PAIN MEDICINE
Volume 6 • Number 6 • 2005

RESEARCH ARTICLES

Predicting Aberrant Behaviors in Opioid-Treated Patients: Preliminary Validation of the Opioid Risk Tool

Lynn R. Webster, MD, and Rebecca M. Webster

Lifetree Pain Clinic and Clinical Research, Salt Lake City, Utah, USA

ABSTRACT

Objective. To provide clinicians with a brief screening tool to predict accurately which individuals may develop aberrant behaviors when prescribed opioids for chronic pain.

Design. One hundred and eighty-five consecutive new patients treated in one pain clinic took the self-administered Opioid Risk Tool (ORT). The ORT measured the following risk factors associated in scientific literature with substance abuse: personal and family history of substance abuse; age; history of preadolescent sexual abuse; and certain psychological diseases. Patients received scores of 0–3 (low risk), 4–7 (moderate risk), or ≥8 (high risk), indicating the probability of their displaying opioid-related aberrant behaviors. All patients were monitored for aberrant behaviors for 12 months after their initial visits.

Results. For those patients with a risk category of low, 17 out of 18 (94.4%) did not display an aberrant behavior. For those patients with a risk category of high, 40 out of 44 (90.9%) did display an aberrant behavior. The authors used the *c* statistic to validate the ORT, because it simultaneously assesses sensitivity and specificity. The ORT displayed excellent discrimination for both the male ($c = 0.82$) and the female ($c = 0.85$) prognostic models.

Conclusion. In a preliminary study, among patients prescribed opioids for chronic pain, the ORT exhibited a high degree of sensitivity and specificity for determining which individuals are at risk for opioid-related, aberrant behaviors. Further studies in a variety of pain and nonpain settings are needed to determine the ORT's universal applicability.

Key Words. Assessment; Screening; Chronic Pain; Opioids; Abuse; Addiction

Introduction

The prevalence of opioid abuse in chronic-pain practices is unknown but is often believed to be no greater than the prevalence of opioid abuse in the general population [1]. Other studies disagree and estimate the danger of abuse for pain patients to be higher than the norm [2,3]. One study puts the prevalence of addictive disorders as high as 60% among patients who sustain major trauma [4].

Patients who abuse opioid prescriptions will generally display one or more aberrant drug-related behaviors [5,6]; however, patients who are not abusing opioids may also display aberrant behaviors (see Table 3 for a list). A request for an early refill, for example, may result from intentional overuse of medication (abuse) or a one-time incident where an individual accidentally destroys a few pills. Most physicians would not consider the latter incident an example of abuse. Nonetheless,

Reprint requests to: Lynn R. Webster, MD, Lifetree Pain Clinic and Clinical Research, 3838 South 700 East, Suite 200, Salt Lake City, UT 84106, USA. Tel: 801-261-4988; Fax: 801-269-9427; E-mail: lynnw@lifetreepain.com.

 1526-2375/05/$15.00/432 432–442

it seems reasonable that the more aberrant behaviors an individual exhibits, the more likely the individual is abusing or is addicted to opioids. For the purposes of this article, abuse means the deliberate overuse of controlled or illegal substances, and addiction means the pursuit of such substances for no medical purpose despite resulting physical or psychological harm. These definitions are rooted in the most recent definitions for abuse and dependence found in the Diagnostic and Statistical Manual for Mental Disorders for 2001, although the authors prefer the term "addiction" to the more confusing and conflicting term "dependence" [7]. Concepts of "tolerance" and "withdrawal" have been separated from the phenomenon of "addiction" in the belief that these first two phenomena may not indicate addiction at all.

A number of screening and diagnostic tools exist to assess for aberrant behaviors that may help clinicians detect when a patient is currently abusing or is addicted to prescription medications [8–22]. Yet there also exists a need for a tool to measure the likelihood of whether a patient will abuse opioids in the future. Because abuse and addiction are diagnosed by observing aberrant behaviors, knowing which patients are at greatest risk for displaying aberrant behaviors can be useful in establishing appropriate levels of monitoring for abuse. This article describes the office-based Opioid Risk Tool (ORT), designed to predict the probability of a patient displaying aberrant behaviors when prescribed opioids for chronic pain.

Methods

All new patients (N = 185; females: 108; males: 77) referred to the first author's pain clinic from January 2000 through May 2001 were asked to complete the self-administered ORT (Table 1), which screened for the presence of several risk factors. The ORT assessed new patients for family and personal history of alcohol; illegal drug and prescription substance abuse; age; history of preadolescent sexual abuse; and specific mental disorders. Each risk factor was weighted and attributed a point value believed to reflect its risk relative to the other risk factors. This was carried out based on the authors' personal clinical experience and a review of the literature on the best-known risk factors associated with abuse [23–53]. These weights were derived entirely before any data used in this study were collected and were not modified after the study began. The validity of the weighting was indirectly assessed in this present study as part of the ORT's validity testing; however, a larger sample size would be required to test the validity of weights attributed to the individual risk factors.

