imagery and physical therapy techniques (ie, acupuncture, hydrotherapy/hot bath) are unclear and merit further elucidation. The greater tendency of women to believe that others should be more solicitous toward their pain experience may also require a tailored intervention involving, for example, family members and/or close friends.

Results from our study show that men and women did not differ according to their overall sociodemographic profile

TABLE 3. Comparisons, Between Women (N=233) and Men (N=137), of Monthly Pain-related Costs (Canadian Dollars) Per Patient Per Expenditure Category

Expenditure Category	Women			Men			P
	Median	Mean	SD	Median	Mean	SD	
Public expenditures	73	219	530	73	186	565	0.698
Private expenditures							
(A) Total out-of-pocket	121	199	233	109	208	335	0.401
(B) Total private third party insurance	131	197	236	138	229	260	0.393
(C) Total time costs (patient + family caregiver)	970	2468	2925	1667	3374	3535	0.590
Total private costs (A + B + C)	1140	2584	2946	1611	3477	3586	0.436
Overall total costs	1362	2749	3029	1764	3564	3610	0.569

except for work status. Being unemployed or on disability was significantly associated with being a man. A study with patients referred to MPTFs also found that men were more frequently on disability leave compared with women.⁵⁴ Other studies failed to find any sex difference in employment status.^{39,41,52,53} In the present study, we dichotomized the work status variable into 2 categories: unemployed/being on disability (temporary or permanent) versus full-time or part-time employed, homemaker, student, and retired. This may have introduced some bias where: (1) women may have described themselves as homemaker even if they were disabled by their CP; and/or (2) men on disability differed from those who were unemployed. Another explanation may be that men were more likely to be unemployed or on disability leave because their pain onset was also significantly more likely to be because of an accident or trauma related to work (medium effect size magnitude). It is also possible that women are less inclined to apply or receive disability benefits than men. All these questions merit further investigation and represent interesting research avenues. Additional studies are needed to develop more comprehensive conceptual models and frameworks that can be tested with sophisticated statistical analyses and thereby allowing further elucidation of the factors that affect and mediate the experience of women and men with CP.

A good number of population-based studies report that women tend to make a larger utilization of health care resources and a greater use of prescribed pain medications than men.^{2,10,13,20,25,34} In patients on waitlists for treatment in MPTFs, our study revealed that both men and women reported having consulted a comparable number of health care professionals in medical, physical, and counseling disciplines. The only exception was in alternative medicine disciplines, for which women reported a greater number of consultations since pain onset. With regards to pain medication, women were also found to take antidepressants, anticonvulsants, and muscle relaxants significantly more frequently than men, and this was true irrespective of their sociodemographic profile and pain characteristics. In a study with CP patients, Turk and Okifuji⁴⁹ did not find sex differences in the use of pain medications with the exception of antidepressants, which were more frequently prescribed to women. It is hard to say if the sex differences in the use of prescribed pain medications are attributable to (1) physicians' prescription bias; (2) men's reluctance to take some types of medication such as antidepressants; or (3) sex-related differences in medication efficacy or adverse side effects. This whole field is clearly understudied and merits further investigation as it may have important clinical implications in terms of analgesic practices.

Even though we did not measure gender differences (eg, masculinity-femininity traits, stereotypes, gender roles) we cannot overlook the fact that our findings are influenced by a more complex and broader politicopsychosocial framework that is encompassed by the North American characteristics ascribed to each sex. It is noteworthy that tertiary pain care studies from different European and North American countries (eg, Canada,^{46,54} USA,^{39,48,52,77} UK,⁴¹ Australia,⁵¹ Denmark⁴⁴) had obtained similar results to ours. To our knowledge, there is no study that has investigated gender role issues related to CP in men and women. Clearly, future research exploring gender factors, when accounting for gender, are required in the pain field.

The second objective of our study was to compare the societal costs of CP in women and men on the waitlists of

MPTFs. The results revealed that the economic burden of their pain was substantial and no significant sex differences emerged in public, private, or total pain-related expenditures. These results compare with those of a recent Danish study with CP patients referred to a MPTF.⁴⁴ In contrast, Weir et al⁵⁴ found that women referred to pain clinics incurred more total direct expenditures and out-of-pocket expenses, whereas men reported higher levels of indirect costs because of loss of income. However, comparing our results with other studies that focus on the costs of CP remains problematic for several reasons.⁵⁶ Most notably, unlike other studies that were not as all-inclusive in their methodology, the costing tool used in the present study considered *all* cost categories of public and private expenditures, including time costs.

The present one has several limitations, some of which have been discussed in 2 earlier publications.^{56,55} Briefly, this study characterized only men and women who were waiting for treatment in tertiary pain clinics. Therefore, our results cannot be generalized to other populations of patients with CP, such as those seeking care from family physicians. The lack of comprehensive diagnostic data on the participants precluded analysis of subgroups of patients with different pain syndromes. Pooling all pain conditions together, rather than focusing on a single one, may have masked some sex differences that would have otherwise emerged. To keep the administration time of the questionnaires within reasonable limits, patients' comorbidities were not assessed in the present study. This is a potential limitation as it is plausible that men and women with CP may differ in this respect. Future studies should consider including and controlling for this factor. Another limitation of this study is the low response rate (24.9%). Nonparticipants—who may or may not have shared common characteristics with our recruited pool of patients—did not provide informed consent to collect data on their demographics or pain history, so it was not possible to assess the presence or absence of differences between them and the study participants. Therefore, severely affected patients may have been overrepresented or underrepresented in the sample of participants who completed the initial questionnaires and the AHCR. Finally, *P*-values from our multivariate regression model should be interpreted with some caution because we used a hierarchical selection procedure coupled to stepwise backward elimination of nonsignificant variables in each block. Although superior to a pure stepwise selection model, the procedure we used may have nevertheless led to too small *P*-values. Our selection model strategies may have over-optimistically selected too many variables, and the observed significant associations will need to be validated in other studies.⁷³

Despite its limitations, our study provides valuable insight into the area of sex and pain. Our results suggest that the burden of illness associated with CP in individuals waiting for treatment in MPTFs is comparable in women and men, with regard to pain severity and interference, quality of life, and psychological well-being. The same appears to be true for the societal costs of their pain. This study suggests that the women and men who are referred to MPTFs do not differ significantly in terms of their pain-related experience. However, the aspects that do actually differ may warrant further clinical attention when it comes to assessing and managing these patients' pain.

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