Hart HF, Stefanik JJ, Wyndow N, et al. The prevalence of radiographic and MRI-defined patellofemoral osteoarthritis and structural pathology: a systematic review and meta-analysis. *Br J Sports Med* 2017;**51**:1195–1208.

Review submitted by: Nicolas Hoover

Purpose:
to perform a systematic review and meta-analysis with the aim to determine the prevalence of PF OA using radiographs and MRI-defined structural PF damage in a variety of study populations.

Methods:
Six databases were searched electronically with no date restrictions but were limited to English language and full text availability. Articles were eliminated by title and abstract review before full text analysis. Cross-sectional and longitudinal studies reporting the prevalence or frequency of PF OA or PF structural damage were included. Reviews, case reports and unpublished studies, as well as non-human studies were excluded. Two reviewers used The Critical Appraisal tool to rate each article. Inter-rater disagreement was discussed and brought to a third reviewer if needed.

Radiographic studies: osteophytes and joint space narrowing via skyline and/or lateral views were used to define PF OA. Data was pooled into the following populations: (1) community-based (individuals randomly recruited from community), (2) knee pain/ symptomatic (individuals recruited based on knee-related symptoms), (3) radiographic and symptomatic OA (individuals recruited based on symptoms and radiographic OA), (4) healthy individuals (no pain, injury or OA), (5) radiographic or high risk of OA (individuals recruited based on radiographic OA or risk of developing radiographic OA without regard to knee pain/symptoms), (6) occupational-based (individuals recruited based on their occupation/sports) and (7) post-traumatic (individuals with previous knee-related trauma, such as ACL injury or reconstruction or meniscal injury). Disease severity was defined as mild, presence of at least mild radiographic PF OA; and definite, presence of defi- nite radiographic PF OA.

MRI studies: MRI-defined structural damage was used to define PF OA, specifically cartilage defect and Bone Marrow Lesion (BML). Authors used the following terms to define cartilage defect: cartilage abnormalities, cartilage defect, full cartilage thickness loss, cartilage pathology and cartilage lesion; and the following terms were used to define BML: marrow abnormalities, marrow lesion and bone marrow edema. Data was pooled into similar populations as above.

Results:
2681 titles were identified. After removal of duplicates, title and abstract analysis, cross-examination of reference lists, and full text review, 85 studies were included. 15 high quality, 16 moderate and 54 low quality studies were identified.

Prevalence of PF OA based on radiography:
Community based population:
Overall prevalence of isolated PF OA: 7% (4 studies)
combined PF and TF OA: 17% (4 studies)
any PF OA: 38% (9 studies)

Sensitivity analysis based on sex: PF OA in women: 41%, in men: 47%

Knee pain or symptomatic population:
overall prevalence of isolated PF OA: 19% (8 studies)
combined PF and TF OA: 34% (7 studies)
any PF OA: 43% (12 studies)
Sex based prevalence of any PF OA: 46% women, 58% men.

Radiographic and symptomatic knee OA population:
overall prevalence of isolated PF OA: 20% (4 studies)
Combined PF and TF OA: 43% (2 studies)
any PF OA: 57% (13 studies)
sex based prevalence of any PF OA: 36% women, 35% men.

Healthy individuals population:
overall prevalence of any PF OA: 17% (4 studies)
Sex based prevalence (women only): 15% (2 studies)

Radiographic knee OA or at risk of developing OA population:
overall prevalence of any PF OA: 48% (4 studies)
Sex based prevalence (women only): 41% (2 studies)

Occupation based population:
Overall prevalence of any PF OA: 21% (4 studies)
Sex based prevalence: 14% men

Post traumatic population:
Overall prevalence of isolated PF OA: 17% (2 studies)
Overall prevalence of any PF OA in injured knee: 27% (19 studies)
Overall prevalence of any PF OA in uninjured knee: 18% (3 studies)

