

Associations of early and middle adulthood physical activity with symptoms of pelvic floor disorders in middle-aged women: an observational study with retrospective physical activity assessment

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Abstract

Objective To investigate associations of early and middle adulthood physical activity (PA) with symptoms of pelvic floor disorders (PFD), i.e. stress urinary incontinence (SUI), urge urinary incontinence (UUI), fecal incontinence (FI), constipation or defecation difficulties (CDD), and feeling of pelvic organ prolapse (POP) among middle-aged women.

Design A cross-sectional, observational study with retrospective physical activity assessment.

Setting University Research Laboratory.

Sample A random population sample of 1098 47-to-55-year-old Finnish women.

Methods PA history, current PA, and demographical and gynaecological variables were assessed using self-report questionnaires. Logistic regression analyses were applied to study associations of past and current PA with PFDs. Associations of demographical and gynaecological variables with PFDs were studied and their potential confounding effect was controlled in multiple logistic regression models.

Main outcome measures Structured questionnaire-assessed retrospective physical activity history at the age of 17–29, current physical activity at middle age, and prevalence of SUI, UUI, FI, CDD and POP.

Results Current PA was not independently associated with the occurrence of the PFDs. Middle-aged women with early adulthood history of competitive sports were more likely to experience UUI (OR 2.161, 95% CI 1.102–4.237, p=0.025) but not SUI, FI or POP, while women with history of regular PA were more likely to experience FI (OR 4.405, 95% CI 1.049–18.493, p=0.043) but not other PFDs.

Conclusions Competitive sports during early adulthood may increase the risk of UUI at middle age. The history of regular PA may increase the risk of FI. Keywords Pelvic floor function, exercise, menopausal women

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Running title: Associations of physical activity with PFDs

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Tweetable abstract Early adulthood competitive or other regular sports may increase the middle age risk of incontinences.

INTRODUCTION

In women, aging-related changes in sex hormones accelerate during middle-age, leading to the permanent cessation of ovarian function.¹ Menopausal decline in serum estrogen concentration may lead to changes in the pelvic floor tissue and potentially to disorders,² such as urinary and fecal incontinences, constipation or defecation difficulties, and pelvic organ prolapse^{3,4,5,6}. In addition to hormonal changes, several factors contribute to the pelvic floor disorders including natural aging of the connective tissue, reproductive history, lifestyle, as well as factors increasing the pressure in abdominal cavity.^{7,8}

The significance of physical activity is broadly studied and due to its numerous health benefits it can be recommended for treating wide range of diseases and conditions.⁹ However, the pelvic floor in women is the rare area of the body where the positive influence of physical activity has been challenged,^{10,11} since pelvic

floor disorders are associated with not only reduced¹² but also notably increased¹³ physical activity. It is debated that while exercise may decrease the risk of incontinences and pelvic organ prolapse by strengthening pelvic floor muscles, it also overloads and stretches the muscles, thus increasing the risk of pelvic floor disorders.¹¹ Large number of girls and women engage in physical activity, and being a potentially modifiable risk factor, its association with pelvic floor disorders needs to be studied.

Several studies have been conducted on the associations of pelvic floor disorders and competitive sports participation in early adulthood,^{14,15,16} but studies on the consequences of strenuous activities during early adulthood to the condition of pelvic floor later in life are scarce. The purpose of the current study is to investigate associations of early and middle adulthood physical activity with stress urinary incontinence, urge urinary incontinence, fecal incontinence, constipation or defecation difficulties, and feeling of pelvic organ prolapse. We hypothesized that high intensity physical activity, such as early adulthood competitive level sport participation, may be a risk-enhancing factor for midlife pelvic floor disorders. In contrast, being in general physically active at midlife may associate with lower risk of having pelvic floor disorders.

