# Exercise and physical activity in the prevention of pre-eclampsia: systematic review

KARINA TAMY KASAWARA, SIMONY LIRA DO NASCIMENTO, MARIA LAURA COSTA, FERNANDA GARANHANI SURITA & JOÃO LUIZ PINTO E SILVA

Scandinavica

Department of Obstetrics and Gynecology, University of Campinas (UNICAMP), Campinas, Brazil

#### Key words

Pregnancy, systematic review, physical activity, exercise, pre-eclampsia

#### Correspondence

Professor João Luiz Pinto e Silva, MD, PhD, Department of Obstetrics and Gynecology, University of Campinas (UNICAMP), Alexander Fleming, 1001, Cidade Universitária – Campinas, São Paulo 13084–971, Brazil. E-mail: psilva@unicamp.br

#### **Conflict of interest**

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Please cite this article as: Kasawara KT, Nascimento SL, Costa ML, Surita FG, Pinto e Silva JL. Exercise and physical activity in the prevention of pre-eclampsia: systematic review. Acta Obstet Gynecol Scand 2012; 91:1147–1157.

Received: 11 November 2011 Accepted: 1 June 2012

DOI: 10.1111/j.1600-0412.2012.01483.x

## Abstract

Exercise and physical activity have been studied and suggested as a way to reduce or minimize the effects of pre-eclampsia. Our aim was to evaluate the association between exercise and/or physical activity and occurrence of pre-eclampsia. We conducted electronic searches without year of publication and language limitations. This was a systematic review designed according to PRISMA. Different databases accessed were as follows: PubMed<sup>®</sup>; Latin-American and Caribbean Literature in Health Sciences (LILACS); Scientific Electronic Library On-line (SciELO); Physiotherapy Evidence Database (PEDro); and ISI web of Knowledge<sup>SM</sup>. The Medical Subject Headings (MeSH) were as follows: ("exercise" OR "motor activity" OR "physical activity") AND ("pre-eclampsia" OR "eclampsia" OR "hypertension, pregnancy-induced"). Inclusion criteria were studies conducted in adults who were engaged in some physical activity. The selection and methodological evaluation were carried out by two independent reviewers. Risk assessment was made by the odds ratio (OR) and incidence of pre-eclampsia in the population who performed physical activity/exercise. A total of 231 articles were found, 214 of which were excluded based on title and full-text, so that 17 remained. Comparison of six case-control studies showed that physical activity had a protective effect on the development of pre-eclampsia [OR 0.77, 95% confidence interval (CI) 0.64–0.91, p < 0.01]. The 10 prospective cohort studies showed no significant difference (OR 0.99, 95% CI 0.93–1.05, p = 0.81). The only randomized clinical trial showed a protective effect on the development of pre-eclampsia in the stretching group (OR 6.34, 95% CI 0.72-55.37, p = 0.09). This systematic review indicates a trend toward a protective effect of physical activity in the prevention of pre-eclampsia.

**Abbreviations:** CI, confidence interval; LILACS, Latin American and Caribbean Literature in Health Sciences; OR, odds ratio; PA, physical activity; PE, pre-eclampsia; PEDro, Physiotherapy Evidence Database; SciELO, Scientific Electronic Library On-line.

# Introduction

Physical activity (PA) is recommended during pregnancy because it may be beneficial to maternal health. Furthermore, it is considered a safe activity for the mother and fetus (1,2). The American College of Obstetricians and Gynecologists (3) recommends moderate-intensity physical exercise every day or at least three times a week, even in pregnant women who were previously inactive (4,5). Exercise and PA have been studied and suggested as a way to reduce or minimize the effects of pre-eclampsia (PE) associated with the prevention and reduction in its incidence or recurrence (6–9). Hypertensive disorders are among the leading causes of maternal morbidity and death, especially in developing countries. However, few well-characterized methodological studies have been carried out (10).

Exercise may contribute to a reduction in blood pressure levels and cardiovascular conditioning in pregnant women (11). It may protect against pre-eclampsia by reducing the maternal concentration of oxidative substances (oxidative stress); stimulating vascularity and placental growth and preventing endothelial dysfunction (12).

Due to the lack of consistent data on this topic, we proposed a systematic review to focus on the effect of exercise and PA on the prevention of pre-eclampsia and its complications. For this we considered exercise as any structured, planned and repetitive form of physical activity, aimed at improving health and maintaining one or more components of physical fitness. Physical activity was defined as any voluntary bodily movement that increased energy expenditure above the basal level (calories expended in the resting state) such as leisure-time or recreational activities, occupational activities or planned physical exercise (sports; 13). The main objective of this study was to evaluate the association between exercise and PA and the development of PE. An additional objective was to recognize the characteristics of activities that could be considered possibly to prevent PE.

# **Material and methods**

This was a systematic review on the effect of exercise and physical activity on the prevention of PE. It was registered at the site PROSPERO (http://www.crd.york.ac.uk/prospero/): CRD42012001975. Inclusion criteria for the analysis were studies conducted in adult humans, with no known disease, who were engaged in some form of PA in order to evaluate the incidence of PE, without limitation to year of publication (up to June, 2011) and language. We considered PA as any voluntary bodily movement that increased energy expenditure above the basal level, such as leisure-time or recreational activities, occupational activities and planned physical exercise (sports; 13). Research was carried out by a systematic search in the following databases: PubMed<sup> $\mathbb{R}$ </sup>; Latin-American and Caribbean Literature in Health Sciences (LILACS); Scientific Electronic Library On-line (Sci-ELO); Physiotherapy Evidence Database (PEDro); and ISI web of Knowledge<sup>SM</sup>. Databases were accessed using the following Medical Subject Headings (MeSH): ("exercise" OR "motor activity" OR "physical activity") AND ("preeclampsia" OR "eclampsia" OR "hypertension, pregnancyinduced"). PRISMA standards (www.equator-network.org) were adhered to.

