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Maternal physical and sedentary activities in relation to reproductive outcomes following IVF

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Abstract

Physical activity could benefit reproductive function through its ability to regulate energy balance and improve insulin sensitivity, but its association with IVF outcomes remains unclear. The aim of this study was to evaluate whether pre-treatment physical and sedentary activity is associated with outcomes of IVF. The Environment and Reproductive Health Study is an ongoing prospective cohort study that enrols subfertile couples at Massachusetts General Hospital Fertility Center. Time spent in physical and sedentary activities in the year before IVF treatment is self-reported using a validated questionnaire. This analysis included 273 women who underwent 427 IVF cycles. Women engaged in a median of 2.8 h per week of moderate-to-vigorous activities. Time spent in moderate-to-vigorous physical activities and total metabolic equivalent task hours before IVF were not associated with probability of implantation, clinical pregnancy or live birth. Of the specific physical activities, only greater time spent in aerobics, rowing, and on the ski or stair machine was associated with higher probability of live birth. Time spent in total and specific

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sedentary activities were not associated with clinical outcomes of IVF. Physical activity is unlikely to have a deleterious effect on IVF success and certain forms of vigorous activity may be beneficial.

Keywords

physical activity; sedentary activity; assisted reproductive technology; in vitro fertilization

Introduction

Physical activity is generally considered to be a health-promoting behaviour as it is associated with reduced risks of cardiovascular disease, diabetes and several cancers in women (Brown *et al.*, 2007). Despite widespread consensus of the importance of physical activity for health, debate continues on the association between physical activity and fertility. Biologically, physical activity can benefit reproductive function through its ability to regulate energy balance and improve insulin sensitivity; however, when energy demand exceeds dietary energy intake, a negative energy balance may occur and may result in hypothalamic dysfunction (Warren and Perlroth, 2001).

Competitive athletes tend to have a higher prevalence of reproductive dysfunction compared with non-athletes, with clinical consequences that may include infertility (Otis *et al.*, 1997; Warren and Perlroth, 2001). Yet, the few studies that have focused on the effect of more moderate physical activity on fertility in the general population have produced mixed results. Data from the Nurses' Health Study II suggest that greater hours of vigorous activity may reduce ovulatory infertility (Rich-Edwards *et al.*, 2002), whereas those from a Norwegian cohort suggest that high intensity and frequency of physical activity increase subfertility (Gudmundsdottir *et al.*, 2009). In a study of physical activity and time to pregnancy, a dose–response relationship was found between increasing vigorous physical activity and delayed time to pregnancy (in all women except those that were overweight and obese), whereas moderate physical activity was associated with a small increase in fecundability regardless of body mass index (BMI) (Wise *et al.*, 2012).

Results from studies specifically on female physical activity and infertility treatment success are equally as mixed. In the first study (Morris *et al.*, 2006), women undergoing infertility treatment who engaged in physical activity for 4 h or more per week for less than 10 years had a 40% reduced likelihood of live birth compared with women not regularly engaged in physical activity. The second study found that moderate physical activity during assisted reproductive technology treatment was associated with higher implantation and live birth rates; however, activity levels before treatment were not associated with clinical outcomes (Kucuk *et al.*, 2010). A third study (Moran *et al.*, 2011), a small trial that randomized overweight women to a lifestyle intervention, including a reduced energy diet and a home-based physical conditioning and walking programme before IVF, observed no differences in pregnancies or live births compared with a group receiving standard treatment. Finally, the two most recent cohort studies showed that regular physical activity carried out before an assisted reproduction cycle was related to improved live birth rates in a cohort of obese patients (Palomba *et al*., 2014) and improved clinical pregnancy rates in a general IVF population (Evenson *et al*., 2014).

The objective of the present study was to investigate pre-treatment physical activity in relation to success of assisted reproduction in a prospective cohort of women undergoing IVF in the USA. We sought to expand on previous studies by investigating the relationship between specific physical and sedentary activities, using a validated assessment tool, with clinical outcomes of infertility treatment in an IVF population with extensive covariate information.

Materials and methods

Study population

Participants were women enroled in the Environment and Reproductive Health (EARTH) Study, an ongoing prospective cohort started in 2006 aimed at identifying determinants of fertility among couples presenting to the Massachusetts General Hospital Fertility Center, Boston, USA. All women who meet eligibility requirements (age 18–46 years and no planned use of donor gametes at enrolment) are invited to participate in the study. About 55% of those referred by physicians ultimately enrol in the study; however, among referred women who research nurses are able to contact, 78% enrol in the study. For this analysis, women were eligible if they had completed at least one IVF cycle by May 2013 (n = 316). Of these, 30 women (9%) were excluded owing to missing physical activity assessment and 13 women (4%) were excluded because they had started their IVF cycle before physical activity assessment. Women missing physical activity assessments were more likely to have IVF cycles cancelled, i.e. low response to treatment or no fertilization, before embryo transfer (26.7% versus 10.1%). All other characteristics were similar to the women included in our analysis. After all exclusions, 273 women contributed a total of 427 IVF cycles. The median (25th percentile, 75th percentile) time between filling out the physical activity assessment and starting an IVF cycle was 157 (70,296) days.

