

### Exploration of Thresholds for PRISM-5-OP Binary Diagnoses of POUD

**Background.** For all substances in DSM-5 SUD, numerous studies showed that the 11 criteria formed inherently dimensional measures<sup>1</sup>. Nevertheless, for all disorders in DSM-5, a diagnostic threshold was needed to assist in clinical decision-making, reimbursements, medical record-keeping, and to estimate prevalence. As is the case for most diagnoses in DSM-IV and DSM-5, no biological test has been available to use as a “gold standard” against which to indicate a valid diagnostic threshold for SUD<sup>2</sup>, and for DSM-5 SUD, no empirical evidence strongly supported any particular threshold as most valid to differentiate between cases and non-cases of SUD. Therefore, the DSM-5 Workgroup designated thresholds that avoided disruption in U.S. national and sub-group prevalence rates to the extent possible<sup>1</sup>. For all substances, a diagnostic threshold of  $\geq 2$  criteria was chosen, which includes mild conditions (2-3 criteria, important for preventive intervention but not indicating addiction), and moderate-to-severe conditions indicated by  $\geq 4$  criteria, which are generally understood as indicating addiction, and which provided the best agreement with the well-validated DSM-IV dependence diagnoses<sup>3-5</sup>.

In the present study, all three POUD criteria sets (completely-unadjusted, DSM-5, pain-adjusted) were dimensional continuous constructs (see factor analyses, e-Table 1). Whether or not the DSM-5 thresholds ( $\geq 2$  criteria,  $\geq 4$  criteria) were optimal to diagnose POUD among those using prescription opioids for chronic pain was unknown. We therefore undertook analyses to determine if the optimal threshold for POUD binary diagnostic measures should be other than  $\geq 2$  criteria to indicate any POUD diagnosis, and  $\geq 4$  criteria to indicate the moderate to severe level that is generally understood to indicate addiction.

**Methods.** For each POUD criteria set (completely-unadjusted, DSM-5, pain-adjusted), receiver operating characteristic (ROC) curve analyses<sup>6</sup> were used to explore for an optimal threshold for a dichotomous POUD diagnosis. The area under the ROC curve (AUC) measures discrimination, i.e. the total ability over all possible cut-points of the diagnostic test (in this case, the criteria set) to predict the presence or absence of another binary variable<sup>7</sup> (here, one of the validators). This analysis included seven binary validators: substance treatment, tampering, prescription for legitimate reason (reverse coded for consistency), personal history of other SUD, family history of DUD, antisocial personality disorder, and internalizing mental disorders. The analyses also included three continuous validators dichotomized at their median values: worst pain in past week (reverse coded), sensation seeking, and impulsivity. The Youden index<sup>8</sup>, a function of sensitivity and specificity, indicates the maximum vertical distance between the ROC curve and the diagonal line of chance. For each validator, the cut-point with the highest Youden value would be considered the “best” (most valid) for a dichotomous diagnosis, since it optimizes diagnostic ability (to “predict” the validator) and provides the most information. Differences between Youden values were tested for significance based on overlapping 95% confidence intervals (CI) from 50 bootstrapped samples

Additionally, a continuous External Composite Validator (ECV) was created from the set of dichotomous validators. A factor analysis model with one factor underlying all dichotomous validators was fit, using full information maximum likelihood estimation, which allowed inclusion of all variables, even those with missing values. The derived factor score estimate, a weighted sum of the validators, was used as a composite validator. Then, for each criteria set, the Spearman correlation between each possible cut-

point (1-10) and the composite validator was calculated, to investigate whether any cut-points were more correlated with the composite validator than the others. Differences between the Spearman correlations were tested based on overlapping 95% CI from 50 bootstrapped samples.

**Results.** Figure 1 and Table 1 show the Youden index values for each of the validators tested at each possible cut-point (1-10 criteria) of the dimensional measures. As shown, a number of cut-points yielded very similar Youden values that did not differ significantly from each other, providing little empirical evidence to support a specific cut-point and making the choice of a single optimal cut-point difficult.

Figure 2 and Table 2 show the correlations of the POUD measures dichotomized across a range of values with the ECV. As with the Youden index, many cut-points showed correlations that did not differ significantly (based on overlapping 95% CI from 50 bootstrapped samples), suggesting no “optimal” cut-points for these inherently dimensional measures.

**Discussion.** As was the case for the DSM-5 SUD measures, the present results did not consistently provide empirical evidence supporting the differential validity of any particular cut-point indicating a diagnostic threshold. Therefore, in the absence of such evidence, for the binary POUD variables we used the standard DSM-5 cut-points:  $\geq 2$  criteria for any POUD diagnosis, and  $\geq 4$  criteria for a moderate-to-severe score suggesting addiction. These cut-points are supported well by the data and have the advantage of being consistent with the thresholds that the field is now using on a widespread basis, and are thus familiar to research and clinical audiences. Ultimately, prospective validation would provide further important information, e.g., whether any particular thresholds at a given point in time predict how patients feel and function medically, psychosocially, and in terms of their opioid use at subsequent follow-ups. A prospective component was not part of the present validation study design, but should be undertaken in future studies.

## References

1. Hasin DS, O'Brien CP, Auriacombe M, et al. DSM-5 criteria for substance use disorders: recommendations and rationale. *Am J Psychiatry*. 2013;170(8):834-851.
2. Kamphuis JH, Noordhof A. On categorical diagnoses in DSM-V: cutting dimensions at useful points? *Psychol Assess*. 2009;21(3):294-301.
3. Hasin D, Hatzenbuehler ML, Keyes K, Ogburn E. Substance use disorders: Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) and International Classification of Diseases, tenth edition (ICD-10). *Addiction*. 2006;101 Suppl 1:59-75.
4. Goldstein RB, Chou SP, Smith SM, et al. Nosologic Comparisons of DSM-IV and DSM-5 Alcohol and Drug Use Disorders: Results From the National Epidemiologic Survey on Alcohol and Related Conditions-III. *J Stud Alcohol Drugs*. 2015;76(3):378-388.
5. Compton WM, Dawson DA, Goldstein RB, Grant BF. Crosswalk between DSM-IV dependence and DSM-5 substance use disorders for opioids, cannabis, cocaine and alcohol. *Drug Alcohol Depend*. 2013;132(1-2):387-390.
6. Shin S. ROC analysis for the evaluation of continuous biomarkers: Existing tools and new features in SAS 9.2. 2012; <http://pharmasug.org/download/papers/SP09.pdf>. Accessed August 8, 2012.
7. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology*. 1982;143(1):29-36.
8. Schisterman EF, Perkins NJ, Liu A, Bondell H. Optimal cut-point and its corresponding Youden Index to discriminate individuals using pooled blood samples. *Epidemiology*. 2005;16(1):73-81.

