Tesis Doctoral Internacional / International Doctoral Thesis

INFLUENCIA DE LOS NIVELES DE SEDENTARISMO Y ACTIVIDAD FÍSICA SOBRE LA CALIDAD DEL SUEÑO DE MUJERES GESTANTES, PERIMENOPÁUSICAS Y CON FIBROMIALGIA

INFLUENCE OF SEDENTARY TIME AND PHYSICAL ACTIVITY LEVELS ON SLEEP QUALITY IN PREGNANCY, PERIMENOPAUSE AND FIBROMYALGIA

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MILKANA M. BORGES COSIC

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Autor: Milkana Borges Cosic
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A mis familias, la de sangre y la que uno escoge…

La doctoranda Dña. **Milkana María Borges Cosic** ha realizado la presente Tesis Doctoral Internacional como beneficiaria de una beca-contrato con cargo al programa de Formación de Profesorado Universitario (FPU14) del Ministerio de Educación, Cultura y Deporte, por resolución de 20 de agosto de 2015, correspondiente a la convocatoria publicada por Resolución de 26 de diciembre de 2014 (BOE-A-2014-13539).

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RESEARCH PROJECTS AND FUNDING

The present Doctoral Thesis was performed as a result of the following research projects:

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ABSTRACT

Sleep disturbances is highly prevalent in the general population, and have a huge impact on adults' quality of life. This disorder is predominantly characterized by dissatisfaction with sleep duration or sleep quality (SQ), difficulties initiating or maintaining sleep, and daytime dysfunction. Moreover, women are at increased risk compared to men to report sleep complaints. In this sense, sleep problems might be improve with breaking time in sedentary behaviours, increasing physical activity (PA) levels or performing physical exercise.

The major aims of the present International Doctoral Thesis were: 1) to examine the association of objectively measured sedentary time (ST) and PA intensity levels with SQ during early pregnancy *(Study I)*, and in perimenopausal women *(Study II)*; 2) to evaluate the influence of a 4-month concurrent exercise training program (resistance and aerobic) compared to a healthy lifestyle counselling on SQ in perimenopausal women *(Study III)*; 3) to examine the association of objectively measured ST and PA intensity levels with SQ in women with fibromyalgia *(Study IV)*; 4) to assess whether those women who meet moderate-to-vigorous PA (MVPA) recommendations have better SQ than their counterparts *(Study IV)*.

To address these aims, four studies were conducted in the context of three research projects: 1) the GESTAFIT (GESTAtion and FITness) project, where 130 early pregnant women participated *(Study I, cross-sectional)*; 2) the FLAMENCO (the Fitness League Against MENopause COst) project randomized controlled trial *(Studies II and III)*, that was divided in two parts: first, a study where 169 perimenopausal women participated *(Study II, cross-sectional)*, and second, a study where a total of 150 women were divided into counselling and exercise groups (both, n=75) (Study III, experimental). The counselling consisted on four conferences about healthy lifestyle; and 3) al-Ándalus project *(Study IV, cross-sectional)*, where 409 women with fibromyalgia were included. Sedentary time and PA intensity levels were objectively assessed with accelerometry and SQ was assessed with the Pittsburgh Sleep Quality Index (PSQI) questionnaire. All measures were used in the three projects. Per protocol and intention-to-treat analyses were presented for the randomized controlled trial.

The main findings and conclusions derived from the studies included in this thesis were: 1) there are not associations between ST and PA intensity levels with SQ in women during early pregnancy *(Study I)* neither in perimenopausal women *(Study II)*; 2) Neither 4-month concurrent exercise training program (resistance and aerobic) nor a healthy lifestyle counselling have effects on SQ in perimenopausal women *(Study III)*; 3) Lower ST and greater PA intensity levels, especially light and total PA, are associated with better SQ components in women with fibromyalgia *(Study IV)*; 4) Women with fibromyalgia who meet physical activity recommendations (150 min/week of MVPA in bouts of ≥10 min) had better SQ than those who do not reach those recommendations *(Study IV)*.

The results of this International Doctoral Thesis enhance our understanding about how reducing ST and increasing PA levels could be a non-pharmacological treatment to improve SQ in women with fibromyalgia, and suggest that these active lifestyle interventions could not be the panacea regarding sleep in pregnant and perimenopausal women. Future studies should confirm or contrast the present findings.

RESUMEN

Los trastornos del sueño son muy frecuentes en la población general y tienen un gran impacto en la calidad de vida de los adultos. Este trastorno se caracteriza principalmente por la insatisfacción con la duración o la calidad del sueño, los problemas para iniciar o mantener el sueño y las dificultades para mantenerse despierto y realizar actividades durante el día. Además, las mujeres tienen mayor riesgo para reportar quejas de sueño que los hombres. En este sentido, los problemas del sueño podrían mejorar disminuyendo el tiempo en conductas sedentarias, aumentando los niveles de actividad física o realizado ejercicio físico.

Los principales objetivos de la presente Tesis Doctoral Internacional fueron: 1) examinar la asociación entre el tiempo de sedentarismo y los niveles de actividad física (medidos objetivamente) con la calidad del sueño en mujeres durante la gestación temprana *(Estudio I)* y en mujeres perimenopáusicas *(Estudio II)*; 2) evaluar la influencia de un programa de entrenamiento de ejercicio concurrente (fuerza y aeróbico) durante 4 meses comparado con consejos acerca de un estilo de vida saludable sobre la calidad del sueño en mujeres perimenopáusicas *(Estudio III)*; 3) examinar la asociación entre el tiempo de sedentarismo y los niveles de actividad física (medidos objetivamente) con la calidad del sueño en mujeres con fibromialgia *(Estudio IV)*; 4) analizar si aquellas mujeres que cumplen las recomendaciones de actividad física moderada-vigorosa tienen mejor calidad del sueño que sus homólogas *(Estudio IV).*

Para abordar estos objetivos, se llevaron a cabo cuatro estudios en el contexto de tres proyectos de investigación: 1) el proyecto GESTAFIT (GESTAtion and FITness), en el que participaron 130 mujeres embarazadas *(Estudio I, transversal)*; 2) el ensayo controlado aleatorizado FLAMENCO (Fitness League Against MENopause COst) que se dividió en dos partes: primero, un estudio en el que participaron 169 mujeres perimenopáusicas *(Estudio II, transversal),* y segundo, un estudio donde 150 mujeres perimenopáusicas se dividieron en dos grupos: grupo de consejos y grupo de ejercicio (ambos, n = 75) *(Estudio III, experimental)*. El asesoramiento consistió en cuatro conferencias sobre cómo mantener un estilo de vida saludable; y 3) el proyecto al-Ándalus *(Estudio IV, transversal),* donde se incluyeron 409 mujeres con fibromialgia. El tiempo de sedentarismo y los niveles actividad física se evaluaron objetivamente con acelerometría y la calidad del sueño se evaluó con el cuestionario Índice de Calidad del

Sueño de Pittsburgh (en inglés, Pittsburgh Sleep Quality Index). Todas las medidas fueron utilizadas en los tres proyectos. Los resultados del ensayo controlado aleatorizado se exploraron tanto por protocolo como en intención de tratar.

Los principales hallazgos y conclusiones derivadas de los estudios incluidos en esta tesis fueron: 1) no se hallaron asociaciones entre el tiempo de sedentarismo y los niveles de actividad física con la calidad del sueño en mujeres durante la gestación temprana *(Estudio I)* ni en mujeres perimenopáusicas *(Estudio II)*; 2) ni un programa de 4 meses de entrenamiento de ejercicio concurrente (fuerza y aeróbico) ni el consejo acerca de un estilo de vida saludable tuvieron efecto en la calidad del sueño en mujeres perimenopáusicas *(Estudio III)*; 3) menores niveles de sedentarismo y mayores niveles de intensidad de actividad física, especialmente ligera y total, fueron asociados con mejores resultados en los componentes de la calidad del sueño en mujeres con fibromialgia *(Estudio IV)*; 4) las mujeres con fibromialgia que cumplían con las recomendaciones de actividad física (150 min/semana de actividad física moderada-vigorosa en *periodos* de ≥10 min) tuvieron mejor calidad del sueño que aquellas que no las cumplían *(Estudio IV)*.

Los resultados de esta Tesis Doctoral Internacional mejoran nuestra comprensión acerca de cómo reducir el tiempo de sedentarismo y aumentar los niveles de actividad física podría ser un tratamiento no farmacológico para mejorar la calidad del sueño en mujeres con fibromialgia, y sugieren que intervenciones basadas en un estilo de vida activo podrían no ser la panacea en mujeres embarazadas y perimenopáusicas. Estudios futuros son necesarios para confirmar o contrastar los presentes hallazgos.

ABBREVIATIONS

ACSM, American College of Sports Medicine

ANCOVA, ANalysis of the COVAriance

BMI, Body Mass Index

CI, Confidence Interval

FLAMENCO, Fitness League Against MENopause COst

GESTAFIT, GESTAtion and FITness

MET, Metabolic Equivalent of Task

MMSE, Mini Mental State Examination

MPA, Moderate Physical Activity

MVPA, Moderato-to-Vigorous Physical Activity

PA, Physical Activity

PSQI, Pittsburgh Sleep Quality Index

RPE, Rate of Perceived Exertion

SD, Standard Deviation

SQ, Sleep Quality

ST, Sedentary Time

I

INTRODUCTION

INTRODUCTION

For most of human history, men’s life have represented those of humans overall, when they are only the 50% of the general population[1]. Specifically, in the scientific research field, studies have been focused on white men data when analysing physiological and psychological characteristics and pathologies, extrapolating the findings to the overall population as if they could directly be applied to women[1]. This is the also called gender data gap.

Men and women are different, and thus, we would expect that their physiological and psychological description, pathological diagnosis and treatment should be also different. However, during decades, in preclinical and clinical studies, male animals and men respectively, have been the only subjects to be studied to diagnose diseases and to test the effectiveness of pharmaceutical treatments[2,3]. Moreover, because of sexist myths about health and pain, women have had more difficulties getting proper diagnoses and treatment for serious conditions, and their pain was more likely to be perceived as "emotional" or "psychogenic" rather than caused by biological factors[3]. For instance, more than 40% of women with autoimmune diseases were diagnosed at the beginning as hypochondriac woman, and they had to wait for 4 years on average to be appropriately diagnosed[2]. Similarly happened with women with endometriosis (with on average 7 years delay in the diagnosis), or with several specific cancers compared with men[2]. Moreover, women had to wait longer to receive a treatment than men in the same clinical manifestations[4], and such as treatments were originally tested only in men, it is not surprising that women could suffer from more side effects than men. Another example of the inequality between men and women in the scientific field is that, according to a Research Gate investigation, there are more than five times as many scientific studies about erectile dysfunction than about premenstrual syndrome. However, 19% of men report suffering from erectile dysfunction at some point in their lives, compared to the 90% of women who have experienced premenstrual syndrome[3]. In this sense, the consequences of living in a world built around male data can be deadly for women[1].

Furthermore, gender-related studies suggest that women are at increased risk compared to men to report sleep complaints[5]. Sleep disturbances[6,7] and, more specifically insomnia disorder[8], is highly prevalent in the general population, a common complaint in clinical practice[9] and have a huge impact on adults' quality of life[10,11]. This disorder is predominantly characterized by dissatisfaction with sleep duration or sleep quality (SQ), difficulties initiating or maintaining sleep, and daytime dysfunction[8]. In this sense, it is plausible the need to research of optimal treatments to reduce sleep disorders and increase SQ in women.

Given the heterogeneity of sleep disturbances, different tools have been developed to measure SQ[12]. Polysomnography is the most objective method to assess sleep disorders. However, it does not allow self-evaluation of SQ, or the impact that sleep disturbances may have on daytime functioning[12]. On the other hand, self-reported SQ questionnaires are a cheap and easy way to explore sleep in large samples, despite it cannot measure how much time people are in the deep restorative sleep phases. In this context, the Pittsburgh Sleep Quality Index (PSQI) is a self-reported questionnaire to assess SQ that has been validated and commonly used in several populations[13–16].

On another note, physical inactivity is a pandemic and a leading risk factor for mortality[17] based on sedentary behaviours (defined as the waking time spent sitting or leaning back[18]). The negative impact of sedentary time (ST) on health in the general population has been widely established[19,20]. Nearly of the 60% of the world population is inactive[21] and this behaviour together with ST increase with age and is more frequent in women than in men[21,22]. In this sense, in Spain, more than half of women are physically inactive (53%)[22].

Contrary, physical activity (PA) is defined as any bodily movement produced by skeletal muscles that requires energy expenditure[23]. Regular and adequate PA is associated with reduced risk of hypertension, coronary heart disease, diabetes, breast and colon cancer, mental disorders and osteoporosis, among others, in adults[23]. The American College of Sports Medicine (ACSM) recommend to engage in at least 150 min/week of moderate-to-vigorous PA (MVPA) for adults[24]. However, the high percentage of women with excessive ST and not reaching the compliance of PA recommendations is worrisome.

The methods traditionally used worldwide to assess sedentary behaviors and PA have been self-report tools[25]. However, questionnaires for this purpose can provide misleading information in the general population[25–27], as well as in other clinical populations[28–30]. Nowadays, accelerometry is considered the best method, if not the gold standard, to measure ST and PA[31] because is a simple, valid, and reliable instrument to assess them objectively in free-living conditions (activities performed at home or community)[31–33].

European countries are experiencing a continuous increase on their pharmaceutical costs[34]. In Spain, pharmacological costs represent 17% of the National Health Expenditures[34]. Previous studies have shown that regular PA reduces health care requirements and thereby leads to significant savings in health-care costs[35,36]. With the objective to promote a healthier lifestyle for all the population, The Spanish Ministry for Health and Consumption designed in 2005 the Strategy for Nutrition, Physical Activity and Prevention of Obesity (NAOS). Moreover, the Spanish National Sports Council launched in 2009 the Integral Plan on Physical Activity and Sport (A + D Plan), incorporating a program designed specifically for women, intending to increase their physical activity levels.

Due to the high prevalence of sleep disorders, and the prevalence of high levels of ST and low levels of PA in women, it may be clinically relevant to assess if ST and PA (objectively measured) are related in different populations of women (i.e. pregnancy, perimenopause or fibromyalgia disease) with SQ. There is limited evidence and studies focused on the relationship of these variables are scarce or inexistent. Moreover, most of them until date have employed different methodologies and concluded contradictory results. For instance, several studies developed in children and adolescents suggest that greater ST might be associated with lower sleep duration[37,38], while others with adult or clinical populations failed to find association[39–41]. Similarly, a study showed that greater PA, particularly regular MVPA, was associated with better SQ in older adults[42], while another study indicated that greater daily activity counts and more minutes in MVPA were related with less sleep time in older women[43]. Notwithstanding, the association between MVPA and total sleep time has been negligible in midlife women[44].

Pharmacological and non-pharmacological (psychological) therapies have been showed to reduce sleep latency, the time spent awake after sleep onset, and increase sleep duration[8]. Moreover, many other non-pharmacological therapies have been proposed to improve SQ in different populations[45–47]. In this sense, exercise (defined as a subcategory of physical activity that is planned, structured, repetitive, and purposeful[23]) has been commonly used as non-pharmacological therapy[48–50]. Therefore, exercise programs had improvements in sleep in adults population[51–53] although it is not fully clear in women.

