WILEY
Online Proofing System Instructions

The Wiley Online Proofing System allows authors and proof reviewers to review PDF proofs, mark corrections, respond to queries, upload replacement figures, and submit these changes directly from the PDF proof from the locally saved file or while viewing it in your web browser.

1. For the best experience reviewing your proof in the Wiley Online Proofing System please ensure you are connected to the internet. This will allow the PDF proof to connect to the central Wiley Online Proofing System server. If you are connected to the Wiley Online Proofing System server you should see the icon with a green check mark above in the yellow banner.


Connected


Disconnected

2. Please review the article proof on the following pages and mark any corrections, changes, and query responses using the Annotation Tools outlined on the next 2 pages.

3. To save your proof corrections, click the "Publish Comments" button appearing above in the yellow banner. Publishing your comments saves your corrections to the Wiley Online Proofing System server. Corrections don't have to be marked in one sitting, you can publish corrections and log back in at a later time to add more before you click the "Complete Proof Review" button below.

4. If you need to supply additional or replacement files bigger than 5 Megabytes (MB) do not attach them directly to the PDF Proof, please click the "Upload Files" button to upload files:

Click Here

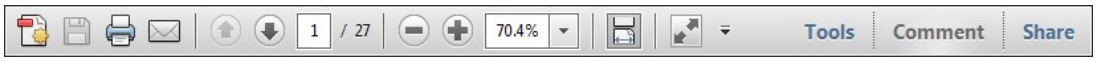
5. When your proof review is complete and you are ready to submit corrections to the publisher, please click the "Complete Proof Review" button below:

Click Here

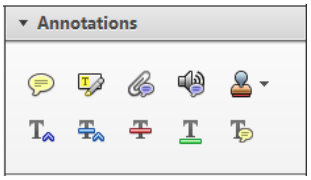
IMPORTANT: Do not click the "Complete Proof Review" button without replying to all author queries found on the last page of your proof. Incomplete proof reviews will cause a delay in publication.

IMPORTANT: Once you click "Complete Proof Review" you will not be able to publish further corrections.

Once you have Acrobat Reader open on your computer, click on the Comment tab at the right of the toolbar:



This will open up a panel down the right side of the document. The majority of tools you will use for annotating your proof will be in the Annotations section, pictured opposite. We've picked out some of these tools below:

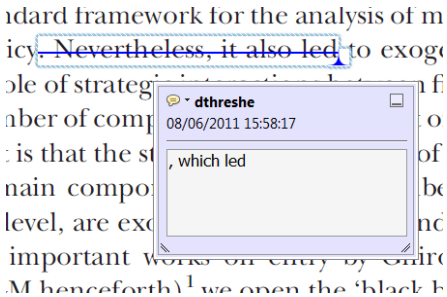


1. Replace (Ins) Tool – for replacing text.

Strikes a line through text and opens up a text box where replacement text can be entered.

How to use it

- Highlight a word or sentence.
- Click on the Replace (Ins) icon in the Annotations section.
- Type the replacement text into the blue box that appears.

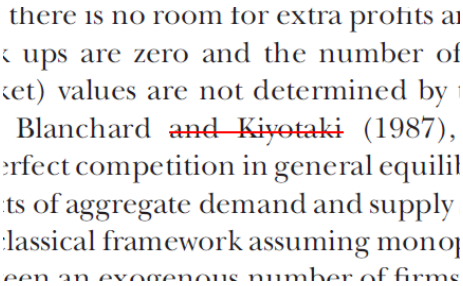


2. Strikethrough (Del) Tool – for deleting text.

Strikes a red line through text that is to be deleted.

How to use it

- Highlight a word or sentence.
- Click on the Strikethrough (Del) icon in the Annotations section.

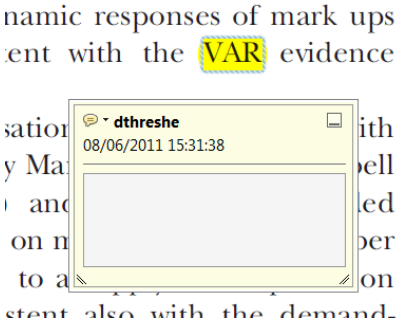


3. Add note to text Tool – for highlighting a section to be changed to bold or italic.

Highlights text in yellow and opens up a text box where comments can be entered.

How to use it

- Highlight the relevant section of text.
- Click on the Add note to text icon in the Annotations section.
- Type instruction on what should be changed regarding the text into the yellow box that appears.

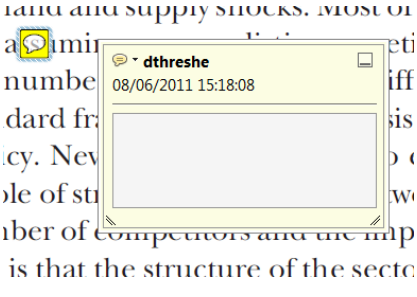


4. Add sticky note Tool – for making notes at specific points in the text.

Marks a point in the proof where a comment needs to be highlighted.

How to use it

- Click on the Add sticky note icon in the Annotations section.
- Click at the point in the proof where the comment should be inserted.
- Type the comment into the yellow box that appears.

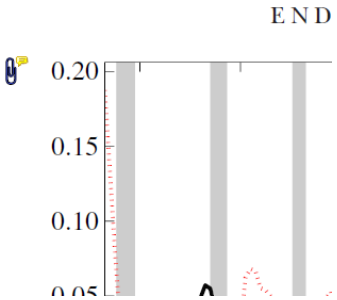


5. Attach File Tool – for inserting large amounts of text or replacement figures.

Inserts an icon linking to the attached file in the appropriate place in the text.

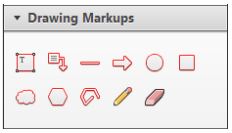
How to use it

- Click on the Attach File icon in the Annotations section.
- Click on the proof to where you'd like the attached file to be linked.
- Select the file to be attached from your computer or network.
- Select the colour and type of icon that will appear in the proof. Click OK.



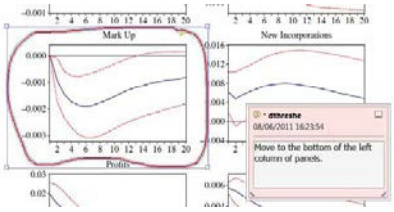
6. Drawing Markups Tools – for drawing shapes, lines and freeform annotations on proofs and commenting on these marks.

