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Physical Pain, Common Psychiatric and Substance Use Disorders, and the Non-Medical Use of Prescription Analgesics in the United States

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Abstract

This study investigated the link between physical pain and non-medical prescription analgesic use (NMPAU), as well as the degree to which this association may vary by the presence of psychiatric and substance use disorders. Data were from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative, in-person probability sample of adults (*n*=43,093) aged 18 or older in the United States (2001–2002). Face-to-face interviews were used to gather information on past-year levels of physical pain (i.e., low, medium, high), in addition to DSM-IV classifications for mood, anxiety, substance use problems (i.e., abuse and/or dependence), and personality disorders. Within the analytic sample of those with valid data (n=42,734), the past-year rate of NMPAU was 1.8%, of which 20% met the DSM-IV criteria for abuse/dependence. Among past-year NMPAUs, 53% was incidental (e.g., less than monthly), but daily use was substantial (13% of NMPAUs). Accounting for our target confounding factors, pain was positively associated ($p<.05$) with an increased probability of non-disordered (i.e., no abuse and/or dependence) and disordered (i.e., abuse and/or dependence) NMPAU in the past year. Within each level of pain, the odds of past-year non-disordered and disordered NMPAU were significantly higher ($p<.05$) for those with disordered alcohol use compared with non-disordered users. This pattern was similar for illicit drugs, although marginally significant ($p=.060$) and specific to disordered NMPAU. In contrast, psychiatric disorders increased the probability of both types of NMPAU, but these associations did not differ by levels of pain. These findings suggest that pain is an independent risk factor for non-disordered and disordered NMPAU, yet its effects are substantially modified by patterns of substance use.

Keywords

Prescription drug abuse; opioids; pain reliever; psychiatric disorders; substance use disorders

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1. INTRODUCTION

Evidence from numerous drug surveillance sources indicates that non-medical use (NMU) of prescription medications, including analgesics, is on the rise (Blanco et al., 2007; Johnston et al., 2004; SAMHSA, 2006c), both nationally and internationally (Kuehn, 2007). According to the 2006 National Survey of Drug Use and Health (NSDUH), prescription analgesics account for the largest percentage of NMU, where approximately 75% of NMU involves prescription analgesic medications (Colliver et al., 2006). Although prescription analgesics are generally acknowledged to be safe and effective treatment options when taken as directed by a physician, concerns have arisen within the medical community about the possibility of Non-Medical Prescription Analgesic Use (NMPAU), which is use occurring outside of the therapeutic context (Cicero and Inciardi, 2005; Mitka, 2000). More specifically, NMPAU may encompass use without a prescription, as well as *with* a prescription but in a manner not intended by a physician. While a balanced approach to addiction risk management and appropriate access to analgesic pain relievers is needed, a more thorough understanding of the prevalence and risk for non-medical use is vital to improving our ability to discern those with the greatest risk of becoming addicted to prescription analgesics (Dowling et al., 2006).

Research investigating the links between pain and the development of NMPAU has been sparse. In one of the earliest works, a meta-analysis conducted by Fishbain et al. (1992) estimated that the rates of NMPAU among individuals suffering from chronic pain ranged from 3.2% to 18.9% (Fishbain et al., 1992). Other researchers have found no association between chronic pain and NMPAU (Edlund et al., 2007; Ives et al., 2006). This suggests that additional work is needed to establish the nature of the association between levels of pain and NMPAU. A diverse range of risk factors should also be included, because the relation between pain and NMU may be spurious and explained by factors that influence both pain and NMU.

Substance use history appears to be among the most potent risk factors for NMPAU, as evidenced by prior studies (Carise et al., 2007; Davis and Johnson, 2008; Potter et al., 2004; Weaver and Schnoll, 2002). For example, in an analysis of the data used in the current study, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), McCabe and colleagues observed that NMPAU was highest among individuals who reported binge drinking or who had an alcohol use disorder (McCabe et al., 2006). However, few studies focusing on NMPAU have incorporated measures of pain. Ives et al. (2006) used a four-item measure of self-reported physical pain, which was unrelated to NMPAU over a 1-year period. They found, however, that chronic pain patients who reported NMPAU were more likely to have a past problem with cocaine or a previous drug conviction compared with chronic pain patients who did not report NMPAU. No measures of psychiatric disorders were included, and the measure of NMPAU did not consider differences between non-disordered and disordered use.

