ASSOCIATION OF SELF-REPORTED PHYSICAL FITNESS DURING PREGNANCY WITH DIFFERENT MARKERS OF MATERNAL-FETAL HEALTH

ASOCIACIÓN DE LA CONDICIÓN FÍSICA AUTO-REPORTADA DURANTE EL EMBARAZO CON DIVERSOS MARCADORES DE SALUD MATERNO-FETAL

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A mi familia, brújula, inspiración y sustento.

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RESEARCH PROJECTS AND FUNDING

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The present International Doctoral Thesis was performed under the framework of the GESTAFIT Project, which received the following funding:

- **GESTAFIT Project 1:** Effects of supervised aerobic and strength training in overweight and grade I obese pregnant women on maternal and fetal health markers: The GESTAFIT Project. Andalucía Talent Hub Program launched by the Andalusian Knowledge Agency, co-funded by the European Union's Seventh Framework Program, Marie Sklodowska-Curie actions (COFUND – Grant Agreement nº 291780) and the Ministry of Economy, Innovation, Science and Employment of the Junta de Andalucía (156.763 €). 01/03/2015 to 28/02/2017. I.P.: Virginia A. Aparicio García- Molina.

- **GESTAFIT Project 2**: Efectos de un programa de ejercicio físico supervisado durante el embarazo sobre la longitud de los telómeros y marcadores de expresión génica relacionados con la adiposidad en la madre y el neonato. Ensayo controlado aleatorizado (PI-0395-2016). Consejería de Salud de la Junta de Andalucía (56.178€). 01/01/2017 to 31/12/2019. I.P.: Virginia A. Aparicio García-Molina.

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PUBLICATIONS

PUBLICATIONS

The present International Doctoral Thesis is composed of eight publications. These eight publications are presented and grouped into different chapters throughout the Doctoral Thesis document, in the following order:

- **CHAPTER I.** Objectively measured physical fitness during pregnancy and body composition and birth-related outcomes (*studies I-II*).

  Study I: Marín-Jiménez, N., Flor-Alemany, M., Baena-García, L., Coll-Risco, I., Castro-Piñero, J., & Aparicio, V. A. (2022). Physical fitness and maternal body composition indices during pregnancy and postpartum: The GESTAFIT Project. *European Journal of Sport Science*, 1-11: **Q1**.

  Study II: Aparicio, V. A, **Marín-Jiménez, N.**, Castro-Piñero, J., Flor-Alemany, M., Coll-Risco, I., & Baena-García, L. Association of body flexibility with the odd of oxytocin administration and caesarean section during labor: The GESTAFIT Project: *European Journal of Sport Science, Submitted (**Q1**).*

- **CHAPTER II.** Self-reported physical fitness during pregnancy and perinatal physical and mental health outcomes (*studies III-VI*).

  Study III: Marín-Jiménez, N., Acosta-Manzano, P., Borges-Cosic, M., Baena-García, L., Coll-Risco, I., Romero-Gallardo, L., & Aparicio, V. A. (2019). Association of self-reported physical fitness with pain during pregnancy: The GESTAFIT Project. *Scandinavian Journal of Medicine & Science in Sports, 29*(7), 1022-1030: **Q1.**

  Study IV: Marín-Jiménez, N., Borges-Cosic, M., Ocón-Hernández, O., Coll-Risco, I., Flor-Alemany, M., Baena-García, L., Castro-Piñero J., & Aparicio, V. A. (2021). Association of self-reported physical fitness with pregnancy related symptoms: The GESTAFIT Project. *International Journal of Environmental Research and Public Health*, *18*(7), 3345: **Q1.**

  Study V: Marín-Jiménez, N., Castro-Piñero, J., Rodríguez-Ayllón, M., Marchán-Rubio, A., Delgado-Fernández, M., & Aparicio, V. A. (2022). The favourable association of self-reported physical fitness with depression and anxiety during pregnancy: The GESTAFIT Project. *European Journal of Sport Science*, *22*(12), 1932-1940: **Q1**.

Study VI: Marín-Jiménez, N., Flor-Alemany, M., Baena-García, L., Corres, P., Molina-Hidalgo C., & Aparicio, V. A. (2023). The role of self-reported physical fitness in emotional well-being and emotional distress during pregnancy: The GESTAFIT Project. *Journal of Sport and Health Science, Submitted **(Q1)***.

CHAPTER III. The influence of the "GESTAFIT" concurrent exercise training protocol on pain and health-related quality of life (*studies VII-VIII*).

Study VII: Aparicio, V. A; **Marín-Jiménez, N**., Flor-Alemany, M., Acosta-Manzano, P., Coll-Risco, I., & Baena-García, L. (2023). Effects of a concurrent exercise training program on low back and sciatic pain and pain disability in late pregnancy. *Scandinavian Journal of Medicine & Science in Sports 3*(7), 1201-1210*:* **Q1**.

Study VIII: Marín-Jiménez, N., Baena-García, L., Coll-Risco, I., Flor-Alemany, M., Castro-Piñero, J., & Aparicio, V. A. (2023). Influence of a concurrent exercise training program on health-related quality of life during advanced pregnancy: The GESTAFIT Project. *Sports Health: A Multidisciplinary Approach: **Q1***.

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ABBREVIATIONS

ABBREVIATIONS

ACOG: American College of Obstetrics and Gynaecology

ACSM: American College of Sport Medicine

ANCOVA: One-way analysis of covariance

BMC: Bone Mineral Content

BMD: Bone Mass Density

BMI: Body Mass Index

CES-D: Center for Epidemiological Studies Depression Scale

CI: Confidence Intervals

DXA: Dual-energy X-ray absorptiometry

GESTAFIT: GESTAtion and FITness

G.W.: Gestational Weeks

GWG: Gestational Weight Gains

HRQoL: Health-Related Quality of Life

IFIS: International FItness Scale

ODI: Oswestry Disability Index

OR: Odds ratio

PA: Physical Activity

PANAS: Positive and Negative Affect Schedule

PANAS-S and PANAS-T (State and Trait)

PCO_2: Partial Pressure of Carbon dioxide

PF: Physical Fitness

pH: Potential of Hydrogen

PO_2: Partial Pressure of Oxygen

PSI: Pregnancy Symptoms Inventory

RCT: Randomized Controlled Trial

SF-36: Short-Form 36 Health Survey

STAI: State Trait Anxiety Index

VAS: Visual Analogue Scale

VO_{2max}: Maximal oxygen intake

ABSTRACT [RESUMEN]

ABSTRACT

Background

Pregnancy is a physiological stage in a woman's life that involves adaptive changes in order to fulfill the demands of the growing new life. Therefore, the study of the effect of the mother's lifestyle, including being physically active, on certain maternal and fetal health markers becomes essential.

Physical fitness is considered a powerful health marker in different general populations (i.e., childhood, adulthood and elderly) and specific populations (i.e., women during perimenopause, people with fibromyalgia and other conditions). Consequently, physical fitness assessment is considered an important prevention and diagnosis tool. Likewise, physical activity and well-designed and adapted exercise programs during gestation means less risk of developing pregnancy-related complications or diseases.

Unfortunately, pregnant women do not meet the physical activity and exercise recommendations during pregnancy, including Spanish pregnant women.

Objectives

The **overall objective** of this International Doctoral Thesis was to assess the influence of physical fitness (i.e., objectively and self-reported measured) and a concurrent exercise intervention (i.e., combining aerobic and resistance training) during pregnancy with different maternal and fetal health markers.

Specifically, this present International Doctoral Thesis aimed to provide knowledge on:

i) The role of objective physical fitness levels during pregnancy on maternal body composition indices.

ii) The role of flexibility levels during early pregnancy on the need of oxytocin administration to induce or stimulate the labor, and the odd of cesarean section.

iii) The role of self-reported physical fitness (measured by the International FItness Scale) on pregnancy-related symptoms such as pain, psychological ill-being and emotional well-being and distress.

iv) The influence of a concurrent (i.e., combining aerobic and resistance training) exercise intervention during pregnancy on pregnancy-related symptoms, such as pain, disability due to pain and health-related quality of life.

Main findings

The **main results** of this Thesis suggest that greater objectively measured physical fitness in early and late pregnancy may promote a better body composition in the postpartum period (**Study I)**; lower flexibility levels at the 16th gestational weeks discriminates among pregnant women who will require oxytocin from those that will not, and with greater risk of cesarean section from those with a vaginal birth (**Study II**); greater self-reported overall physical fitness is associated with reduced bodily, lumbar and sciatic pain, and pain disability during pregnancy (**Study III**); greater self-reported overall physical fitness and its different components, especially cardiorespiratory fitness, have shown a strong relationship with lower incidence and limitations of the most common pregnancy-related symptoms, particularly tiredness-fatigue and poor sleep (**Study IV**); greater self-reported physical fitness is consistently associated with lower outcomes of psychological ill-being, and greater emotional well-being and lower emotional distress during pregnancy (**Studies V** and **VI**); a supervised concurrent exercise program may attenuate low-back and sciatic pain, and ameliorates health-related quality of life deterioration along pregnancy (**Studies VII** and **VIII**).

Conclusions

This International Doctoral Thesis provides evidence on **the positive impact of greater physical fitness levels on several pregnancy-related outcomes**, and highlights **the efficacy of being enrolled in a well-designed concurrent exercise program during pregnancy** as a strategy to provide a healthier and less risky gestational period. The use of physical fitness, especially self-reported physical fitness, is proposed as a clinical and practitioners tool to discriminate among pregnant women at risk of pregnancy-related complications. Health providers should promote and encourage pregnant women to be physically active during gestation.

Contexto

El **embarazo** es una etapa fisiológica en la vida de una mujer que implica cambios adaptativos para cumplir con las demandas de la nueva vida en crecimiento. Por lo tanto, el estudio del efecto del estilo de vida de la madre, incluida la actividad física, sobre ciertos marcadores de salud materna y fetal se vuelve esencial.

La **condición física** se considera un potente marcador de salud en diferentes poblaciones generales (es decir, niños, adultos y ancianos) y poblaciones específicas (es decir, mujeres durante la perimenopausia, personas con fibromialgia y otras afecciones). En consecuencia, la evaluación de la condición física se considera una importante herramienta de prevención y diagnóstico. Asimismo, la actividad física y los programas de ejercicio físico, bien diseñados y adaptados, durante la gestación implican un menor riesgo de desarrollar complicaciones o enfermedades relacionadas con el embarazo.

Desafortunadamente, las mujeres embarazadas no cumplen las recomendaciones de actividad física y ejercicio durante el embarazo, incluidas las embarazadas españolas.

Objetivos

El **objetivo general** de esta Tesis Doctoral Internacional fue evaluar la influencia de la condición física (es decir, medida objetivamente y auto-reportada) y una intervención de ejercicio físico concurrente (es decir, que combina entrenamiento aeróbico y de fuerza) durante el embarazo relacionado con diferentes marcadores de salud materna y fetal.

En concreto, la presente Tesis Doctoral Internacional tuvo como objetivo aportar conocimientos sobre:

i) El papel de los niveles objetivos de condición física durante el embarazo en los índices de composición corporal materna.

ii) El papel de los niveles de flexibilidad durante el embarazo temprano sobre la necesidad de administración de oxitocina para inducir o estimular el trabajo de parto y la probabilidad de cesárea.

iii) El papel de la condición física auto-reportada (medida con la Escala Internacional de Condición Física) sobre los síntomas relacionados con el embarazo, como el dolor, el malestar psicológico y el bienestar y la aflicción emocional.

iv) La influencia de una intervención de ejercicio físico concurrente (es decir, que combina entrenamiento aeróbico y de fuerza) durante el embarazo en los síntomas relacionados con el embarazo, como dolor, discapacidad por dolor y calidad de vida relacionada con la salud.

Principales hallazgos

Los principales resultados de esta Tesis Doctoral Internacional sugieren que una mayor condición física medida objetivamente al principio y al final del embarazo puede promover una mejor composición corporal en el período posparto (**Estudio I**); menores niveles de flexibilidad a las 16 semanas de gestación discrimina entre gestantes que requerirán oxitocina de aquellas que no, y con mayor riesgo de cesárea de aquellas con parto vaginal (**Estudio II**); una mayor condición física general auto-reportada se asocia con una reducción del dolor corporal, lumbar y ciático, y de la discapacidad por dolor durante el embarazo (**Estudio III**); una mayor condición física general auto-reportada y sus diferentes componentes, especialmente la capacidad cardiorrespiratoria, han mostrado una fuerte relación con una menor incidencia y limitaciones de los síntomas más comunes relacionados con el embarazo, particularmente cansancio-fatiga y falta de sueño (**Estudio IV**); una mayor condición física auto-reportada se asocia consistentemente con resultados más bajos de malestar psicológico, y mayor bienestar emocional y menor aflicción emocional durante el embarazo (**Estudios V** y **VI**); un programa de ejercicio físico concurrente supervisado puede atenuar el dolor lumbar y ciático, y mejora el deterioro de la calidad de vida relacionada con la salud durante el embarazo (**estudios VII** y **VIII**).

Conclusiones

Esta Tesis Doctoral Internacional proporciona evidencia sobre el **impacto positivo de mayores niveles de condición física en diferentes marcadores de salud relacionados con el embarazo** y destaca la **eficacia de estar inscrita en un programa de ejercicio físico concurrente, bien diseñado, durante el embarazo** como una estrategia para brindar un período gestacional más saludable y de menor riesgo. El uso de la condición física, especialmente la condición física auto-reportada, se propone como una herramienta clínica y de profesionales del ámbito para discriminar entre las mujeres embarazadas en riesgo de complicaciones relacionadas con el embarazo. Los promotores de salud deben fomentar y alentar a las mujeres embarazadas a realizar actividad física durante la gestación.

KEY CONCEPTS

KEY CONCEPTS

Physical fitness

Physical fitness (PF) is defined as "*a set of attributes or characteristics that people have or achieve that relates to the ability to perform physical activity (PA)*" [1]. More specifically, health-related physical fitness refers to those components of PF that relate to an individual's health status and that can be influenced by regular PA practice. It is defined as "*the state of physical and physiological characteristics that determine risk levels for the premature development of diseases or morbid conditions, usually related to a sedentary lifestyle*" [2].

The American College of Sport Medicine (ACSM) compiles the components of health-related PF as following: *cardiorespiratory fitness, musculoskeletal fitness* (related to muscular fitness and flexibility), *motor fitness*, and *body composition* [1] (see **Table 1**).

Table 1. Physical fitness components and definitions.

COMPONENT	DEFINITION
 ***Cardiorespiratory fitness***	**Cardiorespiratory fitness** refers to the ability of the circulatory and the respiratory systems to supply oxygen during sustained PA [1].
 ***Musculoskeletal fitness***	- **Musculoskeletal fitness** relates to the ability of the muscle to exert force [58]. - **Flexibility** is that component of PF which refers to the ability to move a joint through its full range of motion with ease [59].
 ***Motor fitness***	**Motor fitness** is considered as the performance aspect of PF in daily activities which requires quick reactions, speed of movement, agility, coordination and balance [3].
 ***Body composition***	**Body composition** refers to the relative amount or percentage of body tissues (bone content, fat mass, muscular mass), that are related to health. The most common health-related measure is the total body fat percentage (%BF) [1].

Abbreviations: %BF, Body Fat percentage; PA, Physical Activity; PF, Physical Fitness.

Physical Fitness Assessment

The PF levels can be evaluated both objectively, through laboratory tests and field tests, as well as self-reported, through questionnaires (see **Figure 2**), as shown below:

Objective physical fitness assessment

Laboratory test

Laboratory testing is an objective and accurate method of assessing PF, through reference criteria methods or *gold standard* [4]. However, due to the cost of sophisticated instruments, time constraints and the need for qualified technicians, laboratory testing is limited to sport clubs, schools, population-based studies, and offices or clinical settings.

Field-based test

Field-based PF testing can offer useful and practical alternatives as screening tools, since they are relatively safe and time-efficient, involve minimal equipment and low cost, and can be easily administered to multiple people simultaneously [5, 6]. Nonetheless, this option is not always available mainly due to time or space limitations, and the unlikelihood of being feasible in routine clinical practice.

Self-reported physical fitness

The International FItness Scale (IFIS) is a self-reported questionnaire that assesses the subject's perceived PF levels and has been suggested as a useful, quick, and inexpensive alternative to objectively measured PF assessment [7] (see **Table 2**).

Several researchers have recommended the use of both objective and subjective measures of PF because it can provide information about overestimation or unreal PF levels [8]. Even so, The IFIS has shown acceptable construct discriminant validity and reliability in different populations including children [9], adolescents [10], young [7] and older adults [11], and women with fibromyalgia [12]. Furthermore, the IFIS scale has been validated in pregnant women [13].

Consequently, the IFIS scale could provide health professionals with valuable information on the health of the general population as well as of the pregnant woman.

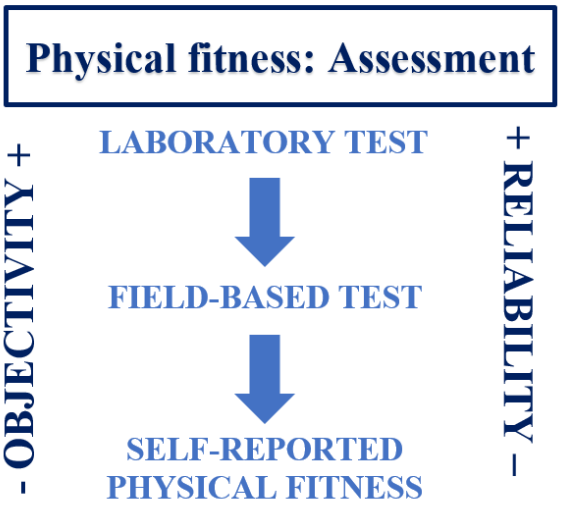

Figure 2. Types of physical fitness assessment.

Table 2. The International FItness Scale (IFIS).

My general physical fitness is:	
Very poor (1)	☐
Poor (2)	☐
Average (3)	☐
Good (4)	☐
Very good (5)	☐
My cardiorespiratory fitness:	
Very poor (1)	☐
Poor (2)	☐
Average (3)	☐
Good (4)	☐
Very good (5)	☐
My muscular strength is:	
Very poor (1)	☐
Poor (2)	☐
Average (3)	☐
Good (4)	☐
Very good (5)	☐
My speed / agility is:	
Very poor (1)	☐
Poor (2)	☐
Average (3)	☐
Good (4)	☐
Very good (5)	☐
My flexibility is:	
Very poor (1)	☐
Poor (2)	☐
Average (3)	☐
Good (4)	☐
Very good (5)	☐

Physical Exercise

Exercise is defined as any PA consisting of planned, structured, and repetitive bodily movements done to improve one or more components of PF [14], being an essential element of a healthy lifestyle.

GENERAL INTRODUCTION

Conspectus of pregnancy

During pregnancy, women undergo continuous adaptive changes, in all spheres, not only from an anatomical-physiological point of view but also in their psychological-social lives. Therefore, knowledge of these changes is essential to ensure a healthy and pleasant pregnancy period.

Main changes in body system

Cardiovascular

Most cardiovascular changes occur early in pregnancy. A reduction in systemic and pulmonary vascular resistance occurs in response to increased circulating levels of progesterone, oestrogen and prostaglandins [15].

During 16th-24th gestational weeks (g.w.) there is an increases in stroke volume peak. Cardiac output gradually increases, eventually by up to 30-50% during the third trimester. The increase in cardiac output is as a result of an increase in heart rate and stroke volume, secondary to ventricular hypertrophy and increased end diastolic volume [15].

In early pregnancy there is a transient reduction in blood pressure, with an amplification of the pulse pressure, since the diastolic pressure is affected more significantly than the systolic pressure [15].

As the pregnancy progresses, diaphragmatic elevation leads to displacement of the heart up and to the left. This can cause electrocardiogram changes, such as left axis deviation and T wave inversion in the lateral leads and lead III. Although these changes are not clinically significant, they may mask other changes secondary to pathological processes. The increase in heart rate necessary to maintain the increased cardiac output may present as sinus tachycardia and may predispose to tachyarrhythmias [15].

Around the 20th g.w. aorto-caval compression by the gravid uterus in the supine position can lead to profound hypotension. Compression of the inferior vena cava produces a reduction in preload resulting in cardiac output [15].

Bone metabolism

During pregnancy and postpartum period, major changes occur in the maternal calcium homeostasis and bone metabolism in order to fulfil the demand of calcium to the fetus and the breastfeeding.

Despite the conflicting reports on bone density changes in pregnancy, it appears to decreases in response to the transfer of calcium to the fetus in combination with decreased renal calcium reabsorption [16], as a compensation, the intestinal calcium absorption is increased caused by high 1,25-dihydroxyvitamin D levels [17].

Endocrine changes

Many of the physiological adaptations of pregnancy are due to the increase in circulating reproductive hormones, such as estrogen and progesterone [15]. In addition, the placenta secretes hormones such as relaxin, human placental lactogen, and human chorionic gonadotropin that contribute to changes in various body systems.

Relaxin is responsible for allowing increased joint laxity during pregnancy and its levels arise in the third trimester in order to prepare the body for birth [18]. Likewise, progesterone also contributes to increased joint laxity during pregnancy [18].

Pregnancy is defined as a "diabetogenic" state. Insulin resistance, secondary to placental secretion of human placental lactogen, can result in gestational diabetes [15, 19]. Moreover, pancreatic β cells suffer hyperplasia during pregnancy, resulting in greater insulin production, which leads to fasting hypoglycemia and postprandial hyperglycemia [19].

Secretion of corticosteroid hormones increased by 30% during pregnancy by the zona fasciculata of the adrenal gland [19]. This increase in cortisol can further contribute to the development of insulin resistance and can also produce changes in skin pigmentation [15].

Leptin regulate food intake, energy expenditure, and body mass accumulations [20]. Leptin during pregnancy is also produced by the placenta.

Biomechanical changes

Changes in posture are naturally developed in order to accommodate the growing fetus, resulting also in some gait alterations and body pain.

The gravid uterus moves the center of gravity forward, increasing lumbar lordosis. Mainly due to the effects of hormones (such as relaxin) to prepare ligaments and joints for birth, may exist axial and appendicular musculoskeletal complaints by compressing or loosening joints [21]. Moreover, there is an increased joint loads (up to 100%) by an increase in the laxity of passive restraints in the pelvis, feet, and other joints [22].

The rib cage expands laterally at 10-15 cm to accommodate the expansion uterus and at the same time preserve the lung function, accompanied by an increase in the subcostal angle and the stretch of the abdominal and intercostal muscles [21].

Changes in spinal curvatures include cervical kyphosis, an exaggerated thoracic kyphosis (due to increased breast tissue) and an increased lumbar lordosis [23].

The pectoral muscles shorten in response to these postural changes, exacerbating depression and rounding of the shoulders [21].

As a result of the increased posterior muscular demands and abdominal mass effect, the flexibility of the transversus abdominis, abdominal oblique, and rectus abdominis muscles increases [21]. Moreover, the linea alba usually stretches and muscle fibers separate [21]. Diastasis recti may begin in the second trimester and typically peaks during the third trimester [21]. At 30^{th} g.w. there is an average separation of 3.4 cm, being even greater at 38^{th} g.w., associated with a deteriorated pelvic stabilization [24].

The anterior pelvic tilt increases during pregnancy to compensate for an increased and displaced anterior body mass, as well as to allow for greater lung capacity, counteracting the expanding mass below the diaphragm [21]. Likewise, the hip abductor and extensor muscles, as well as the ankle plantar flexor muscles, play an important role stabilizing the posture to avoid falling forward [21].

As the center of mass moves anteriorly with increasing uterine mass, the knees must compensate to help maintain upright posture. This is accomplished by hyperextension that can progress to genu recurvatum [21]. The hips also adapt to maintain upright posture, and redistribute weight to increase stability.

Body weight changes

Maternal body composition changes during pregnancy to support healthy development of the fetus. During normal gestation women experiment and increment in usual body weight. The physiological components that contribute to the total gestational weight gains (GWG) are distributed into products of conception: fetus, placenta, and amniotic fluid; and accumulation of maternal tissue: uterine tissue, breast tissue, expansion of blood and plasma volume, and fetus [25]. Therefore, the mean GWG for primiparous women is approximately 12.5 kg, including 3 kg of fat accumulation, suggesting that it supports the increased energy demands during pregnancy lactation [25]. This GWG is distributed at approximately 0.45 kg per week during the second trimester and 0.40 kg per week during the third trimester, according to the report *Nutrition During Pregnancy* (1990) [26]. However, recent studies have indicated higher rates of GWG, especially during second trimester, although pattern of GWG can vary depending on maternal ethnicity and age [26].

Renal and urinary system changes

During pregnancy, several changes occur in the renal system. Kidney size increases by 1 cm at the end of pregnancy, as a result of the increase in vasculature and plasma volume and the renal calyces and ureters are dilated in more than 80% of pregnant women by mid-pregnancy and, more commonly, on the right side [15, 19].

There exists a state of hyperfiltration of the kidneys, with increased effective renal plasma flow around 80% at the end of the first trimester as a result of massive vasodilation from relaxin-mediated nitric oxide release [15, 19]. In early pregnancy there is an increase in urinary frequency and urgency, due to changes in glomerular filtration rate and effective renal plasma flow [15]. The effective renal plasma flow declines during late pregnancy, although frequency and urgency are still present due to the physical compression of the bladder by the growing uterus and fetus.

Water and sodium regulation is also altered during pregnancy. The resistance to the effects of the pressor contributes to a more substantial increase in extracellular volume together with water and sodium retention. In addition, the body retains sodium despite the increase in filtration by the kidneys [15, 19].

Respiratory changes

The diaphragm undergoes an upward displacement as a result of the growing gravid uterus, leading to a decrease in functional residual capacity [15, 19]. This is causes not only from a mechanical perspective but also as hormonal consequence, since progesterone and relaxin induce relaxation to the ligamentous attachments of the lower ribs [15, 19]. In fact, the transverse diameter of the rib cage increases by 2 cm during pregnancy, the chest wall compliance decreases by the third trimester due to increased abdominal content, and the lung compliance remains the same [15]. Functional residual capacity decreases by 20% to 30% during pregnancy, as a result of the elevation of the diaphragm that decreases the decline out of the chest. The inspiratory capacity (maximum inhaled volume of functional residual capacity) increases by 10%, but the total lung capacity remains the same [15, 19].

Increasing progesterone during pregnancy induces important changes in the respiratory system, such as increased sensitivity to carbon dioxide, with changes in the slope of the ventilation curve in response to the changes in alveolar carbon dioxide [15]. On the other hand, estrogen regulates progesterone receptors in the central nervous system, respiratory control center, particularly in the medulla and hypothalamus [15, 19].

During pregnancy there is a state of respiratory alkalosis, with maternal pH ranging between 7.42–7.46 [15, 19]. There is an increase in ventilation, with changes in arterial blood gases [19]. The PaO_2-$PaCO_2$ ratio is altered, with a latter decrease in favor of the CO_2 of the fetus to be transferred to the mother [15, 19]. Furthermore, the respiratory alkalosis would change the oxyhemoglobin curve to the right, which facilitates the oxygen diffusion across the placenta [15, 19].

Main changes in well-being perceptions

Behavioral changes

Most changes in women behavior during pregnancy may be influenced by external recognition of "socially accepted conduct". For instance, women may experience social pressure to outwardly demonstrate their commitment to their pregnancy by restructuring their lifestyle, such as eating healthily or reducing alcohol and smoke consumption [27]. Here plays a role the "social support", since pregnant women seek or receive lay advice from friends, family or health providers, or information or guidance from websites or books, for example, reporting "information overload", especially during early pregnancy [28].

These behavioral changes (added to those produced by physical changes) may induce some well-being alterations, such as greater predisposition to depression, anxiety and stress, fatigue and sleep deprivation, mood swings, affecting also activity patterns and energy expenditure, dietary intake or body weight [20, 29].

A visual summary of the main anatomical-physiological and psychological-social changes that take place during pregnancy is shown below (see **Figure 1**):

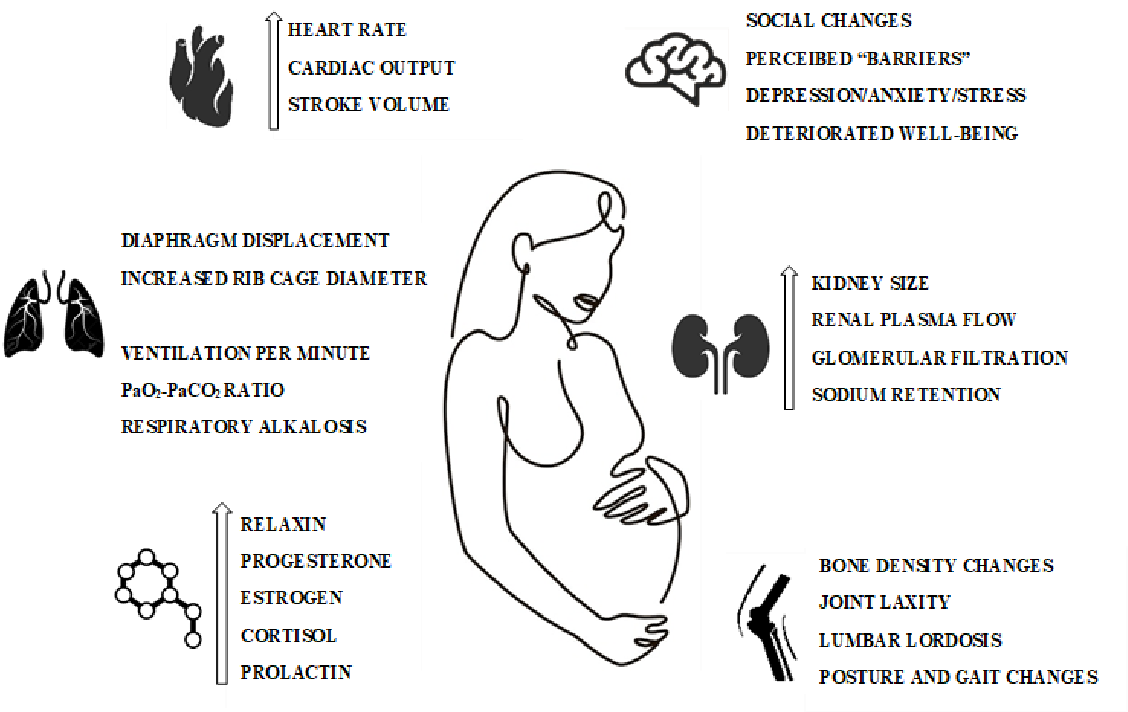

Figure 1. Main anatomical-physiological and psychological-social changes taking place during pregnancy.

Early life programming

Nowadays, emerging evidence postulates that lifestyle factors, such as PA and nutrition, are modulators of risk on non-communicable diseases [30]. In this sense, prevention and management strategies, including individual lifestyle strategies, are globally targeted actions to address this health burden [30]. Most non-communicable diseases are the result of various factors, including genetic, physiological, behavioral, and environmental factors [31]. Following this recognition, new insight about the relationship between the early environment and future disease development is arising, proposing a link between fetal development and the risk of non-communicable diseases in adulthood, especially cardiovascular diseases [32].

This early environment refers to the fetal placental period which is a crucial time that determinate an accurate organogenesis which irreversibly establishes tissue structures, cell distribution, endocrine systems and metabolic activity (i.e. epigenetic programming) [33]. During this process, an organism not only responds to current environmental conditions, but also uses that information to predict future environmental conditions [34]. Therefore, the earliest periods of development in the fetal and infancy period provide indications of the most likely future conditions at a time when there is the greatest degree of developmental plasticity [33].

Thus, "*fetal programming*" or "*early life programming*" refers to the way in which the influence of a specific environmental factor at a specific point may alter the course of fetal development, resulting in lasting modifications in the structure and function of biological systems [33].

The epigenetic programming of fetal development is extremely complex, but it appears that certain exposures can alter epigenetic programming. One the most explored epigenetic processes is the DNA methylation and histone modification, which play a fundamental role in the differentiation of cell structure and function during embryogenesis [35]. Likewise, the early development of the hypothalamic-pituitary-adrenal system, which is also related to the maturation of other systems responsible for the regulation of circadian rhythms, physical growth, and the integration of limbic-cortical processes is also of interest since it plays a role in emotions and stress regulation, or sleep and feeding [36]. In this sense, a dysregulation in the hypothalamic-pituitary-adrenal system response may contribute to postnatal problems, such as elevated stress or altered circadian rhythm [33].

The link between the mother and the fetus is the placenta. Therefore, the impact of such interactions between lifestyle factors and fetal development is explained through maternal and placental mechanisms, such as vascular and metabolic pathways, epigenetic changes in response to blood-borne factors that cross the placenta, or fetal counter-regulatory responses to exposures (such as altered blood glucose or lipid ratios), and activation of hormonal signaling molecules (such as leptin) [33].

Although the effects of lifestyle factors on *early life programming* are complex and need further elucidation, evidence on this maternal pregnancy and pre-pregnancy influence is increasing and, therefore, would become a modifiable target for prevention intervention.

Physically active pregnancy

A healthy lifestyle during pregnancy has becoming a matter of interest due to important implications not only for the mother but also for the fetus health [37]. As stated above, lifestyle factors, such as exercise and nutrition, as well as maternal mental health, are intrinsically related to the fetal environment or *early life programming* [33]. In this sense, being physically active during this period may play a key role [38-40].

Thus, an increase in PA levels or being enrolled in adapted physical exercise during pregnancy promote benefits for both the mother and the fetus [41]. Greater PA levels, or to practice physical exercise decrease the risk of developing some complications or diseases associated with pregnancy, such as excessive GWG [42], cesarean deliveries [43], gestational diabetes [44] and preeclampsia [45] and back and sciatic pain [46]. In fact, the main international guidelines for PA and exercise recommendations during pregnancy, such as the American College of Obstetricians and Gynecologists (ACOG) [47], or the Canadian guideline for PA throughout pregnancy [48], recommend performing at least 30 minutes of moderate-vigorous PA most days of the week. Unfortunately, despite the positive effects of PA and exercise on maternal-fetal outcomes, pregnant women do not meet these guidelines, being this 10% in many countries [49], including Spain [50]. In fact, maternal levels of PA may decline during pregnancy as a result of the significant changes related to pregnancy, such as anatomical, physiological [34], and social and psychological factors [29], contributing to some perceived barriers to being physically active, such as the thinking that resting during pregnancy is the safest behavior [51, 52].

