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Cognitive and emotional factors in chronic low-back pain, fibromyalgia, and comorbid obesity

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Part I: Psychological factors in patients with chronic low-back pain and obesity

List of abbreviations

BMI	Body Mass Index
CLBP	Chronic Low Back Pain
FM	Fibromyalgia
LBP	Low Back Pain
IASP	International Association for the Study of Pain
WC	Waist Circumference
SBST	Star Back Screening Tool
NPRS	Numeric pain rating scale
RMDQ	Roland Morris disability questionnaire
PCS	Pain catastrophizing scale
TSK	Tampa scale of kinesiophobia
EQ-5	European Quality of life instruments
RMSEA	Root Mean Square Error of approximation

TLI	Tucker Lewis Index
CFI	Comparative Fit Index
ICC	Intraclass Correlation Coefficient

Introduction

1. Acute and chronic pain: two different phenomena

Acute and chronic pain are different clinical entities. Acute pain is widely recognized as a survival warning system that alerts to potential tissue damage. It is defined as a physiological response to a harmful chemical, thermal, or mechanical stimulus that is associated with surgical intervention, trauma, or acute illness. Acute pain serves a protective and adaptive function that is typically limited to the duration of healing of the underlying cause. Its biological function is to demand attention and alter behavior by prioritizing escape, protection, and recovery [1]. The biological value of acute pain is lost when it becomes persistent. Indeed, chronic pain is typically non-adaptive, is frequently unrelated to a specific cause, and lasts beyond the expected healing and recovery time [2,3]. Chronic pain is a significant, widespread, and complex problem, and while it is still poorly understood, it is increasingly being viewed as a disease entity in and of itself rather than as "symptom" of another condition [4,5]. It appears to be characterized by pathological changes in the central and peripheral nervous systems [6,7]. Chronic pain conditions can have a significant impact on quality of life and disability [8]. Psychosocial and cognitive variables were found to be strongly related to the transition from acute pain to chronic pain [9].

2. Biomedical model of pain

Pain was once thought to be caused by a direct link between observable organic pathology and patient-reported symptoms. As a result, it was expected that the amount of pain was perfectly

proportional to the amount of tissue damage that was 'causing' the pain. Symptoms such as pain are manifestations of an observable disease, according to the biomedical model, and pathological changes and clinical features are inextricably linked. The primacy of structural pathology has supplanted functional pathology as the primary criterion for disease detection, with behavioral, psychological, and social factors being overlooked. Pain was thought to be dichotomous in the traditional biomedical model: physical (somatogenic) or psychological (psychogenic). Pain that was not directly related to tissue damage or pathological abnormalities was defined as psychogenic pain. Thus, where there was no identifiable pathology, pain could be labeled "psychogenic", and psychological factors were assumed to be the main mechanistic contributors to pain. According to this model, pain is reduced to a complex system of nerve signals, while other factors such as individuals' idiosyncrasies and the psychosocial context are ignored. Indeed, biomedical pain theories have primarily focused on the neurophysiological aspects of pain, particularly the concept of nociception, which reduces painful sensations as a result of nociceptor activation. However, this model did not adequately account for factors related to the subjective experience of individuals. Pain experience is complex, inherently subjective, value-laden, and difficult to determine objectively and empirically, because it is defined by body signals and language, both of which are culturally influenced and subject to different interpretations.

The current understanding of pain is multidimensional and dynamic rather than linear [10]. To optimize treatment, the era of personalized pain medicine underlines the pivotal role of interrelationships between psychological states, social/contextual forces, and neurobiological processes for each patient. Indeed, the International Association for the Study of Pain defines Pain as a distressing sensory and emotional experience that is linked to, or resembles, actual or potential tissue damage [11]. According to the IASP definition, pain can occur even if there is no detectable tissue damage. There are three types of pain: nociceptive, neuropathic, and nociplastic.

Nociceptive pain is caused by the stimulation of nociceptors as a result of a noxious stimulus or a stimulus that may cause tissue damage. This is the most common type of chronic pain, and it includes both primary osteoarthritis and spinal pain [12]. Pain is classified as neuropathic when it is caused by a disease or dysfunction of the somatosensory nervous system [13]. Numbness, tingling, allodynia, and other sensory abnormalities are frequently associated with it. Chronic neuropathic pain, unlike nociceptive pain, is always maladaptive and associated with lower quality of life and higher levels of disability [14]. Nociplastic pain is caused by abnormal pain signal processing in the absence of tissue damage or illness involving the somatosensory system. Fibromyalgia, irritable bowel syndrome, and nonspecific low back pain are all conditions characterized by nociplastic pain, previously, all of these conditions were referred to as functional pain syndromes. These disorders are characterized by abnormal mechanisms such as increased sensory processing and decreased inhibitory pathways.

Table 1. IASP definition of nociceptive, neuropathic and nociplastic pain

	Nociceptive pain	**Neuropathic pain**	**Nociplastic pain**
Causes	Tissue or potential tissue damage	Disease or injury affecting the nervous system	Maladaptive changes that affect nociceptive processing and modulation without objective evidence of tissue or nerve damage
	Somatic: - Bones (bone fracture, metastases); - Muscles (dystonia, muscle spasm); - Joints (osteoarthritis);	Central: - Traumatic (spinal cord injury); - Vascular (stroke); Neurodegenerative (Parkinson's disease);	- Diffuse sensitization (fibromyalgia) - Functional visceral pain (irritable bowel syndrome, bladder pain syndrome)

	- Skin (postoperative pain, burns) Visceral: - Mucosal injury (peptic ulcer) - Obstruction or capsular distension (gallstones, kidney stones) - Ischaemia (angina, mesenteric ischaemia) - Tissue injury (cancer, cirrhosis)	- Autoimmune (multiple sclerosis); - Inflammatory (transverse myelitis) Peripheral: - Infections (HIV, acute herpes zoster or postherpetic neuralgia) - Nerve compression (carpal tunnel syndrome) - Trauma (complex regional pain syndrome type 2) - Metabolic (amyloidosis, nutritional deficiencies) - lschaemic (peripheral vascular disease, diabetes) - Toxic (chemotherapy-induced peripheral neuropathy) - Auto-immune (Guillain-Barré syndrome)	- Regional somatic sensitisation (complex regional pain syndrome type 1, temporomandibular disorder) Altered nociception: - Peripheral sensitisation (proliferation of sodium channels, sympatho-afferent coupling) - Central sensitisation (N-methyl-D-aspartate activation, cortical reorganisation) - Diminished descending inhibition (periaqueductal grey and rostroventromedial medulla) - Immune system activation (glial cells, chemokines, cytokines, and other inflammatory mediators)

		- Genetic (inherited neuropathy)	
Accompanying symptoms	Higher rates of psychopathology including depression and anxiety than controls	Greater psychological distress and concomitant disability than observed in nociceptive pain	Psychological distress affects most individuals. Cognitive symptoms, insomnia, and fatigue are common. Gastrointestinal complaints and sensitivity to other sensory stimuli often occur. Association with multiple sensitivity reactions to chemicals

3. Biopsychosocial model of pain

According to the findings of a study conducted by the American Academy of Pain Medicine's Pain Psychology Task Force, most pain treatments are firmly rooted in the biomedical realm, focusing on nociception while ignoring the other half of the pain definition, which is rooted in psychology [15]. Pain is a public health issue that necessitates a more nuanced approach than many other medical issues. Additionally, effective pain assessment and treatment should be considered a basic human right [15]. The need for more effective pain management has become a key aspect of patient-centered care. The Institute of Medicine's report on Relieving Pain in America [16], as well as the National Pain Strategy [17], emphasizes the importance of treating pain in a more comprehensive manner, as well as improving multidisciplinary pain management. Experts in the field of pain education have advocated for improved pain education in medical schools [18,19], with a focus on the cognitive and affective aspects of pain [20]. New concepts have emerged as a result of the modern trend toward

personalized medicine, such as the redefinition of chronic pain as a multidimensional biopsychosocial phenomenon.

The biopsychosocial model of health and illness, proposed by psychiatrist George Engel in 1977 [21] to emphasize the importance of the mind-body connection, has been applied to a wide range of chronic illnesses. Pain frequently arises in the nervous system in response to physiological stimuli, but the pain experience of each person is determined by a dynamic interaction of biological, psychological, and societal processes. According to the biopsychosocial model, pain and disability are multidimensional and result from dynamic interactions between biological, psychological, and social factors that influence each other. To have a complete understanding of the patient's condition, the interwoven affiliation of the biological, psychological, and social elements unique to each chronic pain patient must be addressed. If any one of these elements is overlooked, standard treatment protocols are found to be inadequate [22,23]. Because patients with the same diagnosis may respond differently to standard treatment, the biopsychosocial approach to assessment and management aims to tailor treatment to the specific needs of the individual. To best assess the individual's unique pain condition, the biopsychosocial model incorporates physical, psychological, social, cognitive, affective, and behavioral measures, as well as their interactions.

Several chronic pain management guidelines [24–27] emphasize the importance of recognizing possible neurobiological mechanisms as well as psychosocial factors, which is consistent with the International Classification of Functioning, Disability and Health (ICF), the framework endorsed by the World Health Organization (WHO) for the description and measurement of health and disability [28]. An interdisciplinary team collaborates at this level to help the patient avoid physical deconditioning and overcome psychological barriers to recovery.

4. Psychological factors in the chronic pain experience

Negative psychosocial factors such as distress, trauma, fear, and catastrophizing have been shown to worsen pain and pain-related outcomes. Among general psychosocial factors, several evidence highlights that symptoms of depression, anxiety, and emotional distress play a significant role in key long-term outcomes of chronic pain, including functional capacity [29,30], healthcare costs [31], mortality [32], and suicide [33]. A growing body of evidence suggests that psychological and physical trauma is associated with chronic pain. There is a strong potential link between traumatic childhood experiences and the development of chronic pain later in life [34].

Although positive psychosocial factors such as social support, active coping skills, acceptance, and self-efficacy have been shown to improve pain and pain-related outcomes. Resilience factors are becoming a more important target for intervention because they are less established and more adaptable to tailored support, although the risk factor side of the biopsychosocial model of chronic pain has received more attention in research and clinical practice. Among pain-specific psychosocial constructs pain coping, kinesiophobia, pain catastrophizing, self-efficacy are the most important [35–39].

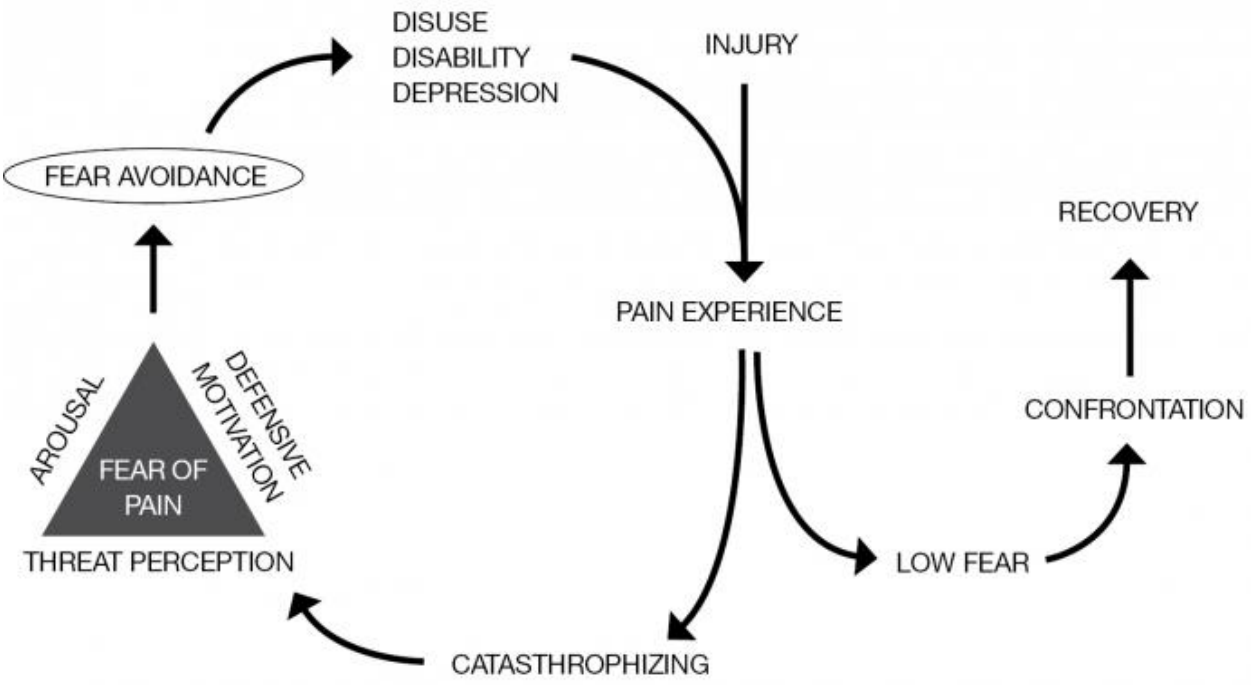
5. Fear avoidance model

A model built according to a biopsychological approach is the fear avoidance model (FAM). The FAM is one of the most important models in pain research and tries to delineate the trajectory that leads people who experience acute pain to experience chronic pain. FAM emphasizes the importance of the beliefs that patients have about pain in increasing fear and avoidance. The most significant model in the context of fear avoidance is the one developed by Vlaeyen et al, initially

formulated for low back pain. When a person experiences an episode of pain, his or her interpretation of pain influences behavior. For example, if a person interprets pain as dangerous, catastrophic, and a sign of pathology, it will lead the subject to an excessive fear of pain and movement associated with pain. In this sense, avoidance will prevent the patient from "correcting" their beliefs about pain. Hypervigilance to pain signals and avoidance are functional in an acute pain setting but become dysfunctional in chronic pain. Avoidance of movement and activities, in addition to causing deconditioning, contributes to psychological distress and isolation.

The FAM proposes two opposing behavioral responses: confrontation and avoidance, and shows how injured patients can become trapped in a downward spiral of increasing avoidance, disability, and pain. The Fear Avoidance Model (FA model) proposes that, for some patients, a negative evaluation of pain as catastrophic leads to fear of situations and movements associated with their pain. This fear leads to avoidance of such situations and movements which have the immediate effect of preventing daily activities which are expected to cause pain from being completed. It also leads to hypervigilance, as evidenced by increased attention to body sensations and difficulty disengaging from such stimuli. One of the key risk factors that is believed to cause long-term problems is fear of movement and reinjury, resulting in avoidance. Avoidance behaviors are initiated in anticipation of pain rather than in response to pain; they may persist because there are fewer opportunities to correct (erroneous) expectations and beliefs about pain as a threatening signal. These avoidance behaviors contribute to physical dysfunction and disability; in fact, they have negative consequences for the musculoskeletal and cardiovascular systems, possibly leading to disuse syndrome. Furthermore, avoidance, which can lead to depression, irritability, frustration, and increased pain. On the contrary, if the injury/pain experience is perceived as nonthreatening, the model suggests that patients will confront and deal with it adaptively, leading to recovery.

Figure 1. Fear Avoidance Model



6. Obesity and chronic pain

A growing body of evidence suggests that pain and obesity are linked. The most widely accepted classification of obesity is a BMI of 30.0kg/m2 or a waist circumference (WC) of 88 cm or 102 cm for abdominal obesity in women and men, respectively [40]. The level of obesity is classified according to these criteria: class I (30–34.9 kg/m2), class II (35-39.9 kg / m2), and class III ($40 kg/m2). Numerous studies have found a link between obesity and chronic pain. According to a community study [41], obesity has been linked to a variety of pain diagnoses: low back pain, fibromyalgia, and abdominal pain. Obesity, on the other hand, is common among chronic pain patients. People who are in a lot of pain have more total fat mass and less total lean mass than those who are not [42]. In their study, Yunus et al. [43] discovered that more than 60% of women with

fibromyalgia were overweight or obese, with 32.2 percent being obese. Another study discovered that people with fibromyalgia had a higher mean BMI than people who were not in pain. According to longitudinal studies, obesity can also be a risk factor for the development of chronic pain. On the other hand, weight gain can be a side effect of chronic pain. Chronic pain is one of the most reported common reasons for weight gain in patients with obesity [44]. The frustration that comes with functional limitations can lead to overeating [45]. Sedentary behavior, insufficient sleep, and side effects of medications are common side effects of chronic pain that can contribute to weight gain in patients with chronic pain [46]. Obesity, according to research, makes chronic pain more problematic in general [47]. In patients with chronic pain, obesity is associated with increased physical disability and psychological distress [48].

7. Chronic low-back pain

Chronic low back pain (CLBP) is a common musculoskeletal condition that causes more functional disability (activity limitation, absenteeism at work, and loss of productivity) than any other condition and has a high rate of recurrence. CLBP is defined as low back pain (LBP; pain below the costal margin and above the gluteal fold) lasting at least 12 weeks [50]. CLBP imposes a significant burden, and current knowledge and treatment approaches are inadequate to alleviate it. Arthritis, chronic low back pain (CLBP), and headaches have all been thought of as separate disorders caused by peripheral pathology in the past [4]. Because pain has historically been viewed as a symptom of an injury or disease, clinicians have focused on identifying etiologic factors to devise a treatment. Beyond the initial triggers, a number of interconnected factors have been identified as contributing to the development and maintenance of pain [16].

Chronic low back pain is increasingly being thought of as a mixed pain syndrome with nociceptive and neuropathic components. There is also a lack of understanding of how different psychosocial factors may contribute to the link between CLBP and disability.

7.1 Chronic low-back pain related disability

Disability resulting from chronic low back pain is a complex and multidimensional phenomenon [51]. It is associated with high health and social costs, in particular loss of productivity, absenteeism from work, and expenditure on health care system [52]. Disability related to chronic low back pain is influenced by a number of factors: perceived pain intensity, psychosocial factors [53–55], occupational factors. Cognitive aspects seem to play a prominent role in influencing the experience of chronic pain. Indeed, the most studied psychological and cognitive aspects are self-efficacy, fear of movement, pain related fear and pain catastrophizing [53,54,56–59].

7.2 Chronic low-back pain and obesity

Obesity and chronic low back pain (CLBP) are two common and debilitating medical conditions [60]. Both conditions come at a high cost to society. The social and financial burden of obesity and CLBP is exacerbated by the costs associated with chronic diseases related to obesity and various CLBP treatments [60–62]. Obesity is becoming more prevalent causing it to be classified as an epidemic [63]. As the morbidity and mortality rates associated with obesity continue to rise, it has become a serious public health concern [64]. Obesity, on the other hand, is not only common, but also costly [41]. Obesity has been linked to several chronic pain conditions [65]. Obesity and pain have traditionally been treated as two distinct fields of study. However, in recent years, the two fields

have merged. This research crossover is significant because people with chronic pain are frequently obese [66], and those who are obese are frequently in pain [67]. As a result, researchers have proposed common physiological pathways that underpin both obesity and pain [66–68]. More importantly, there is evidence of a direct link between obesity and CLBP, indicating that more research is needed [69–72]. Low back pain is more common as BMI rises [73]. Obesity and CLBP research, on the other hand, is scarce and poorly understood.

8. Research project's goals

Chronic pain is a significant problem that affects millions of people. Although the level of perceived pain plays an important role in determining quality of life and associated disability, psychosocial factors also play a role. However, researchers have begun to examine the possible associations between pain, disability, and psychological factors. This type of research is important because it allows us to understand which psychological factors can be addressed. The main areas of research include (1) catastrophizing cognition, (2) coping responses, and (3) beliefs related to pain. In this research project, we focus primarily on two specific factors of FAM, pain catastrophizing, and fear avoidance.

The objective of this doctoral project is to evaluate the association between pain beliefs, pain intensity, and disability in a specific and still poorly studied population, namely, subjects with chronic pain and obesity. In this first part of the project, we will present the studies conducted on individuals with chronic low back pain and obesity. Since the importance of evaluating the whole patient through a biopsychosocial lens, comorbidities, cognitive/emotional/behavioral traits, and QoL/functional impairment must be included. In the first study of this research project, the objective was to validate a questionnaire developed to assess both the physical and psychological

characteristics of the patient's pain experience. In the second study, we evaluated the contribution of pain catastrophizing and kinesiophobia to perceived pain intensity and disability. In the third study, kinesiophobia was then evaluated as a mediator of the relationship between pain intensity and disability.

Study I: Factor structure, validity, and reliability of the STarT Back Screening Tool in Italian obese and nonobese patients with chronic low-back pain

Abstract

The STarT Back Screening Tool (SBST) is a self-report questionnaire that assesses risk factors for disability in chronic back pain patients. It can be used to provide cost-effective stratified care, but reports on its psychometric properties have been mixed. The purpose of this study was to assess the factorial structure and psychometric properties of the STarT Back Screening Tool in Italian (SBST). In a tertiary care hospital and a clinical private center, a cross-cultural adaptation and validation study was conducted. Patients with low back pain, both with obesity and without obesity, were included in the study. Patients completed self-report questionnaires at baseline and after 7 days. The factorial structure, internal consistency, test-retest reliability, and construct validity of the SBST were assessed. The study enrolled a total of 146 patients (62 from Sample 1 and 84 from Sample 2). Confirmatory factor analysis proved that the original two-correlated factors model was adequate. Due to item 2's low correlation with the other items, Cronbach's alpha for the total scale and subscales were both below the cutoffs. Test-retest reliability was adequate. Except for the Roland-Morris Disability Questionnaire, the SBST had moderate correlations with comparison questionnaires. The SBST has good psychometric properties and can be used to identify prognostic factors for patients with back pain.

1. Introduction

Back pain is a very common condition [74,75] and has a significant and negative influence on mobility, sleep, and activity participation [76]. Obesity increases the risk of back pain-related impairment and is a risk factor for back pain due to underlying biological mechanisms. The two disorders share risk factors such as age, gender, race/ethnicity, and lack of physical activity [77–79]. Because back pain becomes chronic and causes long-term disability in 2% to 7% of cases, it is critical to identify people who are at risk of poor treatment outcomes [80,81].

Pharmacological treatment, exercise, manual therapy, and psychological interventions are all common components of rehabilitation [82,83]. These treatments have been shown to reduce pain and impairment, particularly when administered in a multidisciplinary setting [84]. However, between 30% and 40% of patients do not respond to treatment. [85,86]. Demographic factors such as age, physical factors such as pain duration, severity, and disability, and psychological factors such as catastrophizing, anxiety, depression, and kinesiophobia [87,88] are all characteristics that can be used to predict outcomes. Therefore, it becomes critical to quickly risk factors.

The STarT Back Screening Tool (SBST) [89] was developed for this purpose. The SBST has a 9-item that evaluates modifiable physical and psychological risk factors for disability outcomes. The authors propose the following scoring system. Patients with total scores of 0 and 3 are considered low risk, those with overall scores ≥ 4 but with scores <4 in the psychological subscale are considered at medium risk and those with total scores ≥ 4 and scores ≥4 in the psychological subscale at high risk [78,89]. The SBST total scores predict 3- and 6-months disability [89,90], quality of life, work ability [91], and functional recovery after physical treatment [92]. Furthermore, the implementation of stratified care based on SBST scores was clinically and cost effective in the long term [93–95].

The original questionnaire and its translated versions have good or excellent test-retest reliability [90,96–100], construct validity [89,90,96,100] and responsiveness [101]. The internal consistency estimates are more heterogeneous, with some studies reporting good internal consistency [89,96–98] and other studies reporting poor internal consistency [99,102,103]. Surprisingly, the factorial structure has received little attention. To the best of our knowledge, the distinction between physical and psychological items, the absence of additional sources of variability, and the existence of a link between the latent components have not been explicitly confirmed to confirmatory procedures. Knowledge of these features is required to justify the computation of subscale scores and the total score.

The SBST was translated into Italian and has been found to be linguistically accurate, understandable, and acceptable for use by Italian-speaking patients [104]. However, its reliability and construct validity, however, have not been addressed. Validation of the Italian version of the SBST in both patients with and without obesity and low back pain should help determine the best prognosis and treatment options [105]. As a result, the purpose of this study was to evaluate the factorial structure, its internal consistency, test-retest reliability, and construct validity of the Italian version of the SBST.

2. Methods

This investigation was based on data from two samples. During the first week of a 4-week comprehensive rehabilitation program and weight loss management, obese patients admitted to the Istituto Auxologico Italiano's Rehabilitation Unit and Research Laboratory in Biomechanics and Rehabilitation and referred for medical attention for back pain were included in Sample 1. Sample 2 consisted of patients referred to the Accademia Italiana Medicina Osteopatica's training and

clinical internship center. A medical diagnosis of back pain not explained by trauma or other disorders, as well as an age range of 18 to 80 years, were required for both samples.

Back pain was defined as pain or discomfort between the costal margins and the superior gluteal line, with or without leg pain. Patients who were unable to provide their informed consent were not allowed to participate in the study.

After being enrolled, participants were asked to complete a short battery of self-report questionnaires, including the SBST. On a subsequent visit, they were asked to complete the SBST after 7 days. This study was approved by the Institutional Ethical Committee.

3. Measurement Instruments

- The SBST was part of a set of self-report questionnaires given at the start of the study, including the following.
- The Numeric Pain Rating Scale (NPRS) is an 11-point pain scale that measures the intensity of current pain from 0 to 10 (worst possible pain) [106].
- The Roland-Morris Disability Questionnaire (RMDQ) [107,108]. The RMDQ is a valid and reliable measure of physical disability that consists of 24 items that list limitations to everyday activities that are rated on a binary response system ("yes" or "no"). A higher value indicates a higher level of disability.
- The Pain Catastrophizing Scale (PCS) [109,110]. The PCS is a self-report scale that uses 13 items on a 5-point Likert-type scale ranging from 0 ("not at all") to 4 ("extremely") to assess pain catastrophizing ("all the time"). The PCS evaluates the thoughts and feelings that come with pain. We used the total score in this study, with higher values indicating higher levels of catastrophizing [110,111].

- The Tampa Scale of Kinesiophobia (TSK) [112,113]. The TSK is a 17-item questionnaire that was developed as a measure of pain-related fear of movement. It uses a 4-point Likert scale ranging from 1 (“completely disagree”) to 4 (“completely agree”). Higher numbers indicate greater fear of moving.
- The European Quality of Life Instrument (EQ-5D) [114]. The EQ-5D is a five-item self-report questionnaire that assesses mobility, self-care, regular activity, pain/discomfort, and anxiety/depression. The EQ-5D in Italian has been validated, and normative values are now available [115].

After 7 days from baseline, the battery included SBST, NRS and a single question on a 7-point scale ranging from 0 ('No improvement') to 6 ('Complete recovery'), indicating a perception of improvement from baseline.

4. Statistical Analysis

Frequency and percentages were used to investigate categorical variables. Medians and interquartile ranges (IQR) were used to describe ordinal variables, while means and standard deviations were used to describe interval and ratio variables. If necessary, chi-square, Mann-Whitney, and t-tests were used to examine differences in demographic and clinical factors between the two samples. Because missing data accounted for 5% of the total, it was removed from the analyses.

A confirmatory factor analysis evaluating a two correlated factors model distinguishing a physical (items 1 to 4) and a psychosocial (items 5 to 9) subscale was used to assess the structural validity of the SBST [116]. A diagonally weighted least squares estimator with robust standard errors was used to estimate the parameters. If the Root Mean Square Error of Approximation (RMSEA) was

less than 0.06 and the Tucker Lewis Index (TLI) and Comparative Fit Index (CFI) were both greater than 0.95, the model fit was considered adequate [117]. Item loadings were examined to determine the contribution of each item to the respective subscale. Item loadings were considered excellent if ≥.71, very good if <.71 and ≥.63, good if <.63 and ≥.55, fair if <.55 and ≥.45, poor if <.45 and ≥.32 and very poor if <.32 [118].

The Cronbach's alpha was calculated to determine the SBST's and its subscales' internal consistency. The acceptable internal consistency cut-off was 0.70 [119]. Furthermore, the "α if item deleted" technique was used to identify whether removing an item's improved the Cronbach's α coefficient. The Intraclass Correlation Coefficient (ICC) was used to estimate test-retest reliability using the SBST scores at the baseline and after 7 days. Patients who reported during the second administration that their pain had sufficiently, mostly, or completely resolved at the single question investigating their perception of improvement were excluded from this analysis. To calculate the ICC, a two-way mixed-effect ANOVA model with interaction for the absolute agreement between single scores was used ($ICC_{3,k}$) [120]. Values ≤ .5 indicate poor reliability, values >.5 and ≤.75 indicate moderate reliability, values >.75 and ≤.9 indicate good reliability, and values > .90 indicate excellent reliability [121].

A set of prespecified hypotheses about the correlations between the SBST and the comparison questionnaires was formulated to assess construct validity [122]. Pearson's r was used to examine the associations. We expected a moderate correlation (r >.3 and.6) between the SBST total score and the NRS, PCS, TSK, RMDQ, and EQ-5D scales.

The threshold for the identification of significant values was α = .05. The analyses were performed using the R (version 3.6.0) packages lavaan (confirmatory factor analysis) [123], psych [124] (internal consistency and test-retest reliability) and base [125] (correlations).

5. Results

5.1 Description of the sample.

A total of 146 patients were enrolled in Samples 1 and 2, for a total of 62 patients in Sample 1 and 84 patients in Sample 2. The demographic and clinical characteristics of the samples are listed in Table I. Patients in Sample 1 were older and had higher ratings for catastrophizing, disability, and kinesiophobia, as well as higher baseline SBST scores, than patients in Sample 2.

Table 1. Frequencies and descriptive statistics of the sample

		Total sample	Sample 1	Sample 2	
		(n=146)	(n=62)	(n=84)	p-value[a]
Age		55.4 (13.2)	59.1 (8.9)	52.6 (15.2)	<.01
Sex	Male	52 (35.9)	23 (37.1)	29 (34.9)	
	Female	93 (64.1)	39 (62.9)	54 (65.1)	.92[b]
PCS		17 (10.1)	21 (11)	14 (8.3)	<.01
EQ5D		0.7 (0.2)	0.7 (0.2)	0.7 (0.1)	.47
RMDQ		8.5 (5.9)	11.4 (6.2)	6.3 (4.7)	<.01
TSK		27.4 (7.4)	29.5 (7.4)	25.9 (7)	<.01
NRS t0		5.8 (2.2)	6.2 (2.4)	5.5 (2.1)	.06
NRS t1		3.8 (2.4)	3.2 (2.5)	4.2 (2.1)	.01
Perception of improvement		5 [4,6]	3 [2, 5]	4 [3, 6]	<.01[c]
SBST-Ph t0		2.1 (1.2)	2.6 (1.2)	1.8 (1.1)	<.01
SBST-Ps t0		1.1 (1.3)	1.2 (1.5)	0.9 (1)	0.15
SBST total t0		3.2 (2)	3.9 (2.2)	2.7 (1.8)	<.01
SBST-Ph t1		1.5 (1.2)	1.3 (1.3)	1.6 (1.1)	0.10
SBST-Ps t1		0.7 (1.1)	0.6 (1.1)	0.8 (1.1)	0.28
SBST total t1		2.2 (1.9)	1.9 (2.1)	2.4 (1.8)	0.11

Notes. Frequencies and percentages are reported for categorical variables, medians and interquartile ranges for ordinal variables and means and standard deviations for interval or ratio variables.

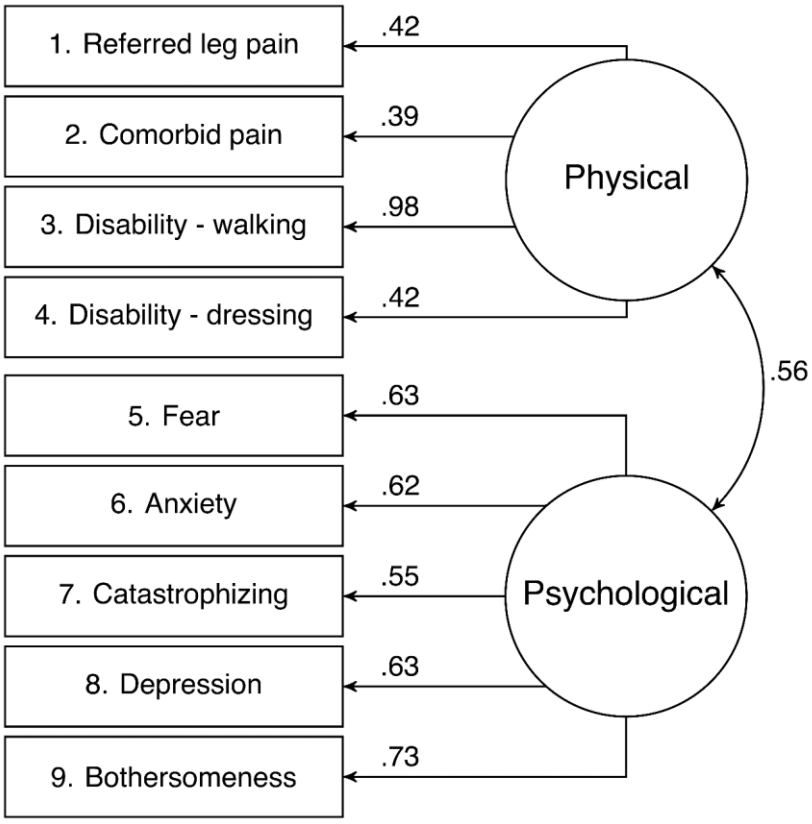
[a] p-values are based on independent sample t-test, if not otherwise specified. [b] based on Chi square test. [c] based on Mann-Wh

Abbreviations: PCS = Pain Catastrophizing Scale, RMDQ = Roland Morris Disability Questionnaire, TSK = Tampa Kinesiophobia, NRS = Numeric Rating Scale, SBST-Ph = Start Back Screening Tool – Physical subscale; SBST-Ps = Start Back Tool – Psychological subscale

5.2 Confirmatory factor analysis

The fit of the two-correlated factors model was adequate: CFI = .98, TLI = .99, RMSEA = .03. Items 1, 3 and 4 had excellent loadings on the physical subscale, whereas item 2 had a very poor loading. Regarding the psychological subscale, item 5 had a fair load, item 6 had a good load, item 8 had a very good load, and items 7 and 9 had excellent loads (Figure 1). The physical and psychological subscale had a correlation of .61. Overall, the two-correlated factors model was considered adequate and subscale scores were used in addition to the total score in the reliability and validity analyses.

Figure 1. Confirmatory factor analysis of the Start Back Screening Tool evaluating a two correlated factors model



5.3 Reliability

The Cronbach's α of the total scale was 0.64 in the total sample. The Cronbach's α in Sample 1 was .68 and in sample 2 was .55. The Cronbach's α of the physical subscale was 0.55 (.58 in sample 1 and .53 in sample 2), whereas the Cronbach's α of the psychological subscale was 0.61 (.73 in sample 1 and .55 in sample 2). The α if item deleted revealed that removing item 2 would increase the internal consistency of the total scale to 0.70 and the one of the physical subscales to 0.65.

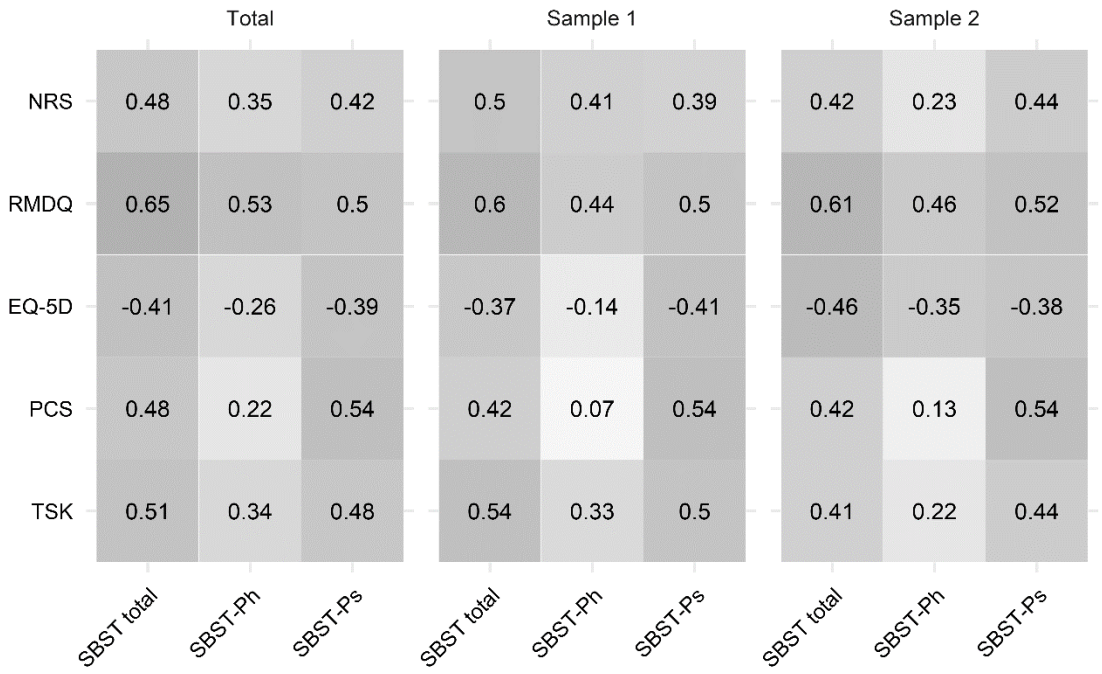
The ICC of the total scale was 0.84 in the total sample, indicating good test-retest reliability. The ICC in Sample 1 and 2 were .85 and .84, respectively. Regarding the physical subscale, the ICC was .77 in the total sample, indicating good test-retest reliability, and .75 and .84 in Sample 1 and 2, respectively. Finally, the ICC of the psychological subscale was .84 in the total sample and .85 and .84 in Sample 1 and 2, respectively. These values indicate good test-retest reliability.

