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## Gender Differences in Risk Factors for Aberrant Prescription Opioid Use

Robert N. Jamison<sup>\*,†</sup>, Stephen F. Butler<sup>‡</sup>, Simon H. Budman<sup>‡</sup>, Robert R. Edwards<sup>\*</sup>, and Ajay D. Wasan<sup>\*</sup>

<sup>\*</sup>Pain Management Center, Department of Anesthesia and Psychiatry, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

<sup>‡</sup>Inflexion, Inc., Newton, MA 02464 USA

### Abstract

This is a longitudinal predictive study to examine gender differences in the clinical correlates of risk for opioid misuse among chronic pain patients prescribed opioids for pain. Two hundred seventy five male and 335 female patients prescribed opioids for chronic noncancer pain were asked to complete a series of baseline questionnaires, including the revised Screener and Opioid Assessment for Pain Patients (SOAPP-R). After five months the subjects were administered a structured prescription drug use interview (Prescription Drug Use Questionnaire; PDUQ), and submitted a urine sample for toxicology assessment. Their treating physicians also completed a substance misuse behavior checklist (Prescription Opioid Therapy Questionnaire; POTQ). At 5-month follow-up, women showed higher scores on the PDUQ ( $p < 0.05$ ), while men had a higher incidence of physician-rated aberrant drug behavior on the POTQ ( $p < 0.05$ ). An item analysis of the SOAPP-R, PDUQ and POTQ showed that women tended to score higher on items relating to psychological distress, while the male patients tended to report having more legal and behavioral problems. These results suggest that risk factors associated with prescription opioid misuse may differ between men and women.

**Perspective**—Understanding gender differences in substance abuse risk among chronic pain patients is important for clinical assessment and treatment. This study suggests that women are at greater risk to misuse opioids due to emotional issues and affective distress, while men tend to misuse opioids due to legal and problematic behavioral issues.

### Keywords

Gender differences; substance abuse; chronic pain; opioids; addiction; aberrant drug behaviors

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There has been a growing use of opioids for the treatment of chronic pain, primarily from providers who prescribe them for chronic noncancer pain.<sup>18</sup> It is also estimated that between 3% and 16% of the general population has a substance use disorder,<sup>14,19,27,29</sup> and increasing notice has been given to the abuse of and dependence on prescription opioid medication.<sup>15, 17,18,28</sup> Some pain centers where opioids are prescribed for pain are overwhelmed with patients who are known or suspected to be abusing their prescribed opioids,<sup>25</sup> and many physicians prescribing pain medication have little training in addiction and/or aberrant drug-related

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<sup>†</sup>Corresponding author. Robert N. Jamison, Ph.D., tel: 617-732-9046; fax: 617-732-9046; RJamison@partners.org

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behavior.<sup>45</sup> These physicians prescribe opioids for patients with chronic pain without an indication of the level of risk for medication abuse.<sup>3</sup> While opioids may be an effective treatment for chronic pain, some providers are reluctant to prescribe opioids because of concerns over tolerance, dependence, and addiction. Optimal use of opioids must include an evaluation of risk associated with potential abuse of opioid medication.<sup>3,46</sup> Opioid misuse and aberrant drug-related behaviors may indicate a treatment adherence issue, or may signal a more serious addiction problem, if accompanied by a lack of control over use despite negative consequences.

There have been an increasing number of investigations on gender differences among chronic pain patients. Studies show that women have a higher incidence of pain<sup>40</sup> and report higher pain intensity compared with men.<sup>2,13,16</sup> Women are also prescribed opioids more often than men,<sup>20,24,34,36</sup> while men demonstrate more substance abuse behavior than women.<sup>21,35,47,48</sup> Women report more depression and sexual abuse than men, and these qualities have been shown to be risk factors for substance misuse.<sup>48</sup> Psychological distress especially has been associated with misuse of prescription medications both in the general population<sup>4</sup> and in chronic pain patients.<sup>23</sup> Overall statistics regarding opioid misuse among men and women, however, are conflicting.<sup>5,8,31,39</sup>

