



Aalborg Universitet

AALBORG UNIVERSITY
DENMARK

Leisure-time physical activity and the risk of suspected bacterial infections

Pape, Kathrine; Ryttergaard, Louise; Rotevatn, Torill Alise; Nielsen, Berit Jamie; Torp-Pedersen, Christian; Overgaard, Charlotte; Bøggild, Henrik

Published in:
Medicine and Science in Sports and Exercise

DOI (link to publication from Publisher):
[10.1249/MSS.0000000000000953](https://doi.org/10.1249/MSS.0000000000000953)

Creative Commons License
CC BY-NC-ND 4.0

Publication date:
2016

Document Version
Publisher's PDF, also known as Version of record

[Link to publication from Aalborg University](#)

Citation for published version (APA):
Pape, K., Ryttergaard, L., Rotevatn, T. A., Nielsen, B. J., Torp-Pedersen, C., Overgaard, C., & Bøggild, H. (2016). Leisure-time physical activity and the risk of suspected bacterial infections. *Medicine and Science in Sports and Exercise*, 48(9), 1737-1744. <https://doi.org/10.1249/MSS.0000000000000953>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

Take down policy

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

Leisure-Time Physical Activity and the Risk of Suspected Bacterial Infections

KATHRINE PAPE¹, LOUISE RYTTERGAARD¹, TORILL ALISE ROTEVATN¹, BERIT JAMIE NIELSEN², CHRISTIAN TORP-PEDERSEN^{1,2}, CHARLOTTE OVERGAARD¹, and HENRIK BØGGILD¹

¹Public Health Epidemiology Group, Department of Health Science Technology, Aalborg University, Aalborg, DENMARK; and ²Department of Clinical Epidemiology, Aalborg University Hospital, Aalborg, DENMARK

ABSTRACT

PAPE, K., L. RYTTERGAARD, T. A. ROTEVATN, B. J. NIELSEN, C. TORP-PEDERSEN, C. OVERGAARD, AND H. BØGGILD. Leisure-Time Physical Activity and the Risk of Suspected Bacterial Infections. *Med. Sci. Sports Exerc.*, Vol. 48, No. 9, pp. 1737–1744, 2016. **Introduction:** The risk of upper respiratory tract viral infections is reduced with increased physical activity, but little information is available regarding bacterial infections. We examined the relationship between leisure-time physical activity and suspected bacterial infections. **Methods:** Information on leisure-time physical activity was obtained from the 2007 and 2010 North Denmark Region Health Surveys of 18,874 Danes and linked to data from nationwide administrative registries. Suspected bacterial infections were determined based on filled prescriptions for antibiotics. Adjusted estimates were calculated using logistic regression models. **Results:** During a 1-yr follow-up, 5368 participants filled at least one antibiotic prescription. There was a statistically significant difference between physical activity level and filling any antibiotic prescriptions among women ($P = 0.003$) but not among men ($P = 0.191$). Logistic regression analysis showed that compared with sedentary behavior, all levels of leisure-time physical activities lowered the likelihood of filling an antibiotic prescription. However, after multivariable adjustments, only estimates of low physical activity were significant (odds ratio [OR] = 0.90, 95% confidence interval [CI] = 0.82; 0.99). Multivariable adjusted subgroup analyses of suspected cystitis showed a decreased likelihood of engaging in low (OR = 0.79, 95% CI = 0.65–0.95) and moderate (OR = 0.68, 95% CI = 0.54–0.87) physical activity. **Conclusion:** Low leisure-time physical activity is associated with a statistically significant 10% lower risk of suspected bacterial infections during a 1-yr follow-up compared with sedentary behavior. Further, low and moderate levels of physical activity were associated with the statistically significant reduction of suspected cystitis. No reduction in suspected respiratory tract infections was statistically significant and associated with physical activity compared with sedentary behavior. **Key Words:** EXERCISE, SEDENTARY LIFESTYLE, COHORT STUDIES, REGISTRIES, CYSTITIS

Despite evidence that physical activity affects the immune system (9,22) and repeated findings of a relationship between physical activity and viral infections (1,5,12,15,20,21), few studies (4,17) with a smaller number of outcomes have examined the relationship between physical activity and risk of bacterial infections. The effect of physical activity on the risk of viral infections is

suggested to be J-shaped (18,19); that is, while the incidence and severity of primarily viral infections, such as upper respiratory tract infections, may be reduced by regular moderate physical activity compared with sedentary behavior, exhaustive high-intensity exercise has been reported to increase the risk of upper respiratory tract infections among athletes (18,19). Among nonathletes, increasing physical activity is associated with a decreased risk of upper respiratory tract infections (15,16). The relationships found between physical activity and viral infections have raised an interest in investigating the more serious infections caused by a wide range of bacteria (3,6,24,31,33). Bacterial infections are a considerable cause of morbidity and mortality worldwide, and they place a burden on the health care system and on society (3,6,24,31,33).

Previous studies (4,17) of leisure-time physical activity and the risk of bacterial infection have primarily focused on a specific disease or specific bacteria and not on bacterial infections in general. The results of those studies indicate a difference between men and women that suggests a sex interaction and the potential confounding of age, sex, body mass index, smoking, and alcohol consumption. Given the high prevalence of bacterial infections (14) and the potential

Address for correspondence: Kathrine Pape, M.Sc., Aalborg University, Niels Jernes Vej 14, Aalborg DK-9220, Denmark; E-mail: kpape@live.dk. Submitted for publication January 2016.

Accepted for publication April 2016.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.acsm-msse.org).

