Physical Activity and the Common Cold in Men Administered Vitamin E and β-Carotene

HARRI HEMILÄ[1], JARMO VIRTAMO[2], DEMETRIUS ALBANES[4], and JAAKKO KAPRIO[1,3]
[1]Department of Public Health, University of Helsinki, Helsinki, FINLAND; [2]Department of Epidemiology and Health Promotion and [3]Department of Mental Health, National Public Health Institute, Helsinki, FINLAND; and [4]Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD

Medicine and Science in Sports and Exercise 2003;35:1815-1820

Published version: http://dx.doi.org/10.1249/01.MSS.0000093616.60899.92
PubMed: http://www.ncbi.nlm.nih.gov/pubmed/14600543

This is a manuscript version of the publication

Harri Hemilä
Department of Public Health, POB 41
University of Helsinki,
FIN-00014
Finland
harri.hemila@helsinki.fi
http://www.ltdk.helsinki.fi/users/hemila

ABSTRACT

Background and Purpose: It has been proposed that moderate regular aerobic training may enhance immunocompetence, whereas excessive training may cause immunosuppression. We evaluated whether physical activity at work, or at leisure, is associated with the risk of the common cold, and whether the antioxidants vitamin E and β-carotene affect common cold risk in physically active people. ***Methods:*** A cohort of 14,401 men aged 50–69 yr and working at study entry was drawn from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study, which examined the effect of vitamin E, 50 $mg \cdot d^{-1}$, and β-carotene, 20 $mg \cdot d^{-1}$, on lung cancer in smokers using a 2 × 2 factorial design. The trial was conducted in southwestern Finland in 1985–1993; the intervention lasted for 6.1 yr (median). Physical activity at work, and the type and frequency of leisure-time exercise were recorded at study entry. The subjects were questioned about common cold episodes 3× yr^{-1}. We modeled the cumulative incidence of colds during a 2-yr follow-up period with Poisson regression, adjusting for potential confounders. ***Results:*** Physical activity at work and at leisure had no association with common cold risk. In subjects with physically load-bearing jobs, neither vitamin E nor β-carotene affected significantly the risk of common cold. In subjects carrying out heavy exercise at leisure, vitamin E and β-carotene increased the risk of colds when compared with placebo. ***Conclusions:*** Contrary to previous suggestions, moderate physical activity is not associated with lower risk of common cold in middle-aged male smokers. It has been previously proposed that antioxidant supplementation might be beneficial for subjects carrying out heavy exercise, but in our study vitamin E and β-carotene increased the risk of colds in subjects carrying out heavy exercise at leisure.

INTRODUCTION

A number of studies have indicated that heavy physical activity may increase the incidence of symptoms commonly associated with upper respiratory infections (URI) (2,17,24). Higher incidence of URI was found within 1–2 wk after a marathon competition when compared to nonrunning controls (20,24,25), but shorter running competitions did not increase subsequent URI incidence (19). Comparisons of marathon runs and shorter running competitions found higher URI incidence after the marathon in one study (3) but not in another (15). Heavy regular exercise has also increased URI incidence in some studies. In 1-yr follow-up studies, elite orienteers (14) and cross-country skiers (8) had a higher URI incidence compared with controls. Adult subjects who were more active runners had a higher URI incidence compared with less active runners (7). Two studies with swimmers found no difference in URI incidence compared with controls, but the studies were small (4,26). A 1-yr prospective study with children practicing swimming, ice hockey, or gymnastics found no difference in URI incidence compared with controls (22). Consequently, several studies have indicated that short-term heavy exertion such as a marathon run and heavy regular exercise may increase the incidence of URI type of symptoms, yet the findings are not consistent.