The ACSM recommends the combination of strength training with the “classical” aerobic exercise[54]. Despite this training protocol has been proposed as the most adequate for improving body compositon[55] and cardiometabolic markers[56], its influence on SQ still unknown in different physiological and pathological circumstances in women.

The purpose of the investigation is to progress and expand scientific knowledge. Hence, bearing in mind the huge differences between both the men and women and that women have been unconsidered through the decades, new adequate investigation paths in health sciences, should consider sex characteristics in the studies and should focus in expanding the knowledge about specific women populations.

Projects/populations

The present International Doctoral Thesis is defined in 3 women populations corresponding to three different projects. GESTAFIT (GESTAtion and FITness) and al-Ándalus projects comprised observational measurements of ST, PA and SQ in pregnant women and women with fibromyalgia, respectively; and FLAMENCO (Fitness League Against MENopause Costs) project, included the same design and variables in perimenopausal women, and the testing of a 4-month concurrent exercise training program on SQ.

The GESTAFIT project: pregnant women

Pregnancy is usually considered by general population as a period of well-being and happiness in a woman's life. However, is also a period of psychological vulnerability[57] where women may be liable to suffering depression[58,59], anxiety[60,61], decreased quality of life[62], or sleep problems[63], among others. More than 75% of the pregnant women suffer insomnia or sleep disturbances[64], with increasing numbers as the pregnancy progresses[65]. During pregnancy, there is an enormous variability in sleep between women.

There is evidence of association of sleep deprivation with a preterm or longer labour, elevated perception of pain or even higher rates of caesarean sections[66] as well as an increased risk of depression[63] in pregnant women. In fact, poor sleep efficiency has been related with poor mental health[67,68] and quality of life[69] during pregnancy. In a sample of preeclampctic pregnant women, some sleep problems including initial insomnia, fragmented sleep, snoring, and lack of getting enough sleep were more common compared to healthy counterparts and non-pregnant women[70]. Thus, it is imperative to change the thought that sleep disturbance is normal and without consequences during the perinatal period[63]. Therefore, it is necessary to mitigate the suffering of sleep disturbances and decreased SQ through amending the modifiable risk factors, and avoiding pharmacological treatments, especially during this period.

Pregnant women spent higher time in sedentary behaviours than their counterparts[71], and most of them spent more than half of their time in sedentary behaviours[72,73]. Although there are considerable variability in studies design and methods of assessing sedentary behaviours[72], several studies have showed an association between increased time in sedentary behaviours with an increased risk for abnormal glucose tolerance, gestational diabetes, preeclampsia[74–76], higher levels of low-density lipoprotein-cholesterol (LDL-C), a larger new-born abdominal circumference[72], and poor mental health[63,67,68]. However, it is unknown whether ST is associated with SQ and whether ST could improve SQ during early pregnancy, and hence, reinforcing positively all pregnancy symptoms.

The new Canadian guidelines for PA throughout pregnancy are pointing out the importance of PA to enhance physical and mental health, and recommends a total of 150 min/week of MVPA in bouts of at least 30 minutes for healthy pregnancies[77]. The truth is that most of pregnant women do not meet PA recommendations[73]. In this sense, the benefits of higher levels of PA for a healthier pregnancy and better quality of life[69,78] are well stablished in this population. However, scarce studies have specifically analysed SQ, despite being a well-being marker during pregnancy. Furthermore, limited studies have approached the topic of PA and SQ during pregnancy. Results suggest little associations between occupational PA and lower odds of very poor SQ, and no associations between overall PA and sleep duration and quality[79,80]. However, these studies have measured PA through self-reported questionnaires. By contrast, in the present Thesis we measure ST, PA intensity levels and total PA through accelerometry, that has been previously used in pregnancy women[81]. Thus, it could be of interest for pregnant women's health to know the relationship between ST and PA levels with SQ during pregnancy *(Study I).*

The FLAMENCO project: perimenopausal women

Climacteric is a period usually comprised between ages of 40 to 65 years, and it incorporates the perimenopause[82] (understood as the time just before, during and after menopause). It is a crucial period for women´s physical and mental health characterized by multiple symptoms as the oestrogen loss characteristic of menopause transition[83–85], frequently related with weight gains and central body-fat accumulation[86], increased hypertension prevalence[87], predispose to a higher incidence of cardiovascular diseases[85], vasomotor symptoms (i.e. hot flushes and night sweats), vaginal dryness[88], vertigo[89], mood fluctuations[90], sleep disturbances[91], and decreased quality of life[92], among others.

From all of this symptoms, the most common problems during perimenopause are sleep disturbances, with around 40-60% of women affected[91] and poor SQ[93]. Thus, sleep is an essential component of health[94,95] and quality of life[96] in midlife women. Many studies have suggested that there is a relationship between poor SQ[97,98] or reduced sleep efficiency[98] with suffering hot flashes, and that women with insomnia present higher rates of climacteric symptoms than those without insomnia[99]. Consequently, menopause might play an important role on women's sleep[100,101]. Therefore, is known that poor sleep is related with increased prevalence of depression[102]. Hence, due to the significance of sleep in women's life during menopause, it is necessary to go in depth into the study of SQ in this population.

Sedentary middle-aged women have more insomnia, severe menopausal symptoms, depressive symptoms, and anxiety, waist circumference, and prevalence of obesity than non-sedentary counterparts[103]. In this sense, there is a higher percentage of obese middle-aged women with sleep disorders and a sedentary lifestyle than non-obese women[104]. Therefore, sleep disorders, sexual dysfunction, and poor quality of life have a prevalence of over 50% in sedentary women during menopause[105], and adult women who are short sleepers seem to be more sedentary[106]. Moreover, reduced ST has been associated with a better cardiovascular profile in perimenopausal women[107]. Hence, it is plausible that a sedentary lifestyle has an enormous impact on physical and mental middle-aged women's health, and that ST and SQ were related in this population. However, it is unknown whether objectively measured ST is associated with SQ during perimenopause.

Regular PA has been associated with decreased risk of cardiovascular disease and type 2 diabetes in middle-aged women, independently of menopause status[108]. Therefore, PA appears to be an effective tool to improve some menopausal symptoms[109], and quality of life[110] in this population and during menopausal transition[111–113]. Meeting PA recommendations has been associated with higher levels of energy and lower levels of fatigue in adults women[114], and higher levels of MVPA per day have been independently related to feelings of vitality in postmenopause[115]. Moreover, moderate levels of PA have been associated with reduced psychosocial and physical menopause symptoms in perimenopausal Korean women[111]. A study in older women also found some bidirectional associations between PA and sleep, and showed that higher daytime activity counts and MVPA the following day were related with worse sleep efficiency[43]. In this sense, a study in midlife women observed that greater activity counts was associated with more sleep duration[44]. It is evidence the importance to perform PA for women's health and the frequent sleep problems that they suffer and perturb their daily lives. Thus, it may be clinically relevant to analyse the association between PA and SQ in menopause. To the best of our knowledge, this Thesis proposed the first study examining the association between all PA intensity levels (measured objectively with accelerometry) with all SQ components in perimenopausal women *(Study II).*

It has been widely demonstrated the exercise benefits on physical and mental health of middle-aged women and women during menopause transition. Exercise programs have been shown to decrease cardiovascular disease and type 2 diabetes risk[85] and to improve bone mineral density, physical fitness, hypertension and dyslipidamia[116], body composition[85,117–119], depression[85,120] and sleep[121,122] in this population. However, regarding SQ, epidemiologic studies have generally shown positive associations of exercise with sleep in middle-aged and menopausal women although in experimental studies there are controversial findings depending on the exercise program type and duration developed. For instance, a 8-week aerobic exercise program was effective on increasing SQ in middle-aged women[123] and a 12-week Pilates exercise program showed improvements on sleep latency and sleep duration[124]. However, different aerobic, stretching, and yoga intervention programmes (12-weeks each other) showed small effects on SQ and subjective SQ in menopausal women[125–127]. A recently review concluded that programmed moderated exercise improved SQ and should be encouraged in middle-aged women[121]. This controversy underlines that the optimal exercise dose has yet to be identified. Thus, research is needed to understand the best exercise modality to optimise SQ during this relevant period. On the other hand, several years of research have already evidenced the need of resistance training together with aerobic exercise in order to improve women health (i.e. cardiovascular health) after menopause[128]. Therefore, a combination of resistance and aerobic training (concurrent program) could ameliorate sleep problems in this period. As far as we know, no prior study has explored this relationship in perimenopausal women *(Study III)*.

The al-Ándalus project: women with fibromyalgia

Fibromyalgia is a heterogeneous and poorly understood disease[129], which has been defined as a complex dimensional disorder characterized by chronic widespread pain regulation[130] as its main symptom[131] and the presence of many other symptoms such as fatigue, stiffness, cognitive problems, depression, anxiety, and sleep problems, among others[131–133]. The American College of Rheumatology recognizes sleep disturbances as an important symptom of fibromyalgia with its inclusion in the updated diagnosis criteria[134]. In fact, patients with fibromyalgia report poorer sleep quality [135], fewer hours of sleep, greater night-time awakenings, and higher non-restorative sleep compared with healthy people and other clinical populations[136]. Moreover, difficulty staying asleep and non-refreshing sleep are distressing symptoms that may impact physical functioning, well-being, and fibromyalgia symptomatology[137]. Thus, the extend symptomatology limits most of daily fibromyalgia patients' activities, such as walking or carrying objects, which entails an impact on patients' quality of life[133,138,139].

The prevalence of fibromyalgia vary depending on the country[140]. In Spain Spanish women/men fibromyalgia proportion of approximately 22:1[141]. This disease usually appears between 40s and 50s[141], which is a crucial period of women´s health due to the oestrogen loss[83–85], relevant metabolic[85,142,143], and mental-health changes[144,145], and sleep disturbances[91]. Thus, fibromyalgia patients incur a significant direct and indirect medical care costs[146,147]. In Spain, the average costs per year and patient is around 5,000€[147]. A prospective study showed that treated patients with fibromyalgia in daily practice improve their clinical symptoms and reduce the costs of the illness[148]. Although the treatment of fibromyalgia is a complex and controversial process, it has been used multiple pharmacologic and non-pharmacologic treatments to reduce fibromyalgia symptomatology[149–151]. The most common non-pharmacologic treatments are exercise interventions[149,152] and psychological-educative programs[151,152]. To be physically active[153] or to perform exercise[154,155] have been proven to have positive benefits in patients with fibromyalgia.

Patients with fibromyalgia present greater levels of ST than controls[153,156]. It has been studied the relationship between ST with the symptomatology and it has been showed that women with fibromyalgia that perform greater levels of ST, had higher pain, fatigue, and overall impact of the disease[157], and worse quality of life[158]. However, it is unknown whether this sedentary behaviour is associated with another important symptom as sleep in this specific population *(Study IV)*.

Patients with fibromyalgia also present lower levels of PA than their counterparts[153,156]. Previous researches in fibromyalgia population have studied the relationship between PA levels assessed with an accelerometer with different symptoms of the disease. Thus, higher levels of objectively measured light PA were associated with lower pain, fatigue, overall impact of the disease[157], and quality of life[158] in women with fibromyalgia. Moreover, women with fibromyalgia who did not meet MVPA recommendations (at least 150 min/week of MVPA) showed increased cardiovascular disease risk[159] and higher levels of MVPA were related with better quality of life[158] in the same population. In the other hand, studies in chronic pain and elderly population showed a direct association between accelerometer-assessed PA and SQ[40,42,160,161]. To the best of our knowledge, there is only one previous study assessing the association of PA and SQ in women with fibromyalgia[135], reporting that self-reported PA levels were associated with SQ. Notwithstanding, in fibromyalgia, there is discordance between self-reported assessments and objective measurements of PA[162]. Indeed, PA questionnaires provide misleading information in this specific population[28]. Consequently, and due to its validity, reliability, and feasibility, the use of objective measures of PA, such as accelerometry, is preferred for these patients[31]. Thus, it is necessary to investigate if objectively measured PA intensity levels are related with SQ in women with fibromyalgia *(Study IV)*.

Aims

The main aims of the present International Doctoral Thesis was to deepen the knowledge on the relationship between sedentary time and physical activity with sleep quality in different populations of women: pregnancy, perimenopausal and women with fibromyalgia, and to examine the effects of a concurrent exercise training program on sleep quality in perimenopausal women. The structure of the work to fulfil the present aims was divided into three projects: the GESTAFIT project, where we worked with pregnant women; the FLAMENCO project, developed in perimenopausal women; and the al-Ándalus Project, performed in a large sample if women with fibromyalgia.

The specific aims of the present International Doctoral Thesis are the following:

The GESTAFIT project: pregnant women

1. To examine the association of objectively measured sedentary time and physical activity intensity levels with sleep quality during early pregnancy *(Study I)*.

The FLAMENCO project: perimenopausal women

2. To examine the association of objectively measured sedentary time and physical activity intensity levels with sleep quality in perimenopausal women *(Study II)*.

3. To evaluate the influence of a 4-month concurrent exercise training program (resistance and aerobic) compared to a healthy lifestyle counselling group on sleep quality in perimenopausal women *(Study III)*.

The al-Ándalus project: women with fibromyalgia

4. To examine the association of objectively measured sedentary time and physical activity intensity levels with sleep quality in women with fibromyalgia *(Study IV)*.

5. To assess whether those women who meet moderate-to-vigorous physical activity recommendations present better sleep quality than their counterparts *(Study IV)*.

Objetivos

El objetivo principal de la presente Tesis Doctoral Internacional fue profundizar en el conocimiento de la relación entre el sedentarismo y la actividad física con la calidad del sueño en diferentes poblaciones de mujeres: embarazadas, perimenopáusicas y con fibromialgia, además de conocer los efectos del ejercicio (entrenamiento aeróbico interválico combinado con fuerza en una misma sesión) sobre la calidad del sueño en mujeres perimenopáusicas. El trabajo para desarrollar los presentes objetivos se dividió en tres proyectos: el proyecto GESTAFIT, donde se trabajó con mujeres durante la gestación temprana; el proyecto FLAMENCO, en el que se intervino en mujeres perimenopáusicas; y el proyecto al-Ándalus, en el que se tomó una amplia muestra de la población andaluza con fibromialgia.

Los objetivos específicos de esta Tesis Doctoral Internacional son los siguientes:

The GESTAFIT project: pregnant women

1. Examinar la asociación entre el tiempo de sedentarismo y los niveles de actividad física con la calidad del sueño en mujeres durante la gestación temprana *(Estudio I)*.

The FLAMENCO project: perimenopausal women

2. Examinar la asociación entre el tiempo de sedentarismo y los niveles de actividad física con la calidad del sueño en mujeres perimenopáusicas *(Estudio II)*.