0195-9131/16/4809-1737/0

MEDICINE & SCIENCE IN SPORTS & EXERCISE®

Copyright © 2016 by the Author(s). Published by Wolters Kluwer Health on behalf of the American College of Sports Medicine. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially.

DOI: 10.1249/MSS.0000000000000953

preventive effect of physical activity, we conducted a large study with a broader and more general focus on bacterial infections. The purpose of the study was to investigate the relationship between different levels of leisure-time physical activity and the risk of suspected bacterial infections, estimated on the basis of filled antibiotic prescriptions. We hypothesized that increased levels of leisure-time physical activity are related with a lower risk of bacterial infections.

METHODS

Data collection. A cohort study based on the residents who completed the North Denmark Region Health Survey in 2007 or 2010 was conducted (28,29). The original aim of the two surveys was to describe the prevalence, distribution, and development of the general health conditions of the citizens of the North Denmark Region. Further, the aim was to provide data material for regional and municipal health planning, for analysis of geographical differences, and for research and methodology development. The information from the respondents was linked in Statistic Denmark with information from multiple nationwide registries via the use of Denmark's unique civil registration number, an identification number assigned to all citizens at birth (30). Written informed consent and ethical approval are not required for anonymized retrospective registry-based studies in Denmark (27,30).

The Civil Registration System (23) includes information about each individual's sex and date of birth. All hospital admissions in Denmark are registered in the National Patient Register (13). Discharge diagnoses are coded using the World Health Organization's *International Statistical Classification of Diseases and Related Health Problems* (ICD-10). Information about all prescriptions filled at Danish pharmacies is held in the Danish National Prescriptions Registry (11) and coded using the World Health Organization's *Anatomical Therapeutic Chemical* (ATC) classifications system (34). Information on educational level was obtained from the Population Education Register (32) and classified using the International Standard Classification of Education (ISCED-2011) (10).

Study population. The health surveys were sent out to two samples of 23,490 and 35,700 citizens in Northern Jutland, Denmark, at two different periods (28,29). The survey was conducted either from November 2006 to February 2007 or from February to March 2010. Both samples were drawn randomly from the Civil Registrations System from populations of 438,014 and 469,998 >16-yr-old Danes, respectively. The samples were cluster samplings stratified according to the sizes of the 11 municipalities of the region. Reminders were sent out twice to those who failed to return the questionnaire. The response rates for the 2007 and 2010 questionnaires were 48.9% and 65.5%, respectively. For participants who had answered both questionnaires, only the first response was included in the study. The sampling design yielded unequal selection probabilities for the citizens of the different municipalities, which could lead to biased parameter

estimates. To correct for the unequal selection probability, in which the citizens of large municipalities were less likely to be selected than the citizens of smaller municipalities, design weights were applied to all analyses. The follow-up period for filled prescriptions was defined as a period of 1 yr, from February 1, 2007, to February 1, 2008, and from March 22, 2010, to March 22, 2011, respectively.

To avoid confounding from chronic diseases that could affect the relationship between leisure-time physical activity and suspected bacterial infections, only participants with no records of cancer (ICD-10 = C00–C96), pharmaceutically treated diabetes (ATC = A10), cardiovascular diseases (ICD-10 = I00–I99), or chronic diseases of the lower respiratory tract (chronic obstructive pulmonary disease and asthma, among others; ICD-10 = J40–J47) at baseline were included. Missing information about physical activity or other covariates led to the exclusion of another 4752 participants. This resulted in a final sample of 18,874 participants (see Fig. 1 for more details).

Assessment of physical activity. In the health survey, self-reported physical activity was assessed using a four-level scale originally constructed by Saltin and Grimby (26), with minor modifications. A single question was used to assess leisure-time physical activity: "If you look at the past year, what would you say best described your leisure-time physical activity?" The participants chose from four levels of physical activity: 1) "regular hard physical training and competitive sports several times per week" (henceforth designated "vigorous physical activity"); 2) "exercise through sports or heavy gardening or similar activities for at least 4 h·wk⁻¹" ("moderate physical activity"); 3) "strolling, riding a bicycle, or other light physical activity for at least 4 h·wk⁻¹ (include also Sunday walks, light gardening, and riding a bicycle/walking to work)" ("low physical activity"); or 4) "reading, watching television, or other sedentary activities" ("sedentary behavior") (28,29).

The survey question from 2007 differed from the 2010 version in that it allowed the participant to choose multiple responses and included a "do not know" category. In this study, the highest level of physical activity level was used, and the "do not know" category was considered missing data.

Identification of suspected bacterial infections. Suspected bacterial infections were based on filled antibiotic prescriptions with the following ATC codes: J01A-G, M, R, and X (34) (see Table, Supplemental Digital Content 1, <http://links.lww.com/MSS/A695>, which list the abbreviations of the ATC codes). We used filled antibiotic prescriptions as an indication of suspected bacterial infection. All relevant antibiotics require a prescription and therefore the capture of relevant prescriptions can be assumed to be complete. Only the first prescription filled during the follow-up period was included in the analyses.