In people not participating in top-level sports, there are few data on the relation of physical activity and the risk of URI. A number of studies have reported various effects, presumed to be beneficial against infections, on the immune system by moderate exercise (2,12,17,24). These findings combined with the increased URI risk by heavy exertion have led to the hypothesis that the relation between physical activity and the risk of infections may follow a "J"-shaped curve (17). According to this hypothesis, moderate exercise would reduce the risk of URI, but heavy exercise would increase the risk of URI, when compared with sedentary lifestyle. However, no large prospective studies with a clinical URI endpoint have tested this "J"-shape hypothesis. A retrospective study with 199 young Dutch adults found no meaningful association between habitual physical activity and URI incidence (28), and two randomized 3- to 4-month trials (18,21) found no statistically significant benefit on URI incidence from moderate exercise, but the latter studies were small (i.e., ≤36 subjects) and lacked statistical power to detect moderate effects.

There is much evidence from human and animal studies indicating that strenuous physical exercise may cause excessive production of free radicals, which may overwhelm the antioxidant defenses (23,29). Antioxidants, in particular vitamin E, have reduced the exercise-induced changes in the markers of oxidative stress (1,6,23,29). Antioxidants vitamin E, β-carotene, and vitamin C have also affected a wide range of immunological parameters in different experimental settings (10,13,16). With the evidence indicating that heavy exercise increases oxidative stress, it is tempting to speculate that this contributes to the risk of infection that could be prevented by antioxidants.

The purpose of the present study was to determine whether physical activity at work or at leisure is associated with the incidence of common cold episodes in middle-aged males, and whether long-term vitamin E or β-carotene supplementation affects the incidence of colds in physically active people.

METHODS

Subjects. The design and methods of the Alpha-Tocopherol Beta-Carotene Cancer Prevention (ATBC) Study examining the effects of vitamin E (α-tocopherol, AT, 50 mg·d^{-1}) and β-carotene (BC, 20 mg·d^{-1}) on the incidence of lung cancer and other cancers have been described in detail elsewhere (30). In brief, the trial participants were recruited in 1985–1988 from the total male population aged 50–69 yr living in southwestern Finland (N = 290,406). To be eligible, participants had to smoke ≥5 cigarettes per day at entry, and potential participants were excluded if they had severe medical problems or if they used supplemental vitamin E, vitamin A, or β-carotene in excess of predefined doses. Those enrolled (N = 29,133) were randomized to one of four intervention groups and administered placebo, AT, BC, or AT+BC. The intervention continued for 5–8 yr (median 6.1 yr) until April 1993 and involved three annual follow-up visits to the local study center. The trial was approved by the review boards of the participating institutions, and all participants gave written informed consent at study entry. Compliance in the study was high: some 80% of participants took more than 95% of their prescribed capsules during their active participation in the trial; there were no differences in capsule consumption among the intervention groups (30).

For the present analysis, we excluded participants not gainfully employed at study entry (N = 12,321) because this is a heterogeneous group comprised of age- and health related retirees, and others unemployed for various reasons for which data were not available. We also excluded participants with missing data on physical activity at work (N = 8), resulting in 16,804 participants working at study entry. The outcome (see below) could not be assessed for participants who did not participate at the 2-yr follow-up visit (N = 2,403) and they were excluded, thus leaving 14,401 participants for the present cohort analysis.

Baseline characteristics. At baseline before randomization, the men completed questionnaires on medical and smoking histories and general background characteristics. A detailed dietary history questionnaire was completed that provided data regarding daily alcohol and coffee consumption (11,30). Dietary data were incomplete and thus not available for 763 subjects of the 14,401.

The baseline questionnaire on physical activity at work and at leisure was a modification of that used originally in the Gothenburg study focusing on cardiovascular diseases (27). The questionnaire asked about physical activity at work during the previous 12 months with the following alternatives and examples being given: 1) very light job: mostly sitting and not walking much, such as work in office at a desk, clocksmith, or radio technician; 2) light job: walking a modest amount but not carrying heavy objects, such as office work that needs walking, foreman, salesman, or light factory work; 3) moderate job: walking a lot and carrying or lifting objects or walking up stairs or uphill, such as carpenter, caretaker of livestock, or moderate factory work; and 4) heavy job: heavy physical work that needs substantial amount of lifting or carrying heavy objects, digging or shoveling, or chopping wood, such as forestry, heavy farm work, heavy construction, and factory work.

