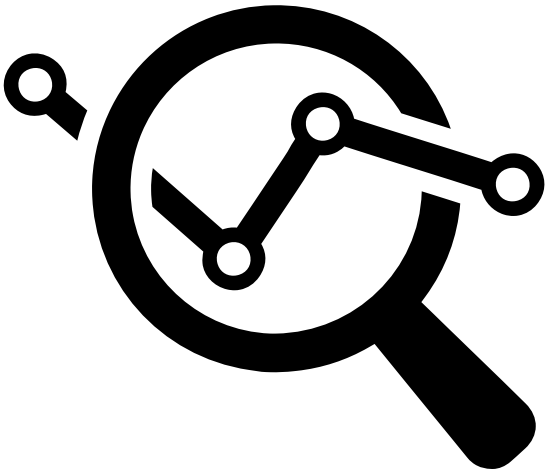
Barbell Medicine Monthly Review



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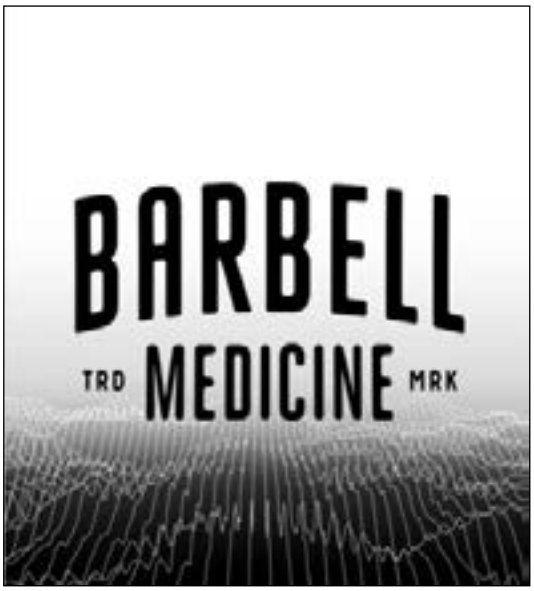

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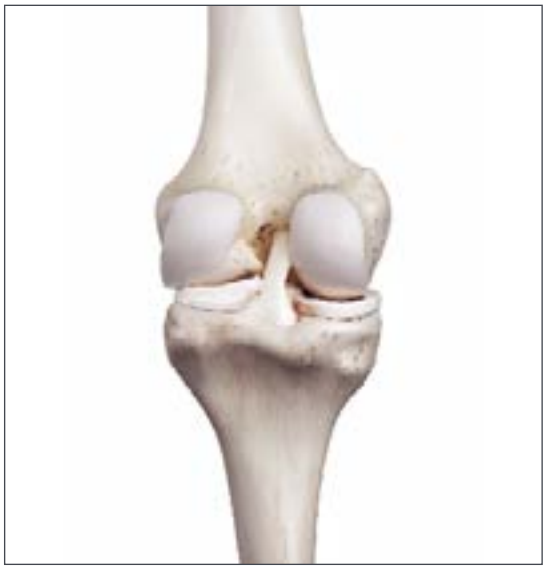

People

Dr. Jordan Feigenbaum

Jordan Feigenbaum is an experienced strength coach who also has his medical degree and residency training. In addition to a veritable laundry list of credentials, Jordan is also an elite powerlifter who currently hold one of the top 20 totals of all-time (source: Powerlifting Watch). If he's not coaching, training, or playing doctor, you'll likely find Jordan hopping a plane to somewhere fun or reading a book.

Dr. Austin Baraki

Dr. Austin Baraki is a practicing Internal Medicine Physician, competitive lifter, and strength coach located in San Antonio, Texas. Originally from Virginia Beach, Virginia, he completed his undergraduate degree in Chemistry at the College of William & Mary, his doctorate in medicine at Eastern Virginia Medical School, and Internal Medicine Residency at the University of Texas Health Science Center in San Antonio. His interests include the application of strength training in the context of complex medical conditions, sarcopenia, pain neuroscience & rehabilitation, as well as cognitive and sport psychology. He enjoys reading, writing, teaching, and spending time with his wife, Dr. Loraine Baraki.

MEET OUR TEAM

Dr. Michael Ray

Dr. Ray is a chiropractor based out of Harrisonburg, VA. He owns and operate Shenandoah Valley Performance Clinic and specializes in the rehabilitation of neuromusculoskeletal issues, associated pain, and dysfunction. He enjoys helping athletes from various backgrounds return to their desired level of ativity. His primary goals for working with clients, educate about their situation and collaboratively design a game-plan to move them from where they are at to where they want to be.

Dr. Derek Miles

Derek is a residency trained physical therapist currently working at Stanford Children's Heal as the Advanced Clinical Specialist in the rehabilitation department. Prior, he worked at the University of Florida for 10 years in sports medicine, treating a variety of athletic injuries from overuse to post-oerative. He is involved in the peer reviewed process for academic journals and has spoked at national level conferences within the physical therapy profession on topics from utiliztion of resistance training in the rehabilitation of endurance athletes to post operative hip progressions. When he is not in the gym or treaing, he can typically found reading, cooking, or brewing beer.

Podcast

Podcast Discussion of February 2020 Issue:

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IS CBD FULL OF PROMISE OR FULL OF SH!T?

BY: DR. JORDAN FEIGENBAUM

Article Reviewed: Inverted U-Shaped Dose-Response Curve of the Anxiolytic Effect of Cannabidiol during Public Speaking in Real Life by Zuardi et al. 2017.

Key Points:

1. Cannabidiol (CBD) is made from the flowers and leaves of one of the *Cannabis species, Cannabis sativa, Cannabis indica*, or *Cannabis ruderalis*. Varieties of these species (e.g., hemp and marijuana) are further categorized by their concentration of THC, the biologically active substance associated with the "high" from marijuana ingestion. It is currently legal to make and distribute hemp-derived products including CBD oil in all states, including interstate commerce. However, it is illegal to make and distribute marijuana-derived products across state lines, although a number of states have their own regulations for legalized marijuana use.
2. While the CBD industry is booming, with an estimated market of $80 billion by 2030. Unfortunately, there are significant concerns with the quality of products in the market and safety in general. For example, when ~80 different commercially available CBD products were tested, only 31% had their CBD concentration labeled accurately.[Bonn-Miller 2017] Over half of all tested samples found additional chemicals in the product that were not on the label. Adverse reactions to CBD are also seen in about ⅓of subjects including diarrhea and liver injury.[VanDolah 2019]
3. The existing evidence on CBD is relatively good for its use in reducing seizure frequency in individuals with drug-resistant seizures. It also *may* be useful for reducing anxiety prior to public speaking. However, there existing data suggests it is not effective for pain, psychiatric conditions, Parkinson's disease, insomnia, or exercise recovery, among others.

Introduction:

Interest in cannabidiol - better known as CBD - has recently exploded in America, with an estimated 1 in 7 adults currently using a CBD-based product. [Brenan 2019] This is big business, with a projected commercial market of $80 billion by 2030 and $20 million in research funding in 2019. [Franck 2019] [Medgadget 2019] Of the nearly 45 million Americans using CBD, 62% report using CBD to treat a medical condition, e.g. pain, anxiety, and depression most commonly. [Corroon 2018] Given its popularity, I thought this month I would dig into the current research on CBD Oil and see if all the hype is warranted.

What is CBD Oil?

In biology, taxonomy is the branch of science that identifies, describes, names, and ultimately classifies different organisms. The taxonomy of CBD starts with *Cannabis*, a genus of the flowering plant family, *Cannabaceae*. There are three major species of the genus Cannabis: *Cannabis sativa, Cannabis indica*, and *Cannabis ruderalis*.

Within these three species there are substantial variations in tetrahydrocannabinol (THC) content, which is the bioactive agent that produces the "high" associated with cannabis ingestion. For example, the variations of cannabis that contain 0.3% or less THC by dry weight are called hemp, whereas the term *marijuana* refers to variations of cannabis that contain more than 0.3% THC by dry weight.

CBD can be produced from the leaves and flowers of either hemp or marijuana. However, there are important compositional and legal differences here. From a composition standpoint, hemp-derived CBD contains high levels of CBD (cannabidiol) and BCP (beta-caryophyllene), neither of which are psychoactive or cause an altered sensory experience, e.g. the "high" associated with marijuana, and have <0.3% THC. Conversely, marijuana-derived CBD contains mainly THC and lower levels of CBD. [White 2019]

Is CBD Legal?

With respect to the legal differences, things get interesting in a hurry! The 1970 Controlled Substances Act originally made it illegal to grow and sell any type of cannabis (including both hemp and marijuana) in the United States. All cannabis products were deemed "Schedule I" drugs, which are defined as having a high potential for abuse and have no currently accepted medical use.

It wasn't until the 2014 Agricultural Act where hemp and marijuana were legally distinguished based on the THC content limits described above, which made it legal for hemp to be grown and distributed in the United States for "research purposes" only. An additional important legal ruling happened in 2014: the Rohrabacher-Farr amendment, which allowed individual states to implement their own rules about cannabis use and distribution, provided it wasn't transported across state lines. Thus, it was still illegal to introduce any supplement or food containing cannabis, including hemp-derived CBD, into interstate commerce. [Agricultural Act of 2014] [Mead 2017]

Subsequently, many Cannabis products were available for sale in select states up until 2018, when the Agricultural Act of 2018 or "Farm Bill" was passed. This bill now made hemp and hemp-derived products (including CBD Oil) legal for sale across states. [VanDolah 2019] As a reminder, hemp is defined as a Cannabis variety that contains <0.3% THC by dry weight whereas marijuana is a variety of Cannabis that contains >0.3% THC. Thus, even if there was a marijuana-derived CBD oil product that contains <0.3% THC after extensive refinement processes, it would still be illegal based on the current laws. In summary, hemp-derived CBD is legal across the nation, but marijuana-derived CBD continues to be illegal regardless of THC content.

Finally, from a medico-legal standpoint there is a huge mess in the supplement industry right now. Under the current Federal Food, Drug, and Cosmetic act, any product (other than a food) that is intended to affect the structure or function of the body of humans or animals, is considered a drug. [FDA 2019] At present, there are less than a handful of FDA-approved products derived from Cannabis:

- Cannabidiol (Epidiolex) is pure 100% CBD that is used to reduce seizure frequency associated with two rare, congenital seizure disorders: Lennox-Gastaut and Dravet syndromes. Epidiolex costs about $13-15 per milliliter and is distributed in 100mL containers, which cost about

$1300-1500.

- Dronabinol (Marinol and Syndros) is a drug that contains synthetic THC and is FDA-approved for treating weight loss in AIDS, as well as chemotherapy-associated nausea and vomiting.
- Nabilone (Cesamet) is another synthetic THC drug that is used for nausea and vomiting associated with chemotherapy.

Despite these relatively narrow therapeutic indications, there are a great number of CBD-containing products being marketed for uses including sleep aids, pain relief, stress reduction, improved recovery from exercise, or as Beam CBD's advertisements claim, "Better everything." These claims are at odds with the current Federal Food, Drug, and Cosmetics Act and as such, the FDA has sent warning letters to over 20 different supplement companies in 2019 alone due various infractions such as improper claims, concentrations of ingredients, or contaminants found upon testing. FDA 2019

For example, in 2016 a multicenter study purchased 84 commercially available CBD products from 31 different companies via the Internet. These products were tested three times each to determine the average concentration of CBD in each product, the accuracy of the ingredients listed on the label, and whether or not there was any THC in the product. The results were concerning:

- The listed CBD concentrations were accurate in only 31% of products. 43% were overdosed relative to what the label stated and 26% were underdosed.
- The labels were found to be accurate in only 12.5% of vaporized products, 25% of tinctures, and 45% of oils.
- THC was found in 21% of samples, with an average concentration of 0.45 mg/mL. Of note, inhaling 2-3mg or ingesting 5-20mg of THC can cause the "high" associated with marijuana use. Bonn-Miller 2017

In summary, while the FDA-approved drugs that are derived from Cannabis have specific medical indications and FDA-enforced quality control and safety guidelines that must be maintained, the commercially available CBD products raise serious concerns about their safety and efficacy. When coupled with their wide-spread usage - 14% of Americans report using a CBD product - this may lead to unexpected problems.

How Does CBD Work?

The cannabis plant contains over 500 different chemicals, which are called cannabinoids. The main cannabinoids derived from the hemp varieties of Cannabis are cannabidiol (CBD) and beta-caryophyllene (BCP). Unfortunately, there isn't much clinical research on what CBD or BCP does in the human body, as most of the existing research has focused on THC. Here's what we know at present:

- The Endocannabinoid System (ECS) is present throughout the body including the brain, nerves, skin, bone, muscle, GI tract, and most of our major organs. It is involved in a wide variety of different processes including appetite, pain, mood, memory, sleep, etc. Witkamp 2014 Acharya 2017
- There are two main cannabinoid receptors, CB1 and CB2. CB1 receptors are widely distributed in most tissues, with the highest concentration in the brain. In contrast, CB2 receptors are concentrated in white blood cells and many organ systems such as the heart, liver, GI tract, and more. CB2 receptors are also located in the brain, but at much lower concentrations than CB1 receptors. Zou 2018
- The body naturally produces its own *endocannabinoids*, e.g. anandamide and 2-arachidonylglycerol, to modulate the ECS.
- Cannabinoids from plants, e.g. THC, CBD, and BCP, also act on the CB1 and CB2 receptors. THC directly binds to CB1 and BCP binds directly to CB2. It appears that CBD doesn't bind to either, yet stimulates both through a mechanism that isn't yet well established. Zou 2018

Overall, CBD likely affects the ECS using CB1 and CB2 receptors as well as other pathways that haven't yet been established, which may be even more important. For example, studies on the FDA-approved drug Epidiolex suggest that the anti-seizure effect of CBD is *not* mediated through its effects on cannabinoid receptors, though the exact mechanism of action remains unknown. VanDolah 2019

How is CBD Administered?

Commercial preparations of CBD can be administered in a number of different ways such as by mouth from a pill, through the oral mucosa via a mist, spray, or drops, via the lungs through an inhaled product, or transdermally through a cream or salve. While there was a single study in the 1980's where CBD was administered in humans via an IV, there are no commercial or prescription formulations of CBD that can be given intravenously. Ohlsson 1986

CBD appears to be well-absorbed orally via a pill, drops placed on or under the tongue, or via a mist sprayed into the mouth. Pills or capsules tend to increase blood levels faster and to higher levels than similarly-dosed drops or aerosolized CBD mists. Blood levels of CBD trend with the amount given in a dose-dependent fashion, e.g. the higher the dose, the higher the concentration of CBD in the blood, though this tends to level off at higher doses. CBD contained within a cigarette or nebulizer has greater bioavailability compared to orally-administered CBD, at 31% compared to 6%. Zhornitsky 2012 Additionally, consuming a meal one hour after oral administration of CBD ingestion tends to increase the absorption and the amount of time the CBD is detectable in the blood. Millar 2018

However, topically-applied CBD preparations do not have any human data indicating they are absorbed effectively. Rather, one mouse and one rat study show absorption of CBD gel through the skin. Rat skin is indeed similar to human skin from an anatomical standpoint. For example, the outer layer of the skin - the stratum corneum - is 18 micrometers thick in both the rat and the human. Additionally, the whole skin is about 2.09 millimeters thick in the rat and about 2.58 millimeters thick in humans. Jung 2015 Nevertheless, human data showing how much CBD is absorbed from topical CBD application are currently lacking.

What Does the Existing Data on CBD Say?

Unlike social media where CBD is often touted as a panacea, the current data on CBD's effects on humans are restricted to seizure disorders, psychosis, pain, Parkinson's disease, and anxiety. With the focus of this month's Research Review being on the effect of CBD on anxiety, we'll review some the other conditions first and save the anxiety discussion for later.

Seizures

At present, the only FDA-approved indication for CBD is to treat drug-resistant seizures. Four, multicenter, double-blind, placebo controlled trials show that prescription CBD, Epidiolex, reduced the frequency of seizures by about half compared to placebo. Devinsky 2017 Devinsky 2018 Devinsky 2016 Hess 2016 It is important to note that the population studied was primarily made up of those with either Lennox-Gastaut or Dravet Syndrome, which are relatively rare conditions that present during childhood and typically arise from genetic disorders. Nevertheless, pharmacologic-grade CBD administration has some solid evidence for these conditions.

Pain

In contrast to the well-controlled data on seizures, the evidence looking at CBD's effects on pain is scant and of very low quality.

For example, a study looked at twelve young women (age 12-24 years) who received the Human Papilloma Virus (HPV) vaccine and subsequently developed dysautonomic syndrome. This is thought to be an autoimmune condition that is characterized by pain, (e.g. headaches, joint and muscle pain, etc.), although its connection to the HPV vaccine is tenuous at best. For example, the largest study evaluating the safety of the HPV vaccine compared ~300,000 young women who received the vaccine to ~700,000 who did not. Those who received the vaccine showed no increases in autoimmune or neurological diseases in those who did not. Dahlstrom 2013

In any case, these 12 women with symptoms of dysautonomic syndrome were given CBD oil as drops under the tongue daily over the course of 3 months. During this time, two women dropped out due to adverse events and another two stopped taking the CBD due to lack of improvement. The remaining 8 individuals showed a statistically significant reduction in body pain and both physical and social functioning compared to their baseline scores at the beginning of the test. Palmieri 2017 That said, this is a very small study that additionally had no placebo-controlled group or a no-treatment group to compare these outcomes to. Did the CBD do anything specifically, or did the condition just run its natural course? This study design

makes it impossible to say.

In fact, there are only two randomized, double-blind, placebo-controlled trials assessing CBD's effect on pain in humans. Researchers out of the UK looked at 24 patients with one of the following conditions: multiple sclerosis (n=18), spinal cord injury (n=4), brachial plexus damage (n=1), and limb amputation due to neurofibromatosis (n=1). Each patient received CBD, THC, CBD + THC, or placebo for 2 weeks during each phase of the trial in a crossover fashion. In other words, each participant would take one agent for 2 weeks before crossing over to another agent for the next 2 weeks, and repeat the process until they'd spent 2 weeks taking each of the possible combinations. Thus, each subject served as their own placebo-matched control.

