Recreational Running with Low Disease Activity Rheumatoid Arthritis

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Introduction

Rheumatoid arthritis (RA) is a chronic, autoimmune disease with a prevalence of 0.5-1% in North American and European countries[1,2] and affects females 2-3 times more often than males.[3] It is characterized by symmetrical inflammation and polyarthralgia of large and small joints secondary to disease processes targeting the synovial membrane, articular cartilage and surrounding bone.[3–5] RA commonly presents in joints of the hands and feet, but may also affect the ankle, knee, elbow and shoulder.[1] The exact cause of RA is unknown. However, RA is theorized to be a combination of genetic and environment factors. In RA, there is an activation of the immune system and creation of an autoimmune response which leads to the synovial membrane being infiltrated with immune cells. This leads to a pro-inflammatory response and an eventual growth of the synovial lining called the "pannus." This inflammatory response can lead to osteoclast and chondrocyte activation causing catabolism of surrounding cartilage and subchondral bone.[3,5] Even though the treatment of RA with methotrexate has been around for 50 years, the dosage and development of other disease-modifying antirheumatic drugs (DMARDs) has vastly advanced over the years.[3] This has led to continual updates of the American College of Rheumatology guidelines for treatment and medical management of RA in the last decade.[6,7] With the addition of targeted synthetic and biologic classes of DMARDs, the options for treatment strategies has expanded.[3,5] Early disease recognition has also been of focus in recent years.[5,7] This has successfully led to a reduction of joint damage in 90% of patients living with RA, and has born the treat-to-target approach with the goal of reaching 50% reduction in disease activity by 3 months and low disease activity or remission by 6 months.[3]

Historically, exercise has been viewed as detrimental to joint surfaces and has been avoided for fear of worsening RA symptoms.[8] In fact, complete bed rest used to be considered as a possibility for treatment,[9] and isometric exercises and mobilization exercises were prescribed cautiously.[10] Today, high-intensity exercise in patients living with RA is still questioned by some healthcare provides,[11] even though it has been demonstrated as safe.[12–14] The changing landscape of medical management has most likely improved the ability for those living with RA to exercise, as low disease activity is a possible outcome.[3]

Exercise in those living with RA should be thought of as crucial to the health of the patient. RA can lead to significant deconditioning secondary to increased pain, fatigue and fear of accelerating joint damage or diseases processes. In turn, this leads to decreased quality of life, social engagement, work capacity and functional ability.[4] Fear of exercise and decreased physical activity can lead to further deconditioning [14] and contribute to increased risk of cardiovascular disease (CVD) along with rising healthcare cost.[5,14] Exercise has shown positive outcomes for quality of life[8] without increasing disease activity,[1,12,13,15–19] yet only 13.8% of RA patients meet recommended levels of physical activity.[14] Physical symptoms are commonly blamed as a main barrier, but lack of advice from medical providers and rheumatology healthcare teams are also influential.[14]

Aerobic and resistance based exercises have long shown to be beneficial for improving health outcomes of RA patients.[1,4,12,13,16–19] Unfortunately, exercise is underutilized in treatment. Although there is evidence for safety of exercise in well managed patients, there is still little structured guidance on implementation.[14,20] The European League Against Rheumatism (EULAR) has set basic recommendations for patients living with RA such that safe and feasible physical activity and exercise routines should include components of muscular strength, cardiorespiratory fitness, neuromotor performance and flexibility.[21] Furthermore, the most valuable exercise program for a patient is one of consistency, and for some, running might represent a great option as it combines elements of aerobic fitness, single limb strength and neuromuscular performance demands with repeated efforts.

Running is one of the most common physical activities globally, consistently ranking in the top 3 sport and leisure time activities.[22] Some individuals with RA may have participated in running prior to diagnosis and have interest in returning to it. Others may have interest in beginning a running program. However, there is little evidence to guide clinicians working with adults with RA wanting to resume or introduce running safely. In the absence of evidence, clinicians may look towards other conditions affecting joints, such as anterior cruciate ligament repair,[23,24] hip arthroscopy,[25] or patellofemoral pain,[26] to guide the gradual progression in return to running activities. Adults with osteoarthritis (OA) may present with similar limitations in strength, range of motion, pain and functional abilities as adults with RA, despite different etiologies.[27,28] Therefore, OA running research analyzing effects on joint health[29–33] may theoretically be used to strengthen confidence in providing guidance about running for individuals with RA. Therefore, the purpose of this narrative review is to present an evidence-informed approach to incorporating running for adults with RA. We will (1) synthesize the evidence regarding safety and benefits of exercise in adults with RA, (2) review current evidence related to safety in running in OA populations, and (3) review clinical considerations when guiding running in adults with RA.

Exercise and Rheumatoid Arthritis

Exercise for adults living with RA has proven to be safe,[1,12,13,16,17,34] which has led to the EULAR to encourage the use of exercise and increases in physical activity as a cornerstone of treatment.[21] In general, aerobic exercise has shown to decrease inflammation[14] and lead to improvements in multiple cardiovascular risk factors[21,35] while increasing aerobic capacity.[4] For those diagnosed with RA, these changes are beneficial to combat the increased CVD risk from disease processes.[3,5,14,36] In addition, high-intensity exercise leads to reductions in joint swelling[12] with trends in decreased pain also noted.[16,17,37] As for resistance training, it has shown to reduce prevalence of cachectic states[13] which is a common condition related to RA.[14] Furthermore, while it has shown little effect on reducing running related injuries,[38–40] it has demonstrated improvements in running performance[38,41] which provides reason for its pursuit. Exercise's positive effects on pain, physical function and fatigue are important findings as these are commonly listed as barriers to exercise for those living with RA.[14,20]

Aerobic, resistive or a combination of both types of exercise has shown to be beneficial for those patients diagnosed with RA.[34,12,17] In general, regular performance of an exercise routine does not require alteration to medication regimens[34,12,17] nor does it lead to evidence of worsening disease activity.[1,4,12,13,16–19] Although the mode of exercise, frequency, duration and intensity varies among studies, exercise consistently leads to no significant difference in rates of joint damage,[16] especially when previous joint impairment is limited or non-existent.[42] Increases in exercise or physical activity results in improvements in function,[12,13,16–18,34,42] aerobic capacity,[1,12,18,34] fatigue,[4,43] muscular strength,[12,16,17,37] and quality of life.[17] Nevertheless, there are some circumstances in which exercise safety should be considered.

As stated, the majority of evidence indicates that exercise is safe for those diagnosed with RA.[1,12,13,16,17,34] However, for some individuals, a risk for further joint damage with exercise must be considered. For instance, adults with RA and existing joint damage demonstrated a 4-40% risk for developing further joint damage after 2-years of participation in 75 minute high-intensity exercise sessions twice per week.[42] In joints with limited or no joint damage, those who exercised were not at higher risk for joint damage across most major joints.[42] This highlights the importance of early diagnosis and treatment for those living with RA to prevent joint structure changes before they occur.

In regard to running, since there is a lack of literature in populations living with RA, other conditions can be used as a template. In those with existing OA, recreational running does not lead to worsening OA.[44] However, other conditions may. A history of joint injury, such as anterior cruciate ligament or meniscal tears, may lead to worsening knee lesions or OA.[31,45] Because of this, when considering running for patients diagnosed with RA, the patient's and provider's knowledge of previous joint health, extent of any joint damage and history of joint injuries should be considered when discussing exercise prescriptions and progressions.

Beyond history of joint injuries, items, such as patient age, disease duration, level of disease activity, prior physical capacity and functional ability are not associated with increased risk of joint damage. Therefore, these could be less of a barrier or concern when beginning a running program. Only greater baseline joint damage has been linked with worsening joint surfaces in those with RA.[42] This again highlights the need for early disease detection and medical treatment. In discussing exercise with a patient's healthcare team, the amount of joint change needs to be considered. Even in joints with previous damage, the lower extremity demonstrates a limited increase in relative risk of further joint changes. However, there are exceptions. When exposed to exercise, the subtalar joints demonstrate a 10-fold (95% CI: 1.3, 79) increase in risk ratio as compared to usual care.[42] In the realm of running, joint surfaces in the foot and ankle may be of greater concern for patients and healthcare providers during progression of a running program than those areas of the hip or knee. Thus, there is a need to thoroughly assess a patient's key problem areas. Nonetheless, worsening joint damage should not necessarily scare patients or providers away from running or exercise, as there are vast systemic and functional benefits to exercise.