## Study selection

The selection and methodological evaluation of the articles were carried out by two independent reviewers (KTK and SLN). Initially, the articles were screened by analysing their titles and/or abstracts. Articles that did not meet the inclusion criteria were excluded. Then full-text articles that potentially addressed the topic were accessed. References of the remaining articles were reviewed to identify articles that were not located due to a limited search strategy. When there was a lack of consensus between the two reviewers, a third reviewer (MLC) was consulted to help overcome disagreement. Data retrieved from selected studies were adapted for use based on a World Health Organization form (14). When studies did not show sufficient data to conduct this review, additional information was extracted from the authors of primary studies by electronic contact before study exclusion.

Risk assessment and comparison of clinical outcome was made by the odds ratio (OR) and incidence of PE in the population who performed physical activity and/or physical exercise. For data analysis, the Comprehensive Meta-Analysis program, version Evaluation (15) was used. The incidence of PE and lack of PE was extracted from studies of groups engaged in physical activity and those who did not take part in any activity. When exercise or physical activity was categorized into "yes" or "no," this value was considered for analysis. When activities were analysed in different categories, the reference value (none) was considered vs. the sum of PE incidence in the remaining categories. The results of these articles were grouped according to type of study, comparing OR values and generating a final odds ratio with a 95% confidence interval (CI). Then articles reporting occupational activities and pre-pregnancy activities were analysed separately among each type of study to observe their effect on the development of PE.

Starting from a limited search strategy, databases were accessed following a sequence: first, the PubMed<sup>®</sup>, then the LILACS database and the SciELO database, followed by the PEDro and ISI Web of Knowledge<sup>SM</sup> databases. When duplicate studies appeared, we considered the first database in which the study was found. The literature search produced a total of 231 articles, with 49 in PubMed, seven in LILACS and 175 in ISI. Of these articles, 178 were excluded based on title, because they did not fulfill the predefined inclusion criteria, 20 were excluded for reasons of patent publication, 15 because they were bibliographic reviews and 143 because of failure to satisfy the topic (Figure 1).

After evaluating the abstracts, we observed that five were duplicate studies. An article was published twice in different journals (16,17). Another was published twice by the same journal, although in different editions (18,19). The abstracts of two other articles were published in annals of conferences and later the full-text article was published with complete data (20–23). One article referred to a letter mentioning the original article (24,25). Only one of the two duplicate articles was included.

Twenty-four studies that did not meet the inclusion criteria were excluded. Five other studies were also excluded because they reported a physical exertion test for assessment of variation in blood pressure as a way to predict PE. As a result, 19 full-text articles remained to be analysed. After full-text analysis, two other studies were excluded for not showing consistent data for analysis. Electronic contact with the main authors was attempted with no success (26,27). For final



Figure 1. Flow chart of study selection process.

analysis, 17 articles remained. The remaining articles were classified according to type of study: six were case–control studies, 10 were prospective cohort studies and one was a randomized clinical trial. Table 1 summarizes the main characteristics and the results of articles included.

# Results

When six articles describing case–control studies were grouped to compare the participation or lack of participation in PA, despite diverse types and intensities, it was observed that PA had a protective effect of around 23% on the development of PE (OR 0.77, 95% CI 0.64–0.91, p < 0.01; Figure 2; 21, 28–32). However, in this type of study, when analysed separately there was an increased risk of PE in women who performed labor activities in both of the studies reporting occupational activity (OR 1.62, 95% CI 1.09–2.42, p = 0.01; Figure 3; 29,30).

Analysing the period of exposure to PA in two case–control studies that evaluated participation in PA in the prepregnancy period, it was demonstrated that exercise performed in the year before pregnancy exerted a protective effect on the development of PE (OR 0.56, 95% CI 0.41–0.76, p < 0.01; Figure 4; 21,31).

Of the 10 articles representative of the prospective cohort studies, two (19,33) failed to show the precise data of women with PE. As the Comprehensive Meta-Analysis program allows the direct inclusion of the odds ratio values, the study power was calculated proportionally to other studies and the results of 10 studies were compared (17,23,34–39). However,

there was no difference between PA and lack of PA (OR 0.99, 95% CI 0.93–1.05, p = 0.81; Figure 5). Separately, ee analysed an article reporting that occupational activity posed a risk for the development of PE (OR 1.28, 95% CI 0.92–1.77, p = 0.13; 40). Regarding the prospective cohort studies in which exposure to PA occurred before pregnancy, we observed that there was no difference (OR 0.85, 95% CI 0.67–1.09, p = 0.21; Figure 6; 23,36,37).

The only randomized clinical trial found in this review evaluated the repercussions of a moderate-intensity 40 min walking exercise program, five times per week vs. a low-intensity 40 min stretching exercise program, five times per week. The pregnant women began activity at 18 weeks gestation. A comparison between the walking group and the stretching group showed that the stretching had a protective effect on the development of PE (OR 6.34, 95% CI 0.72–55.37, p = 0.09; 40).