On each of the last 7 days of each phase, the subjects reported their pain, muscle spasms, bladder function, muscle spasticity, and coordination based on a visual scale that ranged from 0 to 100 (0 = worst to 100 = best). An average score was generated for each patient in each phase and when all the results were in, the CBD group had slightly better pain control: 54.8 in the CBD group compared to 44.5 in the placebo group (again recall 0 = worst and 100 = best in this study). There were no other statistically significant differences between CBD and placebo in any of the other outcomes measured. In addition to the wildly different populations studied here, only 12 of the patients completed the pain assessment for all of the possible interventions. Wade 2003

More recently, researchers out of the Netherlands also used a crossover study design where 20 subjects with fibromyalgia received one of four treatments: THC, THC +CBD, CBD, or placebo. Each week, the subjects got one of the treatments for a **single dose** and then rated their pain. There were no differences between CBD and placebo on any of the pain-related outcomes. van de Donk 2019

Overall, the present data do not clearly support the use of CBD products for pain management. In fact, there seem to be more review articles on CBD than actual trials! Going forward, we'd like to see adequately-powered, randomized, double-blinded, placebo-controlled trials on CBD for specific indications in humans. Right now, the data are severely lacking.

Parkinson's Disease

A single trial investigated the efficacy of CBD on patients with Parkinson's disease and found no benefit in the movement aspects associated with the disorder such as tremor, slow movement, rigidity, and postural instability. Additionally, there was no difference between those receiving CBD or placebo in the Unified Parkinson's Disease Questionnaire-39, a validated questionnaire used to assess the severity of Parkinson's disease in the clinical setting (mainly research). Interestingly, a small subset (n=4) of these subjects had Parksinson's disease-associated sleep behavior disorder did see a reduction in frequency of this condition, which is characterized by nightmares and the muscles being rigid instead of relaxed during sleep. Chagas 2014 Unfortunately, there are no randomized, controlled trials investigating how CBD may affect other sleep conditions such as insomnia or sleep-phase disorders.

Psychosis

At present, there are 3 randomized-controlled trials looking at the efficacy of CBD in patients diagnosed with schizophrenia, a psychiatric condition involving chronic or recurrent psychosis. While all demonstrate an improvement in the symptoms of schizophrenia over time, the trials are small (<100 patients) and the differences between placebo and CBD or traditional antipsychotics and CBD were very small. White 2019

With all that in mind, let's dive into this month's paper on anxiety.

Purpose:

A research group out of Brazil wanted to investigate how CBD affects anxiety. The researchers selected the Test of Speaking in a Real Situation (TPSRS) to generate anxiety. In this study, subjects had 1-minute to prepare a 2-minute speech on "the conditions of one public service of your city" and then present their speech with the other subjects serving as the audience.

Based on previous animal studies, the researchers hypothesized that there would be a "inverted U-shaped" dose-response curve between CBD and effect. An

inverted U-shaped dose-response curve looks like a bell curve and suggests that moderate doses, but not high or low doses, will produce the biggest effects.

Thus, the goal of the study was designed to test the hypothesis that increasing doses of CBD would produce anxiolytic effects in an inverted U-shaped dose-response pattern in healthy volunteers submitted to the TPSRS.

Subjects:

60 men and women aged 18-35 years, with no history of past or current anxiety, psychiatric condition, substance use disorder, or major medical condition were enrolled in the study.

Each subject had their propensity for anxiety measured using the Spielberger State Trait Anxiety Inventory (STAI-trait), which consists of 20 questions about how often someone feels a particular way, e.g. calmed down, safe, tense, annoyed, stunned, upset, etc. The individual can respond with never (1 point), sometimes (2 points), frequently (3 points), or almost always (4 points). Emotions associated with being anxious are scored positively, whereas emotions associated with being calm are scored negatively. Higher scores tend to predict a higher propensity towards anxiety.

The subjects were randomly separated into 5 groups of 12 subjects, each matched for gender (6 men and 6 women), age (average age 22 years), BMI (average 22-23), and STAI-trait score (41-46).

Methods:

The 5 groups received the following:

1. CBD oil 100 mg (99.6% pure CBD powder + corn oil)
2. CBD oil 300 mg (99.6% pure CBD powder + corn oil)
3. CBD oil 900 mg (99.6% pure CBD powder + corn oil)
4. Clonazepam 1 mg
5. Placebo (corn oil)

For reference, clonazepam is a benzodiazepine that is FDA-approved for panic disorder and seizure disorders. There is ample data supporting the use of benzodiazepines, including clonazepam, to reduce each of the three components of panic disorder (attack frequency, anticipatory anxiety, and avoidance). With that said, there is a substantial risk of abuse, addiction, and side effects with benzodiazepines. Of note, the 1 mg dose here is the maximum dose recommended for treating panic disorder per the FDA.

Psychological measurements of anxiety were obtained using the Visual Analog Mood Scale (VAMS), where the individuals rated how they felt by selecting a point on a 100mm line between two pictographic representations of emotions (see Figure 1). Anxiety was assessed by the items calm–excited, relaxed–tense, and tranquil–troubled, whereas sedation was assessed using the items alert–drowsy and attentive–dreamy.

Figure 1: *Pictographic representation of neutral-sad emotions. The line between the two pictures is 100mm and test subjects would mark where they currently felt along the line between the two pictures. The researchers then measured the distance between to determine how anxious and sedate the subjects where during the test.*

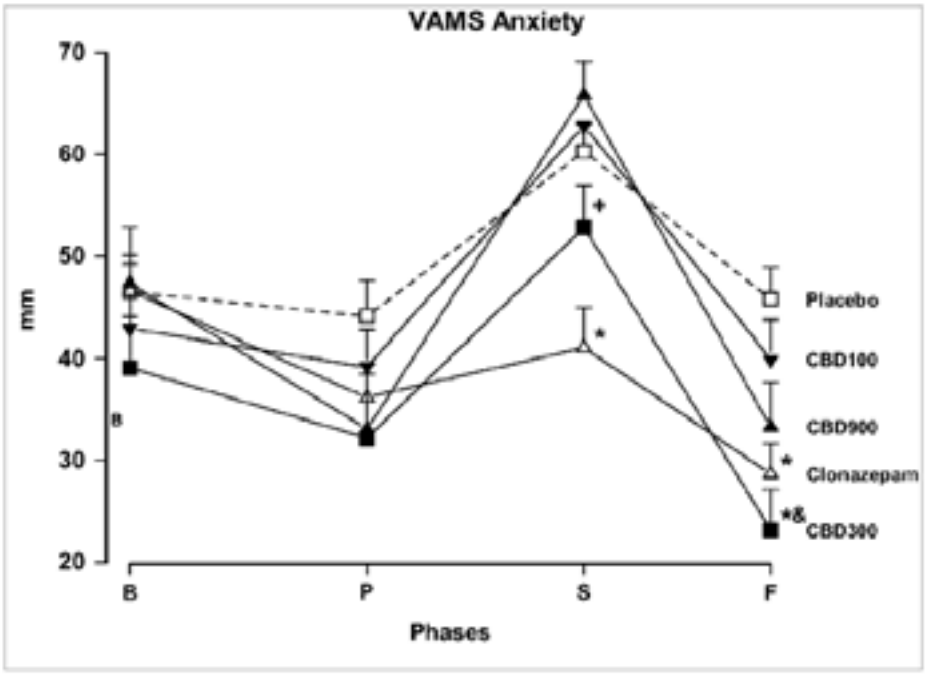


Figure 2: *VAMS-Anxiety results from the experiment. "B" stands for baseline, which is when the medication or placebo was administered. "P" stands for pre-stress, which is prior to when the instructions for the speech test were given. "S" stands for speech, which were measurements taken in the middle of the public speech. "F" stands for final, which were measurements taken one hour after completing the speech test. Asterisks denote statistically significant findings compared to the placebo group. "&" indicates a significant difference compared to the CBD-100 group.*

The VAMS was administered four times in total, once at baseline when the medication or placebo was taken (0 minutes), once prior to the instructions for the public speaking test (80 minutes), once during the speech (153 minutes), and again one hour after the speech (216 minutes). Blood pressure and heart rate were also assessed at these times.

Findings:

Unfortunately, the authors did not provide the raw data for the VAMS scores or physiological data at any point during the experiment.

Based on the above graph and the author's report, we can see that those receiving 300 mg of CBD or 1 mg of clonazepam both had significantly less anxiety during the speech and one hour after the speech as measured by the VAMS. It also appears that clonazepam was significantly better at reducing anxiety than 300 mg of CBD oil during the speech, but not one hour later. With respect to sedation, only clonazepam showed a significant increase in sedation compared to the other groups, however there were no differences between placebo and any of the groups who received CBD (see Figure 3). Finally, there were no significant differences in anxiety between placebo and 100 or 900 mg of CBD at any time point.

The physiological data is shown in Figure 3 (next page). Of note, 300 mg of CBD had significantly higher systolic blood pressure than clonazepam during the speech phase only, but was not significantly different compared to 100 mg of CBD, 900 mg of CBD, or placebo during this time. There were no significant differences in systolic blood pressure at any other time. Additionally, there were no significant differences in heart rate between any of the medications or placebo at any time. Finally, the diastolic blood pressure was significantly higher during the speech phase in those receiving 300 mg of CBD compared to 100 mg of CBD or clonazepam, but not compared to those receiving 900 mg CBD, or placebo. There were no significant differences in diastolic blood pressure at any other time.

Why does this article matter?

Overall, this data suggests that there may be an inverted U-shaped dose-response curve for CBD to reduce anxiety during public speaking. While 300 mg of CBD and clonazepam both reduced as measured by the VAMS test, lower (100 mg of CBD) or higher (900 mg of CBD) did not reduce anxiety. Of course,

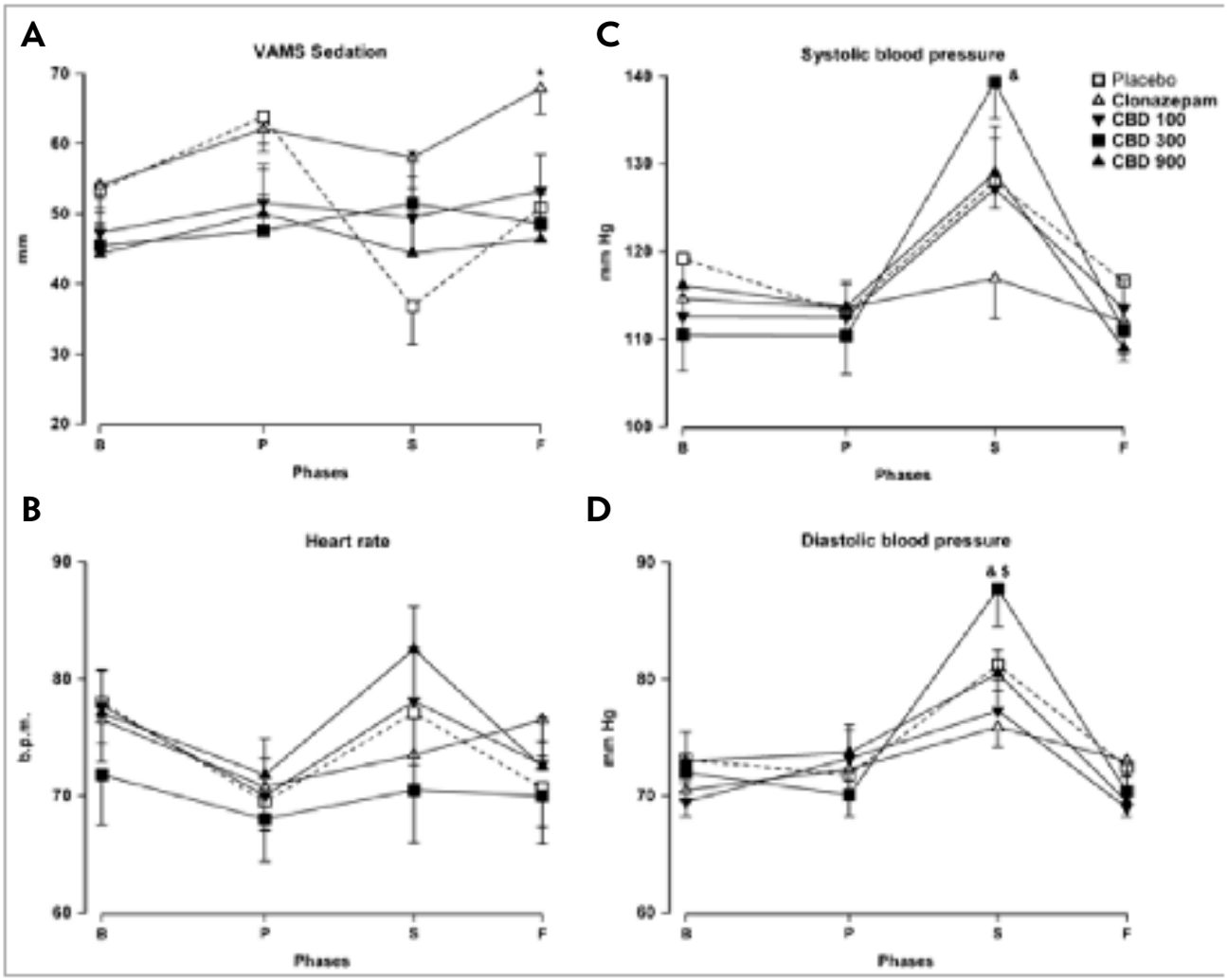


Figure 3: *VAMS-Sedation and physiologic results from the experiment. "B" stands for baseline, which is when the medication or placebo was administered. "P" stands for pre-stress, which is prior to when the instructions for the speech test were given. "S" stands for speech, which were measurements taken in the middle of the public speech. "F" stands for final, which were measurements taken one hour after completing the speech test. Asterisks denote statistically significant findings compared to the placebo group. "&" indicates a significant difference compared to the CBD-100 group. "$" indicates a significant difference to the CBD-100 group.*

this assumes these small changes in the VAMS test are clinically significant. At present, there isn't an established minimal clinically important difference (MCID) for this test. Thus, it's hard to feel confident about these findings.

With that being said, this may be misleading because all of the subjects were of similar size (BMI 22-23) and instead, the appropriate dose for CBD to reduce anxiety during public speaking may be weight-based like it is for the seizure disorders discussed earlier (2.5 mg/kg twice per day). White 2019 Of note, the study reviewed this month is likely underpowered to detect significant differences between CBD dosing, given that there were only 12 subjects in each group. Additionally, there were no statistically significant differences between clonazepam and CBD 300 mg with regards to reducing anxiety, but only the clonazepam increased sedation. Finally, those receiving 300 mg of CBD both had a significant increase in systolic and diastolic blood pressure during the speech phase, which was not seen in the other treatment arms.

Other studies investigating how CBD affects anxiety

outside of public speaking use single-dose CBD, have very small sample sizes, use a wide variety of different CBD doses and routes of administration, and use individuals without anxiety. This makes it difficult to determine what, if any, the chronic impact of CBD on anxiety is, the optimal dose and route of administration, or if CBD can be effective in those diagnosed with a particular anxiety condition. For example, we'd expect those with a diagnosed anxiety condition to potentially benefit more from an anxiolytic (anxiety-reducing) drug than individuals without anxiety. Martin-Santos 2012 Arndt 2017 Hundal 2018

Overall, the data on CBD outside of reducing seizure frequency in those with drug-resistant seizure disorders does not support the notion that CBD is particularly useful for pain, anxiety, neurological conditions such as Parkinson's disease, or psychiatric conditions like schizophrenia. There are no data at this time regarding CBD and the many claims made about it on the Internet such as its effect on exercise performance or recovery and sleep quality or duration in otherwise healthy individuals. There is also a significant concern for adverse reactions including diarrhea (9-20%), anemia (30%), liver injury (8-17%), and interactions with other drugs. Brown 2019 Taken together with the concerns over CBD quality given that less than 1/3 are accurately labeled, I don't think that CBD should be viewed as a panacea, but rather should be approached with caution until better data emerge.

References:

1. Brenan, Megan. "14% Of Americans Say They Use CBD Products." Gallup.com, Gallup, 7 Oct. 2019, news.gallup.com/poll/263147/americans-say-cbd-products.aspx.
2. Corroon J, Phillips JA. A Cross-Sectional Study of Cannabidiol Users. Cannabis Cannabinoid Res. 2018;3(1):152–161. Published 2018 Jul 1. doi:10.1089/can.2018.0006
3. Franck, Tom. "Top Cannabis Analyst on Wall Street Raises Sales Forecast, Names Top 2019 Picks." CNBC, CNBC, 8 Jan. 2019, www.cnbc.com/2019/01/08/top-weed-analyst-on-wall-street-raises-sales-forecast-names-top-picks.html.
4. Jung E.C., Maibach H.I. Animal models for percutaneous absorption. J. Appl. Toxicol. 2015;35:1–10. doi: 10.1002/jat.3004
5. Future, Market Research. "CBD Oil Market Analysis 2019: Hemp Oil and Medical Marijuana to Capture the Largest Share in CBD Oil Industry |." Medgadget, 27 Nov. 2019, www.medgadget.com/2019/11/cbd-oil-market-analysis-2019-hemp-oil-and-medical-marijuana-to-capture-the-largest-share-in-cbd-oil-industry.html.
6. Agricultural Act of 2014, HR 2642, 113th Cong, 2nd Sess (2014). US Government Publishing Office website, https://www.gpo.gov/fdsys/pkg/BILLS-113hr2642enr/pdf/BILLS-113hr 2642enr.pdf
7. White, C. M. (2019). A Review of Human Studies Assessing Cannabidiol's (CBD) Therapeutic Actions and Potential. The Journal of Clinical Pharmacology. doi:10.1002/jcph.1387
8. VanDolah, H. J., Bauer, B. A., & Mauck, K. F. (2019). Clinicians' Guide to Cannabidiol and Hemp Oils. Mayo Clinic Proceedings. doi:10.1016/j.mayocp.2019.01.003
9. Bonn-Miller MO, Loflin MJ, Thomas BF, et al. Labeling accuracy of cannabidiol extracts sold online. JAMA. 2017;318: 1708-1709.
10. Commissioner, Office of the. "FDA Regulation of Cannabis and Cannabis-Derived Products: Q&A." U.S. Food and Drug Administration, FDA, www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd.
11. Witkamp R, Meijerink J. The endocannabinoid system: an emerging key player in inflammation. Curr Opin Clin Nutr Metab Care. 2014;17(2):130-138.
12. Acharya N, Penukonda S, Shcheglova T, Hagymasi AT, Basu S, Srivastava PK. Endocannabinoid system acts as a regulator of immune homeostasis in the gut. Proc Natl Acad Sci U S A. 2017;114(19):5005-5010.

