Prospective Study of Physical Activity and Risk of Asthma Exacerbations in Older Women

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Rationale: The potential role of physical activity in preventing asthma exacerbations is unknown.

Objectives: To investigate the longitudinal association between regular physical activity and asthma exacerbations.

Methods: A total of 2,818 women with asthma from a large U.S. cohort (the Nurses' Health Study) were monitored from 1998 to 2000. Physical activity was self-reported at baseline, using a validated questionnaire, and categorized in quintiles. Exacerbations during follow-up were defined as a self-report of asthma-related hospitalization, emergency department visit, or urgent office visit. Baseline information about severity of asthma, treatment, previous exacerbations, sociodemographic factors, smoking, and other potential confounders was obtained.

Measurements and Main Results: Participants had a mean age of 63 years, and 71% had mild-to-moderate persistent asthma. About half of the women were ever-smokers (48% former, 6% current), and median physical activity was 10 MET-hours/week (equivalent to walking at a brisk pace for 20 minutes three times per week). Risk of exacerbations during follow-up decreased with increasing level of physical activity. In a multivariate logistic regression model, the higher level of physical activity, the lower risk of admission (odds ratio 0.85, 0.81, 0.78, and 0.76, for the 2nd, 3rd, 4th, and 5th quintiles compared with the 1st quintile, P for trend = 0.05). There were no relevant differences on stratifying by age group, smoking status, body mass index, baseline use of inhaled corticosteroids, or previous exacerbations.

Conclusions: Regular physical activity was associated with reduced risk of exacerbations in women with asthma in this longitudinal study.

Keywords: motor activity; exercise; asthma; epidemiology

Regular physical activity is associated with reduced risk of premature mortality and several chronic diseases and conditions, including cardiovascular diseases, diabetes, and colon cancer (1). Despite the large amount of research on the health benefits of physical activity, its effects on respiratory health are mostly unknown. Asthma is among the main causes of morbidity and mortality worldwide, and its exacerbations account for high number of hospital admissions, high costs for the health services, and poor evolution of the disease (2). However, the potential role of physical activity in preventing asthma exacer-

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

The potential role of physical activity in preventing asthma exacerbations is unknown.

What This Study Adds to the Field

This prospective study of older women shows that a higher level of regular physical activity is associated with a lower risk of an asthma exacerbation, independent of asthma severity and other covariates. The results support the recommendation of regular physical activity to most individuals with asthma.

bations is not known. Only a few cross-sectional studies are available, some of which have reported an association between higher levels of regular physical activity and a lower prevalence of asthma symptoms (3, 4), whereas other have not reproduced this association (5–8). These controversial results could be attributed to differences in characteristics of the previous studies or to the inherent difficulty in ascertaining with cross-sectional data whether physical inactivity increases asthma symptoms or whether patients with asthma avoid the practice of physical activity. However, the improvement in cardiopulmonary fitness obtained by physical training in patients with asthma (9) supports the possibility that physical activity could improve asthma (10). The finding that the regular practice of physical activity is associated with a reduced risk of admission for a chronic obstructive pulmonary disease (COPD) exacerbation (11–13), a disease that shares some common pathophysiological and clinical characteristics with asthma, also supports this hypothesis.

The present article aims to investigate the longitudinal association between regular physical activity and subsequent risk of asthma exacerbations, in 2,818 women with asthma from a large U.S. cohort (the Nurses' Health Study).

METHODS

Additional data on study design, subjects, follow-up, measurements and statistical analysis are provided in the online supplement.

Design

This study is a prospective analysis in the Nurses' Health Study (NHS), which began in 1976, when 121,700 female nurses aged 30–55 years living in 11 U.S. states responded to a mailed health questionnaire (14). Every 2 years, the women provide personal information and information on medical risk factors and major medical events. Supplemental questionnaires about asthma and COPD were sent in 1998 and 2000 to all living women who had reported a physician diagnosis of asthma, emphysema, or chronic bronchitis. The institutional review board ap-

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proved the NHS protocols, and informed consent was obtained from all subjects.

