Jan 11, 2023 Version 1

Statistical Analyis Plan for Assessing Psychological Phenotypes of Patients with Low Back Pain in the Military Health System V.1

DOI
dx.doi.org/10.17504/protocols.io.6qpvr4k1ogmk/v1

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Protocol Citation: Daniel I Rhon, Trevor A Lentz, Steven Z George 2023. Statistical Analyis Plan for Assessing Psychological Phenotypes of Patients with Low Back Pain in the Military Health System. **protocols.io** **https://dx.doi.org/10.17504/protocols.io.6qpvr4k1ogmk/v1**

Protocol status: Working
We use this protocol and it's working

Created: January 06, 2023

Last Modified: January 11, 2023

Protocol Integer ID: 74858

Keywords: yellow flags, low back pain, psychological distress, OSPRO, Military Health System, Latent Class Analysis, phenotypes, low back pain in the military health system, care for low back pain, low back pain, psychological phenotypes of patient, assessing psychological phenotype, military health system, details of the the statistical analysis plan, statistical analysis plan, clinical trials of patient, statistical analyis plan, patient, secondary analysis, clinical trial

Funders Acknowledgements:
US Department of Defense BAA/CRMRP
Grant ID: W81XWH-18-1-0475
US Department of Defense MOMRP
Grant ID: W911QY-15-1-0017

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Abstract

This contains the details of the the statistical analysis plan for a secondary analysis using data from 2 clinical trials of patients receiving care for low back pain.

Troubleshooting

Methods

1 **Study Design and Setting**

We will use data already collected from two completed randomized clinical trials for low back pain management in the Military Health System. For this study, we will use baseline data only.

Participants
Individuals seeking care for LBP in primary care (n=510) that participated in two previous trials.[1,2]

Preliminary Work and Background for Analysis Plan
To provide context for psychological status scores (that is, are scores high, low, or average among those with back pain?) and better understand the potentially unique distress characteristics and health care delivery needs of patients with low back pain undergoing conservative care, we will derive a comparison cohort from the Optimal Screening for Prediction of Referral and Outcome (OSPRO) development and validation cohort studies.[3–5]Descriptions of these cohorts were previously published[5]and include intake data from individuals (n = 871) seeking conservative care for a variety of knee, shoulder, low back, or neck pain conditions within the Orthopaedic Physical Therapy Investigator Network, a national network of outpatient physical therapy clinics. Briefly, the OSPRO development cohort (n = 431) was a cross-sectional cohort used to develop the OSPRO Yellow Flag (OSPRO-YF) Assessment tool, described in further detail below. The OSPRO validation cohort (n = 440) was subsequently and separately assembled as a longitudinal cohort to validate the newly-developed OSPRO-YF tool and establish its ability to predict clinical outcomes. Eligibility criteria for both the development and validation cohorts were identical and designed to make the cohort generalizable to outpatient orthopaedic rehabilitation populations. Because these two cohorts had identical eligibility criteria and both had baseline OSPRO-YF scores, we developed a combined sample that included baseline data from both cohorts as a comparison group for this study.

Description of Variables, Outcome Measures, and Data Sources
Demographic information (age, sex, race, ethnicity, education, employment status, marital status, tobacco use, service, rank, and benefit category) and patient-reported measures were collected at baseline. In the OSPRO cohort, baseline demographic variables, pain intensity, and psychological distress measures were available.

Patient Reported Measures

Baseline patient-reported measures include PROMIS Pain Interference, PROMIS Physical Function, PROMIS Sleep Disturbance, and PROMIS Anxiety and Depression

