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The Dose-Response Effects of Aerobic Exercise on Musculoskeletal Injury: A Post Hoc Analysis of a Randomized Trial

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Abstract

In a *post hoc* analysis, we quantified the risk of musculoskeletal injury (MSI) associated with different volumes of aerobic exercise in a randomized trial. Premenopausal women ($n=119$) were randomized to one of three groups: low-dose-aerobic exercise ($150 \text{ min}\cdot\text{wk}^{-1}$), high-dose aerobic exercise ($300 \text{ min}\cdot\text{wk}^{-1}$), or control (usual activity) for five-months. Compared to the control group, the risk of reporting an acute MSI increased with higher volumes of aerobic exercise, with a similar pattern observed for recurrent MSI. The risk of reporting a MSI severe enough to impair activities of daily living did not increase with higher volumes of aerobic exercise. Approximately half of MSI were causally attributed to aerobic exercise. The risk of experiencing an acute or recurrent MSI increase with higher volumes of aerobic exercise, however the risk of experiencing a MSI severe enough to impair activities of daily living does not increase with higher volumes of aerobic exercise.

Keywords

joint; soft-tissue; adverse event; physical activity; impairment

INTRODUCTION

Participation in regular exercise is associated with a decreased risk of experiencing coronary heart disease, stroke, type 2 diabetes, breast and colon cancer, and premature mortality (Blair et al., 1989; Garber et al., 2011). The American College of Sports Medicine (ACSM) and American Heart Association (AHA) recommend healthy adults engage in a dose of 150 minutes-per-week ($\text{min}\cdot\text{wk}^{-1}$) of moderate-intensity aerobic exercise to promote and maintain overall health (Haskell et al., 2007), and a dose of $300 \text{ min}\cdot\text{wk}^{-1}$ of moderate-intensity aerobic exercise for long-term weight maintenance and to maximize the above-described health-benefits (Jakicic et al., 2001).

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Conflicts of Interest:

The authors report no conflicts of interest.

Despite the recognized health-benefits of regular exercise, the risks associated with exercise are less understood. The ACSM/AHA guidelines acknowledge that the relationship between exercise dose and the risk of musculoskeletal injury (MSI) remains unclear (Haskell et al., 2007). The 2008 Physical Activity Guideline Advisory Committee Report to the Surgeon General acknowledged that the number of randomized clinical trials that have systematically reported information on MSI is insufficient (Physical Activity Guidelines Advisory Committee, 2008), and requested that future studies quantify the relationship between exercise dose and MSI because MSI is a common reason why people cease participation in regular exercise (Finch et al., 2001; Koplan et al., 1982). Understanding the relationship between exercise volume and MSI will offer healthcare providers the evidence necessary to balance the risks and benefits of prescribing larger doses of exercise to patients.

This post hoc analysis of data from the Wiser Sister Trial aims to examine the relationship between exercise volume and the risk of MSI in the setting of a randomized controlled clinical trial among premenopausal women. We hypothesized that larger volumes of moderate-intensity aerobic exercise would associate with a higher risk of MSI.

METHODS

Design

The WISER (Women In Steady Exercise Research) Sister study was a randomized controlled trial of premenopausal women at elevated risk of developing breast cancer (Schmitz et al., 2015b). The primary aim of the Wiser Sister study was to assess the dose-response effects of aerobic exercise on estrogen (estrone-1-glucuronide) over five-months. The primary outcome and key secondary outcomes of this study have been published (Schmitz et al., 2015a). This study was approved by the Institutional Review Board at the University of Pennsylvania and registered on clinicaltrials.gov as NCT00892515. All participants provided written informed consent prior to engaging in any study-related activities.

Study Participants

Participants in the Wiser Sister study were healthy, eumenorrheic women, with a 18% lifetime risk for developing breast cancer. For comparison, the average risk of developing breast cancer in the population is 12.4% (McPherson et al., 2000). Detailed participant inclusion and exclusion criteria are published elsewhere (Schmitz et al., 2015b). Pertinent to this analysis, women were excluded if they had a medical condition that would prohibit participation in an aerobic exercise program (i.e., fibromyalgia, post-polio syndrome, unstable cardiopulmonary disease); had a BMI ≥ 30 kg/m²; were attempting to lose weight; were currently pregnant or planning to become pregnant; consumed ≥ 7 alcoholic drinks per week; and were physically active, defined as a self-report of ≥ 75 minutes of moderate- or vigorous-intensity aerobic exercise per week. Women were recruited from the continental United States through non-profit organizations that provide information to people with at-risk for hereditary cancers. Costs for travel (airfare, hotel) to complete in-person measurement visits were paid for by the study.

