Tesis Doctoral Internacional / International Doctoral Thesis

INFLUENCIA DE LOS NIVELES DE ACTIVIDAD FÍSICA, CONDICIÓN FÍSICA Y DE UN PROGRAMA DE EJERCICIO FÍSICO CONCURRENTE DURANTE LA GESTACIÓN SOBRE LOS RESULTADOS MATERNOS Y NEONATALES ASOCIADOS AL PARTO

INFLUENCE OF PHYSICAL ACTIVITY LEVELS, PHYSICAL FITNESS AND A CONCURRENT PHYSICAL EXERCISE PROGRAM DURING PREGNANCY ON MATERNAL AND NEONATAL BIRTH OUTCOMES

PROGRAMA OFICIAL DE DOCTORADO EN MEDICINA CLÍNICA Y SALUD PÚBLICA

DEPARTAMENTO DE ENFERMERÍA

FACULTAD DE CIENCIAS DE LA SALUD

UNIVERSIDAD DE GRANADA

LAURA BAENA GARCÍA

2019

Editor: Universidad de Granada. Tesis Doctorales
Autor: Laura Baena García
ISBN: 978-84-1306-312-6
URI: http://hdl.handle.net/10481/57259

A las mujeres que corren con los lobos

LIST OF CONTENTS

.

RESEARCH PROJECTS AND FUNDING

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

1. GESTAFIT project 1. Effects of supervised aerobic and strength training in overweight and grade I obese pregnant women on maternal and foetal 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 Skłodowska-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.

2. GESTAFIT project 2: Effects of a of supervised physical exercise program during pregnancy on the length of telomeres and markers of gene expression related to adiposity in the mother and the newborn. Randomized controlled trial (PI-0395-2016). Consejería de Salud de la Junta de Andalucía (56.178€). 01/01/2017 al 31/12/2018. I.P.: Virginia A. Aparicio García-Molina

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

ABSTRACT

Recently, the importance of encouraging normal birth and decreasing caesareans sections and instrumental births rates has been pointed out. An example of this is the Strategy for Assistance at Normal Childbirth in the Spanish National Health System, which was developed in 2007 and aims to improve birth outcomes, which in many cases will determine the future health status of both, the mother and newborn. In relation to this, physical activity and physical exercise have shown to be important tools to increase the physical fitness and they could improve maternal and neonatal birth outcomes.

The main aim of this International Doctoral Thesis was to explore the influence of physical activity and physical fitness levels and a supervised concurrent exercise-training program during pregnancy on maternal and neonatal birth outcomes and type of delivery.

To address these objectives, five studies were conducted in the context of the GESTAtion and FITness (GESTAFIT) research project. In *Studies I* and *II*, accelerometers were placed around the hips of the participants for 7 consecutive days. Thus, compliance with the PA guidelines (*Study I*) and the association of sedentary time and different physical activity levels and intensities with birth outcomes (gestational age, length of labour, birth weight and umbilical cord blood gas, among others) and type of delivery (*Study II*) were determined. In *Study III*, the maternal physical fitness was objectively measured in order to explore its association with the same birth outcomes as in *Study II*. In *Study IV*, the self-reported physical fitness was determined through the International FItness Scale and its association with the abovementioned birth outcomes and the oxytocin administration during labour was studied. Finally, in *Study V*, the influence of an exercise program performed from the 17th week of pregnancy until delivery (3 days / week, and 60 minutes / session) consisting of a combination of aerobic and resistance exercises, were explored.

The study sample (n = 135) was divided into a control group (n=85) and an intervention group (n=50).

The main findings and conclusions derived from the five studies included in this Thesis were: I) Although the compliance with the physical activity guidelines was low, greater levels of light, moderate, moderate-to-vigorous, and total physical activity during early second trimester of pregnancy were associated with better maternal and neonatal birth outcomes. Contrary, sedentary time and vigorous physical activity might have a harmful influence on birth outcomes; II) Higher upper-body muscle strength and flexibility during early second trimester of pregnancy were associated to better neonatal birth outcomes and greater cardiorespiratory fitness and flexibility to lower caesarean section rates; III) Pregnant women who reported lower levels of cardiorespiratory fitness and flexibility during late pregnancy were provided with oxytocin (before or during labour) to a greater extent than those who reported higher levels of both physical fitness components; IV) The exercise program performed under the GESTAFIT project was safe for the mother and the new-born. The intervention program extended the duration of the first stage of labour and shortened the second stage, without having a negative impact neither on the Apgar test score nor on the umbilical cord blood gas analysis. Further, greater placental and neonatal weight were found in women who exercised compared to the control group. Finally, the intervention program did not have harmful effects on other studied variables. The findings of this International Doctoral Thesis provide new information about the benefits of physical activity and physical fitness, which could improve maternal and neonatal birth outcomes. For instance, it should be noted that greater sedentary time was associated with worse umbilical cord blood gas profile and better physical fitness was related to more positive neonatal outcomes and lower caesarean rates. On the other hand, self-reported physical fitness could provide important information to health professionals to encourage women to exercise and thus, reduce the use of oxytocin during labour and caesarean section rates.

RESUMEN

En los últimos años, se ha señalado la importancia de fomentar el nacimiento normal y disminuir las tasas de cesáreas, partos instrumentales y otras intervenciones durante el parto. Un ejemplo de esto es la Estrategia de Atención al Parto normal del Sistema Nacional de Salud español, que se desarrolló en 2007 y que tiene como objetivo mejorar los resultados maternos y neonatales asociados al parto, que en muchos casos determinarán el estado de salud futuro de ambos. En este sentido, la actividad física y el ejercicio físico han demostrado ser importantes herramientas para mejorar la capacidad física pudiendo mejorar los resultados maternos y neonatales asociados al parto.

El principal objetivo de esta Tesis Doctoral Internacional fue explorar la influencia de los niveles de actividad física y condición física así como de un programa de ejercicio físico concurrente durante el embarazo sobre los resultados maternos y neonatales ligados al parto y el tipo de parto.

Para abordar estos objetivos se realizaron cinco estudios en el contexto del proyecto de investigación GESTAFIT. En los *estudios I* y *II*, se colocaron acelerómetros alrededor de las caderas de los participantes durante 7 días consecutivos. De esta forma, se evaluaron el cumplimiento las pautas de actividad física (*Estudio I*) y la asociación del tiempo de sedentarismo y los diferentes niveles e intensidades de actividad física con los resultados del parto (edad gestacional, duración del parto, peso al nacer y gasometría en el cordón umbilical, entre otros) y el tipo del parto (*Estudio II*). En el *Estudio III*, la condición física materna se midió objetivamente para explorar su asociación con dichos marcadores. En el *Estudio IV*, se determinó la asociación de la condición física auto-reportada a través de la Escala internacional de Condición Física (IFIS) y su asociación con los resultados del

parto y la administración o no de oxitocina durante dicho trabajo de parto. Finalmente, en el estudio V se exploraron los efectos de un programa de ejercicio físico concurrente realizado desde la semana 17ª de embarazo hasta el parto (3 días / semana y 60 minutos / sesión) que consistió en una combinación de ejercicios aeróbicos interválicos y de fuerza. La muestra del estudio (n = 135) se dividió en un grupo control (n = 85) y un grupo de intervención (n = 50).

Los principales hallazgos y conclusiones derivadas de los cinco estudios incluidos en la presente Tesis Doctoral fueron: I) Si bien el cumplimiento con las pautas de actividad física fue bajo, mayores niveles de actividad física ligera, moderada, moderada-vigorosa y total durante el segundo trimestre de embarazo se asociaron con mejores resultados maternos y neonatales ligados al parto. Al contrario, el tiempo de sedentarismo y la actividad física vigorosa podrían tener una influencia perjudicial en dichos marcadores; II) Mayor fuerza muscular y flexibilidad del tren superior durante el segundo trimestre del embarazo estuvieron asociados con mejores resultados neonatales en el parto y una mayor capacidad cardiorrespiratoria y flexibilidad con una tasa de cesárea más baja; III) A las embarazadas que auto reportaron una menor capacidad cardiorrespiratoria y flexibilidad durante el embarazo tardío se les administró oxitocina (antes y durante el trabajo de parto) en mayor medida que aquellas que reportaron mayores niveles en ambas cualidades físicas; IV) El programa de ejercicio desarrollado bajo el proyecto GESTAFIT, fue seguro para la madre y el recién nacido. El programa de intervención alargó la duración de la primera etapa del trabajo de parto y acortó la segunda, sin tener un impacto negativo ni en la puntuación del test de Apgar ni en los gases de la sangre del cordón umbilical. Además, el peso placentario y neonatal fue mayor en mujeres que realizaron ejercicio comparadas con el grupo control. Finalmente, el programa de intervención no tuvo efectos perjudiciales en otras variables estudiadas.

Los hallazgos de esta Tesis Doctoral Internacional brindan nueva información sobre los beneficios de la actividad física y la condición física en la gestante, los cuales podrían mejorar los resultados maternos y neonatales ligados al parto. Además, se debe tener en cuenta que el tiempo de sedentarismo se asoció con peores valores en la gasometría en sangre de cordón umbilical. Por otro lado, la condición física auto reportada podría ofrecer una información importante a los profesionales de la salud para animar a las mujeres a ejercitarse, lo que podría reducir la necesidad de administración de oxitocina durante el parto y la tasa de cesáreas.

ABBREVIATIONS

ACOG, American College of Obstetricians and Gynaecologists

ANCOVA, analysis of covariance

BMI, body mass index

CI, confidence interval

CO_2, carbon dioxide

CRF, cardiorespiratory fitness

GESTAFIT, GESTAtion and FITness

IFIS, International Fitness Scale

LDL, Low density lipoprotein

METS, metabolic equivalent of task

MVPA, moderate-to-vigorous physical activity

O_2, oxygen

PA, physical activity

PCO_2, partial pressure of carbon dioxide

PF, physical fitness

PO_2, partial pressure of oxygen

PPAQ, Pregnancy Physical Activity Questionnaire

SD, standard deviation

ST, sedentary time

VO_2max, maximal oxygen intake

WHO, World Health Organization

INTRODUCTION

INTRODUCTION

1. Theoretical framework about physical activity, physical fitness and physical exercise during pregnancy and maternal and neonatal birth outcomes

Childbirth is a life-changing event and could positively or negatively affect the future health status of the mother and the newborn[1]. The World Health Organization (WHO) considers prenatal care carried out during pregnancy as one of the most useful tools to reduce the morbidity and mortality associated with childbirth[2]. In this context, the promotion of healthy habits in pregnant women populations is extremely important. One of the main factors to maintain health status being or not pregnant is to do physical activity (PA) and improve physical fitness (PF)[3]. However, sixty percent of the World's population is physically inactive, which comprises a global public health problem[4].

The difference between being physically inactive and having sedentary behaviours must be highlighted. Sedentary behaviours are those that usually are conducted in a sitting posture (such as watching television or reading) and have a metabolic expenditure ≤ 1.5 metabolic equivalent of task (METS)[5]. In this sense, a person can be physically active but spend a lot of time in sedentary behaviour and vice-versa. It has been previously reported that pregnant women spend half of the time in sedentary behaviours, and this has been associated with health issues such as higher levels of low density lipoprotein (LDL) cholesterol and C-reactive protein, and greater abdominal circumference of the newborn[6], among others. For this reason, it is as important to promote the increase of PA as it is to avoid sedentary behaviours in this period of women's lives.

Regarding PA guidelines during pregnancy, the American College of Obstetricians and Gynecologists (ACOG) and the Canadian Society for Exercise Physiology recommend pregnant women without contraindications getting at least 150 minutes of moderate intensity PA per week to obtain health benefits and reduce complications during pregnancy[7,8]. Nevertheless, compliance with PA recommendations has been described as low in different pregnant women populations[9–12]. Physical activity can be evaluated with subjective measures, such as questionnaires, or with objective measures such as pedometers and accelerometers. One of the most used PA questionnaires is the Pregnancy Physical Activity Questionnaire (PPAQ)[13]. Although subjective measures can be useful tools, it is recommended that PA during pregnancy should be measured with accelerometers, which seems to give a more reliable estimate[14,15].

The benefits of PA during pregnancy have been widely described: improved insulin sensibility and lower concentrations of serum triglycerides[16], lower risk of caesarean section[17], better neonatal body composition[18], a more adequate weight gain, and improved maternal cardiorespiratory fitness (CRF)[19].

Physical fitness is an important health marker[20,21] which could improve in pregnant women who perform PA[19] and who exercise during pregnancy[22]. Some of the most studied PF dimensions are muscular strength, CRF and flexibility, which can be measured through objective[23–25] and subjective methods[26].

Muscular strength has been defined as the ability to exert force on an object or against a resistance[27,28]. Greater muscular strength has been related with less bodily pain and pain disability during pregnancy[29] and increased birth weight[30]. However, evidence about the potential associations of maternal muscle strength with other important maternofoetal outcomes such as umbilical cord blood gas or type of birth (vaginal or caesarean section) is still scarce.

Cardiorespiratory fitness is related to lower risk of all-cause mortality[31]. Although a positive relationship has been described between factors such as CRF before pregnancy and general health and physical well-being in women planning pregnancy[32], among others, there have been few studies analysing its association with birth outcomes[33]. In addition, although objective assessing methods are desirable when it comes to increasing research quality, questionnaires could as well be an important tool for health professionals.

Flexibility is defined as the range of motion of a joint or group of joints, as per the skeletal muscles and not any external forces[34] and it probably is the least studied PF dimension in relation to birth outcomes and birth type. Nevertheless, a greater self-reported flexibility during late gestation has been associated with less bodily and sciatic pain[29]. The degree of flexibility could be modified by relaxin levels, which are increased during pregnancy[35]. The effects of relaxin have been studied previously and an important relationship with vascular function –generally producing vasodilators effects[36,37] has been shown, , but this has been not related to childbirth outcomes.

Finally, physical exercise is any type of planned and structured PA and any bodily movement produced by the skeletal muscle contraction that results in energy expenditure[38]. Physical exercise during pregnancy has proven to have a wide margin of safety in women without contraindications, due to maternal and foetal cardiovascular and metabolic adaptations[39]. In addition, strength training and aerobic exercise could have beneficial effects on the health of both the mother and the foetus[40,41]. Unfortunately, the evidence shows that a low percentage of pregnant women exercise during this period[42,43].

Moreover, most training programs conducted during pregnancy have focused only on aerobic[44] or strength[41] training. Notwithstanding, it is possible that the combination of both types of training is the most beneficial for pregnant women and their offspring[22].

Further studies assessing the effects of a concurrent exercise program (aerobic and resistance training) on maternal and foetal birth outcomes are needed.

1.1 Maternal birth outcomes

1.1.1 Gestational age at birth

Gestational age at birth is an important prognostic marker of newborn health status, both in the short and long term. The recommended classification for births occurring after 37 completed weeks of gestation is as follows[45].

- Early term: from 37 to 39 gestational weeks
- Full term: from 39 to 41 gestational weeks
- Late term: from 41 to 42 gestational weeks
- Post-term: more than 42 gestational weeks

Therefore, premature births are those that occur before the 37th gestational week. Approximately 10% of births take place prematurely[46] and the shortening of gestation time has been described as a risk factor for problems related to adaptation to the extrauterine environment[47]. Babies who were born prematurely are more likely to develop chronic kidney diseases, neurodevelopmental deficits, increased blood pressure and cardiac pathologies, reduced sensitivity to insulin and chronic obstructions of the airways, among others[48]. Regarding the association of PA with gestational age at birth, Rêgo et al [49] described that there was no association between both variables. On the other hand, a systematic review published in 2017 by Aune et al.[50] showed that physically active pregnant women could have a 10-14% lower risk of premature birth than sedentary pregnant women.

There seems to be important differences depending on the moment in which PA levels and other maternal variables such as body mass index (BMI) are evaluated. Takami et al.[51] assessed PA before and during pregnancy. The results showed that there was no association between pre-pregnancy PA and preterm birth, but there was a slight increase in the probability of premature birth among women who performed low PA during pregnancy compared to those who were physically more active during this period. Regarding maternal BMI, Straughen et al.[52] concluded that PA during pregnancy had a protective effect on preterm births only for normal-weight women, but this effect disappeared in overweight and obese pregnant women.

On the other hand, prolonged pregnancies may also lead to a higher prevalence of complications. Post-term infants have a higher risk of neurological complications, meconium aspiration, neonatal sepsis and shoulder dystocia, among others[53] and to date no studies have explored whether physical activity could reduce the risk of prolonged gestation.

Given the methodological differences used in these studies, it is difficult to establish a clear answer about the relationship of PA during pregnancy and gestational age at birth, which is of clinical and public health interest (*Study II*).

Finally, to the best of our knowledge, there are no studies that have related maternal PF during pregnancy with gestational age at birth (*Study III*).

1.1.2 Length of the labour

The normal length of a low-risk labour is difficult to define and there are currently doubts about the rigid limits applied to establish when a stage of labour is abnormal, since the timing often varies from one woman to another[54]. Thus, the length of labour could be affected by parity, maternal BMI, birth weight and epidural analgesia, among others[55]. On the one hand, the first stage of labour is usually defined as the period comprising a cervical dilatation from 4 centimetres or more with regular uterine contractions to full dilatation, which is defined by a cervix dilatation of 10 centimetres[56]. The second stage is the one that begins with full cervical dilation and ends with the birth of the baby[56].

Although it has been described that exercise programs during pregnancy could shorten the duration of the labour[57,58], studies analysing the association between PA and the length of labour have reported contradictory results[59–61]. Consequently, studies analysing the association between sedentary time and PA levels with the length of the labour are justified (*Study II*). Finally, no studies have explored the association between maternal PF during pregnancy with the length of the labour (*Study III*).

1.2 Neonatal birth outcomes

1.2.1 Birth weight

Birth weight is an important marker of health status in both the neonatal period and the childhood[62]. Neonatal weight differs from one population to another and seems to be influenced by maternal weight in early pregnancy and parity, among other factors[63]. Some studies have explored the association between PA during pregnancy and this relevant neonatal outcome. A meta-analysis found a modestly lower risk of macrosomia in foetuses of women who had performed moderate-to-vigorous PA (MVPA) during late gestation. However, this lower risk was not observed when PA was performed during early pregnancy. These results are in line with those described by Pathirathna et al.[64], who did not find any association between PA performed between weeks 18 and 24 of gestation and birth weight. Regarding PF, a positive association of muscular strength with birth weight has been previously described[65,66]. Nevertheless, other important PF dimensions, such as CRF and maternal flexibility have been scarcely explored in relation to this neonatal outcome (*Study III*).

1.2.2 The Apgar test

In 1953, Virginia Apgar proposed a method for newborn evaluation after birth[67]. The Apgar test assesses heart rate, respiratory effort, muscle tone, skin colour, and reflex irritability of the newborn. It is done between one and five minutes after birth and the maximum score is 10, which means that the neonate is in the best health conditions. This test is still widely used in all obstetric services[68] and allows a quick and effective assessment of the newborn status with an important prognostic value, especially when it is combined with other data such as umbilical cord blood gas analysis.

Table 1. Signs and definitions of the Apgar Test[67].

	Score		
Sign	**0**	**1**	**2**
Heart rate	Absent	Slow (<100 beats/min)	> 100 beats/min
Respirations	Absent	Weak cry, hypoventilation	Good, strong cry
Muscle tone	Limp	Some reflexion	Active motion
Reflex irritability	No response	Grimace	Cry or active withdrawal
Colour	Blue or pale	Body pink, extremities blue	Completely pink

Although several studies have shown that there is no relationship between the practice of exercise during pregnancy and the Apgar test[69], to the best of our knowledge, there are no studies exploring the association of this neonatal result with maternal PA or PF levels (*Studies II and III*).

1.2.3 Neonatal acid-base balance after birth

The analysis of umbilical cord blood gas after birth is known to be an indicator of foetal acid-base status during labour [70]. The pH analysis is not a reliable indicator by itself, so the gas analysers additionally calculate the partial pressure of oxygen (PO_2) and partial pressure of carbon dioxide (PCO_2) levels to avoid false results [71]. Yeomans et al. [72] previously described the normal values of the arterial and venous blood gases of the umbilical cord which are similar to those described by other authors [73–76]:

Table 2. Normal values of arterial and venous cord blood gases [72].

	Arterial blood	**Venous blood**
pH	7.28±0.05	7.35±0.05
PCO_2 (mmHg)	49±8.4	38±5.6
PO^2 (mmHg)	18±6.2	29±5.9

Values shown as mean±standard deviation. PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen.

Taking blood samples from both the umbilical artery and vein is recommended and allows us to know the cause of the acid-base balance alteration[77]. In the past, the umbilical cord was clamped immediately after birth. Nonetheless, delayed clamping of the umbilical cord at least 30-60 seconds after birth is currently widely recommended. Some of the benefits of this practice are increased levels of haemoglobin and iron deposits, lower risk of necrotising enterocolitis and higher red blood cell volume[78]. In this sense, several studies have shown that umbilical cord blood gases are not affected by delayed clamping[79,80] and it has even been proposed that samples can be taken without clamping with no additional risks[81].

Despite the valuable information that can be obtained from the umbilical blood gases analysis, no previous studies have explored the relationship of this variable with PA or PF during pregnancy (*Studies II and III*).

1.3 Birth type: rates and risks of caesarean section

In 2007, the Spanish Ministry of Health and Consumer Affairs published the Strategy for assistance at normal Childbirth in the Spanish National Health System with the aim of improving care during childbirth, promoting participation and protagonism of women themselves during this process[82]. In addition, it was proposed that programs be implemented to reduce the rate of caesarean sections due to maternal and neonatal risks and the increase in health costs that they entail[82].

Subsequently, in 2016, the Ministry of Health, Consumer Affairs and Social Welfare published the National Statistics of Hospitals, which showed that in Spanish public hospitals, caesarean rate was of 22% of births[83]. This rate is much higher than that recommended by WHO, which states that no more than 15% of births should be by caesarean section[84].

After a caesarean section, women have a higher risk of infection, wound dehiscence, haemorrhage and thrombophlebitis, hysterectomy, admission to intensive care unit and reduced fertility, among other complications, compared with women who had vaginal deliveries[85–87]. On the other hand, neonates born by caesarean section have an increased risk of respiratory problems, allergies and type 1 diabetes[88], among other risks associated with the lack of bacterial colonization by maternal vulvovaginal and rectal flora[89].

Based on these findings, it is relevant to explore maternal variables that might be associated with improvements in maternal and neonatal birth outcomes, and explore their relationship with the type of birth (*Studies II*, *III*, and *IV*). Likewise, it is important to explore the effects that a supervised concurrent physical exercise program during pregnancy could have on these birth-related outcomes (*Study V*).

Hence, the present Doctoral Thesis focuses on the study of the influence of PA, PF and a concurrent physical exercise program during pregnancy on maternal and neonatal birth outcomes and delivery type.

2. Sociodemographic and clinical factors affecting the compliance with physical activity guidelines during pregnancy.

Women usually decrease their daily PA levels when they get pregnant [90]. This decrement in PA levels might be probably explained by the pregnancy symptomatology, fear of harming the foetus, or ignorance about PA guidelines during this period[91,92]. Pregnant women without contraindications for the performance of PA, should achieve at least 150 minutes per week of MVPA, in bouts of at least 10 continuous minutes and with daily amounts of 30 minutes or more[78].

Excessive sedentary time (ST) and low PA levels during pregnancy could negatively affect both the mother and the newborn[6,93]. Nevertheless, compliance with PA guidelines still remains low[10]. In this regard, some studies have identified sociodemographic and clinical characteristics of pregnant women that could condition PA guidelines compliance during this stage, such us BMI, educational level, self-perceived health and socioeconomical status, among others[94–96]. However, most of the studies describing ST and PA levels during pregnancy, and exploring factors which might influence PA guidelines compliance, have been performed by subjective assessment tools, such as self-reported questionnaires[9,10]. Hence, it is not only of clinical and social interest to objectively determine whether Spanish pregnant women meet PA guidelines, but also to explore which sociodemographic and clinical characteristics predispose pregnant women to meet or not PA recommendations. This information might be useful in order to design more tailored interventions focused on increasing PA levels and decreasing sedentary behaviours during this physiological stage. Moreover, the identification of modifiable factors affecting PA levels during pregnancy (*Study I*), might facilitate that future studies focus on more specific lifestyle interventions, as new and alternative therapeutic targets, in order to improve maternal and foetal health[17,94].

3. Association of sedentary time and physical activity during pregnancy with maternal and neonatal birth outcomes.

Uterine blood flow is crucial to meet the nutrient and oxygen requirements of the placenta and the foetus[97]. It should be noted that during delivery, uterine contractions induce metabolic stress in the foetus, whose adaptation can be reflected in the umbilical cord blood gases immediately after birth[71]. Actually, small changes of foetal pH could significantly affect the functioning of the cardiovascular and central nervous system as well as it could be related to worse score in the Apgar test, and a higher risk of neonatal complications in short and long term[98].

Previously, different types and intensities of physical exercise have been related with the neonatal base acid balance, the foetus-placenta blood flow, and the birth weight, among others[99]. To date, it is known that exercise during pregnancy can improve blood perfusion and lower peripheral vascular resistance due to increased angiogenesis, increased endothelial vasodilation[100] and placental uterine perfusion[101]. However, no studies have previously associated different intensities of objectively measured PA with umbilical cord blood gases and other health-related maternal and foetal birth outcomes. Therefore, it seems possible that PA levels during pregnancy might influence utero-placental perfusion, which could be reflected in the acid-base balance of the newborn, as well as ST might have a relevant negative effect on them.

Hence, it is of clinical and social interest to determine whether ST and PA intensity levels are associated with birth outcomes for both, the mother and the newborn (*Study II*). This might guide future studies to focus on specific active lifestyle interventions as new and alternative therapeutic targets in order to avoid adverse birth outcomes, including caesarean sections.

4. Association of objectively measured physical fitness during pregnancy with maternal and neonatal birth outcomes.

Research continues to confirms that exercise during pregnancy contributes to healthier outcomes for both, the mother and the foetus[7,39]. Consequently, exercise is currently recommended in all low risk pregnancies[7]. Exercising during pregnancy has been related to enhanced efficiency of the placenta[102] and placental uterine perfusion[101], a lower rate of caesarean sections[7], and optimal birth weight[99]. Regular exercise is associated with improved PF[103], which is considered a predictor of all-cause mortality in adult populations[104]. Consequently, improved PF is usually observed in women who exercise during pregnancy[22], and is associated with better perinatal health outcomes[32,65]. For instance, maternal handgrip strength (upper-body muscle strength), is positively associated with the newborn birth weight[65]. However, no research to date has specifically looked at the association between other components of PF and many other pregnancy-related outcomes.

It is widely known that umbilical cord blood pH analysis provides vital information about newborn health and reflects its physiological response to any complications that may occur during labour[71]. Accordingly, it would be possible that maternal PF measures are positively associated with improved maternal and neonatal birth outcomes and with less caesarean section rates (*Study III*).

5. Association of self-reported physical fitness during late pregnancy with birth outcomes and oxytocin administration during labour.

