Chronic noncancer pain

Characteristics of patients prescribed opioids by community physicians and referred to a tertiary pain clinic

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Abstract

Objective To describe the characteristics of patients with chronic noncancer pain (CNCP) prescribed opioids by community physicians and referred to a tertiary pain clinic.

Design Cross-sectional, descriptive study.

Setting A tertiary care, hospital-based pain clinic in Toronto, Ont.

Participants A total of 455 consecutive patients newly referred to the pain clinic by community physicians.

Main outcome measures Data on demographic characteristics, pain ratings, and medication intake were obtained using standardized collection forms and retrospective chart review. Patients were classified by diagnosis: group 1 patients had biomedical disorders only, group 2 patients had biomedical disorders and psychological factors, and group 3 patients had psychological factors only. Patients were also categorized based on opioid use: no opioid use (NOU); low opioid use (LOU), with a daily morphine-equivalent dosage (MED) of 200 mg or less; or high opioid use (HOU), with a daily MED of more than 200 mg.

Results In the general study population, 63% of patients were taking opioids, with 1 in 5 exceeding an MED of 200 mg daily. In group 1, 59% of patients used opioids and 10% had HOU; 66% of patients in groups 2 and 3 were taking opioids, with 21% and 26% classified as having HOU. The mean (SD) daily MED for groups 2 and 3 HOU patients combined was significantly higher than that of group 1 HOU patients: 575.7 (472.9) mg/d versus 284.9 (74.6) mg/d, respectively. Men were twice as likely as women to have HOU; Canadian-born patients were 3 times as likely as foreign-born patients to have HOU. Psychoactive drugs were coprescribed in 61% of LOU patients and 76% of HOU patients. Greater opioid use was associated with group 2 and 3 diagnoses, male sex, Canadian-born origin, and high pain scores.

Conclusion Our results indicate that male, Canadian-born CNCP patients presenting with psychological morbidity or comorbidity and reporting higher pain severity ratings were more likely to receive opioids. Additionally, many CNCP patients referred to our tertiary care pain clinic were receiving opioids in excess of a 200-mg/d MED. More studies are needed to determine which factors lead to high-dose opioid prescribing in a subset of this CNCP population.

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EDITOR'S KEY POINTS

- This study sought to characterize patients prescribed opioids for chronic noncancer pain who were referred to a tertiary pain clinic. It demonstrates statistically significant associations between opioid use and a number of patient characteristics. The data also reveal a variety of problematic trends in opioid prescribing.

- Results suggest that physicians continue to prescribe high doses of opioids for large numbers of patients with substantial psychoemotional issues, and many of these patients continue to have high pain ratings, despite high opioid doses. Further, only about one-third of patients diagnosed with neuropathic or musculoskeletal pain were receiving appropriate adjuvant medications, although these findings should be interpreted with caution.

- Psychoactive coprescriptions were often reported in conjunction with opioids. Among those taking high doses of opioids, less than one-quarter (24%) were taking opioids alone; the remainder were taking 1 or more additional psychotropic drugs. Further, 1 in 5 subjects admitted to marijuana use. These data raise concerns that a substantial proportion of patients taking high doses of opioids might be "driving under the influence" of several drugs or substances and at greater risk of causing motor vehicle accidents.

Douleur chronique non cancéreuse

Caractéristiques des patients qui reçoivent des opiacés de médecins de la ville et qui sont dirigés à des cliniques tertiaires de la douleur

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Résumé

Objectif Décrire les caractéristiques des patients à qui les médecins de ville prescrivent des opiacés pour des douleurs chroniques non cancéreuses (DCNC) et qui sont dirigés vers une clinique tertiaire de la douleur.

Type d'étude Étude descriptive transversale.

Contexte Une clinique de la douleur intra-hospitalière prodiguant des soins tertiaires à Toronto, Ontario.

Participants Un total de 455 patients consécutifs nouvellement dirigés à la clinique de la douleur par des médecins de ville.

Principaux paramètres à l'étude Les données sur les caractéristiques démographiques, l'évaluation de la douleur et les médicaments consommés ont été obtenues à l'aide de formulaires standardisés et grâce à une revue rétrospective de dossiers. Les patients étaient classés en fonction du diagnostic : ceux du groupe 1 avaient uniquement des affections biomédicales, ceux du groupe 2 avaient des affections biomédicales et des facteurs psychologiques, et ceux du groupe 3, seulement des facteurs psychologiques. Les patients étaient aussi classés selon leur consommation d'opiacés : aucune utilisation; utilisation faible; utilisation d'au plus 200 mg d'équivalent de morphine par jour (ÉMD); ou utilisation élevée, avec au moins 200 mg d'ÉMD.