Allows shapes, lines and freeform annotations to be drawn on proofs and for comment to be made on these marks.



How to use it

- Click on one of the shapes in the Drawing Markups section.
- Click on the proof at the relevant point and draw the selected shape with the cursor.
- To add a comment to the drawn shape, move the cursor over the shape until an arrowhead appears.
- Double click on the shape and type any text in the red box that appears.



ORIGINAL ARTICLE

Depression symptoms are associated with key health outcomes in women with fibromyalgia: a cross-sectional study

Jesús del POZO-CRUZ,[1] Rosa M. ALFONSO-ROSA,[1] Alejandro CASTILLO-CUERVA,[1] Borja SAÑUDO,[1] Paul NOLAN[2] and Borja del POZO-CRUZ[2]

[1]*Department of Physical Education and Sports, University of Seville, Seville, Spain, and* [2]*Department of Sport and Exercise Science, University of Auckland, Auckland, New Zealand*

Abstract

Aim: To analyze the association between depression severity and other fibromyalgia- (FM) related symptoms such as pain, fatigue, sleep problems, severity of the disease, activity pattern, functional capacity and quality of life.

Method: The sample included 105 Spanish women with FM. Quality of life was assessed by means of the EQ-5D and symptom severity by the Fibromyalgia Impact Questionnaire. Pain, fatigue and unrestful sleep problems were assessed using 0–10 Visual Analog Scales. Activity patterns were determined by using the International Physical Activity Questionnaire while a battery of standardized field-based functional capacity tests was used to assess cardiorespiratory fitness, muscular strength, flexibility, agility and static and dynamic balance. Depression level was assessed and categorized according to the Beck Depression Inventory.

Results: Sixty-two percent of the participants were depressed. Depressed patients exhibited higher pain, fatigue level, sleep problems and severity of the symptoms, reduced levels of lower limb strength and physical activity time and worse quality of life when compared with non-depressed patients ($P < 0.05$). A negative relationship was found between total minutes of physical activity ($P = 0.001$) and caloric expenditure ($P = 0.026$), lower flexibility ($P = 0.005$), hand grip strength ($P = 0.026$) and lower limb strength ($P < 0.001$). A positive relationship was detected between depression and total sitting time ($P = 0.018$). These results were maintained when correlations were adjusted for body mass index.

Conclusions: Depressed women with FM exhibited higher symptom severity and reported worse physical fitness and quality of life than their non-depressed peers.

Key words: depression, fibromyalgia, pain, physical activity, physical fitness, quality of life.

INTRODUCTION

People with fibromyalgia (FM) are characterized by diffuse and widespread musculoskeletal pain[1] which may influence their daily activities. FM significantly reduces health-related quality of life (HRQoL) compared to healthy people[2,3] and people with other rheumatic diseases.[4] FM also contributes to large medical, social and labor costs, resulting in a large impact on society.[5,6]

Correspondence: Borja del Pozo-Cruz, PhD, Department of Sport and Exercise Science, University of Auckland, Building 731 room 340, Tamaki Innovation Campus, 261 Morrin Rd, St Johns, Auckland, Private Bag 92019, Auckland, New Zealand.
Email: b.delpozocruz@auckland.ac.nz

The specific symptoms of FM (i.e., pain, fatigue or sleep problems) contribute to people with FM being less physically active than their peers without FM. As a result, people with FM tend to have decreased physical fitness for their age[7] and are closer to that of healthy older adults.[8]

Additionally, symptoms of depression are common in people with FM. Research shows that the prevalence of mood disorders, including depression, is more than three times higher in FM subjects than in the general population. Depression symptoms appear to increase sensitivity to pain.[9] Although the underlying mechanism mediating depression and pain is not fully understood, different studies support the idea that different brain regions (including the limbic and paralimbic areas) mediate in both conditions and that a bidirectional relationship between pain and depression exists, with the symptoms of one worsening the other or making the other more likely to develop.[10]

Multidisciplinary interventions, including psychological treatment, have been shown to be effective in improving FM-related outcomes and fitness.[11] Depression symptoms appear to increase the sensitivity to pain,[9] leading to reduced physical activity levels and physical function. However, the relationship between depression symptoms and the total amount of physical activity, physical function and FM-related problems is not fully understood. Therefore, the aim of this study was to examine the association of depression symptoms with activity patterns, functional capacity, symptom severity, pain, fatigue, sleep disturbance and quality of life among a sample of women with FM.

PATIENTS AND METHODS

Participants and study design

A cross-sectional study was conducted. Participants in the study were recruited from two local FM associations (Seville, Spain). Researchers contacted the chairperson in each association and informed this person about the study. The chair of each association informed the associated members about the study and the individual members contacted the researchers if they were interested in participating in the study. Potential participants were included in the study if they were diagnosed as having FM by a rheumatologist according to the American College of Rheumatology criteria (1990 criteria)[12] and gave informed consent after receiving detailed information about the aims and study procedures. Exclusion criteria were: having any other rheumatic disease, history of cognitive impairment, severe heart, liver or kidney disease. In addition, those who answered 'yes' to any question on the Physical Activities Readiness Questionnaire (indicating a possible contraindication for physical fitness testing)[13] were also excluded from the study. The study was approved by the Ethics Committee of the University of Seville and was conducted following the ethical guidelines of the Declaration of Helsinki. Out of 125 initial volunteers, 105 participants were finally included in the study. Fifteen participants were excluded because they had other rheumatic diseases and five of them were excluded because they were not diagnosed with FM.

Material and procedures

A general standardized questionnaire was used to collect socio-demographic (i.e., age, educational level, occupational status and income) and clinical data (i.e., number of drugs taken for FM and years since clinical diagnosis) of the participants in the study. Weight, height, and waist and hip circumference were measured so that body mass index (BMI, kg/m^2) and waist-to-hip ratio could be calculated. Body-fat percentage was estimated using a handheld impedance analyzer (Omron BF-306, Omron Healthcare Europe BV, Hoofddorp, the Netherlands) according to the manufacturer's instructions.[14] During the measurement the instrument records impedance from hand to hand to calculate body fat percentage from the impedance value and the pre-entered personal values, including weight, height, age and sex.

