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A prospective study of the association between physical activity and lower urinary tract symptoms in parous middle-aged women: results from the Avon Longitudinal Study of Parents and Children

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Abstract

Purpose

To examine the prospective associations between physical activity and a range of lower urinary tract symptoms (LUTS) in parous middle-aged women.

Materials and Methods

We used prospectively collected data on women participating in the Avon Longitudinal Study of Parents and Children. Physical activity levels were self-reported at mean age of 37.2 years (SD 4.6) and translated into metabolic-equivalents hours per week (MET hours/week). Women reported symptoms of LUTS (stress incontinence, urgency incontinence and mixed incontinence) after 3 (n=4126) and 11.5 (n=2770) years of follow-up.

Results

Prevalence of any LUTS after 3 and 11.5 years of follow-up (mean ages 40.5 years and 49.3 years) was 15% and 23%, respectively. Women in the highest category of physical activity (≥ 43.2 MET hours/week) had lower odds of stress incontinence (adjusted OR (aOR)=0.51; 95% CI 0.32, 0.80) compared to women in the lowest category (0 MET hours/week) after 3 years of follow-up. After 11.5 years of follow-up, women in the highest category of physical activity had lower odds of stress incontinence (aOR= 0.56; 95%CI: 0.39, 0.82), urgency incontinence (aOR= 0.34; 95%CI: 0.20, 0.67) and mixed incontinence (aOR= 0.34; 95%CI: 0.19, 0.63) when compared to women in the lowest physical activity category.

Conclusion

Greater physical activity is associated with reduced odds of LUTS, especially stress incontinence, among middle-aged parous women. Further research is necessary to examine the impact of different types of physical activity on LUTS.

Introduction

Lower urinary tract symptoms (LUTS) are very common and have a major impact on quality of life ^{1 2}. Prevalence estimates of LUTS is 76.3% in North American and European middle-aged women². According to the International Continence Society (ICS), LUTS are divided into storage and voiding symptoms; urinary incontinence (UI) is a storage symptom characterised by involuntary loss of urine ³. UI can be further categorized as stress UI, urgency UI and mixed UI (online Box 1). Other risk factors of LUTS among women include older age, parity, obesity and mode of delivery ⁴⁻⁶.

Existing studies looking at the associations between physical activity and LUTS are mostly cross-sectional with modest sample sizes and limited adjustment for confounders ⁷⁻⁹. Cross sectional studies are limited in their ability to establish the temporal relationship between the exposure and outcome (here physical activity and LUTS, respectively) and may be affected by recall bias due to participants reporting the exposure retrospectively.

Few prospective studies that are better able to establish the direction of the association between physical activity and LUTS have been conducted. A prospective study examined the relation of diet and other lifestyle factors including physical activity, with overactive bladder (OAB) and stress UI in women (n= 6424, median age: 21, range: 18-44 years at baseline) ¹⁰. The study reported lower risk of stress UI and both wet and dry OAB among women who were more physically active after 1 year of follow-up. Another prospective study based on the Nurses' Health Study (NHS) examined physical activity in relation to UI risk in women (n=31,355, mean age: 66, range: 54-79 years at baseline)¹¹. It found that higher levels of physical activity (as measured by averaged MET scores/week) were associated with a reduced risk of UI symptoms after 2 years of follow-up. In the Nurses' Health Study II (mean age: 46, range: 37-54 years at baseline) higher levels of physical activity were associated with a reduced risk of UI symptoms after 14 years of follow-up.

A systematic review assessing the prevalence of UI in female athletes (22 studies, 7,507 women aged 12 to 69 years) aimed to determine how different types of exercise influenced UI¹². The review examined 17 different moderate and high impact sporting activities, and found that gymnastics, volleyball, basketball, tennis and football were associated with the strongest increase in prevalence of UI.

Our study aims to examine the prospective association between physical activity and the risk of developing LUTS in a general population sample of parous middle-aged women.