Patients in the sample were grouped by score into one of three risk categories: high (likely to abuse opioids), moderate (as likely will as won't abuse opioids) or low (unlikely to abuse opioids). The selected cutoff points for these categories are ≥8, 4–7, and 0–3, respectively. Each patient was assigned a pain type based on his or her chief complaint (Table 2). Patients were treated with a

Table 1 Opioid Risk Tool

Item	Mark Each Box That Applies	Item Score If Female	Item Score If Male
1. Family history of substance abuse			
Alcohol	[ ]	1	3
Illegal drugs	[ ]	2	3
Prescription drugs	[ ]	4	4
2. Personal history of substance abuse			
Alcohol	[ ]	3	3
Illegal drugs	[ ]	4	4
Prescription drugs	[ ]	5	5
3. Age (mark box if 16–45)	[ ]	1	1
4. History of preadolescent sexual abuse	[ ]	3	0
5. Psychological disease			
Attention deficit disorder, obsessive-compulsive disorder, bipolar, schizophrenia	[ ]	2	2
Depression	[ ]	1	1
Total		—	—
Total score risk category			
Low risk: 0–3			
Moderate risk: 4–7			
High risk: ≥8			

Table 2 Patient characteristics by risk category

Characteristic	Low Risk (N = 18)	Moderate Risk (N = 123)	High Risk (N = 44)	*P* Value*
Age, mean ±SD (min, max)	50.9 ±14.9 (28, 78)	44.1 ±13.1 (17, 82)	41.1 ±9.2 (20, 64)	0.067
Gender, n (%)				0.540
Female	12 (67)	73 (59)	23 (52)	
Male	6 (33)	50 (41)	21 (48)	
Pain types, n (%)				0.744
Spine: lumbar	6 (33)	43 (35)	23 (52)	
Spine: cervical	1 (6)	9 (7)	1 (2)	
Headache	4 (22)	24 (20)	5 (11)	
Neuropathic	3 (17)	22 (18)	5 (11)	
Musculoskeletal	3 (17)	19 (15)	7 (16)	
Visceral	1 (6)	6 (5)	3 (7)	

* Comparison of three risk groups: Kruskal–Wallis test for age, chi-square test for gender, Fisher–Freeman–Halton test for pain types.

variety of opioids, breakthrough pain medications, and anticonvulsants. The philosophy of treatment was to titrate patients to optimal pain-relief levels with the upper dosage limited only by side effects. Some patients reached several 100 mg of morphine equivalents. Patients were seen weekly until successfully titrated, then monthly thereafter.

Behaviors defined as aberrant used in this study are listed in Table 3. All patients were monitored for aberrant behaviors for 12 months after their initial visits. The first author, also the clinic's medical director, recorded each aberrant behavior as present when it was first documented in the patient's medical chart. The aberrant behavior was documented in the chart by any member of the clinical staff after being observed directly, reported by the patient or a family member or detected by a lab test. This procedure was intended to minimize the authors' subjective interpretation and bias in recording the behaviors.

When possible, a query of the state's prescription-monitoring program was completed before the patient's first visit to assess whether the patient had been receiving opioid prescriptions from more than one physician. Further queries were completed at 6-month intervals and whenever an aberrant behavior triggered a concern by the provider that the patient may be soliciting opioids from other providers.

For tabulation, the authors created a spreadsheet listing new patients and the type and frequency of aberrant behaviors. The authors

Table 3 Aberrant behaviors indicating abuse of opioids prescribed for chronic pain

Aberrant Behaviors	Females (N = 108) n (%)	Males (N = 77) n (%)	*P* Value*
Used additional opioids than those prescribed	8 (7)	8 (10)	0.477
Used additional opioids than those prescribed more than once	6 (6)	8 (10)	0.220
Forged prescription	2 (2)	2 (3)	1.000
Sold prescription	0 (0)	1 (1)	0.416
Admitted to seeking euphoria from opioids	0 (0)	2 (3)	0.172
Admitted to wanting opioids for anxiety	1 (1)	2 (3)	0.571
Overdose and death	0 (0)	5 (6)	0.012
Injected drug	0 (0)	1 (1)	0.416
Abnormal urine/blood screen	12 (11)	10 (13)	0.698
Abnormal urine/blood screen positive for 2 or more substances	2 (2)	1 (1)	1.000
Solicited opioids from other providers	20 (19)	13 (17)	0.775
Unauthorized ER visits	7 (6)	2 (3)	0.309
Concurrent abuse of alcohol	0 (0)	3 (4)	0.070
Unauthorized dose escalation	11 (10)	14 (18)	0.117
Resisted therapy changes/alternative therapy	6 (6)	5 (6)	1.000
Reported lost or stolen prescriptions	6 (6)	5 (6)	1.000
Canceled clinic visit	10 (9)	8 (10)	0.798
Requested early refills	9 (8)	7 (9)	0.857
Requested refills instead of clinic visit	13 (12)	7 (9)	0.525
Abused prescribed drug	11 (10)	11 (14)	0.396
Was discharged from practice†	7 (6)	7 (9)	0.508
No show or no follow-up	12 (11)	11 (14)	0.519
Third party required to manage patient's medications	8 (7)	6 (8)	0.922

* Chi-square test or Fisher's exact test as appropriate.
† Because of egregious aberrant behavior (e.g., forging prescriptions).

thoroughly reviewed each patient's chart after 12 months in the practice to confirm the presence or absence of aberrant behaviors.

Statistical Methods

Several statistical methods were used to compare risk factors and aberrant behaviors between males and females and to determine the predictive value of the risk factors of the ORT.

For statistical comparisons of a categorical variable between two groups, a chi-square test was used, or Fisher's exact test if contingency table cell counts were sparse. The Fisher–Freeman–Halton test is the Fisher's exact test generalized by Freeman and Halton to greater than 2×2 cross-tabulation tables [54].

