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## Examining the factor structure of the Clinical Opiate Withdrawal Scale: A secondary data analysis from the National Drug Abuse Treatment Clinical Trials Network (CTN) 0003

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### Abstract

**Background**—The Clinical Opiate Withdrawal Scale (COWS) is used to assess withdrawal in clinical trials and practice. The aims of this study were to examine the inter-item correlations and factor structure of the COWS in opioid-dependent men and women.

**Methods**—This is a secondary data analysis of the National Drug Abuse Treatment Clinical Trials Network 0003, a randomized clinical trial that compared buprenorphine/naloxone tapering strategies. The trial included 11 sites in 10 US cities. Participants were opioid-dependent individuals (n=516) that had data on the COWS. The COWS at study baseline was analyzed in this study.

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#### Contributors

Barbosa-Leiker conducted the primary analyses and drafted the manuscript. McPherson prepared the dataset, aided in statistical interpretation, and edited all sections of the manuscript. Mamey conducted the preliminary analyses and drafted the tables. Burns aided in the statistical interpretation and edited the results section of the manuscript. Layton assisted in clinical interpretation and wrote parts of the discussion section. Roll aided in the clinical interpretation and edited the introduction and discussion sections of the manuscript. Ling assisted in clinical interpretation and wrote parts of the discussion and conclusion sections.

#### Conflict of Interest

Barbosa-Leiker and McPherson have received research funding from the Bristol-Myers Squibb Foundation. Ling receives research support from Reckitt/Benckiser and Braeburn Pharmaceuticals Inc. and serves as consultant to Reckitt/Benckiser.

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**Results**—Inter-item correlations showed weak to moderate relationships among the items. A 1-factor model did not fit the data for men (comparative fit index (CFI)=.801, root mean square error of approximation (RMSEA)=.073, weighted root mean square residual (WRMR)=1.132) or women (CFI=.694, RMSEA=.071, WRMR=.933), where resting pulse rate was not related to withdrawal for men, and yawning and gooseflesh skin was not related to withdrawal for women. A reduced model comprised of only the 8 items that were significantly related to the construct of withdrawal in both men and women, and an exploratory 2-factor model, were also assessed but not retained due to inconsistencies across gender.

**Conclusions**—When traditional psychometric models are applied to the COWS, it appears that the scale may not relate to a single underlying construct of withdrawal. Further research testing the hypothesized factor structure in other opioid-dependent samples is needed.

### Keywords

Opiate withdrawal; opiate dependence; psychometrics; Clinical Opiate Withdrawal Scale

## 1. INTRODUCTION

Opiate withdrawal scales were developed to examine the patient's physical dependence and physiological readiness prior to methadone or buprenorphine induction, and to compare treatments for withdrawal (Wesson and Ling, 2003). The Clinical Opiate Withdrawal Scale (COWS; Wesson and Ling, 2003) is a common measure used to assess withdrawal in clinical trials and practice, and consists of 11 observed (clinician-rated) and subjective (patient-rated) items. The COWS has been used to assess withdrawal in buprenorphine/naloxone vs. clonidine treatment groups (Ling et al., 2005; Ziedonis et al., 2009) and 7-day vs. 28-day buprenorphine/naloxone tapering schedules (Ling et al., 2009). The COWS has also been used to measure opioid withdrawal severity, where those with high baseline COWS scores, and greater decreases in COWS scores, were more likely to have treatment success compared to those with low baseline COWS scores, regardless of treatment modality (Ziedonis et al., 2009). Interestingly, such relationships were not found in the Ziedonis et al (2009) study when a patient-rated scale of opiate withdrawal, the Adjective Rating Scale of Withdrawal (Bickel et al, 1988a, 1988b; Amass et al., 2000) was used, suggesting that the clinician-rated items are of importance to capture withdrawal.

General clinical guidelines suggest that buprenorphine induction should occur when a patient is physically dependent on opioids and in mild to moderate withdrawal, or waiting for the patient to be in moderate to severe opiate withdrawal (Wesson and Ling, 2003). The items that make up the COWS have been validated in other instruments and the following cut-scores for the COWS have been offered: 5–12 = mild, 13–24 = moderate, 25–36 = moderately severe, and > 36 = severe withdrawal (Wesson and Ling, 2003). Based on clinical experience, Wesson and Ling state that at a score on the COWS of 25, buprenorphine is unlikely to precipitate withdrawal in patients who are physically dependent on opioids (2003).