The intensity of average physical activity during leisure time during the previous 12 months was asked with the following alternatives: 1) light: reading, watching TV, listening radio, or going to movies, mostly activities that are not physically loading; 2) moderate: walking, fishing, hunting, or gardening quite regularly; 3) heavy: actual physical exercises, such as jogging, skiing, swimming, gymnastics, court, and field sports quite regularly.

The average frequency of leisure-time physical activity causing at least modest sweating or shortness of breath during the previous 12 months was asked with the following alternatives: 1) less than once a week, 2) 1–2× wk^{-1}, or 3) 3× wk^{-1} or more.

Outcome and follow-up time. At each 4-monthly follow-up visit, the participants were asked about their health status, including the question "Have you had a common cold since the previous visit, and if so, how many times?" Questions on the occurrence of "other upper respiratory tract infection" and "acute bronchitis" were also asked.

Because the kind of job and physical activity at leisure time can change with time, in particular among subjects aged 50–69 yr, we limited the follow-up time to 2 yr. We calculated the total number of common cold episodes per person (cumulative incidence) during the first 2 yr of the trial as the outcome. There were a total of 27,570 common cold episodes during the 2-yr follow-up in the 14,401 subjects who participated at the 2-yr follow-up visit.

Statistical methods. We limited the analysis of the association between physical activity at work and leisure-time physical activity with the cumulative common cold incidence to the placebo arm of the trial. We modeled these associations using Poisson regression, including relevant baseline characteristics. Age was included as a continuous variable, cigarette smoking, alcohol and coffee consumption, and education were categorized as in Table 1; these variables were associated with the risk of colds in a previous analysis of the ATBC study cohort (11). We calculated the adjusted rate ratio as an estimator of relative risk (RR) and the likelihood ratio-based 95% confidence interval (95% CI) using the SAS PROC GENMOD program (release 8.1, SAS Institute, Inc., Cary, NC).

We also used the Poisson regression model to examine the effects of vitamin E and β-carotene supplementation on the cumulative common cold incidence within the group of 14,401 participants. The supplementation assignments were based on a 2 × 2 factorial design. In subjects with heavy jobs, vitamin E and β-carotene had a statistically significant interaction, and therefore the treatment effects on common cold in these men are shown in the four supplementation groups. As to supplementation, we carried out the analyses following the intention-to-treat principle. Two-tailed P values are used in the text.

RESULTS

The basic characteristics of the participants are shown in Table 1. Forty percent of the participants had moderate or heavy jobs, and 60% took heavy or moderate exercise at leisure time. There was no correlation between the intensity of physical activity at leisure and the intensity of physical activity at work (r = -0.04). In contrast, the Spearman correlation between the intensity of leisure-time physical activity and the frequency of leisure-time physical activity was rather high (r = 0.45). On average the participants had 0.96 common cold episodes per year during the follow-up. No colds during the 2-yr follow-up were reported by 28% of participants, and three or more colds were reported by 29% of participants.

We restricted the examination of the relationship between physical activity on job and the risk of colds to the placebo arm of the trial. Physical activity at work was not significantly associated with the incidence of the common cold (Table 2). Though there was a slight trend toward reduced risk of common cold with increasing physical activity the utmost difference—between the heavy and very light job—was, however, only 7%.

To explore the effect of leisure-time physical activity on the incidence of common cold, we divided the placebo subjects into nine groups on the basis of their average intensity of leisure-time physical activity, and the frequency of leisure-time exercise leading to sweating or shortness of breath (Table 3). We used participants with light leisure time physical activity and infrequent activities leading to sweating or shortness of breath (<1 per week) as the reference group ("sedentary subjects"). The risk of the common cold among participants with heavier and/or more frequent physical activity did not consistently differ from that among sedentary subjects. Participants with heavy exercises 1 to 2× wk^{-1} had 14% lower incidence of common cold episodes compared with the sedentary group, but the small and marginally significant (P = 0.045) difference could be accounted for by multiple comparisons.