The pregnancy related-pain, whether general bodily, lumbar or sciatic, can be so unbearable that it limits the daily activities of the women who suffer from it [53, 54], having to resort to painkillers, some of which are contraindicated or restricted during pregnancy [55]. Moreover, this fact may affect their quality of life by interfering with mental, physical and social activities [56]. Additionally, people suffering from pain appear to be at increased risk of developing comorbidities, such as obesity, depression/anxiety, and early mortality [56, 57]. Likewise, during pregnancy an association has been found between pain and disability, reduced quality of life, higher prevalence of sick leave and risk of postpartum depression [46, 58].

On the other hand, it has been seen that greater PF levels (as a result of the practice of PA or exercise) can imply a decrease in pain during pregnancy [46, 59]. In addition, observational studies have shown the protective effects of PA before pregnancy on the prevention of low back pain [54, 60]. However, it is not known exactly which components of PF are individually associated with less pain in general or during pregnancy [53, 61].

Nowadays, it is well-known that exercise offers an extraordinary potential as therapeutic interventions, being postulated as the real *polypill* [62], with no further side effects (versus traditional pharmacological therapies) in the treatment of certain pathologies [63].

During pregnancy, the role of exercise has not been completely well understood to date. Therefore, traditionally, pregnant women were advised to increase their energy intake and avoid exercise due to concerns regarding fetal risk [64].

Fortunately, growing evidence suggests that physical exercise training during pregnancy might provide beneficial health effects on the mother and fetus (and ulterior newborn) without side effects [65, 66]. For instance, on the mother, exercise during gestation prevents diastasis recti abdominis [67], incidence of cesareans [68], reduce the need for insulin in overweight pregnant with gestational diabetes mellitus [69]. Likewise, maternal exercise may have benefits on the newborn, such as higher neurodevelopment [70, 71], better heart functioning, improved heart rate variability [72], and less body fat [70]. In addition, exercise may improve the pregnant quality of life and reduce stress [73-75], which might protect the fetus [76].

Consequently, it is recommended that primary medical care take PF into account and promote to be physically active during pregnancy to positively influence the pregnancy course, improving maternal-fetal health [77, 78]. Likewise, exercise programs should be proposed as therapeutic intervention to achieve a healthy gestational period.

A physical exercise program for pregnant women

The most specialized and updates guidelines during pregnancy recommend to be enrolled in an exercise program to ensure a healthier pregnancy course and postpartum period [47]. Some of these recommendations include [47]:

- *Women with uncomplicated pregnancies should be encouraged to engage in aerobic and strength conditioning exercises before, during, and after pregnancy.*

- *An exercise program that leads to an eventual goal of moderate-intensity exercise for at least 20–30 minutes per day on most or all days of the week should be developed with the patient and adjusted as medically indicated.*

- *Although an upper level of safe exercise intensity has not been established, women who were regular exercisers before pregnancy and who have uncomplicated, healthy pregnancies should be able to engage in high-intensity exercise programs […].*

However, as cited also by The American College of Obstetricians and Gynecologist: *Additional research is needed to study the effects of exercise on pregnancy-specific conditions and outcomes and to clarify further effective behavioral counseling methods and the optimal type, frequency, and intensity of exercise* [47]. In fact, it is unknown the extent to which supervised exercise programs might improve maternal-fetal physiological and psychological health.

Moreover, despite findings derived from systematic reviews have demonstrated that combining aerobic exercise and resistance training during pregnancy was more effective at improving health outcomes than interventions focused on aerobic exercise alone [48], still most of exercise programs conducted in pregnant women are performed at light-to-moderate exercise intensity, or are based on solely aerobic or strength training.

Therefore, to evaluate the influence of a novel supervised and adapted concurrent (i.e., combining aerobic and resistance training) exercise training program on maternal and fetal health.

Gaps addressed in this International Doctoral Thesis

We identified 4 gaps in this current scientific knowledge that are addressed by the studies included in this thesis book. **Table 3** briefly describes these gaps, together with the contributions of this thesis book.

Table 3. Summary of gaps addressed in this International Doctoral Thesis.

GAP			CONTRIBUTION
CHAPTER I	a	It has not been investigated whether greater PF levels during pregnancy have a positive impact on maternal body composition indices.	Longitudinal study on objectively measured PF in early and late pregnancy related to maternal body composition indices (during pregnancy and postpartum period): **Study I**.
	b	It has not been investigated whether flexibility levels during early pregnancy is associated with the need of oxytocin administration to induce or stimulate labor, and cesarean section.	Longitudinal study on objectively measured flexibility in early pregnancy may predict the need of oxytocin administration during labor, and risk of caesarean: **Study II.**
CHAPTER II	c	It has not been explored whether self-reported PF (measured by the IFIS) is associated with pregnancy-related symptoms, such as pain, psychological ill-being and emotional well-being and distress.	Cross-sectional and longitudinal studies on self-reported PF levels, pregnancy-related symptoms, pain, psychological ill-being and emotional well-being and distress throughout gestation: **Studies III-VI.**
CHAPTER III	d	It has not been investigated whether a concurrent (i.e., combining aerobic and resistance training) exercise intervention during pregnancy is effective on pregnancy-related symptoms such as pain, disability related to pain, and health-related quality of life.	Investigation of the effects of a novel supervised and adapted concurrent exercise training program during pregnancy on pregnancy-related symptoms and health-related quality of life: **Studies VII-VIII.**

Abbreviations: PF, Physical Fitness; IFIS, International FItness Scale.

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AIMS [OBJETIVOS]

AIMS

The **overall aim** of the present Doctoral International Thesis was to assess the influence of physical fitness (i.e., objectively and self-reported measured) and a concurrent (i.e., combining aerobic and resistance training) exercise intervention during pregnancy with different maternal and fetal health markers, on the framed of the GESTAFIT Project (PI-0395-2016). In addition, other related associations were explored.

The **specific aims** of the present International Doctoral Thesis are in eight specific aims (i.e., eight studies):

- **CHAPTER I.** Objectively measured physical fitness during pregnancy and body composition and birth-related outcomes (*studies I-II*).

  Study I: to study the association of physical fitness during pregnancy with gestational weight gain and maternal body fat and bone mineral density in postpartum period.

  Study II: i) to identify whether flexibility levels during the early second trimester of pregnancy may predict the need of oxytocin administration to induce or stimulate labor, and the type of birth (i.e. vaginal or caesarean section); ii) to establish Back-scratch test cut-off points able to improve the accuracy of the need of oxytocin administration and the prognosis of caesarean section to be proposed as a clinician tool.

- **CHAPTER II.** Self-reported physical fitness during pregnancy and perinatal physical and mental health outcomes (*studies III-VI*).

  Study III: to analyze the association of self-reported physical fitness, and its different components, with bodily, lumbar and sciatic pain, and pain disability, during the early second trimester of pregnancy (16^{th} gestational weeks) and late pregnancy (34^{th} gestational weeks).

  Study IV: to analyze the association of self-reported physical fitness level with pregnancy-related symptoms, and its limitations on activities of daily living along pregnancy.

  Study V: to study the association of self-reported physical fitness with depressive symptoms and anxiety levels during the pregnancy course.

Study VI: to explore the association of self-reported physical fitness with emotional well-being and emotional distress along the pregnancy course (i.e., 16th and 34th gestational weeks).

Chapter III. The influence of the "GESTAFIT" concurrent exercise training protocol on pain and health-related quality of life (*study VII*).

Study VII: to explore the influence of a concurrent exercise training program from 17th gestational weeks until birth on low back and sciatic pain, and pain disability at late pregnancy (34th gestational weeks).

Study VIII: to evaluate the influence of a supervised and adapted concurrent exercise training program on health-related quality of life throughout pregnancy (i.e., from 17th gestational weeks until birth).

OBJETIVOS

El **objetivo general** de esta Tesis Doctoral Internacional fue evaluar la influencia de la condición física (es decir, medida objetivamente y auto-reportada) y una intervención de ejercicio físico concurrente (es decir, que combina entrenamiento aeróbico y de fuerza) durante el embarazo relacionado con diferentes marcadores de salud materna y fetal, en el marco del proyecto GESTAFIT (PI-0395-2016). Además, se exploraron otras asociaciones relacionadas.

Los **objetivos específicos** de la presente Tesis Doctoral Internacional se concretan en ocho objetivos específicos (es decir, ocho estudios):

- **CAPÍTULO I.** Condición física medida objetivamente durante el embarazo y composición corporal y resultados relacionados con el nacimiento (*estudios I-II*).

  Estudio I: estudiar la asociación de la condición física durante el embarazo con el aumento de peso gestacional y la grasa corporal materna y la densidad mineral ósea en el período posparto.

  Estudio II: i) identificar si los niveles de flexibilidad durante las primeras etapas del segundo trimestre del embarazo pueden predecir la necesidad de administración de oxitocina para inducir o estimular el parto, así como el tipo de parto (es decir, vía vaginal o mediante cesárea); ii) establecer puntos de corte del test Back-scratch capaces de mejorar la precisión de la necesidad de administración de oxitocina y el pronóstico de cesárea para su propuesta como herramienta clínica.

- **CAPITULO II.** Condición física auto-reportada durante el embarazo y resultados perinatales de salud física y mental (*estudios III-VI*).

  Estudio III: analizar la asociación de la condición física auto-reportada y sus diferentes componentes con el dolor corporal, lumbar y ciático, y la discapacidad por dolor, durante el inicio del segundo trimestre del embarazo (semana 16 de gestación) y al final del embarazo (semana 34 de gestación).

  Estudio IV: analizar la asociación del nivel de condición física auto-reportada con los síntomas relacionados con el embarazo y sus limitaciones en las actividades de la vida diaria durante el embarazo.

  Estudio V: estudiar la asociación de la condición física auto-reportada con los síntomas depresivos y los niveles de ansiedad durante el curso del embarazo.

Estudio VI: explorar la asociación de la condición física auto-reportada con el bienestar emocional y la angustia emocional a lo largo del curso del embarazo (es decir, semanas 16 y 34 de gestación).

CAPÍTULO III. Influencia del protocolo de entrenamiento concurrente "GESTAFIT" sobre el dolor y la calidad de vida relacionada con la salud (*estudios VII-VIII*).

Estudio VII: explorar la influencia de un programa de entrenamiento concurrente desde la semana 17 de gestación hasta el nacimiento sobre el dolor lumbar y ciático, y la discapacidad por dolor al final del embarazo (semana 34 de gestación).

Estudio VIII: evaluar la influencia de un programa de entrenamiento concurrente supervisado y adaptado en la calidad de vida relacionada con la salud durante el embarazo (es decir, desde la semana 17 de gestación hasta el nacimiento).

METHODS

The present Doctoral International Thesis is composed of eight studies. **Chapter I** is focused on objectively measured PF (*studies I-II*), **Chapter II** is focused on self-reported PF (*studies III-VI*), and **Chapter III** is focused on a physical exercise program conducted on pregnant women (*studies VII-VIII*). All these parts address knowledge gaps under the framework of the GESTAFIT Project.

Study design and population

The GESTAFIT Project was initially designed as a randomized controlled trial which was carried out in Granada (southern Spain) between November 2015 and April 2018 (Identifier: NCT02582567) [1]. The main aim of the GESTAFIT Project was to evaluate the effects of a supervised concurrent exercise intervention (*aerobic* + *resistance*) on maternal and fetal health.

The study was carried out at the "Sport and Health University Research Institute", and at the "San Cecilio and Virgen de las Nieves University Hospitals" (Granada, Spain). This project was approved by the Clinical Research Ethics Committee of Granada, Government of Andalusia, Spain (code: GESFIT-0448-N-15).

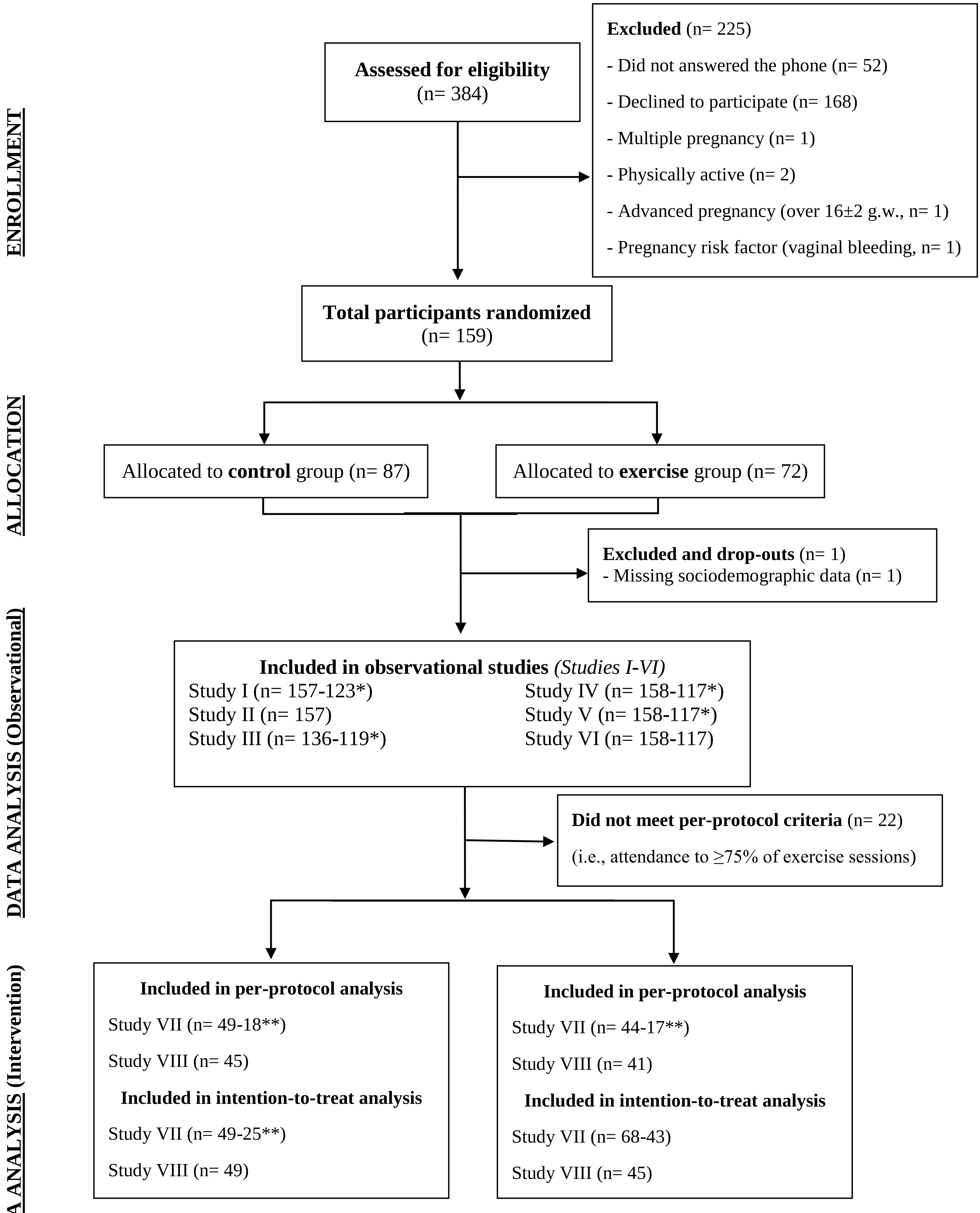
The inclusion and exclusion criteria are detailed in **Table 4**. Briefly, women aged 20-40 years with a normal pregnancy course, and giving birth (singleton) at 37-42th g.w. via spontaneous/vaginal birth, or cesarean section without severe maternal-fetal pathology were included.

Table 4. Inclusion and exclusion criteria in the GESTAFIT Project.

Inclusion criteria
- Pregnant women 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.
Exclusion criteria
- Having acute or terminal illness.
- Having malnutrition.
- Being unable to conduct tests for assessing physical fitness or exercise during pregnancy.
- Having pregnancy risk factors (such as hypertension, type 2 diabetes, etc.).
- Having a multiple pregnancy.
- Having chromosopathy or fetal malformations.
- Having uterine growth restriction.
- Having fetal death.
- Having upper or lower extremity fracture in the past 3 months.
- Suffering neuromuscular disease or presence of drugs affecting neuromuscular function.
- Being registered in another exercise program.
- Performing more than 300 minutes of at least moderate physical activity per week.
-Being engaged in another physical exercise program
- Being unwilling either to complete the study requirements or to be randomized into the control or intervention group*.

**The randomized component was not possible in all the waves of participants due to some difficulties related to the adherence of control women to the intervention.*

Three hundred and eighty-four pregnant women attended their first gynecological visit at the hospital at the 12^{th} g.w. and were informed about the study's aims and procedures. Among them, a total of 159 women were recruited after showing interest in joining the study (see **Figure 3**). All participants signed a written personal informed consent.



**Sample size flow at 16th and 34th gestational weeks. **Less sample size because missing data in some questionnaires.*

Figure 3. Flow-chart of the GESTAFIT Project, distributed by specific study aim.

Sample size calculation

The sample size was estimated based on the change in maternal body weight. The difference in weight-gain changes (between the control and exercise group) from Ruiz et al. [2] as the expected effect size was employed. Thus, to detect a mean difference of 1.04 and standard deviation of 1.15 kg in the weight-gain change with a 90% of statistical power and α=0.05, a total of 52 women (i.e., 26 per group) were necessary.

Randomization and blinding

The study was conducted in three waves for feasibility reasons. In order to allocate participants into the control or exercise group, a computer-generated simple randomization sequence was used (before participants enrolled in the intervention). Nevertheless, the randomized component needed to be broken in the second and third waves to ensure enough adherence to the program; which represents a frequent methodological barrier in antenatal exercise research [3]. Thus, half the women were not randomized but allocated to the control/exercise group according to their personal convenience. Consequently, the GESTAFIT Project was finally characterized by a quasi-experimental design. All the research team personnel were blinded to their allocation into the control/exercise group, excepting those responsible for the training sessions.

Exercise intervention

The exercise intervention consisted of a concurrent supervised-tailored exercise program (from 17th g.w. until birth, 3 days/week, 60 minutes/session) of aerobic and resistance exercises of moderate-to-vigorous (mostly moderate with peaks of vigorous) intensity.

The exercise training program was designed following the standards by the ACOG [4], and the latest scientific evidence [5, 6].

Sessions consisted of a 10-minute warm-up, plus a 40-minute muscular (circuits of resistance exercises and short aerobic blocks) or aerobic block (dance or functional circuits), and finishing with a 10-minute cool-down. Resistance exercises involved anterior and posterior chain dominant, pull, push, and core exercises.

The exercise group started with an informative and movement learning phase (3 sessions): in this **initial phase**, fundamental basic movement patterns were taught (hip and knee dominant, pull and push movements), and theoretical explanations were provided to the participants. Subsequently, the **main exercise training phase** lasted from the 18th until 34th g.w., and was focused on improving or maintaining PF. The **final phase** during the last weeks of pregnancy was focused on the pelvic mobilization (preparation for the birth).

Each exercise session included a **10-min warm-up period** with walks, mobility and activation exercises. The **main part** of the first and last weekly sessions consisted of 40 minutes of exercises organized in two resistance circuits of 15 exercises (40” work/20” rest), alternating with cardiovascular blocks (concurrent training). The second session of the week was focused on aerobic training through dancing, proprioceptive and coordinative circuits, and interval walks. The sessions finished with a **10-min cool-down period** of stretching, breathing, relaxation and myofascial relief [7] (see **Table 5**).

Table 5. Exercise Intervention Protocol conducted on the GESTAFIT Project.

SESION STRUCTURE	CONTENT										
WARM-UP 10 minutes	**Joint mobility and different walk modalities**										
CONDITIONING 40 minutes	**Training week**	**1**	**2-4**	**5-6**	**7-8**	**9-10**	**11-12**	**13-14**	**15-16**	**17-18**	**> 19**
	Gestational week	**17**	**18-20**	**21-22**	**23-24**	**25-26**	**27-28**	**29-30**	**31-32**	**33-34**	**>34**
	Intensity (RPE)		12-13	12-13	13-14	13-14	14-15	14-15	15-16	15-16	
	Monday **CIRCUIT** (muscular and cardiovascular blocks)	Familiarization and acquisition of the basic movement patterns	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	Pelvic movements + integration pattern. Real transfer to birth moment
	Wednesday (cardiovascular block)	Familiarization and acquisition of the basic movement patterns	**Choreographies and aerobic exercises**								Pelvic movements + integration pattern. Real transfer to birth moment
	Friday **CIRCUIT** (muscular and cardiovascular blocks)	Familiarization and acquisition of the basic movement patterns	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	5 RE x 3 1min REST 1 AE 5’ 1min REST 5RE x3 1AE 5’ 1min REST	Pelvic movements + integration pattern. Real transfer to birth moment
COOL-DOWN 10 minutes	**Myofascial release, stretching and relaxation exercises**										

Abbreviations: RPE, rating of perceived exertion; RE, resistance exercise; AE, aerobic exercise; REST, resting; The load will be gradually and individualized increased for each participant to reach the intensity designed for each session.

The intensity of exercises was set at moderate according to the women's perceived effort within the range of 12 to 16 on the Borg scale of perceived exertion ranging from 6 (light effort) to 20 (heavy effort) (see **Figure 4**) [8]. The training sessions were supervised by an experienced exercise specialist. The attendance of the participants to the exercise sessions was recorded to measure adherence to the exercise program.

Rating of Perceived Exertion (RPE) Category Scale	
6	
7	Very, very light
8	
9	Very light
10	
11	Fairly light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Very, very hard
20	

Figure 4. Borg Scale [8].

Control group

Pregnant women allocated into the control group did not participate in the training sessions and were asked to continue with their usual activities. For ethical reasons, the research team held 7 lectures to pregnant women from both groups (exercise and control group) during the duration of the intervention about: 1) the benefits of physical exercise for a better pregnancy, prevention and treatment of cardiovascular diseases and excessive weight gain; 2) ergonomic advises, exercises to perform at home and strategies to increase their daily PA levels; 3) the benefits of the Mediterranean Diet and nutritional education during pregnancy; 4) how to avoid toxics and chemicals during the pregnancy and breastfeeding; 5) pregnancy, postpartum and sex; 6) physical and mental preparation for the birth, what to expect; 7) nutritional education towards breastfeeding. We also used these conferences to maintain control group fidelity until the end of the program.

General procedures

A brief description of the procedures from the GESTAFIT Project which are used in the present Thesis is presented below. More details on all the evaluations conducted can be found elsewhere [1].

Women were evaluated at several time points during pregnancy and postpartum by trained researchers:

- At the 16th and 34th g.w. (2 days/assessment).
- At birth (2 days/assessment),
- And at the early postpartum (i.e., 6 weeks after giving birth) (1 day/assessment).

The general procedures of the GESTAFIT Project are presented in **Figure 5**. At the 16th g.w. sociodemographic and clinical characteristics were assessed with an initial anamnesis. Other questionnaires were also employed to collect self-reported PF and health information related to pain, pregnancy-related symptoms, depressive symptoms and anxiety, or health-related quality of life (HRQoL), among others. Additionally, anthropometrics and objectively measured PF were assessed. Before leaving, participants were given accelerometers (along with a diary to daily report in bed time, water activities, etc.) to wear until the following appointment. At the 17th g.w., the accelerometers along with the diaries were returned, and maternal blood was extracted by a trained nurse.

After the baseline assessment, the exercise intervention was initiated and performed until birth. At the 33rd-34th g.w., the same assessments were performed with identical timing.

After birth, umbilical cord blood samples (from artery and vein) were gathered by midwives, and the placenta and perinatal obstetrics records were collected.

Subsequently (one day after birth), the colostrum was obtained from mothers at the hospital. At the 6th week after giving birth, the mature milk from mothers was collected, maternal and neonatal buccal mucosa cells were extracted, and anthropometrics, body composition, sleep, diet quality, and objective and self-reported PF were evaluated.

Measurements

Sociodemographic and clinical data

Sociodemographic data, including age, number of children, marital status and educational level; and clinical data, including consumption of drugs, such as analgesics or anti-inflammatories (yes/no), or other medication (yes/no) to treat pain during the previous 4 weeks. Illness diagnoses (yes/no) related to pain were also reported, including chronic cervical and lumbar backache, and migraine diagnosis or frequent headache, maternal depression or anxiety diagnosis, abortions and lactation options (exclusive breastfeeding, mixed feeding or formula feeding) were collected.

Body composition indices

Pre-pregnancy body weight was self-reported. On the first and second evaluations, body weight and height were assessed using a scale (InBody R20; Biospace, Seoul, Korea) and a stadiometer (Seca 22, Hamburg, Germany), respectively. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m2), including pre-pregnancy BMI. Moreover, GWG (kg) was calculated as the weight at the 34th g.w. minus weight at the 16th g.w. At the postpartum evaluation, total lean mass, fat mass, fat free mass, android and gynoid fat mass, and bone mineral density (BMD) of the whole body were measured using a dual energy x-ray absorptiometry (DXA) device (Hologic Discovery QDR, Nasdaq: HOLX). Total body BMD was calculated (g/cm^2). Bone T-score was defined as the number of standard deviations [SDs] below the mean value of healthy young women, and the bone Z-score was defined as the number of SDs below the mean of healthy women of the same age [9].

Pain measures

Bodily pain was assessed with two questions of the 36-Item Short Form Health Survey (SF-36) related to general bodily pain. This dimension is standardized in a scale from 0 (*totally painful*) to 100 (*not painful at all*) [10, 11], where greater scores indicate less pain.

Lumbar and sciatic pain were assessed with a visual analogue scale (VAS) [12],, asking the participants to cross out with a mark (perpendicular line) in a 10 cm scale without references. Later, the research team measured the scale with a ruler from 0 mm (*not painful at all)* to 100 mm *(the highest pain)*.

Pain disability was measured with the Oswestry Disability Index (ODI) [13], where the participants are asked about their pain intensity during daily situations, such as lifting, walking, sitting, standing, sleeping or socializing. For each question (10 in total) of six answers, the total score is 5; if the first statement is marked, the score is 0, whereas if the last score is marked, the score is 5. If any question does not have an adequate answer for the participant's situation, the participant may not answer. Then, the disability score is calculated and expressed as percentage. Higher values describe greater functional limitation. Between 0-20%: *minimum functional limitation*; 20-40%: *moderate*; 40-60%: *intense*; 60-80%: *disability*, and above 80%: *maximum functional limitation*.

Pregnancy Related-Symptoms

The Pregnancy Symptoms Inventory (PSI) [14], in the Spanish validated version [15], was used to assess the nature and the frequency of the effects of pregnancy-related symptoms The PSI is a 41-items Likert inventory, self-administered questionnaire that assesses the pregnancy-related symptoms and how frequent these symptoms limit the activities of daily living of pregnant women. Firstly, participants responded to each symptom as “never”, “rarely”, “sometimes” or “often” occurred. A symptom was considered endorsed if the participant indicated “sometimes” or “often”. Consequently, they completed the second part of the questionnaire evaluating how affected they were by that symptom, as “not limited at all”, “limit a little” or “limit a lot” their activities of daily living. A symptom was considered as a limitation if the participant indicated “limit a little” or “limit a lot”. Previous studies summarized the prevalence of these symptoms and its limitations as a “top three” [16] or “top four-five” [14, 15] most reported. Therefore, we chose to explore the "top four" most commonly reported pregnancy-related symptoms [14, 15].

Depressive symptoms

The pregnant antenatal depressive symptoms were assessed with the Center for Epidemiological Studies-Depression Scale (CES-D) questionnaire [17], which includes twenty items assessing depressive symptomatology, collected in eight different subscales:

sadness, loss of interest, appetite, sleep, thinking/concentration, guilt, tiredness, movement and suicidal ideation. Each response ranges from 0 (never) to 3 (most days) and scores range from 0 to 60. A score equal to or greater than 20 indicates risk of clinical depression [18].

Anxiety levels

State-anxiety levels were assessed with the State Trait Anxiety Index (STAI) questionnaire [19], which includes twenty statements, composed of four Likert-scale of 0 (“almost never”) to 3 (“almost always”) and scores range from 0 to 60. STAI evaluates how participants feel at that moment (“right now”). A cut off of 40 has been defined as highly anxious during pregnancy [20].

Emotional well-being and distress

The Spanish adaptation [21] of the Positive and Negative Affect Schedule (PANAS) [21, 22] was used. This is a 20-item questionnaire widely employed to measure emotional well-being and emotional distress. The questionnaire includes two subscales, *positive affect* and *negative affect*, each of which consisting of ten items that express affects such as “active”, “nervous” or “satisfied”. This questionnaire must be answered on a 5-point Likert scale, from 1 = “very slightly or not at all” to 5 = “extremely”. The score ranges from 10 to 50 for both subscales (*positive affect* and *negative affect*). Higher positive scores reflect greater affective well-being and higher negative scores greater emotional distress. This scale was administered in two timeframes, 16^{th} and 34^{th} g.w. Also, two versions of the PANAS questionnaire were used in the current study: (i) PANAS state (PANAS-S, “how do you feel right now”), and (ii) PANAS trait (PANAS-T, ‘‘how do you feel in general”). The PANAS-S assesses relatively short-term fluctuations in mood, while the PANAS-T measures individual long-term differences in affectivity.

Physical fitness tests

Laboratory physical fitness tests

Cardiorespiratory fitness was evaluated through maternal maximal oxygen intake (VO_{2max}). It was estimated with the Modified Bruce treadmill protocol [23, 24], a submaximal, incremental, multistage and continuous treadmill test. The test incorporated progressive increments in the workload (grade and velocity) every 3 min to determine limits of maximal exertion. Women were asked to walk on the treadmill until the maternal heart rate reached 85% [24] of the age-predicted maximal heart rate (Tanaka's equation) [25]. If the participant requested to end the treadmill test, then the test was also stopped before reaching the heart rate value. Although submaximal treadmill testing is common and safe during pregnancy [23, 26], women were secured with a harness during the test to prevent risk of falls.

Field-based physical fitness tests

Upper-body muscular strength was evaluated by handgrip strength, used as a reference to measure global body strength, as described elsewhere [27]. A digital dynamometer (TKK 5101 Grip-D; Takey, Tokyo, Japan) was used. The participants performed the handgrip strength test twice, alternately with both hands. The best value of 2 attempts for each hand was recorded and the average of both hands was used as absolute muscular strength. Relative upper-body muscular strength was calculated as absolute handgrip strength divided by their body weight, measured in each assessment, and used in the analyses as recommended to address the confounding of strength by weight status [28].

Upper-body flexibility was evaluated with the Back-scratch test, as a measure of overall shoulder range of motion. The distance between (or overlap of) the middle fingers behind the back was measured with a ruler [29]. The Back-scratch test outcome is positive for higher flexibility (i.e. hands overlapping behind the back) and negative for lower flexibility (i.e. greater distance between middle fingers behind the back). The best score of 2 attempts for each arm was recorded, and the average of both arms was used for the analyses.

Self-reported physical fitness

Self-reported PF was assessed with the IFIS [30]. The IFIS comprises five Likert-scale questions about the participants perceived overall PF, cardiorespiratory fitness, muscular strength, speed-agility and flexibility. For each question, the ranges from 1 to 5 are "*very poor*", "*poor*", "*average*", "*good*" and "*very good*" [30]. Higher scores indicate greater self-reported PF. This questionnaire has been previously validated [31] and previously used in pregnant population [32-35], and requires 1–5 min to be completed (see **Table 2**).

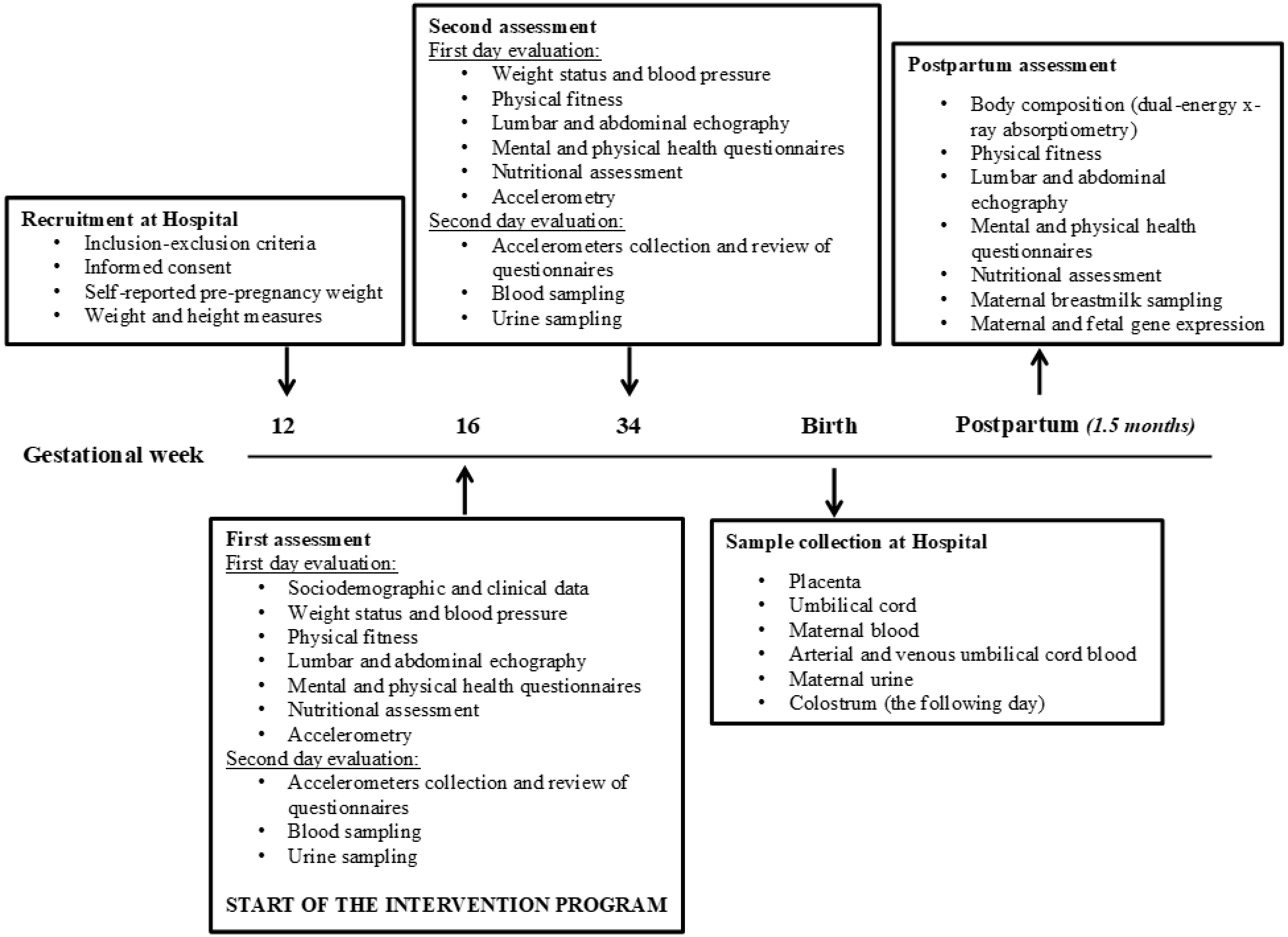


Figure 5. Assessments conducted along the GESTAFIT Project.