Birth and the events that occur during labour may have important implications for both, the mother and the newborn's future health. Some adverse events could be associated with natural reasons —such as placental pathologies[105]— or iatrogenic causes, as a result of interventions carried out by health professionals—such as anaesthesia related problems[106]—. In this sense, it is clinically relevant to describe maternal aptitudes that may be related to an improvement in birth outcomes and a lower risk of iatrogenic injuries during labour. In relation to this, whereas the effects of exercise on birth outcomes have been broadly described[57,101] the association of maternal PF with other important outcomes, such as duration of the different stages of labour and values of umbilical cord blood gases, continue to be scarce, and only its relationship with some maternal and foetal health markers has been previously suggested[32,65].

Moreover, it has been proposed in the last years to avoid interventions that are not necessary during labour[107], such as the administration of oxytocin, commonly used to increase or improve uterine dynamics[108]. It is noteworthy that the use of exogenous oxytocin during labour has been previously associated with an increased risk of uterine hyperactivity and postpartum haemorrhage, pathologies of foetal heart rate, increased morbidity and neonatal mortality and breastfeeding problems, among others[109,110].

In order to study the associations of maternal PF with different health outcomes, PF can be measured in a precise way through objective tests[23,111]. However, this kind of tests requires a lot of time to carry them out, so the development of measuring tools adapted to the health professionals —who usually have less than five minutes of consultation time[112] — is mandatory. For this purpose, the International FItness Scale (IFIS) could be a straightforward and handy clinical tool that might be frequently used to assess self-reported PF[26].

Since pregnancy and labour events have important implications for maternal and foetal health, it is of clinical interest to know which PF components may be potentially associated to better birth outcomes and with a lower prevalence of oxytocin administration to induce or stimulate such labour (*Study IV*).

6. Influence of a concurrent exercise training intervention during pregnancy on maternal and neonatal birth outcomes.

Exercising during pregnancy has been previously associated with more adequate weight gain[113], lower risk of gestational diabetes[114] and chronic diseases[115]. In addition, some studies have shown that physical exercise could influence birth outcomes, such as a shorter duration of labour[116] and lower caesarean rates[117,118].

In relation to the effect of exercise during pregnancy on neonatal birth outcomes, such us the birth weight, the results are contradictory. On the one hand, some studies found a decrease in birth weight in babies whose mothers exercise[43,119,120]. On the other hand, there are studies that did not show any associations or described an increase of foetal weight in exercisers pregnant women[121–123].

This difference could be explained by the type and intensity of the physical training program performed, since programs that do not include muscle strength training do not seem to have an effect on foetal weight[99]. In this sense, the exercise training program that seems to bring more benefits is the combination of strength and aerobic training[22].

However, more studies assessing the effect of a concurrent exercise-training program on maternal and neonatal outcomes are needed (*Study V*).

AIMS/OBJETIVOS

The overall aim of this International Doctoral Thesis was to explore the influence of physical activity and physical fitness levels and a supervised concurrent exercise-training program during pregnancy on maternal and neonatal birth outcomes and type of delivery.

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

1. To describe objectively-measured sedentary time and physical activity levels in a sample of Spanish pregnant women *(Study I)*.
2. To analyse the degree of compliance with PA guidelines during pregnancy *(Study I)*.
3. To explore sociodemographic and clinical factors associated with meeting physical activity guidelines *(Study I)*.
4. To analyse the association of objectively measured sedentary time and physical activity during early second trimester of pregnancy with maternal and neonatal birth outcomes (*Study II)*.
5. To explore if objectively measured sedentary time and physical activity levels differ between women with vaginal or caesarean section deliveries *(Study II).*
6. To analyse the association of physical fitness during early second trimester and late pregnancy with maternal and neonatal birth outcomes *(Study III)*.
7. To investigate if physical fitness during early second trimester and late pregnancy is associated with the type of delivery (i.e. vaginal or caesarean section) *(Study III)*.
8. To explore the associations between self-reported maternal physical fitness and birth outcomes *(Study IV)*.
9. To study whether self-reported maternal physical fitness is related to the administration of oxytocin to induce or stimulate labour *(Study IV).*

10. To analyse the influence of a supervised concurrent exercise-training program from the 17th week of gestation until the end of pregnancy, on maternal and neonatal birth outcomes *(Study V)*.

OBJETIVOS

El objetivo general de esta Tesis Doctoral Internacional fue explorar la influencia de la actividad física y la condición física y de un programa supervisado de entrenamiento físico concurrente durante el embarazo, con marcadores maternos y neonatales asociados al parto y al tipo de parto.

Los objetivos específicos de la presente Tesis Doctoral Internacional fueron los siguientes:

1. Describir los niveles objetivos de tiempo de sedentarismo y de actividad física en una muestra de mujeres embarazadas españolas *(Estudio I)*.

2. Analizar el grado de cumplimiento de las recomendaciones de actividad física durante el embarazo *(Estudio I)*.

3. Explorar los factores sociodemográficos y clínicos asociados con el cumplimiento de las recomendaciones de actividad física *(Estudio I)*.

4. Analizar la asociación los niveles objetivos de tiempo de sedentarismo y de actividad física durante el segundo trimestre del embarazo con marcadores maternos y neonatales asociados al parto *(Estudio II)*.

5. Explorar si los niveles objetivos de sedentarismo y de actividad física difieren entre las mujeres con partos vaginales o con cesárea *(Estudio II)*.

6. Analizar la asociación de la condición física durante el segundo trimestre temprano y el embarazo tardío con marcadores maternos y neonatales asociados al parto *(Estudio III)*.

7. Investigar si la condición física está asociada con el tipo de parto (vaginal o cesárea) *(Estudio III)*.

8. Explorar las asociaciones entre la condición física materna auto-informada y los resultados del parto *(Estudio IV)*.

9. Estudiar si la condición física materna auto-informada está relacionada con la administración de oxitocina para inducir o estimular el parto (*Estudio IV*).

10. Analizar la influencia de un programa de ejercicio físico concurrente desde la 17ª semana de embarazo hasta el final del mismo, sobre marcadores maternos y neonatales asociados al parto (*Estudio V).*

MATERIAL AND METHODS

MATERIAL AND METHODS

Studies design

The summary of the methodology employed in the current International Doctoral Thesis is shown in **Table 3**.

All the studies included are part of the GESTAtion and FITness Project (registration number: NCT02582567). This Project was approved by the Clinical Research Ethics Committee of Granada, Government of Andalusia (Spain) (code: GESTAFIT-0448-N-15, approved on 19/05/2015). The inclusion and exclusion criteria in the GESTAFIT Project are shown in **Table 4.**

Table 3. Summary table of the methodology used of each study of the present International Doctoral Thesis

Study	Study design	Participants	Main variables	Methods
I. Objectively-measured sedentary time and physical activity levels in Spanish pregnant women. Factors affecting the compliance with physical activity guidelines. The GESTAFIT Project.	Cross-sectional	134 pregnant women	Sedentary time Physical activity intensity levels Clinical and sociodemographic factors	Accelerometry (GT3X) Self-reported survey
II. Association of sedentary time and physical activity during pregnancy with maternal and neonatal birth outcomes. The GESTAFIT Project.	Longitudinal	94 pregnant women	Sedentary time Physical activity intensity levels Birth outcomes	Accelerometry (GT3X) Obstetric medical records Cord Blood gas analyser

III. Association of objectively measured physical fitness during pregnancy with maternal and neonatal birth outcomes. The GESTAFIT Project.	Longitudinal	159 pregnant women	Upper and lower-body strength Cardiorespiratory fitness Flexibility Birth outcomes	Hand-Grip test Chair Stand test Bruce test Back-scratch test Obstetric medical records Cord Blood gas analyser
IV. Association of self-reported physical fitness during late pregnancy with birth outcomes and oxytocin administration during labour. The GESTAFIT Project.	Longitudinal	117 pregnant women	Sedentary time Physical activity intensity levels	IFIS Obstetric medical records Cord Blood gas analyser
V. Influence of a concurrent exercise training intervention during pregnancy on maternal and neonatal birth outcomes. The GESTAFIT Project.	Experimental (Randomized Control Trial)	136 pregnant women Intervention group, n=50 Control group, n=86	Birth outcomes	Obstetric medical records Cord Blood gas analyser

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.
*In addition, specific inclusion criteria for data analysis are: pregnancy with single foetus, spontaneous or instrumental vaginal birth, and caesarean without maternofoetal pathology (or any other indication that does not involve maternofoetal risk, such as disproportion, failed induction, no foetal progression or non-cephalic presentation).
Exclusion criteria
- Acute or terminal illness.
- Malnutrition.
- Inability to conduct tests for assessing physical fitness or exercise during pregnancy.
- Underweight.
- Pregnancy risk factors (such as hypertension, type 2 diabetes, etc.).
- Multiple pregnancy.
- Chromosomopathy or foetal malformations.
- Uterine growth restriction.
- Foetal death.
- Upper or lower extremity fracture in the past 3 months.
- Presence of neuromuscular disease or drugs affecting neuromuscular function.
- Being registered in another exercise program.
- Doing more than 300 minutes of at least moderate physical activity per week.
- Unwillingness either to complete the study requirements or to be randomised into the control or intervention group.

Participants

A total of 384 women were contacted at "San Cecilio" and "Virgen de las Nieves" University Hospitals, in Granada (southern Spain) at their first medical visit at 12th week of gestation. The recruitment was performed in three different waves. A final number of 159 women signed an informed consent which included the objectives and procedures of the project. The flow chart of the study participants in the GESTAFIT Project is shown in **Figure 1.**

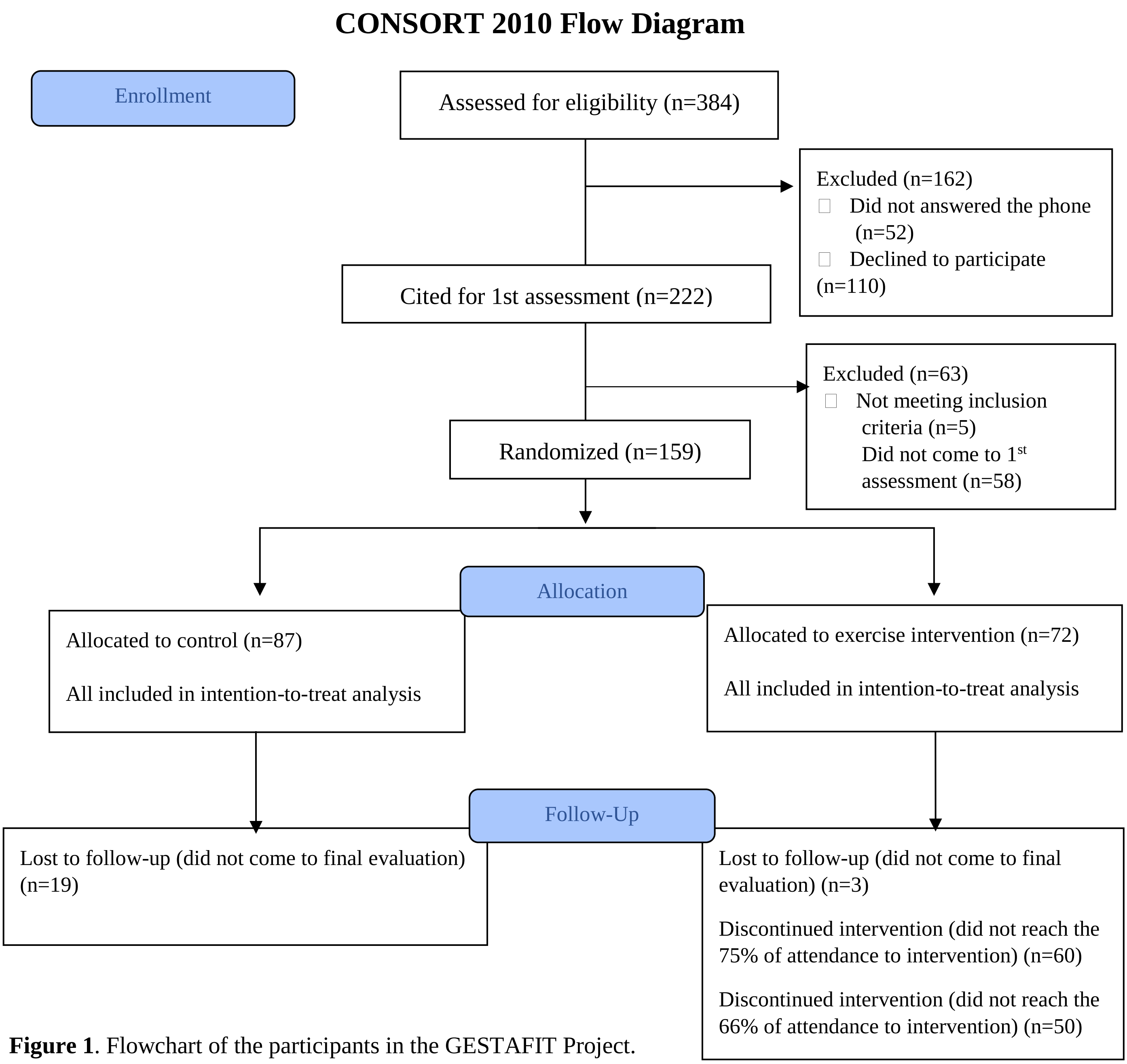

Figure 1. Flowchart of the participants in the GESTAFIT Project.

Procedures

Women were assessed twice (2 days each time) during the study. The first evaluation of the study was completed at 16th gestational week (±2 weeks). Women completed a self-reported questionnaire, anthropometric assessment and PF tests (both, objective measurements and questionnaires). Each participant was given an accelerometer to wear until one and a half week later, when the accelerometers were returned. On week 34th of gestation (±2 weeks), the second assessment for PF tests and height and weight was conducted. Obstetric and gynaecological histories were collected through the "Pregnancy Health Document". Birth and obstetric outcomes for the current pregnancy were collected from the digital medical records. Sampling of the umbilical cord blood occurred immediately after birth. The trainers responsible of the training sessions were the only personnel not blinded to the allocation of participants to the training/control groups.

Outcomes

Sociodemographic and clinical data

The collection of sociodemographic (such as number of children, educational level or marital status), reproductive history, and clinical data (hypertension, diabetes, obesity, etc.) was done through a self-reported survey by the participants. The researchers explained how to fill out this questionnaire properly. This information was gathered by means of an auto administered questionnaire, which also included questions about smoking or alcohol habit and indicators of the socioeconomic status.

Maternal anthropometry

At 16th and 34th gestational weeks, maternal height was measured with a stadiometer (Seca22, Hamburg, Germany) and weight was measured with a scale (InBody R20, Biospace, Seoul, Korea). BMI was calculated as weight (kg) divided by height (m) squared. Weight status groups were based on standard clinical definitions for BMI (normal-weight: 18.5–24.9 kg/m2, overweight/obese: 25.0 kg/m2 or higher). Weight change was calculated as weight at 34th gestational week minus weight at 16th gestational week.

Previous Obstetric History

The “Pregnancy Health Document” is given to all pregnant women by the Andalusian regional government, and it contains obstetric and medical data that were collected for the present study. In this way, information regarding the number and evolution of previous pregnancies, births and gynaecological antecedents were obtained. The gestational age was calculated by the date of last menstruation corrected for cycles of 28 days and subsequently corrected by ultrasound, if needed[124].

Self-reported physical fitness

Self-reported PF was assessed with the *IFIS* questionnaire, which is composed of five Likert-scale questions from 1 (very poor) to 5 (very good) asking the participants about their perceived overall PF, CRF, muscle strength, speed-agility and flexibility in comparison with their counterparts. The participants rated their PF levels as “*very poor*”, “*poor*”, “*average*”, “*good*” and “*very good*”[26]. The higher score indicates greater self-reported PF the participant experiences. This questionnaire is available in different languages at http://profith.ugr.es/IFIS

Physical fitness

Physical fitness was assessed in the following order, to avoid potentially induced fatigue from other tests:

Upper-body muscular strength

Hand grip strength was measured with digital dynamometry (TKK 5101 Grip-D; Takey, Tokyo, Japan), after adjusting by the hand size for an optimal grip, following a protocol described for women[125]. The test was performed twice with both hands, with a rest of 30 seconds and alternating hands. The final value was calculated as a mean of the two values from each hand.

Lower-body muscular strength

Muscular strength of the lower-body was measured through the 30 second Chair Stand test. This test counts the maximum number of repetitions completed in 30 seconds, with a full stand to a sitting position and back straight up as one repetition. The participants performed one trial after a familiarization trial[25].

Flexibility

The Back-scratch test was used to assess upper-body flexibility. The test consists on measuring the overall shoulder range of motion by measuring the distance between the middle fingers come together behind the back. This test was done twice with both hands and the final score was calculated as the mean between the two attempts of each arm[25].

Cardiorespiratory Fitness

Maximal oxygen intake (VO_2max) was estimated (mL/(kg·min)) through the Bruce treadmill protocol, a submaximal, incremental, multistage, continuous treadmill test. The test consists of progressive increments in the workload and velocity every 3 minutes to determine limits of maximal exertion. This test has been previously used and shown to be safe in pregnant women[126,127].

Sedentary time and physical activity levels

Sedentary time and PA levels were objectively assessed with triaxial accelerometry (ActiGraph GT3X+, Pensacola, Florida, US), carried by participants on their hips 24 hours per day for 9 consecutive days. An epoch length of 60 seconds and a frequency rate of 30 Hz were used. The accelerometer was only removed for water activities. The hours of sleep and the time in which they did not wear the accelerometer were subtracted from the total registered time for the whole day (usually 1.440 minutes). To be included in the analysis, a minimum of 10 hours or more of registration was established for 7 days "accelerometer wearing time". Values with recording of ≥20,000 counts/min were excluded because of potential malfunction as well as bouts of 90 continuous minutes of 0 activity intensity counts. A PA notebook was given to participants to report the activities they performed as well as the periods of time in which the accelerometer was removed (for water activities or biking), in order to later collate the accelerometer data.

Accumulated time less than 200 counts per minute (in periods of 10 minutes or more) was used to calculate the ST and it was expressed in minutes per day [128]. The time involved in PA intensity levels (light, moderate, moderate-to-vigorous and vigorous) were calculated based on recommended PA vector magnitude cut points ≥200-2690, ≥2690-6166, ≥2690 and ≥6167 counts/min[129], respectively, and were expressed in min/day. The minutes MVPA bouts per week were also calculated. Bouted MVPA was defined as a period of ≥10 consecutive minutes spent in that behaviour (up to 2 minutes below the cut point allowance). Physical activity categories were established according to the PA recommendations for adults: not meeting PA guidelines <150min/week of bouted MVPA vs. meeting PA guidelines ≥150min/week of bouted MVPA. Data download, reduction, cleaning, and analyses were performed using ActiGraph software (ActiLife v. 6.13.3).

Maternal and neonatal birth outcomes

After birth, we collected information about gestational age at birth, type (i.e. eutocic, instrumental or caesarean section) and onset (i.e. spontaneous, induced or stimulated by oxytocin or prostaglandins) of labour, type of analgesia employed (if any), birth weight, offspring sex and duration of the first and second stages of labour from perinatal obstetric records (partogram). Currently, there is little consensus about when the active phase or first stage of labour begins[130]. The duration of the first stage was defined as the period comprising a cervical dilatation of 4 centimeters or more with regular uterine contractions until full dilatation, which was defined by a dilatation of the cervix of 10 centimeters[131]. The second stage of labour or expulsive period was defined as time from fully dilated cervix to complete delivery of the foetus[131]. Likewise, arterial and venous umbilical cord blood gas analysis and the Apgar score in the newborn were collected from medical records. Placenta was weighted just after delivery with a 3.200 kg Precision Gram Scale.

Oxytocin administration before or during labour

Information about the use of oxytocin during labour was collected from the partogram. In this medical record, midwives usually recorded whether oxytocin is administered or not but the dose and administration time are not frequently collected, so these data were not assessed. Moreover, we consider that oxytocin was administered both, by induction of labour and uterine stimulation, but we did not take into account the administration of this drug during placenta delivery.

Umbilical cord blood gas

Samples of arterial and venous blood from the umbilical cord were collected before the delivery of the placenta to assess pH, partial pressure of carbon dioxide (PCO_2), partial pressure of oxygen (PO_2) and oxygen saturation using a blood analyzer (GEM Premier 4000, Bedford, MA, USA). Double clamping of the umbilical cord was performed by a trained midwife between the first and third minutes of the newborn life, with a minimum distance between both clamps of 10 centimeters. For the extraction of blood, pre-heparinized 1mL syringe was used. The gas analysis was carried out at the time of extraction at room temperature[132].

Randomization

Initially, this study was based on a randomized control trial design that was finally modified because of some difficulties related to the recruitment of overweight-obese pregnant women, and the complexity to maintain women in the control group avoiding high rates of drop out. Women were allocated either to exercise or control group depending on their personal preference and convenience to attend the intervention sessions, and the wave they had been recruited for. These methodological and ethical barriers are frequent in antenatal exercise research[133].

Intervention

Exercise group

Pregnant women into the exercise group participated in a concurrent-training program from the 17th week of pregnancy to the day of delivery (3 days/week, and 60 minutes/session) consisting in a combination of aerobic and resistance exercises of moderate-to-vigorous intensity. This exercise protocol was designed following the ACOG guidelines[134]. The exercise group started with three informative and movement learning sessions. In this way, fundamental basic movement patterns were taught (hip dominant, knee dominant, pull and push movements), and theoretical explanations were provided to the participants. Subsequently, the main exercise training phase lasted from week 18th of pregnancy to week 34th and focused in 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 sessions of the week consisted of 40 min of exercises organized in two resistance circuit 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 exercises and myofascial relief[135]. The attendance to the training sessions was recorded. In addition, the research team gave 7 lectures to the participants during this period with the purpose of providing the women with basic pregnancy health-related information. The exercise program was designed by an expert multidisciplinary team in the field and according to the latest Guidelines in pregnancy[8].

Control group

The participants in the control group did not participate in the exercise sessions, and they were requested to continue with their daily activities. Because of ethical considerations, we also invited women in the control group to these 7 lectures. We also used these meetings to maintain their fidelity until the end of the programme.

Statistical analyses

The statistical approach undertaken to accomplish the aims of the present International Doctoral Thesis is presented below and is summarized in **Table 5**.

We employed descriptive statistics [mean (standard deviation, SD)] for quantitative variables and number of cases and percentage (%) for categorical variables to describe the baseline characteristics of the study sample. All the variables were checked for normality of distribution before the analyses. The statistical analyses were performed with SPSS (IBM SPSS Statistics for Windows, version 20.0; Armonk, NY, USA) and the statistical significance was set at α=0.05.

Study I: the quantitative variable "maternal age" was dichotomized above and below the median (33 years old). The prevalence of compliance with PA recommendations for each categorical variable was assessed through Pearson's chi-squared test. The individual association of the dichotomized dependent variable "meeting/not meeting PA guidelines" with clinical and sociodemographic characteristics of the sample were analysed using binary logistic regressions (Model 1). Sociodemographic and clinical factors were introduced simultaneously in the multiple logistic regression to explore their independent association with meeting PA recommendations (Model 2). Both models were adjusted for accelerometer wear time.

Study II: the association of ST and PA levels with birth-related maternal markers was assessed with partial correlations after adjusting for maternal age, parity, BMI and accelerometer wearing time. The associations of ST and PA levels with duration of first and second stages of labour and neonatal markers were additionally adjusted for epidural analgesia, except for the variable “birth weight” which was only further adjusted for gestational age. Since some variables (food intake, gestational age at birth, birth weight, onset of labour and instrumental delivery) previously showed slight relations with the study variables, we performed secondary analysis to assess their effect as confounders. An analysis of the covariance (ANCOVA) after adjustment for the above mentioned potential confounders (maternal age, parity, BMI and accelerometer wearing time) was employed to explore the differences in ST and PA levels between women who had vaginal deliveries (eutocics and instrumentals) versus caesarean section.

Additionally, standardized effect size statistics were estimated in all the comparisons through Cohen’s *d* and its exact confidence interval. The exact confidence intervals (CI) for Cohen’s d were obtained by means of the non-centrality parameter of the non-central Student’s distribution using Wolfram-Mathematica 8.0. The effect size was interpreted as small (~0.25), medium (~0.5) or large (~0.8 or greater). Finally, such as in the GESTAFIT project, a concurrent physical exercise program was carried out, we have also adjusted all the models for the exercise intervention (control or intervention).

Study III: the association of PF levels with maternal and neonatal outcomes was assessed with partial correlations after adjusting for maternal age, parity and BMI. The associations of PF levels with duration of first and second labour stages, as well as neonatal birth outcomes were also adjusted for epidural analgesia, except for the variable “birth weight” which was only further adjusted for gestational age. Since some variables (gestational age at birth, birth weight, duration of first and second stages of labour, and instrumental delivery) previously showed slight relationship with the study variables, we performed secondary analyses to assess their role as potential confounders.

Changes between pre (16th week) and post (34th week) exercise intervention results of fitness tests were analysed via related measures T-Test. The change (post–pre-value) of cardiorespiratory fitness results (Bruce test) was calculated. Subsequently, the change (post–pre) was included in the linear regression analyses as a dependent variable in separate models, whereas the birth outcomes were included as an independent variable. Depending on the model, the analysis was adjusted for any confounders, for baseline value of cardiorespiratory fitness, and adjusted for baseline value, age, parity, weight change (post – pre) and exercise intervention. The variables showing the duration of first and second labour stages, as well as neonatal birth outcomes were additionally adjusted for epidural analgesia, except for the variable "birth weight" which was only further adjusted for gestational age.

An ANCOVA was employed to explore the differences in PF levels between women who had vaginal deliveries (eutocic and instrumentals) versus caesarean section. We adjusted for the above mentioned potential confounders and additionally adjusted for the place of birth (public or private hospital) [136]. Finally, such as in the GESTAFIT project [137], a concurrent physical exercise program was performed, we have also adjusted all the models for the exercise intervention (control or intervention). Furthermore, standardized effect size statistics were estimated in all the comparisons through Cohen's d and its exact CI. The effect size was interpreted as small (~0.2), medium (~0.5), or large (~0.8 or greater) [138].

We created a clustered overall PF (Z-score) as the mean of the standardized scores [(value – mean)/ standard deviation] of body strength (mean of upper and lower- body strength standardized values), flexibility and CRF at 16 weeks of pregnancy and 34 weeks of pregnancy. Both clustered groups were compared by ANCOVA analysis. We adjusted the analysis for maternal age, parity, maternal BMI at 16th gestational week, exercise intervention and birth place (public or private hospital).

Study IV: The association of self-reported PF with birth outcomes was assessed with partial correlations after adjusting for maternal age, parity, BMI and exercise intervention. The associations of PF levels with duration of first and second labour stages, as well as neonatal birth outcomes were additionally adjusted for epidural analgesia, except for the variable “birth weight” which was only further adjusted for gestational age. Since some variables (adherence to the Mediterranean Diet, gestational age at birth, birth weight, onset of labour, and instrumental delivery) previously showed slight relationship with the study variables, we performed secondary analyses to assess their role as potential confounders.

