Defining Gender Disparities in Pain Management

Linda LeResche ScD

Published online: 6 January 2011
© The Association of Bone and Joint Surgeons® 2011

Abstract

Background Prevalence rates of most musculoskeletal pain conditions are higher among women than men. Reasons for these prevalence disparities likely include sex differences in basic pain mechanisms and gender differences in psychosocial factors.

Questions/purposes The purposes of this review were to (1) identify reasons for differences in pain prevalence between men and women, (2) assess whether musculoskeletal pain conditions are differently treated in men and women, and (3) identify reasons for sex/gender disparities in pain treatment.

Methods A MEDLINE search was conducted using the terms “pain” or “musculoskeletal pain” and “gender differences” or “sex differences” with “health care,” “health services,” and “physician, attitude.” Articles judged relevant were selected for inclusion.

Where Are We Now? Higher pain prevalence in women is consistently observed but not well understood. The relative

contributions of sex differences in pain mechanisms and gender differences in psychosocial factors (eg, coping, social roles) to explaining differences in prevalence are not yet clear. Gender disparities in the amount of healthcare use for pain may be partially explained by the experience of higher-intensity pain in women. Pain intensity also seems to be a major factor influencing treatment, especially the prescription of medications for acute pain. However, clinicians’ gender stereotypes, as well as the clinician’s own gender, appear to influence diagnostic and treatment decisions for more persistent pain problems.

Where Do We Need To Go? The ultimate goal is optimal pain control for each individual, with gender being one difference between individuals.

How Do We Get There? Further research is needed to address all three major purposes, with particular attention to whether gender-specific pain treatment may sometimes be warranted.

The institution of the author (LL) has received funding from Johnson & Johnson (New Brunswick, NJ). The author is an investigator on this grant. The author certifies that she has no other commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

L. LeResche (✉)
Department of Oral Medicine, University of Washington,
Box 356370, Seattle, WA 98195, USA
e-mail: leresche@uw.edu

L. LeResche
Department of Oral Biology, University of Washington,
Seattle, WA, USA

L. LeResche
Group Health Research Institute, Seattle, WA, USA

Introduction

Prevalence rates of many musculoskeletal pain conditions are higher among women than men. For example, in population-based studies, the women to men ratios for headache, neck, shoulder, knee, and back pain average around 1.5 to 1, for orofacial pain conditions about 2 to 1, for migraine headache 2.5 to 1, and for fibromyalgia (a less prevalent but often disabling condition) more than 4 to 1 [25]. Gender differences in pain prevalence emerge during adolescence. Rates of pain conditions increase as girls pass through puberty, whereas rates for adolescent boys are stable or rise less steeply than for girls [28]. Women are more likely than men to experience multiple pains simultaneously [1, 30, 52]. Having multiple pain conditions is

associated with higher levels of disability and psychologic distress than having a single pain condition. These associations are found both in studies controlling for sex [2, 7, 16] and in analyses confined to women [20]. Having multiple pains is also a risk factor for onset of new pain conditions [19, 27, 49].

What factors underlie these differences between men and women in pain prevalence and disability? Pain is inherently multidimensional. Thus, the observed prevalence differences could be due to sex differences in nociceptive pathways, physiology, or perceptual sensitivity. In addition to biologic differences, differences in the pain experience of women and men may be shaped by gender differences in cognitive or emotional appraisal of pain, by pain behaviors and/or by the different social roles of men and women [8]. Research addressing the question of possible sources of sex and gender differences in pain has not been systematic, and many gaps remain in the available data in both the biologic and the psychosocial domains.

Another important question is whether men and women are treated differently by healthcare providers when they present with pain. If gender differences in pain treatment exist, the impulse might be to label these differences as disparities. However, since the ultimate clinical goal is to provide optimal pain management for each patient, it is also essential to know whether, at times, it may be appropriate to provide different treatments to women and men. If different physiologic pain mechanisms or psychosocial factors are at play in the pain experiences of men and women, sex-specific treatments may be warranted.

Finally, when true disparities are found, with one gender receiving inferior treatment for pain, it is essential to understand the sources of these disparities if they are to be corrected. While some research has addressed the question of how patient gender affects healthcare providers' diagnostic and treatment decisions, much remains to be learned about other possible sources of disparities in the management of musculoskeletal pain.