At enrolment, height and weight were measured by a research nurse, from which BMI (kg/m^2) was calculated. Participants also completed a detailed take-home questionnaire focused on lifestyle, medical, and reproductive history. Self-perceived life stress was assessed with four questions on the baseline questionnaire. Each question had five options for response ranging from ‘never’ (0) to ‘very often’ (4). A summary stress score was created by summing across the four questions (range: 0–16). A trained research nurse abstracted clinical information, including infertility diagnosis and treatment protocols, from electronic medical records. The Institutional Review Boards of Massachusetts General Hospital and the Harvard TH Chan School of Public Health approved the study on 5th March 2015 (reference number 1999P008167/MGH). All participants provided written informed consent after a research nurse explained study procedures.

Physical and sedentary activity

Time spent in leisure time physical and sedentary activities was assessed using a validated questionnaire (Wolf *et al*., 1994). Women reported the average time per week during the preceding year spent on any of the following activities: walking, jogging, running, biking, swimming, tennis, squash, weightlifting, aerobics or aerobic exercise equipment, and moderate (e.g. yard work, gardening) and heavy (e.g. digging, chopping) outdoor work. Women also reported the average time per week during the preceding year spent sitting at work, while driving and at home. Each activity question had 13 categories for response ranging from 'never' to '40+ hours per week'. The duration of activity was assigned using the median value for each category. Total physical and sedentary activity (h/week) was calculated by summing across all physical and sedentary activities. Moderate-to-vigorous activity (h/week) was calculated by summing time spent in all physical activities except walking. Vigorous activity included jogging, running, bicycling, swimming, tennis or squash, aerobics or aerobic exercise equipment, and heavy outdoor work. Total metabolic equivalents (h/week) were calculated by multiplying the average metabolic equivalents level of a given activity by its reported duration and summing across all physical activities (Ainsworth *et al.*, 2000). The validity and reproducibility of this questionnaire was assessed in a different cohort by comparison against four 7-day activity recalls collected over the course of 1 year and an identical questionnaire administered a year later (Wolf *et al.*, 1994). The Spearman correlation for total physical activity was 0.79 and for total sedentary activity was 0.41 compared with the activity recalls. The reproducibility coefficient for total physical activity was 0.59 and for total sedentary activity was 0.52, suggesting that physical and sedentary activity is generally stable within a person over time.

Clinical outcomes

Women underwent assisted reproduction techiques via IVF with either conventional insemination or intracytoplasmic sperm injection, as clinically indicated. Implantation was defined as a serum beta HCG level greater than 6 mIU/ml typically measured 17 days (range 15–20 days) after egg retrieval, clinical pregnancy as the presence of an intrauterine pregnancy confirmed by ultrasound at 6 weeks, and live birth as the birth of a neonate on or after 24 weeks gestation.

Statistical analysis

Women were classified into quintiles based on time spent in moderate-to-vigorous and sedentary activities and calculated descriptive statistics for demographic, reproductive and lifestyle characteristics according to quintile of activity. Fisher's exact test, chi-squared test, and Kruskal–Wallis test were used, as appropriate, to test for associations across quintiles. Multivariable generalized linear mixed models with random intercepts were used to evaluate the relationship between physical and sedentary activities and IVF outcomes. These models allowed the inclusion of multiple IVF cycles per woman while accounting for the within-person correlations in IVF treatment outcomes. A binomial distribution and logit link function were specified for the clinical outcomes. Tests for trend across quintiles were conducted using a variable with the median activity level in each quintile as a continuous variable. Physical activity was also evaluated as continuous linear and quadratic variable. All results are presented as population marginal means, adjusted for covariates. Population marginal means can be interpreted as the mean probability of implantation, clinical pregnancy and live birth per quintile of exposure for the average women in our cohort.

Confounding was evaluated using prior knowledge and descriptive statistics from the cohort through the use of directed acyclic graphs. Variables retained in the final model included age, BMI, race, infertility diagnosis and education level. All models were additionally run without adjusting for BMI and infertility diagnosis as we hypothesized these variables to be potential mediators as well as possible confounders of the associations. Effect modification by age, smoking status, initial infertility diagnosis and fertilization type, e.g. intracytoplasmic sperm injection versus traditional insemination, were tested using cross-product terms in the final multivariate models. Of specific interest was effect modification by BMI which we chose to define as BMI 18.5–24.9 versus 25 kg/m^2 or over based on previous literature (Rich-Edwards *et al.*, 2002; Wise *et al.*, 2010). Underweight women (n = 6) were excluded from the normal BMI group, as these women had substantially higher physical activity levels than women with a BMI 18.5–24.9 kg/m^2. Numbers of underweight (six women, 10 IVF cycles) and obese (29 women, 53 IVF cycles) women were insufficient to warrant separate investigation. SAS version 9.4 (SAS Institute, Cary, NC, USA) and a significance threshold of $P < 0.05$ was used for all statistical analyses.