An analysis of the covariance (ANCOVA) was employed to explore the differences in self-reported PF levels between women who were administered versus women who were not administered oxytocin during labour, and it was adjusted for maternal age, parity, BMI, epidural analgesia and birth place (public or private hospital). Elective caesarean sections (elected because of feet or buttocks coming first, n=6) were excluded from the present analyses. We also adjusted all the models for the exercise intervention. Furthermore, standardized effect size statistics were estimated in all the comparisons through Cohen’s *d* and its exact CI.

Study V: Descriptive statistics for continuous and categorical variables were performed to show the sociodemographic and clinical characteristics. To detect potential differences on these outcomes between the groups, the following statistical tests were performed independent sample Student's t-test for continuous variables and the Chi-square test for categorical variables. As initially designed[137], the statistical analysis was conducted on per-protocol basis. Only women who attended at least 75% the exercise sessions were included in the per-protocol analyses. Subsequently, linear regression analyses were used to analyze the differences in maternal and neonatal birth outcomes between the control and exercise group. Birth outcomes were included in the regressions as dependent variables, and the group (control or exercise) as independent variable. After considering relevant confounders suggested by previous literature, Model 1 was adjusted for age, parity, maternal BMI and epidural analgesia (except for placenta weight). Duration of first and second stages of labour was additionally adjusted for oxytocin administration. Birth weight was adjusted for gestational age instead of epidural analgesia. Model 2 was further adjusted for sedentary time, total physical activity and maximal oxygen consumption at 16th gestational weeks. Duration of first and second stages of labour was additionally adjusted for birth weight. In this model, placental weight was adjusted for age, parity, maternal BMI, ST, total PA and muscular strength at 16th weeks of pregnancy. Birth weight was adjusted for smoking status and muscular strength at 16th gestational weeks and maximal oxygen consumption.

Since important variables according to the literature showed a weak or no relationship with the outcomes, these variables were only tested as additional confounders in secondary sensitive analyses (data not shown).

Table 5. Summary table of statistical approach of each study of the present International Doctoral Thesis.

Study	Design	Independent variables	Dependent Variables	Statistical analyses
I	Cross-sectional	Age BMI Marital status Educational level Working status Parity Previous miscarriages	Compliance with PA guidelines	- Pearson's chi-squared test and binary logistic regressions. *Confounders: age, BMI, marital status, educational level, Working status, parity, previous miscarriages and accelerometer wear time.*
II	Longitudinal	Physical activity levels and sedentary time	Maternal and neonatal birth outcomes. Delivery type	-Pearson´s partial correlations and ANCOVA. *Confounders: age, parity, BMI, accelerometer wearing time, epidural analgesia, gestational age, exercise intervention.*
III	Longitudinal	Objectively-measured physical fitness Change (post–pre-value) of cardiorespiratory fitness results	Maternal and neonatal birth outcomes. Delivery type	- Pearson´s partial correlations. -Linear regression analysis with changes (post-pre values of physical fitness variables) as dependent variables (baseline values as confounders). - ANCOVA (of physical fitness tests and clustered overall physical fitness)

				Confounders: age, parity, BMI, epidural analgesia, gestational age, baseline value of cardiorespiratory fitness, age, parity, weight change (post – pre), exercise intervention, birth place.
IV	Longitudinal	Self-reported physical fitness	Maternal and neonatal birth outcomes. Oxytocin administration	-Pearson´s partial correlations and ANCOVA. *Confounders: age, parity, BMI, epidural analgesia, gestational age, exercise intervention, birth place.*
V	Experimental (Randomized Control Trial)	Intervention (control or exercise)	Maternal and neonatal birth outcomes.	- Linear regression analyses *Confounders: age, parity, maternal BMI and epidural analgesia, oxytocin administration, gestational age, sedentary time, total physical activity and maximal oxygen consumption at 16th gestational weeks, smoking status, muscular strength at 16th gestational weeks.*

BMI, Body mass index; ANCOVA, analysis of the covariance.

RESULTS

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

Study I. Objectively-measured sedentary time and physical activity levels in Spanish pregnant women. Factors affecting the compliance with physical activity guidelines. The GESTAFIT Project.

Laura Baena-García, Pedro Acosta-Manzano, Olga Ocón-Hernández, Milkana Borges-Cosic, Lidia Romero-Gallardo, Nuria Marín-Jiménez, V. A. Aparicio. *Submitted to Women & Health.*

The final sample size was composed of 134 Caucasian pregnant women (mean age 33±4.5 years old, BMI: 25±4.1kg/m^2) who had completed valid data for this study. The flow chart of the study participants is shown in **Figure 2**.

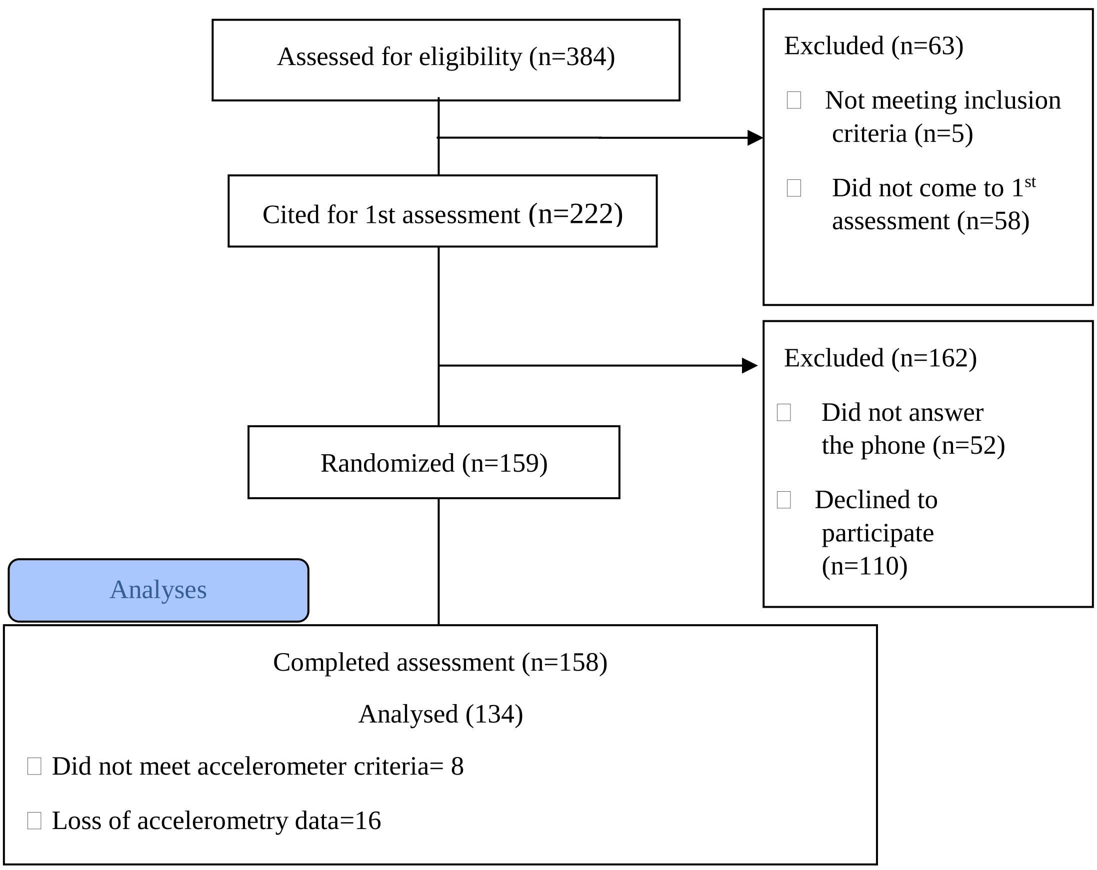

Figure 2. Flowchart of the participants for the specific study I aims.

The sociodemographic and clinical characteristics of the study participants are shown in **Table 6**. Sixty percent of the participants had University degree and most of the sample (70%) worked outside their residence. Around 60% of the women did not have previous births. Women spent ~512 minutes daily in sedentary behaviors, and 85 minutes per week in MVPA (in bouts of at least 10 minutes). They walked on average 7436 steps per day. Only 21.6% of the participants met PA guidelines for pregnancy.

The proportion of women meeting PA guidelines by age groups, BMI, marital, educational and working status, parity and previous miscarriages is shown in **Table 7.** Compliance with PA guidelines was higher in women with University degree and primiparous women (both, $p<0.01$).

The association of sociodemographic and clinical factors during early second trimester of pregnancy potentially affecting meeting PA guidelines is shown in **Table 8.** Having University degree was related with threefold higher odds of meeting PA guidelines in both models (95% confidence interval: 1.354-11 and 1.096-10.428, respectively, both $p<0.05$). Being multiparous was associated to fivefold lower odds of meeting PA guidelines in both models (95% confidence interval 0.091-0.643, and 0.055, 0.605, respectively, both $p<0.01$). Maternal age, BMI, marital and working status and previous miscarriages were not associated with PA guidelines compliance for both models (all, $p>0.05$).

Table 6. Sociodemographic and clinical characteristics of the study I participants (n=134)

Variable	Mean (SD)
Age, years	33 (4.5)
Body mass index at 16th gestational week, Kg/m^2, n (%)	25 (4.1)
Underweight	2 (1.5)
Normal	74 (55.3)
Overweight	41 (30.3)
Obese	17 (12.9)
Married, n (%)	78 (58.2)
Educational status, n (%)	
Below University degree	54 (40.3)
University degree	80 (59.7)
Working outside their residence, n (%)	94 (70.1)
Parity, n (%)	57 (47.2)
Primiparous	79 (59)
Multiparous	55 (41)
Previous miscarriages, n (%)	53 (39.6)
Objectively measured physical activity	
Sedentary time, min/day	512.1 (92.1)
Total PA, min/day	425.2 (892.1)
†*MVPA, min/wk*	84.6 (108.2)
Steps per day	7436 (2410)
Meeting PA guidelines, n (%)	29 (21.6)
Smoker during pregnancy, n (%)	11 (8.2)

Values shown as mean (SD, standard deviation) unless otherwise indicated; min, minute; wk, week; PA, physical activity; †MVPA, moderate-to-vigorous physical activity (in bouts of at least 10 minutes), BMI, body mass index, underweight BMI<18 Kg/m^2; normal weight BMI=18.5-24.9 Kg/m^2; overweight BMI=25-29.9 Kg/m^2; Obese BMI≥30 Kg/m^2

Table 7. Prevalence of pregnant women meeting physical activity guidelines during early second trimester of pregnancy (n=134)

	N (%)	**Pregnant women meeting PA guidelines Frequency**	***P***
Age groups (years)			
21-33	75 (48.3)	14	0.346
34-43	59 (51.7)	15	
Body mass index (kg/m2)			
≤24.9	76 (67.9)	19	0.184
>24,9	58 (32.1)	9	
Marital Status			
Married	78 (18.3)	14	0.222
Single	56 (51.7)	15	
Educational Level			
Below University degree	54 (17.2)	5	**0.004****
University degree	80 (82.8)	24	
Working status			
At home	40 (24.1)	7	0.488
Away from home	94 (75.9)	22	
Parity			
Primiparous	78 (79.3)	23	**0.009****
Multiparous	56 (20.7)	6	
Previuos miscarriages			
No	81 (65.5)	19	0.528
Yes	53 (34.5)	10	

PA guidelines (at least 150 minutes per week of moderate-to-vigorous-intensity physical activity in bouts of at least 10 minutes). BMI, Body mass index; CI, Confidence interval. **$p<0.01$

Table 8. Binary logistic regressions showing the association between sociodemographic and clinical factors with meeting physical activity guidelines (≥150min/week of bouted MVPA) during early second trimester of pregnancy by age group, body mass index, marital status, educational level, working status, parity and previous miscarriages (n=134).

	Model 1			**Model 2**		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***
Age groups (years)						
21-33	Ref.			Ref.		
34-43	1.293	(0.552, 3.303)	0.554	2.07	(0.749, 5.722)	0.161
Body mass index (kg/m2)						
≤24.9	Ref.			Ref.		
>24,9	0.598	(0.245, 1.470)	0.259	0.719	(0.271, 1.905)	0.507
Marital Status						
Married	Ref.			Ref.		
Single	1.330	(0.874, 2.024)	0.184	1.461	(0.889, 2.402)	0.135
Educational Level						
Below University degree	Ref.			Ref.		
University degree	3.859	(1.354, 11)	**0.012***	3.380	(1.096, 10.428)	**0.034***
Working status						
At home	Ref.			Ref.		
Away from home	1.166	(0.433, 3.132)	0.761	0.587	(0.186, 1.855)	0.364
Parity						
Primiparous	Ref.			Ref.		
Multiparous	0.248	(0.091, 0.673)	**0.006****	0.183	(0.055, 0.605)	**0.005****
Previuos miscarriages						
No	Ref.			Ref.		
Yes	0.823	(0.344, 1.996))	0.661	0.784	(0.287, 2.147)	0.636

Model 1 adjusted for accelerometer wear time. Model 2, independent association of meeting PA recommendations adjusted for accelerometer wear time. Ref., reference group. *p<0.05; **p<0.01

Study II. Association of sedentary time and physical activity during pregnancy with maternal and neonatal birth outcomes. The GESTAFIT Project

Laura Baena-García, Olga Ocón-Hernández, Pedro Acosta-Manzano, Irene Coll-Risco, Milkana Borges-Cosic, Lidia Romero-Gallardo, Marta de la Flor-Alemany, Virginia A. Aparicio. Scand J Med Sci Sports. 2019 Mar;29(3):407-414. doi: 10.1111/sms.13337. Epub 2018 Dec 17.

From all the participants who met the eligibility criteria, 161 were cited for the first assessment and 94 Caucasian pregnant women (mean age 32.9±4.6 years old, BMI 24.9 ±4.1kg/m^2) accepted to participate and presented valid data for the present analyses. The flowchart of the participants for this specific study aims is shown in **Figure 3**.

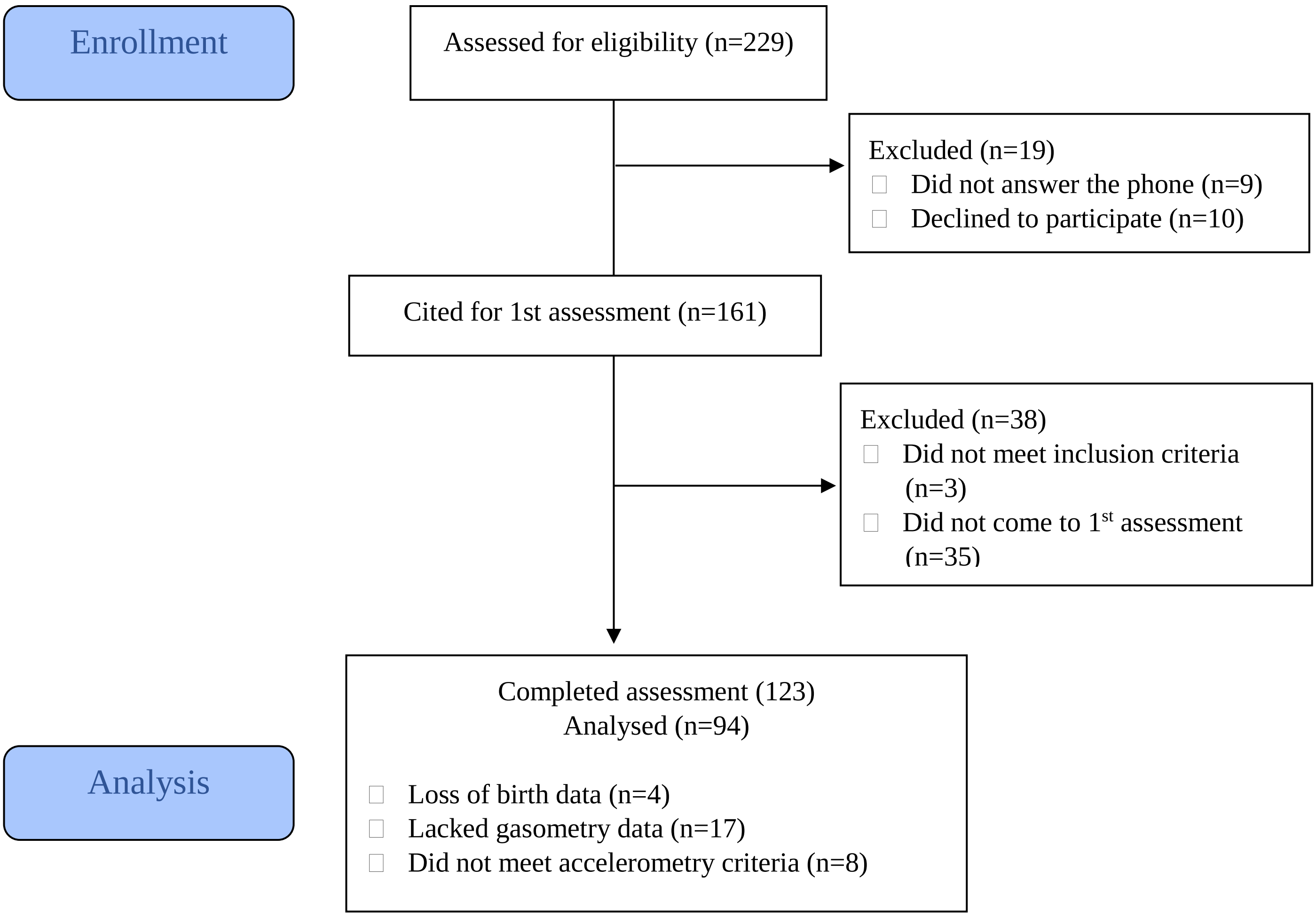

Figure 3. Flowchart of the participants for the specific study II aims.

The sociodemographic and clinical characteristics of the study participants are shown in **Table 9**. Fifty-four percent of the participants had University studies and half of the sample worked full-time (47%). Regarding the type of delivery, 61% of the women had eutocic deliveries, 15% had instrumental deliveries and 24% had caesarean section. The deliveries took place around 39.7±1.2 week of gestation, with a mean neonate body weight at birth of 3310±468.3 grams. Mean Apgar test score at the first minute of life was 8.7±0.9. Participants expend around 3598±682.4 minutes per week in sedentary time, and 95±115.2 minutes per week in MVPA in bouts of at least 10 minutes ¿at 16th weeks of gestation?

Pearson´s partial correlations of ST and PA levels during early pregnancy with labour-related maternal and neonatal markers are shown in **Table 10**. After adjusting for maternal age, parity, BMI, accelerometer wearing time and the exercise intervention, ST was associated with a more acidic cord blood arterial (r=-0.262, p<0.05) and venous (r=-0.267, p<0.05) pH and higher arterial (r=0.335, p<0.01) and venous (r=0-.299, p<0.01) partial pressure of carbon dioxide.
Higher levels of light PA were associated with less acidic venous cord blood pH concentrations (r=0.251, p<0.05). Moderate and bouted MVPA (in bout of at least 10 minutes) were positively associated with arterial oxygen saturation (r=0.251, p<0.05 and r=0.266, p<0.05, respectively). Moderate PA was also associated with greater oxygen saturation in the umbilical artery (r=0.251, p<0.05). Vigorous PA levels were inversely associated with the Apgar test at first minute (r=-0.365, p<0.01), and at five minutes (r=-0.342, p<0.01) of life. Greater total PA was associated with higher arterial cord blood oxygen saturation (r=0.263, p<0.05) and with less acidic venous cord blood pH (r=0.264, p<0.05). Finally, steps per day were associated with lower length of the first stage of labour (r=-0.274, p<0.05), lower neonate body weight (r=-0.208, p<0.05) and greater cord blood arterial oxygen saturation (r=0.318, p<0.05).

Differences on ST and PA levels of the study participants by delivery mode (vaginal or cesarean section) are shown in **Table 11**. A borderline significant difference was observed in ST between women who had cesarean sections and those who had vaginal deliveries (mean difference with 95%CI, *p*=0.091 for the unadjusted model and *p*=0.112 for the adjusted model; Cohen´s *d*=0.39). Women who had cesarean sections spent less minutes on PA than those with vaginal deliveries, regardless of the intensity level: light PA (mean difference with 95% CI *p*=0.088 for the unadjusted model and *p*=0.223 for the adjusted model, Cohen´s *d*=0.29), Moderate PA (mean difference with 95% CI *p*=0.695 for the unadjusted mode and *p*=0.605 for the adjusted model, Cohen´s *d*=0.12), vigorous PA (mean difference with 95% CI *p*=0.046 for unadjusted model and *p*=0.269 for the adjusted model, , Cohen´s *d*=0.26) and MVPA (mean difference with 95% CI *p*=0.489 for the unadjusted model and *p*=0.315 for the adjusted model, Cohen´s *d*=0.24). In addition, women who had caesarean section had less weekly total PA than those who had a vaginal delivery (mean difference with 95% CI *p=0*.073 for the unadjusted model and *p*=0.189 for the adjusted model, Cohen´s *d*=0.31) and less steps per day than those who had a vaginal delivery (mean difference with 95% CI *p*=0.180 for the unadjusted model and *p*=0.199 for the adjusted model, *p*=0.180, Cohen´s *d*=0.31).

Table 9. Sociodemographic and clinical characteristic of the study II participants (n=94)

Maternal outcomes	**Mean ± SD**
Age, years	32.9±4.6
Body mass index at 16th gestational week, Kg/m^2	24.9±4.1
Living with a partner, n (%)	92 (97.9%)
Educational status, n (%)	
Primary or high-school	26 (27.7%)
Professional training	17 (18%)
University studies	51 (54.3%)
Working status, n (%)	
Homework/unemployed	26 (27.6%)
Partial-time employed/student	24 (25.6%)
Full-time employed	44 (46.8%)
Type of delivery, n (%)	
Spontaneous	57 (60.6%)
Instrumental vacuum/forceps	14 (14.9%)
Caesarean	23 (24.5%)
Epidural analgesia, n (%)	67 (62%)
Parity, n (%)	
Nulliparous	58 (61.7%)
Multiparous	36 (38.3%)
Sedentary time and PA, min/week	
Sedentary time	3598±682.4
Light PA	2733±631.2
Moderate PA	255±148.4
Vigorous PA	8±21.5
*Moderate-to-vigorous PA**	95±115.2
Total PA	2997±653.2
Steps per day, mean (SD)	7745±2559.6
Meeting PA guidelines, n (%)	25 (26.6%)
Smoker during pregnancy, n (%)	8 (8.5%)
Neonatal outcomes	
Sex (female, n (%))	47 (50%)
Gestational age at birth, wk	39.7±1.2
Birth weight, grams	3310±468.3
Apgar Test 1 minute	8.7±0.9
Apgar Test 5 minutes	9.6±0.7
Umbilical Cord blood Gas	
Arterial pH	7.2±0.7

Arterial Partial Pressure CO_2, mmHg	50.4±9.9
Arterial Partial Pressure O_2, mmHg	19.7±8.8
Arterial O_2 saturation, %	36.7±22.4
Venous pH	7.3±0.6
Venous Partial Pressure CO_2, mmHg	39.2±7.3
Venous Partial Pressure O_2, mmHg	25.7±7.2
Venous O_2 saturation, %	56.1±17

Values shown as mean ± SD, standard deviation, unless otherwise indicated; CO_2, carbon dioxide; O_2, oxygen *accounted in bouts of at least 10 minutes; min, minute; wk, week; PA, physical activity.

Table 10. Partial correlations of sedentary time and physical activity levels with birth-related maternal and neonatal markers (n=94).

	Sedentary time	**Light PA**	**Moderate PA**	**Vigorous PA**	**MVPA**	**Total PA**	**Steps per day**
Birth outcomes							
Week of gestation (at birth) (n=88)	.120	-.140	-.125	.127	-.105	-.156	**-.286****
Duration of first stage of labour[a] (n=57)	.019	-.134	-.179	-.060	-.191	-.176	**-.264***
Duration of second stage of labour[a] (n=60)	-.123	.105	.066	-.041	.063	.114	.185
Newborn-related outcomes[a]							
Birth weight (n=87)	-.039	.011	-.102	-.168	-.126	-.017	-.089
Apgar Test 1 minute (n=87)	-.018	.027	.034	**-.363****	-.022	.021	.039
Apgar Test 5 minutes (n=87)	-.095	.061	-.034	**-.350****	-.086	.039	-.020
Cord blood arterial pH (n=67)	**-.317****	.240	-.021	.040	-.011	.228	.030
Cord blood arterial partial pressure of CO_2 (n=60)	**.350****	-.204	-.069	-.008	-.073	-.211	-.066
Cord blood arterial partial pressure of O_2 (n=56)	-.171	.197	.174	-.015	.174	.226	.220
Cord blood arterial oxygen saturation (n=59)	-.235	.219	**.252***	.117	**.262***	**.270***	**.307***
Cord blood venous pH (n=80)	**-.334****	**.286****	.092	-.008	.096	**.295****	.168
Cord blood venous partial pressure of CO_2 (n=79)	**.321****	-.192	-.089	.108	-.079	-.201	-.071
Cord blood venous partial pressure of O_2 (n=69)	-.070	.042	.064	-.189	.045	.051	.001

CO_2, Carbon dioxide; O_2, Oxygen; PA, physical activity. Model adjusted for age, parity, maternal body mass index, accelerometer wearing time and exercise intervention. [a] Model additionally adjusted for epidural analgesia. Birth weight was further adjusted for gestational age. *P<0.05; **P<0.01.

Table 11. Differences in sedentary time and physical activity levels (min/week) of the pregnant women by delivery mode (vaginal or caesarean section).

	Vaginal (n=71)	**Caesarean (n=23)**	**P**	**P***	**Effect size *d*-Cohen**
Sedentary time (min/day)	503.3 (11.5)	542.2 (20.1)	0.091	0.112	0.39 (-0.01, 0.79)
Light physical activity (min/wk)	2800.0 (72.6)	2617.1 (127.0)	0.088	0.223	0.29 (-0.10, 0.69)
Moderate physical activity (min/wk)	255.4 (16.4)	237.8 (28.8)	0.695	0.605	0.12 (-0.27, 0.52)
Vigorous physical activity (min/wk)	9.13 (2.5)	3.47 (4.3)	0.046	0.269	0.26 (-0.13, 0.66)
Moderate-to-vigorous physical activity ¥ (min/wk)	99.5 (12.0)	74.6 (21.0)	0.489	0.315	0.24 (-0.15, 0.64)
Total physical activity (min/wk)	3064 (75.8)	2858 (132.8)	0.073	0.189	0.31 (-0.08, 0.71)
Steps per day (number)	7865 (285.7)	7105 (500.2)	0.180	0.199	0.31 (-0.09, 0.71)

*Model adjusted for maternal age, parity, maternal body mass index, accelerometer wearing time and the exercise intervention; Values shown as mean (standard error); ¥, in bouts of at least 10 minutes.

