



Christine Walsh  
Health Quality and Safety Commission  
PO Box 25496  
Wellington 6011

10 August, 2020

Dear Ms. Walsh:

I have been asked by Mrs. Tracey Jourdain to provide a scientific and clinical interpretation of recent prolotherapy reviews. I am happy to do so. As a clinician-scientist at Penn State College of Medicine, I am often asked for such commentary. The aim of my research program is the ethical, translational assessment of novel therapeutic approaches for high impact clinical conditions. This has included prolotherapy for chronic musculoskeletal pain.

In my immediate previous position at the University of Wisconsin (2004-2019), I held continuous external funding since 2004. I am now a professor with tenure, and Vice Chair of Faculty Development, at Penn State College of Medicine, Department of Family and Community Medicine. I am a content leader in the assessment of prolotherapy; my scientific work in this area includes principle investigator on 2 systematic reviews, 3 randomized controlled trials, and numerous descriptive reviews, book chapters and commentaries. I am a collaborating or senior author on dozens more.

Ms. Jourdain wrote to me requesting a comment on the outcomes and clinical recommendations of four prolotherapy reviews. She is aware of my views expressed below. I will provide a note about each review's conclusions and a summary statement about my views on the implications for research and clinical care.

1. The first is by me in 2010. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2831229/>  
It is a straightforward narrative review of prolotherapy for conditions in the three main chronic pain areas for which prolotherapy is used: low back pain, tendinopathy (including lateral epicondylitis (tennis elbow)), and osteoarthritis. It reviews the history and mechanism (such as is known) and safety of prolotherapy, and notes that for several specific conditions, the strength of evidence is "B" using the Strength of Evidence Taxonomy metric, a widely used and respected assessment in primary care (<https://www.aafp.org/afp/2004/0201/p548.html>). Prolotherapy for lateral epicondylitis, received an "A" rating based on consistent patient oriented outcomes in 2 RCTs, though each was limited by small sample size. The strength of evidence for tennis elbow is bolstered by a recent robust RCT by Yelland et al., which reported that prolotherapy, and prolotherapy with physiotherapy, was effective.  
<https://bmcmusculoskeletdisord.biomedcentral.com/articles/10.1186/s12891-019-2905-5>.

We concluded with the cautious statement that “Prolotherapy by an experienced physician is a treatment modality worthy of consideration by primary care physicians for these conditions, especially when patients are refractory to more conventional therapy.”

2. The ACC review by Amanda Bowen is similarly a narrative review of prolotherapy for various indications. <https://www.acc.co.nz/assets/research/bfa40c07d1/prolotherapy-review.pdf>. Studies assessing prolotherapy with some sclerosing agents (for example, polidocanol and sodium tetradecyl sulfate) were not included. It is a sound review and aimed to payment for services decision-making. It was conducted in 2013, four years after my own. In general, the conclusions are “do not purchase”, while acknowledging positive reports for several conditions. The review noted negative findings for prolotherapy used in isolation for low back pain, but did not comment when used with other therapies, as did the Cochrane review (see #4 below). It is reasonable to evaluate prolotherapy in the context of other therapies because chronic low back pain is so complex that best practice standards suggest multimodal care.

Because it relates to funding, the ACC report would benefit from an update on prolotherapy for two conditions. A recent systematic review with meta-analysis by Sit et al. strengthened the evidence base for prolotherapy for knee OA <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4857084/>. Sit and colleagues found that “prolotherapy conferred a positive and significant beneficial effect in the treatment of knee OA”. In a second study assessing a short form of prolotherapy, Sit et al. also reported positive results compared with control, making prolotherapy more accessible to patients because the short form does not require that providers obtain specialized training. <https://www.annfammed.org/content/18/3/235>

Similarly, for lateral epicondylitis, the recent effectiveness study by Yelland et al. found that prolotherapy, and prolotherapy with physiotherapy, were effective. <https://bmcmusculoskeletdisord.biomedcentral.com/articles/10.1186/s12891-019-2905-5>.

3. A comprehensive systematic review of prolotherapy in 2014 was conducted by *Canadian Agency for Drugs and Technologies in Health*. It concluded “Evidence from studies of limited quality suggests that dextrose prolotherapy for the management of musculoskeletal pain including low back pain, tendinopathy, and osteoarthritis may provide pain relief and improve physical function compared with saline injection control, exercise alone, or before prolotherapy treatment.” <https://www.cadth.ca/prolotherapy-management-musculoskeletal-pain-review-clinical-effectiveness>

4. The gold-standard Cochrane review of prolotherapy for low back pain concluded in part, “When combined with spinal manipulation, exercise, and other co-interventions, prolotherapy may improve chronic low-back pain and disability.” <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004059.pub3/full>

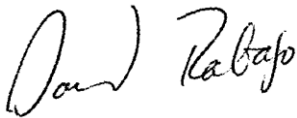
Each of the 4 reviews fairly describes exiting studies in prolotherapy from a particular vantage point, noting limitations of the data and positive findings where they exist. The interpretations and conclusions however, vary somewhat. Three of the four recommend prolotherapy for some conditions. The dissenting ACC review acknowledges positive findings but renders a “do not pay” decision, though it predates at least 3 important studies that may impact conclusions. Given the

import of financial decisions on patient's lives, the review would be more robust if it were updated for knee OA and lateral epicondylitis.

Physicians who treat pain know it's a large and difficult problem. Indeed, musculoskeletal (MSK) health problems are major contributors to the global burden of disease, causing 21.3% of the total medical burden as assessed by the standard metric "years lived with disease".<sup>1,2</sup> We in the medical community are working to find new solutions to this growing problem. Two observations prompt me to recommend prolotherapy to some patients. First, prolotherapy is one such potential pain management solution. While it is not a "cure" for all chronic MSK pain, (we have no such thing) it is clear that prolotherapy provides substantial help to many patients who have exhausted more conventional care options. Second, while research on prolotherapy is ongoing and in an early stage, the evidence for knee OA and tennis elbow is compelling and has prompted medical systems in the US, including the University of Wisconsin, many U.S. Veteran's Administration centers, and elsewhere, to cover prolotherapy for these conditions.

For the research community, promising evidence encourages us to continue to develop and investigate prolotherapy. For the clinical community, patients and stakeholders including payers, the current evidence suggests that the cautious use of prolotherapy, often as part of a comprehensive multimodal care plan, in carefully selected patients whose pain is not alleviated with more conventional therapy, is good patient care.

Most Sincerely,

A handwritten signature in black ink that reads "David Rabago". The signature is written in a cursive, flowing style.

David Rabago, MD  
drabago@pennstatehealth.psu.edu

1. Murray CJ, Vos T, Lozano R. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study. *Lancet (London, England)*. 2013;380:2197-2223.

2. Vos T, Flaxman AD, Naghavi M. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)*. 2013;380:2163-2196