Statistical analyses

Descriptive statistics (mean (standard deviation) for quantitative variables and number of women (%) for categorical variables) were employed to describe baseline characteristics of the participants.

Cross-sectional and longitudinal associations (***studies I-VI***) were explored by performing partial correlations and linear regression (enter method):

- Objectively measured PF components with body composition indices (*study I*)

- Objectively measured flexibility with oxytocin administration and cesarean section (*study II*)

- Pain outcomes (*study III*).

- Pregnancy-related symptoms and limitations due to pain (*study IV*).

- Depressive symptoms and anxiety levels (*study V*).

- Emotional well-being and emotional distress (*study VI*).

Different models were analyzed including potential cofounders. Additionally, since in the GESTAFIT Project [1], a concurrent physical exercise program was carried out until birth, exercise intervention was also included as covariate, in order to correct the possible effect of the exercise program, in those variables assessed at the 34th g.w.

To evaluate the influence of a supervised and adapted concurrent exercise training program on HRQoL throughout pregnancy (***study VII***):

Values of the SF-36, at the 16th g.w. and 34th g.w., were compared to detect differences in these outcomes between the groups, t-test for repeated measures was used.

According to the original protocol [1], the statistical analysis was conducted on a per-protocol basis. Only women who attended ≥75% of the exercise sessions and completed both baseline and follow-up assessments were included in the per-protocol analyses to investigate the clinical efficacy of a concurrent exercise training program on HRQoL. In those participants with missing data at follow-up, specific values were estimated using a mean imputation procedure. Subsequently, the aforementioned statistical analyses were conducted on an intention-to-treat basis to evaluate more realistically the effectiveness of this concurrent exercise-training program when applied to the clinical practice.

We included the changes (34th g.w. – 16th g.w.) in the SF-36 domains as dependent variables in separate models and the group (control= 0 and exercise= 1) as independent variables.

After considering relevant confounders suggested in previous literature, two models were tested. Model I was unadjusted. Model II was adjusted for age, educational status, and GWG (kg).

To evaluate the influence of a supervised and adapted concurrent exercise training program on HRQoL throughout pregnancy (***study VIII***):

The differences between the control and exercise groups on VAS low back, VAS sciatica, and ODI scores were analysed by linear regression analyses on a per protocol-basis as previously designed [1]. Only women who attended at least 75% of the exercise sessions, and completed both baseline and follow-up assessments, were included in the present analyses. The changes (34^{th}-16^{th} g.w.) of these outcomes were included in the linear regression analyses as dependent variables, and the intervention group (control=0 and exercise=1) as independent variable. Model I was unadjusted for age, pre-pregnancy BMI, and baseline values (i.e., values at the 16^{th} g.w.) of pain-related outcomes. Model II was additionally adjusted for gestational weight gain. Multiple imputations were performed to estimate missing data in specific pain outcomes. Subsequently, differences between the control and exercise groups on VAS low back, VAS sciatica, and ODI scores were assessed by linear regression on an intention-to-treat basis according to the CONSORT guidelines. Considering that some authors do not recommend performing imputations when more than 20% of cases are missing [13], multiple imputations were not possible for some ODI subscales.

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

The methods section of the present International Doctoral Thesis is summarized in **Table 6**. This table includes the most relevant methodological features from the scientific studies that compose the present International Doctoral Thesis. For further information of any study, please check the methods section of the corresponding paper.

Table 6. Summary of the main methodological features of the studies of the present International Doctoral Thesis.

Study	Design	Participants	Main predictor/independent variables (instruments)	Outcomes/Dependent variables (instruments)
Study I *Physical fitness and maternal body composition indices during pregnancy and postpartum: The GESTAFIT Project.*	Cross-sectional	157-123* Caucasian pregnant women (age: 32.9 ± 4.6 years)	- Cardiorespiratory fitness (VO_{2max}, Modified Bruce treadmill protocol) - Upper-body muscular strength [digital dynamometer (TKK 5101 Grip-D; Takey, Tokyo, Japan)] - Upper-body flexibility (Back-scratch test)	- Pre-pregnancy body weight (self-reported) - Body weight [scale (InBody R20; Biospace, Seoul, Korea)] - Height [stadiometer (Seca 22, Hamburg, Germany)] - BMI - GWG - Postpartum body composition [DXA device (Hologic Discovery QDR, Nasdaq: HOLX)]
Study II *Association of body flexibility with the odd of oxytocin administration and caesarean section during labor: The GESTAFIT Project.*	Longitudinal	157 Caucasian pregnant women (age: 32.9 ± 4.6 years)	- Upper-body flexibility (Back-scratch test)	- Birth outcomes and oxytocin administration (partogram)

Study III *Association of self-reported physical fitness with pain during pregnancy: The GESTAFIT Project.*	Cross-sectional	136-119** Caucasian pregnant women (age: 32.9 ± 4.6 years)	- Self-reported physical fitness (IFIS)	- Pain and disability (SF-36, VAS, ODI)
Study IV *Association of self-reported physical fitness with pregnancy related symptoms: The GESTAFIT Project.*	Cross-sectional	158-117* Caucasian pregnant women (age: 32.9 ± 4.6 years)	- Self-reported physical fitness (IFIS)	- Pregnancy related-symptoms (Pregnancy Symptoms Inventory)
Study V *The favourable association of self-reported physical fitness with depression and anxiety during pregnancy: The GESTAFIT Project.*	Cross-sectional	158-117*,** Caucasian pregnant women (age: 32.9 ± 4.6 years)	- Self-reported physical fitness (IFIS)	- Depressive symptoms (CES-D) - Anxiety levels (STAI-S)
Study VI *The role of self-reported physical fitness in emotional well-being and distress during pregnancy: The GESTAFIT Project.*	Cross-sectional	158-117*,** Caucasian pregnant women (age: 32.9 ± 4.6 years)	- Self-reported physical fitness (IFIS)	- Positive and negative affect (PANAS)
Study VII *Effects of a concurrent exercise training program on low back and sciatic pain and pain disability in late pregnancy*	Quasi-experimental	93 Caucasian pregnant women: - Exercise group= 49 - Control group= 44 (age: 32.9 ± 4.6 years)	<u>Supervised exercise intervention:</u> - Exercise group: concurrent (aerobic + resistance) training program from the 17^{th} g.w. until birth (3 days/week, 60 minutes/session) of moderate-to-vigorous intensity - Control group: usual care	- Low back and sciatic pain (VAS, ODI)

Study VIII *Influence of a concurrent exercise training program on health-related quality of life during advanced pregnancy: The GESTAFIT Project.*	Quasi-experimental	86 Caucasian pregnant women: - Exercise group= 41 - Control group= 45 (age: 32.9 ± 4.6 years)	Supervised exercise intervention: - Exercise group: concurrent (aerobic + resistance) training program from the 17th g.w. until birth (3 days/week, 60 minutes/session) of moderate-to-vigorous intensity - Control group: usual care	- HRQoL (SF-36)

Note: *Sample size flow at 16th and 34th gestational weeks. **Less sample size because missing data in some questionnaires.
Abbreviations: BMI, Body Mass Index; CES-D, Center for Epidemiological Studies-Depression Scale; DXA, Dual-energy X-ray Absorptiometry; g.w., gestational weeks; GWG, Gestational Weight Gains; HRQoL, Health-Related Quality of Life; IFIS, International FItness Scale; ODI, Oswestry Disability Index; PANAS, Positive and Negative Affect Schedule; SF-36, 36-Item Short Form Health Survey; STAI-S, State Trait Anxiety Index; VAS, Visual Analogue Scale.

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RESULTS and DISCUSSION

CHAPTER I.
Objectively measured physical fitness during pregnancy and body composition and birth-related outcomes

Study I: Physical fitness and maternal body composition indices during pregnancy and postpartum: The GESTAFIT Project.

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RESULTS

The final sample size for this study was composed of 159 Spanish pregnant women. Nonetheless, some of them did not attend the second (at the 34th g.w.) or last evaluation (postpartum) or did not return all the questionnaires duly completed, which meant a loss of data in some outcomes (see **Figure 3**).

The sociodemographic and clinical characteristics of the participants are shown in **Table 7**. The mean age of the women at the recruitment was 32.9 ± 4.6 years old. Most of them were nulliparous (61%) and opted for exclusive breastfeeding (>66%).

Table 7. Sociodemographic and clinical characteristics of the study participants.

Maternal characteristics	**N**	**Mean (SD)**
Age (years)	158	32.9 (4.6)
Marital Status	158	**n (%)**
Married		91 (57.6)
Single		66 (41.8)
Divorced/separated/widow		1 (0.6)
Educational status	158	
Primary or High-school		37 (23.4)
Specialized training		27 (17.1)
University degree		94 (59.5)
Working status	158	
Homework/unemployed		48 (30.4)
Partial-time employed/student		41 (25.9)
Full-time employed		69 (43.7)
Parity	158	**n (%)**
Nulliparous		96 (60.8)
Multiparous		62 (39.2)
Previous abortions		66 (42.0)
Lactation	108	**n (%)**
Exclusive (only breast)		72 (66.7)
Mixed (breast and formula milk)		24 (15.1)
Artificial (only formula milk)		12 (7.5)

Note: Values shown as mean (SD, standard deviation) unless otherwise indicated.

The maternal body composition indices and the PF tests of the participants are shown in **Table 8**. Briefly, women's BMI was 24.2 kg/m^2 during the pre-pregnancy period, and >25.0 kg/m^2 at the 16^{th} g.w. and during the postpartum period. Women's GWG between the 16^{th} g.w. and the 34^{th} g.w. was about 9 kg. Participants' total BMD was 1.06 ± 0.1 g/cm^2 and their bone T-score status was −0.6 ± 1.0 at the postpartum period. Type of lactation (breastfeeding exclusively, mixed or artificial lactation) was additionally included as a potential confounder for bone health outcomes analyses. However, this data no longer changed these results (data not shown).

Table 8. Body composition indices and physical fitness levels of the participants.

Maternal outcomes	**n**	**Mean (SD)**
Height (cm)	157	163 (6.2)
Weight previous to pregnancy (kg)	145	65.1 (12.3)
Pre-pregnancy body mass index (kg/m^2)	145	24.2 (4.2)
Values at 16th g.w.		
Weight at 16th g. w. (kg)	157	67.0 (11.8)
Body mass index at 16th g.w. (kg/m2)	157	25.0 (4.1)
Values at 34th g.w.		
Weight at 34th g. w. (kg)	123	74.6 (10.8)
Gestational weight gains (16th g.w. to 34th g.w.) (kg)	121	8.7 (3.4)
Weight and body composition at postpartum		
Weight at postpartum (kg)	107	68.5 (11.4)
Body mass index at postpartum (kg/m^2)	107	25.5 (4.4)
Total body fat free mass (kg)	110	40.9 (4.7)
Total body lean mass at postpartum (Kg)	110	38.9 (4.7)
Total body fat mass at postpartum (kg)	110	26.2 (7.7)
Total body android fat mass at postpartum (kg)	110	18.8 (0.8)
Total body gynoid fat mass at postpartum (kg)	110	52.1 (1.3)
Total bone mineral density (g/cm^2)		1.06 (0.1)
Bone mineral density T-score*		-0.6 (1.0)
Bone mineral density Z-score		-0.7 (0.9)
Physical fitness tests		**Mean (SD)**
16th g. w.	157	
Cardiorespiratory fitness (75% VO_{2max})		
Upper-body absolute muscular strength; kg/weight (kg)		27.3 (4.3)
Upper-body relative muscular strength; kg/weight (kg)		0.4 (0.1)
Upper-body flexibility (cm)		4.1 (6.2)
34th g. w.	123	
Cardiorespiratory fitness (75% VO_{2max})		
Upper-body absolute muscular strength; kg/weight (kg)		27.2 (4.5)
Upper-body relative muscular strength; kg/weight (kg)		0.4 (0.1)
Upper-body flexibility (cm)		3.9 (6.0)

Note: Values shown as mean (SD, standard deviation) unless otherwise indicated.
*Normal bone is defined as a T-score of −1.0 or higher, osteopenia is defined as between −1.0 and −2.5, osteoporosis is defined as −2.5 or lower [1].
Abbreviations: G. w., gestational weeks.

The linear regression model assessing the associations of PF tests at the 16th g.w. with maternal body composition indices is shown in **Table 9**. In the adjusted model (Model II), greater cardiorespiratory fitness was associated with lower total fat mass, android fat mass, and gynoid fat mass at postpartum (β ranging from −0.230 to −0.311; all, $p < 0.05$). Greater absolute upper-body muscular strength was associated with greater pre-pregnancy BMI, and postpartum body weight, BMI, lean mass, fat free mass, fat mass, gynoid fat mass, T-score and Z-score BMD (β ranging from 0.184 to 0.444; all, $p < 0.05$).

Greater upper-body flexibility was associated with lower pre-pregnancy BMI, and postpartum body weight, BMI, lean mass, fat free mass, fat mass, android fat mass and gynoid fat mass (β ranging from −0.246 to −0.442; all, $p < 0.05$); and with greater postpartum GWG ($\beta = 0.277$, $p < 0.01$). In model I, the results remain the same, except that greater upper-body flexibility was associated with lower T-score ($\beta = -0.198$, $p < 0.05$) and Z-score BMD ($\beta = 0.277$, $p < 0.05$) at postpartum.

Table 9. Linear regression coefficients assessing the association of the physical fitness tests measured at the 16th gestational week with maternal body composition and bone health status.

	Model I			Model II		
	Standardized Coefficients (β)	**Confidence interval 95% (B)**	***P***	**Standardized Coefficients (β)**	**Confidence interval 95% (B)**	***P***
Cardiorespiratory fitness						
Pre-pregancy BMI (kg/m^2)	-0.145	-0.112 (-0.252, -0.029)	0.119	-0.140	-0.108 (-0.249, 0.034)	0.134
GWG (kg)	0.095	0.052 (-0.059, 0.163)	0.352	0.099	0.054 (-0.056, 0.165)	0.331
Weight postpartum (kg)	-0.100	-0.183 (-0.578, 0.212)	0.359	-0.093	-0.170 (-0.563, 0.222)	0.391
BMI postpartum (kg/m^2)	-0.147	-0.110 (-0.270, 0.051)	0.178	-0.141	-0.105 (-0.265, 0.055)	0.195
Total lean mass at postpartum (kg)	0.021	0.015 (-0.143, 0.173)	0.848	0.024	0.018 (-0.139, 0.175)	0.819
Total fat free mass at postpartum (kg)	0.016	0.012 (-0.149, 0.174)	0.881	0.020	0.015 (-0.146, 0.176)	0.853
Total fat mass at postpartum (kg)	-0.255	-0.317 (-0.573, -0.060)	**0.016**	-0.311	-0.250 (-0.563, -0.059)	**0.016**
Total android fat mass at postpartum (kg)	-0.234	-0.029 (-0.055, -0.003)	**0.027**	-0.230	-0.029 (-0.054, -0.003)	**0.028**
Total gynoid fat mass at postpartum (kg)	-0.239	-0.054 (-0.100, -0.007)	**0.024**	-0.234	-0.052 (-0.098, -0.007)	**0.024**
Total BMD at postpartum (g/cm^2)*	-0.070	-0.001 (-0.004, 0.002)	0.515	-0.036	-0.000 (-0.003, 0.002)	0.751
T-score BMD at postpartum*	0.045	0.007 (-0.027, 0.041)	0.674	0.095	0.016 (-0.020, 0.052)	0.388
Z-score BMD at postpartum*	0.052	0.008 (-0.024, 0.039)	0.631	0.104	0.016 (-0.017, 0.049)	0.346
Absolute upper-body strength						
Pre-pregancy BMI (kg/m^2)	0.197	0.192 (0.031, 0.352)	**0.019**	0.203	0.197 (0.037, 0.357)	**0.016**
GWG (kg)	0.185	0.160 (0.005, 0.315)	**0.043**	0.184	0.159 (0.004, 0.315)	**0.044**
Weight postpartum (kg)	0.324	0.987 (0.428, 1.545)	**0.001**	0.311	0.947 (0.393, 1.501)	**0.001**
BMI postpartum (kg/m^2)	0.288	0.339 (0.121, 0.557)	**0.003**	0.277	0.327 (0.109, 0.544)	**0.004**
Total lean mass at postpartum (kg)	0.451	0.561 (0.349, 0.772)	**<0.001**	0.438	0.544 (0.334, 0.755)	**<0.001**
Total fat free mass at postpartum (kg)	0.457	0.580 (0.364, 0.796)	**<0.001**	0.444	0.564 (0.350, 0.779)	**<0.001**
Total fat mass at postpartum (kg)	0.216	0.446 (0.062, 0.829)	**0.023**	0.200	0.411 (0.032, 0.791)	**0.034**
Total android fat mass at postpartum (kg)	0.160	0.034 (-0.006, 0.073)	0.095	0.146	0.031 (-0.009, 0.070)	0.126

Total gynoid fat mass at postpartum (kg)	0.210	0.075 (0.008, 0.142)	**0.028**	0.190	0.068 (0.003, 0.133)	**0.042**
Total BMD at postpartum (g/cm^2)*	0.161	0.003 (-0.001, 0.007)	0.092	0.185	0.004 (0.000, 0.008)	0.068
T-score BMD at postpartum*	0.300	0.075 (0.030, 0.121)	**0.001**	0.300	0.075 (0.027, 0.124)	**0.002**
Z-score BMD at postpartum*	0.309	0.072 (0.030, 0.114)	**0.001**	0.308	0.072 (0.027, 0.117)	**0.002**
Upper-body flexibility						
Pre-pregancy BMI (kg/m^2)	-0.416	-0.287 (-0.392,-0.182)	**<0.001**	-0.414	-0.285 (-0.390,-0.180)	**<0.001**
GWG (kg)	0.274	0.153 (0.055, 0.252)	**0.003**	0.277	0.155 (0.056, 0.254)	**0.002**
Weight postpartum (kg)	-0.355	-0.644 (-0.973, -0.314)	**<0.001**	-0.352	-0.638 (-0.964, -0.313)	**<0.001**
BMI postpartum (kg/m^2)	-0.444	-0.311 (-0.434, -0.189)	**<0.001**	-0.442	-0.310 (-0.431, -0.189)	**<0.001**
Total lean mass at postpartum (kg)	-0.274	-0.202 (-0.339, -0.066)	**0.004**	-0.269	-0.199 (-0.334, -0.064)	**0.004**
Total fat free mass at postpartum (kg)	-0.269	-0.203 (-0.342, -0.064)	**0.005**	-0.265	-0.200 (-0.338, -0.061)	**0.005**
Total fat mass at postpartum (kg)	-0.336	-0.415 (-0.637, -0.192)	**<0.001**	-0.331	-0.408 (-0.626, -0.189)	**<0.001**
Total android fat mass at postpartum (kg)	-0.338	-0.042 (-0.065, -0.020)	**<0.001**	-0.333	-0.042 (-0.064, -0.019)	**<0.001**
Total gynoid fat mass at postpartum (kg)	-0.253	-0.054 (-0.094, -0.015)	**0.008**	-0.246	-0.053 (-0.091, -0.014)	**0.008**
Total BMD at postpartum (g/cm^2)*	-0.043	-0.001 (-0.003, 0.002)	0.657	-0.025	-0.000 (-0.003, 0.002)	0.821
T-score BMD at postpartum*	-0.198	-0.029 (-0.057, -0.002)	**0.039**	-0.195	-0.030 (-0.062, -0.003)	0.072
Z-score BMD at postpartum*	-0.197	-0.027 (-0.053, -0.001)	**0.040**	-0.195	-0.028 (-0.058, -0.003)	0.074

Note: Model I was unadjusted. Model II was adjusted for maternal age. *Model II additionally adjusted for pre-pregnancy body mass index. Bold values, $p< 0.05$.

Abbreviations: BMI, body mass index; GWG, gestational weight gains; BMD, bone mineral density; β, standardized regression coefficient; B, non-standardized regression coefficient.

The linear regression model assessing the associations of PF tests at the 34th g.w. with maternal body composition indices is shown in **Table 10**. In the adjusted model (Model II), greater cardiorespiratory fitness was associated with postpartum lower total fat mass, android fat mass and gynoid fat mass (β ranging from −0.290 to −0.294; all, $p < 0.01$), and with greater T-score and Z-score BMD (β ranging from 0.228 to 0.233; all, $p < 0.05$). In model I, greater cardiorespiratory fitness was additionally associated with lower BMI (β= −0.207, $p < 0.05$), and T-score and Z-score BMD at postpartum were no longer significant ($p > 0.05$). Greater absolute upper-body muscular strength was associated with greater postpartum total lean mass, fat free mass, T-score and Z-score BMD (β ranging from 0.266 to 0.369; all, $p < 0.01$). In model I, the results were unchanged. Greater upper-body flexibility was associated with lower postpartum body weight, BMI, fat mass, android and gynoid fat mass (β ranging from −0.308 to −0.394; all, $p < 0.01$). In model I, the results were unchanged.

The relative upper-body strength was also tested, separately, as previously recommended [2]. The linear regression model assessing the associations of the relative upper-body strength measured at the 16th and 34th g.w. with maternal body composition indices is shown in **Table 11.** At the 16th g.w. (Model II, adjusted), greater relative upper-body strength was associated with lower pre-pregnancy BMI (β= −0.639, $p < 0.001$) and greater GWG (β= 0.271, $p = 0.003$); at the 16th and 34th g.w., greater relative upper-body strength was associated with lower postpartum body weight, BMI, total lean mass, fat free mass, fat mass, and android and gynoid fat mass (β ranging from −0.337 to −0.575; all, $p < 0.05$). In model I, the results were unchanged.

Table 10. Linear regression coefficients assessing the association of the physical fitness tests measured at the 34th gestational week with maternal body composition and bone health status.

	Model I			Model II		
	Standardized Coefficients (β)	**Confidence interval 95% (B)**	***P***	**Standardized Coefficients (β)**	**Confidence interval 95% (B)**	***P***
Cardiorespiratory fitness						
Weight postpartum (kg)	-0.152	-0.359 (-0.877, 0.160)	0.173	-0.115	-0.270 (-0.788, 0.247)	0.302
BMI postpartum (kg/m^2)	-0.207	-0.229 (-0.404, -0.011)	**0.039**	-0.194	-0.176 (-0.373, 0.021)	0.079
Total lean mass at postpartum (kg)	0.029	0.027 (-0.173, 0.227)	0.791	0.085	0.079 (-0.120, 0.278)	0.433
Total fat free mass at postpartum (kg)	0.033	0.032 (-0.174, 0.237)	0.761	0.088	0.083 (-0.122, 0.288)	0.422
Total fat mass at postpartum (kg)	-0.324	-0.522 (-0.854, -0.191)	**0.002**	-0.290	-0.467 (-0.801, -0.134)	**0.007**
Total android fat mass at postpartum (kg)	-0.329	-0.055 (-0.089, -0.021)	**0.002**	-0.293	-0.049 (-0.084, -0.015)	**0.006**
Total gynoid fat mass at postpartum (kg)	-0.318	-0.087 (-0.143, -0.031)	**0.003**	-0.294	-0.081 (-0.138, -0.024)	**0.006**
Total BMD at postpartum (g/cm^2)*	0.127	0.002 (-0.001, 0.005)	0.244	0.207	0.003 (0.000, 0.007)	0.078
T-score BMD at postpartum*	0.141	0.027 (-0.014, 0.067)	0.196	0.233	0.045 (0.001, 0.090)	**0.047**
Z-score BMD at postpartum*	0.130	0.023 (-0.015, 0.060)	0.232	0.228	0.041 (0.000, 0.083)	**0.053**
Absolute upper-body strength						
Weight postpartum (kg)	0.184	0.487 (-0.022, 0.997)	0.061	0.184	0.489 (-0.019, 0.996)	0.059
BMI postpartum (kg/m^2)	0.122	0.125 (-0.074, 0.323)	0.215	0.121	0.124 (-0.075, 0.323)	0.221
Total lean mass at postpartum (kg)	0.364	0.391 (0.199, 0.583)	**<0.001**	0.369	0.397 (0.206, 0.587)	**<0.001**
Total fat free mass at postpartum (kg)	0.369	0.406 (0.210, 0.602)	**<0.001**	0.374	0.412 (0.217, 0.606)	**<0.001**
Total fat mass at postpartum (kg)	0.075	0.134 (-0.208, 0.475)	0.440	0.069	0.123 (-0.217, 0.462)	0.476
Total android fat mass at postpartum (kg)	0.023	0.004 (-0.031, 0.039)	0.808	0.022	0.004 (-0.031, 0.039)	0.822
Total gynoid fat mass at postpartum (kg)	0.083	0.026 (-0.033, 0.085)	0.390	0.067	0.021 (-0.038, 0.079)	0.484
Total BMD at postpartum (g/cm^2)*	0.163	0.003 (0.000, 0.006)	0.090	0.165	0.003 (-0.001, 0.006)	0.100
T-score BMD at postpartum*	0.276	0.060 (0.020, 0.100	**0.004**	0.266	0.057 (0.016, 0.098)	**0.006**
Z-score BMD at postpartum*	0.284	0.057 (0.020, 0.095)	**0.003**	0.274	0.055 (0.017, 0.093)	**0.005**

			Upper-body flexibility			
Weight postpartum (kg)	-0.309	-0.562 (-0.901, -0.223)	**0.001**	-0.308	-0.561 (-0.896, -0.225)	**0.001**
BMI postpartum (kg/m^2)	-0.394	-0.277 (-0.403, -0.151)	**<0.001**	-0.394	-0.277 (-0.403, -0.151)	**<0.001**
Total lean mass at postpartum (kg)	-0.166	-0.125 (-0.268, 0.018)	0.085	-0.162	-0.122 (-0.264, 0.019)	0.089
Total fat free mass at postpartum (kg)	-0.160	-0.123 (-0.270, -0.023)	0.097	-0.156	-0.121 (-0.266, -0.024)	0.101
Total fat mass at postpartum (kg)	-0.342	-0.429 (-0.655, -0.203)	**<0.001**	-0.341	-0.428 (-0.650, -0.205)	**<0.001**
Total android fat mass at postpartum (kg)	-0.339	-0.043 (-0.066, -0.020)	**<0.001**	-0.337	-0.043 (-0.066, -0.020)	**<0.001**
Total gynoid fat mass at postpartum (kg)	-0.320	-0.070 (-0.109, -0.030)	**0.001**	-0.322	-0.070 (-0.109, -0.032)	**<0.001**
Total BMD at postpartum (g/cm^2)*	0.045	0.001 (-0.002, 0.003)	0.642	0.125	0.002 (-0.001, 0.004)	0.242
T-score BMD at postpartum*	-0.095	-0.015 (-0.044, -0.015)	0.326	-0.050	-0.008 (-0.042, -0.025)	0.632
Z-score BMD at postpartum*	-0.099	-0.014 (-0.041, -0.013)	0.308	-0.057	-0.009 (-0.040, -0.023)	0.590

Note: Model I was unadjusted. Model II was adjusted for maternal age, and exercise intervention at the 34th gestational week. *Model II additionally adjusted for pre-pregnancy body mass index. Bold values, $p < 0.05$.

Abbreviations: BMI, body mass index; GWG, gestational weight gains; BMD, bone mineral density; β, standardized regression coefficient; B, non-standardized regression coefficient.

Table 11. Linear regression coefficients assessing the association of the relative upper-body strength measured at the 16th and 34th gestational weeks with maternal body composition and bone health status.

	Model I			Model II		
	Standardized Coefficients (β)	**Confidence interval 95% (B)**	***P***	**Standardized Coefficients (β)**	**Confidence interval 95% (B)**	***P***
Relative upper-body strength (16th g.w.)						
Pre-pregancy BMI (kg/m^2)	-0.639	-32.310 (-38.840, -25.780)	**<0.001**	-0.641	-32.453 (-39.101, -25.804)	**<0.001**
GWG (kg)	0.271	12.266 (4.324, 20.208)	**0.003**	0.283	12.801 (4.793, 20.808)	**0.002**
Weight postpartum (kg)	-0.561	-89.624 (-115.483, -63.764)	**<0.001**	-0.546	-87.316 (-113.060, -61.571)	**<0.001**
BMI postpartum (kg/m^2)	-0.498	-30.771 (-41.240, -20.301)	**<0.001**	-0.487	-30.074 (-40.565, -19.582)	**<0.001**
Total lean mass at postpartum (kg)	-0.353	-22.978 (-34.688, -11.269)	**<0.001**	-0.340	-22.132 (-33.750, -10.513)	**<0.001**
Total fat free mass at postpartum (kg)	-0.350	-23.219 (-35.198, -11.241)	**<0.001**	-0.337	-22.384 (-34.282, -10.486)	**<0.001**
Total fat mass at postpartum (kg)	-0.575	-61.829 (-78.782, -44.876)	**<0.001**	-0.561	-60.377 (-77.089, -43.666)	**<0.001**
Total android fat mass at postpartum (kg)	-0.553	-6.035 (-7.788, -4.283)	**<0.001**	-0.542	-5.915 (-7.656, -4.173)	**<0.001**
Total gynoid fat mass at postpartum (kg)	-0.504	-9.375 (-12.473, -6.278)	**<0.001**	-0.487	-9.064 (-12.092, -6.037)	**<0.001**
Total BMD at postpartum (g/cm^2)*	0.055	0.054 (-0.138, 0.246)	0.579	0.080	0.083 (-0.177, 0.344)	0.528
T-score BMD at postpartum*	0.011	0.138 (-2.374, 2.649)	0.914	0.153	2.033 (-1.226, 5.291)	0.219
Z-score BMD at postpartum*	0.017	0.206 (-2.127, 2.539)	0.862	0.163	2.006 (-1.029, 5.040)	0.193
Relative upper-body strength (34th g.w.)						
Weight postpartum (kg)	-0.529	-92.112 (-121.104, -63.120)	**<0.001**	-0.516	-89.762 (-118.898, -60.627)	**<0.001**
BMI postpartum (kg/m^2)	-0.501	-33.649 (-45.056, -22.241)	**<0.001**	-0.493	-33.087 (-44.614, -21.560)	**<0.001**
Total lean mass at postpartum (kg)	-0.291	-20.447 (-33.402, -7.493)	**0.002**	-0.271	-19.074 (-32.048, -6.100)	**0.004**
Total fat free mass at postpartum (kg)	-0.286	-20.522 (-33.780, -7.264)	**0.003**	-0.267	-19.182 (-32.477, -5.887)	**0.005**
Total fat mass at postpartum (kg)	-0.597	-69.942 (-88.045, -51.839)	**<0.001**	-0.586	-68.687 (-86.736, -50.637)	**<0.001**
Total android fat mass at postpartum (kg)	-0.562	-6.689 (-8.583, -4.795)	**<0.001**	-0.551	-6.560 (-8.466, -4.654)	**<0.001**
Total gynoid fat mass at postpartum (kg)	-0.553	-11.237 (-14.501, -7.974)	**<0.001**	-0.546	-11.104 (-14.309, -7.899)	**<0.001**
Total BMD at postpartum (g/cm^2)*	0.058	0.065 (-0.152, 0.282)	0.554	0.139	0.155 (-0.116, 0.427)	0.260

T-score BMD at postpartum*	0.032	0.449 (-2.287, 3.186)	0.746	0.181	2.564 (-0.809, 5.937)	0.135
Z-score BMD at postpartum*	0.035	0.465 (-2.077, 3.007)	0.717	0.185	2.422 (-0.726, 5.571)	0.130

Note: Model I was unadjusted. Model II was adjusted for maternal age, and exercise intervention at the 34th gestational week. *Model II additionally adjusted for pre-pregnancy body mass index. Bold values, $p < 0.05$

Abbreviations: G.w., gestational weeks; BMI, body mass index; GWG, gestational weight gains; BMD, bone mineral densitsy; β, standardized regression coefficient; B, non-standardized regression coefficient.

DISCUSSION

Our main findings indicate that greater PF in early and late pregnancy was associated with a more adequate GWG during pregnancy, lower adiposity (i.e. total fat mass, fat free mass, lean mass and android and gynoid fat mass) and higher BMD at postpartum period. Specifically, greater cardiorespiratory fitness, relative muscular strength and flexibility during the early second trimester of gestation were strongly associated with better maternal body composition indices.

The recommendations of the Institute of Medicine are the most widely adopted concerning ideal GWG [3], especially for women with overweight and obesity. Pregnant women in our study had a BMI ≥25 kg/m2 at the 16th g.w., and they were close to the median (50th percentile) for GWG recommended at the 34th g.w. [4]. In this context, physical exercise and a healthy diet have been shown to be beneficial lifestyle habits for preventing complications during pregnancy [5, 6], also avoiding the risk of excessive GWG and postpartum increased body weight [5, 6]. Furthermore, adequate PF levels ensure healthier outcomes during pregnancy, birth, and the postpartum period [7-11]. In this sense, our results suggest that, in general, greater PF levels may also promote better body composition during the perinatal period.

Since our study is the first to analyse not only maternal body weight and GWG in relation with PF levels during pregnancy, but also a large number of body composition variables (i.e. adiposity and bone health variables) at the postpartum period, we cannot properly compare our findings with other similar studies. Nevertheless, there are some potential mechanisms that could explain the positive influence of greater PF levels on these body composition parameters.

Gestational-related fat is predominantly accumulated centrally, combining abdominal/truncal and visceral fat, and is strongly associated with cardiometabolic risk factors such as higher blood pressure, adverse lipids concentrations, and reduced insulin sensitivity [12]. As a result, decreasing the amount of accumulated android fat mass during pregnancy is mandatory to prevent these complications [12]. Conversely, the increase in total fat mass during pregnancy is inversely proportional to pregravid obesity [3].

Our results suggest that greater cardiorespiratory fitness in early second trimester of pregnancy is associated with lower postpartum total, android and gynoid fat mass. Aerobic exercise may reflect a person’s cardiorespiratory fitness level through their

VO_{2max} performance [13]. In this regard, intense aerobic exercise results in fat oxidation (and carbohydrate oxidation, both primary sources in aerobic exercise at ≈80% of VO_{2max}) and lipolysis stimulation, linked to central fat reduction [13]. Furthermore, greater cardiorespiratory fitness in late pregnancy was also associated with greater postpartum T-score and Z-score BMD in late pregnancy. Therein, evidence suggests that greater VO_{2max} might promote better bone status in young females, especially in those with overweight [14].

