Review

Tailored exercise programmes for fibromyalgia: a clinical practice guide

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ABSTRACT

Objective. *To evaluate the role of exercise in the management of fibromyalgia syndrome (FM) by addressing its complex pathogenesis involving central sensitisation, autonomic dysfunction, inflammation, and neurological irregularities, and examining how exercise impacts symptom exacerbation caused by external stressors and comorbid conditions.*

Methods. *This review synthesises evidence from current literature focusing on the benefits of structured and personalised exercise programmes in FM management. It discusses the importance of specifying exercise type, intensity, frequency, duration, and progression tailored to individual patient needs and clinical objectives.*

Results. *Regular physical activity effectively mitigates core aetiopathogenetic mechanisms of FM and improves associated conditions such as stress and obesity. It also provides benefits for preventing other chronic diseases, enhancing well-being, and promoting healthy ageing. Structured and personalised exercise programmes that start with a low-demand protocol and gradually increase exercise volume are most beneficial, by improving patient compliance and reducing the risk of adverse effects.*

Conclusion. *Effective management of FM requires a patient-centred approach integrating both pharmacological and non-pharmacological treatments, with exercise playing a pivotal role. Personalised exercise prescriptions that consider FM patients' specific needs and limitations are crucial for optimising treatment outcomes and enhancing quality of life.*

Introduction and pathogenesis

Fibromyalgia (FM) affects about 2% of the general population, predominantly females, without any objectively verifiable pathology. It is characterised by chronic widespread pain, central nervous system pain amplification, and various symptoms including fatigue, cognitive dysfunction, and mood disorders, which significantly impair quality of life and physical performance (1). These symptoms promote a sedentary lifestyle that worsens physical fitness and body composition, creating a vicious cycle of increased pain and disease severity (2). The pathogenesis of FM is multifaceted and partially unclear, involving mechanisms like central sensitisation, a disruption of pain regulatory pathways causing hyperalgesia and allodynia (3), and autonomic nervous system (ANS) dysfunction, which contributes to chronic pain and multisystem symptoms (4). Novel pathways such as small fibre neuropathy, neurotransmitter anomalies (5-7), the gut-brain axis (4, 5), and immune dysfunction also have a role (8). Notably, ANS dysfunction is often characterised by an imbalance favouring sympathetic activity, which may disrupt sleep and increase pain sensitivity (9), while also elevating cardiovascular risk (10). Physical deconditioning, a common outcome in FM, exacerbates muscle ischaemia and peripheral sensitisation, thereby intensifying central sensitisation and perpetuating the condition (11). Furthermore, women with FM generally exhibit higher fat mass, leading to inflammation and worsening symptoms (12). Although some studies suggest cytokine regulation may influence FM pathogenesis, results remain inconclusive (13, 14). FM is also seen as a "functional somatic syndrome", where primary mechanisms like central sensitisation and ANS impairment interact with poor coping strategies, such as reduced exercise and social iso-

lation, thus increasing the risk of non-communicable diseases. Concurrent conditions often exacerbate symptoms, hence complicating diagnosis. Stress and psychosocial factors play significant roles, affecting both pathogenesis and the impact of FM, particularly in terms of mood disorders and life quality (1). Stress responses, influenced by individual differences and coping strategies, can exacerbate symptoms, and become new stressors, potentially leading to decision-making and social behaviour changes that further impair quality of life (15). Accurate and early diagnosis of FM is essential for effective management, including nonpharmacological approaches like psychotherapy and physical reconditioning, to prevent disease progression and reduce its socioeconomic impact (16 -20).

Non-pharmacological interventions are increasingly recognised as essential, often recommended as first-line treatments alongside pharmacological options in EULAR and other guidelines (21, 29-31). Non-pharmacological treatments, including exercise, nutrition, and stress management, address the underlying pathogenetic mechanisms of FM. Exercise is emphasised across all guidelines as critical for managing FM, and is the focus of our discussion, highlighting the criteria to "prescribe exercise".