Subjects

Asthma was defined at baseline (1998 survey) as a self-report of a doctor diagnosis of asthma and the use of medication for asthma within the past 12 months. This definition was previously validated in another cohort of nurses (Nurses' Health Study II), using medical records (15), confirming 95% of asthma cases. To avoid misclassification in asthma diagnosis, we excluded all subjects with COPD, defined by the affirmative response to physician-diagnosed chronic bronchitis, emphysema, or COPD.

Variables and Instruments

Women reported physical activity in 1998 by answering a questionnaire previously validated against a 7-day activities diary (16). The time spent per week at a variety of leisure-time physical activities (such as walking, bicycle, swimming, or tennis) was determined and multiplied by its typical energy expenditure requirements expressed as metabolic equivalents (METs) (17), in which 1 MET is equal to the energy expended at rest. All activities were added together to yield a MET-hours/week score.

Baseline asthma severity measures included symptoms between flares, symptoms in the last 4 weeks, medications in the last 12 months, and days kept from work or usual activities because of asthma. Other variables collected at baseline included the following: smoking status (never, former, and current), pack-years of smoking, secondhand tobacco exposure (at home and/or at work), body mass index, total caloric intake (estimated through a food frequency questionnaire), age, race/ethnicity, spouse's educational attainment, U.S. region, menopause, hormonal replacement therapy, and physician visits.

Exacerbations during follow-up were defined by at least one of the following health care events during a 12-month period in 1999–2000: hospital admissions, emergency department visits, or urgent office visits, for an asthma exacerbation. Exacerbations in the 12-month period in 1997–1998 (before baseline) were also collected to help establish baseline status.

Statistical Analysis

The small number of exacerbations during follow-up precluded the use of a counting approach for the study of the effects of physical activity in the number of asthma exacerbations. Instead, logistic regression was used with having exacerbations (yes/no) as the outcome, and baseline physical activity in quintiles as the exposure. All the variables detailed previously were tested as potential confounders of the association between physical activity and asthma exacerbation (18). Goodness of fit of the models was tested using the Hosmer-Lemeshow test (19). Additional information about statistical analysis, as well as sensitivity analyses, are provided in the online supplement. All analyses were conducted with SAS software, version 9 (SAS Institute, Cary, NC).

RESULTS

From a total of 3,657 women with a self-report of asthma without COPD in 1998, 71 (2%) died and 768 (21%) did not fill out the 2000 asthma questionnaire. (The causes of death were 21% respiratory, 17% cardiovascular, 48% cancer, and 14% other.) Thus, the present analyses were based on 2,818 women with asthma. Table 1 shows their mean age was 63 years, most of them had mild (36%) to moderate (35%) persistent asthma, more than half were former (48%) or current (6%) smokers, and a high proportion were overweight (33%) or obese (32%). Walking, biking, indoor exercise, and other vigorous activities were the most frequently performed, with a median physical activity of 10 MET-hours/week, equivalent to walking at a brisk pace for 20 minutes three times per week. Women who died during follow-up were older at baseline, had more severe asthma, were more likely to be smokers, reported lower total caloric intake, and a lower level of physical activity (see Table