Concerning bone health, women in our study showed normal bone T-score status (-0.6 ± 1.0) at the postpartum period, when compared with non-pregnant women [1]. Calcium homeostasis is markedly altered in pregnant women [15]. Calcium is transferred to the foetus and, although the intestinal calcium absorption is increased [16], it results in a progressive bone loss from early to late pregnancy [17]. The study conducted by To and Wong [17] found that the normal physiological bone loss during pregnancy was significantly more attenuated in active pregnant women compared to their non-exercising counter-partners, supporting that exercise during pregnancy could exert a positive impact on bone metabolism [17]. Moreover, a physically active lifestyle, which is *per se* associated with greater bone mass, promotes a protective effect against bone loss and helps achieving higher peak bone mass [18]. Likewise, an increase in BMD content during pregnancy might prevent maternal skeleton against excessive demineralization and fragility during lactation [16]. In addition to cardiorespiratory fitness, our results suggest that greater absolute upper-body muscular strength in the early second trimester of pregnancy and late pregnancy was also associated with greater bone scores in the postpartum period. In this regard, greater muscular strength is widely associated with greater BMD in those physiological women stages when BMC may diminish, such as the menopausal and postmenopausal period [19]. In lactating women, this positive relationship has been also previously demonstrated [20]. This fact is especially relevant since the application of mechanical stress (e.g., weight-bearing or impact aerobic exercise, such as running or jumping) to the skeleton can preserve and increase BMD, providing a significant contribution in the protection of bone health [21].

Finally, our results indicate that greater levels of flexibility were associated with lower GWG and lower total fat mass in the postpartum period. Greater flexibility levels during pregnancy, especially in late pregnancy to facilitate labour, are mandatory since relaxin is an important vasodilatory hormone during pregnancy [22]. Although the mechanisms are not fully understood yet, it plausible that overweight status induces relaxin-resistance [23]. Therefore, those pregnant women with greater fat mass indices are more likely to have reduced vascular responses, in addition to the possible vasoconstriction phenotype present in overweight status [23]. On the other hand, those pregnant women with greater flexibility during pregnancy could also present higher levels of relaxin, and relaxin seems to contribute to weight reduction [23]. Altogether could partially explain our results.

Although greater PF levels improve by practicing PA or exercise during pregnancy [7, 24], it should be highlighted that women typically reduce their PA levels during pregnancy [25]. In fact, in our study sample, only 22% of the women complied with the PA guidelines [26], which is in line with other studies [7].

To sum up, strategies for promoting greater PF levels through exercise (focusing on resistance training) could be effective to maximize body composition indices during pregnancy, especially in those women with low BMD. Likewise, resistance training may have a positive effect on pregnant women with overweight, promoting better GWG and lower fat mass at postpartum [6].

Study II: Association of body flexibility with the odd of oxytocin administration and caesarean section during labor: The GESTAFIT Project.

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Submitted (European Journal of Sport Science).

RESULTS

Of the 159 women who met the eligibility criteria and completed the first assessment, 157 who had valid data in the Back-scratch test were included for statistical analyses. However, a total of 27 partograms were not found in the informatics system, or could not be collected due to some births occurring in another city. Hence, these participants did not have complete valid data for all the study outcomes.

The sociodemographic and clinical characteristics of the study participants are shown in **Table 12**. The final sample size was composed of 157 Caucasian pregnant women (aged 32.9 ± 4.6 years old, 65.1 ± 12.3 kg of mean weight at 16th g.w.). Most of the participants lived with their partner (97%), had University degrees (60%) and worked full time. Approximately 61% of the sample were nulliparous and 25% had a cesarean section. Births took place around 39.6 ± 1.3 g.w., with a mean neonate body weight of 3.3 ± 0.5 kg. Mean value of the Back-scratch test was 4.0 ± 6 cm.

Table 12. Sociodemographic and clinical characteristic of the study participants.

Maternal characteristics	**n**	**Mean (SD)**
Age (years)	157	32.9 (4.6)
Body mass index at 16th g.w. (kg/m^2)	156	25.0 (4.1)
Weight at 16th g.w. (kg)	156	65.1 (12.3)
		n (%)
Living with a partner	156	152 (97.4)
Educational status	156	
Primary or High-school		36 (23.0)
Specialized training		26 (16.6)
University degree		94 (60.4)
Working status	157	
Homework/unemployed		48 (30.6)
Partial-time employed/student		41 (26.0)
Full-time employed		68 (43.4)
Need of oxytocin administration to induce birth	130	44 (33.8)
Type of birth	141	
Vaginal		106 (75.2)
Caesarean section		35 (24.8)
Birth place	147	
Public Hospital		138 (93.9)
Private Hospital		8 (5.4)
Home		1 (0.7)
Parity	157	
Nulliparous		95 (60.5)
Multiparous		62 (39.5)
Back-scratch test		**Mean (SD)**
16th g.w.	157	4.0 (6.2)
Neonatal outcomes		
Sex [female, n (%)]	138	71 (51.4)
Gestational age at birth, weeks	147	39.6 (1.3)
Birth weight, grams	141	3305 (480.6)
Apgar Test 1 minute	138	8.6 (1.0)
Apgar Test 5 minutes	138	9.6 (0.7)

Note: Values shown as mean (SD, standard deviation) unless otherwise indicated.
Abbreviations: G.w., gestational weeks.

Differences in the Back-scratch test of the pregnant women at the 16th g.w. by oxytocin administration and type of birth are shown in **Table 13**. The mean score in the Back-scratch test were +1.8 cm in women who needed oxytocin administration compared to +5.4 cm in women who did not require its administration (p= 0.001 for the unadjusted model and p= 0.004 for the adjusted model, Cohen´s d= 0.59, 95% CI: 0.2-0.95). The mean cm in the Back-scratch test were +1.6 cm in women who had caesarean sections compared to +5.0 cm in women who had vaginal births (p= 0.004 for the unadjusted model and p= 0.017 for the adjusted model, Cohen´s d= 0.55, 95% CI: 0.2-0.9).

Table 13. Differences in the Back-scratch test of the pregnant women at the 16th gestational week by oxytocin administration and type of birth.

Oxytocin was not administered (n= 85)	**Oxytocin was administered (n= 43)**	***P***	***P****	**Effect size *d*-Cohen (95% CI)**
5.40 (0.68)	1.76 (0.89)	0.001	0.004	0.59 (0.23, 0.95)
Vaginal birth (n= 106)	**Caesarean section (n= 35)**	***P***	***P****	**Effect size *d*-Cohen (95% CI)**
5.04 (0.63)	1.61 (0.89)	0.004	0.017	0.55 (0.21, 0.89)

Note: Values shown as mean (standard error of the mean). *Model adjusted for maternal age, parity, maternal weight, the exercise intervention, epidural analgesia and birth place.
Abbreviations: CI, Confidence interval.

Figure 6 shows the capacity of the Back-scratch test to discriminate between the need of oxytocin administration before or during labor and presence/absence of caesarean section. The AUC to establish the ability of the Back-scratch test to detect the need of oxytocin administration was 0.682 (95% CI: 0.59, 0.78, p= 0.001). The AUC to establish the ability of the Back-scratch test to detect the odd of caesarean section was 0.672 (95% CI: 0.60, 0.77, p= 0.002).

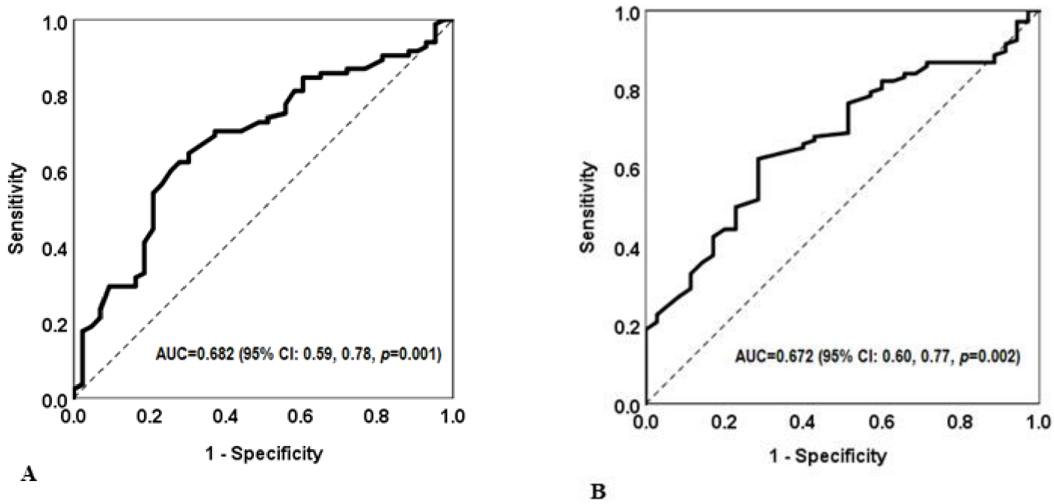

Figure 6. Capacity of the Back-scratch test to discriminate between the need for oxytocin administration before or during labor, and presence/absence of caesarean section.

The thresholds derived from the ROC analysis for the need of oxytocin administration and presence/absence of caesarean section are shown in **Table 14**. The optimal cut-off to discriminate between the need or not of oxytocin administration was +3.6 cm (OR=4.2; 95% CI: 1.9–9.3 for the unadjusted model, and OR: 4.8; 95% CI: 2.0–11.6.7 for the adjusted model). The cut-off points, OR and 95% CI of the Back-scratch test to identifying caesarean presence was tested in an unadjusted model and after adjusting for maternal age and weight, parity, the exercise intervention, epidural analgesia and birth place. The optimal cut-off point to discriminate between presence/absence of caesarean section was +4.1 cm (OR: 4.1; 95% CI: 1.8–9.5 for the unadjusted model, and OR: 4.2; 95% CI: 1.7–10.2 for the model adjusted for the abovementioned potential confounders). We also explored the ability of the back-scratch at 34th g.w. and its predictive capacity remained the same (*data not shown*).

Table 14. Binary logistic regression statistics testing the predictive capacity of the Back-scratch test thresholds derived from the receiver operating characteristics curve analysis for the need of oxytocin administration before or during labor, and presence/absence of caesarean section.

	Low Back-scratch test (based on the cut-off)						
	Cut-off point (cm)	**Unadjusted model**			**Adjusted model***		
		OR	**95% CI**	***P***	**OR**	**95% CI**	***P***
Oxytocin administration	<3.6	4.23	1.92-9.31	<0.001	4.79	1.97-11.6	0.001
Caesarean section	<4.1	4.13	1.80-9.50	0.001	4.15	1.70-10.2	0.002

Note: High Back-scratch test was used as reference; *Model adjusted for maternal age, parity, maternal weight, the exercise intervention, epidural analgesia and birth place.
Abbreviations: OR, odd ratio; CI, confidence interval.

DISCUSSION

The main findings of the present study indicate that lower flexibility levels during early second trimester of pregnancy may be indicators of the need of oxytocin administration before or during labor, and caesarean section.

At 16th g.w., a Back-scratch test score <3.6 cm was associated to ~5 times greater increased odd ratio of requiring exogenous oxytocin administration to induce or stimulate labor. A Back-scratch test score <4.1 cm was associated to ~4 times greater increased odd ratio of having a caesarean section. With the current cut-offs proposed, we provide useful information which makes its use in clinical settings recommendable for a potential tailored prescription of flexibility training programs during pregnancy.

Within the GESTAFIT Project, our group has previously shown that maternal PF is a key factor related to birth outcomes [27-30]. The present results support our previous findings and highlight the importance of implementing PF testing as a complementary tool for the screening of healthy pregnancies. Therefore, considering that the Back-scratch test is efficient in time and equipment, we propose its use as a powerful test to be implemented in routine clinical practice.

Since women who required oxytocin administration have shown lower flexibility during the early second trimester of pregnancy, this PF component seems to be key in preventing the need of this intervention. According to the Spanish Ministry of Health, Social Services and Equality, the prevalence of the use of exogenous oxytocin during spontaneous labor in Spanish public hospitals is 53%, newly much higher than the recommended standards of 5-10% [31]. In the present study, 34% of women were provided with this hormone during labor, which represent almost four times the recommendations. Synthetic oxytocin is extensively employed as a method to induce the labor [32] and a treatment for dystocia of uterine dynamics [33]. However, its use has been related to increased risk of uterine hyperactivity, alterations in the fetal heart rate and postpartum hemorrhage [34]. In addition, other studies have associated the use of oxytocin with sucking problems and early cessation of breastfeeding [35], among other neonatal complications [36].

It has previously shown that maternal flexibility was associated with lower incidence of caesarean sections [28] and those modalities of exercise widely recommended during pregnancy that prioritize flexibility training, such as Yoga, have been related with higher rates of vaginal births [37]. To note is that caesarean sections are clearly associated with greater postpartum complications for the mother and newborn [38, 39]. In our study sample, the 25% of births were caesarean sections, a much higher rate than the one recommended by the World Health Organization, who establishes that rates above 15% do not reduce maternal and neonatal morbidity and mortality [40]. It should as well be taken into account that in Spanish private hospitals the caesarean ratio is higher than in public hospitals, something that we have considered by including the place of birth as potential confounder.

Several mechanisms might partially explain the role of flexibility on the need of oxytocin administration and the type of birth. First, overall bodily flexibility levels may be related to the status of the connective tissue (i.e. ligaments) during pregnancy, which may present greater ligament laxity, necessary for the correct maintenance of pregnancy and the labor progression. Second, those pregnant women with greater flexibility might also present greater serum relaxin concentrations [33], which is also naturally increased during pregnancy [41]. Relaxin is a key hormone during pregnancy that also powerfully increases ligament laxity [42] and, consequently, body flexibility. Third, relaxin also provides vasodilator effects [43], which promotes enhanced blood flow to the fetus and reduces potential alterations in the fetal well-being. Moreover, since relaxin has endothelium-dependent vasodilation effects in the uterine artery [43], it seems feasible that the uteroplacental flow was more efficient during the labor in women with greater relaxin concentrations -and probably also higher body flexibility-. In this line, in a previous study [28], we found that greater maternal flexibility at the 16th g.w. was associated with a more alkaline potential of hydrogen (pH), higher partial pressure of oxygen (PO_2), higher arterial oxygen saturation and lower partial pressure of carbon dioxide (PCO_2) in the arterial umbilical cord blood. Fourth, it seems that high levels of relaxin might also have a determinant role on the appearance of uterine contractions [44, 45]. Finally, although more studies are needed to confirm this hypothesis, it is possible that women with better cardiometabolic status -which has been highly associated with the Back-scratch test scores in several populations [27, 46-48]- showed greater cardiorespiratory fitness [49], and therefore, experienced less fatigue during labor. Less fatigue promotes better uterine dynamic [50], and fatigue is also one of the main clinical reasons to provide this hormone during labor [33].

This study has several clinical implications to highlight. The high capacity of the Back-scratch test to establish the odds of the need of oxytocin administration and caesarean section, and the fact that it is a very accessible tool, reinforces that it should be included as a new complementary pregnancy screening tool. Particularly, the Back-scratch test has a great potential in a clinical setting for several reasons: i) a measuring tape or a rule is all the equipment needed to perform this test, so it is extremely cheap; ii) the procedures for this test are simple and do not require any particular training; iii) typically, PF tests require larger spaces, while the Back-scratch test can be performed in any room without any special requirement; iv) this test is time-efficient, requiring just one minute to perform it, which is a fundamental issue for clinicians, who are usually under time constrains.

To note is that we also checked the ability of the Back-scratch at 34th g.w. and its predictive capacity remained the same. However, as our intention is the promptly detection of these common obstetric risks, we encourage clinicians to assess this test around the 16th g.w. in order to early initiate prevention strategies focused on flexibility. From the GESTAFIT Project team we highly recommend those preventive interventions focused on physical exercise [28, 29, 51], as it exerts strong positive effects on birth-related outcomes such as the prevalence of caesarean sections, gestational age, length of labor stages, birth weight, Apgar test scores and umbilical cord blood gases, among others [28, 29, 51] but also incorporating flexibility training in these pregnant women below the cut-offs.

CHAPTER II.
Self-reported physical fitness during pregnancy and perinatal physical and mental health outcomes

Study III: Association of self-reported physical fitness with pain during pregnancy: The GESTAFIT Project.

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RESULTS

The final study sample size was 159 pregnant women. Nonetheless, some women did not assist to the second evaluation (34th g.w.) or did not return all the questionnaires duly completed, which meant a loss of data in some outcomes (see **Figure 3**). During the second evaluation, when receiving and verifying all questionnaires, we realized of a methodological failure (inadequate printing) in the ODI questionnaires. Thus, in order to be consistent and methodologically strict, we decided not to consider these questionnaires (because of reliability issues), despite the significant loss of sample.

The sociodemographic, anthropometric, and clinical characteristics of the participants are shown in **Table 15**. Most women presented average levels of overall PF and all its components in both, 16th and 34th g.w. Around 8% had previously suffered diagnosed pain, and 37% took medication for pain during the last 4 weeks, being paracetamol the most consumed analgesic (32%).

Table 15. Sociodemographic, anthropometric, and clinical characteristics of the study participants.

Variable	**16th g.w.**	**34th g.w.**
Age (years)	32.9 (4.7)	
Body composition		
Height (cm)	164.0 (6.2)	
Weight (kg), 16th g.w.	67.0 (11.8)	74.6 (10.9)
Body mass index (kg/m^2), 16th g.w.	25.0 (4.1)	27.8 (4.1)
Sedentary time and PA, min/wk		
Sedentary time	3567 (672.1)	
Light PA	2716 (608.6)	
Moderate PA	258 (195.1)	
Moderate-to-vigorous PA[a]	100 (213.5)	
Total PA	2988 (636.7)	
Meeting PA guidelines, n (%)	30 (22.2)	
Self-reported physical fitness		
Overall physical fitness	3.20 (0.77)	3.34 (0.77)
Cardiorespiratory fitness	2.54 (0.92)	2.63 (0.81)
Muscular strength	3.13 (0.77)	3.26 (0.72)
Speed-agility	3.08 (0.81)	2.97 (0.76)
Flexibility	3.14 (1.01)	3.14 (1.03)
Parity	**n (%)**	
Nulliparous	94 (59.5)	
One child	54 (34.2)	
Two children	10 (6.3)	
Marital status	**n (%)**	
Married	90 (57.3)	
Single	67 (42.7)	
Educational status	**n (%)**	
Primary school	18 (11.5)	
High-school	19 (12.1)	
Specialized training	27 (17.2)	
University medium degree	35 (22.3)	
University higher degree	58 (36.9)	
Illness diagnosis	**(yes, n [%])**	
Chronic cervical backache	7 (4.5)	
Chronic lumbar backache	6 (3.8)	
Drug intake	**(yes, n [%])**	
Medication for pain in the last 4 weeks	40 (25.5)	
Ibuprofen	5 (3.2)	
Paracetamol	51 (32.5)	
Diazepam	2 (1.3)	

Note: Values are shown as mean (standard deviation) unless otherwise indicated. [a]Accounted in bouts of at least 10 min. *Abbreviations*: min, minute; PA, physical activity; g.w., gestational weeks.

Bodily, lumbar and sciatic pain, and pain disability of the study sample are shown in **Table 16**. At 16th and 34th g.w., the mean score in the SF-36 bodily pain was 61 and 53, respectively (greater scores mean less pain); the mean of VAS lumbar pain was 22 and 35 mm, and 12 and 21 mm for sciatic pain respectively; the pain disability total score, measured by the ODI questionnaire, was 7% and 12%, respectively.

Table 16. Bodily, lumbar and sciatic pain, and pain disability reported at 16th and 34th gestational weeks.

	Mean (SD)	
Variable	**16th g.w.**	**34th g.w.**
Bodily pain (SF-36)[a] , (0-100)	60.9 (25.4) (n= 133)	53.5 (26.0) (n= 116)
Visual Analogue Scale (VAS)[b] , (0-100)		
Lumbar pain for the last 4 weeks	22.1 (24.5) (n= 136)	35.5 (30.6) (n= 119)
Sciatic (lower member) pain for the last 4 weeks	11.6 (20.8) (n= 136)	21.5 (27.7) (n= 119)
Oswestry Disability Index (ODI)[b] , (0-5)		
Intensity of the pain	0.5 (1.0) (n= 112)	0.6 (1.1) (n= 109)
Pain while standing	0.8 (0.9) (n= 109)	1.1 (1.0) (n= 109)
Pain while carrying out self-care activities	0.3 (0.7) (n= 109)	0.5 (0.7) (n= 109)
Pain while sleeping	0.3 (1.1) (n= 109)	0.6 (0.7) (n= 108)
Pain while liftint weight	0.8 (1.0) (n= 110)	1.1 (1.0) (n= 108)
Pain having sexual activities	0.2 (0.8) (n= 102)	0.8 (1.5) (n= 56)
Pain while walking	0.1 (0.4) (n= 102)	0.4 (0.9) (n= 56)
Limitations of the social life due to pain	0.3 (0.7) (n= 101)	0.6 (1.0) (n= 56)
Pain while seated	0.7 (0.9) (n= 102)	1.2 (1.1) (n= 56)
Pain while traveling	0.4 (0.6) (n= 102)	0.7 (0.9) (n= 56)
Oswestry Disability Index (ODI)[b] total score, (0%-100%)	6.8 (8.7) (n= 141)	12.1 (14.2) (n= 68)

Note: Values shown as mean (SD, standard deviation) unless otherwise indicated. [a]Greater scores indicate lower pain. [b]Greater scores indicate higher pain.
Abbreviations: SF-36, Short Form 36 Survey, g.w., gestational weeks.

Partial correlations of self-reported overall PF and its components with bodily, lumbar and sciatic pain, and pain disability at 16th and 34th g.w. are shown in **Table 17**. At 16th g.w., after adjusting for the aforementioned confounders, greater overall PF was associated with lower bodily and lumbar pain (both, $p < 0.05$), and less pain disability ($p < 0.01$). Greater cardiorespiratory fitness was associated with lower bodily pain ($p < 0.01$), lumbar pain, and the components of ODI questionnaire "pain while standing" and "pain while lifting weight" (all, $p < 0.05$), and less pain disability ($p < 0.01$). Greater muscular strength was associated with lower bodily pain and pain disability (both, $p < 0.05$). Greater speed-agility was associated with lower bodily pain ($p < 0.01$), sciatic pain, and the component of ODI questionnaire "pain having sexual activities" (both, $p < 0.05$). At 34th g.w., greater overall PF was associated with lower bodily and sciatic pain (both, $p < 0.01$) and "pain while sleeping," "pain having sex," "pain while walking," and "limitations of the social life due to pain" (all, $p < 0.05$). Greater cardiorespiratory fitness was associated with lower bodily pain ($p < 0.01$), sciatic pain, and "pain while standing" (both, $p < 0.05$). Greater muscular strength was associated with lower bodily pain, sciatic pain, and "pain while walking" (all, $p < 0.05$). Greater speed-agility was associated with lower bodily and sciatic pain (both, $p < 0.01$). Finally, greater flexibility was associated with lower bodily and sciatic pain (both, $p < 0.05$).

Table 17. Partial correlations of self-reported overall physical fitness and its components with bodily, lumbar and sciatic pain, and pain disability at 16th and 34th gestational weeks.

	Overall fitness	Cardiorespiratory fitness	Muscular strength	Speed-agility	Flexibility
Bodily pain (SF-36)					
16th g.w. (n= 133)	0.184*	0.343**	0.199*	0.232**	0.151
34th g.w. (n= 116)	0.381**	0.313**	0.232*	0.325**	0.207*
VAS					
Lumbar pain					
16th g.w. (n= 136)	-0.176*	-0.191*	-0.151	-0.170	-0.101
34th g.w. (n= 119)	-0.120	-0.086	-0.078	-0.048	-0.012
Sciatic pain					
16th g.w. (n= 136)	-0.103	-0.060	-0.008	-0.190*	0.063
34th g.w. (n= 119)	-0.265**	-0.231*	-0.203*	-0.272**	-0.201*
ODI					
Intensity of the pain					
16th g.w. (n= 122)	-0.001	-0.124	-0.200	0.019	0.067
34th g.w. (n= 109)	-0.121	-0.149	-0.144	-0.104	-0.048
Pain while standing					
16th g.w. (n= 109)	-0.155	-0.244*	-0.006	-0.164	-0.027
34th g.w. (n= 109)	-0.170	-0.208*	-0.150	-0.062	-0.012
Pain while carrying out self-care activities					
16th g.w. (n= 109)	0.050	-0.114	0.430	0.181	0.176
34th g.w. (n= 109)	-0.183	-0.080	-0.130	-0.030	-0.038
Pain while sleeping					

16th g.w. (n= 109)	-0.048	-0.096	-0.065	-0.024	-0.063
34th g.w. (n= 108)	-0.234*	-0.166	-0.113	0.025	-0.085
Pain while lifting weight					
16th g.w. (n= 110)	-0.152	-0.198*	-0.070	-0.065	-0.023
34th g.w. (n= 108)	-0.131	-0.122	-0.046	0.078	-0.010
Pain having sexual activities					
16th g.w. (n= 102)	-0.099	-0.140	-0.183	0.206*	0.064
34th g.w. (n= 56)	-0.309*	-0.235	-0.234	-0.025	-0.008
Pain while walking					
16th g.w. (n= 102)	-0.129	-0.155	-0.420	-0.054	-0.002
34th g.w. (n= 56)	-0.292*	-0.201	-0.367*	-0.218	-0.075
Limitations of the social life due to pain					
16th g.w. (n= 101)	-0.175	-0.118	-0.162	0.102	0.037
34th g.w. (n= 56)	-0.289*	-0.202	-0.136	0.128	0.182
Pain while seated					
16th g.w. (n= 102)	-0.084	-0.069	-0.033	0.101	0.027
34th g.w. (n= 56)	-0.121	-0.232	-0.232	0.066	0.025
Pain while travelling					
16th g.w. (n= 102)	-0.167	-0.195	-0.150	0.037	-0.098
34th g.w. (n= 56)	-0.111	-0.192	-0.233	0.022	0.121
ODI total score					
16th g.w. (n= 122)	-0.271**	-0.301**	-0.196*	-0.037	-0.060
34th g.w. (n= 68)	-0.202	-0.159	-0.228	-0.036	-0.037

Note: Model adjusted for age, body mass index and the exercise intervention. VAS was additionally adjusted for pain medication (16th g.w.). *p< 0.05; **p< 0.01.
Abbreviations: ODI, Oswestry Disability Index; SF-36, 36-Item Short Form Health Survey; VAS, visual analogue scale; g.w., gestational weeks; CRF, cardiorespiratory fitness.

Linear regression models assessing the association of overall PF and its components with bodily, lumbar and sciatic pain, and pain disability at 16th and 34th g.w. are shown in **Table 18**. Regarding the 16th g.w., pregnant women who reported greater overall PF showed lower bodily pain ($p < 0.05$). Bodily pain was also lower in those women with greater cardiorespiratory fitness ($p < 0.001$), muscular strength ($p < 0.05$), and speed-agility ($p < 0.001$). Those who reported greater overall PF showed lower lumbar pain ($p < 0.05$). Lumbar pain was also lower in women with greater cardiorespiratory fitness ($p < 0.05$) and speed-agility ($p < 0.05$), and slightly lower (borderline significance) among those pregnant women with greater muscular strength. ($p = 0.06$). Women with greater speed-agility showed less sciatic pain ($p < 0.05$), whereas no significant association was found for the overall PF nor the rest of PF components (all $p > 0.05$). Pregnant women who reported greater overall PF showed less pain disability ($p < 0.001$). Pain disability was also lower in those with greater cardiorespiratory fitness ($p < 0.001$) and muscular strength ($p < 0.05$). At 34th g.w., women who reported greater overall PF ($p < 0.000$), cardiorespiratory fitness ($p < 0.001$), muscular strength ($p < 0.015$), speed-agility ($p < 0.001$), and flexibility ($p < 0.030$) showed lower bodily pain. Pregnant women who reported greater overall PF ($p < 0.005$), cardiorespiratory fitness ($p < 0.016$), muscular strength ($p < 0.035$), speed-agility ($p < 0.004$), and flexibility ($p < 0.037$) presented lower sciatic pain.

Table 18. Linear regression coefficients assessing the association of self-reported overall physical fitness and its components with bodily pain, lumbar and sciatic pain, and pain disability at 16th and 34th gestational weeks.

	16th g.w.				**34th g.w.**			
	β	**B**	**SE**	***P***	**β**	**B**	**SE**	***P***
Bodily pain (SF-36) (16th g.w., n= 136; 34th g.w., n= 116)								
Overall physical fitness	0.20	6.31	2.98	**0.036**	0.38	13.25	3.09	**0.000**
Cardiorespiratory fitness	0.35	9.41	2.23	**<0.001**	0.31	10.29	3.00	**0.001**
Muscular strength	0.20	6.27	2.33	**0.022**	0.22	8.39	3.39	**0.015**
Speed-agility	0.24	7.62	2.77	**0.007**	0.32	11.37	3.18	**0.001**
Flexibility	0.15	3.74	2.15	0.085	0.20	5.28	2.40	**0.030**
Lumbar pain (VAS) (16th g.w., n= 139; 34th g.w., n= 119)								
Overall physical fitness	-0.18	-5.83	2.83	**0.042**	-0.11	-4.61	3.69	0.215
Cardiorespiratory fitness	-0.19	-5.23	2.24	**0.021**	-0.08	-3.09	3.46	0.374
Muscular strength	-0.15	-4.86	2.60	0.064	-0.07	-3.07	3.83	0.425
Speed-agility	-0.18	-5.65	2.63	**0.033**	-0.04	-1.88	3.78	0.619
Flexibility	-0.10	-2.37	2.04	0.246	-0.12	-0.35	2.72	0.898
Sciatic pain (VAS) (16th g.w., n= 139; 34th g.w., n= 119)								
Overall physical fitness	-0.11	-3.13	2.59	0.229	-0.27	-9.93	3.50	**0.005**
Cardiorespiratory fitness	-0.06	-1.46	2.06	0.481	-0.23	-8.08	3.30	**0.016**
Muscular strength	-0.01	-0.36	2.38	0.879	-0.20	-7.82	3.67	**0.035**
Speed-agility	-0.20	-5.42	2.37	**0.024**	-0.28	-10.36	3.55	**0.004**
Flexibility	-0.06	1.35	1.86	0.472	-0.20	-5.48	2.60	**0.037**
Pain disability (ODI total score) (16th g.w., n= 127; 34th g.w., n= 68)								
Overall physical fitness	-0.29	-3.41	1.12	**0.003**	-0.20	-3.73	2.46	0.135
Cardiorespiratory fitness	-0.29	-2.79	0.84	**0.001**	-0.15	-2.57	2.17	0.243
Muscular strength	-0.18	-2.08	1.01	**0.041**	-0.21	-3.88	2.26	0.092
Speed-agility	-0.02	-0.27	1.04	0.792	-0.03	-0.57	2.21	0.794
Flexibility	-0.06	-0.53	0.80	0.514	0.03	0.50	1.83	0.786

Note: Model adjusted for age, body mass index and the exercise intervention. VAS was additionally adjusted for pain medication (16th g.w.). Bold values, $p < 0.05$.

Abbreviations: β, standardized regression coefficient; B, non-standardized regression coefficient; CI, confidence interval; ODI, Oswestry Disability Index; SE, standard Error; SF-36, 36-Item Short Form Health Survey; VAS, visual analogue scale; g.w., gestational weeks.

DISCUSSION

The findings of the present study indicate that greater self-reported overall PF was associated with less bodily pain, lumbar pain, and disability due to pain during early second trimester of pregnancy (16th g.w.). Greater cardiorespiratory fitness was associated with less bodily and lumbar pain, and pain disability. Greater muscular strength was associated with less bodily pain and pain disability, and speed-agility was associated with less bodily and sciatic pain. Moreover, greater overall PF was associated with less bodily and sciatic pain at late pregnancy (34th g.w.).

To the best of our knowledge, this is the first study exploring the association of self-reported PF with pain in pregnant women. Self-reported PF (measured by the IFIS) has been employed in different populations with [52] and without pain diagnosis [53], inasmuch: it is a reliable tool [52] that may provide useful information about some components of health status [54]. In this regard, IFIS could be employed also in pregnant population and it is being currently validated by our group.

It is widely known that pain induces a reduction in mother's quality of life [55]. Our study shows a mean score in SF-36 bodily pain subscale of 61 in early pregnancy, getting even worse in late pregnancy (scoring 53), whereas the minimum desired score is 70-75 [56, 57]. Nonetheless, other studies involving pregnant women have shown even lower scores in bodily pain dimension [58]. In this regard, it seems that achieving greater levels of overall PF during pregnancy course is imperative, since our results indicate that greater overall PF, cardiorespiratory fitness, muscular strength, speed-agility and flexibility are strongly associated with less bodily pain. Similarly, in other populations where bodily pain is also very high, as women with fibromyalgia, greater levels of overall PF have been related to lower levels of pain [54].

These results are also noteworthy considering that some authors have previously reported that bodily pain is associated with depression during pregnancy, and postpartum depression [59, 60], and previous studies found an inverse association between cardiorespiratory fitness and depression [61].

Low back pain begins in early pregnancy (12th g.w.) and it seems to continue until 34-36th g.w. (late pregnancy) in almost 75% of pregnant women [55]. Pregnant women in our study showed an incremental pain as the course of pregnancy progressed, scoring almost doubly in the VAS at the 34th g.w.. Moreover, our results suggest that pregnant women with greater self-reported overall PF and cardiorespiratory fitness might suffer less lumbar pain in early pregnancy, as well as those with greater overall self-reported PF may also suffer lower sciatic pain in late pregnancy. Our findings are related with previous evidence suggesting that higher levels of PF, especially cardiorespiratory fitness, were strongly associated with a decreased functional limiting low back pain complaints [62].

A recent study has found that women with greater muscular strength levels suffer less low back and bodily pain probably through improvements in musculoskeletal system and balance [63]. These results concur with our findings showing lower bodily and sciatic pain in pregnant women with higher muscular strength, although we could not confirm this association regarding lumbar pain. Moreover, Morino, Ishihara (55) observed that the three motions where the majority of pregnant women felt low back pain were sitting up, standing up from chair, and tossing and turning while supine. Furthermore, specific tasks such as lifting heavy objects and running were identified as additional risk factors for low back pain during pregnancy [55]. These movements/activities associated with pain are stated in some questions from the ODI questionnaire, where we have observed that greater levels of self-reported overall fitness and cardiorespiratory fitness were associated with less pain when performing daily activities.