To obtain information on activity patterns, the International Physical Activity Questionnaire (IPAQ) was used.[15] The short (self-administered, seven items), last-week version of the IPAQ was administered, asking about the time spent being physically active in the last 7 days. Minutes of sitting, walking, moderate-intensity (walking not included) and vigorous-intensity activities were computed so the total metabolic equivalents of task (MET) were calculated as follows: (daily minutes of walking × days per week with walking × 3.3) + (daily minutes of moderate-intensity activity × days per week with moderate-intensity activity × 4.0) + (daily minutes of vigorous activity × days per week with vigorous activity × 8.0).

To assess functional capacity, a battery of fitness tests previously validated in females with FM was used.[16] This battery included the assessment of the cardiorespiratory function, upper and lower body muscular strength, upper and lower body flexibility and static and agility/dynamic balance. The physical fitness tests studied were as follows.

To assess cardiorespiratory function, the 6-min walking test was used.[17] Participants were instructed to walk as far as they could at a fast, comfortable pace in 6 min. The maximum distance (m) walked was recorded as the score of the test. Participants were discouraged from talking during the test and were notified of each passing minute.

A hand grip strength test was used to assess upper body muscular strength.[18] This test was conducted with a digital dynamometer (TKK 5401 Grip-D, Takei Scientific Instruments, Tokyo, Japan). The participants maintained the standard bipedal position during the entire test with the arm in complete extension. Each participant performed the test twice with each hand allowing a 1-min rest period between measures. The peak value was recorded for each trial. The best value of two trials was chosen as score of the test for each arm (dominant and nondominant arm) and an average score of both hands was computed as final hand grip score.

The 30-sec sit to stand (30s-STS) test was used to assess lower body strength.[17] Participants were instructed to perform the task starting and finishing in the seated position. Participants were allowed a practice trial before the beginning of the test. The number of times within 30 sec that the participant could raise to a full stand from a seated position with back straight and feet flat on the floor without pushing off the arms was counted.

Upper-body flexibility was assessed by the 'back scratch' test.[17] This test was assessed twice, alternately with both hands, and the best value was recorded. The average of both hands was used in the analysis.

The modified chair sit and reach test (CST) was used to assess lower body flexibility.[17] A ruler was used to measure the distance between the end of the third digit of the hand and the toes. This value is negative if the fingertip does not reach the toes and positive if fingertip passes the toes. Both sides were measured twice and the maximal score from each leg was recorded. The final score was the average score of both sides.

Motor agility/mobility was assessed by the timed up and go (TUG) test.[17] The participant had to stand up from a chair, walk 2.44 m to and around a cone, and return to the chair in the shortest possible time. The best time of two trials (1-min rest period between each trial) was recorded.

The Fibromyalgia Impact Questionnaire (FIQ) assessed participants' severity of symptoms. This is a reliable and valid questionnaire for the measurement of health status and physical function in Spanish-speaking FM patients, and it has been shown to be responsive to change.[19] The FIQ total score ranges from 0 to 100 with a higher value indicating a greater impact of the disorder.[20]

The Visual Analog Scale (VAS) was used for pain assessment (VAS_{pain}). The VAS_{pain} is a widely used pain evaluation instrument based on a straight line (10 cm long), scaled from 0 to 10, on which the patient marks the intensity of his or her pain. This scale has been also used and validated in FM patients, showing a good reliability and discriminatory power.[21] Another two validated VAS were used for fatigue ($VAS_{fatigue}$)[22] and unrestful sleep ($VAS_{unrestful\ sleep}$).[23]

The Euroqol-5D (EQ-5D)[24] was used to assess participants' HRQoL. The EQ-5D-3L includes five dimensions (mobility, personal care, usual activities, pain/discomfort and anxiety/depression), each of which has three levels (no problems, some problems or extreme problems/unable to), answers ranging from 1 to 3. The juxtaposition of the levels for these five dimensions correlates to a five-digit number, which reflects 243 possible health status values. These health status values can be converted to a health functional index or a 'utility', using time-trade off values ($EuroQol_{utility}$; 1 = full functional quality of life, 0 = death). The EQ-5D-3L also includes a vertical 20-cm VAS which is used by participants to rate their own health between 0 (worst imaginable health state) and 100 (best imaginable health state), thereby providing an overall numerical estimate of their HRQoL.[25]

The Spanish 21-item Beck Depression Inventory (BDI) version was used for depression assessment.[26,27] The BDI is a 21-question multiple-choice self-report inventory, each of which has four brief statements corresponding to normal responses and to mild, moderate and severe depressive symptoms. Respondents choose the statement, scored from 0 to 3, which best describes their feelings over the previous week. Total score is obtained from the sum of the different values across all questions and patients are graded with different depression symptoms. When patients score 17 to 20 points in the BDI, they are considered clinically depressed. The BDI, previously used in FM patients,[28] has shown to be a sensitive measure for depressive symptoms and is simple to administer and code, thus showing good psychometric properties.[26]

Statistical analysis

The SPSS package version 17.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for data analysis. The level of significance was set at $P \leq 0.05$ for all statistical analyses performed. Kolmogorov–Smirnov test was

used to determine the distribution characteristics of the variables. Data are presented as mean (± SD), unless otherwise stated. Student's *t*-test for independent measures (parametric variables) or Mann–Whitney *U*-test (non-parametric variables) were performed to analyze differences between depression-based groups for continuous variables and Chi-square test was used to test these differences for categorical variables. Accordingly, with the distribution of data, the association between depression and functional capacity was assessed using Pearson's correlation coefficients, while the association between depression and activity patterns was analyzed using Spearman's correlation coefficients. As BMI was expected to influence FM-related outcomes, partial correlations adjusted for BMI were also performed.[29] The level of relationship was determined based on the recommendations of Cohen:[30] a coefficient of between 0.1 and 0.29 was considered low; a coefficient between 0.3 and 0.49 was considered moderate; and more than 0.5 was considered high. Additionally, we performed linear regression analyses to get a better understanding of the associations between depression and the main study variables.

RESULTS

Out of 105 women with FM assessed in this study, 62% reported to be clinically depressed according to the BDI. The mean age of participants was 55 (± 9) years, hence, similar to the age of the general Spanish FM population.[31] The majority of the participants were married (63%), working (31%) and reported to have reached primary school studies (41%). The mean BMI was 29.1 (± 8.1) kg/m^2 and had an average body fat percentage of 40% (Table 1). Table 2 describes the level of functional capacity, the activity patterns and the quality of life across the two groups of depression symptoms.