Study III. Association of objectively measured physical fitness during pregnancy with maternal and neonatal birth outcomes. The GESTAFIT Project

Laura Baena-García, Irene Coll-Risco, Olga Ocón-Hernández, Lidia Romero-Gallardo, Pedro Acosta-Manzano, Virginia.A. Aparicio. *Submitted to PloS ONE.*

From all the participants who met the eligibility criteria and accepted to participate, 159 completed the first assessment. Of the 159 women that finally participated in this study, 158 had complete sociodemographic data. The final sample size was composed of 158 Caucasian pregnant women (age 32.9±4.6 years old, BMI 24.9±4.1 kg/m2) who presented valid data for the present analyses. Specifically, at 16 and 34 weeks of pregnancy 156 and 124 women, respectively, participated in the physical fitness tests (**Figure 4**). A total of 18 partograms were not found in the informatics system, or could not be collected due to some births occurred in another city, hence, a total of 141 women had completed valid data for birth outcomes.

Results

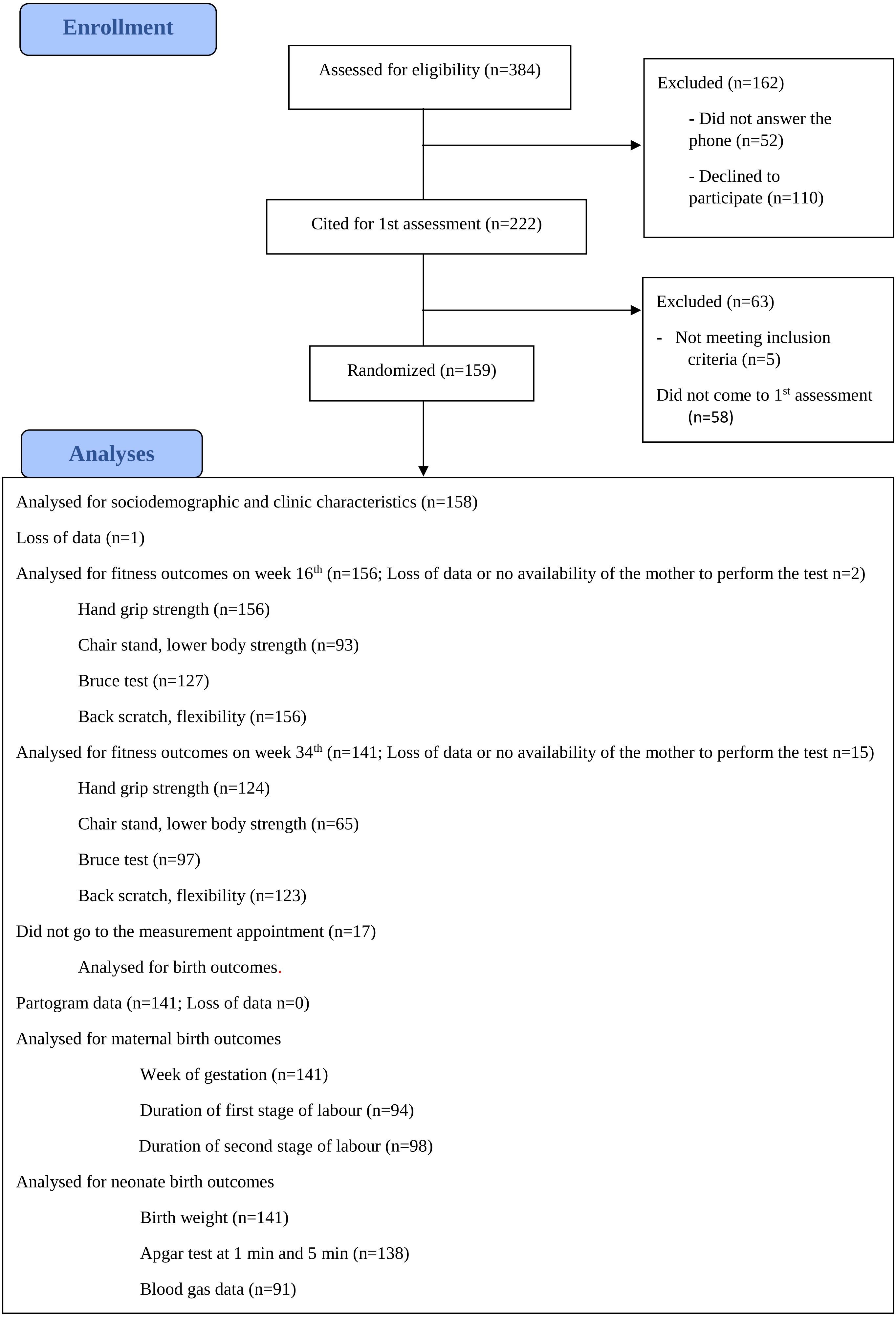
Enrollment
Assessed for eligibility (n=384)
Excluded (n=162)
- Did not answer the phone (n=52)
- Declined to participate (n=110)
Cited for 1st assessment (n=222)
Excluded (n=63)
- Not meeting inclusion criteria (n=5)
Did not come to 1st assessment (n=58)
Randomized (n=159)
Analyses
Analysed for sociodemographic and clinic characteristics (n=158)
Loss of data (n=1)
Analysed for fitness outcomes on week 16th (n=156; Loss of data or no availability of the mother to perform the test n=2)
Hand grip strength (n=156)
Chair stand, lower body strength (n=93)
Bruce test (n=127)
Back scratch, flexibility (n=156)
Analysed for fitness outcomes on week 34th (n=141; Loss of data or no availability of the mother to perform the test n=15)
Hand grip strength (n=124)
Chair stand, lower body strength (n=65)
Bruce test (n=97)
Back scratch, flexibility (n=123)
Did not go to the measurement appointment (n=17)
Analysed for birth outcomes.
Partogram data (n=141; Loss of data n=0)
Analysed for maternal birth outcomes
Week of gestation (n=141)
Duration of first stage of labour (n=94)
Duration of second stage of labour (n=98)
Analysed for neonate birth outcomes
Birth weight (n=141)
Apgar test at 1 min and 5 min (n=138)
Blood gas data (n=91)

Figure 4. Flowchart of the participants for the specific study III aims.

The sociodemographic and clinical characteristics of the study participants are shown in **Table 12**. Most of the participants lived with their partner and more than a half had University degrees and worked full time. Approximately 61% of the sample was nulliparous and 75.6% had vaginal births. Births took place around 39.5±1.3 weeks of gestation, with a mean neonate body weight of 3305±480.6 grams. At 16th and 34th gestational weeks respectively, mean values were similar in upper-body strength (Hand grip); lower-body strength (Chair stand); and 4.1±6.2 cm and 3.9±6 cm in flexibility test (Back scratch), but decreased for cardiorespiratory fitness 22.1±5.5 mL/Kg/min and 17.9±4.9 mL/Kg/min (Bruce). All umbilical cord blood gas mean values were within normal ranges.

Pearson´s partial correlations of physical fitness levels at 16th and 34t^{h} gestational weeks with maternal and neonatal birth outcomes are shown in **Table 13**. Regarding the maternal birth outcomes, physical fitness levels were not associated with these measures at 16th or 34th weeks of gestation. In relation to neonatal birth outcomes, upper-body muscle strength at 16 weeks of gestation was associated with greater birth weight (r=0.191, p<0.05). Lower-body muscle strength was not associated with any maternal and neonatal birth outcome (p>0.05). Greater maternal flexibility at 16th gestational week was associated with a more alkaline pH (r=0.220, p<0.05), higher PO2 (r=0.237, p<0.05), higher arterial oxygen saturation (r=0.242, p<0.05), and lower PCO2 (r=-0.331, p<0.01) in arterial umbilical cord blood. Maternal CRF at 16th weeks was related to higher PO2 (r=0.267, p<0.05) and higher oxygen saturation (r=0.375, p<0.01) in arterial umbilical cord blood. Physical fitness levels at 34 weeks of pregnancy were not associated with any maternal and neonatal birth outcomes (all, p >0.05).

Comparing the fitness levels at 16th and 34th weeks of gestation (**Table 14**) showed no differences in flexibility, upper or lower body strength between the different time-points.

CRF decreased in 4.14 (5.07) mL/(kg*min) from 16 to 34 weeks of gestation (95% CI: 3.014, 5.272; p<0.001).

The associations of the changes in CRF with birth outcomes are shown in **Table 15**. Arterial cord blood PO2 and O2 saturation were inversely associated with the CRF change (B=-0.603; 95% CI: -1.101, -0.105; p=0.019, and B=-1.544; 95% CI: -2.720, -0.368; p=0.011, respectively), with similar results in the model adjusted for baseline CRF, age, parity, weight change and exercise intervention. Model adjusted only for baseline values of CRF showed an inverse association between CRF change and arterial cord blood PO2 (B=-0.622; 95% CI: -1.221, -0.023; p=0.042).

Differences on physical fitness levels at 16^{th} and 34^{th} gestational weeks of the study participants by delivery type (vaginal or caesarean section) are shown in **Table 16**. Regarding 16^{th} week of pregnancy, no significant differences were found on upper and lower-body muscle strength between women who had vaginal deliveries compared to women who had caesarean sections (both, p>0.05). The mean of flexibility levels was +2.4 (4.7) cm in back scratch test in women who had caesarean sections compared to +5.0 (6.2) cm in women who had vaginal births, (p=0.004 for the unadjusted model and p=0.027 for the adjusted model, Cohen´s d=0.44, 95% CI: 0.1, 0.8).

Finally, women who had caesarean sections had a mean of CRF of 18.4 (4.2) ml/kg/min in Bruce test compared to women who had a vaginal delivery, who had 23.3 (5.7) ml/kg/min in CRF (p<0.001, for the unadjusted and p=0.001 for the adjusted model; Cohen´s d=0.90; 95% CI: 0.5, 1.3). In relation to physical fitness at 34^{th} weeks of gestation, flexibility was higher in women who had vaginal births with 4.9 (6.0) cm, than in women with caesarean section, 1.0 (5.8) cm (p=0.005 for the unadjusted model and p=0.033 for the adjusted model, Cohen´s d=0.65; 95% CI: 0.3, 1.0).

Figure 5A and **Figure 5B** show the clustered overall physical fitness at 16th and 34th weeks of gestation, respectively. Relative to women who had vaginal deliveries, women who had caesarean sections presented worse clustered overall physical fitness at 16th (mean difference -0.227, p=0.003; 95% CI: -0.376, -0.078) and at 34th weeks gestation (mean difference -0.223, p=0.018; 95% CI: -0.432, -0.015). Results were similar when elective caesarean sections (elected because of feet or buttocks coming first) were excluded from the analysis.

Table 12. Sociodemographic and clinical characteristic of the study III participants (n=158)

Maternal outcomes	**n**	**Mean (SD)**
Age, years	158	32.9 (4.6)
Body mass index at 16th gestational week, Kg/m^2	158	24.9 (4.1)
Body mass index at 34th gestational week, Kg/m^2	158	27.8 (4.1)
Weight at 16th gestational week, Kg	157	67.04 (11.8)
Weight at 34th gestational week, Kg	123	74.57 (10.8)
Weight change (from 16th to 34th gestational weeks)	121	8.7 (3.4)
		n (%)
Living with a partner,		154 (97.5)
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)
Type of delivery	143	
Spontaneous		83 (58)
Instrumental vacuum/forceps		24 (16.8)
Caesarean section		36 (25.5)
Planned (feet or buttocks coming first)		7 (27.5)
Birth place	147	
Public Hospital		138 (93.9)
Private Hospital		8 (5.4)
Home		1 (0.7)
Parity	158	
Nulliparous		96 (60.8)
Multiparous		62 (39.2)
Physical fitness 16 gestational week		**Mean (SD)**
Upper-body strength (Hand grip), mean (Kg)	156	27.2 (4.2)
Lower-body strength (Chair stand), number of repetitions	93	15.7 (2.4)
Flexibility (Back scratch), mean (cm)	156	4.1 (6.2)
CRF (Bruce), VO_{2max}	127	22.2 (5.5)
Physical fitness at 34th gestational week		

Upper-body strength (Hand grip), mean (Kg)	124	27.2 (4.4)
Lower-body strength (Chair stand), number of repetitions	65	15.9 (2.5)
Flexibility (Back scratch), mean (cm)	123	3.9 (6)
CRF (Bruce), VO_{2max}	97	17.9 (4.9)
Neonatal outcomes		
Sex (female, n (%))	141	72 (51.4)
Gestational age at birth, wk	141	39.5 (1.3)
Birth weight, grams	141	3305 (480.6)
Placental weight, grams	106	573.7 (102.6)
Apgar Test 1 minute	138	8.6 (1)
Apgar Test 5 minutes	138	9.6 (0.7)
Umbilical Cord blood Gas		
Arterial pH	103	7.2 (0.07)
Arterial Partial Pressure CO_2, mmHg	97	51.1 (10.3)
Arterial Partial Pressure O_2, mmHg	92	19.8 (8.9)
Arterial O_2 saturation, %	90	35.6 (21.8)
Venous pH	117	7.3 (0.1)
Venous Partial Pressure CO_2, mmHg	112	39.7 (7.7)
Venous Partial Pressure O_2, mmHg	102	26.3 (9.2)
Venous O_2 saturation, %	97	54.9 (18.4)

Values shown as mean (SD, standard deviation) unless otherwise indicated; BMI, body mass index; CRF, cardiorespiratory fitness; CO_2, carbon dioxide; O_2, oxygen.

Table 13. Partial correlations of physical fitness levels at 16th and 34th weeks of gestation with maternal and neonatal birth outcomes

Maternal outcomes		Upper-body muscle strength	Lower-body muscle strength	Flexibility	Cardiorespiratory fitness
Week of gestation (at birth)	16 g.w.	.008 (n=122)	.163 (n=66)	-.035 (n=121)	.072 (n=98)
	34 g.w.	.052 (n=103)	.040 (n=49)	-.034 (n=102)	-.086 (n=76)
Duration of first stage of labour [a]	16 g.w.	.200 (n=81)	.136 (n=42)	-.037 (n=81)	-.120 (n=66)
	34 g.w.	.132 (n=65)	.085 (n=28)	.023 (n=64)	-.046 (n=46)
Duration of second stage of labour [a]	16 g.w.	-.149 (n=84)	-.011 (n=45)	-.015 (n=84)	-.095 (n=69)
	34 g.w.	-.097 (n=70)	-.166 (n=32)	-.008 (n=69)	.016 (n=50)
Birth outcomes [a]					
Birth weight	16 g.w.	**.191*** (n=122)	.090 (n=66)	.050 (n=121)	-.077 (n=98)
	34 g.w.	.139 (n=103)	-.059 (n=49)	.103 (n=102)	-.076 (n=76)
Apgar Test 1 minute	16 g.w.	-.077 (n=113)	.090 (n=57)	-.033 (n=112)	.084 (n=91)
	34 g.w.	-.114 (n=96)	-.019 (n=43)	-.072 (n=95)	-.093 (n=73)
Apgar Test 5 minutes	16 g.w.	.009 (n=113)	-.095 (n=57)	.081 (n=112)	.096 (n=91)
	34 g.w.	-.038 (n=96)	-.008 (n=43)	.043 (n=95)	-.061 (n=73)
Cord blood arterial pH	16 g.w.	-.048 (n=83)	.175 (n=42)	**.220*** (n=82)	.084 (n=65)
	34 g.w.	.095 (n=70)	-.115 (n=31)	.113 (n=69)	.079 (n=54)
Cord blood arterial PCO_2	16 g.w.	-.056 (n=78)	-.103 (n=37)	**-301****(n=77)	-.140 (n=60)
	34 g.w.	-.096 (n=66)	.260 (n=28)	-.220 (n=65)	-.070 (n=52)
Cord blood arterial PO_2	16 g.w.	.104 (n=74)	-.091 (n=38)	**.237*** (n=73)	**.267*** (n=60)
	34 g.w.	.016 (n=62)	-.188 (n=29)	.162 (n=62)	-.182 (n=48)
Cord blood arterial O_2 saturation	16 g.w.	.015 (n=72)	-.066 (n=36)	**.242*** (n=71)	**.372****(n=57)
	34 g.w.	.016 (n=61)	-.265 (n=27)	.162 (n=60)	-.014 (n=47)
Cord blood venous pH	16 g.w.	.089 (n=95)	.110 (n=47)	.144 (n=94)	.062 (n=76)
	34 g.w.	.204 (n=81)	.099 (n=36)	.102 (n=80)	.041 (n=63)

Cord blood venous PCO_2	16 g.w.	-.113 (n=91)	-.058 (n=43)	-.0158 (n=90)	-.036 (n=72)
	34 g.w.	-.189 (n=78)	-.154 (n=34)	-.030 (n=77)	.013 (n=62)
Cord blood venous PO_2	16 g.w.	-.015 (n=83)	.056 (n=41)	.129 (n=82)	-.018 (n=65)
	34 g.w.	.032 (n=69)	.167 (n=32)	.086 (n=68)	-.160 (n=53)
Cord blood venous O_2 saturation	16 g.w.	.129 (n=73)	.185 (n=38)	.123 (n=77)	0.15 (n=62)
	34 g.w.	.030 (n=70)	.221 (n=29)	.032 (n=65)	-.116 (n=52)

O_2, Oxygen; PO_2, partial pressure of oxygen; PCO_2, partial pressure of carbon dioxide; g.w, gestational week. Model adjusted for age, parity, maternal body mass index, gestational week, and the exercise intervention. Maternal birth outcomes were additionally adjusted for birth weight. [a] Model additionally adjusted for epidural analgesia. Birth weight was further adjusted for gestational age. $^{*}p<0.05$; $^{**}p<0.01$.

Table 14. Maternal physical fitness change from 16th to 34th gestational week

	Mean change in physical fitness (SD)	95% CI	*p*
Flexibility (Back-scratch test), cm	-0.398 (2.68)	(-0.883, -0.086)	0.106
Upper-body muscle strength (Hand-grip test), Kg	-0.261 (2.96)	(-0.793, 0.270)	0.333
Lower-body muscle strength (Chair-stand test), rep	-0.169 (2.51)	(-0.791, 0.453)	0.589
Cardiorespiratory fitness (Bruce test), mL/(kg·min)	-4.14 (5.07)	(-5.272, -3.014)	**<0.001**

SD, standard deviation; CI, Confidence Interval

Table 15. Associations of changes in Cardiorespiratory fitness from 16th to 34th weeks of gestation with birth outcomes

	Unadjusted model			**Model 1**			**Model 2**		
Maternal outcomes	B	95% CI	p	B	95% CI	p	B	95% CI	p
Week of gestation (at birth)	-0.029	(39.26, 39.90)	0.235	-0.049	(-0.111, 0.012)	0.113	-0.068	(-0.137, 0.001)	0.052
Duration of first stage of labour [a]	4.018	(-5.35, 13.38)	0.393	1.545	(-11.35, 14.44)	0.811	3.826	(-5.741, 13.393)	0.423
Duration of second stage of labour [a]	2.270	(-1.44, 5.98)	0.226	2.787	(-1.811, 7.385)	0.230	0.894	(-3.116, 4.904)	0.656
Neonatal outcomes									
Birth weight	5.607	(-13.35, 24.56)	0.557	0.861	(-22.82, 21.54)	0.942	20.176	(-4.763, 45.115)	0.111
Apgar Test 1 minute [a]	-0.026	(-0.69, 0.17)	0.236	-0.038	(-0.092, 0.017)	0.172	-0.027	(-0.086, 0.033)	0.373
Apgar Test 5 minutes [a]	-0.008	(-0.43, 0.27)	0.654	-0.015	(-0.058, 0.029)	0.502	-0.006	(-0.054, 0.043)	0.818
Cord blood arterial pH [a]	0.001	(-0.004, 0.005)	0.773	0.001	(-0.004, 0.006)	0.789	-0.001	(-0.007, 0.005)	0.673
Cord blood arterial PCO_2 [a]	0.130	(-0.449, 0.710)	0.653	0.152	(-0.538, 0.842)	0.661	0.208	(-0.628, 1.044)	0.619
Cord blood arterial PO_2 [a]	-0.603	(-1.101, -0.105)	0.019	-0.622	(-1.221, -0.023)	**0.042***	-0.960	(-1.659, -0.260)	**0.009****
Cord blood arterial O_2 saturation [a]	-1.544	(-2.720, -0.368)	**0.011***	-1.249	(-2.665, 0.167)	0.082	-2.428	(-3.907, -0.650)	**0.007****
Cord blood venous pH [a]	0.001	(0.002, 0.004)	0.536	0.001	(0.003, 0.005)	0.602	0.000	(-0.005, 0.004)	0.905
Cord blood venous PCO_2 [a]	-0.680	(-0.417, 0.282)	0.699	-0.024	(-0.481, 0.433)	0.917	0.095	(-0.426, 0.616)	0.717
Cord blood venous PO_2 [a]	0.154	(-0.266, 0.575)	0.465	-0.071	(-0.632, 0.491)	0.802	0.202	(-0.837, 0.432)	0.523
Cord blood venous O_2 saturation [a]	0.104	(-0.732, 0.940)	0.803	-0.350	(-1.507, 0.806)	0.546	-1.081	(-2.363, 0.200)	0.096

Model 1 was adjusted for baseline value of cardiorespiratory fitness; Model 2 was adjusted for baseline value of cardiorespiratory fitness, maternal age, parity, weight change and exercise intervention; maternal birth outcomes were additionally adjusted for birth weight. [a] Model additionally adjusted for epidural analgesia. Birth weight was further adjusted for gestational age.

$^{*}p<0.05$; $^{**}p<0.01$.

Table 16. Differences in physical fitness of the pregnant women at 16th and 34th weeks of gestation by delivery type.

		Vaginal	Caesarean	*p*	*p**	Effect size *d*-Cohen (95% CI)
Upper-body muscle Strength, kg	16 g.w.	27.6 (4.1) n=102	26.8 (3.7) n=30	0.386	0.160	0.20 (-0.1, 0.5)
	34 g.w.	27.6 (3.7) n=91	26.5 (4.3) n=26	0.216	0.119	0.29 (-0.1, 0.7)
Lower-body muscle Strength, kg	16 g.w.	16.1 (2.5) n=59	15.3 (2.1) n=16	0.102	0.208	0.33 (-0.1, 0.8)
	34 g.w.	16 (2.6) n=50	15.5 (2.2) n=9	0.619	0.426	0.20 (-0.3, 0.7)
Flexibility, cm	16 g.w.	5.0 (6.2) n=102	2.4 (4.7) n=29	0.004	**0.027**	0.44 (0.1, 0.8)
	34 g.w.	4.9 (6.0) n=89	1.0 (5.8) n=26	0.005	**0.033**	0.65 (0.3, 1.0)
Cardiorespiratory fitness, VO_{2max}	16 g.w.	23.3 (5.7) n=86	18.4 (4.2) n=22	<0.001	**0.001**	0.90 (0.5, 1.3)
	34 g.w.	18.4 (4.9) n=72	15.7 (4.8) n=20	0.029	0.081	0.57 (0.2, 1.0)

CI, Confidence interval; g.w., gestational week. *Model adjusted for maternal age, parity, maternal body mass index, exercise intervention and birth place. Values shown as mean (standard deviation).

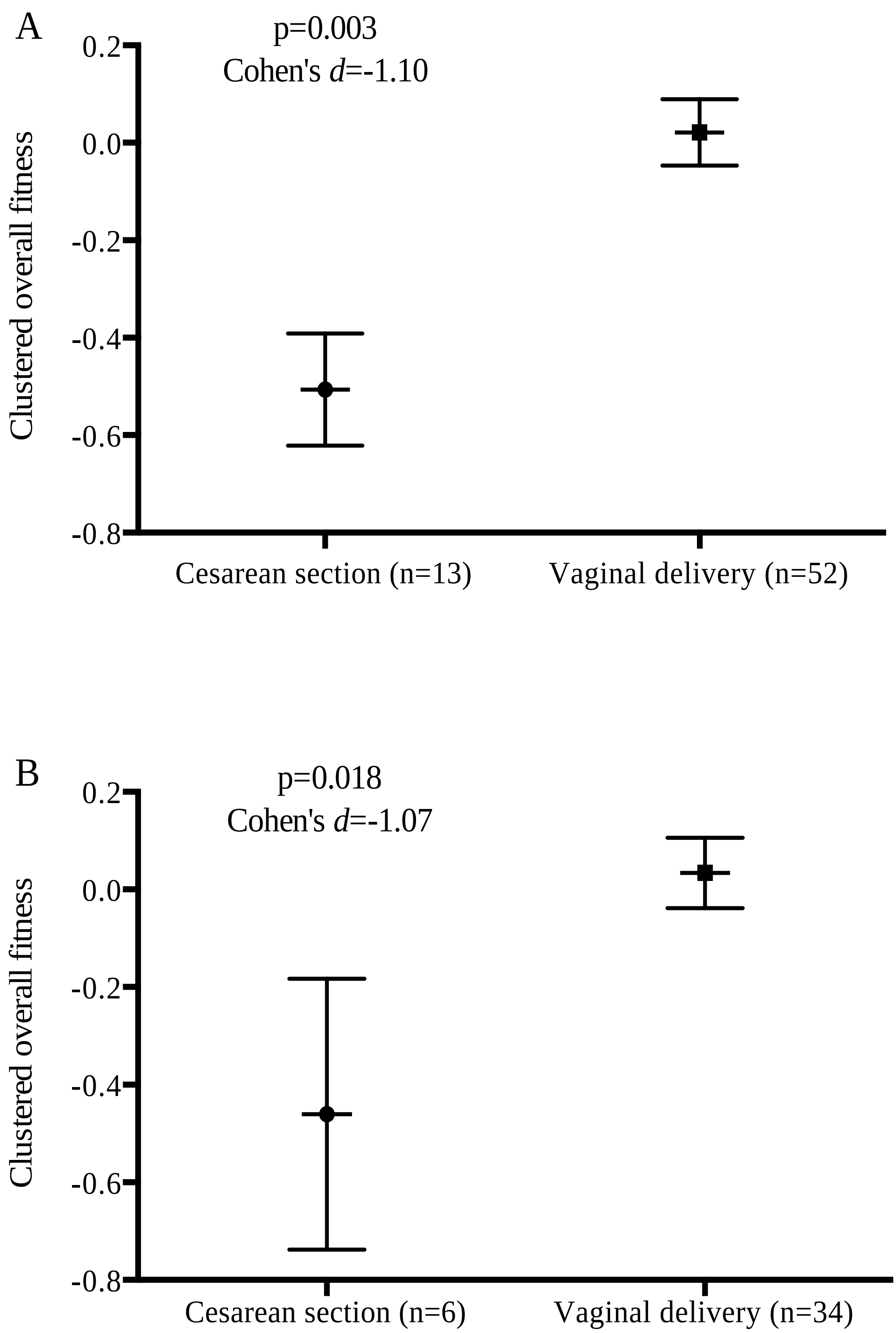

Figure 5. Clustered overall fitness (z-score) at week 16 of pregnancy (Figure A) and at week 34 of pregnancy (Figure B) by caesarean section or vaginal delivery. Dots represent mean and standard deviation. Model adjusted for maternal age, parity, maternal 16th week body mass index, exercise intervention group and birth place.

