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CLINICAL RESEARCH STUDY

AJM Theme AJM Theme Issue: Infectious Disease

Moderate-Intensity Exercise Reduces the Incidence of Colds Among Postmenopausal Women

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ABSTRACT

PURPOSE: Our aim was to assess the effect of a moderate-intensity, year-long exercise program on the risk of colds and other upper respiratory tract infections in postmenopausal women.

SUBJECTS: A total of 115 overweight and obese, sedentary, postmenopausal women in the Seattle area participated.

METHODS: Participants were randomly assigned to the moderate-intensity exercise group or the control group. The intervention consisted of 45 minutes of moderate-intensity exercise 5 days per week for 12 months. Control participants attended once-weekly, 45-minute stretching sessions. Questionnaires asking about upper respiratory tract infections in the previous 3 months were administered quarterly during the course of the year-long trial. Poisson regression was used to estimate the effect of exercise on colds and other upper respiratory tract infections.

RESULTS: Over 12 months, the risk of colds decreased in exercisers relative to stretchers ($P = .02$): In the final 3 months of the study, the risk of colds in stretchers was more than threefold that of exercisers ($P = .03$). Risk of upper respiratory tract infections overall did not differ ($P = .16$), yet may have been biased by differential proportions of influenza vaccinations in the intervention and control groups.

CONCLUSIONS: This study suggests that 1 year of moderate-intensity exercise training can reduce the incidence of colds among postmenopausal women. These findings are of public health relevance and add a new facet to the growing literature on the health benefits of moderate exercise.

KEYWORDS: Colds; Upper respiratory tract infections; Exercise; Postmenopausal women; Prevention; Overweight

The role of regular physical activity in preventing acute illnesses such as colds or other upper respiratory tract infections is not well defined. Improving our understanding of how to prevent these illnesses may help reduce the economic and health burden they impose. With adults in the United States reporting, on average, two to four colds per year,[1] colds are an important source of workplace absenteeism, loss of productivity, and visits to health care providers.[2] The incidence of colds is inversely related to age,[1] is strongly associated with season,[1,3] and may be related to a variety of environmental and genetic factors.[1] Lack of adequate sleep,[4] exposure to children receiving childcare outside the home,[4] poor air quality,[5,6] home dampness,[7] and smoking[8] are among factors associated with an increased risk of colds.

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Research suggests a J-shaped relationship between exercise and the risk of upper respiratory tract infections. Several randomized trials have suggested that moderate-intensity training reduces the severity of upper respiratory tract infections;[9-11] however, most of these studies have been small with intervention periods of at most 15 weeks duration.[9,10,12] The short-term randomized studies that have been conducted to date suggest a relationship between exercise training and the duration of upper respiratory tract infections.[9,10] Yet they have not been able to address whether exercise training can affect the number (incidence) of upper respiratory tract infections. Thus, the objective of the present study was to assess, in a randomized, controlled trial with excellent adherence, the effects of a year-long exercise intervention on the risk of colds and other upper respiratory tract infections.

CLINICAL SIGNIFICANCE

- Research suggests that regular, moderate-intensity physical activity protects against upper respiratory tract infections, but this relationship has not been well established.
- We randomized postmenopausal women to a 1-year exercise training intervention program or stretching control group.
- The probability of self-reported colds was significantly decreased among exercisers compared with stretchers over the course of the year.
- Results from this randomized trial show that postmenopausal women can reduce their risk of colds by engaging in moderate-intensity exercise.

METHODS

Participants were enrolled in a randomized trial of Seattle-area, overweight/obese, nonsmoking, sedentary, postmenopausal women,[13] recruited between 1998 and 2000, who met eligibility criteria for a study of the exercise effect on immune function (n = 115, described in detail in Shade et al.[14]). The exercise prescription consisted of at least 45 minutes of moderate-intensity exercise 5 days per week for 12 months (for details, see Irwin et al.[15]). Control participants attended once-weekly, 45-minute stretching sessions. All participants were asked to maintain their usual diet and exercise habits. Participants provided written informed consent, and the institutional review board approved all study procedures.