Prevalence of PF OA based on MRI:
Community based population:
Isolated PF structural damage based on cartilage defect: 20% (1 study)
Combined PF and TF structural damage from cartilage defect: 44% (1 study)
Isolated PF structural damage based on BML: 18% (1 study)
combined PF and TF structural damage from BML: 22% (1 study)
Any PF structural damage from cartilage defect: 44% (3 studies)
Any PF structural damage from BML: 29% (2 studies)

Knee pain or symptomatic population:
Any PF structural damage from cartilage defect: 52%
Any PF structural damage from BML: 32%
Any PF structural damage based on cartilage defect (age >50): 71%

Radiographic knee OA or at risk of developing OA population:
Any PF structural damage from cartilage defect: 51% in women, 43% in men
Any PF structural damage from BML: 29% in women, 23% in men

Healthy individuals population:
Overall any PF structural damage from cartilage defect: 40% (2 studies)

Radiographic and symptomatic knee OA:
combined PF and TF structural damage from cartilage defect and osteophytes: 75% (1 study)

Post traumatic population:
any PF structural damage based on osteophytes in ACL injured or reconstructed: 29% (2 studies)
any PF structural damage based on cartilage defect in ACL ruptured: 36%
isolated PF structural damage based on cartilage defect in 2 year post op partial medial meniscectomy: 19%

General population:
any PF structural damage based on cartilage defect: 49% or 75%
any PF structural damage based on BML: 45%
any PF structural damage based on osteophytes: 56%

Conclusions:
Meta-analysis revealed that the prevalence of any radiographic PF OA in knee pain or symptomatic populations was 43%, in radiographic TF OA or at risk of TF OA populations was 48%, and radiographic and symptomatic knee OA populations was 57%. The prevalence of any MRI-defined PF structural damage in knee pain or symptomatic population based on BML was 32%, and based on cartilage defect was 52%. The authors conclude that PF OA is an importance source of symptoms in knee OA and is strongly associated with disability. They state that this SR reveals that the prevalence of PF OA is highly based on radiographic and MR imaging in community, symptomatic, radiographic knee OA and traumatic knee OA populations. Their review also revealed a higher prevalence of combined PF OA and TF OA than isolated PF OA. They conclude that signs of PF damage are common and should not be ignored in clinical practice and in research, and that, in the future, MRI might become highly relevant in identifying early disease stages where the disease process might be reversible.

Comments:
In summary, this SR reveals the efficacy and potential benefit for utilizing treatment of the PFJ in symptomatic knee pain and knee OA populations. It also identifies some gaps in the current literature regarding biomechanical and functional impairments associated with PF OA. In my personal practice I have had difficulty with consistency of treatment in patients with PF symptoms. I have noticed that some patients respond well to exercise compared to manual therapy and vice-versa. Some patients respond to treatment rather quickly, while others require several weeks of treatment.
The authors discuss that only a few included studies specifically evaluated interventions to address PF OA including exercise, physical therapy, taping and bracing but that they did provide some evidence for their use. They also note that there are no high-quality studies to support the association between PF pain in younger populations and the development of PF OA, which may be an important direction for future research, especially in identifying the disease process earlier and the potential for reversing or slowing its effects. The addition of MRI for identifying early stages of degeneration is an interesting concept that I am currently indifferent about. On one hand, identifying cartilaginous and boney abnormalities earlier will be beneficial in

understanding and treating PF pain with greater efficiency, but, given the current state of healthcare costs, increasing the volume of MRI use could prove expensive, especially given the lack of a clear definition of PF OA using MRI. I believe that developing clear anatomical and biomechanical definitions should be the first step in the advancement of future research regarding PF OA treatment.

De Oliveira IO, de Vasconcelos RA, Pilz B, Teixeira PE, Ferreira EF, Mello W, Grossi DB. Prevalence and reliability of treatment-based classification for subgrouping patients with low back pain. J Man Manip Ther. 2017;25(3):1-7.

Review submitted by: August Winter

Objective: The objective of this study was to identify the prevalence of subgroups for low back pain in an outpatient setting using the Treatment Based Classification (TBC) system. A secondary aim was to investigate the reliability of classification among clinicians trained with the TBC.