Résultats Dans l'ensemble de la population à l'étude, 63 % des patients prenaient des opiacés et 1 patient sur 5 prenait une dose d'ÉMD excédant 200 mg. Dans le groupe 1, 59 % des patients prenaient des opiacés et 10 % en utilisaient beaucoup; 66 % des patients des groupes 2 et 3 prenaient des opiacés, 21 % et 26 % étant classés comme grands utilisateurs. Pour les patients des groupes 2 et 3 combinés, la moyenne (DS) d'ÉMD était significativement plus élevée que pour les patients du groupe 1 : 575,7 (472,9) mg/d versus 284,9 (74,6) mg/d, respectivement. Les hommes étaient deux fois plus susceptibles que les femmes d'avoir une consommation élevée; les patients d'origine canadienne étaient 3 fois plus susceptibles que ceux d'origine étrangère d'avoir une consommation élevée. Des médicaments psychoactifs étaient prescrits à 61 % des patients faisant un faible usage d'opiacés et à 76 % des grands consommateurs. Il y avait une association entre une plus forte consommation d'opiacés et les diagnostics correspondant aux groupes 2 et 3, le sexe masculin, l'origine canadienne et des scores de douleur élevés.

Conclusion Nos résultats indiquent que les patients de sexe mâle souffrant de DCNC qui présentent des affections psychologiques ou de la comorbidité et qui cotent pour des niveaux de douleur plus élevés sont plus susceptibles de recevoir des opiacés. En outre, plusieurs patients dirigés à notre clinique de soins tertiaires pour des DCNC recevaient des doses d'ÉMD excédant 200 mg. Il faudra d'autres études pour déterminer les facteurs qui amènent à prescrire de fortes doses d'opiacés à un sous-groupe des patients qui souffrent de DCNC.

Cet article a fait l'objet d'une révision par des pairs.
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POINTS DE REPÈRE DU RÉDACTEUR

- Cette étude voulait caractériser les patients à qui des opiacés ont été prescrits pour des douleurs chroniques non cancéreuses et qui ont été dirigés à une clinique tertiaire de la douleur. Les résultats indiquent des associations significatives entre l'utilisation d'opiacés et un certain nombre de caractéristiques des patients. Les données révèlent aussi certaines tendances problématiques dans la prescription d'opiacés.

- Les résultats suggèrent que des médecins continuent de prescrire des doses élevées d'opiacés à un grand nombre de patients qui présentent des problèmes psycho-émotionnels importants, et que plusieurs de ces patients continuent de se plaindre de niveaux élevés de douleur malgré de fortes doses d'opiacés. De plus, à peine le tiers des patients avec un diagnostic de douleur neuropathique ou musculo-squelettique recevaient une médication adjuvante appropriée, quoiqu'il faille interpréter ces observations avec prudence.

- On rapportait souvent des prescriptions de substances psychoactives en association avec des opiacés. Parmi ceux qui consommaient de fortes doses d'opiacés, moins d'un quart (24 %) prenaient seulement des opiacés; les autres prenaient au moins 1 autre agent psychotrope. De plus, 1 sujet sur 5 avouait faire usage de marihuana. Ces données sont préoccupantes du fait qu'un nombre appréciable de patients qui prennent des doses élevées d'opiacés pourraient conduire « sous l'influence » de plusieurs substances ou médicaments, étant ainsi plus à risque de causer des accidents de la circulation.

Chronic non-cancer pain (CNCP) is a serious health problem in the Western world. Patients with CNCP typically first seek care in primary care settings; prevalence estimates vary between 5% and 33%.[1,2] Although many treatments exist for CNCP, opioids represent one of the most controversial options in the physician's armamentarium and continue to be the subject of much debate.[3,4] The use of opioids, which were popularized in the 1980s,[5] particularly for patients with CNCP, has led to an ongoing debate in the medical community and polarized opinions: some advocate generous use of opioids for all noncancer pain, and others underprescribe or refuse to prescribe opioids irrespective of indications.[5-7] With the intention of bridging this divide, the 2010 Canadian guidelines[8] and the American Pain Society and American Academy of Pain Medicine evidence-based guidelines[9] were specifically developed to help inform clinicians about appropriate patient selection, opioid dosing, and potential pitfalls.

In the context of the continuing debate, contrasting beliefs, and recent guidelines on the use of opioids in CNCP, the actual opioid prescribing landscape appears to be shifting, revealing distinct trends.[10] Over the past 10 years or so, opioid prescribing has changed dramatically in Canada and the United States. Per capita, Canada has become the world's third largest consumer of prescription opioids, behind the United States and Belgium,[11] for acute pain, palliative care, and CNCP.[12,13] Alarmingly, coincident with this pattern there has been a rise in the number of patients addicted to opioids seeking treatment at mental health facilities,[14] and the illicit use of prescription opioids has become more common than that of heroin in many Canadian cities.[10,15] Additionally, a more recent study assessing temporal trends in opioid prescribing among those receiving benefits from the Ontario Disability Support Program highlighted 2-year opioid-related mortality rates of 1.6 per 1000 population among individuals prescribed a morphine-equivalent dosage (MED) of less than 200 mg/d; 7.9 per 1000 population among those prescribed an MED of 200 to 400 mg/d; and 9.9 per 1000 population for those prescribed an MED of more than 400 mg/d.[16]

The current study was performed to better understand the characteristics of CNCP patients taking opioids prescribed by community physicians (primary care physicians or consultants) and referred to a tertiary care, hospital-based pain clinic.