Aerobic exercise results in reduced inflammation via decreased expression of inflammatory markers, such as tumor necrosis factor alpha and interleukin-1, and it reduces overall inflammation due to upturns in anti-inflammatory cytokines.[14] Further improvements can occur via reductions in adipose tissue leading to decreased overexpression of inflammatory markers.[14] These positive changes may lead to improved lipid profiles, blood pressure and micro- and macrovascular function.[8] Reduced systemic inflammation and improved vascular function can be beneficial for decreasing risk of co-morbidities and severity of disease processes in RA. As mentioned previously, CVD risk is elevated in those living with RA. In considering dose of exercise for cardiovascular improvements, there is greater evidence in populations without RA. In those populations, any amount of exercise leads to a reduction in cardiovascular risk. However, improvements in maximal oxygen uptake, body composition, total cholesterol and triglyceride profile are seen with a minimum of 30 minutes of running at least 3 times per week.[35] This knowledge can be used when building an exercise program for those living with

RA. If disease activity is low, allowing for safe performance of aerobic exercise for cardiovascular improvements would be beneficial.

Beyond cardiovascular benefits, a meta-analysis by Hu et al reported that aerobic exercise positively altered reports of fatigue,[4] and when resistance training is added, improvements in quality of life, pain, aerobic capacity and physical function are seen without increases in disease activity.[1,4] Positive effects are not limited to acute exercise interventions. In a 2-year program examining bi-weekly, high-intensity exercise involving a range of resistance, low impact and high impact activities, Jong et al reported no difference in use of medications, disease activity, or radiological joint damage in comparison to controls. Similar to other studies, exercise groups noted significant improvements in functional abilities and aerobic fitness. By comparison, usual care groups witnessed a decline during the same time period.[34] This again emphasizes the necessity of exercise to improve aerobic capacity and reduce risk of CVD.

Of specific importance to those living with RA is the knowledge that anywhere from 8-67% of patients suffer from cachexia secondary to disease processes.[14] Historically, there has been the view that aerobic exercise is detrimental to muscle hypertrophy. However, evidence in recent years has shown that aerobic exercise can lead to muscle hypertrophy, decreased protein catabolism and improved mitochondrial function in populations which are not living with RA.[46] This would indicate running may be a beneficial tool to improve muscle hypertrophy and decrease cachexia. Aerobic training in healthy adults does not appear to compromise improvements in muscle hypertrophy or strength when performed with resistance training.[47] To combat common rheumatoid cachexia, Lemmey et al demonstrated that a twice per week progressive resistance training routine promoted positive body composition changes in lean and fat mass that led to a dramatic reduction in those listed as cachectic or cachectic-obese versus control groups.[13] Therefore, perhaps resistance training should be considered for patients with RA that are wishing to pursue running for its ability to further promote muscle hypertrophy and benefit long-term well-being.

Osteoarthritis and Running

Running is a popular form of exercise[22] which is associated with dramatic effects on reducing all-cause and cardiovascular mortality ranging from 27-30% and 30-45% respectively.[48,49] Again, this is critical in light of the elevated risk of CVD in those living with RA[1,3,5] and may provide an avenue to reduce risk. While exercise for individuals living with RA is beneficial,[1,4,12,13,16–19] the primary modes of aerobic or high-intensity interventions used in research investigations were not running and consisted of cycling, walking, swimming or resistive weightbearing exercise.[12,16–19,34,37,50] The lack of studies investigating running for adults with RA may reflect a historical belief that high-impact or plyometric exercise would be detrimental to joint health. Yet, anecdotally, we know that some adults with RA run, competitively and recreationally. In this section, we will review the evidence for the safety and efficacy for running in a population with similar concerns for joint health, adults with osteoarthritis (OA).

Running is a safe mode of recreational exercise and does not increase risk of developing knee or hip OA.[31,45] Moreover, running does not compromise the health of joints with existing OA.[44] In fact, running may be beneficial for joint health. When investigating the internal changes to cartilage volume, cartilage thickness and biomarkers to analyze risk of OA development, it has been found that these areas demonstrate mild or no change.[32] In the event of slight alterations in biomarkers, these return to baseline levels within 1-2 hours after running, even when increasing running duration to >30 minutes.[32] Any changes in cartilage structure are usually only seen immediately after exercise. There is no significant evidence of change at 1 day, week or month time points after termination of running. This means that any changes seen within cartilage of the lower extremity are likely related to the normal fluid exchange allowing for interchange of synovial fluid and maintained cartilage health.[33] This healthy exchange of fluid and nutrients could be why recreational runners have lower prevalence of hip and knee OA (3.5% (95% CI: 3.4%, 3.6%)) compared to sedentary non-runners (10.2% (95% CI: 9.9%, 10.6%))[30] and why recreational runners have a deceased likelihood of undergoing knee surgery due to OA.[29]

Exercises that may contribute to OA development or progression include elite level running[29,30] and sports that involve high loads in conjunction with high volumes of cutting, jumping, pivoting, uneven terrain or unexpected perturbations.[31] In elite level running, intensity and volume of running are considerably higher than recreational running,[30] and may result in loads that exceed tissue capacity.[29,30,45] Elite participation is also associated with greater injury risk, which increases risk of OA as discussed earlier.[29] Muscular fatigue and weakness has also been considered as a risk factor for joint injury as worsening proprioceptive responses and protective mechanisms may result in increased risk of injury.[29,30,45] Although there exists predisposing factors that may lead to joint injury,[45] it would appear that running does not in itself cause damage to cartilage or the overall joint.

Determining Running Readiness, Symptom Monitoring and Exercise Prescription

Before you start

For any individual, beginning an exercise program can be an intimidating task. Any comorbidities can complicate the process of determining appropriate initiation periods, ability to progress and symptom management. When treating an individual living with RA, we must meet the patient where they are presently, both physically and mentally. In considering running as a mode of exercise, disease activity, symptoms, the joints primarily effected and current level of fitness should be considered before moving forward. For most exercise programs, low disease activity in individuals with RA should be a prerequisite. If the individual has inflamed joints and high disease activity, lower level treatment methods, such as low intensity cycling, walking, range of motion exercises or swimming[13,16] should be considered to improve fitness and allow time for RA symptoms to decrease. In addition, communication with the patient's rheumatologist should occur in order to determine low disease activity and safety. To assess disease activity clinically, physicians may use measures such as the clinical disease activity index (CDAI) or simplified disease activity index.[3] The simplified disease activity index score itself can be used to document low disease activity or remission. In addition, there are other blood sample measures that may be used to assess disease activity which are not included in the scope of practice of specific clinicians, such as physical therapists.[51,52] Once lower disease activity has been achieved, progression towards lower impact aerobic exercise and resistance training typically seen in RA research may be pursued prior to engaging in running to allow for an adaptation period and improvements in aerobic capacity.[1,4,12,13,16–19] This author would suggest this to build baseline aerobic fitness with the goal of being able to walk for 30 minutes continuously 3 times per week without discomfort before initiating a running program.[24]

Symptom Tracking and Management

While progressing walking volume, assessment of comfort, disease activity and signs of necessary regression should be monitored. Similar strategies can be used throughout a running program, and these monitoring habits should occur while progressing in intensity, duration, volume or other exercise parameters.