The intensity of PA was difficult to evaluate, owing to the variety of methods used. The included studies quantified and grouped PA intensity as low, medium and high (29,36,38), by a scale of perceived exertion (31,34), by the time engaged in activity (week/month; 17,21,23,28), by the number of times the activity was practiced per week or month (32,35,37,40), employed or unemployed status (30,39) or according to the type of activity performed (19,33).

# Discussion

The results indicate that the performance of recreational and sports PA has a protective effect on the development of PE

Authors (year)	Study design	Sample size	Data collection	Outcome	Exposure definition and period of exposure	Results
Marcoux et al. (1989) (28)	Case-control	172 PE, 254 gestational diabetes and 505 controls	Interview with questionnaire at hospital a few days after delivery	Risk of PE and GH	LTPA, walking (frequent vs. not frequent) and standing position (hours/day) during a regular workday in first 20 weeks of gestation	Standing position not associated with PE or GH; frequent walking associated with a reduced risk of PE (OR 0.6, 95% Cl 0.4–0.9) but not with GH
Irwin et al. (1994) (34)	Cohort	5605 enlisted active duty military women	Records of Retrospective Case-Mix Analysis System (RCMAS), a database of the Defense Manpower Data Center	PIH, hypertension complicating pregnancy, mild or unspecified, severe PE, eclampsia	Occupational exposures: PA classified by job title during pregnancy	Nulliparas had a significantly increased risk ratio for PIH (RR 2.3). Nulliparas employed in jobs involving high levels of PA were at significantly decreased risk of PIH (construction craftsmen, RR 0.37; unskilled laborers RR 0.71). Physical exertion at medium intensity had a high risk ratio for PE (RR 2.5)
Spinillo et al. (1995) (29)	Case-control	160 severe PE and 320 controls	Interview with questionnaire administered at birth	Relation between PA and PE	Four-level scores of PA, type of work, physical intensity (sedentary, moderate or intense), posture and work hours during the first trimester of pregnancy	Moderate or high level of PA associated with PE compared with mild activity (OR 0.2, 95% CI 1.11–3.88)
Sorensen et al. (2003) (21)	Case-control	201 PE and 383 controls	Structured questionnaire during postpartum hospital stay	PE risk	Recreational activities, frequency and average time spent, walking pace, distance and stair climb during first 20 weeks of pregnancy and before pregnancy	During pregnancy: any recreational activity (OR 0. 66, CI 0.47–0.94). The time per week with PA was inversely related to PE risk ( <i>p</i> -value for trend = 0.018). Vigorous activities (OR 0.46, CI 0.27–0.79). Decreased PE risk with increasing energy expenditure PA>31.5 MET h/week (OR 0.44, CI 0.23–0.84, $p = 0.010$ ). Stair climbs daily was inversely associated ( $p = 0.039$ ). Before pregnancy: vigorous PA (OR 0.40, CI 0.23–0.69). PA during both periods (OR 0.59, CI 0.35–0.98).
Saftlas et al. (2004) (30)	Case-control with prospective data collection	44 PE, 172 GH and 2422 controls	Face-to-face interview before 16 weeks gestation	Relation between type of job, exercise or sports, LTPA and PE	Time at work spent sitting, standing and walking; women with sedentary work vs. non-sedentary work; proportion of the time spent sitting; exercise or sports once per week for the 12 months before pregnancy; LTPA; calories expended on LTPA before 16 weeks of gestation	Non-significant reduction in risk of PE in non-sedentary jobs and in the low or moderate sitting categories; GH not associated
Rudra et al. (2005) (31)	Case-control	244 PE and 470 controls	Structured questionnaire on postpartum hospital visits	PE risk	Perception of exertion, intensity and energetic of PA during the year prior to pregnancy	The intensity of recreational PA is strongly and inversely related with PE risk. Moderate exertion referent no or weak (OR 0.54, CI 0.26–1.12). Strenuous exertion (OR 0.2, CI 0.11–0.44). Statistically significant inverse trend: perceived exertion ( $\rho < 0.001$ ); energy expenditure ( $\rho = 0.01$ ).

© 2012 The Authors Acta Obstetricia et Gynecologica Scandinavica © 2012 Nordic Federation of Societies of Obstetrics and Gynecology **91** (2012) 1147–1157