Materials and Methods

Participants

This study included women participating in the Avon Longitudinal Study of Parents and Children (ALSPAC)^{13 14}. Detailed information is available at the cohort website (<http://www.bristol.ac.uk/alspac>), including a fully searchable data-dictionary (<http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary>). Briefly, ALSPAC is a prospective population-based birth cohort study which recruited 14,541 pregnant women residing in the former Avon Health Authority in England, with an estimated date of delivery between April 1991 and December 1992. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. 5,111 women were eligible for the current study because they had information on physical activity and no symptoms of UI at baseline (1999-2001, Figure 1). Of these women, 4,126 had information on LUTS after 3 years of follow-up (2002-2004), and 2770 had information on LUTS after 11.5 years of follow-up (2011-2012).

Physical activity (MET hours/week)

Women were asked to report the average hours in a typical week (>6 hrs, 2-6 hrs, < 2hrs, never) that they carried out diverse types of physical activity in 1999-2001 (8 years and 1 month after recruitment). This time point constituted the baseline for our analysis. Types of physical activity included aerobics, jogging, yoga, squash, tennis/badminton, swimming, brisk walking, weight training, cycling, keep fit exercises and other exercises. We subsequently estimated the metabolic equivalents scores (METs) of these different measures using the estimated energy costs of different types of physical activity in the Compendium of Physical Activity (<https://sites.google.com/site/compendiumofphysicalactivities/>). Keep fit exercises and Other exercises were excluded as we could not assign them METs with confidence.

Activity specific MET-hours per week were calculated by the following equation:

$$MET\text{-hours per week} = activity\ assigned\ METs \times the\ time\ spent\ doing\ an\ activity^* \times frequency$$

Since the response options of the time spent doing an activity (hrs/week) were categorical, we estimated hrs/week as follows: 6 for '≥ 6hrs', 4 for '2– 6hrs', 1 for '< 2hrs' and 0 for 'never'. To derive the total activity score for each participant, we summed up MET hours per week for the different types of physical activity. We divided the MET hours per week into quartiles

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(excluding those women who reported no activity) to obtain a variable with five categories of physical activity levels: 0 (reference group), 0.1-17.2, 17.3-29.2, 29.3-43.2 and greater than 43.2 MET hours/week.

LUTS

Participants responded to whether they had experienced “Problem holding urine when you jump sneeze etc?” and “Passing urine very often?” in the past month in questionnaires administered both 2 years (1996-1998) and 3 years (1997-1999) before baseline. Potential responses were: “*Not at all*”, “*Sometimes*”, “and “*Almost all the time*”. We excluded participants who reported any symptoms of UI on either question in order to study new-onset LUTS.

Three years after baseline (2002-2004), women completed an adapted version of the Bristol Female LUTS questionnaire ¹⁵. At 11.5 years after baseline (2011-2012), women completed an adapted version of the International Consultation on Incontinence Questionnaire on Female LUTS (ICIQ-FLUTS) ¹⁶.

Box 1 lists the LUTS related questions included in the BFLUTS and ICIQ-questionnaire. We were interested in LUTS that specifically have UI as a symptom: stress UI, urgency UI, mixed UI, unexplained UI and nocturnal enuresis. We chose to look at UI-specific symptoms due to the burden of UI in terms of impact on quality of life. Responses to these questions were used to categorize different types of LUTS, including stress UI, urgency UI and mixed UI based on the ICS definitions ³. We originally wanted to include unexplained UI and nocturnal enuresis but did not have a sufficient number of women for a meaningful analysis.

Other variables

Women’s age, occupational social class, education, and parity were self-reported at recruitment (1991-1992). Women’s weight and height were self-reported at baseline (1991-1992). Occupational social class was categorised according to the 1991 British Office of Population and Census Statistics and then binarized into manual and non-manual occupational social class. We categorized women’s education into degree vs other degree (Certificate of Secondary Education, Vocational, Ordinary level, Advanced level).

Statistical analysis

We used logistic regression to estimate the association between physical activity and LUTS subtypes. We tested for evidence of departure from linearity in the relationship between physical activity (MET hours/week) and LUTS subtypes by comparing a model where categories of physical activity were entered as a continuous variable to a model including four dummy variables using a likelihood ratio test.

To minimise selection bias due to including only those participants with complete data (on all of exposure, outcomes and covariables), and in order to increase statistical power, we used multiple imputation to impute missing covariate information for women considered to be eligible for the analysis (i.e. women who provided data on physical activity and LUTS). We generated 20 datasets using multiple imputation by fully conditional specification (chained equations). The imputation model included physical activity, all LUTS outcomes and the covariates mentioned above. The main analysis results were obtained by averaging across the results from each of these 20 datasets using Rubin's rules. The results from the complete case analysis are presented in supplementary tables 3-6 (on request).