13. Zou S, Kumar U. Cannabinoid Receptors and the Endocannabinoid System: Signaling and Function in the Central Nervous System. Int J Mol Sci. 2018;19(3):833. Published 2018 Mar 13. doi:10.3390/ijms19030833
14. Millar, Sophie A., et al. "A Systematic Review on the Pharmacokinetics of Cannabidiol in Humans." Frontiers in Pharmacology, vol. 9, 26 Nov. 2018, doi:10.3389/fphar.2018.01365.
15. Devinsky O, Marsh E, Friedma D, Thiele E, et al. Cannabidiol in patients with treatment-resistant epilepsy: an open-label interventional trial. Lancet Neurol. 2016;15:270-278
16. Hess EJ, Moody KA, Geffrey AL, et al. Cannabidiol as a new treatment for drug-resistant epilepsy in tuberous sclerosis complex. Epilepsia. 2016;57:1617-1624.
17. Devinsky O, Cross JH, Laux L, et al. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. N Engl J Med. 2017;376:2011-2020.
18. Devinsky O, Patel AD, Cross JH, et al. Effect of cannabidiol on drop seizures in the Lennox-Gastaut syndrome. N Engl J Med. 2018;378:1888-1897.
19. Arnheim-Dahlström L, Pasternak B, Svanström H, Sparén P, Hviid A. Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. BMJ. 2013;347:f5906. Published 2013 Oct 9. doi:10.1136/bmj.f5906
20. Palmieri B, Laurino C, Vadala M. Short-term efficacy of CBD-` enriched hemp oil in girls with dysautonomic syndrome after human papillomavirus vaccination. IMAJ. 2017;19:79-84.
21. Wade DT, Robson P, House H, et al. A preliminary controlled study to determine whether whole-plant cannabis extracts can improve intractable neurogenic symptoms. Clin Rehabil. 2003;17:21-29.
22. Chagas MH, Eckeli AL, Zuardi AW, et al. Cannabidiol can improve complex sleep-related behaviours associated with rapid eye movement sleep behaviour disorder in Parkinson's disease patients: a case series. J Clin Pharm Ther. 2014;39(5):564-566.
23. van de Donk T, Niesters M, Kowal MA, Olofsen E, Dahan A, van Velzen M. An experimental randomized study on the analgesic effects of pharmaceutical-grade cannabis in chronic pain patients with fibromyalgia. Pain. 2019;160(4):860–869. doi:10.1097/j.pain.0000000000001464
24. Zhornitsky S., Potvin S. (2012). Cannabidiol in humans-the quest for therapeutic targets. Pharmaceuticals (Basel). 5 529–552. 10.3390/ph5050529
25. Martin-Santos R, Crippa JA, Batalla A, et al. Acute effects of a single, oral dose of d-9-tetrahydrocannabidiol (THC) and cannabidiol (CBD) administration in healthy volunteers. Curr Pharm Design. 2012;18:4966-4979.
26. Arndt, DL, Harriet de Wit H. Cannabidiol does not dampen responses to emotional stimuli in healthy adults. Cannabis and Cannabinoid Res. 2017;2(1):105-113.
27. Hundal H, Lister R, Evans N, et al. The effects of cannabidiol on persecutory ideation and anxiety in a high trait paranoid group. J Psychopharmacol. 2018;32:276-282
28. Brown JD, Winterstein AG. Potential Adverse Drug Events and Drug-Drug Interactions with Medical and Consumer Cannabidiol (CBD) Use. J Clin Med. 2019;8(7):989. Published 2019 Jul 8. doi:10.3390/jcm8070989

MEDICAL REVERSALS & EVIDENCE-BASED MEDICINE

BY: DR. AUSTIN BARAKI

Articles Reviewed: A comprehensive review of randomized clinical trials in three medical journals reveals 396 medical reversals by Herrera-Perez et al. 2019.

Key Points:

1. Traditionally, clinical treatment decisions were based on the prevailing medical models of the time (e.g., the theory of the four humors and other folk models), combined with expert opinion and observational experience of what has seemed to "work" in the past.
2. The Evidence-based Medicine (EBM) movement has led to an increasing emphasis on the use of rigorously performed clinical trials to guide clinical decision making, although it has come with its share of criticism and controversy as well due to a number of real-world limitations.
3. The authors of this study surveyed three leading medical journals from 2003 to 2017 and found 396 randomized, controlled trials of interventions that directly contradicted traditional practices, known as a "medical reversal". Unfortunately despite the clear importance of such work, we also know that such findings and public messaging campaigns regarding low-value care typically do little on their own to influence clinician behavior and practice patterns.

Introduction:

The history of healthcare gives us no shortage of ineffective treatments to discuss, ranging from bloodletting, trepanation, and lobotomies in old times to many seemingly advanced interventions still practiced today. Rather than select any one particular modality to dissect, we'll tackle the topic through a more general lens to illustrate the overall scope of the problem.

Once we think we've arrived at a particular diagnosis, how do we decide what treatment(s) to offer a given patient? Traditionally, such decisions were based on the prevailing medical models of the time (e.g., the theory of the four humors or other folk models), combined with expert opinion and observational experience of what has seemed to "work" in the past. Unsurprisingly, this was a quite limited and relatively unsuccessful approach to the problem for a variety of reasons, as discussed in our article When Logic Fails.

The concept of using evidence from well-conducted scientific research to guide decision making is relatively novel, emerging into the common parlance and medical education only in the 1990s. At this time, the term "Evidence-based Medicine" (EBM) was proposed as an integration of 1) the best research evidence with 2) clinical expertise and 3) patient values (which we've discussed further here).

So, while empirical and observational evidence has certainly played a role in clinical decision making throughout history, the EBM movement emphasized *stratifying* our evidence -- and thus, subsequent conclusions and guidelines -- by their epistemological strength, or Levels of Evidence. This is done using methods such as the "hierarchy of evidence" framework, which is now increasingly shifting to the GRADE framework. Zimerman 2013 Thoma 2015 Sur 2011

This EBM movement is not without limitations or controversy, however, as some have argued that it has led to a myopic focus on only one epistemological approach (specifically randomized, controlled trials) rather than adequately integrating other forms of knowledge into the overall clinical approach. For example, Tonelli argues that: Tonelli 2006

"The failure of the EBM approach centres on its attempt to treat different potential warrants for medical decision making, such as empiric evidence, clinical experience and pathophysiologic rationale, as different in degree, rather than different in kind."

Other criticisms have related to the inherent limitations of science to inform *every* clinical scenario with individual patients, inadequate emphasis on patient values or clinical experience, and many others. Straus 2000 Cohen 2004 Guyatt 2012 Indeed, we routinely run into situations in our daily clinical practices for which we do not have clear evidence to guide decision making, and must resort to these other sources of knowledge (including our "best guesses") to move forward with the individual patient in front of us. Furthermore, there are situations where randomized, controlled trials simply aren't the best epistemological tool for the topic of study, as discussed at length in our 4-part series on nutrition science. (For more discussion on the general topic of epistemology in the context of clinical practice, see here.)

Regardless of the controversy around the EBM model, however, it is clear that medical history is littered with interventions that were initially proposed and offered to patients based on little evidence, biased/confounded evidence, or no evidence at all. For many of these interventions, only subsequent rigorous study (e.g., through randomized, controlled trials) has ultimately revealed their lack of efficacy. The subject of today's article by Herrera-Perez et al. is to examine the frequency of these so-called medical reversals in modern medicine.

Purpose:

The purpose of this article was to identify randomized controlled trials in three leading medical journals that reflected medical reversals from traditional practice,

as a way to help reduce the utilization of low-value care.

Methods:

The authors limited their systematic review to publications in three major medical journals: JAMA and the Lancet (between 2003 and 2017), and the New England Journal of Medicine (between 2011 and 2017).

A total of 3017 articles reporting results of randomized, controlled trials on medical interventions were identified. After excluding 1373 studies on novel interventions, as well as 1229 studies with positive or inconclusive results, a total of 415 articles (14%) with negative results remained. These were classified as "tentative medical reversals", and after further literature review ultimately 396 articles (13% of RCTs) were deemed to represent true medical reversals.

Findings:

As described above, the authors identified 396 randomized, controlled trials of interventions that represented medical reversals from previously established practice. These were identified in three leading medical journals across a limited time period (just 14 years for JAMA/the Lancet, and 6 for NEJM), but represented 13% of all RCTs published in these journals across the time period.

There were some notable findings in the analysis of study characteristics. For example, 366 (92%) of studies were conducted in high-income countries, whereas just 30 (8%) were conducted in low-income countries.

The most frequent topics of study were cardiovascular disease (80 studies, or 20% of total) and public health (48 studies, 12%). The most common interventions studied were medications (129 studies, or 39% of total), followed by procedures (81 studies, 20%), nutritional supplements (53 studies, 13%), medical devices (35 studies, 9%), and systems interventions (30 studies, 8%).

A few of the more notable medical reversals included the following (a full listing of all included reversals is provided in the study & supplemental materials):

Moss et al. 2006. Whereas cancer screening guidelines traditionally recommended women initiate mammographic breast cancer screening at age 40, there was not clear evidence of benefit for women under age 50. This randomized over 160,000 women aged 39-41 to annual mammography versus usual care and found no significant breast cancer mortality benefit for screening at 10.7 years of follow up. A subsequent Cochrane review in 2013 concluded that *"The chance that a woman will benefit from attending screening is small at best, and - if based on the randomised trials - ten times smaller than the risk that she may experience serious harm in terms of overdiagnosis." [Note: Despite this evidence, this intervention continues to be routinely used in practice today.]*

Harris et al. 2013. Given increasing concerns about the development of antibiotic-resistant bacteria ("superbugs"), recommendations emerged for contact precautions (specifically wearing gowns and gloves for all patient contact) in critical care settings. This study randomized 20 ICUs to either these universal contact precautions or to usual care, and found no difference in rates of acquisition of methicillin-resistant S. aureus (MRSA) or vancomycin-resistant enterococcus (VRE) between groups. *[Note: Despite this evidence, this intervention continues to be routinely used in practice today - including in my own residency training in the medical ICU.]*

Friedly et al. 2014. Traditional treatment approaches for back pain symptoms thought to be related to symptomatic lumbar spinal stenosis include epidural corticosteroid injections (CSI). The authors note that "*From 1994 to 2001 there was a 271% growth in usage of the treatment, and the cost went from $24 million to over $175 million*", despite a lack of clear evidence of benefit for this condition. This study randomized 441 individuals to receive injections of epidural CSI plus

anesthetic versus anesthetic alone (a controlled design that should illustrate the specific effects of including a corticosteroid in the injection). At six weeks after randomization, there were no differences in measures of physical function or pain intensity. *[Note: Despite this evidence, this intervention continues to be routinely used in practice today.]*

Katz et al 2013. Patients presenting with knee pain are often found to have meniscal tears on advanced imaging, which frequently prompts surgical evaluation and intervention. This study randomized 351 patients aged 45 and older with meniscal tears and mild-to-moderate osteoarthritis to either surgery plus post-operative physical therapy or physical therapy alone [note: we must point out that this is a poor study methodology due to the lack of blinding with a sham-surgery group]. They found no significant difference in functional improvement after 6 or 12 months. *[Note: Despite this evidence, this intervention continues to be routinely used in practice today, estimated in over 465,000 patients annually in the US].*

Why does this article matter?

Increasing attention is being drawn to low-value medical care via initiatives like the Choosing Wisely Campaign, whereby professional societies provide recommendations against specific interventions that are commonly performed, yet do not provide significant value for patient outcomes.

The authors of this paper argue that such "low-value" practices, defined as practices that are either ineffective or that offer similar effectiveness to lower-cost options, have a number of harmful effects. These include physical and emotional harm to patients, undermining public trust in medicine, and present a significant opportunity cost and financial cost, among others.

The sorts of findings and problems described in today's topic article have been discussed in other analyses of the literature as well. For example, in the world of psychiatry Tajika *et al.* found: Tajika 2015

"Among 83 articles recommending effective interventions, 40 had not been subject to any attempt at replication, 16 were contradicted, 11 were found to have substantially smaller effects and only 16 were replicated. The standardised mean differences of the initial studies were overestimated by 132%."

Similarly, Ioannidis found that out of 49 highly cited original clinical research studies, "*five of 6 highly-cited nonrandomized studies had been contradicted or had found stronger effects vs 9 of 39 randomized controlled trials (P = .008).*" Ioannidis 2005 This has led to strengthening arguments for increasing the proportion of randomized trials in biomedicine in order to more clearly demonstrate efficacy prior to the uptake of new interventions. Collins 2020

Ultimately, we agree with a recent editorial published entitled "The Case for Being a Medical Conservative", wherein the authors argue: Mandrola 2019

"The medical conservative, however, recognizes that many developments promoted as medical advances offer, at best, marginal benefits. We do not ignore value. In a plot of spending vs outcomes, we define marginal advances as "flat of the curve" gain. On the flat part of the curve, additional spending, whether it be on a new drug, device, or diagnostic test, confers little benefit to individual patients or society. The medical conservative adopts new therapies when the benefit is clear and the evidence strong and unbiased ... Most medical decisions, however, come with far less certainty ... When genuine benefit exists for an intervention, it easily withstands critical appraisal."

Unfortunately, as we have discussed elsewhere, individual behavior change is highly complex and difficult to influence, even among healthcare professionals. Clinical decision making is influenced by many factors including legal concerns, patient expectations and the doctor-patient relationship, time, financial incentives, cognitive biases, and many others. For these reasons, information campaigns and comparative scientific evidence have ultimately shown limited effects on practice patterns. Timbie 2012 Colla 2017

We know that patients don't tend to manifest significant behavior change in response to simply providing information about calorie balance in the context of obesity-related behavior change. Similarly, it appears that clinicians don't tend to

significantly change practice patterns in response to information about an intervention's lack of efficacy.

For example, despite a multitude of organizations providing strong Choosing Wisely recommendations against early imaging for nonspecific low back pain, rates of imaging continue to increase in both primary care and emergency department settings. Downie 2019

Several other low-value services have shown modest or no significant change in utilization in response to such public campaigns. Rosenberg 2015

We know that a nuanced, multifactorial approach is required for effective behavior change in the context of lifestyle-related issues such as physical inactivity, obesity, and metabolic syndrome, particularly on an individual level. Similarly, altering clinician practice patterns will require a multifactorial approach both on a large scale and on the individual clinician level. Providing evidence and information is just one factor to consider; as described above, we may require overarching systems interventions to shift legal/malpractice concerns and address financial incentives, clinic-level interventions to address time concerns, and social/public health interventions to address patient expectations (e.g. mass messaging campaigns for low back pain), just to name a few.

As with most things, this is *really complicated*. Essentially all clinicians want to do their best for their patients, but the path to consistent delivery of high-value care is extremely difficult and will require continued diligent effort across multiple levels of society to make progress.

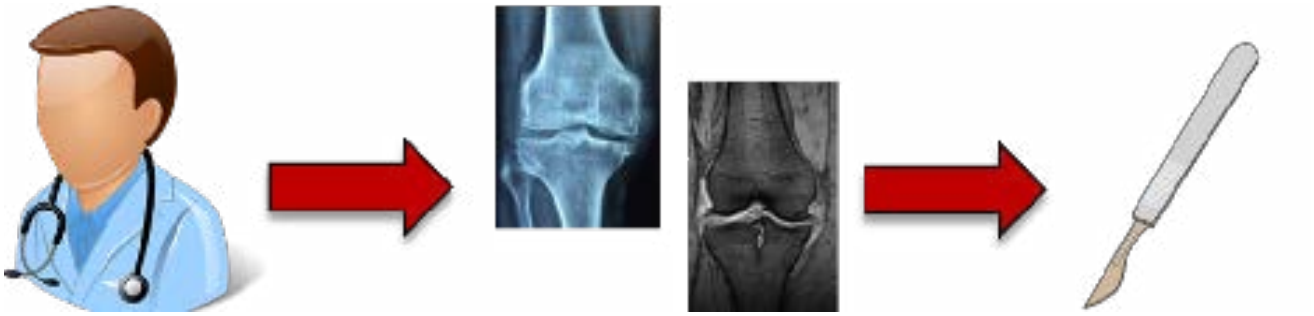
References:

1. Zimmerman. Evidence-Based Medicine: A Short History of a Modern Medical Movement. Virtual Mentor. 2013;15(1):71-76.
2. Thoma et al. A Brief History of Evidence-Based Medicine (EBM) and the Contributions of Dr David Sackett, Aesthetic Surgery Journal, Volume 35, Issue 8, November/December 2015, Pages NP261–NP263
3. Sur et al. "History of evidence-based medicine." Indian journal of urology : IJU : journal of the Urological Society of India vol. 27,4 (2011): 487-9. doi:10.4103/0970-1591.91438
4. Straus, S E, and F A McAlister. "Evidence-based medicine: a commentary on common criticisms." Canadian Medical Association journal. vol. 163,7 (2000): 837-41.
5. Cohen et al. A categorization and analysis of the criticisms of Evidence-Based Medicine. Int J Med Inform. 2004 Feb;73(1):35-43.
6. Tonelli. Integrating evidence into clinical practice: an alternative to evidence-based approaches. J Eval Clin Pract. 2006 Jun;12(3):248-56.
7. Guyatt & Tonelli. The Role of Experience in an Evidence-Based Practice Med Roundtable Gen Med Ed. 2012; 1(1): 75 - 84.
8. Moss SM et al. Effect of mammographic screening from age 40 years on breast cancer mortality at 10 years' follow-up: a randomised controlled trial. Lancet. 2006 Dec 9;368(9552):2053-60.
9. Harris AD et al. Universal glove and gown use and acquisition of antibiotic-resistant bacteria in the ICU: a randomized trial. JAMA. 2013 Oct 16;310(15):1571-80.
10. Friedly JL et al. A randomized trial of epidural glucocorticoid injections for spinal stenosis. N Engl J Med. 2014 Jul 3;371(1):11-21.
11. Katz JN et al. "Surgery versus physical therapy for a meniscal tear and osteoarthritis." The New England Journal of Medicine vol. 368,18 (2013): 1675-84.
12. Tajika et al. Replication and contradiction of highly cited research papers in psychiatry: 10-year follow-up. Br J Psychiatry. 2015 Oct;207(4):357-62.
13. Ioannidis JP. Contradicted and initially stronger effects in highly cited clinical research. JAMA. 2005 Jul 13;294(2):218-28.
14. Collins et al. The Magic of Randomization versus the Myth of Real-World Evidence. N Engl J Med. 2020 Feb 13;382(7):674-678.
15. Mandrola et al. The Case for Being a Medical Conservative. The American Journal of Medicine, Volume 132, Issue 8, 900 - 901.
16. Timbie et al. Five Reasons That Many Comparative Effectiveness Studies Fail To Change Patient Care And Clinical Practice. Health Affairs 2012 31:10, 2168-2175
17. Colla et al. Choosing Wisely Campaign: Valuable For Providers Who Knew About It, But Awareness Remained Constant, 2014–17. Health Affairs 2017 36:11, 2005-2011

18. Downie et al. How common is imaging for low back pain in primary and emergency care? Systematic review and meta-analysis of over 4 million imaging requests across 21 years. British Journal of Sports Medicine. 13 February 2019.
19. Rosenberg et al. Early Trends Among Seven Recommendations From the Choosing Wisely Campaign. JAMA Intern Med. 2015;175(12):1913–1920.
20. O'Keeffe et al. Mass media campaigns are needed to counter misconceptions about back pain and promote higher value care. British Journal of Sports Medicine 2019;53:1261-1262.