Hence, physical exercise which is known as a powerful mechanism to improve PF, could be effective in a combination of primary and posterior prevention of low back pain during pregnancy, reducing its intensity and associated disability, and sick leaves [64, 65]. We have confirmed that greater self-reported overall PF is associated with less pain disability due to lumbar and sciatic pain, assessed by the ODI questionnaire, although lower intensity of pain was not associated with greater self-reported overall PF.

There are many potential mechanisms that might explain a reduction of pain intensity through better PF. Literature has shown that, among healthy adults, aerobic PA reduces pain sensitivity across all types of pain stimuli, and this reduction seems to be the strongest when PA is performed at moderate-to-vigorous intensity [66], that is related to a greater PF status [67]. This could be explained through the hypoalgesic effect that aerobic PA produces, even in population with any type of chronic pain [66]. The exact mechanisms to explain hypoalgesia are still unclear, although one of them is the activation of the endogenous opioid system during exercise [66]. Thus, high intensity or duration of exercise may lead with the liberation of beta-endorphins, producing changes in pain sensitivity [68, 69]. This explanation could also partially justify our results that indicated a reduction in bodily, lumbar and sciatic pain, and pain disability, when higher overall fitness is acquired during pregnancy. These results could also be explained through increasing tissue oxygenation as a result of aerobic PA that may diminish peripheral and central sensitization, thus reducing pain intensity [70]. In this sense, we have also to highlight that only 22% of the sample met PA guidelines during pregnancy. This fact may be associated to some barriers related to inactivity during early pregnancy as fatigue and nauseas [71]. Nevertheless, it has been suggested that being physically active already during early pregnancy may potentially help coping with these symptoms throughout the pregnancy course, by increasing PF [72].

Despite that the pathogenesis and etiology of low back pain during pregnancy is still unclear, and is probably multifactorial [73], several determinants have been identified: GWG and altered posture during pregnancy, ligamentous laxity, and fluid retention within connective tissues [74, 75]. Another possible explanation for our results is that physical inactivity leads to deconditioning, and there is a strong association between reduced muscular function and the development of low back pain in pregnancy [76]. Moreover, people with low back pain presents deficits of the hip musculature, which provokes compensatory lumbo-pelvic movements, slowly movements and an increase of deconditioning, as well as pain [77]. For that reason, it is possible that pregnant women with greater speed-agility may suffer lower sciatic pain, or that those with sciatic pain may be more careful to reduce pain sensitivity through slower movements. Finally, the fact that flexibility has not been associated with any studied outcome is still unclear and need to be further studied [78].

Some studies have drawn attention to a range of issues related to the use of painkillers during pregnancy, which included using contraindicated drugs, self-prescription of painkillers and taking more than the recommended dose for pregnancy [79]. In this sense, the screening of PF levels during pregnancy may facilitate the prescription of tailored exercise programs, focused on increasing specific PF components. It could contribute to beat the pain without the use of painkillers, or through less dose, which could minimize the risk of these drugs on the fetus.

Study IV: Association of self-reported physical fitness with pregnancy related symptoms: The GESTAFIT Project.

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RESULTS

The final sample size was composed of 159 Spanish pregnant women. Nonetheless, the PSI questionnaire was included in the second wave of recruitment, since we considered that information meaningful after the pregnancy-symptoms experienced by our pregnant women and reported to our research team. Therefore, the PSI sample was n= 78, at the 16th g.w., and n= 62, at the 34th g.w. Moreover, some of them did not attend the second evaluation (at the 34th g.w.) or did not return all the questionnaires duly completed, which meant a loss of data in some other outcomes (see **Figure 3**).

Sociodemographic and clinical characteristics of the participants are shown in **Table 19**. The “top four” pregnancy symptoms, reported sometimes or often, at the 16th g.w. were: urinary frequency (92.3%), tiredness-fatigue (85.9%), poor sleep (74.4%) and breast pain (70.5%). At the 34th g.w.: poor sleep (91.9%), urinary frequency (90.3%), tiredness-fatigue (87.1%) and increased vaginal discharge (72.6%). The “top four” frequency of their limitations in activities of daily living at 16th g.w. were: tiredness-fatigue (68.0%), poor sleep (63.2%), urinary frequency (54.6%) and headache (52.7%). At the 34th g.w.: poor sleep (83.6%), tiredness-fatigue (80.7%), urinary frequency (64.5%) and back pain (58.9%).

Table 19. Sociodemographic and clinical characteristics of the study participants.

Maternal characteristics	**n**	**Mean (SD)**
Age (years)	158	32.9 (4.6)
Height (cm)	157	163 (6.21)
Weight at 16th g.w. (kg)	157	67.0 (11.8)
Weight at 34th g.w. (kg)	123	74.6 (10.8)
Body max index at 16th g.w. (kg/ m^2)	157	24.9 (4.14)
Marital Status	158	**n (%)**
Married		91 (57.6)
Single		66 (41.8)
Divorced/separated/widow		1 (0.6)
Educational level	158	
Primary or High-school		37 (23.4)
Specialized training		27 (17.1)
University degree		94 (59.5)
Working status	158	
Homework/unemployed		48 (30.4)
Partial-time employed/student		41 (25.9)
Full-time employed		69 (43.7)
Parity	158	**n (%)**
Nulliparous		96 (60.8)
Multiparous		62 (39.2)
Previous abortions		66 (42.0)
Self-reported physical fitness* (0-5)		
16th g.w.	158	
Overall physical fitness		3.2 (0.7)
Cardiorespiratory fitness		2.5 (0.9)
Muscular strength		3.1 (0.7)
Speed-agility		3.0 (0.8)
Flexibility		3.1 (1.0)
34th g.w.	117	
Overall physical fitness		3.3 (0.7)

Cardiorespiratory fitness		2.6 (0.8)
Muscular strength		3.2 (0.7)
Speed-agility		2.9 (0.7)
Flexibility		3.1 (1.0)
Top four pregnancy symptoms (0-3)	78	**n (%)**
16^{th} g.w.		
Urinary frequency		72 (92.3)
Tiredness-fatigue		67 (85.9)
Poor sleep		58 (74.4)
Breast pain		55 (70.5)
34^{th} g.w.	62	
Poor sleep		57 (91.9)
Urinary frequency		56 (90.3)
Tiredness-fatigue		54 (87.1)
Increased vaginal discharge		45 (72.6)
Top four limitations (0-2)**		
16^{th} g.w.		
Tiredness-fatigue	78	53 (68.0)
Poor sleep	76	48 (63.2)
Urinary frequency	77	42 (54.6)
Headache	72	38 (52.7)
34^{th} g.w.		
Poor sleep	61	51 (83.6)
Tiredness-fatigue	62	50 (80.7)
Urinary frequency	62	40 (64.5)
Back pain	56	33 (58.9)

Note: Values shown as mean (SD, standard deviation) unless otherwise indicated.
*Self-reported physical fitness varies from 1 (“very poor”) to 5 (“very good”).
**As the number of women responding questions varied, the denominator is displayed for each symptom (n). Women who did not experience any of the symptoms did not answer questions about their limitations.

The total 41-items self-reported pregnancy symptoms reported sometimes or often, and the frequency of their limitations in activities of daily living at the 16^{th} and 34^{th} g.w. are shown in **Table 20**.

Table 20. Prevalence of self-reported pregnancy symptoms and limitations to activities of daily living at 16th (n= 78) and 34th (n= 62) gestational weeks.

Items	Pregnancy symptoms						Limitations*							
	16th g.w.			34th g.w.			16th g.w.				34th g.w.			
	Sometimes	Often	Total prevalence	Sometimes	Often	Total prevalence	n	Limit a little	Limit a lot	Total prevalence	n	Limit a little	Limit a lot	Total prevalence
Tiredness-fatigue	38.5	47.4	85.9	33.9	53.2	87.1	78	44.9	23.1	68.0	62	48.4	32.3	80.7
Nausea	25.6	28.2	53.8	16.1	1.6	17.7	70	30.0	17.1	47.1	45	13.3	0.0	13.3
Vomiting	11.5	12.8	24.3	3.2	1.6	4.8	55	18.2	12.7	30.9	45	6.7	2.2	8.9
Reflux	17.9	15.4	33.3	30.6	33.9	64.5	65	12.3	6.2	18.5	53	32.1	9.4	41.5
Constipation	29.5	25.6	55.1	21.0	11.3	32.3	67	19.4	7.5	26.9	53	20.8	0.0	20.8
Hemorrhoids	6.4	5.1	11.5	9.7	6.5	16.2	47	8.5	0.0	8.5	45	8.9	0.0	8.9
Dry mouth	19.2	16.7	35.9	35.5	4.8	40.3	58	8.6	3.4	12.0	54	11.1	0.0	11.1
Food cravings	41.0	5.1	46.1	29.0	1.6	30.6	69	1.9	0.0	1.9	56	3.6	0.0	3.6
Poor sleep	44.9	29.5	74.4	25.8	66.1	91.9	76	47.4	15.8	63.2	61	44.3	39.3	83.6
Restless legs	15.4	9.0	24.4	19.4	21.0	40.4	52	9.6	3.8	13.4	50	26.0	12.0	38.0
Leg cramps	10.3	0.0	10.3	37.1	14.5	51.6	46	8.7	2.2	10.9	56	32.1	7.1	39.2
Snoring	17.9	2.6	20.5	9.7	6.5	16.2	51	3.9	0.0	3.9	51	7.8	0.0	7.8
Urinary frequency	25.6	66.7	92.3	22.6	67.7	90.3	77	42.9	11.7	54.6	62	41.9	22.6	64.5
Incontinence/ leaking urine	12.8	3.8	16.6	17.7	12.9	30.6	53	5.7	11.3	17.0	48	27.1	6.3	33.4
Increased vaginal discharge	37.2	19.2	56.4	37.1	35.5	72.6	70	11.4	1.4	12.8	61	29.5	1.6	31.1
Thrush	5.1	3.8	8.9	1.6	6.5	8.1	41	9.8	7.3	17.1	40	7.5	2.5	10.0
Changes in libido	32.1	23.1	55.2	45.2	21.0	66.2	69	27.5	8.7	36.2	52	26.9	13.5	40.4
Painful veins in vagina	0.0	2.6	2.6	6.5	4.8	11.3	35	5.7	0.0	5.7	40	7.5	5.0	12.5
Carpel tunnel (numb hands)	7.7	5.1	12.8	12.9	12.9	25.8	46	8.7	4.3	13.0	45	24.4	4.4	28.8

Sciatica/ pain down the back of your legs	12.8	12.8	25.6	30.6	16.1	46.7	51	33.3	13.7	47.0	52	30.8	19.2	50.0
Back pain	38.5	24.4	62.9	38.7	25.8	64.5	71	35.2	11.3	46.5	56	33.9	25.0	58.9
Hip or pelvic pain	23.1	6.4	29.5	29.0	22.6	51.6	59	20.3	5.1	25.4	53	32.1	22.6	54.7
Breast pain	29.5	41.0	70.5	16.1	12.9	29.0	71	25.4	4.2	29.6	48	16.7	0.0	16.7
Headache	29.5	29.5	59.0	19.4	4.8	24.2	72	31.9	20.8	52.7	49	24.5	6.1	30.6
Sore nipples	25.6	21.8	47.4	16.1	11.3	27.4	59	20.3	3.4	23.7	46	8.7	0.0	8.7
Dizziness	17.9	6.4	24.3	19.4	6.5%	25.9	57	19.3	7.0	26.3	50	18.0	10.0	28.0
Fainting	1.3	0.0	1.3	0.0	0.0	0.0	31	6.5	0.0	6.5	39	0.0	2.6	2.6
Heart palpitations	24.4	5.1	29.5	22.6	4.8	27.4	51	11.8	2.0	13.8	46	17.4	0.0	17.4
Shortness of breath	12.8	5.1	17.9	29.0	11.3	40.3	50	16.0	4.0	20.0	50	38.0	10.0	48.0
Taste/smell changes	26.9	39.7	66.6	11.3	8.1	19.4	73	19.2	9.6	28.8	45	8.9	0.0	8.9
Forgetfulness	19.2	9.0	28.2	40.3	16.1	56.4	57	17.5	5.3	22.8	54	20.4	5.6	26.0
Feeling depressed	25.6	2.6	28.2	27.4	1.6	29.0	57	15.8	1.8	17.6	49	20.4	2.0	22.4
Anxiety	11.5	7.7	19.2	16.1	4.8	20.9	53	15.1	0.0	15.1	48	22.9	0.0	22.9
Vivid dreams	23.1	11.5	34.6	35.5	8.1	43.6	65	7.7	0.0	7.7	52	11.5	1.9	13.4
Altered body image	26.9	9.0	35.9	35.5	8.1	43.6	58	10.3	0.0	10.3	52	11.5	1.9	13.4
Greasy skin/acne	23.1	16.7	39.8	25.8	22.6	48.4	61	9.8	1.6	11.4	49	24.5	4.1	28.6
Varicose veins	3.8	11.5	15.3	11.3	3.2	14.5	44	9.1	6.8	15.9	41	4.9	2.4	7.3
Brownish marks on face	5.1	6.4	11.5	22.6	14.5	37.1	0	0.0	0.0	0.0	47	21.3	4.3	25.6
Itchy skin	26.9	28.2	55.1	11.3	17.7	29.0	67	14.9	6.0	20.9	49	14.3	0.0	14.3
Changes in nipples	30.8	25.6	56.4	25.8	27.4	53.2	66	10.6	1.5	12.1	54	16.7	5.6	22.3
Stretch marks	9.0	2.6	11.6	30.6	27.4	58.0	44	6.8	0.0	6.8	53	15.1	0.0	15.1
Swollen hands or feet	6.4	3.8	10.2	9.7	6.5	16.2	47	14.9	2.1	17.0	41	4.9	2.4	7.3

Note: *As the number of women responding questions varied, the denominator is displayed for each symptom (n). Women who did not experience any of the symptoms did not answer questions about their limitations. Data on the prevalence of symptoms are shown as a percentage.
Abbreviations: G.w., gestational weeks.

The partial correlations of self-reported overall PF and its components with pregnancy symptoms and limitations to activities of daily living at the 16th and 34th g.w. are shown in **Table 21**.

Table 21. Partial correlations of self-reported overall physical fitness and its components with pregnancy symptoms and limitations to activities of daily living at the 16th and 34th gestational weeks.

Items	Pregnancy symptoms										Limitations*									
	16th g.w. (n= 74)					34th g.w. (n= 23)					16th g.w. (n= 59)					34th g.w. (n= 31)				
	OPF	CRF	MS	S-A	FLEX	OPF	CRF	MS	S-A	FLEX	OPF	CRF	MS	S-A	FLEX	OPF	CRF	MS	S-A	FLEX
Tiredness-fatigue	**-0.277**	**-0.279**	**-0.255**	-0.322	-0.149	-0.349	-0.342	**-0.307**	-0.193	-0.121	-0.074	-0.293	0.113	-0.129	-0.211	-0.188	-0.094	-0.148	-0.273	-0.273
Nausea	-0.177	-0.182	**-0.247**	-0.163	-0.124	-0.478	-0.314	-0.204	**-0.297**	-0.152	0.024	0.066	0.177	0.230	0.215	-0.197	-0.003	**-0.369**	-0.267	-0.018
Vomiting	-0.012	-0.114	-0.057	-0.087	0.101	-0.274	-0.104	-0.218	-0.189	-0.009	0.033	0.060	0.168	0.062	0.074	**-0.390**	0.035	-0.228	-0.342	0.074
Reflux	0.011	0.038	0.032	-0.064	0.051	-0.248	-0.164	-0.055	-0.062	**-0.376**	0.094	0.007	0.419	0.124	-0.009	-0.201	0.147	-0.165	0.008	-0.256
Constipation	-0.040	-0.181	-0.071	0.096	-0.079	-0.194	-0.077	0.137	0.051	0.130	-0.393	-0.616	-0.307	-0.339	-0.343	0.054	0.000	0.257	0.184	0.102
Haemorrhoids	-0.131	-0.040	**-0.315**	0.022	0.087	-0.071	-0.314	-0.143	0.012	0.103						-0.073	-0.159	0.020	0.075	0.068
Dry mouth	-0.142	-0.141	-0.030	-0.042	0.054	-0.292	-0.236	-0.114	-0.161	0.183	-0.185	-0.577	-0.182	0.005	-0.203	**-0.461**	-0.344	**-0.443**	-0.490	-0.220
Food cravings	0.094	0.065	0.006	-0.163	0.038	0.130	0.077	**0.321**	0.187	0.037						-0.026	-0.096	0.028	0.074	0.064
Poor sleep	**-0.408**	-0.191	-0.202	-0.289	-0.022	-0.253	-0.309	-0.072	-0.062	-0.195	-.244	-.214	-0.033	-0.341	-0.318	-0.035	-0.010	-0.147	-0.104	**-0.382**
Restless legs	-0.173	-0.124	0.026	0.036	-0.073	-0.074	-0.130	0.012	-0.120	-0.114	**-0.489**	-0.172	-0.125	-0.131	-0.024	-0.020	-0.112	0.011	0.131	-0.166
Leg cramps	0.034	-0.119	0.042	0.128	-0.055	0.105	0.183	0.175	0.140	0.032						-0.248	0.154	-0.150	-0.276	-0.166
Snoring	-0.056	-0.067	-0.032	0.029	0.141	0.082	-0.067	0.045	-0.096	0.007	-0.005	-0.125	-0.206	0.094	0.056	-0.040	0.051	-0.249	-0.073	0.075
Urinary frequency	**-0.273**	-0.130	-0.093	0.157	-0.089	-0.152	0.017	0.006	0.068	-0.206	-0.413	-0.600	-0.350	-0.417	-0.353	-0.110	0.067	-0.215	-0.146	**-0.459**
Incontinence/ leaking urine	-0.023	-0.129	0.073	-0.187	-0.126	-0.173	-0.093	-0.001	0.025	-0.041	-0.075	0.005	0.286	-0.386	-0.385	-0.110	0.053	-0.082	-0.125	**-0.378**
Increased vaginal discharge	-0.180	-0.035	-0.167	-0.239	-0.211	-0.223	-0.248	0.021	-0.159	**-0.316**	-0.104	-0.041	0.346	-0.283	-0.322	**-0.518**	-0.173	**-0.453**	-0.475	-0.345
Thrush	0.006	-0.094	-0.060	0.176	0.085	-0.054	0.130	0.052	-0.093	-0.238	-0.114	-0.391	-0.273	0.079	0.078	-0.193	-0.006	-0.080	-0.318	**-0.472**
Changes in libido	**-0.268**	-0.201	-0.205	-0.088	-.017	-0.153	0.007	-0.156	-0.149	-0.145	-0.149	-0.021	-0.306	-0.039	-0.037	0.055	0.086	-0.214	0.039	-0.057
Painful veins in vagina	-0.009	0.055	-0.018	-0.257	-0.235	-0.009	0.166	0.072	-0.164	-0.134						0.065	**0.407**	0.247	-0.053	-0.285
Carpel tunnel (numb hands)	**-0.251**	-0.133	**-0.333**	-0.119	0.032	-0.212	-0.189	-0.103	-0.144	0.001	-0.131	0.082	-0.347	-0.088	0.141	-0.153	-0.193	-0.356	-0.132	-0.048
Sciatica/ pain down the back of your legs	-0.058	**-0.267**	-0.218	-0.283	0.018	-0.136	-0.030	-0.136	-0.162	-0.098	0.152	-0.312	0.166	-0.078	-0.180	-0.129	-0.162	-0.111	-0.297	-0.336
Back pain	-0.021	-0.143	0.052	-0.031	0.011	-0.250	-0.215	-0.164	-0.108	-0.177	0.121	-0.355	0.374	0.203	0.034	0.017	-0.239	-0.053	0.061	-0.291
Hip or pelvic pain	-0.187	-0.200	-0.064	-0.243	0.043	-0.385	-0.261	-0.219	-0.154	-0.118	0.005	-0.192	0.020	-0.318	-0.369	-0.214	-0.168	-0.063	-0.046	**-0.463**
Breast pain	-0.045	-0.064	0.030	0.172	-0.134	-0.061	-0.069	-0.018	-0.117	-0.094	-0.011	-0.406	-0.203	0.266	0.266	-0.350	-0.005	-0.302	-0.379	-0.283

Headache	-0.087	-0.046	-0.103	0.115	0.083	-0.303	-0.313	-0.128	-0.229	-0.153	-0.055	-0.086	-0.003	0.151	0.217	-0.338	-0.329	-0.104	-0.272	**-0.403**
Sore nipples	-0.114	-0.166	**-0.248**	0.102	-0.135	-0.117	-0.168	-0.100	0.017	0.090	-0.054	-0.450	0.006	-0.054	-0.132	-0.026	-0.096	0.028	0.074	0.064
Dizziness	-0.176	-0.140	-0.022	0.005	0.081	-0.229	-0.143	0.051	-0.093	0.045	-0.269	-0.122	-0.208	0.135	0.284	-0.080	-0.158	-0.094	-0.202	-0.301
Fainting	-0.150	-0.092	**-0.265**	-0.013	0.076	0.028	-0.018	-0.071	-0.006	-0.207	-0.304	-0.137	-0.519	0.091	0.203	0.173	-0.116	0.180	0.011	-0.185
Heart palpitations	-0.111	-0.050	-0.127	-0.151	0.001	-0.205	-0.012	-0.020	-0.205	-0.099	-0.304	-0.266	-0.130	-0.024	-0.124	0.033	0.207	-0.104	0.070	-0.006
Shortness of breath	-0.088	-0.131	-0.138	-0.178	-0.225	-0.291	-0.250	-0.158	-0.105	0.102	-0.121	-0.197	-0.268	0.188	0.103	-0.068	-0.110	-0.256	-0.093	-0.231
Taste/smell changes	-0.110	-0.128	-0.125	0.059	0.080	-0.185	-0.304	-0.079	-0.095	-0.044	-0.238	-0.213	-0.046	-0.221	-0.261	-0.006	0.002	-0.008	0.029	0.012
Forgetfulness	-0.138	.097	-0.002	-0.070	-0.010	-0.149	-0.094	0.010	-0.039	0.054	-0.287	-0.062	-0.488	-0.208	-0.286	0.111	0.356	-0.114	-0.075	-0.012
Feeling depressed	-0.177	-0.039	**-0.233**	-0.028	0.088	-0.189	-0.250	-0.243	-0.197	-0.018	-0.338	-0.177	-0.240	0.030	0.076	0.122	0.103	-0.114	-0.108	0.087
Anxiety	-0.137	-0.059	-0.138	-0.020	-0.091	-0.348	-0.219	-0.237	**-0.399**	-0.133	-0.294	-0.253	0.025	-0.050	-0.164	-0.343	-0.123	**-0.422**	-0.319	-0.207
Vivid dreams	**0.246**	0.081	**0.467**	-0.035	-0.028	-0.056	0.011	-0.076	-0.241	-0.073	-0.032	-0.102	0.087	-0.327	-0.347	-0.348	-0.091	-0.311	-0.455	**-0.370**
Altered body image	0.148	0.052	0.192	0.297	-0.021	-0.059	0.025	-0.047	**-0.264**	-0.082	0.109	0.165	-0.271	0.109	-0.026	-0.348	-0.091	-0.311	-0.455	**-0.370**
Greasy skin/acne	-0.081	-0.124	0.080	0.066	-0.076	0.016	-0.037	0.067	-0.166	-0.139	**-0.545**	-0.415	-0.573	-0.285	-0.285	0.063	0.041	-0.250	-0.241	-0.156
Varicose veins	0.102	0.070	-0.027	-0.100	-0.009	0.021	0.007	0.232	0.250	0.118						0.177	0.121	0.174	0.215	0.018
Brownish marks on face	-0.057	0.067	0.030	0.114	0.128	0.083	0.057	0.084	0.005	0.162						0.003	-0.053	-0.077	-0.022	0.330
Itchy skin	**-0.298**	**-0.312**	-0.053	-0.064	-0.181	-0.044	-0.058	0.104	0.088	0.195	-0.356	-0.548	-0.052	-0.103	-0.190	-0.105	-0.045	-0.204	-0.065	0.057
Changes in nipples	-0.011	-0.114	-0.176	0.172	0.109	-0.106	0.027	-0.030	-0.119	-0.032	-0.005	-0.125	-0.206	0.094	0.056	-0.028	0.038	-0.198	-0.124	-0.187
Stretch marks	-0.122	-0.121	-0.138	0.039	0.047	-0.313	-0.317	-0.115	-0.204	-0.031						-0.252	-0.140	**-0.368**	-0.231	0.055
Swollen hands or feet	-0.055	-0.060	0.015	-0.053	0.039	-0.114	-0.037	0.071	0.080	0.056	0.147	0.046	0.317	-0.391	-0.369	-0.299	0.020	**-0.632**	-0.287	-0.124

Note: Model adjusted for maternal age and body mass index at the 16th or 34th gestational weeks. *Women who did not experience any of the symptoms did not answer questions about their limitations. Blank space indicates no answer in that item. Bold values, $p < 0.05$.

Abbreviations: G.w., gestational weeks; OPF, Overall physical fitness; CRF, cardiorespiratory fitness; MS, Muscular strength; S-A, Speed-agility; FLEX, Flexibility.

The linear regression model assessing the association of self-reported overall PF and its components with the "top four" reported pregnancy-related symptoms and limitations at the 16th and 34th g.w. are shown in **Table 22**. At the 16th g.w., greater self-reported overall PF was associated with lower incidence of urinary frequency ($\beta = -0.30$, $p = 0.020$). Greater self-reported overall PF, cardiorespiratory fitness, muscular strength and speed-agility were associated with lower incidence of tiredness-fatigue ($\beta = -0.31$, $p = 0.018$; $\beta = -0.29$, $p = 0.018$; $\beta = -0.25$, $p = 0.031$ and $\beta = -0.34$, $p = 0.006$, respectively). Greater self-reported overall PF and speed-agility were associated with lower incidence of poor sleep ($\beta = -0.46$, $p < 0.001$ and $\beta = -0.31$, $p = 0.014$, respectively). Greater self-reported cardiorespiratory fitness and flexibility were associated with lower limitations by tiredness-fatigue ($\beta = -0.34$, $p = 0.006$ and $\beta = -0.25$, $p = 0.035$, respectively). Finally, greater self-reported flexibility was associated with lower limitations by poor sleep ($\beta = -0.28$, $p = 0.021$).

At the 34th g.w., greater self-reported overall PF, cardiorespiratory fitness and muscular strength were associated with lower incidence of tiredness-fatigue ($\beta = -0.32$, $p = 0.013$; $\beta = -0.33$, $p = 0.012$ and $\beta = -0.29$, $p = 0.032$, respectively). Greater self-reported cardiorespiratory fitness was associated with lower incidence of poor sleep ($\beta = -0.31$, $p = 0.019$). Finally, greater self-reported flexibility was associated with lower incidence of increased vaginal discharge ($\beta = -0.31$, $p = 0.023$).

Table 22. Linear regression coefficients assessing the association of self-reported physical fitness and frequent symptoms and limitations at 16th and 34th gestational weeks.

Items	Pregnancy symptoms								Limitations							
	16th g.w.				34th g.w.				16th g.w.				34th g.w.			
	β	**B**	**SE**	***P***	**β**	**B**	**SE**	***P***	**β**	**B**	**SE**	**P**	**β**	**B**	**SE**	***P***
Overall physical fitness																
Urinary frequency	-0.30	-0.22	0.09	**0.020**	-0.09	-0.08	0.11	0.486	-0.18	-0.15	0.11	0.177	-0.07	-0.07	0.13	0.586
Tiredness-fatigue	-0.31	-0.28	0.12	**0.018**	-0.33	-0.32	0.13	**0.013**	-0.16	-0.14	0.12	0.246	-0.26	-0.26	0.13	**0.052**
Poor sleep	-0.46	-0.53	0.14	**<0.001**	-0.26	-0.26	0.13	**0.052**	-0.14	-0.12	0.12	0.300	-0.05	-0.05	0.14	0.705
Breast pain	-0.05	-0.06	0.17	0.709	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Increased vaginal discharge	*N/A*	*N/A*	*N/A*	*N/A*	-0.21	-0.26	0.17	0.134	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Headache	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	-0.14	-0.13	0.14	0.324	*N/A*	*N/A*	*N/A*	*N/A*
Back pain	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	-0.05	-0.05	0.14	0.742
Cardiorespiratory fitness																
Urinary frequency	-0.13	-0.08	0.07	0.278	-0.04	-0.04	0.10	0.728	-0.24	-0.17	0.09	**0.059**	0.10	0.10	0.12	0.436
Tiredness-fatigue	-0.29	-0.22	0.09	0.018	-0.33	-0.30	0.11	**0.012**	-0.34	-0.26	0.09	**0.006**	-0.21	-0.19	0.12	0.120
Poor sleep	-0.20	-0.19	0.12	0.108	-0.31	-0.28	0.12	**0.019**	-0.04	-0.03	0.09	0.769	-0.04	-0.03	0.12	0.779
Breast pain	-0.07	-0.07	0.13	0.593	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Increased vaginal discharge	*N/A*	*N/A*	*N/A*	*N/A*	-0.24	-0.28	0.15	0.076	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Headache	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	-0.15	-0.12	0.11	0.252	*N/A*	*N/A*	*N/A*	*N/A*
Back pain	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	-0.18	-0.18	0.13	0.182
Muscular strength																
Urinary frequency	-0.09	-0.06	0.08	0.440	0.06	0.06	0.11	0.611	-0.10	-0.08	0.10	0.415	-0.07	-0.07	0.13	0.586
Tiredness-fatigue	-0.25	-0.22	0.10	**0.031**	-0.29	-0.27	0.12	**0.032**	-0.20	-0.17	0.10	0.094	-0.22	-0.21	0.13	0.102
Poor sleep	-0.20	-0.22	0.13	0.089	-0.07	-0.07	0.13	0.584	0.01	0.01	0.10	0.939	-0.20	-0.18	0.13	0.153
Breast pain	0.03	0.04	0.14	0.802	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*

Increased vaginal discharge	*N/A*	*N/A*	*N/A*	*N/A*	0.05	0.06	0.17	0.720	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Headache	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	-0.10	-0.09	0.12	0.450	*N/A*	*N/A*	*N/A*	*N/A*
Back pain	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	-0.14	-0.14	0.14	0.328
Speed-Agility																
Urinary frequency	0.16	0.11	0.08	0.189	0.10	0.09	0.10	0.407	0.22	0.17	0.10	0.085	0.03	0.03	0.12	0.801
Tiredness-fatigue	-0.34	-0.28	0.10	**0.006**	-0.18	-0.16	0.12	0.193	-0.18	-0.15	0.11	0.163	-0.15	-0.14	0.12	0.255
Poor sleep	-0.31	-0.32	0.13	**0.014**	-0.06	-0.06	0.12	0.643	-0.15	-0.12	0.10	0.254	-0.05	-0.04	0.12	0.727
Breast pain	0.18	0.21	0.15	0.114	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Increased vaginal discharge	*N/A*	*N/A*	*N/A*	*N/A*	-0.15	-0.17	0.15	0.290	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Headache	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	-0.09	-0.09	0.13	0.481	*N/A*	*N/A*	*N/A*	*N/A*
Back pain	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	0.05	0.04	0.13	0.727
Flexibility																
Urinary frequency	-0.09	-0.05	0.07	0.456	-0.16	-0.12	0.09	0.203	-0.06	-0.04	0.08	0.619	-0.16	-0.13	0.11	0.223
Tiredness-fatigue	-0.15	-0.10	0.08	0.213	-0.10	-0.08	0.10	0.450	-0.25	-0.18	0.08	**0.035**	-0.04	-0.03	0.11	0.766
Poor sleep	-0.02	-0.02	0.11	0.854	-0.20	-0.16	0.11	0.143	-0.28	-0.19	0.08	**0.021**	-0.15	-0.12	0.10	0.267
Breast pain	-0.14	-0.14	0.12	0.260	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Increased vaginal discharge	*N/A*	*N/A*	*N/A*	*N/A*	-0.31	-0.31	0.13	**0.023**	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Headache	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	-0.08	-0.07	0.10	0.517	*N/A*	*N/A*	*N/A*	*N/A*
Back pain	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	-0.13	-0.10	0.11	0.358

Note: Model adjusted for maternal age, body max index at 16th or 34th gestational weeks, and exercise intervention at 34th gestational weeks. Bold values, $p < 0.05$

Abbreviations: G.w., gestational weeks; *N/A*, not applicable. β, standardized regression coefficient; B, non-standardized regression coefficient; SE, Standard Error.

DISCUSSION

Our findings indicate that greater overall self-reported PF was associated with less incidence of pregnancy-related symptoms and its limitations in activities of daily living. Specifically, greater self-reported overall PF, cardiorespiratory fitness, muscular strength and speed-agility were associated with lower incidence of tiredness-fatigue. Moreover, greater self-reported overall PF, cardiorespiratory fitness and speed-agility were associated with lower incidence of poor sleep. Attending its limitations on activities of daily living, greater self-reported cardiorespiratory fitness and flexibility were associated with less tiredness-fatigue during the early second trimester of pregnancy.

The mean age of the women at the time of the recruitment was 32.9 ± 4.6 years old (in the average of Spaniards pregnancy age [80]). Pregnant women showed average level of overall self-reported PF and all its components throughout the pregnancy course. Top prevalence of pregnancy-related symptoms reported by our sample of pregnant women were similar to those found in the original PSI version [81], the Spanish-validated version [82], and other studies investigating pregnancy-related symptoms [83, 84]. In our study, tiredness- fatigue and poor sleep were specially reported as endorsed pregnancy-related symptoms and limitations in activities of daily living along the pregnancy course. The findings of the present study shown that greater PF levels were associated with lower incidence of these two commonly reported pregnancy-related symptoms.

Fatigue has been associated with pregnancy complications and fears, such as depression, risk of caesarean section, fear of childbirth and weak maternal-infant attachment, which may seriously impact maternal-fetal health and quality of life [85]. Moreover, physical, anatomical, physiological and hormonal changes associated with pregnancy, fetal movements and the size of the uterus, may negatively affect sleep patterns [83, 84]. In addition, a high percentage of pregnant women experience fatigue in all trimesters [83], aggravated also by sleep disruptions [83].

Other symptoms, such as increased urinary frequency and vaginal discharge are common urogenital system complaints throughout pregnancy [83], also confirmed in our study sample. The integumentary and vascular systems involve altered levels of circulating hormones, increased intravascular volume, and compression from the enlarging uterus underlie the complex physiological adaptations to the pregnancy course [86], which may also contribute to poor sleep and increased fatigue feelings. Insomuch as these pregnancy-related changes/symptoms are interconnected, it is plausible that improving some of them may also exert a positive impact on others. In this sense, our results show that pregnant women with greater self-reported overall PF levels and its components may experience both, lower incidence and lower limitations in activities of daily living due to tiredness-fatigue and poor sleep.