MATERIALS AND METHODS

Study design and participants

This study utilized the data originated from the cross-sectional, observational study, *Estrogenic Regulation of Muscle Apoptosis (ERMA)* that investigates how hormonal differences over menopausal stages affects the physiological and psychological functioning of middle-aged women. The study data collection proceeded in three phases described in detail in Kovanen et al.¹⁷ and in Figure 1. Briefly, written invitation was sent to 6878 randomly selected women aged 47 to 55 years living in Central Finland. The response rate was 46.9%. In total, 3064 women were willing to participate in ERMA Phase 1 and, in addition to written consent, they returned prequestionnaire which included questions on symptoms of pelvic floor disorders. Thereafter, the exclusion criteria included conditions or use of medications affecting ovarian function, obesity (self-reported body mass index [BMI] > 35 kg/m²), and chronic diseases or medications affecting muscle function. From the eligible participants (n=1627), 1393 gave fasting blood samples (Phase 2) and 1102 of them answered to the main questionnaire survey (Phase 3). The sample size of the present study is 1098, since four main questionnaires were lost due to technical error. The study protocol followed good clinical and scientific practice and the Declaration of Helsinki and was approved by the Ethics Committee of the Central Finland Health Care District (KSSHP Dnro 8U/2014).

Pelvic floor disorders

The occurrence of stress urinary incontinence, urge urinary incontinence, fecal incontinence, constipation or defecation difficulties, and feeling of pelvic organ prolapse within the previous month were assessed by a structured questionnaire at ERMA data collection Phase 1. The specific questions were the following: Have you had within the last month urinary incontinence during physical effort or coughing? Have you had within the last month urge or urgency-related urinary incontinence? Have you had within the last month fecal incontinence? Have you had within the last month constipation or defecation difficulties? Have you had within the last month a feeling that something is falling out of the vagina?

Physical Activity

Early adulthood physical activity and sport participation was assessed with a question: What kind of regular physical activity have you done at different stages of your life?¹⁸ Based on the answers, participants were divided into three groups: no exercise at the age 17–19 and/or 20–29, regular physical activity at the age 17–19 and 20–29, and competitive sport at the age 17–19 and/or 20–29. Current physical activity was evaluated with a structured questionnaire including four questions about the frequency, intensity, and duration of leisure-time physical activity bouts and the average time spent in active commuting.¹⁹ Based on the answers, a metabolic equivalent of a task hours per day (MET-h/d) was calculated to express the intensity and volume of current physical activity.

Demographical descriptives

Age was calculated from the date of birth to the date of answering to the prequestionnaire. BMI was calculated as body mass (kg) divided by height squared (m^2). Body mass and height were measured in the morning of the Phase 3 laboratory visit after overnight fasting and participant wearing only undergarments. Level of education was self-reported with a structured question and participants were classified into two groups based on their answers: those with bachelor level or higher education (tertiary) and those with education lower than bachelor level (secondary). Work-related physical activity was assessed also with a structured question. Based on their answers participants were classified into three groups: mainly sedentary work, work that includes standing and walking, and heavy work that includes also lifting.

Gynaecological variables

Participants were assigned to premenopausal, early and late perimenopausal, and postmenopausal groups according to the slightly modified Stages of Reproductive Aging Workshop (STRAW+10) criteria²⁰ which takes systemic hormone status and self-reported menstrual cycle into account. Menstrual cycle was assessed based on menstrual diary for 6 to 12 months. Follicle stimulating hormone (FSH) and 17β -oestradiol (E_2) levels were determined, but only FSH level was used to aid defining menopausal status, due to the high pulsatile variability of the E_2 level. Self-reported data on gynaecological factors, e.g., gestations, parity, and whether a participant had undergone hysterectomy were collected.

Missing data

The total number of missing data values for the analytical sample including 1098 participants was 419 out of 15372 (2.5%). The percentage of missing values varied from 0 to 16% between the variables. The data was missing due to the invalid and missing measurements as well as unclear or incomplete questionnaire response. Thus, missing data were assumed to occur at random. Multiple imputation was used to create and analyze 50 multiply imputed data sets, and the model parameters were estimated separately for each data set. The used number of iterations for chained equations²¹ was 50. Multiple imputation and pooling of the model estimates were carried out in R²² using the standard settings of the “mice” package.²¹ For comparison, we also performed complete case analysis, but the results were not notably different.

Statistical analysis

Participants characteristics are shown as percentages or as means and standard deviations. The associations of previous and current physical activity with symptoms of pelvic floor disorders were analyzed using logistic regression models. The confounding factors included in the models were age, BMI, education, physical workload, menopausal status, parity, and hysterectomy status, since it is known that demographical factors as well as factors related to gynaecological history may affect pelvic floor disorders and physical activity. The model assumptions were tested using correlation analysis and inspecting residual plots as well as scatter plots between each continuous predictor and the logit values. Statistical analyses were performed using R and IBM SPSS Statistics 22.0 (SPSS Inc., Chicago, IL). The level of significance was set at $p \leq 0.05$.