Table 1. Continued	d.					
Authors (year)	Study design	Sample size	Data collection	Outcome	Exposure definition and period of exposure	Results
Haelterman et al. (2007) (32)	Case-control	102 PE, 99 GH and 4381 controls	Interview by telephone	PE and GH risk	Work schedule, postures, physical exertion, breaks, workspace, job strain, social support and environmental exposures; time spent sitting, standing and walking; frequency of pushing or pulling objects, carrying or lifting loads and stair climbing in a workday	Standing daily at least 1 h consecutively without walking had a higher risk of PE (OR 2.5, 95% CI 1.4–4.6). As the same climbing stairs frequently (OR 2.3, 95% CI 1.2–4.1) and women working more than five consecutive days without a day off (OR 3.0, 95% CI 1.0–9.5)
Longo-Mbenza et al. (2008) (19)	Prospective cohort	238 black pregnant women	Questionnaire about PA and consumption of vegetables and meat	PIH: PE, transient or GH	PA: intense activity (farmers, manual workers), inactivity (sedentary professions) first trimester of pregnancy	Activity during pregnancy provides more protection against PE (RR 0.63, 95% CI 0.33–0.94)
Magnus et al. (2008) (35)	Cohort	59 573	Questionnaire about PA	PE risk	Recreational PA (brisk walking, running, bicycling, attendance at training studios, prenatal aerobics classes, low-impact aerobics classes, high-impact aerobics classes, dancing, skiing, team sports, swimming, walking, horseback riding or other), 14–22 gestational weeks	For PE comparing women who exercise 25 times or more per month with inactive women (OR 0.79, 95% Cl 0.65–0.96). The association was strongest among women whose BMI was <25 kg/m <sup>2</sup> compared with >30 kg/m <sup>2</sup> .
Rudra et al. (2008) (23)	Cohort	2241 pregnant women who began prenatal care before and read English, >18 years old	Structured intreview- administred questionnaire in early pregnancy	Incidence of PE	PA the year before and during early pregnancy, around 7 days before interview (15.1 weeks)	111 developed PE. No association between PA during a week in early pregnancy and PE risk (OR 1.07, CI 0.67–1.69). Any PA in the year before pregnancy (OR 0.55, CI 0.30–1.02). Time spent and energy expenditure were not associated with PE risk. No PA before and during early pregnancy vs. only before (OR 0.73, CI 0.30–1.77) vs. during both (OR 0.76, CI 0.34–1.73) vs. only pregnancy (OR 2.03, CI 0.71–5.81).
Yeo et al. (2008) (40)	Randomized clinical trial	41 walking group, 38 stretching group	Subjects did exercise at home five times a week and reported to the Women's Health Exercise Lab (WHEL) once a week	Incidence of PE and GH in walking and stretching group	40 minutes of exercise (walking or stretching) five times a week, starting at 18 weeks gestation until the end of pregnancy	The difference in the risk for PE in the two groups was not significant ( $\rho = 0.110$ ); the stretchers were 1.8 times as likely to develop GH as the walkers (95% CI 0.89–3.61) but not significant
Østerdal et al. (2009) (17)	Prospective cohort	85139	Telephone interview	PE and severe PE	Exercise reported (0, 1–44, 45–74, 75–149, 150–269, 270–419, $\geq$ 420 min/week) At the 12 and 30 weeks of gestation	270–410 and ≥420 min/week were associated with increased risk of severe pre-eclampsia (OR 1.65, 95% Cl 1.11–2.43; OR 1.78, 95% Cl 1.07–2.95)

© 2012 The Authors

Acta Obstetricia et Gynecologica Scandinavica © 2012 Nordic Federation of Societies of Obstetrics and Gynecology 91 (2012) 1147–1157

Table 1. Continuec						
Authors (year)	Study design	Sample size	Data collection	Outcome	Exposure definition and period of exposure	Results
Hegaard et al. (2010) (36)	Prospective	2793 women	Questionnaire about the year before pregnancy	PE risk	LTPA classified as: sedentary, light or moderate to heavy during the year before pregnancy	Moderate-to-heavy LTPA had a tendency toward a lower risk of PE (OR 0.6, 95% CI 0.3–1.4)
Tyldum et al. (2010) (37)	Cohort	3656	Questionnaire about PA	PE risk	PA (frequency, intensity, duration) pre-pregnancy	No link between pre-pregnancy PA and PE. Women physically active for 120 min/week or more had a tendency for reduced risk for PE (adjusted OR 0.6, 95% CI 0.3–1.2)
Vollebregt et al. (2010) (38)	Prospective co- hort/population based	3679 pregnant women in Amsterdan between January 2003 and March 2004 with a singleton pregnancy and who delivered after 24 weeks	Questionnaires at the first prenatal visit	incidence of PE and GH	PA in leisure time (walking, cycling, playing sports and others activities), time spent in minutes and the intensity (low, moderate and vigorous). PA in early pregnancy (past week, around 15.6 weeks)	Incidence of PE was 3.5% and GH 4.4%. The amount of time or intensity of LTPA was not associated with difference in risk of PE or GH. Women who spent more 585 min (PE: OR 0.6, CI 0.25-1.53) and (GH: OR 0.54, CI 0.22-1.36). Playing sports or total LTPA at high levels (PE: OR 0.43, CI 0.17-1.10) and (GH: OR 0.78, CI 0.36-169).
Chang et al. (2010) (39)	Prospective cohort	20276 postpartum women	Home interview using a structured questionnaire 6 months postpartum	Incidence of PE and GH	Maternal employment during pregnancy (work schedule, working hours per week, job title, type of industry, ownership of work and scale of workplace) during pregnancy	<ol> <li>1.8% with GH, 0.8 with PE and 61% (12 404) worked during pregnancy. There were no statistically significant differences between non-employed and work schedule and work hours for the incidence of PE and GH. GH: non-emp 1.7%, emp 1.8% (OR 1.12, CI 0.90–1.39; adjusted OR 0.98, CI 0.78–1.24). PE: non-emp 0.7%, emp 0.9% (OR 1.27, CI 0.91–1.77; adjusted OR 1.09, CI 0.76–1.55).</li> </ol>
Fortner et al. (2011) (33)	Prospective cohort	1043 self-identified Hispanic pregnant women, age 16–40 years, singleton pregnancy, no prior hypertension or diabetes	interview at prenatal care and from medical records after delivery	incidence of PE and hypertensive disorders (GH and PE)	PA by Kaiser PA Survey (KPAS) stratified in four domains: occupational activities, participation in sports and exercise, active living habits, and household and family care activities in early pregnancy (since onset up time of interview) and during the year before pregnancy	<b>4.8%</b> hypertensive disorders and 2.9% PE. Decrease in the risk of hypertensive disorders with increase sports/exercise in early pregnancy ( <i>p</i> -value for trend = 0.04). High level of active living activity (OR 0.4, Cl 0.1–1.1, $\rho$ = 0.07) and household/care-giving activities (OR 0.4, Cl 0.1–1.3, $\rho$ = 0.07) were associated with a 60% reduction in hypertensive disorders relative to low levels. High level of total PA was associated with a 70% decrease in hypertensive disorders (OR 0.3, Cl 0.1–1.0, $\rho$ = 0.06). No association with pre-preganacy PA.
Abbreviations: BMI, activity; PE, pre-eclar	body mass index; C npsia; PIH, pregnan	l, confidence interval; ncy-induced hypertensi	emp, employed; GH, g on; and RR, relative risk	estational hypertensior	n; LTPA, leisure-time physical activity; non-em	o, non-employed; OR, odds ratio; PA, physica