5.4 Construct Validity

The correlations between the SBST total scale and subscales in the overall sample, as well as Samples 1 and 2, are shown in Figure 2. Most of the sample met all the hypotheses. The only assumptions that were not met were the correlations between the SBST total scale and the RMDQ in the entire sample and Sample 2, which were slightly higher than 60. The correlations between the SBST total scale and subscales in the overall sample, as well as Samples 1 and 2, are shown in Figure 2. Most of the sample met all of the hypotheses. The only assumptions that were not met were the correlations between the SBST total scale and the RMDQ in the entire sample and Sample 2, which were slightly higher than 60.

Figure 2. Correlations between the Start Back Screening Tool and the comparator instruments

Notes. Abbreviations: PCS = Pain Catastrophizing Scale, RMDQ = Roland Morris Disability Questionnaire, TSK = Tampa Scale for Kinesiophobia, NRS = Numeric Rating Scale, SBST-Ph = Start Back Screening Tool – Physical subscale; SBST-Ps = Start Back Screening Tool – Psychological subscale



6. Discussion

The SBST's factorial structure, test-retest reliability, and construct validity were investigated in a group of Italian patients with low back pain and/or obesity. The results show that this instrument assesses the physical and psychological aspects of a patient's pain, as well as its internal consistency, test-retest reliability, and construct validity.

To our knowledge, this is the first study that presents a confirmatory factor analysis of the SBST. Similarly to our study, but using an exploratory procedure, Abedi et al. [116] found that a two-factor model had a good fit with their data. The presence of the two factors is consistent with the authors of the original questionnaire's categorization of the items, which divided them based on their physical or psychological content [89]. The presence of a correlated-factor structure indicates that subscale scores can be calculated, and the moderate correlation between the two subscales supports the use of the total score. Future studies should assess whether the SBST is "unidimensional enough" to allow for the calculation of the total score, to provide a more solid argument for its use [126].

Similarly to other studies on translated versions of the SBST, the internal consistency of the total scale and of the subscales was below the cutoff [99,102,103]. Part of the lack of internal consistency was due to item 2's poor performance, as it had a low correlation with the physical factor in the confirmatory factor analysis, and its removal would improve the total scale and physiological scale's internal consistency, according to another study [99]. This may be due to the fact that this item assesses comorbid neck or shoulder pain, which may be unrelated to other physical aspects of the patient's pain experience. The SBST is not invalidated by its poor internal consistency or the lack of correlations in item 2, and we do not believe it needs to be revised. Because the SBST contains predictors of poor outcomes, its items may be measured using a formative model, in which the content of the construct is defined by its indicators, rather than a reflective model, in which the construct is assumed to be a latent factor influencing the individual's response to the items. Therefore, low correlations between the items could be expected [127]. Because comorbid pain is a significant risk factor for disability, item 2 should not be removed, as this would reduce the predictive power of the questionnaire. As a result, more research into the SBST's and its items'

ability to predict outcomes is required, which could provide a more solid foundation for revising the scale.

Overall, the psychometric properties of the Italian version of the SBST were adequate. The total score and subscale scores of the SBST had good test-retest reliability, indicating that the questionnaire can be used to assess prognostic factors for disability outcomes in both obese and non-obese patients with ABP. This is consistent with other studies finding that SBST has moderate to excellent test-retest reliability [90,96–100]. The construct validity of the SBST was adequate. According to the pre-specified hypotheses, the presence of moderate correlations between the SBST and comparison questionnaires assessing physical and psychological risk factors for physical disability can be used as an indicator that the questionnaire measures a similar construct but does not overlap with them. The presence of a high correlation with RMDQ has been reported elsewhere [90,116] and can be explained by the fact that the presence of multiple risk factors is associated with limitations in daily activities and therefore more disability.

There are a few flaws in this study. The differences between the two samples, which included patients with different clinical manifestations and levels of disability, are the main limitation. Separate reliability and validity analyses on the two samples were part of the solution. The fact that the participants in this study came from a tertiary care hospital and a clinical osteopathic center also limits the applicability of the findings to other clinical settings. The fact that patients received treatments between the first and second administrations of the SBST may have influenced the test-retest analysis. Finally, the SBST is a valid and reliable tool that can be used.

Study II: Kinesiophobia and pain catastrophizing as predictors of disability and pain severity in obesity and chronic low-back pain

Abstract

Patients with chronic low-back pain and obesity have an higher risk of long-term disability. We aimed to explore the contribution of two psychological factors (i.e., kinesiophobia and pain catastrophizing) to disability and pain severity in chronic low-back pain associated to obesity. We assessed pain severity, disability, pain catastrophizing, and kinesiophobia levels through a self-reporting questionnaire in 106 patients with chronic low back pain and obesity. We assess the role of pain catastrophizing and kinesiophobia on pain severity and physical disability using hierarchical regressions. Kinesiophobia, but not pain catastrophing were significantly associated with pain severity and physical disability. In patients with chronic low-back pain and obesity, kinesiophobia may be a critical factor that impact on physical disability and pain severity.

1. Introduction

Obesity is a growing public health issue [128] that has significant personal, community and financial consequences [128]. It is linked to poor physical and psychological well-being [129], and worse physical functioning [130], particularly when combined with other disorders, such as pain conditions [131]. Obesity represents a risk factor for chronic low-back pain (CLBP) [132]. CLBP is pain condition characterized by persistent pain (lasting more than 3 months), with none recognizable mechanical cause [133]. Patients with CLBP and obesity have severe functional limitations [72] and report high levels of disability [134].

Emotional and cognitive factors appear to influence the perception of pain [135]. The Fear Avoidance Model (FAM) [35,136] has received increasing attention in pain research. According to this model, patients who experience acute pain, cognitive and emotional responses to pain, such as pain catastrophizing and kinesiophobia, could influence the development of chronic disability [9,137–139]. Pain catastrophizing is a set of dysfunctional and negative cognitive-emotional responses to actual or anticipated painful sensations [139], which could lead people to magnify the threat of pain and feel helpless [140]. Kinesiophobia is an excessive, and debilitating fear towards movement and physical activity that result from fear of reinjury [141,142]. Fear of movement and catastrophization about pain may be functional for acute pain episodes, but they appear to be maladaptive when pain becomes chronic, because they may perpetuate physical activity aversion, worsening mobility, pain severity, disability, and lowering the pain threshold. Vincent et al. [143] found that in patients with CLBP affected by obesity have higher kinesiophobia than healthy weight individuals. In addition, kinesiophobia was found to be a predictor of disability [144]. In line, high levels of pain catastrophizing appeared to be related to higher levels of disability and pain severity [145]. Although these preliminary findings are presented, more evidence is needed on the contribution of

kinesiophobia and pain catastrophizing to pain severity and physical disability in patients with CLBP and obesity.

In summary, we conducted a cross-sectional study to assess the association of kinesiophobia and pain catastrophizing with physical disability and severity of pain in a sample of patients with obesity and CLBP.

2. Materials and Methods

A cross-sectional study was performed in which 106 individuals were consecutively recruited, from September 2018, 1st to July 2019, 31st, at the start of a month-long hospitalization at the Istituto Auxologico Italiano, U.O. di Riabilitazione Osteoarticolare, S. Giuseppe Hospital, Piancavallo, Italia. The sample size was estimated a priori with G.Power (version 3.1.9.4) [146] setting a medium effect size (0.15), an alpha of 0.05 and a power of .80, resulting in 92 participants. Patients were included according to the following criteria: age in years ≤ 70; obesity [40]; chronic pain in the lower back [147].

Exclusion criteria were: physical or mental inability to provide signed informed consent; low back pain duration < 3 months; diagnosis of fracture, neoplasia, bone metastasis, stenosis; neurogenic or radicular condition; neurological disease; diagnosis of other condition that could explain low back pain; postoperative pain.

This study was approved by the Ethical Committee of Istituto Auxologico Italiano (code 2020_02_18_04). All participants read, understood, and signed an informed consent document. All procedures on human subjects were conducted following the Helsinki Declaration of 1975, as revised in 1983.

2.1 Measures

Pain severity and physical disability were assessed using the following questionnaires:

- Numerical Pain Rating Scale (NPRS) was used to assess pain severity on a 11-point scale. The NPRS is widely used [148] and is a reliable instrument for assessing pain severity [148], in the case of chronic conditions [147]. Higher score indicates higher perceived pain.

- The Italian version [108] of the Roland-Morris Disability Questionnaire (RMDQ) was administered to assess physical disability. The RMDQ has 24 dichotomous items that assess the difficulty of performing daily tasks. Scores ranges from a minimum of 0 to a maximum of 24. The Italian version of the RMDQ showed levels of reliability and validity similar to the original version [108]. Higher levels of physical disability are reflected by higher scores.

The following questionnaire were used to evaluate pain catastrophizing and kinesiophobia:

- The Italian version of The Tampa Scale of Kinesiophobia (TSK) [113] was administered to evaluate kinesiophobia. The TSK has 13 items on a 4-point Likert scale [149]. The TSK is widely used in patients with CLBP [35]. The Italian version of the TSK has a good factorial structure and acceptable psychometric properties [113]. Scores range from 17 to 68, with higher scores indicating higher levels of kinesiophobia [113].

- The Italian version of Pain Catastrophizing (PCS) [110] was usedto evaluate the level of catastrophization about pain. The PCS has 13-items on a 5-point Likert scale (from 0 = “not at all” to 4 = “all the time”). The Italian validation has good psychometric properties in line with the original version [110]. Score ranges from a minimum of 0 to a maximum o52. Higher levels of pain catastrophizing are reflected by with higher scores [110].

2.2 Statistical analysis

Categorical variables were described as counts and percentages, whereas for continuous variables means and standard deviations were computed. The contribution of the TSK score and the PCS score to the variance of the NPRS score and the RMDQ score was evaluated with two independent multiple hierarchical regression. NPRS score (model 1) and RMDQ score (model 2) were entered as dependent variables. In both models, confounding variables, were entered in a first block. The PCS score and TSK score were included in the second block. Confounding variables in model 1 were: gender, age and BMI [150,151]. Confounding variables in model 2 were: sex, age, BMI [150,151] and NPRS scores [152]. ΔR^2 was used to evaluate the amount of variance in the dependent variables explained by factors included in the second blocks compared to the first block. Jamovi (version 1.2)[153] was used to perform the statistical analysis. P-values less than .05 were considered statistically significant.

3. Results

3.1 Participant's characteristics

The sample was composed of 68 women and 38 men. Demographical and clinical factors, as well as scores reported at the questionnaires, are depicted in Table 1.

Table 1. Demographic and clinical characteristics of the sample (n=106)

	N (%)	Mean ± sd
Gender		

Female	68 (64.2)	
Male	38 (35.8)	
Age		57.1±9.67
Body Mass Index (kg/m^2)		39.8 ± 5.58
Numeric Pain Rating Scale (NPRS)		6.15 ± 2.45
Roland Morris Disability Questionnaire (RMDQ)		11.33 ± 6.74
Tampa Scale of Kinesiophobia (TSK)		29.9 ± 7.96
Pain Catastrophizing scale (PCS)		23.5 ± 11.1

3.2 Pain severity

The full model including gender, age, BMI, pain catastrophizing and kinesiophobia as predictors and pain intensity as dependent variable was significant, R^2=0.198, F (5,100) =4.94, p<0.001. The inclusion of the PCS score and the TSK score explained approximately 18% additional variance (ΔR^2=0.177), compared to the first block that included only the confounders. Only the TSK score significantly predicted pain severity (Table 2).

Table 2. Linear regression model evaluating the effect of control factors and psychological components of kinesiophobia and pain catastrophizing on pain severity.

	B	95% CI	p-value
Block 1: Confounding Factors			
Age	-0.009	-0.06 – 0.04	0.700
Gender	-0.524	-1.44– 0.39	0.259
BMI	-0.038	-0.04– 0.12	0.346
Block 2: Psychological variables			

Tampa Scale of Kinesiophobia	0.126	0.07 – 0.18	<0.001*
Pain catastrophizing scale	0.010	-0.03 – 0.05	0.528

3.3 Physical disability

The full model (including sex, age, BMI, pain intensity, pain catastrophizing and kinesiophobia) score was statistically significant, $R^2 = 0.339$, $F(6, 99) = 8.46$, $p < .001$. Pain catastrophizing and kinesiophobis explained approximately 10% additional variance ($\Delta R^2=0.102$). The TSK score was found to significantly predict the RMDQ score (Table 3).

Table 3. Linear regression model evaluating the effect of control factors, kinesiophobia and pain catastrophizing on physical disability.

	B	95% CI	p-value
Model 1: Confounding Factors			
Age	0.084	-0.03 – 0.20	0.162
Sex	-1.424	-3.74 – 0.89	0.226
BMI	-0.06	-0.26 – 0.14	0.555
Numeric Pain Rating Scale	0.741	0.24 – 1.23	0.004*
Model 2: Psychological factors			
Tampa Scale of Kinesiophobia	0.298	0.13 – 0.46	<0.001*

Pain catastrophizing Scale	0.008	-0.09 – 0.11	0.874

4. Discussion

We conducted a cross-sectional study to evaluate the role of kinesiophobia and pain catastrophizing as predictors of physical disability and pain severity in a sample of patients with both obesity and CLBP.

Kinesiophobia is a critical factors of the FAM [137]. Its role in explaining pain severity and physical disability was previously highlighted in patients with both obesity and CLBP [154]. Kinesiophobia results from the fear of injury due to movement or physical activity. As a consequence, patients with high levels of kinesiophobia may avoid pain-inducing movements, increasing disuse and disability [155].

Obesity might be a key factor in explaining the significant contribution of kinesiophobia to pain severity and disability in our sample. Obesity is often associated to respiratory difficulty, greater movement difficulties and discomforts [156]. So, patients with obesity may develop greater fear of movement and activity aversion. Indeed, Vincent et al. [143] that patients with severe obesity and CLBP reported higher levels of kinesiophobia compared to normal weight patients with CLBP [143]. Furthermore, they examined the relationships between LBP, kinesiophobia, and disability in individuals with LBP and overweight [154], and found that the TSK score is a significant predictor of the severity of LBP and perceived disability [154]. Interestingly, this previous evidence and our study shared similar findings, even though individuals with a different range of age were examined. Indeed, Vincent and colleagues evaluated an elderly population, while our sample showed a wider age range.

In contrast, we found that pain catastrophization was not significantly associated with pain severity and physical disability. Our findings are in disagreement with previous results [138,152,157,158]. Nevertheless, previous studies did not specifically examined patients with obesity and CLBP. Moreover, our sample reported moderate and severe degrees of obesity. We might hypothesize that patients with obesity have different pain cognitions and beliefs more predominant than pain catastrophizing. Future studies on obesity and CLBP should evaluate this hypothesis.

Several limitations must be addressed. Because of the cross-sectional design, it is not possible to draw a causal relationship. Longitudinal studies are required to confirm the hypothesis that dysfunctional cognitions contribute to the onset and maintenance of pain and disability in patients with CLBP and obesity. Because the sample was composed of hospitalized patients, there is a risk of selection bias; thus, generalization to patients in different settings should be done with caution. Patients with CLBP and obesity may have different pain coping strategies compared to their healthy weight counterparts. Furthermore, the drug regimen of the enrolled subjects was not evaluated and it has been previously reported [143] that patients with obesity reported greater narcotic consumption to manage pain symptoms compared to normal weight patients. This might suggest that in this specific population, the use of narcotics may be a coping strategy. Furthermore, the presence of emotional eating has not been assessed. Emotional eating might be a pain coping strategy, as previously reported [45]. This behavior might lead to positive energy balance, weight gain, and increased pain and disability, according to a previous study [159].

However, our work has several strengths including the use of validated, reliable survey questionnaire and a sufficient sample size. Furthermore, we examined a clinical population (i.e., people with CBLP and obesity) poorly considered in research.

In sum, psychological factors play a significant role in pain management. In our research, the importance of kinesiophobia in pain severity and physical disability is highlighted. This could be

critical in developing effective pain management rehabilitative programs. Indeed, in patients with obesity and CLBP, kinesiophobia can be a therapeutic target to consider in interdisciplinary pain management programs.

Study III: The mediating role of kinesiophobia in the association between pain severity and disability in patients with obesity and chronic low back pain.

Abstract

Chronic low-back pain and obesity are associated with severe functional limitations, as well as a high level of disability. Kinesiophobia may play a key role in the relationship between pain severity and disability. Our aim was to evaluate the mediating role of kinesiophobia in the relationship between pain severity and disability in patients with chronic low-back pain and obesity. A total of 213 people with chronic low-back pain and obesity completed self-report questionnaires to assess kinesiophobia, pain severity, and disability. Kinesiophobia was found to be a partial mediator of the association between pain severity and disability. According to our results, kinesiophobia is an important psychological factor that should be considered in rehabilitative programs for chronic low-back pain promote better physical functioning in patients with obesity.

1. Introduction

Chronic low-back pain (CLBP) is defined as pain that persist for more than 3 months, contribute to emotional distress, functional disability, and is not explained by another condition [160]. CLBP is the leading cause of disability worldwide [161]. Despite different available treatments, such as surgery and pharmacotherapy [162], its prevalence is increasing. The prevalence of CLBP is directly related to higher body mass index (BMI). Indeed, obesity (defined as BMI ≥30 kg/m^2 [40]) is a risk factor for its development [77,163]. As a reulst, as the obesity rates rise, so do the rates of musculoskeletal disorders [60,63]. Patients with CLBP and obesity face severe functional limitations and reported decrease physical funzioning [72,134] as a result of a dual problem: movement impariment caused by obesity, and pain interference due to CLBP [164]. Obesity and CLBP negatively influence each other; indeed, decreased level of physical activity due to pain contribute to weight gain [143,165]. The perceived pain severity impact on the level of disability in acute low-back [166,167] and chronic low-back pain [168]. However, the reduced physical functioning of patients with acute low-back and chronic low-back pain is not entirely explained by the level of pain intensity [166–168]. Identifying critical factors associated with pain severity and disability is useful to develop rehabilitative programs. However, the mechanisms by which pain causes disability in people with obesity and CLBP are unknown [138,169]. In addition to pain severity, psychological, and social factors contribute to disability, in line with a bio-psycho-social perspective. In chronic pain research, the fear-avoidance model (FAM)[9,137,170] has gained increasingly recognition. The FAM emphasizes the role of cognitive and emotional aspects that impact on the development of chronic pain and disability. Indeed, according to this model [9,137,170] pain severity and disability are associated via psychological components(i.e. pain catastrophizing and kinesiophobia)[9,137,171].

Kinesiophobia is an dysfunctional, irrational fear of movement and physical activities, resulted from a perception of vulnerability due to painful injury or fear of reinjury [35]. As a result, chronic

pain patients might associate movements with the occurrence or exacerbation of pain [170,172], contributing to deconditioning and disuse [137,173]. Kinesiophobia is associated with pain severity [157] and disability [174] in chronic low-back pain patients. It seems that also in patients with both obesity and CLBP, kinesiophobia is a factor related to pain severity [56,175] and disability [56,176]. Moreover, they report higher levels of kinesiophobia, higher disability and decreaed physical functioning compared to their normal-weight patients [144]. In fact, patients with obesity usually report dyspnea, musculoskeletal discomfort, and joint pain during movements [177]. These additional issues might contribute to the perception of the physical activity as unpleasant and pain inducing. Kinesiophobia is associated with pain severity and disability, but it is also a mediating factor that explains their association. The FAM [9,137,170] outline how pain produces disability through kinesiophobia. Cross-sectional mediation studies on chronic back pain patients [168,178] and individuals with a whiplash injury [179] have verified that kinesiophobia is a significant mediator of the relationship between pain severity and disability. Thus, the goal of our study is to verify if kinesiophobia is a psychological factor that can explain how perceived pain produces disability in patients with CLBP and obesity. We performed a cross-sectional study with the goal of evaluating the mediating role of kinesiophobia. As indicated by previous studies in chronic back-pain patients [168,178] we hypothesized that kinesiophobia would be a significant mediator of the association between pain severity and disability in patients with obesity and CLBP.

2. Materials and Methods

The Ethical Committee of Istituto Auxologico Italiano (code 2020_02_18_04) approved the study. All participants read, understood, and signed an informed consent document. All procedures were conducted in accordance with the Helsinki Declaration of 1975, as revised in 1983.

2.1 Participants

We conducted a cross-sectional study. Participants were enrolled at the I.R.C.C.S. Istituto Auxologico Italiano, U.O. di Riabilitazione Osteoarticolare, Ospedale S. Giuseppe, Piancavallo, Italia, from December 1, 2019 to February 31, 2020, at the start of a month-long hospitalization for weight loss and physical therapy.

Patients were enrolled according to the following inclusion criteria: age in years >18 and ≤ 65; obesity, as measured by a body mass index (i.e., BMI computed as the weight in kilograms divided by the square of height in meters: kg/m2) ≥ 30 4; and CLBP, defined as low back pain duration > 3 months [147], diagnosed by a rheumatologist at the beginning of the hospitalization.

Patients were excluded according to the following criteria: physical or mental inability to provide signed informed consent; pain duration < 3 months; diagnosis of another disease that might explain low-back pain; diagnosis of fracture, neoplasia, bone metastasis, stenosis, which might explain the low back pain; postoperative pain; neurogenic or radicular condition; neurological disease.

Demographic and clinical data were gathered using a self-report form administred at the beginning of hospitalization.

2.2 Measures

Disability was measured using the Italian version [108] of the Roland-Morris Disability Questionnaire (RMDQ)[180]. The RMDQ has 24 dichotomous items evaluating the level of difficulty in performing daily activities. The total score ranges from 0 to 24. Higher scores indicate higher

levels of disability. The Italian version of the RMDQ has reliability and validity comparable to the original version [108]. In the current study, internal consistency was good (Cronbach's α=0.82).

The Numerical Pain Rating Scale (NPRS)[181] was administred to evaluate pain severity through an 11-point scale (anchors 0= no pain, 10= worst possible pain). The NPRS is a widely accepted, reliable and valid measure of pain in chronic pain patients [147,148].

Kinesiophobia was evaluated using the Italian version [113] of the Tampa Scale of Kinesiophobia (TSK) [113]. The TSK has 13 items on a 4-point Likert scale ranging from "strongly disagree" to "strongly agree" [149]. Two sub-scales relative to activity avoidance (i.e., belief that activities causing pain should be avoided) and harm (i.e., belief that pain is a sign of bodily damage) can be computed. The total score ranges from 13 to 52 whit higher scores reflecting higher levels of kinesiophobia [113]. The Italian version of the TSK has good factorial structure and acceptable psychometric properties [113]. In the current sample, the internal consistency of this measure was excellent (Cronbach's α=0.90).

2.3 Statistical analysis

Descriptive statistics were calculated in terms of means, standard deviations, and ranges for continuous variables, and frequencies and percentages for categorical variables.

Pearson's correlation was performed to evaluate the relationship between age, BMI, and PNRS, TSK, and RMDQ scores. Point-biserial correlation was performed to evaluate the relationship between age, BMI, PNRS, TSK, and RMDQ scores, as well as sex. Cohen's classification system was used to classify correlation coefficients[182] (.10=small; .30=medium; .50=large). Highly

correlated variables that indicate multicollinearity (r > 0.90), or variables not correlated with pain severity or disability, were excluded from the subsequent mediation analyses.

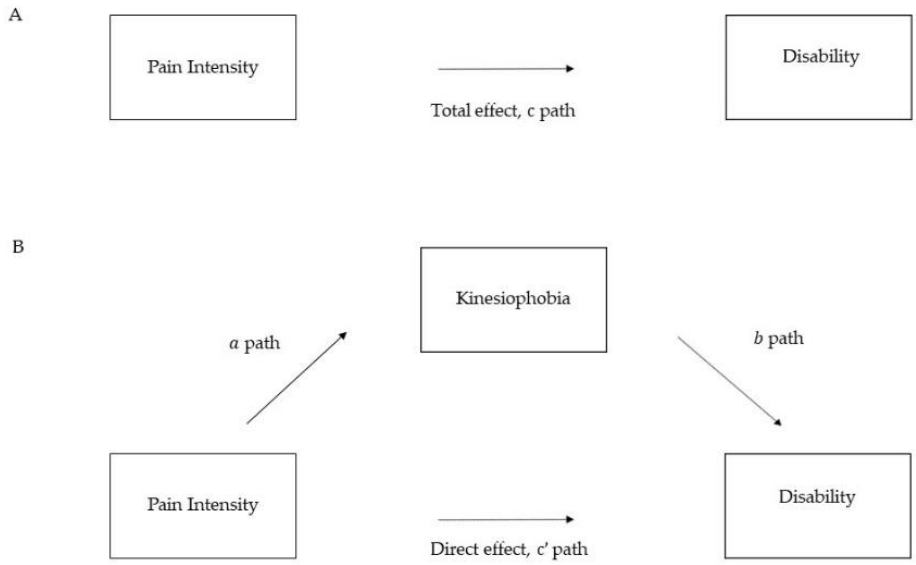
A simple mediation analysis was performed. In our model, kinesiophobia (M) was included as a mediator in the relationship between pain severity (i.e., predictor, X) and disability (i.e., outcome, Y), see Figure 1.

Four steps had to be met to confirm mediation[183] : i) pain severity should be related with disability (total effect; c path= c'+ a x b); ii) pain severity should be related with kinesiophobia (a path); iii) controlling for pain severity, kinesiophobia should be significantly associated with disability (b path); iv) the relationship between pain severity and disability should be reduced (direct effect, c' path) when controlling for kinesiophobia (indirect effect, a x b).

The mediational analysis was performed using Jamovi 1.2 [153]. Bias-corrected bootstrap confidence intervals (CI-BC) for inference about indirect effects was used. It does not require the assumption of normality and reduce the type I error [184,185]. An estimate of the indirect effect was computed from the mean of 5000 bootstrap samples and 95 % CI-BC. The indirect effect is considered statistically significant when confidence intervals (CI-BC) do not include zero.

The empirical power tables proposed by Fritz and Mackinnon [186] for mediation models suggest that the sample size of this study is sufficient for a mediated effect including small-to-medium (.26) a and b paths with a .80 power.

Figure 1. Conceptual diagram of the mediation model tested in this study.



Note. (A) is the primary relationship between pain intensity and disability, with the total effect labeled c. (B) The direct effect (c ') is the effect of pain on disability after controlling for the mediator variables. 'a path' is the association between pain intensity and kinesiophobia. 'b path' is the association between kinesiophobia and disability controlling for pain intensity.

Table 1. Demographic and clinical characteristics of the sample (n=213)

	n (%)	Mean ± sd	Range (min-max)
Sex	M= 68 (31.9); F=145 (68.1)		
Age (in years)	213	56.8± (9.93)	26-65
BMI (Kg/m^2)	213	44.9 ± (8.81)	30-60

PNRS	213	6.21 ± (2.33)	2-10
TSK	213	30.4 ± (7.72)	13-50
RMDQ	213	12.5 ± (5.68)	3-24

Note. M= male; F= female; BMI: Body Mass Index; PNRS: Pain Numeric Rating Scale; TSK: Tampa Scale of Kinesiphobia; RMDQ: Roland Morris Disability Questionnaire.

3. Results

3.1 Participants' characteristics

This study enrolled a total of 213 people. Table 1 summarizes participant demographic and clinical characteristics, as well as means, standard deviations, and ranges for the three primary measures (i.e., PNRS: Pain Numeric Rating Scale; TSK: Tampa Scale of Kinesiphobia; RMDQ: Roland Morris Disability Questionnaire).

3.2 Preliminary data analysis

Correlation coefficients between PNRS, TSK, and RMDQ were less than 0.90 indicating the absence of multicollinearity [187]. Age, sex, and BMI were not significantly correlated with neither NPRS scores nor RMDQ scores (Table 2). As a result, these factors were not entered in the mediation model [188].

Table 2. Pearson and point-biserial correlations coefficients between age, sex and BMI with the measures of pain intensity, kinesiophobia and disability.

	Age (in years)	Sex	BMI	PNRS	TSK	RMDQ
Age (in years)	-					
Sex	0.058	-				
BMI (Kg/m^2)	0.110	-0.035	-			
PNRS	0.057	-0.110	-0.035	-		
TSK	0.055	0.076	0.006	0.281***	-	
RMDQ	0.048	-0.126	0.131	0.275***	0.373***	-

Note. BMI: Body Mass Index; Pain Numeric Rating Scale; TSK: Tampa Scale of Kinesiphobia; RMDQ: Roland Morris Disability Questionnaire. * p < .05, ** p < .01, *** p < .001

3.3 Mediation analysis

A significant total effect of the level of pain severity on the level of disability was found (i, total effect; c path), (b=0.669, SE=0.157, p<.001). Path *a* (ii, association between pain intensity and kinesiophobia), (b=0.931, SE=0.223, p<.001, 95% BC-CI: 0.499, 1.360) and path *b* (iii; association between kinesiophobia and disability), (b=0.236, SE=0.049, p<.001, 95% BC-CI:0.137,0.330) were significant. The indirect effect via kinesiophobia (iv; axb path) was

significant (b=0.220, SE=0.075, p=0.002, 95% BC-CI: 0.094, 0.377). The direct effect (iv; c') was reduced compared to the total effect (c), but remained significant (b =0.449, SE =0.161, p= 0.005).

Our results highlighted that kinesiophobia partially mediate the association between the level of pain severity and the level of disability. Results are reported in Table 3.

Table 3. Results of the simple mediation analysis investigating the level of kinesiophobia as a mediator between the level of pain intensity and the level of disability

Path Estimates						
	b	SE	LLCI	ULCI	Z	p-Value
Effect of pain intensity on kinesiophobia (*a* path)	0.931	0.223	0.499	1.360	4.17	<.001***
Effects of kinesiophobia on disability (*b* path)	0.236	0.049	0.137	0.330	4.77	<.001***
Effect of pain intensity on disability (c')	0.449	0.160	0.126	0.759	2.79	0.005**
Mediation Estimates						
	b	SE	LLCI	ULCI	Z	p
Indirect effect of pain intensity on disability through kinesiophobia (*a* × *b* path)	0.220	0.073	0.094	0.377	3.03	0.002**
Total effect of pain intensity on disability through kinesiophobia (c'+ *a* x *b*)	0.669	0.157	0.356	0.966	4.25	<.001***

Note. SE: standard error; LLCI: lower level of the 95% confidence interval; ULCI: upper level of the 95% confidence interval; Confidence intervals computed with Bias Corrected bootstrap method. *p < .05, ** p < .01, *** p < .001

4. Discussion

In line with previous evidence [56], kinesiophobia is associated with pain severity and disability in patients with obesity and CLBP. This study adds to previous evidence by evaluating kinesiophobia as a mediator. Our hypothesis according which kinesiophobia partially mediates the relationship between pain intensity and disability was confirmed.

Our results are in line with previous evidence [168,178,189] that investigated this relationship in patients with whiplash-associated disorders and CLBP, and they add to the body of evidence supporting the FAM [137,170].

Our findings contribute to a better understanding of the psychological factors that contribute to disability. Intervening solely on perceived pain severity may be ineffective for reducing disability. Pain can be considered a necessary but not sufficient condition for chronic disability, because not all patients with CLBP become chronically disabled [190,191]. Our finding about the role of kinesiophobia as a mediator may help to identify the conditions under which patients develop disability. Pain can cause fear of injury and movement contributing to avoidance, which results in functional impairment [9]. Beside the role of pain severity, the mediating effect of kinesiophobia indicated that the response to the pain (in this case, fear of movement and re-injury) may contribute to disability because kinesiophobia prevents the individual from confronting pain. Indeed, the FAM [9] hypothesizes that confrontation, as opposed to avoidance, is an adaptive pain-coping strategy that leads to fear reduction.

Our results have several clinical implications. The development of tailored treatments for CLBP requires the identification of mechanisms that lead to the development, maintenance, and impact of disability. Kinesiophobia might be a therapeutic target intervention especially in patients with obesity. Indeed, patients with obesity and CLBP might not fully engage in physical therapy and exercise. A gradual exposure to pain-inducing movements might be beneficial to reduce kinesiophobia [192]. Physicians, physical therapists and psychologists might help patients through the physical and psychological transition from living in a "pain-restricted" to a "pain-managed" state [176].

Several limitations must be addressed. We couldn't draw causal relationship because of the cross-sectional design. To overcome this limitation, longitudinal studies should be performed. The sample is not representative of the overall population of patients with obesity and CLBP because we enrolled participants in a care-seeking population recruited from a single center. Because our findings support a partial mediation, the presence of other mediators that were not considered in this study should be examined in future studies.

However, this study has several strengths. Indeed, to our knowledge, this was the first study investigating the role of kinesiophobia in patients with obesity and CBPL. Future research could assess how much kinesiphobia affects behavior by using objective measures, such as the actual level of physical activity levels measured through a pedometer or clinical tests such as the six-minute walking test [193]. The current study adds to our understanding of the psychological factors that influence disability. Kinesiophobia mediated the relationship between pain intensity and disability in people with CLBP and obesity, according to the findings. The importance of kinesiophobia as a factor that should be evaluated and targeted in rehabilitation interventions to reduce disability in CLBP associated with obesity was highlighted by our findings.

Overall conclusion

The goal of the first study was to evaluate the SBST's factorial structure, test-retest reliability, and construct validity in a group of Italian patients with low back pain and/or obesity. The findings indicate that this instrument evaluates the physical and psychological aspects of a patient's pain experience, as well as its internal consistency, test-retest reliability, and construct validity. This tool can be easily implemented in clinical practice in patients with pain to screen those who are at risk for chronic pain, and in patients with chronic pain to monitor improvement following treatment and identify the most influential psychosocial factors on which to intervene. The goal of the second study was to see if kinesiophobia and pain catastrophizing played a role in explaining pain intensity and physical disability in a group of people who had obesity and CLBP. According to the findings, kinesiophobia, but not pain catastrophizing, was found to be a significant predictor of both subjective pain intensity and physical disability. Obesity, we might assume, plays a key role in explaining the importance of kinesiophobia in our sample. As a result of the associated pathologies, such as breathing difficulties, increased movement difficulties, and discomforts, individuals affected by obesity may develop greater aversion and fear of movement.

In contrast, we found that pain catastrophizing was not significantly associated with pain intensity or physical disability; this finding appeared to contradict previous evidence[37,138,157] Our sample, on the other hand, is primarily made up of people who are moderately or severely obese. We can assume that different pain cognitions are more prevalent in obese people than pain catastrophizing. The role of kinesiophobia as a mediator was confirmed in the third study, which added to previous findings. We hypothesized that kinesiophobia mediates the relationship between pain intensity and disability to some extent. Our findings appeared to back up our theory that kinesiophobia plays a role in the relationship between pain intensity and disability. Our findings help us to better

understand the psychological factors that cause disability. Focusing solely on pain intensity, as recently discussed [190,191], may be ineffective in the treatment of chronic pain. Aside from pain intensity, the mediating effect of kinesiophobia suggests that how a person reacts to pain (in this case, fear of movement and reinjury) may play a role in disability. Furthermore, kinesiophobia prevents a person from confronting pain or engaging in fear-inducing movements. A better understanding of the mechanisms that lead to the onset, maintenance, and impact of disability is needed to develop more tailored treatments for CLBP. We proposed that kinesiophobia can be addressed in therapeutic interventions, particularly in the case of associated obesity, because people with obesity and CLBP may not fully engage in treatments (e.g., physical therapy and exercise). Gradual exposure to movements that the patient associates with fear during supervised rehabilitation may be beneficial in reducing kinesiophobia. It is also good to emphasize that having kinesiophobia as a target of the intervention can lead to a double advantage. Allowing the patient to better manage pain and correct their pain expectations and better adhere to rehabilitation programs that include physical activity, with a double benefit, both on pain and obesity, creating a virtuous circle.

Taken together, our results underscore the importance of a multidisciplinary approach that considers psychological aspects in the treatment of chronic low back pain. Screening to identify patients most prone to chronic pain could be useful in improving the trajectory of pain in the chronic phase. It appears from our studies that particularly in the population of CLBP sufferers with obesity kinesiophobia seems to be more significant as a factor than well-established pain catastrophizing. Psychological interventions aimed at the analysis of beliefs related to pain and movement may promote a better adherence to a rehabilitation program that includes physiotherapy and adapted physical activity. Future research will need to assess whether the implementation of psychological interventions targeting this population also impact physical functioning.

Part II: Psychological factors in patients with fibromyalgia and obesity

List of Abbreviations

ACR American College of Rheumatology

BMI Body Mass Index

FM Fibromyalgia

WSP Widespread Pain

WPI Widespread Pain Index

SSS Symptom Severity Scale

Introduction

1. Diagnostic criteria

Fibromyalgia (FM), the most common cause of widespread musculoskeletal pain, is estimated to affect 2% of the general Italian population [194]. It is charactherized by tenderness at specific points, fatigue, stiffness and widespread pain. Diagnosing FM can be difficult, and according to a global survey, it takes an average of 2.3 years to get a diagnosis after the first symptom appears [195].