The purposes of this review are to (1) identify possible reasons for differences in pain prevalence between men and women, (2) assess whether musculoskeletal pain conditions are currently treated differently in men and women, and (3) identify possible reasons for gender disparities in the pain treatment.

Search Strategies and Criteria

Because of the vast scope of the topic, it was not possible to conduct a systematic review of the literature with specific inclusion and exclusion criteria for articles, article quality assessments, data extraction, and summary tables.

Instead, literature searches were conducted on selected topics to supplement the author's own prior research and published literature reviews on prevalence and associated sex and gender variables for specific musculoskeletal pain conditions. All searches were conducted in MEDLINE, with the limit "humans."

Initial searches using the terms "pain" AND "gender differences" and "pain" AND "sex differences" yielded 3696 and 4446 articles, respectively. Searches on "musculoskeletal pain" AND "gender differences" and "musculoskeletal pain" AND "sex differences" returned 175 and 189 articles, respectively. Selected articles from these searches were used to identify possible reasons for gender differences in prevalence (Purpose 1).

To address the second purpose, ie, whether pain is managed differently depending on the gender of the patient, the search was further refined using the terms "musculoskeletal pain" AND "gender differences" AND "health care" (35 articles) or "health services" (33 articles). Similar searches substituting "sex differences" for "gender differences" yielded 41 articles for "health care" and 32 for "health services." Titles from all the searches using the terms "health care" or "health services" were scanned for relevance (eliminating articles on children or not in English), and abstracts were retrieved for the remaining articles. Publications presenting data on sex and gender differences in pain, in summary measures including pain, or in healthcare providers' responses to pain in relation to patient gender were then retrieved and are reviewed here.

Finally, to address one possible reason for gender disparities in the management of pain (Purpose 3), a separate search on "physician" AND "pain" AND "gender" AND "attitude" was conducted. This search yielded 58 articles, of which the most relevant were reviewed and are presented here.

Discussion

Musculoskeletal pain problems are more common in women than in men. However, the reasons for these prevalence differences and how health care may differ for people of different genders is not well understood. This review will focus on where we are now in (1) identifying possible reasons for gender differences in pain prevalence, (2) assessing whether musculoskeletal pain conditions are currently treated differently in men and women, and (3) identifying possible reasons for gender disparities in pain treatment. Since the ultimate clinical goal (where we want to go) is optimal pain management in all individuals, we will also address the question of whether different musculoskeletal pain treatments for people of different sexes

may sometimes be appropriate. Finally, some suggestions will be offered for research that can advance the field toward this goal (ie, how we can get there).

Where Are We Now?

A great deal of research has been directed at understanding the reasons for gender differences in pain prevalence (Purpose 1). At the biologic level, it is clear estrogen influences some clinical pain conditions (ie, migraine [31, 42] and temporomandibular disorder pain [26, 29]), with higher pain occurring during times of low estrogen (around menses) and lower pain at times of high estrogen (late in pregnancy). Experimental evidence suggests the endogenous opioid system differs between sexes and is estrogen-responsive in females, likely influencing pain control [41]. Evidence also indicates some endogenous pain control systems are less robust in women than in men [35]. Some subtypes of opioid analgesics (κ , μ) seem to be more effective in one sex or the other [12, 32]. However, the research is somewhat contradictory, and at this time it is unclear whether the observed biologic differences in opioid response can or should be translated into different treatment recommendations for the two sexes [3]. In the psychosocial sphere, research supports the cultural stereotype that women are more willing than men to report pain [38] and that men and women utilize different patterns of coping strategies when in pain [22, 47]. These generalizations only scratch the surface of research on reasons for gender differences in pain prevalence. A number of recent reviews of the evidence are available (eg, [13, 15]).

Where are we now in addressing the question of whether treatment of pain differs according to the patient's gender (Purpose 2)? Overall, women are more likely to report receiving health care for musculoskeletal pain than men [53]. However, it is possible women seek more health care because they experience greater levels of pain. In one study examining this question, men and women in the community who reported similar levels of pain sought care at similar rates [51]; a second study indicated, after controlling for age and disease severity, women were in fact less likely than men to have consulted their general practitioner for hip pain [21].