1152

© 2012 The Authors Acta Obstetricia et Gynecologica Scandinavica © 2012 Nordic Federation of Societies of Obstetrics and Gynecology **91** (2012) 1147–1157



Figure 2. Forest plot of the risk of pre-eclampsia for any type of physical activity vs. no physical activity in case–control studies. Abbreviations: CI, confidence interval; LTPA, leisure-time physical activity; and PA, physical activity.



Figure 3. Forest plot of the risk of pre-eclampsia for occupational activities in case-control studies. Abbreviations are as for Figure 1.

Study name	Prepregnancy PA		Statisti	cs for e	each stud	ly		Odds	ratio and	95% CI	
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value					
Rudra, 2005 (31)	Recreational PAvs. none	0.39	0.24	0.64	-371	0.00	1	1 -		1	1
Sorensen, 2003 (21)	Recreational PAvs. none	0.70	0.47	1.03	-1.77	0.07					
		0.56	0.41	0.76	-370	0.00	1		◆		
							0.01	0.1	1	10	100

Figure 4. Forest plot of the risk of pre-eclampsia for pre-pregnancy physical activity in case-control studies. Abbreviations are as for Figure 1.

when analysing case–control studies, both in exercises performed during pregnancy and in the pre-pregnancy period. Concerning cohort studies, although some studies demonstrated that PA may exert a protective effect against PE, when the results were combined this association was not confirmed. Clinically, women have to be encouraged to perform exercise and increase their recreational PA during pregnancy to improve maternal health, including a possibility to prevent PE.

The studies were of different types, with diverse methodologies, making data analysis more difficult. These differences are determined by different statistical powers, types of

Study name	Any type of activity		Statis	tics for e	ach study			_	Odds ratio and	95% Cl	
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value					
Irwin, 1994 (34)	Medium/high vs. low physical exertion	0.82	0.62	1.07	-1.41	0.15	- I	1	-+	1	1
Magnus, 2008 (35)	Recreational PA vs. none	0.91	0.83	1.00	-1.84	0.06					
Longo-Mbenza, 2008 (19)	PA vs. none	0.63	0.42	0.94	-2.26	0.02					
Rudra, 2008 (23)	Recreational PA vs. none	0.85	0.56	1.31	-0.70	0.48			-+		
Osterdal, 2009 (17)	PA vs. none	1.10	1.01	1.19	2.19	0.02					
Hegaard, 2010 (36)	LTPA vs. none (before pregnancy)	0.94	0.55	1.62	-0.20	0.83			-		
Tyldum, 2010 (37)	PA vs. none (before pregnancy)	1.04	0.75	1.44	0.28	0.77			+		
Vollebregt, 2010 (38)	LTPA vs. none	0.76	0.46	1.24	-1.08	0.28			-+		
Chang, 2010 (39)	Employed vs. non-employed	1.28	0.92	1.77	1.50	0.13			-	8	
Fortner, 2011 (33)	PA high vs. low	0.20	0.02	1.40	-1.62	0.10		-+-	• +		
		0.99	0.93	1.05	-0.23	0.81			•		
							0.01	0.1	1	10	100

Figure 5. Forest plot of the risk of pre-eclampsia for any type of physical activity vs. no physical activity in cohort studies. Abbreviations are as for Figure 1.



Figure 6. Forest plot of the risk of pre-eclampsia for prepregnacy physical activity in cohort studies. Abbreviations are as for Figure 1.

activity, intensity and periods of exposure to physical activity or exercise. Furthermore, there are differences in the diagnosis of PE; for example, when comparing the Royal College of Obstetricians and Gynaecologists (RCOG) and the Medical Society of Obstetrics Australia and New Zealand (SOMANZ) with the Society of Obstetricians and Gynecologistsof Canada (SOGC) and the American Society of Hypertension (ASH; 41). However, not all articles included information about how the diagnosis of PE had been made.