3. Evaluar la influencia de un programa de entrenamiento de ejercicio concurrente (fuerza y aeróbico) durante 4 meses comparado con consejos acerca de un estilo de vida saludable sobre la calidad del sueño en mujeres perimenopáusicas *(Estudio III).*

al-Ándalus Project: women with fibromyalgia

4. Examinar la asociación entre el tiempo de sedentarismo y los niveles de actividad física con la calidad del sueño en mujeres con fibromialgia *(Estudio IV)*.

5. Analizar si aquellas mujeres que cumplen las recomendaciones de actividad física moderada-vigorosa tienen mejor calidad del sueño que sus homólogas *(Estudio IV).*

MATERIAL AND METHODS

MATERIAL AND METHODS

The summary of the methodology employed in the current International Doctoral Thesis is shown in *table 1*.

Studies design and projects

The cross-sectional study *Sedentary time, physical activity, and sleep quality in women during early pregnancy: the GESTAFIT project (Study I)* is part of the GESTAtion and FITness Project. This Project was approved by the Clinical Research Ethics Committee of Granada, Government of Andalusia (Spain).

The cross-sectional study *Sedentary time, physical activity and sleep quality during perimenopause: the FLAMENCO project (Study II)* and the experimental study *Effects of interval aerobic training combined with strength exercise on sleep during perimenopause: the FLAMENCO project (Study III)* are part of the Fitness League Against MENopause COst Randomized Control Trial Project. The complete methodology of the FLAMENCO project is published elsewhere [163]. The study protocol was reviewed and approved by the Ethics Committee for Research Involving Human Subjects at the University of Granada (no. 861). Moreover, this trial was registered at ClinicalTrials.gov (identifier: NCT02358109).

The cross-sectional study *Sedentary time, physical activity, and sleep quality in fibromyalgia: the al-Ándalus Project (Study IV)* belongs to the al-Ándalus Physical Activity Randomized Controlled Trial Project. The complete methodology of the al-Ándalus project is published elsewhere [164]. The study protocol was reviewed and approved by the Ethics Committee of the Virgen de las Nieves Hospital in Granada (Spain). Furthermore, this trial was registered at ClinicalTrials.gov (identifier: NCT01490281).

Table 1. Summary table of the methodology used of each study of the present International Doctoral Thesis

Project	Study	Study design	Participants	Main variables	Methods
GESTAFIT	I. Sedentary time, physical activity and sleep quality in women during early pregnancy: the GESTAFIT project	Cross-sectional	130 pregnant women	Sedentary time Physical activity intensity levels Sleep quality	Accelerometry (GT3X) PSQI
FLAMENCO	II. Sedentary time, physical activity and sleep quality during perimenopause: the FLAMENCO project	Cross-sectional	169 perimenopausal women	Sedentary time Physical activity intensity levels Sleep quality	Accelerometry (GT3X) PSQI,
	III. Effects of interval aerobic training combined with strength exercise on sleep during perimenopause: the FLAMENCO project	Experimental (Randomized Control Trial)	159 perimenopausal women	Sleep quality	PSQI
Al-Ándalus	IV. Sedentary time, physical activity and sleep quality in fibromyalgia: the al-Ándalus project	Cross-sectional	409 women with fibromyalgia	Sedentary time Physical activity intensity levels Sleep quality	Accelerometry (GT3X) PSQI

PSQI, Pittsburgh Sleep Quality Index

Participants

A total of 384 pregnant women were initially contacted during their 12th gestational week visit at the San Cecilio University Hospital and Virgen de las Nieves University Hospital (Granada, southern Spain). Of those, 222 were cited for the first evaluation and a final sample of 159 women were interested to participate, were informed about the aims, assessments and procedures of the GESTAFIT project, met inclusion and exclusion criteria, and signed an informed consent to participate. Furthermore, only those women with valid and complete data (n=130) were used for the *Study I*. The flow chart of those study participants is shown in *figure 1*.

A total of 214 perimenopausal women from Granada (Southeast Spain) were recruited through primary care centres and press releases published in local newspapers and social media for the FLAMENCO project. One-hundred ninety-eight of these women came to the first evaluation and signed written informed consent after were informed about the study aims, assessments and procedures. Of those, a final sample of 169 women with valid and complete data were included in the *Study II* and the 150, that met all inclusion and exclusion criteria, were randomized into either a counselling (n=75) or exercise (n=75) group in the *Study III*. The flow chart of the *Study II* and *Study III* participants are detailed in *figures 2* and *3*, respectively.

A representative sample of women with fibromyalgia from Andalusia (southern Spain) as described elsewhere [156] was recruited for the al-Ándalus Project. A total of 646 women with fibromyalgia were recruited from Andalusia through fibromyalgia associations, via e-mail and mass-media, read and signed an informed consent form before taking part in the study, and came to the first evaluation. Five-hundred seventeen of those women met inclusion and exclusion criteria and a final sample of 409 had all valid and complete data and were included in the present *Study IV*. The flow chart of those study participants is detailed in *figure 4.*

The inclusion and exclusion criteria of the three projects are shown in *table 2.*

Table 2. Projects inclusion and exclusion criteria

Project	Inclusion	Exclusion
GESTAFIT	-Aged: 25-40 years old with a normal pregnancy course. -Answering "no" to all questions on the PARmed-X for pregnancy. -Being able to walk without assistance. -Being able to read and write properly. -Informed consent: Being capable and willing to provide written consent.	-Acute or terminal illness. -Malnutrition. -Inability to conduct tests for assessing PF or exercise during pregnancy. -Underweight. -Pregnancy risk factors (such as hypertension, type 2 diabetes, etc.). -Multiple pregnancy. -Chromosopathy or foetal malformations. -Uterine growth restriction. -Foetal death. -Upper or lower extremity fracture in the past 3 months. -Presence of neuromuscular disease or drugs affecting neuromuscular function. -Being registered in another exercise program. -Doing more than 300min/week of MPA -Unwillingness either to complete the study requirements or to be randomized into the control or intervention group.
FLAMENCO	-Age: 45–60 years old. -Not to have severe somatic or psychiatric disorders, or diseases that prevent exercise (Answer "no" to all questions on the PAR-Q[165]). -Not to be engaged in regular PA >20min on >3days/week in the last 3 months. -To be able to ambulate without assistance. -To be able to communicate. -Informed consent: To be capable and willing to provide informed consent.	-Acute or terminal illness. -Myocardial infarction in the past 3 months. -Unstable cardiovascular disease or other medical condition. -Upper or lower extremity fracture in the past 3 months. -Unwillingness to either complete the study requirements or to be randomized into control or intervention group. -Presence of neuromuscular disease or drugs affecting neuromuscular function.

-Age: 35-65 years.	-Acute or terminal illness.
-To be diagnosed with fibromyalgia by a rheumatologist and meeting the American College of Rheumatology criteria: widespread pain for more than 3 months, and pain with 4 kg/cm of pressure reported for 11 or more of 18 tender points[166] .	-Myocardial infarction in the past 3 months.
-Not to have other severe somatic or psychiatric disorders, or other diseases that prevent physical loading (Answer "no" to all questions on the -PAR-Q[165]).	-Unstable cardiovascular disease or other medical condition.
-Not to be engaged in regular PA >20min on >3days/week in the last 3 months.	-Upper or lower extremity fracture in the past 3 months.
-Planning to stay in the same Association during the study.	-Unwillingness to either complete the study requirements or to be randomized into control or training group.
-Able to ambulate without assistance.	-Severe dementia (MMSE < 10)
-Able to communicate.	-Presence of neuromuscular disease or drugs affecting neuromuscular function.
-Informed consent: Must be capable and willing to provide consent.	-To be engaged in other physical or psychological treatment.

PAR-Q, Physical Activity Readiness Questionnaire; MPA, moderate physical activity; PA, physical activity; MMSE, Mini Mental State Examination.

Randomization

After the baseline assessments, a total of 150 perimenopausal women voluntarily participated and were randomized into either a counselling (n=75) or exercise (n=75) group. A computer-generated simple randomization sequence was created to allocate the participants to either the counselling or exercise group (1:1). The randomization sequence was prepared by a member of the research team with no clinical involvement in the trial.

Of the 150 perimenopausal women that were randomized into counselling (n=75) and exercise (n=75) groups in the intention-to-treat analyses, 20 and 8 of them dropped out the follow-up in counselling and exercise groups, respectively. A total of 8 women did not attend 75% of the exercise sessions. Moreover, 8 and 3 women of counselling and exercise group, respectively, had missing data in some study variables. Thus, the total number of women used for per-protocol analyses was n=47 for counselling group and n=56 for exercise group. Loss of data is detailed in the flow chart of the *Study III* participants (*figure 3*).