At baseline and 3, 6, 9, and 12 months, participants completed self-administered questionnaires, modified from established, validated instruments,[9,10,16,17] on the number of episodes of allergies, upper respiratory tract infections (colds and flu), and other infections over the past 3 months. Before randomization, women were taught to monitor the occurrence of upper respiratory tract infections and instructed in questionnaire completion and how to distinguish among allergies, colds, and flu. Specifically, subjects were provided the following guidelines: *Allergy symptoms include a runny nose, itchy eyes, and clear discharge from nose. They are not accompanied by a severe sore throat or cough and usually persist for more than 2 weeks. Symptoms may worsen with exposure to house dust, pollen, or pets. Cold symptoms include a runny or stuffy nose, sore throat, coughing, sneezing, and clear or colored discharge. Flu symptoms include fever, general aches and pains, headache, fatigue and weakness, chest discomfort, and cough.* These instructions were partially repeated on the questionnaire (see Appendix in the online version of the *Journal*).

Using these guidelines, women recorded the number and self-defined type of upper respiratory tract infections they experienced during the past 3 months, including whether they visited a physician for diagnosis. We evaluated questionnaire reproducibility among 43 study participants by repeat administration within 5 weeks of the initial response. Thirty-nine (91%) of the selected women returned the repeat questionnaire. Concordance with respect to reporting of upper respiratory tract infections episodes was 74% ($\kappa = 0.44$).

At baseline, 3 months, and 12 months, we collected demographic information, medical history, health habits, reproductive history, physical activity, diet, and anthropometric variables.[15]

Some participants were missing data on colds or other upper respiratory tract infection episodes at 6 and 9 months because no clinic visit took place at that point (44/460 possible assessments were missing, <10%). We addressed this issue of sporadically missing data by using Poisson regression, which allowed for use of data from all available time-points without eliminating individuals with some missing data. Outcomes were modeled as a function of intervention group; indicator variables for 6, 9, and 12 months; and interaction terms between intervention group and each time-point indicator. Colds or other upper respiratory tract infection episodes reported at each visit were considered repeated measures, and we therefore used a generalized estimating equation modification of the Poisson regression model.[18] We assumed an unstructured working correlation matrix, computed robust standard errors, and performed an intention-to-treat analysis, with $P \leq .05$ being considered statistically significant. Results were identical or stronger when restricted to women who had assessments at all four time-points. We also evaluated whether the exercise effect differed by age (<60 vs ≥60 years) or regular multivitamin use, assessed by abstraction of vitamin bottles brought into the clinic at baseline (see Shade et al.[14] for details). All analyses were performed using SAS 8.0 (SAS Institute, Cary, NC) and Stata 8 (StataCorp, College Station, Tex) statistical software. All P values are 2-sided.

RESULTS

Exercisers and stretching controls were comparable at baseline on key demographic variables and self-reported colds

Table 1 Baseline Characteristics of Postmenopausal Exercisers and Stretchers

	Exercisers N = 53	Stretchers N = 62
	n (%)	n (%)
Age (y)		
50 to <55	11 (21)	10 (16)
55 to <60	19 (36)	22 (36)
60 to <65	7 (13)	10 (16)
65 to <70	8 (15)	11 (18)
70 to 75	8 (15)	9 (15)
Mean (SD)	60.5 (7.0)	60.9 (6.8)
Body mass index (kg/m^2)		
24 to <30	29 (53)	34 (55)
30 to <35	15 (28)	22 (36)
≥35	9 (17)	6 (10)
Mean (SD)	30.2 (4.0)	30.3 (3.8)
Regular multivitamin use	25 (47)	32 (52)
Race		
White	46 (87)	55 (89)
Non-white	7 (13)	7 (11)
Season of enrollment		
Spring (March-May)	19 (36)	25 (40)
Summer (June-August)	11 (21)	11 (18)
Fall (September-November)	13 (25)	16 (26)
Winter (December-February)	10 (19)	10 (16)
Number of colds in 3 mo before baseline†		
0	25 (66)	30 (71)
1	12 (32)	12 (29)
2	1 (3)	0 (0)
Mean (SD)	0.37 (0.54)	0.29 (0.46)
Number of any upper respiratory tract infections in 3 mo before baseline†		
0	18 (49)	27 (64)
1	17 (46)	14 (33)
2	2 (5)	1 (2)
Mean (SD)	0.57 (0.60)	0.38 (0.54)
Any allergy episodes	7 (18)	7 (17)
Received influenza immunization		
a) in previous 6 mo	10 (19)	20 (32)
b) during the intervention period	12 (23)	26 (42)