The scarcity of randomized clinical trials may preclude adequate assessment of the effect of an intervention on a certain outcome. The only clinical trial found and included in this systematic review did not show significant results. According to Yeo et al. (40), a limitation of their study was the sample size analysed, which did not reach a p < 0.05 and power > 0.80.

The lack of clinical trials in this topic led us to review case–control studies. The design of these studies, however, has many limitations because they depend on a well-defined selection of cases and controls. Furthermore, patient selection may suffer from a variation in the PE incidence in the study population, making exposure to exercise difficult to assess (42).

Cohort studies are considered ideal to investigate the incidence and natural history of a disease, despite difficulty in controlling for variation in the exposure factor, which may lead to bias. Measurement units of occupational and leisure-time PA during pregnancy are difficult to control (43).

## Characteristics of physical activities and PE

During the selection process of the articles included in this review, we noticed that there was no standardization regarding the definition of PA and physical exercise. Constant conflict has been created because these terms are sometimes used interchangeably. The analysed studies showed a variety of PA, such as occupational activities (29,30,32,39) leisure-time and/or recreational activities (17,21,23,28,30,31,35,36,38), general physical activities (19,33) and physical exercise as sports activities (37,40). There was still heterogeneity among the methods used to assess physical activity. Information was collected by the use of questionnaires, face-to-face interviews and database analysis. Results may be compromised by different frequencies, intensities and duration. The actual effect on the research objective analysed was difficult to evaluate.

Two case–control studies (29,30) assessing occupational activity and a single cohort article (39) reporting that this activity was associated with the risk of developing PE corroborated the findings shown in a review by Bonzini et al. (44). The increase in risk was possibly associated with long working hours, long periods of standing at work and work activity involving considerable physical exertion, particularly at the end of pregnancy. However, the type of occupational activity and risk intensity could not be assessed because the evaluation of activities did not use the same standards, which precluded comparison.

A cohort study by Chang et al. (39) assessed work schedule, hours of work per week, type of occupational activity, type of industry, corporate work and workplace schedule, using a population database named the "Taiwan Birth Cohort Study." In contrast, Spinillo et al. (29) formally analysed the employed or unemployed, type of job, job sector and occupational activity, body position at work, physical intensity levels, working hours per week, time since quitting work and social class of the partner, using a structured questionnaire in pregnant women with severe PE compared with normotensive nulliparous women. This methodology differs from that of Saftlas et al. (30), who evaluated hours of work spent standing, walking and sitting, comparing sedentary occupational activities with non-sedentary occupational activities. Time at work spent sitting was assessed by interview. In this study, employment status was classified as employed or unemployed.

Nevertheless, unemployed pregnant women were not necessarily less active than employed pregnant women. Unemployed woman can perform housework that involves greater physical exertion than a person who spends a large amount of time sitting during a working day. That is why it is so difficult to measure the amount of activity at work, during leisure-time activities or at home doing daily chores.

Considering the diversity of PA in a woman's life, leisuretime activities play a fundamental role during pregnancy. These represent changes in physical and mental behavior introduced during this particular time in a woman's life, regardless of the quantity of PA that had been performed previously (45).

## Intensity of PA

The impact of exercise and PA on the cardiovascular system varies according to the type, duration and level of intensity. Assessment of PA intensity may be performed by measuring the variation in heart rate increase with exertion compared with the heart rate at rest or to maximal heart rate (or peak rate). However, only Yeo et al. (40) measured the impact of PA on the cardiovascular system. The risk of developing PE seems to be reduced with increasing intensity of PA and energy expenditure (21,23,28). However, in this review the intensity of PA could not be analysed adequately, because each study used a different methodology for assessment.

#### Period of exposure to exercise

Both case-control studies evaluating pre-pregnancy PA showed a significant protective effect on the development of PE. Sorensen et al. (21) categorized women into two groups (inactive and active) according to participation in leisuretime PA during the year before pregnancy. An interview was conducted in early pregnancy, which was known to be the most appropriate procedure. Rudra et al. (31) interviewed women in the immediate postpartum period about perceived exertion (Borg scale) in recreational PA performed during the 12 months before pregnancy, categorizing PA in a variety of ways: none to weak (reference), moderate, strenuous and very strenuous to maximal (Figure 3). Prospective cohort studies did not show any difference, highlighting that there were differences in the activities analysed. Hegaard et al. (36) assessed the total quantity of PA, including sports, gardening and walking, classified as sedentary, light and moderate to heavy, and did not find any significant difference due to the low number of women engaged in moderate-to-heavy activities. Rudra et al. (23) evaluated participation in recreational activity, classified as none or any activity. Tyldum et al. (37) investigated the frequency, intensity and duration of exercise such as walking, swimming or participation in sports, although he did not specify the pregestational period evaluated.

However, a reduction in PA is virtually always present during pregnancy. In a study by Evenson et al. (46), 13% of pregnant women in the USA practiced PA before pregnancy, although PA was discontinued at the beginning of pregnancy. Likewise, Owe et al. (47) observed that 46.4% women in Norway exercised before pregnancy and this number decreased to 28% at 17 weeks of gestation. Despite these studies, Evenson et al. (46) observed that 35% of women exercised before pregnancy and continued to exercise throughout pregnancy. When evaluating participation in recreational activities during the year before and in the first 20 weeks of gestation, Sorensen et al. (21) observed that categories such as "before only" and "during only" did not represent protection against PE, while engaging in PA during both periods showed a risk reduction of 41%, compared with women who were sedentary before and during pregnancy (OR 0.59, 95% CI 0.35–0.98). Previously active women should be stimulated to maintain the level of PA during pregnancy, and women who were previously sedentary should be encouraged to begin to perform regular physical exercise, with a gradual increase in intensity as recommended by American College of Obstetricians and Gynecologists (3).

