

Advancing physical therapy interventions by investigating causal mechanisms

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1 **Abstract**

2 In this Point of View, we discuss ways of advancing physical therapy interventions by
3 studying causal mechanisms, and conclude with a clinical scenario to illustrate how a
4 mechanistic study might inform clinical practice.

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6 **Word count:** 1269 + 1 figure

7 Since the inception of patient-centred care,¹ the physical therapy profession has emphasised
8 the importance of patient-reported outcomes such as function and quality of life.²
9 Accordingly, contemporary trials of physical therapy interventions often designate patient-
10 reported outcomes as primary endpoints, while impairment level outcomes are considered
11 secondary.^{3,4} In such trials, it is often assumed that intervening on a set of impairments
12 should yield improvement in outcomes that are relevant and perceptible to everyday
13 functioning. This reflects the fundamental basis of physical therapy practice, as encapsulated
14 by most clinical reasoning frameworks⁵ and by more broadly accepted frameworks from the
15 National Academy of Medicine and World Health Organisation.⁶

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17 Treatments will often have an impact on patient-reported outcomes via the modulation of
18 causal mechanisms at the impairment level. That is, an effective treatment should alleviate
19 impairments that are causally associated with the patient-reported outcome. Conversely, an
20 ineffective treatment might fail to alleviate key impairments, or the treatment might alleviate
21 impairments that are not causally associated with patient-reported outcomes. These concepts
22 are depicted in a series of causal diagrams in Figure 1. This mechanistic approach has
23 informed clinical reasoning, but there is limited evidence to demonstrate that intervening on
24 selected impairments will necessarily yield clinical effect on patient-reported outcomes.^{7,8} To
25 date, only few studies have empirically tested the underlying mechanisms of physical therapy
26 interventions.⁸ The lack of evidence for treatment mechanisms leaves researchers with little
27 information to refine existing treatments, or to devise new treatments based on new targets.
28 This knowledge gap also leaves clinicians to rely on implicit theories to devise and deliver
29 treatments. In this article, we discuss ways of improving physical therapy interventions by
30 studying causal mechanisms and conclude with a clinical scenario illustrating how a
31 mechanistic study might inform practice.

Well conducted randomised controlled trials can provide robust estimates of the average causal effect of a physical therapy intervention.⁹ However, conventional analysis of randomised trials alone cannot explain how an intervention works, or why it does not work.¹⁰ To answer these questions, mechanistic analyses such as ‘causal mediation analyses’ can be embedded into randomised trials.¹¹ The evidence generated from these analyses can play an important role within a comprehensive programme of building, testing, and refining interventions.^{12,13}

In this issue, we see an example of a mechanism evaluation of a clinical trial where [Author] and colleagues test multiple mechanisms of a pain-education intervention that aimed to reduce disability (a patient-reported outcome) in patients with low back pain. [citation] Because pain-education did not offer added benefit over usual care, the aim of their study was to understand why the intervention did not produce the intended effect on disability. In other words, the investigators were interested in identifying where the hypothesised causal mechanisms broke down. In contrary to their hypotheses that pain-education would reduce disability via changes in illness perceptions, catastrophizing, and back pain beliefs, the authors found that none of these impairments mediated the treatment effect. In most part, this was because the treatment did not cause a sufficient change in the hypothesised mediators. This suggests that a stronger causal effect on the mediators might have increased the overall treatment effect on disability.

We also learn from this study that changes in illness perception and catastrophizing were associated with disability, but changes in back pain beliefs were not. This implies that illness perceptions and catastrophizing are important factors that should be targeted in future

iterations of pain-education interventions. The challenge is to devise interventions that can modulate these mediators to a greater magnitude (and for more individuals) so it can have a greater impact on disability. Furthermore, that changes in back pain beliefs were not associated with improvements in disability suggests that re-framing erroneous beliefs is unlikely to reduce disability. However, this finding should be interpreted with caution because the estimate could have been influenced by unknown and unmeasured confounders,¹⁴ and suboptimal implementation of the intervention might have led to insufficient variation in the measure of back pain beliefs. To interpret this data with more confidence, these findings should be replicated in future mechanism studies. Notwithstanding some limitations, [Author et al.] provide useful information that should guide the development of revised forms of pain-education for patients with low back pain.