It is noted that the COWS may be assessed repeatedly so that change in withdrawal due to treatment may be tracked over time. More recently, validation of the COWS was

demonstrated as the scale was found to correlate with the Clinical Institute Narcotic Assessment (CINA) and two visual analog scales (VAS) (bad drug effect and feeling sick) in a sample of opioid-dependent individuals in mild withdrawal (mean peak COWS = 7.6) during a naloxone challenge session, while discriminant validity was demonstrated as the COWS did not correlate with a placebo (Tompkins et al., 2009). This study also reported good internal consistency of the COWS (Cronbach's alpha = .78), and concludes that the COWS is a valid instrument to detect mild opiate withdrawal (Tompkins et al., 2009).

The COWS appears to be a useful tool for clinicians and researchers alike, and it may outperform other opiate withdrawal scales in assessing treatment effects (e.g., Ziedonis et al., 2009). To our knowledge it appears that the factor structure of the COWS has not been assessed. This examination would provide important information regarding the relationship of the COWS items as they make up the construct of withdrawal. Studies consisting of opiate-dependent men and women combined in one sample need verification that measurement properties of the COWS are consistent across gender. Specifically, while we are not testing if COWS levels differ across gender, we are testing the assumption that *measurement* of withdrawal is equivalent for men and women. Therefore, this study sought to advance prior work that utilized the COWS by examining inter-item correlations and the factor structure of the COWS for opioid-dependent men and women at pre-treatment in a clinical trial. As this was the first examination of the factor structure of the COWS, the goal was not to clinically refine the scale, but to apply traditional psychometric analyses to a clinically useful tool to guide future research.

## 2. METHODS

### 2.1 Clinical Trials Network 0003

Participants were from the National Drug Abuse Treatment Clinical Trials Network (CTN) 0003 (Ling et al., 2009). Secondary data analysis employing this study has been reported in previous studies (McPherson et al., 2012, 2014, 2013). This was a randomized, parallel-group, open-label study design for opioid-dependent individuals seeking treatment from 11 outpatient treatment facilities in 10 US cities. This secondary data analysis utilized data at baseline, prior to buprenorphine/naloxone induction, stabilization, and treatment (treatment consisted of two buprenorphine/naloxone taper periods). The COWS was administered by study physicians or nurses. Please see Ling et al. (2009) for a full description of the trial methodology.

### 2.2 Participants

The final intention-to-treat sample consisted of 516 participants who were potentially available for data collection. Sixty-seven percent of the sample was male (male = 347, female = 169). This sample was primarily Caucasian (Caucasian = 366, African American = 56, Hispanic = 35, Multiple = 45, Other = 13, Missing response = 1) with a mean age of 35.91 (SD = 10.45).

## 2.3 Measures

The COWS is an observed (clinician-rated) and subjective (patient-rated) scale of opiate withdrawal signs and symptoms (Wesson and Ling, 2003). The COWS items have been identified as 6 objective items (resting pulse rate, tremor, yawning, pupil size, gooseflesh skin, runny nose or tearing), 1 subjective item (anxiety or irritability), and 4 items that have both objective and subject components (GI upset, sweating, restlessness, bone or joint aches) (Tompkins et al., 2009). Various response categories are used to create individual ratings (e.g., 0–4 for pulse rate [0 = pulse rate 80 or below; 1 = pulse rate 81–100; 2 = pulse rate 101–120; 4 = pulse rate greater than 120]; 0–5 for pupil size [0 = pupils pinned or normal size for room light; 1 = pupils possibly larger than normal for room light; 2 = pupils moderately dilated; 5 = pupils so dilated that only the rim of the iris is visible]), and the ratings are summed to create a total score (Wesson and Ling, 2003). While not specified in study protocol, a pupillometer was used to assess pupil diameter. In this study, COWS total scores were 8.30 (SD = 4.01) for men and 8.86 (SD = 3.84) for women, indicating mild withdrawal for both men and women.