Since our study is the first to analyze the relationship of PF levels with pregnancy-related symptoms, it is not possible to compare the present findings with other similar studies. Nevertheless, pregnancy-related symptoms that caused the largest effect on women's lives such as fatigue-tiredness, sleep disruptions-insomnia, and increased urination need to be deeply explored and understood, preventing women from taking unnecessary pharmacological treatment. Some possible hypothesis about the mechanisms involved in these associations could be proposed. Regarding fatigue-tiredness, there is a lack of studies exploring the influence of PF on fatigue during pregnancy. In general population, greater PA levels have been associated with about 40% reduced risk in experiencing low energy and fatigue [87]. In pregnant women, a recent systematic review and meta-analysis concluded that following a supervised exercise program during pregnancy reduces fatigue [85]. Moreover, a previous study, conducted in general population, showed that those participants with lower self-reported PF had poorer sleep quality [88]. Specifically, poor sleep quality was associated with lower levels of muscular strength, cardiorespiratory fitness and flexibility [89]. Our results showed that those pregnant women with greater self-reported overall PF (especially cardiorespiratory fitness and speed-agility) reported lower incidence of poor sleep. Moreover, those with greater self-reported flexibility also reported lower limitations due to poor sleep. Although further research is needed to elucidate the mechanisms, a possible explanation promoting reduced fatigue and better sleep quality is that exercise plays a role in brain circuitry, neurotransmitters and neuromodulators, regulating motor functioning and mediating mood disturbances, through monoamines, histamine or gabapentin-mediated neurotransmission [87]. In addition, exercise plays a role in the thermoregulatory mechanism, improving vasodilation, decreasing cortisol levels or exerting well-being and a mental-calm state [88], consequently decreasing sleep disturbances.

Regarding urogenital problems, one possible explanation is that pregnant women may have a weak pelvic floor, as it has been studied that a higher BMI is associated with weaker pelvic floor muscles [90], and our participants had an average BMI of 25 kg/ m^2 at the 16th g.w. Moreover, lower PF levels may also exert a negative effect, especially in the later stages of pregnancy, due to the pressure of the growing fetus on the muscles of the utero muscles [91]. In fact, other factors, such as low PF levels and sleep disturbances are also significant contributors to the development of fatigue [92].

Greater PF levels are improved by practicing PA or exercise [7, 93]. The specialized 2019-Canadian Guidelines for physical exercise during pregnancy indicate that “there may be periods when following the guidelines is not possible due to fatigue and/or discomforts of pregnancy” [93]. In fact, common barriers to be physically active during pregnancy include discomforts of pregnancy, among others [25]. Nevertheless, our results suggest that pregnant women with greater self-reported PF levels may suffer from lower frequency and severity of these pregnancy-related symptoms, such as fatigue and discomfort. Therefore, we encourage pregnant women to reach greater PF levels in order to deal with these symptoms and limitations through pregnancy course, although some modification to exercise routines may be necessary [7]. In this sense, women should accomplish with at least 150 min of moderate intensity PA per week, combining aerobic, resistance-strength activities plus pelvic floor training, to obtain meaningful health benefits and reductions in pregnancy-related complications [93]. This should be especially mandatory during pregnancy since we have previously found that only 22% of the Spanish pregnant women complied with these recommendations [26].

Study V: The favourable association of self-reported physical fitness with depression and anxiety during pregnancy: The GESTAFIT Project.

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RESULTS

The present study comprised a total of 158 pregnant women with valid baseline data. Nonetheless, there was a loss of data in some outcomes, due to some of them did not attend the second evaluation (at the 34th g.w.) or did not return all the questionnaires duly (see **Figure 3**).

The sociodemographic, anthropometric and clinical characteristics of the participants are presented in **Table 23**. Data are presented baseline, otherwise indicated. Women's GWG at the 16th and 34th g.w. were 2.1 ± 2.8 kg and 10.6 ± 5.0 kg, respectively. Pregnant women showed an average level of overall self-reported PF and all its components through the pregnancy course. Most women were not at risk of depression either at the 16th or 34th g.w. and neither showed high anxiety levels during the pregnancy course.

Table 23. Sociodemographic, anthropometric and clinical characteristics of the study participants.

Maternal outcomes	**n**	**Mean (SD)**
Age (years)	158	32.9 (4.6)
Height at 16th g.w. (cm)	158	163 (6.21)
Weight at 16th g.w. (kg)	158	67.0 (11.8)
Weight at 34th g.w. (kg)	123	74.6 (10.8)
Gestational weight gains at 16th g.w. (kg)	143	2.1 (2.8)
Gestational weight gains at 34th g.w. (kg)	118	10.6 (5.0)
		n (%)
Marital Status	158	
Living with a partner		154 (97.5)
Educational level	158	
Primary or high-school		37 (23.4)
Specialized training		27 (17.1)
University degree		94 (59.5)
Working status	158	
Homework/unemployed		48 (30.4)
Partial-time employed/student		41 (25.9)
Full-time employed		69 (43.7)
Self-reported Physical Fitness (0-5)		**Mean (SD)**
16th g.w.	142	
Overall physical fitness		3.2 (0.7)
Cardiorespiratory fitness		2.5 (0.9)
Muscular strength		3.1 (0.7)
Speed-agility		3.0 (0.8)
Flexibility		3.1 (1.0)
34th g.w.	117	
Overall physical fitness		3.3 (0.7)
Cardiorespiratory fitness		2.6 (0.8)
Muscular strength		3.2 (0.7)
Speed-agility		2.9 (0.7)
Flexibility		3.1 (1.0)
Parity	158	**n (%)**
Nulliparous		96 (60.8)
Multiparous		62 (39.2)
Previous abortions		66 (42.0)
Previous depression, anxiety or other mental disorder diagnosis (yes)	158	3 (1.9)
CES-D score		**Mean (SD)**
16th g.w.	119	11.53 (8.57)
34th g.w.	116	13.38 (7.60)

Categorization of depressive symptoms (CES-D), *16th g.w.*		**n (%)**
No clinical significance		95 (79.8)
Risk of clinical depression		24 (20.2)
Categorization of depressive symptoms (CES-D), *34th g.w.*		**n (%)**
No clinical significance		90 (77.6)
At risk of clinical depression		26 (22.4)
STAI-S score, 16th g.w., Mean (SD)	142	14.6 (9.8)
STAI-S score, 34th g.w., Mean (SD)	111	17.1 (10.9)
Detection of anxiety disorders (STAI-S), *16th g.w.*		
No highly anxious		138 (97.2)
Highly anxious		4 (2.8)
Detection of anxiety disorders (STAI-S), *34th g.w.*		
No highly anxious		108 (97.3)
Highly anxious		3 (2.7)

Note: Values shown as mean (SD, standard deviation) unless otherwise indicated.
Abbreviations: G.w., gestational weeks; BMI, Body Mass Index; CES-D, Center for Epidemiological Studies-Depression Scale; STAI-S, State Anxiety Inventory.

The linear regression models assessing the association of self-reported overall PF and its components with depressive symptoms and anxiety levels at the 16th and 34th g.w. are shown in **Table 24**. In model 1, women who reported greater overall self-reported PF showed fewer depressive symptoms at the 16th g.w. (β= −0.28, p= 0.004). Greater self-reported cardiorespiratory fitness and muscular strength were associated with lower anxiety levels at the 16th g.w. (β= −0.18, p= 0.042, and β= −0.21, p= 0.017, respectively). Greater overall self-reported PF, cardiorespiratory fitness and speed-agility were associated with lower anxiety levels at the 34th g.w. (β= −0.30, p= 0.003; β= −0.32, p= 0.002; β= −0.31, p= 0.002, respectively). In model 2, women who reported greater overall self-reported PF showed fewer depressive symptoms (β = −0.20, p= 0.035) at the 16th g.w., and lower anxiety levels at the 34th g.w. (β= −0.20, p= 0.041). Greater self-reported cardiorespiratory fitness was associated with lower anxiety levels at the 34th g.w. (β= −0.21, p= 0.030). Greater self-reported muscular strength was associated with lower anxiety levels at the 16th g.w. (β= −0.22, p= 0.014). Finally, greater self-reported speed-agility was associated with lower anxiety levels at the 34th g.w. (β= −0.25, p= 0.009).

Table 24. Linear regression coefficients assessing the association of self-reported overall physical fitness and its components with depressive symptoms and anxiety levels at the 16th and 34th gestational weeks.

	Model 1				Model 2			
	B	**B**	**SE**	***P***	**β**	**B**	**SE**	***P***
Depression (CES-D) (16th g.w., n= 119)								
Overall physical fitness	-0.28	-3.17	1.09	**0.004**	-0.20	-2.24	1.05	**0.035**
Cardiorespiratory fitness	-0.18	-1.75	0.95	0.060	-0.08	-0.73	0.91	0.420
Muscular strength	-0.15	-1.78	1.15	0.120	-0.10	-1.13	1.06	0.290
Speed-agility	-0.07	-0.77	1.05	0.460	-0.03	-0.31	0.99	0.750
Flexibility	-0.01	-0.12	0.83	0.880	0.04	0.36	0.76	0.630
Depression (CES-D) (34th g.w., n= 116)								
Overall physical fitness	-0.15	-1.50	0.94	0.110	-0.05	-0.51	0.90	0.570
Cardiorespiratory fitness	-0.12	-1.19	0.93	0.200	0.02	0.22	0.88	0.790
Muscular strength	-0.00	0.05	1.02	0.950	0.08	0.80	0.95	0.400
Speed-agility	-0.08	-0.86	0.98	0.380	0.01	0.10	0.90	0.910
Flexibility	-0.10	-0.72	0.72	0.320	0.08	0.56	0.68	0.410
Anxiety (STAI-S) (16th g.w., n= 142)								
Overall physical fitness	-0.17	-2.22	1.20	0.060	-0.14	-1.80	1.21	0.140
Cardiorespiratory fitness	-0.18	-2.01	0.98	**0.042**	-0.15	-1.67	0.99	0.090
Muscular strength	-0.21	-2.79	1.16	**0.017**	-0.22	-2.82	1.13	**0.014**
Speed-agility	-0.13	-1.65	1.10	0.130	-0.15	-1.87	1.08	0.080
Flexibility	-0.07	-0.74	0.89	0.400	-0.06	-0.64	0.87	0.460
Anxiety (STAI-S) (34th g.w., n= 111)								
Overall physical fitness	-0.30	-4.08	1.36	**0.003**	-0.20	-2.86	1.38	**0.041**

Cardiorespiratory fitness	-0.32	-4.48	1.33	**0.001**	-0.21	-2.95	1.34	**0.030**
Muscular strength	-0.16	-2.53	1.54	0.100	-0.10	-1.47	1.51	0.330
Speed-agility	-0.31	-4.55	1.43	**0.002**	-0.25	-3.67	1.37	**0.009**
Flexibility	-0.16	-1.72	1.09	0.110	-0.04	-0.39	1.08	0.710

Note: Model 1 adjusted for age and gestational weight gains at 16^{th} and 34^{th} gestational weeks. Model 2 additionally adjusted for sleep quality, exercise intervention at the 34^{th} gestational weeks, educational level, working status and living with a partner. Bold values, $p < 0.05$

Abbreviations: g.w. gestational weeks; CES-D, Center for Epidemiological Studies-Depression Scale; STAI-S, State Anxiety Inventory; β, standardized regression coefficient; B, non-standardized regression coefficient; SE, Standard Error.

The findings of the present study indicate that greater self-reported PF was associated with lower psychological ill-being during pregnancy (i.e. fewer depressive symptoms and lower anxiety levels). Specifically, greater overall self-reported PF was associated with fewer depressive symptoms at the 16th g.w. Greater self-reported cardiorespiratory fitness and muscular strength were associated with lower anxiety levels at the 16th g.w. and overall self-reported PF, cardiorespiratory fitness and speed-agility were associated with lower anxiety levels at the 34th g.w.

These findings have public health and clinical implications, as pregnancy is a period of life in which there is an important prevalence of antenatal depression and anxiety [94-96], impacting not only on the mother's health [94] but also in the newborn development [97].

As far as we know, this is the first study to analyze the association of self-reported overall PF with depressive symptoms and anxiety levels during pregnancy. We have observed that pregnant women with greater self-reported overall PF (understood as the sum of its components) showed fewer depressive symptoms in early second trimester of pregnancy and lower anxiety levels in late pregnancy. In this sense, improving overall PF levels during the pregnancy course (and also before pregnancy) may impact positively not only on the mother's mental health but also on the fetus development. The precise physiological mechanisms associating PF with depression and anxiety are not well established, but it is well known that exercise improves PF [98], being also an effective alternative to treat, as well as to prevent, depressive and anxiety disorders [96, 99-101].

During pregnancy, the neuroendocrine system suffers an over activity led by maternal stress [102], and some studies have reported relatively high levels of anxiety, especially during early and late pregnancy up to the birth [95, 103, 104]. Moreover, there is a strong correlation between maternal and fetal cortisol levels, suggesting that there is a transmission of cortisol through the placenta [95]. In addition to the gestational adverse outcomes [97], the infants exposed to elevated maternal cortisol levels and antenatal anxiety during the fetal period are at increased risk for developing psychological disorders, such as anxiety and behavioral or emotional problems, during the preadolescent period [95].

Exercise may play an important role in the regulation of stress hormones, such as the aforementioned cortisol, via the hypothalamus-pituitary-adrenal axis [102], plus the anti-inflammatory response induced by exercise [105]. In addition, β-endorphins produce an analgesic effect and sense of well-being [106], which may also regulate depression-anxiety symptoms. Indeed, being physically inactive compared with exercising has been associated with more depressive and anxiety symptoms in early [9] and late pregnancy [99]. Moreover, greater overall PF levels promote an increase in circulating brain-derived neurotrophic factor, which might prevent depression promoting neuroplasticity and maintaining brain function [107], as well as improving social factors, sociability [108], self-esteem, self-efficacy, distraction [109], motivation [71] and quality of life [110]. Furthermore, it has been shown that women with greater self-reported PF were less likely to suffer from mental disorders during pregnancy [111], suggesting that adequate PF levels can be used as a tool for the prevention of depression and anxiety during the pregnancy course. Still, longitudinal and intervention studies are necessary to confirm this hypothesis.

Regarding cardiorespiratory fitness, this component has shown a strong association with fewer depressive symptoms [110] in the general population which do not concurs with our findings. In fact, in a previous study conducted at the 16th g.w., we neither found any association between objectively measured cardiorespiratory fitness and outcomes of psychological ill-being [9]. This may be due to factors related to early pregnancy, such as musculoskeletal pain or disability [8], fatigue or nausea [8, 71] or misinformation about safety of PA, resulting in fear of harming the fetus during exercise [71]. Moreover, our study sample reported few risks of clinical depression which may also result in this lack of association.

On the other hand, those pregnant women with greater self-reported cardiorespiratory fitness showed lower anxiety levels in early and late pregnancy. This is in consonance with previous studies showing that greater cardiorespiratory fitness is associated with a reduction in anxiety levels [101]. This fact is especially relevant during late pregnancy, since it has been found that greater cardiorespiratory fitness levels are associated with better maternal birth outcomes and less prevalence of caesarean section [112]. In addition, cardiorespiratory fitness is an important predictor of other maternal mental disorders, such as postpartum depression [113]. Therefore, improving cardiorespiratory fitness during pregnancy is mandatory.

In our study, greater self-reported muscular strength is associated with lower anxiety levels in early pregnancy. Little is known about the effect of muscular strength on pregnancy. Notwithstanding, specialized guidelines during pregnancy recommend to engage in strength training before, during, and after pregnancy [7], suggesting that greater levels of muscular strength may promote better health benefits during this period. Moreover, greater muscular strength has been associated with lower anxiety levels and better mental health in other populations where psychological ill-being impact on their health, such as perimenopausal women [114] and fibromyalgia patients [100]. Regarding speed-agility, it is known that greater self-reported speed-agility is associated with lower depression, anxiety, negative affect and greater optimism in perimenopause [114], and our results show that greater self-reported speed-agility is also associated with lower anxiety levels in late pregnancy.

All in all, being active and reaching greater overall PF levels during pregnancy is an alternative to pharmacological approaches [107], which might improve psychologic well-being [7].

Study VI: The role of self-reported physical fitness in emotional well-being and distress during pregnancy: The GESTAFIT Project.

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Submitted (Sports Health: A Multidisciplinary Approach).

RESULTS

The present study comprised a total of 158 pregnant women with valid baseline data (i.e.,16th g.w.). Nonetheless, there was a loss of data in some outcomes, due to some of them did not attend the second evaluation (at the 34th g.w.) or did not return all the questionnaires duly completed (see **Figure 3**).

The sociodemographic, anthropometric and clinical characteristics of the participants are presented in **Table 25**.

Table 25. Sociodemographic characteristics, anthropometric measures and self-reported physical fitness levels of the study participants.

Maternal outcomes	**n**	**Mean (SD)**
Age (years)	158	32.9 (4.6)
Height (cm)	156	163.9 (6.2)
Weight previous to pregnancy (kg)	145	65.1 (12.3)
Body mass index previous to pregnancy (kg/m^2)	143	24.2 (4.2)
Weight at 16^{th} g. w. (kg)	156	67.0 (11.9)
Weight at 34^{th} g. w. (kg)	123	74.6 (10.9)
Gestational weight gains (pre-pregnancy-16^{th} g.w.)	143	2.1 (2.8)
Gestational weight gains (pre-pregnancy-34^{th} g.w.)	118	10.6 (5.0)
Self-reported physical fitness (0-5)		
16^{th} g. w.	142	
Overall physical fitness		3.2 (0.8)
Cardiorespiratory fitness		2.5 (0.9)
Muscular strength		3.1 (0.8)
Speed-agility		3.1 (0.8)
Flexibility		3.1 (0.8)
34^{th} g. w.	117	
Overall physical fitness		3.3 (0.8)
Cardiorespiratory fitness		2.6 (0.8)
Muscular strength		3.3 (0.7)
Speed-agility		3.0 (0.8)
Flexibility		3.1 (1.0)
PANAS-S		
16^{th} g. w.	143	
Positive affect (10-50)[a]		34.1 (6.7)
Negative affect (10-50)[b]		17.6 (7.1)
34^{th} g. w.	117	
Positive affect (10-50)[a]		32.9 (7.6)
Negative affect (10-50)[b]		18.6 (6.9)
PANAS-T		
16^{th} g. w.	129	
Positive affect (10-50)[a]		33.5 (6.6)
Negative affect (10-50)[b]		18.1 (6.7)
34^{th} g. w.	110	
Positive affect (10-50)[a]		34.2 (7.1)
Negative affect (10-50)[b]		18.9 (6.8)
		n (%)
Living with a partner	158	154 (97.5)
Educational level	158	
Primary or high-school		18 (11.4)
Specialized training		46 (29.1)
University degree		94 (59.5)
Working status	158	
Homework/unemployed student		48 (30.4)
Partial-time employed/student		41 (25.9)
Full-time employed		69 (43.7)

Note: Values shown as mean (SD, standard deviation) unless otherwise indicated. [a], higher scores reflect greater affective emotional health/experience. [b], higher scores reflect greater emotional distress.

Abbreviations: G. w., gestational weeks; PANAS-S, Positive and Negative Affect Schedule-State; PANAS-T, Positive and Negative Affect Schedule-Trait.

Women's GWG at the 16th and 34th g.w. were 2.1 ± 2.8 kg and 10.6 ± 5.0 kg, respectively. Pregnant women showed an average level of overall self-reported PF and all its components thorough the pregnancy course. Almost 90% of the pregnant women had higher studies than primary or high-school and around 70% of them were employed at baseline.

PANAS-S positive affect values were slightly higher at 16th g.w. than at 34th g.w., while PANAS-S negative affect values were slightly higher at 34th g.w. than at 16th g.w. PANAS-T positive affect values were slightly higher at 34th g.w. than at 16th g.w., while PANAS-T negative affect values were similar in both g.w.

Associations of overall self-reported PF and its components with emotional well-being and emotional distress at the 16th g.w. are shown in **Table 26**. In Model II, women who reported greater overall self-reported PF, cardiorespiratory fitness, muscular strength and speed-agility showed greater PANAS-S and PANAS-T positive affect (β ranging from 0.206 to 0.316; all, $p< 0.05$); greater overall self-reported PF, cardiorespiratory fitness, muscular strength and speed-agility were associated with lower PANAS-T negative affect (β ranging from -0.071 to -0.224; all, $p< 0.05$). In Model I, the results remained the same, except for cardiorespiratory fitness, which was no longer associated with PANAS-T negative affect.

Table 26. Association of self-reported overall physical fitness and its components with emotional well-being and emotional distress at the 16th gestational week.

	Model I					**Model II**				
	β	**B**	**95% CI**		***P***	**B**	**B**	**95% CI**		***P***
			Lower	**Upper**				**Lower**	**Upper**	
PANAS-S positive affect (n= 127)										
Overall physical fitness	0.215	1.873	0.323	3.423	**0.018**	0.217	1.891	0.323	3.459	**0.019**
Cardiorespiratory fitness	0.206	1.488	0.210	2.765	**0.023**	0.206	1.491	0.169	2.812	**0.027**
Muscular strength	0.294	2.560	1.075	4.045	**0.001**	0.303	2.634	1.115	4.152	**0.001**
Speed-agility	0.264	2.163	0.757	3.569	**0.003**	0.281	2.303	0.867	3.740	**0.002**
Flexibility	0.065	0.425	-0.739	1.589	0.471	0.070	0.459	-0.731	1.649	0.447
PANAS-S negative affect (n= 127)										
Overall physical fitness	-0.137	-1.279	-2.974	0.415	0.138	-0.139	-1.297	-2.998	0.404	0.134
Cardiorespiratory fitness	-0.145	-1.121	-2.514	0.272	0.114	-0.135	-1.042	-2.472	0.389	0.152
Muscular strength	-0.072	-0.671	-2.342	1.000	0.428	-0.084	-0.782	-2.479	0.916	0.364
Speed-agility	-0.129	-1.135	-2.694	0.424	0.152	-0.140	-1.226	-2.811	0.360	0.128
Flexibility	-0.098	-0.685	-1.936	0.567	0.281	-0.091	-0.636	-1.908	0.636	0.324
PANAS-T positive affect (n= 112)										
Overall physical fitness	0.214	1.849	0.193	3.505	**0.029**	0.218	1.884	0.212	3.557	**0.028**
Cardiorespiratory fitness	0.223	1.651	0.254	3.047	**0.021**	0.215	1.586	0.154	3.017	**0.030**
Muscular strength	0.293	2.498	0.898	4.098	**0.003**	0.316	2.695	1.046	4.344	**0.002**
Speed-agility	0.210	1.671	0.171	3.171	**0.029**	0.229	1.828	0.293	3.363	**0.020**
Flexibility	-0.010	-0.059	-1.234	1.116	0.920	-0.006	-0.039	-1.240	1.162	0.949
PANAS-T negative affect (n= 112)										
Overall physical fitness	-0.203	-1.854	-3.593	-0.116	**0.037**	-0.199	-1.815	-3.541	-0.088	**0.040**
Cardiorespiratory fitness	-0.178	-1.393	-2.887	0.102	0.067	-0.191	-1.489	-2.950	-0.028	**0.046**

Muscular strength	-0.229	-2.068	-3.816	-0.319	**0.021**	-0.213	-1.920	-3.617	-0.223	**0.027**
Speed-agility	-0.249	-2.102	-3.684	-0.519	**0.010**	-0.224	-1.884	-3.438	-0.331	**0.018**
Flexibility	-0.081	-0.521	-1.760	0.718	0.406	-0.071	-0.457	-1.674	0.759	0.458

Note: Model 1 adjusted for age and gestational weight gains at 16th gestational week. Model 2 additionally adjusted for educational level, working status and living with a partner.

Abbreviations: G.w., gestational weeks; PANAS-S, Positive and Negative Affect Schedule-State; PANAS-T, Positive and Negative Affect Schedule-Trait.

Association of self-reported overall PF and its components with emotional well-being and emotional distress at the 34th g.w. are shown in **Table 27**. In Model II, women who reported greater overall self-reported PF showed greater PANAS-S positive affect (β= 0.231, p= 0.024), and greater self-reported cardiorespiratory fitness showed greater PANAS-S positive affect (β= 0.286; p= 0.004); greater overall self-reported PF, cardiorespiratory fitness, muscular strength and speed-agility were associated with lower PANAS-S negative affect (β ranging from -0.192 to -0.243; all p< 0.05); greater overall self-reported PF, speed-agility and flexibility were associated with lower PANAS-T negative affect (β ranging from 0.129 to -0.313; all p< 0.05). In Model I, the results remain the same, except for overall self-reported PF which was further associated with PANAS-T positive affect (β= 0.217, p= 0.030).

Table 27. Association of self-reported overall physical fitness and its components with emotional well-being and emotional distress at the 34th gestational week.

	Model I					Model II				
	β	**B**	**95% CI**		***P***	**β**	**B**	**95% CI**		***P***
			Lower	**Upper**				**Lower**	**Upper**	
PANAS-S positive affect (n= 107)										
Overall physical fitness	0.263	2.629	0.738	4.519	**0.007**	0.231	2.309	0.311	4.306	**0.024**
Cardiorespiratory fitness	0.312	3.027	1.227	4.828	**0.001**	0.286	2.775	0.912	4.638	**0.004**
Muscular strength	0.156	1.693	-0.423	3.809	0.116	0.158	1.711	-0.489	3.912	0.126
Speed-agility	0.166	1.742	-0.278	3.761	0.090	0.163	1.702	-0.330	3.734	0.100
Flexibility	0.124	0.951	-0.532	2.434	0.206	0.108	0.831	-0.679	2.341	0.278
PANAS-S negative affect (n= 126)										
Overall physical fitness	-0.214	-1.929	-3.656	-0.201	**0.029**	-0.243	-2.191	-4.010	-0.372	**0.019**
Cardiorespiratory fitness	-0.217	-1.895	-3.565	-0.225	**0.027**	-0.228	-1.996	-3.725	-0.268	**0.024**
Muscular strength	-0.194	-1.903	-3.800	-0.006	**0.049**	-0.225	-2.204	-4.188	-0.220	**0.030**
Speed-agility	-0.229	-2.165	-3.964	-0.365	**0.019**	-0.238	-2.246	-4.073	-0.420	**0.016**
Flexibility	-0.187	-1.298	-2.623	0.028	0.055	-0.192	-1.330	-2.691	0.031	0.055
PANAS-T positive affect (n= 100)										
Overall physical fitness	0.217	1.961	0.189	3.733	**0.030**	0.185	1.669	-0.205	3.543	0.080
Cardiorespiratory fitness	0.275	2.397	0.713	4.081	**0.006**	0.248	2.159	0.417	3.901	**0.016**
Muscular strength	0.157	1.569	-0.422	3.559	0.121	0.166	1.661	-0.397	3.719	0.112
Speed-agility	0.117	1.121	-0.795	3.038	0.248	0.108	1.038	-0.889	2.965	0.287
Flexibility	0.119	0.821	-0.550	2.192	0.238	0.100	0.690	-0.707	2.087	0.329
PANAS-T negative affect (n= 100)										
Overall physical fitness	-0.247	-2.189	-3.913	-0.465	**0.013**	-0.257	-2.280	-4.102	-0.459	**0.015**
Cardiorespiratory fitness	-0.143	-1.220	-2.919	0.480	0.158	-0.129	-1.103	-2.864	0.657	0.216

Muscular strength	-0.143	-1.397	-3.352	0.558	0.159	-0.159	-1.556	-3.591	0.479	0.132
Speed-agility	-0.305	-2.867	-4.668	-1.066	**0.002**	-0.313	-2.941	-4.757	-1.125	**0.002**
Flexibility	-0.206	-1.393	-2.718	-0.069	**0.039**	-0.209	-1.415	-2.771	-0.060	**0.041**

Note: Model 1 adjusted for age and gestational weight gains at 34th gestational week. Model 2 additionally adjusted for exercise intervention, educational level, working status and living with a partner.
Abbreviations: g.w., gestational weeks; PANAS-S, Positive and Negative Affect Schedule-State; PANAS-T, Positive and Negative Affect Schedule-Trait.

DISCUSSION

Our findings indicate that greater self-reported PF was associated with greater emotional well-being and less emotional distress during pregnancy. Specifically, greater self-reported PF during early pregnancy may especially impact on short-term and long-term fluctuations in positive mood along the pregnancy course. Likewise, greater self-reported PF in late pregnancy seems particularly relevant for reducing negative differences in affectivity measured in a short and long term.

As far as we know, this is the first study confirming that overall self-reported PF plays a role in enhancing greater emotional well-being and lower emotional distress during pregnancy. This has public health and clinical implications, since well-being during pregnancy may be compromised due to pregnancy-related physical and psychological changes [71]. Hence, it seems imperative to find strategies aimed at improving well-being during pregnancy.

Positive and negative affect were measured both *state* and *trait*, reflecting not only how the women may experience such emotional well-being and distress at some points of pregnancy course (i.e., at 16^{th} and 34^{th} g.w., linked to *state*), but also as a longer perspective or women's *trait*. Our results suggest that women with greater PF in early pregnancy not only reflect greater short-term positive affect (i.e., PANAS-S), but may also reflect longer-term positive affect (i.e., PANAS-T).

On the other hand, while the associations found for greater PF levels with positive affect remain significant during the pregnancy course (especially during early pregnancy), the associations of PF levels with negative affect (both *state* and *trait*) are especially relevant during late pregnancy (i.e., at 34^{th} g.w.). Somehow, this fact may be related to the higher rates of anxiety and depression during late pregnancy [95], and some possible fears and worries associated with the term of the pregnancy (such as labor-related pain or to give birth in itself) [115]. Therefore, it seems particularly outstanding to reach adequate PF levels in late pregnancy, to avoid the known possible negative effects of maternal emotional distress on maternal-fetal health [116].

In addition to anxiety, stress or depression, many women experience pregnancy-related symptoms such as fatigue or sleep disruptions [117], which are related to worse quality of life and higher emotional distress [85]. Consequently, these physical and psychological symptoms related to pregnancy are interconnected, and the reduction of one or some of these symptoms may play a role in regulating the others, leading to a more pleasant course of their pregnancy. In this sense, previous studies have found a positive association between greater PF levels and reduced pregnancy-related symptoms (such as pregnancy-related pain or fatigue) [8, 117], better mental health (i.e., lower anxiety and depressive symptoms)[9, 118] and HRQoL [119].

Despite we did not find similar studies investigating the relationship of self-reported PF levels with maternal emotional well-being and emotional distress during pregnancy, some mechanisms have been previously proposed which may explain our findings: First, elevated cortisol (present in physiological states of high physical or mental stress) is a potential biological mechanism leading to health complications in pregnant women, and fetal adverse outcomes (such as premature births or low APGAR scores) [120]. In this sense, exercise may play a key role in the regulation of stress hormones, such as cortisol, via the hypothalamus-pituitary-adrenal axis [102]. Second, exercise also release β-endorphins that produce an analgesic effect and a sense of well-being [106]. Moreover, greater overall PF levels promote improved social factors, sociability [108], self-esteem, self-efficacy, distraction [109], motivation [71] and better quality of life [110]. In conclusion, women with high/adequate PF before pregnancy, or those reaching greater overall PF levels during pregnancy, show greater psychological well-being [7], and may be a key option in the prevention and treatment of maternal distress.

CHAPTER III.
The influence of the "GESTAFIT" concurrent exercise training protocol on pain and health-related quality of life

Study VII: Effects of a concurrent exercise training program on low back and sciatic pain and pain disability in late pregnancy.

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RESULTS

Of the 159 pregnant women who were randomized into the control (n= 87) and exercise (n= 72) groups, 9 and 7 of the control and exercise groups, respectively, did not have valid data in cofounding variables (i.e., pre-pregnancy BMI). A total of 21 women did not attend 75% of the exercise sessions. Thus, the total number of women used for the per-protocol analyses was 93 divided into control (n= 44) and exercise (n= 49) groups. The flowchart of the study participants is shown in **Figure 3**.

Baseline characteristics of the exercise and control groups are shown in **Table 28**. Gestational weight gain was lower in the exercise group ($p= 0.003$). No differences between the control and exercise groups were observed in the rest of the socio-demographic and clinical characteristics (all, $p> 0.05$).

Table 28. Sociodemographic and clinical characteristics of the study participants.

	All women (n= 93)	**Control Group (n= 49)**	**Exercise Group (n= 44)**
Age (years)	33.4 (4.5)	33.5 (4.8)	33.3 (4.2)
Pre-pregnancy body mass index (kg/m^2)	23.6 (3.7)	23.0 (3.2)	24.2 (4.1)
Gestational weight gains (weight at the 34th g.w.-pre-pregnancy) (kg)	11.2 (5.0)	12.6 (5.1)	9.6 (4.4)
Percentage of attendance[a]			85.7 (7.6)
Marital status		**n (%)**	
Married or with partner	55 (59.1)	29 (59.2)	26 (59.1)
Single or living alone	38 (40.9)	20 (40.8)	18 (40.9)
Educational level		**n (%)**	
University studies	61 (65.6)	34 (69.4)	27 (61.4)
Non-university studies	32 (34.4)	15 (30.6)	17 (38.6)
Visual Analogic Scale (VAS)[b] (0-100)			
Low back pain for the last 4 weeks	20.5 (23.6)	19.0 (24.9)	22.2 (22.4)
Sciatic pain for the last 4 weeks (n= 48 vs 44)	10.6 (20.1)	8.1 (16.6)	13.4 (23.1)
Oswestry Disability Index (ODI)[b] (0-5)			
Intensity of the pain	0.2 (0.6)	0.3 (0.8)	0.1 (0.4)
Pain while standing	0.7 (0.9)	0.8 (1.0)	0.6 (0.8)
Pain while carrying out self-care activities	0.1 (0.4)	0.2 (0.4)	0.1 (0.3)
Pain while sleeping	0.2 (0.9)	0.2 (1.0)	0.1 (0.8)
Pain while lifting weight	0.6 (0.8)	0.7 (0.8)	0.5 (0.7)
Pain having sexual activities (n= 40 vs 44)	0.1 (0.5)	0.2 (0.7)	0.1 (0.2)
Pain while walking (n= 40 vs 44)	0.1 (0.2)	0.1 (0.3)	0 (0.0)
Limitations of the social life due to pain (n= 40 vs 44)	0.2 (0.6)	0.3 (0.7)	0.1 (0.4)
Pain while seated (n= 40 vs 44)	0.5 (0.8)	0.5 (0.7)	0.5 (1.0)
Pain while travelling (n= 40 vs 44)	0.3 (0.5)	0.3 (0.5)	0.2 (0.4)
Total score (0-100%) (n= 40 vs 44)	5.6 (7.4)	6.8 (8.6)	4.5 (6.0)
Illness diagnosis		**(yes, n [%])**	
Chronic cervical backache	3 (3.2)	2 (4.1)	1 (2.3)
Chronic lumbar backache	4 (4.3)	3 (6.1)	1 (2.3)
Medication for pain in the last 2 weeks	18 (19.4)	10 (20.4)	8 (18.2)
Drug Intake		**(yes, n [%])**	
Ibuprofen	3 (3.2)	3 (6.1)	0 (0)
Paracetamol	23 (24.7)	12 (24.5)	11 (25.0)
Diazepam	2 (2.2)	1 (2.0)	1 (1.0)

Note: Values shown as mean (standard deviation) unless otherwise indicated. [a]The percentage of attendance in intention-to-treat basis analysis was 77.7% (17.1). [b]Greater scores indicate higher pain.
Abbreviations: G.w., gestational weeks.