In conclusion, our study indicates a protective effect of physical activity on the prevention of PE. It was observed that leisure-time or recreational physical activity was associated with a protective effect. Unfortunately, due to heterogeneity in study results, the optimal intensity of recreational PA that ensures a protective effect on the development of PE could not be assessed. Occupational activity represented a risk for occurrence of PE and has to be studied and analysed separately from the other types of PA. However, further studies with well-defined methodological designs are required to strengthen the evidence that PA and regular physical exercise during pregnancy may have a protective effect against PE.

# Funding

No specific funding.

#### References

- 1. Arena B, Maffulli N. Exercise in pregnancy: how safe is it? Sports Med Arthrosc. 2002;10:15–22.
- Juhl M, Kogevinas M, Andersen PK, Andersen AN, Olsen J. Is swimming during pregnancy a safe exercise? Epidemiology. 2010;21(2):253–8.
- 3. ACOG. Committee on Obstetric Practice. Exercise during pregnancy and the postpartum period. Am Col Obstet Gynecol. 2002;99(1):171–3.
- Wolfe LA, Davies GAL. Canadian Guidelines for exercise in pregnancy. Clin Obstet Gynecol. 2003;46(2):488–95.
- 5. Zavorsky G, Longo LD. Exercise guidelines in pregnancy: new perspectives. Sports Med. 2011;41(5):345–60.
- 6. Weissgerber LT, Wolfe AL, Davies LAG. The role of regular physical activity in preeclampsia prevention. Med Sci Sports Exerc. 2004;36(12), 2024–31.
- Dempsey JC, Butler CL, Williams MA. No need for a pregnant pause: physical activity may reduce the occurrence of gestational diabetes mellitus and preeclampsia. Exerc Sport Sci Rev. 2005;33(3):141–9.
- 8. Weissgerber TL, Wolfe LA, Davies GAL, Mottola MF. Exercise in the prevention and treatment of maternal-fetal

K.T. Kasawara et al.

- 2006;31:661–74.
   Souza VFF, Dubiela A, Serrão Júnior NF. Efeitos do
- souza VFF, Dublea A, Seriao Junio INF, Eleitos do tratamento fisioterapêutico na pré-eclampsia [Effects of physical therapy treatment in preeclampsia]. Fisioter Mov. 2010;23(4):663–72.
- Khan SK, Wojdyla D, Say L, Gulmezoglu AM, Van Look PFA. WHO analysis of causes of maternal death: a systematic review. Lancet. 2006;367:1066–74.
- Yeo S. Prenatal stretching exercise and autonomic responses: preliminary data and a model for reducing preeclampsia. J Nurs Scholarsh. 2010;42(2):113–21.
- Falcao S, Bisotto S, Michel C, Lacasse AA, Vaillancourt C, Gotkowska J, Lavoie JL. Exercise training can attenuate preeclampsia-like features in an animal model. J Hypertens. 2010;28:2446–53.
- Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise and physical fitness: definition and distinction for health-related research. Public Health Rep. 1985;100(2):126–31.
- Jüni P, Altman DG, Egger M. Systematic reviews in health care: assessing the quality of controlled clinical trials. BMJ. 2001;323(7303):42–6.
- Biostat, Inc. Comprehensive meta-analysis. Available online at: http://www.meta-analysis.com/.2006. (accessed 15 August 2011).
- 16. Østerdal ML, Strøm M, Klemmensen AK, Knudsen VK, Juhl M, Halldorsson TI, et al. Moderate to high levels of physical activity in pregnancy may increase risk of severe preeclampsia: prospective cohort. Am J Epidemiol. 2007;165(11):S38.
- Østerdal ML, Strøm M, Klemmensen AK, Knudsen VK, Juhl M, Halldorsson TI, Nybo Andersen AM, Magnus P, Olsen SF. Does leisure time physical activity in early pregnancy protect against pre-eclampsia? Prospective cohort in Danish women. BJOG. 2009;116(1):98–107.
- Longo-Mbenza B, Tshimanga KB, Buassa-bu-Tsumbu B, M'buyamba K Jr. Diets rich in vegetables and physical activity are associated with a decreased risk of pregnancy induced hypertension among rural women from Kimpese, DR Congo. Niger J Med. 2008;17(1):45–9.
- Longo-Mbenza B, Tshimanga KB, Buassa-bu-Tsumbu B, Kabangu MJ. Diets rich in vegetables and physical activity are associated with a decreased risk of pregnancy induced hypertension among rural women from Kimpese, DR Congo. Niger J Med. 2008;17(3): 265–9.
- Sorensen T, Williams M, Lee IM, Dashow E, Luthy D. Physical activity during pregnancy and risk of preeclampsia. Am J Obstet Gynecol. 2001;185(6):S170.
- Sorensen KT, Williams AM, Lee MI, Dashow EE, Thompson LM, Luthy AD. Recreational physical activity during pregnancy and risk of preeclampsia. Hypertension. 2003;41:1273–80.