For continuous variables, a *t*-test was used for comparisons between two groups and a one-way analysis of variance was used for comparisons between three groups. The assumption of normality of these two tests was assessed using the Shapiro–Wilk test, and the assumption of equality of variances was assessed using Levene's test. If either assumption was not satisfied, the nonparametric Wilcoxon–Mann–Whitney test or the Kruskal–Wallis analysis of variance test was substituted respectively.

To validate the ORT, the authors used it to compute a total score for every patient in the sample, the sample serving as the validation dataset (Table 1). Then the total scores, along with the actual observed outcome of one or more aberrant behaviors, were used to compute the concordance index (popularly called the *c* statistic). The *c* statistic was used to validate the ORT, as it simultaneously assesses the sensitivity and specificity [55,56]. The *c* statistic is a measure of the predictive ability (measure of diagnostic discrimination) of a prognostic model. For validating the ORT in this study, the *c* statistic is the likelihood that a patient who exhibits an aberrant behavior will have a higher predicted risk of such a behavior than does a patient who does not exhibit an aberrant behavior [55].

The general rule for interpreting the *c* statistic: $c = 0.5$ suggests no discrimination (i.e., no better than flipping a coin), $0.7 \le c < 0.8$ is considered acceptable discrimination, $0.8 \le c < 0.9$ is considered excellent discrimination, and $c \ge 0.9$ is considered outstanding discrimination [56].

The validation dataset was not large enough to validate directly that the weights assigned to the ORT's risk factors represent the optimal weights. Such a validation would require fitting a multivariable logistic regression model separately for males and females and then basing the ORT weights on the relative size of the regression coefficients. Fitting such a model would require at least 10 patients with an aberrant behavior outcome for every predictor variable in the model to avoid "overfitting" and structural collinearity [55]. The validation dataset only had 37 female patients and 39 male patients with aberrant behaviors, so that only four predictor variables could appropriately be modeled out of the required 10 predictor variables composing the ORT.

Despite the sample size limitation which precluded fitting a multivariable logistic regression model, a large *c* statistic derived from applying the existing ORT would suggest that the weights used in the ORT are sufficiently satisfactory, thereby providing an indirect validation of the weights. This was the approach, then, used in this current validation study.

To account for potential regression-toward-the-mean bias in the *c* statistic calculations, nonparametric bootstrap resampling was used. The bootstrap-resampled *c* statistic is what one would more likely observe in future patients [55,57]. Both the *c* statistic observed for the validation dataset and the *c* statistic computed by nonparametric bootstrap resampling are reported.

To determine if the weights used with the ORT were more predictive than simply summing the items, where every item is assumed to have equal importance, the *c* statistic for the ORT was compared with the *c* statistic derived for the unweighted total score and tested for significance [58].

Results

No difference was found among the three risk groups for age ($P = 0.067$), gender ($P = 0.540$), or pain type ($P = 0.744$) (Table 2). Lumbar spine-related pain was the most common pain type. Headache, neuropathic pain, and musculoskeletal pain were fairly evenly distributed among the three risk groups. Cervical spine-related pain was the least common pain type in all three risk groups.

The most common aberrant behaviors for both men and women were solicited opioids from other providers (males: 17%, females: 19%), unauthorized dose escalation (males: 18%, females: 10%), abnormal urine/blood screen (male: 13%, females: 11%), used additional opioids than those pre-

Table 4 Presence/absence of one or more aberrant behaviors by risk category computed from Opioid Risk Tool (ORT)

Risk Category* by Actual Outcome	Females N (%)	Males N (%)
Patients with no aberrant behaviors	71	38
Low (0–3)†	12 (16.9)	5 (13.2)
Moderate (4–7)	56 (78.9)	32 (84.2)
High (≥8)	3 (4.2)	1 (2.6)
Patients with one or more aberrant behaviors	37	39
Low (0–3)†	0 (0.0)	1 (2.6)
Moderate (4–7)	17 (46.0)	18 (46.2)
High (≥8)	20 (54.0)	20 (51.3)

* Based on total score from ORT.
† Low risk = unlikely to abuse opioids; moderate risk = as likely will as won't abuse opioids; high risk = likely to abuse opioids.

scribed (males 10%, females 7%), used additional opioids than those prescribed more than once (males: 10%, females 6%), no show or no follow-up (males: 14%, females: 11%), abused prescribed drug (males: 14%, females: 10%), and cancelled clinic visit (males: 10%, females: 9%) (Table 3).

For those patients with a risk category of low, 17 out of 18 (94.4%) did not display an aberrant behavior, in close agreement with the category label of "unlikely to abuse opioids" (Table 4). For those patients with a risk category of high, 40 out of 44 (90.9%) did display an aberrant behavior, in close agreement with the category label of "likely to abuse opioids." The data showed that the moderate-risk patients were 2.5 times as likely not to abuse opioid prescriptions as to abuse opioid prescriptions. (35 or 28% did; 88 or 72% did not).