The first diagnostic criteria for fibromyalgia were developed by Smythe in 1979. Subsequently, Bennet in 1981, Yunus in 1981, and Wolfe in 1985 also contributed to their development. Widespread pain fatigue and poor sleep were the main criteria. In 1989, Yunus, Masi, and Aldag published their diagnostic criteria for primary fibromyalgia. They included tender points, widespread pain, pain in seven sites (hands, shoulders, neck, lower back, hips, knees, ankles), fatigue, poor sleep quality, anxiety, and irritable bowel syndrome. Criteria included the presence of pain or stifness in 4 or more anatomic sites for three months or more, for which the presence of another condition that could explain the symptomatology was excluded.

In 1990, the American College of Rheumatology published criteria for the classification of primary and secondary fibromyalgia. The ACR criteria are: widespread pain in at least 11 of the 18 tender points on palpation; widespread pain is defined as pain that at least lasts for 3 months, occurred axially, on the right and left side of the body both above and below the waist. Other symptoms were included, although not mandatory for the diagnosis including fatigue, morning stifness, sleep disturbances. Following the publication of the 1990 criteria, a debate arose about the central role of tender points for diagnosis. In fact, tender points seem to be present even in individuals without widespread pain pain.

Fig. **1.** Tender points locations for the 1990 classfication criteria for fibromyalgia

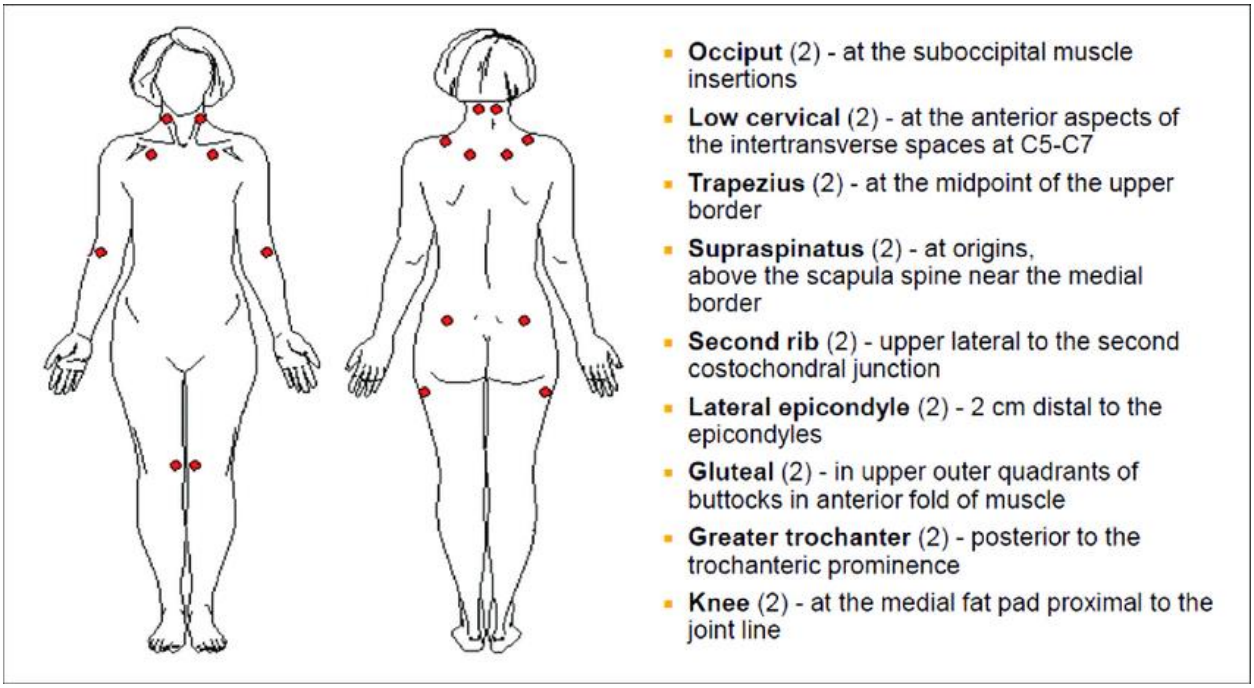


Table 1. ACR 1990 diagnostic criteria

The American College of Rheumatology 1990 criteria for the classification of FM
1. Widespread Pain
Pain is considered widespread when all of the following are present: pain in the left side of the body. Pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition. Shoulder and buttock pain is Considered as pain for each involved side. "Low back" pain is considered lower segment pain.
2. Pain in 11 of 18 tender points sites on digital palpation
Pain, on digital palpation, must be present in at least 11 of the following 18 tender point sites:
Occiput: bilateral, at the suboccipital muscle insertions.
Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at CSX7.
Trapezius: bilateral, at the midpoint of the upper border.
Supraspinarus: bilateral, at origins, above the scapula spine near the medial border.
Second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces Lareral epicondyle: bilateral, 2 cm distal to the epicondyles.
Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle.

Greater trochanter: bilateral, posterior to the trochanteric prominence.

Knee: bilateral, at the medial fat pad proximal to the joint line.

Digital palpation should be performed with an approximate force of 4 kg. For a tender point to be considered "positive" the subject must state that the palpation was painful. "Tender" is not to be considered "painful.

For classification purposes, patients will be said to have fibromyalgia if both criteria are satisfied. Widespread pain must have been present for at least 3 months. The presence of a second clinical disorder does not exclude the diagnosis of fibromyalgia.

The ACR then published in 2010 other diagnostic criteria that were more simple and usable in clinical practice. The widespread pain index (WPI scale), which is designed to indicate the number of body areas (rage 0-19) reported as painful by the patient, replaced the strict tender points examination in the new study. The Symptom Severity Scale was created to finally include the three main core symptoms of FM, in addition to pain: non-refreshed sleep, fatigue, and cognitive problems. SS is calculated by adding the severity of the three symptomatic areas, as well as the overall somatic symptoms.The criteria included a score of at least 7/19 on the widespread pain index scale; at least 5/12 on the symptom severity scale; or at least 3-6 on the widespread index and at least 9/12 on the symptom severity scale. The WPI includes 19 non-articular pain sites; meanwhile, the SSS measures the severity of three major symptoms (fatigue, trouble thinking or remembering, waking unrefreshed), and the severity of the somatic symptoms in general, rated by the physician. While for this classification, the SSS score required physician evaluation, a further change in 2011 removed the physician assessment of the extent of somatic symptoms and replaced it by a summary score of three self-reported symptoms, making it easier to use. This modification enabled researchers to use these criteria in epidemiological and clinical studies without the requirement for an examiner.

Fig. 2 The 2010 ACR diagnostic criteria

Criteria

A patient satisfies modified ACR 2010 fibromyalgia diagnostic criteria if the following 3 conditions are met: (1) Widespread Pain Index ≥ 7 and Symptom Severity Score ≥ 5 or Widespread Pain Index between 3–6 and Symptom Severity Score ≥ 9. (2) Symptoms have been present at a similar level for at least 3 months. (3) The patient does not have a disorder that would otherwise sufficiently explain the pain.

Ascertainment

1). Widespread Pain Index (WPI): Note the number of areas in which the patient has had pain over the last week. In how many areas has the patient had pain? Score will be between 0 and 19.

Shoulder girdle, Lt.	Hip (buttock, trochanter), Lt.	Jaw, Lt.	Upper Back
Shoulder girdle, Rt.	Hip (buttock, trochanter), Rt.	Jaw, Rt.	Lower Back
Upper Arm, Lt.	Upper Leg, Lt.	Chest	Neck
Upper Arm, Rt.	Upper Leg, Rt.	Abdomen	
Lower Arm, Lt.	Lower Leg, Lt.		
Lower Arm, Rt.	Lower Leg, Rt.		

2). Symptom Severity Score: Fatigue; Waking unrefreshed; Cognitive symptoms.

For the each of these 3 symptoms, indicate the level of severity over the past week using the following scale: 0 = No problem; 1 = Slight or mild problems; generally mild or intermittent; 2 = Moderate; considerable problems; often present and/or at a moderate level; 3 = Severe: pervasive, continuous, life-disturbing problems.

The Symptom Severity Score is the sum of the severity of the 3 symptoms (fatigue, waking unrefreshed, and cognitive symptoms) plus the sum of the number of the following symptoms occurring during the previous 6 months: headaches, pain or cramps in lower abdomen, and depression (0–3). The final score is between 0 and 12.

Lastly, after the 2016 revision, fibromyalgia could be diagnosed the following criteria are met: 1) WPI ≥ 7/19 pain sites and SSS ≥ 5/12 or WPI between > 3–6/19 and SSS > 9/12); 2) symptoms have been present at a similar level for at least 3 months; 3) the patient does not have another disorder that would otherwise sufficiently explain the pain; 4) generalized pain, defined as pain in at least 4 of 5 regions, is present.

Fig. 3 Modification to the 2010 ACR criteria

2016 Changes to modified ACR fibromyalgia diagnostic criteria

This revision makes the following changes to the fibromyalgia criteria shown in Table 3.

(1) Changes criterion 1 to "widespread pain index (WPI) ≥ 7 and symptom severity scale (SSS) score ≥ 5 OR WPI 4–6 and SSS score ≥ 9" (WPI minimum must be ≥4 instead of previous ≥ 3).
(2) Adds a generalized pain criterion (criterion 2), and one that is different from the 1990 widespread pain definition. The definition is: "Generalized pain is defined as pain in at least 4 of 5 regions. In this definition, jaw, chest, and abdominal pain are not evaluated as part of the generalized pain definition."
(3) Standardizes and makes 2010 and 2011 criterion (criterion 3) wording the same: "Symptoms have been generally present for at least 3 months."
(4) Removes the exclusion that regarding disorders that could (sufficiently) explain the pain (criterion 4) and adds the following text: "A diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses."
(5) Adds the fibromyalgia symptom (FS) scale as a full component of the fibromyalgia criteria.
(6) Creates one set of criteria instead of having separate physician and patient criteria by replacing the physician estimate of somatic symptom burden with ascertainment of the presence of headaches, pain or cramps in lower abdomen, and depression during the previous 6 months.

Forms and pain maps to aid in ascertainment are available at (https://medicine.umich.edu/sites/default/files/content/downloads/MBM%20w%20SSI%202016.pdf) (Michigan Pain Map) and (https://www.arthritis-research.org/sites/default/files/editor/FM%20Diagnostic%20Criteria%20Survey%20Questionnaire%20%282013%29.pdf) National Data Bank for Rheumatic Diseases (NDB) fibromyalgia diagnosis form.

Many fibromyalgia cases do not exactly match a standardized set of diagnostic criteria. Although some healthcare providers have labeled it as such, it is not thought to be a diagnosis of exclusion. Because there are no universally applicable absolute, definitive diagnostic criteria, providers frequently settle on this diagnosis after ruling out other possibilities [196]. Because symptoms are vague and generalized, diagnosis is difficult and frequently missed. Despite this, almost every patient mentions three main symptoms: pain, fatigue, and sleep disturbance [197]. Pain is usually diffuse, multifocal, deep, gnawing, or burning. It is migratory and waxes and wanes frequently. If this is the case, fibromyalgia should be suspected, as this type of pain is frequently not caused by inflammation or damage in the area of interest.

2. Symptoms

FM is primarily characterized by widespread chronic pain (CWP) in multiple areas of the body. However, a variety of other symptoms are associated with the disease [198,199]. Even though the ACR criteria specify as the main symptoms fatigue, non-restorative sleep, and cognitive disorders,

patients frequently report another pattern of symptomatology: hyperalgesia, stiffness, headache, irritable bowel syndrome, restless leg syndrome, and psychological issues [200].

2.1 Pain

There are specific causes of widespread pain (e.g., inflammatory rheumatic disease and diffuse bone metastases), but there are no specific causes of somatic disease in most patients with CWP [201]. Pain is the primary symptom of FM, which is felt primarily in the musculature and is linked to the sensitization of the CNS pain pathways.

Desmeules et al. [202] found that patients with fibromyalgia have increased sensitivity to a wide range of stimuli (e.g. mechanical, ischemic pressure, or heat and cold). Pain has been linked to distress in some studies, and some psychological factors, such as catastrophizing and hypervigilance, have been shown to influence how we detect pain [203].

Petzke and colleagues conducted a series of studies using randomized pressure stimuli to avoid pain stimuli predictability [204]. They came to the following conclusions: first, when stimuli were randomized, levels of distress had no effect on pressure pain thresholds; second, FM patients were more sensitive than controls, even with randomized stimuli; and third, FM patients did not show more hypervigilance than controls.

Furthermore, pain is aggravated by cold, protracted inactivity; weather changes, and sleep disorders, as often reported by the patients.

2.2 Sleep disturbances

According to one study, 70% of FM patients complained of waking unrefreshed after non-restorative sleep (NRS) [205]. NRS causes energy depletion and fatigue throughout the day, as well as impairments in physical and mental functioning during the day. Patients reported taking longer to fall asleep, as well as frequent waking up during the night, which resulted in an un-refreshed wake-up in the morning, resulting in fewer hours of sleep than healthy controls and/or patients with other diseases [206]. Many clinicians have offered specific treatments for sleep disorders (such as obstructive sleep apnea, upper airway resistance, and periodic limb movement).

2.3 Fatigue

The presence of fatigue and pain in the same person has a long history in medical literature, having been described previously in the ‘neurasthenia' condition, which was once thought to be the previous term for fibromyalgia.

Even though fatigue is a natural part of life, it is one of the most common symptoms of FM, which is described as physically and mentally exhausting. For at least 6 months, it is estimated that about 80% of patients had the same symptoms as those needed to diagnose chronic fatigue syndrome: joint and muscle pain, unrefreshing sleep, sore throat, and fatigue [207]. Due to the many other conditions reported by patients, the cause of fatigue is not fully understood. Sleep disorders, pain, and pharmacological treatments (tricyclic antidepressants and even opioids) could all be identified as precursors. The fatigue is usually worse when you first wake up, improves gradually throughout the morning, and then worsens again in the late afternoon [208]. Although this association has been studied as a positive correlation in other rheumatic conditions, its causality remains unknown [209]. It's also possible that pain contributes to fatigue by exacerbating mood or sleep disorders. Although these findings suggested that a primary sleep disturbance may be at the root of FM symptoms,

another viewpoint is that pain may cause slow-wave sleep disruptions, resulting in unrefreshed wakening and fatigue throughout the day.

2.4 Fibro-fog

The majority of FM patients experience cognitive deficits, particularly short-term memory loss, multitasking difficulties, and poor concentration. The so-called "Fibro-fog" is a cluster of cognitive complaints in FM patients [210]. FM patients rate their cognitive performance as significantly worse when compared to healthy controls or patients with other rheumatic or chronic pain conditions [211]. In any case, it's still unclear whether the subjective complaints reflect an objective function deficit or a patient's uncorrected perception. When FM patients were compared to healthy subjects of the same age, they had lower working memory, free recall, and verbal fluency, but no differences in information processing speed were found. When compared to an older population without FM, the FM sample performed similarly in terms of working memory and free recall, had a lower vocabulary, and processed information faster. It's also worth noting that cognitive delay appears to be linked to pain, but not to anxiety or depression symptomatology [212]. In a recent review, Bertolucci and colleagues found that most FM patients have poor working memory, attention, and executive functions [213]. Furthermore, attention and, in particular, executive function are two functions that lack a universally accepted definition, making it difficult to distinguish minor differences in cognitive impairment. Attention and working memory deficits in FM patients become apparent when distractors or competing stimuli are added to the method [214].

3. Fibromyalgia etiology

Fibromyalgia's etiology and pathogenesis are still poorly understood and several factors appear to be involved, including central and autonomic nervous system dysfunction, neurotransmitters, hormones, immune system, external stressors, psychiatric aspects. The main mechanism involved is central sensitization, which is defined as an increased response to stimulation mediated by CNS signaling [215]. Central sensitization is caused by increased nerve activity, enlarged receptive fields, and enhanced stimulus responses transmitted by primary afferent fibers [216]. The "windup," which reflects the increased excitability of spinal cord neurons, appears to be an important involved phenomenon: after a painful stimulus, subsequent stimuli of the same intensity are perceived as stronger [217]. This occurs normally in everyone, but it is excessive in fibromyalgic patients. The descending inhibitory pain pathways modulate spinal cord responses to painful stimuli are imparide in indiviuals affected by FM and they may play a significant role in the etiopatogenic mechanism. Psychiatric issues appear to play a significant role in the development of fibromyalgia. Patients with fibromyalgia have a higher rate of psychiatric disorders than those with other rheumatic diseases [218]. Anxiety, dysthymia, panic disorders, posttraumatic stress disorder, and depression are the most common [218,219].

4. Disability in fibromyalgia

Fibromyalgia can have a negative impact on almost every aspect of a patient's life, resulting in significant functional impairment and difficulties performing daily and work-related activities [220]. Disability is defined by the International Classification of Functioning, Disability, and Health as a combination of impairments (physical and/or mental function abnormality or loss), activity limitations (difficulties performing various activities), and participation restrictions (difficulties in social life) [221]. Clinical assessments and self-reported questionnaires such as the 36-Item Short-

Form Health Survey, Health Assessment Questionnaire (HAQ), Fibromyalgia Impact Questionnaire (FIQ), and Revised Fibromyalgia Impact Questionnaire can be used to determine the impact of fibromyalgia on quality of life, functionality, and employment ability. Because of the complexity and multi-symptomatic nature of fibromyalgia, a multidimensional assessment is required to evaluate various aspects of a patient's life [222].

5. Treatment

5.1 Pharmacological treatment

Tricyclic antidepressants (TCAs) are designed to raise serotonin and/or norepinephrine levels in the central nervous system. They work by preventing serotonin and norepinephrine from being reabsorbed. The discovery of the alpha-delta NREM sleep abnormality, which was analyzed during a polysomnography study of FM patients, led to the use of TCAs in the treatment of FM. Further research and evidence came from studies on patients' personalities and family histories, which revealed higher rates of affective disorders, particularly depression [223,224]. Arnold and colleagues analyzed 9 placebo-controlled studies of TCAs and found that they had a moderate effect on FM patients' symptomatology [225]. TCAs have recently been largely replaced by a newer class of antidepressants known as Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin and Norepinephrine Dual Reuptake Inhibitors (SNRIs). Fluoxetina was introduced in 1988 to alleviate the side effects (constipation, orthostatic hypotension, dry mouth, and urinary retention) and has since become one of the most widely used SSRIs in the United States, owing to its favorable side effects. The majority of SSRI studies on FM used a randomized placebo-controlled trial, and no significant differences were discovered [226]. Due to its favorable side effects, fluoxetina

was introduced in 1988 to alleviate the side effects (constipation, orthostatic hypotension, dry mouth, and urinary retention). It has since become one of the most widely used SSRIs in the United States. A randomized placebo-controlled trial was used in the majority of SSRI studies on FM, and no significant differences were found [226].The FDA approved pregabalin as the first drug for the treatment of FM. It is a type of antiepileptic drug that is commonly used to treat a variety of chronic pain conditions [227].

5.2 Nonpharmacological treatment

The three most well-studied non-pharmacological treatments for FM patients are psychoeducation, cognitive-behavioral psychotherapy, and physical exercise. These treatments improved overall functioning and continued to do so even after a year [228]. Physical activity is strongly recommended: although it has not been proven which exercise is the best, aerobic exercises combined with stretching elements have been shown to be effective in reducing symptoms and hyperalgesia [229]. In order to engage patients in an exercise treatment that is enjoyable and easy to adhere to, general recommendations suggest starting with a low intensity-impact level. They can also add different types of exercises or gradually increase the intensity level. Reduce the intensity or duration of the exercise while attempting to maintain the frequency to avoid frustration [230]. According to a recent review by Williams [231], pharmacologic treatments improved functional status for just over 10% of patients, indicating that a more multidimensional approach is needed. CBT (cognitive behavioral therapy) is a type of psychotherapy that combines behavior therapy and cognitive psychology. CBT treatment aims to modify the dynamic connection between individuals, their social network, improving their quality of life and better adapting to the disease, according to the biopsychosocial

model of FM disease. CBT therapies typically focus on challenging maladaptive coping strategies (e.g., catastrophizing) and encouraging the development of goals for more adaptive behaviors (e.g., sleep hygiene)[232].

6. Psychosocial factors related to FM

Psychiatric disorders and psychological distress are common features of FM, and they may contribute to the symptomatology's manifestation, persistence, and intensification [200]. Negative events, stressful environments, or physical/emotional traumas may serve as predisposing factors[233]. In FMS, there is evidence of a high prevalence of psychiatric comorbidities (particularly depression, anxiety, borderline personality, obsessive-compulsive personality, and post-traumatic stress disorder), all of which are linked to a poor clinical profile[234,235]. In addition, FMS patients have high levels of negative affect, neuroticism, perfectionism, stress, anger, and alexithymia[236–239].

Personality is also another field of interested in FM[240]. Indeed, several personological carastheristics has been studied. Alexithymia, which literally means "no words for feelings," is a complex personality trait characterized by an inability to recognize and describe one's own feelings, as well as a lack of imagination and a thinking style that is externally oriented[241]. Alexithymia is characterized by a variety of cognitive and emotional characteristics that has been observed in a variety of clinical conditions, particularly psychosomatic disorders[241]. The main features of alexithymia are difficulty identifying and describing subjective feelings, difficulty distinguishing between feelings and bodily sensations of emotional arousal, restricted imagination processes[242]. As a result, alexithymic people have trouble distinguishing physical sensations like somatic manifestations of emotions, and they may misinterpret their emotional arousal as

symptoms of disease[243]. As a result, they are more likely to mistakenly attribute emotional-related physical symptoms to physical disease and to seek medical attention for symptoms for which there are no medical explanations[244]. Increased negative affects, chronic sympathetic hyperarousal, and impaired immune status are thought to result from an inability to emotionally regulate, particularly negative feelings, which can lead to the development or exacerbation of somatic disease and pain [245].

Patients with FM reported higher levels of alexithymia than healthy controls in several previous studies [237,244]. Indeed, alexithymia is thought to play a role in somatoform disorder[246] and chronic pain patients[247]: more specifically, it is thought that alexithymia causes patients to exaggerate bodily sensations, particularly those associated with emotional arousal [248].

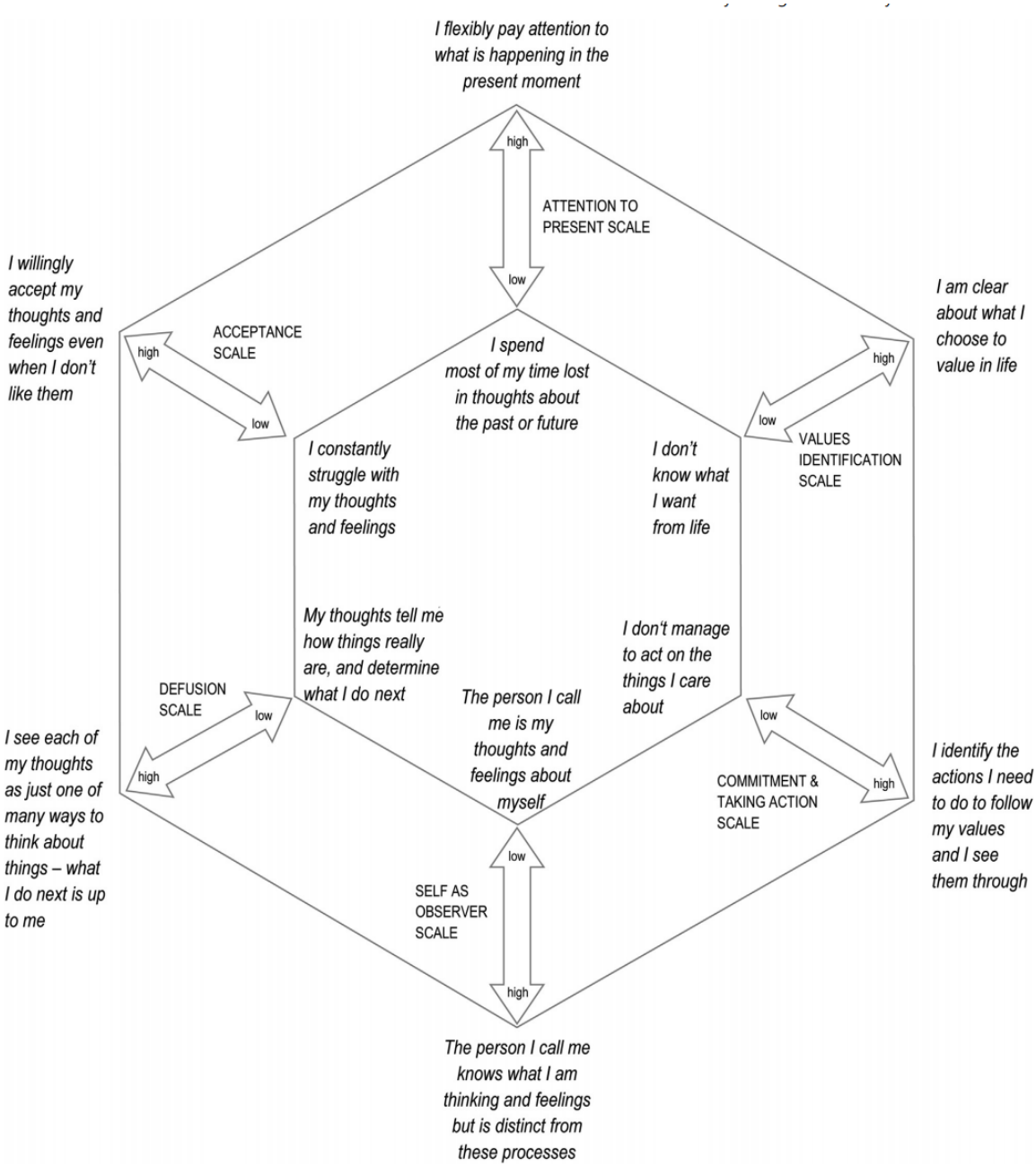
7. Psychological flexibility model

Beside the Fear Avoidance Model, another model has recently gained recognition. The psychological flexibility (PF) model is one that may provide integration, effective guidance for research and treatment development, and fuel progress. The PF model consists of six interconnected processes: acceptance, cognitive defusion, flexible present-focused attention, self-as-observer, values, and committed action [249]. According to McCracken et al. [250], acceptance is the ability to open up to unpleasant experiences and not fight them when doing so serves one's goals The ability to experience a distinction between thoughts and the things they describe, as well as to contact experiences directly without being dominated by the meaning and influences carried in thoughts, is known as cognitive defusion. Moment-to-moment awareness, also known as flexible present-focused attention, is a capacity that can be developed through mindfulness meditation.

The ability to experience a perspective where we are neither defined by nor harmed by our own thoughts and feelings is known as self-as-observer. Values are desires or qualities that we define as important and can be reflected in behavior. They are freely chosen, ongoing, and feed into goals. Committed action is the ability to stick to a goal-oriented course of action that can withstand setbacks and keep moving forward.

In the field of chronic pain, the PF model is still in its infancy. However, some of its six constituent processes are gaining traction, particularly acceptance [251,252]. Unlike the current FA model, which is a disability model with a narrow focus on recovery, the psychological flexibility model is completely symmetrical, presenting both how problems arise and how to solve them[250]. Acceptance, cognitive defusion, flexible awareness of the present, perspective-taking, values, and committed action are all processes of resilience and action for every process of suffering and behavior restriction.

Fig 4. The psychological flexibility model



8. Research project goals

The second part of this thesis project focused on another chronic pain condition, fibromyalgia.

Four studies will be presented. The first study aimed to evaluate the reliability and agreement of a self-administered questionnaire for diagnostic screening for fibromyalgia with a diagnosis made by a rheumatologist.

The second study evaluated the contribution of two psychological variables pain catastrophizing and pain acceptance in explaining self-report disability and performance-based disability.

The third study evaluates the role of pain catastrophizing, kinesiophobia and pain acceptance as mediators of the relationship between pain intensity and pain disability.

The last study evaluated the mediational role of pain catastrophizing, pain acceptance and kinesiophobia in the association between pain severity and disability. Specifically, disability was evaluated using both self-reported and performance based measures.

Study I: The reliability and agreement of the Fibromyalgia Survey Questionnaire in an Italian sample of obese patients

Abstract

The Fibromyalgia Survey Questionnaire (FSQ) was administered in 207 Italian patients with obesity to screen for fibromyalgia (FM). The goal of our study was to evaluate the inter-rater reliability and the agreement between the self-administered FSQ and the clinical interview conducted by a rheumatologist in detecting FM. Patients were randomly assigned to groups A and group B. The patients in group A were firstly interviewed by a rehumatologist and after 48 hours they filled out the self-report FSQ. Patients in group B, on the other hand, filled out the FSQ first and were then interviewed by a rheumatologist 48 hours later. According to the Bland-Altman analysis was satisfactory. Our findings indicated that 33% of our sample met the criteria for a diagnosis of FM. The FSQ is a self-reporting instruments that has good reliability. The FSQ should be used to provide rapid screening for FM.

1. Introduction

Fibromyalgia (FM) is a chronic pain syndrome marked by chronic widespread pain, fatigue, sleep disturbances. This condition in associated with reduced quality of life [253]. FM affects 2.31% of the European population, and 2.22% of the Italian population [254,255].

Weight has a significant impact on symptoms and disability [256–258]. It appears that FM is frequently linked to overweight and obesity [259]. According to several studies, 62–73% of patients with FM are overweight or obese [43,66], in particular higher body mass index (BMI) appears to be positively correlated with disability [260], reduced physical functioning, tender point count, pain sensitivity and sleep disturbances. It is also associated with reduced quality of life, lower tenderness threshold, poor physical functioning [261,262]. Nevertheless, research on patients with obesity and FM needs more evidence.

The diagnosis of FM is a complex process, because of the poly-symptomatology, the different combination and reported symptoms severity [263,264]. The American College of Rheumatology (ACR) proposed several classification criteria. The 2010 ACR criteria consisted of 3 benchmarks:

Criterion 1: Widespread Pain Index (WPI) ≥7 and Symptom Severity Score (SSS) ≥5 or WPI 3–6 and SSS ≥9;

Criterion 2: Symptoms have been present at a similar level for at least 3 months;

Criterion 3: The patient does not have a disorder that would otherwise explain the pain.

The WPI includes 19 non-articular pain sites. The SSS evaluates the severity of three major symptoms: fatigue, trouble thinking or remembering, waking unrefreshed; and the severity of the somatic symptoms in general, rated by the physician. The SSS score required a physician evaluation, that was later change in 2011, removing the physician assessment and replacing it by a score of three self-reported symptoms. These criteria could be easily use in epidemiological and clinical studies without the presence of an examiner.

According to the 2016 ACR criteria, FM could be diagnosed when the following criteria are met: 1) WPI ≥ 7/19 pain sites and SSS ≥ 5/12 or WPI between > 3–6/19 and SSS > 9/12); 2) symptoms have been present at a similar level for at least 3 months; 3) the patient does not have another disorder that could explain the pain; 4) generalized pain, defined as pain in at least 4 of 5 regions, [265].

Despite the improvement of the classification criteria, diagnosing FM remains challenging and diagnostic delays impact on quality of life and psychological well-being, as well as on health care and social costs [266]. The Fibromyalgia Impact Questionnaire-Revised (FIQR) [267] is a measure of disability, specifically in terms of physical functioning, impact of the disease and symptoms. However, this measure is not suitable for the screening for FM, according to the 2010/2011 ACR criteria.

The Fibromyalgia Screening Questionnaire (FSQ) has been developed to assess ACR criteria 1 and 2 using two subscales: the WPI and the SSS [268].

The goal of our study was to evaluate whether the FSQ detect FM accurately in comparison to a clinical interview conducted by a rheumatologist. The clinical interview is based on the 2010 ACR criteria; while the FSQ is based on the 2011 modification of the ACR criteria and evaluates criteria 1 and 2, but not criterion 3, which must be assessed by a rheumatologist.

The goal of this study was to determine the inter-rater reliability and agreement between the Italian translation of the self-administered FSQ and the clinical interview conducted by a rheumatologist [269] in detecting the symptomatology of FM in a sample of Italian patients with obesity and generalized pain.

2. Materials and methods

2.1 Participants and procedures

From May to September 2019, participants were recruited at the Istituto Auxologico Italiano – Istituto di Ricovero e Cura a Carattere Scientifico (Piancavallo, Italy), a clinic specializing in obesity rehabilitation and physical therapy. Patients were asked to participate in the study and provide written informed consent after the study was approved by the Institutional Ethics Committee.

A self-report questionnaire was used to assess demographic data (age, gender, and educational level). A total of 207 obese patients were recruited, with 12 refusing to participate in the study and 6 being excluded from the analyses due to a large number of missing items.

2.2 Materials

Four rheumatologists who are fluent in English and experts in fibromyalgia forward and back translated the FSQ to ensure semantic equivalence between the Italian and English versions. The clinical interview was carried out in accordance with ACR 270 criteria from 2010. All of the patients were randomly assigned to one of two groups: group A was interviewed first by a rheumatologist, and group B was given 48 hours to complete the FSQ. Patients in group B completed the FSQ first, then met with a rheumatologist 48 hours later for an interview.

The questionnaire is divided into two subscales: the WPI is calculated by adding all of the body areas (out of a total of 19) where the patient indicated they had pain in the previous week, ranging from 0 to 19. The SSS is divided into two sections:

Part 1: the patient rates the severity of three somatic symptoms (waking unrefreshed, disturbed cognition, and fatigue) on a scale of 0–3, with a maximum score of 9; Part 2: the patient rates the severity of the following three symptoms (headaches, pain, or cramps) on a 4-point scale (0 absent, 1=slight, 2=moderate, or 3=severe) that occurred in the previous 6 months:

Furthermore, the sum of the two component scores, WPI and SSS, can be used to calculate a poly-symptomatic distress (PSD) scale (Wolfe et al., 2016).

2.3 Statistical Analysis

The Statistical Package for Social Science for Mac was used to conduct all statistical analyses (SPSS-24, IBM SPSS Statistics for Macintosh, IBM Corp., Armonk, NY, USA).

To describe socio-demographic and clinical data, descriptive statistics were used.

Cronbach's alpha was used to assess the internal consistency of the total scales and relative subscales; values of 0.7 and higher were considered desirable [270].

For criteria 1 and 2, a two-way mixed-effect model based on single ratings was used to measure agreement between the two tools using Cohen's kappa statistic and intraclass correlation coefficient (ICC). Each ICC was given a mean estimate as well as a 95 percent confidence interval (CI). We also used Bland-Altman analysis to assess continuous variable agreement (PSD, WPI, and SSS) [271]: The differences between questionnaire and interview measurements were plotted on the y-axis, with the average of the two approaches' measures plotted on the x-axis. The bias, represented by a central horizontal line on the scatter plot, is the mean difference in values obtained with the two approaches. The 95 percent limits of agreement (LOA), expressed as the mean difference 1.96, are shown above and below the horizontal line; the smaller the range between

these two limits, the better the agreement. A Student's t-test was used to compare the values.A level of significance of $p < 0.05$ was considered.

3. Results

Most participants were females (165 vs. 42 males; mean age: 63.2 ± 12.4). All participants were obese, with a level of BMI ≥ 30 (mean ± SD: 40.54 ± 6.45). More than half of the patients (59%) had completed a basic education while only 20 subjects (10%) had completed a tertiary education. Cronbach's alpha of the SSS was .710. Cohen's κ was run to determine if there was an agreement between the FSQ and the clinical interview conducted by a rheumatologist, in satisfying the criteria 1 and 2 for FM (see the above mentioned 2011 ACR criteria). Sixty-nine (33%) subjects were found positive by both FSQ and the interview, vs. 103 patients that did not satisfy the criteria. There was good agreement between the two measurements, $\kappa = .653$ (95% CI, .55 to .757), with a $p < .0005$, index of a substantial strength of agreement [272]. A minor discordant result was found for 16 patients, who were positive for the interview but not for the FSQ measurement.

A high degree of reliability on criterion 1 was also underlined by the interclass correlation. For the PSD scale, the average ICC measure was .899 with a 95% CI from .867 to .923, indicating good reliability (Koo et al., 2016). Similarly, the average ICC measure for WPI was .888 (.853-.915) and for SSS was .851 (95% CI, .804 to .887).

A low bias score between the two assessments was found: regarding PSD, a bias of 0.43 ($p=0.118$) was found with the Bland-Altman 95% limits of agreement of -0.97 and 0.11. Specifically, PSD detected by the FSQ was 12.5 ± 6.61, whereas the mean score at the interview was 13 ± 6.5. WPI scores were 7.41 ± 4.22 by the interview, slightly greater than by patient measures (7.26 ± 4.23) with a difference of 0.134 ($p = .472$). Similar values were found for the SSS, with a bias of. 030 ($p = .062$): mean scores found by the FSQ were 5.29 ± 3.22 vs. 5.59 ± 4.22 by the interview.

4. Discussion

The goal of this study was to evaluate the agreement and inter-rater reliability between the self-administered FSQ and a clinical interview conducted by a rheumatologist in detecting FM symptoms. We recommend the use of FSQ as a valid screening tool because the results show good agreement and inter-rater reliability between the two instruments.

There is currently no consensus on the best way to assess the severity of FM symptoms or to track patients' symptoms, outcomes, or changes. FIQR is a specific questionnaire for FM that addresses several and specific areas for this condition. It has been criticized because it does not fully address all aspects of FM [267] and it may not be sufficiently sensitive to changes.