In order for healthcare professionals, such as physical therapists, to track disease activity during the addition of exercise, measures recommended by the American College of Rheumatology (ACR) could be used. The Patient Activity Scale-II (PAS-II) and the Routine Assessment of Patient Index Data 3 (RAPID3) are 2 of the 5 measures recommended by the ACR.[53] The PAS-II is a combination of the Health Assessment Questionnaire-II, a 10 cm Visual Analog Scale for pain and the Patient Global Assessment,[54] and the ACR provides a PAS-II form and calculator for disease activity on their website.[55] This makes for easy application and use in clinic. As for the RAPID3, it has shown high correlation with other measures that are commonly used to detect disease activity in patients living with RA.[56] A minimal detectable change has been calculated for the RAPID3 as 1.48 points, or 14%, change.[57] However, some studies have reported that the RAPID3 does not always correlate as well with objective disease activity outcome measures as it does subjective.[58] Therefore, other objective measures, such as a joint count found in the CDAI or measures of effusion, could be used to boost clinician confidence. During follow-up appointments with clinicians, other measures, such as the Foot and Ankle Disability Index for function[59] or the IKDC subject knee form[24] to assess the patients function during introduction of running may be used to analyze success of the program in relation to daily life. As always, if the patient has any concerns throughout the process, they should immediately contact their guiding clinician and/or healthcare team.

A combination of methods used in RA and exercise research and other lower extremity conditions have been formed for symptom monitoring and tracking.**(Table 1)** Measures such as visual analog scale (VAS) pain ratings,[16,17,24,60] changes in joint range of motion[60] and joint effusion[59,60] may be implemented for comfort and safety. Figure-of-8 measurements may be used for ankle swelling,[59] and although girth measurements for knee effusion have been used,[24] they may be less reliable when self-administered by the patient. For self-administered tests, the modified stroke test used in anterior cruciate ligament reconstruction (ACLR)[23] may be a suitable alternative for effusion or the implementation of a full crouch by the patient to subjectively assess new stiffness or decreases in range of motion (ROM). Other measure such as soreness rules used in ACLR[23,61] and pain ratings should be used to determine if the patient is ready for progression both during and after running exercise.[24,25] **(Table 2)**

Preferably, no pain would be present during activity, however, it is likely safe to follow pain ratings used in ACLR and patellofemoral pain research during return to running discussed later.[24,25] If pain ratings and soreness criteria are not met during early stages in building aerobic fitness and walking duration, the patient should monitor symptoms and swelling the following day. If swelling or pain is not noted, the patient may repeat the same workout. If swelling and pain is present, the patient should rest for 1-2 days and regress in the intensity, volume or both.[24]

(Table 1) Symptom Tracking

Sign/Symptom/Reasoning	*Test/Measure*
Suspected increased disease activity	Patient Activity Scale-II (PAS-II)[53]
Suspected increased disease activity	RAPID3[53,56,57]
Pain rating	Visual Analog Scale for pain
Ankle edema	Figure of 8
Knee effusion	Modified Stroke Test (Sweep Test)

Pain/soreness and ability to progress activity	ACLR Soreness Rules
Limb edema	Girth Measurements
Subjective joint swelling/restriction	Full Crouch
Additional Clinical Tests	
Functional limitations in relation to disease activity	McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR)[34]
Self-assessed functional capacity	Health Assessment Questionaire[16,17]
Functional abilities in relation to pain	Self-reported Foot and Ankle Score[62]
Functional limitations in relation to lower extremity symptoms/impairments	Rheumatoid Arthritis Outcome Score (RAOS)[63]
Functional abilities	Foot and Ankle Disability Index
Functional abilities	IKDC Questionnaire

Walk-Run Program Design

For those patients living with RA that are looking to initiate a running program, valuable education can be provided in appropriate program design and progression. The optimal dose for reducing cardiovascular risk is in accordance with the American College of Sport Medicine's recommendation of 75 min of vigorous activity or 150 minutes of moderate level activity per week.[64] Therefore, a running program can be developed to help reach this goal in the future. Since evidence for safe progression of a running program does not currently exist in RA populations, clinicians may look towards other return to running programs status post lower extremity surgeries or injuries that are aimed at gradually increasing exercise intensity and volume while monitoring symptoms to minimize negative outcomes.

Of crucial importance is a gradual introduction of aerobic weightbearing exercise. During early stages of a walking or running program, instructions should be provided to avoid running on inclines or declines and to run on softer surfaces to reduce impact loads.[25] Once pain-free walking can be performed, incorporation of a walk-run progression with the participant performing 5 minutes of walking as a warm-up and cooldown can begin.[24] Intervals of 1 minute of walking followed by 1 minute of running at a self-selected, comfortable pace can be used. A gradual progression of increasing running volume by a combination of longer interval duration and an increasing number of repetitions can be employed to accomplish the long-term goal of 30 minutes of continuous running.[25](**Table 3**)

How to Monitor Symptoms During a Walk-Run Program

Symptom monitoring for safe exercise progression discussed earlier should be used during the progression of the walk-run program.**(Table 1)** Similar to before, preferably, no pain would be present during activity. However, setbacks may occur and pain ratings discussed earlier could be used.**(Table 2)** If pain ratings and soreness criteria are not met, the patient should monitor symptoms and swelling the following day. If swelling or pain is not noted, the patient may repeat the same workout. If swelling and pain is present, the patient should rest for 1-2 days and regress to the previous days workout.[24]

(Table 2) Daily Running Safety assessment		**Action suggestions**
Pain Rating[24,26]	2 out of 10 pain (2/10) or less during running	*If greater, discontinue exercise that day, take 2 days off and regress 1 workout*
Pain Duration[24,26]	Should be absent or returned to baseline within 1 hour after running	*If does not return to baseline, take 2 days off and repeat same workout*

Soreness Rules[23]	Soreness after warm-up that continues	*Take 2 days off and regress one day*
	Soreness during warm-up that goes away	*Repeat same run next workout*
	Soreness during warm-up that goes away but returns during session	*Take 2 days off and regress one day*
	No soreness	*Continue with program*

(Table 2) Example Walk-Run Program		**Total Weekly Running Time**	**Total Weekly Time (includes Day 3)**
Week 1	Day 1: (1 min walking/1 min running) x3-4 Day 2: (1 min walking/1 min running) x3-4 Day 3: Rest day/30 min walking Day 4: (1 min walking/1 min running) x4-5 Day 5: (1 min walking/1 min running) x4-5	14-18minutes	58-66 minutes
Week 2	Day 1: (1 min walking/1 min running) x5 Day 2: (1 min walking/1 min running) x6 Day 3: Rest day/30 min walking Day 4: (1 min walking/2 min running) x3 Day 5: (1 min walking/2 min running) x3-4	23-25 minutes	70-73 minutes
Week 3	Day 1: (1 min walking/2 min running) x3-4 Day 2: (1 min walking/2 min running) x4 Day 3: Rest day/30 min walking Day 4: (1 min walking/2 min running) x4-5 Day 5: (1 min walking/2 min running) x5	32-36 minutes	78-84 minutes
Week 4	Day 1: (1 min walking/3 min running) x3-4 Day 2: (1 min walking/3 min running) x4 Day 3: Rest day/30 min walking Day 4: (1 min walking/3 min running) x4-5 Day 5: (1 min walking/3 min running) x5	48-54 minutes	94-102 minutes
Week 5	Day 1: (1 min walking/4 min running) x4 Day 2: (1 min walking/4 min running) x4-5 Day 3: Rest day/30 min walking Day 4: (1 min walking/4 min running) x5 Day 5: (1 min walking/5 min running) x4	72-76 minutes	119-129 minutes
Week 6	Day 1: (1 min walking/5 min running) x5 Day 2: (1 min walking/6 min running) x4-5 Day 3: Rest day/30 min walking Day 4: (1 min walking/6 min running) x5 Day 5: (1 min walking/7 min running) x4	107-113 minutes	155-162 minutes
Week 7	Day 1: (1 min walking/7 min running) x4 Day 2: (1 min walking/9 min running) x3 Day 3: Rest day/30 min walking Day 4: (1 min walking/9 min running) x3 Day 5: (1 min walking/10 min running) x3	112minutes	155 minutes
Week 8	Day 1: (1 min walking/15 min running) + (1 min walking/10 min running) + (1 min walking/5 min running) Day 2: (1 min walking/20 min running) + (1 min walking/10 min running) Day 3: Rest day/30 min walking Day 4: (25 min running) x1 Day 5: (30 min running) x1	115 minutes	150 minutes
-Begin and end each workout with a 5 minute warm-up and cooldown of walking			

-Workouts/Days are meant to be performed in order. Additional 30 minute walk days may be performed between run days or other days of the week. Minimum of 4 run days should be completed each week to allow for adaptation and progression unless injury or concerns arise.