**TABLE S1.** Single-factor model of prescription opioid use disorder criteria as measured by the PRISM-5-OP (N=606)

|  | <b>Completely-unadjusted<sup>a</sup></b> | <b>DSM-5<sup>b</sup></b>  | <b>Pain-adjusted<sup>c</sup></b> |
|--|--|---------------------------|----------------------------------|
|  | <i>Factor loadings</i>                   |                           |                                  |
| <b>Criteria</b>  |  |                           |                                  |
| 1. Hazardous use   | 0.899                                    | 0.891                     | 0.927                            |
| 2. Social/interpersonal problems due to use              | 0.939                                    | 0.936                     | 0.948                            |
| 3. Neglect major roles to use                            | 0.880                                    | 0.874                     | 0.947                            |
| 4. Used larger amounts/longer                            | 0.880                                    | 0.886                     | 0.938                            |
| 5. Persistent desire/ attempts to quit/cut down          | 0.822                                    | 0.818                     | 0.785                            |
| 6. Much time spent using                                 | 0.890                                    | 0.889                     | 0.956                            |
| 7. Continued use despite physical/psychological problems | 0.902                                    | 0.898                     | 0.959                            |
| 8. Activities given up to use                            | 0.862                                    | 0.856                     | 0.953                            |
| 9. Craving   | 0.918                                    | 0.908                     | 0.972                            |
| 10. Withdrawal/ use to avoid withdrawal                  | 0.958                                    | 0.986                     | 0.985                            |
| 11. Tolerance  | 0.787                                    | 0.955                     | 0.980                            |
| <b>Model fit indices</b>                                 |  |                           |                                  |
| Eigenvalues (first four)                                 | 8.78; 0.56;<br>0.37; 0.37                | 9.02; 0.50;<br>0.35; 0.30 | 9.77; 0.40;<br>0.24; 0.18        |
| Comparative fit index (CFI)                              | 0.995                                    | 0.996                     | 0.999                            |
| Root mean square error of approximation (RMSEA) (90% CI) | 0.05 (0.04, 0.06)                        | 0.05 (0.04, 0.07)         | 0.04 (0.03, 0.05)                |

a Completely-unadjusted: all DSM-5 POUD criteria that occurred, regardless of whether prescription opioids were taken only as prescribed or more/other than as prescribed

b DSM-5: all DSM-5 POUD criteria that occurred, except tolerance and withdrawal, which are counted as positive only among patients using opioids in non-prescribed ways

c Pain-adjusted: all DSM-5 POUD criteria that includes the DSM-5 adjustment, and in addition, counted as positive only the criteria that occurred for non-therapeutic reasons (i.e., other than to treat pain, such as to get high)

**TABLE S2.** Youden Index for all possible cut-points

| <b>Cut-Point</b>                                 | <b>Tampering</b>     | <b>Substance treatment</b> | <b>Prescription for legitimate reason<sup>a</sup></b> | <b>Personal history of any other SUD</b> | <b>Antisocial personality disorder</b> | <b>Internalizing mental disorders</b> | <b>Family history of any DUD</b> | <b>Worst pain in past week<sup>a,b</sup></b> | <b>Sensation seeking<sup>b,c</sup></b> | <b>Impulsivity<sup>b,c</sup></b> |
|--|----------------------|----------------------------|---|--|--|---------------------------------------|----------------------------------|--|--|----------------------------------|
| <i>Completely-unadjusted dimensional measure</i> |                      |                            |   |  |  |                                       |                                  |  |  |                                  |
| ≥ 1  | 0.056 (0.000, 0.115) | 0.028 (0.000, 0.074)       | 0.035 (0.000, 0.087)                                  | 0.053 (0.000, 0.126)                     | 0.094 (0.010, 0.177)                   | 0.103 (0.029, 0.177)                  | 0.036 (0.000, 0.088)             | 0.050 (0.000, 0.119)                         | 0.063 (0.000, 0.145)                   | 0.128 (0.024, 0.232)             |
| ≥ 2  | 0.201 (0.137, 0.266) | 0.181 (0.105, 0.257)       | 0.131 (0.046, 0.217)                                  | 0.132 (0.041, 0.223)                     | 0.207 (0.122, 0.292)                   | 0.171 (0.085, 0.257)                  | 0.078 (0.000, 0.159)             | 0.040 (0.000, 0.100)                         | 0.171 (0.066, 0.275)                   | 0.180 (0.055, 0.305)             |
| ≥ 3  | 0.317 (0.251, 0.382) | 0.341 (0.265, 0.416)       | 0.272 (0.186, 0.358)                                  | 0.264 (0.186, 0.342)                     | 0.296 (0.198, 0.395)                   | 0.228 (0.157, 0.298)                  | 0.121 (0.040, 0.202)             | 0.033 (0.000, 0.080)                         | 0.217 (0.118, 0.317)                   | 0.190 (0.089, 0.292)             |
| ≥ 4  | 0.383 (0.320, 0.446) | 0.367 (0.303, 0.431)       | 0.314 (0.240, 0.388)                                  | 0.320 (0.252, 0.388)                     | 0.373 (0.283, 0.463)                   | 0.233 (0.147, 0.319)                  | 0.140 (0.065, 0.216)             | 0.078 (0.013, 0.143)                         | 0.257 (0.155, 0.359)                   | 0.164 (0.065, 0.263)             |
| ≥ 5  | 0.396 (0.339, 0.454) | 0.388 (0.334, 0.442)       | 0.332 (0.259, 0.406)                                  | 0.314 (0.252, 0.377)                     | 0.356 (0.271, 0.441)                   | 0.207 (0.124, 0.290)                  | 0.162 (0.090, 0.234)             | 0.088 (0.025, 0.151)                         | 0.242 (0.145, 0.340)                   | 0.156 (0.063, 0.248)             |
| ≥ 6  | 0.400 (0.339, 0.460) | 0.386 (0.332, 0.439)       | 0.341 (0.267, 0.416)                                  | 0.289 (0.239, 0.339)                     | 0.352 (0.255, 0.449)                   | 0.189 (0.119, 0.259)                  | 0.145 (0.076, 0.215)             | 0.094 (0.036, 0.152)                         | 0.254 (0.160, 0.347)                   | 0.151 (0.067, 0.235)             |
| ≥ 7  | 0.390 (0.328, 0.452) | 0.366 (0.310, 0.422)       | 0.318 (0.235, 0.400)                                  | 0.271 (0.223, 0.319)                     | 0.319 (0.225, 0.412)                   | 0.170 (0.108, 0.232)                  | 0.155 (0.088, 0.222)             | 0.096 (0.039, 0.154)                         | 0.245 (0.163, 0.326)                   | 0.158 (0.085, 0.232)             |
| ≥ 8  | 0.361 (0.295, 0.427) | 0.300 (0.247, 0.353)       | 0.270 (0.200, 0.340)                                  | 0.223 (0.185, 0.262)                     | 0.237 (0.156, 0.318)                   | 0.140 (0.090, 0.190)                  | 0.117 (0.061, 0.174)             | 0.065 (0.013, 0.117)                         | 0.194 (0.128, 0.260)                   | 0.158 (0.091, 0.225)             |
| ≥ 9  | 0.313 (0.253, 0.374) | 0.251 (0.200, 0.302)       | 0.237 (0.175, 0.299)                                  | 0.188 (0.152, 0.225)                     | 0.191 (0.106, 0.276)                   | 0.122 (0.073, 0.171)                  | 0.109 (0.058, 0.159)             | 0.065 (0.016, 0.114)                         | 0.153 (0.093, 0.213)                   | 0.136 (0.076, 0.196)             |
| ≥ 10   | 0.233 (0.170, 0.296) | 0.198 (0.152, 0.243)       | 0.190 (0.130, 0.250)                                  | 0.150 (0.119, 0.182)                     | 0.143 (0.059, 0.226)                   | 0.091 (0.048, 0.134)                  | 0.081 (0.035, 0.127)             | 0.043 (0.000, 0.090)                         | 0.127 (0.070, 0.183)                   | 0.121 (0.065, 0.176)             |
| <i>DSM-5 dimensional measure</i>                 |                      |                            |   |  |  |                                       |                                  |  |  |                                  |
| ≥ 1  | 0.106 (0.036, 0.175) | 0.063 (0.000, 0.130)       | 0.051 (0.000, 0.122)                                  | 0.073 (0.000, 0.156)                     | 0.137 (0.050, 0.224)                   | 0.146 (0.067, 0.225)                  | 0.050 (0.000, 0.117)             | 0.041 (0.000, 0.097)                         | 0.087 (0.000, 0.176)                   | 0.134 (0.024, 0.243)             |
| ≥ 2  | 0.278 (0.212, 0.344) | 0.282 (0.210, 0.353)       | 0.223 (0.136, 0.310)                                  | 0.214 (0.129, 0.298)                     | 0.278 (0.190, 0.366)                   | 0.193 (0.116, 0.269)                  | 0.131 (0.054, 0.208)             | 0.041 (0.000, 0.096)                         | 0.197 (0.093, 0.300)                   | 0.208 (0.087, 0.329)             |
| ≥ 3  | 0.368 (0.306, 0.430) | 0.369 (0.299, 0.439)       | 0.313 (0.236, 0.390)                                  | 0.319 (0.251, 0.387)                     | 0.348 (0.256, 0.441)                   | 0.227 (0.144, 0.309)                  | 0.155 (0.082, 0.227)             | 0.056 (0.000, 0.121)                         | 0.243 (0.139, 0.348)                   | 0.161 (0.057, 0.265)             |
| ≥ 4  | 0.400 (0.337, 0.462) | 0.392 (0.334, 0.449)       | 0.326 (0.252, 0.400)                                  | 0.323 (0.259, 0.386)                     | 0.377 (0.291, 0.464)                   | 0.198 (0.116, 0.280)                  | 0.147 (0.073, 0.222)             | 0.081 (0.022, 0.140)                         | 0.232 (0.131, 0.333)                   | 0.155 (0.064, 0.247)             |
| ≥ 5  | 0.423 (0.369, 0.478) | 0.422 (0.367, 0.477)       | 0.361 (0.288, 0.434)                                  | 0.315 (0.259, 0.371)                     | 0.374 (0.286, 0.462)                   | 0.199 (0.124, 0.275)                  | 0.157 (0.084, 0.231)             | 0.090 (0.032, 0.148)                         | 0.250 (0.156, 0.345)                   | 0.143 (0.054, 0.232)             |
| ≥ 6  | 0.409 (0.348, 0.469) | 0.396 (0.341, 0.451)       | 0.352 (0.278, 0.426)                                  | 0.294 (0.249, 0.339)                     | 0.345 (0.250, 0.440)                   | 0.178 (0.110, 0.246)                  | 0.151 (0.080, 0.222)             | 0.092 (0.035, 0.149)                         | 0.266 (0.186, 0.347)                   | 0.167 (0.090, 0.245)             |
| ≥ 7  | 0.407 (0.344, 0.469) | 0.361 (0.303, 0.419)       | 0.320 (0.239, 0.401)                                  | 0.262 (0.219, 0.304)                     | 0.311 (0.218, 0.404)                   | 0.159 (0.100, 0.218)                  | 0.153 (0.083, 0.222)             | 0.081 (0.025, 0.136)                         | 0.246 (0.169, 0.323)                   | 0.189 (0.116, 0.261)             |
| ≥ 8  | 0.365 (0.299, 0.432) | 0.294 (0.241, 0.346)       | 0.274 (0.205, 0.344)                                  | 0.219 (0.181, 0.258)                     | 0.230 (0.149, 0.311)                   | 0.135 (0.087, 0.184)                  | 0.115 (0.059, 0.171)             | 0.065 (0.013, 0.117)                         | 0.189 (0.125, 0.252)                   | 0.153 (0.087, 0.219)             |