Results

Women in this cohort had mean (standard deviation) age of 35.3 (3.9) years and BMI of 24.0 (4.2) kg/m^2. They engaged in a median (interquartile range) of 2.8 (1.0, 6.0) h/week of moderate-to-vigorous activities and 49.0 (36.0, 62.5) h/week of sedentary activities. Most were white (82%), never smokers (71%), and had a graduate degree (59%). Time spent in moderate-to-vigorous activities and sedentary activities were not correlated ($r_{Spearman}$= 0.08). Level of moderate-to-vigorous physical activity was related to initial infertility diagnosis ($P = 0.04$) (Table 1). Specifically, women in the highest quintile of physical activity were more likely to be diagnosed with an ovulation disorder (13%) or diminished ovarian reserve (16.7%) compared with women in the lowest quintile (3.7% and 11.1%, respectively). All other demographic and reproductive characteristics were similar across quintiles of physical and sedentary activity. Most physical activity was contributed from walking (38%), followed by other activities, e.g. yoga (14%), outdoor activities (12%), running and jogging (12%), weightlifting (8%), aerobics and aerobic exercise equipment (8%), biking (6%), swimming laps (1%) and playing tennis or squash (<1%).

Greater time spent in physical and sedentary activity was unrelated to probability of implantation, clinical pregnancy or live birth after multivariable adjustment (Table 2). For instance, the adjusted difference (95% CI) in the proportion of cycles resulting in live birth comparing women in the 5th versus 1st quintile was 0.11 (−0.02 to 0.22) for total physical activity, 0.03 (−0.09 to 0.15) for moderate-to-vigorous activity, and 0.04 (−0.09 to 0.16) for sedentary activity. Results were consistent regardless of how physical activity was defined. This association was similar when BMI and infertility diagnosis was excluded from the multivariable model. No associations were found when total time spent in physical or sedentary activities was analysed on a continuous level.

When specific physical activities were evaluated, only greater time spent in aerobics, rowing and on the ski or stair machine was significantly associated with higher probability of live birth (Table 3). Specifically, women who engaged in 1.5 h or more a week in those activities had an adjusted difference (95% CI) in proportion of cycles resulting in live birth of 0.16 (95% CI 0.03 to 0.29) compared with women who engaged in 0 hours per week of these activities (*P*-trend = 0.02). Of the sedentary activities, greater time spent sitting at the home was marginally associated with higher probability of live birth (*P*-trend = 0.06) (Table 4); however this association was not statistically significant. All other specific activities, e.g. time spent sitting at work and in the car, were not significantly associated with probability of live birth after IVF.

Evidence was lacking of effect modification of the physical activity and live birth association by age, smoking status, initial infertility diagnosis or insemination method (data not shown). A significant heterogeneity, however, was found in the effect of moderate-to-vigorous and vigorous physical activity on probability of live birth by BMI (*P*-interaction = 0.03 and 0.04, respectively). although vigorous activity was not associated with probability of live birth in overweight or obese women (*P*-trend = 0.23), vigorous activity was positively associated with probability of live birth in women of normal BMI (18.5–24.9 k/m^2) (*P* = 0.02) (Supplementary Table). Specifically, the adjusted proportion of cycles resulting in live birth was 0.49 (95% CI 0.31 to 0.67) for women of normal BMI who exercised vigorously for 4.5 h or more per week compared with 0.32 (95% CI 0.20 to 0.47) for women of normal BMI who did not exercise vigorously. Results were similar after restricting to cycles started within 1 year of physical activity assessment (*n* = 366) and the first IVF cycles per woman (*n* = 273) (data not shown).

Discussion

In this prospective cohort of women undergoing IVF, time spent in physical activities in the year before starting fertility treatment was not significantly associated with probability of implantation, clinical pregnancy or live birth. When specific physical activities were examined, only greater time spent in aerobics, rowing and on the ski or stair machine was significantly associated with higher probability of live birth. Although greater time spent sitting at the home was marginally associated with higher probability of live birth, this association was not statistically significant. Total time spent in sedentary activities was not associated with IVF outcomes.

Results of previous studies on physical activity and outcomes of assisted reproduction have been inconsistent, with two studies finding a beneficial effect (Evenson *et al.*, 2014; Palomba *et al.*, 2014), two finding no effect (Kucuk *et al.*, 2010; Moran *et al.*, 2011), and one finding a detrimental effect (Morris *et al.*, 2006). The accuracy and time frame of physical activity assessment could be one explanation for the heterogeneous results across studies. Physical activity is a hard metric to quantify accurately and, even if it is assessed accurately, there could be differential effects of regular lifetime exercise compared with more recently initiated exercise. For instance, the largest study to date (*n* = 2232), which found a detrimental effect of physical activity 4 h or more per week for less than 10 years compared with women who never exercised, did not find that women who engaged in 1–3 h of exercise per week for 1–9 years or 1–3 h of exercise per week for 10–30 years had less successful IVF outcomes than women who do not exercise (Morris *et al.*, 2006), a pattern with doubtful biological plausibility and more suggestive of chance. It is also important to note that the baseline demographic characteristics, including range and type of physical activity, varied widely across cohorts. It is possible that certain physical activities are beneficial whereas others are not. Similarly, exercise might be positive up to a certain level of activity and then have a deleterious effect above that threshold level of activity. Owing to differing classifications of what constitutes ‘regular’, ‘moderate’, and ‘vigorous’ exercise across studies, results are hard to directly compare. Clearly, more research is needed before strong conclusions concerning physical activity before assisted reproduction technique treatment can be made. As a complex relationship is likely between intensity and duration of exercise, future research should focus on disentangling these effects.