RESULTS

Differences in the reported frequencies of pelvic floor disorders between larger Phase 1 study sample and the smaller Phase 3 sample were minor, indicating good representativeness of the analytical sample (Table 1). About 55% of women reported to have any type of disorder and about 19% experienced more than one pelvic floor disorder type. Most common disorder types were stress urinary incontinence (40%), constipation or defecation difficulties (17%) and urge urinary incontinence (14%). Feeling of pelvic organ prolapse (5%) and fecal incontinence (3%) were less often reported.

Table 2 shows demographical, gynaecological, and physical activity status in total analytical sample and in participants with different types of pelvic floor disorders. The mean age of the participants was 51.2 (SD = 2.0) years. On average, the participants were slightly overweight according to the mean BMI of 25.5

(SD = 3.7). Most (59%) of them had education lower than bachelor level and half (53%) reported their work-related physical activity as light. i.e. mainly sedentary work. Based on serum concentrations of the circulating hormones and bleeding diaries 28% of the women were categorized as premenopausal, 18% early perimenopausal, 19% late perimenopausal, and 35% postmenopausal. The means for number of gestations and parity were 2.5 and 2.0, respectively. About 8% of women had undergone hysterectomy. Groups of women reporting different types of pelvic floor symptoms were fairly similar except that women with feeling of pelvic organ prolapse were less likely to report mainly sedentary work (36%), were more likely to be postmenopausal (41%), had a little bit higher number of gestations (3.2 [SD = 1.8]) and were more likely to have had hysterectomy (20%) than women in other groups. Furthermore, in comparison to other groups, group of women with fecal incontinence had highest BMI (27.1) and lowest education level (74% reported secondary education).

The mean for current physical activity was 4.5 MET-h/d (SD = 3.9) for total analytical sample and ranged from 3.6 to 4.4 MET-h/d for women reporting different types of pelvic floor symptoms. With regard to previous physical activity, 24% of the women were inactive, 67% took part in regular physical activity, and 10% did competitive sports during their early adulthood. Most (90%) of the women reporting fecal incontinence had exercised regularly, but only one of them (3%) recalled that she had practiced competitive sports. Women reporting urge urinary incontinence formed the group with highest number of competitive sport athletes during early adolescent (13%).

Simple logistic regression models indicated higher current physical activity to associate only with lower odds of experiencing stress urinary incontinence (OR 0.96, CI 0.93–0.99, $p=0.023$, Table S1) but not with any other pelvic floor disorder types. However, including early adulthood physical activity, and demographical and gynaecological variables as potential confounding factors into the same model abolished statistical significance of the association (Table 3).

In comparison to not exercising during early adulthood, women with history of competitive sports were more likely to experience urge urinary incontinence according to simple (OR 2.07, CI 1.07–4.00, $p=0.031$, Table S1) and multiple logistic regression models (OR 2.16, CI 1.10–4.24, $p=0.025$, Table 3) controlled for current physical activity and several demographical and gynaecological factors. Early adulthood competitive sport participation did not associate with other pelvic floor dysfunction types. Similarly, women with history of regular physical activity were more likely to experience fecal incontinence (OR 4.41, CI 1.05–18.49 $p=0.043$, Table 3) but no significant associations were found for other pelvic floor disorders

DISCUSSION

Main Findings

In this study, we focused on the association of previous and current physical activity with pelvic floor disorders in middle-aged women. Over half of the women in our total analytical sample had symptoms of urinary or fecal incontinence, constipation or defecation difficulties, or pelvic organ prolapse. We found that higher current physical activity was associated with lower risk of stress urinary incontinence, but association did not remain after adding confounding factors into the same model. Current physical activity was not associated with any other pelvic floor disorder. Women with history of competitive sports were more likely to experience urge urinary incontinence according to pooled simple and multiple logistic regression models controlled with confounders. Early adulthood competitive sport participation did not associate with other pelvic floor dysfunction types. Similarly, women with history of regular physical activity were more likely to experience fecal incontinence but no significant associations were found for other pelvic floor disorders.