THE BEE'S KNEES: AN UPDATED REVIEW OF THE EVIDENCE ON SURGICAL INTERVENTION FOR MENISCUS ISSUES

BY: DR. MICHAEL RAY



Author's Note: Surgical intervention has recently come under fire as the mainstay intervention for knee pain being attributed to the meniscus. Recent guidelines have advocated against surgical interventions in cases presenting with knee osteoarthritis and meniscal changes coined degenerative. This month's article is an update to the prior Logic of Rehab article - The Bee's Knees. We explore recent counterclaims advocating for meniscal surgical intervention based on patient subgroups presenting with particular patient characteristics and their effect on likely outcomes. We also expand the discussion to the young adult (18-40 years of age) and pediatric (less than 18 years of age) populations, assessing current available evidence. Finally we outline our recommended management for those presenting with knee pain being attributed to the meniscus. Although we have evidence of meniscal changes on imaging in asymptomatic populations demonstrating a non-linear and variable relationship with symptoms, the biomedical approach isn't likely to change soon. Hopefully this updated review can aid clinicians with decision making once information about the meniscus is entered into the equation.

Introduction:

The medical machine acts quickly. This is a good thing when situations are dire and life or limb are at stake. However, in less serious situations the expediency of the process may result in a failure to consider all the current evidence regarding diagnosis, treatment options, and their influence on prognosis. The urgency of the process may at first seem reassuring to the patient, instilling confidence that the clinician knows what they are doing. This process *should* be collaborative, but often it becomes authoritative. Patients are expected to make quick decisions as a layperson to the field. Thus, the process necessitates trust. Trust in the clinician, trust in the decision making, and trust that the information being delivered to them is the best we have (hopefully based on current research evidence).

This discussion could quickly become about informed consent; however, for today we'd rather focus on prevalent issues in the musculoskeletal world that are often accompanied with imaging and a question of how we should manage this issue. This article will be all about the bee's knees ... more specifically, the meniscus. We will set out to answer the question: How significant is the meniscus, and when damaged, what should we do about it based on current best evidence?

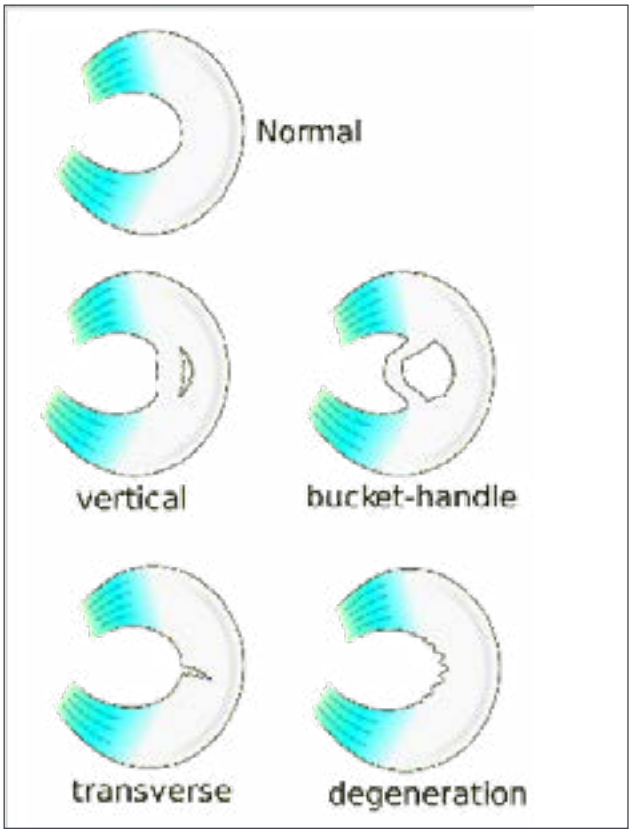
So, what is the meniscus?

The meniscus is a fibrocartilaginous structure located in the tibiofemoral joint. Its anatomy and location are consistent with a function of shock absorption and force transmission. In each knee there is a meniscus on the medial (inner aspect) and lateral (outer aspect) side.

The meniscus may be damaged from traumatic injuries or due to age-related degeneration over time. Meniscal injuries are considered the second most common knee injury, with an incidence of 12% – 14% (61 cases / 100,000 people in U.S.). It is estimated that 10-20% of all orthopedic surgeries involve the knee meniscus (850,000 patients / year). Logerstedt 2010

Classification of meniscal damage is typically based on location and orientation of a tear (see figure at right). Mordecai 2014 Tears can be vertical longitudinal, vertical radial, horizontal, oblique, and complex. Mordecai 2014 A complete vertical tear has the potential to fold over within the joint space, creating what is known as a "bucket-handle" tear. Mordecai 2014 Typically a bucket-handle tear is considered "*unstable*", and classically is thought to provoke mechanical symptoms such as "*locking*" of the joint. Previously, such symptoms were thought to warrant surgical intervention. Silhvonen 2016 However, recent evidence has been emerging that contradicts this usual practice.

The underlying theme that is problematic for addressing this issue is the premise of a structural finding being directly causative of patient symptoms.



If you've been following our work, it should be apparent that things are becoming harder to label as "*pathologies*" or even as *abnormalities* based on radiologic imaging alone. The knee is no different. For example, meniscal damage and osteoarthritis are readily identifiable in asymptomatic populations (no reported pain and/or disability). Recently an article investigated the prevalence of "*abnormal*" imaging findings in 115 asymptomatic individuals (230 knees) using 3 T MRI. To my understanding, this is the largest study to date with high-resolution imaging (typically 1.5 T is utilized) to examine the structures of the knee. Some background data on the included cohort:

- 115 asymptomatic volunteers (51 males, 64 females)
- Median age: 44 years (ranged between 25 - 73 years of age)
- Based out of London
- Median Body Mass Index (BMI): 25 (ranged from 19.6 - 38.1 kg/m2)
- Physical activity (low intensity) was 2 hours / week (ranged from 0 - 4)
- Purposefully included sedentary individuals (not meeting activity guidelines)

The authors' primary findings:

"Nearly all knees (227/230; [97%]) of asymptomatic individuals showed abnormalities in at least one of the knee structures on MRI, of varying grades of severity. These findings included meniscal tears, cartilage abnormalities, bone marrow oedema and tendon and ligament abnormalities." Horga 2020

To further demonstrate these individuals were indeed asymptomatic and functional, the mean Knee Injury and Osteoarthritis Outcome Score (KOOS) for each item was ≥ 90/100. Specific to our discussion, the authors identified 30% prevalence of meniscal tears and 18% of meniscal degeneration in participants' knees. A variety of tear types were identified - horizontal (23% knees), complex (3%), vertical (2%), radial (2%) and bucket handle tears (1%). Finally, 3% of knees demonstrated meniscal extrusion, a situation where the meniscal margin is extending beyond the tibial margin. The authors conclude:

"Our study questions clinical decision-making regarding arthroscopy and its efficacy in reducing symptoms and treatment. The high rate of asymptomatic adults with knee joint abnormalities on MRI may indicate why arthroscopy and other surgical interventions for these do not result in better outcomes than sham surgery. For example, there is no evidence to suggest that meniscectomy benefits patients presenting with meniscal tear symptoms more than sham surgery does. Moreover, meniscectomy and other surgical interventions could lead to further complications or deterioration of the articular cartilage and increase the risk of osteoarthritis." Horga 2020

(For more, *Not Your Image*, references for the knee see Culvenor *et al*, Beals *et al*, Pappas *et al*, van der Heijden *et al*, and Guermazi *et al*).

With this in mind we will now discuss the current evidence regarding the best management of people dealing with knee pain being attributed to meniscal tears given that imaging has likely already been done, regardless of necessity.

Management:

Based on the recent British Journal of Sports Medicine clinical practice guidelines, arthroscopic surgery for meniscal tears in the setting of degenerative knee osteoarthritis is NOT recommended. The guidelines state:

"We make a strong recommendation against the use of arthroscopy in nearly all patients with degenerative knee disease, based on linked systematic reviews; further research is unlikely to alter this recommendation ... This recommendation applies to patients with or without imaging evidence of osteoarthritis, mechanical symptoms, or sudden symptom onset." Siemieniuk 2018

These guidelines include a discussion of a systematic review by Brignardello-Peterson. This is a review article that finds knee arthroscopy is no better than conservative management for patients with degenerative changes. Brignardello-Peterson 2017 The BJSM recommendation falls in line with what the research has been demonstrating on the topic of chronic degenerative meniscal tears.

This paradigm shift will likely continue to take time. Immediately after the BJSM release, an open letter to the editor was written in the Arthroscopy Journal demonstrating a major appeal to authority, post-hoc fallacy, and confirmation bias. Excerpts from the letter:

"I question how the authors have the required knowledge base to critically analyze the articles they have chosen to review. Once again they seem to be predominantly epidemiologists, with the only orthopaedic input coming from an "orthopaedic resident" whose major interest seems to be research methodology. I personally would not have the confidence to cast judgment on a paper from a different specialty of orthopaedics, let alone a subject about which

I do not have an intimate knowledge or extensive professional background." ... "I strongly believe that these (BMJ) conclusions cannot be justified based on the evidence presented and that they are wrong. I would be happy to discuss my detailed reasoning with you further and to introduce you to some of my patients.

"I appreciate that this is anecdotal but in the last two weeks I have seen a 50 year old joiner who was struggling to work because every time he knelt down his knee locked and in desperation had come to see me privately as he had been denied surgical referral after a "normal MRI." After taking out his degenerate bucket handle tear he was back at work after a week." Bollen 2018

Most recently, a 2019 review and meta-analysis by Abram *et al* sought to determine if patients do indeed benefit from arthroscopic partial meniscectomy (APM) over other interventions based on stratification of symptoms and radiological findings. Three adult patient groups with meniscal tears and knee pain were assessed:

- Group A: All patients with any meniscal tear type with or without radiological presence of osteoarthritis
- Group B: Patients with any meniscal tear type without knee osteoarthritis
- Group C: Patients with an "*unstable*" meniscal tear and without knee osteoarthritis

Arthroscopic Partial Meniscectomy was compared to:

- Other surgical interventions such as arthroscopic lavage, sham surgery (*"...procedure requiring an anaesthetic and surgical skin incision but without any knee arthroscopy procedure (diagnostic, washout and other) being performed."*) Abram 2019 and placebo (diagnostic arthroscopy) surgery
- Nonsurgical - physiotherapy and exercise therapy
- Pharmacological - NSAIDS and Intra-articular Steroid Injection
- No intervention - waiting list and active monitoring

Unfortunately, these data are not great. 20 total articles (10 RCTs and 1 cohort study) were included consisting of:

- APM vs Surgical - 2 trials
- APM vs Non-surgical - 7 trials and 1 cohort
- APM vs Pharmacological - 1 trial
- **APM vs No intervention - 0 trials**

The authors state - *"Findings were limited by small sample size, small number of trials and cross-over of participants to APM from comparator interventions."* Abram 2019 We can examine their forest plots (next pages) for a better understanding of findings of APM vs non-surgical interventions (Physiotherapy).

Examining the overall standard mean difference (SMD) for each outcome, we can see how small the difference was between APM vs physiotherapy.

Group	Outcome	APM Total	Control Total	SDM
A	Pain	478	465	0.22 [0.03, 0.40]
A	Knee Function	532	518	0.18 [0.04, 0.33]
A	QoL	183	167	0.43 [0.10, 0.75]
B	Pain	216	186	0.35 [0.04, 0.66]
B	Knee Function	269	238	0.30 [0.06, 0.53]
B	QoL	129	115	0.59 [0.11, 1.07]

Notice, we do not have data on Group C, and this was a theme throughout the article. There was only a single article (cohort study) for group C who were intervened upon with APM after "*failing*" physical therapy. The authors state,

"At 6–12 months, in trials with a non-surgical comparator, there was a small benefit in favour of APM for pain, knee-specific quality of life and function in studies including patients with osteoarthritis. Excluding patients with osteoarthritis, there was a small to moderate benefit in pain, knee-specific quality of life and function.The clinical importance of these differences is, however, uncertain." Abram 2019

Uncertain indeed, and after examining these forest plots, SMDs, and risk of bias, we need to seriously question the benefits being worth it in comparison to risk surgery vs conservative management.

Figure 2.
Pain following arthroscopic partial meniscectomy (APM) versus non-surgical intervention (6 – 12 months).

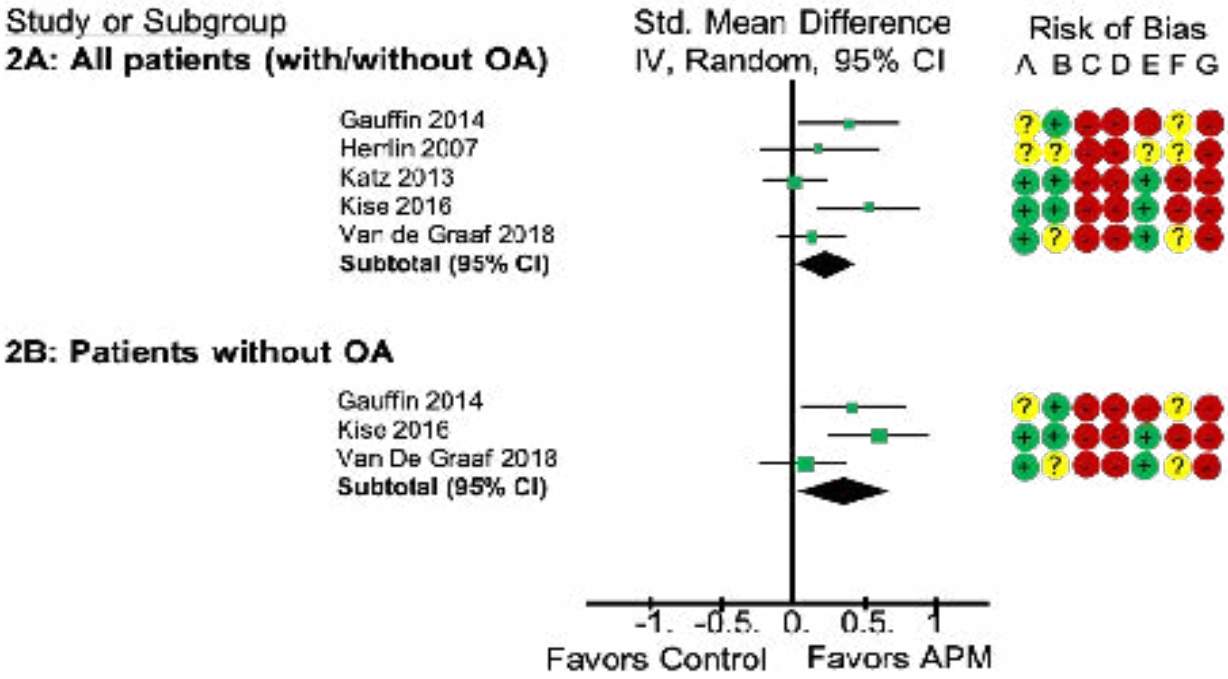


Figure 3.
Function following arthroscopic partial meniscectomy (APM) versus non-surgical intervention (6 – 12 months).

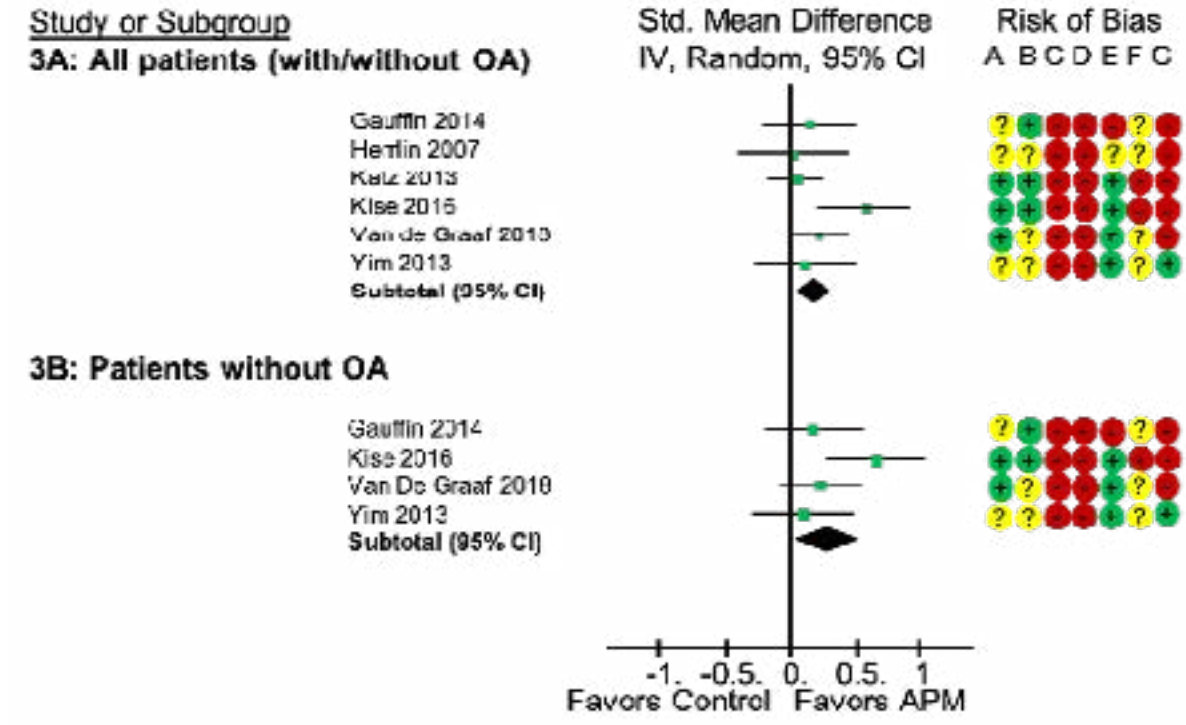
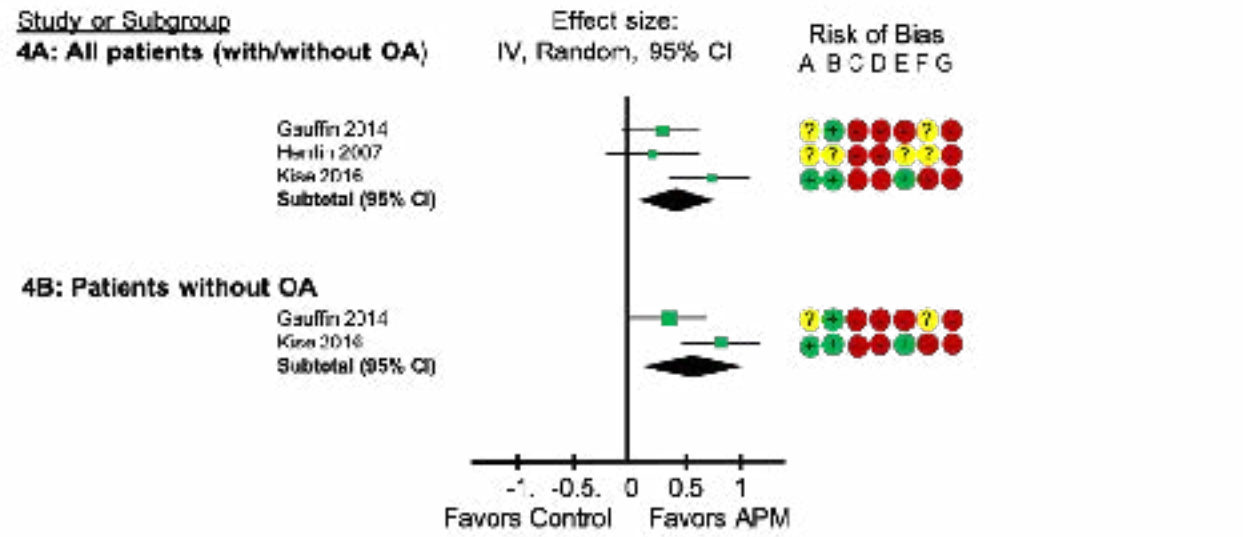


Figure 4.
Knee-specific health-related quality of life following arthroscopic partial meniscectomy (APM) versus non-surgical intervention (6 – 12 months).