Figure 1. Flow chart of participants in the *Study I*

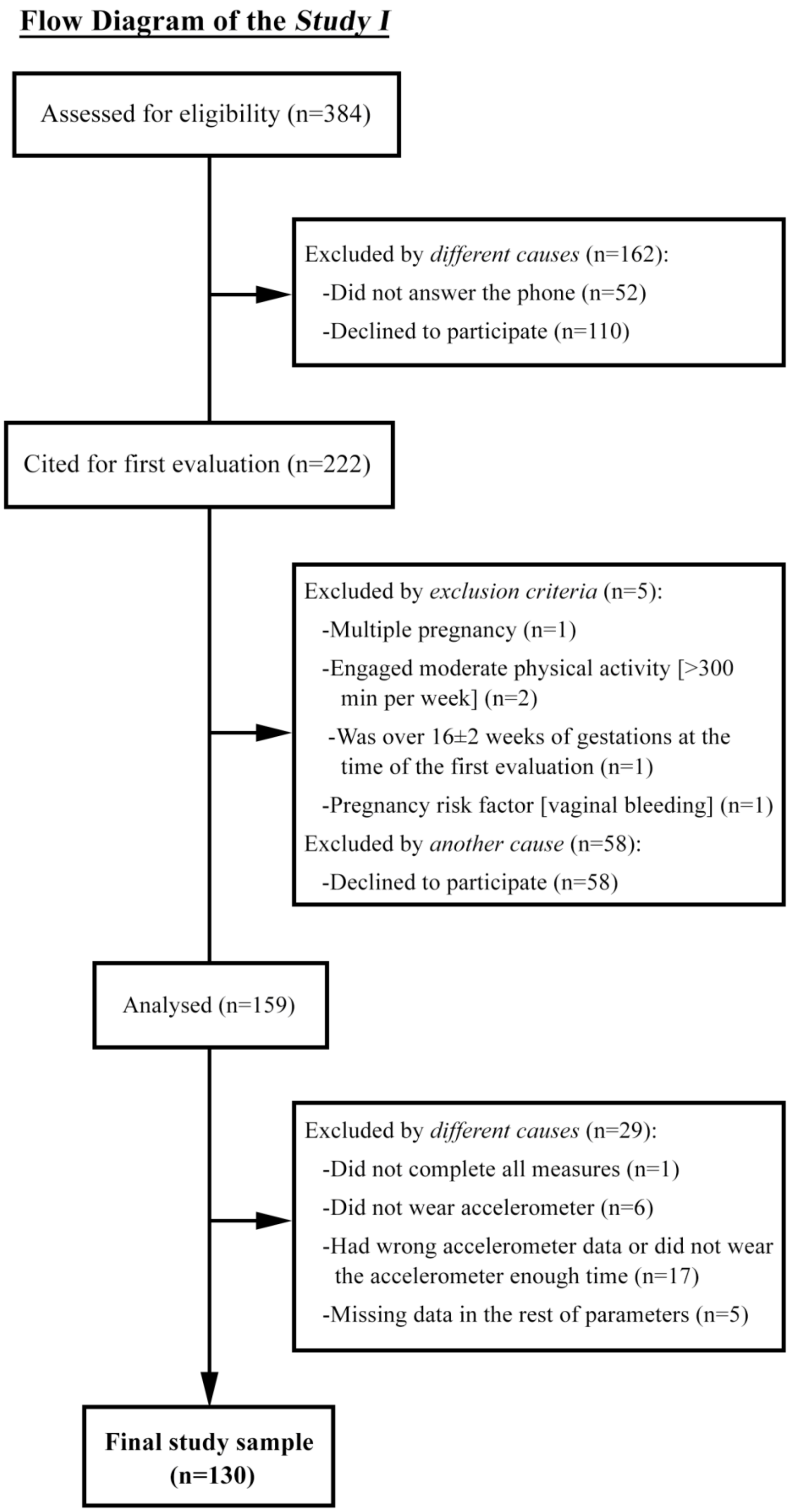


Figure 2. Flow chart of participants in the *Study II*

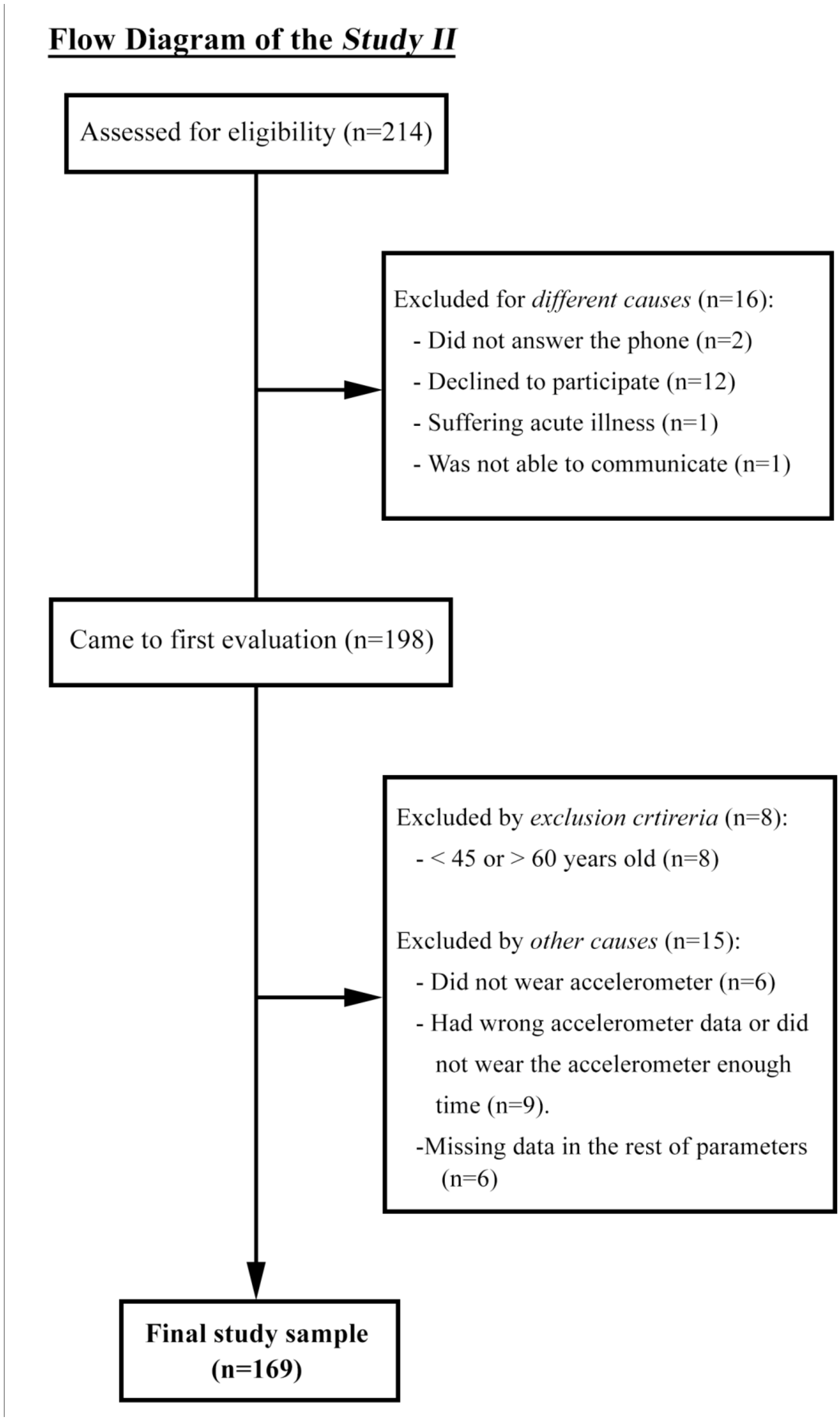


Figure 3. Flow chart of participants in the *Study III*

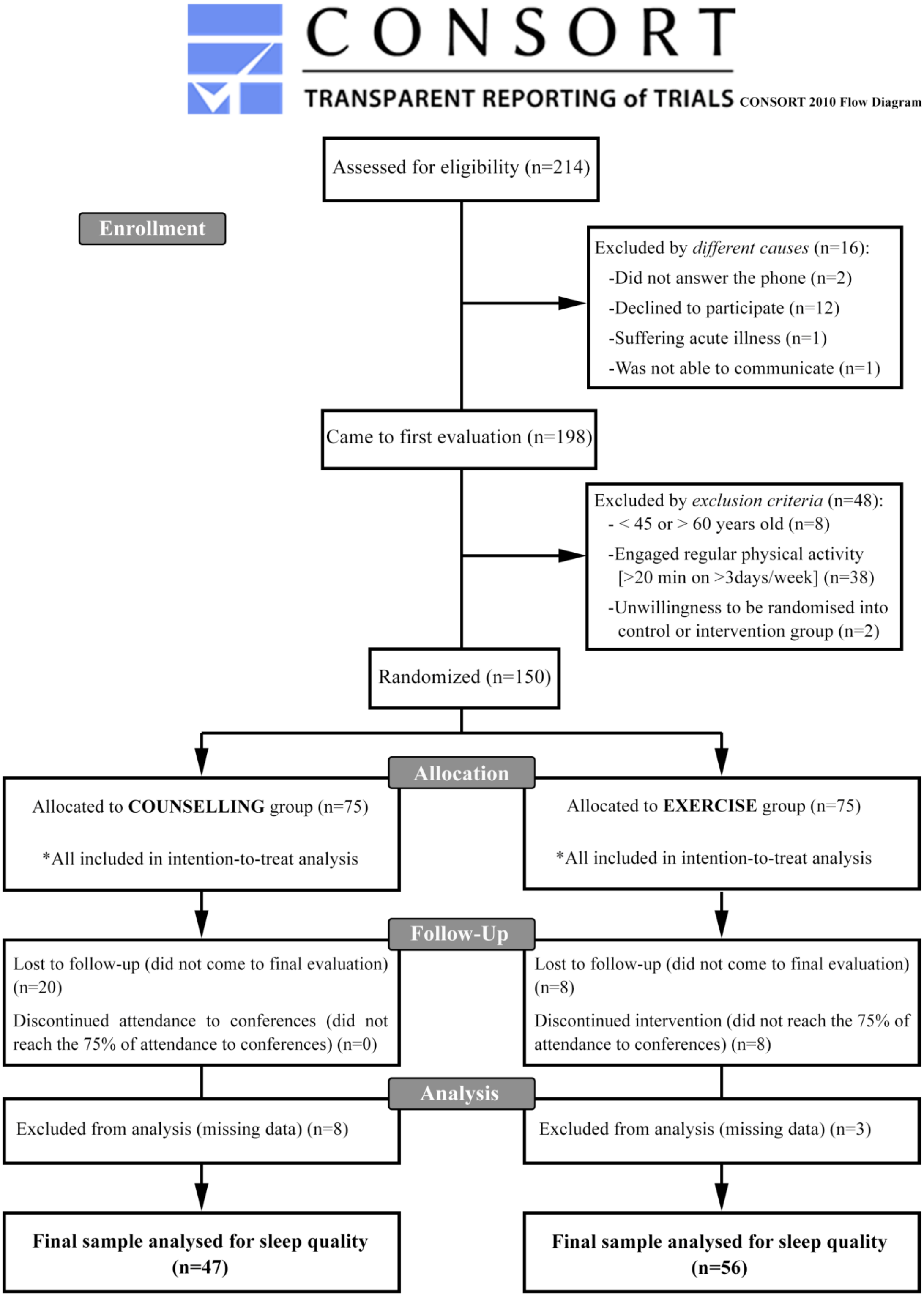
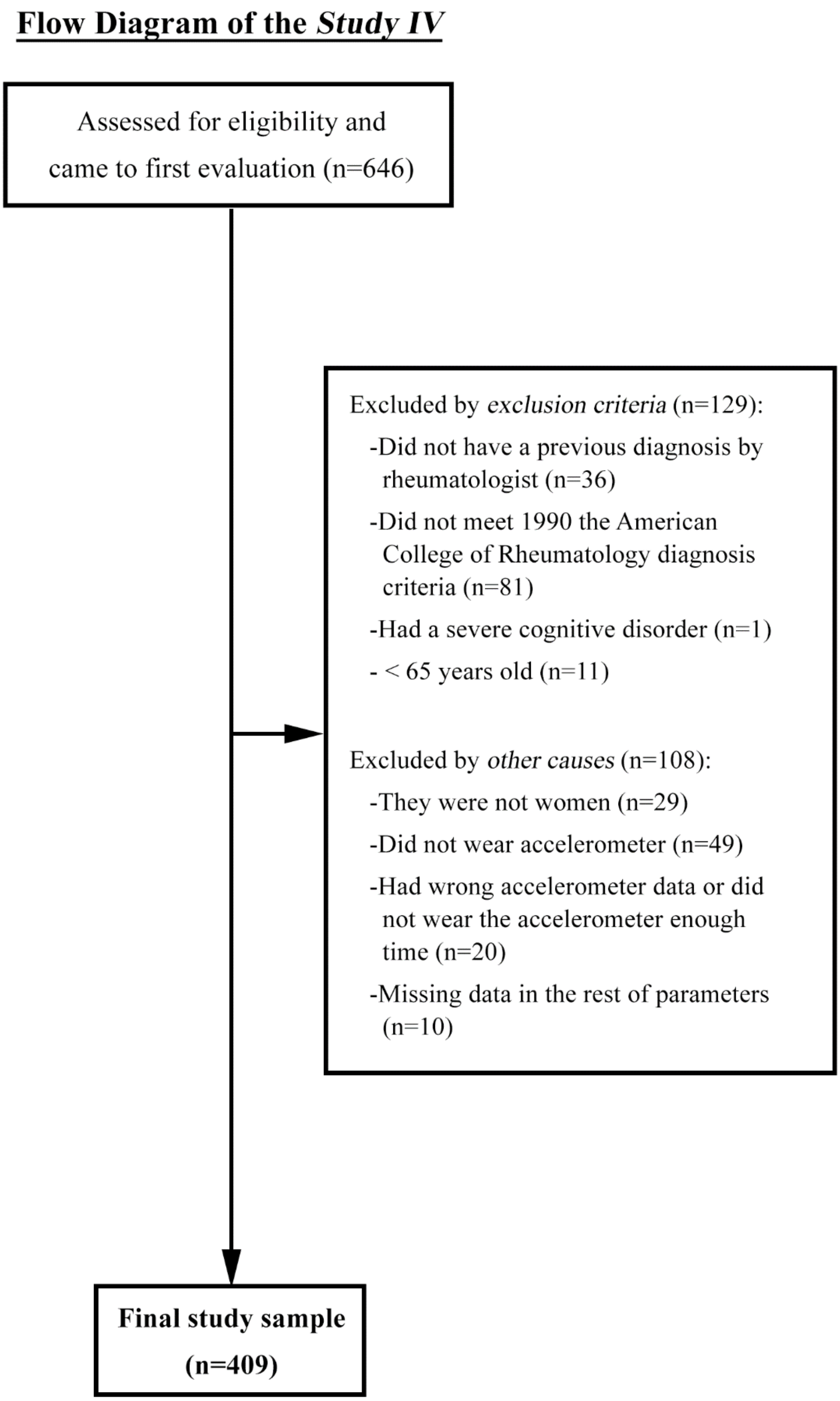


Figure 4. Flow chart of participants in the *Study IV*



Procedures

The evaluation in the GESTAFIT [pregnant women at the 16th gestational week (±2 weeks)] and FLAMENCO (perimenopausal women one week before the intervention and 4-months later, at the end of the programme) projects were carried out in a single day. In al-Ándalus (women with fibromyalgia) the evaluation process was carried out on two non-consecutive days.

For all of these, socio-demographic (age, educational level, marital status, among others), clinical, and other health-related information was self-reported, anthropometry and body composition measures were taken, and different questionnaires were interviewed (i.e. Pittsburgh Sleep Quality Index). Participants were given an accelerometer and a sleep diary that were returned nine days later to the research team.

Furthermore, for the *Studies II and III* The Blatt-Kupperman menopausal index[167] was employed to assess menopause symptomatology and severity, and in the *Study IV* the Mini-Mental State Examination was administered, and the diagnosis of fibromyalgia was confirmed.

Measures

Sociodemographic and clinical data (all studies)

A questionnaire was used to collect the participants' self-reported sociodemographic and clinical data, such as age, educational level, marital status, and menstruation, among others.

Sleep or relaxation medication (all studies)

The intake of sleep or relaxation medications was interviewed as a binary variable (yes/no) in *Studies I and IV* and registered through primary care centres for the *Studies II and III*.

Anthropometry and body composition (all studies)

Weight (kg) and body fat (%) were measured with a bioelectrical impedance analyser (InBody R20, Biospace, Seoul, South Korea). Height (cm) was assessed using a stadiometer (Seca 22, Hamburg, Germany). Weight and height were used to calculate body mass index (weight (kg)/height (m^2).

Sedentary time and physical activity intensity levels (Studies I, II and IV)

The data were collected using a triaxial accelerometer GT3X+ (Actigraph Pensacola, Florida, USA) at a rate of 30 Hz and stored at an epoch length of 60 seconds [168,169]. The participants wore the device on the hip, near the center of gravity, underneath their clothes, and secured with an elastic belt.

Data was recorded during 9 consecutive days, from the day women received the device until the day that they returned it. The wearing time was calculated by subtracting the sleeping time from each day (registered by participants in a dairy where they reported the time they went to bed to sleep and the time they woke up). Bouts of 90 continuous minutes of 0 counts were excluded from the analyses, considered as non-wear periods [170]. The first and last days were excluded from the analyses. Therefore, a total of 7 continuous days with at least 10 valid hours per day were included in the study.

Sedentary time, light, moderate and vigorous PA intensity levels were calculated based on recommended PA vector magnitude cut points [168,169]: 0–199, 200–2689, 2690–6166 and ≥6167, respectively, and were expressed as minutes per day. Total PA was calculated as the sum of light, moderate, and vigorous PA (min/day). A bout of MVPA was defined as spending ≥10 continuous minutes in MVPA (≥2690 cpm). The total time in MVPA in bouts of ≥10 minutes was also calculated. Meeting the bouted PA recommendations required engaging in at least 150 min/week of MVPA accumulated in bouts ≥10 min; conversely, non-bouted PA recommendations did not need to accumulate MVPA in bouts ≥10 min. We used the manufacturer software Actilife™ v.6.11.7 desktop for data download, reduction, cleaning, and analyses purposes.

Sleep quality (all studies)

The Spanish version [171] of the *Pittsburgh Sleep Quality Index* (PSQI) [172] was used to assess the sleep quality. The PSQI is composed by 19 questions about the sleep during the last month yielding seven components: subjective sleep quality, sleep latency, sleep duration, sleep disturbances, sleep efficiency, sleep disturbances, sleep medication and daytime dysfunction. Each component includes items with four-point Likert scales (0-3) where higher scores indicate worse sleep. The sleep quality global score is the sum of all components (score ranges from 0 to 21) and is used to define good and poor sleepers (≤5 and >5, respectively).

The PSQI is reliable and valid in fibromyalgia[14].

Menopause symptoms

Menopause symptoms were measured with the *Blatt–Kupperman Menopausal Index*[167]. This questionnaire consists of 11 items including vasomotor (hot flashes/sweating), paraesthesia, insomnia, nervousness, melancholia, vertigo, weakness (fatigue), arthralgia/myalgia, headaches, palpitation, and formication symptoms. Each item includes four-point Likert scales (0-3) to describe the severity of each complaint. The global score (from 0 to 51) is calculated as the sum of all items by the weighting factor (i.e. sweating/hot flushes item is multiplied by 4, and paraesthesia, fatigue/insomnia and nervousness are multiplied by 2). The severity degree of menopause is categorized as low, mild, moderate or severe depending of the score obtained (<15, 15–20, 20–35, and >35, respectively)

Interventions

Counselling group

The women randomized into the usual care (control group) did not participate in the exercise sessions, and were requested to continue their daily activities. Even so, as an increasing PA levels, exercise and a healthy diet have proven beneficial effects on women health, the research team undertook four conferences (one per month) addressing different topics: 1) benefits of exercise for longevity, prevention, and treatment of diseases; 2) benefits of the Mediterranean Diet and nutritional education; 3) ergonomic advice and exercises to do at home (e.g. resistance training); and 4) strategies to increase daily PA levels. The conferences were also used to maintain the fidelity of the participants until the end of the programme and only usual care group was invited to these conferences. Due to the importance of this type of intervention, the "usual care" group was renamed "counselling" group.

Exercise group

The women randomized into the exercise group participated in a 4-month (3 days/week, and 60 minutes/session) exercise intervention consisting in a moderate-to-vigorous intensity concurrent exercise training program (resistance and aerobic). The exercise intervention was carefully supervised and instructed by qualified exercise professional following the training standards by the ACSM for adults[24].

Each exercise session included: a warm-up period with walks and mobility exercises (10 minutes); the main part which varied across week days (i.e. 3 different models of session) (40 minutes); and a cold-down period of stretching and relaxation exercises (10 minutes). The first session of the week involved circuit training including resistance exercises in a stepped progression throughout the programme. The second session of the week included balance oriented activities (position changes, monopodal and bipodal stances etc.) and aerobic exercises (dancing). The third session of the week combined resistance, aerobic, and coordination exercises within the same session[163].

Heart rate was measured with heart rate monitors (Polar Electro OY, Finland) to control the intensity of the sessions. One third of the participants in the intervention group wore heart rate monitors in 1/3 of the sessions, both randomly selected. Moreover, we used the ratings of perceived exertion (RPE) using the Borg 6-20 RPE[173] scale at the end of all sessions. Intensity (expressed as RPE) was expected to range from 12 to 16.