Previous research has reported a Cronbach's alpha of 0.78 in opioid-dependent individuals, indicating good internal consistency (Tompkins et al., 2009). Additionally, while most noted inter-item correlations have been found to be statistically significant, only restless with anxiety or irritability ( $r = .67$ ), and runny nose/tearing with yawning ( $r = .54$ ) had a moderate to strong correlation (Tompkins et al., 2009).

## 2.4 Statistical Analyses

Inter-item correlations (Spearman's rho) were first assessed for the COWS items. Next, confirmatory factor analysis (CFA) was used to examine a 1-factor model of the COWS in the total sample, and then for men and women separately. This was chosen over exploratory factor analysis given the utility of the COWS total score in clinical and research practices, coupled with previous work on the validity and reliability of the COWS total scores. Therefore, the confirmation of the established use of the COWS was warranted. Additional factor models were explored post hoc.

Model fit was assessed using the comparative fit index (CFI; study criterion = 0.900), the root mean square error of approximation (RMSEA; study criterion = 0.080), and the weighted root mean square residual (WRMR; study criterion = 1.00) (Brown, 2006; Yu, 2002). Additionally, standardized factor loadings were inspected to see which items accounted for at least 9% of the variance in the construct (factor loading of .30) (Kline, 1994). Note that within WLSMV estimation, the factor loadings represent the correlation between  $y^*$  (underlying latent continuous distribution) and the latent continuous factor, which has a variance of 1 (Finney and DiStefano, 2013). Model fit and factor loadings were examined in the gender-specific models regardless of the fit of the model in the total sample to explore potential areas of model strain in the combined sample that may be due to gender differences. Factor loadings in the gender-specific models were examined alongside model fit to explore similarities and differences in the general pattern of significant factor loadings across men and women in order to help identify if each item was related to the construct of withdrawal across gender, a step used to assist with model revision.

All primary statistical testing was conducted in Mplus, Version 6 (Muthén, 1998–2010), using robust weighted least squares (WLSMV) estimator, appropriate in that it assumes that there is a continuous and normal latent response variable (i.e., withdrawal) underling each ordinal manifest variable. Further, WLSMV is a distribution-free estimator and designed to handle ordinal items that may demonstrate a high level of skewness and/or kurtosis. For post hoc 2-factor exploratory factor models, WLSMV using Geomin rotation was used. Factor analyses were also estimated using robust maximum likelihood estimation (MLR); overall patterns of results were similar and therefore results are based on the WLSMV estimation.

### 3. RESULTS

#### 3.1 Inter-item correlations

Inter-item correlations and COWS items descriptive statistics (mean, variance, and number of zeros) are shown in tables 1 and 2. Note that there does not appear to be large discrepancies in the prevalence of zeroes in item responses or item variances across gender. In the total sample (table 1), most items significantly correlated with at least 5 other items. Of note was anxiety or irritability which significantly correlated with all other items, and pupil size, which correlated with all items but resting pulse rate. Conversely, resting pulse rate only significantly correlated with 4 other items (sweating, tremor, anxiety or irritability, and bone or joint aches) and yawning only correlated with 3 items (pupil size, anxiety or irritability, and runny nose or tearing). While most items demonstrated statistically significant relationships with the other items, the highest correlation among the COWS items in the total sample was .30 (restlessness with anxiety or irritability).

Similar patterns of inter-item correlations were found in the male and female (table 2) subsamples with the following exception: pupil size was significantly correlated with 7 other items in the male sample and was not correlated with any other items in the female sample. Note that due to differing sample sizes in the male and female samples, focus should be on the strengths of the relationships among the COWS items in order to avoid misleading conclusions based on *p*-values. In the male sample, the highest correlation among the COWS items was .31 (anxiety or irritability with bone or joints aches), and in the female sample, the highest correlation among the COWS items was .32 (restlessness with anxiety or irritability). Therefore, the largest relationships among COWS items in the total and subsamples were moderate.

#### 3.2 Confirmatory factor analysis

**3.2.1 Total sample**—Results for the total sample indicated that the 1-factor model did not fit the data well ( $X^2 = 164.073$ , CFI = 0.767, RMSEA = 0.073, WRMR = 1.286), with only the RMSEA value meeting the study criterion. In examining the standardized factor loadings (table 3), all items were statistically significantly related to the construct of withdrawal ( $p < .001$ ). The factor loading for “resting pulse rate” was  $<.30$  (loading = .16), while all other factor loadings were  $\geq .30$ . Modification indices showed that model fit could be improved by allowing the residuals for items assessing yawning and runny nose or tearing to correlate. Doing so resulted in improvement of fit ( $X^2 = 122.540$ , CFI = 0.846, RMSEA = 0.060, WRMR = 1.101).