Methods: 429 patients with acute, subacute, and chronic LBP were recruited for the study and initially evaluated by one of thirteen PTs, all of who had advanced training with utilizing the TBC system. This training included an average of eight years using the TBC system in addition to continuing education courses with the TBC developers. All patients completed the FABQ, ODI, NPRS, and Roland Morris Disability Questionnaire. The objective exam consisted of standard lumbar AROM, SIJ and hip screening, and a neurological screen. At the end of each exam the patient was taken through the Mechanical Diagnosis and Therapy McKenzie Protocol, starting with 10-40 repetitions of extension. Lumbar AROM was then performed again, and changes in pain behavior were noted. This was repeated in flexion and lateral shifts in standing. For reliability testing, six of the PTs were given 30 written patient cases and asked to classify them based on the TBC system.

Results: As a group, 66% of patients met the criteria for one subgroup while 21% met the criteria for multiple groups. 13% of patients did not meet the criteria for any of the subgroups. Specific exercise made up 27% of the classifications and stabilization constituted 22%. The most common combined group was flexion and stabilization with 7.5% of the total number of patients. The reliability of the assessed patient cases was 66% between therapists, with a kappa value of 0.62 representing substantial inter-rater agreement.

Conclusions: The vast majority of patients can be classified using the TBC system and in clinicians experienced with using this system there is good inter-rater reliability with classification.

Commentary: This study provides a necessary examination of the practical use of the TBC system in an outpatient setting. It shows that most patients (85%) can actually be classified using this system and that overall agreement among therapists on classification is good. One point in the article that was helpful was the authors' suggestion to begin treatment with one classification but realize that this approach might need to change for patients with a more mixed presentation. Reliability was good among therapists for classification but did involve experienced clinicians trained in using the TBC system. While the article does mention one study investigating novice reliability, I would like to see more evidence to show that this approach is feasible for most clinicians. One important part of this study is the heterogeneity of the patients included. While the authors recorded the types of referrals they received, they did not classify patients based on their acuity. As we know, the majority of research and applicability of the TBC is in acute and subacute populations. Recording the acuity more clearly in the study might have shed light on using this approach with a more chronic population. A final point for this article is the interesting prevalence of combined flexion and stabilization based classifications. These two classification definitions seem more opposed in terms of their criteria and the clinical picture of the patient who meets the criteria. Whether fair or not, this seemingly contradictory classification makes me more weary of trying to use this system for more mixed presentations.

Rice H, Patel M. Manipulation of Foot Strike and Footwear, Increases Achilles Tendon Loading During Running. Am J Sports Med. 2017 Aug;45(10):2411-2417

Review Submitted by: Justin Bittner, PT, DPT

Objective: To determine the effects of both foot strike and footwear on Achilles tendon loading in rearfoot strike runners.

Methods: Twenty-two habitual rearfoot strikers that wore nonminimal running shoes participated in the study. Trials were ran in 3 different footwear conditions: standard shoes, minimal shoes, and barefoot. Participants ran 10 trials per footwear for data collection using markers on 10 anatomic landmarks. With each shoe wear condition, participants ran with a forefoot and rearfoot strike pattern. Ankle plantarflexion moments were calculated by use of inverse dynamics. Achilles tendon force was calculated by the dividing the Achilles tendon moment arm by the internal plantar flexor moment. To compare variance among conditions, a 2-way repeated measures analysis was used.

Results: Achilles tendon impulse was greater when participants ran with a forefoot strike pattern rather than a rearfoot strike pattern in minimal shoes. Achilles tendon impulse considers both the magnitude and duration of Achilles tendon loading during stance. This provides an overall indication of total Achilles tendon loading. Peak dorsiflexion angle was noted to be greater when running with a rearfoot strike pattern regardless of footwear. Regardless of footwear, Achilles tendon loading was higher when participants ran with a forefoot strike pattern. Overall, findings indicate that foot strike influences the magnitude of Achilles tendon loading while the footwear influences the rate.