FM diagnosis is difficult and time-consuming. After presenting FM complaints to a physician for the first time, most patients are diagnosed 2.3 years later [195,273]. The requirement for a physician's examination is a major limitation in understanding FM prevalence and characteristics. As a result, the FSQ may be useful in aiding a physician's diagnosis and expediting the diagnostic process.

Indeed, a screening tool is required for use in situations where an interviewer's presence would be difficult, and it can provide useful information on the overall status of FM symptomatology [274]. The FSQ appears to be an appropriate tool for screening purposes of symptomatology, according to our findings, which are similar to those of Wolfe et al [265].

While the results of the questionnaire and interview appear to be comparable to the SSS and WPI scores, there were minor differences in satisfaction with the diagnosis. However, it is important to remember that the clinical interview is based on the three 2010 criteria, which require the presence of an examiner, whereas the FSQ is based on the 2011 modification of the ACR criteria, which only assesses criteria 1 and 2.

Due to delays and misdiagnosis, patients with FM often undergo unnecessary medical examinations before their diagnosis is finally confirmed, and ineffective and incongruent treatments may be administered.

We found overall good agreement: we found similar values of bias for the PSD and SSS scores, but a significantly lower bias for the WPI scores when compared to Wolfe's [265] results. In addition, we discovered that about a third of the patients met the criteria for FM, which is consistent with a previous study on obese patients that found a prevalence rate of 27.7% [275]. Individuals with fibromyalgia and/or obesity may be on the same syndrome continuum: it is well known that having a high body mass index increases the risk of developing chronic widespread pain [260]; as a result, it's possible to imagine a vicious circle in the behavior of people suffering from obesity and fibromyalgia.

More validation studies in the Italian language and with a larger patient population are needed due to the lack of generalizability of our findings, which were based on a small sample of obese patients.

To summarize, using a self-reporting tool like the FSQ to identify patients with high pain sensitivity can save time. Early detection allows non-pharmacological interventions, such as psychotherapy or physical therapy, to be implemented, potentially lowering national healthcare costs.

Study II: Lower levels of accuracy in recognizing fearful and angry expressions in fibromyalgia.

Abstract

There is a lot of evidence about facial emotion recognition and the role of alexithymic traits in fibromyalgia. Twenty women with fibromyalgia and twenty women who served as controls were tested on their ability to recognize the emotions of fear and anger. A facial emotion recognition task based on implicit behavior was used. A standard psychological questionnaire was also used to assess the level of alexithymic traits. In comparison to the controls, fibromyalgia patients reported a lower level of accuracy in recognizing fearful and angry expressions. The different levels of alexithymic traits could not explain such a difference. Our results were in agreement with some previous evidence in suggesting an altered recognition of others' emotional facial expression in fibromyalgia. However, the behavioral and psychological responses seemed to be strictly in agreement with the subjective emotional experience. Considering the role of emotion recognition on social cognition and psychological well-being in fibromyalgia, we underlined the importance to target this behavior in psychological interventions focused on emotional recognition and regulation.

1. Introduction

Facial emotion recognition is an emotional process that allows individuals to recognize emotions of others when shown through facial expressions. It promotes non-verbal emotional communication, empathy, and social cognition, allowing individuals to efficiently adapt their behavior to the environment [276]. Previous evidence [277,278] in FM is sparse and inconsistent. Previous research assessed the recognition of the facial expressions of happiness, sadness, disgust, fear, surprise, and anger, in samples of women affected by fibromyalgia. Overall, a generalized difficulty in recognizing facial emotional expressions was described. Di Tella and colleagues [278] found a specific difficulty in recognizing expressions of anger and disgust, suggesting an emotion-related impairment. They reported that affected women misrecognized angry facial expressions when they show higher levels of alexithymia. Instead, Weiß and colleagues [277] did not report any effect of alexithymia on their sample's performance. Alexithymia is a trait of emotional functioning peculiarly observed in FM [237,238]. Individuals showing alexithymic traits report difficulty in identifying and communicating feelings, with altered emotional regulation [279,280], and an externally oriented thinking [281,282]. Alexithymic traits may interfere with facial emotion recognition processing [283,284]. However, the results provided by Di Tella and colleagues [278] and Weiß and colleagues [277] regarding the role of alexithymia on facial emotion recognition in FM were heterogeneous. These two studies adopted an *explicit* measure: participants were asked to indicate what was the emotion expressed by the others' faces. However, this procedure might suffer from response's biases (i.e., participants are aware of the experimental question; increased risk of controlled responses) [283,284]. Furthermore, in these studies, multiple primary emotions were investigated at the same time. However, two major criticisms can be leveled at this aspect: the reduced number of trial repetitions, which can be critical in a recognition test, and the reduced ability to draw conclusions about participants' recognition of a specific emotion.

We proposed to investigate facial emotion recognition in FM using an *implicit* task based on an automatic attentional phenomenon known as "redundant target effect" [285]. Since this process is automatic and unaware [286], the task assesses *implicit* behavior. We focused on the two primary emotions of fear and anger. Indeed, individuals with higher levels of alexithymia have more difficulties in recognizing the facial expressions related to these two specific emotions [287]. In the current experimental study, we compared the performance at the implicit facial emotion recognition task [283] of a group of women affected by FM with the performance of a group of pain-free, as controls. If the two groups reported the same behavioral performance on the task, it would suggest that the process of recognition of others' facial expression of fear and anger was preserved in FM.

We also evaluated the presence of alexithymia in our sample, and its impact on facial emotion recognition. In line, with Di Tella and colleagues [278] and other studies relative to non-clinical populations [280], but not with Weiß and colleagues [277], we might expect that those individuals who described themselves as less effective in identifying and communicating their feelings (i.e., higher levels of alexithymia), they might be also less fast and/or accurate in recognizing other's emotional expressions. §IJ'0o

2. Material and methods

This study was approved by the Ethical Committees of the Istituto Auxologico Italiano, IRCCS, Milan, Italy: Protocol n. 21C925_2019 and Città della Salute e della Scienza Hospital, Turin, Italy: Protocol n. CS2/1170. Subjects gave informed written consent, were free to withdraw at any time, and had no prior knowledge of the experiment's rationale. The Fibromyalgia Integrated Outpatient Unit (FIOU), Città della Salute e della Scienza Hospital, Turin, Italy, and the Istituto Auxologico

Italiano, IRCCS, U.O. di Riabilitazione Osteoarticolare, Ospedale S. Giuseppe, Piancavallo, VCO, Italy, recruited participants with fibromyalgia. Healthy volunteers were found through researchers' contacts and word-of-mouth outside of the clinical and academic institutions involved.

2.1 Participants

For this study, 40 women were enrolled. Women participated in this study if they received a diagnosis of FM. We excluded participants according to the following criteria: less than 18 years old, the presence or history of a neurological or severe psychiatric disorder, according to an expert psychiatrist examination. 20 women affected by fibromyalgia were consecutively recruited (Age in years M=48; SD=13; Education in years M=13; SD=1; Body mass index in kg/m^2 M=22.05; SD=2.05). We assessed the level of disability associated with the disease, especially in terms of function, global impact, and symptoms, through the Italian version [288] of the Fibromyalgia Impact Questionnaire - Revised Form (FIQ-R) [267]. The seminal article reported acceptable internal consistency ($\alpha = 0.94$) and all the items had an item-to-total correlation between 0.41 and 0.78.

20 healthy women were enrolled as controls (Age in years M=48; SD=12; Education in years M=15; SD=3; Body mass index in kg/m^2 M=22.02; SD=2.05). We excluded individuals who reported to suffer from FM, but also rheumatic diseases or chronic pain; we also excluded individuals who reported history of a neurological or psychiatric disorder.

2.2 Measures

All participants completed self-report questionnaires to evaluate depression and anxiety. Specifically, the level of depressive symptoms was measured through the Beck Depression Inventory [289,290]. The seminal article reported acceptable internal consistency ($\alpha = 0.86$) as well as acceptable test–retest reliability ($r = 0.93$). Moreover, participants were asked to fill out the State–

Trait Anxiety Inventory [291,292] to assess the current state of anxiety (i.e., trait scale), and the relatively stable aspects of "anxiety proneness," (i.e., state scale). In terms of reliability, it was reported $\alpha = 0.90$ for the trait scale, and $\alpha = 0.93$ for the state scale; moreover, test–retest reliability ranged from 0.73 to 0.86 and 0.16 to 0.62 for scores on the trait and state scales, respectively.

Level of alexithymia. The level of alexithymic traits in our participants was assessed using the Italian version [293] of the Toronto Alexithymia Scale – 20 (TAS-20) [294]. It provides a total score and three sub-scores relative to difficulties in identifying feelings, difficulties in describing feelings, and externally oriented thinking. Individuals indicated the extent to which they agreed or disagreed with each statement on a five-point Likert scale. The questionnaire had acceptable internal consistency ($\alpha = 0.81$); the test–retest reliability was of 0.77.

The implicit facial emotion recognition task. We adopted the implicit facial emotion recognition task described in previous studies [283,284]. This go/no-go task was developed on the basis of the cognitive phenomenon of *redundant target effect* [285]: people respond faster when two identical targets are presented simultaneously rather than when they are presented alone. Moreover, the competitive presence of a non-identical stimulus (i.e., the distractor) affects the efficient recognition of the target, with a lower velocity in detecting the stimuli and a reduction in the level of accuracy. Photographs of male and female faces [295] with either angry, fearful, or neutral expressions, were presented in four different conditions: (i) in the *unilateral condition*, the target (anger/fear) was presented on the right *or* left of the fixation cross; (ii) in the *bilateral condition*, the target was presented simultaneously on the right *and* left of the fixation cross; (iii) in the *neutral incongruent condition*, the emotion target was presented on the right *or* left of the fixation cross along with another but neutral face; (iv) in the *emotional incongruent condition*, the target was

presented on the right *or* left of the fixation cross along with another emotional face. Moreover, in the catch trials, a distractor (represented in half the trials by neutral stimuli, and in the other half by a contrasting emotion) was presented unilaterally, bilaterally, or in opposition to a neutral/emotional stimulus. Participants responded as soon as they noticed the target (regardless of its position or number), pushing a button on the keyboard with the dominant (right) hand. The target emotion was verbally announced by the experimenter at the beginning of each block.

Fear and anger were studied independently in different blocks. Stimuli stayed for a duration of 250 milliseconds. Participants had a maximum of 1500 milliseconds to provide an answer. The inter-stimulus interval varied randomly between 650 and 950 milliseconds. For each condition (unilateral, bilateral, neutral incongruent; emotional incongruent), 32 valid trials and 16 catch trials were presented in four blocks; the block-order was counterbalanced between participants (half of the participants received the order ABBA: anger, fear, fear, anger; the other half, the opposite order BAAB: fear, anger, anger, fear). Overall, 768 trials were administered. There was a short break (two minutes) between each block. *Reaction Time* in milliseconds from stimuli onset was recorded relative to valid trials, and the percentage of *Accuracy* (% hits – % false alarms) were computed.

3. Analysis

3.1 Descriptive characteristics.

An independent sample t-test was used to assess any differences between the two *groups* (participants affected by fibromyalgia vs controls) relative to the demographical characteristics (*Age* and *Education*), the level of *BMI*, and the scores reported on the psychological questionnaires.

The implicit facial emotion recognition task. Fear and anger were studied independently. Reaction time and level of accuracy were independently analyzed. Valid responses faster than 50 milliseconds from stimulus onset were removed from the analysis since they were considered anticipations. A repeated-measures ANOVA with the within-subjects factors of *Condition* (unilateral, bilateral, neutral incongruent, emotional incongruent) and *Gender* (female vs male pictures) and the between-subjects factor of *Group* (participants with fibromyalgia vs controls) was performed. Bonferroni-estimated marginal mean comparisons were applied as post-hoc analyses when the main effect of *Condition* or the interactions were significant.

The main analysis was run again introducing the global score at TAS-20 as covariate, in case of the significant main effect of the between-subjects *Group* or its significant interaction with the between-subjects factors, to verify the role of alexithymia in participants' performance.

4. Results

4.1 Descriptive characteristics and psychological questionnaires

Means, standard deviations, and statistical results are reported in Table 1.

Table 1. Mean (M) and standard deviation (SD) relative to the demographical characteristics and the psychological questionnaires are reported for controls and the participants affected by fibromyalgia. We also report the statistical results (* p value < 0.05).

	Controls	Participants with fibromyalgia	Statistical analyses
	n = 20	n = 20	

	M	SD	M	SD	t	p value	Cohen's d
Age in years	47.9	11.56	47.75	12.66	0.03	0.09	< 0.001
Education in years	14.65	2.85	12.7	1.13	2.84	0.009 *	0.89
Body Mass Index	22.26	1.24	22.05	2.05	0.38	0.7	0.01
Beck Depression Inventory	8	6	15	13	2.2	0.03	0.69
State–Trait Anxiety Inventory							
state-scale	35	9	37	9	-0.48	0.62	0.22
trait-scale	37	12	49	11	3.07	0.004	1.04
Toronto Alexithymia Scale (TAS-20)							
difficulty in identifying feelings	12.15	(4.21)	19.15	(8.05)	3.44	0.002 *	1.08
difficulty describing feelings	10.85	(4.18)	11.85	(4.4)	0.73	0.46	0.23
externally oriented thinking	14.2	(6.18)	15.7	(4.66)	0.86	0.39	0.27
total score	37.2	(12.38)	46.7	(14.06)	2.26	0.029 *	0.71

Participants with fibromyalgia had comparable age with the controls; however, they reported a significant lower level of education. The two groups had comparable body mass index. Participants with fibromyalgia reported significantly higher scores in the Beck Depression Inventory [289,290], and in the trait-scale, but not in the state-scale, relative to the STAI Questionnaire [291,292]. Concerning the Fibromyalgia Impact Questionnaire-Revised Form [267,288], participants with fibromyalgia reported the following scores: about functions, the mean was 17 (SD = 6; range = 6-27); overall impact, the mean was 9 (SD = 5; range = 2-20); symptoms, the mean was 32 (SD = 8; range = 17-47). Moreover, they reported a total score mean of 59 (SD = 17; range = 34-94), which suggested a medium (range 50-70) level of disability associated to the disease [267].

Level of Alexithymia. Means and standard deviations relative to the TAS-20 are reported in Table 1. Affected individuals reported a significantly higher total score in comparison with the controls, as expected. Moreover, we observed a higher score in the scale measuring the individual

difficulties in identifying feelings. Instead, no difference was observed in the scores relative to the other two scales concerning the difficulties in describing feelings and the externally oriented thinking.

Implicit facial emotion recognition task. We report means and standard deviations about the performance of the two groups relative to each experimental condition, split according to the gender (female vs male) of the visual stimuli, relative to the emotion of fear and anger, in Table 2.

Table 2. Implicit Facial Emotion Recognition Task. Mean (M) and standard deviation (SD) for each experimental condition (bilateral, emotional incongruent, neutral congruent) split for the visual stimuli gender (female vs male), relative to the two groups (participants with fibromyalgia vs controls)' performance is reported about the Reaction Time (expressed in milliseconds) and the level of Accuracy (expressed in percentage). The upper part regards the emotion of fear; the lower part, the emotion of and anger.

		Bilateral		Emotional Incongruent		Neutral Incongruent		Unilateral	
		female	male	female	male	female	male	female	male
Fear									
Reaction Time in ms									
Participants with fibromyalgia	M	413	413	428	439	455	419	435	419
	SD	*192*	*159*	*185*	*202*	*160*	*146*	*180*	*126*
Controls	M	368	354	429	411	418	394	372	366
	SD	*117*	*94*	*124*	*143*	*132*	*93*	*87*	*92*
Accuracy in percentage									
Participants with fibromyalgia	M	45.89	55.49	21.63	30.45	20.94	28.92	50.31	58.33
	SD	*19.45*	*19.64*	*20.10*	*19.24*	*23.57*	*16.83*	*19.13*	*19.00*
Controls	M	63.52	66.51	37.57	48.58	39.51	49.83	61.98	69.32
	SD	*19.38*	*14.77*	*22.35*	*16.34*	*22.56*	*17.63*	*18.36*	*12.95*
Anger									
Reaction Time in ms									

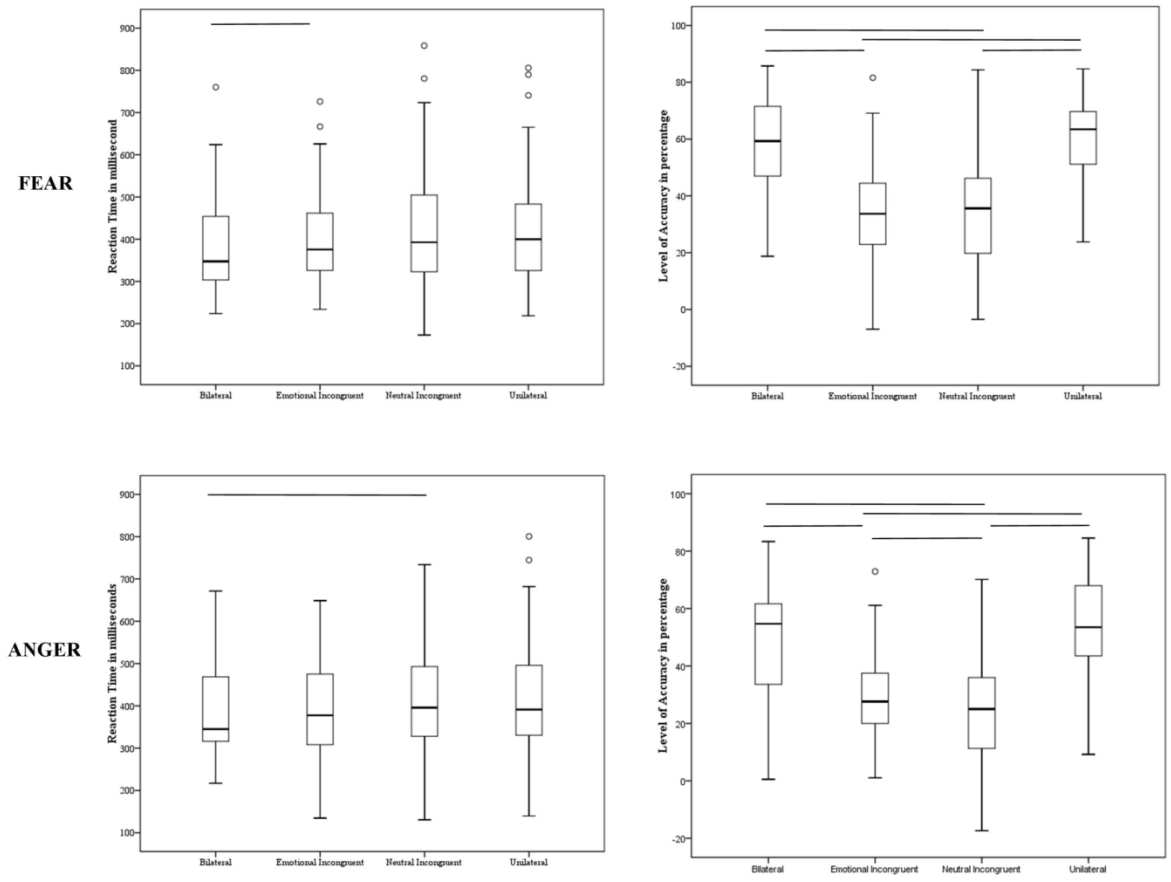
Participants with	M	399	394	384	439	418	436	420	414
fibromyalgia	*SD*	*128*	*156*	*142*	*187*	*141*	*154*	*138*	*155*
Controls	M	374	386	410	423	407	430	375	405
	SD	*98*	*149*	*84*	*166*	*102*	*123*	*103*	*160*
				Accuracy in percentage					
Participants with	M	40.40	43.16	22.29	22.29	15.21	17.43	54.03	44.44
fibromyalgia	*SD*	*28.11*	*21.09*	*14.23*	*13.70*	*21.22*	*15.96*	*22.70*	*21.18*
Controls	M	59.57	55.61	41.28	32.53	33.92	29.76	62.07	56.25
	SD	*18.76*	*16.78*	*17.12*	*20.85*	*17.34*	*23.02*	*17.15*	*19.59*

Fear. The 0.11% of answers provided by the group of participants affected by fibromyalgia's performance and the 0.99% provided by controls were not included in the analysis, since they were anticipations.

Reaction Time. We observed a significant main effect of *Condition* [$F(3,314)=3.84$; $p=0.01$; $\eta_p^2=0.09$]: as shown in the upper part of Figure 1 – left panel, all participants were faster in the bilateral condition in comparison with the emotional incongruent [$p=0.05$], and with the neutral incongruent [$p=0.059$] as a trend. No significant main effect of *Gender* (female pictures M=414; SD=21; male pictures M=401; SD=18) [$F(1,38)=1.46$; $p=0.23$; $\eta_p^2=0.03$] was observed. Focusing on the between-subject factor, no significant main effect of *Group* (participants with fibromyalgia M=427; SD=25; controls M=389; SD=27) [$F(1,38)=0.98$; $p=0.32$; $\eta_p^2=0.002$] emerged. Neither the first level interactions [$p\geq0.33$] neither the second level interaction [$p=0.74$] were significant.

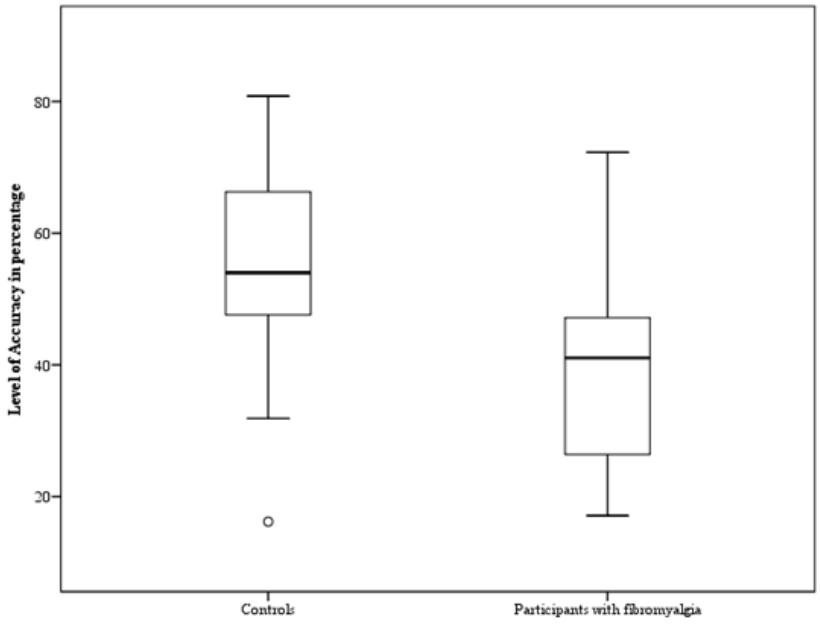
Accuracy. A significant main effect of *Condition* [$F(3,314)=103$; $p<0.001$; $\eta_p^2=0.73$] was reported: as shown in the upper part of Figure 1 – right panel, all participants were significantly more accurate in the bilateral and in the unilateral conditions in comparison with the neutral and emotional incongruent conditions [p always <0.001], in line with the redundant target effect.

Fig 1. Implicit Facial Emotion Recognition Task: the redundant target effect. The upper part regards the emotion of fear; the lower part, the emotion of and anger. For each experimental condition (bilateral, emotional incongruent, neutral congruent, single; x-axis), the mean relative to the Reaction Time expressed in milliseconds on the y-axis (left panels) and the level of Accuracy expressed in percentage on the y-axis (right panels) are depicted. The minimum, the lower quartile, the median, the upper quartile, the maximum, and the outliers are shown. Horizontal lines denote significant differences at $p < 0.05$.



We also observed a significant main effect of *Gender* [$F(1,38)=14.4$; $p=0.001$; $\eta_p^2=0.27$]: participants were less accurate in recognizing fearful expression when expressed by female faces ($M=42.66$; $SD=2.86$) in comparison with male faces ($M=50.92$; $SD=2.26$). Neither the first level interactions [$p \geq 0.17$] neither the second level interaction [$p=0.46$] were significant. A significant main effect of *Group* emerged [$F(1,38)=11.11$; $p=0.002$; $\eta_p^2=0.22$]: as shown in Figure 2, participants with fibromyalgia ($M=38.99$; $SD=15.22$) were significantly less accurate in comparison with the controls ($M=54.6$; $SD=12.36$).

Fig 2. Emotion of Fear. The mean relative to the level of Accuracy expressed in percentage on the y-axis is shown for the two groups (controls vs participants with fibromyalgia). The minimum, the lower quartile, the median, the upper quartile, the maximum, and the outliers are shown.



Since we observed a significant main effect of *Group*, we run again the repeated-measures ANOVA with the within-subjects factors of *Condition* (unilateral, bilateral, neutral incongruent, emotional incongruent) and the between-subjects factor of *Group* (participants with fibromyalgia vs controls) including the global score reported at the TAS-20 as a covariate. We confirmed the significant main effect of *Condition* [$F(3,111)=5.24$; $p=0.002$; $\eta_p^2=0.124$]. Interestingly, the main effect of *Group* still remained significant [$F(1,37)=7.09$; $p=0.011$; $\eta_p^2=0.16$]. The covariate [$F(1,37)=2.23$; $p=0.14$; $\eta_p^2=0.05$] as well as its interaction with the within-subjects factor of *Condition* [$F(3,111)=1.18$; $p=0.31$; $\eta_p^2=0.03$] were not significant. The interaction *Condition*Group* was not significant [$F(3,111)=1.25$; $p=0.29$; $\eta_p^2=0.03$]. These results confirmed

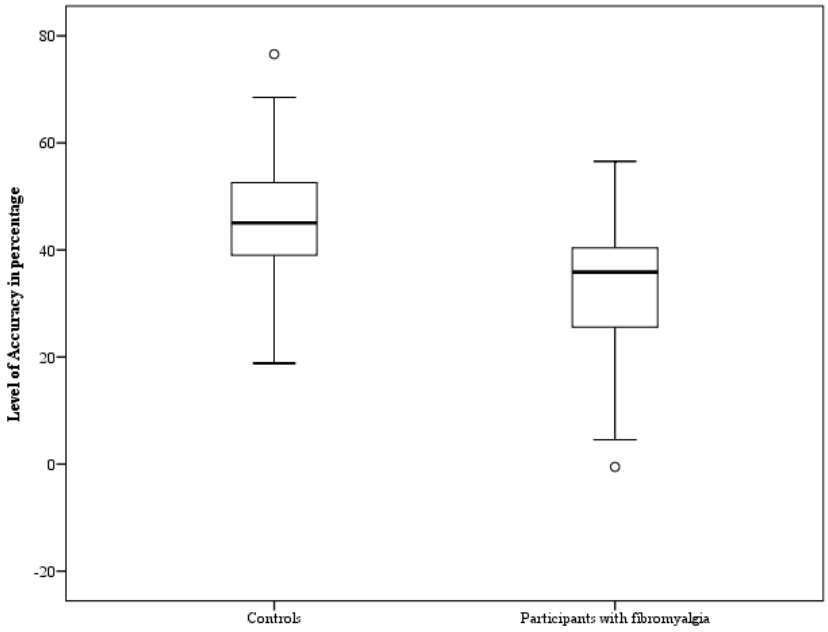
the difference between the two groups, even though when we took into account the different level of alexithymia.

Anger. No answer relative to the group of participants affected by fibromyalgia's performance was excluded; instead, the 0.05% of answers relative to the controls' performance was eliminated since they were anticipations.

Reaction Time. We observed a significant main effect of *Condition* [$F(3,314)=4.85$; $p=0.03$; $\eta_p^2=0.11$]: as shown in the bottom part of Figure 1 – left panel, all participants were significantly faster in the bilateral condition in comparison with the neutral incongruent condition [$p<0.001$]; moreover, a similar - even though no statistically significant - behavior was observed comparing the reaction time relative to the bilateral condition and the emotional incongruent condition [$p=0.058$]. No significant main effect of *Gender* (female pictures M=398; SD=17; male pictures M=415; SD=23) [$F(1,38)=1.66$; $p=0.2$; $\eta_p^2=0.04$] was observed. No significant main effect of *Group* emerged (participants with fibromyalgia M=413; SD=17; controls M=401; SD=31) [$F(1,38)=0.9$; $p=0.76$; $\eta_p^2=0.002$]. Neither the first level interactions [$p\geq0.25$] neither the second level interaction [$p=0.09$] were significant.

Accuracy. We observed a significant main effect of *Condition* [$F(3,314)=122.21$; $p<0.001$; $\eta_p^2=0.76$]: as shown in the bottom part of Figure 1 – right panel, all participants were significantly more accurate in the bilateral and unilateral conditions in comparison with the neutral and emotional incongruent conditions [p always < 0.001], in agreement with the redundant target effect. No significant main effect of *Gender* was observed (female pictures M=41.09; SD=2.66; male pictures M=37.68; SD=2.76) [$F(1,38)=1.65$; $p=0.2$; $\eta_p^2=0.04$] was observed. A significant main effect of *Group* emerged [$F(1,38)=8.71$; $p=0.005$; $\eta_p^2=0.18$]: as shown in Figure 3, participants with fibromyalgia (M=32.4; SD=4.86) were significantly less accurate in comparison with the controls (M=46.37; SD=2.21).

Fig. 3. Emotion of anger. The mean relative to the level of Accuracy expressed in percentage on the y-axis is shown for the two groups (controls vs participants with fibromyalgia). The minimum, the lower quartile, the median, the upper quartile, the maximum, and the outliers are shown.



Neither the first level interactions [p≥0.09] neither the second level interaction [p=0.19] were significant.

Since we observed a significant main effect of *Group*, we run again the repeated-measures ANOVA with the within-subjects factors of *Condition* (unilateral, bilateral, neutral incongruent, emotional incongruent) and the between-subjects factor of *Group* (participants with fibromyalgia vs controls) including the global score reported at the TAS-20 as a covariate. We confirmed the significant main effect of *Condition* [F(3,111)=10.42; p<0.001; η_p^2=0.22]. The main effect of *Group* still remained significant [F(1,37)=6.85; p=0.013; η_p^2=0.15]. Interestingly, the covariate was not significant [F(1,37)=0.12; p=0.73; η_p^2=0.003], as well as its interaction with the within-subjects factor of *Condition* [F(3,111)=25.76; p= 0.35; η_p^2=0.78]. The interaction *Condition*Group* [F(3,111)=1.24; p=0.78; η_p^2=0.009] was not significant. Thus, the main

difference between groups was confirmed (i.e. participants with fibromyalgia less accurate with controls) even though when we took into account the level of alexithymia.

The role of depressive symptoms and anxiety. The two groups were found to report significant different scores at the psychological questionnaires relative to the depressive and trait-anxiety symptoms. To verify if the main results relative to the level of accuracy would be explained by the different psychological functioning between groups, we performed an ANOVA with the within-subjects factors of *Condition* (unilateral, bilateral, neutral incongruent, emotional incongruent) and the between-subjects factor of *Group* (participants with fibromyalgia vs controls) including the psychological scores as covariates.

Fear. When we consider the score relative to the depressive symptoms, we confirmed the significant main effect of *Condition* [$F(3,111)=39.19$; $p<0.001$; $\eta_p^2=0.51$]. Interestingly, the main effect of *Group* still remained significant [$F(1,37)=9.46$; $p=0.004$; $\eta_p^2=0.2$]. The covariate [$F(1,37)=0.004$; $p=0.94$; $\eta_p^2<0.001$] as well as its interaction with the within-subjects factor of *Condition* [$F(3,111)=1.16$; $p=0.32$; $\eta_p^2=0.03$] were not significant. The interaction *Condition*Group* was not significant [$F(3,111)=1.68$; $p=0.17$; $\eta_p^2=0.04$]. When we consider the score relative to trait-anxiety, we confirmed the significant main effect of *Condition* [$F(3,111)=7.33$; $p<0.001$; $\eta_p^2=0.16$]. Interestingly, the main effect of *Group* still remained significant [$F(1,37)=6.87$; $p=0.013$; $\eta_p^2=0.15$]. The covariate [$F(1,37)=0.59$; $p=0.44$; $\eta_p^2=0.01$] as well as its interaction with the within-subjects factor of Condition [$F(3,111)=0.41$; $p=0.74$; $\eta_p^2=0.01$] were not significant. The interaction *Condition*Group* was not significant [$F(3,111)=1.59$; $p=0.19$; $\eta_p^2=0.04$].

Anger. When the score relative to the depressive symptoms was taken into account, we confirmed the significant main effect of *Condition* [$F(3,111)=45.77$; $p<0.001$; $\eta_p^2=0.55$]. The main effect of

Group still remained significant [F(1,37)=10.15; p=0.003; η_p^2=0.21]. The covariate [F(1,37)=1.36; p=0.25; η_p^2=0.03] as well as its interaction with the within-subjects factor of *Condition* [F(3,111)=0.41; p=0.74; η_p^2=0.01] were not significant. The interaction *Condition*Group* was not significant [F(3,111)=1.09; p=0.35; η_p^2=0.02]. When we took into account the score relative to trait-anxiety, we reported again the significant main effect of *Condition* [F(3,111)=4.63; p=0.004; η_p^2=0.11]. Crucially, the main effect of *Group* still remained significant [F(1,37)=10.55; p=0.002; η_p^2=0.22]. The covariate [F(1,37)=1.7; p=0.19; η_p^2=0.04] as well as its interaction with the within-subjects factor of *Condition* [F(3,111)=0.85; p=0.46; η_p^2=0.02] were not significant. The interaction *Condition*Group* was not significant [F(3,111)=0.85; p=0.46; η_p^2=0.02].

These results confirmed that the different level of accuracy between groups was not explained by the level of depressive or state-anxiety symptoms.

5. Discussion

Through an implicit task, we investigated the recognition of fearful and angry facial expressions in women with fibromyalgia compared to women without pain sensations. Both the fibromyalgia patients and the controls reported behavioral performance that was consistent with the attentional phenomenon of the redundant target effect. Participants with fibromyalgia, on the other hand, reported significantly lower accuracy in recognizing fear and anger facial expressions. Despite the different levels of alexithymia between groups, this behavior was still observed. Furthermore, there was no link between this behavior and depressive or anxiety symptoms.

The redundant target effect was observed for all participants when we scored their performance in terms of accuracy. However, when compared to the controls, our fibromyalgia participants had a lower ability to correctly label facial emotion expressions. These findings appeared to be in line

with some previous evidence [277]. We hypothesized that the difficulties in labeling accurately facial expressions in fibromyalgia arise independently from the level of awareness (i.e., higher in [277];lower in our experiment) implied by the task, implying that the disease has a pervasive effect on the emotional processing. Our findings were only partially in agreement with the Di Tella and colleagues [278]. Indeed, they observed a lower level of accuracy in recognizing the facial expressions of anger, but not of fear. Top-down components, such as decision-making about the nature of the emotion expressed by faces, which is largely involved in the case of the facial emotion recognition task, may have a significant impact on accuracy, potentially leading to such heterogeneity. Individual cognitions and beliefs in relation to own emotional perception, as measured by the Toronto Alexithymia Scale – 20 in our study, play a role as well. We can also rule out the possibility that the lower level of accuracy observed in our women with fibromyalgia was due to the higher expression of alexithymic traits.This result was in agreement with Weiß and colleagues [277], but in contrast with Di Tella and colleagues [278], according to whom those individuals affected by fibromyalgia and with higher levels of alexithymia tended to misrecognize angry facial expressions, judging them as expressions of pain. The Toronto Alexithymia Scale – 20 is the most widely used instrument to assess alexithymia. However, because of its self-report nature, this scale is an explicit assessment: the respondents would be aware of their reduced ability to identify and describe feelings in order to report accurately this behavior in the questionnaire [296]. Thus, the questionnaire does not measure the individual emotional capability, but rather its subjective description [297]. Moreover, when individuals suffer from higher levels of alexithymia, as in the case of fibromyalgia, indirect measures of emotional processing might be more suitable to avoid false-negative cases [280]. Also, the behavioral (i.e., the experimental task) and psychological (i.e., the questionnaire) responses might not be strictly in the agreement with each other as well as with the subjective emotional experience, i.e. the feeling. Finally, even though alexithymic traits

and facial emotion recognition are both components of emotional processing, they pertain to two different dimensions. Indeed, the construct of alexithymia highlights the *intra-individual* dimension (i.e. how much I feel and express my emotions) [298,299], although facial emotion recognition refers to the *inter-individual* dimension (i.e. the emotion expressed by the others). Overall, our findings support a methodological approach in which the behavioral measures of emotional processing, as done in our experiment or in [300], are associated with those original measurements.

Since our results, other final considerations should be done. Concentration difficulties, together with decreased other cognitive difficulties (i.e., fibrofog) [301] are commonly reported in fibromyalgia (**Errore. L'origine riferimento non è stata trovata.-Errore. L'origine riferimento non è stata trovata.**) with possible negative side-effects on the experimental performance. The redundant target effect is a psychophysiological unconscious reaction that is triggered by an external event (stimuli) and affects attentional vigilance and behavior. This phenomenon was observed in all of our participants' performances in our study, implying that they (even those with fibromyalgia) have sufficient attentional resources to detect emotional stimuli efficiently. As a result, we ruled out the possibility of sustained and selective visual attention. However, our results relative to the reaction time cannot be discussed in comparison with the previous studies [277,278] in which the performance was not scored in terms of velocity. We suggested extending the investigation of implicit facial emotion recognition to the other primary emotions. Indeed, because we did not test all of them, we cannot say whether the difficulties experienced with fear and anger were also experienced with the other primary emotions. Furthermore, the characteristics of perceived pain should be taken into account, as they have been shown to affect emotion recognition in fibromyalgia patients [302] . When the emotion of fear (rather than anger) was the focus of our research, we discovered that the gender of the visual stimuli had an effect on

the level of accuracy: participants were less accurate in recognizing fearful expressions when expressed by female faces than when expressed by male faces. This result was only partially consistent with previous research findings [283,284]. Nevertheless, the gender effect might be reduced in the case of particular experimental circumstances [303]. Considering that in the present study only women were assessed, in the future male individuals should be tested to deeper understand the role of gender in recognizing facial expressions, even though fibromyalgia is less reported in men [304,305].