|  |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
|--|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| ≥ 9                                      | 0.313 (0.253, 0.374) | 0.251 (0.200, 0.302) | 0.237 (0.175, 0.299) | 0.188 (0.152, 0.225) | 0.191 (0.106, 0.276) | 0.122 (0.073, 0.171) | 0.109 (0.058, 0.159) | 0.065 (0.016, 0.114) | 0.153 (0.093, 0.213) | 0.136 (0.076, 0.196) |
| ≥ 10                                     | 0.235 (0.174, 0.297) | 0.201 (0.158, 0.244) | 0.193 (0.134, 0.252) | 0.147 (0.115, 0.180) | 0.145 (0.062, 0.228) | 0.088 (0.044, 0.132) | 0.084 (0.039, 0.129) | 0.040 (0.000, 0.085) | 0.127 (0.070, 0.183) | 0.121 (0.065, 0.176) |
| <i>Pain-adjusted dimensional measure</i> |                      |                      |                      |                      |                      |                      |                      |                      |                      |                      |
| ≥ 1                                      | 0.309 (0.242, 0.376) | 0.326 (0.257, 0.395) | 0.283 (0.204, 0.363) | 0.257 (0.182, 0.331) | 0.306 (0.215, 0.396) | 0.208 (0.119, 0.297) | 0.133 (0.060, 0.205) | 0.034 (0.000, 0.084) | 0.210 (0.107, 0.314) | 0.174 (0.070, 0.278) |
| ≥ 2                                      | 0.430 (0.365, 0.495) | 0.427 (0.360, 0.493) | 0.361 (0.286, 0.437) | 0.353 (0.294, 0.412) | 0.380 (0.287, 0.474) | 0.210 (0.129, 0.291) | 0.186 (0.106, 0.266) | 0.103 (0.043, 0.163) | 0.240 (0.148, 0.332) | 0.193 (0.106, 0.280) |
| ≥ 3                                      | 0.442 (0.382, 0.503) | 0.450 (0.388, 0.512) | 0.375 (0.298, 0.452) | 0.348 (0.293, 0.404) | 0.395 (0.303, 0.486) | 0.178 (0.100, 0.256) | 0.182 (0.105, 0.260) | 0.126 (0.067, 0.185) | 0.247 (0.159, 0.335) | 0.140 (0.056, 0.225) |
| ≥ 4                                      | 0.453 (0.390, 0.516) | 0.453 (0.394, 0.512) | 0.376 (0.303, 0.449) | 0.337 (0.288, 0.387) | 0.409 (0.317, 0.500) | 0.161 (0.085, 0.237) | 0.181 (0.108, 0.254) | 0.111 (0.055, 0.166) | 0.253 (0.160, 0.346) | 0.162 (0.079, 0.245) |
| ≥ 5                                      | 0.436 (0.375, 0.497) | 0.430 (0.371, 0.489) | 0.378 (0.305, 0.452) | 0.307 (0.263, 0.351) | 0.384 (0.292, 0.476) | 0.167 (0.095, 0.240) | 0.179 (0.113, 0.246) | 0.111 (0.054, 0.169) | 0.239 (0.149, 0.328) | 0.166 (0.081, 0.250) |
| ≥ 6                                      | 0.407 (0.345, 0.468) | 0.383 (0.327, 0.438) | 0.343 (0.267, 0.420) | 0.275 (0.234, 0.316) | 0.320 (0.225, 0.415) | 0.166 (0.103, 0.228) | 0.153 (0.080, 0.225) | 0.083 (0.023, 0.143) | 0.249 (0.173, 0.325) | 0.177 (0.104, 0.251) |
| ≥ 7                                      | 0.388 (0.323, 0.453) | 0.337 (0.278, 0.395) | 0.300 (0.219, 0.380) | 0.250 (0.207, 0.292) | 0.286 (0.191, 0.382) | 0.147 (0.088, 0.206) | 0.149 (0.082, 0.216) | 0.079 (0.025, 0.133) | 0.228 (0.150, 0.306) | 0.172 (0.103, 0.241) |
| ≥ 8                                      | 0.361 (0.298, 0.425) | 0.285 (0.233, 0.338) | 0.262 (0.195, 0.330) | 0.213 (0.174, 0.252) | 0.208 (0.128, 0.287) | 0.129 (0.080, 0.179) | 0.105 (0.049, 0.161) | 0.066 (0.011, 0.121) | 0.181 (0.118, 0.244) | 0.146 (0.081, 0.212) |
| ≥ 9                                      | 0.299 (0.238, 0.361) | 0.245 (0.195, 0.294) | 0.232 (0.171, 0.294) | 0.179 (0.142, 0.215) | 0.187 (0.100, 0.274) | 0.112 (0.063, 0.160) | 0.112 (0.060, 0.164) | 0.052 (0.004, 0.101) | 0.147 (0.086, 0.207) | 0.144 (0.087, 0.202) |
| ≥ 10                                     | 0.206 (0.145, 0.266) | 0.183 (0.141, 0.226) | 0.190 (0.135, 0.245) | 0.134 (0.103, 0.166) | 0.098 (0.021, 0.176) | 0.075 (0.034, 0.115) | 0.070 (0.028, 0.111) | 0.028 (0.000, 0.063) | 0.115 (0.059, 0.171) | 0.110 (0.056, 0.164) |