Risk of Bias Legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data A(attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

APM vs. other surgical interventions:

Two RCTs were included (Silhvonen *et al* and Roos *et al*), totaling 190 patients. Silhvonen's study compared APM vs placebo surgery and Roos's study APM vs sham surgery. Both of these studies excluded patients with OA, meaning their findings fit with groups 1 and 2 above. Overall, these two studies were rated low risk of bias on the Cochrane Collaboration Risk of Bias Tool. However, on one bias assessment, Roos was rated high for allowing 36% of patients to cross-over to APM *before* the final follow-up.

Overall, the authors found Silhvonen *et al* demonstrated no difference between APM and placebo surgery. Roos's findings are a bit less straightforward. At six months there was *"...no improvement in knee pain in comparison with sham surgery at under 6 months (SMD 0.26 [95% CI -0.41 to 0.93]; one trial; 35 patients; GRADE: low)."* But after 12 months - *"...there was a moderate to large improvement in patients receiving APM in comparison with sham surgery (SMD 0.72 [95% CI 0.02 to 1.42]; one trial, 34 patients; GRADE: low) equivalent to a MD of 17.50 (95% CI 1.16 to 33.84) measured using the KOOS pain scale."* Also knee function didn't show improvement in APM vs sham surgery < 6 months nor at > 12 months. Finally, as it relates to knee-specific quality of life and generic quality of life, no difference occurred between APM and sham surgery < 6 months nor at > 12 months.

APM vs. Pharmacologic treatment

A single trial was identified examining APM vs intra-articular corticosteroid injection that fit group 1 above. Related to knee pain and function, no improvement was found between APM and steroid injection at 6 - 12 months, however - *" There was a moderate to large improvement at under 6 months (SMD 0.82 [95% CI 0.41 to 1.23]; MD 2.90 Oxford Knee Score [95% CI 1.50 to 4.30]; one trial; 98 patients; GRADE: low)."*

The authors finally concluded "***Performing APM in all patients with knee pain and a meniscal tear is not appropriate, and surgical treatment should not be considered the first-line***

***intervention**. There may, however, be a small-to-moderate benefit from APM compared with physiotherapy for patients without osteoarthritis. No trial has been limited to patients failing non-operative treatment or patients with an unstable meniscal tear in a non-arthritic joint; research is needed to establish the value of APM in this population." [emphasis ours]* Abram 2019

Lastly - we can't forget evidence demonstrating an increased risk of knee arthroplasty (joint replacement) after undergoing APM. Abram et al retrospectively examined a cohort of 834,393 patients with a history of APM and found:

*"Patients developing a meniscal tear undergoing APM are at greater risk of knee arthroplasty than the general population. This **risk is three-times greater** in the patient's affected knee than in the contralateral knee. Women in the cohort were at double the risk of progressing to knee arthroplasty compared with men."* Abram 2019

Where does this leave us for clinical management?

Rehab clinicians are uniquely poised to handle these cases. During an initial consultation, a discussion should involve patient beliefs about the issue and previous narratives supplied. Although this recent article by Oliveria *et al* focuses on people dealing with persistent hip pain, their line of questioning to explore patient's beliefs is applicable in this context:

1. Explain previous diagnoses given for symptoms and what do the labels mean to the individual (identity beliefs)
2. What does the person think are the causes of their symptoms (cause belief)
3. What consequences the person perceives the symptoms have (consequence beliefs)
4. How long the person expected symptoms to last (timeline beliefs)
5. How much control the person believed they had over their symptoms
6. Actions the person took to address their symptoms
7. How effective the person perceived these actions to be and what they believed it would take to get control over their symptoms (control beliefs)

During this discussion various beliefs such as those regarding imaging findings and/or avoidance of movements can be addressed in the context of the individual's case while setting appropriate expectations and exploring management options.

Therapeutic exercises can then be implemented as needed that are specific to the patient's goals to help return them to previous level of activity. Symptoms will likely improve with time and we simply need to guide the process back to desired activities while setting appropriate expectations and instilling behaviors to cope with any potential future symptoms.

With that said, many patients may be concerned about mechanical symptoms such as "locking". Sihvonen has a study from 2016, Mechanical symptoms as an indication for knee arthroscopy in patients with degenerative meniscus tear: a prospective cohort study. 900 patients recruited, underwent arthroscopy, and followed-up with 1 year later.

The authors found 47% (243 out of 513 cases reporting mechanical symptoms) of participants reported persistent symptoms 12 months post-operatively. Additionally, the sample reporting no mechanical symptoms pre-operatively (282 participants), 11% (32) reported mechanical symptoms at 12-month follow-up. The authors' findings continue to question the attempted validation for meniscal surgery based on mechanical symptoms, often attributed to bucket-handle tears.

Arthroscopic knee surgery for patients dealing with degenerative knee disease remains the most common orthopedic surgical procedure in many countries despite evidence failing to support this approach. There are several common narratives that continue to permeate the field to substantiate the intervention for degenerative knee disease as it relates to the meniscus.

Sihvonen et al explains these narratives in his article, Arthroscopic partial meniscectomy versus placebo surgery for a degenerative meniscus tear: a 2-year follow-up of the randomised controlled trial:

1. Failed conservative management
2. Mechanical Symptoms
3. Unstable tears

The authors compared arthroscopic partial meniscectomy

(APM) versus placebo surgery in participants with mechanical symptoms and those presenting with unastable meniscus tears. The authors found,

".....no statistically significant difference between the APM and placebo surgery for symptomatic patients with a degenerative meniscus tear and no osteoarthritis (OA) in any of the used outcome measures over the course of 24-month follow-up. No evidence could be found to support the prevailing ideas that patients with presence of mechanical symptoms or certain meniscus tear characteristics or those who failed initial conservative treatment are more likely to benefit from APM." Sihvonen 2018

Their findings continue to question the validity of performing meniscal surgery based on mechanical symptoms. At this point, it appears the evidence is almost insurmountable regarding the appropriate plan of care for chronic degenerative meniscal tears.

This raises the question: what about traumatic tears? This is a difficult question to answer, because what designates a trauma? Sihovnen excluded patients who reported acute traumatic injuries in this latest study, but explains how convoluted this line of thinking is and current evidence still isn't supportive:

"Obviously, the concepts 'degenerative' or 'traumatic' in the context of meniscal injuries are very vague by nature. In this trial, all patients with sudden injuries related to their own voluntary muscle activities (such as kneeling, bending or kicking) and patients with a minor twisting of the knee were included. In essence, our criteria for labelling a tear as 'traumatic' required a more substantial event, such as falling from a chair, stairs or bicycle, or slipping on ice." Sihvonen 2018

Many argue there may exist a subgroup of patients who would benefit from surgical intervention for meniscus changes. Perhaps there are specific case context variables we should using to classify a cohort as necessitating surgical intervention. However, that doesn't appear to be the case at this time.

Pihl *et al* published Wild goose chase – no predictable patient subgroups benefit from meniscal surgery: patient-reported outcomes of 641 patients 1 year after surgery. According to the authors, their primary aim was, *"...identify those who might improve after APM [Arthroscopic Partial Meniscectomy], we combined the most logical prognostic factors to develop and validate a prognostic model to predict patients' change in their self-reported outcome 1 year following arthroscopic meniscal surgery."* Pihl 2020

The authors developed their prognostic model from the Knee Arthroscopy Cohort Southern Denmark (KACS), *"...a prospective cohort following patients undergoing knee arthroscopy for a meniscal tear."* Pihl 2020 For this cohort, the KOOS (Knee Injury and Osteoarthritis Outcome Score) was the primary outcome measure of interest and was completed online by patients within 2 weeks pre-surgical intervention and at the 12 week and 52 week marks post-surgical intervention. Specifically, the authors were interested in the mean score change of the KOOS4 from pre-surgical reporting to 52 weeks post-surgical reporting. The KOOS4 aggregates mean scores from the following KOOS subscales: pain, symptoms, Sport/Recreation, and Quality of Life (QOL); the Activities of Daily Living (ADL) subscale is excluded. The authors state ADL subscale is excluded because it is *"...known to display ceiling effects in younger and more active populations."* Pihl 2020 In addition to the KOOS4 the authors included 18 other factors, tracked within the KACS cohort, for their prognostic model, some examples are included in the table on the next page.

Overall, the authors included 641 patients (600 with meniscal resection, 33 with repairs, and 8 with a combination of both surgical interventions). 12% of outcome data was missing at 52 week follow-up (76 patients). Prognostically speaking - the overall finding from their models, *"Our results do not support the existence of specific subgroups of patients with certain preoperative characteristics having larger improvements in patient-reported outcomes after meniscal surgery."* Pihl 2020

A potential limitation to the authors' models is the discrepancy in age groups in their included patient cohort: 150 patients were under the age of 40, whereas 491 patients were over the age of 41. This should diminish our confidence a bit, and the authors even state - *"...younger patients more often have a traumatic meniscal tear (eg, sports-related trauma) in an otherwise normal joint making symptoms more likely to originate from the meniscal tear or be a consequence of loss of*

of meniscus function. This might explain the better apparent predictive performance observed for the models that included only patients aged 40 or younger. However, due to the small sample size, these models were severely overfitted and should be regarded as exploratory, needing to be confirmed." Pihl 2020

The main takeaway is that variables often measured at baseline pre-surgical intervention on the meniscus were poor predictors for patient-reported outcomes post-surgery; these even included those mentioned above such as mechanical symptoms, onset (gradual onset -> traumatic), or knee catching/locking. The authors close by saying,

"Despite considering a large number of clinically relevant factors collected preoperatively, change in patient-reported outcome 1 year following meniscal surgery was not possible to predict. Our results do not support the existence of subgroups with certain characteristics having a particularly favourable outcome after meniscal surgery." Pihl 2020

Van de Graaf *et al* take findings from Chambers et al a step further in their article,

	All (n=641)	40 years or younger (n=150)	41 years or older (n=491)
Variables			
Meniscal tear characteristics			
Duration of symptoms, n(%)			
0 - 3 months	129 (20)	41 (27)	88 (18)
4 - 6 months	181 (28)	24 (16)	157 (32)
7 - 12 months	135 (21)	31 (21)	104 (21)
13 - 24 months	94 (15)	20 (13)	74 (15)
More than 24 months	102 (16)	34 (23)	68 (14)
Symptom onset, n (%)			
Slowly evolved	208 (32)	29 (19)	179 (36)
Semi traumatic	260 (41)	51 (34)	209 (43)
Traumatic	173 (27)	70 (47)	103 (21)
Knee-related symptoms			
Knee catching/locking, n (%)			
Never	301 (47)	61 (41)	240 (49)
Rarely	102 (16)	18 (12)	84 (17)
Sometimes	135 (21)	35 (23)	100 (20)
Often	87 (14)	30 (20)	57 (12)
Always	16 (2)	6 (4)	10 (2)
Able to straighten knee fully, n (%)			
Always	349 (54)	68 (45)	281 (57)
Often	133 (21)	41 (27)	92 (19)
Sometimes	70 (11)	18 (12)	52 (11)
Rarely	32 (5)	7 (5)	25 (5)
Never	57 (9)	16 (11)	41 (8)
Difficulty twisting/pivoting knee, n (%)			
None	13 (2)	6 (4)	7 (1)
Mild	48 (7)	15 (10)	33 (7)
Moderate	89 (14)	25 (17)	64 (13)
Severe	228 (36)	51 (34)	177 (36)
Extreme	263 (41)	53 (35)	210 (43)
Knee instability, n (%)			
Not unstable	107 (17)	22 (15)	85 (17)
Unstable, but not affecting activities	64 (10)	14 (9)	50 (10)
Unstable, slightly affecting activities	125 (19)	30 (20)	95 (19)
Unstable, moderately affecting activities	127 (20)	22 (15)	105 (22)
Unstable, highly affecting activities	199 (31)	57 (38)	142 (29)
Unstable, preventing all activities	19 (3)	5 (3)	14 (3)

Can even experienced orthopaedic surgeons predict who will benefit from surgery when patients present with degenerative meniscal tears? A survey of 194 orthopaedic surgeons who made 3880 predictions. The authors surveyed orthopedic residents and surgeons in the Netherlands and Australia to assess:

- Ability to predict outcomes in patients treated for meniscal tears
- Identify differences between surgeons with vs without expertise in treating patients with knee pain
- Assess differences in predictions between responders vs nonresponders to treatment
- Identify patient characteristics leading surgeons to recommend APM vs non-surgical treatment. Graaf 2019

20 patient profiles were presented to participating orthopedists for review. These patient profiles were representative of participants in the ESCAPE randomized controlled trial comparing physical therapy vs APM, conducted by van der Graaf et al. Each profile included: demographics, symptoms, knee function, pain score, physical examination results, type of meniscus tear verified on MRI, and osteoarthritis level. According to the authors', *"These selected patient profiles represented the top five and bottom five participants from the ESCAPE Trial with complete baseline data from each treatment group..."* Graaf 2019

The orthopedists were asked to designate which treatment, exercise or APM, for each profile. They were then asked to estimate their expected effect of treatment on knee function (5-point Likert scale ranging from strong deterioration to strong improvement) 2 years later for their preferred treatment as well as their non-preferred treatment. The participants were also asked about years of experience, field of expertise, and opinion about the quality of the research literature. Finally, the orthopedists were given a list of patient characteristics and asked how the variables influence their treatment recommendations (exercise therapy or APM), if at all.

It has likely become obvious by now, but the primary outcome was the percentage of correct predictions for treatment outcome. The authors find overall, predictions are no better than coin flip - "*Overall, 50.0% (95% CI 39.6% to 60.4%) of all predictions were correct. This percentage was similar between experienced knee surgeons and the other surgeons, 50.4% (95% CI 48.6% to 52.2%) vs 49.5% (95% CI 48.0% to 51.1%), respectively (p=0.58).*" Graaf 2019

Unsurprisingly, patient characteristics tipping the scales towards preferring APM included:

- bucket handle tears (94% of surgeons)
- knee locking (82%)
- "*Failed*" non-operative treatment (82%),
- traumatic etiology (76%), and
- age <45 years (74%)

However, interestingly, exercise was preferred for patient characteristics including:

- moderate to severe osteoarthritis (96%)
- degenerative etiology (92%)
- lack of obstructive complaints (88%)
- age >45 years (87%), and
- obesity (79%) Graaf 2019

We've already discussed many of the characteristics being viewed as warranting APM and the lack of evidential support for these narratives. The authors end the piece with a final call to action: *"We respectfully recommend that orthopaedic surgeons should rely more on the objective evidence from the literature when choosing treatment options."* Graaf 2019

This is typically where we can argue regarding unique considerations for young adults (18 - 40 years of age), pediatric patients (aged less than 18 years old), and athletes with a timeframe for their return to sport. Unfortunately, there still isn't sufficient evidence to make informed decisions about these populations and the necessity of surgical vs conservative management.

Ferrari *et al* completed a systematic review on meniscal repair in children and adolescents, examining treatment approaches, healing, and outcomes. The authors state:

"In conclusion, meniscal tears in patients 18 years old or younger are not uncommon, and they can be associated with a long period between the onset of symptoms and surgical treatment. Repairs of this injury produced good to

Table 3. Knee Outcome Scores of the Included Pediatric Meniscal Repair Studies

Lead Author	Tegner Before/After	Lysholm Before/After	SF-36 Before/After	IKDC Before/After	Return to Activity
Lucas	3.9/7.1	55.8/85.4	NR/NR	NR/NR	NR
Mintzer	NR/NR	NR/90	NR/70	22 Level 1 4 Level 2	24/26 patients returned 2 had lower level of activity unrelated to symptoms
Kraus	7.8/7.2	NR/95	NR/NR	NR/NR	NR
Vanderhave	NR/8	NR/NR	NR/NR	27 Level 1 13 Level 2	NR
Accadbled	6.8/6.6	65.3/96.3	NR/NR	9 Level A 3 Level B	10/12 patients returned 2 did not return to previous level
Krych	NR/8	NR/NR	NR/NR	65.1/89.4	NR
Schmitt	7.6/7.3	NR/95.7	NR/NR	NR/90.7	11/19 patients returned 2 improved, 6 deteriorated
Krych	1.5/6.2	NR/NR	NR/NR	48/90.3	NR

Tegner (range, 0-10); Lysholm (range, 0-100); SF-36, 36-Item Short Form Health Survey (range, 0-100); IKDC, International Knee Documentation Committee (range, 0-100; level 1, participating in strenuous activities that include jumping, pivoting, and hard cutting; level 2, participating in moderate activities such as heavy manual work and sports such as skiing and tennis; level A, normal; level B, nearly normal); NR, not reported.

excellent outcomes in most patients, regardless of the injury pattern, zone, or technique. Reported complications are minimal, increasing the potential application of this surgical treatment modality. ***Higher quality studies are needed to confirm the findings of this systematic review.***" Ferrari 2019

This review was completed on 8 case series studies and NO randomized controlled trials. We already have good evidence that in other populations meniscal surgery is no better than sham or placebo surgery, which is why we need RCTs to make informed decisions. The authors stated that reported complications were minimal, but yet 44 participants out of 287 total participants went on to have meniscectomy after an initial meniscal repair.