Statistical analyses

The statistical approach undertaken to accomplish the aims of the present International Doctoral Thesis is presented below and is summarized in *table 3*.

Descriptive statistics are shown as mean (standard deviation, SD) for quantitative variables, and number of women (%) for categorical variables. Main variables were checked for normality of distribution before the analyses. Moreover, before the principal analyses, we calculated bivariate correlations to identify potential confounders for each study. Vigorous PA was excluded from the analyses due to the low participants' engagement in this intensity level.

The raw (Spearman) and adjusted (partial) correlations were used to examine the individual association between ST, PA intensity levels [light, moderate and moderate-to-vigorous PA (in bouts of ≥10 min)] and total PA with the components of the PSQI (*Studies I, II and IV)* and the global score (*Studies I and II)* adjusting for the potential cofounders described in *table 3*.

Linear regression analysis was used to explore the individual association of ST, light, moderate, moderate-to-vigorous (in bouts of ≥10 min), and total PA with the SQ global score in separate regression models. We introduced the SQ global score as dependent variable and age, body fat percentage, marital status, educational level, medication for sleep or relaxation regular menstruation, and accelerometer wear time as covariates (S*tudy IV).*

To examine the differences in the SQ global score (i.e., dependent variable) across groups of ST (i.e., independent variable), we compared the tertiles based on the distribution of the data for total ST using the one-way analysis of covariance (ANCOVA). The analyses were adjusted by above mentioned covariates (S*tudy IV).* Similarly, to study the differences in the SQ global score (i.e., dependent variable) across groups of light and total PA (i.e., independent variables in separate models), we compared the tertiles based on the distribution of the data for light and total PA, respectively, using ANCOVA with the same covariates (S*tudy IV).* We used Bonferroni's correction for multiple comparisons when comparing the differences between tertiles. The effect size statistic was calculated in all of the analyses by means of Cohen's *d* (standardized mean difference). The effect size was interpreted as small (~0.25), medium (~0.5), or large (~0.8 or greater).

The differences in SQ across groups of meeting and not meeting the current PA recommendations for adults (non-bouted and bouted MVPA) were compared using ANCOVA with age, total body fat percentage, marital status, educational level, sleep or relaxation medication, and regular menstruation. The Bonferroni's post-hoc analyses for multiple comparisons assessed the differences across groups (S*tudy IV).*

The effects of a 4-month intervention (counselling or exercise) on the components and the global score of the PSQI were assessed in the per-protocol analysis including the counselling group participants (all attended at least 75% of the conferences), and the exercise group participants (with ≥75% attendance at the exercise programme). Changes (post-pre values) in all the outcome variables were calculated. Subsequently, the changes (post-pre) of these outcomes were included in the linear regression analyses as dependent variables in separate models, whereas the group (counselling=0 and exercise=1) was included as an independent variable. Data provided was unadjusted (unadjusted model), adjusted for the baseline value of each variable (model adjusted for baseline values) and adjusted for the baseline values and age, body mass index, marital status, educational level, Blat-Kupperman Menopausal Index global score, and regular menstruation cofounders (model adjusted for baseline values and cofounders). Because of the loss of PSQI values, another analysis assessing the 150 women based on the assigned intervention at the time of randomisation, regardless of adherence and missing data (i.e., intention-to-treat), with a simple imputation made for the missing values, was added *Study III).*

The statistical analyses were conducted with the Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, Version 20.0. IBM Corp, Armonk, New York, USA). The statistical significance was set at $P<0.05$.

Table 3. Summary table of statistical approach of each study of the present International Doctoral Thesis.

Study	Design	Independent variables	Dependent Variables	Statistical analyses
I	Cross-sectional	Sedentary time Physical activity intensity levels	Sleep quality	-Raw (Spearman) and adjusted (partial) correlations. *Confounders: age, body mass index, medication for sleep, and accelerometer wear time.*
II	Cross-sectional	Sedentary time Physical activity intensity levels	Sleep quality	-Raw (Spearman) and adjusted (partial) correlations. *Confounders: age, body mass index, marital status, educational level, medication for sleep, regular menstruation, the Blat-Kupperman Menopausal Index global score, and accelerometer wear time.*
III	Experimental (Randomized Control Trial)	Intervention (counselling or exercise)	Sleep quality	-Multiple imputation for missing values of the variables. -Linear regression with changes (post-pre values of variables) as dependent variables (baseline values as confounders). *Confounders: age, body mass index, marital status, educational level, medication for sleep, regular menstruation, and the Blat-Kupperman Menopausal Index global score.*

IV	Cross-sectional	Sedentary time Physical activity intensity levels	Sleep quality	-Raw (Spearman) and adjusted (partial) correlations. -Linear regression analysis. -ANCOVA to examine the differences in the DV across tertiles based on the distribution of the data for IV. Bonferroni’s correction was used for multiple comparisons when comparing the differences between tertiles. The effect size statistic was calculated by means of Cohen's d (standardized mean difference). -ANCOVA to examine the differences in the DV across groups of meeting or not meeting PA recommendations. The Bonferroni’s post-hoc analyses was used for multiple comparisons assessed the differences across groups. *Confounders: age, body fat percentage, marital status, educational level, medication for sleep or relaxation, regular menstruation, and accelerometer wear time.*

IV, independent variable; DV, dependent variable; B-KMI, Blatt-Kupperman Menopausal Index; ANCOVA, one-way analysis of covariance.

RESULTS

RESULTS

The results of each individual study comprising the present International Doctoral Thesis are presented below.

The GESTAFIT project: pregnant women

Study I. Sedentary time, physical activity and sleep quality in women during early pregnancy: the GESTAFIT project. In progress

The final sample subject to analyses included 130 early pregnant women (33±4.6 years old). *Table 1* shows sociodemographic and clinical characteristics of the study participants. Roughly, 89% of the sample had secondary or University studies, 70% were working, and 22% took sleep medication.

Table 2 shows the association between ST and the PA intensity levels with the SQ components and the global score of the PSQI. Higher levels of moderate PA and MVPA (in bouts ≥10 min) were associated with better sleep efficiency and SQ global score in the raw model (all, $P<0.05$). Moreover, higher MVPA (in bouts ≥10 min) was also associated with better subjective SQ in this model. No associations were found between ST, PA intensity levels, and total PA with any PSQI components and PSQI global score in the adjusted model(all, $P>0.05$).

Table 4. Descriptive characteristics of the early pregnant study sample (n=130)

	Values
Age (years)	33 (4.6)
BMI (kg/m^2)	25.1 (4.2)
Marital status, n (%)	
Married	75 (57.7)
Non married	55 (42.3)
Educational level, n (%)	
Unfinished studies or Primary studies	15 (11.5)
Secondary or University studies	115 (88.5)
Occupational status, n (%)	
Working	90 (69.2)
Housewife	8 (6.2)
Non-working	32 (24.6)
Medication for sleep, *n* (%)	
No	132 (78.1)
Yes	37 (21.9)
PSQI components$^\wedge$	
Sleep quality (0-3)	1.2 (0.7)
Sleep latency (0-3)	0.9 (0.7)
Sleep duration (0-3)	0.8 (0.7)
Sleep efficiency (0-3)	0.5 (0.8)
Sleep disturbances (0-3)	1.5 (0.5)
Sleep medication (0-3)	0.1 (0.3)
Daytime dysfunction (0-3)	0.9 (0.7)
Global score (0-21)	5.9 (3.1)
Sedentary time and PA levels (min/day, accelerometry)	
Sedentary time	512.5 (92.5)
Light PA	387.6 (86.6)
Moderate PA	35.2 (20.5)
MVPA (min/week, in bouts ≥10 min)	84.88 (108.8)
Total PA	423.7 (89.7)

Values expressed as mean (standard deviation) unless otherwise indicated.
BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index; PA, physical activity; MVPA, moderate-to-vigorous physical activity; min, minute.
$^\wedge$ Lower values indicate better sleep quality.

Table 5. Raw (Spearman) and adjusted (partial) correlations between sedentary time and physical activity (PA) intensity levels with sleep quality components and the global score in women during early pregnancy (n=130).

	Subjective sleep quality		Sleep latency		Sleep duration		Sleep efficiency		Sleep disturbances		Sleep medication		Daytime dysfunction		Global score	
	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted
Sedentary time, *r*	-.003	.054	.016	.084	.064	-.018	.043	.064	-.142	-.050	-.148	-.027	-.013	-.016	.005	.032
Light PA, *r*	-.035	-.014	-.089	-.063	.105	.040	-.049	-.030	.023	.069	-.004	.014	.037	.032	-.032	-.004
Moderate PA, *r*	-.160	-.156	-.149	-.101	-.104	-.088	**-.239****	-.145	-.114	-.072	.097	.058	-.111	-.073	**-.200***	-.114
MVPA[∞], r	**-.214***	-.135	-.155	-.045	-.091	-.043	**-.205***	-.036	-.122	-.044	-.111	-.078	-.048	.010	**-.233****	-.063
Total PA, *r*	-.061	-.054	-.097	-.084	.109	.018	-.080	-.064	.014	.050	.000	.027	.021	.016	-.051	-.032

Raw, Spearman correlation; Adjusted, partial correlation controlled for age, body mass index, medication for sleep, and accelerometer wear time. MVPA, moderate-to-vigorous physical activity. [∞]MVPA in bouts ≥10 min.

*P < 0.05; *P < 0.01

The FLAMENCO project: perimenopausal women

Study II. Sedentary time, physical activity and sleep quality during perimenopause: the FLAMENCO project. In progress

The final sample subject to analyses included 169 perimenopausal women (52.5±4.1 years old). *Table 6* shows sociodemographic and clinical characteristics of the study participants. Roughly, 73% of the sample had secondary or university studies, 78 % did not take sleep medication, and 72% did not have a regular menstruation.

Table 7 shows the association between ST and the PA intensity levels with the SQ components and the global score of the PSQI. Higher levels of ST were associated with less sleep duration and worse SQ global score in the raw model (all, $P<0.05$). Moreover, higher levels of light and total PA were associated with better sleep efficiency, and total PA was associated with less sleep medication also in the raw model (all, $P<0.05$). No associations were found between ST, PA intensity levels, and total PA with any PSQI components and PSQI global score in the adjusted model (all, $P>0.05$).

Table 6. Descriptive characteristics of the perimenopausal study sample (n=169)

	Values
Age (years)	52.5 (4.1)
BMI (kg/m^2)	27.1 (4.3)
Marital status, n (%)	
Married	118 (69.8)
Non married	51 (30.2)
Educational level, n (%)	
Unfinished studies or Primary studies	45 (26.6)
Secondary or University studies	124 (73.4)
Occupational status, n (%)	
Working	89 (52.7)
Housewife	41 (24.3)
Non-working	39 (23.1)
Medication for sleep, *n* (%)	
No	132 (78.1)
Yes	37 (21.9)
Regular menstruation, n (%)	
No	122 (72.2)
Yes	47 (27.8)
Blatt-Kupperman Menopausal Index[#]	
Global Score (0-51)	15.3 (10.6)
PSQI components[^]	
Sleep quality (0-3)	1.7 (0.8)
Sleep latency (0-3)	1.1 (1.0)
Sleep duration (0-3)	1.5 (0.9)
Sleep efficiency (0-3)	0.8 (1.0)
Sleep disturbances (0-3)	1.5 (0.7)
Sleep medication (0-3)	0.6 (1.0)
Daytime dysfunction (0-3)	0.6 (0.6)
Global score (0-21)	7.5 (3.0)
Sedentary time and PA levels (min/day, accelerometry)	
Sedentary time	474.0 (90.7)
Light PA	424.7 (81.3)
Moderate PA	58.1 (28.1)
MVPA (min/week, in bouts ≥10 min)	190.1 (161.1)
Total PA	486.0 (92.5)

Values expressed as mean (standard deviation) unless otherwise indicated.
BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index; PA, physical activity; MVPA, moderate-to-vigorous physical activity; min, minute.
[#] Lower values indicate better menopausal symptomatology.
[^] Lower values indicate better sleep quality.

Table 7. Raw (Spearman) and adjusted (partial) correlations between sedentary time and physical activity (PA) intensity levels with sleep quality components and the global score in perimenopausal women (n=169).

	Subjective sleep quality		Sleep latency		Sleep duration		Sleep efficiency		Sleep disturbances		Sleep medication		Daytime dysfunction		Global score	
	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted
Sedentary time, *r*	-.056	-.010	.022	.032	**.189***	.094	.041	.092	.113	.118	.120	.088	.037	-.074	**.156***	.118
Light PA, *r*	.056	.020	-.080	-.032	-.058	-.153	**-.184***	-.116	-.116	-.082	-.127	-.057	.079	.106	-.135	-.127
Moderate PA, *r*	.002	-.002	-.012	-.002	.095	.099	.043	-.012	-.150	-.135	-.073	-.101	-.035	-.050	-.015	-.034
MVPA[∞], r	.038	-.002	-.044	-.047	.035	.061	.061	-.017	-.146	-.155	-.103	-.104	-.063	-.073	-.063	-.062
Total PA, *r*	.049	.010	-.069	-.032	-.022	-.094	**-.157***	-.092	-.136	-.118	**-.155***	-.088	.066	.074	-.133	-.118

Raw, Spearman correlation; Adjusted, partial correlation controlled for age, body mass index, marital status, educational level, medication for sleep, regular menstruation, Blat-Kupperman Menopausal Index global score and accelerometer wear time. MVPA, moderate-to-vigorous physical activity. [∞]MVPA in bouts ≥10 min.
*$P < 0.05$

Study III. Effects of interval aerobic training combined with strength exercise on sleep during perimenopause: the FLAMENCO project. In progress

The baseline characteristics of the study participants by groups (counselling or exercise) are shown in *table 8*. Women, who were 52.6±4.5 years old, had a mean BMI of 27.6 Kg/m^2 in the counselling group and 27.2 Kg/m^2 in the exercise group. Counselling and exercise groups scored a mean of 15.0 and 16.7 points, respectively, in the Blatt-Kupperman index assessed at baseline, both groups being mildly affected by menopause[167]. Less than 30% of the women had regular menstruation at the time of the first evaluation. Roughly, almost 70% of the women were married and worked full or part-time, almost 70% had finished secondary or University studies.

Per-protocol analyses

Table 9 shows the per-protocol analyses of sleep changes between pre and post intervention for counselling and exercise groups. For this specific study, per-protocol analysis was considered as the main one, as a high number of data had to be imputed. There were no associations between groups for any PSQI variables in any regression model (unadjusted, adjusted for baseline values nor adjusted for baseline values and cofounders) (all, P>0.05). The same trend was observed in both groups for all components and the global score of the PSQI (i.e., greater values in postest for subjective SQ and sleep efficiency, meaning worse sleep after the 4-month intervention, and lower values in postest for the rest variables of the PSQI, meaning better sleep).

Intention-to-treat analyses

Table 10 shows the intention-to-treat analyses of sleep changes between pre and post intervention for counselling and exercise groups. The exercise group decreased sleep disturbances (B=0.102, P<0.05) compared to the counselling after adjusting for baseline values. The rest of intention to treat results showed a similar trend than per-protocol analyses for all variables.