The literature on whether healthcare providers prescribe medications differently based on the patient's sex also suggests the level of the patient's pain is an important mediating factor. An early study found women treated for pain in the emergency room are more likely than men to receive medication and to receive more potent medication. However, these differences were entirely explained by higher reported pain in women [36]. More recent research found prescribing of analgesics overall and opioids in

particular in the emergency department did not differ by the sex of the patient after controlling for the presence of chronic pain (among other variables) [18]. Another study in multiple emergency departments found analgesic administration was not different for male and female patients, although women presenting with severe pain were more likely than men to receive analgesics [40]. Outside of the emergency setting, evidence suggests higher rates of use of prescription analgesics among women, especially elderly women [34, 39]. Prescribing patterns for opioid pain medications can also differ by patient gender, with higher rates of long-term opioid use in women [4].

Health professionals also interact with musculoskeletal pain patients around issues of recovery and disability. Although there is little research on how and whether patients' interactions with healthcare professionals influence these issues, it is clear gender influences both the probability and the patterns of pain-related disability. When disability is defined in terms of limitations in activities of daily living and work absence, it appears women have higher rates of pain-related disability [50], even after controlling for psychiatric comorbidities, potential psychologic mediators, and pain severity [45]. It is unclear whether women or men are more likely to experience employment disability associated with pain conditions. One large US national study of employed people showed the overall productive time lost due to pain did not differ by gender, but women were more likely to lose work time due to headache and men due to back pain [44]. On the other hand, studies of long-term disability outcomes consistently indicate women with disabling musculoskeletal injuries recover less quickly [9, 33, 43] and return to work later than men [10]. However, women may be more likely to stay at work once they return [6]. A conceptual review of gender issues in prolonged disability related to musculoskeletal pain explores the complex themes underlying these observed differences, documenting how a person's gender role influences paths through pain and rehabilitation in complex ways [5].

Where are we now in understanding how the gender stereotypes and possible biases of healthcare providers influence the diagnostic and treatment modalities they prescribe for women and men with similar pain problems (Purpose 3)? Most of the research we have in this area has used standardized patient vignettes or simulations to assess providers' beliefs and proposed behaviors (eg, whether to prescribe an opioid analgesic) while controlling for all possible patient factors other than sex. Recent research using "virtual human" technology suggests females are judged by US healthcare students as having more pain than males, even after controlling for race, age, and facial expressions of pain [46]. In this study, the patient's gender accounted for 12% of the variance in judged pain intensity

and 16% of the variance in judged pain unpleasantness. Since women do report higher pain levels than men, judgments in this study may have been influenced by the students' prior experiences. In a Swedish study undertaken as part of a national examination of physician interns, vignettes of two identical cases of neck pain were presented at different testing centers, one with a woman's and one with a man's first name [17]. Examinees stated what history questions they would ask and what diagnostic and treatment procedures they would propose. The female case was more likely to receive nonspecific somatic symptom diagnoses, such as tendinitis and myalgia; the female case was also more likely to be "asked" about psychosocial variables (especially family aspects) as part of the history taking. Laboratory tests were suggested more often for the male case, and diagnostic referral to a physiotherapist or orthopaedist, as well as prescriptions for pain medications or psychoactive drugs, were more likely to be suggested for the female case. Female physicians proposed more diagnoses (particularly of nonspecific physical symptoms) in the female case, and female physicians were more likely to ask psychosocial questions, especially for the female case, than their male counterparts. In this vignette study, male physicians were somewhat more likely than female physicians to "prescribe" analgesics or psychoactive drugs. This is similar to the findings of an observational study of actual physician behavior in the management of nontraumatic complaints of arm, neck, and shoulder pain in general practice, in which male physicians prescribed medication more frequently than female physicians [11]. Patient gender did not influence prescribing in this study. Finally, a study of Michigan physicians that used patient vignettes [14] found physicians were more likely to provide optimal treatment for men (versus women) with acute postoperative pain or with cancer pain, but care suggested for chronic pain patients did not differ by patient gender. (The influence of physician gender on clinical decision making was not examined in this study.) Overall, there is little research on how patient gender influences healthcare providers' judgments about pain severity and appropriate diagnosis and treatment. However, the existing literature suggests women are likely to be treated differently from men, simply by virtue of their sex. In some cases the disparity may favor men, but in others it may favor women (eg, in evaluation of psychosocial aspects of pain, which is appropriate treatment).