Participants reporting clinical depression symptoms exhibited lower-limb body strength ($P = 0.012$) than non-clinically depressed participants. Depressed participants also exhibited lower upper-limb body strength scores than their peers without clinical depression symptoms; however, this was not statistically significant ($P = 0.089$). As shown by Pearson's correlation coefficient, there were inverse relationships between depression symptoms and upper- ($r = -0.243/P = 0.026$) and lower- ($r = -0.425/P < 0.001$) limb strength and with lower-limb flexibility ($r = -0.304/P = 0.005$) (Fig. 1). With the exception of lower-limb body flexibility, these relationships were maintained when correlation analyses were controlled by BMI (upper [$r = -0.268/P = 0.025$] and lower [$r = -0.382/P = 0.001$] limb strength).

Table 1 Characteristics in women with fibromyalgia ($n = 105$)

Variable	Total sample ($n = 105$)
Age (years)	55.26 (9.34)
Years since clinical diagnosis	9.23 (6.20)
Number of drugs for fibromyalgia (median IQR)†	1 (2)
Body composition	
BMI (kg/m^2)	29.07 (8.11)
Body fat (%)	39.60 (6.75)
WHR	0.88 (0.07)
Marital status, *n* (%)	
Unmarried	16 (17.80)
Married	57 (63.30)
Widowed	8 (8.90)
Divorced	6 (6.70)
Separated	3 (3.30)
Occupational status, *n* (%)	
Housewife	22 (24.40)
Working	28 (31.10)
Unemployed	14 (15.60)
Retired	26 (28.90)
Educational status, *n* (%)	
Unfinished studies	27 (30.00)
Primary school	37 (41.10)
Secondary school	11 (12.20)
University degree	15 (16.70)
Income per month, *n* (%)	
< 1200 €	75 (83.30)
1201–1800 €	10 (11.10)
> 1800 €	5 (5.60)

Values are means (standard deviation), unless otherwise indicated. FM, fibromyalgia; BMI, body mass index; WHR, waist-to-hip ratio; VAS: visual analog scale from 0 to 10; IQR, interquartile range; †painkillers, antidepressants and sleeping pills.

Similarly, depressed FM participants displayed lower levels of physical activity ($P = 0.049$) and caloric expenditure ($P = 0.027$) when compared with non-depressed participants (Table 2). In addition, an inverse relationship between depression and the amount of physical activity level and a direct relationship between depression symptoms and sitting time ($\rho = 0.335/P = 0.001$) (Fig. 1) was found. After correction for BMI, depression symptoms were related to total caloric expenditure ($r = -0.306/P = 0.010$) along with the total amount of physical activity ($r = -0.248/P = 0.037$). However, the relationship between depression and sitting time was not present after corrections for BMI ($P > 0.05$).

Table 2 Physical function, activity patterns and quality of life by depression status groups (n = 105)

Variables	Clinical depression FM group (n = 60)	Non-clinical depression FM group (n = 45)	P
Physical function			
Cardiorespiratory function (6-min waking test, m)	416.63 (83.60)	427.37 (57.65)	0.549†
Muscular function			
Upper body (handgrip strength, kg)	17.28 (4.99)	19.40 (5.62)	0.089†
Lower body (30-s chair-to-stand test, number of stands)	7.72 (2.44)	9.30 (2.75)	0.012†
Flexibility			
Upper body (back-scratch test, cm)	−5.66 (10.76)	−5.03 (7.80)	0.782†
Lower body (chair sit-and-reach test, cm)	−5.70 (14.68)	−2.67 (14.06)	0.369†
Balance			
Static (30-s blind flamingo test, failures)	9.78 (5.74)	7.74 (7.19)	0.187†
Dynamic/agility (time up-and-go test, s)	6.80 (1.86)	6.99 (1.84)	0.650†
Activity patterns (IPAQ)			
Total minutes of physical activity (min)	46.83 (43.21)	71.84 (57.84)	0.049†
Total caloric expenditure (MET/min)	699.68 (479.81)	1213.05 (1076.61)	0.027†
Total sitting time (min)	365.00 (215.28)	302.00 (180.50)	0.213†
Quality of Life (EQ-5D)			
VAS (0–100 mm)	43.86 (20.16)	52.27 (14.93)	0.047†
EQ-5D$_{\text{UTILITY}}$	0.50 (0.25)	0.51 (0.23)	0.850†

Values are means (standard deviation). FM, fibromyalgia; IPAQ, International Physical Activity Questionnaire; PA, physical activity; MET, Metabolic equivalent of task; EQ-5D, European quality of life questionnaire; VAS (0–100 mm), Visual Analog Scale from the EQ-5D where lower results represent a worse quality of life; P, P-value from Student's t-test for independent measurements†or Mann–Whitney U-test‡.

Clinically depressed FM participants showed lower self-reported quality of life as measured with VAS (0.047) (Table 2) and higher self-reported severity of the symptoms ($P < 0.001$), pain ($P < 0.001$), fatigue ($P = 0.027$) and sleep problems ($P = 0.002$) than those without clinical depression symptoms (Fig. 2).

According to the linear regression analysis, 30% of the total variance in depression symptoms is associated with: strength (upper and lower) and agility/dynamic balance; 7% with total caloric expenditure; 33% with self-care and anxiety/depression EQ-5D dimensions; 39% with severity of the symptoms; 12% with pain or restful sleep problems; and 11% with fatigue. The final regression model depicts that self-care and anxiety/depression dimensions and severity of the symptoms account for 51% of the total depression symptoms variance (Table 3).