SD = standard deviation.

*None of the differences are statistically significant at the $\alpha = 0.05$ level, except for influenza immunization.

†Reporting of colds and other upper respiratory tract infections episodes in the 3 months before the baseline visit may be artificially high because of lack of instruction in how to track qualifying episodes.

and other upper respiratory tract infection episodes (Table 1). On average, study participants were 61 years old and had a body mass index of 30 kg/m^2. Intervention participants exercised an average of 3.8 days/week, for a total of 166 minutes/week, meeting 85% of their exercise time goal. Exercisers wore heart-rate monitors and showed significant increases in cardiopulmonary fitness (VO_2 max).[15]

The exercise intervention decreased the risk of self-reported colds relative to controls (Figure 1). Over 12 months, the risk of colds decreased modestly in exercisers and increased modestly in stretchers (Figure 1, $P = .02$ for overall difference). In the final 3 months of the study, the risk of colds in stretchers was more than 3-fold higher than that of exercisers ($P = .03$). More stretchers than exercisers had at least one cold during the 12-month study period (48.4% vs 30.2%), and among women reporting at least one cold, stretchers tended to report colds more frequently than exercisers (Table 2). No statistically significant exercise effect was observed for upper respiratory tract infections overall, which included flu episodes and unknown types of upper respiratory tract infections ($P = .16$).

Exercise reduced the risk of colds in multivitamin non-users ($P = .02$), whereas there was a suggested increase in users ($P = .07$). However, this difference in effects between the two groups was not statistically significant ($P = .11$ for the interaction). We did not observe significant differences in the exercise effect by age group (results not shown).

DISCUSSION

The results from this randomized, controlled trial show that moderate-intensity exercise training over the course of 1 year can reduce the incidence of colds among postmenopausal, nonsmoking, previously sedentary women. The lack of effect on upper respiratory tract infections overall (which included flu episodes) may be because more stretchers than exercisers were vaccinated against influenza in the 6 months before baseline. Further, more stretchers (42%) than exercisers (23%) reported vaccination during the intervention period ($P = .03$). In addition, it is possible that susceptibility to colds, in contrast to influenza, may be more easily modifiable by host immunity. Although it seems that differences in the risk of colds between exercisers and stretchers in our study were partly attributable to an increase in colds in stretchers, this increase was not statistically significant. Attending exercise or stretching classes on a regular basis may increase exposure to infectious agents as the result of social contacts, and thus the decrease among exercisers may be even more relevant.

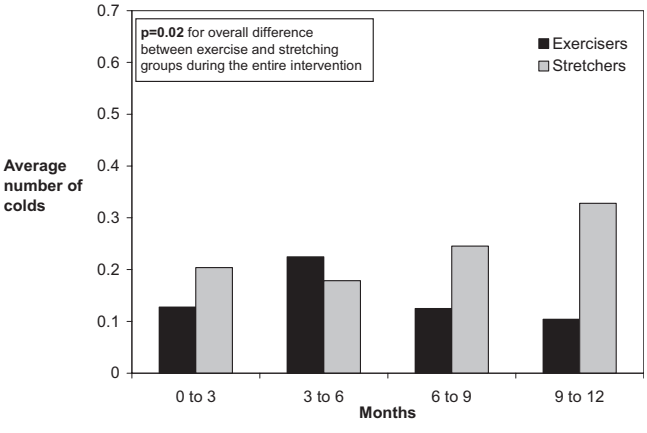

Figure 1 Number of colds in postmenopausal exercisers and stretchers assessed quarterly throughout the 12-month intervention period.