Little has been written about gender differences and assessment of misuse of prescription opioid medication. Given that some risk characteristics for opioid misuse (e.g., depression) are differentially prevalent as a function of sex, and that many features of substance abuse behavior are different in men and women,<sup>42</sup> it may be important to document whether the risk factors that predict opioid misuse are to some degree sex-specific. There are hints in the general substance abuse literature that some of the factors affecting relapse differ between the sexes, with relapse among women more closely tied to psychological distress and interpersonal processes compared to men.<sup>42</sup> The purpose of this study was to examine, among persons prescribed opioids for pain, gender differences in: 1) the rates and characteristics of problematic opioid use, 2) the profile of risk factors for potential opioid misuse, and 3) longitudinal predictive associations between risk factors and subsequent misuse behaviors. It was hypothesized that indices of substance misuse (e.g., physician documentation, aberrant urine screens, etc.) would be higher among men relative to women, and that the predictors of that misuse would differ across the sexes, with opioid misuse among women more closely related to affective distress.

## Materials and Methods

### Patient participants

The Human Subjects Committees of each of the hospitals approved this study's procedures. Chronic noncancer pain patients were recruited from pain management centers in five states (Massachusetts, New Hampshire, Pennsylvania, Ohio, and Indiana) as part of a larger study.<sup>7</sup> Patients prescribed opioids for their pain were informed about the study and invited to participate. All subjects signed an informed consent form and were assured that the information obtained through their questionnaire responses and from the urine toxicology screens would remain confidential and would not be part of their clinic record. Participant patients were paid with a \$50 gift certificate for completing the measures.

We were interested in capturing patient behaviors related to both *substance misuse* (defined here as the use of any addictive drug in a manner other than how it is indicated or prescribed), and *substance abuse* (defined as the use of any substance when such use is unlawful, or when such use is detrimental to the user or the others but is not unlawful).<sup>1</sup> Prescription opioid addiction in patients with pain is a primary, chronic, neurobiologic disease that is characterized by behaviors that include impaired control, compulsive use, continued use despite harm, and

craving.<sup>1</sup> Typically, research in this area uses a multi-modal assessment of substance misuse and abuse, and in the present study, aberrant drug-related behavior was defined as any behavior that suggested the presence of substance abuse or addiction. We utilized three modes of assessment, ranging from objective findings on urine toxicology assays, to quasi-objective physician ratings of aberrant drug-related behavior, to patients self-report during a structured interview.

### Baseline Measures

**Screener and Opioid Assessment for Pain Patients (SOAPP-R)<sup>7</sup>** —The SOAPP-R is a 24-item, self-administered screening instrument revised from the original SOAPP v.1.<sup>6</sup> used to help determine risk potential for aberrant drug-related behavior. Items are rated from 0=never to 4=very often, and their sum is the total SOAPP-R score. Test-retest reliability was .71 with a coefficient alpha of 0.74. The SOAPP-R has been shown to have good predictive validity, with an area under the curve ratio of 0.88 (95% confidence interval [CI], .81-.95). A cutoff score of 18 shows adequate sensitivity (.86) and specificity (.73). The SOAPP-R was empirically derived and incorporates subtle items. Support has been found for the internal reliability and predictive validity of the SOAPP-R.<sup>7</sup>

**The Brief Pain Inventory (BPI)<sup>10</sup>** —The BPI is a well-known, self-report, multidimensional pain questionnaire. The BPI provides information about pain history, intensity, and location as well as the degree to which the pain interferes with daily activities, mood, and influences enjoyment of life. Scales (rated from 1 to 10) indicate the intensity of pain at its worst, at its least, average pain, and pain “right now.” Test-retest reliability for the BPI reveals correlations of .93 for worst pain, .78 for usual pain, and .59 for pain now. Research suggests the BPI has adequate validity and has been adopted in many countries for clinical pain assessment, epidemiological studies, and in studies of the effectiveness of pain treatment. Although originally developed to assess cancer pain, the BPI has been validated for use for patients with chronic noncancer pain.<sup>37</sup>

