Appraisal   Trial Protocol

Understanding how pain education causes changes in pain and disability: protocol for a causal mediation analysis of the PREVENT trial

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Abstract

Introduction: Pain education is a complex intervention developed to help clinicians manage low back pain. Although complex interventions are usually evaluated by their effects on outcomes, such as pain or disability, most do not directly target these outcomes; instead, they target intermediate factors that are presumed to be associated with the outcomes. The mechanisms underlying treatment effects, or the effect of an intervention on an intermediate factor and its subsequent effect on outcome, are rarely investigated in clinical trials. This leaves a gap in the evidence for understanding how treatments exert their effects on outcomes. Mediation analysis provides a method for identifying and quantifying the mechanisms that underlie interventions. **Aim**: To determine whether the effect of pain education on pain and disability is mediated by changes in self-efficacy, catastrophisation and back pain beliefs. **Design**: Causal mediation analysis of the PREVENT randomised controlled trial. **Participants and setting**: Two hundred and two participants with acute low back pain from primary care clinics in the Sydney metropolitan area. **Intervention**: Participants will be randomised to receive either 'pain education' (intervention group) or 'sham education' (control group). **Measurements**: All outcome measures (including patient characteristics), primary outcome measures (pain and disability), and putative mediating variables (self-efficacy, catastrophisation and back pain beliefs) will be measured prior to randomisation. Putative mediators and primary outcome measures will be measured 1 week after the intervention, and primary outcome measures will be measured 3 months after the onset of low back pain. **Analysis**: Causal mediation analysis under the potential outcomes framework will be used to test single and multiple mediator models. A sensitivity analysis will be conducted to evaluate the robustness of the estimated mediation effects on the influence of violating sequential ignorability – a critical assumption for causal inference. **Discussion and significance**: Mediation analysis of clinical trials can estimate how much the total effect of the treatment on the outcome is carried through an indirect path. Using mediation analysis to understand these mechanisms can generate evidence that can be used to tailor treatments and optimise treatment effects. In this study, the causal mediation effects of a pain education intervention for acute non-specific low back pain will be estimated. This knowledge is critical for further development and refinement of interventions for conditions such as low back pain.

Trial registration: Australian New Zealand Clinical Trials Registry (ACTRN). **Registration number:** 12612001180808. **Was this trial prospectively registered:** Yes. **Date of trial registration:** 6 November 2012. **Funded by:** Australian National Health & Medical Research Council (NHMRC). **Funder approval number:** NHMRC grant number APP1047827. **Anticipated completion date:** December 2016. **Provenance:** Not invited. Peer reviewed. **Correspondence:** James McAuley, Neuroscience Research Australia (NeuRA) and University of New South Wales, Barker Street, Randwick, NSW 2031, Australia. Email: j.mcauley@neura.edu.au.

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