Table 2 Total Number and Relative Risk of Colds and All Upper Respiratory Tract Infections*

	All Exercisers (N = 53)	All Stretchers (N = 62)	Multivitamin Nonusers		Multivitamin Users	
			Exercisers (N = 23)	Stretchers (N = 28)	Exercisers (N = 25)	Stretchers (N = 32)
Number of colds over 12 mo	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
0	26 (49)	19 (31)	14 (61)	5 (18)	9 (36)	14 (44)
1	11 (21)	15 (24)	4 (17)	8 (29)	5 (20)	7 (22)
2	3 (6)	13 (21)	1 (4)	6 (21)	2 (8)	7 (22)
3	2 (4)	2 (3)	0 (0)	1 (4)	2 (8)	1 (3)
Number of colds between	RR (95% CI)		RR (95% CI)		RR (95% CI)	
0-3 mo	0.62 (0.24-1.59)		0.20 (0.03-1.50)		1.38 (0.40-4.79)	
3-6 mo	1.26 (0.56-2.86)		1.24 (0.27-5.77)		1.35 (0.50-3.63)	
6-9 mo	0.51 (0.20-1.28)		0.15 (0.02-1.11)		1.19 (0.37-3.76)	
9-12 mo	0.32 (0.13-0.81)		0.13 (0.02-1.00)		0.49 (0.15-1.61)	
P value†	0.02		0.02		0.07	
			P = .11 for interaction			
Number of upper respiratory tract infections†‡ over 12 mo	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
0	14 (26)	11 (18)	6 (26)	2 (7)	5 (20)	9 (28)
1	9 (17)	18 (29)	4 (17)	8 (29)	5 (20)	10 (31)
2	11 (21)	11 (18)	5 (22)	6 (21)	4 (16)	5 (16)
3	1 (2)	6 (10)	0 (0)	2 (7)	1 (4)	4 (13)
4	5 (9)	3 (5)	3 (13)	2 (7)	2 (8)	1 (3)
5	1 (2)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
6	1 (2)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)
Number of upper respiratory tract infections†‡ between	RR (95% CI)		RR (95% CI)		RR (95% CI)	
0-3 mo	0.95 (0.49-1.86)		0.72 (0.30-1.74)		1.41 (0.48-4.11)	
3-6 mo	2.19 (1.04-4.61)		2.10 (0.65-6.77)		2.54 (0.98-6.60)	
6-9 mo	0.94 (0.58-1.55)		0.72 (0.33-1.59)		1.31 (0.69-2.50)	
9-12 mo	0.71 (0.39-1.28)		1.06 (0.46-2.42)		0.46 (0.19-1.16)	
P value†	0.16		0.57		0.16	
			P = .20 for interaction			

RR = relative risk; CI = confidence interval.

*The total possible number of assessments was 212 for exercisers and 248 for stretchers (four time-points multiplied by the number of individuals). In exercisers, 9.4% of assessments were missing, compared with 9.7% in stretchers.

†*P* values for overall difference between exercise and stretching groups during the entire intervention period based on Poisson regression, which includes persons who have data missing at one or more time-points.

‡Includes colds, flu, unknown, and other upper respiratory tract infections.