Study IV. Association of self-reported physical fitness during late pregnancy with birth outcomes and oxytocin administration during labour. The GESTAFIT Project

Laura Baena-García, Nuria Marín-Jiménez, Lidia Romero-Gallardo, Milkana Borges-Cosic, Olga Ocón-Hernández, Eloísa Ramírez-Sánchez de la Blanca, Virginia A. Aparicio. *Submitted to Midwifery*.

From the 159 women who signed the informed consent and met the inclusion criteria, 158 had complete sociodemographic data. The final sample size was composed of 117 Caucasian pregnant women (age 33.1±4.5 years old, BMI 24.6±4.1 kg/m2) who presented valid data for the present analyses (**Figure 6**).

Sociodemographic and clinical data, and self-reported PF components of the study sample are shown in **Table 17**. Most of the participants lived with their partners (98.3%) and more than a half had University degrees (63.2%). Broadly, participants rated their PF levels as "*average*", except for CRF, which was classified as "*poor*", compared to their peers. Regarding delivery outcomes, 77.3% had vaginal births and nearly a quarter had caesarean sections. Around 58% of participants were nulliparous and 27.8% were administered oxytocin before or during the labour. They gave birth around the 40th gestational week and neonates had a birth weight average of 3338±428 grams.

Pearson´s partial correlations of self-reported PF levels at 34th gestational week, with pregnancy and neonatal birth outcomes are shown in **Table 18**. After adjusting for potential confounders, speed-agility showed a significant positive association with arterial and venous cord blood pH (both, p<0.05). Greater overall PF and MS showed some evidence of borderline statistical significance with higher cord blood venous pH (both, $p<0.100$). Nonetheless, flexibility was no associated with any birth outcomes (all, $p>0.05$). Finally, maternal outcomes, birth weight, Apgar test and partial pressure of CO_2, O_2, and oxygen saturation in both umbilical blood vessels, were no associated with any self-reported PF component (all, $p>0.05$).

Differences on self-reported PF levels at 34th gestational week of the study participants by oxytocin administration before or during labour are shown in **Table 19.** Women who were not administered oxytocin showed greater CRF compared to women who needed oxytocin (of 2.73±0.7 versus 2.32±0.8, respectively, $p=0.044$ for the unadjusted model and $p=0.013$ for the adjusted model, Cohen´s $d=0.55$; 95% CI: 0.14, 0.93). Greater flexibility was shown in women who were not given oxytocin compared to women who were given oxytocin (of 3.27±1.1 versus 2.75±0.9, respectively, $p=0.013$ for the unadjusted model and $p=0.040$ for the adjusted model, Cohen´s $d=0.51$; 95% CI: 0.09, 0.89). No significant differences were found in self-reported overall fitness, MS and speed-agility between women who were not administered and those who were administered oxytocin during the labour (all, $p>0.05$).

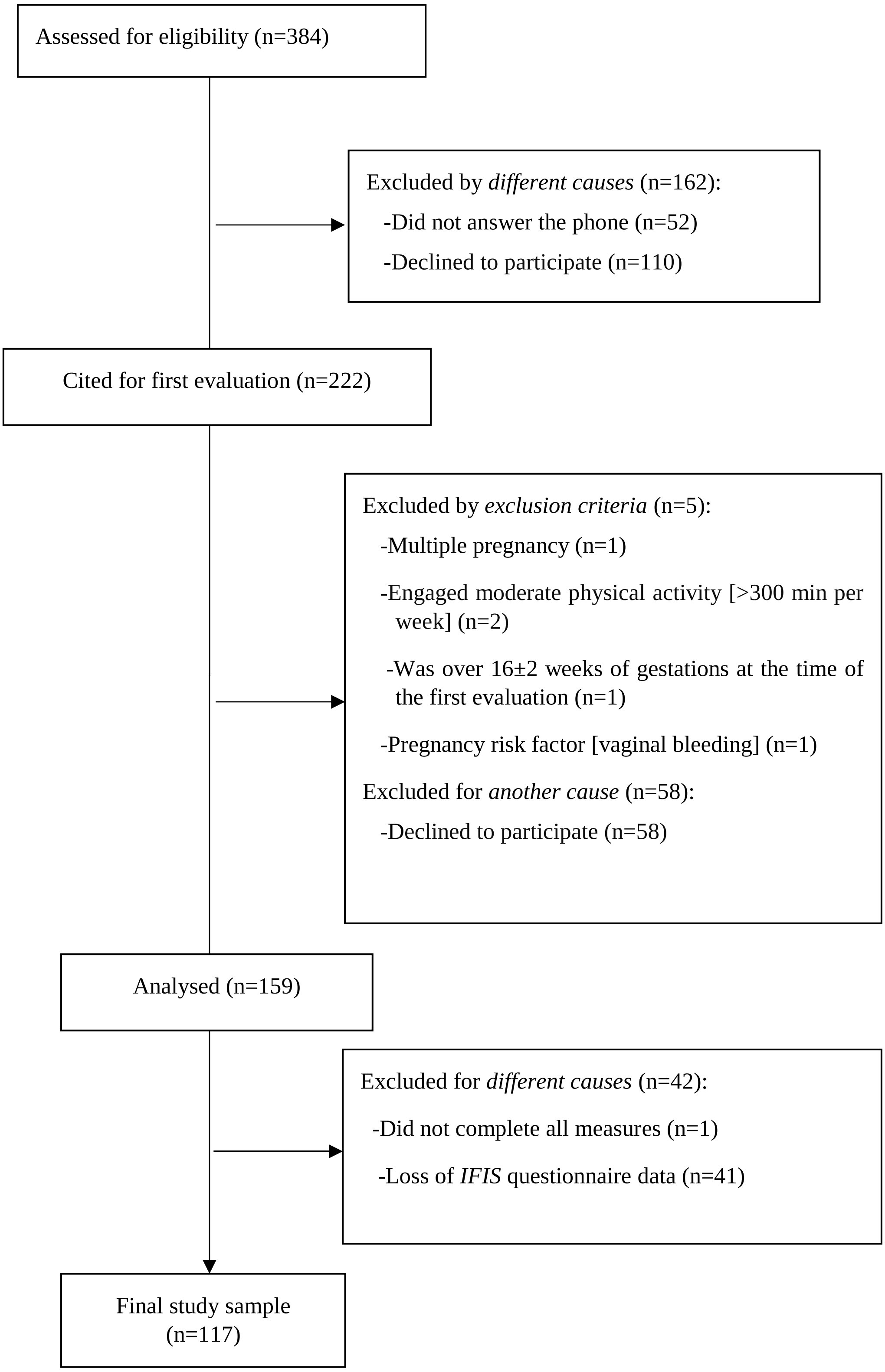

Figure 6. Flowchart of the participants for the specific study IV aims.

Table 17. Sociodemographic and clinical characteristic of the study IV participants (n=117)

Maternal outcomes	**n**	**Mean (SD)**
Age, years	117	33.1 (4.5)
Body mass index at 16th gestational week, Kg/m²	117	24.6 (4.1)
Body mass index at 34th gestational week, Kg/m²		27.8 (4.1)
		n (%)
Living with a partner,		115 (98.3)
Educational status	117	
Primary or high-school		24 (20.6)
Specialized training		19 (16.2)
University degree		74 (63.2)
Working status	117	
Homework/unemployed		34 (29.1)
Partial-time employed/student		34 (29.1)
Full-time employed		49 (41.8)
Self-reported Physical Fitness (0-5)		
34th gestational week	117	
Overall physical fitness		3.3 (0.7)
Cardiorespiratory fitness		2.6 (0.8)
Muscular strength		3.3 (0.7)
Speed-agility		3.0 (0.7)
Flexibility		3.1 (1.0)
Type of delivery	110	
Spontaneous		65 (59.1)
Instrumental vacuum/forceps		20 (18.2)
Caesarean section		25 (22.7)
Oxytocin administered during labour, n %		30 (27.8)
Birth place	115	
Public Hospital		108 (93.9)
Private Hospital		6 (5.2)

Home		1 (0.9)
Parity	117	
Nulliparous		68 (58.1)
Multiparous		49 (41.9)
Neonatal outcomes	110	
Sex (female, n (%))		55 (50)
Gestational age at birth, wk		39.5 (1.2)
Birth weight, grams		3338.5 (428.7)
Apgar Test 1 minute		8.6 (1.1)
Apgar Test 5 minutes		9.6 (0.7)
Umbilical Cord blood Gas		
Arterial pH	80	7.2 (0.07)
Arterial Partial Pressure CO_2, mmHg	75	51.6 (10.7)
Arterial Partial Pressure O_2, mmHg	72	19.5 (9.4)
Arterial O_2 saturation, %	69	34.6 (22.8)
Venous pH	93	7.3 (0.1)
Venous Partial Pressure CO_2, mmHg	89	39.7 (7.7)
Venous Partial Pressure O_2, mmHg	80	26.2 (8.5)
Venous O_2 saturation, %	77	54.7 (18.0)

Values shown as mean (SD, standard deviation) unless otherwise indicated; BMI, body mass index; CO_2, carbon dioxide; O_2, oxygen.

Table 18. Partial correlations of self-reported physical fitness levels at 34[th] gestational week with materna and neonatal birth outcomes

	Overall Fitness	Cardiorespiratory Fitness	Muscular strength	Speed-agility	Flexibility
Maternal outcomes					
Week of gestation (at birth) (n=101)	.018	.083	.087	.070	.014
Duration of first stage of labour [a] (n=63)	-.014	-.063	.013	.061	.085
Duration of second stage of labour [a] (n=69)	-.021	-.069	-.040	.103	.152
Neonatal outcomes [a]					
Birth weight (n=101)	-.009	-.112	.053	.070	.003
Apgar Test 1 minute (n=95)	.101	.075	-.072	.034	-.048
Apgar Test 5 minutes (n=95)	-.081	-.042	.002	-.107	-.177
Cord blood arterial pH (n=69)	.109	.056	.154	**.232***	-.017
Cord blood arterial partial pressure of CO_2 (n=65)	-.044	.005	-.094	-.165	0.049
Cord blood arterial partial pressure of O_2 (n=62)	-.006	-.156	.042	-.020	-.102
Cord blood arterial oxygen saturation (n=59)	-.051	-.110	.045	-.023	-.130
Cord blood venous pH (n=81)	.207	.091	.214	**.239***	-.028
Cord blood venous partial pressure of CO_2 (n=78)	-.074	.024	-.183	-.130	.040

Cord blood venous partial pressure of O_2 (n=69)	.094	-.062	.130	.133	.034
Cord blood venous O_2 saturation (n=66)	.127	.011	.108	.033	.109

O_2, Oxygen; PO_2, partial pressure of oxygen; PCO_2, partial pressure of carbon dioxide. Model adjusted for age, parity, maternal body mass index, gestational week, and the exercise intervention. Maternal birth outcomes were additionally adjusted for birth weight. [a] Model additionally adjusted for epidural analgesia. Birth weight was further adjusted for gestational age. [*]$p<0.05$.

Table 19. Differences in self-reported physical fitness of the pregnant women at 34th gestational week by oxytocin administration before or during labour.

	Oxytocin was not administered (n=78)	Oxytocin was administered (n=30)	P	P*	Effect size *d*-Cohen (95% CI)
Overall fitness	3.38 (0.8)	3.25 (0.7)	0.067	0.348	0.16 (-0.22,0.55)
Cardiorespiratory fitness	2.73 (0.7)	2.32 (0.8)	**0.044**	**0.013**	0.55 (0.14, 0.93)
Muscular strength	3.27 (0.7)	3.29 (0.7)	0.966	0.982	-0.014 (-0.37, 0.35)
Speed-agility	2.95 (0.7)	2.96 (0.6)	0.967	0.728	0.0 (-0.51, 0.37)
Flexibility	3.27 (1.1)	2.75 (0.9)	**0.013**	**0.040**	0.51 (0.09, 0.89)

CI, Confidence interval. *Model adjusted for maternal age, parity, maternal body mass index, exercise intervention, birth place and epidural analgesia. Values shown as mean (standard deviation)

Study V. Influence of a concurrent exercise training intervention during pregnancy on maternal and neonatal birth outcomes. The GESTAFIT Project

Laura Baena-García, Milkana Borges-Cosic, Irene Coll-Risco, Lidia Romero-Gallardo, Pedro Acosta-Manzano, Olga Ocón-Hernández, Marta de la Flor-Alemany, Nuria Marín-Jiménez, Virginia A. Aparicio. *In progress.*

From all the initially interested participants (n=384), the final study sample included in the per-protocol analyses (>75% of attendance) was comprised of 135 pregnant women who were divided into control (n=86), (age 33.1±4.8 years old, BMI 24.8±4.1 kg/m^2), and exercise group (n=50), (age 33.1±4.1 years old, BMI 24.7±4.1 kg/m^2). The flow chart of the *Study V* participants is shown in **Figure 7**.

The sociodemographic and clinical characteristics of pregnant women are shown in **Table 20.** Roughly, almost all women lived with their partners and more than half had a University degree. Almost 30% of births in the control group occurred by caesarean section compared to 18.8% of caesarean sections in the exercise group. No differences were found in the baselines data between the control and exercise groups (all, $p>0.05$).

The effects of the concurrent exercise intervention on maternal and neonatal birth outcomes are shown in **Table 21.** In the unadjusted model, no significant differences were found between groups in maternal and neonatal birth outcomes (all, $p>0.05$). In the regression analyses of Model 1, the differences for duration of first stage of labour became non-significant, but showed evidence ¿close to? statistical significance ($p=0.06$). In the model 2, the exercise group increased 80.8 minutes the duration of first stage of labour (95% CI, 5.313 to 156.313 $p=0.037$) and decreased 29.1 minutes the duration of second stage of labour (95% CI, -55.71 to -2.573 $p=0.032$). Finally, the exercise group was associated with greater placental weight (53.32 grams, 9.99 to 96.66, $p=0.017$) and greater birth weight (167.41 grams, 14.189 to 320.64, $p=0.033$) as compared with the control group.

The effects of the concurrent exercise intervention on delivery type are shown in **Table 22.** Non-statistically significant differences were found in relation to the type of delivery between the control group and the exercise group, neither in the unadjusted model nor after adjusting for potential confounders (both, $p>0.05$).

CONSORT
TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram

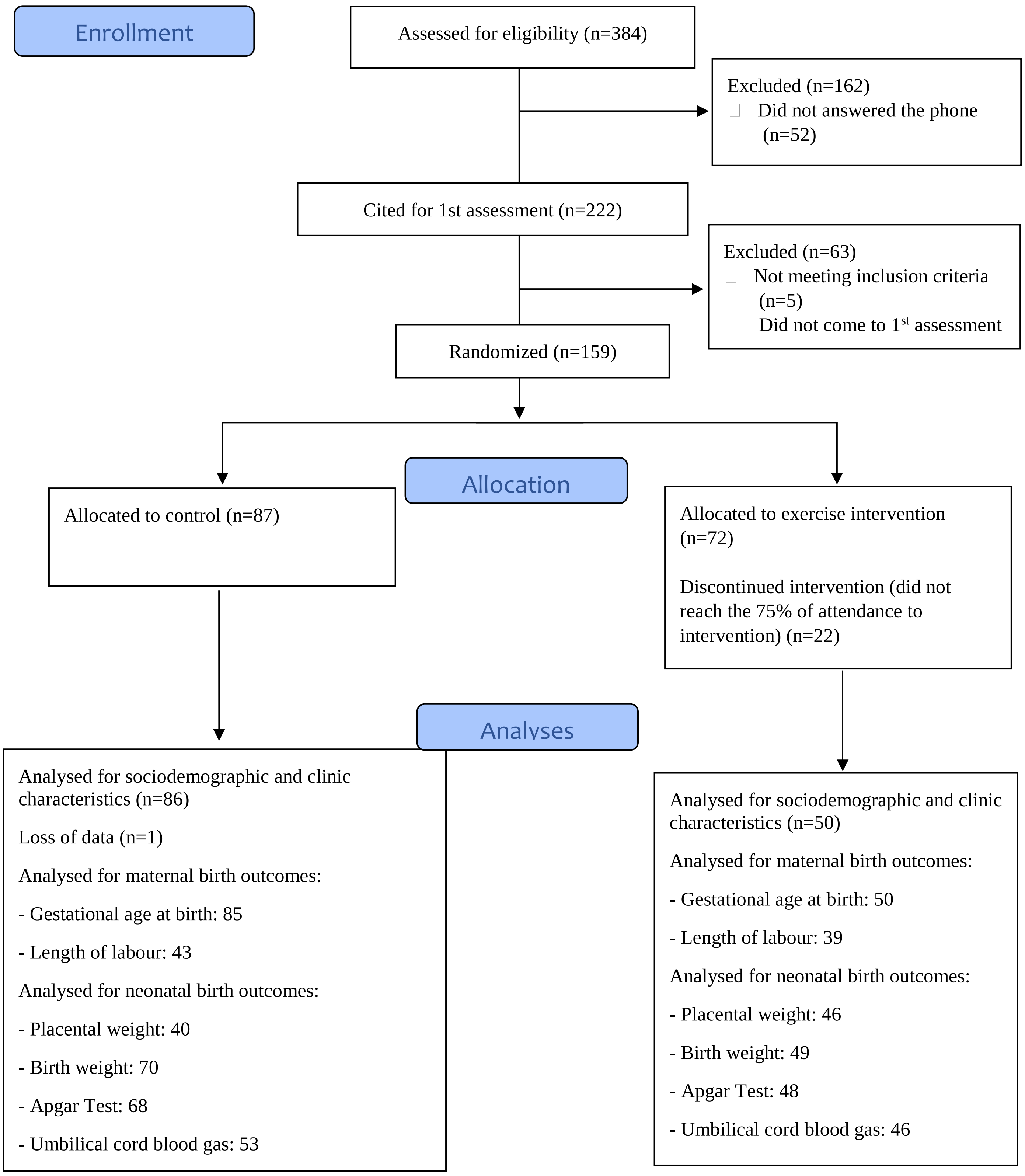

Figure 7. Flowchart of the participants for the specific study V aims.

Table 20. Sociodemographic and clinical characteristics of the study IV participants (n=135)

Maternal outcomes	**Counselling group (n=86)**	**Exercise Group (n=50)**	**p-value**
Age, years	33.3 (4.8)	33.1 (4.1)	0.837
Body mass index at 16 gestational week, Kg/m^2	24.8 (4.1)	24.7 (4.1)	0.926
CRF (Bruce), VO_{2max} at 16 gestational week, mL/(kg·min)	21.4 (5.1)	22.7 (5.8)	0.21
Sedentary time at 16 gestational week, min/day	498.07 (101)	532.3 (84.6)	0.056
Total physical activity at 16 gestational week, min/day	432.05 (94.2)	417.21 (86.3)	0.359
Living with a partner, n %	84 (96.6%)	50 (100%)	0.277
Educational status, n %			0.973
Primary or high-school	19 (22.1%)	9 (18%)	
Specialized training	14 (16.3%)	9 (18%)	
University degree	53 (61.6%)	94 (64%)	
Type of delivery, n %			0.375
Eutocic	41 (57.7%)	29 (60.4%)	
Instrumental vacuum/forceps	9 (12.7%)	24 (16.8)	
Caesarean section	21 (29.6%)	9 (18.8%)	
Caesarean section due to suspected loss of fetal well-being	8 (40%)	0 (0%)	
Birth place, n %			0.632
Public Hospital	71 (94.7%)	47 (94%)	
Private Hospital	3 (4%)	3 (6%)	
Home	1 (1.3%)	0 (0%)	
Parity, n %			0.194
Nulliparous	50 (58.8%)	35 (70%)	
Multiparous	35 (41.2%)	15 (30%)	
Epidural analgesia during labour, n %	41 (61.2%)	35 (74.5%)	0.161
Oxytocin administration during labour, n %	20 (32.3%)	14 (29.2%)	0.728
Duration of first stage of labour	202.21 (137.2)	241.9 (172.4)	0.261
Duration of second stage of labour	94.1 (69.2)	93 (65.4)	0.939
Neonatal outcomes			
Sex (female), n %	36 (41.4%)	24 (48%)	0.879
Gestational age at birth, wk	39.4 (1.5)	39.7 (1.1)	0.220
Birth weight, grams	3218.9 (545.9)	3375.5 (378.9)	0.084
Placental weight	550.74 (84.3)	590.26 (110.9)	0.065

Apgar Test 1 minute	8.5 (1.1)	8.6 (0.9)	0.720
Apgar Test 5 minutes	9.5 (0.7)	9.7 (0.6)	0.402
Umbilical Cord blood Gas			
Arterial pH	7.2 (0.08)	7.2 (0.06)	0.169
Arterial Partial Pressure CO_2, mmHg	52.4 (11.1)	51.7 (9.6)	0.760
Arterial Partial Pressure O_2, mmHg	19.9 (8.7)	19.9 (8.4)	0.307
Arterial O_2 saturation, %	39.9 (21.8)	32.7 (21.1)	0.811
Venous pH	7.3 (0.08)	7.3 (0.06)	0.788
Venous Partial Pressure CO_2, mmHg	39.5 (8.1)	38.5 (6.7)	0.529
Venous Partial Pressure O_2, mmHg	27.1 (9.8)	25.1 (7.2)	0.298
Venous O_2 saturation, %	54.8 (19.4)	57.1 (16.7)	0.576

Values shown as mean (SD, standard deviation) unless otherwise indicated; BMI, body mass index; CRF, cardiorespiratory fitness; CO_2, carbon dioxide; O_2, oxygen.

Table 21. Per-protocol analyses showing the effect of the concurrent exercise program on maternal and neonatal birth outcomes (n=135)

	Mean difference (SE)	**Unadjusted model**					**Model 1**					**Model 2**				
		β	B	95% CI		*P*	*β*	B	95% CI		*P*	*β*	B	95% CI		*P*
Maternal outcomes																
Week of gestation at birth	-.312 (0.239)	.113	.312	-.189	.813	0.220	.052	.139	-.376	.654	0.594	.058	.135	-.397	.667	0.615
Duration of first stage of labour[a]	-39.73 (35.69)	.129	39.73	-30.132	109.593	0.261	.185	54.994	-2.949	112.936	0.062	.250	80.853	5.313	156.313	**0.037**
Duration of second stage of labour[a]	1.140 (14.87)	-.009	-1.14	-30.823	28.544	0.939	-.104	-13.595	-38.373	11.183	0.227	-.226	-29.172	-55.771	-2.573	**0.032**
Neonatal outcomes																
Placental weight	-39.52 (21.1)	.197	39.52	-3.239	82.286	0.065	.213	41.633	-1.118	84.384	0.056	.286	53.328	9.99	96.667	**0.017**
Birth weight	-157.22 (90.23)	.159	157.224	-21.477	335.926	0.084	.129	127.972	-23.381	279.324	0.097	.168	167.414	14.189	320.64	**0.033**
Apgar test 1 minute	-0.072 (0.194)	.034	.072	-.326	.471	0.720	.044	.098	-.336	.532	0.656	.020	.039	-.421	.500	0.865
Apgar test 5 minutes	-0.114 (0.131)	.079	.114	-.155	.383	0.402	.069	.100	-.182	.382	0.483	.126	.199	-.166	.564	0.280
Cord blood arterial pH	0.023 (0.016)	-.150	-.023	-.057	.01	0.169	-.130	-.021	-.056	.015	0.254	-.154	-.023	-.064	.017	0.258
Cord blood arterial PCO_2	0.726 (2.329)	-.035	-.727	-5.453	4.0	0.760	-.016	-.346	-5.436	4.744	0.893	-.045	-.938	-6.989	5.114	0.756
Cod blood arterial PO_2	2.03 (1.97)	-.119	-2.03	-5.963	1.903	0.307	-.156	-2.702	-6.950	1.545	0.208	-.095	-1.756	-7.489	3.976	0.539

Cord blood arterial O_2 saturation	1.195 (4.951)	-.028	-1.196	-11.1	8.709	0.811	-.050	-2.127	-12.697	8.443	0.689	-.028	-1.199	-13.587	11.189	0.846
Cord blood venous pH	-0.004 (0.015)	.027	.004	-.026	.035	0.788	.024	.004	-.027	.034	0.817	-.003	.00	-.033	.032	0.978
Cord blood venous PCO_2	0.974 (1.529)	-.066	-.975	-4.037	2.087	0.529	-.009	-.136	-3.353	3.081	0.933	.055	.752	-2.925	4.429	0.683
Cord blood venous O_2	1.962 (1.872)	-.114	-1.963	-5.687	1.762	0.298	-.134	-1.947	-5.311	1.418	0.253	-.205	-3.146	-7.622	1.330	0.164
Cord blood venous O_2 saturation	-2.240 (3.995)	.062	2.241	-5.709	10.191	0.576	.023	.800	-7.339	8.938	0.845	-.025	-.879	-11.017	9.259	0.862

SE, standard error; Results show mean difference between counselling and exercise groups regarding maternal and neonatal birth outcomes (standard error). O_2, Oxygen; PO_2, partial pressure of oxygen; PCO_2, partial pressure of carbon dioxide. Model 1 was adjusted for age, parity, maternal body mass index and epidural analgesia. [a] Additionally adjusted for oxytocin administration. Birth weight was adjusted for gestational age instead of epidural analgesia. Model 2 was further adjusted for sedentary time and total physical activity at 16 gestational weeks. Duration of first and second stages of labour were additionally adjusted for birth weight. Birth weight was adjusted for smoking status and muscular strength at 16 gestational weeks instead of epidural analgesia and maximal oxygen consumption. β, standardized beta. Only women with available data and participants exercise group who attended ≥75% of the exercise sessions were included.

Table 22. Binary logistic regressions showing the association between control and exercise groups with delivery type (vaginal or caesarean section)

	Unadjusted model			Adjusted Model		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***
Groups						
Counselling Group	Ref.			Ref.		
Exercise Group	0.818	(0.337, 1.987)	0.658	0.639	(0.248, 1.648)	0.354

[a] Model adjusted for maternal age, body mass index, parity and birth place. Ref., reference group.

DISCUSSION

DISCUSSION

Summary of the main findings

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

The main results of the present International Doctoral Thesis showed that the compliance with PA guidelines during the early second trimester of pregnancy was low, especially in women without a University degree and those with children (*Study I*). Moreover, greater ST at 16th gestational weeks was associated with a more acidic arterial and venous pH, and vigorous PA was inversely associated with the Apgar score test (*Study II*). Contrary, at 16th gestational weeks, different PA levels *(Study II)* and greater flexibility and CRF *(Study III)* as well as self-reported speed-agility at late pregnancy *(Study IV)* were associated with better values in umbilical cord blood gases. Finally, higher muscular strength at early second trimester of pregnancy was related to greater neonatal birth weight.

Regarding the delivery type, women who had caesarean section showed a borderline significant greater ST and less PA levels at 16th week of pregnancy than women with vaginal deliveries (*Study II*). Nevertheless, women who had caesarean section showed lower CRF at 16th gestational weeks and lower flexibility both, during the early second trimester and late pregnancy, than women who had vaginal births (*Study III*). Finally, women who were administered with oxytocin, to induce or stimulate the labour, showed lower self-reported flexibility and CRF at 34th gestational weeks than women who did not need this drug (*Study IV*).