Women were placed into one of three groups using computerized randomization: low-dose aerobic exercise (150 min·wk⁻¹), high-dose aerobic exercise (300 min·wk⁻¹), or control (usual activity) using blocked randomization in a 1:1:1 ratio.

Aerobic Exercise Intervention

The primary modality of aerobic exercise used in this study was walking. Women randomized to the low-dose or high-dose groups were prescribed aerobic exercise using study-provided treadmills in their homes (Smooth 5.65, Smooth Fitness, King of Prussia, PA). Prior to engaging in exercise, all participants received instructions from a certified personal trainer regarding appropriate warm-up, cool-down, stretches, and proper footwear for injury prevention. The prescribed doses of aerobic exercise were 150 min·wk⁻¹ for the low-dose group, consistent with guidelines to promote and maintain overall health (Haskell et al., 2007), and 300 min·wk⁻¹ for the high-dose group, consistent with guidelines to promote weight maintenance and maximize overall health (Jakicic et al., 2001). The low-dose group increased weekly volume of aerobic exercise to 150 min·wk⁻¹ over the first four-weeks of the study. The high-dose group increased weekly volume of aerobic exercise to 150 min·wk⁻¹ over the first four-weeks of the study, and then increased to 300 min·wk⁻¹ by week 10 of the study. Both the low-dose and high-dose groups engaged in aerobic exercise that was 65–70% of their age predicted heart rate maximum (HR_{max}) for the first four-weeks of the study, and increased to 70–80% of HR_{max} from week five to the end of the study. These heart rate ranges are consistent with that of moderate-intensity aerobic exercise. Participants wore a heart rate monitor (RS400, Polar USA, Lake Success, NY) to objectively record exercise adherence and intensity. Participants also completed self-reported exercise logs. Study staff reviewed the heart rate information and self-reported exercise logs to guide exercise progression. Adherence and alterations in the exercise prescription due to illness, MSI, travel, etc., were coordinated by a certified personal trainer who had weekly contact with the participants. Additional details about the exercise prescription are provided elsewhere (Schmitz et al., 2015b).

Measurements

Measurements were completed at baseline and after five-months by trained staff blinded to treatment allocation, following standardized protocols. Demographic characteristics were self-reported. Caloric consumption was quantified using three-day food records using the Nutrition Data System for Research software (Nutrition Coordinating Center, University of Minnesota, 2009 version). Physical activity was assessed using the Modifiable Physical Activity Questionnaire (Kriska et al., 1990). Total treadmill time from the Bruce protocol was used to quantify aerobic fitness (Bruce et al., 1973). Anthropometric measures included height, weight, and body composition using dual energy x-ray absorptiometry (QDR 4500 Discovery A, Hologic, Bedford MA).

Musculoskeletal Injury Questionnaire

At the end of the study, a survey assessed self-reported MSI that occurred over the five-month period (survey included as supplementary material). The content of the MSI questionnaire was developed in accordance with the National Institutes of Health adverse event reporting guidelines (National Institutes of Health, 2010), and has been used in prior

randomized trials of weightlifting exercise (Brown et al., 2012; Warren and Schmitz, 2009). The MSI survey asked questions related to the incidence of injury over the study period, type of injury (joint or soft-tissue), anatomic location of injury, relatedness to exercise, severity of injury, and if the injury impaired activities of daily living (Brown et al., 2012; Warren and Schmitz, 2009). The questionnaire was multiple choice but did allow for free-text responses should none of the provided choices be applicable. The questionnaire was developed with input from exercise physiology, rehabilitation medicine, and internal medicine experts. We calculated three definitions of MSI: 1) acute MSI, defined as an injury that occurred one time; 2) recurrent MSI, defined as an injury that occurred two or more times; and 3) MSI that impaired daily activities, defined as any acute or recurrent injury that impeded activities required for daily living. In exploratory analysis we examined the three above definitions of injury separately for joint-specific and soft-tissue-specific injuries.