Strengths and limitations

The present study had several strengths. It was conducted in a large homogenous cohort of relatively healthy Finnish women, which permits precise measurements without a need to control potential confounders (e.g. ethnicity, health or income). On the contrary, our results may not be generalizable to more heterogenous

populations. Unique to our study was the exact determination of menopause status of the participants by FSH measurements and menstrual bleeding diaries. This enabled us to adjust the models with menopause status, and reliably evaluate its association with pelvic floor disorders. Furthermore, the extend of this study is exceptional: five different pelvic floor disorders were studied among the large observational cohort including retrospective data for early adulthood physical activity.

The study had also some limitations. The experienced symptoms of pelvic floor disorders were asked by postal query in an early stage of the study. We were not able to study if this timing has influenced the willingness of the participants to report the conditions that may be considered sensitive. In addition, the threshold to report pelvic floor disorders may vary, since the manner women experience symptoms most likely differs from person to person, and the symptoms may also remain unrecognized.^{23,24}

Pelvic floor disorders have been associated with higher BMI,^{25,26,27} however, women with BMI>35 kg/m² were excluded from the analytical study sample, thus the results cannot be generalized to severely obese individuals. However, there were no obvious difference in the prevalence of any type of pelvic floor disorder among large Phase 1 study sample in which BMI was not exclusion criteria and among the analytical sample. Another limitation is that previous and current physical activity were self-reported, which may result some recalling or reporting bias by underestimating the number of low and overestimating the number of high physically active participants.²⁸

Interpretation

Due to the hormonal changes and natural aging, middle-aged women are at high risk for developing pelvic floor disorders. The prevalence rates of urinary incontinence increase steadily with age.^{29,30,31} Previous studies^{31,31} reveal a 30–40% prevalence among middle-aged women, which is in line with the present study, since symptoms of stress urinary incontinence were reported by 40% of women. In previous studies^{25,32,13} current leisure activity was associated with lower odds of stress urinary incontinence; whereas the lack of exercise increases these odds. Similarly, in the current study, we found an association between current physical activity and stress urinary incontinence, nevertheless, the association did not remain after controlling for past physical activity as well as demographical and gynaecological variables. Competitive sport in early adulthood was associated with urge urinary incontinence, and association remained after controlling for confounding factors. Previously, Townsend et al.³³ found that long-term moderate physical activity is inversely associated with urge urinary incontinence in 37–54 years old women, instead, according to Danford et al.³⁴ long-term total physical activity is not related to incidence of urge urinary incontinence in older women.

Fecal incontinence is estimated to affect 7–15% of community-dwelling women, and its prevalence rises with age.³⁵ Deviating from previous estimates, the prevalence of the symptoms of fecal incontinence was only 3% in our sample. Physical activity has an effect on colonic motor function,^{36,37} and changes in function may be proportional to the amount of activity.³⁸ Lower physical activity has been associated with fecal incontinence in women ages 62–87 years.³⁹ Similarly, in the National Health and Nutrition Examination Study, adults with greater perceived severity of fecal incontinence engaged in less moderate-to-vigorous physical activity.⁴⁰ In contrary, there is some evidence to suggest that brisk physical activity, running in particular, may predispose to gastrointestinal disturbance.^{41,42} According to Vitton et al.⁴³ 18–40 years old women who engaged in high-intensity sport for over 8 hours a week had significantly higher risk of fecal incontinence than less active women. Interestingly, we did not find an association on physical activity with fecal incontinence in simple logistic regression analyses, however, after adding current physical activity, and demographical and gynaecological variables in the model, we found that women with history of regular physical activity were more likely to experience fecal incontinence. Competitive sports or inactivity in young adulthood or current physical activity in middle-age were not associated with these symptoms. It is noteworthy, that the small prevalence of fecal incontinence may affect the results and, in addition, women reporting the symptoms were older, had higher BMI and lower education compared to women who had some other type of pelvic floor disorder.

The global prevalence of constipation is reported to be 14% in adult population.⁴⁴ The risk of constipation is higher in women than in men and increases with age.^{44,45} In addition, menopausal transition is associated with gastrointestinal symptoms, such as constipation.⁴⁶ In our study symptoms of constipation or defecation difficulties were reported by 19% of middle-aged women. As stated before, physical activity affects colonic motor function, therefore, the effect of physical activity on constipation seems likely. However, study results are inconsistent: In National Health and Nutrition Examination Survey⁴⁷ recreational physical activity was not strongly associated with constipation on a population level. Meshkinpour et al.⁴⁸ implemented an exercise intervention and concluded that regular exercise does not play a role in the management of constipation. Neither did we found an association on previous or current physical activity with constipation or defecation difficulties. In contrary, Dukas et al.⁴⁹ conclude that moderate physical activity is associated with substantial reduction in the prevalence of constipation in women, and Tack et al.⁵⁰ state that physical inactivity is one of the many causes contributing to constipation.