Demographic and lifestyle characteristics. Information regarding age and sex was identified through the Civil Registration System. We calculated body mass index (weight in

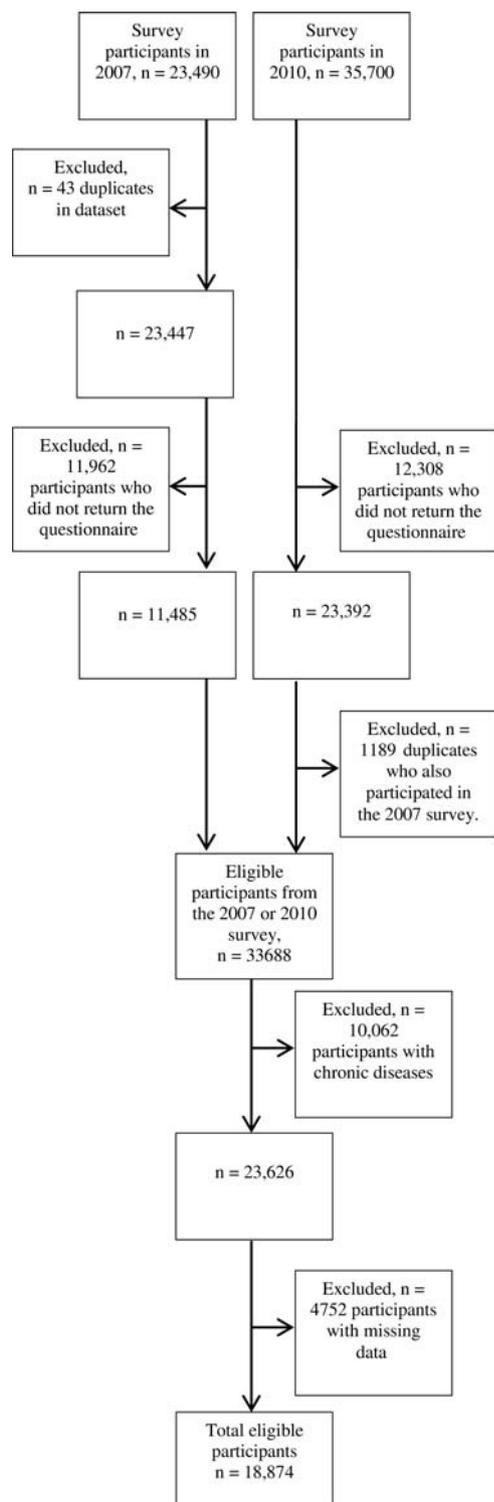


FIGURE 1—Flowchart of the study selection process of participants who completed the North Denmark Region Health Survey from 2007 or 2010.

kilograms divided by the square of height in meters) based on self-reported weight and height in the survey and grouped the participants into four categories: $<18.5 \text{ kg}\cdot\text{m}^{-2}$ (underweight), ≥ 18.5 to $<25 \text{ kg}\cdot\text{m}^{-2}$ (normal weight), ≥ 25 to $<30 \text{ kg}\cdot\text{m}^{-2}$ (overweight), and $\geq 30 \text{ kg}\cdot\text{m}^{-2}$ (obese) (31). Smoking status and weekly alcohol consumption were also obtained through

the health survey. Smoking status was classified as “current,” “past,” or “never.” Alcohol consumption was divided into four categories according to the Danish Health and Medicines Authority’s recommendations (7) based on sex and weekly consumption and define alcohol intake (women/men) as follows: no consumption ($0/0 \text{ U}\cdot\text{wk}^{-1}$), low risk ($<7/<14 \text{ U}\cdot\text{wk}^{-1}$), moderate risk ($7\text{--}14/14\text{--}21 \text{ U}\cdot\text{wk}^{-1}$), and high risk ($>14/>21 \text{ U}\cdot\text{wk}^{-1}$).

The participants were grouped into five educational levels according to the highest educational level achieved based on the ISCED-2011 (10). The ISCED-2011 classification consists of eight levels, and we operationalized these into five levels corresponding to the Danish educational system (8): A) early childhood education, primary education, and lower secondary education (ISCED levels 0–2); B) general upper secondary education and high school programs (ISCED level 3); C) vocational upper secondary education and vocational training and education (ISCED level 3); D) short- or medium-length higher education, first-cycle program tertiary education, and bachelor’s degree or equivalent (ISCED level 5–6); and E) long-term higher education, second-cycle programs, master’s degree or equivalent, or third-cycle programs: doctoral and PhD programs or equivalent (ISCED levels 7–8) (32). Because of small numbers in category E, it was combined with category D.

Data analysis and statistics. Descriptive baseline data are shown in terms of counts and percentage stratified by sex and physical activity level. Age is presented as the mean \pm SD. The chi-square test was used to analyze group differences at baseline for associations between categorical variables, whereas *t*-tests were used to analyze age. Because there was no difference between the participating men and women, survey-weighted logistic regression models were adjusted for sex and age to examine the relationship between leisure-time physical activity and antibiotic prescriptions for suspected bacterial infections. Although no interaction between sex and physical activity was detected in the fully adjusted regression model ($P = 0.117$), sex-stratified models were produced for comparisons with previous studies (4,15,17,21). Sedentary behavior was used as the reference in all models. The significance level was set at $P < 0.05$, and 95% confidence intervals (CI) were calculated. Adjustments were conducted for age, body mass index, smoking status, alcohol consumption, and educational level in the multivariate logistic regressions. Furthermore, adjustments for the two different survey periods and the different municipalities were performed. The adjustments did not show any differences and were thus not included in the final analyses.

Subgroup analyses were performed for the illnesses associated with the most frequently used antibiotic treatments in the study (cystitis and respiratory tract infections) using logistic regression models. Antibiotics prescribed to treat several bacterial infections in different subgroups were not included. All levels of physical activity above sedentary behavior were merged together in the analyses of respiratory tract infections. In the analyses of cystitis, body mass index categories 1 and 2 were merged together for men because of

a small number of outcomes. We performed a sensitivity analysis of those who filled three or more prescriptions during the year. We also performed a sensitivity analysis using multivariate imputation by chained equations of those who were excluded because of missing data ($n = 4752$). Further, we examined the robustness of the exposure by examining whether the participants who had completed both questionnaires had changed their physical activity level during the 3 yr between surveys. SAS 9.4 software (SAS Institute, Inc., Cary, NC) was used for all data management, and all statistical analyses were performed using R Studio software version 0.98.1062 (R Studio, Inc., ©2009–2013, part of the R statistical software package, version 3.2.2, Development Core Team, Boston, MA).