In summary, higher pain prevalence in women is consistently observed but not well understood. The relative contributions of sex differences in pain mechanisms and gender differences in psychologic and social factors (eg, coping, social roles) to explaining differences in prevalence are not yet clear. Gender disparities in the amount of healthcare use for pain may be partially explained by the

experience of higher-intensity pain in women. Pain intensity also seems to be a major factor influencing treatment, especially the prescription of medications for acute pain. However, clinicians' gender stereotypes, as well as the clinician's own gender, appear to influence diagnostic and treatment decisions for more persistent pain problems.

Where Do We Need To Go?

The ultimate goal of the clinician should be optimal pain management for each patient, taking sex and gender (which may vary among members of the same sex) into account as individual difference factors to be considered in the complex calculus of diagnostic and treatment decisions. Achieving this goal requires that research be conducted with the aim of developing a better understanding of how basic pain mechanisms may differ in the two sexes, as well as the diverse ways in which gender differences currently influence diagnostic and treatment decisions. In addition, optimal pain management requires that clinicians understand and examine their own gender stereotypes and be prepared to evaluate whether these stereotypes result in less-than-optimal pain management for certain individuals.

How Do We Get There?

Purpose 1: Although there are hundreds of published studies on pain prevalence, much remains to be learned about gender differences in the prevalence of musculoskeletal pain conditions. Information is needed on whether women's higher prevalence rates are a result of higher rates of onset or longer duration of pain. Additionally, it is important to take into account not only gender- but also age-specific prevalence patterns, which differ for different pain conditions. For example, across the adult lifespan, joint pain prevalence rises with age for both genders, rates of abdominal pain and tension-type headache decrease, and rates of migraine and temporomandibular disorder pain show a bell curve, with prevalence peaking between 40 and 50 years old [24]. These age differences in prevalence patterns may provide clues concerning factors that influence the rates of onset or persistence of these pain conditions in women and men. Finally, the degree to which the higher rates of pain in women reflect gender differences in willingness to report pain versus biologic differences in pain perception and nociceptive mechanisms is an important subject for future research as tools, such as brain imaging, become available to address this question.

The data reviewed suggest a number of areas for further research on the reasons for observed gender differences in pain. Research on gender differences and their causes is

needed at all levels, including studies of basic nociceptive mechanisms, psychologic vulnerabilities and responses to pain, and societal factors that influence pain experience and pain treatment.

There is growing evidence that similar neurobiologic mechanisms, specifically endogenous opioid systems, underlie the regulation of responses to physical and emotional stressors [37] and that these systems are influenced by estradiol [41]. Further studies are needed to confirm whether estradiol/pain relationships found in initial research on migraine and facial (temporomandibular) pain hold for other clinical pain conditions. If these relationships are confirmed, the next step would be additional studies aimed at understanding how estradiol influences clinical pain. Other hormones, such as progesterone and testosterone, should also be explored for their possible roles in modulating pain in humans. If differential pain mechanisms are confirmed, this could eventually lead to new treatments specifically tailored for each gender. In the meantime, clinical trials of pain medications should be powered, if possible, to analyze for possible gender differences in outcomes; such differences might provide additional evidence indicating different pain or pain modulation mechanisms are operating in men and women [12, 15].

Research is needed on how comorbid conditions, which differentially affect men and women, contribute to gender differences in pain and response to pain treatment. Persons with pain, particularly those with multiple pain conditions, are at increased risk of depression [7], a relationship found worldwide [16]. Women are more likely than men to experience multiple pain problems [25, 28], and base rates of depression in the population are higher for women than for men [23]. Somatic symptoms other than pain are also more common in women [48]. These comorbidities likely affect treatment outcomes for pain, but research on gender differences in pain treatment outcomes often does not take these factors into account [15].

Cognitive factors and coping strategies may also explain some of the observed gender differences in pain. For example, in one study of elderly patients with arthritis [22], women reported higher pain levels and greater pain-related disability than men. However, women in this sample were more likely to cope with pain by catastrophizing, and when catastrophizing was controlled for statistically, the gender differences in pain and disability disappeared. These results are intriguing and call for additional research on how cognitive factors contribute to gender differences in clinical pain in other samples, including younger persons with different pain conditions.