Oddly, Liechti *et al* also did a systematic review on the pediatric population with the same exact 8 case series studies. When re-reading the data from this systematic review three additional factors worth mentioning became apparent:

1. Although Ferrari et al is quoted above with 44 cases of meniscectomies after repair, Liechti et al reports - *"A total of 52 failures in 301 total menisci were reported (17.3% failure rate) at a mean time of 16.6 months after initial surgery. Of these, 41 patients underwent partial meniscectomy at the time of revision surgery whereas 9 patients underwent re-repair."* Liechti 2019 Re-examining Ferrari et al's table 2 the following post-repair interventions were identified:
   - 43 partial meniscectomies
   - 7 re-repairs
   - 1 meniscal debridement
2. The outcome assessments are not well reported across studies, which makes it difficult to make bold claims in the conclusion such as -
   - Liechti *et al* - *"The available data suggest that arthroscopic repair of a meniscal tear in the pediatric population is an effective treatment option that has a low failure rate, provides good clinical outcomes, and preserves meniscal tissue."* Liechti 2019
   - Ferrari *et al* - *"In conclusion, meniscal tears in patients 18 years old or younger are not uncommon, and they can be associated with a long period between the onset of symptoms and surgical treatment. Repairs of this injury produced good to excellent outcomes in most patients, regardless of the injury pattern, zone, or technique."* Ferrari 2019

Examining the outcome data (table 3 above) gives a bit of a different story, mainly not well tracked or reported, from Liechti et al: The Tegner was developed to be administered in conjunction with the Lysholm specifically in ACL tear populations, but has also been used in meniscus tear situations. Collins 2011 Some of the studies show Tegner not changing, not reported, or improvement - a mixed bag. Lysholm is mostly not reported, not reported at baseline, or does show improvement pre-post operation. SF-36 wasn't reported at all. IKDC is reported in the majority of studies as an overall score, Level 1, Level 2, A, or B format. Finally we see return to activity,

with some not even tracking this information. I find the above listed conclusions a bit disproportionate in confidence comparatively to what Table 3 above shows. Again, without well conducted randomized controlled trials, it's difficult to know if the results we do see from these reviews are due to the surgical intervention itself, can't be achieved with other interventional like education, time, and activity modification, or are merely masking natural history and regression to the mean.

Lastly and importantly - many of these meniscus tears co-occurred with ACL tears, from Liechti et al, *"This review of a total of 301 meniscal tears (134 medial, 127 lateral, 32 both medial and lateral, 8 location unspecified) demonstrated **172 concomitant anterior cruciate ligament (ACL) tears and 1 ACL-deficient knee** in the included studies" [emphasis ours]* This should lead us to further question these reviews' findings and their external validity to situations solely presenting with meniscal tears.

Thorlund recently released this study, Risk factors, diagnosis and non-surgical treatment for meniscal tears: evidence and recommendations: a statement paper commissioned by the Danish Society of Sports Physical Therapy (DSSF). The authors state:

"No randomised trials comparing non-surgical treatments with surgery in patients younger than 40 years of age or patients with traumatic meniscal tears were identified." Thorlund 2018

This is a major problem. Currently, it would seem we allow youth surgical intervention on meniscus for unsupported narratives. However, it looks like we will have some evidence very soon. Thorlund *et al* states at the end of the article:

"Given the lack of evidence there is a need for high-quality randomised trials comparing surgical and non-surgical treatments of meniscal tears in younger patients and patients with a traumatic tear. Two such studies, one Dutch and one Danish, are currently underway." Thorlund 2018

Recently Skou and Thorlund released a feasibility study titled, *A 12-week supervised exercise therapy program for young adults with a meniscal tear: Program development and feasibility study.* The authors examined the feasibility of exercise therapy in young adults aged 18 - 40 years of age.

- 6 patients were recruited with MRI confirmed meniscal alteration and deemed eligible for surgical intervention by orthopedist
- Exclusion occurred if history of prior knee injury in same knee, clinical suspicion of displaced bucket-handle tear with MRI confirmation, or complete rupture of one or more knee ligaments

Exercise intervention was a 12-week group based program with supervision. Participants had 2 exercise sessions per week that lasted approximately 60 - 90 minutes. Sessions included the following:

- 5 minute warm-up on stationary bike
- 2 exercises used within first weeks with primary focus to reduce swelling and increase ROM
- 8 neuro-muscular exercises for lower extremities
- 4 strengthening exercises for lower extremities

The full protocol can be reviewed HERE. On one hand, I certainly think we can question the utility of some of these exercises and how individualized our prescriptions need to be, on the other hand I think this perhaps is a good path to reframe from the idea that meniscus tear in this population must mean surgical correction.

The authors did find overall improvement in patient's symptoms and function as demonstrated by subjective reporting and the KOOS (see next page for table 2), and no patient elected for surgery after the 12 week exercise therapy.

There are obvious limitations here, small sample size, lack of control, and only males were included. However, as a feasibility study, this is a step towards achieving better quality studies to further reveal if exercise therapy should be the mainstay for this cohort over the often traditional surgical intervention.

Without prospective studies and randomized control trials, we can't speak confidently on a potential natural history and regression to the mean for symptoms being attributed to

Table 2. Improvements in outcomes from baseline to 3 months (n=6)

Variable	Baseline	3 months	Improvements	P-value
Catching or locking of knee, n (%)				0.63
Never	3 (50)	5 (83)		
Once a month	2 (33)	1 (17)		
Once a week	0 (0)	0 (0)		
Several times/week	1 (17)	0 (0)		
Daily	0 (0)	0 (0)		
KOOS, median (mean; range)				
Pain	68.1 (69.9; 61.1 to 88.9)	86.1 (87.0; 80.6 to 94.4)	15.3 (17.1; 0.0 to 33.3)	0.06
Symptoms	66.1 (67.9; 50 to 92.9)	83.9 (83.3; 64.3 to 100.0)	10.7 (15.5; - 10.7 to 50.0)	0.60
ADL	76.5 (77.0; 63.2 to 89.7)	95.6 (95.3; 88.2 to 100.0)	16.2 (18.4; 2.9 to 36.8)	0.03
Sport/Rec	52.5 (52.6; 45.0 to 60.0)	77.5 (79.2; 60.0 to 95.0)	22.5 (26.7; 10.0 to 45.0)	0.03
QOL	43.8 (46.9; 43.8 to 56.3)	56.3 (58.3; 50.0 to 75.0)	9.4 (11.5; - 6.3 to 31.3)	0.22

meniscal changes. Chambers *et al* examined the available evidence on natural history in the pediatric population and states several limitations of current available data:

"It is quite difficult to parse the natural history of meniscus tears from the current literature. There are patients who have meniscal injuries which are unrecognized, there are patients who have meniscal injuries with malalignment issues which may predispose to mechanical problems such as arthritis and most of the patients who have a symptomatic meniscus tear have surgical treatment of their injuries." Chambers 2019

One major issue is our eagerness to peer beneath the surface with MRIs in search of something to structurally fix, which may drive up perceived incidence rates of meniscal alterations despite also having evidence of asymptomatic presentations. For youth athletes, we are left with an even more pressing question of whether intervention on the meniscus via repair or partial or full meniscectomy actually alters natural history. Based on Chambers *et al*'s conclusions, it appears to be a complex matter with a ¯_(ツ)_/¯ for now:

"It will be very difficult, in a setting where there are physicians who are adept at diagnosing meniscus tears, have access to advanced imaging and have the means to treat meniscus tears that any natural history study will ever be performed. Perhaps a study could be performed in an underserved area of the world, with capture of all of the variables contributing to long-term problems, but none has been performed at this time." Chambers 2019

In other words, just because we can find and correct a structural change, we don't know that we've actually had any meaningful effects beyond placebo-like contextual effects, natural history, and regression to the mean. It is unlikely our biomedical paradigm for approaching these symptoms will be greatly altered any time soon. For now, based on the current totality of evidence, our best bet is conservative management via education and goal directed activity for knee symptoms being attributed to meniscal issues, regardless of population. Perhaps future evidence will emerge identifying subsets of populations warranting meniscal surgery, but as of now the evidence doesn't appear supportive.

The premise that surgery is warranted requires identifying specific indications for surgery from a biological perspective, which is difficult given the current research suggesting the problems with identifying clear biological symptom "drivers" (see references in introduction). When and how much does "biology" matter? We are not entirely sure, and don't have enough evidence to make informed decisions regarding the topic outside of extreme traumatic situations. Given what we've seen thus far with long-term outcomes after ACL reconstruction – our skepticism for the idea that that surgery MUST be done is high.

References:

1. Culvenor AG, Øiestad BE, Hart HF, Stefanik JJ, Guermazi A, Crossley KM. Prevalence of knee osteoarthritis features on magnetic resonance imaging in asymptomatic uninjured adults: a systematic review and meta-analysis. British journal of sports medicine. 2018;
2. Beals CT, Magnussen RA, Graham WC, Flanigan DC. The Prevalence of Meniscal Pathology in Asymptomatic Athletes. Sports medicine (Auckland, N.Z.). 2016; 46(10):1517-24.
3. Pappas GP, Vogelsong MA, Staroswiecki E, Gold GE, Safran MR. Magnetic Resonance Imaging of Asymptomatic Knees in Collegiate Basketball Players: The Effect of One Season of Play. Clinical journal of sport medicine : official journal of the Canadian Academy of Sport Medicine. 2016; 26(6):483-489.
4. van der Heijden RA, de Kanter JL, Bierma-Zeinstra SM, et al. Structural Abnormalities on Magnetic Resonance Imaging in Patients With Patellofemoral Pain: A Cross-sectional Case-Control Study. The American journal of sports medicine. 2016; 44(9):2339-46.
5. Guermazi A, Niu J, Hayashi D, et al. Prevalence of abnormalities in knees detected by MRI in adults without knee osteoarthritis: population based observational study (Framingham Osteoarthritis Study) BMJ. 2012; 345(aug29 1):e5339-e5339.
6. Horga LM, Hirschmann AC, Henckel J, et al. Prevalence of abnormal findings in 230 knees of asymptomatic adults using 3.0 T MRI Skeletal Radiol. 2020.
7. Logerstedt DS, Snyder-Mackler L, Ritter RC, Axe MJ, Godges J. Knee Pain and Mobility Impairments: Meniscal and Articular Cartilage Lesions J Orthop Sports Phys Ther. 2010; 40(6):A1-597.
8. Mordecai SC. Treatment of meniscal tears: An evidence based approach WJO. 2014; 5(3):233-.
9. Sihvonen R, Englund M, Turkiewicz A, Järvinen T. Mechanical symptoms as an indication for knee arthroscopy in patients with degenerative meniscus tear: a prospective cohort study Osteoarthritis and Cartilage. 2016; 24(8):1367-1375.
10. Siemieniuk RAC, Harris IA, Agoritsas T, et al. Arthroscopic surgery for degenerative knee arthritis and meniscal tears: a clinical practice guideline Br J Sports Med. 2018; 52(5):313-313.
11. Brignardello-Petersen R, Guyatt GH, Buchbinder R, et al. Knee arthroscopy versus conservative management in patients with degenerative knee disease: a systematic review BMJ Open. 2017; 7(5):e016114-.
12. Bollen S. An Open Letter to the Editor of The BMJ Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2018; 34(1):8-11.
13. Sihvonen R, Paavola M, Malmivaara A, et al. Arthroscopic partial meniscectomy versus placebo surgery for a degenerative meniscus tear: a 2-year follow-up of the randomised controlled trial. Annals of the rheumatic diseases. 2018; 77(2):188-195.
14. Ferrari M, Murphy C, Gomes J. Meniscus Repair in Children and Adolescents: A Systematic Review of Treatment Approaches, Meniscal Healing, and Outcomes J Knee Surg. 2018;
15. Thorlund JB, Juhl CB, Ingelsrud LH, Skou ST. Risk factors, diagnosis and non-surgical treatment for meniscal tears: evidence and recommendations: a statement paper commissioned by the Danish Society of Sports Physical Therapy (DSSF) Br J Sports Med. 2018; 52(9):557-565.
16. van Yperen DT, Reijman M, van Es EM, Bierma-Zeinstra SM, Meuffels DE. Twenty-Year Follow-up Study Comparing Operative Versus Nonoperative Treatment of Anterior Cruciate Ligament Ruptures in High-Level Athletes Am J Sports Med. 2018; 46(5):1129-1136.
17. I R de Oliveira B, Smith AJ, O'Sullivan PPB, et al. 'My hip is damaged': a qualitative investigation of people seeking care for persistent hip pain Br J Sports Med. 2020.

18. Pihl K, Ensor J, Peat G, et al. Wild goose chase – no predictable patient subgroups benefit from meniscal surgery: patient-reported outcomes of 641 patients 1 year after surgery Br J Sports Med. 2020; 54(1):13-22.
19. Chambers HG, Chambers RC. The Natural History of Meniscus Tears Journal of Pediatric Orthopaedics. 2019; 39:S53-S55.
20. van de Graaf VA, Bloembergen CH, Willigenburg NW, et al. Can even experienced orthopaedic surgeons predict who will benefit from surgery when patients present with degenerative meniscal tears? A survey of 194 orthopaedic surgeons who made 3880 predictions. British journal of sports medicine. 2019.
21. van de Graaf VA, Noorduyn JCA, Willigenburg NW, et al. Effect of Early Surgery vs Physical Therapy on Knee Function Among Patients With Nonobstructive Meniscal Tears JAMA. 2018; 320(13):1328-.
22. Liechti DJ, Constantinescu DS, Ridley TJ, Chahla J, Mitchell JJ, Vap AR. Meniscal Repair in Pediatric Populations: A Systematic Review of Outcomes. Orthopaedic journal of sports medicine. 2019; 7(5):2325967119843355.
23. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Ou Arthritis Care Res. 2011; 63(S11):S208-S228.
24. Abram SGF, Hopewell S, Monk AP, Bayliss LE, Beard DJ, Price AJ. Arthroscopic partial meniscectomy for meniscal tears of the knee: a systematic review and meta-analysis. British journal of sports medicine. 2019.
25. Abram SGF, Judge A, Beard DJ, Carr AJ, Price AJ. Long-term rates of knee arthroplasty in a cohort of 834 393 patients with a history of arthroscopic partial meniscectomy. The bone & joint journal. 2019; 101-B(9):1071-1080.

STRETCHY TAPE IS NOT HELPING ATHLETES, NO MATTER WHAT COLOR.

BY: DR. DEREK MILES

Article Reviewed: Does the patients' expectations on kinesiotape affect the outcomes of patients with a rotator cuff tear? A randomized controlled clinical trial by Analay et al. 2018.

Key Points:

1. Research on kinesiotape has dramatically increased over the prior decade but this was mostly predicated on public exposure to the product after the 2008 Olympics.
2. Kinesiotape does not have supporting evidence for utility in the literature but, it has been shown to influence outcomes when individuals believe it is going to work.
3. While contextual factors such as beliefs can influence outcomes, it creates an issue when those factors go against the clinical utility of a modality.

Introduction:

It seems with recent Summer Olympiads, a new product or intervention hits the market that athletes tout as the *game changer* that will give them a competitive edge or help them train through an injury. With the coming summer Olympics in Tokyo, no doubt a new *best* will hit the market that clinicians will spend ample time debunking.

There are often athlete profile pieces that delve into their training regimens and recovery protocols that quote medical and rehabilitation professionals touting a new technique that is bleeding edge. The issue with this being, the lay public is often unaware these techniques almost always lack any scientific basis for their utilization. The 2008 Olympics was one of the first instances of this when volleyball player Kerry Walsh-Jennings was seen donning bright pink and blue tape. This event seems as much related to the fact that kinesiotape donated 50,000 rolls of tape to 58 countries as any perceived efficacy of the tape. The same article linked above reports that prior to this donation the kinesiotape website was generating 600 views/day, but as of the 2012 publication of that piece, they were averaging 345,000 views daily.

For a donation supposed to help athletes, the return on monetary investment for the company was substantial. According to a Marketwatch Report, as of 2019 the kinesiotape market is $180 million a year, expected to grow to $310 million a year by 2024. While this may sound like a good financial investment, the product itself does not come with sound evidence supporting its use. Kinesiotape, compared to many passive modalities, has been extensively researched, with the vast majority generated in the last 12 years. A Pubmed search for "kinesiotape" yielded 775 total papers, but as it is obvious from figure 1, the 2008 Olympics certainly sparked an interest in the intervention.

When the search is narrowed to higher levels of evidence such as systematic reviews and meta-analyses, the degree to which kinesiotape's effectiveness quickly diminishes further. A 2012 meta-analysis by Williams et al for "treatment and prevention" of sports injuries found *"there was little quality evidence to support the use of KT over other types of tape in the management and prevention of sports injuries."* Williams 2012 A systematic review from the same year on kinesiotape's role in the treatment of musculoskeletal injuries found "insufficient" evidence to support its use. Mostafavifar 2012 There is an interesting point made by the authors that I will explore as it relates to the current review. They state, "a perceived benefit cannot be discounted." If this perceived benefit detracts away from interventions that possess evidential backing and instill a belief in a patient that something "works" when it is more the belief that it works, this creates obstacles to best care.