We restricted the analyses of Tables 2 and 3 to participants aged 50–59 yr without any significant association between physical activity and the risk of colds (data not shown).

In participants with heavy job activity, vitamin E, and β-carotene had statistically significant interaction (P = 0.037). However, the risks of common cold in the active intervention groups did not differ significantly from that of the placebo group (Table 4).

In participants who carried out heavy exercise at leisure, β-carotene and vitamin E–β-carotene combination increased common cold risk by 25% (P = 0.001) and 21% (P = 0.005), respectively, compared with the placebo group (Table 4). The risk of colds was nonsignificantly 10% higher in vitamin E group compared with the placebo group.

DISCUSSION

Physical activity at work or at leisure had no material association with the incidence of colds in middle-aged male smokers. In participants who were exercising heavily 1 to 2× wk^{-1}, the incidence of colds was 14% lower compared with the sedentary group, but the difference was marginally significant and it may be explained by the multiple comparisons. Furthermore, if heavy exercise would reduce common cold risk by 14% with an annual incidence of one common cold episode per person, then seven persons need to exercise heavily 1 to 2× wk^{-1} for 1 yr in order to prevent one common cold episode. Thus, the cost-benefit ratio is very low for such intervention even if the slight difference were real.

The present analysis was restricted to a 2-yr follow-up with a presumption that the kind of work and the leisure-time exercise habits reported at the baseline of the study did not considerably change within that time frame. We repeated the analyses with a restriction to participants aged 50–59 yr to further reduce the possibility that, for example, retirement would render the baseline information less accurate, but the findings were similar. Vitamin E and β-carotene supplementation did not reduce the risk of colds in participants with heavy jobs or in participants carrying out heavy exercise at leisure; in contrast, these two antioxidants increased the risk of colds in the latter subjects.

In our study, no virological or serological tests were carried out to explore the etiological causes of the self reported colds. However, it is the subjective symptoms rather than positive laboratory findings that lead a subject to stay off work or to withdraw from participation in a sports competition, and therefore the subjective outcome is considerably more relevant for public health purposes. Furthermore, the manifestations of the common cold are so typical that self-diagnosis is usually correct (5). Nevertheless, differences in the subjective perception of colds may contribute to bias between different physical activity groups. For example, subjects with heavy jobs or subjects practicing heavy exercise can differ in their reporting of colds when compared with sedentary subjects. Given the lack of material findings for activity level, it seems, however, unlikely that such potential biases or physical activity misclassification could be large enough to camouflage quantitatively meaningful true differences between the physical activity groups.

A potential limitation of our study is the heterogeneous outcome, self-reported colds, which may contain a variety of viral respiratory episodes of different severity. The heterogeneity of the outcome, however, should not affect our conclusions. To assume that physical activity would affect the incidence of certain specific kinds of colds (e.g., severe colds or colds caused by a certain virus) would require that physical activity would equivalently increase the incidence of colds in the complementary group (e.g., mild colds or colds caused by other viruses) to generate the flat response. Such a possibility seems highly improbable.

A large number of studies have found diverse effects on the immune system by moderate physical exercise considered to be positive against infections (2,12,17,24). Only few small studies have examined the association between moderate exercise and the risk of URI, but none of them found significant benefit from moderate exercise (18,21,28). On the other hand, there are several studies that have reported elevated risk of URI type of symptoms in subjects carrying out exceptionally heavy acute or regular exercise (2,17,24). Based on the assumption that the effects of moderate exercise on the immune system are positive, when compared with sedentary subjects, and on the rather consistent increase in the URI type of symptoms in exceptionally stressed subjects, the relationship between physical activity and URI risk was hypothesized to resemble the "J"-shape (17).

Our large-scale cohort study does not support a reduction in URI risk by moderate exercise as implied by the "J"-curve hypothesis. In our study, when physical activity increases from sedentary level at work or at leisure, there are no indications of substantial reduction in common cold risk.