TABLE 1. BASELINE CHARACTERISTICS OF WOMEN WITH ASTHMA FROM THE NURSES' HEALTH STUDY

	n = 2,818*
Age, mean (SD)	62.7 (6.9)
Asthma exacerbations in past year (1997–1998), n (%)†	839 (29.8)
Number of asthma exacerbations in past year, mean (SD)	0.7 (1.5)
Asthma severity, n (%)‡	
Mild intermittent	570 (20.2)
Mild persistent	1,004 (35.6)
Moderate persistent	975 (34.6)
Severe persistent	267 (9.5)
Smoking habits, n (%)	
Never-smokers	1,290 (45.8)
Former smokers	1,361 (48.3)
Current smokers	165 (5.8)
Pack-years among ever-smokers, mean (SD)	21.0 (19.5)
Exposure to secondhand smoke at work and/or at home, n (%)	1,733 (71.3)
Total caloric intake, mean (SD)	1,774 (532)
Body mass index (kg/m ²), mean (SD)	28.1 (5.9)
Body mass index, n (%)	
<20 kg/m ²	112 (4.0)
20–24.9 kg/m ²	850 (30.4)
25–29.9 kg/m ²	929 (33.2)
≥30 kg/m ²	903 (32.3)
Physical activity	
Walking, n (%)	2,302 (81.7)
Jogging, n (%)	56 (2.0)
Running, n (%)	25 (0.9)
Biking, n (%)	603 (21.4)
Swimming, n (%)	300 (10.6)
Tennis, n (%)	67 (2.4)
Calisthenics sport, n (%)	502 (17.8)
Low-intensity exercise, n (%)	936 (33.2)
Other vigorous activities, n (%)	1,042 (37.0)
Flights of stairs, n (%)	2,818 (100.0)
Physical activity (MET-h/wk), mean (SD)	16.6 (20.9)
Physical activity (MET-h/wk), median (p25–p75)	9.8 (2.9–22.3)
Physical activity, n (%)	
<1 MET-h/wk—no physical activity	369 (13.1)
1–2.9 MET-h/wk—light physical activity (e.g., walking slowly for 20 min three times per wk)	338 (12.0)
3–5.9 MET-h/wk—moderate physical activity (e.g., walking at brisk pace [4 mph] for 20 min three times per wk)	367 (13.0)
6–11.9 MET-h/wk—moderate-vigorous physical activity (e.g., jogging at 6 mph for 20 min three times per wk)	524 (18.6)
12–29.9 MET-h/wk—vigorous physical activity (e.g., jogging at 6 mph for 20 min daily)	736 (26.1)
≥30 MET-h/wk—very vigorous physical activity (e.g., jogging at 6 mph for 1 h daily)	484 (17.2)

Definition of abbreviations: MET, metabolic equivalent (MET-h/wk is the sum of the average time per week spent in each activity × MET value of each activity); p25–p75, 25th and 75th percentiles.

* Some values are missing for certain variables: 2 in asthma severity, 775 in secondhand smoking, 24 in BMI, and 2 in pack-years.

† At least one hospitalization, emergency room visit, and/or urgent office visit for exacerbation of asthma.

‡ Based on frequency of symptoms between flares, symptoms in the last 4 weeks and days kept from work or usual activities because of asthma.

E1 in the online supplement). Women who did not answer the 2000 questionnaire had a higher proportion and number of previous asthma exacerbations, were more likely to be smokers, had higher body mass index, and reported a lower physical activity level (Table E1).

A total of 621 (22%) women with asthma suffered at least one exacerbation in the period 1999–2000. Among them, 67, 128, and 552 had reported at least one hospital admission, one

TABLE 2. DISTRIBUTION OF ASTHMA EXACERBATIONS PER YEAR (1999–2000) ACCORDING TO TERTILES OF BASELINE (1998) REGULAR PHYSICAL ACTIVITY, IN WOMEN WITH ASTHMA FROM THE NURSES' HEALTH STUDY

	All Subjects (<i>n</i> = 2,818) <i>n</i> (%)	Physical Activity, Tertile 1 (<i>n</i> = 978) <i>n</i> (%)	Physical Activity, Tertile 2 (<i>n</i> = 907) <i>n</i> (%)	Physical Activity, Tertile 3 (<i>n</i> = 933) <i>n</i> (%)	<i>P</i> Value
All asthma exacerbations*					
0	2,197 (78.0)	732 (74.8)	721 (79.5)	744 (79.7)	0.004
1	290 (10.3)	99 (10.1)	103 (11.4)	88 (9.4)	
2	172 (6.1)	72 (7.4)	45 (5.0)	55 (5.9)	
≥3	159 (5.6)	75 (7.7)	38 (4.2)	46 (4.9)	
Hospital admissions for an asthma exacerbation†					
0	2,751 (97.6)	948 (96.9)	890 (98.1)	913 (97.9)	0.064
1	53 (1.9)	21 (2.1)	16 (1.8)	16 (1.7)	
2	5 (0.2)	5 (0.5)	0 (0)	0 (0)	
≥3	9 (0.3)	4 (0.4)	1 (0.1)	4 (0.4)	
Emergency department visits for an asthma exacerbation‡					
0	2,690 (95.5)	933 (95.4)	869 (95.8)	888 (95.2)	0.830
1	92 (3.3)	31 (3.2)	27 (3.0)	34 (3.6)	
2	25 (0.9)	10 (1.0)	9 (1.0)	6 (0.6)	
≥3	11 (0.4)	4 (0.4)	2 (0.2)	5 (0.5)	
Urgent office visits for an asthma exacerbation§					
0	2,266 (80.4)	757 (77.4)	741 (81.7)	768 (82.3)	0.004
1	283 (10.0)	101 (10.3)	100 (11.0)	82 (8.8)	
2	153 (5.4)	63 (6.4)	39 (4.3)	51 (5.5)	
≥3	116 (4.1)	57 (5.8)	27 (3.0)	32 (3.4)	