**Marlow-Crowne Social Desirability Scale - Short Form (M-C)<sup>30</sup>** —This 13-item questionnaire was designed to measure social desirability, which is a test of response bias, i.e., whether a subject is more or less likely to tell you what you want to hear. This measure was completed by all subjects and was included to test items’ tendency to be associated with patients’ desire to answer questions in a socially desirable way. A lower score is indicative of less response bias. Reynolds<sup>30</sup> found this scale to be a viable substitute for the regular 33-item Marlow-Crowne scale.<sup>12</sup>

### End-of-study Measures

**Prescription Drug Use Questionnaire (PDUQ)<sup>11</sup>** —Self-report of patient status was obtained using the PDUQ. This 42-item structured interview is an acceptable substance abuse assessment measure for pain patients.<sup>33</sup> Based on the American Society of Addiction Medicine’s (ASAM) definition of addiction in chronic pain patients, the PDUQ is a 20-minute interview where the patient is asked about his or her pain condition, opioid use patterns, social and family factors, family history of pain and substance abuse syndromes, patient history of substance abuse, and psychiatric history. In an initial test of the psychometric properties of the PDUQ, the standardized Cronbach’s  $\alpha$  was .79, suggesting acceptable internal consistency. Compton and her colleagues suggested that subjects who scored below 11 “did not meet criteria for a substance disorder,” while those with a score of 15 or greater “had a substance use disorder.” For purposes of this study, those patients who obtained a score of 11 points or higher on the PDUQ interview were identified as being at risk for a substance use disorder.

**Prescription Opioid Therapy Questionnaire (POTQ)<sup>26</sup>**—This is an 11-item scale adapted from the Physician Questionnaire of Aberrant Drug Behavior completed by the treating clinician to assess misuse of opioids.<sup>26</sup> The items reflect the behaviors outlined by Chabal et al.<sup>9</sup> that were indicative of substance abuse. The participant patient's chart was made available to the treating physician to facilitate accurate recall of information. Providers answered yes or no to eleven questions indicative of misuse of opioids, including multiple unsanctioned dose escalations, episodes of lost or stolen prescriptions, frequent unscheduled visits to the pain center or emergency room, excessive phone calls, and inflexibility around treatment options. Patients who were positively rated on two or more of the items met criteria for prescription opioid misuse. Clinicians were asked to complete the POTQ for each of their patients at the end of the 5-month follow-up period.

**Urine toxicology screens**—Subjects were requested to provide a urine sample and inform staff of their current medication at the end of the study. The subjects were given a specimen cup and instructed to provide a urine sample (~30 -75 ml of urine) without supervision in the clinic bathroom. The research assistant (RA) at each center collected and shipped the sample to a central Quest Diagnostics lab ([www.questdiagnostics.com](http://www.questdiagnostics.com)). This was a radioimmunoassay screen followed by gas chromatography mass spectroscopy confirmation of positive results. The results of the urine toxicology were sent directly to the research team. The treating physician and the clinic did not have access to the results. The report included evidence of 6-MAM (heroin), codeine, dihydrocodeine, morphine, oxycodone, oxymorphone, hydrocodone, hydromorphone, meperidine, methadone, propoxyphene, buprenorphine, fentanyl, tramadol, amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, phencyclidine, and ethyl alcohol. Urine screen results were classified as either positive (illicit or non-prescription substances detected) or negative (clean urines).