Higher age and postmenopausal status are risk factors for pelvic organ prolapse.^{27,51,52} In epidemiological surveys, reported prevalences varies widely between 1–31% for self-reported symptoms and up to 65% for clinically confirmed prolapse.⁵³ Explanations for the discrepancies between clinical signs of pelvic organ prolapse and experienced symptoms might lie in the personal sphere or in the social circumstances.²⁴ In our sample, 5% of women reported symptoms. We did not find association between previous or current physical activity and pelvic organ prolapse, which is in line with some previous studies.^{27,54,55,56} However, association of physical activity and pelvic organ prolapse is somewhat controversial subject, since Braekken et al.⁵⁶ concluded that postmenopausal women with pelvic organ prolapse had participated less in exercise when they were younger, and, according to Nygaard et al.,⁵⁴ strenuous physical activity during teenage years may result higher odds of pelvic organ prolapse in middle-age.

CONCLUSION

Pelvic floor disorders are complex and dynamic phenomenon related not only with demographical and gynaecological factors but also modifiable lifestyle factors such as physical activity. In order to gain greater insight, longitudinal studies on development of pelvic floor disorders over lifespan are necessary.

The present study showed that competitive sports during early adulthood may increase the middle age risk of urge urinary incontinence but not stress urinary incontinence. History of regular physical activity in early adulthood, or the amount of current physical activity are not associated with urinary incontinences in middle-age. Women with history of regular physical activity are more likely to experience fecal incontinence. Past or current physical activity are not associated with constipation or defecation difficulties neither with pelvic organ prolapse.

Disclosure of interest

The authors report no conflict of interest.

Contribution to authorships

MAK, MH and MK contributed to data analysis, data interpretation and manuscript writing. SS, PA and EKL contributed to the study design, data interpretation and manuscript editing. AK, MH, MK, SS, PA and EKL contributed to critical manuscript revision. All authors agree with the final version and agree to be accountable for the integrity of the data published.

Ethics approval

The Ethics Committee of the Central Finland Health Care District approved the study; 9 October 2014 (KSSHP Dnro 8U/2014).

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Supporting Information

Table S1. Pooled simple logistic regression models ($n = 1098$).

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Table 1. Frequencies of pelvic floor disorders in Phase 1 sample and in analytical sample.

Variables	Phase 1 sample $n=3064$	Analytical sample $n=1098$
Any type of disorder, n (%)	1671 (54.7)	605 (55.2)
Missing data, n	7	2
Stress urinary incontinence, n (%)	1179 (38.7)	440 (40.3)
Missing data, n	17	6
Urge urinary incontinence, n (%)	405 (13.3)	149 (13.6)
Missing data, n	24	6
Fecal incontinence, n (%)	97 (3.2)	34 (3.1)
Missing data, n	17	8
Constipation or defecation difficulties, n (%)	593 (19.5)	189 (17.3)
Missing data, n	19	6
Feeling of pelvic organ prolapse, n (%)	152 (5.0)	56 (5.1)
Missing data, n	17	4
Number of pelvic floor disorders, n (%)		
None	1386 (45.5)	491 (45.0)
One	1081 (35.5)	397 (36.4)
Two or more	577 (19.0)	202 (18.5)
Missing data, n	20	8

Table 2. Descriptive data in total analytical sample and in participants with different types of pelvic floor disorders.