The link between NMPAU and psychiatric disorders other than substance use, specifically, mood, anxiety, and personality disorders, is also well established. Huang et al. (2006) explored the role of psychiatric comorbidity and NMPAU using the NESARC data, and found that individuals with a lifetime history of NMPAU abuse or dependence were 3 times as likely to have a lifetime anxiety disorder than were those without an NMPAU disorder (Huang et al., 2006). Other work using the NESARC data has reported that rates of anxiety disorders were prevalent among a polydrug class that included lifetime prescription drug abuse (Agrawal et al., 2007). None of these studies, however, included pain in the pathway linking psychiatric disorders to the NMPAU.

One exception was a study conducted by Edlund and colleagues (2007), which used a multivariate approach to control for the potentially confounding effects of mental and substance

use disorders on the relation between pain and NMPAU (Edlund et al., 2007). Their study examined rates of NMPAU and dependence among Veterans Affairs (VA) patients in the southern United States. Substance use and psychiatric disorders were diagnosed using a chart extraction of patient diagnoses. The authors identified three conditions (back pain, migraine, and arthritis) associated with high physical pain. In adjusted models, nonopioid substance use was the strongest predictor of NMPAU, followed by mental disorders. Although nonsignificant, the presence of back pain or arthritis elevated the risk of disordered NMPAU. Note that this study was limited to a VA treatment-seeking sample and did not examine non-disordered levels of NMPAU nor differences in NMPAU by levels of pain.

We can summarize the nature of the relation between pain and NMPAU as follows: (a) the association is largely inconsistent across studies; (b) rates of NMPAU are higher among those with substance use and psychiatric disorders; and (c) levels of physical pain are higher among those with psychiatric and substance use disorders compared with those without these disorders (France, 1989; Gureje et al., 2008; Kessler et al., 2008; King, 1995; Sheu et al., 2008). Taken together, it is possible that the association between physical pain and NMPAU may be spurious because it shares a common underlying cause, perhaps due to psychiatric disorders and/or substance use. However, prior work has not included quantitative assessments of pain in relation to a comprehensive set of factors as an approach to understand the underlying mechanisms linking pain and NMPAU. Past studies have also primarily been limited to patient samples, or failed to compare the effects of risk factors across different usage types of NMU, such as (1) use defined by diagnostic abuse and/or dependence and (2) lower levels of use that may be defined as non-disordered because of infrequent use at lower quantities relative to disordered use. However, non-disordered use is still harmful because it exposes the user to many dangerous side effects, which may increase as these prescription medications are taken in combination with other drugs.

To fill these conceptual gaps, the purpose of the current paper is to first identify differences in rates of NMPAU by levels of pain, and how these associations may persist when controlling for possible confounders related to substance use and psychiatric disorders using cross-sectional data derived from the NESARC. Although cross-sectional data cannot be used to isolate the causal linkages, it can be used to help establish the nature of the relations in terms of the direct effect of a given factor on an outcome, such as pain, accounting for candidate confounding factors, thereby excluding a spurious relationship. A second aim entails examining whether the association between pain and NMPAU is increased or decreased by the presence of psychiatric and substance use disorders that have been previously documented as risk factors for NMPAU. Cross-sectional studies are also useful for identifying effect modification, as temporal priority between the risk factor (e.g., pain) and its modifying factor (e.g., psychiatric disorders or substance use) need not be established. Finally, we also examine these questions in relation to two types of NMPAU: non-disordered use and disordered use, given that the relations may vary by levels of use.

2. METHODS

2.1 Sample

The National Institute on Alcohol Abuse and Alcoholism (NIAAA), with support from the National Institute on Drug Abuse (NIDA), conducted the NESARC to produce data on the prevalence, risk factors, and consequences of alcohol abuse (Grant et al., 2003a; Grant et al., 2004). The study also contains comprehensive assessments of common mental and substance use disorders. The NESARC sampling frame included the noninstitutionalized population aged 18 or older residing in the contiguous United States, the District of Columbia, or Hawaii. In addition to the enumeration of family dwellings (e.g., houses, apartments) in the sampling frame, the following group-quarters housing units also were included: boarding houses,

rooming houses, nontransient hotels and motels, shelters, facilities for housing workers, college dormitories, and group homes, including elder care facilities. The design also oversampled minority populations to increase precision, ensure adequate cell sizes for variables with low event rates, and ensure representation of major racial and ethnic categories.

The sampling weights provided in the NESARC public use data set were constructed to adjust for probability of selection into the study and nonresponse. The overall response rate was 81%. Post-stratification weights were derived from the 2000 U.S. Census to ensure that the sample was representative of the U.S. population, based on the sampling targets noted in the previous paragraph. Between August 2001 and May 2002, 180 interviewers from the U.S. Census Bureau conducted in-person interviews using computer-assisted interviewing (CAI) methods; the research protocol, including the informed consent procedure, was approved by the Institutional Review Boards from the U.S. Census Bureau and the U.S. Office of Management and Budget (Grant et al., 2003b). These efforts resulted in an unweighted sample size of 43,093.