* All asthma exacerbations include hospital admissions, emergency department visits, or urgent office visits for an exacerbation of asthma.

† From the total of 67 patients admitted because of an asthma exacerbation, 17 also reported an emergency department visit, 18 also reported an urgent office visit, and 24 reported both.

‡ From the total of 128 patients reporting an emergency department visit because of an asthma exacerbation, 17 also reported an admission, 43 also reported an urgent office visit, and 24 reported both.

§ From the total of 552 patients reporting an urgent office visit because of an asthma exacerbation, 18 also reported an admission, 43 also reported an emergency department visit, and 24 reported both.

emergency department visit, or one urgent office visit, respectively (Table 2). The numbers of total exacerbations and urgent office visits were inversely related to the level of physical activity, whereas the numbers of hospital admissions and emergency department visits were not (Table 2). The proportion of women with exacerbations decreased with increasing level of physical activity (Table 3). In a multivariate logistic regression model, the higher the level of physical activity, the lower the risk of exacerbation. Compared with the first quintile of physical activity, the odds ratios for the second, third, fourth, and fifth quintiles of activity were 0.85, 0.81, 0.78, and 0.76, respectively (*P* for trend = 0.05). The adjusted predicted

probability of exacerbation (and 95% confidence intervals) was plotted against physical activity (Figure 1), and shows that the higher the physical activity, the lower the probability of asthma exacerbation.

Stratification by age group, smoking status, body mass index group, baseline use of inhaled corticosteroids, or previous exacerbations did not reveal any relevant differences in the association between physical activity and asthma exacerbation, although statistical significance was lost in many models, most likely due to a reduction in statistical power. The inclusion of respiratory deaths yielded again a statistically significant inverse association between physical activity and asthma exacerbation (adjusted odds

TABLE 3. CRUDE AND ADJUSTED LONGITUDINAL ASSOCIATION BETWEEN BASELINE (1998) REGULAR PHYSICAL ACTIVITY AND ASTHMA EXACERBATIONS (1999–2000) IN WOMEN WITH ASTHMA FROM THE NURSES' HEALTH STUDY

	Median Physical Activity (MET-h/wk)	<i>n</i>	Patients with Exacerbations, <i>n</i> (%)	Crude OR (95% CI)	Adjusted OR (95% CI)*
Physical activity					
Quintile 1	0.8	605	157 (26)	1.00	1.00
Quintile 2	4.1	558	124 (22)	0.82 (0.62–1.07)	0.85 (0.64–1.13)
Quintile 3	10.2	558	122 (22)	0.80 (0.61–1.05)	0.81 (0.61–1.08)
Quintile 4	20.2	553	111 (21)	0.72 (0.54–0.94)	0.78 (0.59–1.05)
Quintile 5	40.8	544	107 (20)	0.70 (0.53–0.92)	0.76 (0.57–1.02)
<i>P</i> for trend:				0.007	0.050

Definition of abbreviations: CI = confidence interval; OR = odds ratio.

* Multivariate logistic regression model adjusted for age, previous asthma exacerbations (hospital admissions, emergency department visits, or urgent office visits for an exacerbation of asthma), and asthma severity (based on symptoms between flares, symptoms in the last 4 wk, and days kept from work or usual activities because of asthma). Other potential confounders (such as smoking status, pack-years, secondhand tobacco exposure, total energy intake or body mass index) were not finally included because they were not related to the outcome or modified OR estimates for physical activity.

ratios for the second, third, fourth, and fifth quintiles were 0.81, 0.79, 0.74, and 0.73, respectively; P for trend = 0.02) (see Table E2 in the online supplement).