Table 8. Descriptive characteristics of the perimenopausal women study sample (n=150)

	Counselling Group (n=75)	**Exercise Group (n=75)**
Age (years)	52.6 (4.5)	52.7 (4.4)
BMI (kg/m^2)	27.6 (4.2)	27.6 (4.8)
Marital status, n (%)		
Married	55 (73.3)	50 (66.7)
Non married	20 (26.7)	25 (33.3)
Educational level, n (%)		
Unfinished studies or Primary studies	23 (30.7)	20 (26.7)
Secondary or University studies	52 (69.3)	55 (73.3)
Occupational status, n (%)		
Working	42 (56.0)	37 (49.4)
Housewife	19 (25.3)	19 (25.3)
Non-working	14 (18.7)	19 (25.3)
Medication for sleep, *n* (%)		
No	53 (70.7)	56 (74.7)
Yes	22 (29.3)	19 (5.3)
Regular menstruation, n (%)		
No	53 (70.7)	56 (74.7)
Yes	22 (29.3)	19 (25.3)
Blatt-Kupperman Menopausal Index#		
Global Score (0-51)	15.0 (10.2)	16.7 (10.8)
Moderate-to-vigorous PA (min/week)	180 (145)	179 (157)

Values expressed as mean (standard deviation) unless otherwise indicated. BMI, body mass index; PA, Physical activity.

Lower values indicate better menopausal symptomatology.

Table 9. Per-protocol analyses showing the effect of a 4-month concurrent exercise training program on sleep quality components and the global score in perimenopausal women (n=103).

	Changes in counselling group (n=47)	Changes in exercise group (n=56)	**Unadjusted model**				**Model adjusted for baseline values**				**Model adjusted for baseline values and cofounders**			
			β	B	95% CI	*P*	*β*	B	95% CI	*P*	*β*	B	95% CI	*P*
Subjective SQ	0.085 (0.619)	0.304 (0.851)	0.145	0.187	-0.100 .473	0.200	0.047	0.071	-0.198; 0.339	0.602	0.019	0.029	-0.242; 0.300	0.833
Sleep latency	-0.532(1.249)	-0.625 (1.168)	-0.055	-0.130	-0.579 0.319	0.567	0.028	0.068	-0.304; 0.440	0.717	0.020	0.048	-0.298; 0.393	0.785
Sleep duration	-1.106 (1.026)	-1.392 (0.947)	-0.147	-0.288	-0.656 0.081	0.124	-0.024	-0.047	-0.261; 0.167	0.665	-0.034	-0.068	-0.288; 0.153	0.544
Sleep efficiency	0.936 (2.004)	0.910 (1.791)	0.010	0.037	-0.676 0.749	0.919	0.031	0.117	-0.454; 0.688	0.686	0.017	0.065	-0.533; 0.662	0.831
Sleep disturbances	-0.447 (0.746)	-0.661 (0.640)	-0.140	-0.192	-0.450 0.065	0.142	0.062	0.087	-0.045; 0.218	0.193	0.061	0.085	-0.053; 0.223	0.223
Sleep medication	-0.042 (0.624)	-0.125 (0.833)	-0.059	-0.185	-0.360 0.189	0.539	-0.012	-0.017	-0.279; 0.244	0.895	-0.022	-0.032	-0.305; 0.204	0.816
Daytime dysfunction	-0.106 (0.699)	-0.196 (0.553)	-0.066	-0.081	-0.316 0.153	0.493	0.004	0.005	-0.211; 0.221	0.964	-0.004	-0.004	-0.233; 0.224	0.970
Global score	-2.149 (2.949)	-2.625 (2.832)	-0.104	-0.590	-1.666 0.485	0.279	0.005	0.031	-0.858; 1.920	0.945	0.003	0.204	0.890; 0.920	0.974

Cofounders: age, body mass index, marital status, educational level, medication for sleep, regular menstruation, and the Blatt-Kupperman Menopausal Index global score. *β*, standardized regression coefficient; B, non-standardized regression coefficient; CI, confidence interval.

Table 10. Intention-to-treat analyses showing the effect of a 4-month concurrent exercise training program on sleep quality components and the global score in women during perimenopause (n=150).

	Changes in counselling group (n=75)	Changes in exercise group (n=75)	**Unadjusted model**				**Model adjusted for baseline values**				**Model adjusted for baseline values and cofounders**			
			β	B	95% CI	*P*	*β*	B	95% CI	*P*	*β*	B	95% CI	*P*
Subjective SQ	0.565 (0.849)	0.298 (0.880)	0.160	0.256	0.000; 0.512	0.050	0.054	0.087	-0.120; 0.294	0.408	0.009	0.015	-0.248; 0.278	0.912
Sleep latency	-0.608 (1.217)	-0.628 (1.159)	0.014	0.033	-0.342; 0.408	0.862	0.037	0.085	-0.190; 0.361	0.542	-0.003	-0.008	-0.331; 0.314	0.960
Sleep duration	-1.079 (1.158)	-1.340 (1.995)	-0.105	-0.209	-0.528; 0.111	0.199	-0.045	-0.089	-0.243; 0.066	0.258	-0.040	-0.079	-0.281; 0.122	0.438
Sleep efficiency	0.915 (1.833)	1.034 (1.693)	0.046	0.158	-0.398; 0.714	0.575	0.083	0.283	-0.131; 0.697	0.178	0.046	0.170	-0.376; 0.717	0.538
Sleep disturbances	-0.490 (0.846)	-0.640 (0.659)	-0.080	-0.109	-0.331; 0.112	0.331	0.075	0.102	0.011; 0.194	**0.029**	0.076	0.103	-0.021; 0.226	0.102
Sleep medication	-0.122 (0.881)	-0.099 (0.828)	0.036	0.059	-0.208; 0.327	0.662	0.047	0.077	-0.137; 0.292	0.479	-0.020	-0.029	-0.276; 0.218	0.818
Daytime dysfunction	0.090 (0.784)	-0.180 (0.589)	-0.142	-0.180	-0.385; 0.024	0.084	-0.035	-0.045	-0.213; 0.123	0.599	0.036	0.003	-0.011; 0.017	0.682
Global score	-2.509 (3.041)	-2.685 (2.811)	-0.019	-0.113	-1.062; 0.836	0.814	0.041	-0.241	-0.442; 0.925	0.487	-0.015	-0.081	-0.927; 0.764	0.849

Cofounders: age, body mass index, marital status, educational level, medication for sleep, regular menstruation, and the Blatt-Kupperman Menopausal Index global score. *β*, standardized regression coefficient; B, non-standardized regression coefficient; CI, confidence interval.

The al-Ándalus project: women with fibromyalgia

Study IV. Sedentary time, physical activity and sleep quality in fibromyalgia: the al-Ándalus project.

(Scandinavian Journal of Medicine & Science in Sports, 2019, 29(2):266-274, doi: 10.1111/sms.13318)

The final sample subject to analyses included 409 women with fibromyalgia (51.4±7.6 years old). *Table 11* shows sociodemographic and clinical characteristics of the study participants. Roughly, 57% of the sample had unfinished or primary education, 73% took sleep or relaxation medication, and 69% did not have a regular menstruation.

Table 12 shows the association between ST and the PA intensity levels with the SQ components of the Pittsburgh Sleep Quality Index. Several significant small correlations were observed. More ST was associated with worse subjective SQ, sleep duration, sleep disturbances, and daytime dysfunction (all, $P<0.05$). All of the PA intensity levels were correlated with better subjective SQ, sleep latency, sleep medication, and daytime dysfunction (all, $P<0.05$). Light PA and total PA were associated with sleep efficiency and sleep disturbances (all, $P<0.05$). After adjusting for the corresponding covariates, all correlations remained unchanged (all, $P<0.05$) except for the correlations of ST with sleep disturbances, light PA with sleep latency, and moderate and moderate-to-vigorous PA with sleep medication (all $P>0.05$). The individual associations of ST and PA intensity levels with SQ global score are shown in *Table 13* (all separate analyses). Sedentary time was independently associated with worse SQ global score (B=0.118, $P<0.05$), and light PA and total PA were independently associated with better SQ global score (B=-0.157, B=-0.163, respectively; all, $P<0.01$).

The SQ global score across tertiles of ST, light PA, and total PA are plotted in *figure 5.* The post-hoc analyses showed that patients with fibromyalgia with the highest number of minutes in ST (3rd tertile) presented worse SQ global scores than those from the 2nd tertile (14.0 vs 12.8, F=3.766, $P<0.05$, Cohen's d=-0.24). Regarding light PA, the participants who spent less time in PA (1st tertile) showed worse SQ global scores than those from the 2nd and 3rd tertiles (14.1 vs 12.9 and 12.8, F=5.186, all $P<0.01$, Cohen's *d*=0.33 and *d*=0.35, respectively). With respect to total PA, the participants who spent less time in PA (1st tertile) showed worse SQ global scores than those from the 2nd and 3rd tertiles (14.2 vs 12.8 and 12.8, F=5.186, all P<0.01, Cohen's *d*=0.42 and *d*=0.40, respectively).

The differences in SQ global scores across groups of both patients meeting (bouted or non-bouted) and not meeting the PA recommendations are presented in *figure 6*. The post-hoc analyses showed that the women who met the bouted PA recommendations displayed better SQ than the patients who did not meet the recommendations (bouted or non-bouted) (mean difference =1.49; P<0.05).

Table 11. Descriptive characteristics of the women with fibromyalgia study sample (n=409)

	Values	
Age (years)	51.4	(7.6)
BMI (kg/m^2)	28.4	(5.4)
Total body fat (%)	40.1	(7.6)
Time since fibromyalgia diagnosis, *n* (%)		
Less than 5 years	165	(40.3)
More than 5 years	233	(57.0)
Missing data	11	(2.7)
Marital status, *n* (%)		
Married	312	(76.3)
Single, separated, divorced, or widowed	97	(23.7)
Educational level, *n* (%)		
Unfinished or Primary education	235	(57.5)
Secondary or University education	174	(42.5)
Sleep or relaxation medication, *n* (%)		
No	111	(27.1)
Yes	298	(72.9)
Regular menstruation, *n* (%)		
No	282	(68.9)
Yes	127	(31.1)
Sleep quality (PSQI) ^		
Subjective sleep quality (0-3)	2.1	(0.8)
Sleep latency (0-3)	2.0	(0.9)
Sleep duration (0-3)	1.8	(0.9)
Sleep efficiency (0-3)	1.6	(1.2)
Sleep disturbances (0-3)	2.1	(0.6)
Sleep medication (0-3)	2.1	(1.3)
Daytime dysfunction (0-3)	1.5	(0.8)
Sleep quality global score (0-21)	13.3	(3.9)
Sedentary time and physical activity intensity levels		
Sedentary time	460.1	(104.0)
Light PA	418.4	(91.7)
Moderate PA	43.8	(29.5)
MVPA (min/week, in bouts ≥10 min)	85.5	(111.9)
Total PA	462.6	(105.6)

All values are expressed as mean (standard deviation) unless otherwise indicated.
BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index; PA, physical activity; MVPA, moderate-vigorous physical activity; min, minute.
^ Lower values indicate better sleep quality.

Table 12. Raw (Spearman) and adjusted (partial) correlations between sedentary time and physical activity (PA) intensity levels with sleep quality components in women with fibromyalgia (n=409).

	Subjective sleep quality		Sleep latency		Sleep duration		Sleep efficiency		Sleep disturbances		Sleep medication		Daytime dysfunction	
	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted	Raw	Adjusted
Sedentary time, *r*	**.133****	**.111***	.086	.087	**.150****	**.167*****	-.004	-.002	**.098***	.058	.093	.044	**.179*****	**.135****
Light PA, *r*	**-.133****	**-.115***	**-.113***	-.085	-.026	-.021	**-.139****	**-.142****	**-.147****	**-.101***	**-.203*****	**-.133****	**-.161****	**-.160****
Moderate PA, *r*	**-.136****	**-.102***	**-.110***	**-.104***	-.042	-.024	-.062	-.046	-.064	-.022	**-.107***	-.006	**-.136****	**-.121***
MVPA$^{\infty}$, r	**-.137****	**-.107***	**-.112***	**-.105***	-.041	.002	-.062	-.022	-.064	-.018	**-.109***	-.011	**-.136****	**-.123****
Total PA, *r*	**-.148****	**-.130****	**-.126***	**-.105***	-.022	-.025	**-.133****	**-.138****	**-.138****	**-.096***	**-.185*****	**-.120****	**-.159****	**-.176*****

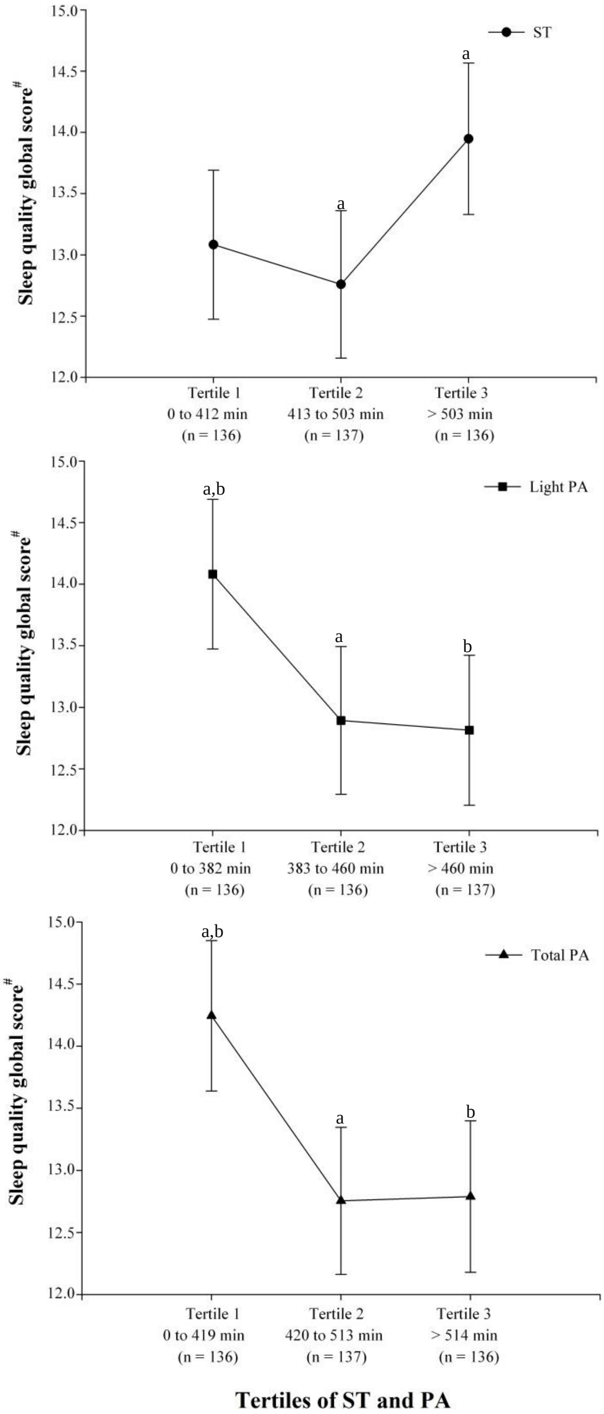
Raw, Spearman correlation; Adjusted, partial correlation controlled for age, total body fat percentage, marital status, educational level, sleep or relaxation medication, regular menstruation, and accelerometer wear time. MVPA, moderate-vigorous physical activity. $^{\infty}$MVPA in bouts ≥10 min
*P < 0.05; **P < 0.01; ***P<0.001.