Our findings build on the work by Nieman et al.,[9,10,17] who showed that exercise training can reduce the number of days with upper respiratory tract infection symptoms overall[10] or per episode.[9] The long duration of our trial enabled us to investigate whether exercise can reduce the number (incidence) of upper respiratory tract infection and cold episodes. Unfortunately, the current design did not permit the measurement of upper respiratory tract infections by daily health-logs, as used in past research[9,10,17] because of participant burden. A previous cross-sectional study on upper respiratory tract infections that compared highly conditioned individuals with those randomized to walking or calisthenic exercise found the incidence of upper respiratory tract infections to be significantly less common among highly conditioned individuals, with walkers and calisthenic exercisers having the intermediate and highest risk of upper respiratory tract infections, respectively.[17] In that study, review of the symptoms revealed that the upper respiratory tract infection cases could be almost exclusively described as the common cold. Thus, our results, which show an effect specifically for colds, are consistent with these past investigations.

Brisk walking amounted to 51.8% of facility-based and 73.7% of home-based activity among exercisers.[15] Nieman et al.[19] showed that walking for 30 minutes can increase leukocyte counts temporarily and suggested that walking may reduce the risk of upper respiratory tract infections by increasing the number of episodes in which leukocytes counts are transiently higher. Another possible mechanism is through an increase in salivary immunoglobulin (Ig) A, a key component of mucosal immunity. An inverse relationship between salivary IgA concentration or secretion rate

and the risk of upper respiratory tract infections in athletes has been described.[20,21] Despite a transient decrease of IgA with high-intensity exercise,[21-25] elite athletes may have higher salivary IgA concentrations than sedentary persons.[26] Results from intervention studies,[27,28] including one randomized trial,[28] suggest that salivary IgA levels increase after engaging in a moderate-intensity exercise program for several months. However, findings from studies comparing active individuals with sedentary individuals are inconsistent, as are studies evaluating serum IgA.[26,29-31]

In our study, the protective exercise effect seemed confined to women who did not regularly use multivitamins. Several epidemiologic studies suggest that multivitamin use may be immune-enhancing, although the data from randomized, controlled trials are not entirely consistent.[32-34] Our findings suggest that women who do not use multivitamins may derive greater protection against colds from exercise.

The present study has several strengths, including its relatively long intervention period and large size compared with previous studies. Further, adherence was excellent. We do, however, note several limitations. Because participants did not keep daily logs of infections and allergies, reliance on memory may have introduced error. The reproducibility of the occurrence of episodes was good, whereas the self-reported duration of such episodes did not prove reproducible in this setting and thus could not be evaluated. Participants may not have classified colds, flu, and other upper respiratory tract infections accurately; however, both exercisers and stretching controls received identical instructions, and any error in the reporting should have biased our findings toward observing no effect.

Our trial is the first to report on the effects of a year-long, moderate-intensity exercise training program on the incidence of upper respiratory tract infections. Although we did not find an effect overall on upper respiratory tract infections, our study suggests that moderate-intensity training can reduce the risk of colds in postmenopausal, nonsmoking, overweight or obese women. This finding is of clinical relevance and adds a new facet to the growing literature on the health benefits of moderate exercise.

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P.A.T.H.
(Physical Activity for Total Health)

OFFICE USE ONLY: AFFIX LABEL HERE

Visit ___Baseline ___3-month
DATE RECEIVED: ___/___/_____
REVIEWED BY: _____ ☐1 SELF ☐2 Group ☐3 Interview
☐4Assisted

Please fill in the date when you complete this questionnaire:

Date: _____/_____/_____
Month Day Year

This questionnaire asks about any cold, flu, or allergies you've experienced over the past 3 months.

ALLERGIES, COLDS AND OTHER INFECTIONS

1. In the past 3 months, did you have any **allergy episodes**? (Allergy symptoms include a runny nose, itchy eyes, and clear discharge from you nose. They are not accompanied by a severe sore throat or cough and usually persist for more than 2 weeks. Symptoms may worsen with exposure to house dust, pollen, or pets).

☐1 No ☐2 Yes

If yes, about how long was the total time period (from beginning to end) during which you had any allergy symptoms?
Please fill in the number of days, weeks, or months.

____ days or ____ weeks or ____ months

2. In the past 3 months, did you have any **cold sores**?

☐1 No ☐2 Yes

If yes, how many episodes of cold sores?