95% CI are generated from 50 bootstrapped samples.

a Reverse coded for consistency with other validators

b continuous scales were dichotomized by their median values

c N=313

**TABLE S3.** Correlation of External Composite Validator and all potential cut-points of the dimensional measures (N=606)

| Cut-Point | Spearman's correlation (95% CI)        |                        |                                |
|-----------|--|------------------------|--------------------------------|
|           | Completely-unadjusted binary diagnosis | DSM-5 binary diagnosis | pain-adjusted binary diagnosis |
| ≥ 1       | 0.073 (-0.006, 0.152)                  | 0.129 (0.048, 0.209)   | 0.374 (0.309, 0.440)           |
| ≥ 2       | 0.231 (0.158, 0.303)                   | 0.330 (0.262, 0.397)   | 0.511 (0.449, 0.573)           |
| ≥ 3       | 0.390 (0.320, 0.459)                   | 0.443 (0.384, 0.503)   | 0.539 (0.483, 0.595)           |
| ≥ 4       | 0.457 (0.397, 0.518)                   | 0.474 (0.417, 0.531)   | 0.547 (0.495, 0.599)           |
| ≥ 5       | 0.481 (0.426, 0.535)                   | 0.517 (0.467, 0.567)   | 0.539 (0.487, 0.591)           |
| ≥ 6       | 0.498 (0.444, 0.551)                   | 0.517 (0.464, 0.569)   | 0.514 (0.461, 0.568)           |
| ≥ 7       | 0.496 (0.440, 0.551)                   | 0.502 (0.447, 0.556)   | 0.486 (0.429, 0.542)           |
| ≥ 8       | 0.453 (0.403, 0.503)                   | 0.453 (0.403, 0.502)   | 0.442 (0.393, 0.492)           |
| ≥ 9       | 0.413 (0.362, 0.464)                   | 0.413 (0.362, 0.464)   | 0.408 (0.355, 0.460)           |
| ≥ 10      | 0.353 (0.295, 0.411)                   | 0.358 (0.303, 0.413)   | 0.333 (0.277, 0.388)           |

Since the composite validator is a continuous measure, correlation was reported instead of Youden index (appropriate for categorical measures).  
95% CI were generated from 50 bootstrapped samples.

| <b>TABLE S4.</b> Characteristics of the validation and test-retest samples, overall and by type of site |                   |                             |                     |                                |                            |                     |
|---|-------------------|-----------------------------|---------------------|--------------------------------|----------------------------|---------------------|
|   | Validation sample |                             |                     | Test-retest reliability sample |                            |                     |
|   | All (N=606)       | Substance treatment (N=258) | Pain clinic (N=348) | All (N=206)                    | Substance treatment (N=97) | Pain clinic (N=109) |
|   | Prevalence (%)    |                             |                     |                                |                            |                     |
| <b>Demographic Characteristic</b>   |                   |                             |                     |                                |                            |                     |
| Age   |                   |                             |                     |                                |                            |                     |
| 20-29   | 13.7              | 26.4                        | 4.3                 | 11.7                           | 20.6                       | 3.7                 |
| 30-39   | 20.8              | 39.5                        | 6.9                 | 26.2                           | 43.3                       | 11.0                |
| 40-49   | 15.0              | 15.9                        | 14.4                | 18.0                           | 20.6                       | 15.6                |
| ≥50   | 50.5              | 18.2                        | 74.4                | 44.2                           | 15.5                       | 69.7                |
| Sex   |                   |                             |                     |                                |                            |                     |
| Male  | 49.8              | 65.5                        | 38.2                | 49.0                           | 63.9                       | 35.8                |
| Female  | 50.2              | 34.5                        | 61.8                | 51.0                           | 36.1                       | 64.2                |
| Race  |                   |                             |                     |                                |                            |                     |
| White   | 77.9              | 74.8                        | 80.2                | 79.1                           | 74.2                       | 83.5                |
| Black   | 7.4               | 6.6                         | 8.0                 | 6.8                            | 9.3                        | 4.6                 |
| Hispanic  | 11.2              | 15.1                        | 8.3                 | 11.7                           | 14.4                       | 9.2                 |
| Other   | 3.5               | 3.5                         | 3.4                 | 2.4                            | 2.1                        | 2.8                 |
| Education   |                   |                             |                     |                                |                            |                     |
| No College  | 30.7              | 46.5                        | 19.0                | 33.5                           | 49.5                       | 19.3                |
| Some College  | 69.3              | 53.5                        | 81.0                | 66.5                           | 50.5                       | 80.7                |
| Marital   |                   |                             |                     |                                |                            |                     |
| Neither   | 54.1              | 72.1                        | 40.8                | 53.4                           | 66.0                       | 42.2                |
| Living together   | 11.4              | 14.3                        | 9.2                 | 13.1                           | 16.5                       | 10.1                |
| Married   | 34.5              | 13.6                        | 50.0                | 33.5                           | 17.5                       | 47.7                |
| Employment  |                   |                             |                     |                                |                            |                     |
| None  | 76.1              | 77.9                        | 74.7                | 76.7                           | 76.3                       | 77.1                |
| Any   | 23.9              | 22.1                        | 25.3                | 23.3                           | 23.7                       | 22.9                |
| Health Insurance  |                   |                             |                     |                                |                            |                     |
| Public  | 76.9              | 90.7                        | 66.7                | 79.6                           | 91.8                       | 68.8                |
| Private   | 35.8              | 13.2                        | 52.6                | 34.0                           | 13.4                       | 52.3                |
| Mode of PRISM-5-OP Interview  |                   |                             |                     |                                |                            |                     |
| In-person   | 50.2              | 100.0                       | 13.2                | 54.4                           | 100.0                      | 13.8                |
| Phone   | 49.8              | 0.0                         | 86.8                | 45.6                           | 0.0                        | 86.2                |
| <b>Validators</b>   |                   |                             |                     |                                |                            |                     |
| <b>Binary</b>   |                   |                             |                     |                                |                            |                     |