Benefit of exercise in fibromyalgia patients

Physical exercise is a critical component in the prevention and management of chronic non-communicable diseases, as well as in enhancing well-being, health aging, and quality of life (22-24). Notably, aerobic exercise and adequate quantity and quality of muscle mass are inversely correlated with mortality; being cardiorespiratory fitness a prime predictor of all-cause mortality (Fig. 1) (25).

For FM patients, exercise is a proven therapeutic strategy, directly addressing etiopathogenetic mechanisms and indirectly improving related behaviours like stress and lifestyle habits (2, 21, 26-30). It also mitigates risks associated with cardiometabolic, oncologic, and musculoskeletal diseases prevalent among FM patients. Understanding exercise's mechanisms can lead to better adherence through tailored exercise prescriptions that induce hypoalgesia and regulate major body systems including immunological, hormonal, and autonomic functions (31, 32). Exercise improves cardiac autonomic control - which can be evaluated through non-invasive methods like spectral analysis of heart rate variability - in athletes, healthy individuals, and patients with various chronic conditions (33-35). This is particularly relevant as autonomic nervous system impairment, influenced by factors like chronic stress and unhealthy lifestyle, plays a significant part in FM (1, 15,16). The reduction of fat mass through aerobic exercise is crucial, especially since FM patients often have higher obesity rates (36, 37). This approach, combined with healthy nutrition, improves body composition and autonomic, immunological, and hormonal functions, hence enhancing life quality and reducing chronic disease risks (36-38). Strength and flexibility exercises also provide significant benefits in FM by improving muscle strength and flexibility, counteracting fatigue, and alleviating muscle pain and improves sleep (39-42). Moreover, exercise may mitigate a high genetic risk for chronic diseases through epigenetic effects, potentially applicable in FM (43, 44). It can act as a catalyst for positive behavioural changes, by encouraging other healthy practices like balanced nutrition and stress management (22, 45, 46). Despite the proven benefits, the integration of exercise into clinical practice for FM is limited by socio-cultural, economic, and organisational barriers, as well as the absence of effective and sustainable intervention programmes (16, 47). Traditional advice on exercise often does not translate into practical benefits for FM patients, who might experience symptom exacerbation post-exercise without perceiving tangible improvements.

From subject's assessment to exercise prescription

Intervention programmes based on physical exercise can be considered effective when they modulate the pathogenetic mechanisms of diseases (16). According to the available literature, the most effective programmes result from a structured and personalised exercise prescription, encompassing a clear definition of modality, intensity, frequency, duration, and progression (this latter one particularly relevant in FM) of physical activity, tailored to FM patients' conditions, needs and clinical goals (23, 27, 47, 48). A correct exercise prescription, which requires specific competencies (16, 48) and which is pertinent to the physician, should focus on the single patient/subject, rather than on a specific disease/condition, by considering all the clinical features and possible contraindications. In the present paper, we focus on practical aspects of exercise prescription in FM which may be useful to physicians (rheumatologist, sport and exercise physicians, internal medicine physicians, etc.) who would like to use exercise to manage FM. Other exercise professionals (exercise physiologists, physiotherapists) have the important specific role of helping the patient in applying the prescription and of following up the patient over time.

Subject assessment

A correct assessment of subjects' clinical conditions and lifestyle is crucial to establish clinical goals as well as exclude any contraindication/barrier to some types/intensities of exercise. Further, it may be helpful to get some parameters, such as maximal and basal heart rate, to be utilised for a correct exercise prescription, in those FM patients capable of performing a stress test. Besides, subject assessment may be important to verify the results obtained after exercising, which - even if small - represent a motivational tool able to foster an individual proactive role.