In the present study, a significant interaction of BMI on the effect of physical activity on live birth was observed, such that only women of normal BMI seemed to benefit from vigorous activity. Moreover, the positive association between vigorous activity and IVF success in normal-weight women was present even after accounting for BMI. If this is indeed a true biological effect, it suggests that physical activity may affect fertility via mechanisms other than body weight regulation. For instance, regular physical activity is known to be an effective therapeutic intervention to improve glucose homeostasis and insulin sensitivity (Hawley, 2004). As insulin sensitizers seem to have beneficial effects on ovulatory function and fertility, even among women with little to no clinical evidence of polycystic ovary syndrome (Ibanez *et al.*, 2001; van Santbrink *et al.*, 2005), it is possible that improved glucose regulation is the mechanism through with physical activity is exerting its beneficial effects. Routine physical activity is also associated with improved psychological well-being, e.g. through reduced stress, anxiety and depression. As previous studies have demonstrated that increased stress and anxiety negatively influence live birth rates (Klonoff-Cohen *et al.*, 2001), this could be another possible mechanism through which vigorous activity positively affects IVF success. We explored this pathway by controlling for our assessment of perceived stress; however, results were similar, suggesting that this pathway was not likely driving our link between physical activity and IVF outcomes in normal weight women.

What is unclear is why we found a lack of association between physical activity and live birth in overweight and obese women. Although speculative, it is possible that overweight and obese women with high amounts of exercise did not couple this with increased energy intake, leading to negative energy balance where the energy requirements of reproductive functions could not be met (Loucks *et al.*, 1998). We tried to address this possibility by comparing energy intakes in the subset of women who completed a Food Frequency Questionnaire. Although the calorie intakes were not appreciably lower in highly active overweight and obese women, the Food Frequency Questionnaire is not the best tool to assess energy balance as its estimate of total energy intake correlates poorly with doubly-labelled water (the gold standard of energy intake assessment) (Subar *et al.*, 2003). An alternate suggestion is that the detrimental effects of excess body weight might outweigh the beneficial effects of vigorous exercise in overweight and obese women. Of note, the interaction between BMI and vigorous activity on fertility has been shown in two previous studies. Among a large cohort of nurses, vigorous activity had a protective association with ovulatory infertility among women in the normal weight range but not among women who were underweight or overweight (Rich-Edwards *et al.*, 2002). In contrast, among a cohort of Danish women planning pregnancy, vigorous physical activity was associated with reduced

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fecundity in all subgroups of women with the exception of overweight and obese women (Wise *et al.*, 2012).

The use of a single physical activity questionnaire to characterize exposure was a limitation of our present study, as it could have led to misclassification during follow-up. Although this type of misclassification is likely to be non-differential, it would tend to attenuate effects to the null. Iin particular, this bias might affect the analyses of sedentary activity given the low validation coefficients shown in previous studies. We also only assessed typical physical activity over the previous year and not specifically during the month before or during IVF treatment. Therefore, our results are only applicable to that time period of interest. Additionally, we assumed that any changes in activity immediately before or during IVF are similar across women. Because of the observational nature of our study, we cannot rule out residual or unmeasured confounding as an explanation for our results. Although we tried to account for many potential confounding factors in our adjusted models, it is possible that there were other variables not measured or accounted for in our analyses. The size of our cohort limited our power to detect small differences in effect (which could be one explanation for the null findings) and conduct sub-group analyses. Moreover, in the instances where we did explore potential interactions, it is possible that sparse data or chance could be creating the appearance of interaction. Although prevalence of obesity was lower compared with other fertility patient cohorts in the USA (Shah *et al.*, 2011; Schliep *et al.*, 2015), our study participants were comparable in age and ethnicity, suggesting that results may be generalizable to other couples seeking infertility treatment (Stephen and Chandra, 2000). Finally, women who did not fill out the physical activity assessment were more likely to fail early in their treatment cycle. If these women also differed from the women included in our cohort in physical activity level, this could have resulted in selection bias.

The strengths of our study include its prospective design and the use of a previously validated activity questionnaire. We also benefited from having a wide range of physical activity in our population; however, few women in our cohort reported no physical activity compared with some previous studies. Finally, the standardized assessment of a wide variety of participant characteristics increased the ability to adjust for confounding.

In conclusion, our study suggests that overall physical activity in the year before starting fertility treatment is unlikely to have a deleterious effect on outcomes of IVF. Moreover, certain forms of physical activity may be beneficial and certain sub-groups of women such as those of normal BMI may benefit from vigorous physical activity before IVF treatment initiation. Further research is needed to investigate this association in other populations with a particular emphasis on understanding the interplay of timing, intensity, type, and duration of exercise before IVF treatment initiation that are associated with the greatest success.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Biography

Audrey Gaskins received her doctorate of science in epidemiology and nutrition from the Harvard TH Chan School of Public Health in 2014. She is currently in her second year of a postdoctoral fellowship in the Department of Nutrition at the same institution. Her major areas of interest are male and female infertility, assisted reproduction and adverse pregnancy outcomes.