Experimental study (Study V)

The concurrent exercise training program performed from the 17th gestational week until delivery increased the first stage of labour duration and shortened the second stage. In addition, placental and neonatal weight were greater in the intervention group. In relation to the delivery type, no significant differences were found between the exercise and control group.

Discussion of main findings with previous literature

Study I. Objectively-measured sedentary time and physical activity levels in Spanish pregnant women. Factors affecting the compliance with physical activity guidelines. The GESTAFIT Project.

The main finding of this study indicates that having a University degree and being primiparous seem to significantly increase the odd ratio of compliance with PA guidelines during early second trimester of pregnancy. Moreover, less than 22% of the pregnant women complied with PA guidelines.

Spain is one of the countries with the highest sedentary rates in the European region (27% for men and 33% for women), according to the World Health Survey data on PA[139]. In our study, participants spent on average 8.5 hours per day in sedentary behaviors. This result is consistent with values described by Ruifrok et al.[140], who also objectively measured ST in early pregnant women from The Netherlands. This could have important clinical consequences since increasing ST during pregnancy has been previously associated with higher levels of LDL cholesterol and C-reactive protein and a greater abdominal circumference in the newborn, among others[6]. In this sense, one of the most effective tools to reduce ST is to increase PA. Nevertheless, time spent in MVPA was much lower than recommended[7], since the average time performing this PA level was around 85 minutes per week. This mean is lower than that found in American pregnant women during the same trimester of pregnancy[141], differences which were also previously observed in general adult population[142].

Furthermore, pregnant women included in our study walked 7436 steps per day on average. This number is substantially lower than that described in other studies, in which pregnant women walked an average between 9600[143] and 11000[144] steps per day in this stage of pregnancy. This data may be partially due to cultural differences between Spain and other European countries, as similar data regarding general population[145]. Nevertheless, in both studies the accelerometer was placed around the participants' arms instead of the hips, so the steps could have been overestimated by the movements of the upper body.

The low percentage of women meeting PA guidelines in our sample (22%) was below to that described by Broberg et al.[9], who observed 38% of compliance in their cohort of Danish women, which could be newly explained by cultural differences, as Danish population is physically more active than Spanish population[145]. However, Amezcua et al.[10] carried out a study in a cohort of pregnant women from Granada (the same city area than the present study) and they observed a 20% PA guidelines compliance during 20-22th weeks of pregnancy, which is similar to our rates. To note is that in both studies, the amount and intensity of PA was assessed by self-reported questionnaires, and this methodology may present information and memory bias, which is one reason why questionnaires have shown to be unreliable in the measurement of PA during pregnancy[15,146]. Santos et al.[11] determined the degree of compliance with different international guidelines on PA in a sample of Portuguese pregnant women with the same accelerometer than us (i.e. ActiGraph GT3X+), and concluded that the compliance of the ACOG guidelines was 4%. This huge difference may be explained by to the fact that Portuguese adult population is even a less active population[145,147] than Spanish adult population, but more studies are needed to verify these findings.

Moreover, our findings suggest that having a University degree is associated with meeting PA guidelines during early second trimester of pregnancy, which concurs with other studies performed in pregnant women from Nordic Countries[94] and Spain[96]. It should be noted that a higher educational level has been widely associated with a decrease in health risk habits in the adult population[148], especially regarding physical inactivity[149]. In addition, and in agreement with similar studies, having children seem to decrease the possibilities of meeting PA guidelines[90,96]. In this sense, we hypothesized that it may be due to having less leisure time which would favors more physically active behaviors.

We have not found other associations previously described in the literature in relation to greater PA guidelines compliance regarding age[150], marital status[95], BMI[94], previous miscarriages[9] or working status. On the other hand, it is important that health professionals carry out an adequate counseling of PA importance during pregnancy to improve maternal and fetal health[8]. Indeed, a study conducted in the United Kingdom[151] described that most midwives knew specific contraindications regarding clinical and obstetrics characteristics and PA intensities during pregnancy, but only 2% knew PA guidelines for this period. However, several studies have described that the trend is to decrease PA during gestation[150], so it is necessary to start having adequate levels of PA during the first weeks of pregnancy individualized according to the characteristics of the pregnant women.

Considering that only 22% of the women who participated in the present study met PA guidelines, we may considerate that there is still a long way for behavioural change regarding ST and PA in order to reduce future health problems in both, the mother and the newborn.

Study II. Association of sedentary time and physical activity during pregnancy with maternal and neonatal birth outcomes. The GESTAFIT Project.

As far as we know, this is the first study exploring the association of objectively measured ST and PA intensity levels during early second trimester of pregnancy with birth outcomes. A major finding of the present study is that more ST is associated with a lower pH as well as higher partial pressure of carbon dioxide in both umbilical artery and vein. Likewise, higher levels of total, moderate, MVPA and steps per day are associated with greater umbilical arterial oxygen saturation, and greater total and light PA are related to higher levels of venous cord blood pH. It is also noteworthy that women who had caesarean sections showed a trend to more ST during early second trimester of pregnancy.

We found that greater number of steps per day were associated with shorter duration of the first stage of labour, lower gestational age and better oxygen saturation in the umbilical artery. Avoiding a prolonged duration of the first stage of labour is important, since it has been associated with more obstetric interventions, instrumented deliveries, and caesareans sections[152]. In addition, the shorter time of cervical dilatation might have influenced the better saturation of oxygen in the umbilical artery after delivery, which is a positive sign of foetal well-being, since uterine contractions during labour produce acute restrictions of blood flow from the placenta to the foetus[71]. Findings regarding the associations of steps per day with the labour length cannot be commented with regard to other studies, since it has never been explored in pregnant women. It is possible that women who walked more during second trimester of pregnancy, were more active during late pregnancy too. Hence, since aerobic exercise performed regularly during pregnancy shortens the first phase of labour[58], a plausible explanation could be that PA, which is a similar stimulus to aerobic walking, even at low intensity[153], might influence the shortening of the first stage of labour.

In agreement with our results, Ruifrok et al.[140] observed that objectively measured ST was not associated with gestational age or birth weight. We also observed that greater ST during early second trimester pregnancy was associated with higher arterial partial pressure of carbon dioxide (PCO_2), and more acidic pH in both arterial and venous cord blood. This is a relevant finding because umbilical arterial cord blood gas at birth is a gold standard in the determination of the acid-base balance in the foetus[75]. Consequently, measuring PCO_2 in the umbilical cord blood is useful to identify foetal acidosis[154]. Rate of CO_2 production is proportional to foetal oxygen consumption [155] and the higher cord blood PCO_2 and decrease in pH indicate a state of foetal acidosis[71]. If this acidosis is reflected exclusively in the umbilical artery, it would be a consequence of the own labour, or other acute situations, and usually affects only peripheral tissues[156]. However, venous umbilical cord blood gas indicates the state of the placenta, so that increases of PCO_2 and decreases of pH could be related to a chronic decrease in blood flow, probably from the mother to the placenta[157]. Therefore, our results suggest that higher ST might be related with increased foetal acidosis during delivery, which may be indicative of a worse placental perfusion[101].

Otherwise, in this study, vigorous PA has been associated with a worse score in the Apgar test at one and five minutes of life. Apgar test has been shown to be effective on predicting neonatal morbidity and mortality in term babies with normal birth weight[68]. Low scores in the Apgar test have also been related to dysfunctions in cognitive ability[158]. This finding requires further studies and should be considered by health professionals in the counselling and monitoring of pregnant women.

Results regarding the positive associations found between total and bouted MVPA with neonatal outcomes suggest that the practice of total PA or MVPA may have beneficial influence on the newborn. Currently, more studies are needed to explore which specific maternal factors, including sedentary behaviours and PA, could influence placental blood flow. However, several studies suggest that regular exercise during pregnancy increases placental growth and its ability to perfuse oxygen and nutrients to the foetus[159]. These statements are consistent with our findings, in which oxygen saturation was better in women with greater low to moderate PA levels, perhaps because increasing PA has a similar effect on placental angiogenesis during early pregnancy. The increase in PA intensity (which indirectly represents the muscle mass involved in the contractile activity, such as increased aerobic exercise intensity) might lead to a generally transient reduction of uterine-placental blood flow, which could overcome the compensatory mechanisms of the placenta[160]. This could have influenced the lower score in the Apgar test observed in those newborns whose mothers performed more minutes of vigorous PA but it was not related to worse umbilical cord blood gas parameters. Other studies have previously evaluated the association of PA with other neonatal parameters, such as birth weight[161]. However, more studies are needed to analyse the association of vigorous PA with the Apgar test score for a better understanding of these results.

Finally, findings observed in relation to ST and PA levels among different types of delivery (i.e. caesarean or vaginal) need to be highlighted. Although we did not confirm statistically significant differences, women who had caesarean sections showed a tendency to present higher ST and lower PA levels than those with vaginal deliveries (borderline significant and clinically meaningful). These differences between vaginal and caesarean deliveries could have been stronger with a larger sample size. In fact, Nielsen et al.[17] found a decrease in the rate of caesarean sections in women who had greater PA levels during the first and second trimesters of pregnancy. These results could be explained by an improvement in placental function in exercised pregnant women[101]. Indeed, the study carried out by Jackson et al. [162] found that PA during mid pregnancy increased the parenchymal component of the placenta as well as capillary and total vascular volumes. Moreover, our results suggest that newborns of more active women have a better acid-base balance, which might reduce the risk of caesarean section due to loss of foetal well-being.

It should be noted that 24.5% of births in the present study occurred by caesarean section, which is similar to the rate described in the pregnant population of the same geographical area [163]. However, the World Health Organization establishes that caesarean rates above 10-15% are not associated with a reduction in maternal or neonatal morbidity and mortality[84], so its abuse is not clinically justified. This is clinically relevant because caesarean incidence rates in Spain are extremely high, which implies greater health costs and risk for both, the mother and the newborn[164,165]. In a study carried out in Canada, a saving of $27 million, in just four years, was achieved by implementing a program aimed at reducing caesarean sections[166]. Taking also into account that only a quarter of the women who participated in the present study met PA recommendations, we may considerate that there is still a large room for behavioural changes in order to improve maternal and neonatal birth outcomes.

Study III. Association of objectively measured physical fitness during pregnancy with maternal and neonatal birth outcomes. The GESTAFIT Project.

To the best of our knowledge, this is the first study assessing the association of objectively measured physical fitness during pregnancy with birth outcomes related to delivery and the neonate. We hypothesized that maternal PF measures are positively associated with improved maternal and neonatal birth outcomes and with vaginal deliveries. Although no differences were seen in maternal outcomes, 16th gestational week upper-body strength was related to greater birth weight, and in the same stage of pregnancy, CRF and flexibility were positively associated with arterial umbilical cord blood gas. One of the major findings of this study is that caesarean rates are associated with decreased CRF, flexibility, and clustered overall physical fitness at 16 and 34 weeks of pregnancy compared to women who had vaginal deliveries.

Our findings of increased maternal upper-body muscle strength at 16 weeks of gestation associated with greater neonate birth weight is in agreement with Bisson et al. [30]. On one hand, increased birth weight can be related to an increased risk of foetal macrosomia, or birth weight greater than four kilograms[167]. In this study sample, only five neonates (3.5%) were macrosomic and among them, only two of the mothers showed higher handgrip strength than the mean of the sample (27.3±4.2 Kg). Therefore, maternal upper-body muscle strength does not seem to be related to a pathological increase in birth weight, but to a normal and healthy range of birth weight. Importantly, Dodds et al.[168] found that neonates with higher birth weight had more muscle strength later in childhood. Thus, the increases in birth weight may be due to increases in neonatal muscle mass. A potential mechanism for the relationship between maternal muscle strength and neonatal birth weight could be related to changes in placental function. Lewis et al.[169] reported that women with less arm muscle area also had decreased placental amino acid transport, which is essential for appropriate foetal development[169]. Another possible explanation for the change in birth weight is increased placental angiogenesis, as it occurs in pregnant women who perform exercise training[101]. Further research will need to be done with more specific and longitudinal body composition analysis of offspring in order to determine if maternal PF leads to with healthier weights in offspring's at later stages of life[23]. However, we performed the present analysis introducing placental weight as a confounder, and the results did not change (data not shown).

Since the 16th gestational week measures of CRF and flexibility were positively associated with arterial umbilical cord blood gas, these may relate to the status of connective tissue, i.e. ligaments, during pregnancy. For example, serum relaxin levels are increased during pregnancy[35], which increases ligament laxity[170], necessary for the correct maintenance of pregnancy and the labour progression[171]. For this reason, the association between flexibility at 16th gestational week and better umbilical cord blood gas could be explained by increased levels of relaxin in pregnant women with greater flexibility[172]. Since relaxin has endothelium-dependent vasodilation effects in the cardiovascular system[36], and more specifically in the uterine artery[173], it seems feasible that during pregnancy, the uteroplacental flow was more efficient during the labour in women with highest relaxin receptors expression. This result is clinically important since lower arterial pH levels (pH<7.20) in the umbilical cord blood are strongly associated with increased neonatal morbidity and mortality[174]. Mukai et al.[175] measured the oxygen saturation in the cranial tissue during the crowning of the foetus and five minutes after birth. The authors described that foetuses with better oxygen saturation during labour, also had better oxygen saturation at five minutes after birth [175]. This result, as well as the higher levels of arterial PO_2 in neonates of mothers with greater flexibility, may be related to a better blood perfusion from the mother to the foetus. This possibility is in agreement with Ramírez et al.[102] who found that exercise, which is closely related to physical fitness, during pregnancy decreased placenta weight, but increased its efficiency. This fact could also explain the positive association observed between maternal VO_{2max} and PO_2 and oxygen saturation in the arterial umbilical cord. A higher VO_{2max} means a greater capacity of the cardiorespiratory system to supply, transport and optimize the blood flow of oxygen, and is usually observed in more physically active people[176]. Thus, it is plausible that this would provide increased oxygen to the foetus. Indeed, placental changes expressed in active pregnant women are associated with improvements in placental perfusion[101]. However, more studies are needed to verify this association.

Regarding delivery type, women who had caesarean sections had lower flexibility and CRF and worse clustered overall PF during pregnancy than women who had vaginal births. Regarding the association of flexibility with delivery type can be explained via the vasodilator effects of relaxin[173], which may promotes a better blood flow to the foetus and decreases alterations in foetal well-being. There are no studies that directly relate maternal flexibility with type of delivery, but one of the modalities of exercise widely performed during pregnancy, such as yoga, that includes flexibility training, has been associated with less labour pain, shortening of labour stages and lower caesarean sections[177]. Additional studies are needed to contrast these results.

Moreover, regarding CRF, the relation between a higher maternal VO_{2max} and greater arterial PO_2 and arterial O_2 saturation in cord blood and a lower rate of caesarean section has been never reported. Labour is a major physical effort that often lasts greater than 7 hours[178]. Therefore, women with lower CRF and less ability of the respiratory and circulatory systems to supply oxygen to the body during a strenuous work have a higher prevalence of caesarean sections.

Finally, the findings about the lower caesarean rate in women with better clustered overall PF during pregnancy are extremely important. Caesarean sections are associated with a greater number of postpartum complications for mother and neonate [88,165]. More than one in four of the births in our study sample were by caesarean delivery, which is an extremely high number according to the proposals of the WHO [84]. However, the results of the present study are encouraging. Lower rates of caesarean sections and better neonatal outcomes could be promoted by increasing maternal physical fitness, which is also associated with better health of women and offspring in the future.

In this regard, it is of clinical relevance to determine if the assessment of PF levels during pregnancy might provide medical care supplementary information regarding the maternofoetal health at birth.

Study IV. Association of self-reported physical fitness during late pregnancy with birth outcomes and oxytocin administration during labour. The GESTAFIT Project.

To the best of our knowledge, this is the first study exploring the association of maternal self-reported PF levels in late pregnancy with birth outcomes, and the use of oxytocin during the labour. Although most of the PF components assessed through the IFIS questionnaire were not associated with maternal and neonatal birth outcomes, greater speed-agility was associated with a more alkaline pH in both, umbilical artery and vein. One of the major findings of the present study is that those women who required oxytocin before or during labour showed lower self-reported CRF and flexibility in late pregnancy.

In this study, no association was found between maternal gestational week at birth, and duration of first and second stages of labour with PF components. As far as we know, there are no previous studies analyzing the influence of self-reported maternal PF with birth outcomes, so the reliable comparison of the present findings is extremely difficult. Nevertheless, our results do not concur with those described by Kardel et al. [116], who observed a relationship of CRF (through the objective measurement of the VO_{2max}) at 35-37th gestational weeks, with shorter labour in nulliparous women. It should be taken into account that the mean CRF of our sample was reported as "poor", and it is possible that the shortening of labour was related to slightly higher values of this PF dimension. On the other hand, two studies have previously found a positive association of maternal muscle strength with birth weight[30,65], but in both cases the importance of the second trimester of pregnancy is highlighted for this association to be positive. It is possible that this finding was not found in late pregnancy, since in the third trimester maternal muscle strength tends to decrease[65].

Notwithstanding, we found that greater self-reported speed-agility was related with more alkaline pH in both umbilical vessels. During labour, many women experience fatigue, which is associated with both, physical and mental discomfort[178]. For this reason, we hypothesize that women who feel themselves more agile, might be more likely to have an active labour with greater changes of body position, that leads to an improvement of birth outcomes[179,180]. These results should be interpreted with caution and more studies are needed to confirm these associations.

After adjusting for substantial potential confounders, we found that women who were administered oxytocin during labour had lower CRF and flexibility than women who did not need this drug. CRF has been positively associated with endogenous oxytocin levels in pregnant women [181]. Moreover, labour is a strenuous process that often has a long duration and usually produces a huge physiological fatigue[178]. In this sense, it has been described that fatigue during labour is related to alterations in uterine dynamics[182], which is one of the indications for the administration of synthetic oxytocin[183]. Although more studies are needed to confirm this, it is possible that women with greater CRF experienced less fatigue during labour and, therefore, showed a better uterine dynamic, so that they did not need exogenous oxytocin administration.

Regarding flexibility, no previous studies have associated this PF dimension with the use of oxytocin. A possible explanation to our findings could be that women with greater self-reported flexibility during pregnancy could also have higher levels of relaxin[35]. Thus, as this hormone has vasodilators effects when acting on its receptors in the uterine artery[173], it is possible that the increase in uterine vascularization improves its dynamics during labour. Finally, it seems that high levels of relaxin could also have an important implication in the appearance of uterine contractions during pregnancy[184,185], although the mechanisms are not fully understood yet[186].

According to the data of the Spanish Ministry of Health and Social Policy and Equality, the prevalence of exogenous oxytocin use during spontaneous labour in Spanish public hospitals is 53%, much higher than the recommended standard of 5-10%[187]. Among the women who presented valid data for the analysis of differences in PF by oxytocin administration, almost one in four had been provided with this hormone during labour, so these rates are still higher than recommended. Synthetic oxytocin is widely used as a treatment for dystocia of uterine dynamics[183] and as a method to induce the labour[188]. However, its use has been related to an increased risk of uterine hyperactivity, abnormalities in the fetal heart rate and postpartum hemorrhage[189]. In addition, other studies have associated the use of oxytocin during birth with sucking problems of the neonate and early cessation of breastfeeding [190], among others neonatal problems[109].

Altogether, the findings of the present study are clinically relevant. The IFIS could be employed as an easy and quick clinical tool by nurses to assess women who should receive health education, in order to improve their PF and avoid, in this way, the potential need to be administered oxytocin before or during the future labour. Nevertheless, more studies are needed to confirm the findings of our study.

Study V. Influence of a concurrent exercise training intervention during pregnancy on maternal and neonatal birth outcomes. The GESTAFIT Project.

The major finding of this study was that the intervention group had longer duration of the first stage and shorter duration of second stage of labour and greater placental and neonatal weight than control group. No differences were found in the rest of the birth outcomes studied or in the type of birth between both groups.

Although the exercise program had no effect on gestational age at birth, our results can be interpreted positively, since there were only three premature deliveries (at 34th, 35th and 36th gestational weeks) and all belonged to women in the control group. Physical exercise during pregnancy has been previously described in a systematic review as a protective factor for preterm delivery[191]. Moreover, Huang et. al[192] also described a lower risk of preterm birth in women who exercised at moderate intensity during pregnancy. However, other studies found no association between exercise and gestational age at birth[123].

Regarding duration of labour, our results are in agreement with that described by Sanda et al.[61], who found a longer first stage of labour in women who performed a physical exercise program twice a week. In contrast, Perales et al.[57] found that pregnant women from the intervention group had a shorter first stage of labour. However, this effect was only statistically significant in the unadjusted model, but this relationship disappeared when they adjusted for confounders. Other study did not find differences between pregnant women who trained and control group[193]. The methodological differences of each exercise program and even the different definitions of the stages of labour do not allow a reliable comparison. Studies evaluating the effects of physical exercise on the duration of the second stage of labour, are even scarcer. One study found no differences between both groups[61] and another study found that physically more active pregnant women had a longer duration of the second stage of labour[60]. We performed these analyses with the total duration of labour and there were no differences between both groups (data not shown). Therefore, it seems that although cervical dilation time was longer, the total time of labour was not affected. On the other hand, the shortening of the second stage of labour is a positive finding, since the prolongation of this stage is related to instrumental deliveries, caesarean sections, shoulder dystocia, postpartum haemorrhage and low scores in the Apgar test, among others[194,195].

Interestingly, placentas and neonates of the mothers in the exercise group weighed more after adjusting for potential confounders. Performing moderate-intensity physical exercise regularly during pregnancy has been shown to increase maternal plasma volume, vascularity of the intervillous space, and placental weight and functionality[196–198]. Nevertheless, physical exercise at a more vigorous intensity or with more frequent training sessions could have the opposite effect, decreasing the placental size[99,199]. In this sense, placental weight is positively associated with birth weight[200–203], so both findings are correlated. Regarding birth weight, only 5 foetuses presented macrosomia (more than 4000 grams of weight[167]), three of them belonged to the control group and two of them to the intervention group, but none of those mothers were diabetic. For this reason, we can conclude that the concurrent training program did not have a negative effect on the neonatal birth weight. This finding is consistent with that described by Juhl et al.[43] who concluded that pregnant women who exercised had a lower risk of having small-for-gestational-age neonates.

Finally, we did not find any differences in the rest of the birth outcomes studied. Although previous studies have not found effects of the exercise in the Apgar test[44,204], the findings regarding the effects on the mode of delivery are still controversial[61,117,205,206] and studies exploring the relationship between physical training during pregnancy and umbilical cord blood gas after birth are scarce or non-existent. It is important to note that the training program did not imply any perinatal risk for the mother nor the foetus. Performing a well-designed exercise program during pregnancy, supervised by professionals, is safe and provides health benefits for both, the mother and the neonate[22,123,204]. Notwithstanding, the interpretation of our results is complicated due to the methodological difference used in the design of the intervention programs of other studies. In addition, the results shown are preliminary, derived exclusively from the per-protocol analysis, so they should be interpreted with caution.

LIMITATIONS AND STRENGTHS

LIMITATIONS AND STRENGTHS

Limitations

In *Studies I-V,* the sample sizes were relatively small, and there were data loss due to several reasons.

In *Studies I-IV* the cross-sectional design precludes determination of causality.

In *Studies I* and *II,* accelerometry does not register activities such as biking or swimming, but pregnant women did not report to practice these activities in their personal PA notebook.

In *Study III,* there are no validated tests for the evaluation of physical fitness in pregnant women. Therefore, we have employed those that have been used in previous research with pregnant women[25,125,207].

In *Study IV,* although the IFIS scale has proven to be a reliable tool in other populations[208,209], subjective measures tend to overestimate some dimensions.

In *Study V,* the randomized component of this study was broken and there could be selection biases, although we try to avoid them. However, the methodological quality could be more determinant than the randomization design. Only interested women participated in the study. Important secondary analyzes should be included, such as the consumption of carbohydrates during pregnancy, which could be especially important in relation to placental and neonatal weight. The results are derived only from per-protocol analysis, so they are preliminary findings that need to be completed in order to be interpreted properly.

Strengths

In *Study I*, one of the important strengths is that the measurement tool used to assess ST and PA levels (i.e. accelerometry) is widely valid and reliable. It also should be noted that a strict inclusion criteria was used related to the accelerometer wearing time, and all pregnant women included had seven valid days with at least ten hours of time recorded.

In *Study II*, it was provided a comprehensive examination of the association of objectively measured ST and PA during early second trimester of pregnancy with maternal and foetal relevant birth outcomes. The analysis of different PA intensities (including vigorous PA levels) is a strength, since it has previously been pointed out that the analysis of vigorous PA together with moderate PA could mask the true effects of a higher PA intensity[18]

In *Studies II-V*, the measurement of gases in the artery umbilical cord blood is a gold standard in the determination of the acid-base status in the foetus, and paired samples were taken (venous and arterial blood) that allow us a better interpretation of the results.

In *Study III*, provides a comprehensive examination of the association of physical fitness levels objectively measured during pregnancy with maternal and neonatal birth outcomes (e.g. acid balance base of the newborn, and delivery type).

In *Study IV*, shows a useful and quick tool that can be used by health professionals to detect pregnant women with low physical fitness, to encourage them to exercise and might decrease the administration of oxytocin during labour.

In *Study V*, the concurrent exercise program was a novel individually-tailored intervention which was designed according to the latest Guidelines in pregnancy[7,8] by an expert multidisciplinary team. Moreover, the exercise training was strictly supervised throughout the entire study, and the attendance, intensity and other related parameters were monitored periodically.

CONCLUSIONS/CONCLUSIONES

CONCLUSIONS

General conclusion

The findings of this International Doctoral Thesis suggest that decreasing sedentary time and increasing physical activity during pregnancy was related to better neonatal birth outcomes, especially in relation to the values of umbilical cord blood gases. In addition, maternal muscle was positively associated with birth weight and cardiorespiratory fitness and flexibility were related to better neonatal outcomes and lower rates of caesareans. Broadly, a supervised concurrent physical training program promoted a better maternal birth outcomes and improved placental and neonatal weight. Moreover, it did not have any harmful effect on the type of delivery or other maternal and neonatal outcomes.

Specific conclusions

1. Pregnant women without a University degree and more children require special attention from health professionals, since these factors could be related to a greater extent with physical inactivity.

2. Greater physical activity levels of light-to-moderate intensity as well as steps per day are associated with better maternal and neonatal birth outcomes. Contrary, sedentary time and vigorous physical activity could have a harmful influence on birth outcomes.

3. Pregnant women with more upper-body muscle strength have neonates with greater birth weight. Likewise, greater cardiorespiratory fitness and flexibility during pregnancy is related to enhanced gas values in the umbilical artery. Lower flexibility, clustered fitness and cardiorespiratory fitness during pregnancy is associated to more caesarean sections.

4. Greater self-reported speed-agility is related with a more alkaline pH in arterial and venous umbilical cord blood gas. Moreover, women who have lower self-reported cardiorespiratory fitness and flexibility during late pregnancy have more prevalence of oxytocin administration during labour.