**3.2.2 Male sample**—In males, the 1-factor model did not fit the data well ( $X^2 = 126.038$ , CFI = 0.801, RMSEA = 0.073, WRMR = 1.132), with only the RMSEA value meeting the study criterion. The item that assessed resting pulse rate did not load significantly on the factor, while all other items loaded significantly on the factor ( $p < .001$ ). The factor loading for resting pulse rate was  $<.30$  (loading = .11), as well as for tremor (loading = .26). All other factor loadings were  $\geq .30$ . As with the total sample, modification indices pointed to correlating residuals for items assessing yawning and runny nose or tearing. While fit improved ( $X^2 = 107.121$ , CFI = 0.845, RMSEA = 0.066, WRMR = 1.038), the factor loading for resting pulse rate remained nonsignificant.

**3.2.3 Female sample**—In females, the 1-factor model did not fit the data well ( $X^2 = 81.188$ , CFI = 0.694, RMSEA = 0.071, WRMR = 0.933), with the CFI well below the study criterion. The items that assessed yawning and gooseflesh skin did not load significantly on the factor, while all other items loaded significantly on the factor ( $p < .05$ ). The factor loading for resting pulse rate was  $<.30$  (loading = .24), as well as for yawning (loading = .06), pupil size (loading = .21), and gooseflesh skin (loading = .17). All other factor loadings were  $\geq .30$ . Again, modification indices suggested correlating residuals for yawning and runny nose or tearing, and model fit improved ( $X^2 = 59.315$ , CFI = 0.866, RMSEA = 0.047, WRMR = .783) with only the CFI not meeting study criterion. However, adding this correlated residual did not change the nonsignificant factor loadings for yawning and gooseflesh skin.

### 3.3 Post hoc exploratory models

**3.3.1 Reduced 1-factor model**—A reduced, 1-factor model of the COWS was analyzed where only items that had significant factor loadings for both men and women were included; resting pulse rate, yawning, and gooseflesh skin were not included in the model. For the total sample, this model did not fit the data well ( $X^2 = 65.724$ , CFI = 0.874, RMSEA = 0.067, WRMR = 1.014) with the CFI and WRMR not meeting study criterion while all factor loadings were statistically significant and  $>.30$ . For the male sample, fit was adequate ( $X^2 = 56.935$ , CFI = 0.865, RMSEA = 0.073, WRMR = .943) with only the CFI not meeting study criterion and all factor loadings were statistically significant and  $>.30$ . For the female sample, the reduced model fit the data well ( $X^2 = 28.233$ , CFI = 0.917, RMSEA = 0.049, WRMR = .688) with all fit indices meeting study criterion, however, in this model pupil size was no longer significantly related to the construct of withdrawal. All other factor loadings were statistically significant and  $>.30$ .

**3.3.2 Exploratory 2-factor model**—A 2-factor exploratory factor analysis of all COWS items was also run to see if the items would fall into 2 possible constructs (e.g., primary vs. secondary symptoms, observed vs. subjective times, etc.). In the total sample and male sample, a second factor of a single primary item (yawning) and positively cross-loaded items (pupil size and runny nose or tearing) emerged. In the female sample, a second factor of 2 items (yawning and runny nose) and 1 cross-loaded item (restlessness) arose. Therefore, items assessing yawning (for men and women) and runny nose (for women only) were driving this 2<sup>nd</sup> factor. Clinically, yawning and runny nose are not indicative of a separate construct intended to be measured by the COWS or related to meaningful construct of



withdrawal. Further, 1–2 items typically do not warrant a psychometrically-sound second factor. Thus, a 2-factor model was deemed invalid for the COWS.

#### 4. DISCUSSION

We applied traditional psychometric theory to the COWS, a clinically useful instrument to measure opiate withdrawal. This research first examined the relationships among the COWS items. While most items were indeed related, the relationships were weak to moderate, with correlations  $.32$  across all subsamples. This is similar to what has been found in previous research (Tompkins et al., 2009), which described the low to moderate correlations as demonstration of content validity in that the items covered a wide range of withdrawal symptoms. Additionally, one may not expect inter-item correlations to be strong since opioids affect individuals differently and individuals, in turn, develop tolerance to opioid effects differently.