References

Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR Jr, Schmitz KH, Emplaincourt PO, Jacobs DR Jr, Leon AS. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc. 2000; 32:S498–504. [PubMed: 10993420]

Brown WJ, Burton NW, Rowan PJ. Updating the evidence on physical activity and health in women. Am J Prev Med. 2007; 33:404–411. [PubMed: 17950406]

Evenson KR, Calhoun KC, Herring AH, Pritchard D, Wen F, Steiner AZ. Association of physical activity in the past year and immediately after in vitro fertilization on pregnancy. Fertil Steril. 2014; 101:1047–1054. [PubMed: 24524834]

Gudmundsdottir SL, Flanders WD, Augestad LB. Physical activity and fertility in women: the North-Trondelag Health Study. Hum Reprod. 2009; 24:3196–3204. [PubMed: 19801570]

Hawley JA. Exercise as a therapeutic intervention for the prevention and treatment of insulin resistance. Diabetes Metab Res Rev. 2004; 20:383–393. [PubMed: 15343584]

Ibanez L, Valls C, Ferrer A, Marcos MV, Rodriguez-Hierro F, de Zegher F. Sensitization to insulin induces ovulation in nonobese adolescents with anovulatory hyperandrogenism. J Clin Endocrinol Metab. 2001; 86:3595–3598. [PubMed: 11502783]

Klonoff-Cohen H, Chu E, Natarajan L, Sieber W. A prospective study of stress among women undergoing in vitro fertilization or gamete intrafallopian transfer. Fertil Steril. 2001; 76:675–687. [PubMed: 11591398]

Kucuk M, Doymaz F, Urman B. Effect of energy expenditure and physical activity on the outcomes of assisted reproduction treatment. Reprod Biomed Online. 2010; 20:274–279. [PubMed: 20113966]

Loucks AB, Verdun M, Heath EM. Low energy availability, not stress of exercise, alters LH pulsatility in exercising women. J Appl Physiol (1985). 1998; 84:37–46. [PubMed: 9451615]

Moran L, Tsagareli V, Norman R, Noakes M. Diet and IVF pilot study: short-term weight loss improves pregnancy rates in overweight/obese women undertaking IVF. Aust N Z J Obstet Gynaecol. 2011; 51:455–459. [PubMed: 21806596]

Morris SN, Missmer SA, Cramer DW, Powers RD, McShane PM, Hornstein MD. Effects of lifetime exercise on the outcome of in vitro fertilization. Obstet Gynecol. 2006; 108:938–945. [PubMed: 17012457]

Otis CL, Drinkwater B, Johnson M, Loucks A, Wilmore J. American College of Sports Medicine position stand. The Female Athlete Triad. Med Sci Sports Exerc. 1997; 29:i–ix.

Palomba S, Falbo A, Valli B, Morini D, Villani MT, Nicoli A, La Sala GB. Physical activity before IVF and ICSI cycles in infertile obese women: an observational cohort study. Reprod Biomed Online. 2014; 29:72–79. [PubMed: 24813759]

Rich-Edwards JW, Spiegelman D, Garland M, Hertzmark E, Hunter DJ, Colditz GA, Willett WC, Wand H, Manson JE. Physical activity, body mass index, and ovulatory disorder infertility. Epidemiology. 2002; 13:184–190. [PubMed: 11880759]

Schliep KC, Mumford SL, Ahrens KA, Hotaling JM, Carrell DT, Link M, Hinkle SN, Kissell K, Porucznik CA, Hammoud AO. Effect of male and female body mass index on pregnancy and live birth success after in vitro fertilization. Fertil Steril. 2015; 103:388–95. [PubMed: 25497445]

Shah DK, Missmer SA, Berry KF, Racowsky C, Ginsburg ES. Effect of obesity on oocyte and embryo quality in women undergoing in vitro fertilization. Obstet Gynecol. 2011; 118:63–70. [PubMed: 21691164]

Stephen EH, Chandra A. Use of infertility services in the United States: 1995. Fam Plann Perspect. 2000; 32:132–137. [PubMed: 10894259]

Subar AF, Kipnis V, Troiano RP, Midthune D, Schoeller DA, Bingham S, Sharbaugh CO, Trabulsi J, Runswick S, Ballard-Barbash R, Sunshine J, Schatzkin A. Using intake biomarkers to evaluate the extent of dietary misreporting in a large sample of adults: the OPEN study. Am J Epidemiol. 2003; 158:1–13. [PubMed: 12835280]

van Santbrink EJ, Hohmann FP, Eijkemans MJ, Laven JS, Fauser BC. Does metformin modify ovarian responsiveness during exogenous FSH ovulation induction in normogonadotrophic anovulation? A placebo-controlled double-blind assessment. Eur J Endocrinol. 2005; 152:611–617. [PubMed: 15817918]

Warren MP, Perlroth NE. The effects of intense exercise on the female reproductive system. J Endocrinol. 2001; 170:3–11. [PubMed: 11431132]

Wise LA, Rothman KJ, Mikkelsen EM, Sorensen HT, Riis A, Hatch EE. An internet-based prospective study of body size and time-to-pregnancy. Hum Reprod. 2010; 25:253–264. [PubMed: 19828554]

Wise LA, Rothman KJ, Mikkelsen EM, Sorensen HT, Riis AH, Hatch EE. A prospective cohort study of physical activity and time to pregnancy. Fertil Steril. 2012; 97:1136–1142. [PubMed: 22425198]

Wolf AM, Hunter DJ, Colditz GA, Manson JE, Stampfer MJ, Corsano KA, Rosner B, Kriska A, Willett WC. Reproducibility and validity of a self-administered physical activity questionnaire. Int J Epidemiol. 1994; 23:991–999. [PubMed: 7860180]

Table 1

Baseline characteristics of 273 women in Environment and Reproductive Health (EARTH) Study by quintile of moderate-to-vigorous and sedentary activity.