As it relates to specific conditions, a 2019 meta-analysis for kinesiotape in the treatment of chronic non-specific low back pain found *"no evidence to support the use of KT tape in clinical practice for patients with non-specific low back pain."* Luz Junior 2019 A 2020 meta-analysis by Ghozy et al also found no utility for kinesiotape in the treatment of shoulder pain and disability, concluding *"there is insufficient evidence to support the use of kinesiotape in clinical practice as a treatment for shoulder pain."* Ghozy 2020

At this point, it would seem reasonable to conclude that kinesiotape should not be a part of clinical practice, yet clinicians and patients believe that it works so it persists. A demonstration is best seen in a response to the 2014 systematic review by Parreira Pdo et al which is aptly titled

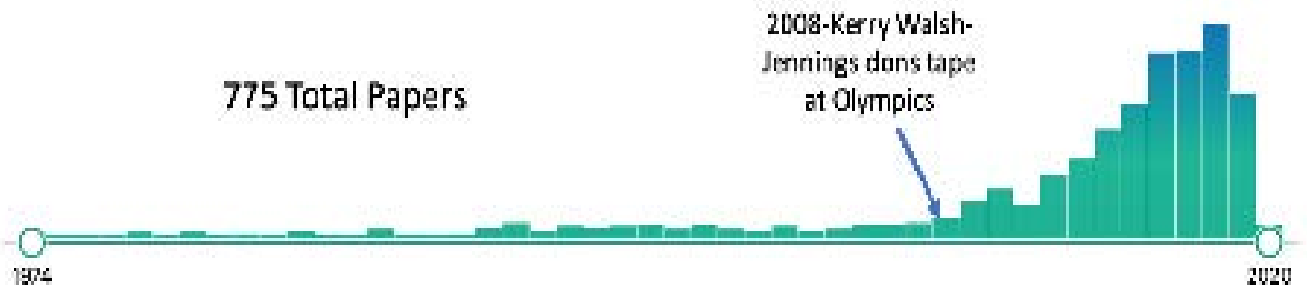


Figure 1: Number of publications per year regarding kinesiotape in peer reviewed literature.

"Current evidence does not support the use of kinesiotaping in clinical practice: a systematic review." Parreira Pdo 2014 The response to the paper included one penned by Ester de Ru in which she commends the authors for their thorough methods, then states the conclusions are flawed as they failed to consider *"the more than 10 taping possibilities."* de Ru 2014 This is a common trope used across interventions to defend a pet technique. It has led to the dichotomy between "adjustment" and "manipulation," which are the same, "dry needling" and "acupuncture," which are the same, and the various concoctions of orthobiologics which lack evidence but have regenerative medicine practitioners lamenting that even though evidence is lacking, their recipe works. de Ru sums these findings nicely at the end of her piece (emphasis mine):

"Currently, numerous professionals persist in using this tape because of the perceived positive effect in the daily clinic. On the other hand, researchers are telling us that it doesn't work. We must be missing something."

The overall body of evidence does not support the use of kinesiotape at this time, there is a widespread perception among both clinicians and patients that the tape "works." This month's review of the paper by Analay et al sought to look at that perception and analyze what happens when patients are informed that a treatment does not work, versus when they are told that it does. If kinesiotape does possess an effect for some clinicians, it is quite possible that this effect is more related to what they believe that the tape is supposed to help with, versus what actually happens.

Methods:

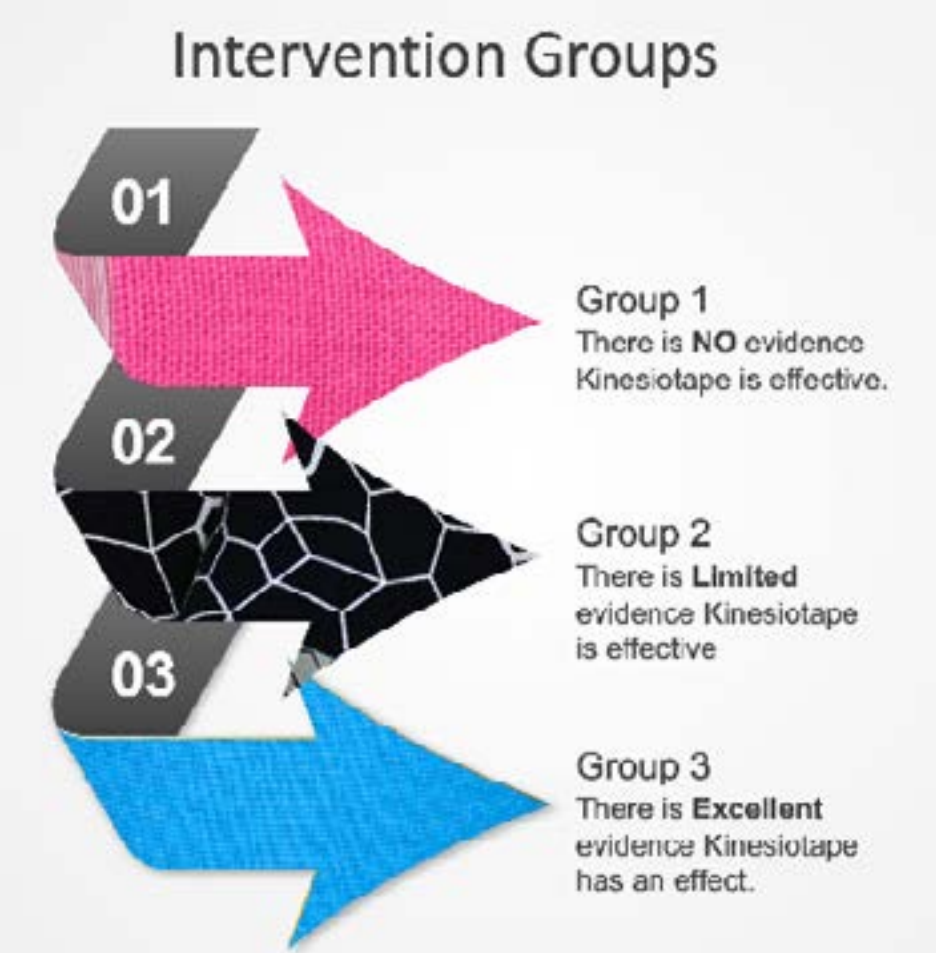
This is a prospective, double-blind, randomized controlled trial. The study was conducted from January 2016 to January 2017 with 110 participants recruited. The ***inclusion criteria*** for the study was if they had a partial rotator cuff diagnosed by an orthopedic surgeon, magnetic resonance imaging (MRI) evidence of a rotator cuff tear, symptoms for at least three months, no radiographic signs of the glenoid, greater or lesser tuberosity, absence of shoulder instability, an insufficient response to non-operative management (corticosteroid injections, non-steroidal anti-inflammatories (NSAIDs), rest, and physical therapy), a positive Hawkins-Kennedy test, and a positive empty can test.

Subjects needed to be between 18-50 years old and have difficulty performing activities of daily living (ADLs). ***Exclusion criteria*** included presence of inflammatory joint disease, rheumatological conditions, osteoarthritis of the humerus, prior history of shoulder surgery, or an inability to complete questionnaires.

Patients were randomized into one of three groups using a "research randomizer" program. The aim was to have 33 participants in each group using sequentially numbered index cards assigning group, sealed by an investigator with no other role in the study. Next the physiotherapist delivering the intervention opened the cards and divided the groups according to intervention. The interventions were then applied by the same physiotherapist. The outcomes assessment was then performed by a different physiotherapist, unaware of group assignment, 30 minutes and 24 hours after the intervention.

The primary outcome measure was pain intensity, assessed via visual analog scale (VAS). Secondary outcome measures were pain at rest, pain during activities of daily living, and pain at night all assessed via individual VAS. Carlsson 1983 Their pain-free range of motion for active and passive shoulder forward flexion, abduction, and scapular plane internal and external rotation range of motion were then assessed using a goniometer. Clarkson 1989 Function was assessed using the disability of the arm, shoulder, and hand questionnaire and the American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form. Hudak 1996 Celik 2013 Michener 2002

Rest and activity were assessed prior to kinesiotaping (time point 1) and 30 minutes after (time point 2). The night pain, range of motion, and patient reported outcome measures, were assessed at time points one and



two as well as 24 hours after taping (time point 3).

Interventions:

The main intervention for this study was not the taping, but rather the instructions given while taping. The subjects all received the same standardized kinesiotape application from a "certified" practitioner who was blinded to group assignment. The taping method used was suggested by Kenso Kase, the original founder of kinesiotape, for rotator cuff pathology. [Kase 2003] Standard, 5cm tape was used for all applications. The intervention groups can be seen in figure 2.

Subjects who were taking NSAIDs or analgesic medication were instructed not to do so for the 24 hours of the study.

Data Analysis

The authors performed a power analysis assuming a clinically important improvement in symptoms of 20 mm on a 0-to-100mm scale with a standard deviation of 25 mm. At a 95% confidence interval and 80% power, they would need 26 individuals per group or 78 total. The authors then factored in a 25% drop out rate as is typical to raise the number of participants needed to ninety-nine.

Baseline demographics were compared using analysis of variance (ANOVA) of continuous data and the chi-squared test of independence for categorical data to assess adequacy of randomization. The effects of treatment on visual analog scale were determined using a 3-by-3 mixed-model repeated measures ANOVA with treatment groups as the between-subject factor and time as the within-subject factor. Range of motion and patient reported outcome measures were analyzed using a 3-by-2 mixed-model repeated measure ANOVA with treatment groups as the between subjects and time as the within-subject factor. Intention-to-treat analysis was performed with missing

data. Before and 24hrs after kinesiotape, values within the group were compared using paired-sample t-test in dependent groups.

The results before and after kinesiotape were also directly compared with reported minimum clinically important differences (MCIDs) in the literature. Established MCIDs for outcomes are as follows:

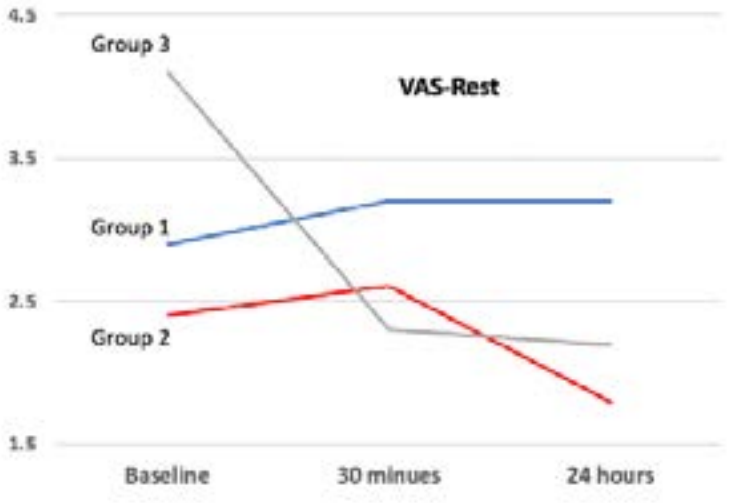
- VAS 20 mm
- Disability of the Arm, Shoulder, and Hand Questionnaire 10.2
- American Shoulder and Elbow Surgeons Standardized Shoulder Assessment 6.4

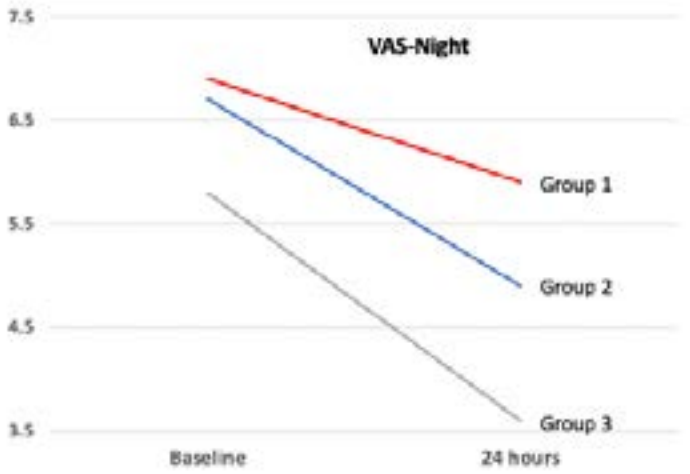
The authors determined effect sizes from the differences in the means of the baseline and follow-up data divided by the standard deviation at the baseline with effect sizes of 0.2, 0.5, and 0.8 considered small, medium, and large, respectively.

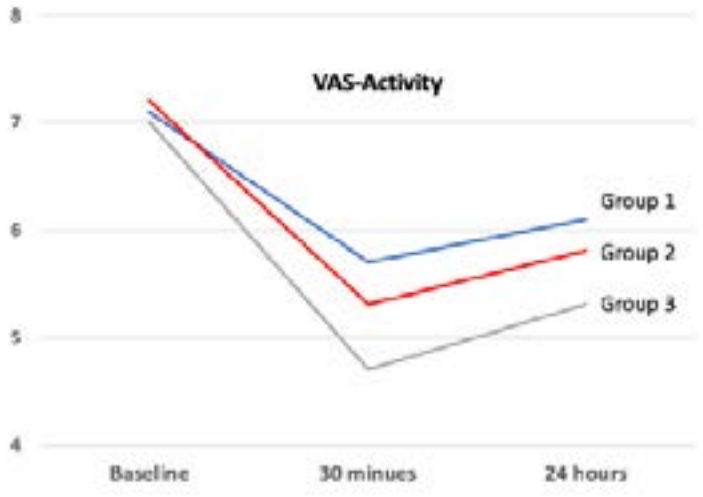
Results:

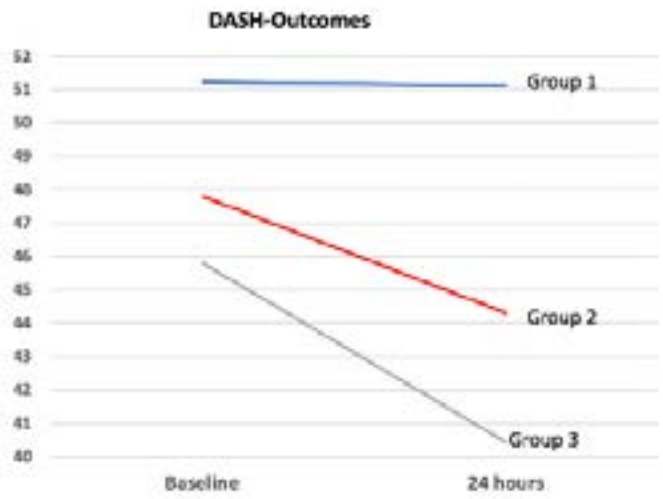
The authors were able to recruit 99 patients (mean +/- SD age 50.92+/-10.28 years with 36% male) according to their inclusion criteria. The mean duration of symptoms was 11.77 +/- 18.5 months. There were no differences in baseline demographic traits between groups. The group-by-time interaction for the 3-by-3 mixed-model repeated measure ANOVA was not statistically significant between the three groups in VAS. There was no significant difference between the three groups in VAS, patient reported outcome measures, or range of motion at baseline. For intra-group measures, group 2 had an improvement in the VAS-rest after 30 minutes (p=0.02). Group 3 demonstrated an improvement after 30 minutes (p=0.01) and after one day in VAS (p=0.01).

For range of motion measures, flexion increased in only in group 3 after 24 hours (0.02). Patient reported outcome measures were improved in both groups 2 and 3 after 24 hours. Small, but clinically important differences were found for VAS activity and night only in group 3.









Why This Study Matters

The Design

There are multiple layers as to why this study matters. First, I want to go through the methods of this study, regardless of what they were studying, and discuss what these authors did *right*. Figure 1 demonstrates a massive uptick in the amount of research on the subject over the last decade. The issue is that most of that research is low-level case studies that do not add anything to the evidence for the utility of the intervention. There are a number of case reports on the intervention, from treatment of Achilles tendinopathy in a badminton player who had previously received ultrasound, TENS, and stopping sport to the effects of kinesiotape on acute non-specific low back pain in a 60 year old individual.[Lee 2012] [Lee 2017] I do not say this to discount the role of case studies entirely, but in the first instance, the individual was provided treatments shown to be ineffective in the management of tendinopathy and the second was an instance of acute injury. With any acute injury, there is a high probability of regression to the mean occurring where natural history will resolve the issue without any additional intervention.

The current study is a double-blind, randomized control trial which presents numerous advantages when determining the efficacy of a treatment. The double-blind nature of the design means that both the participant, and the assessor are unaware of the nature of the intervention. If an assessor knows which group and individual is in, it can influence outcomes like goniometric measurement. We all contain biases as to the varying efficacy of treatments. If the assessor's bias is that a treatment works, that may affect the measurement they take when assessing joint angle. Blinding the assessor to the intervention is a way with which to mitigate that bias. The standard error of measure for most goniometer measurements is approximately 5 degrees and it would be easy to obtain a little more range with no nefarious intentions whatsoever.

The randomized controlled trial also possesses benefits when studying the efficacy of an intervention. Randomization assists in eliminating the risk of bias for individuals assigning to a group in which they would *perceive* benefit more. This may not have played as much of a role in the current study as the intervention was the dialogue associated with kinesiotape.