We repeated analyses restricting activities to those classified as high intensity (METs ≥ 6 or more). These included aerobics, jogging, squash, tennis/badminton, swimming and cycling. All analyses were done using STATA/MP 15 (Statacorp, Texas).

Results

Table 1 shows the distribution of women's characteristics, physical activity and LUTS in the two different study samples used for the analysis of LUTS at 3 years (mean age 40.5 years; SD 4.5) and 11.5 years (mean age 49.3 years; SD 4.4) after baseline. At both time points, the most common LUTS was stress UI (9% and 13% respectively).

Supplementary tables 7 and 8 (on request) show the distribution of characteristics across categories of physical activity in the samples included in the analysis of LUTS at 3 years and at 11.5 years of follow up, respectively. Mean age increased and BMI decreased across levels of physical activity. There was no difference in the probability of being from a manual occupational social class by physical activity while the probability of having a university degree decreased across categories of physical activity at both time points. Parity also varied somewhat across physical activity categories.

Physical activity and LUTS at 3 years of follow up

The associations between physical activity and LUTS at 3 years after baseline are presented in Table 2. There was evidence of a non-linear relationship between physical activity and risk of stress UI. Women in the highest category of physical activity (≥ 43.2 MET hours/week) had a 50% reduction in the odds of reporting stress UI at 3 years of follow-up compared to inactive women in both the unadjusted and adjusted models. There was no strong evidence of any relationship between physical activity and urgency UI. There was evidence of reduced odds of mixed UI among women in the highest category of physical activity (aOR=0.48; 95%CI: 0.24, 0.99).

Physical activity and LUTS at 11.5 years of follow up

The associations between physical activity levels and LUTS 11.5 years after baseline are presented in Table 3. There was evidence of a non-linear relationship between physical activity and stress UI, mixed UI and urgency UI. Women in the highest category of physical (≥ 43.2 MET hours/week) had reduced odds of reporting stress UI (aOR=0.56; 95%CI 0.39, 0.82), urgency UI (aOR=0.34; 95%CI 0.20, 0.67) and mixed UI (aOR=0.34; 95%CI 0.19, 0.63) compared to women with zero MET hours/week. Lower odds of stress UI were also found for women with 17.3-29.2 MET hours/week of physical activity, while lower odds of urgency UI and mixed UI were observed among women with both 0.1-17.2 MET hours/week and 17.3-29.2 MET hours/week.

Tables 4 and 5 present results of high intensity analysis which are similar to the main results. Supplementary tables 5 and 6 (on request) show the complete case results which are similar to the main results.

Discussion

We found evidence for a decreased burden of LUTS at 3 and 11.5 years of follow-up, among middle-aged parous women who reported higher levels of physical activity. The odds of stress UI and mixed UI were lower among women in the highest category of physical activity, as compared to those in the lowest category, after both 3 and 11.5 years of follow-up. We also observed lower odds of urgency UI after 11.5 years of follow-up.

Strengths and limitations

Strengths of our study include its sample size, its prospective design, the use of validated questionnaires to assess LUTS, our ability to investigate multiple UI subtypes and our adjustment for multiple potential confounders. Our study included data on LUTS at two time points, 8.5 years apart.

Attrition is a limitation of this study, but we used multiple imputation to minimise selection bias due to missing information on potential confounders. We did not have information on some types of LUTS (urge) to exclude those with prevalent disease at baseline. We therefore cannot completely exclude the possibility of reverse causation affecting estimated associations between physical activity and LUTS. Physical activity (as well as potential confounders) was assessed once and may have changed during the follow-up period, i.e. between baseline and outcome assessment. We relied on self-reported physical activity to estimate MET-hours of physical activity per week. This might have introduced misclassification in our exposure, resulting in biased estimates. It seems plausible that women might over-report time spent on physical activity, which would result in underestimation of the true effect sizes. ALSPAC participants are predominantly white, and they are all parous. The results might therefore not be generalizable to other ethnicities and to nulliparous women.