2.2 Instrument and Measures

The NESARC assessed past-year non-medical use of prescription opioid pain relievers (excluding methadone and heroin) using a single question: “In the past year, did you use [drug] without a prescription, in greater amounts, more often, or longer than prescribed, or for a reason other than a doctor said you should use them?” The instrument also captured information on other substances of abuse, including alcohol, marijuana, cocaine, hallucinogens, inhalants, and the NMU of other prescription medications, including stimulants, benzodiazepines, and tranquilizers. Psychiatric diagnoses aligned with common DSM-IV diagnoses were generated using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-version 4 (AUDADIS-IV) (Grant et al., 2003b). This instrument is a structured diagnostic interview designed to be administered by lay interviewers, and studies have shown acceptable levels of reliability for psychiatric disorders (Grant et al., 2003a).

To increase sample size for conditions that occurred in the past year, we collapsed disorders within broad classes of mood (major depressive disorder, dysthymia, bipolar I and II) and anxiety (generalized anxiety disorder, panic disorder, with and without agoraphobia, social phobia, and specific phobia). For these disorder classes, substance-induced and medical illness–induced exclusionary criteria were followed. We also included adult antisocial personality disorder, given its strong and consistent relation to stages of drug use found in prior studies (Cottler et al., 1995; Kidorf et al., 2004).

The assessments for past-year (i.e., previous 12 months) substance use problems were categorized by type of substance, including alcohol, illicit drugs (i.e., marijuana, crack/cocaine, heroin, hallucinogen, inhalants) and prescription drugs (i.e., benzodiazepines, tranquilizers, stimulants). For prescription drugs and illicit drugs, three patterns of use were created: (a) no past-year use; (b) non-disordered use in the past year, defined by a failure to meet the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV) criteria (APA, 1994)) for abuse and/or dependence on prescription analgesics; and (c) disordered use in the past year, defined by meeting the criteria for abuse and/or dependence. Given the licit nature of alcohol, only two patterns were of interest: (a) no use/any use; and (b) abuse/dependence in the past year.

Physical pain was assessed using a subscale from the 12-item short form self-report scale (SF-12) of health-related quality of life (HRQL) (Ware et al., 1996). The physical pain subscale uses a single item, measured on a five-point scale (e.g., not at all, a little bit, moderately, quite a bit, and extremely) to capture the amount in which physical pain interferes with daily activities. The psychometric properties of the SF-12 instrument have been demonstrated in numerous empirical studies, and the instrument is designed to produce scores that are normed

to the U.S. population (Ware et al., 1996). The normed scores are derived from a Item Response Theory model, and represented as t-scores that are linear transformations with a mean of 50 and a standard deviation of 10 in the general U.S. population. Following the SF-12 scoring guidelines, the continuous diagnostic criteria were collapsed to classify pain into three levels, corresponding conceptual categories of interference based on high (extremely/a lot of interference), moderate (moderate amount of pain interference) and low (a little bit/not at all interference).

2.3 Analyses

We first estimated the prevalence of stages of past-year NMPAU by self-reported levels of physical pain using cross-tabulations. The corresponding case-weights were used to create estimates of the U.S. population prevalence rate for adults aged 18 or older. We report a rounded estimate in thousands, given the lack of precision associated with the calculation of a more specific estimate. We also examined respondents' self-reported frequency of use, measured in number of days of NMPAU in the past year. We collapsed the response options into four categories: 1 to 2 days per year, a couple of times per year, monthly, and every day or almost daily.

Following our research questions, we characterized the independent associations between self-reported physical pain and patterns of past-year NMU, controlling for potentially confounding effects of *past-year* psychiatric and substance-use risk factors. We chose to examine the primary outcome of NMPAU as an ordered response variable representing types of use (i.e., no use, non-disordered use, disordered use). We used the standard logistic regression model, using a forced entry of all independent variables simultaneously, to estimate the conditional probability of being in a particular stage relative to a prior stage in the past 12 months. These probabilities, and corresponding odds ratios, were estimated as a function of the covariates of interest.

Two specific comparisons were identified. First, we examined whether there were differences between those with no NMPAU in the past year and those using at non-disordered levels. Second, we examined the differences between those meeting the criteria for abuse or dependence (i.e., disordered use) and those endorsing any lower pattern of use (i.e., non-disordered use and no-use) in the past year. These estimates were calculated via the standard logistic model, and the demographic control variables included age, sex, race, education, marital status, and income. To focus the presentation of results on the main study variables, the effects of the demographic controls are not shown in the tables.