Statistical Analysis

Continuous variables are summarized with means and standard deviations. Categorical variables are summarized with counts and percentages. Relative risks (RR) and 95% confidence intervals (95% CI) of MSI were calculated using a generalized linear model. Randomized group assignment was treated as a categorical variable in the regression model to quantify the risk of MSI for the low-dose and high-dose exercise groups, as compared to the control group. The test of a dose-response effect of MSI with volume of exercise was assessed across the three groups using randomized group assignment as an ordinal variable in the regression model. We calculated the attributable risk to estimate the percentage of MSI causally related to exercise (Macera and Powell, 2001). Attributable risk was calculated as the risk difference of injury between the exercise group (low-dose or high-dose) and control group, divided by the incidence of injury in the exercise group, then multiplied by 100. We calculated the number needed to injure: the number of women who would need to be prescribed exercise for five-months to cause one MSI that would have not otherwise occurred (Barratt et al., 2004). The number needed to injure was calculated as the inverse of the risk difference between the exercise group (low-dose or high-dose) and control group. The software package Stata 14.1 (StataCorp LP, College Station, TX) was used for all statistical analyses. $P < 0.05$ was used to indicate statistical significance for all analyses.

RESULTS

The WISER Sister study randomized 139 women to the three study groups (Figure 1), and 122 successfully completed the study (88%). MSI questionnaire data were missing on three women (two in the low-dose group and one in the high-dose group); consequently, this analysis includes 119 of the 122 women who completed the study (98%). The most common reason for attrition was lack of time, and no participants cited MSI as a reason for attrition.

Demographic and Clinical Characteristics

Demographic and clinical characteristics are presented in Table 1. Age ranged from 18–49 years, 11% self-reported non-white race, and 56% were employed full time. BMI ranged from 17.5–42.5 kg/m².

Exercise Adherence Characteristics

Women randomized to low-dose aerobic exercise completed 85% of their prescribed exercise dose, averaging 127 ± 51 min·wk⁻¹ of exercise. Women randomized to high-dose aerobic exercise completed 81% of their prescribed exercise dose, averaging 214 ± 73 min·wk⁻¹ of exercise. Maximal aerobic fitness improved in dose-response fashion across the three study groups ($P < 0.001$) (Schmitz et al., 2015a).

Acute Musculoskeletal Injury

Acute MSI outcomes are described in Table 2. Among all three groups, 45 women (38%) reported an acute MSI. The risk of experiencing an acute MSI increased in dose-response fashion ($P_{\text{trend}} = 0.001$). Compared to the control group, the low-dose [RR: 2.08 (95% CI: 1.03–4.20); $P = 0.040$] and high-dose [RR: 2.76 (95% CI: 1.44–5.30); $P = 0.002$] groups were more likely to report an acute MSI. Among the low-dose and high-dose exercise groups, 52% and 63% of acute MSI were causally attributed to exercise training, respectively. Approximately 5 and 3 women would need to be prescribed low-dose or high-dose exercise for five-months to cause one incident acute MSI, respectively.

Recurrent Musculoskeletal Injury

Among all three groups, 34 women (28%) reported a recurrent MSI. The risk of experiencing a recurrent MSI increased in dose-response fashion ($P_{\text{trend}} = 0.032$). Compared to the control group, the low-dose [RR: 1.72 (95% CI: 0.77–3.82); $P = 0.184$] and high-dose [RR: 2.22 (95% CI: 1.06–4.66); $P = 0.035$] groups were likely to report a recurrent MSI. Among the low-dose and high-dose groups, 42% and 55% of recurrent MSI were causally attributed to exercise training, respectively. Approximately 8 and 5 women would need to be prescribed low-dose or high-dose exercise for five-months to cause one incident recurrent MSI, respectively.