Where the authors really succeeded in conducting an excellent study was in their preset power analysis. Many studies are *underpowered* meaning there are not sufficient subjects from which to run the statistical analysis they hope to achieve. Prior to conducting the study, the authors set what they considered clinically meaningful results; VAS changes of 20mm, PROM outcome measures at MCID then set α and β accordingly. A full explanation of this is beyond the scope of this review but this is an *extremely* important step to conducting a well founded study. The α value is the probability of rejecting the null hypothesis when the null hypothesis is true, or the probability of finding a result when there is not one. This happens often, for various reasons, but among them is having too few participants in your cohort with which to adequately detect if a difference exists. Beta, on the other hand, is the probability that you will dismiss a "true" result when the data comes back negative. These two

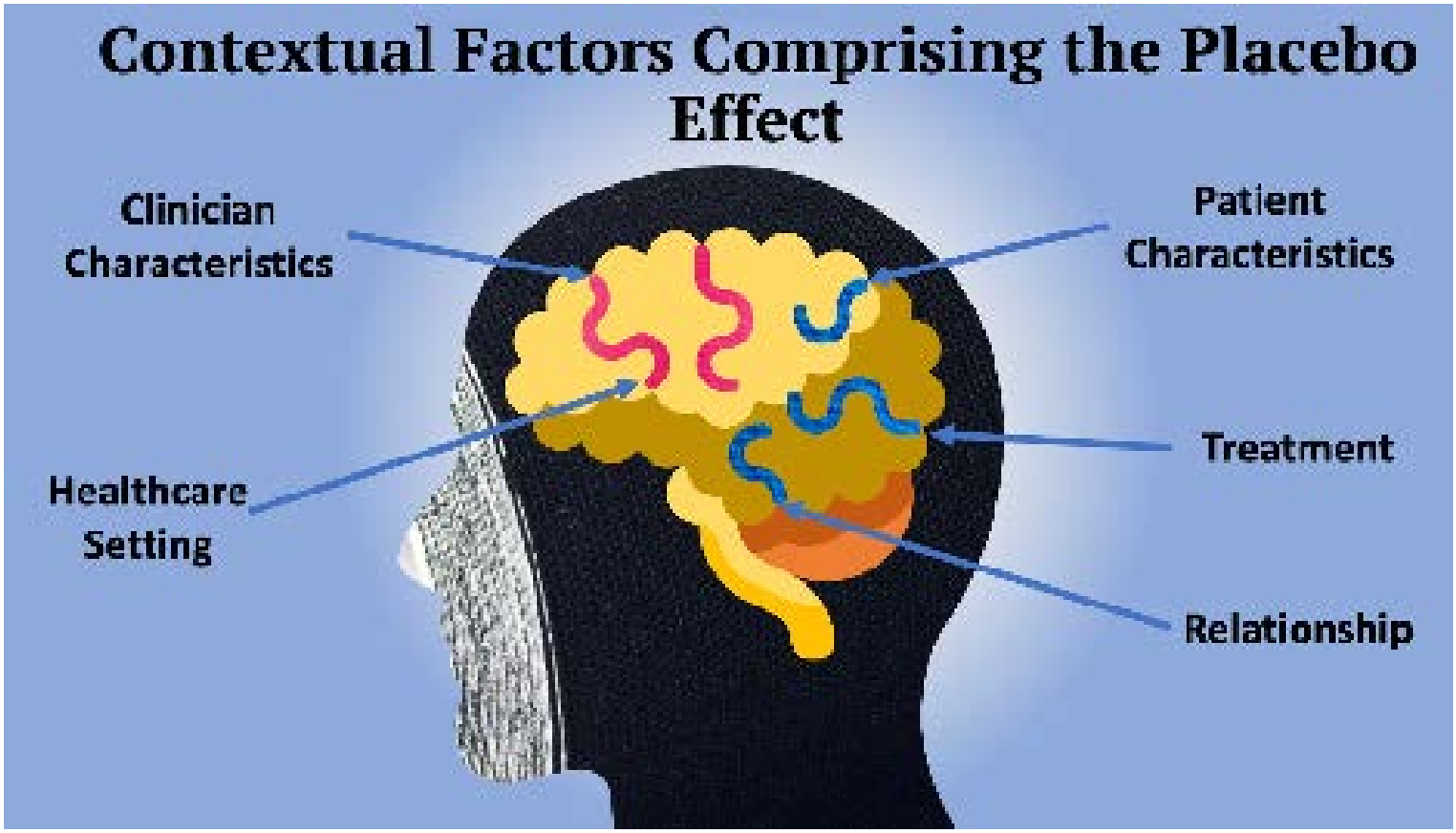


Figure 3- Contributing factors to enhancing a placebo effect as contextual factors.

factors allow authors to calculate, prior to running an experiment the proper number of subjects in order to best determine if an effect exists. This is how the authors of this study came to decide that each cohort needed 26 subjects but they then took this a step further, accounting for the normal drop out rate and adjusted their cohort. Kudos to the authors for a well designed set up.

In lay terms an experiment can be thought of where a coin is flipped to determine heads or tails. The probability of this with a normal coin is 50% so the expectation would be that there would be an equal number of heads and tails flipped. However, if the experiment was set up to only contain 4 flips, there will be instances where the results would conclude that "coin lands on heads every flip." The same could be said for 6 flips, etc....it is only with a large sample size, that the true probability of the flip will be seen. The same can be said for experiments such as this where if only 8 subjects were in each group, there is a chance that one group possesses a higher distribution of people who respond more to a treatment. This can skew results and give the false impression that there is an effect, when none exists.

The Premise

The main purpose of this study was to determine the effect of setting expectations verbally on the effectiveness of kinesiotape in individuals with a rotator cuff tear. Many treatments are often compared to *placebo* as a means of determining their efficacy in randomized controlled trials however, this may miss an important component of what constitutes a placebo. By definition, a placebo has "no therapeutic effect" which is somewhat paradoxical as we often discuss the placebo and nocebo *effects*. The paradox led to the study of *contextual factors* as they related to influencing treatment effects. Rossettini has presented a framework for the influence these factors play in determining either an enhanced or muted placebo effect as displayed in figure 3. Rossettini 2018

The current study played on clinician characteristics and the treatment in how kinesiotape was framed to the participant. There was no baseline data as to how much patient characteristics would play a role as a question of "how much do you believe kinesiotape will help your symptoms," would discern. What is seen is that all groups, even the group told explicitly kinesiotape is not effective, experienced an immediate decrease in symptoms on at least *some* variables. The effect has been seen across other modalities as well with Linde *et al* demonstrating a larger association to treatment effect on the *belief* that acupuncture works, versus the method of acupuncture used ("true" vs. sham). Linde 2007 Analysis of manual therapy techniques has also shown a relationship between patient expectations and achieving positive results. Bishop 2011

If expectations are a primary driver of outcomes, and patient characteristics heavily influence those expectations, it does raise two important questions; 1) where do those patient expectations come from and 2) if they exist upon arrival to clinic, is it the responsibility of the clinician to acquiesce to those expectations if they are aware of the evidence regarding kinesiotape lacking efficacy. The answer to question 1 is rather obvious if any time is spent on social media or watching sports. We live in a society predicated on "quick fixes" and with high exposure to celebrities and athletes. It is intentional that kinesiotape often comes in brightly colored strips. It is *meant* to garner attention. When accounting for the fact that kinesiotape donated 50,000 rolls of brightly colored tape it becomes rather obvious where patients would obtain the idea the tape works. Fifty-thousand rolls likely pales in comparison to an athlete with over a million follows being seen running up and down the court with the tape on his shoulder.

If a patient arrives at the clinic having seen these athletes donning tape, or after searching Instagram for quick fixes, what should a clinician do? I would argue that the clinician should fall back to one of the cornerstones of any treatment plan, education. First, there should be a discussion as to why the athlete *perceives* the tape to work. Working through those beliefs is one of the best ways with which to *change* those beliefs. A large issue with the tape in general is the unfounded claims associated with it's application. If athletes believe they need the tape to "activate" muscles or "inhibit" pain, that is problematic. Those beliefs need to be examined, but not attacked. Belief change takes time and both clinicians and patients are predisposed to overestimating the benefit of treatments. Hoffman 2017 Hoffman 2015

Clinicians and coaches should also be aware that kinesiotape settled a class action lawsuit due to the inflation of their claims. Rocktape is currently facing similar litigation for its claims. As a result, the vernacular on many of the kinesiology tape websites has dramatically changed. Rocktape even goes so far as to admit that a purpose for their "brightly colored tape" is "bringing more customers to your door." This is not having an athlete's best interests in mind, it is a borderline multilevel marketing scheme meant to fool athletes into thinking something is happening. The piece linked above also cites the Kalron *et al* as stating *"moderate evidence was found supporting an immediate reduction in pain while wearing the KT,"* which is does.Kalron 2013 The same study then goes on to conclude *"there is no firm evidence-based conclusion of the effectiveness of this application on the majority of movement disorders within a wide range of pathologic disabilities."* This would seem to call into question how much that moderate effect matters. A letter to the editor was also penned by Saltychev *et al* in which they conducted a meta-analysis on the data aggregated by Kalron. They found substantial heterogeneity in the data for the immediate effects of the tape and moderate heterogeneity for delayed but *also* found the results of taping to be insignificant. Saltychev 2013

The premise of the current study was that the application of kinesiotape does not matter so much as *how* the application is sold to the patient. While de Ru, in her letter to the editor, layed out numerous possible methods for kinesiotape to work from "biotensegrity" to "fascial lines" and "muscle trains" literally ***none*** of that has the smallest shred of evidential backing. Biotensegrity is a bullshit term concocted by Steven Levin, MD based upon the architectural principles of Buckminster Fuller. Somehow Levin conflates the principles of a static structure with those of a dynamic system such as human movement. But, this raises an important point as it relates to contextual factors, the more complex something sounds, the more value is typically assigned to it. This is seen with exercise prescription discussing working in the sagittal plane for anti-rotation strengthening of the lateral fascial line or some other overly complex explanation. All of that verbiage to say

"we're going to perform an exercise where you twist."

With each successive methodology disproven, the mythology of kinesiotape lives on like a hydra sprouting two new narratives for every one shot down. While "inhibition" and "activation" have been all but discarded, now there are stories of "fascial gliding." In each instance, it is just a fancier way of saying "this is why I think this works." These types of narratives do have an effect on the outcome, but it comes at the expense of athletes now believing their fascia is stuck, or some arbitrary line needs intervened upon. Prior to a reader citing the systematic review by Wilke *et al*, the methodological quality of that "study" is horrendous at best. [Wilke 2016] It is the peer reviewed equivalent of laying in your backyard, looking up in the sky, and agreeing that Callisto kinda looks like a bear, if you tilt your head to the right, and squint your eyes, and attended the right continuing education course prior to looking at the sky.

The Findings

There was a clear trend towards improved results for Group 3 across all domains that was not seen in the other two groups. Pain, metrics of range of motion, and patient reported outcomes scores all improved from hearing that a treatment is effective. One of the common tropes used to justify the use of passive modalities is that they "show short term pain relief." This study would add credence to it not being a specific modality, but rather what is conveyed in terms of effectiveness of the modality. In instances such as this, should we not just skip the modality and convey to the athlete that they are going to be okay. How often is tape, cupping, dry needling, IASTM or other modalities applied under the premise of "you do not need this?" Instead, the modalities tend to be conveyed as a *means* to get better where the actual path is based upon staying moving within the constraints of the injury, and staying calm through the process.

To be explicitly clear, there is ***no good evidence*** for the use of kinesiotape in either the rehabilitation of sport injuries, or to increase performance. The *thought* that kinesiotape is effective (or any modality for that matter) plays a larger role than any presupposed polysyllabic narrative attached, stuck if you will, to the intervention. Passive interventions in general are typically given under the premise of speeding up healing, but this has never been supported. With high reinjury rates for many common maladies seen in sport, it is likely better to be honest with athletes that healing does take time, and to use *valid* objective measures to determine readiness for return to sport.

In the instance of Olympic athletes donning tape, like they are sure to do in the upcoming 2020 games, it is ridiculous to think that years of hard work would need to be held together by a piece of stretchy tape. These athletes have spent countless hours training, recovering, embodying their sport and with that will come aches and pains. Healthcare practitioners do not need to apply a piece of tape in order to give them a competitive edge. Adding a "you did it" sticker to a test after you have aced it does *feel good*, but it was ultimately the hard work put in that achieved the "A" and the sticker is nothing but validation of that work.

To Summarize:

The current study demonstrates that the *belief* associated with a treatment likely plays more of a role than the mechanism of treatment for passive modalities such as kinesiotape. This is likely a contributing factor to the personal stories associated with kinesiotape "working" for athletes and the success attributed to it by practitioners. A paper by Cuijpers and Christea from 2016 gives an overview on ways with which to prove a treatment works, even when it does not according to the evidence. [Cuijpers 2016] The authors lay out steps with which to increase the likelihood of achieving a positive result in research outcomes, but the themes should be too familiar to those touting new interventions.

1. **Have a strong allegiance to your treatment:** This takes advantage of the principle of clinical *equipoise*, where a clinician's belief that an intervention works will sway it towards working. [Cook 2011] If a new intervention is making an impact on social media, there is an endorsement among other clinicians, and a clinician just attended a continuing education course touting the effectiveness, odds are the clinician will *believe* the treatment works, thus increasing the effectiveness. A meta-analysis by Miller *et al* demonstrated that this belief has a strong relationship to effect

sizes in clinical trials. Miller 2008 This is where steps must be taken to be certain that the intervention has an effect, and it is not the imparting of beliefs from the clinician.

2. **Increase expectations in athletes:** As the current study demonstrates, increasing patient expectations increases effectiveness of interventions. The phenomenon is seen across placebo research as well such as the study reviewed earlier this year in BMR on placebo injections for runners. Ross 2015 The issue here emerges that it is not just the treating clinician that influences these expectations. With the rise of social media, many of these expectations are set long before an athlete enters a clinic. Cuijpers also recommends (tongue in cheek) that expectations can be increased by penning books on the intervention, going to conferences and setting up large booths to attract attention, or, perhaps I may suggest giving 50,000 rolls of your brightly colored product to athletes right before one of the most televised sporting events of the year. It now becomes the role of the clinician to shape those expectations to that which evidence supports. It becomes an ethical grey area to provide a treatment we know lacks efficacy under the guise of athlete expectations. The argument of "what is the harm" forgets that there is a monetary cost incurred with needing an intervention as well as the probability of a belief emerging that something needs *fixed* on the athlete.

3. **Use 'weak spots" of randomized controlled trials:** The authors go on to lay out 10 means of increasing the likelihood of positive results. Power calculations have already been addressed, but it is also worth briefly mentioning the phenomenon of p-hacking. Mead 2015 While the cutoff point of $p<0.05$ is arbitrary ($p=0.51$ suddenly becomes insignificant), there are means of hedging towards a *significant* finding by conducting trials with multiple outcomes. If a study contains 20 outcomes measures, the likelihood of one of those measures being *statistically significant* increases then the authors will only report that outcome measure as a positive result. The result is a study where measures of pain and disability scores show no significant effect, but an author can report as an immediate increase in shoulder abduction range of motion could warrant the utility of an intervention. Thelen 2008

The overwhelming evidence at this juncture is kinesiotape lacks utility in the treatment of injuries. Five systematic reviews and meta-analyses conclude that there is little use for kinesiotape in rehabilitation and it is time we admit to ourselves, and our athletes.

Williams (2012): *"there was little quality evidence to support the use of KT over other types of elastic taping in the management or prevention of sports injuries."*

Mostafavifar (2012): *"This systematic review found insufficient evidence to support the use of KT following musculoskeletal injury, although a perceived benefit cannot be discounted."*

Da Luz Junior (2019): *"Very low to moderate quality evidence shows that KT was no better than any other intervention for most the outcomes assessed in patients with chronic nonspecific low back pain. We found no evidence to support the use of KT in clinical practice for patients with chronic nonspecific low back pain."*

Ghozy (2019): *"There is insufficient evidence to support the use of kinesio taping in clinical practice as a treatment for shoulder pain."*

Silva Parreira (2014): *"Overall, Kinesio Taping was no better than sham taping/placebo and active comparison groups. In all comparisons where Kinesio Taping was better than an active or a sham control group, the effect sizes were small and probably not clinically significant or the trials were of low quality."*

References:

1. Analay Akababa Y, Kaya Mutlu E, Altun S, et al. Does the Patients' Expectations on Kinesiotape Affect the Outcomes of Patients With a Rotator Cuff Tear? A Randomized Controlled Clinical Trial. Clin Rehabil, 32 (11), 1509-1519 Nov 2018.
2. Williams, S. Whatman, C, Hume P, et al. Kinesio Taping in Treatment and Prevention of Sports Injuries: A Meta-Analysis of the Evidence for Its Effectiveness. Sports Med, 42 (2), 153-64 2012 Feb 1.

3. Mostafavifar M, Wertz J, Borchers J. A systematic review of the effectiveness of kinesio taping for musculoskeletal injury. Phys Sportsmed. 2012;40(4):33–40. doi:10.3810/psm.2012.11.1986.
4. Luz Júnior MAD, Almeida MO, Santos RS, Civile VT, Costa LOP. Effectiveness of Kinesio Taping in Patients With Chronic Nonspecific Low Back Pain: A Systematic Review With Meta-analysis. Spine (Phila Pa 1976). 2019;44(1):68–78.
5. Ghozy S, Dung NM, Morra ME, et al. Efficacy of kinesio taping in treatment of shoulder pain and disability: a systematic review and meta-analysis of randomised controlled trials [published online ahead of print, 2019 Dec 9]. Physiotherapy. 2019;107:176–188.
6. Parreira Pdo C, Costa Lda C, Hespanhol LC Jr, Lopes AD, Costa LO. Current evidence does not support the use of Kinesio Taping in clinical practice: a systematic review. J Physiother. 2014;60(1):31–39.
7. de Ru E. Review of Kinesio Taping ignored other models and techniques. J Physiother. 2014;60(3):176.
8. Kase K, Wallis J and Kase T. Clinical therapeutic applications of the Kinesio taping method. Albuquerque, NM:Universal Printing & Publishing Inc., 2003.
9. Carlsson AM. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. Pain. 1983;16(1):87–101.
10. Clarkson HM and Gilewich GB. Musculoskeletal assessment:joint range of motion and manual muscle strength. Philadelphia, PA: Williams & Wilkins, 1989.
11. Hudak PL, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG) [published correction appears in Am J Ind Med 1996 Sep;30(3):372]. Am J Ind Med. 1996;29(6):602–608.
12. Celik D, Atalar AC, Demirhan M, Dirican A. Translation, cultural adaptation, validity and reliability of the Turkish ASES questionnaire. Knee Surg Sports Traumatol Arthrosc. 2013;21(9):2184–2189.
13. Michener LA, McClure PW, Sennett BJ. American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form, patient self-report section: reliability, validity, and responsiveness. J Shoulder Elbow Surg. 2002;11(6):587–594.
14. Lee JH, Yoo WG. Treatment of chronic Achilles tendon pain by Kinesio taping in an amateur badminton player. Phys Ther Sport. 2012;13(2):115–119.
15. Lee JH. The short-term effectiveness of balance taping on acute nonspecific low-back pain: A case report. Medicine (Baltimore). 2017;96(51):e9304.
16. Rossettini G, Carlino E, Testa M. Clinical relevance of contextual factors as triggers of placebo and nocebo effects in musculoskeletal pain. BMC Musculoskelet Disord. 2018;19(1):27. Published 2018 Jan 22.
17. Linde K, Witt CM, Streng A, et al. The impact of patient expectations on outcomes in four randomized controlled trials of acupuncture in patients with chronic pain. Pain. 2007;128(3):264–271.
18. Bishop MD, Bialosky JE, Cleland JA. Patient expectations of benefit from common interventions for low back pain and effects on outcome: secondary analysis of a clinical trial of manual therapy interventions. J Man Manip Ther. 2011;19(1):20–25.
19. Hoffmann TC, Del Mar C. Clinicians' Expectations of the Benefits and Harms of Treatments, Screening, and Tests: A Systematic Review. JAMA Intern Med. 2017;177(3):407–419.
20. Hoffmann TC, Del Mar C. Patients' expectations of the benefits and harms of treatments, screening, and tests: a systematic review. JAMA Intern Med. 2015;175(2):274–286.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