Table 5 Risk factors for opioid-related aberrant behavior (items composing the Opioid Risk Tool)

Risk Factor	Females (N = 108) n (%)	Males (N = 77) n (%)	*P* Value*
Family history of substance abuse			
Alcohol	54 (50)	53 (69)	0.011
Illegal drugs	21 (19)	12 (16)	0.499
Other (prescription drugs)	10 (9)	2 (3)	0.070
Personal history of substance abuse			
Alcohol	17 (16)	22 (29)	0.035
Illegal drugs	14 (13)	13 (17)	0.457
Prescription drugs	23 (21)	12 (16)	0.328
Age ≤45	62 (57)	43 (56)	0.832
History of preadolescent sexual abuse	43 (40)	6 (8)	<0.001
Psychological disease			
Attention deficit disorder, obsessive-compulsive disorder, bipolar, or schizophrenia	28 (26)	13 (17)	0.144
Depression	77 (71)	44 (57)	0.046

* Chi-square test.

Table 6 Number of aberrant behaviors

	Females (N = 108) n (%)	Males (N = 77) n (%)	*P* Value*
Total number of aberrant behaviors			
0	71 (66)	38 (49)	
1–2	15 (14)	20 (26)	
≥3	22 (20)	19 (25)	
Median (25th, 75th percentiles)	0 (0, 2)	1 (0, 2)	0.057
Range (min–max)	0–14	0–13	
Total number of aberrant behaviors			
0	71 (66)	38 (49)	
≥1	37 (34)	39 (51)	0.026
Total number of aberrant behaviors			
0–2	86 (80)	58 (75)	
≥3	22 (20)	19 (25)	0.487

* Wilcoxon–Mann–Whitney test for the first comparison, chi-square test for last two comparisons.

Therefore, the label of "as likely will as won't abuse opioids" reflects cautious patient management.

The need for gender-specific numerical weights for the risk factors composing the ORT is indirectly supported by the difference in prevalence of these risk factors between genders (Table 5). The capacity of a risk factor to impact an outcome will, in part, depend on the prevalence of other risk factors, especially potent ones [59]. For example, a fivefold greater prevalence of a history of preadolescent sexual abuse was observed among females relative to males (females: 40%, males: 8%, $P < 0.001$).

Most aberrant behaviors considered in the validation dataset were essentially equally common among males and females (Table 3). When cumulated, however, males had a greater incidence of at least one aberrant behavior (females: 34%, males: 51%, $P = 0.026$) (Table 6). No significant gender difference was observed in the incidence of at least three aberrant behaviors (females: 20%, males: 25%, $P = 0.487$). Of the total sample, 41% displayed at least at least one aberrant behavior.

The female prognostic model had $c = 0.85$ and the male model had $c = 0.82$ (Table 7). The

Table 7 Discrimination performance of Opioid Risk Tool total score

	Observed *c* Statistic (95% CI)*	Bootstrapped *c* Statistic (95% CI)*
Males	0.82 (0.73–0.91)	0.82 (0.72–0.90)
Females	0.85 (0.78–0.93)	0.85 (0.77–0.92)

The observed *c* statistic is the estimate computed for the validation dataset. The bootstrapped *c* statistic is the estimate derived from nonparametric bootstrap resampling, which is less subject to regression toward the mean bias.
* 95% confidence interval for *c* statistic.

Table 8 Percent of one or more aberrant behaviors for each total score from the Opioid Risk Tool

Probability Category	Total Score	Females c/n (%)	Males c/n (%)
Low (0–3)	0–1	0/3 (0)	0/3 (0)
	2	0/7 (0)	0/0 (0)
	3	0/2 (0)	1/3 (33)
Moderate (4–7)	4	2/17 (12)	4/22 (18)
	5	4/28 (14)	4/8 (50)
	6	6/12 (50)	6/10 (60)
	7	5/16 (31)	4/10 (40)
	8	2/3 (67)	4/4 (100)
High (≥8)	9	4/5 (80)	6/6 (100)
	10	4/5 (80)	1/2 (50)
	11–18	10/10 (100)	9/9 (100)
	Total	37/108	39/77

c = count of patients with that total score who had one or more aberrant behaviors; n = number of patients with that total score; % = c/n × 100.

observed *c* statistic estimates were identical to the bootstrapped *c* statistic estimates.

The ORT, with its present item weights, outperformed the unweighted total score of the items, where each item was given a weight of one if the risk factor was present. For females, the ORT exhibited significantly greater discrimination ($c = 0.85$) than its unweighted counterpart ($c = 0.77$, $P = 0.046$). For males, the ORT exhibited greater discrimination ($c = 0.82$) than its unweighted counterpart ($c = 0.78$), but failed to reach statistical significance ($P = 0.234$).

Table 8 lists the percent of one or more aberrant behaviors by gender for each total score from the ORT. The number and percent of aberrant behaviors generally increased with the total score. All patients with a score of 11 or more displayed at least one aberrant behavior. Of patients in the high-risk group, 90.9% displayed aberrant behaviors. Although 33% of males who had a score of 3 (in the low-risk group) displayed at least one aberrant behavior, this represented only one patient. Patients with a score of 2 or lower did not display aberrant behaviors.

Discussion

It is difficult to predict which patients are at risk for abusing the opioids prescribed for chronic pain. Of the currently available diagnostic tools, such as the Addiction Severity Index (ASI) [8–10] and the Structured Clinical Interview for DSM-IV (SCID) [11–14], many take a long time to administer and require unique skills to interpret. This makes them impractical for most physicians. By contrast, brief screening tools are less cumbersome but have two frequent problems: 1) they are designed to identify patients who already have problems with substances, not to predict who may develop problems; and 2) they are not designed to screen specifically for opioid abuse. For example, the widely used alcohol-screening tool CAGE (from the key words "Cut," "Annoyed," "Guilty," "Eye") [15] has not proven to be effective in predicting opioid abuse [16]. Likewise, a tool called TICS (from Two-Item Conjoint Screening tool), a two-question measure of sensitivity to substance abuse [17], is neither opioid-specific nor designed to be predictive, as is the ORT.