Musculoskeletal Injury that Impaired Daily Activities

Among all three groups, 16 women (13%) reported a MSI that impaired daily activities. The risk of experiencing a MSI that impaired daily activities did not increase in dose response fashion ($P_{\text{trend}} = 0.350$). Compared to the control group, the low-dose [RR: 1.87 (95% CI: 0.57–6.14); $P = 0.299$] and high-dose [RR: 1.78 (95% CI: 0.54–5.83); $P = 0.344$] groups were not more likely to report a MSI that impaired daily activities. Among the low-dose and high-dose groups, 47% and 44% of MSI that impaired daily activities were causally attributed to exercise training, respectively. Approximately 13 and 14 women would need to be prescribed low-dose or high-dose exercise for five-months to cause one incident MSI to impair daily activities, respectively. None of the variables listed in Table 1 modified the relationship between exercise dose and the risk of MSI.

Exploratory Analyses: Individual Joint and Soft-Tissue Injury Endpoints

The effects of acute joint-specific injury increased in dose-response fashion ($P_{\text{trend}} = 0.009$), but not acute soft-tissue-specific injury ($P_{\text{trend}} = 0.344$). Restricting the analysis to recurrent joint-specific injury showed a dose-response effect ($P_{\text{trend}} = 0.049$), but not recurrent soft-tissue-specific injury ($P_{\text{trend}} = 0.805$). The effects of acute or recurrent joint-specific injury

that impaired daily activities ($P_{\text{trend}}=0.325$) and acute or recurrent soft-tissue-specific injury that impaired daily activities ($P_{\text{trend}}=0.836$), did not increase in dose response fashion.

Location of Injury

The anatomical location of joint and soft-tissue injury is displayed in Table 3. MSI of the knee and ankle were most common in the exercise groups, whereas MSI of the back was most common in the control group. Though not statistically significant, a pattern of increasing frequency of acute and recurrent knee injuries was observed with higher volumes of aerobic exercise.

DISCUSSION

The risk of experiencing an acute or recurrent MSI increased with higher volumes of moderate-intensity aerobic exercise; however, the risk of experiencing a MSI severe enough to impair activities of daily living did not increase with higher volumes of moderate-intensity aerobic exercise. Nonetheless, these data do indicate that if healthcare providers prescribe aerobic exercise to their patients MSIs will occur. Because MSI is a frequently cited reason people cease participation in exercise (Finch et al., 2001; Koplan et al., 1982), the development of an infrastructure to guide patients in the safe progression of exercise to minimize injury risk may be warranted. These findings, derived from a randomized clinical trial setting, fill a gap in the literature regarding the risk of MSI associated with aerobic exercise. An awareness of the relationship between exercise dose and the risk of MSI may assist healthcare providers to determine the risk-to-benefit ratio of prescribing larger doses of aerobic exercise to patients.

Our findings on the dose-response relationship of aerobic exercise and MSI are similar to observational studies, where much of the evidence regarding the risk of MSI has been derived (Gilchrist et al., 2000; Hootman et al., 2001; Hootman et al., 2002; Koplan et al., 1982; Morrow et al., 2012). Among 909 community-dwelling women, the risk of reporting a MSI over three-years increased with volume of exercise, such that women who engaged in 150 min·wk⁻¹ and 300 min·wk⁻¹ of exercise were 1.4- and 1.7-fold more likely to experience a MSI compared to women who exercised <150 min·wk⁻¹, respectively (Morrow et al., 2012). Our study sample included a population at high risk of developing a MSI from exercise. Female gender, younger age, sedentary lifestyle, and overweight or obesity are known risk factors for MSI (Physical Activity Guidelines Advisory Committee, 2008). The WISER Sister participants were women, with a mean age of 35, who were sedentary or physically inactive at baseline, and 48% were overweight or obese (BMI ≥ 25.0 kg/m²).

Few reports have varied the definition of MSI to delineate the specific mechanisms of injury associated with exercise. The primary outcome of this analysis was MSI, defined as a composite of joint-specific injury and soft-tissue-specific injury. However, in secondary analyses, our data indicated that the risk of joint-specific injury and soft-tissue-specific injury may differ, such that the risk of joint-specific injury increases, whereas the risk soft-tissue-specific injury does not increase, with volume of weight-bearing aerobic exercise, such as treadmill walking prescribed in this study. There is evidence that joint-specific injuries of the lower-extremities are more common than soft-tissue injuries for non-contact,

repetitive activities such as aerobic exercise (Hammes et al., 2015; Hootman et al., 2002; Koplan et al., 1982).