Biomechanical strategies to manage loading in running

When beginning a running program, determining what alterations a patient may need to make in running technique may be pursued based on clinical presentation and joints affected. For instance, one may alter cadence,[65–70] use 'run softer' cueing,[71–73] change foot strike patterns,[74–79] trunk flexion[80,81] or even footwear[82–85] to decrease forces felt at the joints of the foot, ankle or knee. Although, trunk flexion has been proposed as a treatment method of patellofemoral pain,[80] it results in an increase distance of center of mass to center of pressure on initial contact and increases rates of loading, peak braking forces and impact transients which have been linked with amplified risk of injury.[81] Therefore, this training method is not recommended by this author and will not be covered in this review. As for strength training[38–41,86] and neuromuscular control[87] programs, these have been implemented to decrease running related overuse injuries with varying and limited success. Therefore, the main areas that will be of focus during the remainder of this review will be: impact forces and loading rates, cadence alterations, 'run softer' gait training, foot strike patterns and shoe wear for their feasibility, ease of implementation and evidence of load management.

Impact Forces and Loading Rates

Determining strategies to reduce running related injuries (RRI) is difficult. Many commonly thought prevention strategies, such as strength training or impact load reduction, have not shown to prevent running related injuries.[38–40,88] Other variables, such as cadence, stride length or ground contact time, have not been found to be significantly different between those with or without a history of RRI.[89] What occurs more often is the targeting of biomechanical factors related to running once an injury arises. Impact forces and loading rates are commonly 2 of these variables.

Impact forces during exercise are often proposed as a risk in the development of OA. However, when comparing low impact cycling to higher impact running there have been discrepencies.[90,91] Greater impact peak forces and loading rates are associated with some running related injuries.[92] Interventions to reduce loading rates and impact forces have been targeted to diminish injury severity and frequency when analyzing runners.[71,72] However, others have suggested that these impact related variables may not be the cause of RRI.[88,93] In a systematic review, Ceyssens et al noted inconsistent and moderate level evidence that average or instantaneous loading rate have no significant effect of RRI development. They also found there is strong evidence that vertical impact peaks are not associated with RRI.[88] Similar results have been found in another meta-analysis which reported no significant difference in vertical impact peak when comparing injured versus uninjured runners prospectively. In addition, the authors reported conflicting evidence for influence of vertical impact peak, average loading rates or instantaneous loading rates in the development of RRI.[93] Thus, these variables may not be key as preventative measures. Nonetheless, if a patient begins to present with a RRI or increased joint swelling, impact variables may be targeted as a treatment procedure. The implementation of increased cadence or 'run softer' in the following sections are areas that should be considered.

Running Cadence

Increasing running cadence is an intervention that ought to be attempted first to reduce loading rates and impact forces. It is relatively easy to apply and alters loading rates and impact forces with minimal resources needed.[65–70] Running cadence is defined as a step rate most often written as a steps/minute. For a step, it is the time from when the right foot strikes the ground until the left foot strikes the ground or vice versa. Therefore, we are counting each individual ground strike. For example, if a runner has a cadence of 160 steps/min, this means the left foot made contact with the ground 80 times and the right foot made contact 80 times. Gait retraining to increase cadence by 5-10% can decrease impact peak, vertical average loading rate, vertical instantaneous loading rate,[65,68,94] decrease eccentric knee joint work,[94] peak knee flexion,[69] vertical oscillations and ground contact time.[65] In essence, increasing running cadence reduces peak loads at all joints of the lower extremity during ground contact. Furthermore, increased running cadence may reduce excessive contralateral hip drop or increased hip adduction that may be seen by some as a running impairment.[69,94] This can be accomplished without the need of complicated neuromuscular interventions. In several studies, increased running cadence is associated with improvements in patellofemoral pain[69] and decreased pain reports during running[82] during 4 and 12 week follow-ups respectively.

How to increase cadence

Cadence alterations are frequently accomplished both in and out of clinic. In the clinic, running cadence alterations can be introduced by use of a treadmill. Participants will simply be asked to run at a comfortable and preferred speed for 5 minutes. During this time period, the clinician may either count the number of foot strikes over the course of a minute or match the patients pace to a metronome to determine step rate.[69] After this is determined, the clinician would calculate a step rate that is 7.5-10% greater than the preferred cadence without altering treadmill speed.[67–69,94] For instance, if the patient's original step rate was 155 steps per min and treadmill speed was 6 mph, the goal during retraining would be to increase to ~166-171 steps per minute with the treadmill speed at 6 mph. The clinician may set a metronome for 170 steps per minute and ask the patient to match their cadence to the new step rate.[69] This metronome feedback could be performed continuously for 5-10 minutes. After this point, feedback would be removed and only reintroduced during the next 5-10 minutes as needed if the clinician feels the step rate is faltering. Out of the clinic, patients can continue implementing alterations by use of a metronome application on a smartphone or by use of a smart watch that tracks step rate.[68,94]

'Run Softer' Gait Training

In conjunction with increasing cadence, cues to "run softer" can decrease the force that occurs during ground contact. Gait retraining aimed at running softer has shown to decrease tibial peak positive acceleration almost immediately within a session.[73] Higher tibial peak positive acceleration during impact has been found in runners that suffer from stress fractures[73] indicating that reduction may lead to decreased RRI. Longer 'run softer' retraining of 8 sessions with guidance on self-maintenance techniques has led to maintained reductions in vertical instantaneous loading rate, vertical average loading rate and peak vertical impact at 2 weeks and 12 months.[71,72] 'Run softer' cues decreased RRI by 62% in novice runners completing an average weekly volume of >8km with no history of injury in the previous 6 months.[71] Although some studies relied on accelerometers for data collection and biofeedback,[71,72] the same results have been achieved with the use of verbal cues from experienced clinicians alone.[73] Furthermore, verbal cueing has frequently been used in conjunction with other feedback measures, such as mirrors, to address other running form alterations with success.[87]

How to improve ability to 'run softer'

In order to train the ability to 'run softer' in clinic, the patient would run on a treadmill at a self-selected comfortable pace for a warm-up of 5-10 minutes. After, the clinician would provide the patient verbal cues to "run softer" or "make your foot strikes quieter" based on subjective observation. For 10 minutes, the clinician would provide feedback every 30-60 second based on the performance within that time period.[73] The patient would then try to maintain this running pattern for an additional 5-10 minutes with verbal cues only provided if the patient significantly deviates.

Foot strike

Other options to reduce impact force or loading rates would be transitioning to a forefoot strike (FFS) pattern during running. Some studies argue that a FFS running pattern leads to an increased cadence naturally; however, the evidence for this conflicting.[74,76,77] While FFS has been shown to produce lower vertical average loading rate and vertical instantaneous loading rate,[74,76] and ground reaction forces[74,76,78] as compared to a rearfoot strike, a systematic review and meta-analysis by Anderson et al noted that there is limited evidence that a transition to a FFS pattern leads to significant decreases in vertical average loading rate, peak vertical impact or peak vertical loading rate.[77] More importantly, transitioning to a FFS will lead to decreased demands of the knee and increase the stress around the foot and ankle.[75,77,78] Shifting loads to the ankle and foot may result in new injury, such as metatarsal stress fractures, foot pain or Achilles tendon injuries.[95] In altering foot strike, clinicians should consider the joints and areas of the body that are the most problematic for the patient. If a person living with RA primarily reports impairments at the knee, then an FFS may be an option if cadence increases or 'run softer' techniques cannot be accomplished. However, altering foot strike patterns should be gradual and approached carefully.