These preliminary findings show that the ORT predicted which patients were at highest risk of displaying aberrant behaviors when prescribed opioids for the treatment of chronic pain in the author's practice. The ORT displayed excellent discrimination for both males and females for interpreting the *c* statistic (see Statistical Methods section). In addition, the observed *c* statistic estimates were identical to the bootstrapped *c* statistic estimates, suggesting the ORT will discriminate just as well in future patients. Although the ORT provides information regarding potential risk factors that might have universal applicability, the validity of the ORT across practices with different demographics remains to be assessed.

The weights assigned to the risk factors reflect the well-documented link between substance abuse and the risk factors studied. Many individual risk factors for substance abuse are not included in the ORT, in keeping with the goal of providing clinicians with an assessment that is both effective and brief. The risk factors were chosen for what was believed to be their predictive power based on a review of related scientific literature. Part of the focus of future testing should be to ensure which factors are indeed most predictive of aberrant, drug-related behaviors and whether the significant results from this preliminary study can be duplicated. It is possible the weights will be adjusted to their optimal values after further testing.

What follows is a brief review of the literature pertaining to the risk factors studied.

Several studies show genetic and environmental links to developing alcohol abuse and other drug addiction [23–36]. Even biological children of alcohol-dependent parents adopted and raised in nonalcoholic environments show a two- to ninefold increased risk of developing alcohol abuse or dependency [31]. The ORT attributed more relative risk to family history of alcohol abuse among men than women. This is based on evidence of a

higher prevalence of alcohol abuse among men, coupled with evidence that the risk of a person related to an alcoholic-developing alcoholism is greater when the relative and the alcoholic are of the same sex [32].

Alcohol abuse is included as a risk factor based on evidence of polysubstance abuse among alcoholics [35]. However, alcohol abuse was not weighted as heavily as a personal or family history of prescription drug abuse. One study showed that while an abuser of one drug is more likely than nonabusers to go on to abuse a different category of drug, most of the genetic influence on heroin/opioid abuse is specific to heroin/opioids and not shared with other drugs. The same research showed that genetic influence in the abuse of marijuana, stimulants, and sedatives is shared across drugs [29]. The high degree of genetic influence on opioid abuse is the reason why prescription drug abuse (both personal and family history) is weighted most heavily. Illegal drug abuse was considered next in line as being predictive of opioid abuse [36], followed by alcohol abuse. In one study, polysubstance abusers admitted for alcohol-abuse treatment rated their nonalcohol drug use as more problematic than their drinking [35]. The authors also reported that those who used nonalcoholic substances tended to abuse alcohol less.

The age range included on the ORT reflects findings that drug dependence or abuse rates tend to rise with age to peak in the twenties, then fall off at middle age [37].

Substance abuse has been associated with numerous psychological disorders [38–53]. It is generally accepted that women who experienced preadolescent sexual abuse have increased risk for mental and substance-abuse disorders [42]. Preadolescent sexual abuse gives rise to posttraumatic stress disorder (PTSD), which is associated with substance abuse and is two to three times more common in women than in men. Some 30–59% of women in drug abuse treatment have been reported to have PTSD [47].

The select group of mental disorders included on the ORT were chosen based on the prevalence of their association with substance abuse found in the literature [48–52]. Regier et al. found that having a lifetime mental disorder is associated with more than twice the risk of having an alcohol disorder and over four times the risk of having another drug-abuse disorder [51]. Thus, the ORT weighting scale was supported by the literature and proved to be very predictive of abuse in the current sample but may need to be revised to more optimal levels after further research.

A limitation of the study is that the clinician who recorded aberrant behaviors in a patient's chart was not blinded to that patient's ORT score. Because the study took place in a clinical setting, the ORT score was visible as part of a patient's medical history. Future studies should eliminate this limitation to avoid any possibility of bias on the part of the recording clinician.

Another limitation of the current validation study was the small sample size relative to the number of risk factors. A second validation study therefore with a much larger sample size is called for to determine if the weights assigned to the ORT are optimal or if they need to be modified. Furthermore, the ORT should be tested in multiple pain clinics and in nonpain clinic settings to further assess its applicability to a wider population.

It has been demonstrated that for many scales, a simple total score of the items without weights works just as well as a weighted scale [60]. The ORT, with its present weights, exhibited greater discrimination than its unweighted counterpart for both male and female patients, being significantly so in females. Therefore, even though the weights were not empirically derived, which will require a further study, the present weights appear to have merit at this stage of development.

The ORT yielded additional useful findings. The data suggest that the prevalence of aberrant behaviors related to abuse or addiction among patients treated for chronic pain with opioids is much higher than previously reported. A fifth of the women and a quarter of the men in the total sample displayed three or more aberrant behaviors. It should be noted that the authors recorded only those aberrant behaviors that were observed. Other behaviors that might indicate abuse might have gone undetected or were not recorded because they did not fit the list of behaviors chosen to measure.