Purpose 2: Research is critically needed on how actual clinical practice (diagnostic tests ordered, treatment approaches employed) varies by patient gender. In these studies, attention should be paid to (1) whether gender

appears to influence the practice, (2) whether the observed findings (of a relationship with gender or of no gender difference) change when pain level is taken into account, and importantly, (3) whether treatment outcomes differ by gender.

Purpose 3: Few studies have addressed how social factors and gender stereotypes might influence pain treatment. Of necessity, many of these studies have relied on written vignettes to standardize all factors other than gender, and most clinicians have been aware they were participating in a study of their clinical judgments. Studies that are closer to the actual clinical encounter, as well as less obtrusive to clinicians, might produce somewhat different results.

As this brief review has demonstrated, the field of gender differences in pain provides a wealth of research opportunities for basic, clinical, and social scientists. Although basic and human experimental studies have uncovered possible gender differences in pain mechanisms, data are scarce on gender differences and disparities in the management of clinical pain. Further research on these issues is critically needed so clinicians can appropriately take gender into consideration when tailoring treatment to provide optimal pain control for each individual.

Acknowledgments I thank the editors and anonymous reviewers for helpful suggestions.

References

1. Berkley KJ. Sex differences in pain. *Behav Brain Sci.* 1997; 20:371–380.
2. Buchman AS, Shah RC, Leurgans SE, Boyle PA, Wilson RS, Bennett DA. Musculoskeletal pain and incident disability in community-dwelling older adults. *Arthritis Care Res (Hoboken).* 2010;62:1287–1293.
3. Cairns BE, Gazerani P. Sex-related differences in pain. *Maturitas.* 2009;63:292–296.
4. Campbell C, Weisner C, LeResche L, Ray T, Saunders K, Merrill JO, Banta-Green C, Sullivan MD, Silverberg MJ, Boudreau D, Von Korff M. Age and sex trends in long-term opioid analgesic use for non-cancer pain. *Am J Public Health.* 2010;100:2541–2547.
5. Côté D, Coutu MF. A critical review of gender issues in understanding prolonged disability related to musculoskeletal pain: how are they relevant to rehabilitation? *Disabil Rehabil.* 2010;32: 87–102.
6. Crook J, Moldofsky H. The probability of recovery and return to work from work disability as a function of time. *Qual Life Res.* 1994;3(Suppl 1):S97–S103.
7. Dworkin SF, Von Korff MR, LeResche L. Multiple pains and psychiatric disturbance: an epidemiologic investigation. *Arch Gen Psychiatry.* 1990; 47:239–244.
8. Dworkin SF, Von Korff M, LeResche L. Epidemiologic studies of chronic pain: a dynamic-ecologic perspective. *Ann Behav Med.* 1992;14:3–11.
9. Egol KA, Tejjwani NC, Walsh MG, Capla EL, Koval KJ. Predictors of short-term functional outcome following ankle fracture surgery. *J Bone Joint Surg Am.* 2006;88:974–979.

