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ORIGINAL ARTICLE ***Reproductive epidemiology***

Physical activity and fertility in women: the North-Trøndelag Health Study

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BACKGROUND: Changes in the state of energy balance owing to changes in physical activity may affect the reproductive system. We evaluated the association between physical activity (PA) and fertility and parity in healthy women.

METHODS: A population-based health survey (HUNT 1) was conducted during 1984–1986 in Nord-Trøndelag county, Norway, with follow-up from 1995 to 1997 (HUNT 2). The study included 3887 women, <45 years old in HUNT 2. PA was assessed by baseline questionnaire, and fertility and parity by questionnaire at follow-up. Data focused on overall occurrence of infertility in the population (without biological confirmation).

RESULTS: Increased frequency, duration and intensity of PA were associated with increased subfertility, and frequency of PA was associated with voluntary childlessness ($P < 0.01$). After adjusting for age, parity, smoking, and marital status, women who were active on most days were 3.2 times more likely to have fertility problems than inactive women. Exercising to exhaustion was associated with 2.3 times the odds of fertility problems versus low intensity. Women with highest intensity of PA at baseline had the lowest frequency of continuing nulliparity and highest frequency of having three or more children during follow-up ($P < 0.05$). Sensitivity analysis including body mass index as confounder did not alter the results. No associations were found between lower activity levels and fertility or parity.

CONCLUSION: Increased risk of infertility was only found for the small group of women reporting the highest levels of intensity and frequency of PA. Awareness of the possible risks of infertility should be highlighted among non-athletic women who exercise vigorously.

Key words: epidemiology / exercise / infertility / physical activity / women

Introduction

Infertility is defined as the inability of a couple to conceive within 1 year of trying to become pregnant (Kumar *et al*., 2007). Recent estimates of the prevalence of infertility range from 3.5 to 16.7% in more developed nations and from 6.9 to 9.3% in less developed nations (Boivin *et al*., 2007). In Norway, the lifetime infertility prevalence has been estimated to be 6.6% (Rostad *et al*., 2006).

A variety of lifestyle factors, such as smoking (Hughes and Brennan 1996; Augood *et al*., 1998; Hull *et al*., 2000), psychological stress (Hjollund *et al*., 1999), caffeine (Wilcox *et al*., 1988) and alcohol consumption (Gill, 2000; Eggert *et al*., 2004) and extremely low or high body mass index (BMI) (Rich-Edwards *et al*., 2002; Hassan and Killick 2004; Norman *et al*., 2004) have been proposed as causes of infertility. Consequences of infertility may include psychosocial problems (Greil, 1997; Boivin, 2003), higher risks of breast and ovarian cancer (Jensen *et al*., 2008) and high financial costs for those trying infertility treatment (Jain and Hornstein 2003). In addition, childlessness has been related to mortality disadvantages (Grundy and Kravdal, 2008). It is suggested that one-third of the incidences of couple infertility can be related to male reproductive problems (Meacham *et al*., 2007).

Reproductive dysfunction is reported to have a higher prevalence in athletes than non-athletes (Russell *et al*., 1984; Otis *et al*., 1997), with clinical consequences that may include infertility (Warren *et al*., 2001). Less is known about the effects of physical activity (PA) on female fertility in the general population, in contrast to the relatively well-known beneficial effects of regular PA for numerous undesirable health outcomes, including the prevention of premature death (Bouchard and Blair 1999; Warburton *et al*., 2006). Only a few studies have focused on the general population. In a cohort study, the Nurses' Health Study II, more hours of vigorous exercise were associated with reduced risk of ovulatory infertility (Rich-Edwards *et al*., 2002; Chavarro *et al*., 2007) while Morris *et al*. (2006) found that women who had enrolled on a fertility treatment programme and reported exercising 4 h or more per week for 1–9 years previously were 40% less likely to have a live birth, almost three times more likely to experience cycle cancellation, and twice as likely to have an implantation failure or pregnancy loss than women who had reported not exercising. More moderate exercise together with weight loss has been found to be positive in fertility treatment in obese women (Clark *et al*., 1995). The effect of PA on fertility may therefore be positive up to a certain level and have a negative effect above that threshold level of activity. A similar pattern is suggested for bone health: physically active individuals have been found to have a lower risk of low bone mineral density and fractures, while the risk of stress fractures is increased with high-volume training (Kohrt *et al*., 2004). This may occur through the direct effects of activity on hormones which stimulate bone formation or indirectly via effects on estrogen and menstrual function, a condition often coupled with negative energy availability in an interrelationship known as the female athlete triad (Nattiv *et al*., 2007).