METHODS

This cross-sectional descriptive study was conducted at the Comprehensive Pain Program (CPP), an academic tertiary care pain clinic of University Health Network in Toronto, Ont. The study sample comprised a series of consecutive patients referred to the CPP between June 2008 and April 2009 by primary care physicians or treating consultants. Although the specific reasons for referral varied among patients, another study from our clinic showed that the 3 main reasons Ontario family physicians refer patients to pain clinics include nerve blocks (which our clinic does not offer), expertise in diagnosis and management of CNCP, and opioid management.[17] The study was approved by the Research Ethics Board of the University Health Network.

Data collection

Data were gathered using standardized data collection forms completed by each patient at the time of his or her first visit to the CPP and through a retrospective chart review, which included findings of previous tests and interventions as well as results of investigations ordered during follow-up visits. The data set included demographic data (including country of birth classified according to the *2005 World Population Data Sheet*[18] classifications); responses to the Short Form of the McGill Pain Questionnaire (SFMGPQ) and verbal pain ratings on a numerical rating scale (NRS) ranging from 0 to 10 for the primary pain site at time of consultation; history of original and current pain complaints; and results of a detailed neuromusculoskeletal examination by physicians with expertise in chronic pain management.

Data about medication intake at the time of entry into the CPP included classes of drugs with psychotropic effects (tricyclic antidepressants, other antidepressants, anticonvulsants, and sedatives or hypnotics, all recorded separately) and type and dose of opioids prescribed. All medications were reported using generic names. Equianalgesic dose information for opioids was obtained from the Canadian guidelines for safe and effective use of opioids for CNCP.[8] The average prescribed daily dose (in milligrams) of oral morphine or equivalent was calculated for each patient. Patients were categorized into 3 groups: no opioid use (NOU); low opioid use (LOU), with a daily MED of 200 mg or less; or high opioid use (HOU), with a daily MED of more than 200 mg. These categories were based on the "watchful dose" of 200-mg MED recommended by the 2010 Canadian guidelines.[8] The Canadian guidelines[8] suggested that, based on a literature review of randomized controlled trials, most CNCP patients could be treated with doses well below 200 mg. This dose benchmark was further supported by the American Academy of Pain Management guidelines.[9] Although this level is not synonymous with "optimal" dosing, opioid administration above this dose has been associated with increased mortality,[16] and it therefore serves as a well-recognized benchmark to categorize opioid users. Opioids were classified as weak (propoxyphene, meperidine, codeine, and tramadol alone or in combination with acetaminophen) or strong

(morphine, fentanyl, hydromorphone, and oxycodone preparations alone or in combination with acetaminophen or acetylsalicylic acid). Patients taking tramadol were excluded from morphine equivalency calculation, as an accurate conversion ratio between morphine and tramadol has not been well established; these patients were nonetheless considered to have LOU. Onset of action, such as controlled-release or sustained-release versus immediate-release, was also recorded. Midway through the study, we began collecting data on routine marijuana use.

Diagnostic classification was based on the *Diagnostic and Statistical Manual of Mental Disorders,* fourth edition, text revision, categories of pain disorders. Diagnoses were retrieved retrospectively from chart review including the original consultation review of accompanying documentation, as well as, when necessary, additional information and findings of investigations collected during subsequent follow-up visits. Patients were categorized into 1 of the following groups:

- group 1 patients had chronic pain disorder associated with a general medical condition (*not* a psychiatric disorder);
- group 2 patients had chronic pain disorder associated with both a general medical condition and psychological factors; or
- group 3 patients had chronic pain disorder associated with psychological factors (no relevant physical pathology, with available technology, could be documented at the time of evaluation).

Group 3 was not considered a diagnosis of exclusion but rather required a combination of history or physical examination findings, the absence of abnormal investigation findings (eg, radiology, electrophysiology), and the presence of abnormal behavioural signs, including but not limited to discordance between reported disability and clinical findings; substantial mood or anxiety disorders and other psychological or psychosocial variables were documented separately. The above diagnostic classification for groups 1, 2, and 3 has been described in detail in a previous publication from our program.[19]

Statistical analysis

Statistical analyses were conducted using SAS (Statistical Analysis System, version 9.2) and SPSS (Statistical Package for the Social Sciences, version 16.0). Descriptive statistics were used to examine demographic, diagnostic, and pharmacoepidemiologic data. Inferential statistical tests (Pearson χ^2 test, *t* tests, and ANOVA [analysis of variance]) were applied to determine the association between the variables. Where applicable, effect sizes (Cohen *d* and η^2) were also calculated. Bonferroni correction was used to compare significant differences between means within a group; χ^2 goodness-of-fit test was used for the ratio analysis. At a 95% confidence interval, statistical significance was indicated by $P<.05$. Denominators vary owing to missing data.