RESULTS

The baseline characteristics of the 18,874 participants according to their leisure-time physical activity level and sex are presented in Table 1. During 1 yr of follow-up, 5368 participants (22.4% of the men and 34.1% of the women) filled at least one antibiotic prescription. There was a statistically significant difference between physical activity level and filling any antibiotic prescriptions among the women ($P = 0.003$) but not among the men ($P = 0.191$). The men and women who participated in vigorous physical activity were significantly younger than the participants in the other exposure groups. The percentage of current smokers and those with a body mass index higher than $25 \text{ kg}\cdot\text{m}^{-2}$ was lower among the participants with higher levels of physical activity. Age, body mass index, smoking status, and alcohol consumption significantly differ in relation to

antibiotic prescription. The odds ratio (OR) estimates of the relationship between leisure-time physical activity and suspected bacterial infections (Fig. 2, models A and B) showed that compared with sedentary behavior, all levels of physical activity lowered the risk of filling an antibiotic prescription. Estimates of low (OR = 0.86, 95% CI = 0.78–0.94) and moderate (OR = 0.83, 95% CI = 0.75–0.93) physical activity were significant after adjustment for sex and age. In the multiaadjusted analysis, the estimate of moderate physical activity was attenuated (OR = 0.90, 95% CI = 0.80–1.00) whereas the estimate of low physical activity (OR = 0.90, 95% CI = 0.82–0.99) remained significant. The risk of filling an antibiotic prescription in relation to vigorous physical activity was not as pronounced as for the other physical activity levels. Although vigorous physical activity was not significant in any of the models, the results suggest a U-shaped relationship between leisure-time physical activity and the risk of suspected bacterial infections.

None of the results for men in either model A¹ or model B¹ (Fig. 2) were statistically significant. However, OR values showed that low and moderate levels of physical activity were associated with a lower risk of filling an antibiotic prescription, whereas vigorous leisure-time physical activity was associated with an increased risk, when compared with sedentary behavior.

Age-adjusted estimates (Fig. 2, model A²) showed that women who engaged in low (OR = 0.80, 95% CI = 0.71–0.91), moderate (OR = 0.81, 95% CI = 0.70–0.94), and vigorous (OR = 0.81, 95% CI = 0.62–1.05) leisure-time physical activity were less likely to fill a prescription for antibiotics compared with women with sedentary behavior. Estimates of vigorous physical activity were not statistically significant in

TABLE 1. Demographic and lifestyle characteristics of a cohort of Danes living in the North Region of Denmark based on two health questionnaires completed in either 2007 or 2010.

Physical activity	Men						Women					
	Sedentary	Low	Moderate	Vigorous	Total	P	Sedentary	Low	Moderate	Vigorous	Total	P
n (%)	1304 (14.2)	4699 (51.2)	2643 (28.8)	533 (5.8)	9179 (100)	<0.001	1323 (13.6)	6375 (65.8)	1686 (17.4)	311 (3.2)	9695 (100)	<0.001
Age, mean (SD)	45.4 (15.9)	50.4 (14.9)	45.4 (15.6)	29.4 (13.4)	47.0 (16.0)	<0.001	46.8 (17.0)	48.1 (15.6)	43.0 (16.3)	28.4 (14.3)	46.4 (16.3)	<0.001
Filled antibiotics prescriptions, n (%)												
No	994 (76.2)	3631 (77.3)	2087 (79.0)	409 (76.7)	7121 (77.6)		815 (61.6)	4263 (66.9)	1109 (65.8)	198 (63.7)	6385 (65.9)	
Yes	310 (23.8)	1068 (22.7)	556 (21.0)	124 (23.3)	2058 (22.4)	0.191	508 (38.4)	2112 (33.1)	577 (34.2)	113 (36.3)	3310 (34.1)	0.003
Body mass index, n (%)												
<18.5 kg·m ⁻²	16 (1.2)	30 (0.6)	9 (0.3)	11 (2.1)	66 (0.7)		49 (3.7)	171 (2.7)	52 (3.1)	20 (6.4)	292 (3.0)	
≥18.5–<25 kg·m ⁻²	423 (32.4)	1753 (37.3)	1220 (46.2)	355 (66.6)	3751 (40.9)		610 (46.1)	3568 (56.0)	1122 (66.5)	224 (72.0)	5524 (57.0)	
≥25–<30 kg·m ⁻²	558 (42.8)	2266 (48.2)	1157 (43.8)	148 (27.8)	4129 (45.0)		376 (28.4)	1880 (29.5)	391 (23.2)	62 (19.9)	2709 (27.9)	
≥30 kg·m ⁻²	307 (23.5)	650 (13.8)	257 (9.7)	19 (3.6)	1233 (13.4)	<0.001	288 (21.8)	756 (11.9)	121 (7.2)	5 (1.6)	1170 (12.1)	<0.001
Smoking status, n (%)												
Never smokers	523 (40.1)	2102 (44.7)	1382 (52.3)	365 (68.5)	4372 (47.6)		620 (46.9)	3352 (52.6)	1011 (60.0)	221 (71.1)	5204 (53.7)	
Current smokers	489 (37.5)	1256 (26.7)	607 (23.0)	102 (19.1)	2454 (26.7)		408 (30.8)	1494 (23.4)	305 (18.1)	47 (15.1)	2254 (23.2)	
Former smokers	292 (22.4)	1341 (28.5)	654 (24.7)	66 (12.4)	2353 (25.6)	<0.001	295 (22.3)	1529 (24.0)	370 (21.9)	43 (13.8)	2237 (23.1)	<0.001
Education, n (%)												
Basic school	483 (37.0)	1348 (28.7)	702 (26.6)	268 (50.3)	2801 (30.5)		469 (35.4)	2009 (31.5)	495 (29.4)	187 (60.1)	3160 (32.6)	
High school	63 (4.8)	136 (2.9)	124 (4.7)	59 (11.1)	382 (4.2)		93 (7.0)	354 (5.6)	155 (9.2)	32 (10.3)	634 (6.5)	
Vocational	515 (39.5)	2246 (47.8)	1215 (46.0)	133 (25.0)	4109 (44.8)		441 (33.3)	2277 (35.7)	495 (29.4)	49 (15.8)	3262 (33.6)	
Short/medium/long length	243 (18.6)	969 (20.6)	602 (22.8)	73 (13.7)	1887 (20.6)	<0.001	320 (24.2)	1735 (27.2)	541 (32.1)	43 (13.8)	2639 (27.2)	<0.001
Alcohol intake per week, n (%)												
None	170 (13.0)	399 (8.5)	153 (5.8)	59 (11.1)	781 (8.5)		382 (28.9)	1280 (20.1)	239 (14.2)	51 (16.4)	1952 (20.1)	
<7 women, <14 men	839 (64.3)	3371 (71.7)	1909 (72.2)	312 (58.5)	6431 (70.1)		693 (52.4)	3637 (57.1)	1007 (59.7)	152 (48.9)	5489 (56.6)	
>7–<14 women, >14–<21 men	126 (9.7)	490 (10.4)	316 (12.0)	71 (13.3)	1003 (10.9)		157 (11.9)	1038 (16.3)	320 (19.0)	70 (22.5)	1585 (16.3)	
>14 women, >21 men	169 (13.0)	439 (9.3)	265 (10.0)	91 (17.1)	964 (10.5)	<0.001	91 (6.9)	420 (6.6)	120 (7.1)	38 (12.2)	669 (6.9)	<0.001