How to switch to forefoot strike

In order to prepare a patient for the process of altering from a rearfoot strike to FFS, clinicians may wish to use a strengthening protocol prior to the transition to prepare musculature of the feet and lower extremities. Clinicians may consider double leg or single leg heel raises, toe spreading or towel curl exercises for multiple sets of 10-20 repetitions. For a more in depth protocol, refer to the supplementary material used by Futrell et al.[76] In transitioning to a FFS, a more minimally cushioned shoe is frequently used to decreased risk of excessive supination on initial contact.[76] In transitioning to a FFS, patients are simply asked to strike the ground with their forefoot. The success of this can be visually confirmed by the clinician.[78] The use of tibial accelerometers have been used in research to audibly and visual indicate when a FFS pattern is achieved based on impact.[76] However, in clinic, verbal cues to "strike the ground with the ball of your foot" may be used. The addition of a mirror in front of a treadmill may also assist patients in visually being able to see their own corrections and running form.[96]

Shoe wear

Although there may be some biomechanical alterations between shoes, patient preference and comfort based on their symptoms should be the main deciding factors. There are 3 main types of shoe wear that can be considered when beginning a running program: minimalist, traditional and maximal. Minimalist shoe wear tends to alter foot strike patterns and yields a FFS which will result in similar outcomes listed earlier with greater loads at the metatarsophalangeal joints and ankle.[84] If a FFS is not adopted, minimalist footwear results in increased vertical average loading rate.[85] However, runners tend to alter their biomechanics by landing in a more plantarflexed position[85] leading to an anterior center of pressure on the foot and likely reducing internal knee extensor moments and tibiofemoral loading.[84] Thus, the location of our patients symptoms in relation to joints within the body would dictate the foot strike style used.

If traditional, maximal and minimal running shoes all demonstrate a 4mm heel-to-toe drop, peak eversion ends up being greatest in minimal and maximal cushioned shoes. As for dorsiflexion, traditional and maximal cushioned running shoes increase dorsiflexion at initial contact. However, minimal shoes demonstrate greater dorsiflexion excursion, and the second largest peak dorsiflexion. If a patient presents with dorsiflexion and eversion limitation, maximally or minimally cushioned shoes may be inappropriate.[85] Although heel-to-toe drop may alter biomechanics, such as greater knee adduction, excursion and flexion at midstance with higher drop categories,[84] there are no significant differences in RRI between 0 mm, 6 mm and 10 mm drop shoes.[83,84] Outside of injuries, patient range of motion limitations should be considered since an 11mm heel lift has been shown to reduce peak ankle dorsiflexion during running by 20%.[97]

How to select a running shoe

The primary purpose of a running shoe should be based around comfort. Selecting a shoe based on personal comfort alone can provide an injury risk reduction of >50%.[97] Selecting a running shoes based on plantar shape, arch height or other factors has not consistently shown to reduce the risk of running related injury.[97–99] With that said, a patient's ankle range of motion, foot structure and injury history should be assessed prior to shoe selection as heel-to-toe drops may effect dorsiflexion range of motion[97] and guidance can be given towards shoes that may be more comfortable based of toe box shape.

Discussion

Individuals living with low disease activity rheumatoid arthritis can safely perform resistive and aerobic exercise at low or high intensities without evidence of change in disease activity[1,4,12,13,16–19] or medication usage.[34,12,17] In fact, consistent exercise routines are beneficial to those living with RA as they have shown to reduce joint swelling,[12] improve aerobic capacity[12,18,34] and quality of life.[17] Furthermore, aerobic exercise leads to decreased expression of inflammatory markers,[14] blood pressure, improved lipid profiles and vascular function[8] leading to a reduced risk of cardiovascular disease, which is a known complication of RA.[5,14] Running is a widely popular form of exercise globally[22] with many cardiovascular benefits[48,49] that could reduce CVD risk in those with RA.

Overall, recreational running is a safe mode of exercise, and does not cause or lead to worsening joint destruction on its own.[44] However, much research is still needed, as there are currently no published randomized control trials in relation to running and RA which makes clinical application and development of accurate running volume or intensity for exercise prescriptions difficult, as these are currently lacking.[29,30,44] Future research should not only examine the safety of running with RA, but it should also analyze the effects of running volume, frequency and intensity that is deficient in other running research of those living without RA.

In the meantime, a slow and progressive running program under the guidance of a clinician may be pursued. Similar to return to running after knee surgical procedures, programs aimed at protecting joint structures during early phases of soft tissue or graft healing can likely guide clinical reasoning. Attention should be given to the need of progression or regression of exercises as it relates to signs of increased stress, such as pain ratings,[16,17,24,60] changes in joint range of motion[60] and joint effusion.[59,60] In addition to gradual progression of activity with symptom monitoring, gait modifications through cadence alteration and 'run softer' cueing can be incorporated to improve the comfort and success in return to running. Future research of these interventions in an RA populations will be crucial in determining the safest and most feasible method of running in those living with RA. Detailed and high quality randomized controlled trials are needed to not only guide clinicians in running activities for those living with RA but exercise as well. Medication regimens and treatments are consistently changing and updated literature is needed to provide the highest quality of care to this population.

References

1. Azeez M, Clancy C, O'Dwyer T, Lahiff C, Wilson F, Cunnane G. Benefits of exercise in patients with rheumatoid arthritis: a randomized controlled trial of a patient-specific exercise programme. *Clin Rheumatol*. 2020;39(6):1783-1792. doi:10.1007/s10067-020-04937-4

2. Silman AJ, Pearson JE. Epidemiology and genetics of rheumatoid arthritis. *Arthritis Res*. 2002;4 Suppl 3:S265-72. doi:10.1186/ar578

3. Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis: A review. *JAMA*. 2018;320(13):1360-1372. doi:10.1001/jama.2018.13103

4. Hu H, Xu A, Gao C, Wang Z, Wu X. The effect of physical exercise on rheumatoid arthritis: An overview of systematic reviews and meta-analysis. *J Adv Nurs*. 2021;77(2):506-522. doi:10.1111/jan.14574

5. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet*. 2016;388(10055):2023-2038. doi:10.1016/S0140-6736(16)30173-8

6. Singh JA, Saag KG, Bridges SL, et al. 2015 american college of rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26. doi:10.1002/art.39480

7. Fraenkel L, Bathon JM, England BR, et al. 2021 american college of rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2021;73(7):924-939. doi:10.1002/acr.24596

8. Metsios GS, Stavropoulos-Kalinoglou A, Kitas GD. The role of exercise in the management of rheumatoid arthritis. *Expert Rev Clin Immunol*. 2015;11(10):1121-1130. doi:10.1586/1744666X.2015.1067606

9. Smith RD, Polley HF. Rest therapy for rheumatoid arthritis. *Mayo Clin Proc*. 1978;53(3):141-145.

10. Milazzo S. The treatment of rheumatoid arthritis. *Aust Fam Physician*. 1977;6(8):936-950.

11. Munneke M, de Jong Z, Zwinderman AH, et al. High intensity exercise or conventional exercise for patients with rheumatoid arthritis? Outcome expectations of patients, rheumatologists, and physiotherapists. *Ann Rheum Dis*. 2004;63(7):804-808. doi:10.1136/ard.2003.011189

12. van den Ende CH, Hazes JM, le Cessie S, et al. Comparison of high and low intensity training in well controlled rheumatoid arthritis. Results of a randomised clinical trial. *Ann Rheum Dis*. 1996;55(11):798-805. doi:10.1136/ard.55.11.798

13. Lemmey AB, Marcora SM, Chester K, Wilson S, Casanova F, Maddison PJ. Effects of high-intensity resistance training in patients with rheumatoid arthritis: a randomized controlled trial. *Arthritis Rheum*. 2009;61(12):1726-1734. doi:10.1002/art.24891