Aberrant behaviors have been described as less predictive or more predictive of abuse [5]. Alternatively, we suggest aberrant behaviors exist on a continuum from nonexistent to egregious. The authors are not aware of a consensus on what is deemed egregious behavior compared with what would be considered relatively inconsequential behavior. This is an area ripe for research. Passik and Kirsh found little agreement among doctors as to how to interpret certain behaviors but found the most common factors among the abusers they

studied to be unscheduled visits, multiple phone calls to the clinic, unsanctioned dose escalations, and obtaining opioids from more than one source [61]. In a separate study of pain physicians' perceptions, Passik et al. found wide variation in the perception of 13 drug-related behaviors but noted that physicians found illegal activity the most troubling [62]. Selling prescription drugs and forging prescriptions were the top two behaviors considered most indicative of abuse by physicians. Compton suggested three behaviors were predictive of addictive disease: the tendency to increase analgesic dose or frequency, to have a preferred route of administration, and to consider oneself an addict [19]. It is apparant that patients who inject oral medication are displaying more egregious behavior than the individual who uses an occasional extra pill for breakthrough pain. Therefore, although 41% of the current study's total sample displayed at least one aberrant behavior, the importance of this number should not be overstated as the severity of the behaviors varies.

The egregious behaviors are likely to be consistent with behaviors that meet the criteria from the DSM-IV-TR for "dependency" or addiction. It would seem logical that patients with opioid addiction would display multiple egregious behaviors. In a prior, similar study, the author reported that patients who are in the ORT's high-risk group displayed an average of 4.21 aberrant behaviors compared with an average of 0.81 aberrant behaviors in the moderate-risk group over the same time interval [6]. In that study, the high-risk group also demonstrated multiple aberrant behaviors sooner than the moderate- and low-risk groups. While it took an average of nearly 11 months to see three or more aberrant behaviors in the moderate-risk group, it took only about 4 months for the high-risk group. The current study also demonstrated that patients categorized as high risk for abusing opioids demonstrated more aberrant behaviors than the moderate- or low-risk groups (Table 8).

The more egregious the behavior, the greater the likelihood egregious abuse or addiction is taking place. Likewise, the quantity of behaviors can be a prime indicator, with greater numbers of aberrant behaviors likely indicating that significant abuse or addiction is taking place. However, no single indicator clearly marks an addict. Instead, there exists a large gray area, a diagnostic no-man's land, where a patient can display strong indications of addiction, yet not be a true addict. It is probably fair to state that while all addicts are abusers, not all abusers are addicts (see Figure 1).

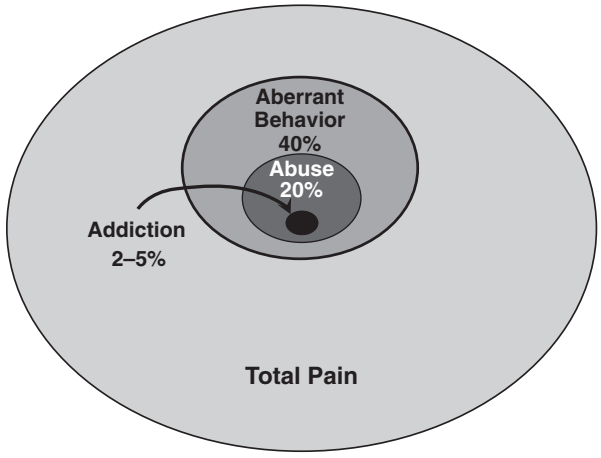

Figure 1 Relationships among aberrant behavior, abuse, and addiction in total pain population.

Even aberrant behaviors that suggest abuse or addiction may only reflect a patient's attempt to feel normal. The phrase *chemical copers* refers to patients who, knowingly or unknowingly, inappropriately use opioids to treat a comorbid disease such as depression or anxiety. Although not technically an addict, such a person, fearing withdrawal, is abusing a drug and may even be buying it illegally. In addition, some patients who demonstrate aberrant behavior in an attempt to feel normal are only displaying *rational abuse* of the type that arises from under-treated pain or a failure of treatment management. While a chemical coper's function may not improve as a result of misusing medication, a rational abuser's function and mental status tend to improve.

Despite these cautions, the potential for drug abuse or addiction clearly exists for pain patients as it does for the population at large. Given this reality, it is vital that patients be adequately assessed for abuse potential. The purpose is not to deny high-risk patients adequate pain treatment but to ensure that their psychological and substance-abuse disorders are also treated, and that their opioid intake is closely monitored. In the absence of a laboratory test to detect abuse or addiction, the observation of behavior is the best avenue open to clinicians who wish to avoid contributing to opioid abuse.

Conclusion

Accurately predicting behavior is difficult regardless of the behavior one is trying to predict. In predicting who will abuse opioids, however,

known risk factors may help determine the general probabilities of who may display behavioral cues suggesting abuse or addiction.

This article documents the results of a preliminary study showing the instrument was predictive in the setting in which it was administered and indicates the instrument may have broad applicability. Using the ORT, this study found that patients who had a high probability of abusing opioids demonstrated more aberrant behaviors than the moderate- or low-risk groups (Tables 4, 8). In the sample tested, the ORT demonstrated validity and accuracy in predicting who is at high risk and at low risk for opioid-related, aberrant behavior.

By having a clinical instrument to assess the probability of an individual developing aberrant behavior, the clinician can tailor the monitoring of patients according to their risk profiles. More importantly, patients who are at high risk could be identified before opioid treatment and directed to appropriate counseling or treatment of the disorders that make them high risk. It is hoped this awareness would result in better clinical outcomes and less abuse.