- Clinical assessment

Proper medical screening is crucial for FM patients, involving a comprehensive evaluation of the patient's age, clinical condition, cardiac risk factors, and the intended exercise intensity (23, 48). Assessing disease severity, level

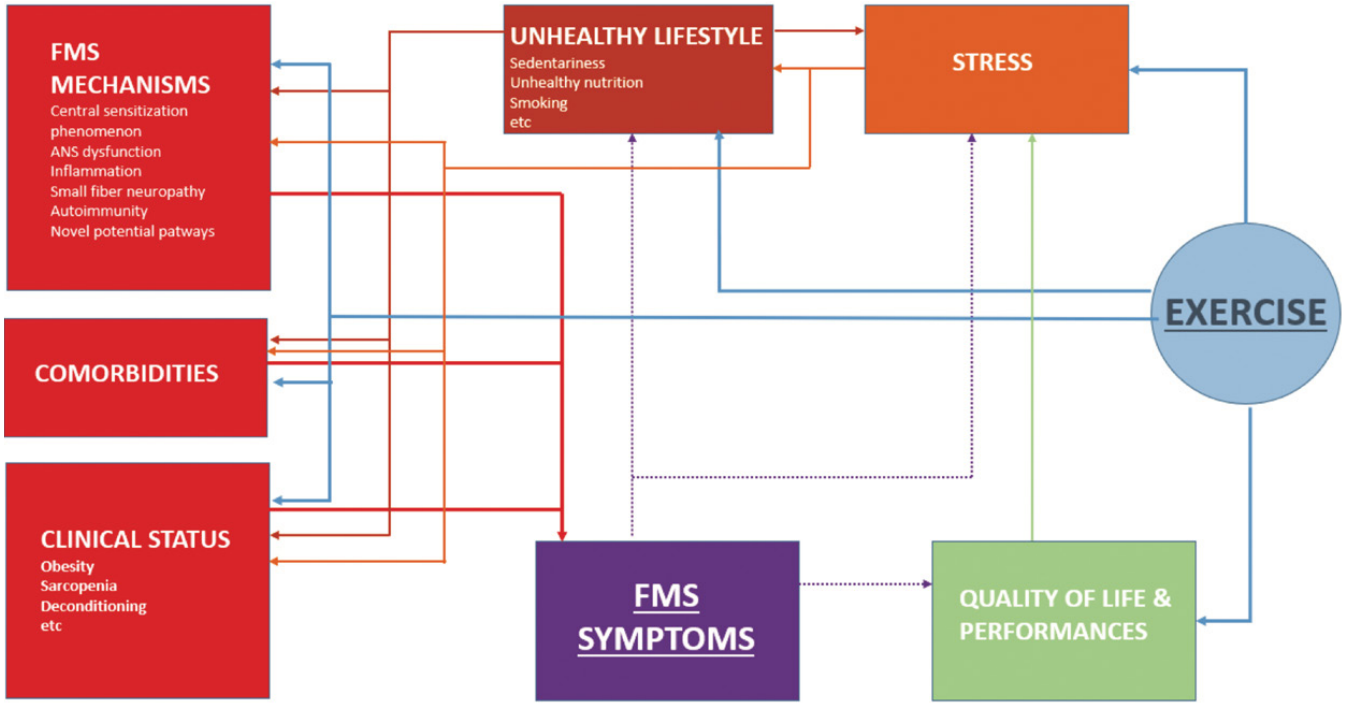

Fig. 1. Pathways by which exercise may counteract FM symptoms aetiopathogenesis.
Complex mechanisms underlying FM, comorbidities, patient's clinical status, lifestyle and stress determine FM symptoms, which, in turn, may negatively affect the quality of life and physical performance thus resulting in an unhealthy lifestyle, sedentariness and stress, which in turn can worsen physical fitness, muscular strength, and body composition, with consequent negative effects on pain, disease severity and quality of life in a sort of "vicious circle". Exercise may positively improve many mechanisms underlying FM and comorbidities, may manage obesity, sarcopenia and deconditioning, may reduce stress and improve lifestyle and quality of life, with consequent reduction of symptoms.

Table I. Scores related to the five disease severity categories of the three specific clinimetric instruments for FM [modified from (49)].