### **Aberrant Drug Behavior Index (ADBI)**

Patients were classified as to whether they engaged in aberrant medication-related behavior, which relates positively to opioid medication abuse. Since there is no gold standard for identifying which patients are and which are not abusing their prescription medications,<sup>33</sup> we classified patients into categories of aberrant drug-related behavior by triangulating three perspectives, self report via structured interview, physician report, and urine toxicology results. The ADBI is based on positive scores on the self-reported PDUQ, the physician-reported POTQ, and the urine toxicology results. A positive rating on the PDUQ is an accumulated score higher than 11. A positive rating on the POTQ is given to anyone who has two or more physician-rated aberrant behaviors.<sup>6</sup> A positive rating from the urine screens is given to anyone with evidence of having taken an illicit substance (e.g., cocaine) or an additional opioid medication that was not prescribed. We chose not to count the omission of a prescribed opioid medication from the urine screen results as a positive rating because of multiple factors that can contribute to this result (e.g., subject ran out the medication before the urine screen). We also did not classify urines that were rejected by the lab. Urine screen results were confirmed based on chart review of prescription history and a comparison between self-report at the time of the urine screen and the toxicology report. Those with positive scores on the PDUQ were given a positive ADBI. If this score (PDUQ < 11) was negative, then positive scores on both the urine toxicology screen and on the POTQ ( $\geq 2$ ) was necessary to achieve a positive ADBI. This allowed for triangulation of data to identify those patients who admitted to aberrant drug-related behavior and those who underreported aberrant behavior (e.g., low PDUQ scores, but positive POTQ and abnormal urine screen results).

### **Statistical Analyses**

All data were analyzed with SPSS (Statistical Package for the Social Sciences; Chicago, IL) v.15.0. Relations among demographic data, interview items, and questionnaire data were

analyzed using Pearson product moment correlations, and Chi-square and t-test analyses depending whether the variables were ordinal or numerical. A discriminant function analysis was run to determine which items among the questionnaire items and which outcome data were most useful in identifying gender differences among the subjects. Predictive analyses using the SOAPP-R items involved t-tests performed separately in men and women.

## Results

### Patient characteristics

Six hundred twenty-two (N=622) patients who were taking long-term opioid medication for chronic noncancer pain participated in this study. The average age of the patients was 50.4 years (SD=13.0; range 21-89), 54.8% were women, 46.1% were married, 80.1% Caucasian, 72.5% had a high school education, and 66.8% reported low back pain as their primary pain site. Their average pain rating was 5.96 (SD=1.83; least=4.53, SD = 2.31; worst = 7.19, SD=2.15; now = 5.74, SD=2.29). The patients were prescribed immediate-release (53.6% oxycodone with acetaminophen; 15.5% hydrocodone; 9.5% oxycodone; 7.2% morphine; 7.1% hydromorphone; 3.6% codeine; 3.6% propoxyphene), and sustained-release (43.3% oxycodone; 22.7% methadone; 20.6% transdermal fentanyl; 13.4% morphine) opioids for pain. Twenty-seven percent were taking both long and short-acting opioids for pain.

Differences on demographic data, pain intensity ratings, and Marlow-Crowne scores between male and female subjects are presented in Table 1. Average scores on the Marlow-Crowne for all the subjects were 8.68 (SD=2.68; range 0-13). Scores on the PDUQ averaged 8.62 (SD=4.51; range 1-28) and physicians' ratings of drug misuse behavior on the POTQ averaged 0.97 (SD = 1.72; range 0-10). Twenty four percent of the patients (N= 115) had positive scores of two or more on the POTQ (males = 28.1%; females = 20.5%) while 29.1% (N = 130) scored an 11 or higher on the PDUQ (males = 23.8%; females = 33.3%). Three hundred fifty-six subjects (58.1%) had results from a urine toxicology screen and 37.1% of these (N=134) had positive urines. Most were positive for having evidence of an unprescribed drug (27.2%). Three percent were positive for cocaine. Fifteen percent had evidence of missing drug or the urine screen was rejected by the lab. As outlined in the ADBI criteria above, 158 (25.8%) of the subjects had missing data on two or more variables (PDUQ, POTQ, urine toxicology results) and as a result were excluded from the final analyses. Four hundred fifty-five (N=455; 74.2%) of the 613 patients with a positive or negative ADBI were included in the outcome analyses. Using the algorithm for the ADBI, 155 (34.1%) were positive and 300 (65.9%) were negative. No differences were found on the ADBI for gender, age, race, education, duration of opioids, or average pain intensity. Patients with a positive ADBI reported more often being single ( $X^2=11.02$ ;  $df=4$ ;  $p<0.05$ ), disabled because of the pain ( $X^2=11.14$ ;  $df=1$ ;  $p<0.001$ ), receiving disability benefits ( $X^2=12.61$ ;  $df=1$ ;  $p<0.001$ ).

