



Upper respiratory tract infection is reduced in physically fit and active adults

David C Nieman,¹ Dru A Henson,² Melanie D Austin,¹ Wei Sha³

¹Human Performance Laboratory, Appalachian State University, North Carolina Research Campus, Kannapolis, North Carolina, USA

²Department of Biology, Appalachian State University, Boone, North Carolina, USA

³Bioinformatics Research Center, University of North Carolina at Charlotte, North Carolina Research Campus, Kannapolis, North Carolina, USA

Correspondence to

David C Nieman, Director, Human Performance Laboratory, North Carolina Research Campus, Plants for Human Health Institute, 600 Laureate Way, Kannapolis, NC 28081, USA; niemandc@appstate.edu

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ABSTRACT

Objective Limited data imply an inverse relationship between physical activity or fitness level and the rates of upper respiratory tract infection (URTI). The purpose of this study was to monitor URTI symptoms and severity in a heterogeneous group of community adults and contrast across tertiles of physical activity and fitness levels while adjusting for potential confounders.

Design A group of 1002 adults (ages 18–85 years, 60% female, 40% male) were followed for 12 weeks during the winter and fall seasons while monitoring URTI symptoms and severity using the Wisconsin Upper Respiratory Symptom Survey. Subjects reported frequency of aerobic activity, and rated their physical fitness level using a 10-point Likert scale. A general linear model, with adjustment for seven confounders, was used to examine the effect of exercise frequency and fitness level on the number of days with URTI and severity of symptoms.

Results The number of days with URTI during the 12-week period was significantly reduced, 43% in subjects reporting ≥ 5 days/week aerobic exercise compared to those who were largely sedentary (≤ 1 day/week) and 46% when comparing subjects in the high versus low fitness tertile. URTI severity and symptomatology were also reduced 32% to 41% between high and low aerobic activity and physical fitness tertiles.

Conclusions Perceived physical fitness and frequency of aerobic exercise are important correlates of reduced days with URTI and severity of symptoms during the winter and fall common cold seasons.

INTRODUCTION

Upper respiratory tract infection (URTI) is caused by more than 200 different viruses, especially rhinoviruses and coronaviruses.^{1–3} The National Institute of Allergy and Infectious Diseases reports that people in the USA suffer 1 billion colds each year with an incidence of 2–4 for the average adult and 6–10 for children.¹ URTI imposes an estimated \$40 billion burden in direct and indirect costs on the US economy.²

Lifestyle habits and demographic factors such as mental stress,⁴ lack of sleep,⁵ poor nutrient and energy status,⁶ and old age⁷ have all been associated with impaired immune function and/or elevated risk of infection. Low to high exercise workloads have a unique effect on immunosurveillance and URTI risk. Regular moderate exercise training stimulates a recirculation of cells from the innate immune system and decreases URTI risk, while sustained and intense exertion induces immune dysregulation, inflammation, oxidative stress and increases URTI risk.^{8–18}

Several lines of evidence provide support for the linkage between moderate exercise training and improved immunosurveillance leading to decreased URTI rates including data from surveys of physically active individuals,^{8, 9} animal-based studies,¹⁰ epidemiologic investigations,^{11–15} randomised training studies with previously sedentary subjects^{16–19} and acute exercise bouts with pre- and post-exercise immune measures.^{20, 21}

A few epidemiologic reports have retrospectively or prospectively compared URTI incidence in groups of moderately active and sedentary individuals.^{11–15} Collectively, the epidemiologic studies support reduced URTI rates in physically active or fit individuals, but the primary criticism has been that URTI incidence and symptomatology were not measured with validated methods in any of the studies. A 1-year epidemiological study of 547 adults showed a 23% reduction in URTI risk in those engaging in regular versus irregular moderate-to-vigorous physical activity.¹¹ URTI episodes were recorded during four 3-month retrospective reports provided by the subjects during clinic visits, but URTI symptomatology was not measured. A cohort of 1509 Swedish men and women aged 20–60 were followed for 15 weeks during the winter/spring, with subjects in the upper tertile for physical activity experiencing an 18% reduction in URTI risk.¹⁵ Subjects were contacted every 3 weeks via email and requested to report whether or not they experienced URTI episodes and the occurrence of seven symptoms.

The purpose of this study was to study the relationship between both physical activity and physical fitness level with URTI during a 12-week period in a heterogeneous group of 1002 men and women using the Wisconsin Upper Respiratory Symptom Survey (WURSS).²² The WURSS is a reliable, valid and responsive daily logging system that was designed and developed to comprehensively measure all significant health-related dimensions that are negatively affected by the common cold. Important potential confounders were recorded at baseline and adjusted for in statistical modelling to determine the relationship between low-to-high tertiles of physical activity and fitness with URTI incidence and severity of symptoms.