The definitions of MSI in this analysis differ in two ways from prior reports using the same self-report questionnaire (Brown et al., 2012; Warren and Schmitz, 2009). First, we did not restrict the definition of MSI to include only events that lasted longer than one week. This is important because short-term or transient yet recurring injuries exert a negative influence on participation and willingness to exercise (Hootman et al., 2001; Hootman et al., 2002; Physical Activity Guidelines Advisory Committee, 2008). Second, we did not restrict the definition of MSI to events that participants self-attributed to exercise. This inclusive definition of MSI allowed for direct comparison of injury rates between the two exercise groups and the control group. The randomized design permitted our analysis to account for MSI that occurred in the control group. The study asked women randomized to the control group to maintain their usual levels of activity. Despite absence of a structured, progressive aerobic exercise program, 20%, 18%, and 9%, of women in the control group reported an acute, recurrent, or MSI that impaired daily activities, respectively. In the absence of a randomized controlled trial, the proportion of MSI causally attributed to aerobic exercise training would consequently be overestimated. Depending on the definition used in our analysis, 42–63% of MSI may be causally attributed to aerobic exercise training.

The ACSM created the Exercise is Medicine initiative calling for physicians to prescribe exercise to their patients (Sallis, 2009). Exercise is associated with reductions in the risk of experiencing coronary heart disease, stroke, type 2 diabetes, breast and colon cancer, and risk of premature mortality (Blair et al., 1989; Garber et al., 2011). All of these above-described associations have dose-response relationships, such that larger volumes of exercise provide more favorable health-benefits. Despite these known dose-response relationships, healthcare providers may be cautious to prescribe larger doses of exercise out of concern that their patients will become injured and cease participating in exercise altogether (Finch et al., 2001; Powell et al., 1998). Our data may be useful to providers to balance the risks and benefits of prescribing larger volumes of aerobic exercise to their patients. Providers who consider prescribing exercise should know that the risk of experiencing an acute or recurrent MSI will increase with exercise dose, but the risk of experiencing a MSI severe enough to impair daily activities does not increase in dose-response fashion. Muscle strengthening activities may lower the risk of experiencing an MSI during aerobic exercise (Naclerio et al., 2015; Theodorou et al., 2016), perhaps by mediating the inflammatory (C-reactive protein) and muscle damage (creatine kinase and lactate dehydrogenase) responses that occur during and immediately after aerobic exercise (Souglis et al., 2015). Both the ACSM/AHA guidelines (Haskell et al., 2007), and the 2008 Physical Activity Guideline Advisory Committee Report to the Surgeon General (Physical Activity Guidelines Advisory Committee, 2008), concluded that the risks of MSI from exercise are outweighed by the potential health-benefits. Our data provide quantitative evidence to substantiate the viewpoint that the benefits of progressive moderate-intensity aerobic exercise outweigh the risks with respect to MSI.

Despite the strengths of our study, there are limitations that should be acknowledged to add context to our findings. The major limitation of our study was the self-report MSI

questionnaire which was administered at a single time point at the end of the study. Our questionnaire did not inquire as to when the MSI occurred; therefore we are unable to determine when MSI are mostly likely to occur over a five-month period. The analysis of the self-report MSI questionnaire was not pre-specified as a secondary outcome in the study protocol. Therefore our report should be interpreted conservatively as a *post hoc* analysis. Our findings may be subject to recall bias, such as differential reporting between the control and exercise groups. Women in the exercise groups may be more likely to remember MSI experienced during exercise training, which would overestimate the risk of MSI associated with exercise. Another limitation of our study was that we did not corroborate self-reported MSI with physician evaluation or diagnostic imaging. Over 83% of exercise-related MSI are not reported to a physician, which makes the use of a self-report survey advantageous (Kaplan et al., 2014; Koplan et al., 1982). We did not ask about MSI sustained before entering the study. It is known that prior MSI increases the risk for a recurrent MSI (Physical Activity Guidelines Advisory Committee, 2008). Randomization is known to balance both measured and unmeasured variables across groups; therefore the proportion of women with a prior MSI would be similar across the three groups. Though our study sample included premenopausal women at high-risk of developing breast cancer, we believe our findings may be applicable to premenopausal women broadly.