Table 29 shows the per-protocol basis analyses of VAS low back, VAS sciatica, and ODI score changes between pre-and post-intervention for control and exercise groups. In model I, VAS low back and VAS sciatica scores increased by 4.1 and 4.2 mm, respectively, in the exercise group from 16^{th} to 34^{th} g.w., whereas they increased by 26.0 and 17.1 mm, respectively, in the control group. Consequently, the exercise group increased 21.9 and 12.9 mm less than the control group in the VAS low back (between-group differences (B): 95% CI: -33.6 to -10.2 mm; p< 0.001) and the VAS sciatica score (between-group differences: 95% CI (B): -21.8 to -4.0 mm; p= 0.005), respectively. Regarding the ODI, pain while sleeping, lifting weight, and limitations of the social life due to pain scores increased by 0.03, 0.2, and 0.1 in the exercise group whereas it increased by 0.8, 0.7 and 1.0 in the control group, respectively. Consequently, the exercise group increased 0.7, 0.5 and 0.7 less than control group in pain while sleeping score (between-group differences (B): 95% CI: -1.4 to -0.01; p= 0.025), pain while lifting weight score (between-group differences (B): 95% CI: -0.9 to -0.01; p= 0.016) and limitations of the social life due to pain (between-group differences(B): 95% CI: -1.3 to -0.06; p= 0.032) scores. Furthermore, ODI total score increased by 5.7% in the exercise group from 16^{th} to 34^{th} g.w. whereas it increased by 12.6% in the control group. Consequently, the exercise group increased 6.9% less than the control group the ODI total score (between-group differences (B): 95% CI: -13.9 to 0.053%; p= 0.052). After additionally adjusting for GWG results remained the same except for ODI-limitations of the social life and ODI total score. Intention-to-treat basis analyses depicted similar results (see **Table 30**).

Table 29. Per-protocol analyses showing the association of the changes on Visual Analogic Scale and the Oswestry Disability Index from 16th to 34th gestational weeks with the intervention group (control or exercise group) in pregnant women.

			Model I				Model II			
	Changes within control group Post-Pre	**Changes within exercise group Post-Pre**	**β**	**B**	**Between-group difference (95% CI)**	***P***	**Β**	**B**	**Between-group difference (95% CI)**	***P***
Visual Analogic Scale (VAS)[a], (0-100 mm)										
Low back pain for the last 4 weeks (n= 49 vs 44)	26.0 (4.0)	4.1 (4.2)	-0.33	-21.89	-33.60 to -10.18	**<0.001**	-0.30	-19.38	-31.50 to -7.25	**0.002**
Sciatic pain for the last 4 weeks (n= 48 vs 44)	17.1 (3.0)	4.2 (3.2)	-0.29	-12.91	-21.79 to -4.02	**0.005**	-0.26	-11.80	-21.14 to -2.47	**0.014**
Oswestry Disability Index (ODI)[a], (0-5)										
Intensity of the pain (n= 48 vs 38)	0.3 (0.2)	0.4 (0.2)	0.04	0.11	-0.44 to 0.66	0.690	0.01	0.04	-0.53 to 0.62	0.873
Pain while standing (n= 48 vs 38)	0.3 (0.1)	0.5 (0.2)	0.10	0.23	-0.17 to 0.64	0.253	0.14	0.30	-0.11 to 0.72	0.148
Pain while carrying out self-care activities (n= 48 vs 38)	0.3 (0.1)	0.2 (0.1)	-0.09	-0.12	-0.42 to 0.17	0.410	-0.07	-0.09	-0.40 to 0.21	0.537
Pain while sleeping (n= 47 vs 38)	0.8 (0.2)	0.03 (0.2)	-0.22	-0.73	-1.37 to -0.09	**0.025**	-0.24	-0.81	-1.48 to -0.15	**0.016**
Pain while lifting weight (n= 47 vs 38)	0.7 (0.1)	0.2 (0.2)	-0.24	-0.51	-0.93 to -0.09	**0.016**	-0.21	-0.45	-0.88 to -0.01	**0.042**
Pain having sexual activities (n= 22 vs 21)	1.0 (0.3)	0.3 (0.3)	-0.29	-0.82	-1.74 to 0.08	0.075	-0.29	-0.84	-1.91 to 0.21	0.113
Pain while walking (n= 22 vs 21)	0.6 (0.1)	0.2 (0.1)	-0.21	-0.35	-0.77 to 0.07	0.105	-0.23	-0.37	-0.87 to 0.12	0.140
Limitations of the social life due to pain (n= 22 vs 21)	0.8 (0.2)	0.1 (0.2)	-0.30	-0.66	-1.27 to -0.06	**0.032**	-0.27	-0.60	-1.30 to 0.10	0.093
Pain while seated (n= 22 vs 21)	1.0 (0.2)	0.6 (0.2)	-0.18	-0.33	-0.90 to 0.24	0.247	-0.18	-0.32	-0.98 to 0.33	0.326
Pain while travelling (n= 22 vs 21)	0.5 (0.2)	0.3 (0.2)	-0.11	-0.06	-0.62 to 0.38	0.637	-0.05	-0.09	-0.68 to 0.48	0.735
Oswestry Disability Index (ODI)[a] total score, (0-100%) (n= 18 vs 17)	12.6 (2.3)	5.7 (2.4)	-0.30	-6.91	-13.88 to 0.05	**0.052**	-0.25	-5.73	-13.79 to 2.32	0.158

Note: Values shown as mean (standard error). Model I was adjusted for baseline values, age and pre-pregnancy body mass index. Model II was additionally adjusted for gestational weight gains (i.e., weight at the 34th gestational week-pre-pregnancy weight). Mean results show the differences between post-pre intervention (i.e., 34th gestational week-16th gestational week) after adjusting for baseline values, age and pre-pregnancy body mass index for each variable, with negative values indicating a reduction in the post evaluation compared to pre-evaluation. [a]Greater scores indicate higher pain. Bold values, $p < 0.05$.
Abbreviations: β, standardized regression coefficient; B, non-standardized regression coefficient.

Table 30. Intention-to-treat analyses showing the association of the changes on Visual Analogic Scale and Oswestry Disability Index from 16th to 34th gestational weeks with the intervention group (control or exercise group) in pregnant women.

			Model I				Model II			
	Changes within control group Post-Pre	**Changes within exercise group Post-Pre**	**β**	**β**	**Between-group difference (95% CI)**	***P***	**β**	**B**	**Between-group difference (95% CI)**	***P***
Visual Analogic Scale (VAS)[a], (0-100 mm)										
Low back pain for the last 4 weeks (n= 49 vs 68)	24.7 (4.0)	2.7 (3.4)	-0.331	-21.937	-32.381 to -11.493	**<0.001**	-0.295	-19.501	-30.535 to -8.467	**0.001**
Sciatic (lower member) pain for the last 4 weeks (n= 48 vs 68)	16.7 (3.3)	4.4 (2.8)	-0.258	-12.349	-20.982 to -3.716	**0.005**	-0.230	-11.031	-20.249 to -1.814	**0.019**
Oswestry Disability Index (ODI)[a] total score, (0-100%) (n= 25 vs 43)	10.9 (2.3)	4.2 (1.8)	-0.267	-6.651	-12.492 to -0.811	**0.026**	-0.205	-5.107	-12.136 to 1.923	**0.151**

Note: Values shown as mean (standard error). Model I was adjusted for baseline values, age and pre-pregnancy body mass index. Model II was additionally adjusted for gestational weight gains (i.e., weight at the 34th gestational week-pre-pregnancy weight). Mean results show the differences between post-pre intervention (i.e., 34th gestational week-16th gestational week) after adjusting for baseline values, age and pre-pregnancy body mass index for each variable, with negative values indicating a reduction in the post evaluation compared to pre-evaluation. [a]Greater scores indicate higher pain. Bold values, $p < 0.05$.

Abbreviations: β, standardized regression coefficient; B, non-standardized regression coefficient.

DISCUSSION

The main findings of this intervention study suggest that the concurrent exercise training program developed within the GESTAFIT Project improved low back and sciatic pain, as well as limitations due to pain, compared to the control group. Specifically, the exercise group had a lower increase in VAS-low back and VAS-sciatic pain than the control group through pregnancy. Regarding ODI subscales, the exercise group worsened less than the control group in pain while sleeping, pain while lifting weight, and limitations of the social life due to pain. Furthermore, the exercise group increased 7% less than the control group the ODI total score.

It is widely documented that pain negatively affects the quality of life during pregnancy [55], and it is also associated with anxiety and depression levels [121, 122], thus, all kind of safe pain-prevention and pain-release strategies are specially welcome in this physiological period. Pain usually increases throughout gestation [123], and musculoskeletal problems are common complaints, especially during late pregnancy [124]. Low back pain generally begins in early pregnancy and it seems to continue and increase until late pregnancy in almost 75% of pregnant women [55]. Similarly, in the present study, pain increased as the course of pregnancy progressed, with women scoring almost doubly at the 34th g.w. However, pain increased in a lower range in the exercise group. we have contrasted that this concurrent exercise-training program decreased low back pain by 22% and sciatic pain by 13% in comparison with the control group.

Overall, systematic reviews and meta-analyses [64, 125, 126], have concluded that exercise during pregnancy can be useful at preventing or decreasing low back, pelvic girdle, lumbopelvic pain, and some pain-related disabilities. However, a recent meta-analysis[16] stood out that prenatal exercise (i.e. aerobic, yoga, specific strengthening, general strengthening or a combination of different types of exercise) did not reduce low back, pelvic girdle or lumbopelvic pain during pregnancy [127]. Nonetheless, exercise seems to strongly prevent new episodes of sick leave due to lumbopelvic pain during pregnancy [64], and we have confirmed that our concurrent exercise training protocol also reduced pain-related limitations while sleeping and lifting weight, and limitations of social life due to pain. Notwithstanding, these findings must be confirmed by further research as these reviews included few studies, and most of them were uniquely focused on pelvic and core muscle-stabilizing exercises, or low volume and intensity aerobic activities, whereas we developed a multicomponent exercise training program. In this sense, to highlight is the similar supervised intervention performed by Haakstad and Bø [128], where the authors developed a 60 minutes exercise session that consisted of 35 minutes of aerobic training followed by 15 minutes of strength training, at least twice per week, for a minimum of 12 weeks. Contrary to our findings, they found no differences between the intervention and control group in low back pain, which could be partially explained by the shorter duration of the program, and the lower time dedicated to resistance training within their exercise protocol. On the other hand, in agreement with our study, no negative effects of the intervention were reported [128]. Unfortunately, no studies so far have reported the influence of prenatal exercise on sciatic pain to confirm or contrast our positive findings.

Some studies have also drawn attention to the inadequate use of painkillers during pregnancy, which included the intake of contraindicated drugs, self-prescription of painkillers, or taking more than the recommended dose for pregnancy [79]. In this context, exercise during pregnancy might struggle pain without the use of painkillers, or through lower doses, which could reduce fetal exposure to the risks associated with these drugs. In fact, in a recent study performed in pregnant women, the median usage of Paracetamol as an analgesic to control back pain in the control group was 500 mg higher than in the exercise group [129].

Despite the exact mechanisms to explain exercise-induced hypoalgesia are still unclear, there are potential factors that might explain this lower pain through the concurrent exercise program. First, it is widely demonstrated that aerobic exercise reduces pain sensitivity across all types of pain [66], even in populations without chronic pain [66]. One of these mechanisms is the activation of the endogenous opioid system [66] as aerobic exercise may promote the liberation of beta-endorphins, inducing positive changes in pain sensitivity or analgesia [68, 69]. For instance, a recent study [130] has contrasted that aerobic exercise-related enhancements in endogenous pain inhibition, in part endogenous opioid-related, likely contributed to chronic low back pain reduction [130]. Similarly, the hypoalgesic mechanism of aerobic exercise based on cycling seems to involve the enhancement of the central descending inhibitory function [131]. Second, increasing tissue oxygenation as a result of aerobic exercise may diminish peripheral and central sensitization, therefore reducing pain intensity [132]. Third, since a growing body of evidence implicated the amygdala as a critical node in emotional affective aspects of chronic pain, a study performed in mice has suggested that voluntary running may promote pleasant emotion and hypoalgesia through plastic changes in the amygdala [133]. Fourth, also in rats exposed to voluntary running, a recent study has proposed that the therapeutic efficacy of exercise in low back pain is mediated, at least in part, at the epigenetic level [134]. Fifth, our exercise protocol promoted lower excessive GWG (data under review), which has been associated with greater low back pain during pregnancy [135]. Indeed, in the statistical model II, additionally adjusted for GWG, the exercise improvements were attenuated, and differences in ODI total score and social limitations due to pain disappeared. Sixth, exercise during pregnancy promotes psychological well-being, decreasing stress, anxiety and depression levels [136], and this better emotional status might be associated with less pain perception [137]. Lastly, the improved muscle function induced by resistance training has been associated with lower low back pain in pregnancy [76]. For instance, core muscle strengthening (also performed in the present study exercise program) in patients with low back pain after caesarean section decreased low back pain intensity and disability. The anti-inflammatory role of myokines [138], such as irisin might also have partially promoted this analgesic effect [139, 140]. Therefore, the combination of aerobic exercise with resistance training can provide additional effects on pain prevention through different relief pathways [141]. In agreement with this hypothesis, our group previously contrasted in this study sample that greater overall PF and its components (mainly cardiorespiratory fitness and muscle strength) were associated with less bodily, low back, and sciatic pain, and reduced pain disability during pregnancy [64]. A recent study has also found that women with greater muscular strength suffer less low back and bodily pain probably through improvements in the musculoskeletal system and balance [63].

Study VIII: Influence of a concurrent exercise training program on health-related quality of life during advanced pregnancy: The GESTAFIT Project.

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RESULTS

Flow chart of the study participants is shown in **Figure 3.** From 159 participants, 73 women discontinued the study (did not attended the second evaluation at 34th g.w.), or did not return all the questionnaires duly completed, which meant a loss of data in some outcomes. A total of 86 pregnant women divided into control (n= 45) (age 33.3 ± 4.9 years old) and exercise groups (n= 41) (age 33.0 ± 4.3 years old) were included in the present analysis. The baseline characteristics of the study participants are listed in **Table 31**. No differences were found between exercise and control groups in baseline characteristics (all $p > 0.05$). Nevertheless, the HRQoL of the pregnant women, regardless of their allocation in the exercise or the control group, suffered a deterioration in the majority of SF-36 domain scores as the pregnancy progressed (see **Table 32**).

Table 31. Sociodemographic and clinical characteristics of the study participants.

	Control Group (n= 45)	**Exercise Group (n= 41)**	***P***
Age (years)	33.3 (4.9)	33.0 (4.3)	0.792
Percentage of attendance*		86.1 (6.4)	
Marital status			
Living with a partner	26 (57.8)	24 (58.5)	0.943
Single	19 (42.2)	17 (41.5)	
Educational level			
Non-University studies	15 (33.3)	16 (39.0)	0.583
University studies	30 (66.7)	25 (61.0)	
Gestational weight gains (kg)**	12.5 (5.3)	9.6 (4.6)	**0.009**
SF-36			
Physical functioning (0-100)	80.4 (14.3)	85.0 (14.2)	0.143
Physical role (0-100)	62.4 (23.3)	70.0 (25.2)	0.165
Bodily pain (0-100)	59.4 (27.6)	67.8 (23.8)	0.134
General health (0-100)	75.9 (15.8)	81.7 (15.6)	0.091
Vitality (0-100)	52.6 (17.7)	54.6 (16.9)	0.606
Social functioning (0-100)	78.1 (21.3)	81.1 (21.9)	0.516
Emotional role (0-100)	90.4 (16.9)	93.5 (11.3)	0.320
Mental health (0-100)	76.3 (13.8)	77.6 (12.8)	0.670
Physical component summary	45.3 (7.6)	48.5 (7.9)	0.056
Mental component summary	51.3 (7.1)	51.6 (7.1)	0.812

Note: Values shown as mean (SD, standard deviation) unless otherwise indicated. *Percentage of attendance in an intention-to-treat analysis (attendance to the 75% of the exercise sessions)= 75.3% (19.6). **Gestational weight gains between 16th gestational week and 34th gestational week.
Abbreviations: SF-36, Short Form 36 Health Survey questionnaire.

Table 32. Short Form 36 Health Survey scores at the 16th vs 34th gestational weeks.

	Total cohort (n= 86)			**Control (n= 45)**			**Intervention (n= 41)**		
	16th g.w.	**34th g.w.**	***P***	**16th g.w.**	**34th g.w.**	***P***	**16th g.w.**	**34th g.w.**	***P***
Physical function (0-100)	82.6 (14.4)	66.7 (20.0)	**<0.001**	80.4 (14.3)	56.6 (20.3)	**<0.001**	85.0 (14.2)	77.8 (12.6)	**0.003**
Physical role (0-100)	66.1 (24.4)	54.6 (24.6)	**<0.001**	62.6 (23.3)	48.9 (23.7)	**0.002**	70.0 (25.2)	60.8 (24.4)	**0.052**
Bodily pain (0-100)	63.4 (26.1)	53.4 (25.2)	**<0.001**	59.4 (27.6)	48.2 (26.2)	**0.005**	67.8 (23.8)	59.1 (23.0)	**0.028**
General health (0-100)	78.6 (15.9)	79.2 (18.5)	0.724	75.9 (15.8)	77.2 (17.6)	0.528	81.7 (15.6)	81.4 (19.5)	0.903
Vitality (0-100)	53.6 (17.2)	51.9 (17.5)	0.385	52.6 (17.7)	50.9 (17.0)	0.466	54.6 (16.9)	53.0 (18.2)	0.608
Social functioning (0-100)	79.5 (21.5)	77.5 (22.3)	0.444	78.1 (21.3)	72.2 (23.7)	0.150	81.1 (21.9)	83.2 (19.5)	0.528
Emotional role (0-100)	91.9 (14.5)	91.4 (14.1)	0.774	90.4 (16.8)	91.9 (13.0)	0.522	93.5 (11.3)	90.9 (15.5)	0.286
Mental health (0-100)	76.9 (13.2)	74.9 (15.8)	0.230	76.3 (13.8)	74.3 (13.6)	0.314	77.6 (12.8)	75.6 (18.1)	0.473
Physical component summary	46.8 (7.9)	41.4 (9.5)	**<0.001**	45.3 (7.7)	37.9 (9.1)	**<0.001**	48.5 (7.9)	45.2 (8.4)	**0.019**
Mental component summary	51.4 (7.1)	52.9 (7.6)	0.076	51.3 (7.1)	53.6 (6.4)	**0.028**	51.6 (7.1)	52.1 (8.8)	0.695

Note: Values are shown as mean (SD). Bold values, p< 0.05 or p< 0.01.

Abbreviations: G.w., gestational weeks.

Table 33 shows the per-protocol analyses of HRQoL changes between pre- and post-intervention for control and exercise groups. In the adjusted model (Model II), the exercise group decreased in the physical functioning 16.1 points less than the control group (between-group differences (B): 95% CI: 9.02 to 23.22; $p < 0.001$), and in the SF-36 *physical component summary* decreased 4.5 points less than the control group (between-group differences (B): 95% CI: 0.65 to 8.28; $p = 0.022$). In Model I, the results remain the same.

Table 33. Per-protocol analyses showing the association of the changes on Short Form 36 Health Survey questionnaire a concurrent exercise program with the intervention group (control or exercise group) in pregnant women.

			Model I		Model II	
	Changes within control group Post-Pre (n= 45)	**Changes within exercise group Post-Pre (n= 41)**	**Between-Group Difference (B) (95% CI)**	***P***	**Between-Group Difference (B) (95% CI)**	***P***
SF-36						
Physical functioning (0-100)	-23.9 (16.4)	-7.2 (14.6)	16.694 (10.004 to 23.384)	**<0.001**	16.117 (9.018 to 23.216)	**<0.001**
Physical role (0-100)	-13.8 (28.1)	-9.1 (29.2)	4.604 (-7.691 to 16.898)	0.459	6.580 (-6.356 to 19.517)	0.315
Bodily pain (0-100)	-11.2 (25.2)	-8.7 (24.3)	2.497 (-8.142 to 13.136)	0.642	2.931 (-8.367 to 14.229)	0.607
General health (0-100)	1.3 (14.1)	-0.3 (15.3)	-1.626 (-7.915 to 4.663)	0.609	-0.547 (-7.211 to 6.117)	0.871
Vitality (0-100)	-1.7 (15.2)	-1.5 (18.9)	0.142 (-7.185 to 7.470)	0.969	-1.194 (-8.885 to 6.497)	0.758
Social functioning (0-100)	-5.8 (26.7)	2.1 (21.5)	7.967 (-2.491 to 18.426)	0.134	9.946 (-1.067 to 20.959)	0.076
Emotional role (0-100)	1.5 (15.4)	-2.6 (15.6)	-4.124 (-10.788 to 2.541)	0.222	-3.741 (-10.713 to 3.230)	0.289
Mental health (0-100)	-2.0 (13.2)	-1.9 (17.2)	0.049 (-6.495 to 6.593)	0.988	-0.584 (-7.390 to 6.221)	0.865
Physical component summary	-7.4 (8.2)	-3.3 (8.6)	4.094 (0.495 to 7.693)	**0.026**	4.468 (0.655 to 8.282)	**0.022**
Mental component summary	2.3 (6.8)	0.5 (8.1)	-1.800 (-4.992 to 1.393)	0.265	-1.886 (5.231 to 1.459)	0.265

Note: Values are shown as mean (standard deviation). Model I was unadjusted. Model II was adjusted for age, educational status, and gestational weight gains (kg). Mean results show the differences between post-pre intervention (i.e., 34th gestational week-16th gestational week) for each variable with negative values indicating a reduction in the post-evaluation compared to pre-evaluation; Bold values, p< 0.05 or p< 0.01.

Per-protocol analyses were performed including only women who attended ≥75% of the exercise sessions. The within-group post-pre intervention changes (from the exercise training group minus the control group) are presented for Model I.

Abbreviations: SF-36, Short Form 36 Health Survey questionnaire; B, non-standardized regression coefficient.

Because of the substantial percentage of missing data (average= 31.4%), multiple imputations were not possible for some outcomes. Intention-to-treat analyses have been added to **Table 34** to be as transparent as possible. In model II (adjusted), the exercise group decreased in the SF-36 physical functioning 14.2 points less than the control group (between-group differences (B): 95% CI: 7.72 to 20.73; $p < 0.001$), the exercise group decreased in the SF-36 social functioning 10.03 points less than the control group (between-group differences (B): 95% CI: 0.39 to 19.68; $p = 0.042$), and decreased in the SF-36 *physical component summary* 3.58 points less than the control group (between-group differences (B): 95% CI: 0.31 to 6.85; $p = 0.032$). In model I, the results remain the same, except for SF-36 social functioning ($p > 0.05$).

Table 34. Intention to treat analyses showing the association of the changes on Short Form 36 Health Survey questionnaire a concurrent exercise program with the intervention group (control or exercise group) in pregnant women.

			Model I		Model II	
	Changes within control group Post-Pre (n= 45)	**Changes within exercise group Post-Pre (n= 41)**	**Between-Group Difference (B) (95% CI)**	***P***	**Between-Group Difference (B) (95% CI)**	***P***
SF-36						
Physical functioning (0-100)	-23.7 (16.2)	-9.0 (16.3)	14.691 (8.460 to 20.923)	**<0.001**	14.225 (7.717 to 20.733)	**<0.001**
Physical role (0-100)	-14.1 (27.9)	-11.5 (26.4)	2.604 (-7.785 to 12.993)	0.620	4.844 (-5.905 to 15.593)	0.374
Bodily pain (0-100)	-10.2 (25.2)	-7.5 (23.9)	2.702 (-6.678 to 12.082)	0.569	2.528 (-7.312 to 12.367)	0.612
General health (0-100)	1.5 (13.9)	0.3 (13.9)	-1.215 (-6.562 to 4.132)	0.653	-0.804 (-6.414 to 4.806)	0.777
Vitality (0-100)	-1.7 (14.9)	-1.7 (19.1)	0.015 (-6.658 to 6.688)	0.996	-0.343 (-7.340 to 6.653)	0.923
Social functioning (0-100)	-6.4 (26.3)	0.8 (23.1)	7.189 (-2.209 to 16.588)	0.132	10.035 (0.392 to 19.677)	**0.042**
Emotional role (0-100)	1.4 (15.1)	-2.6 (15.5)	-3.972 (-9.847 to 1.903)	0.183	-3.718 (-9.701 to 2.264)	0.221
Mental health (0-100)	-1.9 (12.9)	-0.6 (15.7)	1.270 (-4.315 to 6.854)	0.653	1.259 (-4.585 to 7.103)	0.670
Physical component summary	-7.3 (8.2)	-3.9 (8.1)	3.373 (0.258 to 6.488)	**0.034**	3.579 (0.311 to 6.846)	**0.032**
Mental component summary	2.2 (6.7)	0.9 (7.7)	-1.262 (-4.046 to 1.522)	0.371	-0.961 (-3.870 to 1.948)	0.514

Note: Values are shown as mean (standard deviation). Model I was unadjusted. Model II was adjusted for age, educational status, and gestational weight gains (kg). Mean results show the differences between post-pre intervention (i.e., 34th gestational week-16th gestational week) for each variable with negative values indicating a reduction in the post-evaluation compared to pre-evaluation. Bold values, p< 0.05 or p< 0.01.
Abbreviations: SF-36, Short Form 36 Health Survey questionnaire; B, non-standardized regression coefficient.

DISCUSSION

The main findings of these secondary analyses from the GESTAFIT Project suggest that this concurrent exercise program attenuated HRQoL decline across pregnancy. Specifically, the program positively influenced the SF-36 physical functioning, the SF-36 social functioning, and the SF-36 *physical component summary*. Therefore, following a concurrent exercise program might ameliorate the SF-36 *physical component summary* deterioration, being of great importance during the pregnancy period, since it is known that HRQoL in general, and physical function in particular, decreases as pregnancy progresses [142-144]. Thus, our findings are broadly consistent with other studies involving active pregnant women (i.e., practicing PA or engaging in an exercise-training program).

In line with our results, a 3-month supervised aerobic exercise program improved the SF-36 physical functioning domain and the SF-36 *physical component summary* more in the exercise group than in the control group [145]. Likewise, a 4-month water exercises (aerobic+strength) program, ameliorated all domains except for the SF-36 mental health domain and the SF-36 *mental component summary* [142].

Nevertheless, some studies have failed to show differences between groups when following an exercise program [143, 146-150]. In this regard, some protocol differences could explain this lack of results. First, regarding the length of the intervention, our exercise program involved 17 weeks, while other programs were developed during shorter periods (11-12 weeks) [143, 146, 147]. Likewise, the initiation time of the exercise programs also differs between studies, without a specific time period for starting. For instance, ranging from 14^{th}-24^{th} g.w. [150], 18^{th}-22^{th} g.w. [147], or only indicating <20^{th} g.w. [149], making more difficult the proper comparison between studies. Moreover, pregnant women suffer the majority of anatomical and physiological changes mainly during the early second trimester of gestation, and it may predispose them to have worse HRQoL results [71, 151] related to physical functioning. This fact could partially explain the lack of results of the study by O'Connor et al. [143], where pregnant women exercised from the 22^{nd} to the 34^{th} g.w. Second, some exercise programs were designed as home-based training [146-148, 150]. Although lack of time is a frequent barrier that may be supplied by exercising at home [71], is also noteworthy that a supervised exercise program (in a sport or research center) may contribute to higher opportunities to interact and consult with exercise professionals. Furthermore, increasing pregnant women's interest and motivation to participate in the exercise program, thereby increasing the impact of exercise on their HRQoL. This circumstance is especially important since a low motivation is a major barrier to exercise in pregnant women [71]. Third, the low adherence to the exercise program found in some studies (33-55%) [147, 148] might also explain the insufficiency of positive findings. Fourth, all studies were designed in isolation as uniquely resistance or aerobic (cycling or water-based) training [143, 146-150], whereas our study included both components. In fact, it has been found that aerobic training exerts additional improvements on HRQoL during pregnancy [144]. Moreover, the latest Guidelines for exercise during pregnancy recommend combining aerobic and resistance training (concurrent) in this population [24]. To summarize, the timing of assessments, the program initiation or length, its compliance, and the design of these exercise programs could contribute to the differences found between studies. In addition, there is not a specific tool to assess HRQoL in pregnant population, which also difficult proper comparisons between studies.

According to a recent systematic review, the physical components of the HRQoL might be key during pregnancy since it seems to especially decrease as pregnancy progresses [151]. Therefore, exercise programs during pregnancy may be focused on improving these physical components, which might exert improvements in the anatomical, morphological and musculoskeletal systems of pregnant women. Thereby, exercise might imply an improvement in the functionality, motor tasks, and activities of daily living that might be compromised [152], especially during late pregnancy, where the functional ability of the trunk during gait declines [152]. Therefore, as shown in our exercise program design, weight-bearing and resistance exercises should be included to strengthen the musculoskeletal system through core-based exercises, and consequently enhance its functionality along the pregnancy course.

The exact mechanisms by which physical functioning improves is still unknown, although musculoskeletal health is an important aspect of function which improves through greater PF levels [153]. Furthermore, multicomponent activities and functional exercises, such as those that combine aerobic, strength, endurance, and flexibility, translate into general improvements in daily living functioning, which has been widely shown especially in older populations [154, 155]. Hence, our intervention program integrates all these tasks and, therefore, could imply such an improvement.

Finally, the SF-36 social functioning domain improved in the exercise group 10 points more than in the control group (34th g.w. minus 16th g.w.). This finding is worth mentioning since it demonstrates that, despite the isolation process that may be perceived during pregnancy caused by changes in social lifestyle compared to pre-pregnancy [151], enrolling in an exercise program might encourage contact with other pregnant women, empowering their autonomy, competence and support, facilitating positive interactions, making women feel especially valued and so decreasing the impact of gestation, or thus, improving social life [71, 156]. Thus, the results showed in “intention to treat analyses” indicate that the benefits of the exercise program on the social functioning might had been also mediated by another mechanism inherent to being physically active itself (more than the social contact of the participants), such as the release of β-endorphins, producing a sense of well-being [106]. Moreover, exercise promotes improved social factors, sociability [108], self-esteem, self-efficacy, distraction [109], motivation [71] and general HRQoL [110]. Therefore, these mechanisms may partially explain why positive significant results were found even attending less than 75% of the exercise sessions. In addition, the fact that our exercise program was conducted by an exercise specialist is a further advantage over home-based training, since it comprises encouraging participants to do their best. Furthermore, the supervised exercise program also implies peer support, facing with lack of motivation derived from individual training. In this sense, healthcare providers and sport specialists should encourage women to participate in more social group-based exercise activities to maximize the effectiveness of exercising during pregnancy [144, 156].

REMARKABLE DISCUSSION

In the present International Doctoral Thesis, relevant gaps related to being physically active during pregnancy have been addressed.

As stated in the **Introduction section:** ***Conspectus of pregnancy***, the anatomical and physiological changes that occurs during gestation could trigger undesired effects on women's health, leading to an uncomfortable gestation.

On the other hand, despite growing scientific evidence is emerging in this field, still exact mechanism to explain our findings are arousing and, therefore, under debate. Nevertheless, some of them are common and derive from the physiological benefits of being physically active and enrolled in specific concurrent exercise programs along gestation.

Therefore, we thought it might be important for the readers to summarize the most common physiologic mechanisms that could explain our findings to a better understanding of why it is key to encourage pregnant women to follow a healthy lifestyle, especially to be active, during the prenatal period (and even before pregnancy).

In this context, we should understand "*being physically active*" and their underlying mechanisms as any stimulus that imply movement (to a greater or lesser extent), although it is known that the greater the physical stimulus, the greater the health benefits (in most cases). Thus, in this case we will talk interchangeably of *PA*, *PF* and *exercise*, even knowing that in practice these terms are not synonymous (*see* ***Key Concepts section*** *for specific definitions*).

Finally, although the different body systems work synergistically to maintain body homeostasis, we have tried to divide it into parts to facilitate its reading.

The potential physiological mechanisms related to the findings derived from this International Doctoral Thesis are summarized in **Table 35**:

Table 35. Potential physiological mechanisms related to the findings derived from this International Doctoral Thesis.

BODY SYSTEMS	CONTRIBUTION TO THE THESIS FINDINGS	
Cardiovascular and respiratory systems 	   	✓ Aerobic exercise results in fat oxidation (and carbohydrate oxidation, both primary sources in aerobic exercise at ≈80% of VO_{2max}) and lipolysis stimulation, linked to central fat reduction [13]. ✓ Greater VO_{2max} might promote better bone status in young females, especially in those with overweight [14]. ✓ It is possible that women with greater cardiorespiratory fitness experienced less fatigue during birth, promoting better uterine dynamic [50]. ✓ Aerobic PA reduces pain sensitivity across all types of pain stimuli, with a greater reduction when it is performed at moderate-to-vigorous intensity [66]. This could be explained through the hypoalgesic effect of aerobic activity. Although the exact mechanisms to explain hypoalgesia are still unclear, one of them is the activation of the endogenous opioid system during exercise [66].
Musculoskeletal system 		✓ Greater muscular strength is widely associated with greater bone mineral density in those physiological women stages when bone mineral content may diminish, such as the menopausal and postmenopausal period [19]. ✓ The application of mechanical stress (e.g., weight-bearing or impact aerobic exercise) to the skeleton can preserve and increase bone mineral density, providing a significant contribution in the protection of bone health [21].