Independent samples t-tests were run between male and female patients and scores on the PDUQ, POTQ, urine screen results, and the ADBI (Table 2). Females tended to report more misuse behaviors on the PDUQ while males were noted to have more physician-rated aberrant behaviors than females ( $p<0.05$ ). No gender differences were found on urine toxicology screens or on the combined ADBI results. Analyses were also run between those subjects who had an ADBI (complete; N=455) and those who did not have an ADBI (missing; N=158) on the demographic variables, and pain ratings to determine if there was a selection bias for those with incomplete data. All differences between those with complete data and those with missing data were nonsignificant except that those with a missing ADBI were younger (48.1 vs. 51.1;  $p<0.05$ ). Individual item analyses were also performed to identify in what ways male and female subjects differed on the individual items of the outcome measures (PDUQ and POTQ; Table 3). In general, those items used to assess risk for substance misuse that have to do with history of physical and sexual abuse, psychiatric diagnoses and history, and family concerns

were rated more frequently by women than by men, while men had more direct concerns about addiction and physician-rated unexpected positive urine screens.

We were also interested in examining gender differences on the SOAPP-R, since this had not been reported previously and the item analyses would lend some insight as to the ways men and women may differ in their risk for opioid misuse (Table 4). In general, those items used to assess risk for substance misuse that have to do with history of physical and sexual abuse, psychiatric diagnoses and history, and mood disorder were rated more frequently by women than by men. Additional analyses were run for a prospective prediction of problematic outcomes consisting of aberrant urine screens or physician-related aberrant behavior. The SOAPP-R item that was most predictive for women was counting pain pills (#6), while for men having close friends who use alcohol or drug (#13), having a bad temper ((#14), being consumed by the need for medication (#15), having legal problems ((#18), attending AA or NA meetings (#19), and history of treatment for drug or alcohol problems (#24) were each significantly predictive of problematic opioid use ( $p < 0.05$ ).

A discriminant analysis was performed incorporating all of the variables on the SOAPP-R by gender and resulted in a combined Wilk's Lambda of .905 ( $X^2=56.71$ ;  $p < 0.0001$ ) and a canonical correlation of .31. The 20 variables that indicated significant gender differences (2 listed on Table 1, 2 on Table 2, 8 on Table 3, and 8 on Table 4) were entered into a stepwise discriminant function analysis. The analysis yielded a single discriminant function, and resulted in correct classification of 70.2% of the patients with a Wilks' Lambda of .771 ( $X^2=92.00$ ;  $p < 0.0001$ ) and canonical correlation of .49. From this initial group of variables, three items from the substance misuse risk-assessment questionnaires included in the step-wise procedure were found to be the best in distinguishing between the genders, with positive responses in women being much more predictive of opioid misuse compared with men (Have you ever been physically or sexually abused? Has anyone ever suggested that your pain or other physical symptoms are caused by psychological problems? Did you have psychological or psychiatric problems prior to the onset of your chronic pain?).

We also evaluated the capability of individual SOAPP-R items (at baseline) to predict problematic outcomes (after 5 months), separately in men and women. For this analysis, because the SOAPP-R items and PDUQ items both involve self-report on the part of subjects (and thus share substantial method variance), we utilized only the non-self-report outcomes at follow-up: urine toxicology screening data, and physician report of problematic behavior on the POTQ. For this analysis, outcomes at follow-up were classified as "Aberrant" if either the urine screen contained at least 1 aberrant finding, or the POTQ score  $\geq 2$ , or both. In contrast, outcomes were classified as "Normal" if the urine screen did not contain an aberrant finding, and the POTQ score  $< 2$ . T-tests revealed that one of the SOAPP-R items was predictive only for women, while six of the items were only predictive for men. The item that was predictive for women referred specifically to the medication-specific behavior of counting pills, while the majority of items that were predictive for men appeared to be related to a history of drug and alcohol abuse (i.e., having close friends who abuse drugs or alcohol, a history of legal problems and treatment for drug and alcohol abuse).