DISCUSSION

The current study shows that Spanish women with FM who have clinical depression according to the BDI report lower levels of quality of life, physical fitness (especially muscle strength), greater amounts of sitting time and are less physically active than their non-clinically depressed peers. Moreover, symptom severity is increased with higher levels of depression. Although small, the study sample was equally distributed among depressed symptoms groups, thus allowing for making proper comparisons between groups. The fact that 62% of our sample reported to be clinically depressed and 41% of our participants had completed primary school level study may reflect what other studies have shown in this regard,[10,32]

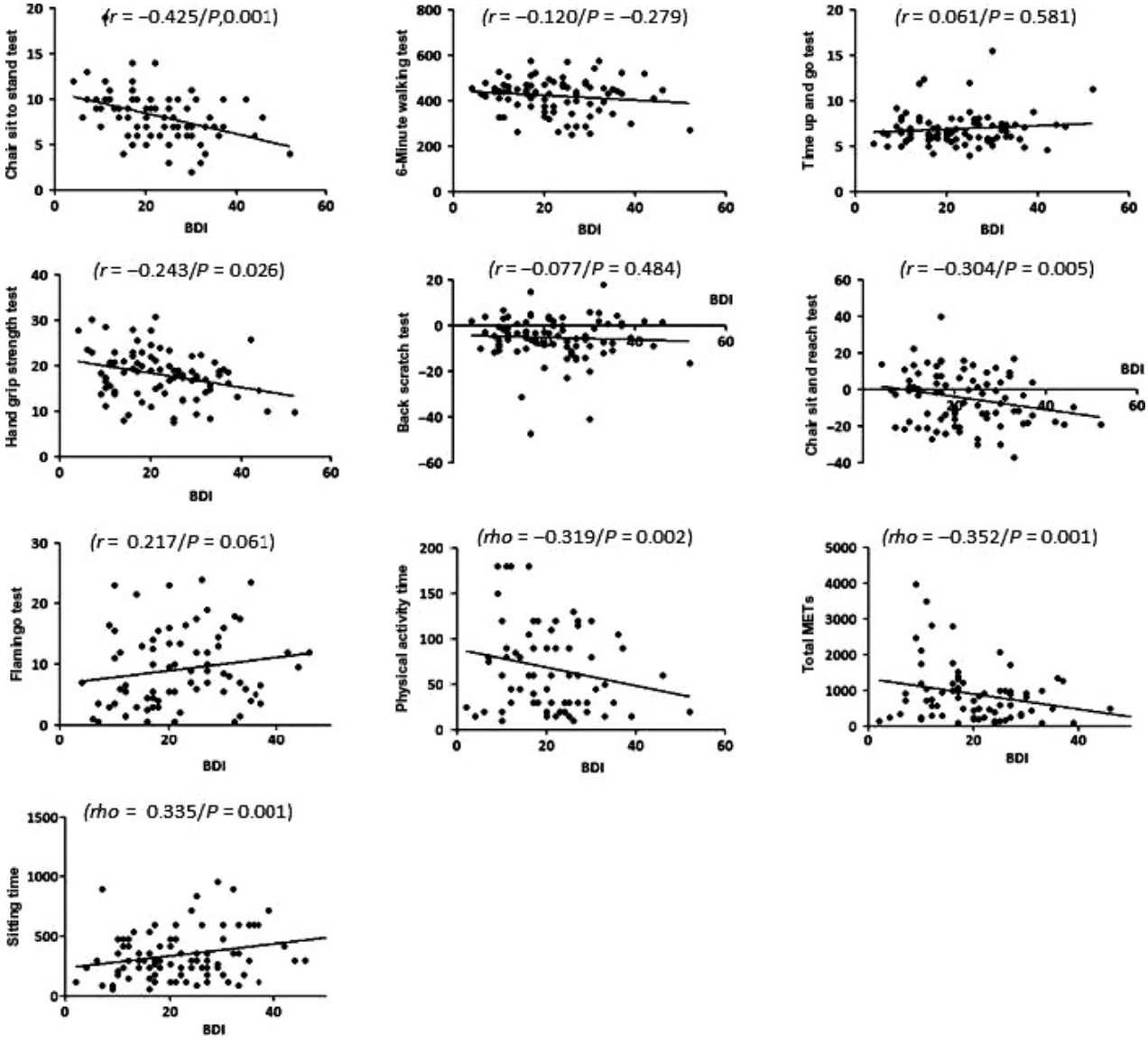


Figure 1 Correlation between functional capacity (chair sit-to-stand test, 6-min walking test, time up-and-go test, hand grip, back-scratch test, chair sit-and-reach test and flamingo test), physical activity (min/week and total METs), sitting time (min/week) and depression (BDI). BDI, Beck Depression Inventory; MET, metabolic equivalent of task; *r*, Person correlation coefficient; rho, Spearman correlation coefficient.

It has been suggested that depression may be responsible for an increase in sensory amplification in FM, that may contribute to physical and pain comorbidities in people exhibiting higher depression symptoms.[9] Our results demonstrate that depressed participants self-reported more pain than those without depression. This is an important finding as physical activity and sedentary behaviors seem to be related to central nervous system regulation of pain in FM.[33]

In this study, the depressed FM participants exhibited lower levels of physical activity, thus had a lower caloric expenditure than their non-depressed FM peers. This is consistent with previous research where correlations have been established between the amount of physical activity and BDI scores.[34] Therefore, it is important to identify people with FM who exhibit depression symptoms as they are more likely to be less physically active. This is especially important as people with FM are often