Comparison of our findings with previous studies

A prospective study of women aged 54-79 years reported an inverse association between physical activity and UI incidence after two years of follow up ¹¹. In a second study of 30,135 middle-aged women (mean age 46 years) in the Nurses' Health Study II, results indicated a decrease in risk of stress and urgency UI among women with higher physical activity after 12 years of follow-up ¹⁷. Findings from the Leicestershire MRC study (n= 6424; median age 21 years) also reported lower risk of stress UI and wet and dry OAB among women who were more physically active ¹⁰.

Findings from a systematic review of studies in female athletes indicated that women who performed high-impact physical activity were more likely to report UI ¹². Compared with women in the community, athletes exercise for long periods and may engage in strenuous activities, which might damage pelvic floor muscles. High-impact physical activity, such as trampolining and gymnastics, may also increase the risk of developing UI due to strain on pelvic floor muscles ^{18 19}. Notably, when we restricted our analysis to high-intensity physical

activity, results were not substantially altered. However, this could be because our analysis was not limited to high impact activities.

Possible mechanisms explaining the association between physical activity and LUTS

There are different plausible mechanisms that might explain why women who are more physically active have a lower burden of LUTS. For example, women with higher physical activity could be more aware of their overall health. They could also be engaging in Kegel pelvic floor exercises which might directly decrease the risk of LUTS by strengthening of the muscles. Unfortunately, we do not have information on pelvic floor exercises to explore this in more detail. Physical activity may directly reduce the risk of developing UI by strengthening the pelvic floor muscles ²⁰, or it may act through lower BMI which in turn is associated with lower intra-abdominal pressure ²¹. However, after adjusting for BMI measured concurrently to the assessment of outcomes, results were still similar, suggesting that mediation by BMI did not fully account for associations between physical activity and LUTS.

Conclusion

Our study adds to the limited evidence-base concerning the association between physical activity and LUTS. Performing exercises such as jogging or swimming equivalent to 6 hours or more throughout the week (equivalent to ≥ 43.2 MET-hrs/week) could reduce the risk of developing stress UI by 49% (95% CI: 20%, 68%) compared to women who do not exercise at all. Our study has shown that performing higher physical activity is associated with a lower odds of developing urgency UI. The effect of physical activity on urgency UI should be further investigated in a large independent sample as our confidence interval was wide due to the small sample. Further research is necessary to examine the impact of different types and intensities of physical activity on LUTS.

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Abbreviations	
ALSPAC	Avon longitudinal study of parents and children
BMI	Body mass index
BFLUTS	Bristol female LUTS questionnaire
ICIQ-FLUTS	International Consultation on Incontinence Questionnaire on Female LUTS
LUTS	Lower urinary tract symptoms
UI	Urinary Incontinence
MET hours s/week	Metabolic equivalents hours per week
aOR	Adjusted odd ratio
Stress UI	Stress urinary incontinence
Urgency UI	Urgency urinary incontinence
OAB	Overactive bladder

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Table 1. Characteristics of women with data on LUTS at 3 and 11.5 years of follow up.

	2002-2004 (3 years follow up) N=4126	2011-2012 (11.5 years follow up) N=2770
Age, Mean (SE)	40.5 (0.1)	49.3 (0.1)
BMI, Mean (SE)	24.6 (0.1)	24.3 (0.1)
Parity, %		
1	48	48
2	36	37
3+	16	15
Occupational Social Class, %		
Manual	84	82
Non-manual	16	18
University Degree, %		
Yes	73	91
No	27	9
Physical activity (MET hours/week), %		
0	14	12
0.1-17.2,	24	23
17.3-29.2,	23	23
29.3-43.2	19	21
≥43.2	20	21
Stress UI, %		
Yes	9	13
No	91	87
Urgency UI, %		
Yes	3	4
No	97	96
Mixed UI, %		
Yes	3	6
No	97	94

Table 2. Associations of physical activity with risk of LUTS (by subtype) at 3 years of follow-up (Multiple Imputation)