Next we created interaction terms to determine whether the associations between pain and patterns of NMPAU varied by levels of each past-year psychiatric and substance-use risk factor. Similar to our approach above, we estimated these models using the standard logistic model. Because the risk factors were ordinal measures, multiple interaction terms were required to estimate the interactive effect between separate levels of each risk factor and three levels of physical pain. We calculated an overall-effect test (Wald-F test) that captured the simultaneous effect of these interactions. Six sets of interaction terms were tested, one for each psychiatric and substance-use characteristic. For statistically significant interaction tests, the expected conditional probabilities were then calculated for each level within a given factor. This coefficient is interpreted as the probability, ranging from 0–1.0, of the expected response for an individual conditional on his belonging to a particular group (e.g., presence of high pain and an alcohol use disorder). This coefficient is adjusted for the mean values on all control variables (e.g., race, gender) included in the model that is used to derived the expected probability value. Population percentages may be recovered by multiplying the conditional probabilities by 100.

Less than 1% of the data was missing for key study variables (e.g., self-reported pain), and no significant differences were observed between missing (n=359) and complete (n=42,734) cases on available demographic and psychiatric characteristics. All descriptive and inferential analyses were conducted using SUDAAN (release 9.2,) using the sample weights and Taylor series linearizaton to account for the multistage probability sampling design.

3. RESULTS

Overall, the prevalence of NMPAU (Table 1) for prescription pain relievers in the past year was 1.8%, which translates into an estimated 3.7 million adults. The majority of these cases (80%, 2.96 million) did not meet the criteria for disordered use, defined by DSM-IV abuse and/or dependence. However, approximately 20% (733,000) of those who had used prescription analgesics non-medically in the past year did meet the criteria for disordered use, although the percentage of the total adult population is relatively small (<1%). Slightly less than 50% of all NMPAUs consumed on multiple occasions, such as monthly or more (1.7 million). Less than one-third of all NMPAUs (1.2 million) consumed only once or twice in the past year.

We examined the rates of NMPAU by different levels of pain (Table 1), and observed a positive association between pain and the rates of NMU ($p<.05$). Within the group exhibiting high pain, approximately 2.7% reported any NMPAU, compared with 2.4% in the moderate pain group and 1.3% in the no or minimal pain group. This represented a population estimate of 683,000, compared with 1.1 million NMPAUs with moderate pain and 1.8 million NMPAUs with no-or-minimal-pain. Similarly, disordered use was more common in the high-pain group (.75%) compared with the moderate (0.56%) and no-or-minimal-pain groups (0.21%).

Table 2 reports the multivariate associations between pain, psychiatric and substance-use risk factors, and types of past-year NMPAU. More specifically, the strong and positive associations between physical pain and NMPAU observed in the bivariate cross-tables (Table 1) remained significant after introduction of the substance use and psychiatric correlates. Compared with those classified as having no physical pain, the odds of non-disordered NMPAU in the past year were significantly higher for those with moderate (O.R.=1.66, 95% C.I.=1.22–2.25) and high (O.R.=2.18, 95% C.I.=1.56–3.03) levels of pain. This pattern was similar for disordered use, where compared with those with no physical pain, use was higher for those with moderate (O.R.=2.38, 95% C.I.=1.17–4.81) and high (O.R.=3.97, 95% C.I.=2.06–7.64) levels of physical pain. Overall, this suggests that physical pain exerts an independent influence, net of potentially confounding influences of demographic, psychiatric, and substance-use characteristics.

Substance use patterns also were significantly related to types of NMPAU, with prescription drugs (i.e., stimulants, benzodiazepines, tranquilizers) among the strongest predictors of both non-disordered and disordered NMPAU. Findings for the associations between psychiatric disorders and types of NMPAU, also shown in Table 2, reveal that mood disorders and anti-social personality disorder (ASPD) were not significantly related to non-disordered NMPAU ($p>.05$), but were positively and significantly associated ($p<.05$) with disordered NMPAU. In contrast, anxiety disorders were positively and significantly associated ($p<.05$) with non-disordered NMPAU but were not significantly related to disordered use. More specifically, anxiety disorders appeared to be more strongly associated with lower levels of NMPAU whereas mood disorders and ASPD were more strongly predictive of more harmful levels of use.