PA plays an important role in maintaining energy balance and it has been suggested that changes in the status of energy balance due to changes in PA may affect the reproductive system (Redman, 2006). In addition, there are some indications that weight loss via PA may protect ovarian function by increasing insulin resistance and changing the hormone profile (Norman *et al*., 2004).

The purpose of this study is to evaluate the association between PA and fertility status and parity in healthy, premenopausal, Norwegian women.

Methods

All residents in the county of Nord-Trøndelag, Norway, men and women aged ≥20 years, were invited to participate in the Nord-Trøndelag Health Study in 1984–1986 (HUNT 1) and in the follow-up study in 1995–1997 (HUNT 2).

Among those eligible for HUNT 1, 77 310 (90.8%) returned a health-related questionnaire and 74 977 (88.1%) participated in the health examination. At the examination, participants filled out a second questionnaire, including questions regarding PA.

In HUNT 2, 71.3% of the original cohort from HUNT 1 participated. Participants were sent a comprehensive health-related questionnaire by mail. Assessments at the screening station included measurements of height and weight. At the examination, participants received a more detailed questionnaire evaluating demographics, medication use, diet, reproductive history, infertility, menstrual history, history of gynaecological surgery and pregnancy.

In total, 24 837 women participated in both surveys. Of those, 5986 women were <45 years old at HUNT 2, and therefore considered premenopausal. We excluded women who reported serious conditions or diagnoses known to affect capability for PA or reproductive function at baseline, as summarized in Fig. 1, leaving 3887 women in our study.

Weekly frequency, intensity and duration of leisure time PA was assessed using a self-reported questionnaire in HUNT 1 (http://www.ntnu.no/eksternwebEN/aboutntnu/facultiesanddepartments/dmf/HUNT/questionnaires/) (Table I). The questions regarding PA have been validated for men with good reliability and test and retest validity (Kurtze *et al*., 2008). Based on the reported intensity, duration and frequency, an index of PA was calculated: detailed descriptions are presented in previously published papers (Augestad *et al*., 2004; Augestad *et al*., 2006). With division at the 33.3th and 66.6th percentiles of the index, leisure time PA was categorized into low, moderate and high levels. Occupational PA was assessed by asking the women if they felt physically tired from occupational work (almost never, seldom, often, almost always). Age, education, marital status, smoking, and alcohol consumption were reported at baseline. BMI (kg/m^2) was computed from measured height and weight.

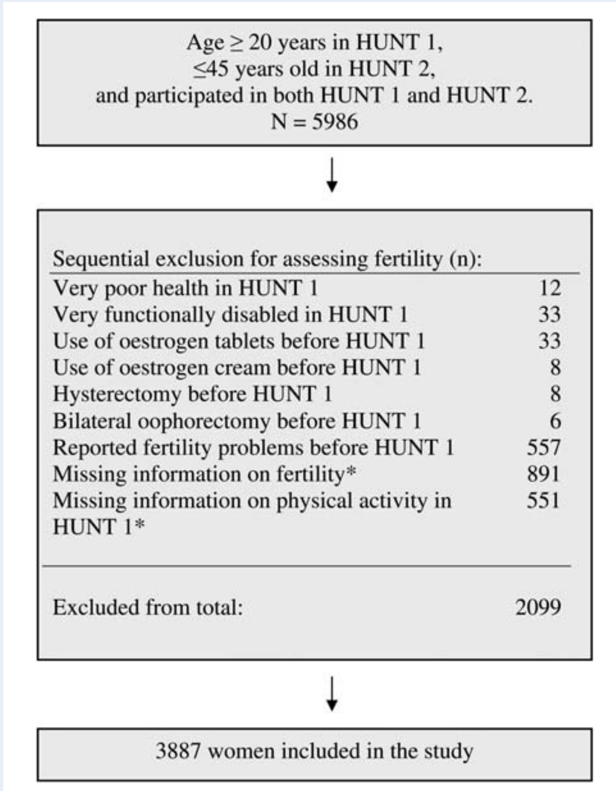

Figure 1 Sequential exclusion of participants in the study of physical activity and fertility. *No response to questions needed for classification.

Fertility status and reproductive history were assessed by a self-reported questionnaire in HUNT 2. Questions included inability to conceive within 1 year of trying (and at what age), parity, age at childbirth(s), contraceptive use and menstruation and pregnancy status.