The major findings of our study are that acute and recurrent MSI increase in dose-response fashion with volume of aerobic exercise. However, MSI severe enough to impair daily activities do not increase in dose-response fashion with volume of aerobic exercise. The proportion of MSI causally attributed to progressive moderate-intensity aerobic exercise training ranges from 42 to 63%, depending on the definition of MSI used. Healthcare providers now have quantitative data from a randomized controlled clinical trial to inform their decision making and balance the risks and benefits of prescribing two common doses of aerobic exercise to their patients.

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Figure 1.
Flow of participants

Table 1

Demographic and clinical characteristics

Characteristic	Overall (N=119)	Control (N=45)	Low-Dose (N=36)	High-Dose (N=38)
Age, yr	34.8±6.6	34.5±7.5	36.2±5.4	34.0±6.4
Race				
White	106 (89%)	38 (84%)	34 (94%)	34 (89%)
Other	13 (11%)	7 (16%)	2 (6%)	4 (11%)
Employed full time, % yes	67 (56%)	24 (53%)	22 (61%)	21 (55%)
Caloric consumption, kcals/day	1,845±528	1,840±554	1817±578	1879±450
Physical activity (MET-hr/wk)	8.3±7.6	8.3±6.5	8.9±9.5	7.5±6.7
Treadmill time, seconds	499±94	482±99	496±81	523±96
Body mass, kg	71.9±16.3	74.1±16.4	72.5±17.1	69.0±15.3
Body mass index, kg/m ²	26.0±6.0	26.8±6.2	26.1±6.1	25.1±5.7
Body fat, %	37.0±6.8	37.6±7.0	37.9±6.3	35.5±6.8
Lean mass, kg	44.4±6.2	45.3±5.8	44.1±6.5	43.7±6.2

Data are means ± standard deviation. There were no differences across randomized groups.

Table 2

Musculoskeletal Injury with Varying Definitions

Definition of Outcome	N (%)	Relative Risk (95% CI)	P	Excess % of Injury Attributable To Exercise (95% CI)	Number Needed To Injure*
Acute musculoskeletal injury					
Control	9 (20%)	1 — Referent	—	—	—
Low-Dose	15 (42%)	2.08 (1.03–4.20)	0.040	52% (3–76)	5
High-Dose	21 (55%)	2.76 (1.44–5.30)	0.002	63% (31–81)	3
$P_{\text{trend}}=0.001$					
Recurrent musculoskeletal injury					
Control	8 (18%)	1 — Referent	—	—	—
Low-Dose	11 (31%)	1.72 (0.77–3.82)	0.184	42% (–29–74)	8
High-Dose	15 (40%)	2.22 (1.06–4.66)	0.035	55% (5–78)	5
$P_{\text{trend}}=0.032$					
Acute or recurrent musculoskeletal injury that impaired daily activities					
Control	4 (9%)	1 — Referent	—	—	—
Low-Dose	6 (17%)	1.87 (0.57–6.14)	0.299	47% (–75–84)	13
High-Dose	6 (16%)	1.78 (0.54–5.83)	0.344	44% (–85–83)	14
$P_{\text{trend}}=0.350$					
Acute joint injury					
Control	8 (18%)	1 — Referent	—	—	—
Low-Dose	11 (31%)	1.72 (0.78–3.82)	0.184	42% (–29–74)	8
High-Dose	17 (45%)	2.52 (1.22–5.17)	0.012	60% (18–81)	4
$P_{\text{trend}}=0.009$					
Recurrent joint injury					
Control	6 (13%)	1 — Referent	—	—	—
Low-Dose	8 (22%)	1.67 (0.64–4.37)	0.299	40% (–57–77)	11
High-Dose	12 (32%)	2.37 (0.98–4.37)	0.055	58% (–2–82)	6
$P_{\text{trend}}=0.049$					
Acute or recurrent joint injury that impaired daily activities					
Control	2 (4%)	1 — Referent	—	—	—