RESULTS

Demographics

The study population consisted of 455 subjects (248 women and 207 men), with a mean (SD) age of 48.2 (14.2) years. Sixty-one percent of subjects identified Canada as their country of birth. A total of 26% of subjects indicated that they were employed; 45% were unemployed; and 29% identified themselves as retirees, housewives, or students. More than 44% of patients attended postsecondary institutions, while the remainder attained high school education or less. Mean (SD) pain intensity for the primary pain complaint was rated as 6.4 (2.6) using the NRS, with a mean (SD) duration of 64.7 (79.2) months. Most patients had more than 1 pain complaint. Low back pain was the most common complaint (35% of subjects); however, only 8% of this subgroup reported this area as their sole site of pain.

Diagnostic classification

Diagnostically, 32% of patients were placed in group 1, 49% in group 2, and 20% in group 3. When analyzed by diagnosis, group 1 (with pure biomedical pathology) contained the highest percentage of employed patients and retirees. As shown in **Table 1,** groups 2 and 3 had a significantly greater proportion of subjects receiving disability payments from the Workplace Safety and Insurance Board or the Ontario Disability Support Program ($P<.001$). Additionally, patients in group 1 reported significantly lower pain ratings than those in groups 2 and 3 did ($P<.001$) and selected fewer words in the moderate and severe pain intensity categories of the SFMGPQ ($P<.01$).

Opioid and other drug consumption

Of the total sample, 63% of patients were taking opioids prescribed by their family doctors or other physicians, with almost 1 in 5 (19%) exceeding an MED of 200 mg/d. However, opioid consumption varied significantly among the diagnostic groups. When all opioid users (LOU and HOU combined) were compared across diagnostic groups, the difference in mean MED proved to be statistically significant ($P<.001$), with the lowest daily opioid consumption found in the biomedical group and the highest consumption in the group with no detectable peripheral pathology (**Table 2**). In group 1, 59% of the patients were taking opioids, with 10% of these opioid users exceeding a 200-mg/d MED. Most of the group 1 opioid users (89%), however, consumed relatively low daily doses: mean (SD) MED of 39.6 (40.6) mg/d.

Table 1. Demographic characteristics, pain ratings, and sources of disability payments by diagnostic group

CHARACTERISTIC	GROUP 1, BIOMEDICAL DIAGNOSIS (N = 139)	GROUP 2, BIOMEDICAL DIAGNOSIS AND PSYCHOLOGICAL FACTORS (N = 214)	GROUP 3, PSYCHOLOGICAL FACTORS (N = 88)
Female to male ratio	1.3	1.1	1.2
Disability payment source, % (mean [SD] age of patients, y)*			
• CPP	46.0 (68.0 [10.3])	13.9 (59.8 [16.4])	11.5 (55.7 [14.5])
• LTD	19.2 (49.6 [7.8])	15.3 (51.2 [8.2])	11.5 (41.2 [14.6])
• WSIB	17.6 (45.7 [8.3])	37.2† (46.6 [7.1])	40.1† (43.4 [10.9])
• ODSP	6.9 (50.2 [8.7])	19.0† (44.0 [11.5])	21.2† (40.6 [13.7])
Mean (SD) SFMGPQ score‡	6.8 (3.9)	9.0§ (3.6)	9.2§ (3.8)
Mean (SD) NRS primary pain rating‖	5.2 (2.6)	7.0† (2.2)	6.5† (2.8)
Mechanisms of pain, %			
• NP	51.0	31.3	NA¶
• MSK	41.7	54.7	NA¶
• NP and MSK	5.0	9.4	NA¶
• Visceral	2.2	3.3	NA¶
Most common etiology (proportion of patients)	Mechanical low back pain (13.7); nerve injury (10.8)	Mechanical low back pain (13.6); nerve injury (8.4); regional myofascial pain (10.3)	NA

CPP—Canada Pension Plan, LTD—long-term disability, MSK—musculoskeletal, NA—not applicable, NP—neuropathic pain, NRS—numerical rating score, ODSP—Ontario Disability Support Program, SFMGPQ—Short Form of the McGill Pain Questionnaire, WSIB—Workplace Safety and Insurance Board.
*Group 1, n = 74; group 2, n = 137; group 3, n = 52.
†Statistically significant ($P<.001$) by Bonferroni correction for the difference between group 1 and groups 2 and 3. No difference was found between groups 2 and 3.
‡Score is the number of words selected from the moderate and severe pain intensity categories of the SFMGPQ; higher scores suggest more severe pain.
§Statistically significant ($P<.01$) by Bonferroni correction for the difference between group 1 and groups 2 and 3. No difference was found between groups 2 and 3.
‖Primary pain was rated on a scale of 0 to 10.
¶Not detectable with available technology (electrophysiological and imaging studies).