In conclusion, we found that fibromyalgia patients had difficulty decoding angry and fearful facial expressions. Nonetheless, psychophysical affective responses that were consistent with the emotional stimulation were observed at a very low level. This behavior was discovered to be unrelated to the level of alexithymic traits as measured by a self-report questionnaire, implying that behavioral and psychological responses may not be entirely consistent with subjective emotional experience. Empathy and adaptive behaviors in social interactions are mediated by the ability to decode other people's emotions efficiently. It may play a role in fibromyalgia patients' psychological well-being if it is impaired.

Study III: The role of pain catastrophizing and pain acceptance in performance-based and self-reported physical functioning in individuals with fibromyalgia and obesity.

Abstract

Physical dysfunction is one of the most serious consequences of fibromyalgia, especially when comorbid obesity is present. Psychological factors are known to influence how people perceive their physical health (i.e., subjective physical health). Physical function, on the other hand, is a multifaceted concept that encompasses both subjective and objective functioning. It's unclear what role psychological factors play in performance-based (i.e., objective) functioning. The purpose of this study is to investigate the contribution of pain catastrophizing and pain acceptance to both self-reported and performance-based physical functioning. In this cross-sectional study, 160 people filled out self-report pain catastrophizing, pain acceptance, and pain severity questionnaires. Physical functioning was assessed using a self-report measure and a performance-based test. At both self-reported and performance-based levels, higher pain catastrophizing and lower pain acceptance were linked to poorer physical functioning. Our findings back up previous research that shows a link between pain catastrophizing and pain acceptance and self-reported physical functioning. This study adds to the existing body of knowledge by revealing new information about the role of psychological factors in performance-based physical functioning. Multidisciplinary interventions that address pain catastrophizing and pain acceptance are recommended and could help women with FM and obesity improve their perceived and performance-based functioning.

1. Introduction

Fibromyalgia (FM) is a chronic pain syndrome that primarily affects women [265,306]. It's marked by widespread pain, fatigue, cognitive impairment, and a loss of physical function. Although the cause of FM is unknown, central sensitization may play a significant role [301,307]. However, it appears that a combination of genetic/biological and psychosocial factors is required to explain how this disease develops and persists [308,309].

One of the most serious consequences of FM is impaired physical functioning [265,310,311]. Physical functional capacity reduction is a significant impediment to daily activities [312–314] and has a negative impact on the quality of life of those who are affected [301,315]. Women with FM, for example, have difficulty performing activities that are necessary for them to remain physically independent, necessitating the assistance of others [312].

The reduced physical functioning is further exacerbated when patients have comorbid obesity [262,316,317]. Obesity is a significant factor to consider in FM because of its high prevalence in this population, which can be attributed in part to FM patients' decreased activity levels [262,310,318]. Obesity adds to the burden of FM-related disability [262]. Obesity is linked to increased pain intensity and reduced physical function in FM patients [262,316,318–320]. Patients with FM and obesity have severe functional impairements as a result of a combination of two issues: FM-related persistent pain and obesity-related restricted movement [262,321–323]. As a result, the two conditions can interact and exacerbate one another. FM-related chronic pain and fatigue can lead to sedentary behavior, physical inactivity, and weight gain, all of which can have a negative impact on physical functioning and pain levels, creating a vicious cycle [66].

In recent years, there has been a growing consensus that it is more important to improve physical functioning in people with chronic pain than it is to reduce pain severity [324–326]. Efforts are being made to shift the focus of pain management from pain reduction to quality of life improvement, in

line with this concept [326–328]. As a result, in recent decades, pain research has focused on modifiable psychological factors (i.e., pain-related cognitions and beliefs about pain), which help to explain individual differences in the adaptation to chronic pain. Among these factors pain catastrophizing and pain acceptance have been the most studied [22,56,57,329,330].

Pain catastrophizing is defined as a set of dysfunctional and negative cognitive-emotional responses to actual or anticipated pain sensations [139]. According to the Fear-Avoidance Model, which is a theoretical model that explains how pain-related cognitions affect pain experience [137,169,170], pain catastrophizing is a key cognitive factor linked to poor functioning. Indeed, the tendency to exaggerate the threat value of pain sensations and ruminate on painful experiences, combined with the tendency to feel helpless during pain episodes (i.e., pain catastrophizing), has been linked to activity aversion and fear of movement [170]. As a result, catastrophizers engage in several safety behaviors, such as movement avoidance, guarded movement, to prevent the worsening of pain [9]. As a result, a cycle of avoidance, deconditioning, and increased disability develops [310,331,332].

In patients with FM, catastrophization about pain has been observed [333] and has been strongly linked with physical impairment in FM and other pain disorders [334–337]. The role of pain catastrophizing in patients with chronic pain and comorbid obesity, on the other hand, is less clear. Patients with severe obesity and osteoarthritis, according to Somers et al., have higher levels of pain catastrophizing than those with less severe obesity and overweight [338]. Shelby and colleagues observed that higher levels of pain catastrophizing were associated with greater disability in older adults with overweight, obesity, and osteoarthritis [145]. Whereas, in a sample of patients with obesity and chronic low back pain, we recently found that there is no link between pain catastrophizing and physical disability [56]. The participants' characteristics in terms of age, clinical condition, and level of obesity, among other things, could explain the contradictory and

heterogeneous results. The lack of evidence on the role of pain catastrophizing in people with FM and comorbid obesity, on the other hand, justifies more research.

Another psychological factor that has gotten more attention in chronic pain research is pain acceptance [339], which refers to the willingness to experience painful sensations without attempting to avoid them, as well as the willingness to continue significant activities despite the presence of pain [340]. While the Fear Avoidance Model regards pain catastrophizing as a significant contributor to physical disability, the Psychological Flexibility Model of pain regards pain acceptance as a critical factor in pain adaptation [341]. The Psychological Flexibility Model emphasizes the importance of an individual's ability to change or persist with a behavior while taking into account personal goals, values, and competing psychological influences (such as pain acceptance) and situational conditions [341]. According to this framework, engaging in value-oriented behaviors despite unpleasant experiences such as pain is critical to living a full and meaningful life. [250]. Indeed, it appears that pain acceptance facilitates participation in valued activities and the pursuit of personal goals [342], which could limit pain interference with daily activities and reduce perceived disability [339,342,343].

In pain research, pain catastrophizing and pain acceptance may be important to take into account. Previous research has primarily focused on identifying psychological factors that have a negative impact on physical disability in patients with chronic pain [57,138,168,333,344,345]. However, resilience factors have gained interest in pain research in recent years [346]. Pain acceptance has been identified as critical component in chronic pain adaptation. In fact, pain acceptance is increasingly being targeted in rehabilitative programs that emphasize resource promotion rather than the modification of dysfunctional behaviors [347]. In conclusion, while pain catastrophizing might negatively impact the process of adaptation to chronic pain, pain acceptance might facilitate it. [348].

The majority of research on physical functioning in patients with chronic pain and FM has relied on self-report measures.[326,334,357,358,349–356]. Performance-based measures evaluate actual functional ability rather than perceived functional ability. In research they have largely been neglected, because they are time-consuming and required the presence of an examiner. Self-report and performance-based measures provide distinct but complementary information about physical functioning [359]. Physical function is a multidimensional concept that include both subjective and objective aspects. [326,360–362]. Psychological factors contribute more to subjective aspects that involve cognitive evaluation (such as perceived functioning) than to actual performance in daily activities [363]. Because previous studies assessed subjective perceptions, they may have revealed strong associations between psychological factors and self-report measures of physical functioning. Importantly, in individuals with diverse musculoskeletal chronic pain, performance-based and self-reported physical function are not significantly correlated [360]. Furthermore, a study found that people with FM have lower subjective physical functioning than they do objective performance [364]. To advance interdisciplinary interventions for chronic pain, research that evaluates and compares the contribution of psychological factors to perceived and performance-based functioning outcomes is required.

In summary, the purpose of this study is to look into the effects of pain catastrophizing (vulnerability factor) and pain acceptance (resilience factor) on physical functioning in people with FM and comorbid obesity. We hypothesized that pain catastrophizing [334–336,343,345] would be associated with decreased physical functioning, while pain acceptance would be associated with better physical functioning [339,349,357,365]. We also hypothesized that psychological variables would contribute more to perceived functioning than to performance-based functioning [363].

2. Materials and Methods

2.1 Procedure and participants

A cross-sectional study was carried out. G. Power was used to perform an a priori power analysis (version 3.1.9.4) [146] to determine the sample size required to detect statistical significance. With a conservative small-to-medium effect size of the predictors (0.10), an alpha of 0.05, and a power of 0.90, a sample size of n = 130 was needed to detect the hypothesized effects.

From January to September 2019, 160 women were recruited in a row at the start of a one-month hospitalization program for weight loss and physical therapy at the IRCCS Istituto Auxologico Italiano's Orthopaedic Rehabilitation Unit (Piancavallo, Italy). Before beginning a physical therapy and nutritional rehabilitative program for weight loss, data was collected during the first week of the diagnostic assessment.

Participants were eligibile for this study if they met the following criteria: (a) had a FM diagnosis provided by a rheumatologist according to Wolfe et al. criteria [265]; (b) met the American College of Rheumatology (ACR) Research Criteria for fibromyalgia [366,367], as measured by the Fibromyalgia Survey Questionnaire in its Italian version [344]; (c) were over the age of 18; and (d) were able to complete the questionnaires and sign an informed consent form.

Patients were excluded if they (a) had psychiatric disorders with psychotic symptoms or severe personality disorders; (b) had previously or were currently receiving psychological treatment for FM; or (c) had comorbid acute pain conditions or comorbid chronic pain conditions other than FM.

2.2 Measures

Data on socio-demographics and clinical outcomes. Participants completed a self-report protocol that included their age, weight, and height (in centimeters), job status (employed, unemployed, or disability pension), years of education, current opioid use, and pain duration (in years).

Fibromyalgia symptomatology. The Italian version of the Fibromyalgia Survey Questionnaire (FSQ) [344] was used to assess the ACR Fibromyalgia Research Criteria [366,367]. This measure, which is recommended in research [366,368], was administered to evaluate the level of symptomatology required to confirm the diagnosis of FM. Individuals must meet the following Research Criteria: (1) Widespread Pain Index ≥ 7 and Symptom Severity Scale score ≥ 5 OR Widespread Pain Index of 4–6 and Symptom Severity Scale score ≥ 9; (2) symptoms have generally been present for at least 3 months.

Pain severity. The Numeric Pain Rating Scale (NPRS) [181] was used to assess pain severity levels. It consists of an 11-point scale (anchors 0= no pain; 10= worst possible pain). The Numeric Pain Rating Scale is a well-validated and widely used measure of pain severity in chronic pain conditions [148].

Pain catastrophizing. The Pain Catastrophizing Scale (PCS) [369] is a self-report measure of pain-related catastrophic thinking. It consists of 13 items on a five-point Likert scale (from 0 = "not at all" to 4 = "all the time"). The total score ranges from 0 to 52, with higher scores indicating higher levels of pain catastrophizing [370]. The Italian version [370] has psychometric properties comparable to the original version. In the current study, internal consistency was excellent (Cronbach's α = 0.89).

Pain acceptance. The Chronic Pain Acceptance Questionnaire (CPAQ) is a measure of pain acceptance [252,371,372] that consists of 20 items scored on a 7-point Likert scale (0= 'Never true' to 6= 'Always true'). The maximum total score is 120, with higher scores indicating greater acceptance. The Italian version of the questionnaire was used [373], which, in line with the original

version, has obtained good psychometric properties. In the present study, the internal consistency of this measure was excellent (Cronbach's $\alpha = 0.90$).

Self-report physical functioning limitations. The Physical Functioning subscale of the Fibromyalgia Impact Questionnaire- Revised was used to assess self-reported physical functioning limitations (PF-FIQR). The FIQR consists of 21 items. The items are scored on an 11-point numeric rating scale ranging from 0 to 10, with 10 representing the "worst" functioning scores. All questions concern the operation of the previous seven days. Higher total scores indicate a greater impact of the disease as well as poorer functioning. The FIQR evaluates three domains: (a) "physical function," (b) "overall impact," and (c) "symptoms." The total score, which evaluates the impact of FM on overall functioning, can also be calculated. Given the purpose of the current study, the physical function subscale was used. The FIQR's physical functioning subscale, in particular, includes 9 items designed to assess the degree of physical impairment. This scale has previously been used in research [331,364,374,375]. The physical functioning subscale of the FIQR has a score range of 0 to 30, with higher scores indicating poor physical functioning. The FIQR and its subscales have excellent psychometric properties and discriminant ability. Internal consistency was high in the current study (Cronbach's = 0.82).

Performance-based physical functioning. The 6-Minute Walking Test (6MWT) is a performance-based test that assesses the ability to walk for a set distance and is a simple and low-cost measure of physical function. The 6MWT has been used in research with persons with FM [331,375,376] with good applicability and reliability findings [331,377]. In this test, the participant must walk for six minutes along a 45.7-meter-long rectangular course. Walking distance is measured in meters, with higher scores indicating improved physical performance. The distance walked during the 6MWT was found to be shorter in females with FM when compared to healthy women (i.e., discriminant validity) [312]. Moreover, the 6MWT has good reproducibility and is recommended for assessing

walking ability in obese individuals.[378]. Obese women were also found to walk significantly shorter distances during the 6MWT than their normal-weight counterparts [379,380].

2.3 Statistical analysis

Categorical variables were described using counts and percentages, while continuous variables were described using means and standard deviations. Height in meters and weight in kilograms were used to compute Body Mass Index (i.e., BMI, as the weight in kilograms divided by the square of height in meters (kg/m2)[40]), which is considered as an indicator of obesity (BMI ≥ 30)[40]. Pearson bivariate analyses were used to examine the relationships between the Numeric Pain Rating Scale (i.e., pain severity), the Pain Catastrophizing Scale (i.e., pain catastrophizing), the Chronic Pain Acceptance Questionnaire (i.e., pain acceptance), the Fibromyalgia Impact Questionnaire's Physical functioning scale (i.e., self-reported physical functioning), and the 6-Minute Walking Test (i.e., performance-based physical functioning).

We used multivariate hierarchical regression analyses to answer our research question, as has been done in previous studies. We checked the data's normality, linearity, homoscedasticity, and multicollinearity assumptions before performing multivariate regression. To assess the contribution of pain catastrophizing and pain acceptance to self-reported physical functioning limitations, pain catastrophizing and pain acceptance were separately introduced as dependent factors in two separate regressions. In both models, age [381,382], opioid use [382,383], and pain duration [384,385] were entered into the first step as covariates to control for their relationship with the outcome measures. Pain severity was entered in the second step, because of its association with physical functioning [331,386]. In the third and final step, pain catastrophizing and pain acceptance were entered concurrently. The change in explained variance (R2) was used to assess the additional variance of

the dependent variables accounted for by the variables in each block. The significance was determined using a p.05. criterion. The Jamovi software was used to analyze the data [153].

3. Results

Table 1 shows the characteristics of the participants.

Table 1. Means and standard deviations of sociodemographic characteristics and clinical measures. The theoretical range and actual range are reported. N=160

Sociodemographic characteristics			N=160
Age in years (mean± SD)			43.6±7.25
Body mass index (mean± SD)			44.3±7.15
Pain duration in years (mean± SD)			7.08±2.70
Current opioid use (%)			13.1%
Employeed (%):			71.9%
Full-time			22.5%
Part-time			49.4%
Clinical measures	Theoretical range	Sample's range	Mean ±SD
Widespread Pain Index	0-19	7-18	13.8±2.70
Symptoms Severity	0-12	5-11	8.13±1.85
Numeric Pain Rating Scale	0-10	3-9	5.67±1.58
Pain Catastrophizing Scale	0-52	0-44	27.3±10.3
Chronic Pain Acceptance Questionnaire	0-120	21-74	51.7±11.2
Physical Functioning subscale	0-30	9-29	17.7±4.77
6-Minute Walking Test in meters	NA*	201-402	306±59.4

Note. *NA: not applicable.

3.1 Correlations

Table 2 shows Pearson's correlations between measures. Catastrophizing about pain and accepting pain were both significantly and negatively correlated (r=-.49, p<.001). Pain catastrophizing was

found to be significantly and positively related to pain severity (r=.42, p<.001), perceived limitations in physical functioning (r=.43, p<.001), and performance-based physical functioning (r=-.57, p<.001). Pain acceptance, on the other hand, was significantly and negatively related to pain severity (r=-.39, p<.001) and limitations in physical functioning (r=-.47, p<.001); whereas it was positively related to performance-based physical functioning (r=.52, p<.001). Perceived physical limitations were negatively related to performance-based physical functioning (r=-.53, p<.001), because higher scores on the self-reported physical functioning limitations measure indicate greater disability, whereas higher scores on the performance-based test indicate better physical functioning.

Table 2. Pearson correlation coefficients between study variables. N=160

	1.	2.	3.	4.
1. Pain severity (NPRS)	-			
2. Pain catastrophizing (PCS)	.42*	-		
3. Pain acceptance (CPAQ)	-.39*	-.49*	-	
4. Self-reported physical functioning limitations (PF-FIQR)	.36*	.43*	-.47*	-
5. Performance-based physical functioning (6MWT)	-.38*	-.57*	.52*	-.53*

Note. NPRS: Numeric Pain Rating Scale; PCS: Pain Catastrophizing Scale; CPAQ: Chronic Pain Acceptance Questionnaire; PF-FIQR: Physical Functioning subscale of the Fibromyalgia Impact Questionnaire; 6MWT: 6 Minute Walking Test. * p < .001.

3.2 Hierarchical regression relative to self-reported disability

Self-reported physical functioning limitations were used as the dependent variable in the first multivariate hierarchical regression study (Table 3). The demographic characteristics (i.e., pain duration, age, current opioid use, and body mass index) included in the first step explained a nonsignificant 4% (R^2= 0.04) variance of self-report physical functioning limitations in the first

step (F (4,155) =1.78; p =0.14). Pain severity, which was included in the second step, significantly contributed an additional 12% of the explained variance (ΔF (1,154) = 22.60; p < .001; ΔR^2 =0.12) of self-report physical functioning limitations. The third step, which included pain catastrophizing and pain acceptance, significantly explained an additional 17% of the variance of self-reported physical functioning limitations (ΔF (2,152) = 20.10; p < .001; ΔR^2 =0.17).

In the final model, opioid use (B = 2.66, p=.006), pain acceptance (B = −0.13, p < .001), and pain catastrophizing (B = 0.12, p = <.001) contributed unique variance to the prediction of self-reported physical functioning limitations. When the contribution of pain catastrophizing and pain acceptance was taken into account, pain severity, which was significantly associated with self-reported physical functioning limitations in the second step, became nonsignificant.

Table 3. Multivariate hierarchical regression predicting self-report physical functioning limitations.

	Step 1		**Step 2**		**Step 3**	
Factors	B (SE)	*p*	B (SE)	*p*	B (SE)	*p*
Pain duration	-0.04 (0.14)	.792	0.02 (0.13)	856	-0.07 (0.12)	.566
Age	-0.01(0.05)	.826	0.02 (0.05)	.707	-0.01(0.04)	.929
Current opioid use	2.86(1.13)	.012	2.70 (1.06)	.110	2.66 (0.95)	.006
Body Mass Index	0.01 (0.05)	.897	-0.04 (0.05)	.400	-0.09 (0.23)	.054
Pain severity			1.09 (0.23)	<.001	0.44 (0.23)	.060
Pain catastrophizing					0.12(0.04)	.003
Pain Acceptance					-0.13 (0.03)	<.001

3.3 Hierarchical regression relative to performance-based functioning

The dependent variable in a second multivariate hierarchical regression was performance-based physical functioning (Table 4). The first step, which included demographic variables (i.e., pain duration, age, current opioid use, body mass index), explained a significant 12% (R^2=0.12) variance of performance-based physical functioning (F (4,155) =5.23, p=<0.001). In the second step, pain severity contributed an additional 14% variance of performance-based physical functioning (ΔF (1,154) =28.9; p<.001; ΔR^2 =0.139). Next, pain catastrophizing and pain acceptance included in the third step significantly explained an additional 23% variance of performance-based physical functioning (ΔF (2,152) = 33.3; p < .001; ΔR^2 =0.226).

Pain duration, current opioid use, and pain severity were significantly associated with performance-based physical functioning in the final model. Additionally, both pain catastrophizing (B = −0.364; p < .001) and pain acceptance (B =0.272; p = <.001) uniquely and significantly contributed to performance-based physical functioning.

Table 4. Multivariate hierarchical regression predicting performance-based physical functioning.

	Step 1		**Step 2**		**Step 3**	
Factors	B (SE)	*p*	B (SE)	*p*	B (SE)	*p*
Pain duration	-3.85 (1.66)	.022	-4.65 (1.54)	.003	-3.37 (1.30)	.010
Age	-1.07 (0.62)	.089	-1.16 (0.58)	.045	-0.81 (0.49)	.099
Current opioid use	-37.79 (13.47)	.006	-35.68 (0.59)	.005	-35.99 (10.43)	<.001
Body Mass Index	-1.02 (0.63)	.109	-0.36 (0.59)	.544	0.29 (0.51)	.574

Pain severity	-14.46 (2.69)	<.001	-5.05 (2.54)	.048
Pain catastrophizing			-2.21 (0.43)	<.001
Pain Acceptance			1.45 (0.37)	<.001

4. Discussion

The goal of this research was to evaluate the contribution of pain catastrophizing and pain acceptance to self-reported and performance-based physical functioning in people with FM and obesity. When measured using a self-report and a performance-based measure, we found that higher pain catastrophizing and lower pain acceptance were significantly associated with poorer physical functioning. Even after controlling for body mass index, pain duration, current opioid use, and pain severity, both pain catastrophizing and pain acceptance were significant predictors of self-report and performance-based physical functioning. However, contrary to our expectations, psychological variables had a greater impact on performance-based physical functioning than on self-reported physical functioning.

Research has shown that pain catastrophizing and pain acceptance are important predictors of self-reported physical functioning in samples with acute [387,388] and chronic pain [388,389], including FM [334,390–393]. Our findings are in line with the evidence presented previously. Previous research, on the other hand, has primarily focused on subjective functional capacity measures. Our study adds to the body of knowledge by combining a self-report measure with a performance-based test that provides a more objective assessment of physical function. Psychological factors play a role in both perceived and actual physical functioning, according to the findings of this study. Importantly, both pain catastrophizing and pain acceptance played a separate role in the prediction of self-report and performance-based functioning, implying that the two factors are likely to

influence physical functioning in different ways. Finally, the fact that both psychological factors had a significant impact on physical functioning when combined in a multivariate analysis supports the idea that they should be targeted separately in multidisciplinary interventions. Furthermore, this supports the validity of various psychological models for understanding pain, such as the Fear-Avoidance Model and the Psychological Flexibility Model.

Individuals who catastrophize tend to appraise pain as a catastrophic and harmful experience and frequently ruminate and feel hopeless about it [336,394]. According to the findings, the tendency to catastrophize about pain may have a negative impact on both an individual's perception of what they are capable of in terms of physical performance (i.e., what I think I can do) and their actual physical performance (i.e., what I can do). We propose a mechanism for why this could happen. Pain catastrophizing might increase the level of attention and awareness of painful sensations [395], thus increasing protective behaviors. Individuals with chronic pain who catastrophize engage in a variety of safety behaviors (e.g., activity avoidance, movement restriction, and guarded movement) to prevent the worsening of pain symptoms [9]. Obesity, in turn, might increase avoidance in chronic musculoskeletal pain conditions [396]. Individuals' beliefs that being overweight causes additional damage or increases pain appear to play an additional role in limiting activity, which combined with skin friction, discomfort, respiratory difficulties [397] might result in the avoidance of movements and in turn impediment to weight loss [396].

On the other hand, the willingness to continue with important activities despite pain (i.e., acceptance) may have a positive impact on both subjective and actual physical functioning [339,342,343]. Patients who accept pain as an unpleasant experience that they are willing to experience in order to achieve their goals are more likely to move and participate in significant activities despite the pain. Furthermore, acceptance may facilitate chronic pain adaptation by focusing on one's personal goals rather than pain control, preventing the use of pain-avoidance behaviors

[339,342,343]. Taking all of the preceding into account, reducing pain catastrophizing and increasing pain acceptance through psychological interventions may assist people with chronic pain in reducing the use of unnecessary and harmful protective behaviors that perpetuate a cycle of avoidance, deconditioning, and increased disability [310,331,332].

We found a significant and moderate relationship between the self-reported measure of physical function and the performance-based test. Our findings are similar to those of Mannerkorpi and colleagues [331]. However, they contradict Greenberg and colleagues' findings, which found no significant relationship between subjective and objective measures of physical functioning in people with different types of chronic pain [360]. These disparities could be attributed to differences in sample characteristics or measurements used across studies, or they could indicate that the relationship between subjective and objective components of physical functioning is modulated differently in clinical conditions. While this is acknowledged, more research is required to determine the extent to which self-report and objective measures of functioning are associated in different populations due to the scarcity of existing studies. Such studies are significant because they investigate whether a subjective assessment of physical functioning can be used as a reliable alternative measure to objective tests of physical functioning, which are typically more time-consuming.

The contribution of psychological factors was greater for performance-based physical functioning than for self-reported physical functioning, which was an interesting and unexpected finding. While, psychological aspects have a greater impact on factors that require cognitive evaluation [363]. The results could be explained by the fact that the performance-based test was both interpreted as painful and actually painful to perform. As a result, paying attention to a potential or actual pain-inducing movement may cause the repertoire of pain-related cognitive/coping strategies to become more prominent and influential in motivating different behaviors. Individuals who tend to

catastrophize about pain, for example, may be encouraged to restrict movement when they experience pain in real-world situations, whereas those who accept pain may be encouraged to continue moving. More research is needed to confirm this hypothesis, which could lead to an exciting new line of research in the future.

The body mass index was not significantly related to self-reported and performance-based physical functioning. This result contradicted previous evidence [43,261,262]. It should be noted, however, that the variability in Body Mass Index in our sample was limited because only obese people were included. Furthermore, recent research has suggested that the BMI is an insufficient and oversimplified measure that fails to adequately capture the complexity of obesity [72,398]. Different obesity indices, such as adiposity level and adipose tissue distribution, could be used in future studies [399,400].

Current opioid use was found to be significantly associated with both self-report and performance-based physical functioning, among other control factors. Individuals on opioid therapy may become reliant on the medication as a result of their poor subjective and objective physical functioning. Instead, only performance-based physical functioning was significantly related to the duration and severity of pain. The biological function of pain is to alter behavior by prioritizing protection and avoidance [1], and it seems likely that pain has a more pronounced effect on physical performancethan on its perception [401]. Regarding pain duration, it's possible that people with a longer history of chronic pain have developed dysfunctional coping strategies over time (such as avoiding movement and activities due to pain persistence despite treatment) that lead to deconditioning and disuse, worsening their ability to move [137,173].

This study's findings could have a number of clinical implications. Measures of pain catastrophizing and pain acceptance should be included in the assessment of biopsychosocial aspects of pain in FM and obesity, according to our findings, to provide a more complete picture

of the factors that significantly affect physical functioning. Furthermore, our findings suggest that pain catastrophizing and pain acceptance should be treatment targets in psychological evidence-based interventions aimed at improving physical functioning in people with FM and obesity. In support of this hypothesis, Baranoff and colleagues [339] highlighted how changes in pain catastrophizing and pain acceptance accounted for changes in self-reported and performance-based disability in individuals with chronic pain, primarily located in the low back. Importantly, because both pain catastrophizing and pain acceptance are significant predictors of both perceived and actual physical functioning, multidisciplinary interventions targeting both factors are likely to improve both aspects of functional capacity. More research is required to test this hypothesis in individuals with FM, especially when it is associated with obesity.

Finally, it is important to note that the willingness to move and engage in physical activity is critical in the management of both FM and obesity. Physical activity improves physical functioning in individuals with FM [402–407] as well as in those with obesity [408–410]. Consequently, current and previous research supports the idea that it might be beneficial to reduce pain catastrophizing and enhance pain acceptance in order to promote adherence to physical activity and a healthy, active lifestyle in individuals with FM and obesity. More research is needed to determine what other factors might be important in promoting physical activity compliance.

This study has some limitations. We did not include a control group (for example, individuals who are only affected by FM or obesity. In addition, we focused only on two psychological factors. While both are important factors according to the pain literature, other psychological factors, such as kinesiophobia [57] or pain self-efficacy [411], might also play a role in physical functioning. Furthermore, while the self-report questionnaire used referred to a period in the past (e.g., the previous week), the performance-based measure was based on the present moment. While most available measures refer to this timeframe, the development of self-report measures that refer to

the current time of assessment could be used to mitigate this mismatch. In addition, the pain severity measure used in this study assesses the intensity of perceived pain at the time of completion. Since there can be variability in levels of perceived pain in fibromyalgia even within a single day [412–414], measures that assess medial pain intensity over a week could be implemented to address this limitation. Finally, because we focused on individuals with FM and obesity as a comorbid condition, the findings might not be generalizable to other populations.

Our findings suggest that pain catastrophizing and pain acceptance should be addressed to improve performance-based and self-reported physical functioning in individuals with FM and obesity. If these components are ignored, rehabilitative interventions may neglect critical factors associated with the maintenance of poor physical functioning and physical health.

Study IV: Pain catastrophizing, pain acceptance and kinesiophobia as mediators of the relationship between pain severity and disability.

Abstract

The aim of the current study was to evaluate the mediational role of pain catastrophizing, pain acceptance and kinesiophobia in the association between pain severity and disability. Also, disability was evaluated using both self-reported and performance based measures. 165 patients with obesity and fibromyalgia was recruited. Two multiple mediation model was performed. According to our results in the association between pain severity and self-reported disability, pain acceptance and kinesiophobia played a significant role. While in the relationship between pain intensity and performance based physical functioning pain catastrophizing and kinesiophobia resulted as significant mediators. It appears that pain intensity has an impact on disability only when psychological factors are taken into account. Also perceived and actual physical functioning are influenced by different psychological factors.

1. Introduction

In addition to widespread and persistent pain, patients with fibromyalgia experience other distressing symptoms, such as fatigue, poor sleep quality, cognitive problems, and mood disorders [415]. The etiology of FM is still unclear, but it appears that a complex interplay of genetic, biological, and psychological factors plays a role in its development and maintenance [308]. FM has a negative impact on the quality of life [314] and is related to impaired physical functioning [315]. Decline in physical functioning is one of the main consequences of FM and it is related with severity of perceived pain [416,417]. Hovewer, research showed that reducing pain intensity does not result in a proportional improvement in physical functioning [178,351,418,419]. In line with this, both pharmacological and non-pharmacological interventions that improve physical functioning do not consistently reduce perceived pain intensity [420]. The inconsistencies in the relationships suggest that the relationship between pain severity and physical functioning may be mediated by other factors (e.g. psychological factors)[421]. It is critical to identify these mediating factors because research shows that improvements in physical functioning can lead to a reduction in pain intensity by reversing or preventing deconditioning and disuse. Thus, focusing on the variables that mediate the relationship between pain intensity and physical functioning could help improve functioning and, in turn, decrease pain severity.

Cognitive, affective, and behavioral factors contribute to disability in several chronic pain conditions [137,169,170]. The Fear Avoidance Model [170] and the Psychological Flexibility Model [250,340] are two of the most well-known model devised for describing how psychological factors influence the progression of physical disability. According to the FAM, pain catastrophizing and kinesiophobia are two factors that have a negative impact on the development of physical disability [56,57,138,334,335]. Indeed, individuals who appraise pain as catastrophic (i.e., pain catastrophizing)

experience pain-related fear which leads to avoidance of movement and activities associated with pain (i.e., kinesiophobia) [157,422]. Specifically, pain catastrophizing is defined as an exaggerated and negative appraisal of pain that occurs in response to actual or anticipated pain experiences [139,369]. For example, individuals who are prone to catastrophization, magnify the threat value of pain, ruminate on pain experiences and feel helpless. Kinesiophobia refers to an excessive, irrational, and debilitating fear of physical movement and activity resulting from a feeling of vulnerability due to painful injury or reinjury [423]. Thus, individuals might develop cognitions and beliefs that physical activity will result in more pain and re/injury. Pain catastrophizing and kinesiophobia, when combined, might lead to aversion to movement and activities, which contributes to disability and disuse, in the long run [170]. As a result, the patient is trapped in a vicious cycle of increasing pain and disability.

On the contrary, pain acceptance is one of the key mechanisms that could have a positive impact on physical functioning [391], according to the Psychological Flexibility model [252]. It is defined as a willingness to live with pain without trying to reduce, avoid or try to change it. This means that individuals are willing to engage in valued activities and to focus on personal goals despite pain.

It is unclear which of these factors has a greater impact on FM physical functioning. Early detection of either of these factors in FM patients may help to prevent or even reverse functional decline.

Most of the studies focus on self-reported (i.e. subjective perception) physical functioning. Even though this is an important aspect to consider, it appears that there might be a mismatch between self-reported and performance-based physical functioning (e.g. six minute walking test). It has been suggested that these two type of measurements provide different and complementary information [360]. Thus, different psychological factors might influence subjective physical functioning and physical performance. It is interesting to consider whether these two aspects of

physical functioning (i.e. self-reported and performance-based) are influenced by different factors. This would allow us to design treatments that intervene on specific, evidence-based targets to improve both the perceived aspect of functioning and physical performance. The importance of improved physical function as a primary outcome in the treatment of chronic pain is widely recognized. It is critical to assess and improve physical functioning in a comprehensive manner, taking into account both the self-reported and performance-based physical functioning, in line with the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMPAACT) guidelines [324]

However, to our knowledge, no study has tested the mediating effects of multiple psychological factors such as pain catastrophizing, kinesiophobia, and pain acceptance on the association between pain intensity and disability (both self-reported and performance-based) in individuals with FM. This type of study would allow us to compare the relative importance of these three psychological factors as mediators. Based on previous results on chronic low back pain [57], heterogeneous chronic pain [424,425] and FM patients [334], we hypotesized that pain catastrophizing, kinesiophobia, and pain acceptance would mediate the relationship between pain intensity and physical functioning.

2. Methods

2.1 Procedure and participants

A cross-sectional study was performed. Power analysis. We consecutively recruited one hundred and sixty-five individuals at the start of a one-month-long hospitalization for physical rehabilitation and weight loss. The recruitment process began in June 2020 and ended in July 2021 at the IRCCS Istituto Auxologico Italiano, U.O. di Riabilitazione Osteoarticolare, Ospedale S.

Giuseppe, Piancavallo, Italy. Data was collected during the first week of diagnostic assessment, prior to the start of any physical therapy and nutritional intervention.

Participants were eligible if they met the following criteria: (a) had previously been diagnosed with FM by a rheumatologist [265]; (b) met the American College of Rheumatology (ACR) Research Criteria [366,367], as measured by the Fibromyalgia Survey Questionnaire [344]; (c) were between the ages of 18 to 60 ; and (d) could sign an informed consent form. Patients were excluded if they (a) had psychiatric disorders with psychotic symptoms; (b) had a diagnosed personality disorder; (c) had previously received psychological intervention for FM management; (d) had comorbid acute or chronic pain conditions other than FM.

2.2 Measures

Participants filled out a self-report form with sociodemographic information such as age, weight (in kilograms), and height (in centimeters),

Pain intensity. The Numeric Pain Rating Scale (NPRS) was used to assess pain severity levels. It is a well validated and widely used measure for pain severity in chronic pain conditions. It is composed by 11-point scale where 0 = no pain and 10= worst possible pain.

Pain catastrophizing. The Pain Catastrophizing Scale (PCS) [369] is a measure of catastrophic thinking about pain. It comprises 13 items on a five-point Likert scale, from 0 = "not at all" to 4 = "all the time". The total score ranges from 0 to 52, with higher scores corresponding to higher levels of pain catastrophizing [370]. The Italian version [370] shows psychometric properties similar to the original version. Internal consistency was excellent in the current study (Cronbach's $\alpha = 0.90$).

Pain acceptance. The Chronic Pain Acceptance Questionnaire (CPAQ) is a self-report measure of pain acceptance [252,371,372]. It consists of 20 items on a 7-point Likert scale, from 0= "never true" to

6= “always true”). The maximum total score is 120, with higher scores corresponding to higher levels of pain acceptance. The Italian version of the questionnaire [373] has psychometric properties in line with the original version. In the present study, the internal consistency of this measure was excellent (Cronbach’s α = 0.89).

Fear of movement. The Italian version [113] of the Tampa Scale of Kinesiophobia (TSK) [113] was used to evaluate kinesiophobia. The TSK consists of 13 items ranging from “strongly disagree” to “strongly agree”, on a 4-point Likert scale [149]. The TSK has two sub-scales relative to activity avoidance (i.e., belief that activities that cause pain should be avoided) and harm (i.e., belief that pain is a sign of bodily damage). The total score ranges from 13 to 52 with higher scores indicating higher levels of kinesiophobia [113]. The TSK has been validated in chronic LBP [35]. The Italian version of the TSK shows a good factorial structure and acceptable psychometric properties [113]. In the current study, the internal consistency of this measure was excellent (Cronbach’s α=0.90).