General and Pain-related Psychological Distress

The OSPRO-YF Assessment Tool is a multidimensional screening tool for general and pain-related psychological distress.[5]Using patient responses to each item, it accurately calculates estimates for what a patient would score on 11 full-length questionnaires measuring psychological constructs across three different domains. The three domains along with their associated psychological constructs (in parentheses) are: negative mood (depression, trait anxiety, trait anger), negative coping (fear-avoidance for work, fear-avoidance for physical activity, pain catastrophizing, kinesiophobia, and pain anxiety), and positive affect and coping (pain self-efficacy, self-efficacy for rehabilitation, and pain acceptance). The OSPRO-YF then uses those score estimates to identify the presence of a yellow flag for each of the 11 constructs. A yellow flag is a psychosocial prognostic factor for the development of disability after the onset of musculoskeletal pain. The presence of a yellow flag is based on meeting a score threshold for each of the full-length questionnaire score estimates. Score thresholds were established based on the sample distribution of full-length questionnaire scores in the previously described OSPRO development cohort.[5]Score estimates for negative mood and negative coping questionnaires within the top quartile of OSPRO development cohort scores indicate a yellow flag, whereas score estimates for positive affect and coping questionnaires that fall into the bottom quartile (suggesting higher psychological distress) indicate a yellow flag. For instance, if the quartile threshold for the Tampa Scale of Kinesiophobia (a negative coping questionnaire) is 30, then patients with a score estimate greater than 30 on the Tampa Scale of Kinesiophobia would have a yellow flag for kinesiophobia. This process results in 0 to 11 possible yellow flags. There are different versions of the tool, with the 10-item version representing the ideal combination of high accuracy and low response burden.[6]The 10-item OSPRO-YF version was collected in both trials. The OSPRO-YF has good internal validity, reliability, and predictive validity for persistent pain, disability, quality of life, and healthcare use. Using OSPRO-YF responses at the initial evaluation, we will calculate 11 full-length psychological questionnaire score estimates and the presence or absence of a yellow flag based on each of the 11 score estimates.

2 **AIMS**

In a cohort of patients seeking care for low back pain in the Military Health System
*Aim 1:*Describe rates of general and pain-related psychological distress
*Aim 2:*Derive common psychological distress phenotypes.

3 **Description of Statistical Analysis and Sample Size**

Complete data will be available n ≤ 510 patients. To address our first question, we plan to compare OSPRO-YF full-length questionnaire score estimate means and 95% confidence intervals between the LBP cohort and the OSPRO cohort. As a sensitivity analysis to account for age-related differences between the cohorts, we developed a subset of the OSPRO cohort younger than 50 years to provide a comparison group with a similar age distribution as the military cohort. Although MCIDs are a preferred metric for interpreting the magnitude of differences between groups,[7]MCIDs for military populations do not exist for many of the full-length psychological questionnaires estimated by the OSPRO-YF. In the absence of MCIDs, we will use Cohen's d, which standardizes mean differences so they can be easily compared across different questionnaires. In the social sciences, Cohen's d values have been described as large (0.8), medium (0.5), and small (0.2).[8]The larger the value the potentially more clinically meaningful the difference may be, however interpretation is still highly context dependent.
To address our second question, we will use latent class analysis to derive psychological distress phenotypes in the military cohort based on the presence or absence of 11 yellow flag indicators. Psychological distress phenotypes are characterized by specific mood, belief, and behavioral factors that differentiate subgroups within a population.[9]Latent class analysis is a probability clustering technique that identifies unobserved latent classes defined by the distribution of binary indicators; in this case, the presence or absence of 11 different yellow flags. To allow for proper model identification, sparsely distributed indicators will be excluded if present in less than 5% of the analytic sample to ensure that a sufficient number of respondents with each psychological characteristic were included.

To select the best class size, we will first assess model fit for different numbers of classes using the model-fit likelihood ratio chi-square statistic (L^2), which is a measure of how similar model-based frequencies are to observed frequencies. The associated p value formally assesses the model's fit, with $p < 0.05$ indicating poor fit. Additional measures of model parsimony include the Bayesian information criterion and Akaike information criterion, based on the L^2, with lower values indicating better models. Additional criteria we will use to determine the optimal class solution include the proportion of classification errors, class size (more than 5% of the sample), and interpretability of classes (clinical relevance of psychological characteristic combinations), particularly when other criteria do not produce a clearly superior model. We will account for pairwise associations among variables (local dependence) by modeling the direct effect of parameters associated with large bivariate residuals (that is, more than 1) in the model. After selecting a best-fit latent class model, we will assign participants to the groups based on the highest posterior probability estimates.

We will compare demographic information (age, sex, race, ethnicity, education, employment status, marital status, tobacco use, service, rank, and benefit category) and

patient-reported measures (PROMIS Pain Interference, PROMIS Physical Function, PROMIS Sleep Disturbance, and PROMIS Anxiety and Depression) across phenotypes/clusters using the appropriate parametric or non-parametric tests (e.g., one-way ANOVA or Kruskal-Wallis H test). All analyses will be conducted using IBM SPSS Statistics for Windows (Version 27.0. Armonk, NY: IBM Corp), except for the latent class analysis, which will be conducted with Latent Gold software version 6.0 (Statistical Innovations, Belmont, MA, USA). Statistical significance will be set at p = 0.05.

As this is a cross-sectional analysis including only baseline data, we will exclude cases that are missing the relevant variables of interest.

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