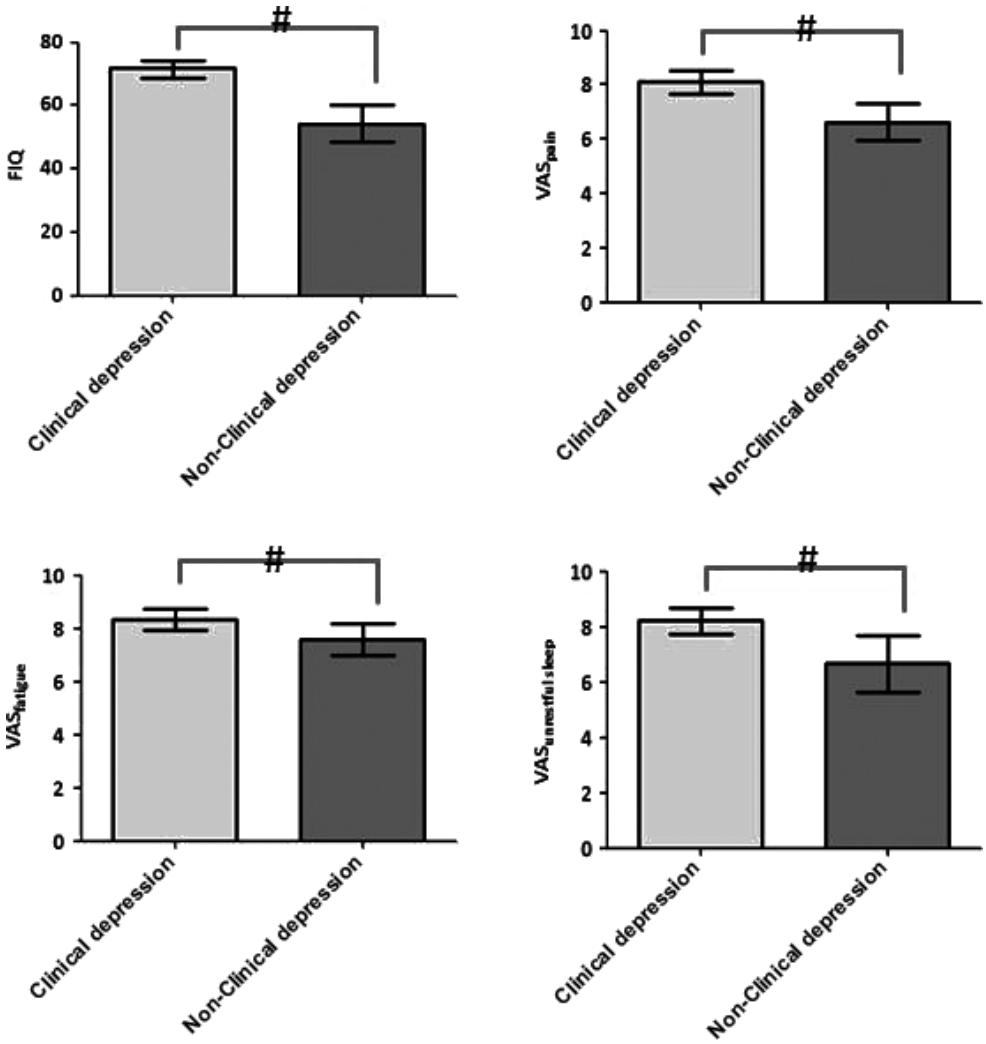


Figure 2 Self-reported severity of the symptoms, pain, fatigue and sleep problems by clinical depression symptoms. # denotes statistical significant differences (after Student's *t*-test for independent measurements) between the two groups.

less physically active than their age-matched peers.[7] However, despite differences in reported activity levels, there was no difference between the two group's cardiorespiratory function. The reason for this apparent anomaly may be two-fold: (i) cardiorespiratory function was measured via the 6-min walk test which is not a particularly sensitive measure; and (ii) the intensity of physical activity was not assessed, resulting in an inability to determine how much activity took place at vigorous, moderate or low intensities. Future studies may wish to include more sensitive measures of cardiorespiratory function (i.e., VO_2max test) and physical activity (i.e., accelerometry) to establish this relationship more clearly.

Additionally, there is a large body of literature that has shown increasing physical activity in FM patients may improve depression symptoms.[35] Recently, Fontaine *et al.*[36] found that after a short-term lifestyle intervention, those FM patients who increased their physical activity levels also improved depression symptoms and pain at 12-month follow-up. Improving physical activity levels appears to be of tremendous use for people with FM to improve depression symptoms.

To the best of our knowledge, only one previous study (40) analyzed the influence of depression symptoms on the functional level within a FM sample.[37] The authors found that depression severity was associated with physical function. Those with higher depression

Table 3 Predictive linear regression models of depression level (BDI) among women with fibromyalgia (n = 105)

Variables	Beta	SE	ST Beta	P
Model 1: Functional capacity (r = 0.54; r^2 = 0.30)				
Chairs sit to stand test	−2.010	0.473	−0.515	< 0.001
Hand grip strength test	−0.622	0.230	−0.325	0.001
Time up and go test	−4.206	1.222	−0.458	0.009
Constant	77.242	12.199		< 0.001
Model 2: Health-related quality of life (r = 0.57; r^2 = 0.33)				
Self-care	7.888	1.888	0.393	< 0.001
Anxiety/depression	7.543	2.410	0.295	0.002
Constant	−3.417	4.375		0.437
Model 3: Impact of the disease (r = 0.62; r^2 = 0.39)				
FIQ	0.410	0.054	0.626	< 0.001
Constant	−4.974	3.661		0.178
Model 4: Pain (r = 0.35; r^2 = 0.12)				
VAS_{pain}	1.942	0.558	0.348	0.001
Constant	7.181	4.344		0.102
Model 5: Fatigue (r = 0.33; r^2 = 0.11)				
$VAS_{fatigue}$	2.139	0.635	0.338	0.001
Constant	4.601	5.236		0.382
Model 6: Unrestful sleep (r = 0.34; r^2 = 0.12)				
$VAS_{unrestful\ sleep}$	1.539	0.444	0.347	0.001
Constant	10.049	3.559		0.006
Model 7: Activity Pattern (r = 0.26; r^2 = 0.07)				
Total METs	−0.003	0.001	−0.261	0.026
Constant	23.197	1.664		< 0.001
Model 8: All study variables (r = 0.71; r^2 = 0.51)				
Self-care	5.374	2.236	0.287	0.020
Anxiety/depression	6.301	2.320	0.293	0.009
FIQ	0.189	0.070	0.317	0.009
Constant	−10.825	4.504		0.020

BDI, beck depression inventory; FIQ, fibromyalgia impact questionnaire; MET, metabolic equivalent of task.

levels had lower functional levels. This is consistent with our results showing that participants reporting higher levels of self-reported depression also depicted reduced levels of muscle strength. This is an interesting finding as previous studies have determined the contribution of better strength scores for severity of the symptoms[16,38] and quality of life.[39] Taken together, we suggest that increasing the participant's fitness (especially strength levels) may lead to improvements in the psychological dimension, reinforcing the value of exercise interventions in people with FM.[40] However, we cannot rule out that other non-exercise based interventions that help with depressive symptoms would not improve physical activity and therefore physical fitness.

As expected, symptom severity was increased in those FM participants who reported increased levels of depression,[41] which is also reflected by the increased pain and fatigue in this group. On the other hand, an increase of sleep problems across BDI-depression symptoms groups as assessed by $VAS_{unrestful\ sleep}$ was found.[42] These results could also partially explain the lower quality of life in participants with clinical depression symptoms. In line with these results, our regression analysis showed that the severity of symptoms and self-reported quality of life account for 51% of the variance in reported BDI-depression symptoms.