	Total cohort	Moderate-to-vigorous activity		Sedentary activity	
Quintile (range of activity, h/week)	**–**	**Q1 (<0.7)**	**Q5 (≥7.2)**	**Q1 (<29)**	**Q5 (≥66)**
N	273	54	54	53	55
Age, years	35.3 (3.9)	35.5 (4.5)	35.4 (3.7)	35.1 (4.4)	35.6 (3.6)
BMI, kg/m^2	24.0 (4.2)	24.6 (4.3)	24.0 (4.7)	23.9 (4.7)	24.4 (4.5)
Ever smoker, *n* (%)	78 (28.7)	16 (29.6)	16 (29.6)	15 (28.3)	15 (27.3)
White/Caucasian, *n* (%)	224 (82.1)	43 (79.6)	47 (87.0)	39 (73.6)	46 (83.6)
Education level, *n* (%)					
Less than college	24 (8.8)	5 (9.3)	8 (14.8)	9 (17.0)	4 (7.3)
College degree	89 (32.6)	17 (31.5)	17 (31.5)	18 (34.0)	19 (34.5)
Graduate degree	160 (58.6)	32 (59.3)	29 (53.7)	26 (49.1)	32 (58.2)
Currently employed, *n* (%)	262 (96.0)	50 (92.6)	53 (98.1)	48 (90.6)	53 (96.4)
Moderate-to-vigorous activity, h/week	4.3 (4.6)	0.2 (0.3)	11.9 (4.4)[a]	3.8 (4.7)	4.7 (4.6)
Sedentary activity, h/week	48.6 (21.7)	43.3 (22.6)	49.7 (18.6)	16.9 (7.2)	78.8 (11.6)[a]
Self-perceived stress[b]	5.7 (3.1)	5.5 (3.5)	5.8 (3.2)	5.6 (3.0)	6.1 (3.4)
Infertility diagnosis, *n* (%)					
Female factor	86 (31.5)	18 (33.3)	21 (38.9)[a]	19 (35.8)	17 (30.9)
Ovulation disorders	23 (8.4)	2 (3.7)	7 (13.0)	4 (7.5)	4 (7.3)
Diminished ovarian reserve	25 (9.2)	6 (11.1)	9 (16.7)	4 (7.5)	5 (9.1)
Tubal	20 (7.3)	5 (9.3)	2 (3.7)	8 (15.1)	4 (7.3)
Endometriosis	16 (5.9)	5 (9.3)	2 (3.7)	2 (3.8)	4 (7.3)
Uterine	3 (1.1)	0 (0.0)	1 (1.9)	1 (1.9)	0 (0.0)
Male factor	92 (33.7)	21 (38.9)	16 (29.6)	18 (34.0)	17 (30.9)
Unexplained	94 (34.4)	15 (27.8)	17 (31.5)	16 (30.2)	21 (38.2)
Treatment protocol, *n* (%)					
Antagonist	21 (7.7)	6 (11.1)	4 (7.4)	4 (7.5)	5 (9.1)
Flare	35 (12.9)	9 (16.7)	6 (11.1)	5 (9.4)	5 (9.1)
Luteal phase agonist	216 (79.4)	39 (72.2)	44 (81.5)	44 (83.0)	45 (81.8)

	Total cohort	Moderate-to-vigorous activity		Sedentary activity	
Quintile (range of activity, h/week)	**–**	**Q1 (<0.7)**	**Q5 (≥7.2)**	**Q1 (<29)**	**Q5 (≥66)**
Day 3 FSH, IU/L[c]	7.1 (2.1)	7.1 (2.0)	7.2 (2.4)	7.4 (2.2)	7.0 (2.0)
Embryo transfer day, *n* (%)					
No embryos transferred	25 (9.2)	3 (5.6)	8 (14.8)	6 (11.3)	5 (9.1)
Day 2	14 (5.1)	3 (5.6)	3 (5.6)	1 (1.9)	1 (1.8)
Day 3	127 (46.5)	28 (51.9)	25 (46.3)	25 (47.2)	26 (47.3)
Day 5	89 (32.6)	14 (25.9)	15 (27.8)	18 (34.0)	18 (32.7)
Egg donor or cryo cycle	18 (6.6)	6 (11.1)	3 (5.6)	3 (5.7)	5 (9.1)
Number of embryos transferred, n (%)					
No embryos transferred	25 (9.2)	3 (5.6)	8 (14.8)	6 (11.3)	5 (9.1)
1 embryo	34 (12.5)	7 (13.0)	8 (14.8)	6 (11.3)	5 (9.1)
2 embryos	157 (57.5)	27 (50.0)	28 (51.9)	30 (56.6)	30 (54.5)
3+ embryos	39 (14.3)	11 (20.4)	7 (13.0)	8 (15.1)	10 (18.2)
Egg donor or cryo cycle	18 (6.6)	6 (11.1)	3 (5.6)	3 (5.7)	5 (9.1)

Data are presented as mean (standard deviation) unless otherwise noted.

[a] $P < 0.05$ across all quintiles.