Table 13. Associations of sedentary time and physical activity (PA) intensity levels with sleep quality global score in women with fibromyalgia (n=409)

	β	B	95% CI		*P*
Sedentary time	0.118	0.004	0.001	0.008	**0.014**
Light PA	-0.157	-0.007	-0.011	-0.003	**0.001**
Moderate PA	-0.081	-0.011	-0.023	0.001	0.085
MVPA[∞]	-0.078	-0.003	-0.006	0.000	0.098
Total PA	-0.163	-0.006	-0.009	-0.003	**0.001**

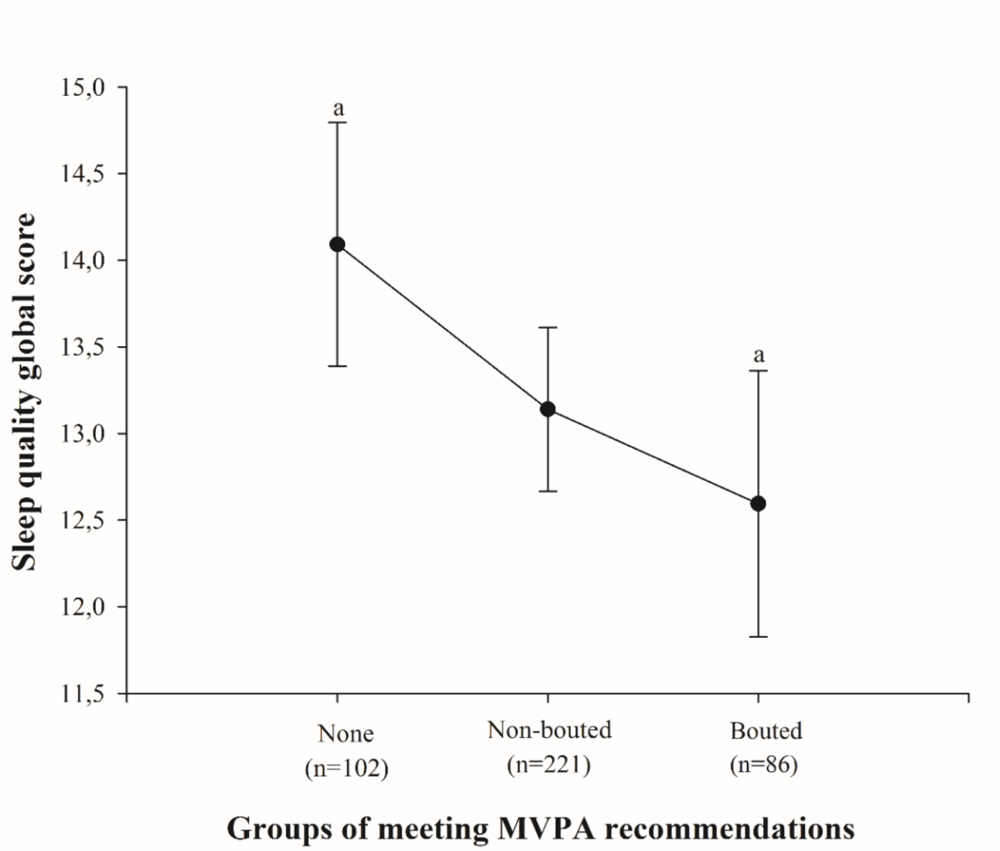
Results of separate regression analyses controlled for age, total body fat percentage, marital status, educational level, sleep or relaxation medication, regular menstruation, and accelerometer wear time. *β*, standardized regression coefficient; B, non-standardized regression coefficient; CI, confidence interval; PA, physical activity; MVPA, moderate-vigorous physical activity; [∞]MVPA in bouts ≥10 min

Figure 5. Differences in the sleep quality (SQ) global score across tertiles of sedentary time (ST), light and total physical activity (PA).



Low (1), middle (2), and high (3) scores on sedentary time (ST), light and total physical activity (PA) with sleep quality global score from the Pittsburgh Sleep Quality Index in women with fibromyalgia study sample (n=409). The estimated means (dots) and 95% confidence intervals (CIs, error bars) represent values after adjustment for age, total body fat percentage, marital status, educational level, sleep or relaxation medication, regular menstruation, and accelerometer wear time. Common superscripts indicate significant differences (P<0.05) between the components with the same letter after Bonferroni's correction. # Lower values indicate better sleep quality.

Figure 6. Differences in the sleep quality (SQ) global score across groups of meeting and not meeting physical activity (PA) recommendations for adults.



Association between the engagement in moderate-to-vigorous physical activity (MVPA) recommendations, with or without accounting for a minimum of 10 min bouts, with sleep quality global score from the Pittsburgh Sleep Quality Index in women with fibromyalgia study sample (n=409). None: <150 min/week MVPA (either non-bouted or bouted); Non-bouted: meeting 150min/week non-bouted MVPA; Bouted: meeting 150 min/week bouted MVPA. The estimated means (dots) and 95% confidence intervals (CIs, error bars) represent values after adjustment for age, total body fat percentage, marital status, educational level, sleep or relaxation medication, regular menstruation, and accelerometer-wear time. [a] indicate significant differences (P<0.05) between the components after Bonferroni's correction.
Lower values indicate better sleep quality.

DISCUSSION

D

DISCUSSION

Summary of the main findings

Cross-sectional studies (Studies I, II, and IV)

The main results of the present International Doctoral Thesis showed that there were no associations between ST, PA intensity levels, and total PA with any PSQI components and the PSQI global score neither in women during early second trimester of pregnancy *(Study I)* nor in perimenopausal women *(Study II).* However, in women with fibromyalgia (*Study IV)* we found a relevant association of ST and PA (especially light and total PA) with SQ and its components. Furthermore, the results indicated that meeting PA recommendations (i.e. more than 150 min/week in bouts ≥10 min) was associated with better SQ in women with fibromyalgia.

Experimental study (Study III)

The main findings for the per-protocol analysis about the effects of a 4-month concurrent exercise training program, compared with a counselling intervention, showed a trend to better SQ but no clear significant effects between groups for any PSQI variables. After imputed the missing data (intention-to-treat analysis), results did not change, except for the *model adjusted for baseline values,* where the exercise group significantly decreased sleep disturbances compared to the counselling group.

Discussion of main findings with previous literature

The GESTAFIT project: pregnant women

Study I. Sedentary time, physical activity and sleep quality in women during early pregnancy: the GESTAFIT project

To the best of our knowledge, the relationship between objectively measured ST and PA intensity levels with SQ and its components have not been previously studied during pregnancy, although two cross-sectional studies analysed the association between non objectively measured PA levels with sleep duration and SQ in this population[79,80].

In the present study, we observed no association between any PA intensity levels with sleep duration. According to us, no associations were found between light, moderate, and vigorous PA intensity levels with shorter sleepers (vs. medium and longer) in a sample of pregnant Hispanic women with a risk of type 2 diabetes[80]. Furthermore, in the same study, no associations were found between women who reported high occupational or transportation activity with the odds of reporting long (vs. medium) sleep duration, and between occupational, transportation, and sports or exercise activity with short (vs. medium) sleep duration[80]. In contrast, Hawkins et al. (2018)[80] showed that women with the highest levels of household PA had more possibility of short (vs. medium) sleep duration compared to those with the lowest levels[80], and Borodulink et al. (2010)[79] showed that higher occupational PA was associated with greater sleep duration[79].They also found that women with higher indoor household PA were less likely to report normal sleep duration (vs. short)[79]. In addition, our findings showed no association between any PA intensity levels nor sports and exercise activities with SQ. These findings are in agreement with the others studies developed in pregnant women[79,80]. Nevertheless, Hawkins et al. (2018)[80] also found an association between higher levels of household or caregiving activity with higher odd of very poor SQ, although this odd decreased when occupational activity increased. Thus, pregnant women with high occupational activity had less probability of very poor SQ compared to women that reported no occupational activity[80].

There is a disparity in the scarce findings related with PA levels and sleep during pregnancy. These opposite directions in terms of the associations on the results could be explained by the different methodologies and approaches used in the studies. Specifically, the tools used to measure PA clearly differed between studies. For instance, in the study by Borodulink et al. (2010)[79] the authors assessed PA with an interview about the past week. Conversely, Hawkins et al. (2018)[80] assessed PA with the self-reported Pregnancy Physical Activity Questionnaire that ask about the type of PA where the participant is engaged. Instead, we used accelerometry, which is a simple, valid, and reliable instrument[31–33] that has been considered the gold standard to measure PA[31]. Moreover, in pregnancy it has been demonstrated that self-reported questionnaires over-estimate PA, and objective devices (as accelerometers) should be used, when it is possible[30]. Additionally, in contrast with others[79,80], we measured the different intensities of PA but we did not report the specific types of activities that women performed (i.e. household or caregiving, occupational, transportation, and sport or exercise).

Other potential explanations of the contradictory results found could be the studies' sample size, and the time when participants were evaluated. The relatively small sample size of the current study compared with the ones by Borodulink et al. (2010)[79] (n=1259) and Hawkins et al. (2018)[80] (n=251) may partially explain the lack of significant differences in our study sample. Moreover, in the present study, women were assessed at the 16th gestational week (±2 weeks) while in Borodulink et al. (2010)[79] and Hawkins et al. (2018)[80] studies, participants were evaluated at 27th-30th and 26th gestational week respectively. Previous researches have showed that both PA[174] and SQ[65] decreases during pregnancy. In this sense, PA and SQ data of pregnant women in the second and third gestational trimesters may not be fully comparable.

As far as we know, there are no previous studies analysing ST and the rest of PSQI components in pregnancy to properly compare such data with our results. Moreover, due to the scarce literature in PA and SQ in pregnant, and the wide disparity with the findings, we cannot affirm that PA is an effective non-pharmacological treatment for sleep problems in this population. Further research should investigate whether duration, and intensity of objectively measured PA is associated with SQ, or their components, in bigger and representative samples of pregnant women. Furthermore, additional studies are needed to understand the relationship between ST and SQ in this population.

The FLAMENCO project: perimenopausal women

Study II. Sedentary time, physical activity and sleep quality during perimenopause: the FLAMENCO project

Similarly to this study, many others have analysed the association of ST and PA with sleep in clinical and non-clinical populations. Although we expected a clear relationship between these variables, our results did not confirm our hypothesis. In fact, no association was found between ST and daytime dysfunction (which is in agreement with similar studies performed in middle-aged and older adults[175], overweight adults with obstructive sleep apnea[41], and healthy adults[40,176]). However, a study in a big cohort of adults (n=42,489) stablished that those individuals who spent more time in sedentary behaviours showed higher daytime dysfunction[177]. Furthermore, we also observed no association between ST and sleep efficiency as in a similar study performed in adult women[178]. In contrast, Madden et al. (2014)[179] found a weak association between ST and sleep efficiency in active older adults, despite their sample size was small (n=54). Regarding to PA intensity levels, we found significant associations with light and total PA in the raw model. However, when we further adjusted for potential confounders, the significance was not maintained. This lack of association concurs with two prospective studies performed in adults[177] and older women[43]. The mixed findings of the above mentioned studies could be explained by the studies' measurements tools, samples sizes, and populations. Moreover, sixty percent of these studies employed objective instruments (accelerometry)[40,41,43,178,179] to assess ST and PA levels whereas self-reported questionnaires were used in the largest samples (n>1000)[175–177]. Additionally, there is a high variability between the studies' methodology. For instance regarding the sample sizes (being n=54 the smallest[178] and n=42,489 the largest[177]) and type of population (mostly men[40,41,176,177,179], and where perimenopausal women were not studied or representative). Finally, recent studies performed in children[38], adults[106], and women with fibromyalgia[180] observed that greater levels of ST were related with less sleep duration. However, our results only confirmed this association newly in the raw model. Therefore, our data concur with a prospective study developed in adult women that found no association between ST and sleep duration[178]. However, due to the fact that perimenopause is a crucial period for women's life with a specific physiological situation characterized by vasomotor symptoms (i.e. hot flushes and night sweats)[88], among others, that could affect sleep, similar researches in perimenopausal women are warranted to more adequately compare the findings of the current study.

Regarding to PA, our results indicate no association between any PA intensity levels and sleep duration, which is in agreement with the study by Mitchell et al. (2016)[178]. Nevertheless, in a prospective study developed in older women, Gabriel et al. (2016)[181] found that women with higher daytime PA showed reduced likelihood of reporting short (<7 hours) or long (>9 hours) sleep that night. Similarly, Kishida and Elavsky (2016)[44] concluded that greater activity counts were associated with greater sleep duration in midlife women, although this association was negligible for MVPA. Moreover, total PA and sleep medication were related in the raw model of the present study but we did not find previous studies to compare our results. The loss of significance in some correlations in the raw model after adjusting for confounders such as total PA and medication may explain the absence of some significant findings. Indeed, we used eight covariates in the adjusted model, and this relatively high number of confounders in a moderately small sample (n=169) could skew some of the results.

During menopause, women normally present poor SQ[93]. We analysed the potential association between ST and PA intensity levels with SQ and we did not find any association. In contrast, several studies have showed that higher time spent in sedentary behaviours was associated with worse SQ in different populations[176,177,180,182]. Moreover, our research group has previously showed positive associations between light and total PA with better SQ, and no associations for the rest of PA intensity levels in women with fibromyalgia[180]. Despite to the differences between participants of the present study and our study developed in fibromyalgia patients[180], some characteristics are shared: First, the methodology used in both studies (including measurement tools and statistical analyses), and second, in both studies the mean age of the women was around 52 years old and approximately 70% of them had no regular menstruation, which means they were in a similar physiological situation (similar menopausal stage). However, in the current study we did not find significant associations despite of the multiple correlations observed in the study performed with fibromyalgia patients. To note is that the different sample size could have interfered in the effect size and power of such associations in favour of the fibromyalgia sample. For instance, the partial correlation coefficient found between higher ST and less sleep duration in fibromyalgia patients was quite similar to that observed in our perimenopausal sample (i.e. perimenopausal women: $P>0.05$, $r=0.189$ vs. women with fibromyalgia $P<0.001$, $r=0.167$). The same phenomena occurs regarding the association between light PA and sleep efficiency (perimenopausal women: $P>0.05$, $r=-0.184$; women with fibromyalgia $P<0.01$, $r=-0.142$), among others. Future researches with larger samples of perimenopausal women are needed to corroborate the trend in the current findings.