Table 2. Daily opioid consumption by diagnostic group: *Mean (SD) MED of HOU subjects in groups 2 and 3 combined was greater than that of group 1 HOU subjects (575.7 [472.9] mg/d vs 284.9 [74.6] mg/d, respectively; P<.001).*

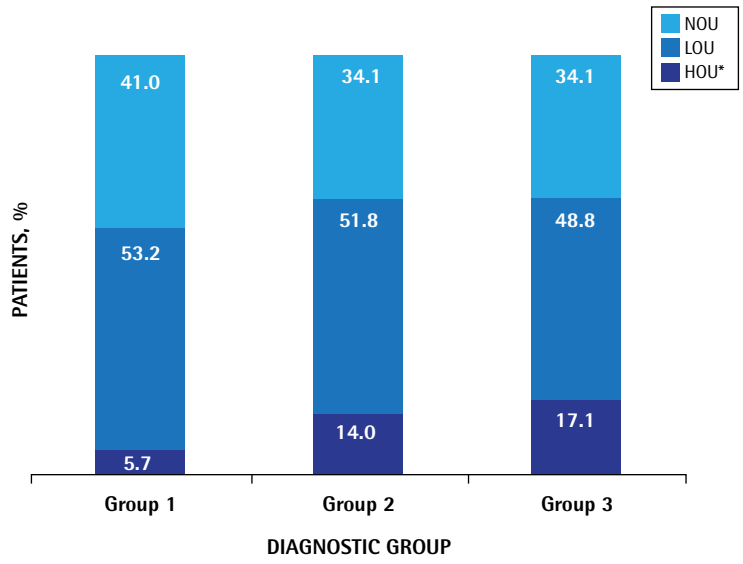
OPIOID GROUP	GROUP 1, BIOMEDICAL DIAGNOSIS (N = 65)	GROUP 2, BIOMEDICAL DIAGNOSIS AND PSYCHOLOGICAL FACTORS (N = 100)	GROUP 3, PSYCHOLOGICAL FACTORS (N = 38)
Mean (SD) daily MED for all opioid users, mg	66.5 (89.2)	162.6 (287.8)	219.4 (410.5)
HOU			
• Mean (SD) daily MED, mg	284.9 (74.6)	543.7 (405.5)	639.7 (596.3)
• Range of daily MEDs, mg	200-409	203-1864	200-2340
LOU			
• Mean (SD) daily MED, mg	39.6 (40.6)	47.6 (49.2)	53.5 (49.0)
• Range of daily MEDs, mg	0.4-175	2-198	0.5-180

HOU—high opioid use, LOU—low opioid use, MED—morphine-equivalent dosage.

In contrast, 66% of patients in each of the other 2 groups were taking opioids, with 21% and 26% of these exceeding a 200-mg/d MED in groups 2 and 3, respectively (**Figure 1**). Mean (SD) daily MED opioid consumption in group 2 and 3 HOU subjects combined was much higher than that of group 1 HOU subjects: 575.7 (472.9) mg/d versus 284.9 (74.6) mg/d, respectively ($P<.001$). Although there were no significant differences in mean (SD) NRS scores between LOU (6.6 [2.4]) and HOU (7.1 [2.1]) patients, opioid users had significantly higher pain ratings than NOU (5.7 [2.7]) patients did ($P<.01$).

Men were twice as likely as women to have HOU, and subjects born in Canada were 3 times more likely

Figure 1. Diagnostic group and opioid use



HOU—high opioid use, LOU—low opioid use, NOU—no opioid use.
*Patients with HOU represent 9.8% of group 1, 21.3% of group 2, and 25.9% of group 3 opioid users.

to have HOU than foreign-born subjects were. While no difference was found between the daily opioid dose of men and women in the HOU group, women in the LOU group consumed a significantly lower ($P<.05$) daily MED than men in the LOU group did (**Table 3**). Similarly, while the daily opioid MED was similar between Canadian-born and foreign-born subjects in the HOU group, foreign-born subjects in the LOU group were receiving a significantly lower ($P<.05$) opioid dose than Canadian-born subjects in the LOU group were (**Table 4**).

The most frequently prescribed opioids in rank order were calculated separately for the HOU and LOU groups. The top 5 opioids prescribed to HOU subjects consisted of controlled-release oxycodone (55%), fentanyl patches (42%), oxycodone in combination with acetaminophen or acetylsalicylic acid (33%), immediate-release oxycodone (18%), and hydromorphone (15%). The top 5 opioids in the LOU group were codeine in combination or codeine alone (42%), with 93% of codeine preparations prescribed as combinations; oxycodone in combination with acetaminophen or acetylsalicylic acid (37%); controlled-release oxycodone (15%); tramadol (13%); and long-acting hydromorphone (5%).

Psychoactive coprescriptions (tricyclic antidepressants, other antidepressants, anticonvulsants, and sedatives or hypnotics) were often reported in conjunction with opioids. In the LOU group 39% of patients were taking opioids alone, while 32%, 20%, and 9% were receiving 1, 2, and 3 or more additional psychotropic drugs, respectively. In the HOU group, less than one-quarter (24%) were taking opioids alone, while 40%, 20%, and 16% received 1, 2, and 3 or more additional psychotropic drugs, respectively.

Of those asked (n=296), 19% acknowledged using marijuana occasionally or regularly. Marijuana use was more frequently identified among group 3 ($P<.01$), Canadian-born ($P<.05$), or unemployed ($P<.05$) subjects, and users were younger (mean [SD] age 41.1 [10.4] years) than nonusers (49.0 [13.7] years; $P<.001$) and reported higher SFMGPQ pain scores ($P<.05$). No differences in sex or opioid use were observed in this group.