Conclusions: The authors here add that the increased loading of the Achilles tendon with forefoot strike and minimal shoes could contribute to Achilles tendinopathy. They also state that studies should be done using participants whom are habitual forefoot strikers.

Commentary: Although anatomically and biomechanically it makes sense that the Achilles tendon is loaded more in a person running with a forefoot strike pattern in minimal footwear, this study helps to reinforce those ideas. Achilles tendinopathy is reported to be 2.3 times more in people who run barefoot vs. shod runners. This study brought to light what Irene Davis said at AAOMPT 2015. She said one was not superior to the other (forefoot vs. rearfoot striking) and that anyone can be a barefoot runner but they need to train their foot and LE to be. She also mentioned that this is very patient specific and can be different for everyone. This study was specifically looking at the Achilles tendon and the effects of strike pattern and footwear on its loading. For patients wishing to transition to minimalist shoes, we should be sure to recommend a prolonged transition for the patient. This way the Achilles tendon can be progressively loaded to adapt to new forces on it. This may consist of a day or 2 per week in more of a minimalist shoe, while wearing their normal shoe for Education on tendinopathy and referencing this study can be used to help the patient understand the kinematics on the ankle and its effects on Achilles loading.

Bove A, Baker N, Livengood H, King V, Machino J, Popchak A, Fitzgerald G. Task-Specific Training for Adults With Chronic Knee Pain: A Case Series. J Orthop Sports Phys Ther. 2017;47(8)548-556.

Review submitted by: Katie Stokely

Objective: Evidence-based guidelines recommend the use of exercises including strengthening, flexibility, and joint mobility to improve pain and function in people with chronic knee pain. Recent research has shown that impairment-based exercises have limited positive effects on performance of specific tasks such as walking, stair negotiation and transfers. Currently, evidence supporting task specific training is limited to people with neurological disorders and little has been done to examine task specific performance on general function for people with chronic knee pain. Therefore, the purpose of this study was to describe task specific training for people with chronic knee pain who report change in pain and physical function via clinical outcome measures.

Study Design: Case Series, Therapy, Level 5.

Methods: Five females and two males participated in this study. Inclusionary criteria required that patients be over the age of forty, report chronic knee pain, had moderate difficulty with functional tasks based on the Knee Injury and Osteoarthritis Outcomes Score (KOOS), and self-reported diagnosis of knee OA. People were excluded if they receive physical therapy within six months of the beginning of trial treatment, intra-articular knee injections, or history or myocardial infarction or neurological disorder. Physical therapist participating in this study were trained in the novel task specific approach. Participant outcomes measures were assessed at baseline, eight, twelve, and sixteen session. Two pain rating outcomes, one confidence outcome, and three performance outcome-based assessments were utilized. Participants could receive up to sixteen therapy sessions if needed. They were trained on sit to stand transfers, floor transfers, and stair negotiation. Task complexity was modified based on participants' ability and task-limiting impairments were addressed as needed.

Results: The majority of participants demonstrated improvement on the KOOS with regards to pain and activities of daily living (ADL) (sit to stand transfers, floor transfers, and stairs. Participants reported confidence in performance of these tasks improved 19% from baseline to follow-up. Five of the seven patients met the MDIC for change in the 30-second chair raise test. Three saw clinically important improvement on the stair-climb test. Outcomes that showed changes to stair negotiation were less consistent than sit to stand and floor transfers.

Conclusion: Those with chronic knee pain may benefit from task specific training to improve functional ability and decrease pain. Larger and randomized control trials need to be performed to compare task specific training to impairment based treatment.

Commentary: Improvements in the KOOS pain and ADL subscale were noticeably higher than studies that did not focus on task specific training. This study presents an easy to follow guideline on how to progress task specific training for people who struggle with sit to stand transfers, stair negotiation, and floor transfers. It also highlights that impairment based treatment with performance of exercises in isolation may not translate to improved function and reduced disability due to motor planning, cognitive, and perceptual deficits. Finally, the authors make a nice discussion point related to the need to examine central nervous system modulation as it relates to chronic pain and how this may need to be addressed in this population group for optimal outcomes.