[b] Assessed on a scale from zero (least stressed) to 16 (most stressed).

[c] Data are missing for 38 women (35 missing by design: cryo cycles, donor egg cycles and early cancellations).

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Table 2

Associations between physical and sedentary activity and clinical outcomes of IVF in 273 women (427 initiated cycles) from the Environment and Reproductive Health (EARTH) Study.[a]

	Implantation	Clinical pregnancy	Live birth
Quintile (range)	**Adjusted mean proportions (95% CI)[b]**		
Total physical activity, h/week			
Q1 (0–2.5)	0.50 (0.38 to 0.62)	0.41 (0.31 to 0.53)	0.32 (0.22 to 0.43)
Q2 (2.6–5.1)	0.65 (0.51 to 0.77)	0.57 (0.44 to 0.69)	0.44 (0.31 to 0.58)
Q3 (5.2–7.9)	0.55 (0.42 to 0.67)	0.52 (0.41 to 0.64)	0.39 (0.28 to 0.52)
Q4 (8.0–−12.5)	0.60 (0.47 to 0.71)	0.52 (0.41 to 0.64)	0.40 (0.29 to 0.53)
Q5 (12.6–59.2)	0.61 (0.48 to 0.72)	0.51 (0.39 to 0.63)	0.36 (0.25 to 0.49)
P-trend	0.42	0.64	0.94
Total METs, MET-h/week			
Q1 (0–10.0)	0.46 (0.34 to 0.58)	0.37 (0.27 to 0.49)	0.28 (0.19 to 0.39)
Q2 (10.1–23.2)	0.67 (0.53 to 0.79)	0.61 (0.48 to 0.73)	0.45 (0.32 to 0.59)
Q3 (23.4–32.8)	0.54 (0.41 to 0.66)	0.47 (0.36 to 0.59)	0.36 (0.25 to 0.48)
Q4 (32.9–53.2)	0.63 (0.50 to 0.74)	0.58 (0.46 to 0.69)	0.48 (0.35 to 0.60)
Q5 (53.3–188.8)	0.61 (0.48 to 0.72)	0.51 (0.40 to 0.63)	0.36 (0.25 to 0.48)
P-trend	0.21	0.30	0.60
Moderate-to-vigorous activity, h/week			
Q1 (0–0.7)	0.57 (0.44 to 0.69)	0.48 (0.36 to 0.60)	0.33 (0.22 to 0.46)
Q2 (0.8–2.4)	0.58 (0.45 to 0.70)	0.52 (0.40 to 0.64)	0.44 (0.32 to 0.57)
Q3 (2.5–3.9)	0.53 (0.40 to 0.66)	0.48 (0.36 to 0.60)	0.35 (0.24 to 0.48)
Q4 (4.0–7.0)	0.58 (0.45 to 0.70)	0.52 (0.40 to 0.64)	0.38 (0.26 to 0.50)
Q5 (7.1–24.5)	0.59 (0.47 to 0.71)	0.51 (0.39 to 0.62)	0.39 (0.28 to 0.51)
P-trend	0.72	0.78	0.80
Vigorous activity, h/week			
Q1 (0)	0.52 (0.41 to 0.63)	0.47 (0.36 to 0.57)	0.36 (0.26 to 0.47)
Q2 (0.1–0.5)	0.64 (0.49 to 0.76)	0.52 (0.38 to 0.65)	0.35 (0.23 to 0.49)
Q3 (0.6–1.9)	0.48 (0.36 to 0.61)	0.40 (0.29 to 0.53)	0.34 (0.23 to 0.47)
Q4 (2.0–4.4)	0.67 (0.54 to 0.77)	0.61 (0.49 to 0.72)	0.42 (0.30 to 0.55)
Q5 (4.5–19.5)	0.60 (0.48 to 0.71)	0.52 (0.41 to 0.63)	0.41 (0.29 to 0.54)
P-trend	0.38	0.35	0.35
Sedentary activity, h/week			
Q1 (0.2–28.5)	0.55 (0.43 to 0.67)	0.52 (0.41 to 0.63)	0.38 (0.27 to 0.51)
Q2 (28.6–45.5)	0.65 (0.52 to 0.75)	0.51 (0.40 to 0.63)	0.36 (0.26 to 0.49)
Q3 (45.6–52.9)	0.51 (0.38 to 0.64)	0.44 (0.32 to 0.57)	0.32 (0.21 to 0.45)
Q4 (53.0–65.9)	0.54 (0.41 to 0.67)	0.49 (0.36 to 0.62)	0.39 (0.27 to 0.53)
Q5 (66.0–123.5)	0.59 (0.46 to 0.71)	0.52 (0.40 to 0.64)	0.43 (0.30 to 0.56)
P-trend	0.93	0.93	0.57

[a]All analyses were run using generalized linear mixed models with random intercepts, binomial distribution and logit link function.

[b]Data are presented as predicted marginal means adjusted for age, body mass index, race, infertility diagnosis (female, male, unexplained), and education (high school or less, college, graduate).

MET, metabolic equivalent task.