Of the 138 patients diagnosed with neuropathic pain, 59% (81 of 138) were taking opioids. Only one-third of these opioid users (35%, 28 of 81) were taking anticonvulsant drugs or tricyclic antidepressants (adjuvant neuropathic medications). Similarly, only one-third (33%, 19 of 57) of neuropathic pain patients who were not taking opioids were prescribed adjuvant neuropathic medications appropriate for their conditions. Of those patients with musculoskeletal pain,

Table 3. Daily opioid consumption by sex

OPIOID GROUP	WOMEN	MEN
HOU		
• Number*	19	36
• Mean (SD) daily MED, mg	465.9 (493.4)	563.3 (414.7)
• Range of daily MEDs, mg	200-2340	200-1864
LOU		
• Number†	107	99
• Mean (SD) daily MED, mg	39.4‡ (39.4)	54.3‡ (53.1)
• Range of daily MEDs, mg	0.4-180	0.5-198

HOU—high opioid use, LOU—low opioid use, MED—morphine-equivalent dosage.
*The ratio of women to men was 0.52:1.00.
†The ratio of women to men was 1.10:1.00.
‡While there was a significant difference ($P<.05$) in daily opioid consumption between LOU men and women, such sex differences were not found in the HOU group.

Table 4. Daily opioid consumption in Canadian-born and foreign-born participants

OPIOID GROUP	CANADIAN-BORN PARTICIPANTS	FOREIGN-BORN PARTICIPANTS
HOU		
• Number	46	9
• Mean (SD) daily MED, mg	538.2 (441.1)	485.7 (466.6)
• Range of daily MEDs, mg	200-2340	206-1620
LOU		
• Number	135	71
• Mean (SD) daily MED, mg	52.9* (50.1)	34.7* (37.8)
• Range of daily MEDs, mg	0.4-198	1-188

HOU—high opioid use, LOU—low opioid use, MED—morphine-equivalent dosage.
*While there was a significant difference ($P<.05$) between Canadian-born and foreign-born participants in the LOU group, such a difference was not found in the HOU group.

65% (114 of 175) were taking opioids, with one-third of these (29%, 33 of 114) also receiving nonsteroidal anti-inflammatory drugs (NSAIDs). Similar numbers, of NOU patients with musculoskeletal pain (34%, 21 of 61) were taking NSAIDs.

DISCUSSION

This study demonstrates statistically significant associations between opioid use and a number of patient characteristics. Specifically, CNCP patients who were male, born in Canada, with psychological morbidity or comorbidity and higher pain severity ratings, were more likely to receive opioids. Additionally, of those who exceeded the 200-mg/d MED watchful dose, the mean MED was significantly lower for group 1 subjects than it was for group 2 and 3 patients with psychological factors involved in their presentation.

While other studies have reported that emotional distress is a prominent factor leading to use of prescription opioids,[20] these data are the first (to the best of our knowledge) to correlate underlying biomedical pathology (or lack thereof) and opioid prescribing habits in Ontario. The results noted for groups 2 and 3 reinforce findings reported in previous publications suggesting that physicians continue to prescribe high doses of opioids for large numbers of patients with substantial psychoemotional issues.[21] Furthermore, we noted that despite high opioid doses, patients in groups 2 and 3 maintained high pain ratings. Although we have indicated that group 3 patients had minimal or no biomedical pathology (detectable with current technology), functional neuroimaging research has documented an interface between the central nervous system and emotional factors in these individuals. However, our data suggest that this type of pain does not respond well to even high doses of opioids. Moreover, while our findings do not necessarily suggest that patients not taking opioids or taking low-dose opioids are appropriately managed, they are consistent with other studies that report greater overall benefits with the use of low-dose opioids.[10]

The preponderance of male subjects receiving opioid prescriptions and, in particular, high-dose opioids, is noteworthy, as sex differences in opioid dosing have not been reported previously. The association between HOU and Canadian-born origin has been reported before in a distinct sample of injured workers referred to our clinic by the Workplace Safety and Insurance Board.[22] One explanation for this finding could be that foreign-born individuals have not been offered opioids owing to language or other barriers. However, the data tend to refute this stance, as in the LOU group almost 40% of users were foreign-born, suggesting that these individuals do not appear to have difficulty obtaining or tolerating low opioid doses. Another possible explanation is that foreign-born patients, owing to cultural or other reasons, are reluctant to accept "too many opioids" for fear of addiction or other adverse effects of these drugs.