DISCUSSION

This is the first longitudinal study assessing the relation between the regular practice of physical activity and risk of asthma exacerbations. In our population of female U.S. health professionals, with an average low-risk lifestyle (20, 21) (not smoking, exercising daily, and eating a healthy diet), we found that a higher level of regular physical activity is associated with a lower risk of an asthma exacerbation. This association was independent of asthma severity and other covariates, and was consistent after different stratifications and sensitivity analyses, although statistical significance was lost in some models, most likely due to a reduction in statistical power.

The association between physical activity and respiratory symptoms in patients with asthma has been examined in several cross-sectional studies (3–8). Those including adult subjects yielded an association between higher physical activity level and lower asthma symptoms (3, 4), as we found. The studies with null results were conducted in children (6–8), and/or used less reliable measures of asthma (defined as wheezing) (7) or physical activity (defined from single questions about TV watching [6] or sports playing [8]), suggesting that differences in subjects' age or study design may be responsible for the seemingly discrepant results. The possibility that sex plays any role in these inconsistent results is difficult to ascertain: whereas one of the previously mentioned studies yielded similar associations between physical activity and asthma symptoms in men and women (3), the other found statistically significant associations only in men (4). Finally, the cross-sectional design of all previous studies also makes their interpretation and comparisons with current results difficult. Data from the population-based cross-sectional European Community Respiratory Health Survey (28 to 57 yr old; 51% men) had shown reduced bronchial hyperresponsiveness among the most physically active subjects (22), which is in agreement with our findings given that bronchial hyperresponsiveness is a feature of asthma exacerbations (23). In addition, because bronchial hyperresponsiveness has been considered an epiphenomenon of airway inflammation (24), it is likely that the effect of physical activity in asthma exacerbations is partly mediated by inflammation, as has been suggested for many chronic diseases (25). Finally, the follow-up of the population-based Copenhagen City Heart Study (mean age, 52 yr; 43% male) showed that regular physical activity may attenuate lung function decline, an association that was stronger in subjects with asthma than in the general population (26), pointing to the possibility of patients with asthma as a specific subgroup being more sensitive to the effects of physical activity. A systematic review of physical training for patients with asthma found that physical training programs can improve cardiopulmonary fitness (maximal oxygen uptake and maximal expiratory ventilation) even without changing lung function (9). It should be noted that the mechanisms underlying short-term results obtained by rehabilitation programs may differ from the mechanisms underlying the long-term effects of regular physical activity, both of them deserving further specific research that is beyond the scope of epidemiological studies.

Despite the physical activity benefits for asthma that can be inferred from existing data, and despite the mention of the importance of physical activity both in the National Asthma Education and Prevention Program (27) and in the Global Initiative for Asthma (23) 2007 guidelines, the potential of physical activity as a treatment to improve evolution of the

Figure 1. Adjusted probability (and 95% confidence intervals) of asthma exacerbation according to physical activity. From a logistic regression model with physical activity as a continuous variable, and adjusted for age, previous asthma exacerbations, and asthma severity. Outliers (women with physical activity >95th percentile) were excluded.

disease is not addressed in any of these guidelines. The present study provides additional evidence in support of the recommendation of regular practice of physical activity in individuals with asthma, a recommendation that could also have benefits for many other health outcomes (1). The dose (duration, frequency, intensity, or type) of physical activity to be recommended cannot be derived from a single study. Our results suggest an inverse and linear relationship for asthma exacerbations, as has been found for all-cause mortality or total cardiovascular disease (28). However, the evaluation of dose-response relationships between physical activity and health outcomes is a complex issue that has not yet been solved for diseases such as cancer, hypertension, or hypercholesterolemia (28). It is especially worth mentioning that fear of an exercise-induced asthma attack may lead to the avoidance of physical activities by individuals with asthma. Unfortunately, our data did not include information about exercise-induced asthma exacerbations, thus not allowing us to study the effects of physical activity in this specific subgroup of patients. However, despite the potential difference in the physiological response to a strenuous exercise challenge in comparison with the regular practice of moderate physical activity, our results show that physical activity even of high intensity appears to have pulmonary benefits.