## Discussion

The results of this study suggest that men and women demonstrate similar degrees of aberrant drug-related behavior, although gender differences were found in the risk factors for misuse of prescription opioids and in the way men and women are classified as having aberrant drug-related behavior. From the results of a structured interview (PDUQ), women tended to endorse items that are based more on emotional issues and affective distress compared with men. Conversely, men had higher scores on opioid misuse behaviors such as associating with others

who abuse drugs and alcohol and engaging in criminal behavior. The discriminant analyses showed that women with aberrant drug-related behavior were much more likely to admit to a history of sexual or physical abuse, or a prior history of psychiatric or psychological problems, than were men. These results are in agreement with past research that highlighted the importance of sexual and physical abuse history in predicting opioid misuse.<sup>47-48</sup> These same studies also showed that women with a significant history of anxiety and depression tend to do less well in properly managing opioids prescribed for pain, possibly because of the tendency to self-medicate a mood disorder using opioids. Men in the present study, on the other hand, reported fewer mood problems and seemed to be more prone toward behavioral problems leading to opioid misuse. It is especially noteworthy that specific problematic aberrant opioid-related behaviors, assessed at follow-up, were more frequent in women when assessed using a self-report interview (i.e., the PDUQ), but were more frequent in men when assessed by treating physicians. Given that many PDUQ items involve psychological distress, this finding may be explained, in part, by sex differences that are observed consistently across the lifespan: women are more likely than men to report distress.<sup>49</sup> In contrast, men are more likely than women to display problematic social and interpersonal behaviors,<sup>49</sup> and these may alert physicians to potential medication-related problems. It is also noteworthy that over a third of the subjects were positive on the ADBI and had abnormal urine screens, in keeping with previous studies.<sup>25</sup>

A smaller number of pain patients may have an addiction disorder and may require more intensive services from a substance abuse center. These individuals would likely endorse items that are much more problematic such as 'Do you believe that you are addicted to your pain medicine?', 'Have any family members ever expressed concern that you might be addicted to your pain medication?', and 'To your knowledge, have you ever been diagnosed as having an alcohol or drug problem.' Gender differences were not found on these items, suggesting that the frequency of a frank addiction disorder may be unaffected by gender. Indeed, other factors such as a personal or family history of substance abuse, age, and psychiatric history<sup>26-43-44</sup> may be substantially more powerful determinants than gender of the development of such opioid addiction. Surprisingly, some demographic factors were not useful in differentiating men and women. In particular, age, duration of opioid therapy, pain intensity, social desirability, and overall SOAPP-R scores were not predictive of gender differences. As found in this study and noted elsewhere, a greater percentage of women prescribed opioids for chronic pain tend to be unmarried (divorced or separated) compared with men.<sup>13</sup> It is unknown if this is related to the negative effects of chronic pain or if women prone to chronic pain also prefer not to be married. We also note that the incidence of headaches was found to be greater in women than in men in keeping with other studies.<sup>32</sup> Overall, however, few demographic differences were found among men and women and demographic factors were not found to play a role in predicting opioid misuse separately for men or women.

While the summary score of the SOAPP-R has been shown to be useful in predicting prescription opioid misuse,<sup>7</sup> gender differences were found on individual items of the SOAPP-R (Table 4). For instance, women who are more preoccupied about the number of their remaining opioids (pill counts) showed a greater likelihood of behavioral opioid misuse. In contrast, a number of individual SOAPP-R items were found to predict aberrant drug behavior for men. In particular, outward irritability, associating with others who have problems with drugs or alcohol, having legal problems, attending Alcoholics Anonymous meetings, and getting treatment for drug or alcohol problems were associated more with abnormal urines and physician-rated behavioral problems in men than in women. These results reflect, in part, the behavioral indicators of opioid misuse rather than self-report indices. A recent, comprehensive review of the published literature on predictors of prescription opioid misuse suggested that three clusters of variables appeared to be most strongly predictive: a history of substance abuse, a history of legal problems, and history of psychiatric disorders.<sup>41</sup> In the present study, items

related to a history of substance abuse and legal problems seem, at baseline, to be predictive of subsequent aberrant drug-related behaviors, but only among men.