5. The concurrent exercise training program of moderate intensity is safe and promotes a heavier placenta and neonate, a longer first stage of labour and a shorter second stage.

CONCLUSIONES

Conclusión general

Los hallazgos de esta Tesis Doctoral Internacional sugieren que la disminución del tiempo de sedentarismo y el aumento de la actividad física durante el embarazo se relacionaron con mejores resultados neonatales asociados al parto, especialmente en relación con los valores de los gases de la sangre del cordón umbilical. Además, la fuerza muscular materna se asoció positivamente con el peso al nacer y la capacidad cardiorrespiratoria y la flexibilidad se relacionaron con mejores resultados neonatales y menores tasas de cesáreas. En términos generales, un programa supervisado de entrenamiento físico concurrente promovió mejores resultados neonatales ligados al parto y mejoró el peso placentario y neonatal. Además, no tuvo ningún efecto perjudicial sobre el tipo de parto u otros resultados maternos y neonatales.

Conclusiones especificas

1. Las mujeres embarazadas sin estudios universitario y aquellas que tienen hijos requieren la atención especial de los profesionales de la salud, ya que estos factores podrían estar relacionados en mayor medida con la inactividad física.

2. Los mayores niveles de actividad física de intensidad ligera a moderada, así como los pasos por día, se asocian con mejores resultados de parto maternos y neonatales. Por el contrario, el tiempo de sedentarismo y la actividad física vigorosa podrían tener una influencia perjudicial en los resultados de parto.

3. Las mujeres embarazadas con más fuerza muscular en tren superior tienen neonatos con mayor peso al nacer. Del mismo modo, una mayor capacidad cardiorrespiratoria y flexibilidad durante el embarazo se relacionan con mejores valores de los gases en la arteria umbilical. Menor flexibilidad, fitness agrupado y capacidad cardiorrespiratoria durante el embarazo se asocian con más tasa de cesáreas.

4. Una mayor velocidad-agilidad auto-reportada se relaciona con un pH más alcalino en arteria y venas umbilicales. Además, las mujeres que tienen menor capacidad cardiorrespiratoria auto-informada y flexibilidad durante el embarazo tardío tienen una mayor prevalencia de administración de oxitocina durante el trabajo de parto.

5. El programa de entrenamiento físico concurrente de intensidad moderada es seguro y promueve que la placenta y el recién nacido pesen más, una primera etapa del parto más larga y una segunda etapa más corta.

REFERENCES

REFERENCES

1. Excellence (NICE) National Institute for Health and Clinical. Intrapartum apartum care for health healthy y women and babies. *Nice*. 2014;(December):1-58. file:///C:/Users/Dr Harris/AppData/Local/Mendeley Ltd./Mendeley Desktop/Downloaded/National Institute for Health and Clinical Excellence - 2014 - Intrapartum apartum care for health healthy y women and babies.pdf.

2. Barrientos J, García D, Gómez A, et al. Recomendaciones de la OMS sobre atención prenatal para una experiencia positiva del embarazo Resumen de orientación. *SCLMFyC*. 2007:10-70. http://www.laalamedilla.org/guias/embarazo.pdf.

3. Myers J, McAuley P, Lavie CJ, Despres JP, Arena R, Kokkinos P. Physical Activity and Cardiorespiratory Fitness as Major Markers of Cardiovascular Risk: Their Independent and Interwoven Importance to Health Status. *Prog Cardiovasc Dis*. 2015:306-314. doi:10.1016/j.pcad.2014.09.011

4. World Health Organization. Inactividad física: un problema de salud pública mundial. *Bol Epidemiol*. 2015;06:1-7. http://www.who.int/dietphysicalactivity/factsheet_inactivity/es/.

5. Sedentary Behaviour Research Networ. Letter to the Editor: Standardized use of the terms “sedentary” and “sedentary behaviours.” *Appl Physiol Nutr Metab*. 2012:540-542. doi:10.1139/h2012-024

6. Fazzi C, Saunders DH, Linton K, Norman JE, Reynolds RM. Sedentary behaviours during pregnancy: A systematic review. *Int J Behav Nutr Phys Act*. 2017;14(1). doi:10.1186/s12966-017-0485-z

7. American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 650: Physical Activity and Exercise During Pregnancy and the Postpartum Period. *Obs Gynecol*. 2015;126(6):e135-e142. doi:10.1097/AOG.0000000000001214

8. Mottola MF, Davenport MH, Ruchat SM, et al. No. 367-2019 Canadian Guideline for Physical Activity throughout Pregnancy. *J Obstet Gynaecol Canada*. 2018;40(11):1528-1537. doi:10.1016/j.jogc.2018.07.001

9. Broberg L, Ersbøll AS, Backhausen MG, Damm P, Tabor A, Hegaard HK. Compliance with national recommendations for exercise during early pregnancy in a Danish cohort. *BMC Pregnancy Childbirth*. 2015;15(1). doi:10.1186/s12884-015-0756-0

10. Amezcua-Prieto C, Lardelli-Claret P, Olmedo-Requena R, Mozas-Moreno J, Bueno-Cavanillas A, JimÉnez-MoleO'N JJ. Compliance with leisure-time physical activity recommendations in pregnant women. *Acta Obstet Gynecol Scand*. 2011;90(3):245-252. doi:10.1111/j.1600-0412.2010.01050.x

11. Santos PC, Abreu S, Moreira C, et al. Impact of compliance with different guidelines on physical activity during pregnancy and perceived barriers to leisure physical activity. *J Sports Sci*. 2014;32(14):1398-1408. doi:10.1080/02640414.2014.893369

12. Petersen AM, Leet TL, Brownson RC. Correlates of physical activity among pregnant women in the United States. *Med Sci Sports Exerc*. 2005;37(10):1748-1753. doi:10.1249/01.mss.0000181302.97948.90

13. Coll-Risco I, Camiletti-Moirón D, Acosta-Manzano P, Aparicio VA. Translation and cross-cultural adaptation of the Pregnancy Physical Activity Questionnaire (PPAQ) into Spanish. *Journal of Maternal-Fetal and Neonatal Medicine*. 2018.

14. Bell R, Tennant PWG, McParlin C, et al. Measuring physical activity in pregnancy: A comparison of accelerometry and self-completion questionnaires in overweight and obese women. *Eur J Obstet Gynecol Reprod Biol*. 2013;170(1):90-95. doi:10.1016/j.ejogrb.2013.05.018

15. Harrison CL, Thompson RG, Teede HJ, Lombard CB. Measuring physical activity during pregnancy. *Int J Behav Nutr Phys Act*. 2011;8(1):19. doi:10.1186/1479-5868-8-19

16. van Poppel MNM, Oostdam N, Eekhoff MEW, Wouters MG a J, van Mechelen W, Catalano PM. Longitudinal relationship of physical activity with insulin sensitivity in overweight and obese pregnant women. *J Clin Endocrinol Metab*. 2013;98(7):2929-2935. doi:10.1210/jc.2013-1570

17. Nielsen EN, Andersen PK, Hegaard HK, Juhl M. Mode of Delivery according to Leisure Time Physical Activity before and during Pregnancy: A Multicenter Cohort Study of Low-Risk Women. *J Pregnancy*. 2017;2017. doi:10.1155/2017/6209605

18. Bisson M, Tremblay F, St-Onge O, et al. Influence of maternal physical activity on infant's body composition. *Pediatr Obes*. 2017;12:38-46. doi:10.1111/ijpo.12174

19. Melzer K, Schutz Y, Soehnchen N, et al. Effects of recommended levels of physical activity on pregnancy outcomes. *Am J Obstet Gynecol*. 2010;202(3). doi:10.1016/j.ajog.2009.10.876

20. Kennedy AB, Lavie CJ, Blair SN. Fitness or Fatness: Which Is More Important? *JAMA*. 2018. doi:10.1001/jama.2017.21649

21. McAuley PA, Blaha MJ, Keteyian SJ, et al. Fitness, Fatness, and Mortality: The FIT (Henry Ford Exercise Testing) Project. *Am J Med*. 2016;129(9):960-965. doi:10.1016/j.amjmed.2016.04.007

22. Perales M, Santos-Lozano A, Ruiz JR, Lucia A, Barakat R. Benefits of aerobic or resistance training during pregnancy on maternal health and perinatal outcomes: A systematic review. *Early Hum Dev*. 2016:43-48. doi:10.1016/j.earlhumdev.2016.01.004

23. Bohannon RW. Muscle strength: Clinical and prognostic value of hand-grip dynamometry. *Curr Opin Clin Nutr Metab Care*. 2015. doi:10.1097/MCO.0000000000000202

24. Åstrand P-O, Ryhming I. A Nomogram for Calculation of Aerobic Capacity (Physical Fitness) From Pulse Rate During Submaximal Work. *J Appl Physiol*. 1954. doi:10.1152/jappl.1954.7.2.218

25. Rikli R, Jones C. Development and validation of a functional fitness test for community-residing older adults. *Gerontologist*. 2013;53(2):255-267. doi:10.1093/geront/gns071

26. Ortega FB, Ruiz JR, España-Romero V, et al. The International Fitness Scale (IFIS): Usefulness of self-reported fitness in youth. *Int J Epidemiol*. 2011. doi:10.1093/ije/dyr039

27. Stone MH. POSITION STATEMENT: Explosive Exercise and Training. *Natl Strength Cond Assoc J*. 2004. doi:10.1519/0744-0049(1993)015<0007:eeat>2.3.co;2

28. Siff MC. Biomechanical Foundations of Strength and Power Training. In: *Biomechanics in Sport*. ; 2008. doi:10.1002/9780470693797.ch6

29. Marín-Jiménez N, Acosta-Manzano P, Borges-Cosic M, et al. Association of self-reported physical fitness with pain during pregnancy. The GESTAFIT Project. *Scand J Med Sci Sports*. 2019;29(7):1022-1030. doi:10.1111/sms.13426

30. Bisson M, Alméras N, Plaisance J, et al. Maternal fitness at the onset of the second trimester of pregnancy: Correlates and relationship with infant birth weight. *Pediatr Obes*. 2013;8(6):464-474. doi:10.1111/j.2047-6310.2012.00129.x

31. Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA*. 2009;301(19):2024-2035. doi:10.1001/jama.2009.681

32. Engberg E, Tikkanen HO, Koponen A, et al. Cardiorespiratory fitness and health-related quality of life in women at risk for gestational diabetes. *Scand J Med Sci Sports*. 2018;28(1):203-211. doi:10.1111/sms.12896

33. Kardel KR, Johansen B, Voldner N, Iversen PO, Henriksen T. Association between aerobic fitness in late pregnancy and duration of labor in nulliparous women. *Acta Obstet Gynecol Scand*. 2009;88(8):948-952.

doi:10.1080/00016340903093583

34. Holt J, Holt LE, Pelhan T. Flexibility redefined. *XIIIth Int Symp Biomech Sport*. 1996:170-174.

35. Petersen LK, Vogel I, Agger AO, Westergård J, Nils M, Uldbjerg N. Variations in serum relaxin (hRLX-2) concentrations during human pregnancy. *Acta Obstet Gynecol Scand*. 1995;74(4):251-256. doi:10.3109/00016349509024444

36. Leo CH, Jelinic M, Ng HH, et al. Vascular actions of relaxin: nitric oxide and beyond. *Br J Pharmacol*. 2017:1002-1014. doi:10.1111/bph.13614

37. Jelinic M, Marshall SA, Leo CH, Parry LJ, Tare M. From pregnancy to cardiovascular disease: Lessons from relaxin-deficient animals to understand relaxin actions in the vascular system. *Microcirculation*. 2018:e12464.

38. ACSM. *ACSM Guidelines for Exercise Testing and Prescription*. Vol 37.; 2014. doi:9781609136055

39. May L, Newton E. Adaptation of Maternal-Fetal Physiology to Exercise in Pregnancy: The Basis of Guidelines for Physical Activity in Pregnancy. *Clin Med Insights Women's Heal*. 2017;23(10). doi:10.1177/1179562X17693224

40. O'Connor PJ, Poudevigne MS, Cress ME, Motl RW, Clapp JF. Safety and efficacy of supervised strength training adopted in pregnancy. *J Phys Act Health*. 2011;8(3):309-320.

41. Petrov Fieril K, Glantz A, Fagevik Olsen M. The efficacy of moderate-to-vigorous resistance exercise during pregnancy: A randomized controlled trial. *Acta Obstet Gynecol Scand*. 2015;94(1):35-42. doi:10.1111/aogs.12525

42. Owe KM, Nystad W, Skjaerven R, Stigum H, BØ K. Exercise during pregnancy and the gestational age distribution: A cohort study. *Med Sci Sports Exerc*. 2012;44(6):1067-1074. doi:10.1249/MSS.0b013e3182442fc9

43. Juhl M, Olsen J, Andersen PK, Nøhr EA, Andersen AMN. Physical exercise during pregnancy and fetal growth measures: a study within the Danish

National Birth Cohort. *Am J Obstet Gynecol*. 2010;202(1):63.e1-8. doi:10.1016/j.ajog.2009.07.033

44. Ghodsi Z, Asltoghiri M. Effects of aerobic exercise training on maternal and neonatal outcome: A randomized controlled trial on pregnant women in Iran. *J Pak Med Assoc*. 2014;64(9):1053-1056.

45. Spong CY. Defining "term" pregnancy: Recommendations from the defining "term" pregnancy workgroup. *Obstet Gynecol Surv*. 2013:2445-2446. doi:10.1097/01.ogx.0000435519.66840.48

46. Luyckx VA. Preterm Birth and its Impact on Renal Health. *Semin Nephrol*. 2017;37(4):311-319. doi:10.1016/j.semnephrol.2017.05.002

47. White SW, Newnham JP. Is it possible to safely prevent late preterm and early term births? *Semin Fetal Neonatal Med*. 2019:33-36. doi:10.1016/j.siny.2018.10.006

48. Luu TM, Rehman Mian MO, Nuyt AM. Long-Term Impact of Preterm Birth: Neurodevelopmental and Physical Health Outcomes. *Clin Perinatol*. 2017:305-314. doi:10.1016/j.clp.2017.01.003

49. Rêgo AS, Alves MTSS de B e, Batista RFL, et al. Physical activity in pregnancy and adverse birth outcomes. *Cad Saude Publica*. 2016;32(11):e00086915. doi:10.1590/0102-311x00086915

50. Aune D, Schlesinger S, Henriksen T, Saugstad OD, Tonstad S. Physical activity and the risk of preterm birth: a systematic review and meta-analysis of epidemiological studies. *BJOG An Int J Obstet Gynaecol*. 2017:1816-1826. doi:10.1111/1471-0528.14672

51. Takami M, Tsuchida A, Takamori A, et al. Effects of physical activity during pregnancy on preterm delivery and mode of delivery: The Japan Environment and Children's Study, birth cohort study. *PLoS One*. 2018;13(10):e0206160. doi:10.1371/journal.pone.0206160

52. Straughen JK, Sealy-Jefferson S, Bazydlo M, Helmkamp L, Misra DP.

Physical Activity and Risk of Preterm Birth in a Cohort of African American Women. *Women's Heal Issues*. 2018;28(6):488-494. doi:10.1016/j.whi.2018.04.001

53. Chantry a a, Lopez E. [Fetal and neonatal complications related to prolonged pregnancy]. *J Gynecol Obstet Biol Reprod (Paris)*. 2011;40(8):717-725. doi:10.1016/j.jgyn.2011.09.007

54. Abalos E, Oladapo OT, Chamillard M, et al. Duration of spontaneous labour in 'low-risk' women with 'normal' perinatal outcomes: A systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2018:123-132. doi:10.1016/j.ejogrb.2018.02.026

55. Piper JM, Bolling DR, Newton ER. The second stage of labor: Factors influencing duration. *Am J Obstet Gynecol*. 1991:976-979. doi:10.1016/0002-9378(91)90452-W

56. Blix E, Kumle M, Øian P. What is the duration of normal labour? *Tidsskr den Nor Laegeforening*. 2008;128(6):686-689.

57. Perales M, Calabria I, Lopez C, Franco E, Coteron J, Barakat R. Regular Exercise Throughout Pregnancy is Associated with a Shorter First Stage of Labor. *Am J Heal Promot*. 2016;30(3):149-154. doi:10.4278/ajhp.140221-QUAN-79

58. Barakat R, Franco E, Perales M, López C, Mottola MF. Exercise during pregnancy is associated with a shorter duration of labor. A randomized clinical trial. *Eur J Obstet Gynecol Reprod Biol*. 2018;224:33-40. doi:10.1016/j.ejogrb.2018.03.009

59. Gawade P, Pekow P, Markenson G, Plevyak M, Goh W, Chasan-Taber L. Physical activity before and during pregnancy and duration of second stage of labor among Hispanic women. *J Reprod Med*. 2009;54(7):429-435. http://www.ncbi.nlm.nih.gov/pubmed/19691259.

60. Kondo Y, Sawa R, Ebina A, et al. Influence of Habitual Physical Activity During Late Pregnancy on the Duration of Labor. *J Phys Act Heal*.

2016;14(3):203-207. doi:10.1123/jpah.2016-0163

61. Sanda B, Vistad I, Sagedal LR, Haakstad LAH, Lohne-Seiler H, Torstveit MK. What is the effect of physical activity on duration and mode of delivery? Secondary analysis from the Norwegian Fit for Delivery trial. *Acta Obstet Gynecol Scand*. 2018;97(7):861-871. doi:10.1111/aogs.13351

62. McGuire SF. Understanding the Implications of Birth Weight. *Nurs Womens Health*. 2017:45-49. doi:10.1016/j.nwh.2016.12.005

63. Reeves S, Bernstein IM. Optimal Growth Modeling. *Semin Perinatol*. 2008:148-153. doi:10.1053/j.semperi.2007.11.001

64. Pathirathna ML, Sekijima K, Sadakata M, Fujiwara N, Muramatsu Y, Wimalasiri KMS. Effects of Physical Activity During Pregnancy on Neonatal Birth Weight. *Sci Rep*. 2019;9(1):6000. doi:10.1038/s41598-019-42473-7

65. Żelaźniewicz A, Pawłowski B. Maternal hand grip strength in pregnancy, newborn sex and birth weight. *Early Hum Dev*. 2018;119(March):51-55. doi:10.1016/j.earlhumdev.2018.03.004

66. Bisson M, Alméras N, Plaisance J, et al. Maternal fitness at the onset of the second trimester of pregnancy: Correlates and relationship with infant birth weight. *Pediatr Obes*. 2013;8(6):464-474. doi:10.1111/j.2047-6310.2012.00129.x

67. Apgar V, York N. A Proposal for a'New Method of Evaluation.of the Newborn Infant.*. *Curr Res Anesth Analg*. 1953;32:250-259.

68. Finster M, Wood M. The Apgar score has survived the test of time. *Anesthesiology*. 2005;102(4):855-857. doi:10.1097/00000542-200504000-00022

69. Davenport MH, Meah VL, Ruchat SM, et al. Impact of prenatal exercise on neonatal and childhood outcomes: A systematic review and meta-analysis. *Br J Sports Med*. 2018:1386-1396. doi:10.1136/bjsports-2018-099836

70. James LS, Weisbrot IM, Prince CE, Holaday DA, Apgar V. The acid-base

status of human infants in relation to birth asphyxia and the onset of respiration. *J Pediatr*. 1958;52(4):379-394. doi:10.1016/S0022-3476(58)80058-X

71. Armstrong L, Stenson BJ. Use of umbilical cord blood gas analysis in the assessment of the newborn. *Arch Dis Child Fetal Neonatal Ed*. 2007;92(4):430-434. doi:10.1136/adc.2006.099846

72. Yeomans ER, Hauth JC, Gilstrap LC, Strickland DM. Umbilical cord pH, Pco2, and bicarbonate following uncomplicated term vaginal deliveries. *Am J Obstet Gynecol*. 1985;151(6):798-800. doi:10.1016/0002-9378(85)90523-X

73. Victory R, Penava D, Da Silva O, Natale R, Richardson B. Umbilical cord pH and base excess values in relation to adverse outcome events for infants delivering at term. *Am J Obstet Gynecol*. 2004;191(6):2021-2028. doi:10.1016/j.ajog.2004.04.026

74. Helwig JT, Parer JT, Kilpatrick SJ, Laros J. Umbilical cord blood acid-base state: What is normal? In: *American Journal of Obstetrics and Gynecology*. ; 1996:1807-1812. doi:10.1016/S0002-9378(96)70214-4

75. Thorp JA, Rushing RS. UMBILICAL CORD BLOOD GAS ANALYSIS. *Obstet Gynecol Clin North Am*. 1999;26(4):695-709. doi:http://dx.doi.org/10.1016/S0889-8545(05)70107-8

76. Riley RJ, Johnson JWC. Collecting and analyzing cord blood gases. *Clin Obstet Gynecol*. 1993:13-23. doi:10.1097/00003081-199303000-00005

77. Thorp JA, Dildy GA, Yeomans ER, Meyer BA, Parisi VM. Umbilical cord blood gas analysis at delivery. *Am J Obstet Gynecol*. 1996;175:517-522.

78. Committee Opinion No. 684: Delayed Umbilical Cord Clamping After Birth. *Obstet Gynecol*. 2017;129(1):e5-e10. doi:10.1097/AOG.0000000000001860

79. De Paco C, Florido J, Garrido MC, Prados S, Navarrete L. Umbilical cord blood acid-base and gas analysis after early versus delayed cord clamping in neonates at term. *Arch Gynecol Obstet*. 2011;283(5):1011-1014.

doi:10.1007/s00404-010-1516-z

80. Tang J, Fullarton R, Samson SL, Chen Y. Delayed cord clamping does not affect umbilical cord blood gas analysis. *Arch Gynecol Obstet*. 2019:719-724. doi:10.1007/s00404-019-05048-5

81. Xodo S, Xodo L, Berghella V. Delayed cord clamping and cord gas analysis at birth. *Acta Obstet Gynecol Scand*. 2018:7-12. doi:10.1111/aogs.13233

82. Spanish Ministry of Health and C affaires. Strategy for Assitance at Normal Childbirth in the National Health System 2007. 2008. http://www.msssi.gob.es/organizacion/sns/planCalidadSNS/pdf/equidad/estrategiaPartoNormalEnglish.pdf.

83. Ministerio de Sanidad C y BS. Estadística de hospitales. Tablas nacionales. Año 2016. (Página 32). 2016. http://www.msssi.gob.es/estadEstudios/estadisticas/estHospiInternado/inforAnual/home.htm.

84. Organización Mundial de la Salud. *Declaración de La OMS Sobre Tasa de Cesárea*.; 2015. doi:10.1016/j.rhm.2015.07.007

85. Villar J, Carroli G, Zavaleta N, et al. Maternal and neonatal individual risks and benefits associated with caesarean delivery: Multicentre prospective study. *Br Med J*. 2007;335:1025. doi:10.1136/bmj.39363.706956.55

86. Kulas T, Bursac D, Zegarac Z, PlaninicRados G, Hrgovic Z. New Views on Cesarean Section, its Possible Complications and Long-Term Consequences for Children's Health. *Med Arch*. 2013;67(6):460-463. doi:10.5455/medarh.2013.67.460-463

87. Gurol-Urganci I, Bou-Antoun S, Lim CP, et al. Impact of Caesarean section on subsequent fertility: a systematic review and meta-analysis. *Hum Reprod*. 2013:1943-1952. doi:10.1093/humrep/det130

88. Boutsikou T, Malamitsi-Puchner A. Caesarean section: Impact on mother and child. *Acta Paediatr Int J Paediatr*. 2011:1518-1522. doi:10.1111/j.1651-

2227.2011.02477.x

89. Carrapato MRG, Ferreira AM, Wataganara T. Cesarean section: the pediatricians' views. *J Matern Neonatal Med*. 2017:2081-2085. doi:10.1080/14767058.2016.1237496

90. Fell DB, Joseph KS, Armson BA, Dodds L. The impact of pregnancy on physical activity level. *Matern Child Health J*. 2009;13(5):597-603. doi:10.1007/s10995-008-0404-7

91. Duncombe D, Wertheim EH, Skouteris H, Paxton SJ, Kelly L. Factors related to exercise over the course of pregnancy including women's beliefs about the safety of exercise during pregnancy. *Midwifery*. 2009;25(4):430-438. doi:10.1016/j.midw.2007.03.002

92. Petrov Fieril K, Fagevik Olsen M, Glantz A, Larsson M. Experiences of Exercise During Pregnancy Among Women Who Perform Regular Resistance Training: A Qualitative Study. *Phys Ther*. 2014;94(8):1135-1143. doi:10.2522/ptj.20120432

93. Baena-García L, Ocón-Hernández O, Acosta-Manzano P, et al. Association of sedentary time and physical activity during pregnancy with maternal and neonatal birth outcomes. The GESTAFIT Project. *Scand J Med Sci Sports*. 2018;29(3):407-414. doi:10.1111/sms.13337

94. Lindqvist M, Lindkvist M, Eurenius E, Persson M, Ivarsson A, Mogren I. Leisure time physical activity among pregnant women and its associations with maternal characteristics and pregnancy outcomes. *Sex Reprod Healthc*. 2016;9:14-20. doi:10.1016/j.srhc.2016.03.006

95. Gaston A, Vamos CA. Leisure-time physical activity patterns and correlates among pregnant women in Ontario, Canada. *Matern Child Health J*. 2013;17(3):477-484. doi:10.1007/s10995-012-1021-z

96. Amezcua-Prieto C, Olmedo-Requena R, Jiménez-Mejías E, Mozas-Moreno J, Lardelli-Claret P, Jiménez-Moleón JJ. Factors associated with changes in leisure time physical activity during early pregnancy. *Int J Gynaecol Obstet*.