	Remission	Mild disease	Moderate disease	Severe disease	Very severe disease
FIQR	0–23	24–40	41–63	64–82	>83
FAS 2019mod	0–12	13–20	21–28	29–33	>33
PDS	0–5	6–15	16–20	21–25	>25

of deconditioning, and functioning is essential, by means of tools like the Fibromyalgia Impact Questionnaire Revised (FIQR) (49) and the Fibromyalgia Assessment Status modified (FAS 2019mod) (50, 51), alongside the Polysymptomatic Distress Scale (PDS) (51) to gauge symptom severity and distribution (49).
Table I reports the scores related to the five categories of the three specific clinimetric instruments for FM.

Exercise capacity
(measure of the ability to perform maximal aerobic exercise): Fatigue and pain may limit the possibility of performing tests to assess exercise capacity, such as cardiopulmonary stress test (to define VO_{2max} and anaerobic threshold), or even the simple maximal exercise test with 12-lead ECG recording (to check cardiac risk and to define maximal heart rate). In patients with important limitations of functioning, easier-to-perform tests may be employed, such as 6-minute walking test (52).

Muscle strength:
(measure of the ability of a muscle to generate force): Muscle strength can be evaluated using the handgrip strength test, provided that the patient's conditions permit it (53).
Physical performance: Assessments like the Short Physical Performance Battery (SPPB) (54-56) are used according to the patient's severity of disease. These tests include assessment of gait speed, balance, and chair stand tests (55, 57).
Body composition: Body composition is ideally measured using dual-energy x-ray absorptiometry (DXA), though bioelectrical impedance analysis (BIA) is a more accessible alternative in clinical settings. BIA measures fat mass percentage and calculates fat-free mass with algorithms (58).

- Lifestyle assessment
Lifestyle factors are assessed using ad hoc questionnaires that cover areas like physical activity, nutrition, stress perception, alcohol consumption, smoking, and sleep (16, 59-61). Objective methods, such as wearable devices, may help to quantify physical activity as well as monitor training improvement or motivate adherence to the prescribed programme.

Goal setting
Clinical goals must be defined for a correct exercise prescription, according to both subjects' initial requests and physician's considerations derived