The results of the interaction tests between psychiatric and substance-use disorders by levels of pain are presented in Table 3. None of the interactions between psychiatric disorders and

levels of pain were statistically significant for either type of NMPAU. Recall that the use of other prescription medications non-medically was the strongest predictor of both types of NMPAU. However, these effects did not vary by levels of pain, for either non-disordered (Wald-F=0.37, *p*=.689) or disordered (Wald-F=2.59, *p*=.200) levels of NMPAU.

The findings for the interaction tests between illicit drug use and physical pain revealed only a marginally significant effect and only for disordered NMPAU (Wald-F=2.39, *p*=.061) but not for non-disordered use (Wald-F=1.73, *p*=.161). The probability of past-year disordered NMU was highest among those with high pain and disordered illicit drug use (pr=.04) compared with all other combinations of pain and types of illicit drug use. Additional inspection of the expected conditional values suggested that the probability of having high pain with no past-year illicit drug use was significantly higher (pr=.004) than for those with low pain and disordered use of illicit drugs (pr=.011).

The presence of an alcohol-use disorder significantly modified the risk of self-reported physical pain in the likelihood of both types of past-year NMPAU. To illustrate, the rates of NMPAU were significantly higher among those with an alcohol-use disorder compared with those without an alcohol-use disorder within each level of pain. The effect also appeared stronger for disordered NMPAU compared with non-disordered NMPAU, given that the magnitude of the differences in the predicted probabilities were substantially larger for disordered NMPAU.

4. DISCUSSION

This study contributes new knowledge regarding the nature of the association between self-reported physical pain and NMPAU. It goes beyond prior research by (1) examining a comprehensive range of psychiatric disorders and substance-usage patterns, (2) exploring different stages of NMPAU (e.g., non-disordered and disordered), and (3) using a population-based sample of U.S. adults.

Four key findings are of relevance. First, we observed a linear association between levels of pain and NMPAU for both non-disordered and disordered use. Second, this relation persisted upon introduction of potentially confounding substance-use and psychiatric characteristics, suggesting that pain is independently associated with NMPAU. Third, substance use was among the most potent factors associated with NMPAU, and its effect was modified by levels of pain. Fourth, psychiatric disorders were uniquely related to types of NMPAU. The presence of an anxiety disorder was associated only with non-disordered NMPAU, whereas mood and ASPD were associated only with disordered NMPAU. Associations with NMPAU also were not affected by levels of pain. The implications of each of these findings are discussed further below.

4.1 Association Between Pain and NMPAU

This study reveals a positive relation between pain and NMPAU, with increases in pain associated with a higher probability of NMPAU. Although NMPAU also appeared more common among those with *high physical pain*, this group accounted for a smaller percentage of total NMPAU in the U.S. Our findings are inconsistent with prior research that has failed to detect an association between the presence of pain and the NMPAU specifically (Edlund et al., 2007; Ives et al., 2006). As noted in the Introduction, our results may differ because much of this prior research has focused on chronic pain, using clinical samples, whereas the current study employed a community-based sample with greater variability in the range of self-reported pain. Furthermore, the relation between pain and NMPAU was consistent across stages of use, and persisted after controlling for a large range of confounders. These findings are important because they exclude the possibility of a spurious relation due to comorbidity between pain with psychiatric and substance-use disorders.

An important consequence of the cross-sectional study design is that we can only document the existence of an independent contribution of pain to NMPAU and are unable to examine the temporal course between pain and NMPAU. Respondents reporting current NMPAU may have been prescribed medications for a legitimate medical condition and, over time, began using these medications non-medically. Conversely, it is also plausible that respondents began NMPAU and then developed subsequent medical conditions associated with higher levels of physical pain. Although longitudinal data may shed light on these causal pathways, further investigations should also focus on the motivations for NMPAU. The independent effect of pain may suggest that patients with legitimate medical conditions are undertreated and therefore, are using medications outside of the therapeutic context to treat pain symptoms. However, a study conducted by Tsao et al. (2007) reported that among an HIV-positive sample, high levels of pain were associated with non-medical use specifically for other reasons than to treat pain (Tsao et al., 2007). Thus, self-medication of pain may be only one motivation for NMPAU; other motivations may include the feelings of euphoria and disassociation.

