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Are you translating research into clinical practice? What to think about when it does not seem to be working

Myles Calder Murphy
The University of Notre Dame Australia, myles.murphy@nd.edu.au

William Gibson
The University of Notre Dame Australia, william.gibson@nd.edu.au

G. Lorimer Moseley

Ebonie Kendra Rio

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Research translation? What to think about when it's not working

Myles Murphy [1,2]

William Gibson [1]

G. Lorimer Moseley[3]

Ebonie Rio [4]

Affiliations

[1] School of Physiotherapy, The University of Notre Dame Australia, Fremantle, WA, Australia

[2] SportsMed Subiaco, St John of God Health Care, Subiaco, WA, Australia

[3] IIMPACT in Health, University of South Australia, Adelaide, South Australia, Australia

[4.] La Trobe Sports and Exercise Medicine Research Centre, La Trobe University, Bundoora, VIC, Australia

Corresponding author

Corresponding Author: Myles Murphy, School of Physiotherapy, University of Notre Dame Australia, 19 Mouat Street (PO Box 1225), Fremantle, Western Australia, 6959, Australia.

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Introduction

The value of clinical research can be lost in translation and implementation. One often overlooked issue concerns how easily clinicians can determine whether their patient is similar to research participants and, *ipso facto,* whether their treatment will have the same effects as those reported in a research study. This editorial presents five questions and clinical tips for clinicians facing these issues.

Who are the research participants?

The characteristics of a research study's participants can be considered their 'clinical phenotype'. The field dedicated to more precisely matching treatments to clinical phenotypes is 'precision medicine'.[1] Defining clinical phenotypes remains a great challenge in musculoskeletal research because a gold standard diagnostic test is commonly absent. For example, the single leg decline squat is provocative for anterior knee pain but is not diagnostic for patellar tendinopathy.[2] Even where agreement exists as to a patient group having the same condition (e.g. rotator cuff tendinopathy), different clinical phenotypes (e.g. positive versus negative empty can test) within that group represent heterogenous populations, with potentially variable responses to interventions.

Clinical tip: Don't rely on the title or abstract of a paper. Review the methods section for details on more precise clinical phenotypes (or not), including how the condition was diagnosed and other features such as physical activity, education, cognitive or socioeconomic characteristics.[3] Does your patient match the clinical phenotype(s) in the study?

Are those with comorbidities excluded?

Research studies usually involve stricter inclusion criteria than clinical practice does. This may mean your patient will not nicely match the research cohort. For example, the presence of comorbid

conditions such as depression or other areas of pain (Appendix A), often means exclusion from research studies because these conditions can confound results (via known - e.g. impaired descending inhibition - and unknown mechanisms), necessitating bigger samples and more resources,[4] but such comorbidities are common in clinical presentations.

Clinical tip: Clarify whether your patient would satisfy the inclusion and exclusion criteria of the study. Consider comorbidities when planning and interpreting your intervention.

What non-specific treatment effects could be at play?

Non-specific treatment effects are those that occur in response to an intervention but are not mediated by the intended active, or unique, component of the intervention.[5] Non-specific effects become more likely as the outcome of interest moves towards clinically relevant metrics such as pain, quality of life and return to sport or work. For example, although pain modulation with exercise is often attributed to injury healing or aggravation, which reflects a biomedical tissue-focussed interpretation, there are other aspects of exercise that are also likely to change pain.[5] Relevant here are contemporary understandings of pain as providing a protective buffer for tissues (rather than a 'read out of tissue state'), the size of which depends on complex and multifactorial processes across bio-, psycho- and social domains.[5,6]

Clinical tip: Consider all possible mechanisms by which a study's treatment could cause a change in outcome, not just the mechanism mentioned in the title.

Does the authors' interpretation match their study design?

We recently conducted a case-series investigating the effect of an isometric squat in-season training program for jumping and landing athletes with patellar tendinopathy.[7] We observed a decrease in pain over the 4-week intervention period. Our design allowed us to conclude that pain decreased during the course of the intervention, but not that pain decreased *because* of the intervention or any

part thereof. In addition to the passing of time, many non-specific effects may have been at play (e.g. expectations of effect, different training structure and timing, increased care). The important clinical consideration of such studies is that the specificity with which results can be explained by mechanisms is limited by the extent to which the design isolates those mechanisms from others. That is, to gain the study's effect with your patient may require replication of the intended active component (isometric squats in the above example) *and* everything else not controlled for in the study.

Clinical tip: Look for potential non-specific treatment mechanisms that can be replicated or estimated, for example by providing positive, accurate messaging and referring the patient to the published research.

Are too many assessments spoiling your result?

The sensitivity of pain processing can be rapidly and substantially modified by a wide range of factors from across the biopsychosocial spectrum.[8] It is important to remember the potential effect of multiple assessments, especially pain provocation tests and the order in which they are conducted. For example: imagine one performs a pain provocation test, then assesses pain; then assesses mechanical sensitivity via palpation; then implements an intervention; then reperforms the provocation test, palpation and finally reassess pain. Any or all the assessments could modify sensitivity, clouding the value of the final pain reassessment. Multiple assessments can both increase or decrease an apparent treatment effect, just as repeated pain provocation tests can *increase or decrease* pain, dependent on myriad of intra- and inter-individual factors.

Clinical tip: Understand how assessments (e.g. palpation of the painful structure) can influence peripheral and central sensitivity. Select a single assessment most likely to detect the effect you intend to induce.

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CONTRIBUTORSHIP

All authors have contributed substantially to the manuscript and approved the manuscript for this submission. MM and ER conceptualised the review. MM, WG, GLM and ER have written the manuscript.

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