Descriptive baseline data are stratified by sex and level of physical activity during leisure time, and P values are provided for the differences between physical activity levels.

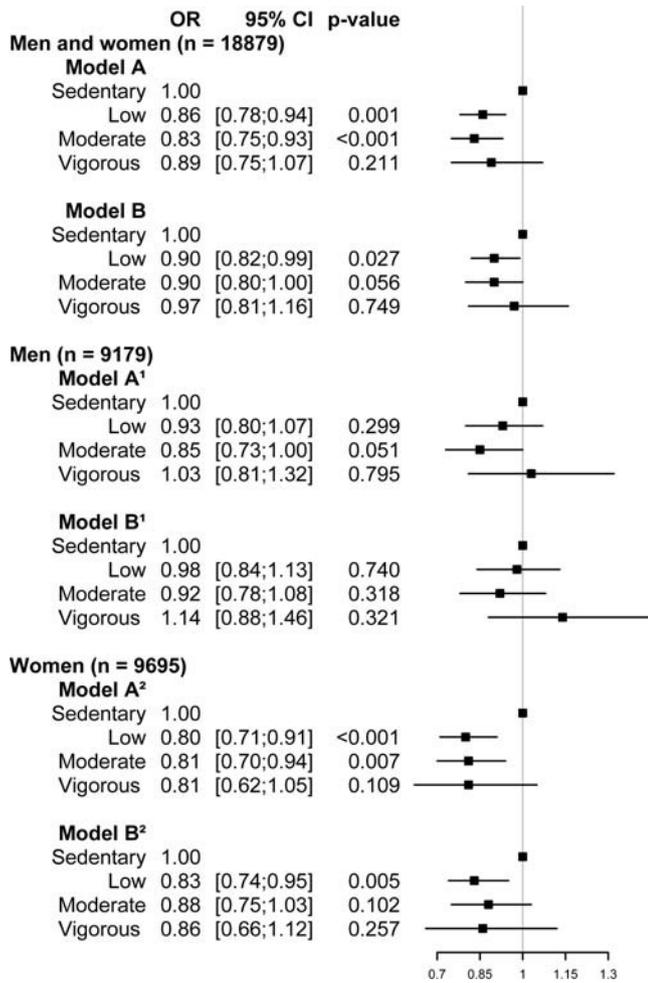


FIGURE 2—Logistic regressions analysis showing OR, 95% CI, *P* values, and forest plots for the relationships between different levels of leisure-time physical activity and the risk of filling an antibiotic prescription in the following year. The population studied was Danes living in the North Region of Denmark who completed a health questionnaire in either 2007 or 2010. Model A: OR adjusted for age and sex. Model A^{1,2}: OR adjusted for age. Model B: OR adjusted for age, sex, body mass index, smoking status, alcohol consumption, and educational level. Model B^{1,2}: OR adjusted for age, body mass index, smoking status, alcohol consumption, and educational level.

the multiadjusted model (model B²), and the relationships were attenuated for moderate leisure-time physical activity (OR = 0.88, 95% CI = 0.75–1.03); however, a similar pattern was found for the OR estimates.

The results for the analyses of the subgroup with suspected cystitis were insignificant for both men and women participating in vigorous physical activity and for men who participated in low physical activity. However, all levels of physical activity were associated with a lower risk of filling an antibiotic prescription compared with sedentary behavior (Table 2). All estimates of the subgroup analysis of suspected respiratory tract infections were statistically insignificant (Table 2). However, all estimates showed that physical activity either lowered the risk of filling an antibiotic prescription or had no influence compared with sedentary behavior.