We classified women as fertile if they conceived within 1 year of attempting to become pregnant and gave birth, and infertile if they did not conceive within 1 year, regardless of any subsequent pregnancies (Kumar *et al*., 2007). Infertile women were further classified as subfertile if the time to pregnancy exceeded 1 year of trying, and as involuntarily childless if they reported problems with conceiving within 1 year and there had been no childbirth. Voluntarily childlessness was assumed if neither problems with becoming pregnant nor childbirth were reported.

Fertility status and parity for different levels of baseline variables were compared using descriptive and chi-square statistics. We modelled the probability of fertility problems (subfertility or involuntary childlessness) using unadjusted and adjusted logistic regression. For infertility, odds ratio (ORs) estimates were obtained by maximum likelihood with associated 95% confidence intervals (CIs). We were concerned there might be some link between PA and age and therefore performed subgroup analyses for young women, <30 years of age, because of the higher prevalence of infertility in this group.

The associations of baseline measurements with parity were examined in women who were nulliparous in HUNT 1. Comparisons were made using ordinal regression models, adjusting for potential confounders. In these analyses parity was treated as a three-level variable: nulliparous, one to two children and more than two children.

Table I Baseline characteristics of the healthy Norwegian female study population

Characteristic	*n* within level	Fertile, 3511 (90.3%)	Subfertile, 197 (5.1%)	Involuntary childless, 27 (0.7%)	Voluntary childless, 152 (3.9%)	*P*-value
Age, *n*						
20–25 years	1247	1048 (84.0)	120 (9.6)	13 (1.0)	66 (5.3)	0.000
26–30 years	1632	1502 (92.0)	62 (3.8)	10 (0.6)	58 (3.6)	
31–35 years	1008	961 (95.3)	15 (1.5)	4 (0.4)	28 (2.8)	
BMI						
<18.5	151	132 (87.4)	10 (6.6)	1 (0.7)	8 (5.3)	0.001
18.5–24.9	3007	2743 (91.2)	138 (4.6)	24 (0.8)	102 (3.4)	
25–29.9	579	511 (88.3)	38 (6.6)	1 (0.2)	29 (5.0)	
30.0–34.9	114	98 (86.0)	7 (6.1)	0	9 (7.9)	
35.0<	31	22 (71.0)	4 (12.9)	1 (3.2)	4 (12.9)	
Frequency of PA						
Never	272	258 (94.9)	6 (2.2)	1 (0.4)	7 (2.6)	0.000
<1 per week	1252	1144 (91.4)	60 (4.8)	8 (0.6)	40 (3.2)	
1 per week	1210	1109 (91.7)	55 (4.5)	9 (0.7)	37 (3.1)	
2–3 per week	890	778 (87.4)	50 (5.6)	8 (0.9)	54 (6.1)	
Nearly every day	263	222 (84.4)	26 (9.9)	1 (0.4)	14 (5.3)	
Intensity of PA						
Take it easy	1418	1298 (91.5)	57 (4.0)	8 (0.6)	55 (3.9)	0.000
Lose breath	1363	1215 (89.1)	80 (5.9)	11 (0.8)	57 (4.2)	
To exhaustion	94	76 (80.9)	14 (14.9)	0 (0.0)	4 (4.2)	
Duration of PA						
<15 min	440	403 (91.6)	24 (5.5)	2 (0.5)	11 (2.5)	0.001
15–30 min	937	860 (91.8)	30 (3.2)	5 (0.5)	42 (4.5)	
30–60 min	1261	1124 (89.1)	71 (5.6)	12 (1.0)	54 (4.3)	
>60 min	305	260 (85.2)	30 (9.8)	0 (0.0)	15 (4.9)	
PA index						
Low	989	916 (92.6)	38 (3.8)	5 (0.5)	30 (3.0)	0.000
Moderate	968	885 (91.4)	39 (4.0)	7 (0.7)	37 (3.8)	
High	880	752 (85.5)	72 (8.2)	7 (0.8)	49 (5.6)	
Physically tired from work						
Never	432	380 (88.0)	22 (5.1)	3 (0.7)	27 (6.2)	0.097
Seldom	1546	1413 (91.4)	74 (4.8)	11 (0.7)	48 (3.1)	
Often	1365	1261 (92.4)	54 (4.0)	5 (0.4)	45 (3.3)	
Almost always	268	246 (91.8)	13 (4.9)	2 (0.7)	7 (2.6)	
Smoking						
Never	1563	1388 (88.8)	73 (4.7)	12 (0.8)	90 (5.8)	0.001
Former	761	703 (92.4)	37 (4.9)	4 (0.5)	17 (2.2)	
Current	1549	1409 (91.0)	85 (5.5)	11 (0.7)	44 (2.8)	
Alcohol consumption prev. 14 days						
Never	2038	1857 (91.1)	88 (4.3)	80 (3.9)	13 (0.6)	0.170
1–4 times	1746	1560 (89.3)	102 (5.8)	71 (4.1)	13 (0.6)	
5–10 times	35	30 (85.7)	4 (11.4)	0	1 (2.9)	
>10 times	55	52 (94.5)	2 (3.6)	1 (1.8)	0	
Marital status						
Unmarried	1352	1056 (78.1)	134 (9.9)	22 (1.6)	140 (10.4)	0.000
Married	2377	2312 (97.3)	53 (2.2)	5 (0.2)	7 (0.3)	
Previously married	97	90 (92.8)	7 (7.2)	0 (0.0)	0 (0.0)	