Acknowledgments

Statistical analysis by Gregory J. Stoddard, Section of Biostatistics, University of Utah School of Medicine. Manuscript review and editing by Beth Dove.

References

1 Weaver M, Schnoll S. Abuse liability in opioid therapy for pain treatment in patients with an addiction history. Clin J Pain 2002;18(Suppl. 4): 561–9.
2 Chabal C, Erjavec MK, Jacobsen L, Mariano A, Chaney E. Prescription opiate abuse in chronic pain patients: Clinical criteria, incidence and predictors. Clin J Pain 1997;13:150–5.
3 Manchikanti L, Pampati V, Damron K, et al. Prevalence of opioid abuse in interventional pain medicine practice settings: A randomized clinical evaluation. Pain Physician 2001;4:358–65.
4 Savage SR. Assessment for addiction in pain-treatment settings. Clin J Pain 2002;18(Suppl. 4): 528–38.
5 Portenoy RK. Opioid therapy for chronic nonmalignant pain: A review of the critical issues. J Pain Symptom Manage 1996;11(4):203–17.
6 Webster LR, Webster RM. Predicting Aberrant Drug-Related Behavior in Chronic Pain Patients. New York: International Conference on Pain and Chemical Dependency; 2002.
7 American Psychiatric Association. DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders. 4th edition. Washington, DC: American Psychiatric Association; 2001.
8 McLellan AT, Luborsky L, O'Brien CP, Woody GE. An improved diagnostic instrument for substance abuse patients: The Addiction Severity Index. J Nerv Ment Dis 1980;168:26–33.
9 McLellan AT, Luborsky L, Cacciola J, Griffith J. New data from the Addiction Severity Index: Reliability and validity in three centers. J Nerv Ment Dis 1985;173:412–23.
10 McLellan AT, Kushner H, Metzger D, et al. The fifth edition of the Addiction Severity Index. J Subst Abuse Treat 1992;9:199–213.
11 Spitzer RL, Williams JB, Mirian G, First M. Instruction Manual for the Structured Interview for DSM-III-R. New York: Biometrics Research Department, New York State Psychiatric Institute; 1989.
12 Spitzer RL, Williams JB, Gibbon M, First MB. The structured clinical interview for DSM-III-R (SCID) I: History, rationale and description. Arch Gen Psychiatry 1992;49:624–9.
13 Williams JB, Gibbon M, First M, et al. The structured clinical interview for DSM-III-R (SCID) II: Multisite test-retest reliability. Arch Gen Psychiatry 1992;49:630–6.
14 Kranzler H, Kadden R, Babor TF, Tennen H, Rounsaville BJ. Validity of the SCID in substance abuse patients. Addiction 1996;91:859–68.
15 Ewing JA. Detecting alcoholism: The CAGE questionnaire. JAMA 1984;252:1905–7.
16 Atluri S, Sudarshan G. A screening tool to determine the risk of prescription opioid abuse among patients with chronic non-malignant pain. Pain Phys 2002;5:4.
17 Brown RL, Leonard T, Saunders LA, Papasouliotis O. A two-item screening test for alcohol and other drug problems. J Fam Pract 1997;44:151–60.
18 Butler SF, Budman SH, Fernandez K, Benoit C, Jamison RN. Validation of a screener and opioid assessment for patients with pain. Poster Presented to the 6th International Conference on Pain and Chemical Dependency, Brooklyn, NY; 2004.
19 Compton P, Darakjian J, Miotto K. Screening for addiction in patients with chronic pain and a "problematic" substance use: Evaluation of a pilot assessment tool. J Pain Symptom Manage 1998;16(6): 355–63.
20 Bastiaens L, Riccardi K, Sakhrani D. The RAFFT as a screening tool for adult substance use disorders. Am J Drug Alcohol Abuse 2002;28(4):683–93.
21 Gavin DR, Ross HE, Skinner HA. Diagnostic validity of the Drug Abuse Screening Test in the assessment of DSM-III drug disorders. Br J Addict 1989;84:301–7.
22 Sutherland G, Edwards G, Taylor C, et al. The measurement of opiate dependence. Br J Addict 1986;81:483–94.