Sensitivity analysis. The sensitivity analyses that included three or more filled antibiotic prescriptions (outcomes = 1615) produced results similar to those of the main analyses for one or more filled antibiotic prescriptions (outcomes = 5368), but with wider CI values. The sensitivity analyses, with use of multivariate imputation by chained equations of those who were excluded because of missing data (*n* = 4752), produced statistically significant results for low physical activity and the risk of filling an antibiotic prescription for suspected bacterial infection (OR = 0.91, 95% CI = 0.84–0.99). The results for suspected cystitis were significant for participating in low (OR 0.79, 95% CI = 0.65–0.95) and moderate (OR = 0.68, 95% CI = 0.54–0.87) physical activity and insignificant result for suspected respiratory tract infections. The results were similar as those of the main analyses, however with smaller CI values.

Of the respondents who participated in both surveys, 63.6% reported unchanged levels of physical activity during the 3-yr follow-up period. Among those who reported a different physical activity level, only 3.27% changed by more than one level.

DISCUSSION

This study suggests that low physical activity is associated with a lower risk of suspected bacterial infections during a 1-yr follow-up period. The results were primarily driven by a reduction in suspected cystitis infections in women. There was no statistically significant sex interaction; however, there were very few suspected cystitis infections among the men. For comparison with previous studies (4,15,17,21) that most often presented separate analyses of sex, we performed analyses of men and women together and stratified.

Among the men, none of the results were statistically significant; however, our results suggest a J-shaped tendency. This is a tendency in which vigorous physical activity was associated with a higher risk of suspected bacterial infections, whereas low and moderate levels of physical activity were associated with a lower risk of suspected bacterial infections compared with sedentary behavior. A prospective study (4) of age and lifestyle factors that focused on community-acquired pneumonia found that the risk of pneumonia among nonathletic men was U-shaped; however, the findings were insignificant. The J-shaped tendency among men in our study is similar to the findings from earlier studies of primarily viral infections among athletes (1,4,5,12,15–17,20,21). Our findings regarding vigorous physical activity could indicate that our population-based sampling included some participants who were involved in a physical activity level equivalent to that of athletes, which could explain why our results show patterns similar to those found among athletes.

Multiadjusted results were only statistically significant for low physical activity among women. Estimates for the different physical activity levels remained to decrease the risk of suspected bacterial infections; however, the smaller number of respondents in these groups could potentially

TABLE 2. Subgroup logistic regressions analyses showing OR, 95% CI, and *P* values for different levels of physical activity during leisure time and the risk of filling an antibiotics prescription for specific bacterial infections (cystitis or respiratory tract infections).

	Physical activity	Both (n = 18,874)				Men (n = 9179)				Women (n = 9695)			
		OR	95% CI	CI	P	OR	95% CI	CI	P	OR	95% CI	CI	P
Cystitis													
Model 1 ^a		1				1				1			
	Sedentary	0.81	0.67	0.98	0.029	0.73	0.40	1.30	0.285	0.81	0.67	0.99	0.041
	Low	0.72	0.57	0.91	0.006	0.41	0.19	0.88	0.022	0.76	0.60	0.98	0.031
	Moderate	0.82	0.55	1.23	0.341	0.88	0.19	4.12	0.873	0.84	0.55	1.28	0.412
Model 2 ^a		1				1				1			
	Sedentary	0.79	0.65	0.95	0.014	0.72	0.39	1.34	0.306	0.78	0.64	0.95	0.015
	Low	0.68	0.54	0.87	0.002	0.41	0.18	0.92	0.030	0.71	0.55	0.92	0.008
	Moderate	0.67	0.45	1.02	0.062	0.88	0.18	4.22	0.873	0.66	0.43	1.02	0.062
	Vigorous												
Respiratory tract infection													
Model 1 ^b		0.91				0.87				0.93			
	Nonsedentary	0.97	0.81	1.02	0.095	0.93	0.73	1.03	0.095	1.01	0.80	1.09	0.376
Model 2 ^b		0.97				0.93				1.01			
	Nonsedentary	0.97	0.87	1.09	0.641	0.93	0.78	1.10	0.369	1.01	0.86	1.17	0.934

The population studied comprised Danes living in the North Region of Denmark who completed a health questionnaire in either 2007 or 2010.

Model 1^{a,b}: OR adjusted for age and, in the group "both," for age and sex.

Model 2^{a,b}: OR adjusted for age, body mass index, smoking status, alcohol consumption, and educational level and, in the group "both," also for sex.

explain the lower precision. A prospective study (4) of age and lifestyle factors focusing on community-acquired pneumonia found that the risk of pneumonia decreased with increased physical activity, but only among younger women, and after adjusting for body mass index, the relation was attenuated. A later expansion of the study (17) with 1265 female cases of pneumonia extending and expanding the first study (4) of 305 female cases found that women who exercised more frequently were less likely to develop pneumonia; however, after adjusting for body mass index, smoking, and alcohol use, these results were insignificant. Our results remained significant for women participating in low leisure-time physical activity after adjustment for all covariables unlike previous studies (4,17). This could possibly be explained by the broader focus on bacterial infections in general, which contributed to more robust estimates.

A strong relationship was found between low and moderate levels of physical activity and lower risk of filling an antibiotic prescription for cystitis in both men and women. All estimates were statistically insignificant because of the risk of filled antibiotic prescriptions used to treat respiratory tract infections; however, the tendency for all physical activity levels was either lowering the risk or had no influence.