Continued

Table I Continued

Characteristic	*n* within level	Fertile, 3511 (90.3%)	Subfertile, 197 (5.1%)	Involuntary childless, 27 (0.7%)	Voluntary childless, 152 (3.9%)	*P*-value
Education						
<10 years	1090	1021 (93.7)	33 (3.0)	6 (0.6)	30 (2.8)	0.000
10–12 years	2258	2024 (89.6)	132 (5.8)	15 (0.7)	87 (3.9)	
>12 years	510	442 (86.7)	31 (6.1)	5 (1.0)	32 (6.3)	
Parity						
0	786	510 (64.9)	97 (12.3)	27 (3.4)	152 (19.3)	0.000
1≤	3095	2995 (96.8)	100 (3.2)			

PA, physical activity. Fertility status based on self-reported problems with conceiving within 1 year and childbirths at follow-up. *P*-values indicate results of the Pearson's chi-square test. *n* (%).

In all of the above analyses, models were run separately for each of the PA variables (frequency, intensity, duration and index). Full multivariate models were run at first. Variables were subsequently removed from the models if their removal did not affect the coefficient estimates of the remaining variables in the model or the overall significance of the model.

Based primarily on *a priori* considerations, we considered the following baseline measurements as potential confounders: age (5-year categories), parity, i.e. when assessing the probability of infertility (nulliparous, not nulliparous) (Sternfeld *et al*., 1999; Miller *et al*., 2002), smoking (never, former, current), frequency of alcohol consumption during the 14 days prior to participation in the study (never, 1–4 times, 5–10 times, >10 times) marital status (unmarried, married, previously married) and education (<10, 10–12, >12 years).

Women with an unusually high or low BMI tend to have greater risk of infertility. Because women with high or low BMI may be either less likely or more likely to be physically active, baseline BMI may be considered a potential confounder of the relationship between PA and fertility. However, BMI might also be considered an intermediate variable in that PA could affect BMI and, in turn, fertility status. We therefore did not include BMI as an independent variable in the primary (*a priori*) analyses, because its inclusion might have biased the estimated association between PA and fertility status. However, to assess whether inclusion of BMI affected the estimated association with fertility status, we also conducted additional (sensitivity) analyses that included this variable, treating it as categorical (World Health Organization categorization of under-, normal- and overweight, obesity and severe obesity) at baseline. Statistical significance was set at $P < 0.05$.

The study was approved by the Norwegian Regional Committee for Ethics in Medical Research and the Norwegian Data Inspectorate and each subject gave written informed consent prior to participation.

Results

Baseline characteristics and their bivariate relations to fertility status at follow-up are shown in Table I. The mean baseline age was 27.2 years (range 20–35) and mean BMI was 22.7 kg/m^2 (range 14.5–44.1). Overall, 90.1% of the women were classified as fertile, 5.1% as subfertile, 0.7% as involuntary childless and 3.9% as voluntary childless. A total of 62.4% of infertile women reported having visited a medical doctor for fertility problems.

The frequency of subfertility decreased with increased age, as did voluntary childlessness. The relationships of BMI categories with subfertility and voluntary and involuntary childlessness were approximately J-shaped, and subfertility was least common in the normal weight group (BMI: 18.5–24.9). Based on the univariate analyses, women classified as fertile were more often married and had less than 10 years of education. Voluntarily childless women were more often unmarried, non-smokers, with more than 12 years of education. Subfertility was least common among married women (Table I).