Potential limitations of the current study include likely misclassification of the disease, the outcome, or the exposure; selection bias; and residual confounding. The asthma diagnosis was self-reported by registered nurses, and an earlier validation study confirmed a high percentage of confirmed diagnoses (95%) (15). Nevertheless, we specifically excluded all subjects with a concomitant diagnosis of emphysema, chronic bronchitis, or COPD to minimize misclassification. Exacerbations were also self-reported, and therefore subject to potential misclassification. A key strength of studying registered nurses is that they have a higher level of education and demonstrated health interest, thus improving the quality of data obtained from questionnaires. Differences in the effect of physical activity among the several types of exacerbation were not addressed because of the reduction in statistical power and potential misclassification. The validity of self-reported physical activity by the NHS questionnaire had been previously assessed against activity diaries with correlation coefficients ranging from 0.41 to 0.79 (16). Indeed, the NHS questionnaire has been used to study

the effects of regular physical activity on several health outcomes (29–32). Overall, nondifferential misclassification of the disease, the outcome, or the exposure in this prospective study would bias the estimates toward a lack of association between physical activity and exacerbations, thus underestimating the true association. Although women who died during follow-up or did not fill out the follow-up questionnaire (year 2000) had reported a lower level of physical activity at baseline (year 1998), the inclusion of respiratory deaths in the exacerbated group did not yield differences in the association between physical activity and asthma exacerbation, thus suggesting that survival bias did not play a relevant role in the present analysis. Finally, a certain degree of residual confounding cannot be ruled out, specifically due to misperceptions in the asthma severity.

In summary, we found that regular physical activity was associated with reduced risk of asthma exacerbations in a well-characterized cohort of older U.S. women. This finding helps to address ongoing uncertainty about the respiratory benefits of physical activity, in comparison with the abundant literature on the health benefits of exercise for other chronic diseases (1). The results support the inclusion of physical activity advice in asthma guidelines as well as the promotion of research about the effects of exercise training programs on the clinical course of asthma.