A number of limitations need to be recognized in this study. Since a cross-sectional design was used, a causative interpretation is not possible. Another shortcoming is that the population of this study represents a convenience sample defined by the inclusion criteria, which may introduce selection bias. Moreover, we have not analyzed differences regarding depression grades due to the small number of participants falling into these subgroups. Therefore, given the small sample size of our

study it is difficult to give definitive conclusions; however, the results give us an indication of what further research may show.

Another drawback of the study is the lack of clinical data regarding the management of participants in the study. However, because they all were part of an association of FM patients, non-pharmacological treatments may be standardized across all participants. Medication might be considered as a potential confounder, so results should interpreted with caution.

Finally, the lack of a group of healthy individuals limits further direct comparisons. Future larger prospective cohort studies, including age-matched healthy groups, are required to confirm the relationships demonstrated in the current study. Longitudinal studies implementing depression interventions in depressed women with FM are also warranted to clarify the relationships between the effects of such interventions on these outcomes.

Notwithstanding these limitations, to our knowledge this is the first study analyzing the relationship between depression symptoms and key health outcomes in women with FM, therefore helping to progress the understanding of the management in this population. In conclusion, depression symptoms appear to be related to symptom severity and sitting time, lower levels of physical activity and caloric expenditure and worse quality of life and lower-limb strength in female FM patients. These findings suggest that the assessment of depression may be useful for the management and monitoring of FM patients[43,44] and reinforce the potential use of interdisciplinary long-term interventions, including exercise and psychological strategies for reducing the severity of the symptoms within this population group.

ACKNOWLEDGMENTS

We, the authors, we would like to thank the staff from the local associations involved in the study for their contribution in the recruitment process of patients participating in the research and for providing the facility for testing.

AUTHORS CONTRIBUTION

BdPC and JdPC conceptualized the study, analyzed data and drafted the article. BS critically reviewed the article. ACC and RAR collected and critically reviewed the article. PN critically reviewed the article. All authors approved the final version.

REFERENCES

1 Cassisi G, Sarzi-Puttini P, Alciati A *et al.* (2008) Symptoms and signs in fibromyalgia syndrome. *Reumatismo* **60** (Suppl. 1), 15–24.
2 Ovayolu N, Ovayolu O, Karadag G (2011) Health-related quality of life in ankylosing spondylitis, fibromyalgia syndrome, and rheumatoid arthritis: a comparison with a selected sample of healthy individuals. *Clin Rheumatol* **30** (5), 655–64.
3 Reisine S, Fifield J, Walsh S, Dauser D (2004) Employment and quality of life outcomes among women with fibromyalgia compared to healthy controls. *Women Health* **39** (4), 1–19.
4 Wolfe F, Michaud K, Li T, Katz RS (2010) EQ-5D and SF-36 quality of life measures in systemic lupus erythematosus: comparisons with rheumatoid arthritis, noninflammatory rheumatic disorders, and fibromyalgia. *J Rheumatol* **37** (2), 296–304.
5 Sabariego C, Brach M, Stucki G (2011) Determinants of major direct medical cost categories among patients with osteoporosis, osteoarthritis, back pain or fibromyalgia undergoing outpatient rehabilitation. *J Rehabil Med* **43** (8), 703–8.
6 Robinson RL, Birnbaum HG, Morley MA, Sisitsky T, Greenberg PE, Claxton AJ (2003) Economic cost and epidemiological characteristics of patients with fibromyalgia claims. *J Rheumatol* **30** (6), 1318–25.
7 Tudor-Locke C, Washington TL, Hart TL (2009) Expected values for steps/day in special populations. *Prev Med* **49** (1), 3–11.
8 Panton LB, Kingsley JD, Toole T *et al.* (2006) A comparison of physical functional performance and strength in women with fibromyalgia, age- and weight-matched controls, and older women who are healthy. *Phys Ther* **86** (11), 1479–88.
9 Geisser ME, Strader Donnell C, Petzke F, Gracely RH, Clauw DJ, Williams DA (2008) Comorbid somatic symptoms and functional status in patients with fibromyalgia and chronic fatigue syndrome: sensory amplification as a common mechanism. *Psychosomatics* **49**(3), 235–42.
10 Alciati A, Sgiarovello P, Atzeni F, Sarzi-Puttini P (2012) Psychiatric problems in fibromyalgia: clinical and neurobiological links between mood disorders and fibromyalgia. *Reumatismo* **64** (4), 268–74.
11 Scascighini L, Toma V, Dober-Spielmann S, Sprott H (2008) Multidisciplinary treatment for chronic pain: a systematic review of interventions and outcomes. *Rheumatology (Oxford)* **47** (5), 670–8.
12 Wolfe F, Smythe HA, Yunus MB *et al.* (1990) The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* **33** (2), 160–72.