- 22. Rudra CB, Sorensen TK, Williams MA. A prospective analysis of recreational physical activity and preeclampsia risk. Am J Epidemiol. 2007;165(11):S38.
- 23. Rudra CB, Sorensen TK, Luthy DA, Williams MA. A prospective analysis of recreational physical activity and preeclampsia risk. Med Sci Sports Exerc. 2008;40(9): 1581–8.
- Joles JA, Poston L. Can exercise prevent preeclampsia? J Hypertens. 2010;28(12):2384–5.
- Lavoie JL, Gutkowska J. Can exercise prevent preeclampsia? J Hypertens. 2011;29(7):1465.
- Martin CL, Brunner LR. Physical activity and hypertensive complications during pregnancy: findings from 2004 to 2006 North Carolina Pregnancy Risk Assessment Monitoring System. Birth. 2010;37(3):202–10.
- Stutzman SS, Brown CA, Hains SMJ, Godwin M, Smith GN, Parlow JL, Kisilevsky BS. The effects of exercise conditioning in normal and overweight pregnant women on blood pressure and heart rate variability. Biol Res Nurs. 2010;12(2):137–48.
- Marcoux S, Brisson J, Fabia J. The effect of leisure time physical activity on the risk of preeclampsia and gestational hypertension. J Epidemiol Community Health. 1989;43:147–52.
- Spinillo A, Capuzzo E, Colonna L, Piazzi G, Nicola S, Baltaro F. The effect of work activity in pregnancy on the risk of severe preeclampsia. Aust N Z J Obstet Gynaecol. 1995;35(4):380–5.
- Saftlas FA, Logsden-Sackett N, Wang W, Woolson R, Bracken BM. Work, leisure-time physical activity, and risk of preeclampsia and gestational hypertension. Am J Epidemiol. 2004;160(8):758–65.
- Rudra CB, Williams MA, Lee IM, Miller RS, Sorensen TK. Perceived exertion during prepregnancy physical activity and preeclampsia risk. Med Sci Sports Exerc. 2005;37(11):1836–41.
- 32. Haelterman E, Marcoux S, Croteau A, Dramaix M. Population-based study on occupational risk factors for preeclampsia and gestational hypertension. Scand J Work Environ Health. 2007;33(4):304–17.
- 33. Fortner RT, Pekow PS, Whitcomb BW, Sievert LL, Markenson G, Chasan-Taber L. Physical activity and hypertensive disorders of pregnancy among Hispanic women. Med Sci Sports Exerc. 2011;43(4):639–46.
- 34. Irwin DE, Savitz DA, Standre KA, Hertzpicciotto I. Study of occupational risk-factors for pregnancy-induced

hypertension among active-duty enlisted navy personnel. Am J Ind Med. 1994;25(3):349–59.

- Magnus P, Trogstad L, Owe KM, Olsen SF, Nystad W. Recreational physical activity and the risk of preeclampsia: a prospective cohort of Norwegian women. Am J Epidemiol. 2008;168(8):952–7.
- 36. Hegaard HK, Ottesen B, Hedegaard M, Petersson K, Henriksen TB, Damm P, Dykes AK. The association between leisure time physical activity in the year before pregnancy and pre-eclampsia. J Obstet Gynaecol. 2010;30(1):21–4.
- Tyldum EV, Romundstad PR, Slørdahl SA. Pre-pregnancy physical activity and preeclampsia risk: a prospective population-based cohort study. Acta Obstet Gynecol Scand. 2010;89(3):315–20.
- Vollebregt KC, Wolf H, Boer K, van der Wal MF, Vrijkotte TG, Bonsel GJ. Does physical activity in leisure time early in pregnancy reduce the incidence of preeclampsia or gestational hypertension? Acta Obstet Gynecol Scand. 2010;89(2):261–7.
- Chang PJ, Chu LC, Hsieh WS, Chuang YL, Lin SJ, Chen PC. Working hours and risk of gestational hypertension and pre-eclampsia. Occup Med (Lond). 2010;60(1):66–71.
- 40. Yeo S, Davidge ST, Ronis DL, Antonakos CS, Hayashi R, O'Leary S. A Comparison of walking versus stretching exercise to reduce the incidence of preeclampsia: a randomized clinical trial. Hypertens Pregnancy. 2008;27:113–30.
- Steegers EAP, Dadelszen PV, Duvekot JJ, Pijnenborg R. Pre-eclampsia. Lancet. 2010;376:631–44.
- 42. Schulz KF, Grimes DA. Case-control studies: research in reverse. Lancet. 2002;359:431–4.
- 43. Grimes DA, Schulz KF. Cohort studies: marching towards outcomes. Lancet. 2002;359:341–5.
- 44. Bonzini M, Coggon D, Palmer T. Risk of prematurity, low birthweight and pre-eclampsia in relation to working hours and physical activities: a systematic review. Occup Environ Med. 2007;64:228–43.
- 45. Tendais I, Figueiredo B, Mota J, Conde A. Physical activity, health-related quality of life and depression during pregnancy. Cad Saude Publica. 2011;27(2):219–28.
- Evenson KR, Savitz DA, Huston SL. Leisure-time physical activity among pregnant women in the US. Paediatr Perinat Epidemiol. 2004;18:400–7.
- Owe KM, Nystad W, Bø K. Corralates of regular exercise during pregnancy: the Norwegian Mother and Child Cohort Study. Scand J Med Sci Sports. 2009;19:637–45.