Past research suggests that women tend to be more open, to admit to more problematic behavior, and to seek psychological treatment more than men.<sup>22,38</sup> It is possible that the results of this study reflect gender differences in willingness to admit to behavior captured through the self-reported SOAPP-R and PDUQ. Even though no gender differences were evident in the number of abnormal urine screens and in the ADBI, it is possible that women misuse their opioid medication in a different way compared with men. For instance, women may tend to overuse their prescription opioids because they are distressed and the medication is used to help stabilize their mood and to help them relax. Men may be affected more by environmental factors of associating with others who are prone to use illicit substances.

These results may be useful in guiding treatment decisions. Among women with evidence of significant affective distress, the treatment of their mood disorder could be seen as a priority in reducing the misuse of oral opioids. Future studies may demonstrate that women respond better than men to antidepressant medication and individual and group cognitive/behavioral therapy. Education about avoiding the use of opioids as a way to deal with anxiety and sleep disturbances due to stress may also be important. Conversely for men, closer monitoring of behavior including monthly urine screens, pill counts, and compliance monitoring may have greater efficacy in reducing the misuse of opioids. Stressing the importance of complying with the opioid therapy agreement, of not running out of medication early, and insisting on interventions to keep all opioid medications secure with behavioral consequences of misuse such as more frequent dosing and clinic visits, may be more useful in reducing aberrant drug behavior among men.

There are limitations of this study that deserve mention. First, the results are correlational, and no causal relationship can be claimed between gender and showing aberrant drug-related behavior. Also, the patients were recruited from multidisciplinary pain centers, were older, mostly disabled, and had pain for many years. These results may not generalize to pain patients who are younger, less chronic, or cared for in primary care settings. Second, we did not analyze the outcome variables based on type of opioid used. General classes of opioids used at the initial onset of the study were recorded, but exact medications and doses were not recorded. It is possible that gender differences existed on the type of medication used and misused. Third, although objective measures such as toxicology screens and physician ratings were obtained, much of the information in determining aberrant drug behavior was based on self-report and there was likely a tendency to under-report on these measures. Also, gender biases of the physicians may have influenced the results of their ratings of prescription opioid misuse, although this could not be directly confirmed. Finally, not all subjects completed the measures and many had missing urine toxicology screens. Reasons for missing urine toxicology reports included discontinuation of treatment and not returning to the clinic, protocol omissions by the clinic staff, and patient refusal. We did not assess the exact reason for missing urines in each clinic. Although those who were younger tended to have missing data more often than older subjects, we do not believe that this significantly biased the results. Future studies in which all subjects are tracked for a period of time with limited missing data are needed.

Despite these limitations, the results of this study suggest that the correlates of problematic opioid use may differ as a function of sex, with women more likely to endorse psychological distress leading to aberrant drug-related behavior and men less likely to report emotional issues but more likely to have a history of substance abuse and legal problems that predispose them to misuse. A recent review has concluded that identifying chronic pain patients at the greatest risk for opioid abuse and misuse remains a difficult challenge, and requires much additional research.<sup>41</sup> We hope that the present findings may help to guide additional work evaluating



potential sex-specific predictors of such misuse. Given the prominence of sex differences in a variety of pain-related processes,<sup>16</sup> we may eventually arrive at a method for tailoring risk assessment and risk-reducing interventions in part as a function of gender. Such a conclusion must, of course, await additional research in this area.

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**Table 1**

Patient Demographic and Descriptive Characteristics between Male and Female Patients (N=613)