|   | Validation sample |                             |                     | Test-retest reliability sample |                            |                     |
|---|-------------------|-----------------------------|---------------------|--------------------------------|----------------------------|---------------------|
|   | All (N=606)       | Substance treatment (N=258) | Pain clinic (N=348) | All (N=206)                    | Substance treatment (N=97) | Pain clinic (N=109) |
| Lifetime substance treatment  | 48.0              | 100.0                       | 9.5                 | 47.1                           | 100.0                      | 0.0                 |
| Family history of any DUD <sup>a</sup>  | 38.6              | 59.3                        | 23.3                | 41.8                           | 62.9                       | 22.9                |
| Personal history of other SUD   | 66.7              | 99.2                        | 42.5                | 67.5                           | 97.9                       | 40.4                |
| Lifetime antisocial personality disorder  | 18.2              | 39.2                        | 2.6                 | 18.9                           | 37.1                       | 2.8                 |
| Lifetime internalizing mental disorders <sup>b</sup>  | 66.3              | 84.1                        | 53.2                | 59.7                           | 73.2                       | 47.7                |
| Ever tampered with medication   | 29.0              | 61.6                        | 4.9                 | 29.6                           | 56.7                       | 5.5                 |
| Prescription for legitimate reason  | 66.7              | 31.4                        | 92.8                | 64.1                           | 32.0                       | 92.7                |
| <b>Continuous</b>   | Mean (SD)         | Mean (SD)                   | Mean (SD)           | Mean (SD)                      | Mean (SD)                  | Mean (SD)           |
| Worst pain level in past week   | 6.53 (3.90)       | 5.31 (4.18)                 | 7.43 (3.42)         | 6.35 (3.97)                    | 5.32 (4.30)                | 7.27 (3.41)         |
| Sensation seeking <sup>c</sup>  | 2.67 (0.95)       | 3.30 (0.95)                 | 2.27 (0.70)         | 2.94 (1.03)                    | 3.23 (0.97)                | 2.09 (0.69)         |
| Impulsivity <sup>c</sup>  | 0.72 (0.58)       | 0.98 (0.66)                 | 0.56 (0.46)         | 0.81 (0.59)                    | 0.94 (0.59)                | 0.45 (0.42)         |
| <p>a DUD= any SUD except alcohol<br/> b major depressive disorder, persistent depressive disorder, generalized anxiety disorder, PTSD<br/> c N's for these scales: whole sample=313; addiction treatment=121; pain clinic=192; reliability sub-sample=86; addiction treatment=64; pain clinic=22.</p> |                   |                             |                     |                                |                            |                     |



**TABLE S5.** Differential effects of adjusting PRISM-5-OP prescription opioid use disorder (POUD) criteria for therapeutic intent/pain relief in patient treatment settings: pain clinics vs. addiction treatment settings

| Individual Criteria   | DSM-5 POUD criteria for patients treated in pain clinics |   |                  |         | DSM-5 POUD criteria for patients treated in addiction settings |   |                  |         | Difference in associations of unadjusted vs adjusted criteria between patients in addiction treatment vs. pain clinics |         |
|---|--|---|------------------|---------|--|---|------------------|---------|--|---------|
|   | % Unadjusted for therapeutic intent/pain relief          | % Adjusted for therapeutic intent/pain relief | aOR <sup>a</sup> | p-value | % Unadjusted for therapeutic intent/pain relief                | % Adjusted for therapeutic intent/pain relief | aOR <sup>b</sup> | p-value | Ratio of aORs <sup>c</sup>   | p-value |
| 1. Hazardous use  | 2.3  | 1.1   | 0.49             | 0.048   | 26.0   | 25.2  | 0.96             | 0.154   | 1.95   | 0.065   |
| 2. Social/interpersonal problems due to use                 | 3.4  | 1.7   | 0.48             | 0.015   | 36.8   | 36.4  | 0.98             | 0.316   | 2.02   | 0.018   |
| 3. Neglected major roles to use                             | 9.8  | 2.3   | 0.21             | <.001   | 36.8   | 35.7  | 0.95             | 0.081   | 4.48   | <.001   |
| 4. Used larger amounts/longer                               | 9.5  | 3.4   | 0.34             | <.001   | 42.6   | 41.9  | 0.97             | 0.156   | 2.87   | <.001   |
| 5. Persistent desire or repeated attempts to quit/cut down  | 40.5   | 18.7  | 0.33             | <.001   | 53.1   | 38.8  | 0.55             | <.001   | 1.66   | <.001   |
| 6. Much time spent using                                    | 9.8  | 2.3   | 0.21             | <.001   | 39.9   | 39.5  | 0.98             | 0.316   | 4.69   | <.001   |
| 7. Continued use despite physical OR psychological problems | 7.8  | 2.0   | 0.24             | <.001   | 40.3   | 39.9  | 0.98             | 0.316   | 4.10   | <.001   |
| 8. Activities given up to use                               | 19.0   | 5.2   | 0.23             | <.001   | 45.0   | 43.8  | 0.95             | 0.081   | 4.23   | <.001   |
| 9. Craving  | 18.4   | 7.8   | 0.37             | <.001   | 56.2   | 55.4  | 0.97             | 0.156   | 2.63   | <.001   |
| 10. Withdrawal OR use to avoid withdrawal                   | 10.6   | 2.9   | 0.24             | <.001   | 56.2   | 53.9  | 0.91             | 0.013   | 3.71   | <.001   |
| 11. Tolerance   | 34.5   | 6.6   | 0.13             | <.001   | 51.6   | 48.4  | 0.88             | 0.004   | 6.76   | <.001   |