14. Metsios GS, Kitas GD. Physical activity, exercise and rheumatoid arthritis: Effectiveness, mechanisms and implementation. *Best Pract Res Clin Rheumatol*. 2018;32(5):669-682. doi:10.1016/j.berh.2019.03.013

15. Hu A, Koh B, Teo M-R. A review of the current evidence on the sensitivity and specificity of the Ipswich touch test for the screening of loss of protective sensation in patients with diabetes mellitus. *Diabetol Int*. 2021;12(2):145-150. doi:10.1007/s13340-020-00451-9

16. Häkkinen A, Sokka T, Lietsalmi A-M, Kautiainen H, Hannonen P. Effects of dynamic strength training on physical function, Valpar 9 work sample test, and working capacity in patients with recent-onset rheumatoid arthritis. *Arthritis Rheum*. 2003;49(1):71-77. doi:10.1002/art.10902

17. Lourenzi FM, Jones A, Pereira DF, Santos JHCAD, Furtado RNV, Natour J. Effectiveness of an overall progressive resistance strength program for improving the functional capacity of patients with rheumatoid arthritis: a randomized controlled trial. *Clin Rehabil*. 2017;31(11):1482-1491. doi:10.1177/0269215517698732

18. Westby MD, Wade JP, Rangno KK, Berkowitz J. A randomized controlled trial to evaluate the effectiveness of an exercise program in women with rheumatoid arthritis taking low dose prednisone. *J Rheumatol*. 2000;27(7):1674-1680.

19. Hurkmans E, van der Giesen FJ, Vliet Vlieland TP, Schoones J, Van den Ende ECHM. Dynamic exercise programs (aerobic capacity and/or muscle strength training) in patients with rheumatoid arthritis. *Cochrane Database Syst Rev*. 2009;(4):CD006853. doi:10.1002/14651858.CD006853.pub2

20. Veldhuijzen van Zanten JJCS, Rouse PC, Hale ED, et al. Perceived Barriers, Facilitators and Benefits for Regular Physical Activity and Exercise in Patients with Rheumatoid Arthritis: A Review of the Literature. *Sports Med*. 2015;45(10):1401-1412. doi:10.1007/s40279-015-0363-2

21. Rausch Osthoff A-K, Niedermann K, Braun J, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. *Ann Rheum Dis*. 2018;77(9):1251-1260. doi:10.1136/annrheumdis-2018-213585

22. Hulteen RM, Smith JJ, Morgan PJ, et al. Global participation in sport and leisure-time physical activities: A systematic review and meta-analysis. *Prev Med*. 2017;95:14-25. doi:10.1016/j.ypmed.2016.11.027

23. Adams D, Logerstedt DS, Hunter-Giordano A, Axe MJ, Snyder-Mackler L. Current concepts for anterior cruciate ligament reconstruction: a criterion-based rehabilitation progression. *J Orthop Sports Phys Ther*. 2012;42(7):601-614. doi:10.2519/jospt.2012.3871

24. de Fontenay BP, van Cant J, Gokeler A, Roy J-S. Reintroduction of running after ACL reconstruction with a hamstring graft: can we predict short-term success? *J Athl Train*. Published online October 8, 2021. doi:10.4085/1062-6050-0407.21

25. Kraeutler MJ, Anderson J, Chahla J, et al. Return to running after arthroscopic hip surgery: literature review and proposal of a physical therapy protocol. *J Hip Preserv Surg*. 2017;4(2):121-130. doi:10.1093/jhps/hnx012

26. Esculier J-F, Bouyer LJ, Dubois B, et al. Is combining gait retraining or an exercise programme with education better than education alone in treating runners with patellofemoral pain?A randomised clinical trial. *Br J Sports Med*. 2018;52(10):659-666. doi:10.1136/bjsports-2016-096988

27. Ross C. A comparison of osteoarthritis and rheumatoid arthritis: diagnosis and treatment. *Nurse Pract*. 1997;22(9):20, 23-24, 27. doi:10.1097/00006205-199709000-00003

28. Kettunen JA, Kujala UM. Exercise therapy for people with rheumatoid arthritis and osteoarthritis. *Scand J Med Sci Sports*. 2004;14(3):138-142. doi:10.1111/j.1600-0838.2004.00396.x

29. Timmins KA, Leech RD, Batt ME, Edwards KL. Running and Knee Osteoarthritis: A Systematic Review and Meta-analysis. *Am J Sports Med*. 2017;45(6):1447-1457. doi:10.1177/0363546516657531

30. Alentorn-Geli E, Samuelsson K, Musahl V, Green CL, Bhandari M, Karlsson J. The Association of Recreational and Competitive Running With Hip and Knee Osteoarthritis: A Systematic Review and Meta-analysis. *J Orthop Sports Phys Ther*. 2017;47(6):373-390. doi:10.2519/jospt.2017.7137

31. Driban JB, Hootman JM, Sitler MR, Harris KP, Cattano NM. Is participation in certain sports associated with knee osteoarthritis? A systematic review. *J Athl Train*. 2017;52(6):497-506. doi:10.4085/1062-6050-50.2.08

32. Dong X, Li C, Liu J, et al. The effect of running on knee joint cartilage: A systematic review and meta-analysis. *Phys Ther Sport*. 2021;47:147-155. doi:10.1016/j.ptsp.2020.11.030

33. Khan MCM, O'Donovan J, Charlton JM, Roy J-S, Hunt MA, Esculier J-F. The Influence of Running on Lower Limb Cartilage: A Systematic Review and Meta-analysis. *Sports Med*. 2022;52(1):55-74. doi:10.1007/s40279-021-01533-7

34. de Jong Z, Munneke M, Zwinderman AH, et al. Is a long-term high-intensity exercise program effective and safe in patients with rheumatoid arthritis? Results of a randomized controlled trial. *Arthritis Rheum*. 2003;48(9):2415-2424. doi:10.1002/art.11216

35. Foulds HJA, Bredin SSD, Charlesworth SA, Ivey AC, Warburton DER. Exercise volume and intensity: a dose-response relationship with health benefits. *Eur J Appl Physiol*. 2014;114(8):1563-1571. doi:10.1007/s00421-014-2887-9

36. Peter WF, Swart NM, Meerhoff GA, Vliet Vlieland TPM. Clinical practice guideline for physical therapist management of people with rheumatoid arthritis. *Phys Ther*. 2021;101(8). doi:10.1093/ptj/pzab127

37. Flint-Wagner HG, Lisse J, Lohman TG, et al. Assessment of a sixteen-week training program on strength, pain, and function in rheumatoid arthritis patients. *J Clin Rheumatol*. 2009;15(4):165-171. doi:10.1097/RHU.0b013e318190f95f

38. Brushøj C, Larsen K, Albrecht-Beste E, Nielsen MB, Løye F, Hölmich P. Prevention of overuse injuries by a concurrent exercise program in subjects exposed to an increase in training load: a randomized controlled trial of 1020 army recruits. *Am J Sports Med*. 2008;36(4):663-670. doi:10.1177/0363546508315469

39. Baltich J, Emery CA, Whittaker JL, Nigg BM. Running injuries in novice runners enrolled in different training interventions: a pilot randomized controlled trial. *Scand J Med Sci Sports*. 2017;27(11):1372-1383. doi:10.1111/sms.12743

40. Toresdahl BG, McElheny K, Metzl J, Ammerman B, Chang B, Kinderknecht J. A randomized study of a strength training program to prevent injuries in runners of the new york city marathon. *Sports Health*. 2020;12(1):74-79. doi:10.1177/1941738119877180

41. Blagrove RC, Howatson G, Hayes PR. Effects of Strength Training on the Physiological Determinants of Middle- and Long-Distance Running Performance: A Systematic Review. *Sports Med*. 2018;48(5):1117-1149. doi:10.1007/s40279-017-0835-7