Self-reported disability. The Physical Functioning subscale of the Fibromyalgia Impact Questionnaire- Revised was used to assess self-reported disability (PF-FIQR). The FIQR is a 21-item measure with a numeric rating scale of 0 to 10, with 10 corresponding to “worst” functioning scores. All questions concern the functioning of the previous seven days. The FIQR evaluates three domains: (a) "physical function," (b) "overall impact," and (c) "symptoms." The total score evaluates the impact of FM on overall functioning, with higher total scores indicating a greater impact of the disease and poorer functioning. Given the purpose of the current study, the physical function subscale was used. The FIQR's physical functioning subscale includes 9 items that assess the degree of physical impairment. This scale has previously been used in research.[333,366,376,377]. The physical functioning subscale of the FIQR has a score range of 0 to 30, with higher scores

indicating poor physical functioning. The FIQR and its subscales have good psychometric properties and discriminant ability. In the current study, internal consistency was good (Cronbach's $\alpha = 0.82$).

Performance based physical functioning. The 6-Minute Walking Test (6MWT) is a performance-based test that is used to assess the ability to walk. It is a quick and inexpensive measure of physical functioning. The 6MWT has been used in research with persons with FM [333,377,378] with good applicability and reliability findings [333,379]. In this test, the participant is required to walk for six minutes along a rectangular course of 45.7 meters. Walking distance in meters is measured and higher scores indicate better physical performance. The distance walked during 6MWT and has been found to be shorter in females with FM than in healthy women (i.e., discriminant validity) [314]. The 6MWT has good reproducibility and is recommended for assessing walking ability in individuals with obesity [380]. Women with obesity have also been found to walk significantly shorter distances during the 6MWT than their normal-weight counterparts [381,382].

2.3 Statistical analysis

For continuous variable, descriptive statistics were calculated in terms of means, standard deviations and ranges, and for categorical variables, in terms of frequencies and percentages.

Preliminary, to identify potential covariates, Pearson's correlation was used to verify the relationship between age, BMI, and scores at clinical measures. We used point-biserial correlation to study the association with sex. Correlation coefficients were classified according to Cohen [182] (.10=small; .30=medium; .50=large). Prior to perform the main analyses, the multicollinearity the independent factors and the mediators scores was tested.

Pearson's correlation coefficients were performed to analyze the relationships between variables. sociodemographic characteristics that showed significant association in bivariate analyses with the outcome variable were included in the multiple mediation analysis to control confounding variables.

We performed two multiple mediation models. In the first model, we evaluated pain catastrophizing, pain acceptance, and kinesiophobia as mediators (i.e., M) of the effect of pain intensity (i.e., X) on self-reported physical functioning (i.e., Y). In the second model, we evaluated pain catastrophizing, pain acceptance, and kinesiophobia as mediators of the effect of pain intensity on performance-based physical functioning. The mediation analysis calculated the direct effect, the indirect effect, and the total effects (Preacher & Hayes, 2008). The effect of X (i.e., pain intensity) on Y (i.e., physical functioning) is referred to as the direct effect (c'path). The effect of X on Y via M (i.e., pain catastrophizing, pain acceptance, kinesiophobia) is referred to as indirect effects (ab paths). Path a represents the effect of X on M, whereas path b is the effect of M on Y controlling the effect of X. Lastly, we determined the total effect of X on Y (c path), which is the sum of the direct effect and indirect effects (Preacher & Hayes, 2008). The paths were quantified with unstandardized regression coefficients (B) since they are the preferred metric in causal modeling and standardized coefficients are considered uninterpretable. To test the significance of the indirect effects, bias-corrected (BC- CIs) bootstrap confidence intervals were computed following the procedures recommended by Preacher and Hayes (2008). The bootstrap estimates were based on 5000 bootstrap samples and a 95% CI was used.

3. Results

3.1 Sample characteristics

Table 1 summarizes demographic and clinical characteristics of the sample.

Table 1. Means, standard deviations of sociodemographic variables and clinical measures.

Sociodemographic Variables			N=165
Age in years (mean± SD)			43.8±7.26
BMI (mean± SD)			44.4±7.22
Pain duration in years (mean± SD)			7.13±2.71
Current opioid use (%)			20%
Employeed (%)			49.7%
Clinical variables	Theoretical range	Actual range	Mean ±SD
NPRS	0-10	3-10	5.71±1.59
PCS	0-52	0-44	26.9±10.7
CPAQ	0-120	21-74	51.5±11.5
TSK	13-52	23-53	38.8±9.05
PF-FIQR	0-30	9-29	17.8±4.75
6MWT in meters	NA	201-402	304±59.8

Note. BMI: Body Mass Index; FSQ-WPI; NPRS: Numeric Pain Rating Scale; PCS: Pain Catastrophizing Scale; CPAQ: Chronic Pain Acceptance Questionnaire; TSK: Tampa Scale of Kinesiophobia; PF-FIQ: Physical Functioning subscale of the Fibromyalgia Impact Questionnaire; 6MWT: 6 Minute Walking Test.

3.2 Correlations

Table 2 shows correlation coefficients among the control factors and clinical factors

Table 2. Correlation coefficients among demographic variable (i.e., age, BMI, pain duration, current opioid use, work status), pain intensity (NPRS), pain catastrophizing (PCS), pain acceptance (CPAQ), self-reported physical functioning (PF-FIQR) and performance-based physical functioning (6MWT).

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.

1. Age	-									
2. BMI	0.03	-								
3. Pain duration	0.03	0.03	-							
4. Opioid use	0.17	0.10	-0.14	-						
5. Work status	-0.01	0.10	-0.03	0.02	-					
6. NPRS	-0.01	0.21**	-0.08	0.03	0.01	-				
7. PCS	0.09	0.20**	0.05	-0.05	-0.02	0.38***	-			
8. CPAQ	-0.07	-0.19**	-0.07	0.01	0.08	-0.39***	-0.52***	-		
9. TSK	0.12	0.26***	0.09	0.06	-0.05	0.46***	0.55***	-0.64***	-	
10. PF-FIQR	0.06	0.031	-0.03	0.04	-0.14	0.35***	0.44***	- 0.50***	0.54***	-
11. 6MWT	-1.87*	-0.16*	-0.02*	-0.12	0.01	-0.40**	-0.57***	0.54***	-0.70***	-0.54***

Note. NPRS: Numeric Pain Rating Scale; PCS: Pain Catastrophizing Scale; CPAQ: Chronic Pain Acceptance Questionnaire; TSK: Tampa Scale of Kinesiophobia; PF-FIQ: Physical Functioning subscale from the Fibromyalgia Impact Questionnaire; 6MWT: 6 Minute Walking Test. * $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

3.3 Mediation analysis

Table. 3 Mediation estimates of pain intensity on self-reported physical functioning

Indirect effect of pain intensity (NPRS) on self-reported physical functioning (PF-FIQR) via mediators				
	B	SE	LLCI	ULCI
Pain catastrophizing (PCS)	0.155	0.117	-0.040	0.426
Pain acceptance (CPAQ)	0.298	0.119	0.050	0.527
Kinesiophobia (TSK)	0.404	0.136	0.160	0.706

Direct effect of pain intensity (NPRS) on self-reported physical functioning (PF-FIQR)				
	B	SE	LLCI	ULCI
	0.249	0.202	-0.137	0.655

Total effect of pain intensity (NPRS) on self-reported physical functioning (PF-FIQR) via mediators				
	B	SE	LLCI	ULCI

	1.046	0.218	0.620	1.474

Mediation estimates of pain intensity on performance-based physical functioning

Indirect effect of pain intensity (NPRS) on performance-based physical functioning (6MWT) via mediators

	B	SE	LLCI	ULCI
Pain catastrophizing (PCS)	-3.328	1.384	-6.732	-1.177
Pain acceptance (CPAQ)	-1.399	1.120	-4.028	0.510
Kinesiophobia (TSK)	-8.265	1.504	-11.460	-5.582

Direct effect of pain intensity (NPRS) on performance-base physical functioning (6MWT)

B	SE	LLCI	ULCI
-1.854	2.253	-6.118	2.746

Total effect of pain intensity (NPRS) on performance-based physical functioning (6MWT) via mediators

B	SE	LLCI	ULCI
-14.845	2.695	-20.127	-9.563

Note. NPRS: Numeric Pain Rating Scale; PCS: Pain Catastrophizing Scale; CPAQ: Chronic Pain Acceptance Questionnaire; TSK: Tampa Scale of Kinesiophobia; PF-FIQ: Physical Functioning subscale from the Fibromyalgia Impact Questionnaire; 6MWT: 6 Minute Walking Test.

4. Discussion

According to our results, the level of perceived pain intensity affects the physical functioning of people with FM and obesity only when the cognitive and emotional aspects of pain interpretation and response are considered. However, these psychological factors differentially explain the relationship between pain intensity and self-reported and performance-based physical functioning. Specifically, the relationship between pain intensity and self-reported physical functioning appears to be fully mediated by pain acceptance and kinesiophobia, with no significant role for pain catastrophizing. On the other hand, the relationship between pain intensity and performance-based physical functioning is fully mediated by kinesiophobia and pain catastrophizing. During the 6

minute walking test, the psychological aspects of potential harm and pain worsening due to movement might become more salient. In fact, pain catastrophizing and kinesiophobia might serve a protective function against pain and its worsening by encouraging avoidance and restriction of movement. It is possible that a repertoire of protective responses, including pain catastrophizing and kinesiophobia, leads to safety-seeking behavior such as avoidance. Pain is a salient and attention-demanding signal that prompts protective action to avoid or minimize its impact. These protective actions are functional in the case of acute pain and real threat, but they paradoxically increase suffering and disability in the case of chronic pain, by avoiding pain confrontation. In the case of kinesiophobia, some evidence suggests that even just imagining performing a movement associated with pain can elicit fear. It also appears that fear of movement does not need to be learned by experience, but rather through observation or verbal instruction. Surprisingly, pain catastrophizing did not have a significant role as a mediator. Pain catastrophizing is one of the most consistent predictor of pain related disability in chronic pain. Hovewer, the current findings are in line with our previous results on invidiuals with chronic low-back pain and obesity. Also in this study pain catastrophizing did not result as a significant predictor of disability. Instead, more of the "dispositional" component could be highlighted during the compilation of the self-report instrument. To improve physical functioning in this population, focusing only on pain reduction may not be as effective as focusing also on the subject's cognitive and emotional reactions to the pain experience. Our results reinforce previous evidence presenting self-reported and performance-based functioning as two complementary methods that provide different information and also appear to be influenced by different psychological factors. Moreover, to improve the self-reported and objective dimensions of physical functioning, the target factors should be differentiated in interventions. It seems therefore that an integration between the two models is desirable, because both variables of the FAM and psychological flexibility model have relevance

in mediating the relationship examined, and could be effective targets for intervention to respond in a more functional way to the experience of pain and promote better functioning.

Overall conclusion

The first study of this project aimed to evaluate the reliability and agreement between a self-report questionnaire on fibromyalgia-related symptoms and the diagnosis made by a rheumatologist. This tool can be used as a screening tool to identify at risk individuals, and speed up the diagnosis of fibromyalgia, allowing for early interventions. It can also be used to keep track of the progress during multidisciplinary interventions.

Furthermore, the second study showed that psychological factors, specifically, pain catastrophizing and pain acceptance, contribute significantly to disability in both self-report and performance-based forms. In addition, their role as mediators (in conjunction with kinesiophobia) in the relationship between pain intensity and disability, both self-report and performance based, was investigated. Taken together, our results emphasize the significance of psychological factors and their impact on disability. As a result, we stress the importance of a multidisciplinary approach, that includes pain acceptance, catastrophizing and kinesiophobia as targets. In addition, it appears that these factors should be consider differentialy depending on the dimension of disability being consider, whether the perceived or performance-based aspects.

Further longitudinal and prospective studies are needed to clarify and confirm the causal direction of the psychological components. In addition, future research should evaluate if interventions directed to psychological factors such as pain catastrophizing, kinesiophobia and pain acceptance

have a significant impact also on the improvement of physical functioning, always evaluating a self-report and an objective aspect.

References

1. Attridge N, Noonan D, Eccleston C, Keogh E. The disruptive effects of pain on n-back task performance in a large general population sample. *Pain*. 2015;156(10):1885-1891. doi:10.1097/j.pain.0000000000000245
2. Bonica JJ. *The Management of Pain.* Philadelphia: Lea & Febiger; 1953.
3. Merksey H BN. *Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms*. 2nd ed. Seattle WA: IASP Press; 1994.
4. Aziz Q, Barke A, Bennett MI, et al. A classification of chronic pain for ICD-11. *Pain*. 2015;156(6):1003-1007.
5. Tracey I, Bushnell MC. How Neuroimaging Studies Have Challenged Us to Rethink: Is Chronic Pain a Disease? *J Pain*. 2009;10(11):1113-1120. doi:10.1016/j.jpain.2009.09.001
6. Woolf CJ. Central sensitization: Implications for the diagnosis and treatment of pain. *Pain*. 2011;152(SUPPL.3):S2-S15. doi:10.1016/j.pain.2010.09.030
7. Henry DE, Chiodo AE, Yang W. Central nervous system reorganization in a variety of chronic pain states: A review. *PM R*. 2011;3(12):1116-1125. doi:10.1016/j.pmrj.2011.05.018
8. Rice ASC, Smith BH, Blyth FM. Pain and the global burden of disease. *Pain*. 2016;157(4):791-796. doi:10.1097/j.pain.0000000000000454
9. Vlaeyen JWS, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain : a state of the art. *Pain*. 2000;85(3):317-332.
10. Ebert, M., & Kerns R. *Behavioral and Psychopharmacologic Pain Management.* Cambridge: Cambridge University Press.; 2010. doi:doi:10.1017/CBO9780511781445
11. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of

Pain definition of pain: concepts, challenges, and compromises. *Pain*. 2020;161(9):1976-1982. doi:10.1097/j.pain.0000000000001939

12. DiBonaventura MD, Sadosky A, Concialdi K, et al. The prevalence of probable neuropathic pain in the US: Results from a multimodal general-population health survey. *J Pain Res*. 2017;10:2525-2538. doi:10.2147/JPR.S127014
13. Finnerup NB, Haroutounian S, Kamerman P, et al. Neuropathic pain: An updated grading system for research and clinical practice. *Pain*. 2016;157(8):1599-1606. doi:10.1097/j.pain.0000000000000492
14. Spahr N, Hodkinson D, Jolly K, Williams S, Howard M, Thacker M. Distinguishing between nociceptive and neuropathic components in chronic low back pain using behavioural evaluation and sensory examination. *Musculoskelet Sci Pract*. 2017;27:40-48. doi:10.1016/j.msksp.2016.12.006
15. Darnall BD, Scheman J, Davin S, et al. Pain psychology: A global needs assessment and national call to action. *Pain Med (United States)*. 2016;17(2):250-263. doi:10.1093/pm/pnv095
16. Institute of Medicine (US). Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. In: Washington (DC): National Academies Press (US); 2011.
17. Interagency Pain Research Coordinating Committee. National Pain Strategy. 2016:1-83. http://www.painaustralia.org.au/images/pain_australia/NPS/National Pain Strategy 2011.pdf.
18. Watt-Watson J, Murinson BB. Current challenges in pain education. *Pain Manag*. 2013;3(5):351-357. doi:10.2217/pmt.13.39
19. Mezei L, Murinson BB. Pain education in North American Medical Schools. *J Pain*.

2011;12(12):1199-1208. doi:10.1016/j.jpain.2011.06.006

20. Murinson BB, Mezei L, Nenortas E. Integrating cognitive and affective dimensions of pain experience into health professions education. *Pain Res Manag*. 2011;16(6):421-426. doi:10.1155/2011/424978

21. Engel GL. The need for a new medical model: A challenge for biomedicine. *Science (80-)*. 1977;196:129-136. doi:10.1521/pdps.2012.40.3.377

22. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The Biopsychosocial Approach to Chronic Pain: Scientific Advances and Future Directions. *Psychol Bull*. 2007;133(4):581-624. doi:10.1037/0033-2909.133.4.581

23. Gatchel RJ and Maddrey AM. The Biopsychosocial Perspective of Pain. In: L RJ and L, ed. *Healthcare Psychology Handbook.* American Psychological Association Press.; 2004.

24. Stanos SP, Bruckenthal P, Barkin RL. Strategies to reduce the tampering and subsequent abuse of long-acting opioids: potential risks and benefits of formulations with physical or pharmacologic deterrents to tampering. *Mayo Clin Proc Innov Qual Outcomes*. 2012;87(7):683-694. doi:10.1016/j.mayocp.2012.02.022

25. Dworkin RH, Connor ABO, Audette J, et al. Recommendations for the Pharmacological Management of Neuropathic Pain : An Overview and Literature Update. *Mayo Clin Proc*. 2010;85(3):S3-S14. doi:10.4065/mcp.2009.0649

26. Rolfs RT, Johnson E, Williams NJ, Sundwall DN. Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain. *J Pain Palliat Care Pharmacother*. 2010;24(3):219-235. doi:10.3109/15360288.2010.503265

27. Fitzcharles MA, Ste-Marie PA, Goldenberg DL, Pereira JX, Abbey S, Choinière M, Ko G, Moulin DE, Panopalis P, Proulx J SY. 2012 Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome : Executive summary. *2013*. 2013;18(3):119-127.

28. World Health Organization. *Towards a Common Language for Functioning, Disability and Health: ICF, The International Classification of Functioning, Disability and Health 2002*.; 2002. http://www.who.int/classifications/icf/icfbeginnersguide.pdf.

29. Howe CQ, Robinson JP, Sullivan MD. Psychiatric and Psychological Perspectives on Chronic Pain. *Phys Med Rehabil Clin N Am*. 2015;26(2):283-300. doi:10.1016/j.pmr.2014.12.003

30. Hall AM, Kamper SJ, Maher CG, Latimer J, Ferreira ML, Nicholas MK. Symptoms of depression and stress mediate the effect of pain on disability. *Pain*. 2011;152(5):1044-1051. doi:10.1016/j.pain.2011.01.014

31. Baumeister H, Knecht A, Hutter N. Direct and indirect costs in persons with chronic back pain and comorbid mental disorders-A systematic review. *J Psychosom Res*. 2012;73(2):79-85. doi:10.1016/j.jpsychores.2012.05.008

32. Macfarlane GJ, McBeth J SA. Widespread body pain and mortality: prospective population based study. *BMJ*. 2001;323(7314):662-665.

33. Hassett AL, Aquino JK, Ilgen MA. The risk of suicide mortality in chronic pain patients. *Curr Pain Headache Rep*. 2014;18(8):1-7. doi:10.1007/s11916-014-0436-1

34. Jones GT, Power C, Macfarlane GJ. Adverse events in childhood and chronic widespread pain in adult life: Results from the 1958 British Birth Cohort Study. *Pain*. 2009;143(1-2):92-96. doi:10.1016/j.pain.2009.02.003

35. Vlaeyen JW, Kole-Snijders AM, Boeren RG, van Eek H. Fear of movement /(re) injury in chronic low back pain and its relation to behavioral performance. *Pain*. 1995;62(3):363-372.

36. Vowles KE, McCracken LM EC. Patient functioning and catastrophizing in chronic pain: the mediating effects of acceptance. *Heal Psychol*. 2008;27(2S):136-143.

37. Giusti EM, Lacerenza M, Manzoni GM, Castelnuovo G. Psychological and psychosocial predictors of chronic post-surgical pain: a systematic review and meta-analysis. *Pain*. 2020;In press. doi:10.1097/j.pain.0000000000001999

38. Lami MJ, Martínez MP, Miró E, Sánchez AI, Guzmán MA. Catastrophizing, Acceptance, and Coping as Mediators Between Pain and Emotional Distress and Disability in Fibromyalgia. *J Clin Psychol Med Settings*. 2018;25(1):80-92. doi:10.1007/s10880-018-9543-1

39. Perrot S, Poiraudeau S, Kabir M, et al. Active or Passive Pain Coping Strategies in Hip and Knee Osteoarthritis ? Results of a National Survey of 4 , 719 Patients in a Primary Care Setting. 2008;59(11):1555-1562. doi:10.1002/art.24205

40. World Health Organization Technical Report Series. *Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation on Obesity*. Geneva; 2000.

41. Abram SE. Chronic Pain, Overweight, and Obesity: Findings from a Community-Based Twin Registry. *Yearb Anesthesiol Pain Manag*. 2011;2011:353-354. doi:10.1016/j.yane.2010.10.008

42. Yoo JJ, Cho NH, Lim SH, Kim HA. Relationships between body mass index, fat mass, muscle mass, and musculoskeletal pain in community residents. *Arthritis Rheumatol*. 2014;66(12):3511-3520. doi:10.1002/art.38861

43. Yunus MB, Arslan S, Aldag JC. Relationship between body mass index and fibromyalgia features. *Scand J Rheumatol*. 2002;31(1):27-31. doi:10.1080/030097402317255336

44. Ferguson S, Al-Rehany L, Tang C, Gougeon L, Warwick K, Madill J. Self-reported causes of weight gain: Among prebariatric surgery patients. *Can J Diet Pract Res*. 2013;74(4):189-192. doi:10.3148/74.4.2013.189

45. Amy Janke E, Kozak AT. The more pain i have, the more i want to eat: Obesity in the

context of chronic pain. *Obesity*. 2012;20(10):2027-2034. doi:10.1038/oby.2012.39

46. Knutson KL, Van Cauter E. Associations between sleep loss and increased risk of obesity and diabetes. *Ann N Y Acad Sci*. 2008;1129:287-304. doi:10.1196/annals.1417.033

47. Forhan M, Gill S V. Obesity, functional mobility and quality of life. *Best Pract Res Clin Endocrinol Metab*. 2013;27(2):129-137. doi:10.1016/j.beem.2013.01.003

48. Marcus DA. Obesity and the Impact of Chronic Pain. *Clin J Pain*. 2004;20(3):186-191. doi:10.1097/00002508-200405000-00009

49. Hagen KB, Tambs K, Bjerkedal T. A prospective cohort study of risk factors for disability retirement because of back pain in the general working population. *Spine (Phila Pa 1976)*. 2002;27(16):1790-1796. doi:10.1097/00007632-200208150-00019

50. Rubinstein SM, Van Middelkoop M, Assendelft WJJ, De Boer MR, Van Tulder MW. Spinal manipulative therapy for chronic low-back pain: An update of a cochrane review. *Spine (Phila Pa 1976)*. 2011;36(13):2-5. doi:10.1097/BRS.0b013e3182197fe1

51. Salvetti M de G, Pimenta CA de M, Braga PE, Corrêa CF. Disability related to chronic low back pain: Prevalence abd associated factors. *Rev da Esc Enferm*. 2012;46(SPL. ISS.):16-23. doi:10.1590/S0080-62342012000700003

52. Luo X, Pietrobon R, Sun SX, Liu GG, Hey L. Estimates and Patterns of Direct Health Care Expenditures among Individuals with Back Pain in the United States. *Spine (Phila Pa 1976)*. 2004;29(1):79-86. doi:10.1097/01.BRS.0000105527.13866.0F

53. Woby SR, Urmston M, Watson PJ. Self-efficacy mediates the relation between pain-related fear and outcome in chronic low back pain patients. *Eur J Pain*. 2007;11(7):711-718. doi:10.1016/j.ejpain.2006.10.009

54. Swinkels-Meewisse IEJ, Roelofs J, Oostendorp RAB, Verbeek ALM, Vlaeyen JWS. Acute low back pain: Pain-related fear and pain catastrophizing influence physical

performance and perceived disability. *Pain*. 2006;120(1-2):36-43. doi:10.1016/j.pain.2005.10.005

55. Sardá J, Nicholas MK, Asghari A, Pimenta CAM. The contribution of self-efficacy and depression to disability and work status in chronic pain patients: A comparison between Australian and Brazilian samples. *Eur J Pain*. 2009;13(2):189-195. doi:10.1016/j.ejpain.2008.03.008

56. Varallo G, Giusti EM, Scarpina F, Cattivelli R, Capodaglio P, Castelnuovo G. The Association of Kinesiophobia and Pain Catastrophizing with Pain-Related Disability and Pain Intensity in Obesity and Chronic Lower-Back Pain. *Brain Sci*. 2020;11(1):11. doi:10.3390/brainsci11010011

57. Varallo G, Scarpina F, Giusti EM, et al. Does Kinesiophobia Mediate the Relationship between Pain Intensity and Disability in Individuals with Chronic Low-Back Pain and Obesity ? *Brain Sci*. 2021;11(684).

58. Woby SR, Watson PJ, Roach NK, Urmston M. Are changes in fear-avoidance beliefs , catastrophizing , and appraisals of control , predictive of changes in chronic low back pain and disability ? 2004;8:201-210. doi:10.1016/j.ejpain.2003.08.002

59. Williams DA, Kuper D, Segar M, Mohan N, Sheth M, Clauw DJ. Internet-enhanced management of fibromyalgia: A randomized controlled trial. *Pain*. 2010;151(3):694-702. doi:10.1016/j.pain.2010.08.034

60. Freburger JK, Holmes GM, Agans RP, et al. The rising prevalence of chronic low back pain. *Arch Intern Med*. 2009;169(3):251-258. doi:10.1001/archinternmed.2008.543

61. Andersson GB. Epidemiological features of chronic low-back pain. *Lancet*. 1999;354(9178):581-585. doi:10.1016/b978-0-7236-0490-7.50029-x

62. Cassidy JD, Co P, Carroll LJ, Kristman V. Incidence and course of lower back pain in the

general population. *Spine (Phila Pa 1976)*. 2005;30(24):1-7. http://graphics.tx.ovid.com.ezproxy.library.ubc.ca/ovftpdfs/FPDDNCIBDBAHIL00/fs047/ovft/live/gv024/00007632/00007632-200512150-00021.pdf%5Cnpapers2://publication/uuid/D3654C88-41D7-4CA2-90E7-F48754E31665.

63. Janke EA, Collins A, Kozak AT. Overview of the relationship between pain and obesity: What do we know? Where do we go next? *J Rehabil Res Dev*. 2007;44(2):245-261. doi:10.1682/JRRD.2006.06.0060

64. Garaulet M, Ordovás JM, Madrid JA. The chronobiology, etiology and pathophysiology of obesity. *Int J Obes*. 2010;34(12):1667-1683. doi:10.1038/ijo.2010.118

65. Taylor FR. Obesity, migraine, and chronic migraine: Possible mechanisms of interaction. Views and reviews. *Headache*. 2007;47(9):1355. doi:10.1111/j.1526-4610.2007.00927.x

66. Okifuji A, Hare BD. The association between chronic pain and obesity. *J Pain Res*. 2015;8:399-408. doi:10.2147/JPR.S55598

67. Arranz LI, Rafecas M, Alegre C. Effects of obesity on function and quality of life in chronic pain conditions. *Curr Rheumatol Rep*. 2014;16(1). doi:10.1007/s11926-013-0390-7

68. Hitt HC, McMillen RC, Thornton-Neaves T, Koch K, Cosby AG. Comorbidity of Obesity and Pain in a General Population: Results from the Southern Pain Prevalence Study. *J Pain*. 2007;8(5):430-436. doi:10.1016/j.jpain.2006.12.003

69. Heuch I, Hagen, Kurt, Heuch I, Nygaard Ø, Zwart J. The Impact of Body Mass Index on the Prevalence of low back pain. *Spine (Phila Pa 1976)*. 2010;35(7):764-768.

70. Leboeuf-Yde C. Body Weight and Low Back Pain. *Spine (Phila Pa 1976)*. 2000;25(2):226. doi:10.1097/00007632-200001150-00015

71. Nilsen TIL, Holtermann A, Mork PJ. Physical exercise, body mass index, and risk of

chronic pain in the low back and neck/shoulders: Longitudinal data from the nord-trøndelag health study. *Am J Epidemiol*. 2011;174(3):267-273. doi:10.1093/aje/kwr087

72. Urquhart DM, Berry P, Wluka AE, Strauss BJ, Wang Y, Proietto J, Jones G, Dixon JB, Cicuttini FM, Wang Y, Proietto J, Cicuttini FM. Increased Fat Mass Is Associated With High Levels of Low Back Pain Intensity and Disability. *Spine (Phila Pa 1976)*. 2011;36(16):1320-1325. doi:10.1097/BRS.0b013e3181f9fb66

73. Smuck M, Kao MCJ, Brar N, Martinez-Ith A, Choi J, Tomkins-Lane CC. Does physical activity influence the relationship between low back pain and obesity? *Spine J*. 2014;14(2):209-216. doi:10.1016/j.spinee.2013.11.010

74. Ferreira ML, Machado G, Latimer J, Maher C, Ferreira PH, Smeets RJ. Factors defining care-seeking in low back pain--a meta-analysis of population based surveys. *Eur J Pain*. 2010;14(7):747.e1-7. doi:10.1016/j.ejpain.2009.11.005

75. Maher C, Underwood M, Buchbinder R. Non-specific low back pain. *Lancet*. 2017;389(10070):736-747. doi:10.1016/S0140-6736(16)30970-9

76. De Souza LH, Frank AO. Experiences of living with chronic back pain: The physical disabilities. *Disabil Rehabil*. 2007;29(7):587-596. doi:10.1080/09638280600925852

77. Heuch I, Heuch I, Hagen K, Zwart JA. Body mass index as a risk factor for developing chronic low back pain: A follow-up in the nord-trøndelag health study. *Spine (Phila Pa 1976)*. 2013;38(2):133-139. doi:10.1097/BRS.0b013e3182647af2

78. Solovieva S, Viikari-juntura E, Shiri R, Karppinen J. Meta- and Pooled Analyses The Association Between Obesity and Low Back Pain : A Meta-Analysis. *Am J Epidemiol*. 2010;171(2):135-154. doi:10.1093/aje/kwp356

79. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and Trends in Obesity Among US Adults, 1999-2000. *JAMA*. 2002;288(14):1723-1727.

doi:10.1001/jama.288.14.1723

80. da C Menezes Costa L, Maher CG, Hancock MJ, McAuley JH, Herbert RD, Costa LOP. The prognosis of acute and persistent low-back pain: a meta-analysis. *C Can Med Assoc J = J l'Association medicale Can*. 2012;184(11):E613-24. doi:10.1503/cmaj.111271

81. James SL, Abate D, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 Diseases and Injuries for 195 countries and territories, 1990-2017: A systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1789-1858. doi:10.1016/S0140-6736(18)32279-7

82. Shipton EA. Physical Therapy Approaches in the Treatment of Low Back Pain. *Pain Ther*. 2018;7(2):127-137. doi:10.1007/s40122-018-0105-x

83. National Institute for Health and Care Excellence. *Low Back Pain and Sciatica in over 16s.*; 2020.

84. Kamper SJ, Apeldoorn AT, Chiarotto A, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain: Cochrane systematic review and meta-analysis. *BMJ*. 2015;350:h444. doi:10.1136/bmj.h444

85. Cecchi F, Negrini S, Pasquini G, et al. Predictors of functional outcome in patients with chronic low back pain undergoing back school, individual physiotherapy or spinal manipulation. *Eur J Phys Rehabil Med*. 2012;48(3):371-378.

86. Helmhout PH, Staal JB, Heymans MW, Harts CC, Hendriks EJM, de Bie RA. Prognostic factors for perceived recovery or functional improvement in non-specific low back pain: secondary analyses of three randomized clinical trials. *Eur Spine J*. 2010;19(4):650-659. doi:10.1007/s00586-009-1254-8

87. Hayden JA, Chou R, Hogg-Johnson S, Bombardier C. Systematic reviews of low back pain prognosis had variable methods and results: guidance for future prognosis reviews. *J*

Clin Epidemiol. 2009;62(8):781-796.e1. doi:10.1016/j.jclinepi.2008.09.004

88. George SZ, Beneciuk JM. Psychological predictors of recovery from low back pain: a prospective study. *BMC Musculoskelet Disord*. 2015;16(1):49. doi:10.1186/s12891-015-0509-2

89. Hill JC, Dunn KM, Lewis M, et al. A primary care back pain screening tool: Identifying patient subgroups for initial treatment. *Arthritis Care Res*. 2008;59(5):632-641. doi:10.1002/art.23563

90. Ben Ami N, Weisman A, Yona T, Shashua A, Hill J, Pincus T. STarT back tool retained its predicting abilities in patients with acute and sub-acute low back pain after a transcultural adaptation and validation to Hebrew. *Musculoskelet Sci Pract*. 2020;46:102134. doi:10.1016/j.msksp.2020.102134

91. Forsbrand MH, Grahn B, Hill JC, Petersson IF, Post Sennehed C, Stigmar K. Can the STarT Back Tool predict health-related quality of life and work ability after an acute/subacute episode with back or neck pain? A psychometric validation study in primary care. *BMJ Open*. 2018;8(12):e021748. doi:10.1136/bmjopen-2018-021748

92. Katzan IL, Thompson NR, George SZ, Passek S, Frost F, Stilphen M. The use of STarT back screening tool to predict functional disability outcomes in patients receiving physical therapy for low back pain. *Spine J*. 2019;19(4):645-654. doi:10.1016/j.spinee.2018.10.002

93. Hall JA, Jowett S, Lewis M, Oppong R, Konstantinou K. The STarT Back stratified care model for non-specific low back pain. *Pain*. 2020;Publish Ah(00). doi:10.1097/j.pain.0000000000002057

94. Hill JC, Whitehurst DGT, Lewis M, et al. Comparison of stratified primary care management for low back pain with current best practice (STarT Back): A randomised

controlled trial. *Lancet*. 2011. doi:10.1016/S0140-6736(11)60937-9

95. Whitehurst DGT, Bryan S, Lewis M, Hill J, Hay EM. Exploring the cost-utility of stratified primary care management for low back pain compared with current best practice within risk-defined subgroups. *Ann Rheum Dis*. 2012. doi:10.1136/annrheumdis-2011-200731

96. Yılmaz Yelvar GD, Dalkılıç M, Çırak Y, Parlak Demir Y, Karadüz BN, Parlak MM. Validity and reliability of Turkish version of STarT Back Screening Tool. *Agri Agri Dernegi'nin Yayin organidir = J Turkish Soc Algol*. 2019;31(4):163-171. doi:10.14744/agri.2019.99266

97. Schmidt P-A, Naidoo V. Cross-cultural adaptation and validation of the STarT back screening tool in isiZulu. *South African J Physiother*. 2020;76(1):1402. doi:10.4102/sajp.v76i1.1402

98. Raimundo A, Parraça J, Batalha N, et al. Portuguese translation, cross-cultural adaptation and reliability of the questionnaire «Start Back Screening Tool» (SBST). *Acta Reumatol Port*. 2017;42(1):38-46.

99. Robinson HS, Dagfinrud H. Reliability and screening ability of the StarT Back screening tool in patients with low back pain in physiotherapy practice, a cohort study. *BMC Musculoskelet Disord*. 2017;18(1):9-15. doi:10.1186/s12891-017-1553-x

100. Luan S, Min Y, Li G, et al. Cross-cultural adaptation, reliability, and validity of the chinese version of the STarT back screening tool in patients with low back pain. *Spine (Phila Pa 1976)*. 2014;39(16). doi:10.1097/BRS.0000000000000413

101. Wideman TH, Hill JC, Main CJ, Lewis M, Sullivan MJL, Hay EM. Comparing the responsiveness of a brief, multidimensional risk screening tool for back pain to its unidimensional reference standards: the whole is greater than the sum of its parts. *Pain*.

2012;153(11):2182-2191. doi:10.1016/j.pain.2012.06.010

102. Karstens S, Krug K, Hill JC, et al. Validation of the German version of the STarT-Back Tool (STarT-G): a cohort study with patients from primary care practices. *BMC Musculoskelet Disord*. 2015;16:346. doi:10.1186/s12891-015-0806-9

103. Piironen S, Paananen M, Haapea M, et al. Transcultural adaption and psychometric properties of the STarT Back Screening Tool among Finnish low back pain patients. *Eur spine J Off Publ Eur Spine Soc Eur Spinal Deform Soc Eur Sect Cerv Spine Res Soc*. 2016;25(1):287-295. doi:10.1007/s00586-015-3804-6

104. Maggiani A, Abenavoli A. Italian Translation and Cross-Cultural Adaptation of a Back Pain Screening Questionnaire (Start Back Screening Tool). *Ann Ig*. 2019;31(1):69-75. doi:10.7416/ai.2019.2260

105. Hay EM, Dunn KM, Hill JC, et al. A randomised clinical trial of subgrouping and targeted treatment for low back pain compared with best current care. The STarT Back Trial Study Protocol. *BMC Musculoskelet Disord*. 2008;9(1):58. doi:10.1186/1471-2474-9-58

106. Jensen MP, Turner JA, Romano JM, Fisher LD. Comparative reliability and validity of chronic pain intensity measures. *Pain*. 1999;83(2):157-162. doi:10.1016/s0304-3959(99)00101-3

107. Roland M, Morris R. A study of the natural history of back pain. Part I: development of a reliable and sensitive measure of disability in low-back pain. *Spine (Phila Pa 1976)*. 1983;8(2):141-144. doi:10.1097/00007632-198303000-00004

108. Padua L, Ceccarelli E, Romanini E, Zanoli G, Bondì R. Italian version of the Roland Disability Questionnaire , specific for low back pain : cross-cultural adaptation and validation. *Eur Spine J*. 2002;11(2):126-129. doi:10.1007/s005860100262

109. Sullivan M, Bishop S, Pivik J. The pain catastrophizing scale: development and

validation. *Psychol Assess*. 1995. doi:10.1037/1040-3590.7.4.524

110. Monticone M, Baiardi P, Ferrari S, et al. Development of the Italian version of the Pain Catastrophising Scale (PCS-I): cross-cultural adaptation, factor analysis, reliability, validity and sensitivity to change. *Qual Life Res*. 2012;21(6):1045-1050. doi:10.1007/s11136-011-0007-4

111. Meroni R, Piscitelli D, Bonetti F, et al. Rasch Analysis of the Italian version of Pain Catastrophizing Scale (PCS-I). *J Back Musculoskelet Rehabil*. 2014. doi:10.3233/BMR-140564

112. Kori S, Miller R, Todd D. Kinesophobia: a new view of chronic pain behaviour. *Pain Manag*. 1990.

113. Monticone M, Giorgi I, Baiardi P, Barbieri M, Rocca B, Bonezzi C. Development of the Italian Version of the Tampa Scale of Kinesiophobia (TSK-I): Cross-Cultural Adaptation , Factor Analysis , Reliability , and Validity. *Spine (Phila Pa 1976)*. 2010;35(12):1241-1246.