Kennedy, Ewan, et al. "Clinical characteristics and outcomes of treatment of the cervical spine in patients with persistent post-concussion symptoms: a retrospective analysis." ***Musculoskeletal science and practice*** **29 (2017): 91-98.**

Reviewed by: Erik Lineberry, DPT

Background: Concussion is typically defined as a mild brain injury, and yet the brain is unlikely to be the only source of persistent post-concussion symptoms. Concurrent injury to the cervical spine in particular is acknowledged as a potential source of common persistent symptoms such as headache, dizziness and neck pain.

Objectives: To describe the cervical spine findings and outcomes of treatment in a series of patients with persistent post-concussion symptoms, and describe the clinical characteristics of a cervicogenic component when it is present.

Design: Retrospective chart review of a consecutive series of patients with concussion referred to a physiotherapist for cervical spine assessment.

Method: Patient charts for all patients over a calendar year referred by a concussion service provider to a physiotherapist for cervical spine assessment were de-identified and transferred to the research team. Clinical data were independently extracted by two research assistants and analyzed using descriptive statistics.

Results: Data were analyzed from 46 patient charts. Those with a cervicogenic component (n= 32) were distinguished from those without a cervicogenic component (n= 14) by physical examination findings, particularly pain on manual segmental examination. Physiotherapy treatment of the cervicogenic component (n= 21) achieved improvements in function (mean increase of 3.8 in the patient-specific functional scale), and pain (mean decrease of 4.6 in the numeric pain-rating scale).

Conclusions: The clinical characteristics described give preliminary support to the idea that the cervical spine may contribute to persistent post-concussion symptoms, and highlight the value of physiotherapy assessment and treatment of the cervical spine following a concussive injury.

Commentary: This retrospective review looked to determine if treatment of the cervical spine could be an effective treatment for patients with post-concussion symptoms. An examination algorithm was used to determine if the patients' symptoms were cervicogenic. The article stated the importance of using both subjective and objective findings to rule in/out cervicogenic component due to the overlap in reported subjective findings with concussion and cervicogenic presentations. 81% of cases with cervicogenic component show mild or end-range cervical AROM restrictions and all cases show restricted segmental motion with reproduced pain. However only 56% showed neck pain. This highlights the importance of screening cervical spine for patients presenting with concussion-like symptoms. The study makes it clear that symptoms may be present due to head injury as well. The goal of the study was to highlight a patient population with persistent post-concussion symptoms that may benefit from cervical intervention. Due to the study design the population was biased with patients already diagnosed with concussion that were referred to PT. The take home point from the article was that we should be screening for cervical dysfunction in these patients and treated as soon as possible to reduce the risk of patients' symptoms becoming worse or persistent.

Table 1
Methods for categorising physical examination and treatment data.

Characteristic	Categories	Notes
Neck AROM	Full range (no restriction), end-range restriction (end-range restriction only), mild restriction (at least one movement limited to 75% of normal), moderate restriction (at least one movement limited to 50% of normal), and severe restriction (at least one movement limited to 25% of normal). Movement restriction was documented as due to pain or stiffness.	Extracted from a diagram of movement
Neck pain during AROM	Yes/No	Based on any note of pain on AROM movement diagram (as opposed to stiffness)
Segmental findings of pain	Yes/No	Any findings of pain in the cervical and thoracic spine were considered a 'segmental finding of pain'
Segmental level(s) of pain	Upper cervical (occiput-C3), lower cervical (C4-C7), thoracic (T1-12), or mixed (a combination of findings in any two categories).	
Segmental sidedness of pain	Unilateral, bilateral	Segmental findings of pain were considered bilateral if affecting both sides of the spine, or documented as central pain.
Tenderness on palpation	Head, neck, thoracic (including the shoulder), and general (affecting more than one region).	
Outcome of assessment	'Received further treatment', 'referred on', 'did not return', or 'no further treatment required'	Patients 'referred on' for cervical spine treatment typically lived out of town, or had an existing preferred provider.
Type of treatment	Manual therapy, acupuncture, stability exercises, or a combination of these.	Based on information from the pilot. Note patients also routinely received education, case management and advice, but for research purposes data extraction was limited to physical treatment.