In addition, perimenopause is a crucial period for women's life with a specific physiological situation characterized by many different symptoms[88]. The most well studied symptom in this population are vasomotor manifestations (e.g. hot flashes and night sweats)[91,183,184]. Previous studies in middle age women have demonstrated that vasomotor symptoms were related with higher sleep problems[98,185–189], and that decreasing vasomotor symptoms improved SQ[184]. The current results showed no association between PA levels and sleep, and several studies have indicated a weak associations between PA levels and vasomotor symptoms in women during the menopause transition[126,190]. However, different studies have revealed the effectiveness of substitutive hormonal therapy to improve SQ[102,184]. Thus, considering the relationship between vasomotor symptoms and sleep, an effective and indirect treatment for a better sleep during perimenopause could be hormonal treatments[185].

Study III. Effects of interval aerobic training combined with strength exercise on sleep during perimenopause: the FLAMENCO project

Recent reviews performed in healthy populations have demonstrated the benefits of exercise on sleep[122,191]. These studies have determined that improvements of exercise on sleep are immediate[122], and that sleep and exercise influence each other through complex, reciprocal interactions including multiple physiological and psychological pathways[191]. A review in middle-aged women also concluded that sleep improved after different exercises programs[121]. Similarly, several intervention studies in middle-aged women have demonstrated the benefits of exercise on women's sleep[123,124,192]. For example, an 8-week aerobic exercise program[123], and 16-week of moderate walking exercise or yoga[192] improved SQ in this middle-aged population. Moreover, an intervention program based on 12-weeks of Pilates also increased middle-aged women's sleep latency and duration[124].

According to the above mentioned studies and previous literature, aerobic training seems to be the most recommended type of exercise intervention to ameliorate sleep problems. A 24-week[52] and a 12-week[126] aerobic training programs improved SQ and the perceived quality of sleep, respectively, in menopausal women. Moreover, after a yearlong, a moderate aerobic exercise program showed benefits on subjective SQ in postmenopausal women, and a yearlong stretching intervention reduced sleep medication and the time to fall asleep in the same population[125]. In contrast, Buchanan et al. (2017)[127], the only study that employed objectively measured registry (actigraphy) to assess sleep, found no significant effects of a 12-week yoga or aerobic exercise interventions on sleep in menopausal women with hot flashes.

Hence, the positive role of exercise on SQ appears to be widely demonstrated despite of our findings. Some factors could explain the lack of significant improvements in our study and thus the absence of differences found between both counselling and exercise groups could have various interpretations. First, although the present study strictly followed the Consort guidelines for Randomized Controlled Trials during the entire intervention, the inclusion of a counselling group instead of a control group for ethical reasons may have masked the potential positive results in this regard. We believe that most of the positive changes regarding sleep observed in the counselling group were due to a high and unexpected acceptance and follow-up of the lifestyle conferences given to the participants. The lecturers provided participants with professional advices on the importance of having an active behaviour and the benefits of exercise for longevity. We also informed to the counselling group on how to improve their nutritional habits. Moreover, supplementary intention-to-treat analyses showed similar tendencies for most of variables, except for the adjusted model for baseline values, where we observed higher effects in the concurrent exercise training compared to the counselling intervention in sleep disturbances. We consider relevant to take this significant value like a starting point for future researches.

Furthermore, as previously stated, aerobic training is the most used exercise intervention employed until date to reduce sleep problems, despite of the ACSM guidelines for general population[54], which recommend the inclusion of resistance training. However, little is known about the possible benefits of an intervention consisting in a moderate-to-vigorous intensity concurrent exercise training program (resistance and aerobic exercise) on sleep in perimenopause, as we performed in the present study. After consideration of all the factors above mentioned, and the relative physically active status of the participants at baseline in the present study, future studies should be carried out with concurrent exercise training interventions (at different intensities) in sedentary perimenopausal women. Studies should also compare their findings about the effects of exercise on sleep with a usual care group (without counselling intervention), in search of better results.

The al-Ándalus project: women with fibromyalgia

Study IV. Sedentary time, physical activity and sleep quality in fibromyalgia: the al-Ándalus project

The observed association between ST and daytime dysfunction differs from findings of previous studies that indicated a lack of association between ST and daytime sleepiness in healthy adults[40] as well as in overweight adults with obstructive sleep apnea [41]. The lack of findings in previous studies may be due to the time lag in the data collection protocol between sleep and accelerometry assessments[40], or to the small sample size (n=62)[41], which prevented from finding a small correlation. However, our findings may also suggest that the association between ST and daytime dysfunction might be specific for fibromyalgia. A previous study by McClain et al.[40] also observed that the frequency of daytime sleepiness was associated with reduced levels of MVPA in women from 20 to 39 and ≥60 years old. Due to the fact that our data are correlational, they may reflect a mutual influence of ST, lower PA, and disturbed sleep. These observations are in agreement with the hypothesis that women with fibromyalgia who present less pain, worries, and time in sedentary behaviours or more PA might sleep better and feel less sleepy during the day.

The patients with fibromyalgia who spent more time in ST had shorter sleep duration. This is in disagreement with previous studies performed in healthy adults and people with the metabolic syndrome[39,40]. Saleh and Janssen[39] employed accelerometry to assess sleep duration, but the participants removed the display before going to bed. Consequently, the sleep duration was a proxy measure as non-wear time at night, which may have overestimated sleep time. Nonetheless, our results are consistent with other studies in children[37,38] and with a study with European adults, where short sleepers (<6 hours per night) spent more minutes per day sitting in front of screens (computer or tablet) than normal sleepers (6-8 hours per night)[193]. Thus, our findings could support that those women with fibromyalgia that show more ST spend more time in screen behaviours (computer, tablet, or television) and, therefore, have a shorter sleep duration. Finally, regarding ST and PA intensity levels, we observed a trend showing that those women with lower ST and greater PA levels have better subjective SQ (meaning better SQ perception). This is relevant in this population due to the fact that fibromyalgia patients usually underestimate their SQ[194], so reducing ST and increasing PA might improve SQ perception.

Therefore, we suggest that ST and SQ seem to be related in this population. In agreement with our results, Kakinami et al.[182] observed that more time spent in sedentary activities was associated with poorer SQ in young adults. Regarding MVPA, a study in a small sample of healthy adults ≥65 years old (n=60) showed that MVPA was associated with better SQ[42]. Slightly in contrast, we observed (in our larger sample) no direct association between MVPA (in bouts of ≥10 min) and the SQ global score. Nevertheless, when we compared women who did and did not meet the PA recommendations (i.e. 150 min/week of MVPA in bouts ≥10 min), we observed that those who did, presented a better SQ global score. For the remaining PA intensity levels, in contrast with our findings, a study performed in rheumatoid arthritis patients [195] and others in young adults Kakinami et al.[182] did not find an association between PA and sleep. To note is that both studies assessed PA levels by questionnaires whereas we have employed objectively measured PA. Andrews et al.[160] observed that, in patients with chronic pain, high-intensity activities and high fluctuations in PA were associated with poorer sleep at night. Thus, they suggested that PA could be a key treatment for sleep complaints (i.e. awakes or SQ). With the categorization of groups by tertiles, we observed that women with fibromyalgia with the highest ST and the lowest light and total PA presented a greater SQ global score, meaning poorer SQ, than the other groups. Moreover, exercise intervention studies have observed a positive effect of exercising on SQ in patients with fibromyalgia[196]. Furthermore, exercise appears to be a useful non-pharmacological treatment to improve fibromyalgia symptomatology[197].

Among the mediators that might explain the associations of ST and PA levels with SQ are hormonal changes, structural and functional neurological changes, and modifications in the autonomic nervous system functioning. During PA, the sympathetic autonomic nervous system is stimulated[198]. However, after PA there is a physiological response that includes a decrease in this sympathetic tone and a shift towards parasympathetic activity, which promotes muscular and nervous relaxation[199,200]. Partially as a consequence of this parasympathetic activity, PA is shown to decrease the heart rate and to have antihypertensive effects which also facilitate sleep[201]. Moreover, PA induces body and mental relaxation and has a clear anxiolytic effect[202], thus decreasing stress levels[202], which may all together promote a better SQ[203]. It is also plausible that those women with high levels of ST and low levels of PA have less hours of slow wave sleep[204]. Disturbed slow-wave sleep may increase fibromyalgia severity[205].

Decades of research led to the current concept that chronic pain encompasses multiple and mutually interacting biological, psychological, and social factors. These include –but are not limited to– nature of pain, peripheral and central pain processing mechanisms, physical disability, sleep disturbances, obesity and other health risks, psychological resilience and vulnerabilities (emotions, cognitions, behaviour), and social factors (work, support, facilities, financial resources)[206]. The relations between all factors of this biopsychosocial model are recognized to be dynamic and reciprocal, with mutually influencing pathways in which changes of one component may induce change in all. The weight of the distinct factors differs between individuals. Following this model, it is likely that PA influences sleep and that sleep influences PA, as indicated in a prospective study in chronic pain and insomnia participants, suggesting that people's perception about their SQ may condition their PA levels[161]. Also, another study observed in a middle-aged to elderly population that regular moderate exercise was associated with a reduction in the prevalence and risk of symptoms of disturbed sleep [207]. Our results suggest that high intensity levels of PA are not essential to reduce sleep disturbances in patients with fibromyalgia; but light PA might be helpful. Overall, our data and those of other studies indicate that the reduction of ST, enhanced light PA, and improved sleep are potential beneficial targets in the management of fibromyalgia.

LIMITATIONS AND STRENGTHS

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Limitations

In *Studies I, II and IV,* the cross-sectional design does not allow to establish causal relationships. Future longitudinal studies are warranted to confirm these results.

In *Studies I, II and IV,* the accelerometer does not discriminate some specific physical activity activities such as cycling, swimming, or weight lifting.

In *Studies I, II and IV,* the use of new methods to process accelerometer data (e.g.: Lyden's Sojourns method) might provide greater validity than ActiGraph software data processing, especially to distinguish between ST and light PA[208].

In *Study IV,* future studies should use self-reported questionnaires to check whether different types of physical activity present distinctive associations with sleep parameters.

In *Studies I, II, III and IV,* although valid and reliable in women with fibromyalgia[14] and pregnancy[15], the PQSI questionnaire is not an objective measure of sleep and cannot, for instance, measure how much time people are in the deep restorative sleep phases.

In *Study IV,* due to the small sample (n=29), men were not included

In *Studies II and III*, women included in the studies were not particularly affected by menopause (mild severity) and showed moderate-high PA levels, which hinder the extrapolation to women severely affected by menopause, or with poor physical activity levels.

In Study III, for ethical reasons, the control group received the above mentioned educational conferences. Consequently, we lacked a control group with no stimulus at all with which we could compare the real efficacy of our intervention. Hence, results should be interpreted with caution. Although the counselling women did not participate in the exercise intervention, the conference about increasing PA to improve their health, life expectancy, and prevent pathologies, may have been more influential than initially expected.

Strengths

In *Studies I, II and IV*, an objective quantification of sedentary time and/or physical activity levels, given that self-reported measures have shown poor reliability and validity (i.e. in general population[25,26], pregnant women[209] or in fibromyalgia population[28]).

In *Studies I, II and IV,* the accelerometer criteria employed were stricter than those used in previous studies[153].

In *Study IV,* the large and representative study sample[133].

In *Study III,* the intention-to-treat analyses, those being potentially important as they replicate how this kind of programmes would work in real life. Per-protocol analyses were also included, being able to isolate and evaluate the clinical efficacy of the present concurrent exercise training program.

In *Study III*, the design of this study as a randomized controlled trial that is considered the gold standard for evaluating efficacy in clinical research. Furthermore, this randomized controlled trial was strictly supervised during all stages of the study, and the intensities of the training sessions were monitored periodically.

CONCLUSIONS / CONCLUSIONES

CONCLUSIONS

Overall, the findings of the present International Doctoral Thesis suggest that sedentary time and physical activity are related with sleep quality in women with fibromyalgia where those that spend less time in sedentary behaviours and more time to perform physical activity sleep better. However, in women during early pregnancy and perimenopausal women no association was found between the variables above mentioned. Furthermore, they are not effects of a 4-month concurrent exercise training program on sleep quality in perimenopausal women.

The *specific conclusions* of each individual study are presented below.

The GESTAFIT project: pregnant women

1. There are not associations between sedentary time and physical activity intensity levels with sleep quality in women during early pregnancy *(Study I)*.

The FLAMENCO project: perimenopausal women

2. There are not associations between sedentary time and physical activity intensity levels with sleep quality in perimenopausal women *(Study II)*.
3. Neither 4-month concurrent exercise training program (resistance and aerobic) nor a healthy lifestyle counselling have effects on sleep quality in perimenopausal women *(Study III).*

The al-Ándalus project: women with fibromyalgia

4. Lower sedentary time and greater physical activity intensity levels are associated with better components of the sleep quality in women with fibromyalgia *(Study IV)*.
5. Lower sedentary time and greater light and total physical activity levels are associated with better sleep quality in women with fibromyalgia *(Study IV)*.
6. Women with fibromyalgia who meet physical activity recommendations (150 min/week of MVPA in bouts of ≥10 min) had better sleep quality than those who do not reach those recommendations *(Study IV)*.

CONCLUSIONES

En general, los resultados de la presente Tesis Doctoral Internacional sugieren que los niveles de sedentarismo y actividad física están relacionados con la calidad del sueño en mujeres con fibromialgia, mostrando que aquellas que dedican menos tiempo a comportamientos sedentarios y mayor tiempo a realizar actividad física, duermen mejor. Sin embargo, en mujeres durante la gestación temprana y perimenopáusicas, no se ha hallado asociación entre las variables citadas anteriormente. Además, no se han encontrado efectos en un programa de 4 meses de entrenamiento de ejercicio concurrente sobre la calidad del sueño en mujeres perimenopáusicas.

Las *conclusiones específicas* de cada estudio están presentadas a continuación.

El proyecto GESTAFIT: mujeres gestantes

1. No se hallaron asociaciones entre el tiempo de sedentarismo y los niveles de actividad física con la calidad del sueño en mujeres durante la gestación temprana *(Estudio I)*.

El proyecto FLAMENCO: mujeres perimenopáusicas

2. No se hallaron asociaciones entre el tiempo de sedentarismo y los niveles de actividad física con la calidad del sueño en mujeres perimenopáusicas *(Estudio II)*.
3. Ni un programa de 4 meses de entrenamiento de ejercicio concurrente (fuerza y aeróbico) ni el consejo acerca de un estilo de vida saludable tuvieron efecto en la calidad del sueño en mujeres perimenopáusicas *(Estudio III).*

El proyecto al-Ándalus: mujeres con fibromialgia

4. Menores niveles de sedentarismo y mayores niveles de intensidad de actividad física fueron asociados con mejores resultados en los componentes de la calidad del sueño en mujeres con fibromialgia *(Estudio IV).*

5. Menores niveles de sedentarismo y mayores niveles de actividad física ligera y

total fueron asociados con mejor calidad del sueño en mujeres con fibromialgia *(Estudio IV)*.

6. Las mujeres con fibromialgia que cumplían con las recomendaciones de actividad física (150 min/semana de actividad física moderada-vigorosa en *periodos* de ≥10 min) tuvieron mejor calidad del sueño que aquellas que no las cumplían *(Estudio IV)*.

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