Outcome	Physical activity Categories MET hours/week*	N	N cases (%)	Unadjusted OR (95% CI)	Adjusted OR** (95% CI)	Non-Linearity Test P-value
Stress UI						
	1 (0 MET hours/week)	577	47 (8)	Ref	Ref	0.010
	2	955	61 (6)	0.83 (0.59, 1.16)	0.80 (0.54, 1.18)	
	3	955	62 (6)	0.74 (0.53, 1.05)	0.72 (0.48, 1.07)	
	4	803	51 (8)	0.72 (0.50, 1.03)	0.80 (0.53, 1.21)	
	5	835	34 (4)	0.50 (0.34, 0.74)	0.51 (0.32, 0.80)	
Urgency UI						
	1	577	23 (4)	Ref	Ref	0.382
	2	956	25 (3)	0.65 (0.36, 1.15)	0.63 (0.34, 1.14)	
	3	955	25 (3)	0.65 (0.36, 1.15)	0.70 (0.40, 1.27)	
	4	803	20 (2)	0.62 (0.33, 1.13)	0.70 (0.38, 1.30)	
	5	835	20 (2)	0.59 (0.32, 1.08)	0.67 (0.35, 1.25)	
	per category			0.90 (0.78, 1.03)	0.94 (0.81, 1.08)	
Mixed UI						
	1	577	47 (8)	Ref	Ref	0.010
	2	955	61 (6)	0.83 (0.59, 1.16)	0.80 (0.54, 1.18)	
	3	955	62 (6)	0.74 (0.53, 1.05)	0.72 (0.48, 1.07)	
	4	803	51 (8)	0.72 (0.50, 1.03)	0.80 (0.53, 1.21)	
	5	835	34 (4)	0.50 (0.34, 0.74)	0.48 (0.24, 0.99)	
	per category					
* Category 1: 0 MET hours/week, Category 2: 0.1- 17.2 MET hours/week, Category 3: 17.3-29.2 MET hours/week, Category 4: 29.3-43.2 MET hours/week, Category 5: ≥43.2 MET hours/week						
** Confounders included for the adjusted models are age, parity, BMI, university degree and social status.						

Table 3. Associations of physical activity with risk of LUTS (by subtype) at 11.5 years of follow-up (Multiple Imputation)

Outcome	Physical activity categories MET hours/week*	N	N cases (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)**	Non-Linearity Test P-value
Stress UI						
	1 (0 MET hours/week)	275	58 (21)	Ref	Ref	0.026
	2	494	86 (17)	0.79 (0.57, 1.09)	0.78 (0.55, 1.11)	
	3	530	78 (15)	0.66 (0.47, 0.92)	0.65 (0.45, 0.93)	
	4	477	84 (18)	0.80 (0.57, 1.12)	0.89 (0.62, 1.26)	
	5	474	59 (12)	0.51 (0.35, 0.72)	0.56 (0.39, 0.82)	
Urgency UI						
	1	343	37 (11)	Ref	Ref	0.027
	2	633	44 (7)	0.61 (0.38, 0.96)	0.55 (0.33, 0.92)	
	3	637	38 (6)	0.53 (0.33, 0.86)	0.54 (0.32, 0.90)	
	4	574	41 (7)	0.65 (0.40, 1.04)	0.78 (0.47, 1.30)	
	5	583	23 (4)	0.33 (0.19, 0.56)	0.34 (0.20, 0.67)	
Mixed UI						
	1	274	25 (10)	Ref	Ref	0.006
	2	492	29 (6)	0.58 (0.36, 0.94)	0.55 (0.33, 0.91)	
	3	530	31 (6)	0.56 (0.34, 0.91)	0.55 (0.33, 0.92)	
	4	477	27 (6)	0.57 (0.35, 0.93)	0.63 (0.38, 1.07)	
	5	473	15 (3)	0.32 (0.18, 0.57)	0.34 (0.19, 0.63)	
* Category 1: 0 MET hours/week, Category 2: 0.1- 17.2 MET hours/week, Category 3: 17.3-29.2 MET hours/week, Category 4: 29.3-43.2 MET hours/week, Category 5: ≥43.2 MET hours/week						
** Confounders included for the adjusted models are age, parity, BMI, university degree and social status.						