<sup>a</sup> Odds ratio, adjusted versus unadjusted criterion in patients treated in pain clinics, controlling for age, sex, race/ethnicity, education, marital status, employment, health insurance.  
<sup>b</sup> Odds ratio, adjusted versus unadjusted criterion in patients treated in addiction settings, controlling for age, sex, race/ethnicity, education, marital status, employment, health insurance.  
<sup>c</sup> Differences in effect for adjusted vs. unadjusted criteria between patients in addiction treatment and patients in pain clinics, presented as ratios of odds ratios

**TABLE S6.** Associations of completely-unadjusted and DSM-5 PRISM-5-OP dimensional measures of prescription opioid use disorder (POUD) with convergent and discriminant validators (N=606)

|   | Association of validators with completely-unadjusted POUD dimensional measure <sup>a</sup> |         | Association of validators with DSM-5 <sup>b</sup> POUD dimensional measure <sup>b</sup> |         | Difference in associations of completely-unadjusted <sup>a</sup> and DSM-5 <sup>b</sup> dimensional POUD measures with validators |         |
|---|--|---------|---|---------|---|---------|
|   | Mean ratio (95% CI) <sup>c</sup>   | p-value | Mean ratio (95% CI) <sup>c</sup>  | p-value | Ratio of mean ratios (95% CI) <sup>d</sup>  | p-value |
| <b>Convergent validators</b>                |  |         |   |         |   |         |
| Addiction treatment                         | 1.97 (1.58, 2.46)  | <.0001  | 2.45 (1.94, 3.10)   | <.0001  | 1.24 (1.19, 1.30)   | <.0001  |
| Family history of any DUD <sup>e</sup>      | 1.23 (1.02, 1.49)  | 0.0320  | 1.33 (1.09, 1.63)   | 0.0054  | 1.08 (1.04, 1.12)   | <.0001  |
| Personal history of other SUD               | 1.64 (1.33, 2.01)  | <.0001  | 1.96 (1.56, 2.45)   | <.0001  | 1.19 (1.13, 1.27)   | <.0001  |
| Antisocial Personality Disorder             | 1.40 (1.13, 1.73)  | 0.0024  | 1.56 (1.25, 1.96)   | <.0001  | 1.12 (1.08, 1.15)   | <.0001  |
| Internalizing mental disorders <sup>f</sup> | 1.65 (1.34, 2.02)  | <.0001  | 1.75 (1.40, 2.19)   | <.0001  | 1.06 (1.01, 1.12)   | 0.0226  |
| Tampering <sup>g</sup>                      | 1.68 (1.34, 2.10)  | <.0001  | 1.97 (1.56, 2.50)   | <.0001  | 1.18 (1.14, 1.21)   | <.0001  |
| Sensation-seeking <sup>h,i</sup>            | 1.29 (1.09, 1.53)  | 0.0036  | 1.39 (1.16, 1.67)   | 0.0004  | 1.08 (1.04, 1.12)   | <.0001  |
| Impulsivity <sup>h,i</sup>                  | 1.37 (1.10, 1.69)  | 0.0040  | 1.48 (1.18, 1.85)   | 0.0006  | 1.08 (1.04, 1.13)   | 0.0002  |
| <b>Discriminant validators</b>              |  |         |   |         |   |         |
| Worst pain in past week <sup>i</sup>        | 0.99 (0.96, 1.01)  | 0.410   | 0.96 (0.93, 0.99)   | 0.009   | 0.97 (0.95, 0.98)   | <.001   |
| Prescription for legitimate reason          | 0.73 (0.58, 0.92)  | 0.0079  | 0.63 (0.50, 0.80)   | 0.0001  | 0.86 (0.83, 0.89)   | <.0001  |

CI = confidence interval  
a Completely-unadjusted: a count of all DSM-5 OUD criteria that occurred, regardless of whether prescription opioids were taken only as prescribed or more/other than as prescribed  
b DSM-5: a count of all DSM-5 OUD criteria that occurred, except tolerance and withdrawal, which were counted as positive only among patients using opioids in non-prescribed ways  
c The mean ratio is the ratio of the mean value for the dimensional measure among those with the validator and without the validator, i.e. the exponentiated regression coefficient from the correlated-outcomes negative binomial regression model, controlling for covariates (age, sex, race, education, marital status, employment, health insurance).  
d The difference in the validator effect for DSM-5 vs. completely-unadjusted is presented as the ratio of mean ratios. If this term is statistically significantly different from 1, differential effects are present, meaning that one criteria set shows stronger association than the other.  
e DUD= any SUD except alcohol  
f includes major depression, persistent depression, generalized anxiety disorder, post-traumatic stress disorder  
g Ever tampered with prescribed opioid medication  
h N=314  
i Continuous measure; ratio indicates change for a one-unit increase in the scale

**TABLE S7. PRISM-5-OP binary diagnostic measures of current (past 12 months) Prescription Opioid Use Disorder (POUD): Associations of DSM-5 and completely-unadjusted POUD with convergent and discriminant validators (N=606)**