Clinical scenario

Here we present a clinical scenario illustrating how the findings of a mediation analysis might inform clinical practice.

Clinical problem: You are an outpatient physical therapist working at a secondary care hospital. You are scheduled to see a patient who has rheumatoid arthritis of her hand and reports marked pain and loss of function. You are aware of a randomised trial that has demonstrated efficacy of an exercise program for improving hand function in this population.¹⁵ The trial intervention comprised of seven mobility exercises and four strengthening exercises. However, from this you are not sure which of these exercises are essential components to the intervention. To help understand which exercises would most likely lead to functional improvements, you search for evidence of the underlying mechanisms of this multicomponent exercise program.

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83 *Solution and caveats:* A mechanism study suggests that grip strength partially mediated the
84 overall treatment effect.¹⁶ You look for the key effects in this study - the total, indirect, and
85 direct effects. The total effect (4.35 [95% CI: 1.51 to 7.19]) represents the entire effect of the
86 treatment on hand function; the indirect effect (0.85 [0.10 to 1.60]) represents the effect of
87 the treatment on hand function that is channelled through grip strength; and the direct effect
88 (3.50 [0.71 to 6.29]) encompasses all other mechanisms that are not channelled through grip
89 strength. Therefore, the proportion mediated through grip strength is the fraction of the total
90 effect that is explained by the indirect effect ($0.85/4.35 = 20\%$). These findings suggest that
91 strengthening exercises should be retained in the implementation of this exercise program. If
92 you had limited time and resource, one option would be to concentrate on strengthening
93 exercises as there is proof of this causal mechanism.

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95 Furthermore, the study suggests that other mechanisms account for a far greater proportion
96 (80%) of the overall treatment effect. One plausible mechanism is joint mobility, but the
97 intervention did not demonstrate substantial effects on five different measures of mobility,
98 and these mobility measures were not associated with hand function. You speculate whether
99 this finding was due to a lack of precision in the mobility measures, or whether it was due to
100 a lack of causal effect of the intervention on mobility. Based on this data alone, you decide
101 not to rule out the possibility of mobility as an important mechanism. In summary, these
102 results suggest that unless there are reasons to prioritise treatment components (e.g. due to
103 practice restrictions on treatment duration and/or frequency), you should implement the full
104 exercise program as originally designed by the investigators. With limited available evidence,
105 you have a partial understanding for the underlying mechanisms of the exercise program. The
106 unknown mechanisms may be explained by more complex constructs such as dexterity, or

107 alternative psychological or behavioural factors such as self-efficacy or motivation. However,
108 you can only speculate until more data emerge to support or refute these potential causal
109 mechanisms.

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111 In this point-of-view, we highlight the merits of using mechanistic evidence to guide the
112 development of physical therapy interventions, and present a case scenario that illustrates
113 how mechanistic studies might influence clinical practice. The recent shift towards patient-
114 centred care may have downplayed the importance of impairment-level measures in physical
115 therapy trials. A mechanistic approach that links impairment-level measures to patient-
116 reported outcomes provides deeper causal explanations for how physical therapies may (or
117 may not) work. Generating and implementing this evidence will be important for the
118 scientific progression of physical therapy interventions.

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167 **Figure 1. Causal diagrams illustrating potential scenarios of when an intervention**
168 **would be effective or ineffective.** Black solid arrows represent positive causal effects; the
169 red solid arrow represents a negative causal effect; broken lines represent null causal effects;
170 ‘Complex intervention’ refers to interventions that are made up of multiple components; the
171 first model on the left panel assumes that the intervention does not have a causal effect on
172 harmful mechanisms; all models on the right panel assume that the intervention does not
173 work through unknown/unmeasured mechanisms.