In this sample, the item assessing anxiety or irritability correlated with most other items, while resting pulse rate and yawning only correlated with a few others. Interestingly, pupil size related to almost all other items in the male sample and was not correlated with any other items in the female sample. It does not appear that the prevalence of zeroes in item responses, or differences across item variances, explain these differences. The differences between men and women and the dissimilar pattern of relationships for this particular item on the opiate withdrawal scale may be related to other sex differences in nociception and opioid antinociception observations. For example, there are significant gender differences in pain sensitivity where women are more likely than men to experience persistent pain, pain of more intense severity and longer duration, and demonstrate greater responsiveness to opioid antinociceptive properties (Gintzler et al., 2012). Sex differences have also been reported during acute naloxone-precipitated withdrawal in opioid-dependent individuals (Chopra et al., 2008). These sex differences may also lead to different characteristics during opiate withdrawal as measured by the COWS.

The factor structure of the COWS was next examined to determine the dimensionality, as well as the strength of the items with the construct of withdrawal, for the total sample, and then for men and women separately. Correlated residuals were added to the model for each subsample and while fit improved, as expected, the additional parameter did not alleviate the issues with differing nonsignificant loadings across gender (data not shown). It appears that resting pulse rate is not related to withdrawal for men, while yawning and gooseflesh skin is not related to withdrawal for women. These effects are physiologically mediated by cranial, sympathetic and parasympathetic system nerves with their cell bodies in the spinal cord. While speculative, it is possible the sex differences observed in these COWS items may be related to the observation that, at least in rat spinal cord, mu-opioid receptor-coupled regulation of the release of endomorphin 2 has also been found to be sexually dimorphic (Chakrabarti et al., 2012). An examination of the strength of the factor loadings across men and women provides additional information on differences in the relationship between the items and the construct of withdrawal across gender. Notable discrepancies in factor loadings across gender can be seen for items assessing sweating, tremor, yawning, pupil size, gooseflesh skin, and runny nose or tearing. However, it is important to note that the



factor model did not fit the sample as a whole or for men and women separately, and therefore differences across gender may lessen, or completely go away, once an acceptable factor model is demonstrated.

Next, a reduced model comprised of only the 8 items that were significantly related to the construct of withdrawal in both men and women (deleting resting pulse rate, yawning, and gooseflesh skin from the model) was analyzed. This reduced model adequately fit for the men, but while the model fit well for women, pupil size was no longer related to withdrawal. Reducing the COWS may not be clinically helpful since different individuals will tend to be more or less sensitive to opioid effects in different physiological systems. Therefore, the clinical usefulness of the entire tool should remain the primary focus in this line of research.

Lastly, an exploratory factor analysis was then used to assess the possibility of a 2-factor model. This model proved to be invalid as a substantive second factor did not emerge.

#### 4.1 Limitations

The primary limitation to this study is that all data analyzed came from a single clinical trial, CTN0003. Participants in this study were in mild withdrawal (Ling et al., 2009); more intense withdrawal may produce different results. Additional analyses using data from other trials is essential before clinical conclusions can be drawn about the ability of the COWS to equivalently measure withdrawal across men and women. While this research only reports on the COWS items at a single time-frame within the clinical trial, additional psychometric analyses were performed for each stage of the trial and results were similar to the baseline assessment (data not shown). As a good-fitting factor model was not found in the combined or gender-specific samples, caution is needed when examining gender differences across models. Lastly, only general applications of classical test theory were used in analyses. Other types of modeling, such as finite mixture modeling, may be better suited for the COWS and should be explored.

#### 4.2 Conclusions

This research failed to find a single model where all items were related to the construct of withdrawal (i.e., statistically significant or meaningful factor loadings) for men and women in mild withdrawal. Further research testing the hypothesized factor structure in other opioid-dependent samples, particularly in samples with greater variation in COWS scores and for those in moderate opioid withdrawal, is needed. The COWS was developed to rate severity within each item because that corresponds with clinical severity within the individual on each item; that may not be necessarily the case across items. The composite score simply acknowledges that some individual will show more, or less, withdrawal symptoms within certain physiological systems and may therefore not assess a single construct of withdrawal. It is our hopes that this research will lead to further psychometric testing of this clinically useful scale.