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References

1. U.S. Department of Health and Human Services. Physical Activity and Health: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996.
2. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004;59:469–478.
3. Ford ES, Heath GW, Mannino DM, Redd SC. Leisure-time physical activity patterns among US adults with asthma. *Chest* 2003;124:432–437.
4. Kilpeläinen M, Terho EO, Helenius H, Koskenvuo M. Body mass index and physical activity in relation to asthma and atopic diseases in young adults. *Respir Med* 2006;100:1518–1525.
5. Chen Y, Dales R, Krewski D. Leisure-time energy expenditure in asthmatics and non-asthmatics. *Respir Med* 2001;95:13–18.
6. Romieu I, Mannino DM, Redd SC, McGeehin MA. Dietary intake, physical activity, body mass index, and childhood asthma in the Third National Health And Nutrition Survey (NHANES III). *Pediatr Pulmonol* 2004;38:31–42.
7. Eijkemans M, Mommers M, de Vries SI, van Buuren S, Stafleu A, Bakker I, Thijs C. Asthmatic symptoms, physical activity, and overweight in young children: a cohort study. *Pediatrics* 2008;121:e666–e672.
8. Corbo GM, Forastiere F, De Sario M, Brunetti L, Bonci E, Bugiani M, Chellini E, La Grutta S, Migliore E, Pistelli R, et al.; Sidria-2 Collaborative Group. Wheeze and asthma in children: associations with body mass index, sports, television viewing, and diet. *Epidemiology* 2008;19:747–755.
9. Ram FS, Robinson SM, Black PN, Picot J. Physical training for asthma. *Cochrane Database Syst Rev* [serial on the Internet]. 2005 [accessed March 2009];4:CD001116. Available from <http://www.cochrane.org/reviews/clibintro.htm>
10. Lucas SR, Platts-Mills TA. Physical activity and exercise in asthma: relevance to etiology and treatment. *J Allergy Clin Immunol* 2005;115:928–934.
11. Garcia-Aymerich J, Farrero E, Felez MA, Izquierdo J, Marrades RM, Antó JM; EFRAM Investigators. Risk factors of readmission to hospital for a COPD exacerbation: a prospective study. *Thorax* 2003;58:100–105.
12. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population-based cohort study. *Thorax* 2006;61:772–778.
13. Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Physical activity and hospitalization for exacerbation of COPD. *Chest* 2006;129:536–544.
14. Colditz GA, Martin P, Stampfer MJ, Willett WC, Sampson L, Rosner B, Hennekens CH, Speizer FE. Validation of questionnaire information on risk factors and disease outcomes in a prospective cohort study of women. *Am J Epidemiol* 1986;123:894–900.
15. Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. *Arch Intern Med* 1999;159:2582–2588.
16. Wolf AM, Hunter DJ, Colditz GA, Manson JE, Stampfer MJ, Corsano KA, Rosner B, Kriska A, Willett WC. Reproducibility and validity of a self-administered physical activity questionnaire. *Int J Epidemiol* 1994;23:991–999.
17. Ainsworth BE, Haskell WL, Leon AS, Jacobs OR Jr, Montoye HJ, Sallis JF, Paffenbarger RS Jr. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc* 1993;25:71–80.
18. Rothman KJ, Greenland S. Modern epidemiology. Philadelphia: Lippincott-Raven; 1998.
19. Hosmer DW, Lemeshow S. Applied logistic regression. New York: John Wiley & Sons; 1989.
20. Chiuve SE, Rexrode KM, Spiegelman D, Logroscino G, Manson JE, Rimm EB. Primary prevention of stroke by healthy lifestyle. *Circulation* 2008;118:947–954.
21. van Dam RM, Li T, Spiegelman D, Franco OH, Hu FB. Combined impact of lifestyle factors on mortality: prospective cohort study in US women. *BMJ* 2008;337:a1440.
22. Shaaban R, Leynaert B, Soussan D, Antó JM, Chinn S, de Marco R, Garcia-Aymerich J, Heinrich J, Janson C, Jarvis D, et al. Physical activity and bronchial hyperresponsiveness: European Community Respiratory Health Survey II. *Thorax* 2007;62:403–410.
23. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention, 2007. Available from: <http://www.ginasthma.org> [accessed March 2009].
24. Grootendorst DC, Rabe KF. Mechanisms of bronchial hyperreactivity in asthma and chronic obstructive pulmonary disease. *Proc Am Thorac Soc* 2004;1:77–87.
25. Handschin C, Spiegelman BM. The role of exercise and PGC1 α in inflammation and chronic disease. *Nature* 2008;454:463–469.
26. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study. *Am J Respir Crit Care Med* 2007;175:458–463.
27. National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the diagnosis and management of asthma. Full Report 2007. Washington DC: U.S. Government Printing Office, 2007.
28. Kesaniemi YK, Danforth E Jr, Jensen MD, Kopelman PG, Lefèbvre P, Reeder BA. Dose-response issues concerning physical activity and health: an evidence-based symposium. *Med Sci Sports Exerc* 2001;33(6, Suppl):S351–S358.
29. Martínez ME, Giovannucci E, Spiegelman D, Hunter DJ, Willett WC, Colditz GA; Nurses' Health Study Research Group. Leisure-time physical activity, body size, and colon cancer in women. *J Natl Cancer Inst* 1997;89:948–955.
30. Bertone ER, Willett WC, Rosner BA, Hunter DJ, Fuchs CS, Speizer FE, Colditz GA, Hankinson SE; Nurses' Health Study. Prospective study of recreational physical activity and ovarian cancer. *J Natl Cancer Inst* 2001;93:942–948.
31. Townsend MK, Danforth KN, Rosner B, Curhan GC, Resnick NM, Grodstein F. Physical activity and incident urinary incontinence in middle-aged women. *J Urol* 2008;179:1012–1016.
32. Maruti SS, Willett WC, Feskanich D, Rosner B, Colditz GA. A prospective study of age-specific physical activity and premenopausal breast cancer. *J Natl Cancer Inst* 2008;100:728–737.