Concluding from our results, the effects of moderate exercise on diverse laboratory measures of immune function reported in several studies (2,12,17,24) may have little practical significance on the URI risk in the general population.

Our study is limited to 50- to 69-yr-old male smokers who were overall fairly sedentary or engaged mainly in physical exercise secondary to other free time activities; only 6% of the participants carried out actual heavy exercise at leisure. Therefore, our study cannot address the question whether highly intense and/or protracted sporting activities such as a marathon run, or strenuous regular competitive sports training among young subjects, increases the incidence of symptoms commonly associated with URI, as implied by the latter part of the "J"-curve. Nevertheless, our study indicates that in middle-aged men, URI risk is not materially increased by physical activity when their exercise is classified heavy in their own social context.

Heavy exercise increased the biochemical markers of oxidative damage in several studies with animals and humans, and these changes were diminished by antioxidants, in particular by vitamin E (1,6,23,29). Furthermore, antioxidants vitamin E, β-carotene and vitamin C have improved the functions of the immune system in a large number of studies (10,13,16). We examined whether vitamin E or β-carotene supplementation might decrease the incidence of colds in participants categorized as performing heavy activity at work or in participants carrying out heavy exercise at leisure under the assumption that oxidative stress may be increased under such conditions and the immune system might be protected by antioxidant supplementation. In participants categorized as having a heavy job, vitamin E and β-carotene supplementations had statistically significant interaction in their effects on the common cold risk, but none of the three antioxidant groups materially differed from the placebo group. In participants carrying out heavy leisure-time exercise, risk of colds was increased in the three antioxidant groups compared with the placebo group. These findings are inconsistent with the notion that vitamin E or beta-carotene might be beneficial for subjects enduring heavy physical stress.

We must be cautious when extrapolating findings to subjects differing from our study population, but given the tendency of vitamin E and β-carotene to increase common cold risk in subjects carrying out heavy exercise, it seems unlikely that these antioxidants could yield substantial benefit in young athletes practicing more heavily than our subjects. A third antioxidant, vitamin C, is also of interest in relation to conditions of physical stress; e.g., in a recent study, vitamin C prevented exercise-induced oxidative changes (1). In three small randomized placebo-controlled trials with subjects under heavy acute physical stress, vitamin C supplementation decreased the incidence of colds, and combining the results of the three trials yielded an average of 50% reduction ($P = 0.001$) in the risk of colds by vitamin C (9). By contrast, large-scale trials of sedentary subjects showed no effect on the common cold incidence by vitamin C (10), explicitly indicating that any putative effects by this third antioxidant are limited to specific conditions. Evidently, more research on vitamin C in physically active people would seem to be warranted, but based on the present findings, it is unlikely that vitamin E or β-carotene supplementation will provide any beneficial effects against URI in physically stressed subjects.

The ATBC study was supported by U.S. Public Health Service contract N01-CN-45165 from the United States National Cancer Institute.