Increased frequency of PA was associated with increased subfertility and voluntary childlessness. A similar relationship was observed between intensity and longer duration of PA and subfertility but less so with voluntary childlessness. In the unadjusted analyses, a high level of PA, according to our calculated index, was associated with increased subfertility and voluntary childlessness. Due to missing answers however, the PA index could not be calculated for just over 1000 women. Tiredness from occupational activity was not found to be associated with fertility status (Table I).

The observed relationships between PA variables and fertility status followed the same trend as those reported above, after controlling for suspected confounding factors: age, parity, smoking and marital status (Table II). Additional control for education and alcohol consumption did not meaningfully affect the ORs. In particular, women who were active on most days of the week were 3.2 times more likely to be infertile than inactive women. Exercising to exhaustion was associated with 2.3 times the odds of infertility compared with lower levels of intensity. For duration, there was decreased risk of infertility in those whose exercise was moderate (16–30 and 30–60 min) compared with the shortest duration of less than 15 min. Women who, according to the index of PA, were highly active had an OR of 1.5 for infertility compared women with low or moderate levels of activity.

The alternative analysis, designed to assess the sensitivity of results to alternative models, in which we included BMI as a potential confounding factor, did not result in notably different parameter estimates, consistent with the small differences in BMI across the groups in the PA variables.

In a subgroup analysis restricted to women up to 30 years of age in whom subfertility was more common (6.3%) than in the older age group (1.5%), we found that these younger women were more likely than older women to exercise every day, exercise to exhaustion or exercise for more than 60 min. Among the young women, subfertility was reported by 23.7% of those exercising to the level of exhaustion and by 11.1% of those who reported exercising almost every day.

Table II Unadjusted and adjusted ORs from logistic regression for fertility problems (subfertility or involuntary childlessness)

PA	Unadjusted OR (95% CI)	Adjusted OR# (95% CI)
Frequency		
Never*	1.0	1.0
<Once a week	2.2 (1.0–4.8)	2.1 (0.9–4.7)
Once a week	2.1 (1.0–4.7)	2.0 (0.9–4.5)
2–3 times a week	2.6 (1.2–5.9)	2.0 (0.9–4.6)
Almost every day	4.3 (1.9–10.1)	3.2 (1.3–7.6)
Intensity		
Easy*	1.0	1.0
Sweating and out of breath	1.3 (1.1–1.9)	1.1 (0.8–1.6)
Exhaustion	3.3 (1.8–6.2)	2.3 (1.2.–4.5)
Duration		
<15 min*	1.0	1.0
16–30 min	0.3 (0.2–0.6)	0.3 (0.2–0.5)
30–60 min	0.6 (0.3–1.0)	0.5 (0.3.–0.9)
>60 min	0.9 (0.5–1.6)	0.6 (0.3–1.2)
PA index		
Low*	1.0	1.0
Medium	1.0 (0.7–1.7)	0.9 (0.6–1.5)
High	2.1 (1.5–3.2)	1.5 (1.0–2.3)

PA, physical activity.
#Adjusted for age, parity, smoking and marital status.
*Reference category OR, odds ratio; CI, confidence interval.

In this subgroup there was a u-shaped relationship between duration of exercise and subfertility. Among women who reported <15 min or >60 min duration, the frequency of subfertility was 12.6 and 12.4%, respectively, while 3.9% of women exercising for 16–30 min and 7.0% of those exercising for 30–60 min reported subfertility.

In this subgroup, adjusted logistic analysis showed similar but somewhat stronger relationships than in the study group as a whole. The OR for infertility was 3.5 (CI: 1.3–9.0) for women who exercised almost every day and women who exercised to the level of exhaustion had 3.0 (CI: 1.3–6.0) times the risk of infertility compared with those taking it easy. The trend between the calculated index of PA, occupational activity or other variables did not differ meaningfully from patterns observed in the analyses that included all age groups.

Women who were nulliparous at baseline were significantly younger than women who had given birth (24.0 versus 26.5; $P < 0.001$). They had higher occurrence of frequent PA, higher intensity and longer duration of activity ($P < 0.001$ for all). Nulliparous women were less likely to feel tired from occupational activity. They had higher education at baseline, and were more likely to be non-smokers and unmarried than women who had given birth ($P < 0.001$ for all). The two groups did not differ on baseline BMI.

For women who were nulliparous at baseline, the mean number of children born between baseline and follow-up investigations was 1.5 (range 0–4). A total of 179 women were still nulliparous at follow-up, of whom 152 (84.9%) reported voluntary childlessness. In descriptive analyses of this group, continued nulliparity at follow-up was associated with greater age and with lower or higher than normal BMI. Parity during follow-up was also related to education. However, it should be noted that at baseline, 93.7% of women with <10 years education had already given birth (Table I). For women who had not given birth at baseline, we found similar ORs of infertility as for the whole sample but the 95% CIs were larger and included 1 in all instances (data not shown).