A noticeable trend was observed in the use of high-dose opioids in combination with other psychoactive coprescriptions and illicit substance use. In this sample, more than one-third of individuals consuming high-dose opioids received at least 2 other psychoactive medications concurrently, while 1 in 5 of the total study group admitted to using cannabis. The results might be underestimating the true prevalence of marijuana use, as patients could have been reluctant to disclose use of illicit substances. While we did not specifically investigate marijuana use for analgesia, the statistically significant associations with group 3 diagnosis, younger age, higher unemployment, Canadian-born origin, and higher pain ratings suggest that psychosocial or demographic factors could contribute to marijuana use in CNCP. Beyond the issue of possible addiction (which was not assessed), our findings are also concerning for their possible effects on driving, as certain patients taking opioids or opioids in combination with other psychoactive drugs might be "driving under the influence" and at greater risk of causing motor vehicle accidents.[23-25] The latter could lead to liability issues on behalf of the prescribing physicians.

In contrast to the multiple psychoactive preparations taken, only one-third of opioid users with neuropathic or musculoskeletal pain pathology received

adjuvant neuropathic medications or NSAIDs, respectively, for their underlying pathology. These findings should be interpreted with caution. Patients might have experienced treatment failure or complications with these medications resulting in the discontinuation of the adjuvant medication before referral. Alternatively, these patients might have been offered opioids as the drug of choice instead of drugs appropriate for the underlying pain conditions.

Limitations

First, the findings might not be generalizable to all patients in a pain clinic setting or to most CNCP patients treated in the community. Patients referred to a tertiary pain clinic are often recalcitrant and represent a specific subset of patients with CNCP. These patients are typically unresponsive to nonopioid interventions and might represent a biased sample with greater levels of comorbidity requiring more complex pharmacotherapeutic management. However, as all patients originated from community settings, the data are likely to represent at least a subgroup of patients found within primary and secondary care practices who are referred to pain clinics. Second, medication dosages might not be an accurate representation of true patient intake levels. Data were gathered through patient history and file review, and there might have been cases where medication intake was underreported or even overreported. Previous publications, though, report that the concordance between patient report and medical records for current medication intake is generally high.[26,27] Of note, the data were not designed to detect opioid diversion; therefore, no claims can be made about whether patients were actually taking the medications prescribed. A third limitation of the study relates to referral bias. The reported associations were based on small effect sizes, and some of the most important factors affecting opioid prescribing in the study population could relate to referring physician bias. Physicians referring patients to the clinic might have "inherited" patients taking opioids from other prescribers, realized that pain management continued to be unsuccessful despite increasing doses of opioids, expressed concerns about regulatory authorities or questioned the amount of opioids prescribed by other physicians, and referred the patients to the CPP for management. However, accurate information to further delineate the exact nature of this bias could not be retrieved from the available data. Future research might need to focus on prescribers in an effort to understand the characteristics of physicians who tend to prescribe high doses of opioids.

Conclusion

While a 2003 Canadian publication reported that 37% of primary care physicians were unwilling to prescribe opioids even for moderate to severe CNCP,[28] this study demonstrated that a substantial number of community physicians do prescribe opioids frequently and in high doses for questionable indications. Physicians therefore must carefully weigh the risks and benefits when prescribing opioids, particularly when considering doses over the watchful 200-mg/d MED. While the study reveals problematic trends in opioid prescribing in general, many patients who could benefit from an appropriate prescription of opioids continue to be deprived of this option (eg, the elderly who are highly undertreated despite a high prevalence of chronic pain).[29] Opioids are indicated when administered to the right patient for the right reason and in appropriate levels. Despite current efforts to better educate health care professionals about the proper use of opioids for CNCP, many challenges still exist. The evidence for the benefits of long-term opioids in CNCP remains weak[30]; however, the empirical evidence for less-than-ideal opioid prescribing practices continues to mount.

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Competing interests
None declared

Contributors
All the authors contributed to the concept and design of the study; data gathering, analysis, and interpretation; and preparing the manuscript for submission.

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References

1. Reid MC, Engles-Horton LL, Weber MA, Kerns RD, Rogers EL, O'Connor PG. Use of opioid medications for chronic noncancer pain syndromes in primary care. *J Gen Intern Med* 2002;17(3):173-9.
2. Upshur CC, Luckmann RS, Savageau JA. Primary care provider concerns about management of chronic pain in community clinic populations. *J Gen Intern Med* 2006;21(6):652-5.
3. Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. *CMAJ* 2006;174(11):1589-94.
4. Gardner-Nix J. Principles of opioid use in chronic noncancer pain. *CMAJ* 2003;169(1):38-43.
5. Harden RN. Chronic opioid therapy: another reappraisal. *APS Bulletin* 2002;12(1):8-10.
6. Practice guidelines for chronic pain management: a report by the American Society of Anesthesiologists Task Force on Pain Management, Chronic Pain Section. *Anesthesiology* 1997;86(4):995-1004.
7. Wilson PR. Opioids and chronic pain. *Clin J Pain* 1997;13(1):1-2.
8. National Opioid Use Guideline Group. *Canadian guideline for safe and effective use of opioids for chronic non-cancer pain*. Hamilton, ON: National Pain Centre; 2010. Available from: **http://nationalpaincentre.mcmaster.ca/opioid/**. Accessed 2011 Feb 22.
9. Chou R. 2009 clinical guidelines from the American Pain Society and the American Academy of Pain Medicine on the use of chronic opioid therapy in chronic noncancer pain: what are the key messages for clinical practice? *Pol Arch Med Wewn* 2009;119(7-8):469-77.
10. Sullivan MD, Edlund MJ, Fan MY, DeVries A, Brennan Braden J, Martin BC. Trends in use of opioids for non-cancer pain conditions 2000-2005 in commercial and Medicaid insurance plans: the TROUP study. *Pain* 2008;138(2):440-9. Epub 2008 Jun 10.
11. Zacny JP, Lichtor SA. Nonmedical use of prescription opioids: motive and ubiquity issues. *J Pain* 2008;9(6):473-86. Epub 2008 Mar 14.