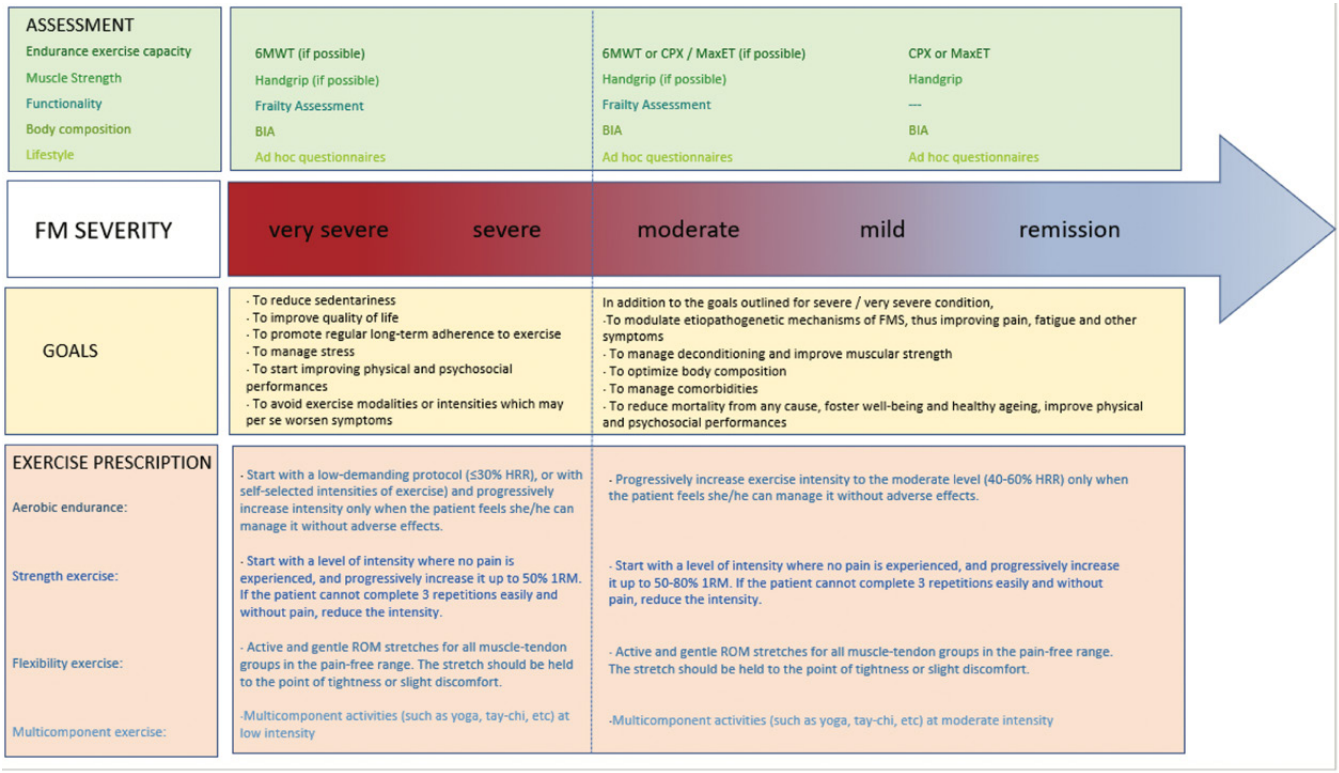

Fig. 2. Proposed model of assessment and exercise prescription for FM patients according to disease severity status, considering the clinical goals to reach.

from clinical assessment. Different clinical goals require different modalities and/or intensity of exercise. This may explain, albeit in part, the observation that aerobic or strength exercise alone cannot completely overcome all the negative effects of FM, while a combination of them could achieve or even surpass the effects of the two separate exercise programmes (62-64).

Exercise prescription

According to the World Health Organisation 2020 guidelines and several other sources (22-24, 48), to promote and maintain health, all healthy adults aged 18 to 65 years need to reach a weekly target range of 150–300 min of moderate-intensity or 75–150 min of vigorous-intensity physical activity (if adequately trained). In addition, every adult should perform activities that maintain or increase muscular strength and endurance for a minimum of two days weekly (22-24, 48, 65, 66). Very high doses of exercise (frequently performed also using anaerobic metabolic pathways) are not associated with health benefits (67-68) (Fig. 2).

For FM patients, especially those with high disease severity, following these guidelines can be challenging due to barriers like fatigue, pain, mood disorders, and often economic and time constraints (48, 69); therefore, these recommendations should serve as long-term goals rather than immediate starting points.

Exercise prescription needs to be tailored to patient's clinical status and needs, starting with modalities and doses that can be sustained by the patient (Fig. 2). Some patients need to begin with an exercise dose (especially in terms of intensity) immediately below their current capacity, and progressively increment it up to the level capable of granting benefits as per the defined goal (70-72). Exercise progression is crucial in FM. Intervention often should simply aim at the reduction of sedentariness (*i.e.* taking any opportunity to perform physical activity, such as walking at any pace and reducing the time spent sitting) and/or even physiotherapy. In this initial phase, the main challenge is maintaining patient motivation, and small results, such as leaving home in order to simply walk, may represent a significant motivational tool toward the execution of a real exercise programme.

A proper exercise prescription for FM patients requires defining the type of exercise, intensity, duration, frequency, and a plan for progressively increasing the exercise dose to achieve the desired health benefits.

- Exercise modality

The type of activity to perform to reach the set goals, based on physiological and biomechanical demands (73).

- Aerobic exercise refers to activity performed at an intensity that allows metabolism of stored energy to occur mainly through aerobic glycolysis. Alongside the glycolytic pathway, fat metabolism (b-oxidation) is also involved during aerobic exercise. Aerobic exercise involves large muscle groups performing dynamic activities and resulting in substantial increases in heart rate and energy expenditure. Examples of aerobic exercise include walking, cycling, running, and swimming, performed at low to moderate intensity (23).
- Anaerobic exercise refers, in contrast, to movement performed at high intensity that cannot be sustained by oxygen delivery alone and requires metabolism of stored energy to be

processed largely by anaerobic glycolysis. Examples are speed running, or a sustained isometric muscle contraction that, even if is not working maximally, does not entirely depend upon oxygen (23).