AROM = Active range of movement.

Characteristics	Cervicogenic component (n = 32)	No cervicogenic component (n = 14)
Mean age (Range, SD)	26.9 (Range 12–62, Standard deviation 11.9)	25.8 (Range 16–59, Standard deviation 12.7)
Male gender	15 (47%)	6 (43%)
Ethnicity	NZ European 29 (91%)	NZ European 10 (71%)
	Other European 3 (9%)	Other European 1 (7%)
	Maori 0	Maori 1 (7%)
	Asian 0	Asian 2 (14%)
Work status	Full time work 10 (31%)	Full time work 2 (14%)
	Part time work 2 (6%)	Part time work 2 (14%)
	Student 17 (53%) *(Polytech 1 (3%), School 7 (22%), University 9 (28%))*	Student 9 (64%) *(Polytech 0, School 2 (14%), University 7 (50%))*
	Retired 1 (3%)	Retired 0
	Unemployed 2 (6%)	Unemployed 1 (7%)
Time since injury	Less than one month 5 (16%)	Less than one month 2 (14%)
	1-3 months 19 (59%)	1-3 months 10 (71%)
	4-6 months 2 (6%)	4-6 months 1 (7%)
	More than six months 3 (9%)	More than six months 1 (7%)
	Unclear 3 (9%)	Unclear 0
Cause of injury	Transport accident 5 (16%)	Transport accident 3 (21%)
	Fall 9 (28%)	Fall 2 (14%)
	Mechanical force 13 (41%) *(Sport related 10 (31%), Non sport related 3 (9%))*	Mechanical force 3 (21%) *(Sport related 3 (21%), Non sport related 0)*
	Assault 5 (16%)	Assault 6 (43%)
Headache symptoms	Yes 31 (97%)	Yes 14 (100%)
Dizziness symptoms	Yes 17 (53%)	Yes 6 (43%)
Subjective neck pain	Yes 18 (56%)	Yes 3 (21%)
Subjective neck stiffness	Yes 12 (38%)	Yes 14 (100%)
Neck AROM	Full range 6 (19%)	Full range 14 (100%)
	End of range restriction 8 (25%)	
	Mild restriction 14 (44%)	
	Moderate restriction 4 (13%)	
	Severe restriction 0	
Neck pain during AROM	Yes 21 (66%)	Yes 0
	No 11 (34%)	No 14 (100%)
Segmental findings of pain	Yes 32 (100%)	Yes 1 (7%)
	No 0	No 13 (93%)
Segmental level(s) of pain	Upper cervical 24 (75%)	Thoracic 1
	Lower cervical 1 (3%)	
	Mixed 7 (22%)	
Segmental sidedness of pain	Bilateral 18 (56%)	Bilateral 1
	Unilateral 14 (44%)	
Tenderness on palpation	Neck 26 (81%)	Head 1 (7%)
	General 6 (19%)	Thoracic 1 (7%)
		Nil 12 (86%)
Outcome of assessment	Received further treatment 21 (66%)	No treatment required 14
	Referred on for neck treatment 8 (25%)	
	No further contact 1 (3%)	
	No treatment required 2 (6%)	

Duchesne E, Dufresne SS, Dumont NA. Impact of Inflammation and Anti-inflammatory Modalities on Skeletal Muscle Healing: From Fundamental Research to the Clinic. Phys Ther. 2017;97(8):807-817.