REFERENCES

1. ASHTON, T., I. S. YOUNG, J. R. PETERS, et al.
Electron spin resonance spectroscopy, exercise, and oxidative stress: an ascorbic acid intervention study.
J. Appl. Physiol. 87:2032–2036, 1999.
http://dx.doi.org/10.1007/s004210050366
2. BRENNER, I. K. M, P. N. SHEK, and R. J. SHEPHARD. Infection in athletes.
Sports Med. 17:86–107, 1994.
http://dx.doi.org/10.2165/00007256-199417020-00002
3. CASTELL, L. M., J. R. POORTMANS, and E. A. NEWSHOLME.
Does glutamine have a role in reducing infections in athletes? Eur. J. Appl. Physiol. 73:488–490, 1996.
http://dx.doi.org/10.1007/BF00334429
4. GLEESON, M., D. B. PYNE, W. A. MCDONALD, et al.
Pneumococcal antibody responses in elite swimmers. Clin. Exp. Immunol. 105: 238–244, 1996.
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2200502
5. GWALTNEY, J. M. The common cold. In: Principles and Practice of Infectious Diseases, 4th Ed.,
G. L. Mandell, J. E. Bennett, and R. Dolin (Eds.). New York: Churchill Livingstone, 1995, pp. 561–566.
6. HARTMANN, A., A. M. NIESS, M. GRUNERT-FUCHS, B. POCH, and G. SPEIT.
Vitamin E prevents exercise-induced DNA damage.
Mutat. Res. 346:195–202, 1995.
http://dx.doi.org/10.1016/0165-7992(95)90035-7
7. HEATH, G. W., E. S. FORD, T. E. CRAVEN, C. A. MACERA, K. L. JACKSON, and R. R. PATE.
Exercise and the incidence of upper respiratory tract infections.
Med. Sci. Sports Exerc. 23:152–157, 1991.
http://dx.doi.org/10.1249/00005768-199102000-00002
8. HEIR, T., and S. LARSEN. The influence of training intensity, airway infections and environmental conditions on seasonal variations in bronchial responsiveness in cross-country skiers.
Scand. J. Med. Sci. Sports 5:152–159, 1995.
http://dx.doi.org/10.1111/j.1600-0838.1995.tb00029.x
9. HEMILÄ, H.
Vitamin C and common cold incidence: a review of studies with subjects under heavy physical stress.
Int. J. Sports Med. 17:379–383, 1996.
http://dx.doi.org/10.1055/s-2007-972864
http://helda.helsinki.fi/handle/10250/7983
http://www.ncbi.nlm.nih.gov/pubmed/8858411
10. HEMILÄ, H., and R. M. DOUGLAS.
Vitamin C and acute respiratory infections.
Int. J. Tuberc. Lung Dis. 3:756–761, 1999.
http://www.ingentaconnect.com/content/iuatld/ijtld/1999/00000003/00000009/art00004
http://www.ncbi.nlm.nih.gov/pubmed/10488881
11. HEMILÄ, H., J. KAPRIO, D. ALBANES, O. P. HEINONEN, and J. VIRTAMO.
Vitamin C, vitamin E, and beta-carotene in relation to common cold incidence in male smokers.
Epidemiology 13:32–37, 2002.
http://dx.doi.org/10.1097/00001648-200201000-00006
http://www.jstor.org/pss/3703244
http://helda.helsinki.fi/handle/10138/18059
http://www.ncbi.nlm.nih.gov/pubmed/11805583
12. HOFFMAN-GOETZ, L., and B. K. PEDERSEN. Exercise and the immune system.
Immunol. Today 15:382–387, 1994.
http://dx.doi.org/10.1016/0167-5699(94)90177-5
13. HUGHES, D. A. Effects of carotenoids on human immune function.
Proc. Nutr. Soc. 58:713–718, 1999.
http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=800112
http://www.ncbi.nlm.nih.gov/pubmed/10604207
14. LINDE, F. Running and upper respiratory tract infections.
Scand. J. Sports Sci. 9:21–23, 1987.
15. MACERA, C. A., D. R. DAVIS, R. R. PATE, K. L. JACKSON, and J. WOODS.
Postrace morbidity among runners.
Am. J. Prev. Med. 7:194–198, 1991.
http://www.ncbi.nlm.nih.gov/pubmed/1756054