10. Faber E, Burdorf A, Bierma-Zeinstra SM, Miedema HS, Koes BW. Determinants for improvement in different back pain measures and their influence on the duration of sickness absence. *Spine (Phila Pa 1976)*. 2006;31:1477–1483.
11. Feleus A, Bierma-Zeinstra SM, Bernsen RM, Miedema HS, Verhaar JA, Koes BW. Management decisions in nontraumatic complaints of arm, neck, and shoulder in general practice. *Ann Fam Med*. 2009;7:446–454.
12. Fillingim RB, Gear RW. Sex differences in opioid analgesia: clinical and experimental findings. *Eur J Pain*. 2004;8:413–425.
13. Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL 3rd. Sex, gender and pain: a review of recent clinical and experimental findings. *J Pain*. 2009;10:447–485.
14. Green CR, Wheeler JR, LaPorte F. Clinical decision making in pain management: contributions of physician and patient characteristics to variations in practice. *J Pain*. 2003;4:29–39.
15. Greenspan JD, Craft RM, LeResche L, Arendt-Nielsen L, Berkley KJ, Fillingim RB, Gold MS, Holdcroft A, Lautenbacher S, Mayer EA, Mogil JS, Murphy AZ, Traub RJ; Consensus Working Group of the Sex, Gender, and Pain SIG of the IASP. Studying sex and gender differences in pain and analgesia: a consensus report. *Pain*. 2007;132(Suppl 1):S26–S45.
16. Gureje O, Von Korff M, Kola L, Demyttenaere K, He Y, Posada-Villa J, Lepine JP, Angermeyer MC, Levinson D, de Girolamo G, Iwata N, Karam A, Borges GL, de Graaf R, Browne MO, Stein DJ, Haro JM, Bromet EJ, Kessler RC, Alonso J. The relation between multiple pains and mental disorders: results from the World Mental Health Surveys. *Pain*. 2008;135:82–91.
17. Hamberg K, Risberg G, Johansson EE, Westman G. Gender bias in physicians' management of neck pain: a study of the answers in a Swedish national examination. *J Womens Health Gend Based Med*. 2002;11:653–666.
18. Heins JK, Heins A, Grammas M, Costello M, Huang K, Mishra S. Disparities in analgesia and opioid prescribing practices for patients with musculoskeletal pain in the emergency department. *J Emerg Nurs*. 2006;32:219–224.
19. Jinks C, Jordan KP, Blagojevic M, Croft P. Predictors of onset and progression of knee pain in adults living in the community: a prospective study. *Rheumatology*. 2008;47:368–374.
20. John MT, Miglioretti DL, LeResche L, Von Korff M, Crichtlow CW. Widespread pain as a risk factor for dysfunctional temporomandibular disorder pain. *Pain*. 2003;102:257–263.
21. Jüni P, Low N, Reichenbach S, Villiger PM, Williams S, Dieppe PA. Gender inequity in the provision of care for hip disease: population-based cross-sectional study. *Osteoarthritis Cartilage*. 2010;18:640–645.
22. Keefe FJ, Lefebvre JC, Egert JR, Affleck G, Sullivan MJ, Caldwell DS. Relationship of gender to pain, pain behavior, and disability in osteoarthritis patients: the role of catastrophizing. *Pain*. 2000;87:325–334.
23. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen HU, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. *Arch Gen Psychiatry*. 1994;51:8–19.
24. LeResche L. Gender considerations in the epidemiology of chronic pain. In: Crombie IK, Croft PR, Linton SJ, LeResche L, Von Korff M, eds. *Epidemiology of Pain*. Seattle, WA: IASP Press; 1999:43–52.
25. LeResche L. Epidemiologic perspectives on sex differences in pain. In: Fillingim RB, ed. *Sex, Gender and Pain: Progress in Pain Research and Management*. Vol 17. Seattle, WA: IASP Press; 2000:233–249.
26. LeResche L, Mancl L, Sherman JJ, Gandara B, Dworkin SF. Changes in temporomandibular pain and other symptoms across the menstrual cycle. *Pain*. 2003;106:253–261.
27. LeResche L, Mancl LA, Drangsholt MT, Huang G, Von Korff M. Predictors of onset of facial pain and temporomandibular disorders in early adolescence. *Pain*. 2007;129:269–278.
28. LeResche L, Mancl LA, Drangsholt MT, Saunders K, Korff MV. Relationship of pain and symptoms to pubertal development in adolescents. *Pain*. 2005;118:201–209.
29. LeResche L, Sherman JJ, Huggins KH, Saunders K, Mancl LA, Lentz G, Dworkin SF. Musculoskeletal orofacial pain and other signs and symptoms of temporomandibular disorders during pregnancy: a prospective study. *J Orofac Pain*. 2005;19:193–201.
30. Leveille SG, Zhang Y, McMullen W, Kelly-Hayes M, Felson DT. Sex differences in musculoskeletal pain in older adults. *Pain*. 2005;116:332–338.
31. Marcus DA. Clinical review: interrelationships of neurochemicals, estrogen, and recurring headache. *Pain*. 1995;62:129–139.
32. Paller CJ, Campbell CM, Edwards RR, Dobs AS. Sex-based differences in pain perception and treatment. *Pain Med*. 2009;10:289–299.
33. Pernold G, Mortimer M, Wiktorin C, Tornqvist EW, Vingård E; Musculoskeletal Intervention Center-Norråljä Study Group. Neck/shoulder disorders in a general population: natural course and influence of physical exercise: a 5-year follow-up. *Spine (Phila Pa 1976)*. 2005;30:E363–E368.
34. Pokela N, Bell JS, Lihavainen K, Sulkava R, Hartikainen S. Analgesic use among community-dwelling people aged 75 years and older: a population-based interview study. *Am J Geriatr Pharmacother*. 2010;8:233–244.
35. Popescu A, LeResche L, Truelove EL, Drangsholt MT. Gender differences in pain modulation by diffuse noxious inhibitory controls—a systematic review. *Pain*. 2010;150:309–318.
36. Raftery KA, Smith-Coggins R, Chen AH. Gender-associated differences in emergency department pain management. *Ann Emerg Med*. 1995;26:414–421.
37. Ribeiro SC, Kennedy SE, Smith YR, Stohler CS, Zubieta JK. Interface of physical and emotional stress regulation through the endogenous opioid system and mu-opioid receptors. *Prog Neuropsychopharmacol Biol Psychiatry*. 2005;29:1264–1280.
38. Robinson ME, Riley JL 3rd, Myers CD, Papas RK, Wise EA, Waxenberg LB, Fillingim RB. Gender role expectations of pain: relationship to sex differences in pain. *J Pain*. 2001;2:251–257.
39. Sadowski CA, Carrie AG, Grymonpre RE, Metge CJ, St John P. Access and intensity of use of prescription analgesics among older Manitobans. *Can J Clin Pharmacol*. 2009;16:e322–e330.
40. Safdar B, Heins A, Homel P, Miner J, Neighbor M, DeSandre P, Todd KH; Pain and Emergency Medicine Initiative Study Group. Impact of physician and patient gender on pain management in the emergency department—a multicenter study. *Pain Med*. 2009;10:364–372.
41. Smith YR, Stohler CS, Nichols TE, Bueller JA, Koeppe RA, Zubieta JK. Pronociceptive and antinociceptive effects of estradiol through endogenous opioid neurotransmission in women. *J Neurosci*. 2006;26:5777–5785.
42. Somerville BW. The influence of progesterone and estradiol upon migraine. *Headache*. 1972;12:93–102.
43. Spies-Dorgelo MN, van der Windt DA, Prins AP, Dziedzic KS, van der Horst HE. Clinical course and prognosis of hand and wrist problems in primary care. *Arthritis Rheum*. 2008;59:1349–1357.
44. Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the UW workforce. *JAMA*. 2003;290:2443–2454.
45. Stubbs D, Krebs E, Bair M, Damush T, Wu J, Sutherland J, Kroenke K. Sex differences in pain and pain-related disability among primary care patients with chronic musculoskeletal pain. *Pain Med*. 2010;11:232–239.