Pubmed Link: https://www.ncbi.nlm.nih.gov/pubmed/28789470

Review Submitted by: Scott Resetar, PT, DPT

Objective: PT's in the UK and other smaller jurisdictions have recently been given the right to prescribe NSAIDs. In addition, many PT's have contradictory beliefs about use of NSAIDs after musculoskeletal injuries. Some believe you should use NSAIDs over acetaminophen, while a minority believe that you should withhold NSAIDs in the early period of a musculoskeletal injury.

Muscle Regeneration: Because the nuclei of the muscle cells cannot divide anymore, muscle regeneration is ensured by a population of muscle stem cells, named satellite cells. You can also obtain muscle regeneration from hypertrophy, but this process plateaus much sooner than the satellite cell mechanism. Following an injury, satellite cells activate and become myoblasts that proliferate extensively for the first few days

Resolution of the Inflammatory Process: Contrary to the original belief that the dampening of the inflammatory response is a passive process caused by the arrest of proinflammatory factor secretion, recent discoveries showed that resolution of inflammation is an active step that involves complex cellular and molecular interactions. At the cellular level, it was shown that macrophages switch from a pro-inflammatory phenotype (M1 macrophages) to an anti-inflammatory phenotype (M2 macrophages) approximately 2 days after a muscle injury. M1 macrophages phagocytose muscle cell debris and release pro-inflammatory factors that stimulate myoblast proliferation. On the other hand, M2 macrophages release anti-inflammatory molecules and growth factors that stop myoblast proliferation and stimulate their differentiation, fusion, and myofiber growth. A similar switch was also observed at the molecular level during muscle regeneration, where the biosynthesis of proinflammatory lipid mediators is progressively replaced by antiinflammatory and pro-resolving lipid mediators. This programmed class-switching of lipid mediators supports the idea that the resolution of inflammation is predetermined from the beginning of the inflammatory response. Particularly, the enzyme cyclooxygenase (COX)-2 is directly implicated in this lipid mediator class-switching. Both proinflammatory and anti-inflammatory molecules are generated by COX-2 at different stages of the inflammatory process, which is particularly important because COX-2 is the enzyme targeted by NSAIDs. Since physical therapists are frequently treating patients consuming NSAIDs, they should be aware that COX-2 inhibition does not only blunt the proinflammatory response but also inhibit the resolution of inflammation, which has a direct effect on muscle healing.

NSAIDs and Acute Muscle Healing: Inhibition of COX-2 with specific inhibitors or using COX-2-deficient animal models demonstrated that blocking this pathway diminishes proliferation, differentiation and fusion of satellite cells, and results in impaired skeletal muscle growth, delayed skeletal muscle repair and increased fibrosis. In human, administration of NSAIDs failed to improve the efficacy of physical therapist treatment following acute hamstring injury. There is accumulating evidence indicating that the dampening of the inflammatory process during acute injuries leads to impaired muscle growth and regeneration in animals and humans. Notably, anti-inflammatory properties of a treatment are commonly confounded with its analgesic effect. It may be more beneficial to focus on pain reduction via non-anti-inflammatory modalities versus analgesics in the acute stage.

The Chronic Inflammatory Process: The persistence of proinflammatory signals affects the regenerative capacity of satellite cells and consequently impairs skeletal muscle healing leading to inappropriate repair mechanisms, such as muscle fibrosis and fat accumulation. This process is affected by local and systemic factors

A. Systemic Factors: Aging is related to a higher concentration of pro-inflammatory systemic factors (also called "inflammaging"), which impairs the resolution of the inflammatory process and contributes to different diseases. In addition to slowing down the repair process, there is evidence indicating that this chronic low-grade inflammatory state is associated with a reduction in the synthesis and an upregulation in the degradation of contractile proteins in muscle fibers

B. Local Factors: A second injury to an already regenerating muscle can desynchronize the healing process. Successive muscle injuries separated by 4 days led to a prolonged and persistent inflammatory response, while muscle injuries separated by 10 days caused an exaggerated production of the pro-fibrotic factor TGF-beta (transforming growth factor-beta), which led to muscle fibrosis. Altogether, there is growing evidence that local interference of the myogenic process strongly impair muscle healing