23 Meller WH, Rinehart R, Cadoret RJ, Troughton E. Specific familial transmission in substance abuse. Int J Addict 1988;23(10):1029–39.
24 Tsuang MT, Lyons MJ, Eisen SA, et al. Genetic influences on DSM-III-R drug abuse and dependence: A study of 3,372 twin pairs. Am J Med Genet 1996;67:473–7.
25 Jang KL, Livesley WJ, Vernon PA. Alcohol and drug problems: A multivariate behavioural genetic analysis of comorbidity. Addiction 1995;90:1213–21.
26 Lewis DC, ed. Personality pathology, family history of alcoholism linked. DATA: The Brown University of Addiction Theory and Application 1999;18:3.
27 Prescott CA, Aggen SH, Kendler KS. Sex-specific genetic influences on the comorbidity of alcoholism and major depression in a population-based sample of US twins. Arch Gen Psychiatry 2000;57:803–11.
28 Schuckit MA. Biological, psychological and environmental predictors of the alcoholism risk: A longitudinal study. J Stud Alcohol 1998;59:485–94.
29 Tsuang MT, Lyons MJ, Meyer JM, et al. Co-occurrence of abuse of different drugs in men: The role of drug-specific and shared vulner-abilities. Arch Gen Psychiatry 1998;55:967–72.
30 Zickler P. Twin studies help define the role of genes in vulnerability to drug abuse. NIDA Notes 1999;14(4).
31 Belcher S, Shinitzky HE. Substance abuse in children: Prediction, protection, prevention. Arch Pediatr Adolesc Med 1998;152(10):952–60.
32 Prescott CA. Sex Differences in the Genetic Risk for Alcoholism. National Institute on Alcohol Abuse and Alcoholism (NIAAA) Publications 2003. Available at: http://www.niaaa.nih.gov/publications/arh26-4/264-273.htm (accessed November 2003).
33 Bohman M. Some genetic aspects of alcoholism and criminality: A population of adoptees. Arch Gen Psychiatry 1978;35:269–76.
34 Goodwin DW. Alcoholism and genetics: The sins of the fathers. Arch Gen Psychiatry 1985;42:171–4.
35 Staines GL, Magura S, Foote J, Deluca A, Kosanke N. Polysubstance abuse among alcoholics. J Addict Dis 2001;20:53–69.
36 Lewis DC, ed. Study: Abusers of one drug are at risk of abusing others. DATA: The Brown University Digest of Addiction Theory and Application 1999;18:3.
37 Substance abuse and Mental Health Services Administration. Results from the 2003 National Survey on Drug Use and Health: National Findings. Rockville, MD: Office of Applied Studies, NSDUH Series H-25, DHHS Publication No. SMA 04-3964, 2004.
38 Burke JD, Burke KC, Rae DS. Increased rates of drug abuse and dependence after onset of mood or anxiety disorders in adolescence. Hosp Community Psychiatry 1994;45:5.
39 Christie KA, Burke JD, Jr., Regier DA, et al. Epidemiologic evidence for early onset of mental disorders and higher risk of drug abuse in young adults. Am J Psychiatry 1988;145(8):971–5.
40 Horowitz HA, Overton WF, Rosenstein D, Steidl JH. Comorbid adolescent substance abuse: A maladaptive pattern of self-regulation. Adolesc Psychiatry 1992;18:465–83.
41 Ross HE, Glaser FB, Glaser MD, Germanson T. The prevalence of psychiatric disorders in patients with alcohol and other drug problems. Arch Gen Psychiatry 1988;45:1023–31.
42 Kendler KS, Bulik CM, Silberg J, et al. Childhood sexual abuse and adult psychiatric and substance use disorders in women: An epidemiological and co-twin control analysis. Arch Gen Psychiatry 2000;57(10):953–9.
43 Lewis DC, ed. Dual diagnosis: Patients report interplay of substance use, PTSD symptoms. DATA: The Brown University Digest of Addiction Theory and Application 1999;18(3).
44 Mullen PE, Martin JL, Anderson JC, Romans SE, Herbison GP. Childhood sexual abuse and mental health in adult life. Br J Psychiatry 1993;163:721–32.
45 Zickler P. Childhood sex abuse increases risk for drug dependence in adult women. NIDA Notes 2002;17(1).
46 Bifulco A, Brown GW, Adler Z. Early sexual abuse and clinical depression in adult life. Br J Psychiatry 1991;159:115–22.
47 Swan N. Exploring the role of child abuse in later drug abuse. NIDA Notes 1998;13(2).
48 Farrell M, et al. Nicotine, alcohol and drug dependence and psychiatric comorbidity. Br J Psychiatry 2001;179:432–7.
49 Merikangas KR, Gelernter CS. Comorbidity for alcoholism and depression. Psychiatr Clin North Am 1990;13(4):613–22.
50 Schuckit MA. New findings in the genetics of alcoholism. JAMA 1999;281(20):1875–6.
51 Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug use. JAMA 1990; 264(19):2511–8.
52 Stocker S. Medications reduce incidence of substance abuse among ADHD patients. NIDA Notes 1999;14(4).
53 Webster L. Assessing abuse potential in pain patients. Medscape Neurol Neurosurg 2004;6(1).
54 Conover WJ. Practical Nonparametric Statistics. 2nd edition. New York: John Willey & Sons; 1980:165–9.
55 Harrell FE Jr. Regression Modeling Strategies with Applications to Linear Models, Logistic Regression and Survival Analysis. New York: Springer-Verlag; 2001.
56 Hosmer DW, Lemeshow S. Applied Logistic Regression. 2nd edition. New York: John Wiley & Sons; 2000.

57 Harrell FE Jr., Lee KL, Mark DB. Multivariable prognostic models: Issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Statist Med 1996;15:361–87.
58 DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating curves: A nonparametric approach. Biometrics 1988;44:837–45.
59 Rothman KJ. Epidemiology: An Introduction. Oxford: Oxford University Press; 2002:11–2.
60 Streiner DL, Norman GR. Health Measurement Scales: A Practical Guide to Their Development and Use. New York: Oxford University Press; 1995.
61 Passik SD, Kirsh KL. Commentary: The need to identify predictors of aberrant drug-related behavior and addiction in patients being treated with opioids for pain. Pain Med 2003;4(2):185–8.
62 Passik SD, Kirsh KL, Whitcomb LA, Dickerson P, Theobald DE. Pain clinicians' rankings of aberrant drug-taking behaviors. J Pain Palliat Care Pharmacother 2002;16(4):39–49.