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### Highlights

- We assessed the factor structure of the Clinical Opiate Withdrawal Scale (COWS).
- A 1-factor model did not fit the data for opioid-dependent men or women.
- The COWS may not relate to a single underlying construct of withdrawal.
- Further testing of the factor structure in opioid-dependent samples is needed.

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**Table 1**

Inter-item correlations of the Clinical Opiate Withdrawal Scale (COWS) in the total sample (N = 516).

	Resting pulse rate	GI upset	Sweating	Tremor	Restlessness	Yawning	Pupil size	Anxiety or irritability	Bone or joint aches	Gooseflesh skin	Mean (variance)	Number of zeros (%)
Resting pulse rate	---	---	---	---	---	---	---	---	---	---	.46 (.37)	309 (59.9)
GI upset	.05	---	---	---	---	---	---	---	---	---	.97 (.84)	188 (36.4)
Sweating	.11*	.22**	---	---	---	---	---	---	---	---	.96 (.45)	122 (23.6)
Tremor	.15**	.11**	.17**	---	---	---	---	---	---	---	.69 (.90)	308 (59.7)
Restlessness	.00	.03	.17**	.11*	---	---	---	---	---	---	.96 (.94)	168 (32.6)
Yawning	.00	.04	.02	-.07	.11**	---	---	---	---	---	.56 (.54)	294 (57.0)
Pupil size	.00	.10*	.18**	.09*	.12**	.22**	---	---	---	---	.67 (.58)	256 (49.6)
Anxiety or irritability	.09*	.17**	.15**	.14**	.30**	.10*	.10*	---	---	---	1.01 (.39)	92 (17.8)
Bone or joint aches	.11**	.22**	.15**	.09*	.07	.03	.09*	.27**	---	---	.84 (.41)	154 (29.8)
Gooseflesh skin	.07	.09	.21**	.05	.09*	.06	.09*	.17**	.07	---	.55 (1.50)	427 (82.8)
Runny nose or tearing	-.04	.16**	.17**	.01	.18**	.28**	.12**	.16**	.10*	.14**	.83 (.70)	158 (30.6)

\* p .05

\*\* p .01

\*\*\* p .001

Inter-item correlations of the Clinical Opiate Withdrawal Scale (COWS) in the female sample (n = 169) above the diagonal and in the male sample (n = 347) below the diagonal with means (variances) and number of zeros (%) presented in the final rows and columns.

**Table 2**

	Resting pulse rate	GI upset	Sweating	Tremor	Restlessness	Yawning	Pupil size	Anxiety or irritability	Bone or joint aches	Gooseflesh skin	Runny nose or tearing	Female mean (variance)	Female number of zeros (%)
Resting pulse rate	---	.04	.15*	.20*	-.07	-.01	.13	.16*	.12	.02	.03	.56 (.50)	93 (55.0)
GI upset	.05	---	.13	.12	.10	-.04	-.02	.19*	.25*	.10	.10	.97 (.86)	62 (36.7)
Sweating	.08	.26**	---	.13	.14	.01	.01	.08	.07	.18*	.20**	.96 (.36)	33 (19.5)
Tremor	.11*	.10*	.19**	---	.18*	-.06	.06	.16*	.11	.05	-.02	.74 (1.11)	103 (60.9)
Restlessness	.04	-.01	.18**	.07	---	.04	.14	.32**	.09	-.01	.21*	.94 (.97)	56 (33.1)
Yawning	.01	.08	.03	-.07	.15**	---	.13	-.03	-.11	.01	.26**	.56 (.57)	99 (58.6)
Pupil size	-.08	.15**	.26**	.10	.11*	.27**	---	.03	.10	.06	.05	.73 (.66)	78 (46.2)
Anxiety or Irritability	.05	.15**	.17**	.13**	.30**	.16**	.14**	---	.19*	.08	.10	1.02 (.40)	29 (17.2)
Bone or joint aches	.10	.20**	.18**	.07	.07	.10	.07	.31**	---	.03	.04	.88 (.43)	47 (27.8)
Gooseflesh skin	.08	.09	.23**	.06	.15**	.09	.11*	.21**	.09	---	.05	.71 (1.81)	131 (77.5)
Runny nose or tearing	-.07	.19**	.16**	.03	.17**	.29**	.15**	.19**	.13*	.19**	---	.79 (.59)	53 (31.4)
Male mean (variance)	.41 (.30)	.97 (.84)	.96 (.50)	.66 (.80)	.97 (.92)	.56 (.53)	.64 (.53)	1.01 (.39)	.82 (.40)	.47 (1.34)	.85 (.87)	---	---
Male number of zeros (%)	216 (62.2)	126 (36.3)	89 (25.6)	205 (59.1)	112 (32.3)	195 (56.2)	178 (51.3)	63 (18.2)	107 (30.8)	296 (85.3)	105 (30.3)	---	---