16. MORIGUCHI, S., and M. MURAGA.
Vitamin E and immunity.
Vitam. Horm. 59:305–336, 2000.
http://dx.doi.org/10.1016/S0083-6729(00)59011-6
17. NIEMAN, D. C.
Exercise, upper respiratory tract infection, and the immune system.
Med. Sci. Sports Exerc. 26:128–139, 1994.
http://dx.doi.org/10.1249/00005768-199402000-00002
18. NIEMAN, D. C., D. A. HENSON, G. GUSEWITCH, et al.
Physical activity and immune function in elderly women.
Med. Sci. Sports Exerc. 25:823–831, 1993.
http://dx.doi.org/10.1249/00005768-199307000-00011
19. NIEMAN, D. C., L. M. JOHANSSEN, and J. W. LEE.
Infectious episodes in runners before and after a roadrace.
J. Sports Med. Phys. Fitness 29:289–296, 1989.
http://www.ncbi.nlm.nih.gov/pubmed/2635263
20. NIEMAN D. C., L. M. JOHANSSEN, J. W. LEE, and K. ARABATZIS.
Infectious episodes in runners before and after the Los Angeles marathon.
J. Sports Med. Phys. Fitness. 30:316–328, 1990.
http://www.ncbi.nlm.nih.gov/pubmed/2266764
21. NIEMAN D. C., S. L. NEHLSEN-CANNARELLA, P. A. MARKOFF, et al.
The effects of moderate exercise training on natural killer cells and acute upper respiratory tract infections.
Int. J. Sports Med. 11: 467–473, 1990.
http://dx.doi.org/10.1055/s-2007-1024839
22. OSTERBACK, L., and Y. QVARNBERG.
A prospective study of respiratory infections in 12-year-old children actively engaged in sports.
Acta Paediatr. Scand. 76:944 –949, 1987.
http://dx.doi.org/10.1111/j.1651-2227.1987.tb17269.x
23. PACKER, L. Oxidants, antioxidant nutrients and the athlete.
J. Sports Sci. 15:353–363, 1997.
http://dx.doi.org/10.1080/026404197367362
24. PETERS, E. M. Exercise, immunology and upper respiratory tract infections.
Int. J. Sports Med. 18:S69–S77, 1997.
http://dx.doi.org/10.1055/s-2007-972702
25. PETERS E. M., and E. D. BATEMAN. Ultramarathon running and upper respiratory tract infections.
S. Afr. Med. J. 64:582–584, 1983.
http://www.ncbi.nlm.nih.gov/pubmed/6623247
26. PYNE, D. B., M. S. BAKER, P. A. FRICKER, W. A. MCDONALD, R. D. TELFORD, and M. J. WEIDEMANN.
The effects of an intensive 12-wk training program by elite swimmers on neutrophil oxidative activity.
Med. Sci. Sports Exerc. 27:536–542, 1995.
http://dx.doi.org/10.1249/00005768-199504000-00011
27. SALTIN, B., and G. GRIMBY. Physiological analysis of middle-aged and old former athletes.
Circulation 38:1104–1115, 1968.
http://circ.ahajournals.org/cgi/content/short/38/6/1104
28. SCHOUTEN, W. J., R. VERSCHUUR, and H. C. G. KEMPER.
Physical activity and upper respiratory tract infections in a normal population of young men and women.
Int. J. Sports Med. 9:451–455, 1988.
http://dx.doi.org/10.1055/s-2007-1025050
29. SEN, C. K. Oxidants and antioxidants in exercise.
J. Appl. Physiol. 79:675–686, 1995.
http://jap.physiology.org/cgi/content/abstract/79/3/675
30. THE ALPHA-TOCOPHEROL, BETA-CAROTENE CANCER PREVENTION STUDY GROUP.
The effect of vitamin E and beta-carotene on the incidence of lung cancer and other cancers in male smokers.
N. Engl. J. Med. 330:1029–1035, 1994.
http://dx.doi.org/10.1056/NEJM199404143301501
http://atbcstudy.cancer.gov/pdfs/atbc33010291994.pdf

TABLE 1. Baseline characteristics of working participants, ATBC study

Characteristic	No. of Subjects
All subjects	14401 (100%)
Age (years)	
50-54	7466 (52%)
55-59	4897 (34%)
60-64	1715 (12%)
65-69	323 (2%)
Smoking (cigarettes/day)	
5-14	2509 (17%)
15-24	6806 (47%)
25-34	3839 (27%)
≥35	1247 (9%)
Alcohol intake [a]	
None	1190 (8%)
Any	12448 (87%)
Coffee intake (ml/day) [a]	
≤299	1697 (12%)
300-599	4789 (33%)
≥600	7152 (50%)
Education	
Elementary school or less	10678 (74%)
More than elementary school	3723 (26%)
Physical activity at work	
Very light	3490 (24%)
Light	4670 (33%)
Moderate	4030 (28%)
Heavy	2211 (15%)
Physical activity at leisure [a]	
Light	6025 (42%)
Moderate	7455 (52%)
Heavy	916 (6%)
Frequency of physical activity at leisure leading to sweating [a]	
<1 /week	8415 (59%)
1-2 /week	4342 (30%)
≥3 /week	1628 (11%)