42. Munneke M, de Jong Z, Zwinderman AH, et al. Effect of a high-intensity weight-bearing exercise program on radiologic damage progression of the large joints in subgroups of patients with rheumatoid arthritis. *Arthritis Rheum*. 2005;53(3):410-417. doi:10.1002/art.21165

43. Cramp F, Hewlett S, Almeida C, et al. Non-pharmacological interventions for fatigue in rheumatoid arthritis. *Cochrane Database Syst Rev*. 2013;(8):CD008322. doi:10.1002/14651858.CD008322.pub2

44. Lo GH, Musa SM, Driban JB, et al. Running does not increase symptoms or structural progression in people with knee osteoarthritis: data from the osteoarthritis initiative. *Clin Rheumatol*. 2018;37(9):2497-2504. doi:10.1007/s10067-018-4121-3

45. Ni G-X. Development and Prevention of Running-Related Osteoarthritis. *Curr Sports Med Rep*. 2016;15(5):342-349. doi:10.1249/JSR.0000000000000294

46. Konopka AR, Harber MP. Skeletal muscle hypertrophy after aerobic exercise training. *Exerc Sport Sci Rev*. 2014;42(2):53-61. doi:10.1249/JES.0000000000000007

47. Schumann M, Feuerbacher JF, Sünkeler M, et al. Compatibility of Concurrent Aerobic and Strength Training for Skeletal Muscle Size and Function: An Updated Systematic Review and Meta-Analysis. *Sports Med*. 2022;52(3):601-612. doi:10.1007/s40279-021-01587-7

48. Pedisic Z, Shrestha N, Kovalchik S, et al. Is running associated with a lower risk of all-cause, cardiovascular and cancer mortality, and is the more the better? A systematic review and meta-analysis. *Br J Sports Med*. 2020;54(15):898-905. doi:10.1136/bjsports-2018-100493

49. Lee D-C, Pate RR, Lavie CJ, Sui X, Church TS, Blair SN. Leisure-time running reduces all-cause and cardiovascular mortality risk. *J Am Coll Cardiol*. 2014;64(5):472-481. doi:10.1016/j.jacc.2014.04.058

50. Häkkinen A, Sokka T, Kotaniemi A, Hannonen P. A randomized two-year study of the effects of dynamic strength training on muscle strength, disease activity, functional capacity, and bone mineral density in early rheumatoid arthritis. *Arthritis Rheum*. 2001;44(3):515-522. doi:10.1002/1529-0131(200103)44:3<515::AID-ANR98>3.0.CO;2-5

51. Bykerk VP, Massarotti EM. The new ACR/EULAR remission criteria: rationale for developing new criteria for remission. *Rheumatology (Oxford)*. 2012;51 Suppl 6:vi16-20. doi:10.1093/rheumatology/kes281

52. Felson DT, Smolen JS, Wells G, et al. American College of Rheumatology/European League against Rheumatism provisional definition of remission in rheumatoid arthritis for clinical trials. *Ann Rheum Dis*. 2011;70(3):404-413. doi:10.1136/ard.2011.149765

53. England BR, Tiong BK, Bergman MJ, et al. 2019 update of the american college of rheumatology recommended rheumatoid arthritis disease activity measures. *Arthritis Care Res (Hoboken)*. 2019;71(12):1540-1555. doi:10.1002/acr.24042

54. Parekh K, Taylor WJ. The patient activity scale-II is a generic indicator of active disease in patients with rheumatic disorders. *J Rheumatol*. 2010;37(9):1932-1934. doi:10.3899/jrheum.100008

55. Disease Activity & Functional Status Assessments. Accessed April 16, 2022. https://www.rheumatology.org/Practice-Quality/Clinical-Support/Quality-Measurement/Disease-Activity-Functional-Status-Assessments

56. Muñoz JGB, Giraldo RB, Santos AM, et al. Correlation between rapid-3, DAS28, CDAI and SDAI as a measure of disease activity in a cohort of Colombian patients with rheumatoid arthritis. *Clin Rheumatol*. 2017;36(5):1143-1148. doi:10.1007/s10067-016-3521-5

57. Uhlig T, Kvien TK, Pincus T. Test-retest reliability of disease activity core set measures and indices in rheumatoid arthritis. *Ann Rheum Dis*. 2009;68(6):972-975. doi:10.1136/ard.2008.097345

58. Boone NW, Sepriano A, van der Kuy P-H, Janknegt R, Peeters R, Landewé RBM. Routine Assessment of Patient Index Data 3 (RAPID3) alone is insufficient to monitor disease activity in rheumatoid arthritis in clinical practice. *RMD Open*. 2019;5(2):e001050. doi:10.1136/rmdopen-2019-001050

59. Delahunt E, Bleakley CM, Bossard DS, et al. Clinical assessment of acute lateral ankle sprain injuries (ROAST): 2019 consensus statement and recommendations of the International Ankle Consortium. *Br J Sports Med*. 2018;52(20):1304-1310. doi:10.1136/bjsports-2017-098885

60. Rambaud AJM, Ardern CL, Thoreux P, Regnaux J-P, Edouard P. Criteria for return to running after anterior cruciate ligament reconstruction: a scoping review. *Br J Sports Med*. 2018;52(22):1437-1444. doi:10.1136/bjsports-2017-098602

61. Brinlee AW, Dickenson SB, Hunter-Giordano A, Snyder-Mackler L. ACL Reconstruction Rehabilitation: Clinical Data, Biologic Healing, and Criterion-Based Milestones to Inform a Return-to-Sport Guideline. *Sports Health*. Published online December 13, 2021:19417381211056870. doi:10.1177/19417381211056873

62. Ortega-Avila AB, Ramos-Petersen L, Cervera-Garvi P, Nester CJ, Morales-Asencio JM, Gijon-Nogueron G. Systematic review of the psychometric properties of patient-reported outcome measures for rheumatoid arthritis in the foot and ankle. *Clin Rehabil*. 2019;33(11):1788-1799. doi:10.1177/0269215519862328

63. Bremander ABI, Petersson IF, Roos EM. Validation of the Rheumatoid and Arthritis Outcome Score (RAOS) for the lower extremity. *Health Qual Life Outcomes*. 2003;1:55. doi:10.1186/1477-7525-1-55

64. McMullen CW, Harrast MA, Baggish AL. Optimal running dose and cardiovascular risk. *Curr Sports Med Rep*. 2018;17(6):192-198. doi:10.1249/JSR.0000000000000491

65. Adams D, Pozzi F, Willy RW, Carrol A, Zeni J. Altering cadence or vertical oscillation during running: effects on running related injury factors. *Int J Sports Phys Ther*. 2018;13(4):633-642. doi:10.26603/ijspt20180633

66. Schubert AG, Kempf J, Heiderscheit BC. Influence of stride frequency and length on running mechanics: a systematic review. *Sports Health*. 2014;6(3):210-217. doi:10.1177/1941738113508544

67. Davis IS, Tenforde AS, Neal BS, Roper JL, Willy RW. Gait retraining as an intervention for patellofemoral pain. *Curr Rev Musculoskelet Med*. 2020;13(1):103-114. doi:10.1007/s12178-020-09605-3

68. Wang J, Luo Z, Dai B, Fu W. Effects of 12-week cadence retraining on impact peak, load rates and lower extremity biomechanics in running. *PeerJ*. 2020;8:e9813. doi:10.7717/peerj.9813

69. Bramah C, Preece SJ, Gill N, Herrington L. A 10% increase in step rate improves running kinematics and clinical outcomes in runners with patellofemoral pain at 4 weeks and 3 months. *Am J Sports Med*. 2019;47(14):3406-3413. doi:10.1177/0363546519879693

70. Chumanov ES, Wille CM, Michalski MP, Heiderscheit BC. Changes in muscle activation patterns when running step rate is increased. *Gait Posture*. 2012;36(2):231-235. doi:10.1016/j.gaitpost.2012.02.023