Women who reported the highest intensity of PA at baseline had the lowest frequency of continuing nulliparity and highest frequency of having three or more children during follow-up ($P < 0.05$). In the unadjusted analysis, there was also a tendency towards less continuing nulliparity and higher parity among those women with longer durations of PA and higher scores on the PA index (Table III).

There was a significant tendency towards higher parity among women with the highest intensity of PA compared with moderate intensity in an ordinal regression analysis, adjusting for age and education. Women reporting low intensity of activity did not significantly differ from the high intensity group. The model was subsequently run including BMI but no meaningful changes to the parameter estimates were observed. In another subgroup analysis excluding those women who were voluntarily childless in HUNT 2, although the direction of this association was the same, the relationship was no longer significant ($P = 0.07$).

Frequency of PA or tiredness from occupational activity was not related to parity.

Discussion

In this study we examined the association between PA and fertility status and parity in healthy premenopausal Norwegian women. We found that women with the highest levels of frequency or intensity of PA had increased risk of infertility. We did not, however, see a trend for increased risk of infertility for the submaximal levels of intensity or frequency of PA. Moreover, the highest level of our index of PA, indicating the total load of exercise, was related to increased likelihood of infertility in adjusted analyses. There was decreased risk of infertility for women reporting moderate duration of activity in our adjusted analyses, compared with women reporting activity duration of less than 15 min. Our estimate of 5.8% prevalence of infertility is somewhat lower than earlier reports from the same study population in which lifetime infertility prevalence has been estimated to be 6.6% (Rostad *et al.*, 2006). The women in our sample were younger than in the Rostad *et al.* (2006) study and some may still experience infertility in their remaining reproductive years.

Although we showed that high intensity of PA was related to increased risk of infertility, there was also a trend of having three or more children during the follow-up period among women who reported the highest level of PA intensity at baseline. A possible explanation may be that women who did high intensity training at baseline and experienced infertility problems adjusted their activity level to a lower intensity level. Alternatively, although if intense PA had a negative effect on the first trial for conception, hormonal changes during and following pregnancy may have counteracted that negative effect in later pregnancies. The likelihood of fertility problems in our study was, however, not notably different for nullipara women compared with those who had already given birth. This may suggest that the

Table III Baseline characteristics of women who were nulliparous at baseline (*n* = 786)

		No childbirth, 179 (22.8)	1–2 children, 458 (58.3)	3 or more children, 149 (19.0)	*P*-value
Age					
20–25 years	561	79 (14.1)	358 (63.8)	124 (22.1)	0.000
26–30 years	179	68 (38.0)	88 (49.2)	23 (12.8)	
31–35 years	46	32 (69.6)	12 (26.1)	2 (4.3)	
BMI					
<18.5	31	9 (29.0)	16 (51.6)	6 (19.4)	0.005
18.5–24.9	616	126 (20.5)	371 (60.2)	119 (19.3)	
25–29.9	113	30 (26.5)	59 (52.2)	24 (21.2)	
30.0–34.9	15	9 (60.0)	6 (40.0)	0	
35.0<	9	5 (55.6)	4 (44.4)	0	
Frequency of PA					
Never	38	8 (21.1)	27 (71.1)	3 (7.9)	0.668
<1 per week	200	48 (24.0)	114 (57.0)	38 (19.0)	
1 per week	216	46 (21.3)	126 (58.3)	44 (20.4)	
2–3 per week	255	62 (24.3)	142 (55.7)	51 (20.0)	
Nearly every day	77	15 (19.5)	49 (63.6)	13 (16.9)	
Intensity of PA					
Take it easy	222	63 (28.4)	125 (56.3)	34 (15.3)	0.013
Lose breath	361	68 (18.8)	224 (62.0)	69 (19.1)	
To exhaustion	30	4 (13.3)	16 (53.3)	10 (33.3)	
Duration of PA					
<15 min	67	13 (19.4)	46 (68.7)	8 (11.9)	0.151
15–30 min	187	47 (25.1)	101 (54.0)	39 (20.9)	
30–60 min	283	66 (23.3)	169 (59.7)	48 (17.0)	
>60 min	97	15 (15.5)	58 (59.8)	24 (24.7)	
PA index					
Low	131	35 (26.7)	80 (61.1)	16 (12.2)	0.256
Moderate	204	44 (21.6)	121 (59.3)	39 (19.1)	
High	276	56 (20.3)	163 (59.1)	57 (20.7)	
Physically tired from work					
Never	120	30 (25.0)	75 (62.5)	15 (12.5)	0.459
Seldom	242	59 (24.4)	138 (57.0)	45 (18.6)	
Often	227	50 (22.0)	130 (57.3)	47 (20.7)	
Almost always	47	9 (19.1)	32 (68.1)	6 (12.8)	
Smoking					
Never	411	102 (24.8)	220 (53.5)	89 (21.7)	0.030
Former	108	21 (19.4)	64 (59.3)	23 (21.3)	
Current	264	55 (20.8)	172 (65.2)	37 (14.0)	
Alcohol consumption prev. 14 days					
Never	334	93 (27.8)	183 (54.8)	58 (17.4)	0.044
1–4 times	422	84 (19.9)	252 (59.7)	86 (20.4)	
5–10 times	15	1 (6.7)	13 (86.7)	1 (6.7)	
>10 times	10	1 (10.0)	7 (70.0)	2 (20.0)	
Marital status					
Unmarried	717	162 (22.6)	417 (58.2)	138 (19.2)	0.500
Married	40	12 (30.0)	21 (52.5)	7 (17.5)	