|   | Association of validators with Completely-unadjusted binary diagnosis |         |                                  |         | Association of validators with DSM-5 binary diagnosis |         |                                  |         | Difference in association between binary diagnoses |         |                                    |         |
|---|---|---------|----------------------------------|---------|---|---------|----------------------------------|---------|--|---------|------------------------------------|---------|
|   | ≥2 criteria   |         | ≥4 criteria                      |         | ≥2 criteria   |         | ≥4 criteria                      |         | ≥2 criteria  |         | ≥4 criteria                        |         |
|   | Odds Ratio (95% CI) <sup>a</sup>                                      | p-value | Odds Ratio (95% CI) <sup>a</sup> | p-value | Odds Ratio (95% CI) <sup>a</sup>                      | p-value | Odds Ratio (95% CI) <sup>a</sup> | p-value | Ratio (95% CI) of ORs <sup>b</sup>                 | p-value | Ratio (95% CI) of ORs <sup>b</sup> | p-value |
| <b>Convergent validators</b>                |   |         |                                  |         |   |         |                                  |         |  |         |                                    |         |
| Substance treatment                         | 1.59 (1.05, 2.42)   | 0.030   | 3.48 (2.14, 5.67)                | <.001   | 2.50 (1.64, 3.82)                                     | <.001   | 4.67 (2.79, 7.82)                | <.001   | 1.57 (1.33, 1.86)                                  | <.001   | 1.34 (1.10, 1.64)                  | 0.005   |
| Family history of any DUD <sup>c</sup>      | 1.14 (0.81, 1.62)   | 0.450   | 1.35 (0.89, 2.04)                | 0.155   | 1.44 (1.01, 2.03)                                     | 0.041   | 1.47 (0.97, 2.23)                | 0.069   | 1.26 (1.07, 1.47)                                  | 0.005   | 1.09 (0.95, 1.24)                  | 0.211   |
| Personal history of other SUD               | 1.24 (0.84, 1.84)   | 0.278   | 3.42 (1.98, 5.92)                | <.001   | 1.80 (1.20, 2.70)                                     | 0.004   | 4.22 (2.34, 7.62)                | <.001   | 1.45 (1.16, 1.81)                                  | <.001   | 1.23 (0.93, 1.63)                  | 0.142   |
| Internalizing mental disorders <sup>d</sup> | 1.74 (1.21, 2.51)   | 0.003   | 2.64 (1.68, 4.15)                | <.001   | 1.94 (1.34, 2.81)                                     | <.001   | 2.22 (1.41, 3.47)                | <.001   | 1.11 (0.91, 1.36)                                  | 0.284   | 0.84 (0.77, 0.92)                  | <.001   |
| Antisocial Personality Disorder             | 1.69 (1.04, 2.74)   | 0.035   | 2.72 (1.65, 4.48)                | <.001   | 2.26 (1.40, 3.66)                                     | <.001   | 2.91 (1.78, 4.76)                | <.001   | 1.34 (1.18, 1.53)                                  | <.001   | 1.07 (0.92, 1.23)                  | 0.371   |
| Tampering <sup>e</sup>                      | 1.65 (1.06, 2.57)   | 0.028   | 2.88 (1.80, 4.60)                | <.001   | 2.29 (1.47, 3.56)                                     | <.001   | 3.33 (2.07, 5.34)                | <.001   | 1.39 (1.21, 1.59)                                  | <.001   | 1.16 (1.02, 1.31)                  | 0.027   |
| Sensation-seeking <sup>f,g</sup>            | 1.43 (1.05, 1.94)   | 0.023   | 1.92 (1.31, 2.83)                | <.001   | 1.66 (1.22, 2.26)                                     | 0.001   | 1.89 (1.28, 2.79)                | 0.001   | 1.16 (1.02, 1.32)                                  | 0.020   | 0.98 (0.92, 1.06)                  | 0.645   |
| Impulsivity <sup>f,g</sup>                  | 1.73 (1.1, 2.73)  | 0.018   | 1.31 (0.78, 2.2)                 | 0.311   | 1.86 (1.18, 2.94)                                     | 0.008   | 1.33 (0.79, 2.24)                | 0.278   | 1.08 (0.84, 1.38)                                  | 0.571   | 1.02 (0.91, 1.14)                  | 0.741   |
| <b>Discriminant validators</b>              |   |         |                                  |         |   |         |                                  |         |  |         |                                    |         |
| Worst pain in past week <sup>e</sup>        | 1.03 (0.98, 1.07)   | 0.253   | 0.97 (0.92, 1.01)                | 0.177   | 1.00 (0.96, 1.04)                                     | 0.933   | 0.96 (0.91, 1.01)                | 0.084   | 0.97 (0.95, 0.99)                                  | 0.003   | 0.99 (0.98, 1.01)                  | 0.224   |
| Prescription for legitimate reason          | 0.87 (0.57, 1.32)   | 0.505   | 0.48 (0.31, 0.75)                | 0.001   | 0.58 (0.38, 0.89)                                     | 0.012   | 0.43 (0.27, 0.67)                | <.001   | 0.67 (0.59, 0.77)                                  | <.001   | 0.88 (0.77, 1.01)                  | 0.068   |

CI = confidence interval; DUD = drug use disorder; SUD = substance use disorder

a The odds ratio (OR) is the exponentiated regression coefficient from the logistic regression model, controlling for covariates (age, sex, race, education, marital status, employment, health insurance)

b The difference in the validator effect for DSM-5 vs. completely-unadjusted is presented as the ratio of the odds ratios. If this term is statistically significantly different from 1, differential effects are present, and one criterion set shows stronger association than the other.

c DUD= any SUD except alcohol

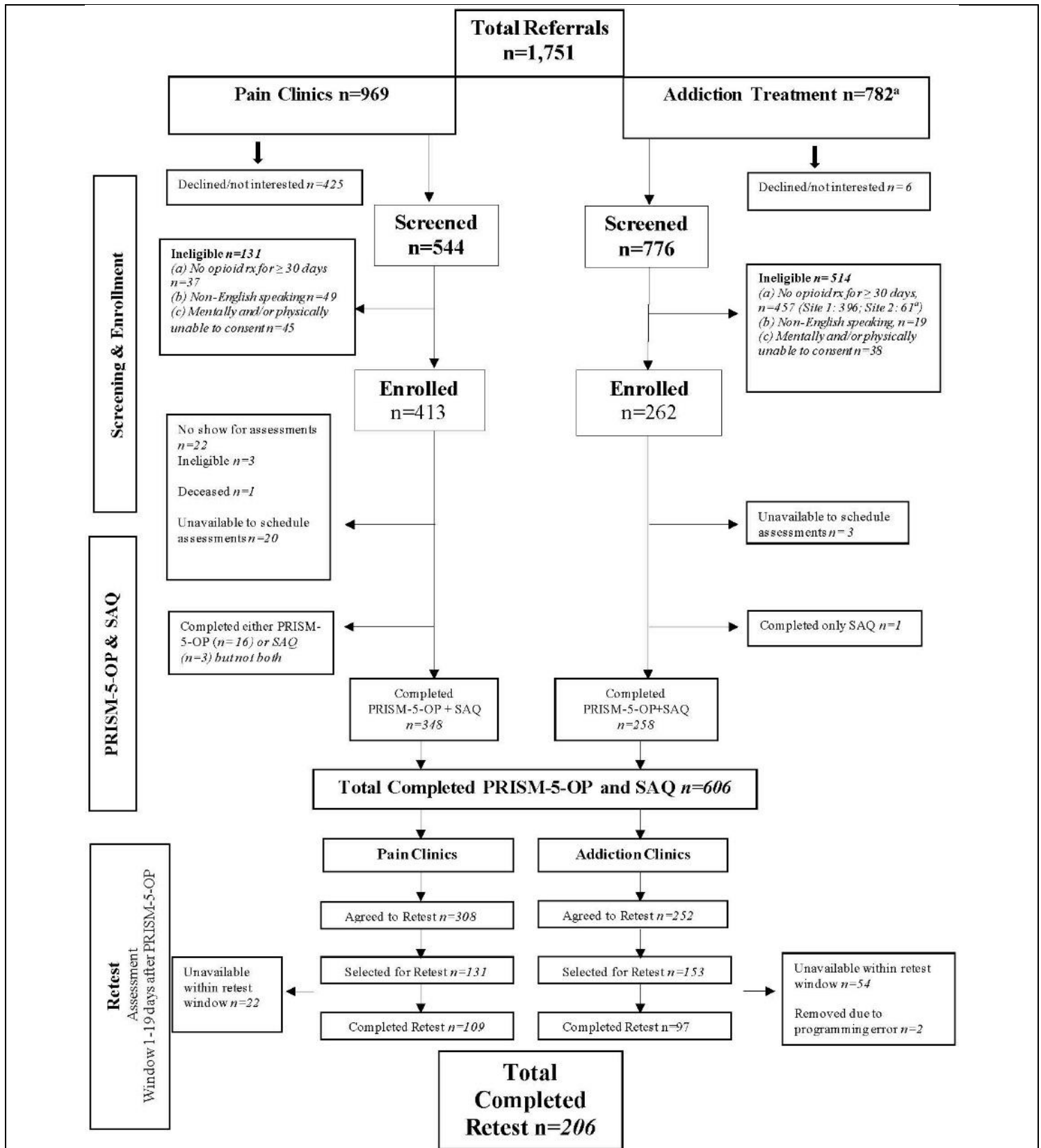
d includes major depression, persistent depression, generalized anxiety disorder, post-traumatic stress disorder

e Ever tampered with prescribed opioid medication

f N=313

g Continuous measure; odds ratio indicates change for a one-unit increase in the scale