4.2 Substance-Use Patterns

Although the nature of the relations between pain and NMPAU is likely complex, it also appears to vary by substance-use pattern. Disordered alcohol use (e.g., abuse and/or dependence) modified the associations between pain and NMPAU for both stages of NMPAU. However, illicit drug use/disorders were related only to disordered NMPAU. One explanation is that alcohol-use problems typically have higher prevalence rates than either illicit drug abuse or dependence (SAMHSA, 2006c). Compared with alcohol, illicit drug use may reflect a greater level of deviance, and the combination of non-medical use of prescription analgesics with other drugs may indicate more compulsive drug-seeking behavior. In additional analyses not shown, we confirmed that rates of non-disordered NMPAU were higher for those with alcohol abuse compared with those with alcohol dependence, drug abuse, and drug dependence, decreasing respectively. Conversely, rates of disordered NMPAU were lowest among alcohol abusers. Overall, these findings highlight differences in risk for NMPAU among specific subgroups of substance users. One topic of speculation would be that a high level of alcohol in the system is associated with loss of motor control (e.g., falling down) and disinhibition that sometimes result in aggression and fighting. Occasional use of analgesics may occur among alcohol abusers or those dependent on alcohol in such instances to relieve pain resulting from the consequences of alcohol-related behaviors.

4.3 Mood, Anxiety, and Anti-Social Personality Disorders

Our results indicate that the presence of psychiatric disorders other than substance use related disorders, was associated with a higher risk of NMPAU. While these findings are consistent with prior research (Huang et al., 2006; Regier et al., 1990), the specificity of these relations to types of NMPAU is a unique contribution of this work. There is a high co-occurrence between mood and anxiety disorders (Kessler et al., 2008). Yet we observed that anxiety disorders were associated solely with non-disordered use, whereas mood disorders were linked only to disordered use. Individuals with mood disorders may use prescription analgesics in higher doses and over longer periods of time to deal with the unrelenting symptoms, thus increasing the probability of addiction. In addition, somatic complaints are often a common component of mood disorders and may motivate NMPUA (Dowling et al., 2006). In contrast, the symptoms of anxiety disorders may include less physical pain, be more situation-specific, and wax and wane over time.

The finding that the association between pain and NMPAU did not differ by mood and anxiety disorders seems to contradict a recent study by Sullivan et al. (2005). Using the Healthcare for Communities Study (HCC), physical pain was measured with the SF-12 measure and dichotomized into high (extremely/a lot) and low (moderately/a little bit/not at all). Regular

use of prescription opioids was the outcome, but the question in the HCC restricted use to prescriptions that were prescribed for the respondent. Interactions were observed such that rates of prescription opioids were highest among those with high pain and a mental health (MH) disorder (22.3%); followed by high pain, no MH disorder (10.8%); low pain/MH disorder (5.6%); and low pain/no MH disorder (1%). Their findings, which used a community-based sampling design similar to that of the NESARC, suggest that those with a psychiatric disorder and high levels of pain were the most likely group to receive and use prescription pain medications. Our findings, however, indicate that these differences in rates of exposure are not necessarily reflected in rates of NMU.

4.4 Limitations

Several limitations should be considered when evaluating findings from this study. Cross-sectional data are always of concern in that this design greatly limits causal inferences. As noted above, we were unable to resolve whether pain occurred temporally prior to the initiation of psychiatric disorders and substance use or was subsequent to the onset of these conditions. Our analyses excluded those reporting that their psychiatric disorders were the direct cause of a medical condition as an attempt to place the effect of pain on the pathway temporally prior to psychiatric disorders. The link between a medical condition and the onset of a psychiatric condition was self-identified by the respondent in the survey question, and is certainly subject to bias. Yet, this provides a tenable approach to attempt to control for causal ordering. The NESARC is a longitudinal study, and the release of the second wave of data (circa fall 2008) will permit a more thorough probing of the temporal ordering of onset and course. However, even the 3-year time lag between waves may not allow for sufficient time to accrue a large and diverse sample size of individuals with different patterns of NMU, pain perceptions, and psychiatric and substance use disorders to fully replicate this work. Therefore, additional longitudinal studies are needed to evaluate the effects of a smaller set of risk factors identified by our work on stages of NMPAU.

Second, physical pain was derived using a rather brief, self-report measure contained in the SF-12. Pain is usually categorized by its course, such as acute or chronic, and can be further subdivided into region (e.g., chronic back pain, cancer, non-cancerous pain). It is also a wholly subjective phenomenon, and there are numerous pain-related assessment scales that measure intensity using different question forms, such as numerical, verbal, or visual aids (Jensen, 2006; Nielson et al., 2008). Given that there is no clear consensus on the best measurement of pain, we are unable to comment on how our results would be affected if another rating scale were used. Further, we can only speculate how the likelihood of NMPAU may differ by type (e.g., chronic or acute) or anatomical site (e.g., back) of pain. Such information would provide important insight into the specificity of pain in elevating the risk of NMPAU.