Definition of Outcome	N (%)	Relative Risk (95% CI)	P	Excess % of Injury Attributable To Exercise (95% CI)	Number Needed To Injure*
Low-Dose	5 (14%)	3.13 (0.64–15.17)	0.158	68% (–55–93)	11
High-Dose	4 (11%)	2.37 (0.46–12.22)	0.303	58% (–118–92)	16
$P_{\text{trend}}=0.325$					
Acute soft-tissue injury					
Control	4 (9%)	1 — Referent	—	—	—
Low-Dose	5 (14%)	1.56 (0.45–5.40)	0.480	36% (–121–82)	20
High-Dose	6 (16%)	1.78 (0.54–5.83)	0.344	44% (–85–83)	14
$P_{\text{trend}}=0.344$					
Recurrent soft-tissue injury					
Control	4 (9%)	1 — Referent	—	—	—
Low-Dose	3 (8%)	0.94 (0.22–3.92)	0.930	6% (–292–78)	—
High-Dose	4 (11%)	1.18 (0.32–4.42)	0.801	15% (–215–77)	61
$P_{\text{trend}}=0.805$					
Acute or recurrent soft-tissue injury that impaired daily activities					
Control	3 (7%)	1 — Referent	—	—	—
Low-Dose	2 (6%)	0.83 (0.15–4.72)	0.837	17% (–372–85)	—
High-Dose	3 (8%)	1.18 (0.25–5.53)	0.830	16% (–294–82)	81
$P_{\text{trend}}=0.836$					

*The number of women that would need to be prescribed the respective dose of exercise for five menstrual cycles to cause one incident injury that would not otherwise have occurred.

Table 3

Musculoskeletal Injury Anatomic Location Characteristics

Type and Location of Injury	Control			High-Dose			P	Control			High-Dose			P		
	N (%)			N (%)				N (%)			N (%)					
	Acute	Low-Dose	Recurrent	Acute	Low-Dose	Recurrent		Acute	Low-Dose	Recurrent	Acute	Low-Dose	Recurrent			
Joint							.078						.380			.619
Wrist	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)		1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Back	2 (25%)	0 (0%)	0 (0%)	1 (6%)	0 (0%)	1 (8%)		1 (17%)	0 (0%)	1 (8%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Knee	4 (50%)	6 (54%)	13 (76%)	13 (76%)	5 (63%)	10 (83%)		3 (50%)	5 (63%)	10 (83%)	1 (50%)	2 (40%)	3 (75%)	0 (0%)	0 (0%)	
Hip	0 (0%)	3 (27%)	0 (0%)	0 (0%)	1 (13%)	0 (0%)		0 (0%)	1 (13%)	0 (0%)	0 (0%)	2 (40%)	0 (0%)	0 (0%)	0 (0%)	
Ankle	1 (13%)	2 (18%)	3 (18%)	3 (18%)	2 (25%)	1 (8%)		1 (17%)	2 (25%)	1 (8%)	0 (0%)	1 (20%)	1 (25%)	0 (0%)	0 (0%)	
Soft-tissue							.163									.486
Neck	0 (0%)	1 (20%)	0 (0%)	0 (0%)	1 (33%)	0 (0%)		0 (0%)	1 (33%)	0 (0%)	2 (67%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)	
Arms	1 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)		1 (25%)	0 (0%)	0 (0%)	1 (33%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Back	3 (75%)	1 (20%)	1 (17%)	1 (17%)	0 (0%)	0 (0%)		3 (75%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Gluteus	0 (0%)	0 (0%)	1 (17%)	1 (17%)	0 (0%)	1 (25%)		0 (0%)	0 (0%)	1 (25%)	0 (0%)	0 (0%)	1 (33%)	0 (0%)	0 (0%)	
Upper leg	0 (0%)	0 (0%)	1 (17%)	1 (17%)	0 (0%)	1 (25%)		0 (0%)	0 (0%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Lower Leg	0 (0%)	3 (60%)	3 (50%)	3 (50%)	2 (67%)	2 (50%)		0 (0%)	2 (67%)	2 (50%)	0 (0%)	1 (50%)	2 (67%)	0 (0%)	0 (0%)	

* Injuries that impaired daily activities (IDA)