[a] Data on alcohol and coffee consumption was missing from 763 participants, physical activity at leisure from 5, and the frequency of physical activity at leisure from 16 participants.

TABLE 2. Relative risk of the common cold in relation to physical activity at work during 2-year follow-up, ATBC study, placebo arm

Physical activity at work	No. of subjects	Relative risk of colds		Colds per year
		RR	(95% CI)[a]	
Very light	869 (25%)	1.00	(reference)	1.02
Light	1129 (33%)	0.97	(0.91-1.04)	0.98
Moderate	973 (28%)	0.96	(0.90-1.03)	0.96
Heavy	502 (14%)	0.93	(0.85-1.02)	0.90

[a] Poisson regression model; adjusted for age, cigarettes per day, consumption of alcohol and coffee, and education. Data on diet was missing from 188 subjects who are excluded.
Abbreviations: RR, relative risk; CI, confidence interval.

TABLE 3. Relative risk of the common cold in relation to physical activity at leisure time during 2-year follow-up, ATBC study, placebo arm

Average Physical Activity at Leisure	Frequency of Exercise Causing Sweating or Shortness of Breath		
	<1/week	**1-2/week**	**≥3/week**
Light			
Relative Risk of Colds			
RR (95% CI) [a]	1.00 (reference)	0.97 (0.87-1.07)	1.01 (0.83-1.23)
Colds per year	0.97	0.94	0.99
No. of subjects	1198 (34%)	226 (6.5%)	52 (1.5%)
Moderate			
Relative Risk of Colds			
RR (95% CI) [a]	1.01 (0.95-1.08)	0.99 (0.93-1.06)	1.05 (0.96-1.16)
Colds per year	0.99	0.98	1.01
No. of subjects	832 (24%)	683 (20%)	268 (8%)
Heavy			
Relative Risk of Colds			
RR (95% CI) [a]	1.11 (0.71-1.64)	0.86 (0.74-1.00)	0.95 (0.80-1.12)
Colds per year	1.04	0.84	0.91
No. of subjects	11 (0.3%)	119 (3.4%)	81 (2.3%)

[a] Poisson regression model; adjusted for age, cigarettes per day, consumption of alcohol and coffee, and education. Data on physical activity at leisure was missing from 3 subjects, and data on diet was missing from 188 subjects, who are excluded.
Abbreviations: RR, relative risk; CI, confidence interval.

TABLE 4. Effect of vitamin E and β-carotene supplementation on common cold incidence during 2-year follow-up in physically active subjects, ATBC study

Physical activity	Intervention			
	Placebo	**Vitamin E**	**β-Carotene**	**Vitamin E and β-Carotene**
Heavy job activity				
(2211 subjects) [a]				
Relative Risk of Colds				
RR (95% CI) [b]	1.00 (ref.)	1.08 (0.99-1.18)	1.00 (0.92-1.10)	0.95 (0.87-1.04)
Colds per year	0.92	0.99	0.92	0.87
Heavy exercise at leisure				
(916 subjects)				
Relative Risk of Colds				
RR (95% CI) [b]	1.00 (ref.)	1.10 (0.96-1.27)	1.25 (1.09-1.44)	1.21 (1.06-1.38)
Colds per year	0.86	0.95	1.08	1.04

[a] Vitamin E and β-carotene supplementation had statistically significant interaction: $\chi^2(1\ df) = 4.4$; $P = 0.037$.
[b] Poisson regression model comparing intervention to placebo, unadjusted model.
RR, relative risk; CI, confidence interval.