13 Thomas S, Reading J, Shephard RJ (1992) Revision of the Physical Activity Readiness Questionnaire (PAR-Q). *Can J Sport Sci* **17** (4), 338–45.
14 Deurenberg P, Andreoli A, Borg P *et al.* (2001) The validity of predicted body fat percentage from body mass index and from impedance in samples of five European populations. *Eur J Clin Nutr* **55** (11), 973–9.
15 Craig CL, Marshall AL, Sjostrom M *et al.* (2003) International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* **35** (8), 1381–95.
16 Aparicio VA, Carbonell-Baeza A, Ruiz JR *et al.* (2013) Fitness testing as a discriminative tool for the diagnosis and monitoring of fibromyalgia. *Scand J Med Sci Sports* **23**, 415–23.
17 Rikli J (2001). *Senior Fitness Test Manual. Human Kinetics Champaign, Chicago.*
18 Rodriguez F, Gusi N, Valenzuela A, Nacher S, Nogues J, Marina M (1998) Evaluation of health-related fitness in adults (I): background and protocols of the AFISAL-INEFC Battery [in Spanish]. Apunts **52**, 54–76.
19 Esteve-Vives J, Rivera Redondo RJ, Isabel Salvat Salvat M, de Gracia Blanco M, de Miquel CA (2007) [Proposal for a consensus version of the Fibromyalgia Impact Questionnaire (FIQ) for the Spanish population]. *Reumatol Clín* **3** (1), 21–4.
20 Bennett R (2005) The Fibromyalgia Impact Questionnaire (FIQ): a review of its development, current version, operating characteristics and uses. *Clin Exp Rheumatol*, **23** (5Suppl.39), S154–62.
21 Marques AP, Assumpcao A, Matsutani LA, Pereira CA, Lage L (2008) Pain in fibromyalgia and discrimination power of the instruments: Visual Analog Scale, Dolorimetry and the McGill Pain Questionnaire. *Acta Reumatol Port* **33** (3), 345–51.
22 Crawford BK, Piault EC, Lai C, Bennett RM (2011) Assessing fibromyalgia-related fatigue: content validity and psychometric performance of the Fatigue Visual Analog Scale in adult patients with fibromyalgia. *Clin Exp Rheumatol*, **29** (6Suppl.69), S34–43.
23 Boomershine CS, Emir B, Wang Y, Zlateva G (2011) Simplifying Fibromyalgia Assessment: The VASFIQ Brief Symptom Scale. *Ther Adv Musculoskelet Dis* **3** (5), 215–26.
24 The EuroQol Group (1990) EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* **16** (3), 199–208.
25 Brooks R (1996) EuroQol: the current state of play. *Health Policy* **37** (1), 53–72.
26 Sanz J, Vázquez C (1998) Reliability, validity and normative data of Beck Depresión Inventory. *Psicithema* **10**, 303–18.
27 Nuevo R, Dunn G, Dowrick C *et al.* (2009) Cross-cultural equivalence of the Beck Depression Inventory: a five-country analysis from the ODIN study. *J Affect Disord* **114** (1–3), 156–62.
28 Lopez-Rodriguez Mdel M, Castro-Sanchez AM, Fernandez-Martinez M, Mataran-Penarrocha GA, Rodriguez-Ferrer ME (2012) Comparison between aquatic-biodanza and stretching for improving quality of life and pain in pations with fibromyalgia. *Aten Primaria* **44** (11), 641–9.
29 Aparicio VA, Ortega FB, Carbonell-Baeza A, Camiletti D, Ruiz JR, Delgado-Fernandez M (2011) Relationship of weight status with mental and physical health in female fibromyalgia patients. *Obes Facts* **4** (6), 443–8.
30 Cohen J (1988). *Statistical Power Analysis for the Behavioural Sciences, 2nd edn. Lawrence Erlbaum Publishers, Hillsdale, NJ.*
31 Mas AJ, Carmona L, Valverde M, Ribas B (2008) Prevalence and impact of fibromyalgia on function and quality of life in individuals from the general population: results from a nationwide study in Spain. Clin Exp Rheumatol **26** (4), 519–26.
32 Bjorkegren K, Wallander MA, Johansson S, Svardsudd K (2009) General symptom reporting in female fibromyalgia patients and referents: a population-based case-referent study. *BMC Public Health* **9**, 402.
33 Ellingson LD, Shields MR, Stegner AJ, Cook DB (2012) Physical activity, sustained sedentary behavior, and pain modulation in women with fibromyalgia. *J Pain* **13** (2), 195–206.
34 Gowans SE, Dehueck A, Voss S, Silaj A, Abbey SE (2004) Six-month and one-year followup of 23 weeks of aerobic exercise for individuals with fibromyalgia. *Arthritis Rheum* **51** (6), 890–8.
35 Busch AJ, Webber SC, Brachaniec M *et al.* (2011) Exercise therapy for fibromyalgia. *Curr Pain Headache Rep* **15** (5), 358–67.
36 Fontaine KR, Conn L, Clauw DJ (2011) Effects of lifestyle physical activity in adults with fibromyalgia: results at follow-up. *J Clin Rheumatol* **17** (2), 64–8.
37 Jones CJ, Rutledge DN, Aquino J (2010) Predictors of physical performance and functional ability in people 50 + with and without fibromyalgia. *J Aging Phys Act* **18** (3), 353–68.
38 Aparicio VA, Ortega FB, Heredia JM, Carbonell-Baeza A, Sjostrom M, Delgado-Fernandez M (2011) Handgrip strength test as a complementary tool in the assessment of fibromyalgia severity in women. *Arch Phys Med Rehabil* **92** (1), 83–8.
39 Tomas-Carus P, Hakkinen A, Gusi N, Leal A, Hakkinen K, Ortega-Alonso A (2007) Aquatic training and detraining on fitness and quality of life in fibromyalgia. *Med Sci Sports Exerc* **39** (7), 1044–50.
40 Carbonell-Baeza A, Aparicio VA, Ortega FB *et al.* (2011) Does a 3-month multidisciplinary intervention improve pain, body composition and physical fitness in women with fibromyalgia? *Br J Sports Med* **45** (15), 1189–95.

41 Alves AM, Natour J, Assis MR, Feldman D (2012) Assessment of different instruments used as outcome measures in patients with fibromyalgia. *Rev Bras Reumatol* **52** (4), 501–6.
42 Munguia-Izquierdo D, Legaz-Arrese A (2012) Determinants of sleep quality in middle-aged women with fibromyalgia syndrome. *J Sleep Res* **21** (1), 73–9.
43 de Miquel CA, Campayo J, Florez MT *et al.* (2010) Interdisciplinary consensus document for the treatment of fibromyalgia. *Actas Esp Psiquiatr* **38** (2), 108–20.
44 Hughes L (2006) Physical and psychological variables that influence pain in patients with fibromyalgia. *Orthop Nurs* **25**(2), 112–9; quiz 20–1.

Author Query Form

Journal: APL

Article: 12564

Dear Author,
During the copy-editing of your paper, the following queries arose. Please respond to these by marking up your proofs with the necessary changes/additions. Please write your answers on the query sheet if there is insufficient space on the page proofs. Please write clearly and follow the conventions shown on the attached corrections sheet. If returning the proof by fax do not write too close to the paper's edge. Please remember that illegible mark-ups may delay publication.

Many thanks for your assistance.

Query reference	Query	Remarks
1	**AUTHOR: Please convert € to US$ in Table 1, throughout.**	
2	**AUTHOR: What is the significance of (40) in sentence To the best of our. . .?**	
3	**AUTHOR: Please check journal title for reference [26].**	
4	**AUTHOR: Figure 1 is of low resolution. Please supply a high resolution version (at least 300 dpi for halftones and 600 dpi for line art figures at final size) with your proof corrections.**	
5	**AUTHOR: Figure 2 is of low resolution. Please supply a high resolution version (at least 300 dpi for halftones and 600 dpi for line art figures at final size) with your proof corrections.**	
6	**AUTHOR: Please confirm that given names (red) and surnames/family names (green) have been identified correctly.**	