Variable	Male (N= 276)	Female (N = 335)	p
Age	50.19 ±12.30	50.52 ±13.62	NS
Married (% yes)	54.3	40.3	X <sup>2</sup> =22.59***
Race (% Caucasian)	84.8	77.6	NS
High school graduate (% yes)	88.4	91.3	NS
Recv disability (SSI, WC; % yes)	57.6	56.0	NS
Litigation (% active)	9.9	10.7	NS
Pain site (% low back)	64.5	63.3	NS
Pain site (% head)	5.8	10.7	X <sup>2</sup> =8.28*
Pain relief from meds <sup>‡</sup> (%)	33.7±28.15	30.7±30.72	NS
Pain adequately treated (% yes)	78.2	72.9	NS
Yrs taking opioids	6.63 ±11.73	5.44 ±8.25	NS
Pain: <sup>‡</sup> Worst (24 hrs; 0-10)	7.16 ±2.10	7.20 ±2.20	NS
Least (24 hrs; 0-10)	4.38 ±2.24	4.60 ±2.35	NS
Average (24 hrs; 0-10)	5.89 ±1.93	6.00 ±1.75	NS
Now (0-10)	5.57 ±2.22	5.86 ±2.34	NS
Marlow-Crowne Score (total)	8.45 ±2.63	8.86 ±2.71	NS
SOAPP-R	24.97±11.44	26.39±11.89	NS

NS = nonsignificant

<sup>‡</sup> 0=no pain; 10=pain as bad as you can imagine<sup>‡</sup> 0=no relief; 10=complete relief

\* p&lt;0.05

\*\*\* p&lt;0.001

**Table 2**

Gender Differences on the Prescription Drug Use Questionnaire (PDUQ), Physician's Opioid Treatment Questionnaire (POTQ), Urine Toxicology Results, and the Aberrant Drug Behavior Index (ADBI)

Variable	N	Male (N=217)	Female (N=263)	p
PDUQ total	(480)	7.83 ±3.80	8.74 ±4.48	t=2.31*
POTQ total	(480)	1.14 ±1.82	.82 ±1.63	t=1.99*
Abnormal Urine	(355)	33.6%	37.4%	NS
ADBI <sup>‡</sup>	(453)	31.0%	36.7%	NS

\* p<0.05

<sup>‡</sup> Aberrant Drug Behavior Index = (positive scores on the PDUQ, or positive scores on the POTQ and urine toxicology screen)

**Table 3**

Differences Between Male and Female Patients on Individual Items of the Prescription Drug Use Questionnaire (PDUQ)

Variable	Male (N=275)	Female (N=335)	p
<b>Items Favoring Women:</b>			
<i>PDUQ (% yes):</i>			
Phys/sexual abuse history	11.5	32.1	$X^2=25.90^{***}$
Have psych problems	16.6	34.5	$X^2=17.93^{***}$
Pain caused by psych problems	3.1	14.3	$X^2=15.72^{***}$
Diagnosed with a psych problem	45.1	60.3	$X^2=10.21^{**}$
Saved unused meds	24.0	36.3	$X^2=7.70^{**}$
Family concerned re meds	6.8	14.7	$X^2=6.73^{**}$
<b>Items Favoring Men:</b>			
<i>PDUQ (% yes)</i>			
Addicted to pain meds	27.5	17.5	$X^2=6.30^*$
<i>POTQ (% yes)</i>			
Positive urine screen	15.3	8.4	$X^2=5.43^*$

\*  
p<0.05\*\*  
p<0.01\*\*\*  
p<0.001

**Table 4**

Differences between Male and Female Patients on Individual Items of the Screener and Opioid Assessment for Pain Patients (SOAPP-R)

Variable	Male (N=275)	Female (N=335)	p
<b>Items Favoring Women:</b>			
<i>SOAPP-R (0-4) <sup>‡</sup>:</i>			
Things are too overwhelming	1.65±	1.86±	t=3.55***
Got into arguments/got hurt	1.25±	1.65±	t=3.21**
Impatient with your MDs	1.55±	1.85±	t=3.12**
Sexually abused	.62±	.83±	t=2.56*
Concerned people judge you	1.98±	2.26±	t=2.42*
<b>Items Favoring Men:</b>			
<i>SOAPP-R (0-4) <sup>‡</sup>:</i>			
History of being arrested	.59±	.37±	t=3.51***
Had a bad temper	.91±	.69±	t=2.88**
Friends w/ alcohol/drug problems	.98±	.78±	t=2.37*

<sup>‡</sup>How often are you...

\* p<0.05

\*\* p<0.01

\*\*\* p<0.001