The findings of this study add knowledge to the area of exercise and immunology. We found a significant protective effect of low physical activity compared with sedentary behavior during leisure time on the risk of suspected bacterial infections in general, without significant interactions between the sexes. Furthermore, we showed that both low and moderate levels of physical activity were related to a statistically significant lower risk of suspected cystitis compared with sedentary respondents. These results indicate that practitioners should be aware of physical activity as a potential preventive factor for bacterial infections in the work of disease prevention and health promotion.

Study limitations and strengths. A limitation of the study is the possibility of a general physician confusing a bacterial infection with a viral infection, leading to the mistaken prescription of an antibiotic. Similarly, not all who are infected with a bacterial infection will be treated with antibiotics.

However, these misclassifications would be nondifferential and not related to the different levels of physical activity. Another limitation of the present study is the use of a relatively simple single-item question to assess self-reported physical activity (26). Although the instrument's predictive validity for several health outcomes has been found acceptable (2,25), a more detailed measurement of physical activity in terms of frequency and intensity is desirable when studying the relationships between physical activity and bacterial infections; nonetheless, we showed that the measure was relatively stable during a 3-yr period (and was not subject to differential changes). Furthermore, filling antibiotic prescriptions was the only measurement of suspected bacterial infections included in this study, which not necessarily reflect the total occurrence of bacterial infections in a population because of the limitations. We considered including clinical hospital diagnoses of bacterial infections and abnormal C-reactive protein and white blood cell levels indicative of infections. However, less than 2% of the study population was identified with a suspected bacterial infection based on diagnoses (*n* = 92) or blood samples (*n* = 199) during the 1-yr follow-up, and no meaningful analyses were conducted because of low precision, which may have been related to the small number of outcomes.

A major strength of the present study is its access to nationwide registries, which allowed us to obtain information about all types of antibiotics and thus analyze a wide range of bacterial infections rather than just a few bacterial diseases or bacteria strains. Furthermore, the registries allowed us to exclude participants who were sedentary because of a history of cancer, diabetes, cardiovascular diseases, or chronic diseases of the lower respiratory tract. The large sample and the inclusion of both men and women with complete follow-up in the registries and a large number of outcomes also add strength to the study.

CONCLUSION

Low leisure-time physical activity is related to a statistically significant lower risk of filling any antibiotic prescriptions during a 1-yr follow-up period compared with

sedentary behavior. A lower risk of filling an antibiotic prescription for suspected cystitis was related to both low and moderate levels of leisure-time physical activity compared with sedentary behavior. No statistically significant reduction in suspected respiratory tract infections was associated with physical activity compared with sedentary behavior.

The authors thank the employees of the Public Health and Epidemiology. The authors thank the employees of the Public Health and Epidemiology Group at the Department of Health Science and Technology at Aalborg University for their support and help. The

North Denmark Region Health Survey 2007 and 2010 was founded by the North Denmark Region.

K. P., C. T. P., C. O., H. B., L. R., and T. A. R. conceived the concept for the study and are accountable for its design. K. P. conducted the data management process and statistical analyses with help and guidance from C. T. P., B. J. N., and H. B. K. P. drafted the manuscript. K. P., L. R., T. A. R., B. J. N., C. T. P., C. O., and H. B. contributed to the interpretation of the data. All of the authors revised the text for important intellectual content, approved the final manuscript, and are accountable for all aspects of the work.

The authors declare that there are no conflicts of interest. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