71. Chan ZYS, Zhang JH, Au IPH, et al. Gait Retraining for the Reduction of Injury Occurrence in Novice Distance Runners: 1-Year Follow-up of a Randomized Controlled Trial. *Am J Sports Med*. 2018;46(2):388-395. doi:10.1177/0363546517736277

72. Bowser BJ, Fellin R, Milner CE, Pohl MB, Davis IS. Reducing Impact Loading in Runners: A One-Year Follow-up. *Med Sci Sports Exerc*. 2018;50(12):2500-2506. doi:10.1249/MSS.0000000000001710

73. Creaby MW, Franettovich Smith MM. Retraining running gait to reduce tibial loads with clinician or accelerometry guided feedback. *J Sci Med Sport*. 2016;19(4):288-292. doi:10.1016/j.jsams.2015.05.003

74. Almeida MO, Davis IS, Lopes AD. Biomechanical Differences of Foot-Strike Patterns During Running: A Systematic Review With Meta-analysis. *J Orthop Sports Phys Ther*. 2015;45(10):738-755. doi:10.2519/jospt.2015.6019

75. Xu Y, Yuan P, Wang R, Wang D, Liu J, Zhou H. Effects of Foot Strike Techniques on Running Biomechanics: A Systematic Review and Meta-analysis. *Sports Health*. 2021;13(1):71-77. doi:10.1177/1941738120934715

76. Futrell EE, Gross KD, Reisman D, Mullineaux DR, Davis IS. Transition to forefoot strike reduces load rates more effectively than altered cadence. *J Sport Health Sci*. 2020;9(3):248-257. doi:10.1016/j.jshs.2019.07.006

77. Anderson LM, Bonanno DR, Hart HF, Barton CJ. What are the Benefits and Risks Associated with Changing Foot Strike Pattern During Running? A Systematic Review and Meta-analysis of Injury, Running Economy, and Biomechanics. *Sports Med*. 2020;50(5):885-917. doi:10.1007/s40279-019-01238-y

78. Kuhman D, Melcher D, Paquette MR. Ankle and knee kinetics between strike patterns at common training speeds in competitive male runners. *Eur J Sport Sci*. 2016;16(4):433-440. doi:10.1080/17461391.2015.1086818

79. Willson JD, Ratcliff OM, Meardon SA, Willy RW. Influence of step length and landing pattern on patellofemoral joint kinetics during running. *Scand J Med Sci Sports*. 2015;25(6):736-743. doi:10.1111/sms.12383

80. Teng H-L, Powers CM. Sagittal plane trunk posture influences patellofemoral joint stress during running. *J Orthop Sports Phys Ther*. 2014;44(10):785-792. doi:10.2519/jospt.2014.5249

81. Warrener A, Tamai R, Lieberman DE. The effect of trunk flexion angle on lower limb mechanics during running. *Hum Mov Sci*. 2021;78:102817. doi:10.1016/j.humov.2021.102817

82. Bonacci J, Hall M, Saunders N, Vicenzino B. Gait retraining versus foot orthoses for patellofemoral pain: a pilot randomised clinical trial. *J Sci Med Sport*. 2018;21(5):457-461. doi:10.1016/j.jsams.2017.09.187

83. Malisoux L, Chambon N, Urhausen A, Theisen D. Influence of the Heel-to-Toe Drop of Standard Cushioned Running Shoes on Injury Risk in Leisure-Time Runners: A Randomized Controlled Trial With 6-Month Follow-up. *Am J Sports Med*. 2016;44(11):2933-2940. doi:10.1177/0363546516654690

84. Sun X, Lam W-K, Zhang X, Wang J, Fu W. Systematic Review of the Role of Footwear Constructions in Running Biomechanics: Implications for Running-Related Injury and Performance. *J Sports Sci Med*. 2020;19(1):20-37.

85. Hannigan JJ, Pollard CD. Differences in running biomechanics between a maximal, traditional, and minimal running shoe. *J Sci Med Sport*. 2020;23(1):15-19. doi:10.1016/j.jsams.2019.08.008

86. Taddei UT, Matias AB, Ribeiro FIA, Bus SA, Sacco ICN. Effects of a foot strengthening program on foot muscle morphology and running mechanics: A proof-of-concept, single-blind randomized controlled trial. *Phys Ther Sport*. 2020;42:107-115. doi:10.1016/j.ptsp.2020.01.007

87. Letafatkar A, Rabiei P, Afshari M. Effect of neuromuscular training augmented with knee valgus control instructions on lower limb biomechanics of male runners. *Phys Ther Sport*. 2020;43:89-99. doi:10.1016/j.ptsp.2020.02.009

88. Ceyssens L, Vanelderen R, Barton C, Malliaras P, Dingenen B. Biomechanical Risk Factors Associated with Running-Related Injuries: A Systematic Review. *Sports Med*. 2019;49(7):1095-1115. doi:10.1007/s40279-019-01110-z

89. Brindle RA, Taylor JB, Rajek C, Weisbrod A, Ford KR. Association Between Temporal Spatial Parameters and Overuse Injury History in Runners: A Systematic Review and Meta-analysis. *Sports Med*. 2020;50(2):331-342. doi:10.1007/s40279-019-01207-5

90. Bjerre-Bastos JJ, Nielsen HB, Andersen JR, et al. A biomarker perspective on the acute effect of exercise with and without impact on joint tissue turnover: an exploratory randomized cross-over study. *Eur J Appl Physiol*. 2021;121(10):2799-2809. doi:10.1007/s00421-021-04751-z

91. Bjerre-Bastos JJ, Nielsen HB, Andersen JR, et al. Does moderate intensity impact exercise and non-impact exercise induce acute changes in collagen biochemical markers related to osteoarthritis? - An exploratory randomized cross-over trial. *Osteoarthr Cartil*. 2021;29(7):986-994. doi:10.1016/j.joca.2021.02.569

92. Johnson CD, Tenforde AS, Outerleys J, Reilly J, Davis IS. Impact-Related Ground Reaction Forces Are More Strongly Associated With Some Running Injuries Than Others. *Am J Sports Med*. 2020;48(12):3072-3080. doi:10.1177/0363546520950731

93. Vannatta CN, Heinert BL, Kernozek TW. Biomechanical risk factors for running-related injury differ by sample population: A systematic review and meta-analysis. *Clin Biomech (Bristol, Avon)*. 2020;75:104991. doi:10.1016/j.clinbiomech.2020.104991

94. Willy RW, Buchenic L, Rogacki K, Ackerman J, Schmidt A, Willson JD. In-field gait retraining and mobile monitoring to address running biomechanics associated with tibial stress fracture. *Scand J Med Sci Sports*. 2016;26(2):197-205. doi:10.1111/sms.12413

95. Daoud AI, Geissler GJ, Wang F, Saretsky J, Daoud YA, Lieberman DE. Foot strike and injury rates in endurance runners: a retrospective study. *Med Sci Sports Exerc*. 2012;44(7):1325-1334. doi:10.1249/MSS.0b013e3182465115

96. Roper JL, Harding EM, Doerfler D, et al. The effects of gait retraining in runners with patellofemoral pain: A randomized trial. *Clin Biomech (Bristol, Avon)*. 2016;35:14-22. doi:10.1016/j.clinbiomech.2016.03.010

97. Mestelle Z, Kernozek T, Adkins KS, Miller J, Gheidi N. Effect of heel lifts on patellofemoral joint stress during running. *Int J Sports Phys Ther*. 2017;12(5):711-717.

98. Knapik JJ, Trone DW, Tchandja J, Jones BH. Injury-reduction effectiveness of prescribing running shoes on the basis of foot arch height: summary of military investigations. *J Orthop Sports Phys Ther*. 2014;44(10):805-812. doi:10.2519/jospt.2014.5342

99. Knapik JJ, Swedler DI, Grier TL, et al. Injury reduction effectiveness of selecting running shoes based on plantar shape. *J Strength Cond Res*. 2009;23(3):685-697. doi:10.1519/JSC.0b013e3181a0fc63