The traditional subdivision in binary terms such as endurance or strength exercise may be useful from a practical clinical point of view.

- Endurance activity entails the rhythmic motion of large muscle groups in aerobic activities (walking, jogging, swimming, etc.) (73), which depend primarily on the aerobic energy-generating process (74). It can be performed at low to high intensity according to subject's fitness level (*i.e.* exercise capacity). Endurance aerobic activities contribute to improving cardiorespiratory fitness, reducing cardio-metabolic-oncologic risk, decreasing fat mass as well as improving wellness and maintaining health (23, 47, 48, 73). They also may counteract many symptoms of FM, particularly pain, fatigue, sleep, mood disorders, and stress. Aerobic endurance programmes in FM patients need a minimum duration of three-four weeks in order to produce positive effects (75) and should become part of patient's lifestyle.
- Strength exercise involves activities that use low- to moderate-repetition movements against resistance, such as weightlifting (73). Strength exercise is primarily prescribed in order to increase strength and muscle mass, and physical independence. In FM it was associated with improvement of symptoms and quality of life (76). Nevertheless, the intensity of this exercise modality must be tailored to patient's disease severity and physical performance. Pain tolerance and perceived exertion need to be taken into account in the progression of intensity (75). It is also important to minimise the eccentric component of dynamic strength (resistance) exercises to lessen exercise-induced muscle microtrauma, particularly during a symptom flare-up (77), and teach FM individuals how to perform each exercise correctly to reduce the potential for injury (77).
- Flexibility and muscle stretching exercises aim at improving joint range of motion (flexibility) as well as decreasing muscle tension. They are mainly prescribed in order to relieve muscle pain associated to muscle tension (often present in FM patients), to improve joint range and prevent injuries. The effects of stretching on FM typical symptoms (pain, fatigue, depressed mood) are not clearly established (75), but there seems to be headroom for the application of this exercise modality. ACSM recommends (77) a stretching routine once or twice a week, with progression up to five times a week, for all pain-free muscle groups.
- Balance exercises improve the ability to maintain the body's centre of gravity within its base of support, and they are primarily prescribed in order to reduce the risk of falls and injury (78).
- Multicomponent physical activity refers to any exercise regimen that includes multiple forms of physical activity, combining all types of exercise (aerobic, muscle strengthening, flexibility and balance training) generally at low or moderate intensities (24). This modality of physical activity also encompasses mind-body exercises, which combine movement, concentration, and breath control (79), with the latter being a typical component of relaxation training programme (16, 80-82). Multicomponent physical activity is particularly suitable for FM patients (79, 81), especially for those with high disease severity.

- *Exercise intensity: the effort needed to reach the goal*

- Endurance aerobic exercise: a cardiopulmonary exercise test (CPX) would be required to establish cardiorespiratory fitness (VO_{2max}) and subsequently the exercise intensity as percent of it (16, 22-24, 48, 65). However, in clinical practice, by leveraging the approximate linear relationship between the increase of O_2 consumption and the increase of heart rate (HR), the exercise intensity is usually indicated as training heart rate, which can be calculated from resting heart rate and actual maximal heart rate – measured by conventional maximal exercise stress test – using Heart Rate Reserve (HRR) formula (Table II) (23, 24, 83-85). If even this test is not available, predefined tables might be used to estimate the training HR. Training intensity can also be expressed as a percentage of maximal heart rate (HRmax) recorded during an exercise test (23) or might be predicted on the basis of the equation (HRmax = 220 - age) (23). Nevertheless, the use of predefined tables or prediction equations for HRmax, is not recommended, because there is a large standard deviation around the regression line between age and HRmax, and exercise intensity cannot be actually tailored (23). These equations must not be used in subjects under chronotropic drugs and/or particularly deconditioned (84) such as FM patients. Alternatively, empirical tools may be helpful (Table II), especially in the initial phase of a training programme for a sedentary/deconditioned subject with low exercise capacity. Notably, moderate exercise intensity is required to get significant benefits from endurance aerobic exercise. Even lower intensity may be useful, particularly at the beginning of intervention in deconditioned subjects (86) as FM patients, being able to improve quality of life and some symptoms (79). Benefits will increase at higher intensities as long as exercise remains aerobic (87, 88). In FM endurance aerobic exercise intensity needs to be tailored to patient's clinical condition, generally starting with a lower intensity than that recommended by guidelines (71-74), and progressively increasing it to moderate level, by leveraging empirical tools to define it. The quantification of a personalised training HR may be considered only in those FM patients capable of performing a maximal exercise test.
- Strength exercise: defining the intensity is quite difficult since it depends on several factors, such as the resistance to win (*e.g.* a weight to lift), the speed of movement and the number