46. Stutts LA, Hirsh AT, George SZ, Robinson ME. Investigating patient characteristics on pain assessment using virtual human technology. *Eur J Pain*. 2010;14:1040–1045.
47. Unruh AM, Ritchie J, Mersky H. Does gender affect appraisal of pain and pain coping strategies? *Clin J Pain*. 1999;15:31–40.
48. Von Korff M, Dworkin SF, LeResche L, Kruger A. An epidemiologic comparison of pain complaints. *Pain*. 1988;32:173–183.
49. Von Korff M, LeResche L, Dworkin SF. First onset of common pain symptoms: a prospective study of depression as a risk factor. *Pain*. 1993;55:251–258.
50. Von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. *Pain*. 1992;50:133–149.
51. Von Korff M, Wagner EH, Dworkin SF, Saunders KW. Chronic pain and use of ambulatory health care. *Psychosom Med*. 1991;53:61–79.
52. Wijnhoven HA, de Vet HC, Picavet HS. Prevalence of musculoskeletal disorders is systematically higher in women than in men. *Clin J Pain*. 2006;22:717–724.
53. Wijnhoven HA, de Vet HC, Picavet HS. Sex differences in consequences of musculoskeletal pain. *Spine (Phila Pa 1976)*. 2007;32:1360–1367.