114. The EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy (New York)*. 1990;16(3):199-208.

115. Scalone L, Cortesi PA, Ciampichini R, et al. Italian population-based values of EQ-5D health states. *Value Heal*. 2013;16(5):814-822. doi:10.1016/j.jval.2013.04.008

116. Abedi M, Manshadi FD, Khalkhali M, et al. Translation and validation of the Persian version of the STarT Back Screening Tool in patients with nonspecific low back pain. *Man Ther*. 2015;20(6):850-854. doi:10.1016/j.math.2015.04.006

117. Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Struct Equ Model A Multidiscip J*. 1999;6(1):1-55. doi:10.1080/10705519909540118

118. Tabachnick BG, Fidell LS, Ullman JB. *Using Multivariate Statistics*. Vol 5. Pearson Boston, MA; 2007.

119. Prinsen CAC, Mokkink LB, Bouter LM, et al. COSMIN guideline for systematic reviews of patient-reported outcome measures. *Qual Life Res*. 2018;27(5):1147-1157. doi:10.1007/s11136-018-1798-3

120. Qin S, Nelson L, McLeod L, Eremenco S, Coons SJ. Assessing test–retest reliability of patient-reported outcome measures using intraclass correlation coefficients: recommendations for selecting and documenting the analytical formula. *Qual Life Res*. 2019;28(4):1029-1033. doi:10.1007/s11136-018-2076-0

121. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med*. 2016;15(2):155-163. doi:10.1016/j.jcm.2016.02.012

122. Reeve BB, Wyrwich KW, Wu AW, et al. ISOQOL recommends minimum standards for patient-reported outcome measures used in patient-centered outcomes and comparative effectiveness research. *Qual Life Res*. 2013;22(8):1889-1905. doi:10.1007/s11136-012-0344-y

123. Rosseel Y. {lavaan}: An {R} Package for Structural Equation Modeling. *J Stat Softw*. 2012;48(2):1-36.

124. Revelle W. psych: Procedures for Psychological, Psychometric, and Personality Research. 2019.

125. R Core Team. R: A Language and Environment for Statistical Computing. 2017.

126. Reise SP, Scheines R, Widaman KF, Haviland MG. Multidimensionality and Structural Coefficient Bias in Structural Equation Modeling: A Bifactor Perspective. *Educ Psychol Meas*. 2013;73(1):5-26. doi:10.1177/0013164412449831

127. Bollen KA, Diamantopoulos A. In defense of causal-formative indicators: A minority report. *Psychol Methods*. 2017;22(3):581-596. doi:10.1037/met0000056

128. Haslam DW, James WP. Obesity. *Lancet*. 2005;366(9492):1197-1209.

129. Doll HA, Petersen SE, Stewart-Brown SL. Obesity and Physical and Emotional Well-Being : Associations between Body Mass Index , Chronic Illness , and the Physical and Mental Components of the SF-36 Questionnaire. *Obes Res*. 2000;8(2):160-170.

130. Davison KK, Ford ES, Cogswell ME, Dietz WH. Percentage of Body Fat and Body Mass Index Are Associated from NHANES III. *J Am Geriatr Soc*. 2002;50(11):1802-1809.

131. Giusti EM, Spatola C, Brunani A, et al. ISPRM/ESPRM Guidelines on Physical and Rehabilitation Medicine (PRM) professional practice for adults with obesity and related comorbidities. *Eur J Phys Rehabil Med*. 2020;In press.

132. Zhang TT, Liu Z, Liu YL, Zhao JJ, Liu DW, Tian QB. Obesity as a Risk Factor for Low Back Pain: A Meta-Analysis. *Clin spine Surg*. 2018;31(1):22-27. doi:10.1097/BSD.0000000000000468

133. International Association for the Study of Pain. *Classification of Chronic Pain - Description of Chronic Pain Syndromes and Definitions of Pain Terms*. 2nd editio. (Merskey H, Ed. NB, eds.). Seattle, WA 98105 USA: IASP PRESS • SEATTLE; 2002.

134. Tukker A, Visscher TLS, Picavet HSJ. Overweight and health problems of the lower extremities : osteoarthritis , pain and disability. *Public Heal Nutr*. 2008;12(3):359-368. doi:10.1017/S1368980008002103

135. Bushnell MC, Čeko M, Low LA. Cognitive and emotional control of pain and its disruption in chronic pain. *Nat Rev Neurosci*. 2013;14(7):502-511. doi:10.1038/nrn3516

136. Meulders A. From fear of movement-related pain and avoidance to chronic pain disability: a state-of-the-art review. *Curr Opin Behav Sci*. 2019;26:130-136.

doi:10.1016/j.cobeha.2018.12.007

137. Goossens EJB, Linton SJ, Crombez G, Leeuw M, Boersma K, Vlaeyen JWS. The Fear-Avoidance Model of Musculoskeletal Pain : Current State of Scientific Evidence. *J Behav Med*. 2007;30(1):77-94. doi:10.1007/s10865-006-9085-0

138. Giusti EM, Manna C, Varallo G, et al. The Predictive Role of Executive Functions and Psychological Factors on Chronic Pain after Orthopaedic Surgery : A Longitudinal Cohort Study. *Brain Sci*. 2020;10(10):1-10.

139. Quartana, PJ; Campbell, CM; Edwards R. Pain catastrophizing : a critical review. *Expert Rev Neurother*. 2010;9(5):745-758. doi:10.1586/ERN.09.34.Pain

140. Chaves, J.F.; Brown JM. Spontaneous Cognitive Strategies for the Control of Clinical Pain and Stress. *J Behav Med*. 1987;10(3):263-276.

141. Larsson C, Hansson EE, Sundquist K, Jakobsson U. Kinesiophobia and its relation to pain characteristics and cognitive affective variables in older adults with chronic pain. *BMC Geriatr*. 2016:1-7. doi:10.1186/s12877-016-0302-6

142. Knapik A, Saulicz E. Kinesiophobia – Introducing a New Diagnostic Tool by. *J Hum Kinet*. 2011;28(June):25-31. doi:10.2478/v10078-011-0019-8

143. Vincent HK, Omli MR, Day T, Hodges M, Vincent KR, George SZ. Fear of Movement , Quality of Life , and Self-Reported Disability in Obese Patients with. *Pain Med (United States)*. 2011;35(12):154-164.

144. Vincent HK, Omli MR, Day T, Hodges M, Vincent KR, George SZ. Fear of Movement, Quality of Life, and Self-Reported Disability in Obese Patients with chronic lumbar pain. *Pain Med (United States)*. 2011;12(1):154-164.

145. Shelby RA, Somers TJ, Keefe FJ, Pells JJ, Dixon KE, Blumenthal JA. Domain Specific Self-Efficacy Mediates the Impact of Pain Catastrophizing on Pain and Disability in

Overweight and Obese Osteoarthritis Patients. *J Pain*. 2008;9(10):912-919. doi:10.1016/j.jpain.2008.05.008

146. Erdfelder E, Faul F, Buchner A. Statistical power analyses using G * Power 3 . 1 : *Behav Res Methods*. 2009;41(4):1149-1160. doi:10.3758/BRM.41.4.1149

147. Institute for Clinical Systems Improvement. *Adult Acute and Subacute Low Back Pain Diagnosis Algorithm*.; 2018.

148. Breivik H, Borchgrevink PC, Allen SM, et al. Assessment of pain. *Br J Anaesth*. 2008;101(1):17-24. doi:10.1093/bja/aen103

149. Woby SR, Roach NK, Urmston M, Watson PJ. Psychometric properties of the TSK-11 : A shortened version of the Tampa Scale for Kinesiophobia. *Pain*. 2005;117:137-144. doi:10.1016/j.pain.2005.05.029

150. Majedi H, Amini MH, Yousefshahi F, Majedi M, Rahimi M, Orandi A. Predicting Factors of Pain Duration in Patients with Chronic Pain : A Large Population-based Study. *Anesth Pain Med*. 2020;10(1):1-6. doi:10.5812/aapm.95776.Research

151. Cimmino MA, Ferrone C, Cutolo M. Epidemiology of chronic musculoskeletal pain. *Best Pract Res Clin Rheumatol*. 2011;25(2):173-183. doi:10.1016/j.berh.2010.01.012

152. Sanchis-alfonso JDV, Lo L. Influence of kinesiophobia and catastrophizing on pain and disability in anterior knee pain patients Influence of kinesiophobia and catastrophizing on pain and disability in anterior knee pain patients. *Knee Surg Sport Traumatol Arthrosc*. 2013;21(7):1562-1568. doi:10.1007/s00167-012-2238-5

153. jamovi (version 1.2). The Jamovi Project. 2020. https://www.jamovi.org.

154. Vincent, HK; Seay, AN; Montero, C; Conrad, BP; Hurley, RW; Vincent K. Kinesiophobia and Fear Avoidance Beliefs in Overweight Older Adults with Chronic Low Back Pain, Relationship to Walking Endurance: Part II. *Am J Phys Med Rehabil*. 2014;92(5):439-445.

155. Vlaeyen JWS, Kole-snijders AMJ, Annemarie M, Ruesink R, Heuts PHTG. The Role of Fear of Movement /(Re) Injury in Pain Disability. *J Occup Rehabil*. 1995;5(4):235-252.

156. van der Hulst, M; Vollenbroek-Hutten, MM; Rietman, JS; Schaake, L; Groothuis-Oudshoorn, KG; Hermens H. Back Muscle Activation Patterns in Chronic Low Back Pain During Walking : A '" Guarding "' Hypothesis. *Clin J Pain*. 2010;26(1):30-37.

157. Picavet HSJ, Vlaeyen JWS, Schouten JSAG. Pain Catastrophizing and Kinesiophobia : Predictors of Chronic Low Back Pain. *Am J Epidemiol*. 2002;156(11):1028-1034. doi:10.1093/aje/kwf136

158. Giusti EM, Lacerenza M, Manzoni GM, Castelnuovo G. Psychological and psychosocial predictors of chronic postsurgical pain: a systematic review and meta-analysis. *Pain*. 2020;in press.

159. Janke EA, Jones E, Hopkins CM, Ruggieri M, Hruska A. Catastrophizing and anxiety sensitivity mediate the relationship between persistent pain and emotional eating. *Appetite*. 2016;103:64-71. doi:10.1016/j.appet.2016.03.022

160. Barke A, Schiller J, Rief W, et al. The IASP classification of chronic pain for ICD-11. *Pain*. 2018;160(1):88-94. http://www.ncbi.nlm.nih.gov/pubmed/30586076.

161. Hoy D, March L, Brooks P, et al. The global burden of low back pain: Estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis*. 2014;73(6):968-974. doi:10.1136/annrheumdis-2013-204428

162. Darnall BD, Ziadni MS, Roy A, et al. Comparative Efficacy and Mechanisms of a Single-Session Pain Psychology Class in Chronic Low Back Pain: Study Protocol for a Randomized Controlled Trial. *Trials*. 2018;19(1):1-15. doi:10.1186/s13063-018-2537-3

163. Heuch I, Heuch I, Hagen K, Zwart JA. A comparison of anthropometric measures for assessing the association between body size and risk of chronic low back pain: The HUNT

study. *PLoS One*. 2015;10(10):1-15. doi:10.1371/journal.pone.0141268

164. Wasser JG, Vasilopoulos T, Zdziarski LA, Vincent HK. Exercise Benefits for Chronic Low Back Pain in Overweight and Obese Individuals. *PM R*. 2017;9(2):181-192. doi:10.1016/j.pmrj.2016.06.019

165. Vincent HK, Adams MCB, Vincent KR, Hurley RW. Musculoskeletal Pain , Fear Avoidance Behaviors , and Potential Interventions to Manage Pain and Maintain Function. 2013;38(6):481-491. doi:10.1097/AAP.0000000000000013

166. Lee H, Hübscher M, Moseley GL, et al. How does pain lead to disability? A systematic review and meta-analysis of mediation studies in people with back and neck pain. *Pain*. 2015;156:988-997. doi:10.1097/j.pain.0000000000000146

167. Mühlhauser Y, Vogt L, Niederer D. How and how fast does pain lead to disability? A multilevel mediation analysis on structural, temporal and biopsychosocial pathways in patients with chronic nonspecific low back pain. *Musculoskelet Sci Pract*. 2020;49(May):102199. doi:10.1016/j.msksp.2020.102199

168. Marshall PWM, Schabrun S, Knox MF. Physical activity and the mediating effect of fear, depression, anxiety, and catastrophizing on pain related disability in people with chronic low back pain. *PLoS One*. 2017;12(7):1-15. doi:10.1371/journal.pone.0180788

169. Keefe FJ, Rumble ME, Scipio CD, Giordano LA, Perri LCM. Psychological aspects of persistent pain: Current state of the science. *J Pain*. 2004;5(4):195-211. doi:10.1016/j.jpain.2004.02.576

170. Crombez G, Eccleston C, Damme S Van, Vlaeyen JWS, Karoly P. Fear-Avoidance Model of Chronic Pain. *Clin J Pain*. 2012;28(6):475-483.

171. Wideman TH, Asmundson GGJ, Smeets RJEM, Zautra AJ, Simmonds MJ, Sullivan MJL, Haythornthwaite JA ER. Rethinking the fear avoidance model: toward a multidimensional

framework of pain-related disability. *Pain*. 2013;154(11):2262-2265.

172. Lethem J, Slade PD, Troup JDG, Bentley G. Outline of a fear-avoidance model of exaggerated pain perception-I. *Behav Res Ther*. 1983;21(4):401-408. doi:10.1016/0005-7967(83)90009-8

173. Celletti C, Castori M, La Torre G, Camerota F. Evaluation of kinesiophobia and its correlations with pain and fatigue in joint hypermobility syndrome/Ehlers-Danlos syndrome hypermobility type. *Biomed Res Int*. 2013;2013. doi:10.1155/2013/580460

174. Luque-suarez A, Martinez-calderon J, Falla D. Role of kinesiophobia on pain , disability and quality of life in people suffering from chronic musculoskeletal pain : a systematic review. *Br J Sport Med*. 2018;53:1-8. doi:10.1136/bjsports-2017-098673

175. Vincent HK, Seay AN, Montero C, Conrad BP, Hurley RW, Vincent KR. Kinesiophobia and fear-avoidance beliefs in overweight older adults with chronic low-back pain: Relationship to walking endurance - Part II. *Am J Phys Med Rehabil*. 2013;92(5):439-445. doi:10.1097/PHM.0b013e318287633c

176. Vincent HK, Lamb KM, Day TI, Tillman SM, Vincent KR, George SZ. Morbid Obesity Is Associated With Fear of Movement and Lower Quality of Life in Patients With Knee Pain-Related Diagnoses. *PMRJ*. 2010;2(8):713-722. doi:10.1016/j.pmrj.2010.04.027

177. Vincent HK, Vincent KR, Seay AN, Hurley RW. Functional impairment in obesity: a focus on knee and back pain. *Pain Manag*. 2011;1(5):427-439. doi:10.2217/pmt.11.39

178. Costa LDCM, Maher CG, McAuley JH, Hancock MJ, Smeets RJEM. Self-efficacy is more important than fear of movement in mediating the relationship between pain and disability in chronic low back pain. *Eur J Pain*. 2011;15(2):213-219. doi:10.1016/j.ejpain.2010.06.014

179. Kamper SJ, Maher CG, Menezes Costa LDC, McAuley JH, Hush JM, Sterling M. Does

fear of movement mediate the relationship between pain intensity and disability in patients following whiplash injury? A prospective longitudinal study. *Pain*. 2012;153(1):113-119. doi:10.1016/j.pain.2011.09.023

180. Roland MO. The natural history of back pain. *Practitioner*. 1983;227(1381):1119-1122.

181. Ritter PL, González VM, Laurent DD, Lorig KR. Measurement of pain using the visual numeric scale. *J Rheumatol*. 2006;33(3):574-580.

182. Cohen J. Set Correlation and Contingency Tables. *Appl Psychol Meas*. 1988;12(4):425-434. doi:10.1177/014662168801200410

183. RM Baron; DA Kenny. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol*. 1986;51(6):1173-1182.

184. Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav Res Methods*. 2008;40(3):879-891. doi:10.3758/BRM.40.3.879

185. Hayes AF. *Introduction to Mediation, Moderation and Conditional Process Analysis*. New York: Guiford Press; 2013.

186. Fritz MS, MacKinnon DP. Required sample size to detect the mediated effect. *Psychol Sci*. 2007;18(3):233-239. doi:10.1111/j.1467-9280.2007.01882.x

187. Tabachnick B FL. *Using Multivariate Statistics*. Boston, MA: Pearsons

188. Tabachnick B FL. *Using Multivariate Statistics*. Boston, MA: Pearson Education Limited; 2013.

189. Gheldof ELM, Vinck J, Van den Bussche E, Vlaeyen JWS, Hidding A, Crombez G. Pain and pain-related fear are associated with functional and social disability in an occupational setting: Evidence of mediation by pain-related fear. *Eur J Pain*. 2006;10(6):513.

doi:10.1016/j.ejpain.2005.07.005

190. Ballantyne JC, Sullivan MD. Intensity of Chronic Pain — The Wrong Metric? *N Engl J Med*. 2015;373(22):2098-2099. doi:10.1056/nejmp1507136

191. Sullivan MD, Ballantyne JC. Must we reduce pain intensity to treat chronic pain? *Pain*. 2016;157(1):65-69. doi:10.1097/j.pain.0000000000000336

192. GK F. Therapeutic exercise for knee osteoarthritis: considering factors that may influence outcome. *Eura Medicophys*. 2005;41(2):163-171.

193. American Thoracic Society. American Thoracic Society ATS Statement : Guidelines for the Six-Minute Walk Test. *Am J Respir Crit Care Med*. 2002;166:111-117. doi:10.1164/rccm.166/1/111

194. Salaffi F, Farah S, Di Carlo M, et al. The Italian Fibromyalgia Registry: a new way of using routine real-world data concerning patient-reported disease status in healthcare research and clinical practice. *Clin Exp Rheumatol*. 2020;38(1):65-71. doi:10.1136/annrheumdis-2020-eular.5535

195. Perrot S, Choy E, Ginovker A, et al. A patient survey of the impact of fibromyalgia and the journey to diagnosis. *BMC Health Serv Res*. 2010;10(1). doi:10.1186/1472-6963-10-102

196. Sim J, Madden S. Illness experience in fibromyalgia syndrome: A metasynthesis of qualitative studies. *Soc Sci Med*. 2008;67(1):57-67. doi:10.1016/j.socscimed.2008.03.003

197. Aaron LA, Burke MM, Buchwald D. Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder. *Arch Intern Med*. 2000;160(2):221-227. doi:10.1001/archinte.160.2.221

198. Weigent DA, Bradley LA, Blalock JE, Alarcon GS. Current Concepts in the Pathophysiology ofAbnormal Pain Perception In Fibromyalgia. *Am J Med Sci*.

1998;315(6):405-412. doi:10.1016/s0002-9629(15)40358-1

199. Sluka KA, Clauw DJ. Neurobiology of fibromyalgia and chronic widespread pain. *Neuroscience*. 2016;338(June):114-129. doi:10.1016/j.neuroscience.2016.06.006

200. Aguglia A, Salvi V, Maina G, Rossetto I, Aguglia E. Fibromyalgia syndrome and depressive symptoms: Comorbidity and clinical correlates. *J Affect Disord*. 2011;128(3):262-266. doi:10.1016/j.jad.2010.07.004

201. Rustøen T, Wahl AK, Hanestad BR, Lerdal A, Paul S, Miaskowski C. Prevalence and characteristics of chronic pain in the general Norwegian population. *Eur J Pain*. 2004;8(6):555-565. doi:10.1016/j.ejpain.2004.02.002

202. Desmeules JA, Cedraschi C, Rapiti E, et al. Neurophysiologic evidence for a central sensitization in patients with fibromyalgia. *Arthritis Rheum*. 2003;48(5):1420-1429. doi:10.1002/art.10893

203. Sullivan MJL, D'Eon JL. Relation Between Catastrophizing and Depression in Chronic Pain Patients. *J Abnorm Psychol*. 1990;99(3):260-263. doi:10.1037/0021-843X.99.3.260

204. Petzke F, Clauw DJ, Ambrose K, Khine A, Gracely RH. Increased pain sensitivity in fibromyalgia: Effects of stimulus type and mode of presentation. *Pain*. 2003;105(3):403-413. doi:10.1016/S0304-3959(03)00204-5

205. Cassisi G, Sarzi-Puttini P, Alciati A, et al. I segni e i sintomi della sindrome fibromialgica. *Reumatismo*. 2007;60(SUPPL. 1):15-24. doi:10.4081/reumatismo.2008.1s.15

206. Diaz-Piedra C, Di Stasi LL, Baldwin CM, Buela-Casal G, Catena A. Sleep disturbances of adult women suffering from fibromyalgia: Asystematic review of observational studies. *Sleep Med Rev*. 2015;21:86-99. doi:10.1016/j.smrv.2014.09.001

207. Evengård B, Klimas N. Chronic fatigue syndrome: Probable pathogenesis and possible treatments. *Drugs*. 2002;62(17):2433-2446. doi:10.2165/00003495-200262170-00003

208. Roehrs T, Diederichs C, Gillis M, et al. Nocturnal sleep, daytime sleepiness and fatigue in fibromyalgia patients compared to rheumatoid arthritis patients and healthy controls: A preliminary study. *Sleep Med*. 2013;14(1):109-115. doi:10.1016/j.sleep.2012.09.020

209. Crosby LJ. Factors which contribute to fatigue associated with rheumatoid arthritis. *J Adv Nurs*. 1991;16(8):974-981. doi:10.1111/j.1365-2648.1991.tb01803.x

210. Williams DA, Clauw DJ, Glass JM. Perceived cognitive dysfunction in fibromyalgia syndrome. *J Musculoskelet Pain*. 2011;19(2):66-75. doi:10.3109/10582452.2011.558989

211. Glass JM. Review of Cognitive Dysfunction in Fibromyalgia: A Convergence on Working Memory and Attentional Control Impairments. *Rheum Dis Clin North Am*. 2009;35(2):299-311. doi:10.1016/j.rdc.2009.06.002

212. Yunus MB. Central Sensitivity Syndromes: A New Paradigm and Group Nosology for Fibromyalgia and Overlapping Conditions, and the Related Issue of Disease versus Illness. *Semin Arthritis Rheum*. 2008;37(6):339-352. doi:10.1016/j.semarthrit.2007.09.003

213. Bertolucci PHF, De Oliveira FF. Cognitive impairment in fibromyalgia. *Curr Pain Headache Rep*. 2013;17(7). doi:10.1007/s11916-013-0344-9

214. Dick BD, Verrier MJ, Harker KT, Rashiq S. Disruption of cognitive function in Fibromyalgia Syndrome. *Pain*. 2008;139(3):610-616. doi:10.1016/j.pain.2008.06.017

215. Yunus MB. Towards a model of pathophysiology of fibromyalgia: aberrant central pain mechanisms with peripheral modulation. *J Rheumatol*. 1992;19(6):846-850.

216. Staud R, Smitherman ML. Peripheral and central sensitization in fibromyalgia: pathogenetic role. *Curr Pain Headache Rep*. 2002;6(4):259-266. doi:10.1007/s11916-002-0046-1

217. Li J, Simone DA, Larson AA. Windup leads to characteristics of central sensitization. *Pain*. 1999;79(1):75-82. doi:10.1016/S0304-3959(98)00154-7

218. Giesecke T, Williams DA, Harris RE, et al. Subgrouping of Fibromyalgia Patients on the Basis of Pressure-Pain Thresholds and Psychological Factors. *Arthritis Rheum*. 2003;48(10):2916-2922. doi:10.1002/art.11272

219. Epstein SA, Kay G, Clauw D, et al. Psychiatric disorders in patients with fibromyalgia: A multicenter investigation. *Psychosomatics*. 1999;40(1):57-63. doi:10.1016/S0033-3182(99)71272-7

220. Schweiger V, Del Balzo G, Raniero D, De Leo D, Martini A, Sarzi-Puttini P PE. Current trends in disability claims due to fibromyalgia syndrome. *Clin Exp Rheumatol*. 2017;105(3):119-126.

221. Prodinger B, Salzberger T, Stucki G, Stamm T, Cieza A. Measuring Functioning in People with Fibromyalgia (FM) Based on the International Classification of Functioning, Disability and Health (ICF)-A Psychometric Analysis. *Pain Pract*. 2012;12(4):255-265. doi:10.1111/j.1533-2500.2011.00488.x

222. Ben-Yosef M, Tanai G, Buskila D, Amital D, Amital H. Fibromyalgia and Its Consequent Disability. *Isr Med Assoc J*. 2020;22(7):446-450.

223. Burckhardt CS, O'Reilly CA, Wiens AN, Clark SR, Campbell SM, Bennett RM. Assessing depression in fibromyalgia patients. *Arthritis Rheum*. 1994;7(1):35-39. doi:10.1002/art.1790070108

224. Cole JA, Rothman KJ, Cabral HJ, Zhang Y, Farraye FA. Migraine, fibromyalgia, and depression among people with IBS: A prevalence study. *BMC Gastroenterol*. 2006;6:4-11. doi:10.1186/1471-230X-6-26

225. Arnold LM, Keck PE, Welge JA. Antidepressant treatment of fibromyalgia. A meta-analysis and review. *Psychosomatics*. 2000;41(2):104-113. doi:10.1176/appi.psy.41.2.104

226. Mazza M, Mazza O, Pomponi M, et al. What is the effect of selective serotonin reuptake

inhibitors on temperament and character in patients with fibromyalgia? *Compr Psychiatry*. 2009;50(3):240-244. doi:10.1016/j.comppsych.2008.08.004

227. Arnold LM, Russell IJ, Diri EW, et al. A 14-week, Randomized, Double-Blinded, Placebo-Controlled Monotherapy Trial of Pregabalin in Patients With Fibromyalgia. *J Pain*. 2008;9(9):792-805. doi:10.1016/j.jpain.2008.03.013

228. Goldenberg DL, Burckhardt C, Crofford L. Management of Fibromyalgia Syndrome. *Jama*. 2004;292(19):2388-2395. http://www.ncbi.nlm.nih.gov/pubmed/15547167.

229. Jones KD, Adams D, Winters-Stone K, Burckhardt CS. A comprehensive review of 46 exercise treatment studies in fibromyalgia (1988-2005). *Health Qual Life Outcomes*. 2006;4:2-7. doi:10.1186/1477-7525-4-67

230. Busch AJ, Webber SC, Brachaniec M, et al. Exercise therapy for fibromyalgia. *Curr Pain Headache Rep*. 2011;15(5):358-367. doi:10.1007/s11916-011-0214-2

231. Williams DA. Psychological and behavioural therapies in fibromyalgia and related syndromes. *Best Pract Res Clin Rheumatol*. 2003;17(4):649-665. doi:10.1016/S1521-6942(03)00034-2

232. Williams D. Cognitive and behavioral approaches to chronic pain. In: D W, DJ C, eds. *Fibromyalgia & Other Central Pain Syndromes.* Philadelphia: Lippincott Williams & Wilkins; 2005:343-352.

233. Häuser W, Galek A, Erbslöh-Möller B, et al. Posttraumatic stress disorder in fibromyalgia syndrome: Prevalence, temporal relationship between posttraumatic stress and fibromyalgia symptoms, and impact on clinical outcome. *Pain*. 2013;154(8):1216-1223. doi:10.1016/j.pain.2013.03.034

234. Galvez-Sánchez CM, Montoro CI, Duschek S, Reyes del Paso GA. Depression and trait-anxiety mediate the influence of clinical pain on health-related quality of life in

fibromyalgia. *J Affect Disord*. 2020;265(November 2019):486-495. doi:10.1016/j.jad.2020.01.129

235. Raphael KG, Janal MN, Nayak S, Schwartz JE, Gallagher RM. Psychiatric comorbidities in a community sample of women with fibromyalgia. *Pain*. 2006;124(1-2):117-125. doi:10.1016/j.pain.2006.04.004

236. Sayar K, Gulec H, Topbas M. Alexithymia and anger in patients with fibromyalgia. *Clin Rheumatol*. 2004;23(5):441-448. doi:10.1007/s10067-004-0918-3

237. Di Tella M, Castelli L. Alexithymia and fibromyalgia: Clinical evidence. *Front Psychol*. 2013;4(DEC):1-5. doi:10.3389/fpsyg.2013.00909

238. Ghiggia A, Romeo A, Tesio V, et al. Alexithymia and depression in patients with fibromyalgia: When the whole is greater than the sum of its parts. *Psychiatry Res*. 2017;255(October 2016):195-197. doi:10.1016/j.psychres.2017.05.045

239. Di Tella M, Ghiggia A, Tesio V, et al. Pain experience in Fibromyalgia Syndrome: The role of alexithymia and psychological distress. *J Affect Disord*. 2017;208:87-93. doi:10.1016/j.jad.2016.08.080

240. Wolfe F, Haüser W, Walitt BT, Katz RS, Rasker JJ, Russell AS. Fibromyalgia and physical trauma: The concepts we invent. *J Rheumatol*. 2014;41(9):1737-1745. doi:10.3899/jrheum.140268

241. Taylor GJ. Recent developments in alexithymia theory and research. *Can J Psychiatry*. 2000;45(2):134-142. doi:10.1177/070674370004500203

242. Kooiman CG, Bolk JH, Rooijmans HGM, Trijsburg RW. Alexithymia Does Not Predict the Persistence of Medically Unexplained Physical Symptoms. *Psychosom Med*. 2004;66(2):224-232. doi:10.1097/01.psy.0000116714.38868.06

243. van Middendorp H, Lumley MA, Jacobs JWG, van Doornen LJP, Bijlsma JWJ, Geenen

R. Emotions and emotional approach and avoidance strategies in fibromyalgia. *J Psychosom Res*. 2008;64(2):159-167. doi:10.1016/j.jpsychores.2007.08.009

244. Tuzer V, Bulut SD, Bastug B, Kayalar G, GöKa E, BeStepe E. Causal attributions and alexithymia in female patients with fibromyalgia or chronic low back pain. *Nord J Psychiatry*. 2011;65(2):138-144. doi:10.3109/08039488.2010.522596

245. Huber A, Suman AL, Biasi G, Carli G. Alexithymia in fibromyalgia syndrome: Associations with ongoing pain, experimental pain sensitivity and illness behavior. *J Psychosom Res*. 2009;66(5):425-433. doi:10.1016/j.jpsychores.2008.11.009

246. Lumley MA, Neely LC, Burger AJ. The assessment of alexithymia in medical settings: Implications for understanding and treating health problems. *J Pers Assess*. 2007;89(3):230-246. doi:10.1080/00223890701629698

247. Celikel FC, Saatcioglu O. Alexithymia and anxiety in female chronic pain patients. *Ann Gen Psychiatry*. 2006;5:1-5. doi:10.1186/1744-859X-5-13

248. Steinweg DL, Dallas AP, Rea WS. Fibromyalgia: Unspeakable Suffering, A Prevalence Study of Alexithymia. *Psychosomatics*. 2011;52(3):255-262. doi:10.1016/j.psym.2010.12.022

249. Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and Commitment Therapy: Model, processes and outcomes. *Behav Res Ther*. 2006;44(1):1-25. doi:10.1016/j.brat.2005.06.006

250. McCracken LM, Morley S. The psychological flexibility model: A basis for integration and progress in psychological approaches to chronic pain management. *J Pain*. 2014;15(3):221-234. doi:10.1016/j.jpain.2013.10.014

251. Vowles KE, Witkiewitz K, Sowden G, Ashworth J. Acceptance and commitment therapy for chronic pain: Evidence of mediation and clinically significant change following an

abbreviated interdisciplinary program of rehabilitation. *J Pain*. 2014;15(1):101-113. doi:10.1016/j.jpain.2013.10.002

252. Vowles KE, McCracken LM. Acceptance and Values-Based Action in Chronic Pain: A Study of Treatment Effectiveness and Process. *J Consult Clin Psychol*. 2008;76(3):397-407. doi:10.1037/0022-006X.76.3.397

253. Bazzichi L, Giacomelli C, Consensi A, et al. One year in review 2020: Fibromyalgia. *Clin Exp Rheumatol*. 2020;38(1):S3-S8.

254. Cabo-Meseguer A, Cerdá-Olmedo G, Trillo-Mata JL. Fibromyalgia: Prevalence, epidemiologic profiles and economic costs. *Med Clin (Barc)*. 2017;149(10):441-448. doi:10.1016/j.medcli.2017.06.008

255. De Angelis R, Salaffi F, Grassi W. Prevalence of spondyloarthropathies in an Italian population sample: A regional community-based study. *Scand J Rheumatol*. 2007;36(1):14-21. doi:10.1080/03009740600904243

256. Khaodhiar L, Ling PR, Blackburn GL, Bistrian BR. Serum levels of interleukin-6 and C-reactive protein correlate with body mass index across the broad range of obesity. *J Parenter Enter Nutr*. 2004;28(6):410-415. doi:10.1177/0148607104028006410

257. Okifuji A, Turk DC. Stress and psychophysiological dysregulation in patients with fibromyalgia syndrome. *Appl Psychophysiol Biofeedback*. 2002;27(2):129-141. doi:10.1023/A:1016243710507

258. DJ Wallace. Is there a role for cytokine based therapies in fibromyalgia. *Curr Pharm Des*. 2006;12(1):17-22.

259. Ursini F, Naty S, Grembiale RD. Fibromyalgia and obesity: The hidden link. *Rheumatol Int*. 2011;31(11):1403-1408. doi:10.1007/s00296-011-1885-z

260. Creed F. A review of the incidence and risk factors for fibromyalgia and chronic

widespread pain in population-based studies. *Pain*. 2020;161(6):1169-1176. doi:10.1097/j.pain.0000000000001819

261. Neumann L, Lerner E, Glazer Y, Bolotin A, Shefer A, Buskila D. A cross-sectional study of the relationship between body mass index and clinical characteristics, tenderness measures, quality of life, and physical functioning in fibromyalgia patients. *Clin Rheumatol*. 2008;27(12):1543-1547. doi:10.1007/s10067-008-0966-1

262. Okifuji A, Donaldson GW, Barck L, Fine PG. Relationship between fibromyalgia and obesity in pain, function, mood, and sleep. *J Pain*. 2010;11(12):1329-1337. doi:10.1016/j.jpain.2010.03.006

263. Salaffi F, Mozzani F, Draghessi A, et al. Identifying the symptom and functional domains in patients with fibromyalgia: Results of a cross-sectional Internet-based survey in Italy. *J Pain Res*. 2016;9:279-286. doi:10.2147/JPR.S100829

264. Lawrence RC, Helmick CG, Arnett FC, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheum*. 1998;41(5):778-799. doi:10.1002/1529-0131(199805)41:5<778::AID-ART4>3.0.CO;2-V

265. Goldenberg DL, Russell IJ, Russell AS, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum*. 2016;46(3):319-329. doi:10.1016/j.semarthrit.2016.08.012

266. Di Franco M, Iannuccelli C, Bazzichi L, et al. Misdiagnosis in fibromyalgia: A multicentre study. *Clin Exp Rheumatol*. 2011;29(6 SUPPL. 69).