	Total analytical sample ($n=1098$)	Stress urinary incontinence ($n=4$)
<i>Demographical descriptives</i>		
Age, mean (SD)	51.2 (2.0)	51.0 (2.0)
Body mass index, mean (SD)	25.5 (3.7)	26.2 (3.8)
Missing data, n	171	77
Education, n (%)		
Secondary	643 (58.6)	273 (62.0)
Tertiary	455 (41.4)	167 (38.0)
Physical workload, n (%)		
Light	535 (53.0)	204 (50.0)

	Total analytical sample (<i>n</i> =1098)	Stress urinary incontinence (<i>n</i> =4
Moderate	203 (20.1)	80 (19.6)
Heavy	271 (26.9)	124 (30.4)
Missing data, <i>n</i>	89	32
<i>Gynecological variables</i>		
Menopausal status, <i>n</i> (%)		
Premenopausal	304 (27.7)	136 (30.9)
Early perimenopausal	198 (18.0)	94 (21.4)
Late perimenopausal	209 (19.0)	68 (15.5)
Postmenopausal	387 (35.2)	142 (32.3)
Gestations, mean (SD)	2.5 (1.6)	2.7 (1.6)
Missing data, <i>n</i>	7	4
Parity, mean (SD)	2.0 (1.2)	2.1 (1.3)
Missing data, <i>n</i>	2	2
Hysterectomy, <i>n</i> (%)		
No	1007 (91.8)	402 (91.4)
Yes	90 (8.2)	38 (8.6)
Missing data, <i>n</i>	1	0
<i>Physical activity</i>		
Previous PA (age 17–29), <i>n</i> (%)		
No exercise	234 (23.7)	97 (24.3)
Regular PA	658 (66.7)	266 (66.7)
Competitive sport	94 (9.5)	36 (9.0)
Missing data	112	41
Current PA (MET-h/d), mean (SD)	4.5 (3.9)	4.2 (3.6)
Missing data	7	3

Table 3. Pooled multiple logistic regression model estimates (*n* =1098)

	Stress urinary incontinence		Urge urinary incontinence		Fec
	OR (95 % CI)	<i>p</i> value	OR (95 % CI)	<i>p</i> value	OR
<i>Physical activity</i>					
Previous PA (age 17–29)					
No exercise (ref)	1		1		1
Regular PA	0.95 (0.69–1.30)	0.746	1.48 (0.92–2.39)	0.104	4.41
Competitive sport	0.96 (0.58–1.59)	0.868	2.16 (1.10–4.24)	0.025	1.57
Current PA (MET-h/d)	0.97 (0.94–1.01)	0.143	0.97 (0.92–1.02)	0.243	0.95
<i>Demographical descriptives</i>					
Age	0.94 (0.88–1.01)	0.071	1.06 (0.97–1.17)	0.219	1.25
Body mass index	1.09 (1.05–1.14)	<0.001	0.98 (0.93–1.04)	0.517	1.11
Education					
Secondary (ref)	1		1		1
Tertiary	0.90 (0.69–1.18)	0.453	0.95 (0.65–1.40)	0.813	0.55
Physical workload					
Light (ref)	1		1		1
Moderate	1.11 (0.78–1.56)	0.565	1.18 (0.72–1.95)	0.513	1.05
Heavy	1.36 (0.99–1.87)	0.061	1.51 (0.96–2.36)	0.072	0.95
<i>Gynecological variables</i>					
Menopausal status					

	Stress urinary incontinence		Urge urinary incontinence		Feca
Premenopausal (ref)	1		1		1
Early perimenopausal	1.07 (0.74–1.55)	0.729	1.13 (0.66–1.92)	0.657	0.92
Late perimenopausal	0.58 (0.39–0.85)	0.006	0.84 (0.48–1.49)	0.554	0.49
Postmenopausal	0.77 (0.55–1.10)	0.149	1.06 (0.65–1.73)	0.823	0.58
Parity	1.12 (1.01–1.24)	0.031	1.03 (0.90–1.19)	0.649	1.14
Hysterectomy					
No (ref)	1		1		1
Yes	0.94 (0.59–1.49)	0.794	1.48 (0.83–2.63)	0.183	1.18

	Stress urinary incontinence	Stress urinary incontinence	Urge urinary incontinence
	OR (95 % CI)	<i>p</i> value	OR (95 % CI)
<i>Physical activity</i>			
Previous PA (age 17–29)			
No exercise (ref)	1		1
Regular PA	0.95 (0.69–1.30)	0.746	1.48 (0.92–2.39)
Competitive sport	0.96 (0.58–1.59)	0.868	2.16 (1.10–4.24)
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<i>Gynecological variables</i>			
Menopausal status			
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Hysterectomy			
No (ref)	1		1
Yes	0.94 (0.59–1.49)	0.794	1.48 (0.83–2.63)

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