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Causal mechanisms in the clinical course and treatment of back pain

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A B S T R A C T

In recent years, there has been increasing interest in studying causal mechanisms in the development and treatment of back pain. The aim of this article is to provide an overview of our current understanding of causal mechanisms in the field. In the first section, we introduce key concepts and terminology. In the second section, we provide a brief synopsis of systematic reviews of mechanism studies relevant to the clinical course and treatment of back pain. In the third section, we reflect on the findings of our review to explain how understanding causal mechanisms can inform clinical practice and the implementation of best practice. In the final sections, we introduce contemporary methodological advances, highlight the key assumptions of these methods, and discuss future directions to advance the quality of mechanism-related studies in the back pain field.

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Introduction

Experiencing back pain without knowing its cause can be highly distressing for the patient. Disappointingly, research so far has failed to provide robust causal explanations to mitigate these uncertainties. Poor understanding of causal factors has stifled the development of effective treatments. This is because treatment targets have only been informed by assumptions or implicit theories rather than empirical evidence for well-defined causal mechanisms. For the past 16 years, landmark papers in the field have repeatedly highlighted the paucity of evidence on the causes of low back pain [1–3]. This is despite back pain researchers ranking research into the mechanisms and causes of low back pain as one of the highest research priorities to advance the field [4].

By understanding causal mechanisms in the clinical course of back pain, we can identify important factors that can be targeted in treatment. Although pain and disability are important outcomes for the patient, they are not the typical targets of treatments. Treatments are devised to target hypothesised intermediary factors (or mediators) that are causally linked to patient-relevant outcomes such as pain and disability. In other words, treatments generally exert their effects on pain and disability through indirect pathways, which we refer to as 'causal mechanisms'. In a recent mechanism evaluation study, Fordham et al. showed that cognitive behavioural therapy (exposure) reduced disability (outcome) through changes in self-efficacy, fear avoidance and physical functioning (mediators) but not through improvements in mental functioning [5]. This information gained from a mechanism evaluation is particularly useful in understanding how treatments work or why they fail.

By understanding causal mechanisms, treatments can be adapted and refined to improve their clinical efficacy and facilitate implementation. Recently, there has been increasing interest in generating evidence for causal mechanisms in the back pain field [6]. The aim of this article is to provide an overview of current understanding of causal mechanisms in the clinical development and treatment of back pain. This article is divided into five sections (1. Key concepts and terminology; 2. Overview of mechanism evaluations in the field; 3. Application to clinical practice and implementation; 4. Methodological considerations; 5. Future directions).

Key concepts and terminology

Many empirical studies in health research aim to establish *whether* an exposure causes an outcome [7]. For example, a randomised trial might aim to establish whether an exercise programme (exposure) causes less disability (outcome). However, merely establishing a single causal association is often insufficient to explain *how* or *why* an exposure causes an outcome [8]. This approach to understanding causation is often criticised as the 'black-box' approach because the underlying causal mechanisms are unknown [9,10]. In the above example, there is no explanation for *how* an exercise programme causes less disability. To overcome this limitation, we can use certain design characteristics and analyses in clinical studies to evaluate causal mechanisms and help explain *how* or *why* a causal association occurs [10].

A causal mechanism is the pathway that links an exposure (which could be a treatment or observed variation in clinical exposure) to an outcome [9]. To identify a causal mechanism, a theoretically plausible intermediate variable (often called a mediator) that lies on the causal path between the exposure and outcome needs to be identified. Then, mediating effects (or indirect effects) caused by that selected mediator can be estimated, often by conducting a form of mediation analysis [10].

Mediation analysis can quantify causal mechanisms by decomposing the causal effect of the exposure on the outcome (total effect) into indirect and direct effects. The indirect effect is the causal effect of the exposure on the outcome that is channelled through the selected mediator [8,10,11], and the direct effect encompasses all other unspecified mechanisms. Quantitatively, the total effect is the sum of the indirect and direct effects, hence the term 'effect decomposition'. By decomposing the total effect into indirect and direct effects, we can gain insight into *why* an exposure causes an outcome. Importantly, mediation analyses are causal analyses. Thus, it is always necessary to consider the role of confounders in these analyses.

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