267. Bennett RM, Friend R, Jones KD, Ward R, Han BK, Ross RL. The revised fibromyalgia impact questionnaire (FIQR): Validation and psychometric properties. *Arthritis Res Ther*. 2009;11(4):1-14. doi:10.1186/ar2783

268. Häuser W, Jung E, Erbslöh-Möller B, et al. Validation of the fibromyalgia survey

questionnaire within a cross-sectional survey. *PLoS One*. 2012;7(5):3-8. doi:10.1371/journal.pone.0037504

269. Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res*. 2010;62(5):600-610. doi:10.1002/acr.20140

270. Nunnally, J. C. and Bernstein IH. The Assessment of Reliability. *Psychom Theory,*. 1994;3:248-292.

271. Bland, J. M., Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;i:310.

272. Altman DG. *Practical Statistics for Medical Research.* New York: Chapman & Hall/CRC Press.; 1999.

273. Marcus DA, Bernstein C, Albrecht KL. Brief, Self-Report Fibromyalgia Screener Evaluated in a Sample of Chronic Pain Patients. *Pain Med (United States)*. 2013;14(5):730-735. doi:10.1111/pme.12114

274. Shir Y, Ménard H, Fitzcharles M-A, Ste-Marie PA, Wolfe F, Panopalis P. The 2010 American college of rheumatology fibromyalgia survey diagnostic criteria and symptom severity scale is a valid and reliable tool in a French speaking fibromyalgia cohort. *BMC Musculoskelet Disord*. 2012;13(1). doi:10.1186/1471-2474-13-179

275. Arreghini M, Manzoni GM, Castelnuovo G, Santovito C, Capodaglio P. Impact of fibromyalgia on functioning in obese patients undergoing comprehensive rehabilitation. *PLoS One*. 2014;9(3). doi:10.1371/journal.pone.0091392

276. Ekman P, Davidson RJ. Afterword: Are there basic emotions? *Nat Emot Fundam Quest*. 1994;99(3):46-47.

277. Weiß S, Winkelmann A, Duschek S. Recognition of facially expressed emotions in

patients with fibromyalgia syndrome. *Behav Med*. 2013;39(4):146-154. doi:10.1080/08964289.2013.818932

278. Di Tella M, Castelli L, Colonna F, et al. Theory of mind and emotional functioning in Fibromyalgia syndrome: An investigation of the relationship between social cognition and executive function. *PLoS One*. 2015;10(1):1-16. doi:10.1371/journal.pone.0116542

279. Taylor GJ, Bagby RM. New Trends in Alexithymia Research. *Psychother Psychosom*. 2004;73(2):68-77. doi:10.1159/000075537

280. Jongen S, Axmacher N, Kremers NAW, et al. An investigation of facial emotion recognition impairments in alexithymia and its neural correlates. *Behav Brain Res*. 2014;271:129-139. doi:10.1016/j.bbr.2014.05.069

281. Taylor GJ, Parker JDA, Michael Bagby R, Acklin MW. Alexithymia and somatic complaints in psychiatric out-patients. *J Psychosom Res*. 1992;36(5):417-424. doi:10.1016/0022-3999(92)90002-J

282. Sifneos PE. The prevalence of "Alexithymic" characteristics in psychosomatic patients. *Psychother Psychosom*. 1973;22(2-6):255-262. doi:10.1159/000286529

283. Scarpina F, Varallo G, Castelnuovo G, Capodaglio P, Molinari E, Mauro A. Correction to: Implicit facial emotion recognition of fear and anger in obesity (Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity, (2020), 10.1007/s40519-020-01010-6). *Eat Weight Disord*. 2020. doi:10.1007/s40519-020-01042-y

284. Marzoli SB, Molinari E, Mauro A, Castelnuovo G, Scarpina F, Melzi L. Explicit and Implicit Components of the Emotional Processing in Non-organic Vision Loss: Behavioral Evidence About the Role of Fear in Functional Blindness. *Front Psychol*. 2018;9(April):1-12. doi:10.3389/fpsyg.2018.00494

285. Miniussi C, Girelli M, Marzi CA. Neural site of the redundant target effect:

Electrophysiological evidence. *J Cogn Neurosci*. 1998;10(2):216-230. doi:10.1162/089892998562663

286. Diano M, Celeghin A, Bagnis A, Tamietto M. Amygdala response to emotional stimuli without awareness: Facts and interpretations. *Front Psychol*. 2017;7(JAN):1-13. doi:10.3389/fpsyg.2016.02029

287. Prkachin GC, Casey C, Prkachin KM. Alexithymia and perception of facial expressions of emotion. *Pers Individ Dif*. 2009;46(4):412-417. doi:10.1016/j.paid.2008.11.010

288. Fausto Salaffi, Franco Franchignoni, Andrea Giordano, Alessandro Ciapetti, Piercarlo Sarzi-Puttini MO. Psychometric characteristics of the Italian version of the revised Fibromyalgia Impact Questionnaire using classical test theory and Rasch analysis. *Clin Exp Rheumatol*. 2013;31.

289. Sica, C., & Ghisi M. *The Italian Versions of the Beck Anxiety Inventory and the Beck Depression Inventory-II: Psychometric Properties and Discriminant Power*. (Lange MA, ed.). Nova Science Publishers.; 2007.

290. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An Inventory for Measuring Depression The difficulties inherent in obtaining. *Arch Gen Psychiatry*. 1960;4(6):561-571.

291. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR JG. *Manual for the State-Trait Anxiety Inventory*. Palo Alto: Consulting Psychologists Press; 1983.

292. Macor A, Pedrabissi L SM. Ansia di stato e di tratto: ulteriore contributo alla verifica della validita psicometrica e teorica dello STAI forma Y di Spielberger. *Psychol Sci*. 1990;15:67-74.

293. Bressi C, Taylor G, Parker J, et al. Cross validation of the factor structure of the 20-item Toronto Alexithymia Scale: An Italian multicenter study. *J Psychosom Res*.

1996;41(6):551-559. doi:10.1016/S0022-3999(96)00228-0

294. Bagby RM, Parker JDA, Taylor GJ. The twenty-item Toronto Alexithymia scale-I. Item selection and cross-validation of the factor structure. *J Psychosom Res*. 1994;38(1):23-32. doi:10.1016/0022-3999(94)90005-1

295. Ekman P FW. *Pictures of Facial Affect.* Consulting Psychologists Press.; 1976.

296. Parling T, Mortazavi M, Ghaderi A. Alexithymia and emotional awareness in anorexia nervosa: Time for a shift in the measurement of the concept? *Eat Behav*. 2010;11(4):205-210. doi:10.1016/j.eatbeh.2010.04.001

297. Mauss IB, Robinson MD. Measures of emotion: A review. *Cogn Emot*. 2009;23(2):209-237. doi:10.1080/02699930802204677

298. van Middendorp H, Lumley MA, Moerbeek M, Jacobs JWG, Bijlsma JWJ, Geenen R. Effects of anger and anger regulation styles on pain in daily life of women with fibromyalgia: A diary study. *Eur J Pain*. 2010;14(2):176-182. doi:10.1016/j.ejpain.2009.03.007

299. Greenwood KA, Thurston R, Rumble M, Waters SJ, Keefe FJ. Anger and persistent pain: Current status and future directions. *Pain*. 2003;103(1-2):1-5. doi:10.1016/S0304-3959(03)00132-5

300. González-Roldán AM, Muñoz MA, Cifre I, Sitges C, Montoya P. Altered psychophysiological responses to the view of others' pain and anger faces in fibromyalgia patients. *J Pain*. 2013;14(7):709-719. doi:10.1016/j.jpain.2013.01.775

301. Clauw DJ. Fibromyalgia: A clinical review. *JAMA - J Am Med Assoc*. 2014;311(15):1547-1555. doi:10.1001/jama.2014.3266

302. Fischer-Jbali LR., Montoro CI, Montoya P, Halder W DS. Central nervous activity during implicit processing of emotional face expressions in fibromyalgia syndrome. *Brain Res*.

2021.

303. Brody LR HJ. Gender and emotion in context. In: *Handbook of Emotions*. ; 2008:395-408.

304. Rodham K, Rance N, Blake D. A qualitative exploration of carers' and "patients" experiences of fibromyalgia: one illness, different perspectives. *Musculoskeletal Care*. 2010;8(2):68-77. doi:10.1002/msc.167

305. Buskila D, Neumann L, Alhoashle A, Abu-Shakra M. Fibromyalgia syndrome in men. *Semin Arthritis Rheum*. 2000;30(1):47-51. doi:10.1053/sarh.2000.8363

306. Marques AP, Sousa A De, Matsutani LA, Lee S, Yuan K, Assumpc A. Prevalence of fibromyalgia : literature review update. *Rev Bras Reum*. 2017;7(4):356-363. doi:10.1016/j.rbre.2017.01.005

307. Siracusa R, Di Paola R, Cuzzocrea S, Impellizzeri D. *Fibromyalgia: Pathogenesis, Mechanisms, Diagnosis and Treatment Options Update*. Vol 22.; 2021. doi:10.3390/ijms22083891

308. Stisi S, Cazzola M, Buskila D, et al. Etiopathogenetic mechanisms of fibromyalgia syndrome. *Reumatismo*. 2011;60(1s):25-35. doi:10.4081/reumatismo.2008.1s.25

309. Ghiggia A, Torta R, Tesio V, Di Tella M, Romeo A, Colonna F, Geminiani GC, Fusaro E, Batticciotto A CL. Psychosomatic syndromes in fibromyalgia. *Clin Exp Rheumatol*. 2017;105(3):106-111.

310. Bennett RM, Jones J, Turk DC, Russell IJ, Matallana L. An internet survey of 2,596 people with fibromyalgia. *BMC Musculoskelet Disord*. 2007;8:1-11. doi:10.1186/1471-2474-8-27

311. Turk DC, Dworkin RH, Revicki D, et al. Identifying important outcome domains for chronic pain clinical trials: An IMMPACT survey of people with pain. *Pain*. 2008;137:276-285. doi:10.1016/j.pain.2007.09.002

312. Jones J, Rutledge DN, Jones KD, Matallana L RD. Self-assessed physical function levels of women with fibromyalgia: a national survey. *Womens Heal Issues*. 2008;18(5):406-412. doi:10.1016/j.whi.2008.04.005

313. Kingsley JD, Panton LB, Toole T, Sirithienthad P, Mathis R, McMillan V. The effects of a 12-week strength-training program on strength and functionality in women with fibromyalgia. *Arch Phys Med Rehabil*. 2005;86(9):1713-1721. doi:10.1016/j.apmr.2005.04.014

314. Verbunt JA, Pernot DHFM, Smeets RJEM. Disability and quality of life in patients with fibromyalgia. *Health Qual Life Outcomes*. 2008;6(8). doi:10.1186/1477-7525-6-8

315. Costa I da S, Gamundí A, Miranda JGV, França LGS, de Santana CN, Montoya P. Altered functional performance in patients with fibromyalgia. *Front Hum Neurosci*. 2017;11(January):1-9. doi:10.3389/fnhum.2017.00014

316. Aparicio VA, Ortega FB, Carbonell-Baeza A, Camiletti D, Ruiz JR, Delgado-Fernández M. Relationship of weight status with mental and physical health in female fibromyalgia patients. *Obes Facts*. 2011;4(6):443-448. doi:10.1159/000335293

317. Kim CH, Luedtke CA, Vincent A, Thompson JM, Oh TH. Association of body mass index with symptom severity and quality of life in patients with fibromyalgia. *Arthritis Care Res*. 2012;64(2):222-228. doi:10.1002/acr.20653

318. Vincent A, Clauw D, Oh TH, hipple MO, Toussaint LL. Decreased physical activity attributable to higher body mass index influences fibromyalgia symptoms. *PM R*. 2014;6(9):802-807. doi:10.1016/j.pmrj.2014.02.007

319. Kim CH, Luedtke CA, Vincent A, Thompson JM, Oh TH. Association between body mass index and response to a brief interdisciplinary treatment program in fibromyalgia. *Am J Phys Med Rehabil*. 2012;91(7):574-583. doi:10.1097/PHM.0b013e318255665c

320. Arranz L, Canela MÁ, Rafecas M. Relationship between body mass index, fat mass and lean mass with SF-36 quality of life scores in a group of fibromyalgia patients. *Rheumatol Int*. 2012;32(11):3605-3611. doi:10.1007/s00296-011-2250-y

321. D'Onghia M, Ciaffi J, Lisi L, Mancarella L, Ricci S, Stefanelli N, Meliconi R UF. Fibromyalgia and obesity: A comprehensive systematic review and meta-analysis. *Semin Arthritis Rheum*. 2021;51(2):409-424.

322. Wearing SC, Hennig EM, Byrne NM, Steele JR HA. The biomechanics of restricted movement in adult obesity. *Obes Rev*. 2006;7(1):13-24.

323. Larsson UE, Mattsson E. Functional limitations linked to high body mass index, age and current pain in obese women. *Int J Obes*. 2001;25(6):893-899. doi:10.1038/sj.ijo.0801553

324. Turk DC, Dworkin RH, Allen RR, et al. Core outcome domains for chronic pain clinical trials : IMMPACT recommendations. 2003;106:337-345. doi:10.1016/j.pain.2003.08.001

325. Turk DC, Dworkin RH. What should be the core outcomes in chronic pain clinical trials ? *Arthritis Res Ther*. 2004;6:151-154. doi:10.1186/ar1196

326. Jackson W, Zale EL, Berman SJ, et al. Physical functioning and mindfulness skills training in chronic pain: A systematic review. *J Pain Res*. 2019;12:179-189. doi:10.2147/JPR.S172733

327. Severeijns R, Sc M, Vlaeyen JWS, et al. Pain Catastrophizing Predicts Pain Intensity , Disability , and Psychological Distress Independent of the Level of Physical Impairment. 2001:165-172.

328. Pincus T, Burton AK, Vogel S, Field AP. A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. *Spine (Phila Pa 1976)*. 2002;27(5):109-120. doi:10.1097/00007632-200203010-00017

329. Segura-Jiménez, V.; Borges-Cosic, M.; Soriano-Maldonado, A.; Estévez-López, F.;

Alvarez-Gallardo IC. H-C, M.; Delgado-Fernández, M.; Ruiz JR. Association of sedentary time and physical activity with pain , fatigue , and impact of fibromyalgia : the al- Andalus study. *Scand J Med Sci Sport*. 2015;27:83-92. doi:10.1111/sms.12630

330. Crombez G, Vlaeyen JWS, Heuts PHTG, Lysens R. Pain-related fear is more disabling than pain itself : evidence on the role of pain-related fear in chronic back pain disability. 1999;80:329-339.

331. Mannerkorpi K, Svantesson U BC. Relationships between performance-based tests and patients' ratings of activity limitations, self-efficacy, and pain in fibromyalgia. *Arch Phys Med Rehabil*. 2006;87(2):259-264. doi:10.1016/j.apmr.2005.10.013

332. Gaudreault N, Boulay P. Cardiorespiratory fitness among adults with fibromyalgia. *Breathe*. 2018;14(2):e25-e33. doi:10.1183/20734735.019717

333. Edwards RR, Cahalan C, Mensing G, Smith M HJ. Pain, catastrophizing, and depression in the rheumatic diseases. *Nat Rev Rheumatol*. 2011;7(4):216-224.

334. Paschali M, Lazaridou A, Paschalis T, Napadow V, Edwards RR. Modifiable Psychological Factors Affecting Functioning in Fibromyalgia. *J Clin Med*. 2021;10(4):803. doi:10.3390/jcm10040803

335. Suso-Ribera C, García-Palacios A, Botella C, Ribera-Canudas MV. Pain catastrophizing and its relationship with health outcomes: Does pain intensity matter? *Pain Res Manag*. 2017;2017. doi:10.1155/2017/9762864

336. Edwards RR, Bingham CO, Bathon J, Haythornthwaite JA. Catastrophizing and pain in arthritis, fibromyalgia, and other rheumatic diseases. *Arthritis Care Res*. 2006;55(2):325-332. doi:10.1002/art.21865

337. Larice S, Ghiggia A, Di Tella M, et al. Pain appraisal and quality of life in 108 outpatients with rheumatoid arthritis. *Scand J Psychol*. 2020;61(2):271-280. doi:10.1111/sjop.12592

338. Somers TJ, Keefe FJ, Carson JW, et al. Pain catastrophizing in borderline morbidly obese and morbidly obese individuals with osteoarthritic knee pain. 2008;13(5).

339. Baranoff J, Hanrahan SJ, Kapur D, Connor JP. Acceptance as a process variable in relation to catastrophizing in multidisciplinary pain treatment. *Eur J Pain (United Kingdom)*. 2013;17(1):101-110. doi:10.1002/j.1532-2149.2012.00165.x

340. Thompson M, McCracken LM. Acceptance and related processes in adjustment to chronic pain. *Curr Pain Headache Rep*. 2011;15(2):144-151. doi:10.1007/s11916-010-0170-2

341. Vowles KE, McCracken LM, Sowden G, Ashworth J. Psychological flexibility in coping with chronic pain: Further examination of the brief pain coping inventory-2. *Clin J Pain*. 2014;30(4):324-330. doi:10.1097/AJP.0b013e31829ea187

342. Mccracken LM. Learning to live with the pain : Acceptance of pain predicts adjustment in persons with chronic pain. *Pain*. 1998;74:21-27. doi:10.15064/jjpm.38.6_441

343. Vowles KE, McCracken LM EC. Patient functioning and catastrophizing in chronic pain: the mediating effects of acceptance. *Heal Psychol*. 2008;27(2S):S136-43.

344. Varallo G, Ghiggia A, Arreghini M, Capodaglio P, Manzoni GM. The reliability and agreement of the Fibromyalgia Survey Questionnaire in an Italian sample of obese patients. *Front Psychol*. 2020:2-6.

345. Keefe FJ, Brown GK, Wallston KA, Caldwell DS. Coping with rheumatoid arthritis pain: catastrophizing as a maladaptive strategy. *Pain*. 1989;37(1):51-56. doi:10.1016/0304-3959(89)90152-8

346. Ramírez-Maestre C, de la Vega R, Sturgeon JA, Peters M. Editorial: Resilience Resources in Chronic Pain Patients: The Path to Adaptation. *Front Psychol*. 2019;10(December):1-3. doi:10.3389/fpsyg.2019.02848

347. Sturgeon JA, Zautra AJ. Resilience: A new paradigm for adaptation to chronic pain. *Curr*

Pain Headache Rep. 2010;14(2):105-112. doi:10.1007/s11916-010-0095-9

348. Sturgeon JA, Zautra AJ. Psychological Resilience , Pain Catastrophizing , and Positive Emotions : Perspectives on Comprehensive Modeling of Individual Pain Adaptation. *Curr Pain Headache Rep*. 2013;17(3). doi:10.1007/s11916-012-0317-4

349. Craner JR, Sperry JA, Koball AM, Morrison EJ, Gilliam WP. Unique Contributions of Acceptance and Catastrophizing on Chronic Pain Adaptation. *Int J Behav Med*. 2017;24(4):542-551. doi:10.1007/s12529-017-9646-3

350. Yu L, Kioskli K ML. The Psychological Functioning in the COVID-19 Pandemic and Its Association With Psychological Flexibility and Broader Functioning in People With Chronic Pain. *J Pain*. 2021;4(S1526-5900(21)00032-8).

351. Suso-Ribera C, Camacho-Guerrero L, Osma J, Suso-Vergara S, Gallardo-Pujol D. A reduction in pain intensity is more strongly associated with improved physical functioning in frustration tolerant individuals: A longitudinal moderation study in chronic pain patients. *Front Psychol*. 2019;10(APR):1-12. doi:10.3389/fpsyg.2019.00907

352. Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP. Associations between psychosocial factors and pain intensity, physical functioning, and psychological functioning in patients with chronic pain: A cross-cultural comparison. *Clin J Pain*. 2014;30(8):713-723. doi:10.1097/AJP.0000000000000027

353. Goesling J, Henry MJ, Moser SE, et al. Symptoms of Depression Are Associated with Opioid Use Regardless of Pain Severity and Physical Functioning among Treatment-Seeking Patients with Chronic Pain. *J Pain*. 2015;16(9):844-851. doi:10.1016/j.jpain.2015.05.010

354. Matos M, Bernardes SF, Goubert L. The relationship between perceived promotion of autonomy/dependence and pain-related disability in older adults with chronic pain: the

mediating role of self-reported physical functioning. *J Behav Med*. 2016;39(4):704-715. doi:10.1007/s10865-016-9726-x

355. Jensen MP, Nielson WR, Turner JA, Romano JM, Hill ML. Readiness to self-manage pain is associated with coping and with psychological and physical functioning among patients with chronic pain. *Pain*. 2003;104(3):529-537. doi:10.1016/S0304-3959(03)00092-7

356. Karasawa Y, Yamada K, Iseki M, et al. Association between change in self-efficacy and reduction in disability among patients with chronic pain. *PLoS One*. 2019;14(4):1-10. doi:10.1371/journal.pone.0215404

357. Kanzler KE, Pugh JA, McGeary DD, et al. Mitigating the Effect of Pain Severity on Activity and Disability in Patients with Chronic Pain: The Crucial Context of Acceptance. *Pain Med (United States)*. 2019;20(8):1509-1518. doi:10.1093/pm/pny197

358. Dibenedetto DJ, Wawrzyniak KM, Finkelman M, et al. Relationships between Opioid Dosing, Pain Severity, and Disability in a Community-Based Chronic Pain Population: An Exploratory Retrospective Analysis. *Pain Med (United States)*. 2019;20(11):2155-2165. doi:10.1093/pm/pny240

359. Terwee CB, Slikke RMA Van Der, Lummel RC Van, Benink RJ, Meijers WGH, Vet HCW De. Self-reported physical functioning was more influenced by pain than performance-based physical functioning in knee-osteoarthritis patients. *J Clin Epidemiol*. 2006;59(7):724-731. doi:10.1016/j.jclinepi.2005.11.019

360. Greenberg J, Mace RA, Popok PJ, et al. Psychosocial correlates of objective, performance-based, and patient-reported physical function among patients with heterogeneous chronic pain. *J Pain Res*. 2020;13:2255-2265. doi:10.2147/JPR.S266455

361. World Health Organization. *World Report on Disability*. Geneva; 2011.

362. Taylor AM, Phillips K, Patel K V., et al. *Assessment of Physical Function and*

Participation in Chronic Pain Clinical Trials: IMMPACT/OMERACT Recommendations. Vol 157.; 2016. doi:10.1097/j.pain.0000000000000577

363. Suso-Ribera C, Martínez-Borba V, Martín-Brufau R, Suso-Vergara S, García-Palacios A. Individual differences and health in chronic pain: Are sex-differences relevant? *Health Qual Life Outcomes*. 2019;17(1):1-11. doi:10.1186/s12955-019-1182-1

364. Estévez-López F, Álvarez-Gallardo IC, Segura-Jiménez V, et al. The discordance between subjectively and objectively measured physical function in women with fibromyalgia: association with catastrophizing and self-efficacy cognitions. The al-Ándalus project. *Disabil Rehabil*. 2018;40(3):329-337. doi:10.1080/09638288.2016.1258737

365. Ramírez-Maestre C, Esteve R, López-Martínez A. Fear-Avoidance, Pain Acceptance and Adjustment to Chronic Pain: A Cross-Sectional Study on a Sample of 686 Patients with Chronic Spinal Pain. *Ann Behav Med*. 2014;48(3):402-410. doi:10.1007/s12160-014-9619-6

366. Wolfe F, Clauw DJ, Fitzcharles MA, et al. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: A modification of the ACR preliminary diagnostic criteria for fibromyalgia. *J Rheumatol*. 2011;38(6):1113-1122. doi:10.3899/jrheum.100594

367. Wolfe F. Fibromyalgia research criteria. *J Rheumatol*. 2014;41(1):187. doi:10.3899/jrheum.131224

368. Gómez-Perretta C, González-Villar A, Romero-Yuste S, et al. Convergence between the 1990 and 2010 ACR diagnostic criteria and validation of the Spanish version of the Fibromyalgia Survey Questionnaire (FSQ). *Rheumatol Int*. 2014;35(1):141-151. doi:10.1007/s00296-014-3074-3

369. Sullivan, M. J. L., Bishop, S. R., & Pivik J. The Pain Catastrophizing Scale: Development

and validation. *Psychol Assess*. 1995;7(4):524–532.

370. Monticone M, Baiardi P, Ferrari S, Rocca B, Vanti C. Development of the Italian version of the Pain Catastrophising Scale (PCS-I): cross-cultural adaptation , factor analysis , reliability , validity and sensitivity to change. *Spine (Phila Pa 1976)*. 2012;35(12):1241-1246. doi:10.1007/s11136-011-0007-4

371. McCracken LM, Yang SY. The role of values in a contextual cognitive-behavioral approach to chronic pain. *Pain*. 2006;123(1-2):137-145. doi:10.1016/j.pain.2006.02.021

372. Mccracken LM, Vowles KE, Eccleston C. Acceptance of chronic pain : component analysis and a revised assessment method. 2004;107:159-166. doi:10.1016/j.pain.2003.10.012

373. Bernini O, Pennato T, Cosci F, Berrocal C. The psychometric properties of the chronic pain acceptance questionnaire in italian patients with chronic pain. *J Health Psychol*. 2010;15(8):1236-1245. doi:10.1177/1359105310365576

374. Ayán C, Martín V, Alonso-Cortés B, Alvarez MJ, Valencia M BM. Relationship between aerobic fitness and quality of life in female fibromyalgia patients. *Clin Rehabil*. 2007;21(12):1109-1113.

375. Carbonell-Baeza A, Ruiz JR, Aparicio VA, Ortega FB D-FM. The 6-minute walk test in female fibromyalgia patients: relationship with tenderness, symptomatology, quality of life, and coping strategies. *Pain Manag Nurs*. 2013;14(4):193-199. doi:10.1016/j.pmn.2011.01.002

376. Carbonell-Baeza A, Aparicio VA, Ortega FB, Cuevas AM, Alvarez IC, Ruiz JR D-FM. Does a 3-month multidisciplinary intervention improve pain, body composition and physical fitness in women with fibromyalgia? *Br J Sport Med*. 2011;45(15):1189-1195.

377. Pankoff B, Overend T, Lucy D WK. Validity and responsiveness of the 6 minute walk test

for people with fibromyalgia. *J Rheumatol*. 2000;27(11):2666-2670.

378. Larsson UE RS. The six-minute walk test in outpatients with obesity: reproducibility and known group validity. *Physiother Res Int*. 2008;13(2):84-93.

379. Mattsson E, Evers Larsson U, Rössner S. Is walking for exercise too exhausting for obese women? *Int J Obes*. 1997;21(5):380-386. doi:10.1038/sj.ijo.0800417

380. de Souza SAF, Faintuch J, Fabris SM, et al. Six-minute walk test: functional capacity of severely obese before and after bariatric surgery. *Surg Obes Relat Dis*. 2009;5(5):540-543. doi:10.1016/j.soard.2009.05.003

381. Hunter J. Demographic variables and chronic pain. *Clin J Pain*. 2001;17(4):14-19. doi:10.1097/00002508-200112001-00006

382. Ferrari S, Vanti C, Pellizzer M, Dozza L, Monticone M, Pillastrini P. Is there a relationship between self-efficacy, disability, pain and sociodemographic characteristics in chronic low back pain? A multicenter retrospective analysis. *Arch Physiother*. 2019;9(1):1-9. doi:10.1186/s40945-019-0061-8

383. Fillingim RB, Doleys DM, Edwards RR, Lowery D. Clinical characteristics of chronic back pain as a function of gender and oral opioid use. *Spine (Phila Pa 1976)*. 2003;28(2):143-150. doi:10.1097/00007632-200301150-00010

384. Rijken M, Spreeuwenberg P, Schippers J, Groenewegen PP. The importance of illness duration, age at diagnosis and the year of diagnosis for labour participation chances of people with chronic illness: Results of a nationwide panel-study in the Netherlands. *BMC Public Health*. 2013;13(1):1-13. doi:10.1186/1471-2458-13-803

385. Chaney JM, Uretsky DL, Mullins LL, et al. Differential effects of age and illness duration on pain-depression and disability-depression relationships in rheumatoid arthritis. *Int J Rehabil Heal*. 1996;2(2):101-112. doi:10.1007/bf02213445

386. Carbonell-Baeza A, Aparicio VA, Sjöström M, Ruiz JR D-FM. Pain and functional capacity in female fibromyalgia patients. *Pain Med*. 2011;12(11):1667-1675.

387. Ramírez-Maestre C, Esteve R, Ruiz-Párraga G, Gómez-Pérez L, López-Martínez AE. The Key Role of Pain Catastrophizing in the Disability of Patients with Acute Back Pain. *Int J Behav Med*. 2017;24(2):239-248. doi:10.1007/s12529-016-9600-9

388. Wertli MM, Eugster R, Held U, Steurer J, Kofmehl R, Weiser S. Catastrophizing - A prognostic factor for outcome in patients with low back pain: A systematic review. *Spine J*. 2014;14(11):2639-2657. doi:10.1016/j.spinee.2014.03.003

389. Ferreira-Valente A, Solé E, Sánchez-Rodríguez E, et al. Does Pain Acceptance Buffer the Negative Effects of Catastrophizing on Function in Individuals with Chronic Pain? *Clin J Pain*. 2021;37(5):339-348. doi:10.1097/AJP.0000000000000930

390. Catala P, Suso-Ribera C, Gutierrez L, Perez S, Lopez-Roig S PC. Is thought management a resource for functioning in women with fibromyalgia irrespective of pain levels? *Pain Med*. 2021.

391. Tangen SF, Helvik AS, Eide H, Fors EA. Pain acceptance and its impact on function and symptoms in fibromyalgia. *Scand J Pain*. 2020;20(4):727-736. doi:10.1515/sjpain-2020-0049

392. Rodero B, Casanueva B, Luciano J V., Gili M, Serrano-Blanco A, García-Campayo J. Relationship between behavioural coping strategies and acceptance in patients with fibromyalgia syndrome: Elucidating targets of interventions. *BMC Musculoskelet Disord*. 2011;12. doi:10.1186/1471-2474-12-143

393. Trainor H, Baranoff J, Henke M, Winefield H. Functioning with fibromyalgia: The role of psychological flexibility and general psychological acceptance. *Aust Psychol*. 2019;54(3):214-224. doi:10.1111/ap.12363

394. Gracely RH, Geisser ME, Giesecke T, et al. Pain catastrophizing and neural responses to pain among persons with fibromyalgia. *Brain*. 2004;127(4):835-843. doi:10.1093/brain/awh098

395. Roelofs J, Peters ML, McCracken L VJ. The pain vigilance and awareness questionnaire (PVAQ): further psychometric evaluation in fibromyalgia and other chronic pain syndromes. *Pain*. 2003;101(3):299-306. doi:10.1016/S0304-3959(02)00338-X

396. Cooper L, Ells L, Ryan C MD. Perceptions of adults with overweight/obesity and chronic musculoskeletal pain: An interpretative phenomenological analysis. *J Clin Nurs*. 2018;27(5-6):e776-e786.

397. Hulens M, Vansant G, Claessens AL, Lysens R, Muls E. Predictors of 6-minute walk test results in lean, obese and morbidly obese women. *Scand J Med Sci Sport*. 2003;13(2):98-105. doi:10.1034/j.1600-0838.2003.10273.x

398. Han TS, Schouten JSAG, Lean MEJ, Seidell JC. The prevalence of low back pain and associations with body fatness, fat distribution and height. *Int J Obes*. 1997;21(7):600-607. doi:10.1038/sj.ijo.0800448

399. Donnelly JE, Smith B, Jacobsen DJ, et al. The role of exercise for weight loss and maintenance. *Best Pract Res Clin Gastroenterol*. 2004;18(6 SPEC.ISS.):1009-1029. doi:10.1016/j.bpg.2004.06.022

400. Egger G, Dixon J. Non-nutrient causes of low-grade, systemic inflammation: Support for a “canary in the mineshaft” view of obesity in chronic disease. *Obes Rev*. 2011;12(5):339-345. doi:10.1111/j.1467-789X.2010.00795.x

401. Hodges PW, Smeets RJ. Interaction between pain, movement, and physical activity: Short-term benefits, long-term consequences, and targets for treatment. *Clin J Pain*. 2015;31(2):97-107. doi:10.1097/AJP.0000000000000098

402. Busch AJ, Barber KA, Overend TJ, Peloso PM SC. Exercise for treating fibromyalgia syndrome. *Cochrane Database Syst Rev*. 2007;17(4).

403. Fontaine KR, Conn L CD. Effects of lifestyle physical activity on perceived symptoms and physical function in adults with fibromyalgia: results of a randomized trial. *Arthritis Res Ther*. 2010;12(2).

404. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis*. 2017;76(2):318-328. doi:10.1136/annrheumdis-2016-209724

405. Da Costa D, Abrahamowicz M, Lowensteyn I, Bernatsky S, Dritsa M, Fitzcharles MA DP. A randomized clinical trial of an individualized home-based exercise programme for women with fibromyalgia. *Rheumatol (Oxford)*. 2005;44(11):1422-1427. doi:10.1093/rheumatology/kei032

406. Meiworm L, Jakob E, Walker UA, Peter HH KJ. Patients with fibromyalgia benefit from aerobic endurance exercise. *Clin Rheumatol*. 2000;19(4):253-257.

407. Rooks DS, Silverman CB, Kantrowitz FG. The effects of progressive strength training and aerobic exercise on muscle strength and cardiovascular fitness in women with fibromyalgia: A pilot study. *Arthritis Care Res*. 2002;47(1):22-28. doi:10.1002/art1.10180

408. Petridou A, Siopi A, Mougios V. Exercise in the management of obesity. *Metabolism*. 2019;92:163-169. doi:10.1016/j.metabol.2018.10.009

409. Oppert JM, Bellicha A CC. Physical activity in management of persons with obesity. *Eur J Intern Med*. 2021;S0953-6205. doi:10.1016/j.ejim.2021.04.028

410. Johns DJ, Hartmann-Boyce J, Jebb SA AP. Diet or exercise interventions vs combined behavioral weight management programs: a systematic review and meta-analysis of direct comparisons. *J Acad Nutr Diet*. 2014;114(10):1557-1568. doi:10.1016/j.jand.2014.07.005

411. Alamam DM, Leaver A, Alsobayel HI, Moloney N, Lin J MM. Low Back Pain-Related Disability Is Associated with Pain-Related Beliefs Across Divergent Non-English-Speaking Populations: Systematic Review and Meta-Analysis. *Pain Med*. 2021;24.

412. Williams DA, Gendreau M, Hufford MR, Groner K, Gracely RH, Clauw DJ. Pain assessment in patients with fibromyalgia syndrome: A consideration of methods for clinical trials. *Clin J Pain*. 2004;20(5):348-356. doi:10.1097/00002508-200409000-00010

413. Clauw DJ, Crofford LJ. Chronic widespread pain and fibromyalgia: What we know, and what we need to know. *Best Pract Res Clin Rheumatol*. 2003;17(4):685-701. doi:10.1016/S1521-6942(03)00035-4

414. Harris RE, Williams DA, McLean SA, et al. Characterization and consequences of pain variability in individuals with fibromyalgia. *Arthritis Rheum*. 2005;52(11):3670-3674. doi:10.1002/art.21407

415. Goldenberg DL, Russell IJ, Russell AS, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum*. 2016;46(3):319-329. doi:10.1016/j.semarthrit.2016.08.012

416. Kop WJ, Lyden A, Berlin AA, et al. Ambulatory monitoring of physical activity and symptoms in fibromyalgia and chronic fatigue syndrome. *Arthritis Rheum*. 2005;52(1):296-303. doi:10.1002/art.20779

417. Bigatti SM, Hernandez AM, Cronan TA, Rand KL. Sleep disturbances in fibromyalgia syndrome: Relationship to pain and depression. *Arthritis Care Res*. 2008;59(7):961-967. doi:10.1002/art.23828

418. Gauthier N, Thibault P, Sullivan MJL. Individual and relational correlates of pain-related empathic accuracy in spouses of chronic pain patients. *Clin J Pain*. 2008;24(8):669-677. doi:10.1097/AJP.0b013e318173c28f

419. Bendayan R, Ramírez-Maestre C, Ferrer E, López A, Esteve R. From acute to chronic back pain: Using linear mixed models to explore changes in pain intensity, disability, and depression. *Scand J Pain*. 2017;16:45-51. doi:10.1016/j.sjpain.2017.02.009

420. Häuser W, Petzke F, Sommer C. Comparative Efficacy and Harms of Duloxetine, Milnacipran, and Pregabalin in Fibromyalgia Syndrome. *J Pain*. 2010;11(6):505-521. doi:10.1016/j.jpain.2010.01.002

421. Steiner JL, Bigatti SM, Slaven JE AD. The Complex Relationship between Pain Intensity and Physical Functioning in Fibromyalgia: The Mediating Role of Depression. *J Appl Biobehav Res*. 2017;22(4).

422. Lundberg M, Frennered K, Hägg O, Styf J. The impact of fear-avoidance model variables on disability in patients with specific or nonspecific chronic low back pain. *Spine (Phila Pa 1976)*. 2011;36(19):1547-1553. doi:10.1097/BRS.0b013e3181f61660

423. Swinkels RAHM, Verbeek ALM, Vlaeyen JWS, et al. Psychometric properties of the Tampa Scale for kinesiophobia and the fear-avoidance beliefs questionnaire in acute low back pain. 2003;8:29-36. doi:10.1054/math.2002.0484

424. Esteve R, Ramírez-Maestre C, López-Marínez AE. Adjustment to chronic pain: the role of pain acceptance, coping strategies, and pain-related cognitions. *Ann Behav Med*. 2007;33(2):179-188.

425. Martinez-Calderon J, Flores-Cortes M, Clavero-Cano S, et al. The Role of Positive Psychological Factors in the Association between Pain Intensity and Pain Interference in Individuals with Chronic Musculoskeletal Pain: A Cross-Sectional Study. *J Clin Med*. 2020;9(10):3252. doi:10.3390/jcm9103252

426. Thompson CG, Kim RS, Aloe AM, Becker BJ. Extracting the Variance In flation Factor and Other Multicollinearity Diagnostics from Typical Regression Results. *Basic Appl Soc*

Psych. 2017;39(2):81-90. doi:10.1080/01973533.2016.1277529