Table II. Classification of endurance activity intensity.

		INTENSITY					
	EFFORT	Very light light	Light light	Moderate moderate	High hard	Very hard very hard	Maximal maximal
Relative intensity	VO_2max (%) HRR* (%)	<25	25-44	45-59	60-84	≥85	100
	Maximal HR (%) RPE	<30 <9	30-49 9-10	50-69 11-12	70-89 13-16	≥90 >16	100 20
Absolute intensity	INTENSITY METs	Sedentary** 1-1.5	Light 1.6-2.9	Moderate 3.0-5.9	Vigorous 6-9	 ≥9	
Empirical tools		• at rest with limited added movement	• no noticeable change in breathing • can sustain activity for 1 hour or more	• breathing is faster but compatible with speaking full sentences, but not singing • increased sweating • can sustain activity for 30-60 min • walking at least 100 step·min - 1	• feeling "out of breath", breathing very hard, incompatible with carrying on a conversation comfortably • increased sweating • can sustain activity for up 30 min	• feels like giving 100% All out burst of between 1 and 2 min • intensity cannot be sustained for more than 10 min	• it is impossible to sustain the
Examples		• sittings • reclining or lying • watching TV • using a PC • driving a car	• walking slowly • light work while standing • playing an instrument	• brisk walking (5-6 km/h) • slow cycling (15 km/h) • ballroom dancing • recreational swimming	• jogging • running • biking > 15 km/h • swimming laps • single tennis	• training or competing in most competitive sports • racing or any all-out activity (*e.g.* running, rowing, swimming, skiing and high intensity intervals)	
Training zone ***		Aerobic	Aerobic	Aerobic	Aerobic+ Lactate	Aerobic + Lactate +Anaerobic	Anaerobic

Modified from (23, 73, 45, 83-85].

VO_{2max}: maximal aerobic capacity; HRR: heart rate reserve = Maximal heart rate – resting HR; METs indicates metabolic equivalents. 1 MET = 3.5 mL O2 kg-1 min-1.

*% heart rate reserve (HRR): calculate HRR target by (HRR×%value)+resting HR; RPE, rating of perceived exertion (20 value Borg score).

**Sedentary behaviour is defined as any waking behaviour which is characterised by an energy expenditure ≤ 1.5 Mets.

***Adapted from reference (84), using training zones related to aerobic and anaerobic thresholds. Low-intensity exercise is below the aerobic threshold; moderate is above the aerobic threshold but not reaching the anaerobic zone; high intensity is close to the anaerobic zone; and very intense exercise is above the anaerobic threshold. The duration of exercise will also largely influence this division in intensity (23).

of repetitions and it is generally defined using 1RM (*i.e.* the maximum amount of weight that a person can lift for one repetition, or the maximum amount of force that can be generated in one maximal contraction) or using 5RM (the maximum amount of weight that can be performed 5 times) (23). Usually, greater resistance implies a lower speed of movement and number of repetitions, resulting in a relatively higher effort. A lower repetition range with a heavier weight (anaerobic) may better optimise muscular strength and power, whereas a higher repetition range with a lighter weight may better enhance muscular endurance. In FM patients, strength exercise intensity needs to be adapted to individual clinical condition and, generally, tends to be low, in order to avoid the worsening of symptoms. In fact, patients need to experience no pain while performing exercise (77).