12. International Narcotics Control Board. *Part four: statistical information on narcotic drugs*. Vienna, Austria: International Narcotics Control Board; 2004. Available from: **www.incb.org/pdf/e/tr/nar/2004/narcotics_part4.pdf**. Accessed 2006 Oct 17.
13. Fischer B, Rehm J, Patra J, Cruz MF. Changes in illicit opioid use across Canada. *CMAJ* 2006;175(11):1385-7.
14. Sproule B, Brands B, Li S, Catz-Biro L. Changing patterns in opioid addiction. Characterizing users of oxycodone and other opioids. *Can Fam Physician* 2009;55:68-69.e1-5. Available from: **www.cfp.ca/cgi/reprint/55/1/68.** Accessed 2011 Feb 14.
15. Dhalla IA, Mamdani MM, Sivilotti ML, Kopp A, Qureshi O, Juurlink DN. Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. *CMAJ* 2009;181(12):891-6. Epub 2009 Dec 7.
16. Gomes T, Juurlink DN, Dhalla IA, Mailis-Gagnon A, Paterson JM, Mamdani MM. Trends in opioid use and dosing among the socio-economically disadvantaged. *Open Med* 2011;5(1):13-22.
17. Lakha SF, Yegneswaran B, Furlan JC, Legnini V, Nicholson K, Mailis-Gagnon A. Referring patients with chronic noncancer pain to pain clinics. Survey of Ontario family physicians. *Can Fam Physician* 2011;57:e106-12.
18. Mailis-Gagnon A, Yegneswaran B, Nicholson K, Lakha SF, Papagapiou M, Steiman AJ, et al. Ethnocultural and sex characteristics of patients attending a tertiary-care pain clinic in Toronto, Canada. *Pain Res Manage* 2007;12(2):100-6.
19. Mailis-Gagnon A, Nicholson K, Yegneswaran B, Zurowski M. Pain characteristics of older adults 65 years of age and older referred to a tertiary care pain clinic. *Pain Res Manag* 2008;13(5):389-94.
20. Breckenridge J, Clark JD. Patient characteristics associated with opioid versus nonsteroidal anti-inflammatory drug management of chronic low back pain. *J Pain* 2003;4(6):344-50.
21. Braden JB, Sullivan MD, Ray GT, Saunders K, Merrill J, Silverberg MJ, et al. Trends in long-term opioid therapy for noncancer pain among persons with a history of depression. *Gen Hosp Psychiatry* 2009;31(6):564-70. Epub 2009 Aug 27.
22. Mailis-Gagnon A, Arvantaj A, Mitrovic B, Lakha SF, Mailis N. Prescription of opioids and other psychotropic drugs in injured chronic pain workers identified by Workers Safety and Insurance Board (WSIB) as management problems. *Pain Res Manag* 2008;(13)2:142-3.
23. Dubois S, Bédard M, Weaver B. The association between opioid analgesics and unsafe driving actions preceding fatal crashes. *Accid Anal Prev* 2010;42(1):30-7. Epub 2009 Jul 19.
24. Engeland A, Skurtveit S, Mørland J. Risk of road traffic accidents associated with the prescription of drugs: a registry-based cohort study. *Ann Epidemiol* 2007;17(8):597-602. Epub 2007 Jun 18.
25. Lagarde E, Chastang JF, Lafont S, Coeuret-Pellicer M, Chiron M. Pain and pain treatment were associated with traffic accident involvement in a cohort of middle-aged workers. *J Clin Epidemiol* 2005;58(5):524-31.
26. Solomon DH, Stedman M, Licari A, Weinblatt ME, Maher N, Shadick N. Agreement between patient report and medical record review for medications used for rheumatoid arthritis: the accuracy of self-reported medication information in patient registries. *Arthritis Rheum* 2007;57(2):234-9.
27. Tisnado DM, Adams JL, Liu H, Damberg CL, Chen WP, Hu FA, et al. What is the concordance between the medical record and patient self-report as data sources for ambulatory care? *Med Care* 2006;44(2):132-40.
28. Morley-Forster PK, Clark AJ, Speechley M, Moulin DE. Attitudes toward opioid use for chronic pain: a Canadian physician survey. *Pain Res Manag* 2003;8(4):189-94.
29. Landi F, Onder G, Cesari M, Gambassi G, Steel K, Russo A, et al. Pain management in frail, community-living elderly patients. *Arch Intern Med* 2001;161(22):2721-4.
30. Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. *Pain* 2004;112(3):372-80.

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