The Impact of Anti-inflammatory Drugs on Muscle Healing in Chronic Inflammation: Contrary to what is observed in acute muscle injuries, the use of anti-inflammatory drugs may have potential beneficial effects on some chronic muscle disorders. For instance, the administration of prednisone following repeated lab induced injury, was shown to blunt the chronic inflammatory condition, which diminished the production of TGF-beta and reduced muscle fibrosis. Thus, STEROIDAL anti-inflammatory drug (SAID) administration restored the balance in the inflammatory process and improved muscle regeneration. The positive effects of SAIDs are limited in time and are progressively lost after a few months to years. Part of this time-limited effect might be caused by the fact that while SAIDs are very efficient at downregulating inflammatory activity, their prolonged use can have harmful side effects. For instance, glucocorticoids activate cellular signaling pathways involved in protein degradation, which promotes muscle atrophy. Moreover, SAIDs reduce the proliferation and differentiation of myoblasts . While NSAIDS can have some benefits in local inflammation, they are ineffective in systemic inflammatory conditions.

As a result of this review, the authors propose a concept map for the use of anti-inflammatory modalities in a clinical setting (Fig. 3).

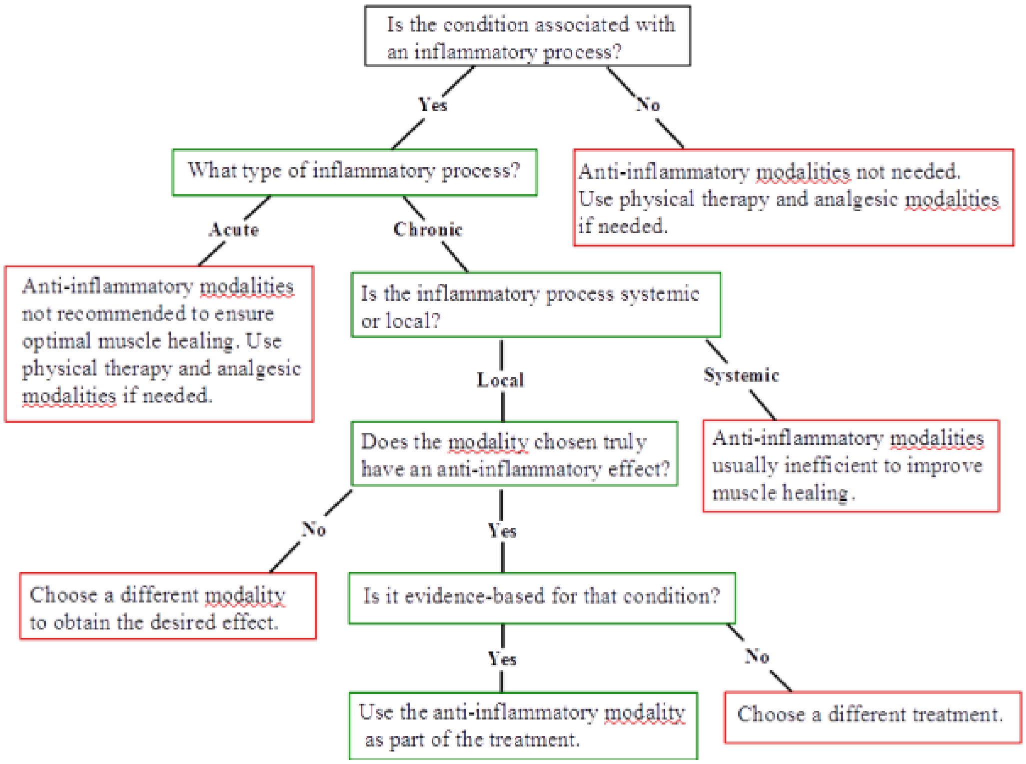

Figure 3. Concept map for the use of anti-inflammatory modalities. This decision-making tree shows the general guidelines for the evidence-based use of anti-inflammatory modalities for the treatment of muscle disorders in a clinical setting.