- Exercise duration: the duration of an exercise session is particularly important for endurance exercise, which should last at least 30 min every day (at moderate intensity) for improving health. In unfit subjects, such as many FM patients, even shorter duration at moderate intensity – especially if repeated during the day - may grant some benefits as compared to inactive individuals (24, 86). Longer periods may be required to reach specific goals: for instance, 60 min/day of endurance moderate exercise is required to lose fat mass (89).
- Exercise frequency: how many times the subject needs to exercise.

Endurance aerobic exercise needs to be performed ideally every day, at least 5 days weekly – if the exercise intensity is light-moderate – or 3 days/week at aerobic vigorous intensity (23, 73, 45, 85). Importantly, a high frequency is recommended in order to improve metabolic control in diabetic and obese patients (48, 90).

Strength exercise requires exercising the same muscular group for 2–3 non-consecutive days/week, in order to permit muscular recovery (48, 65), which is of paramount importance in FM patients.

- Exercise progression: to drive the subject toward the planned exercise dose in order to reach the established goal (73, 48, 91). Progression is vital for fostering subject compliance in all subjects, especially in those with FM. It consists in modulating intensity, frequency, and duration of exercise according to subject's training level, disease severity, preference, and characteristics. The prescription of a structured exercise programme should be always accompanied by a reduction of sedentary behaviour, by taking any opportunity during regular daily chores, or working time, to perform physical activity even at light intensity (24, 92). Sedentariness reduction often represents the first step, particularly in unfit subjects.
- Exercise execution: exercise may be executed in different places (home, fitness centres, swimming pool, outdoor, indoor, etc) in relation to subjects' preferences/needs. Temperature- and humidity-controlled rooms are preferred in order to minimise exacerbation of symptoms (77). Supervised or group exercise should be encouraged, especially in the beginning, to provide a social support system for reducing physical and emotional stress and promoting adherence (77).

Conclusion

Research extensively demonstrates the significant role of exercise in managing FM, with numerous studies and meta-analyses highlighting its benefits (27, 93). It is crucial to remember that many mechanisms contribute to the specific FM symptoms, and that an exercise protocol can be effective only if able to positively modify them, by considering all the clinical goals reported above. All exercise modalities may have a role, in particular endurance aerobic exercise and strength exercise. Overall, exercise represents a strategy not simply to treat FM but actually to improve the health of an individual being *also* affected with FM. According to FM severity, Figure 2 summarises the main assessment tools, which may provide useful data for defining clinical goals as well as the exercise modality/dose required to achieve them.

Key points in exercise prescription for FM

1. Tailored Prescription: Exercise plans should be customised according to the patient's clinical condition, FM severity, fitness level, and personal preferences.
2. Comprehensive Planning: A successful prescription defines the modality (type), intensity (effort), duration (how long), frequency (how many times weekly) and progression (how to titrate exercise dose up to the desired one) to gradually increase the exercise dose as tolerated by the patient.
3. Inclusive of All Exercise Forms: While endurance and strength exercises are fundamental, flexibility exercises and multicomponent activities like yoga and tai-chi might also be incorporated.
4. Gradual Progression: Starting with low-intensity protocols and cautiously increasing intensity ensures manageable exercise and does not lead to adverse effects.
5. Addressing Psychosocial Factors: Exercise can mitigate the negative impacts of psychosocial stress and unhealthy lifestyles which are common among FM patients.
6. Holistic Health Improvement: Exercise transcends mere symptom management; it enhances overall health for individuals afflicted with FM (94, 95).

In summary, exercise is a transformative approach that extends beyond treating FM symptoms to improve holistic health. This strategic approach requires careful consideration of patient-specific factors to optimise outcomes. This is achieved by adopting a prescriptive method similar to that used for medical prescriptions, ensuring a tailored and personalised prescription of each exercise (like a pharmaceutical treatment).

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