Continued

Table III *Continued*

		No childbirth, 179 (22.8)	1–2 children, 458 (58.3)	3 or more children, 149 (19.0)	*P*-value
Education					
<10 years	82	36 (43.9)	39 (47.6)	7 (8.5)	0.000
10–12 years	555	102 (18.4)	341 (61.4)	112 (20.2)	
>12 years	140	37 (26.4)	76 (54.3)	27 (19.3)	

PA, physical activity. Childbirths during follow-up reported in questionnaire. *P*-values indicate results of the Pearson's chi-square test. *n*(%).

possible detrimental effects of high intensity exercise are reversible and not permanent. Unfortunately, our data did not allow further consideration of this matter.

There have only been a few studies regarding the effect of PA on fertility status and parity in the general female population. Our results are somewhat comparable to results of a retrospective case–control study which found a 6.2-fold increased risk of infertility in women who exercised vigorously (defined as aerobic activities with estimated energy requirements of 6 kcal/min) for at least 60 min per day (Green *et al*., 1986). There are also reports of lutheal phase alterations, which may lead to infertility, among recreational runners with at least 2 h per week of exercise and running 32 km/week (De Souza *et al*., 2003). The recreational runners in the De Souze study had lower BMI and fat mass than sedentary controls and the results were related to short-term negative energy balance and hypometabolic state, similar to but not as extensive as seen in amenorrheaic athletes.

Results from the Nurse's Health Study indicate reduced risk of ovulatory infertility in women doing vigorous exercise for at least 30 min daily (Chavarro *et al*., 2007). An earlier report of the same cohort indicated a 7% relative risk reduction for ovulatory infertility for each additional hour of vigorous exercise per week (Rich-Edwards *et al*., 2002). Thus, there is a considerable divergence in study results. The mean age in our study group was approximately 5 years lower than in the women in the Nurse's Health Study and this may explain the difference in results to some extent, as we found younger women more likely to report both highest intensity of PA and infertility than older ones.

PA can improve body composition, glucose homeostasis and insulin sensitivity (Warburton *et al*., 2006). Exercise-induced weight loss has been shown to improve metabolic function and hormonal profiles, and often leads to significant increase in fertility (Clark *et al*., 1995; Norman *et al*., 2004). In our study, adjustment for BMI did not significantly alter the increased risk of infertility associated with the highest intensity or frequency of activity. Thus, the effect of PA may largely act through a mechanism that does not involve BMI to a significant extent.

It is possible that in normal weight women, high loads of exercise, not coupled with increased energy intake, lead to negative energy balance where the energy requirements of reproductive functions cannot be met (Loucks *et al*., 1998). This may explain our finding of increased infertility risk among women doing high intensity training or very frequent exercise sessions.