REFERENCES

- Ahmadinejad Z, Alijani N, Mansori S, Ziaee V. Common sports-related infections: a review on clinical pictures, management and time to return to sports. *Asian J Sports Med.* 2014;5(1):1–9.
- Aires N, Selmer R, Thelle D. The validity of self-reported leisure time physical activity, and its relationship to serum cholesterol, blood pressure and body mass index. A population based study of 332,182 men and women aged 40–42 years. *Eur J Epidemiol.* 2003;18(6):479–85.
- Atkinson IW, Wolfe S, Hamborsky J. Pneumococcal disease. In: Centers for Disease Control and Prevention, editor. *Epidemiology and Prevention of Vaccine-Preventable Diseases.* Washington, DC: Public Health Foundation; 2012. pp. 233–48.
- Baik I, Curhan GC, Rimm EB, Bendich A, Willett WC, Fawzi WW. A prospective study of age and lifestyle factors in relation to community-acquired pneumonia in us men and women. *Arch Intern Med.* 2000;160(20):3082–8.
- Bermon S. Airway inflammation and upper respiratory tract infection in athletes: is there a link? *Exerc Immunol Rev.* 2007;13:6–14.
- Blasi F, Mantero M, Santus P, Tarsia P. Understanding the burden of pneumococcal disease in adults. *Clin Microbiol Infect.* 2012; 18(5 Suppl):7–14.
- Danish Health Authority and Medicines Agency. *Alcohol—Stop before 5 Units—It Can Make a Difference. Our 7 Recommendations about Alcohol* [Internet]. 2014; [cited 2015 Jun 29]. Available from: <http://sundhedsstyrelsen.dk/en/health/alcohol>.
- European Commission. Denmark: Overview. [Internet]. 2015; [cited 2015 Aug 17]. Available from: <https://webgate.ec.europa.eu/fpfis/mwikis/eurydice/index.php/Denmark:Redirect>.
- Harris MD. Infectious disease in athletes. *Curr Sports Med Rep.* 2011;10(2):84–9.
- Jensen VM, Rasmussen AW. Danish education registers. *Scand J Public Health.* 2011;39(7 Suppl):91–4.
- Kildemoes HW, Sørensen HT, Hallas J. The Danish National Prescription Registry. *Scand J Public Health.* 2011;39(7 Suppl): 38–41.
- Klentrou P, Cieslak T, MacNeil M, Vintinner A, Plyley M. Effect of moderate exercise on salivary immunoglobulin A and infection risk in humans. *Eur J Appl Physiol.* 2002;87(2):153–8.
- Lynge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public Health.* 2011;39(7 Suppl):30–3.
- Mathers C, Fat DM, Boerma T. *The Global Burden of Disease: 2004 Update.* Geneva (Switzerland): World Health Organization; 2008. p. 146.
- Matthews CE, Ockene IS, Freedson PS, Rosal MC, Merriam PA, Hebert JR. Moderate to vigorous physical activity and risk of upper-respiratory tract infection. *Med Sci Sports Exerc.* 2002; 34(8):1242–8.
- Moreira A, Delgado L, Moreira P, Haahtela T. Does exercise increase the risk of upper respiratory tract infections? *Br Med Bull.* 2009;90(1):111–31.
- Neuman MI, Willett WC, Curhan GC. Physical activity and the risk of community-acquired pneumonia in US women. *Am J Med.* 2010;123(3):281.e7–11.
- Nieman DC. Current perspective on exercise immunology. *Curr Sports Med Rep.* 2003;2(5):239–42.
- Nieman DC. Special feature for the Olympics: effects of exercise on the immune system: exercise effects on systemic immunity. *Immunol Cell Biol.* 2000;78(5):496–501.
- Nieman DC, Johanssen LM, Lee JW, Arabatzis K. Infectious episodes in runners before and after the Los Angeles Marathon. *J Sports Med Phys Fitness.* 1990;30(3):316–28.
- Nieman DC, Nehlsen-Cannarella SL, Markoff PA, et al. The effects of moderate exercise training on natural killer cells and acute upper respiratory tract infections. *Int J Sports Med.* 1990;11(6):467–73.
- Pedersen BK, Hoffman-Goetz L. Exercise and the immune system: regulation, integration, and adaptation. *Physiol Rev.* 2000;80(3): 1055–81.
- Pedersen CB. The Danish Civil Registration System. *Scand J Public Health.* 2011;39(7 Suppl):22–5.
- Randall B. Increasing US mortality from infectious diseases. *JAMA* 1996;275(18):1399–400.
- Saltin B. Physiological effects of physical conditioning. In: Hansen A, Schnohr P, Rose G, editors. *Ischaemic Heart Disease: The Strategy of Postponement.* Chicago: Year Book Medical Publishers; 1977. pp. 104–15.
- Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes comparison with still active athletes of the same ages. *Circulation.* 1968;38(6):1104–15.
- The Danish Data Protection Agency. Datatilsynet: Compiled version of the Act on Processing of Personal Data [Internet]. 2007; [cited 2015 Dec 8]. Available from: <http://www.datatilsynet.dk/english/the-act-on-processing-of-personal-data/read-the-act-on-processing-of-personal-data/compiled-version-of-the-act-on-processing-of-personal-data/>.
- The North Denmark Region, Pedersen J Friis K, et al. *Sundhedsprofil 2010: Trivsel, sundhed og sygdom i Nordjylland. [Health Profile 2010: Well-being, Health and Disease in Northern Jutland].* Aalborg: 2010. Available from: http://www.rm.dk/Sundhed/Til-sundhedsfaglige-og-samarbejdspartnere/Sundhedsfremme-og-forebyggelse/Sundhedsprofil/Sundhedsprofil-2010/Resultater/~media/Rn_dk/Sundhed/Til%20sundhedsfaglige%20og%20samarbejdspartnere/Sundhedsfremme%20og%20forebyggelse/Sundhedsprofil/2010/Sundhedsprofil_2010.ashx.
- The North Denmark Region, The National Institute of Public Health, University of Southern Denmark, Rasmussen NK, et al. *Sådan står det til med sundheden i Nordjylland : Sundhedsprofil for Region Nordjylland og 11 nordjyske kommuner. [This is the state of health in Northern Jutland: Health Profil of the North Denmark Region and 11 municipalities in Northern Jutland].* Aalborg: The North Denmark Region; 2007. Available from: <http://www.rm.dk/Sundhed/Til-sundhedsfaglige-og-samarbejdspartnere/Sundhedsfremme->

og-forebyggelse/Sundhedsprofil/Sundhedsprofil-2007/Resultater/~/
media/Rn_dk/Sundhed/Til%20sundhedsfaglige%20og%20
samarbejdspartnere/Sundhedsfremme%20og%20forebyggelse/
Sundhedsprofil/2007/Sundhedsprofil2007.ashx.

30. Thygesen LC, Daasnes C, Thaulow I, Brønnum-Hansen H. Introduction to Danish (nationwide) registers on health and social issues: structure, access, legislation, and archiving. *Scand J Public Health*. 2011;39(7 Suppl):12–6.
31. Torres A, Peetermans WE, Viegi G, Blasi F. Risk factors for community-acquired pneumonia in adults in Europe: a literature review. *Thorax*. 2013;68(11):1057–65.
32. United Nations Educational Scientific and Cultural Organization (UNESCO), UNESCO Institute for Statistics. *International Standard Classification of Education: ISCED 2011*. Montreal: UNESCO Institute for Statistics; 2012. Available from: <http://www.uis.unesco.org/Education/Documents/iscsed-2011-en.pdf>.
33. Varon E, Mainardi JL, Gutmann L. *Streptococcus pneumoniae*: still a major pathogen. *Clin Microbiol Infect*. 2010;16(5):401.
34. WHO Collaborating Centre for Drug Statistics Methodology. *Guidelines for ATC Classification and DDD Assignment 2013*. Oslo: WHO Collaborating Centre for Drug Statistics Methodology; 2012. p. 276.