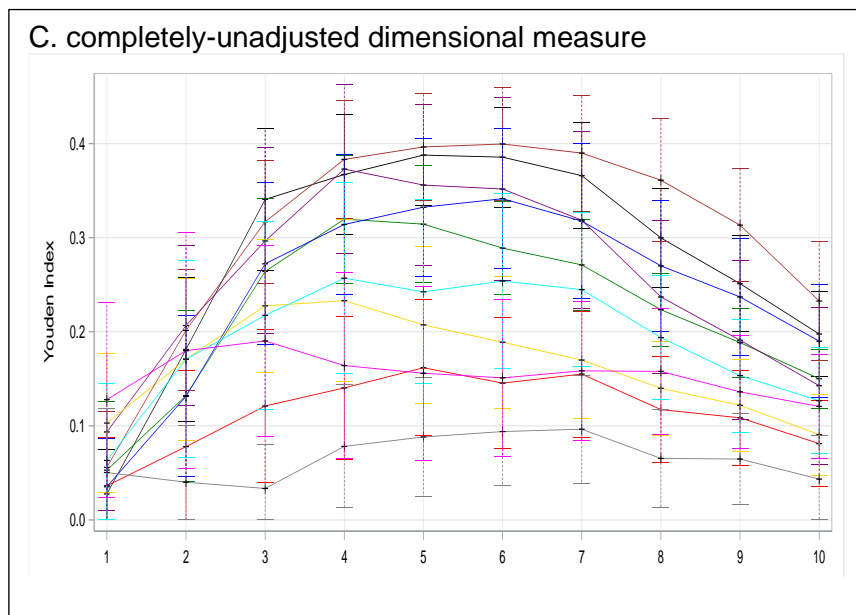
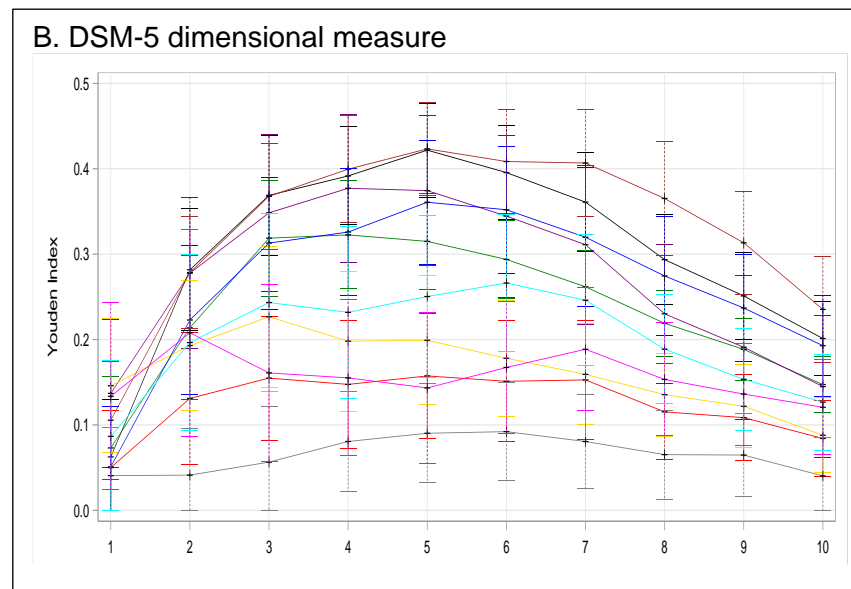
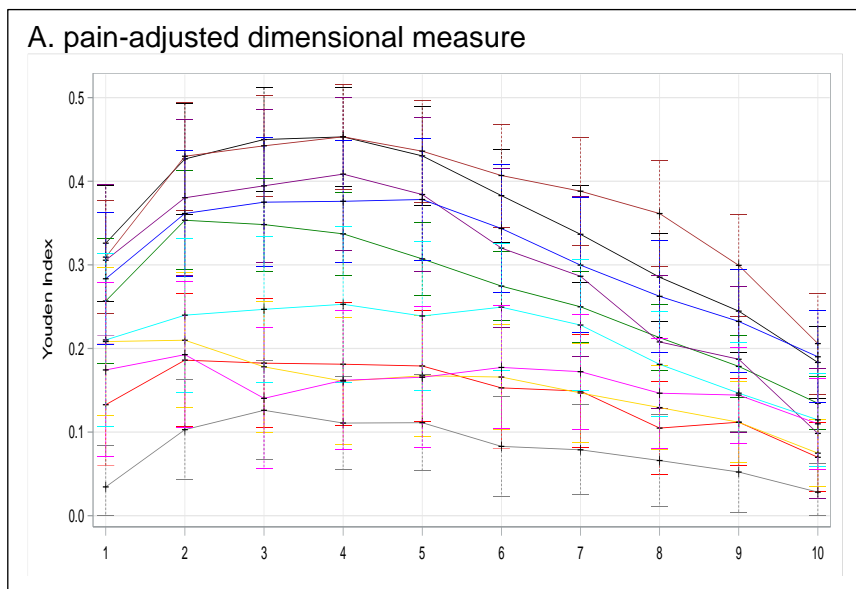
**FIGURE S1. Recruitment, screening and enrollment details**



<sup>a</sup> At Site 2, the number of referred patients was not collected during 9 of the 14 months of enrollment. For these 9 months, we estimated the total number of patients referred and total number ineligible based on the numbers for the 5 months during which these data were collected. We calculated the ratio of referred to screened patients and based on the known number of total screened patients, we then calculated the estimated total number of referred patients. The same process was conducted to estimate the number ineligible during these months. The numbers in the flowchart represent the totals, including the actual numbers during the 5 months for which we had data, and the 9 months for which we estimated the numbers of ineligible and referred.

PRISM-5-OP: Psychiatric Research Interview for Substance and Mental Disorder, DSM-5 Opioid version; SAQ: Self-Administered Questionnaire; rx: prescription

**FIGURE S2.** Youden index across all possible cut-points



**Legend for all panels:**

**Validators**

- Tampering
- Substance treatment
- Prescription for legitimate reason\*
- Personal history of other SUD
- Antisocial personality disorder
- Family history of any DUD
- Internalizing mental disorders
- Worst pain in past week\*
- Sensation seeking
- Impulsivity

\*Reverse coded for consistency with other validators  
Cut-points are shown on the x-axis.

**FIGURE S3.** Correlation of External Composite Validator (ECV) and all potential cut-points