Table 4. Associations of high intensity physical activity with risk of LUTS (by subtype) at 3 years of follow-up (Multiple Imputation)

Outcome	Physical activity Categories MET hours/week*	N	N cases (%)	Unadjusted OR (95% CI)	Adjusted** OR (95% CI)	Non-Linearity Test P -value
Stress UI						
	1 (0 MET hours/week)	1557	148 (10)	Ref	Ref	0.027
	2	669	68 (10)	1.07 (0.79, 1.45)	1.10 (0.81, 1.51)	
	3	1020	79 (8)	0.80 (0.60, 1.06)	0.87 (0.64, 1.17)	
	4	286	21 (7)	0.75 (0.47, 1.21)	0.87 (0.54, 1.40)	
	5	594	33 (6)	0.56 (0.38, 0.82)	0.65 (0.44, 0.97)	
Urgency UI						
	1	1557	48 (3)	Ref	Ref	0.524
	2	669	16 (2)	0.79 (0.44, 1.40)	0.86 (0.48, 1.54)	
	3	631	17 (3)	0.87 (0.50, 1.53)	1.00 (0.56, 1.76)	
	4	675	17 (3)	0.80 (0.46, 1.40)	0.90 (0.51, 1.60)	
	5	594	15 (3)	0.81 (0.45, 1.45)	0.93 (0.51, 1.70)	
	per category			0.93 (0.82, 1.04)	0.97 (0.86, 1.86)	
Mixed UI						
	1	1557	54 (3)	Ref	Ref	0.493
	2	669	18 (3)	0.78 (0.45, 1.32)	0.77 (0.45, 1.32)	
	3	1020	22 (2)	0.61 (0.37, 1.01)	0.61 (0.37, 1.01)	
	4	286	8 (3)	0.80 (0.38, 1.70)	0.80 (0.38, 1.70)	
	5	594	14 (2)	0.67 (0.37, 1.22)	0.67 (0.37, 1.21)	
	per category			0.89 (0.78, 1.02)	0.95 (0.83, 1.10)	
* Category 1: 0 MET hours/week, Category 2: 0.1- 17.2 MET hours/week, Category 3: 17.3-29.2 MET hours/week, Category 4: 29.3-43.2 MET hours/week, Category 5: ≥43.2 MET hours/week ** Confounders included for the adjusted models are age, parity, BMI, university degree and social status.						

Table 5. Associations of high intensity physical activity with risk of LUTS (by subtype) at 11.5 years of follow-up (Multiple imputation)

Outcome	Physical activity categories MET hours/week*	N	N cases (%)	Unadjusted OR (95% CI)	Adjusted OR**(95% CI)	Non-Linearity Test P-value
Stress UI						
	1 (0 MET hours/week)	429	47 (11)	Ref	Ref	0.073
	2	717	61 (9)	0.80 (0.59, 1.08)	0.83 (0.62, 1.13)	
	3	772	62 (8)	0.84 (0.65, 1.10)	0.90 (0.69, 1.17)	
	4	633	51 (8)	0.90 (0.60, 1.34)	0.97 (0.65, 1.46)	
	5	659	34 (5)	0.60 (0.43, 0.85)	0.68 (0.48, 0.96)	
Urgency UI						
	1	961	77 (8)	Ref	Ref	0.251
	2	475	29 (6)	0.76 (0.49, 1.19)	0.78 (0.50, 1.23)	
	3	717	46 (6)	0.80 (0.55, 1.17)	0.88 (0.60, 1.29)	
	4	206	11 (5)	0.65 (0.34, 1.24)	0.73 (0.38, 1.42)	
	5	411	20 (5)	0.56 (0.34, 1.94)	0.67 (0.40, 1.12)	
	per category			0.90 (0.79, 1.02)	0.94 (0.81, 1.06)	
Mixed UI						
	1	429	22 (5)	Ref	Ref	0.121
	2	718	12 (2)	0.81 (0.52, 1.28)	0.83 (0.53, 1.32)	
	3	772	19 (2)	0.72 (0.48, 1.08)	0.77 (0.51, 1.17)	
	4	633	20 (3)	0.66 (0.33, 1.30)	0.73 (0.37, 1.46)	
	5	660	13 (2)	0.59 (0.35, 1.01)	0.70 (0.41, 1.20)	
	per category			0.84 (0.73, 1.00)	0.93 (0.79, 1.10)	
* Category 1: 0 MET hours/week, Category 2: 0.1- 17.2 MET hours/week, Category 3: 17.3-29.2 MET hours/week, Category 4: 29.3-43.2 MET hours/week, Category 5: ≥43.2 MET hours/week ** Confounders included for the adjusted models are age, parity, BMI, university degree and social status.						

Figure 1. Flow chart showing the women included in the study