		✓ The anti-inflammatory role of myokines [138], such as irisin might have partially promoted this analgesic effect in the reduction of pain [139, 140].
Endocrine system 	    	✓ It plausible that overweight status induces relaxin-resistance [23], and relaxin seems to contribute to weight reduction [23]. ✓ Relaxin also provides vasodilator effects [43], which promotes enhanced blood flow to the fetus and reduces potential alterations in the fetal well-being. ✓ Since relaxin has endothelium-dependent vasodilation effects in the uterine artery [43], it seems feasible that the uteroplacental flow was more efficient during the birth in women with greater relaxin concentrations. Thus, high levels of relaxin might also have a determinant role on the appearance of uterine contractions [44, 45]. ✓ Relaxin seems to be associated with a more alkaline pH, higher PO_2, higher arterial oxygen saturation and lower PCO_2 in the arterial umbilical cord blood [28]. ✓ High intensity or duration of exercise may lead with the liberation of beta-endorphins, producing changes in pain sensitivity [68, 69]. ✓ Exercise may play an important role in the regulation of stress hormones, such as cortisol, via the hypothalamus-pituitary-adrenal axis [102], plus the anti-inflammatory response induced by exercise [105].
		✓ Exercise plays a role in brain circuitry, neurotransmitters and neuromodulators, regulating motor functioning and mediating mood disturbances, through monoamines, histamine or gabapentin-mediated neurotransmission [87]. Thus, exercise promotes reduced fatigue and better sleep quality.

Nervous and limbic systems 	✓ Exercise plays a role in the thermoregulatory mechanism, improving vasodilation, decreasing cortisol levels or exerting well-being and a mental-calm state [88], consequently decreasing sleep disturbances.  ✓ Greater overall PF levels promote an increase in circulating brain-derived neurotrophic factor, which might prevent depression promoting neuroplasticity and maintaining brain function [107], as well as improving social factors, sociability [108], self-esteem, self-efficacy, distraction [109], motivation [71] and quality of life [110]. In addition, β-endorphins produce an analgesic effect and sense of well-being [106], which may also regulate depression-anxiety symptoms.  ✓ Aerobic exercise increases tissue oxygenation and may diminish peripheral and central sensitization, therefore reducing pain intensity [132]. ✓ Running may promote pleasant emotion and hypoalgesia through plastic changes in the amygdala [133], and a growing body of evidence implicated the amygdala as a critical node in emotional affective aspects of chronic pain.

Abbreviations: PA, Physical Activity; PCO_2, partial Pressure of Carbon dioxide; PF, Physical Fitness; pH, potential of Hydrogen; PO_2, partial Pressure of Oxygen; VO_{2max}, Maximal oxygen intake.

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LIMITATIONS AND STRENGTHS

LIMITATIONS AND STRENGTHS

The studies included in this International Doctoral Thesis present some limitations that should be taken into account when interpreting their results. Likewise, this International Doctoral Thesis also presents strengths, which are summarized below.

General limitations

I. Objective PF was evaluated through field-based tests. Although field-based PF tests are widely used and provide valid and reliable information [157], when possible, laboratory tests (i.e. *gold-standards*) [157] should be administered to reduce error in assessment, especially in research contexts. To note, the PF tests were chosen based on current recommendations for PF assessment in pregnant population [158].

II. The field-based PF tests are still not validated in pregnancy.

III. Some caution should be taken into account since, although we have analysed absolute and relative muscular strength to control the interpretation of confounding parameters, such as changes in body composition during pregnancy (i.e. the higher the body mass the greater the absolute muscular strength) [2], there is a lack of reliable measures of strength in this specific population.

IV. Results of Studies I-VI are derived from a cross-sectional and longitudinal design, the associations found cannot be explained via a causal pathway.

V. We did not have the possibility of measuring pre-pregnancy variables, such BMD (due to the impossibility of knowing the intention to get pregnant), or pain problems, and neither BMD changes during pregnancy because of the harmful effects of radiation during pregnancy.

VI. Our sample of pregnant women only included young Caucasian women with a high educational level, so our results cannot be extrapolated to other types of populations.

VII. Although analyses were performed controlling for potential confounders (i.e., age, educational status, working status, living with a partner, parity, exercise intervention, etc.), it is possible that there exist other unstudied confounders that affect the outcomes studied.

General strengths

I. Relative large sample in cross-sectional and longitudinal studies.

II. The vast majority of our results are novel in the pregnant population, documenting a strong association between objective and self-reported PF and pregnancy-related outcomes.

III. Despite the fact that people tend to overestimate their PF, we assessed PF through a self-reported questionnaire (i.e., the IFIS), since it has been found to be a reliable tool, and it has been validated in pregnant women [10].

IV. Both, the Back-scratch test and the IFIS questionnaire could be used in clinical settings as easy, quick and economical tools to measure and monitor a healthier and lower-risk gestational period.

V. Cross-sectional, longitudinal, and intervention analyses have been tested to elucidate pregnancy-related outcomes across different g.w., providing a wide overview of the gestational and postpartum period, and asserting the findings found in the different studies included in this International Doctoral Thesis.

VI. Per-protocol analyses were tested to investigate the clinical efficacy of a concurrent exercise training program on different pregnancy-related outcomes, but also intention-to-treat analyses to evaluate more realistically the effectiveness of this program when applied to the clinical practice.

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CONCLUSIONS [CONCLUSIONES]

CONCLUSIONS

Considering the eight gaps identified in this International Doctoral Thesis, the conclusions related to these gaps, organized by chapters and studies, are summarizes in **Table 36**.

Table 36. Conclusions of the present International Doctoral Thesis, linked to the identified gaps.

CONCLUSIONS	
CHAPTER I	**Gap I.** (i) Greater physical fitness levels have shown a strong relationship with better body composition during the perinatal period (i.e. appropriated gestational weight gains, less adiposity and greater bone mass) (*study I*).
	Gap II. (ii) Lower flexibility levels discriminates among pregnant women who will require oxytocin from those that will not, and with greater risk of caesarean section from those with a vaginal birth. The early identification of pregnant women who fail to meet the suggested standards in the Back-scratch test can help for a better pregnancy monitoring and might help to easily, quickly and cheaply identify these relevant birth-related complications to initiate preventive strategies (*study II*).
CHAPTER II	**Gap III.** (iii) Greater self-reported and its components are associated with less bodily, lumbar and sciatic pain, and pain disability during pregnancy. Maintaining or improving physical fitness levels throughout the pregnancy course might prevent pregnancy-related pain (*study III*).
	Gap IV. (iv) Greater self-reported overall physical fitness and its different components, especially cardiorespiratory fitness, have shown a strong relationship with lower incidence and limitations of the most common pregnancy-related symptoms, particularly tiredness-fatigue and poor sleep (*study IV*).

	Gap V. (v) Greater self-reported physical fitness is consistently associated with lower psychological ill-being during pregnancy. Specifically, greater self-reported overall physical fitness is associated with fewer depressive symptoms at the 16th gestational week. Moreover, greater cardiorespiratory fitness is associated with lower anxiety levels during the pregnancy course; greater muscular strength with lower anxiety levels at the 16th gestational week; and greater overall physical fitness and speed-agility with lower anxiety levels at the 34th gestational week (*study V*).
	Gap VI. (vi) Greater self-reported physical fitness is consistently associated with better emotional well-being (positive affect) and less emotional distress (negative affect) during pregnancy (*study VI*).
CHAPTER III	**Gap VII.** (vii) A supervised concurrent exercise program (i.e., aerobic + resistance training) during pregnancy may attenuate low back and sciatic pain during pregnancy. Moreover, the exercise group showed better scores in pain while sleeping and lifting weight, and limitations of the social life due to pain (*study VII*).
	Gap VIII. (viii) A supervised concurrent exercise program during pregnancy ameliorates health-related quality of life deterioration compared with the control group. Specifically, improvements were observed in the SF-36 physical functioning, the SF-36 social functioning, and the SF-36 *physical component summary*. Therefore, engaging in a well-structured group-based exercise program, preferably combining aerobic + resistance training, might be proposed as a clinical and public health tool to maintain adequate health-related quality of life levels during this relevant stage for maternal-fetal health status (*study VIII*).

Three general lines can conclude the findings found in the present International Doctoral Thesis:

- Greater **physical fitness** levels positively impact on several pregnancy-related outcomes. Specifically, **the Back-scratch test** can be proposed as an easy, quick and cheap tool to identify relevant birth-related complications in clinical settings.
- Likewise, **the International Fitness Scale** is proposed as a clinical and practitioners tool to discriminate among pregnant women at risk of pregnancy-related complications.
- **A supervised concurrent exercise program** (aerobic + resistance training) throughout gestation provides fewer perinatal complications and better quality of life and emotional state during this period.

Teniendo en cuenta los ocho gaps identificados en esta Tesis Doctoral Internacional, las conclusiones relacionadas con estos gaps, organizados por capítulos y estudios, se resumen en la **Tabla 37**.

Tabla 37. Conclusiones de la presente Tesis Doctoral Internacional, vinculadas a los gaps identificados.

CONCLUSIONES	
CAPÍTULO I	**Gap I.** (i) Mayores niveles de condición física han mostrado una fuerte relación con una mejor composición corporal durante el período perinatal (i.e. ganancias de peso gestacionales apropiadas, menor adiposidad y mayor masa ósea) (*estudio I*).
	Gap II. (ii) Menores niveles de flexibilidad discriminan entre las mujeres embarazadas que requerirán oxitocina de las que no, y con mayor riesgo de parto por cesárea de las que tienen un parto vaginal. La identificación temprana de mujeres que no cumplen con los estándares sugeridos en el test Back-scratch puede ayudar a un mejor seguimiento del embarazo y podría ayudar a identificar de manera fácil, rápida y económica estas complicaciones relevantes relacionadas con el parto para iniciar estrategias preventivas (*estudio II*).
CAPÍTULO II	**Gap III.** (iii) Mayor condición física auto-reportada y sus componentes se asocian con menos dolor corporal, lumbar y ciático, y dolor incapacitante durante el embarazo. Mantener o mejorar los niveles de condición física durante el curso del embarazo podría prevenir el dolor relacionado con el embarazo (*estudio III*).
	Gap IV. (iv) Una mayor condición física auto-reportada general y sus diferentes componentes, especialmente la capacidad cardiorrespiratoria, han mostrado una fuerte relación con una menor incidencia y limitaciones de los síntomas más comunes relacionados con el embarazo, en particular el cansancio-fatiga y la falta de sueño (*estudio IV*).

	Gap V. (v) Una mayor condición física auto-reportada se asocia consistentemente con un menor malestar psicológico durante el embarazo. Específicamente, una mayor condición física auto-reportada general se asocia con menos síntomas depresivos en la semana 16 de gestación. Además, una mayor capacidad cardiorrespiratoria se asocia con menores niveles de ansiedad durante el curso del embarazo; mayor fuerza muscular con menores niveles de ansiedad en la semana 16 de gestación; y una mayor condición física general y velocidad-agilidad con niveles de ansiedad más bajos de ansiedad en la semana 34 de gestación (*estudio V*).
	Gap VI. (vi) Una mayor condición física auto-reportada se asocia consistentemente con un mejor bienestar emocional (afecto positivo) y menos malestar emocional (afecto negativo) durante el embarazo (*estudio VI*).
CAPÍTULO III	**Gap VII.** (vii) Un programa de ejercicio concurrente supervisado (es decir, entrenamiento aeróbico + de fuerza) durante el embarazo puede atenuar el dolor lumbar y ciático durante el embarazo. Además, el grupo de ejercicio mostró mejores puntuaciones en dolor al dormir y levantar peso, y limitaciones en la vida social debido al dolor (*estudio VII*).
	Gap VIII. (viii) Un programa de ejercicio concurrente supervisado durante el embarazo mejora el deterioro de la calidad de vida relacionada con la salud en comparación con el grupo control. Específicamente, se observaron mejoras en el funcionamiento físico del SF-36, el funcionamiento social del SF-36 y el *resumen del componente físico* del SF-36. Por lo tanto, la participación en un programa de ejercicio grupal bien estructurado, preferiblemente que combine entrenamiento aeróbico y de fuerza, podría proponerse como una herramienta clínica y de salud pública para mantener niveles adecuados de calidad de vida relacionada con la salud durante esta etapa relevante para el estado de salud materno-fetal (*estudio VIII*).

Tres líneas generales pueden concluir los hallazgos encontrados en la presente tesis doctoral:

- Mayores niveles de **condición física** impactan positivamente en varios resultados relacionados con el embarazo. Específicamente, **el test Back-scratch** puede proponerse como una herramienta fácil, rápida y económica para identificar complicaciones relevantes relacionadas con el parto en entornos clínicos.
- De igual forma, **la Escala Internacional de Condición Física** se propone como una herramienta clínica y de profesionales del ámbito para discriminar entre las mujeres embarazadas en riesgo de complicaciones relacionadas con el embarazo.
- **Un programa de ejercicio concurrente supervisado** (entrenamiento aeróbico + fuerza) a lo largo de la gestación proporciona menos complicaciones perinatales y una mejor calidad de vida y estado emocional durante este periodo.

FUTURE RESEARCH DIRECTIONS

FUTURE RESEARCH DIRECTIONS

The studies derived from the present International Doctoral Thesis elucidate important scientific knowledge on future directions aimed at the prevention and early detection of pregnant women who are inactive or whose PF is not adequate, and those who may experience pregnancy-related symptoms. Therefore, they can benefit from a physically active pregnancy through the improvement of their PF and physical exercise programs adapted to this important period for women's lives.

Consequently, future studies should aim:

(i) To contrast whether increasing PF levels through a specific exercise program could decrease pregnancy-related outcomes and promote maternal-fetal health benefits along the pregnancy course. In particular, to test whether greater flexibility levels may enhance better labor-related outcomes.

(ii) To explore the specific influence of exercise programs on maternal-fetal health based on concurrent training (and even plus and optimal Mediterranean Diet adherence, as it was a complementary aim of the GESTAFIT Project) prior to pregnancy, if possible, and not only during pregnancy but also on postpartum period. This will help us to understand if exercise programs initiated early in pregnancy (i.e., when the mother has a predominant noticeable influence on intrauterine programming, and the main biological processes take place) could be more effective than those initiated at early second trimester of pregnancy.

(iii) To study also the effectiveness of greater PF levels and being enrolled in a well-designed exercise program during gestation in different pregnant populations (i.e. other ethnicities, body composition profiles, socioeconomic status or health conditions) on maternal-fetal health.

(iv) To stablish specific self-reported and objective PF cut-off points as clinical tools to identify pregnant women at risk of potential pregnancy-related symptoms who can benefit of an exercise program during gestation to reduce possible harmful effects. This will help advise clinicians about how to promote a healthy gestation in primary care.

(v) To propose lifestyle strategies that could face with the high rates of withdrawals in lifestyle interventions, implementing interventions that consider the usual barriers to being physically active during pregnancy, thereby favoring successful adherence of women to these interventions. Thus, health care providers, physical therapists and physical exercise specialists should advise and encourage pregnant women to being physically active during this stage.

In addition, despite is not a main aim of the present International Doctoral Thesis, future research should also be aimed in developing a specific field-based test battery to assess pregnant women' physical fitness level, based on scientific evidence, valid, reliable and safe. Of note, we are currently validating some of the field-based PF tests employed in the GESTAFIT Project with gold standard methods.

TAKE-HOME MESSAGES

As a group commitment to transfer scientific knowledge to society, *take-home messages* summarizing the clinical and practical relevance of the findings derived of this present International Doctoral Thesis seems imperative.

Therefore, the following figure (**Figure 7**) gathers this valuable information for the readers.

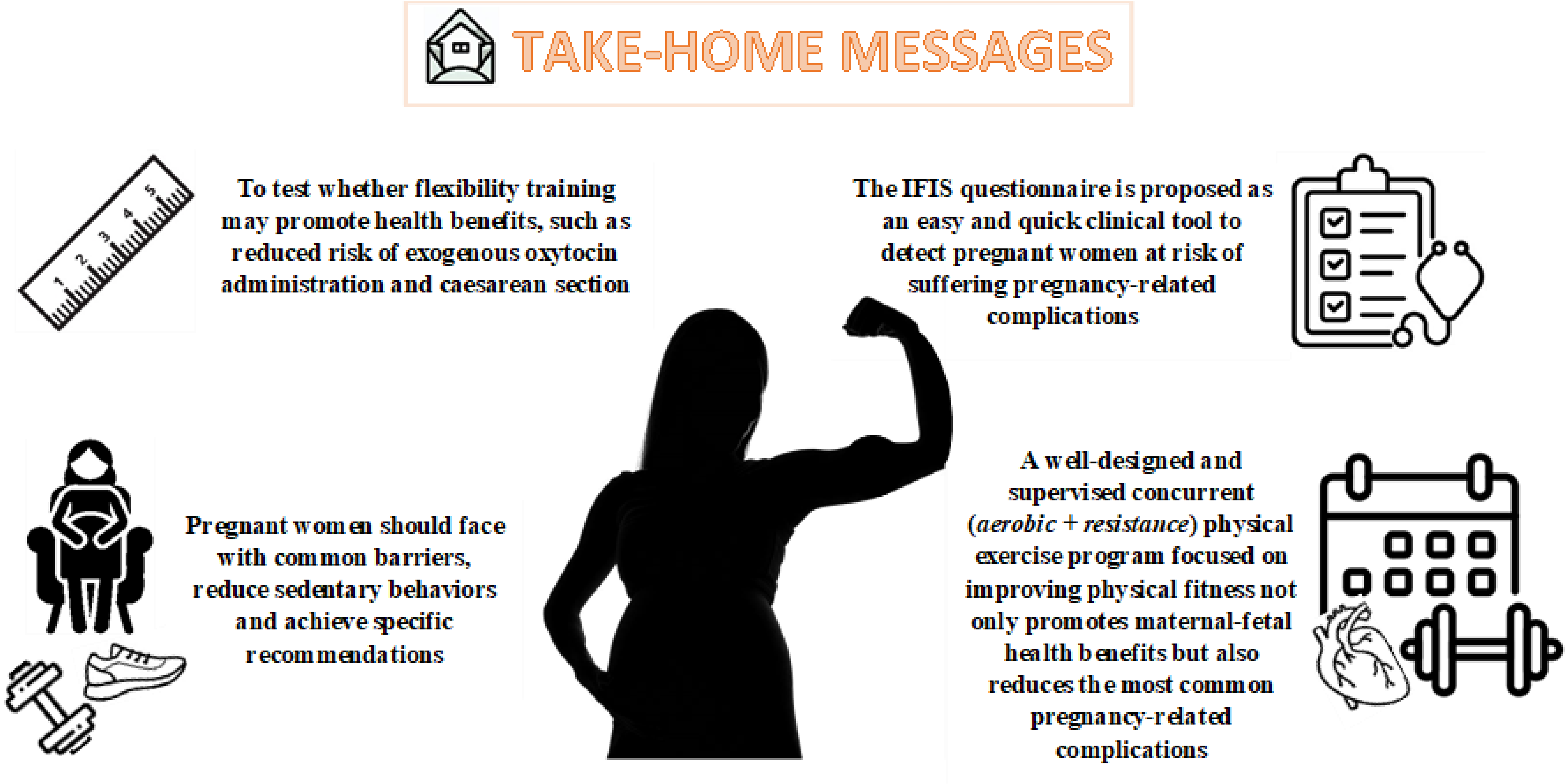

Figure 7. Take-home messages derived from this International Doctoral Thesis.

Abbreviations: IFIS, The International FItness Scale.

ANNEXES

SHORT CV

CURRICULUM VITAE [SHORT CV]

Personal Data

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Education and training

2017-*2023* PhD candidate in Biomedicine. University of Granada, Spain.

2019-2022 PhD in Health Sciences. University of Cádiz, Spain.

2017-2018 Master´s degree in Research on Physical activity and Health Specializing in Physical Activity and Health. University of Granada, Spain.

2016-2017 Master's Degree in Teaching Compulsory and Pre-University Secondary Education, Vocational Training and Language Teaching. Specializing in Physical Education. University of Granada, Spain.

2011-2016 Bachelor´s Degree in Sport Sciences. University of Granada, Spain.

Erasmus Student Internship - 9 months at University of Tallin, Estonia (2015-2016).

National fellowships

2019-2022 Regional Government of Andalusia and University of Cadiz: Research and Knowledge Transfer Fund (PPIT-FPI19).

National internships

2019 Faculty of Sport Sciences, Polytechnic University of Madrid. Professor Rocio Cupeiro Coto (3 months).

International internships

2022 Funding: Erasmus+ Programme (K107) for teaching. Center: Tbilisi State University, Georgia (1 week).

2021 Funding: University of Cadiz: Research and Knowledge Transfer Fund. Center: Karolinska Institutet, Sweeden. Professor Marie Löf (3 months).

2019 Funding: Erasmus+ Programme (K103) for teaching. Center: University of Tallin, Estonia (1 week).

Participation in research projects

Researcher 2020–…

Project Title & Design: Influencia de un programa de ejercicio físico concurrente durante el embarazo sobre la composición corporal, condición física y desarrollo motor. Acronym: GESTAFITOS.

Principal Investigator: Virginia A Aparicio.

Department of Physical Education and Sport, University of Granada, Spain.

Funding: I+D+I projects in the framework of FEDER Andalucia, 2014-2020 (6.400€).

Researcher 2019–…

Project Title & Design: Health-related physical fitness test battery design for the adult population: The ADULT-FIT Project.

Principal Investigator: José Castro Piñero and Magdalena Cuenca García.

Department of Physical Education and Sport, University of Cadiz, Spain.

Funding: Spanish Ministry of Economy, Industry, and Competitiveness (112.000€)

Researcher 2017–2019

Project Title & Design: Effects of a supervised physical exercise intervention during pregnancy on telomere length and gene expression markers related to adiposity in the mother and neonate. A randomized controlled trial.

Principal Investigator: Virginia A Aparicio.

Department of Physical Education and Sport, University of Granada, Spain.

Funding: Spanish Ministry & European Funding (*MSCA-COFUND* 56000€)

Researcher 2015–2017

Project Title & Design: Influence of physical activity levels, physical fitness and nutritional habits of the pregnant women on diverse foetal and maternal health markers" Acronym: GESTAFIT.

Principal Investigator: Virginia A Aparicio.

Department of Physical Education and Sport, University of Granada, Spain.

Funding: Spanish Ministry & European Funding (100000€).

Student Assistant-Collaborator 2015–2018

Project Title & Design: Cost-effectiveness of an exercise intervention program in perimenopausal women. The Fitness League Against MENopause COst (FLAMENCO) randomized controlled trial.

Principal Investigator: Virginia A Aparicio.

Department of Physical Education and Sport, University of Granada, Spain.

Funding: Spanish Ministry (38500€).

Scientific and organizing committee member activities

2019 XII Simposio Internacional de Fuerza y Proyecto IRONFEMME / I NSCA Spain National Conference, Madrid, Spain. Organization coordinator (volunteer) and mediator.

2019 24th Annual Congress of the European College of Sports Sciences, Prague, Czech Republic. Volunteer.

Reviewer activity

Nuria Marín Jiménez has contributed as reviewer of indexed journals, such as *Journal of Science and Medicine in Sport*, *Clicmateric*, *Women & Health*, *Journal of Obstetrics and Gynaecology* and *RETOS*.

Publications (*not included as part of this Doctoral Thesis*)

1. Marín-Jiménez, N., Sánchez-Parente S., Expósito-Carrillo, P., Jiménez-Iglesias J., Álvarez-Gallardo, IC., Cuenca-García, M., Castro-Piñero, J. (2023). Criterion-related validity and reliability of the 2-km walk test and the 20-m shuttle run test in adults: The role of sex, age and physical activity level. *Journal of Science and Medicine in Sport, 26*(4-5), 267-276.

2. Marín-Jiménez, N., Flor-Alemany, M., Ruiz-Montero, P. J., Coll-Risco, I., & Aparicio, V. A. (2023). Effects of concurrent exercise on health-related quality of life in middle-aged women. *Climacteric*, 1-7.

3. Flor-Alemany, M., Migueles, J. H., Acosta-Manzano, P., **Marín-Jiménez, N.**, Baena-García, L., & Aparicio, V. A. (2023). Assessing the Mediterranean diet adherence during pregnancy: Practical considerations based on the associations with cardiometabolic risk. *Pregnancy Hypertension*, *31*, 17-24.

4. Marín-Jiménez, N., Cruz-Leon, C., Sanchez-Oliva, D., Jimenez-Iglesias, J., Caraballo, I., Padilla-Moledo, C., ... & Castro-Piñero, J. (2022). Criterion-Related Validity of Field-Based Methods and Equations for Body Composition Estimation in Adults: A Systematic Review. *Current Obesity Reports*, 1-14.

5. Cuenca-García, M., **Marín-Jiménez, N.**, Perez-Bey, A., Sanchez-Oliva, D., Camiletti-Moiron, D., Alvarez-Gallardo, I. C., ... & Castro-Pinero, J. (2022). Reliability of field-based fitness tests in adults: a systematic review. *Sports Medicine*, *52*(8), 1961-1979.

6. Baena-García L, Flor-Alemany M, **Marín-Jiménez N**, Aranda P, Aparicio VA. A 16-week multicomponent exercise training program improves menopause-related symptoms in middle-aged women. The FLAMENCO Project randomized control trial. *Menopause*, 2022; 29(5), 537-544.

7. Marín-Jiménez, N., Cruz-León, C., Perez-Bey, A., Conde-Caveda, J., Grao-Cruces, A., Aparicio, V. A., ... & Cuenca-García, M. (2022). Predictive Validity of Motor Fitness and Flexibility Tests in Adults and Older Adults: A Systematic Review. *Journal of Clinical Medicine*, *11*(2), 328.

8. Romero-Parra N, Maestre-Cascales C, **Marín-Jiménez N**, et al. Exercise-Induced Muscle Damage in Postmenopausal Well-Trained Women. *Sports Health.* 2021; 13(6):613-621.

9. Flor-Alemany M, Acosta P, **Marín-Jiménez N**, Baena-García L, Aranda P, Aparicio VA. Influence of the degree of adherence to the mediterranean diet and its components on cardiometabolic risk during pregnancy: The GESTAFIT Project. *Nutrition, Metabolism and Cardiovascular Diseases.* 2021; 31(8):2311-2318.

10. Aparicio VA, Flor-Alemany M, **Marín-Jiménez N**, Coll-Risco I, Aranda P. A 16-week concurrent exercise program improves emotional well-being and emotional distress in middle-aged women: the FLAMENCO Project randomized controlled trial. *Menopause.* 2021; 28(7):764-771.

11. Ruiz-Montero P, **Marín-Jiménez N**, Borges-Cosic M, Aparicio V. Association of objectively measured physical fitness with health-related quality of life of mid-life women: the FLAMENCO Project. *Climacteric.* 2021; 24(3):282-288.

12. Baena-García L, Acosta-Manzano P, Ocón-Hernández O, Borges-Cosic M, Romero-Gallardo L, **Marín-Jiménez N**, Aparicio, VA. Objectively measured sedentary time and physical activity levels in Spanish pregnant women. Factors affecting the compliance with physical activity guidelines. *Women & Health.* 2021; 61(1):27-37.

13. Castro-Piñero, J., **Marín-Jiménez, N.**, Fernández-Santos, J. R., Martin-Acosta, F., Segura-Jiménez, V., Izquierdo-Gómez, R., ... & Cuenca-Garcia, M. (2021). Criterion-Related validity of field-based fitness tests in adults: a systematic review. *Journal of Clinical Medicine*, *10*(16), 3743.

14. Baena-García L, **Marín-Jiménez N**, Romero-Gallardo L, et al. Association of Self-Reported Physical Fitness during Late Pregnancy with Birth Outcomes and Oxytocin Administration during Labour: The GESTAFIT Project. *International Journal of Environmental Research and Public Health.* 2021; 18(15):8201.

15. Marín-Jiménez N, Ruiz-Montero PJ, De la Flor-Alemany M, Aranda P, Aparicio VA. Association of objectively measured sedentary behavior and physical activity levels with health-related quality of life in middle-aged women: The FLAMENCO Project. *Menopause.* 2020; 27(4):437-443.

16. Flor-Alemany M, Nestares T, Alemany-Arrebola I, **Marín-Jiménez N**, Borges-Cosic M, Aparicio VA. Influence of Dietary Habits and Mediterranean Diet Adherence on Sleep Quality during Pregnancy: The GESTAFIT Project. *Nutrients.* 2020; 12(11):3569.

17. Flor-Alemany M, **Marín-Jiménez N**, Nestares T, Borges-Cosic M, Aranda P, Aparicio V. Mediterranean diet, tobacco consumption and body composition during perimenopause. the FLAMENCO Project. *Maturitas.* 2020; 137:30-36.

18. Flor-Alemany M, **Marín-Jiménez N**, Coll-Risco I, Aranda P, Aparicio VA. Influence of dietary habits and Mediterranean diet adherence on menopausal symptoms. The FLAMENCO Project. *Menopause.* 2020; 27(9):1015-1021.

19. Aparicio VA, **Marín-Jiménez N**, Coll-Risco I, et al. Doctor, ask your perimenopausal patient about her physical fitness; association of self-reported physical fitness with cardiometabolic and mental health in perimenopausal women: the FLAMENCO Project. *Menopause.* 2019; 26(10):1146-1153.

Teaching experience

Lecturer at University of Cadiz (200 h)

- Actividad Física para Grupos de Población Específica
- Actividad Física y Salud
- Aula Universitaria de Mayores
- Dinamización y Recreación en Piscinas y Playas
- Enseñanza y Aprendizaje de la Educación Física
- Expresión Corporal
- Fisiología del Ejercicio 2
- Fundamentos de la Educación Física
- Fundamentos de las Habilidades Motrices
- Fundamentos de los Deportes Individuales 1
- Nuevas Tendencias del Fitness y el Wellness
- Trabajo Fin de Grado
- Valoración de la Condición Física relacionada con la Salud

Lecturer at Karolinska Institutet (10 h)

- Diet, Physical Activity and Fitness - assessment and evaluation (Master's Program in Nutrition Science).

Lecturer at University of Granada (2 h)

- Máster propio en alimentación, ejercicio y deporte para la salud (Food & Fit).

Other merits

I am part of the consolidated research group **CTS158-Galeno** (*visit page*), with a dynamic national and international participation, leading to strong scientific publications.

Twenty-seven communications or posters both in national and international **conferences**, recently being invited as a speaker at a symposium.

Also, Given the current need to transfer scientific knowledge to society, I have publicized the results of my research being involved in the **3-Minutes Thesis Contest** (University of Granada, 2019), and winning a **science monologue** (*interview*). Moreover, I actively participate in the **European Researchers' Night**, and I have participated as an instructor at the **International Doctoral Summer School in Nutrition and Exercise for a Healthier Pregnancy** (Canal URG-University of Granada, 2018).

LIST OF STUDIES INCLUDED

and quality indexes

All the authors gave their approval for the presentation of the included studies as part of the current Doctoral Thesis, and their resignation to present these studies as part of another Doctoral Thesis at any other University.

Nuria Marín Jiménez states her contribution in the included studies as follows:

- **Studies I, III, IV, V, VI and VIII:** Nuria Marín Jiménez contributed in the acquisition of the data, the creation of the databases, performed the data analyses, proceeded with the presentation of the results, and wrote the manuscript, being the first author.
- **Studies II and VII:** Nuria Marín Jiménez contributed in the acquisition of the data, the creation of the databases, the elaboration of the manuscripts' figures, gave critical discussion of the manuscript, and contributed in the final manuscript as accepted, being the second author and/or the corresponding author.

1. Marín-Jiménez, N., Flor-Alemany, M., Baena-García, L., Coll-Risco, I., Castro-Piñero, J., & Aparicio, V. A. (2022). Physical fitness and maternal body composition indices during pregnancy and postpartum: The GESTAFIT Project. *European Journal of Sport Science*, 1-11. doi.org/10.1080/17461391.2022.2115405: **Q1**.

2. Aparicio, V. A, **Marín-Jiménez, N.,** Castro-Piñero, J., Flor-Alemany, M., Coll-Risco, I., & Baena-García, L. Association of body flexibility with the odd of oxytocin administration and caesarean section during labor: The GESTAFIT Project. *Submitted: European Journal of Sport Science:* **Q1***.

3. Marín-Jiménez, N., Acosta-Manzano, P., Borges-Cosic, M., Baena-García, L., Coll-Risco, I., Romero-Gallardo, L., & Aparicio, V. A. (2019). Association of self-reported physical fitness with pain during pregnancy: The GESTAFIT Project. *Scandinavian Journal of Medicine & Science in Sports*, *29*(7), 1022-1030. doi.org/10.1111/sms.13426: **Q1**.

4. Marín-Jiménez, N., Borges-Cosic, M., Ocón-Hernández, O., Coll-Risco, I., Flor-Alemany, M., Baena-García, L., Castro-Piñero J., & Aparicio, V. A. (2021). Association of self-reported physical fitness with pregnancy related symptoms: The GESTAFIT Project. *International Journal of Environmental Research and Public Health*, *18*(7), 3345. doi.org/10.3390/ijerph18073345: **Q1**.

5. Marín-Jiménez, N., Castro-Piñero, J., Rodríguez-Ayllón, M., Marchán-Rubio, A., Delgado-Fernández, M., & Aparicio, V. A. (2022). The favourable association of self-reported physical fitness with depression and anxiety during pregnancy: The GESTAFIT Project. *European Journal of Sport Science*, *22*(12), 1932-1940. doi.org/10.1080/17461391.2021.1986141: **Q1**.

6. Marín-Jiménez, N., Flor-Alemany, M., Baena-García, L., Corres, P., Molina-Hidalgo C., & Aparicio, V. A. (2023). The role of self-reported physical fitness in emotional well-being and emotional distress during pregnancy: The GESTAFIT Project. *Journal of Sport and Health Science*, Submitted*:* **Q1***.

7. Aparicio, V. A; **Marín-Jiménez, N**., Flor-Alemany, M., Acosta-Manzano, P., Coll-Risco, I., & Baena-García, L. (2023). Effects of a concurrent exercise training program on low back and sciatic pain and pain disability in late pregnancy. *Scandinavian Journal of Medicine & Science in Sports 3*(7), 1201-1210. doi.org/10.1111/sms.14353: **Q1**.

8. Marín-Jiménez, N., Baena-García, L., Coll-Risco, I., Flor-Alemany, M., Castro-Piñero, J., & Aparicio, V. A. (2023). Influence of a concurrent exercise training program on health-related quality of life during advanced pregnancy: The GESTAFIT Project. *Sports Health: A Multidisciplinary Approach*. doi/10.1177/19417381231189730: **Q1**.

**Studies II and VI are currently submitted for publication in high-impact science journals.*