\* *p* .05

\*\* *p* .01

\*\*\* *p* .001

**Table 3**

Standardized [unstandardized] factor loadings (standard errors) in the 1-factor model of the Clinical Opiate Withdrawal Scale (COWS) across gender

<b>Full scale (11 items)</b>	<b>Total sample</b>	<b>Men</b>	<b>Women</b>
Resting pulse rate	.16(.06) ** [1.00(.00)]	.11(.07) [1.00(.00)]	.24 * (.12) [1.00(.00)]
GI upset	.39(.05) *** [2.38(.95)]	.40(.06) *** [3.45(2.22)]	.37 ** (.09) [1.56(.85)]
Sweating	.48(.05) *** [2.96(1.17)]	.51(.06) *** [4.48(2.88)]	.36 ** (.09) [1.51(.81)]
Tremor	.30(.05) *** [1.84(.80)]	.26(.07) *** [2.26(1.55)]	.40 ** (.09) [1.69(.90)]
Restlessness	.46(.05) *** [2.85(1.17)]	.43(.06) *** [3.73(2.47)]	.58 ** (.07) [2.41(1.22)]
Yawning	.32(.06) *** [1.98(.83)]	.41(.06) *** [3.61(2.31)]	.06(.10) [.24(.43)]
Pupil size	.37(.06) *** [2.28(.98)]	.45(.07) *** [3.93(2.62)]	.21 * (.10) [.87(.65)]
Anxiety or irritability	.56(.05) *** [3.44(1.35)]	.59(.05) *** [5.13(3.27)]	.54 ** (.08) [2.23(1.12)]
Bone or joint aches	.41(.05) *** [2.52(1.02)]	.42(.06) *** [3.71(2.38)]	.40 ** (.10) [1.66(.93)]
Gooseflesh skin	.44(.06) *** [2.69(1.11)]	.56(.08) *** [4.87(3.14)]	.17(.11) [.70(.64)]
Runny nose or tearing	.47(.05) *** [2.90(1.17)]	.51(.06) *** [4.47(2.90)]	.33 ** (.10) [1.38(.80)]
<b>Reduced scale (8 items)</b>			
GI upset	.40 *** (.05) [1.00(.00)]	.42 *** (.06) [1.00(.00)]	.36 *** (.09) [1.00(.00)]
Sweating	.47 *** (.05) [1.17(.18)]	.53 *** (.06) [1.26(.20)]	.33 *** (.10) [.91(.33)]
Tremor	.33 *** (.05) [.83(.16)]	.31 *** (.07) [.74(1.17)]	.38 *** (.08) [1.05(.36)]
Restlessness	.48 *** (.05) [1.21(.20)]	.41 *** (.06) [.99(.20)]	.65 *** (.07) [1.79(.53)]
Pupil size	.33 *** (.06) [.83(.18)]	.42 *** (.07) [.99(.21)]	.18(.10) [.50(.30)]
Anxiety or irritability	.58 *** (.05) [1.46(.24)]	.60 *** (.06) [1.44(.23)]	.52 *** (.08) [1.45(.47)]
Bone or joint aches	.44 *** (.05) [1.11 (.18)]	.46 *** (.06) [1.10(.19)]	.38 *** (.10) [1.06(.36)]
Runny nose or tearing	.39 *** (.06) [.98 (.18)]	.42 *** (.07) [1.00(.19)]	.33 *** (.10) [.90(.35)]

\*  
p .05

\*\*  
p .01

\*\*\*  
p .001.

P-values based on standardized factor loadings.