____ number of cold sore episodes

3. In the past 3 months, did you have any episodes of **vomiting, diarrhea, or nausea**?

☐1 No ☐2 Yes

If yes, how many episodes?

____ number of vomiting and diarrhea episodes

What was the average number of days per episode?

____ days

4. In the past 3 months, did you have any **cold or flu episodes**? (Symptoms include a sore throat, runny or stuffy nose, coughing, sneezing, fever, headache, general aches and pains, fatigue and discomfort).

☐1 No ☐2 Yes

If yes, how many cold or flu episodes?

____ number of cold or flu episodes in the past 3 months

Please fill out ONE of the following pages for EACH episode of cold or flu:

If you had **no cold or flu episodes** during the past 3 months you are now finished with this questionnaire.

Appendix (continued)

Please think about your MOST RECENT cold or flu episode in the past 3 months and fill out the box below:

10. What type of illness was this?
- ☐1 Cold
- ☐2 Flu
- ☐3 Don't know (please describe symptoms)
- ☐4 Other (please describe symptoms)

_____

11. During what month (s) did this occur? _____

12. Did you see a doctor about this illness?
☐1 No ☐2 Yes

↓

13. If yes, what did the doctor say (did he or she give it a medical name)?

_____

14. Were you in bed because of this illness?
☐1 No ☐2 Yes → _____ number of days

15. Aside from days in bed (if any) were you away from work or restricted in your usual activities?
☐1 No ☐2 Yes → _____ number of days

16. How many total days did you have ANY symptoms (including cough, a runny or stuffy nose, general aches and pains, headaches, or others?

_____ Total number of days

17. How sick did you feel? Please circle a number below, where a "1" indicates "not very sick", and a "10" indicates "extremely sick".

Not very sick **Extremely sick**

1 2 3 4 5 6 7 8 9 10

Appendix (continued)

If you had more than one cold or flu episode, please think about the PREVIOUS cold or flu episode in the past 3 months and fill out the box below.

18. What type of illness was this?
- ☐1 Cold
- ☐2 Flu
- ☐3 Don't know (please describe symptoms)
- ☐4 Other (please describe symptoms)

_____

19. During what month (s) did this occur? _____

20. Did you see a doctor about this illness?
☐1 No ☐2 Yes

21. If yes, what did the doctor say (did he or she give it a medical name)?

_____

22. Were you in bed because of this illness?
☐1 No ☐2 Yes _____ number of days

23. Aside from days in bed (if any) were you away from work or restricted in your usual activities?
☐1 No ☐2 Yes _____ number of days

24. How many total days did you have ANY symptoms (including cough, a runny or stuffy nose, general aches and pains, headaches, or others?

_____ Total number of days

25. How sick did you feel? Please circle a number below, where a "1" indicates "not very sick", and a "10" indicates "extremely sick".

Not very sick **Extremely sick**

1 2 3 4 5 6 7 8 9 10

Appendix (continued)

If you had more than two cold or flu episodes, please think about the PREVIOUS cold or flu episode in the past 3 months and fill out the box below.

26. What type of illness was this?
- ☐1 Cold
- ☐2 Flu
- ☐3 Don't know (please describe symptoms)
- ☐4 Other (please describe symptoms)

_____

27. During what month (s) did this occur? _____

28. Did you see a doctor about this illness?
☐1 No ☐2 Yes

↓

29. If yes, what did the doctor say (did he or she give it a medical name)?

_____

30. Were you in bed because of this illness?
☐1 No ☐2 Yes → _____ number of days

31. Aside from days in bed (if any) were you away from work or restricted in your usual activities?
☐1 No ☐2 Yes → _____ number of days

32. How many total days did you have ANY symptoms (including cough, a runny or stuffy nose, general aches and pains, headaches, or others?

_____ Total number of days

33. How sick did you feel? Please circle a number below, where a "1" indicates "not very sick", and a "10" indicates "extremely sick".

Not very sick **Extremely sick**

1 2 3 4 5 6 7 8 9 10

Appendix (continued)