Third, NMPAU was defined in the NESARC under a broad, therapeutic rubric of prescription pain relievers rather than by identifying which drug and formulation was used. Several studies have reported that differences in the prevalence rates of NMU by brand, scheduling, and formulation (Novak et al., 2007; SAMHSA, 2006a; 2006b). These studies typically do not examine market penetration and drug discrimination, so they cannot be used to establish abuse liability. They do, however, provide insight into market surveillance of NMU's drug patterns, and raise the fundamental question of which pain medications are used most commonly by NMUs.

Fourth, the NESARC did not gather information on access to medications. This information would provide insight into whether NMPAUs are abusing their own medications, or obtaining them fraudulently through other sources, such as from peers, by faking symptoms to obtain medications, or through Internet pharmacies. This distinction is critical, as it would provide

estimates of the numbers of patients exhibiting disordered use that began with a legitimate prescription for pain relief.

4.5 Policy Implications

In light of these methodological issues, our results touch on a number of broader implications that extend beyond the scope of this work. There are many excellent discussions of the policy and clinical implications of NMPAU, including regulatory control (Zacny et al., 2003) and the role of formulation as a preclinical strategy to reduce abuse potential (Balster and Bigelow, 2003). Of more direct relevance to the findings presented here is the need for clinicians to thoroughly identify the factors associated with NMU. As information identifying subgroups at high risk accumulates, so does the need for tools that effectively aid in the screening for risk potential. This is especially salient given that patients presenting with risk factors identified by our research (e.g., psychiatric disorders and substance-use histories) have been documented in other studies as being more likely to receive a prescription for opioid analgesics compared with those with these disorders (Sullivan et al., 2005). Recent work has begun to develop clinically friendly instruments that can be administered prior to a patient's receiving a prescription analgesic (Butler et al., 2006; Butler et al., 2004; Wu et al., 2006). In parallel, the World Health Organization has developed a stepwise approach for the treatment of pain, which links the selection and dosage of pain medications by levels and chronicity of pain (Reid and Davies, 2004). Yet future longitudinal work, perhaps incorporating biological information with comprehensive pain assessments, may help generate information that can be used in new behavioral and pharmacological formulations to reduce the abuse liability of NMPAU.

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Table 1

Population estimates for past year non-medical prescription analgesic use (NMPAU)

	Total			No Pain[a]			Moderate Pain[a]			High Pain[a]		
	n= 42,734[b]			n= 27,393[b]			n= 9,732[b]			n= 5,609[b]		
	Pop Est[c]	%[d]	SE[d]	Pop Est[c]	%[d]	SE[d]	Pop Est[c]	%[d]	SE[d]	Pop Est[c]	%[d]	SE[d]
Past year NMPAU												
No NMPAU	202,437,000	98.2	0.1	132,582,000	98.6	0.1	45,510,000	97.6	0.3	24,346,000	97.3	0.3
Any NMPAU	3,699,000	1.8	0.1	1,873,000	1.4	0.1	1,143,000	2.4	0.3	683,000	2.7	0.3
Non-disordered[e]	2,965,000	1.4	0.1	1,590,000	1.2	0.1	880,000	1.9	0.2	495,000	2.0	0.3
Disordered[f]	733,000	0.4	0.1	283,000	0.2	0.1	263,000	0.6	0.1	187,000	0.7	0.2
TOTAL	206,136,000			134,454,000			46,653,000			25,029,000		
Frequency of NMPAU												
1 to 2 days per year	1,156,000	31.3	2.2	771,000	41.2	3.1	264,000	23.1	4.0	121,000	3.7	0.11
Couple times per year	797,000	21.5	1.9	444,000	23.7	2.6	234,000	20.5	3.8	119,000	4.3	0.13
Monthly	1,247,000	33.7	2.1	547,000	29.2	2.9	465,000	40.7	4.8	235,000	34.4	5.7
Every day or almost daily	499,000	13.5	1.7	111,000	5.9	1.5	180,000	15.7	3.0	208,000	30.5	4.5

[a] SF-12 physical pain subscale.

[b] Unweighted sample size.

[c] Population estimate based on weighted estimates to U.S. population aged 18 or older, rounded to nearest thousand (2000 Census). Estimates do not sum to total due to rounding

[d] Estimates (%=percent, SE=standard error) based on weighted sample and calculated within each row. Design adjustments performed using SUDAAN (release 9.2).

[e] Non-disordered non-medical use defined as use in the past year without DSM-IV past year opioid abuse or dependence.

[f] Disordered non-medical use defined as DSM-IV abuse or dependence in the past year among past year users.