2013;121(2):127-131. doi:10.1016/j.ijgo.2012.11.021

97. Mayhew TM, Charnock-Jones DS, Kaufmann P. Aspects of human fetoplacental vasculogenesis and angiogenesis. III. Changes in complicated pregnancies. *Placenta*. 2004;25(2-3):127-139. doi:10.1016/j.placenta.2003.10.010

98. Omo-Aghoja L. Maternal and fetal acid-base chemistry: A major determinant of perinatal outcome. *Ann Med Health Sci Res*. 2014;4(1):8-17. doi:10.4103/2141-9248.126602

99. Clapp JF. The effects of maternal exercise on fetal oxygenation and feto-placental growth. In: *European Journal of Obstetrics Gynecology and Reproductive Biology*. ; 2003:80-85. doi:10.1016/S0301-2115(03)00176-3

100. Schuler G, Adams V, Goto Y. Role of exercise in the prevention of cardiovascular disease: Results, mechanisms, and new perspectives. *Eur Heart J*. 2013;34(24):1790-1799. doi:10.1093/eurheartj/eht111

101. Reyes LM, Davenport MH. Exercise as a therapeutic intervention to optimize fetal weight. *Pharmacol Res*. 2018;132(April):160-167. doi:10.1016/j.phrs.2018.04.016

102. Ramírez-Vélez R, Bustamante J, Czerniczyniec A, Aguilar De Plata AC, Lores-Arnaiz S. Effect of exercise training on enos expression, NO production and oxygen metabolism in human placenta. *PLoS One*. 2013;8(11):e80225. doi:10.1371/journal.pone.0080225

103. Norris R, Carroll D, Cochrane R. The effects of aerobic and anaerobic training on fitness, blood pressure, and psychological stress and well-being. *J Psychosom Res*. 1990;34(4):367-375. doi:10.1016/0022-3999(90)90060-H

104. Barry VW, Baruth M, Beets MW, Durstine JL, Liu J, Blair SN. Fitness vs. fatness on all-cause mortality: A meta-analysis. *Prog Cardiovasc Dis*. 2014;56(4):382-390. doi:10.1016/j.pcad.2013.09.002

105. Roescher AM, Timmer A, Erwich JJHM, Bos AF. Placental pathology,

perinatal death, neonatal outcome, and neurological development: A systematic review. *PLoS One*. 2014:e89419. doi:10.1371/journal.pone.0089419

106. Khaskheli MN, Baloch S, Sheeba A. Iatrogenic risks and maternal health: Issues and outcomes. *Pakistan J Med Sci*. 2014;30(1):111-115. doi:10.12669/pjms.301.4062

107. Lothian JA. Healthy Birth Practice #4: Avoid Interventions Unless They Are Medically Necessary. *J Perinat Educ*. 2014;23(4):198-206. doi:10.1891/1058-1243.23.4.198

108. Page K, McCool WF, Guidera M. Examination of the Pharmacology of Oxytocin and Clinical Guidelines for Use in Labor. *J Midwifery Women's Heal*. 2017:425-433. doi:10.1111/jmwh.12610

109. Burguet A, Rousseau A. Oxytocin administration during spontaneous labor: Guidelines for clinical practice. Chapter 6: Fetal, neonatal and pediatric risks and adverse effects of using oxytocin augmentation during spontaneous labor. *Rev Sage - Femme*. 2017;46(6):523-530. doi:10.1016/j.sagf.2016.10.007

110. Brimdyr K, Cadwell K, Widström AM, et al. The Association Between Common Labor Drugs and Suckling When Skin-to-Skin During the First Hour After Birth. *Birth*. 2015;42(4):319-328. doi:10.1111/birt.12186

111. Mottola MF, Davenport MH, Brun CR, Inglis SD, Charlesworth S, Sopper MM. V̇O2peak prediction and exercise prescription for pregnant women. *Med Sci Sports Exerc*. 2006;38(8):1389-1395. doi:10.1249/01.mss.0000228940.09411.9c

112. Irving G, Neves AL, Dambha-Miller H, et al. International variations in primary care physician consultation time: A systematic review of 67 countries. *BMJ Open*. 2017:e017902. doi:10.1136/bmjopen-2017-017902

113. Lamina S, Agbanusi E. Effect of aerobic exercise training on maternal weight gain in pregnancy: a meta-analysis of randomized controlled trials. *Ethiop J Health Sci*. 2013;23(1):59-64.

114. Cordero Y, Mottola MF, Vargas J, Blanco M, Barakat R. Exercise is associated with a reduction in gestational diabetes mellitus. *Med Sci Sports Exerc*. 2015;47(7):1328-1333. doi:10.1249/MSS.0000000000000547

115. James M. Pivarnik (Chair), Chambliss HO, Clapp JF, et al. Impact of Physical Activity during Pregnancy and Postpartum on Chronic Disease Risk. *Med Sci Sport Exerc*. 2006;38(5):989-1006. doi:10.1249/01.mss.0000218147.51025.8a

116. Kardel KR, Johansen B, Voldner N, Iversen PO, Henriksen T. Association between aerobic fitness in late pregnancy and duration of labor in nulliparous women. *Acta Obstet Gynecol Scand*. 2009;88(8):948-952. doi:10.1080/00016340903093583

117. Bungum TJ, Peaslee DL, Jackson AW, Perez MA. Exercise during pregnancy and type of delivery in nulliparae. *J Obstet Gynecol Neonatal Nurs*. 2000;29(3):258-264. doi:10.1111/j.1552-6909.2000.tb02047.x

118. Silveira LC da, Segre CA de M. Physical exercise during pregnancy and its influence in the type of birth. *Einstein (Sao Paulo)*. 2012;10(4):409-414. http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=23386078&site=ehost-live.

119. Barakat R, Pelaez M, Cordero Y, et al. Exercise during pregnancy protects against hypertension and macrosomia: Randomized clinical trial. *Am J Obstet Gynecol*. 2016;214(5):649.e1-649.e8. doi:10.1016/j.ajog.2015.11.039

120. Hopkins SA, Baldi JC, Cutfield WS, McCowan L, Hofman PL. Exercise training in pregnancy reduces offspring size without changes in maternal insulin sensitivity. *J Clin Endocrinol Metab*. 2010;95(5):2080-2088. doi:10.1210/jc.2009-2255

121. Hegaard HK, Rode L, Katballe MK, Langberg H, Ottesen B, Damm P. Influence of pre-pregnancy leisure time physical activity on gestational and postpartum weight gain and birth weight–a cohort study. *J Obstet Gynaecol (Lahore)*. 2017;37(6):736-741. doi:10.1080/01443615.2017.1292227

122. Huang L, Fan L, Ding P, et al. The mediating role of placenta in the

relationship between maternal exercise during pregnancy and full-term low birth weight. *J Matern Neonatal Med*. 2018;31(12):1561-1567. doi:10.1080/14767058.2017.1319936

123. Nascimento SL, Surita FG, Cecatti JG. Physical exercise during pregnancy: A systematic review. *Curr Opin Obstet Gynecol*. 2012:387-394. doi:10.1097/GCO.0b013e328359f131

124. Date ED. Committee opinion no 611: method for estimating due date. *Obstet Gynecol*. 2014;124(4):863-866. doi:10.1097/01.AOG.0000454932.15177.be

125. Ruiz-Ruiz J, Mesa JLM, Gutiérrez A, Castillo MJ. Hand size influences optimal grip span in women but not in men. *J Hand Surg Am*. 2002;27(5):897-901. doi:10.1053/jhsu.2002.34315

126. Santos IA, Stein R, Fuchs SC, et al. Aerobic exercise and submaximal functional capacity in overweight pregnant women: A randomized trial. *Obstet Gynecol*. 2005;106(2):243-249. doi:10.1097/01.AOG.0000171113.36624.86

127. Barker D, Mason G, Schlosshan D, McLoughlin H, Tan L-B. Maximal exercise testing can be safely used to assess pregnant cardiac patients. *Am J Obstet Gynecol*. 2005;193(6):S80. doi:10.1016/j.ajog.2005.10.790

128. Aguilar-Farías N, Brown WJ, Peeters GMEEG. ActiGraph GT3X+ cut-points for identifying sedentary behaviour in older adults in free-living environments. *J Sci Med Sport*. 2014;17(3):293-299. doi:10.1016/j.jsams.2013.07.002

129. Sasaki JE, John D, Freedson PS. Validation and comparison of ActiGraph activity monitors. *J Sci Med Sport*. 2011;14(5):411-416. doi:10.1016/j.jsams.2011.04.003

130. Hanley GE, Munro S, Greyson D, et al. Diagnosing onset of labor: A systematic review of definitions in the research literature. *BMC Pregnancy Childbirth*. 2016;16(71). doi:10.1186/s12884-016-0857-4

131. World Health Organization. Integrated Management Of Pregnancy And Childbirth (IMPAC), Managing Complications in Pregnancy and

Childbirth :A guide for midwives and doctors. 2007. https://apps.who.int/iris/bitstream/handle/10665/43972/9241545879_eng.pdf;jsessionid=A9D0A603FB51DE6712D869D03F08D979?sequence=1.

132. Butterwegge M, Kappen R, Rath W. [Changes in umbilical cord blood acid-base status after delivery in dependence on time intervall--a continuing forensic problem]. *Z Geburtshilfe Neonatol*. 2012;216(6):253-258. doi:10.1055/s-0032-1323794

133. Kehler AK, Heinrich KM. A selective review of prenatal exercise guidelines since the 1950s until present: Written for women, health care professionals, and female athletes. *Women and Birth*. 2015:e93-8. doi:10.1016/j.wombi.2015.07.004

134. ACOG Committee Obstetric Practice. ACOG Committee opinion. Number 267, January 2002: exercise during pregnancy and the postpartum period. *Obstet Gynecol*. 2002.

135. Aparicio VA, Ocón O, Diaz-Castro J, et al. Influence of a Concurrent Exercise Training Program During Pregnancy on Colostrum and Mature Human Milk Inflammatory Markers: Findings From the GESTAFIT Project. *J Hum Lact*. 2018;34(4):789-798. doi:10.1177/0890334418759261

136. Morris T, McNamara K, Morton CH. Hospital-ownership status and cesareans in the United States: The effect of for-profit hospitals. *Birth*. 2017;44(4):325-330. doi:10.1111/birt.12299

137. Aparicio VA, Ocón O, Padilla-Vinuesa C, et al. Effects of supervised aerobic and strength training in overweight and grade I obese pregnant women on maternal and foetal health markers: the GESTAFIT randomized controlled trial. *BMC Pregnancy Childbirth*. 2016;16(1):290. doi:10.1186/s12884-016-1081-y

138. Nakagawa S, Cuthill IC. Effect size, confidence interval and statistical significance: A practical guide for biologists. *Biol Rev*. 2007:591-605. doi:10.1111/j.1469-185X.2007.00027.x

139. Guthold R, Ono T, Strong KL, Chatterji S, Morabia A. Worldwide Variability in Physical Inactivity. A 51-Country Survey. *Am J Prev Med*. 2008;34(6):486-494. doi:10.1016/j.amepre.2008.02.013

140. Ruifrok AE, Althuizen E, Oostdam N, et al. The relationship of objectively measured physical activity and sedentary behaviour with gestational weight gain and birth weight. *J Pregnancy*. 2014;2014. doi:10.1155/2014/567379

141. Evenson KR, Wen F. Prevalence and correlates of objectively measured physical activity and sedentary behavior among US pregnant women. *Prev Med (Baltim)*. 2011;53(1-2):39-43. doi:10.1016/j.ypmed.2011.04.014

142. Dumith SC, Hallal PC, Reis RS, Kohl HW. Worldwide prevalence of physical inactivity and its association with human development index in 76 countries. *Prev Med (Baltim)*. 2011;53(1-2):24-28. doi:10.1016/j.ypmed.2011.02.017

143. Berntsen S, Richardsen KR, Mørkrid K, Sletner L, Birkeland KI, Jenum AK. Objectively recorded physical activity in early pregnancy: A multiethnic population-based study. *Scand J Med Sci Sport*. 2014;24(3):594-601. doi:10.1111/sms.12034

144. Marshall MR, Montoye AHK, George AJ. Pregnancy walking cadence does not vary by trimester. *Gait Posture*. 2018;65:81-85. doi:10.1016/j.gaitpost.2018.06.175

145. TNS Opinion & Social at the request of the Directorate-General for Education and Culture of the European Comission. *Special Eurobarometer 412: Sport and Physical Activity: Report*.; 2014. doi:10.2766/73002

146. O'Neill B, McDonough SM, Wilson JJ, et al. Comparing accelerometer, pedometer and a questionnaire for measuring physical activity in bronchiectasis: A validity and feasibility study? *Respir Res*. 2017;18(1):16. doi:10.1186/s12931-016-0497-2

147. Camoes M, Lopes C. [Factors associated with physical activity in the Portuguese population]. *RevSaude Publica*. 2008;42(2):208-216.

148. Laaksonen M, Talala K, Martelin T, et al. Health behaviours as explanations for educational level differences in cardiovascular and all-cause mortality: A follow-up of 60 000 men and women over 23 years. *Eur J Public Health*. 2008. doi:10.1093/eurpub/ckm051

149. Friis K, Lasgaard M, Rowlands G, Osborne RH, Maindal HT. Health Literacy Mediates the Relationship Between Educational Attainment and Health Behavior: A Danish Population-Based Study. *J Health Commun*. 2016;21(Sup2):54-60. doi:10.1080/10810730.2016.1201175

150. Liu J, Blair SN, Teng Y, Ness AR, Lawlor DA, Riddoch C. Physical activity during pregnancy in a prospective cohort of British women: Results from the Avon longitudinal study of parents and children. *Eur J Epidemiol*. 2011;26(3):237-247. doi:10.1007/s10654-010-9538-1

151. Hopkinson Y, Hill DM, Fellows L, Fryer S. Midwives understanding of physical activity guidelines during pregnancy. *Midwifery*. 2018;59:23-26. doi:10.1016/j.midw.2017.12.019

152. Ängeby K, Wilde-Larsson B, Hildingsson I, Sandin-Bojö A-K. Prevalence of Prolonged Latent Phase and Labor Outcomes: Review of Birth Records in a Swedish Population. *J Midwifery Womens Health*. 2018;63(1):33-44. doi:10.1111/jmwh.12704

153. Ruchat SM, Davenport MH, Giroux I, et al. Walking program of low or vigorous intensity during pregnancy confers an aerobic benefit. *Int J Sports Med*. 2012;33(8):661-666. doi:10.1055/s-0032-1304635

154. Neonatal Professional Committee of Chinese Medical Doctor Association. [Experts' consensus on the criteria for the diagnosis and grading of neonatal asphyxia in China]. *Zhongguo Dang Dai Er Ke Za Zhi*. 2013;15(1):1. doi:10.7499/j.issn.1008-8830.2013.01.002

155. Blechner JN. Maternal-fetal acid-base physiology. *Clin Obstet Gynecol*. 1993;36(1):3-12. doi:10.1097/00003081-199303000-00004

156. Hagelin A, Leyon J. The effect of labor on the acid-base status of the

newborn. *Acta Obstet Gynecol Scand*. 1998;77(8):841-844. doi:10.1080/j.1600-0412.1998.770810.x

157. Johnson JWC, Richards DS, Cook WA, Hopwood HG, Devoe LD. The etiology of fetal acidosis as determined by umbilical cord acid- base studies. In: *American Journal of Obstetrics and Gynecology*. Vol 177. ; 1997:274-282. doi:10.1016/S0002-9378(97)70187-X

158. Ehrenstein V, Pedersen L, Grijota M, Nielsen GL, Rothman KJ, Sørensen H. Association of Apgar score at five minutes with long-term neurologic disability and cognitive function in a prevalence study of Danish conscripts. *BMC Pregnancy Childbirth*. 2009;9. doi:10.1186/1471-2393-9-14

159. Krause Neto W, Gama EF. Exercise Effect on Placental Components: Systematic Review and Meta-Analysis. *Rev Bras Med do Esporte*. 2015;21(6):485-489. doi:10.1590/1517-869220152106142913

160. Erkkola RU, Pirhonen J., Kivijarvi AK. Flow velocity waveforms in uterine and umbilical arteries during submaximal bicycle exercise in normal pregnancy. *Obstet Gynecol*. 1992;79(4):611-615.

161. Takito MY, D'Aquino Benício MH, de Cassya Lopes Neri L. Physical activity by pregnant women and outcomes for newborns: A systematic review. *Rev Saude Publica*. 2009;43(6):1-10. doi:10.1590/S0034-89102009005000074

162. Jackson MR, Gott P, Lye SJ, Ritchie JW, Clapp JF. The effects of maternal aerobic exercise on human placental development: placental volumetric composition and surface areas. *Placenta*. 1995;16(2):179-191. doi:10.1016/0143-4004(95)90007-1

163. Márquez-Calderón S, Ruiz-Ramos M, Juárez S, López JL. Caesarean delivery in Andalusia, Spain. Relationship with social, clinical and health services factors (2007-2009). *Rev Esp Salud Publica*. 2011;85(2):205-215. doi:10.1590/S1135-57272011000200008

164. Kodakkattil S, Annaiah TK. Re: Perinatal and maternal morbidity and mortality among term singletons following midcavity operative vaginal

delivery versus caesarean delivery. *BJOG: An International Journal of Obstetrics and Gynaecology*. 2017:1491-1492.

165. Hobbs AJ, Mannion CA, McDonald SW, Brockway M, Tough SC. The impact of caesarean section on breastfeeding initiation, duration and difficulties in the first four months postpartum. *BMC Pregnancy Childbirth*. 2016;16(1):90. doi:10.1186/s12884-016-0876-1

166. Bermúdez-Tamayo C, Johri M, Chaillet N. Budget impact of a program for safely reducing caesarean sections in Canada. *Midwifery*. 2018;60:20-26. doi:10.1016/j.midw.2018.01.022

167. Araujo Júnior E, Peixoto AB, Zamarian ACP, Elito Júnior J, Tonni G. Macrosomia. *Best Pract Res Clin Obstet Gynaecol*. 2017:83-96. doi:10.1016/j.bpobgyn.2016.08.003

168. Dodds R, MacDonald-Wallis C, Kapasi T, et al. Grip strength at 4 years in relation to birth weight. *J Dev Orig Health Dis*. 2012;3(2):111-115. doi:10.1017/S204017441100081X

169. Lewis RM, Greenwood SL, Cleal JK, et al. Maternal muscle mass may influence system A activity in human placenta. *Placenta*. 2010;31(5):418-422. doi:10.1016/j.placenta.2010.02.001

170. Dehghan F, Haerian BS, Muniandy S, Yusof A, Dragoo JL, Salleh N. The effect of relaxin on the musculoskeletal system. *Scand J Med Sci Sport*. 2014:34-48. doi:10.1111/sms.12149

171. Parry LJ, Vodstrcil LA. Relaxin physiology in the female reproductive tract during pregnancy. *Adv Exp Med Biol*. 2007:34-48. doi:10.1007/978-0-387-74672-2_4

172. Hisaw FL. Experimental relaxation of the pubic ligament of the guinea pig. *Exp Biol Med*. 1926;185(1):76-80. doi:10.3181/00379727-23-3107

173. Vodstrcil LA, Tare M, Novak J, et al. Relaxin mediates uterine artery compliance during pregnancy and increases uterine blood flow. *FASEB J*.

2012;26(10):4035-4044. doi:10.1096/fj.12-210567

174. Malin GL, Morris RK, Khan KS. Strength of association between umbilical cord pH and perinatal and long term outcomes: Systematic review and meta-analysis. *BMJ*. 2010. doi:10.1136/bmj.c1471

175. Mukai M, Uchida T, Itoh H, Suzuki H, Niwayama M, Kanayama N. Tissue oxygen saturation levels from fetus to neonate. *J Obstet Gynaecol Res*. 2017;43(5):855-859. doi:10.1111/jog.13295

176. Dyrstad SM, Anderssen SA, Edvardsen E, Hansen BH. Cardiorespiratory fitness in groups with different physical activity levels. *Scand J Med Sci Sport*. 2016;26(3):291-298. doi:10.1111/sms.12425

177. Jahdi F, Sheikhan F, Haghani H, et al. Yoga during pregnancy: The effects on labor pain and delivery outcomes (A randomized controlled trial). *Complement Ther Clin Pract*. 2017;27:1-4. doi:10.1016/j.ctcp.2016.12.002

178. Tzeng YL, Kuo SY, Tsai SH. Childbirth-Related fatigue during labor: An important but overlooked symptom. *J Nurs*. 2013;60(6):16-21. doi:10.6224/JN.60.6.16

179. Lawrence A, Lewis L, Hofmeyr GJ, Dowswell T, Styles C. Maternal positions and mobility during first stage labour (Review). *Cochrane Collab*. 2013. doi:10.1002/14651858.CD004896.pub2

180. J.K. G. Woman’s position during second stage of labour. *Cochrane Database Syst Rev*. 2000.

181. Irianti S, Ginandjar AB, Krisnadi SR, Effendi JS, Nataprawira D, Gandamihardja S. Aerobic Exercise and Its Effect on Oxytocin Level and Labor Progression. In: *IOP Conference Series: Materials Science and Engineering*. ; 2017. doi:10.1088/1757-899X/180/1/012177

182. Ebrahimzadeh S, Golmakani N, Kabirian M, Shakeri MT. Study of correlation between maternal fatigue and uterine contraction pattern in the active phase of labour. *J Clin Nurs*. 2012;21(11-12):1563-1569. doi:10.1111/j.1365-

2702.2012.04084.x

183. Dupont C, Carayol M, Le Ray C, et al. Oxytocin administration during spontaneous labour: Guidelines for clinical practice. Guidelines short text. *Rev Sage - Femme*. 2017;45(1):56-61. doi:10.1016/j.sagf.2016.11.006

184. Pupula M, MacLennan AH. Effect of porcine relaxin on spontaneous, oxytocin-driven and prostaglandin-driven pig myometrial activity in vitro. *J Reprod Med*. 1989;34(10):819-823.

185. Pantelis A, Sotiriadis A, Chatzistamatiou K, Pratilas G, Dinas K. Serum relaxin and cervical length for prediction of spontaneous preterm birth in second-trimester symptomatic women. *Ultrasound Obstet Gynecol*. 2018;52(6):763-768. doi:10.1002/uog.18972

186. Marshall SA, Senadheera SN, Parry LJ, Girling JE. The Role of Relaxin in Normal and Abnormal Uterine Function during the Menstrual Cycle and Early Pregnancy. *Reprod Sci*. 2017:342-354. doi:10.1177/1933719116657189

187. Ministry of Health and Social Policy and Equality. Report on Attention to Delivery and Birth in the National Health System [Spanish]. 2012:103. http://www.msssi.gob.es/organizacion/sns/planCalidadSNS/pdf/InformeFinalEAPN_revision8marzo2015.pdf.

188. Penfield CA, Wing DA. Labor Induction Techniques: Which Is the Best? *Obstet Gynecol Clin North Am*. 2017:509-521. doi:10.1016/j.ogc.2017.08.011

189. Rousseau A, Burguet A. Oxytocin administration during spontaneous labor: Guidelines for clinical practice. Chapter 5: Maternal risk and adverse effects of using oxytocin augmentation during spontaneous labor. *Rev Sage - Femme*. 2017. doi:10.1016/j.sagf.2016.11.003

190. Olza Fernández I, Marín Gabriel M, Malalana Martínez A, Fernández-Cañadas Morillo A, López Sánchez F, Costarelli V. Newborn feeding behaviour depressed by intrapartum oxytocin: A pilot study. *Acta Paediatr Int J Paediatr*. 2012;101(7):749-754. doi:10.1111/j.1651-2227.2012.02668.x

191. Di Mascio D, Magro-Malosso ER, Saccone G, Marhefka GD, Berghella V. Exercise during pregnancy in normal-weight women and risk of preterm birth: a systematic review and meta-analysis of randomized controlled trials. *Am J Obstet Gynecol*. 2016:561-571. doi:10.1016/j.ajog.2016.06.014

192. Huang L, Fan L, Ding P, et al. Maternal exercise during pregnancy reduces the risk of preterm birth through the mediating role of placenta. *J Matern Neonatal Med*. 2019;31(12):1561-1567. doi:10.1080/14767058.2017.1372415

193. Salvesen KÅ, Stafne SN, Eggebø TM, Mørkved S. Does regular exercise in pregnancy influence duration of labor? A secondary analysis of a randomized controlled trial. *Acta Obstet Gynecol Scand*. 2014;93(1):73-79. doi:10.1111/aogs.12260

194. Matta P, Turner J, Flatley C, Kumar S. Prolonged second stage of labour increases maternal morbidity but not neonatal morbidity. *Aust New Zeal J Obstet Gynaecol*. 2018. doi:10.1111/ajo.12935

195. Laughon SK, Berghella V, Reddy UM, Sundaram R, Lu Z, Hoffman MK. Neonatal and maternal outcomes with prolonged second stage of labor. In: *Obstetrics and Gynecology*. ; 2014:57-67. doi:10.1097/AOG.0000000000000278

196. Clapp JF, Kim H, Burciu B, Lopez B. Beginning regular exercise in early pregnancy: Effect on fetoplacental growth. *Am J Obstet Gynecol*. 2000;183(6):1484-1488. doi:10.1067/mob.2000.107096

197. Clapp JF, Kim H, Burciu B, Schmidt S, Petry K, Lopez B. Continuing regular exercise during pregnancy: Effect of exercise volume on fetoplacental growth. *Am J Obstet Gynecol*. 2002;186(1):142-147. doi:10.1067/mob.2002.119109

198. Clapp JF. Exercise during pregnancy: A clinical update. *Clin Sports Med*. 2000;19(2):273-286. doi:10.1016/S0278-5919(05)70203-9

199. Hilde G, Eskild A, Owe KM, Bø K, Bjelland EK. Exercise in pregnancy: an association with placental weight? *Am J Obstet Gynecol*. 2017;2016(2):168.e1-168.e9. doi:10.1016/j.ajog.2016.10.018

200. Winick M, Coscia A, Noble A. Cellular grow in human placenta: I. Normal Placental Growth. *Pediatrics*. 1967;39(2):248-251.

201. Crawford MA, Doyle W, Meadows N. Gender differences at birth and differences in fetal growth. *Hum Reprod*. 1987;2(6):517-520. doi:10.1093/oxfordjournals.humrep.a136581

202. Thame M, Osmond C, Wilks R, Bennett FI, Forrester TE. Second-trimester placental volume and infant size at birth. *Obstet Gynecol*. 2001;98(2):279-283. doi:10.1016/S0029-7844(01)01414-4

203. Thame M, Osmond C, Bennett F, Wilks R, Forrester T. Fetal growth is directly related to maternal anthropometry and placental volume. *Eur J Clin Nutr*. 2004;58(6):894-900. doi:10.1038/sj.ejcn.1601909

204. Barakat R, Perales M, Bacchi M, Coteron J, Refoyo I. A program of exercise throughout pregnancy. is it safe to mother and newborn? *Am J Heal Promot*. 2014;29(1):2-8. doi:10.4278/ajhp.130131-QUAN-56

205. Barakat R, Ruiz JR, Stirling JR, Zakynthinaki M, Lucia A. Type of delivery is not affected by light resistance and toning exercise training during pregnancy: A randomized controlled trial. *Obstet Gynecol Surv*. 2010;65(4):209-210. doi:10.1097/OGX.0b013e3181d3ddf8

206. White E, Pivarnik J, Pfeiffer K. Resistance Training during Pregnancy and Perinatal Outcomes. *J Phys Act Heal*. 2014;11(6):1141-1148. doi:10.1123/jpah.2012-0350

207. Bruce RA, Kusumi F, Hosmer D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. *Am Heart J*. 1973;85(4):546-562. doi:10.1016/0002-8703(73)90502-4

208. Ortega FB, Ruiz JR, España-Romero V, et al. The International Fitness Scale (IFIS): Usefulness of self-reported fitness in youth. *Int J Epidemiol*. 2011;40(3):701-711. doi:10.1093/ije/dyr039

209. Álvarez-Gallardo IC, Soriano-Maldonado A, Segura-Jiménez V, et al.

International fitness scale (IFIS): Construct validity and reliability in women with fibromyalgia: The al-ándalus project. *Arch Phys Med Rehabil*. 2016;97(3):395-404. doi:10.1016/j.apmr.2015.08.416