Our study is population based, not depending on cases seeking help from a clinic, and can be viewed as a cohort study. The prospective assessment of the effect of baseline PA on subsequent fertility problems hopefully contributes to avoiding selection bias of cases and reporting bias of activity levels. However, there were possible limitations. We did not try to identify different causes of infertility with biological testing but focused on the overall occurrence in the population and this may have biased our results. Green *et al*. (1986) found that among infertile women who had never conceived, high intensity exercise for more than 60 min/day was associated with even higher risk of infertility after excluding cases with evidence of tubal dysfunction. Differences in measurement methods for infertility may contribute to differences in results, to some extent. Also, not all women who participated in the baseline survey did so in the follow-up survey. If non-participation at follow-up was jointly associated with PA and infertility, bias may have resulted. Many women did not answer questions regarding fertility status and we cannot exclude the possibility that those women differed from women who did answer; this could have affected our results. Our analysis found, however, that women who did not answer questions regarding fertility status in the follow-up study had somewhat lower intensity and duration of PA at baseline than women who did answer those questions, although this difference was not statistically significant. Because data on fertility status were collected retrospectively, recall bias may have occurred. Nevertheless, since fertility status is of high personal interest, precise recollection of its aspects may be likely. Other sources of bias may have been spousal infertility and change of partner, which we could not control for in our data.

PA may affect fertility merely temporary or more permanently in the reproductive life, but our study did not obtain information at the time when women tried to conceive. Although we excluded women who reported infertility at baseline we cannot be certain whether the level of PA reported at baseline was maintained until trying to conceive.

In epidemiological studies, the intensity of PA can be assessed as absolute or relative intensity. Metabolic equivalent task is frequently used to refer to absolute intensity indicating the energy cost of an activity. PA-related energy expenditure has been associated with morbidity and mortality (Helmrich *et al*., 1994; Manini *et al*., 2006; Mora *et al*., 2007). Besides being an important determinant of health, data on energy expenditure also facilitate study result comparisons and interpretation of findings into meaningful units, although misreporting errors have been observed (Mahabir *et al*., 2006). Relative intensity can be described by use of the Borg scale (Borg, 1982) or other measures of how intense the exercise is perceived by each subject. In the current study, information regarding PA was based on a self-reported questionnaire that allowed for subjective interpretation of PA variables. It may therefore suffer from misclassification of activity by factors such as age, social situations and seasonal variation (Vanhees *et al*., 2005). Including a large number of study subjects and classifying subjects into wide categories, e.g. low, moderate, high score on activity can compensate for the effects of misclassification (Shephard, 2003). The questions regarding intensity and duration of PA in the current study have previously been validated in a small sample of women and men over a wide age range (Wisloff *et al*., 2006). The results indicate a positive association between reported intensity and the measures of oxygen uptake during exercise. Taking it easy corresponded to an intensity of approximately 55% of the maximal oxygen uptake, independent of activity duration up to 90 min. Intensity descriptions of loosing breath and exercising to the level of exhaustion corresponded to 71–75 and 76–90%, respectively, of the maximum oxygen uptake. Relative intensity decreased when duration of exercise was increased. A study of reliability and validity of the questions including only men found good reliability and kappa statistics of 0.69–0.82 between test and retest (Kurtze *et al*., 2008), although these results are not necessarily valid for women. It seems likely that any measurement error in the assessment of PA should not depend on fertility status and would tend to bias results toward the null. In our study, there were many missing responses on both PA and fertility. For instance, our PA index could not be calculated for just over 1000 women in our study sample. In summary, we found that women who were active on most days of the week had a threefold risk of infertility compared with inactive women. The increased risk of infertility was only found for the most extreme intensity and frequency of PA, perhaps representing women who exercised at levels comparable to elite athletes. While we did not find any associations between lower levels of activity and fertility status or parity, other studies have found regular moderate PA to improve reproductive function. It could therefore be suggested that moderate PA has little or perhaps even a positive direct effect on fertility. This should undoubtedly be confirmed, as it may possibly affect fertility by other means than biological, for example via positive effects on self-esteem and improved mental health. Psychosocial interventions, particularly those emphasizing skills training, such as relaxation training, have been found effective in infertility treatment (Boivin 2003) and the positive psychological effects of regular PA on mental well-being have been reported in numerous studies (Scully *et al*., 1998; Kull 2002). Results on the association between high levels of PA and fertility status are conflicting. We found increased risk of infertility in women who reported doing PA almost every day and in those reporting exercising to the level of exhaustion. Although it cannot be concluded from this study, it seems likely that fertility may be positively affected by PA up to a certain level after which the energy requirements of the activity outweigh the positive effects, resulting in infertility. It is also possible that this threshold level applies merely at an individual level, perhaps in combination with energy availability, and cannot be identified at the population level.

The potential role of regular PA in the prevention and treatment of infertility needs further investigation. However, awareness of the possible risks of infertility should be highlighted among non-athletic women who exercise vigorously.

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