Table 2

Multivariable correlates (odds ratios) of past year non-medical use (NMU) of prescription pain relievers

	Non-disordered NMPAU[a]			Disordered NMPAU[b]		
	O.R.[c]	95% C.I.[c]	Sig[c]	O.R.[c]	95% C.I.[c]	Sig[c]
SF-12 Physical pain						
None	1.00			1.00		
Moderate	1.66	1.22–2.25	.002	2.38	1.17–4.81	.017
High	2.18	1.56–3.03	<.001	3.97	2.06–7.64	<.001
Past year prescription drug NMU[d]						
No use	1.00			1.00		
Non-disordered use	15.76	11.39–21.79	<.001	5.41	2.13–13.73	<.001
Disordered use	11.74	6.11–22.56	<.001	35.63	16.68–76.07	<.001
Past year disordered alcohol use						
No	1.00			1.00		
Yes	2.58	1.90–3.51	<.001	3.59	2.20–5.87	<.001
Past year illicit drug use[e]						
No use	1.00			1.00		
Non-disordered use	4.27	2.98–6.11	<.001	1.72	0.70–4.22	.233
Disordered use	3.17	1.92–5.23	<.001	3.63	1.35–9.75	.011
Past year mood disorder (MD)						
No	1.00			1.00		
Yes	0.82	0.56–1.22	.325	1.98	1.13–3.46	.018
Past year anxiety disorder (AD)						
No	1.00			1.00		
Yes	1.48	1.07–2.04	.017	1.03	0.54–1.96	.922
Anti-social personality disorder (ASPD)						
No	1.00			1.00		
Yes	1.07	0.71–1.62	.737	2.09	1.23–3.55	.007

[a] Non-disordered non-medical use defined as use in the past year without DSM-IV past year opioid abuse or dependence.

[b] Disordered non-medical use defined as DSM-IV abuse or dependence in the past year among past year users.

[c] Estimates (odds ratios, confidence intervals, and significance level) shown control for other variables in model and age, sex, race, education, and income; 1.0 denotes reference category. Design adjustments performed using SUDAAN (release 9.2).

[d] Includes stimulants, benzodiazepines, and tranquilizers.

[e] Includes cocaine/crack, heroin, marijuana, inhalants, and hallucinogens.

Table 3

Interactions between physical pain and selected risk factors on past year nonmedical use of prescription pain relievers

	Non-disordered NMPAU[a]				Disordered NMPAU[b]			
	Wald F[c]	Sig[c]	Conditional probability[c]	SE[c]	Wald F[c]	Sig[c]	Conditional probability[c]	SE[c]
Pain by past year prescription drug (RX)[d]	0.37	.689			2.59	.200		
Pain by past year Disordered alcohol use	12.36	<.001			17.08	<.001		
No pain, non-disordered use			.01	.001			.001	.001
No pain, disordered use			.02	.001			.006	.002
Mod pain, non-disordered use			.01	.001			.004	.001
Mod pain, disordered use			.03	.010			.008	.002
High pain, non-disordered use			.02	.001			.005	.002
High pain, disordered use			.04	.010			.014	.005
Pain by past year illicit drug use[e]	1.73	.161			2.39	.061		
No pain, no use							.001	.001
No pain, non-disordered use							.002	.001
No pain, disordered use							.011	.004
Mod pain, no use							.004	.001
Mod pain, non-disordered use							.011	.006
Mod pain, disordered use							.080	.003
High pain, no use							.004	.001
High pain, non-disordered use							.012	.006
High pain, disordered use							.041	.026
Pain by past year mood disorder (MD)	0.58	.563			0.92	.403		
Pain by past year anxiety disorder (AD)	2.16	.124			2.27	.112		
Pain by anti-social personality disorder (ASPD)	1.40	.254			0.132	.879		

	Non-disordered NMPAU[a]				Disordered NMPAU[b]			
	Wald F[c]	Sig[c]	Conditional probability[c]	SE[c]	Wald F[c]	Sig[c]	Conditional probability[c]	SE[c]

[a] Non-disordered non-medical use defined as use in the past year without DSM-IV past year opioid abuse or dependence.

[b] Disordered non-medical use defined as DSM-IV abuse or dependence in the past year among past year users.

[c] Estimates (Wald F, significance levels, conditional probability and standard error of conditional probability) control for other variables in model and age, sex, race, education, and income; 1.0 denotes reference category. Design adjustments performed using SUDAAN (release 9.2).

[d] Includes stimulants, benzodiazepines, and tranquilizers.

[e] Includes cocaine/crack, heroin, marijuana, inhalants, and hallucinogens.