Table 3

Associations between specific physical activities and probability of live birth in 273 women (427 initiated IVF cycles) from the Environment and Reproductive Health (EARTH) Study.[a]

Category (range)	Number of women	Number of live births/total cycles (%)	Adjusted proportion of live births (95% CI[b]
Walking for exercise, h/week			
Q1 (<0.5)	71	44/114 (38.6)	0.38 (0.28 to 0.49)
Q2 (0.5–2.4)	63	42/99 (42.4)	0.40 (0.29 to 0.53)
Q3 (2.5–4.9)	53	29/83 (34.9)	0.28 (0.18 to 0.41)
Q4 (≥5.0)	86	61/131 (46.6)	0.41 (0.31 to 0.53)
P-trend			0.63
Outdoor activities, h/week			
Q1 (0)	110	61/162 (37.7)	0.34 (0.25 to 0.44)
Q2 (0.1–0.9)	71	55/115 (47.8)	0.45 (0.34 to 0.57)
Q3 (≥1)	92	60/150 (40.0)	0.37 (0.28 to 0.47)
P-trend			0.77
Running and jogging, h/week			
Q1 (0)	136	90/212 (42.5)	0.40 (0.31 to 0.49)
Q2 (0.1–1.4)	67	40/107 (37.4)	0.32 (0.23 to 0.44)
Q3 (≥1.5)	70	46/108 (42.6)	0.37 (0.27 to 0.49)
P-trend			0.83
Other activities, h/week			
Q1 (0)	206	138/325 (42.5)	0.39 (0.32 to 0.47)
Q2 (0.1–1.4)	30	14/43 (32.6)	0.28 (0.16 to 0.45)
Q3 (≥1.5)	37	24/59 (40.7)	0.35 (0.23 to 0.50)
P-trend			0.55
Weightlifting, h/week			
Q1 (0)	151	95/229 (41.5)	0.37 (0.29 to 0.46)
Q2 (0.1–0.9)	42	25/59 (42.4)	0.40 (0.26 to 0.55)
Q3 (≥1)	80	56/139 (40.3)	0.38 (0.28 to 0.48)
P-trend			0.95
Aerobics, rowing and ski or stair machine, h/week			
Q1 (0)	176	105/268 (39.2)	0.35 (0.28 to 0.43)
Q2 (0.1–1.4)	46	29/79 (36.7)	0.33 (0.22 to 0.47)
Q3 (≥1.5)	51	42/80 (52.5)	0.51 (0.38 to 0.64)
P-trend			0.02
Bicycling, h/week			
Q1 (0)	180	111/286 (38.8)	0.35 (0.28 to 0.43)
Q2 (0.1–0.9)	40	28/59 (47.5)	0.43 (0.29 to 0.58)
Q3 (≥1)	53	37/82 (45.1)	0.43 (0.31 to 0.56)
P-trend			0.24
Tennis and squash, h/week			

Category (range)	Number of women	Number of live births/total cycles (%)	Adjusted proportion of live births (95% CI[b]
None	251	162/388 (41.8)	0.38 (0.31 to 0.46)
Any	22	14/39 (35.9)	0.29 (0.16 to 0.47)
P-trend			0.93
Swimming laps, h/week			
None	241	152/371 (41.0)	0.37 (0.31 to 0.45)
Any	32	24/56 (42.9)	0.38 (0.24 to 0.54)
P-trend			0.29

[a]All analyses were run using generalized linear mixed models with random intercepts, binomial distribution, and logit link function.

[b]Data are presented as predicted marginal means adjusted for age, body mass index, race, infertility diagnosis (female, male, unexplained) and education (high school or less, college, graduate).

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Table 4

Associations between specific sedentary activities and probability of live birth in 273 women (427 initiated IVF cycles) from the Environment and Reproductive Health (EARTH) Study.[a]

Category (range)	Number of women	Number of live births/total cycles (%)	Adjusted proportion of live births (95% CI)[b]
Sitting at home, h/week			
Q1 (≤8.5)	72	39/114 (34.2)	0.33 (0.23 to 0.43)
Q2 (9–15.5)	68	44/110 (40.0)	0.36 (0.26 to 0.48)
Q3 (16–24.5)	59	39/92 (42.4)	0.37 (0.25 to 0.50)
Q4 (≥25)	73	54/111 (48.6)	0.46 (0.35 to 0.57)
P-trend			0.06
Sitting at work, h/week			
Q1 (≤ 5)	60	42/100 (42.0)	0.41 (0.30 to 0.53)
Q2 (6–26)	89	55/135 (40.7)	0.35 (0.26 to 0.46)
Q3 (27–36)	70	44/104 (42.3)	0.36 (0.26 to 0.48)
Q4 (> 36)	53	35/88 (39.8)	0.37 (0.26 to 0.50)
P-trend			0.68
Sitting in the car, h/week			
Q1 (≤ 1.5)	63	37/95 (38.9)	0.38 (0.27 to 0.49)
Q2 (2–5)	90	53/142 (37.3)	0.35 (0.26 to 0.46)
Q3 (8.5)	76	55/123 (44.7)	0.39 (0.28 to 0.51)
Q4 (>8.5)	43	31/67 (46.3)	0.42 (0.29 to 0.57)
P-trend			0.49

[a]All analyses were run using generalized linear mixed models with random intercepts, binomial distribution, and logit link function.

[a]Data are presented as predicted marginal means adjusted for age, body mass index, race, infertility diagnosis (female, male, unexplained), and education (high school or less, college, graduate).