METHODS

Subjects

Male and female subjects (N=1023), 18–85 years of age, were recruited via mass advertising from the community, with 1002 subjects completing

all requirements for the 12-week study. During recruitment, subjects were stratified by gender (approximately 40% male, 60% female), age (approximately 40% young adult or 18–39 years of age, 40% middle-aged or 40–59 and 20% older or 60 and over) and body mass index (BMI) groups (approximately one-third each for normal or 18.5–24.9, overweight or 25–29.9 and obese or ≥ 30 kg/m²) to ensure representation of these various subgroups. Half of the subjects were studied during a 12-week period from January to April 2008 and the second half from August to November 2008. Subjects had to be non-institutionalised, and women were excluded if pregnant or lactating. No other exclusion criteria were employed. Several papers have been published from this study, with a focus on quercetin supplementation and inflammation, oxidative stress, plasma quercetin response, immune function and URTI.^{23–26} Quercetin supplementation at two doses (500 and 1000 mg/day) compared to placebo had no influence on immune function or URTI,^{24, 26} and the data from this study were subsequently reanalysed to investigate the influence of perceived physical fitness and exercise frequency on URTI after adjustment for important confounders. Written informed consent was obtained from each subject and the Appalachian State University institutional review board approved all experimental procedures.

Research design

Two weeks prior to the start of the study, subjects provided demographic and lifestyle habit information using a comprehensive survey developed and posted by the investigative team on SurveyMonkey.com (Portland, Oregon, USA). Subjects without internet access were mailed a printed version of the questionnaire, with instructions to complete all questions prior to their first lab session. Subjects reported to the lab at the start and end of the 12-week study, with height measured with a stadiometer, and body mass measured using a Tanita scale (Tanita, Arlington Heights, Illinois, USA). Pre- and post-study height and body mass data were averaged, with BMI calculated as kg/m².

Information on dietary patterns was obtained through a semi-quantitative food frequency questionnaire for food groups including fruit, vegetables, cereals, meat, dairy and fat. Subjects checked a box representing typical daily consumption. Specifically, questions asked ‘On average, how many servings of...do you eat per day?’ Serving size information was provided for each food group in accordance to the MyPyramid Food Guide,²⁷ and then subjects checked a box representing how many servings they consumed on an average day. Of the various food groups, only fruit intake was found to have a significant relationship to the URTI measures. For fruit intake the questionnaire answers were reduced to tertiles of one or fewer servings per day, twice daily and three or more servings per day.

Perceived physical fitness levels were reported in response to the question, ‘In general, compared to other persons your age, rate how physically fit you are’. Subjects responded using a 10-point Likert scale, with 1 denoting ‘not at all physically fit’, 5 ‘somewhat physically fit’ and 10 ‘extremely physically fit’, similar to Gerber *et al.*²⁸ Responses to this question used in prior studies correlate well with measures of objective physical fitness, perceived well-being and sleep habits.²⁹ Subjects were grouped into perceived physical fitness tertiles, with 1–5 corresponding to low fitness, 6–7 to medium fitness and 8–10 to high fitness.

Leisure-time exercise frequency habits were assessed through answers to this categorical question taken from the National Health Interview Survey³⁰: ‘Outside of your normal work or daily responsibilities, how often do you engage in exercise that at least moderately increases your breathing and heart rate, and makes you sweat, for at least 20 min (such as brisk walking, cycling, swimming, jogging, aerobic dance, stair climbing, rowing, basketball, racquetball, vigorous yard work)’. Response categories included are seldom or never, less than 1, 1–2, 3–4 or 5 or more times per week. Subjects were grouped into leisure-time aerobic exercise frequency tertiles of ≤ 1 , 1–4, or ≥ 5 times per week.

Recent exposure to stressful events was assessed through answers to the following question taken from the National Center for Health Statistic’s General Well-Being Schedule questionnaire³¹: ‘During the past month, would you say that you experienced (‘a lot’, ‘moderate’, ‘relatively little’ or ‘almost no’) stress?’ Subjects were grouped into stress tertiles based on their answers, with subjects answering ‘relatively little’ or ‘almost no’ stress being grouped together in the low stress tertile.

Upper respiratory tract infection

The WURSS was used to assess URTI incidence and symptomatology.²² The WURSS is an empirically derived, patient-oriented, illness specific, quality-of-life evaluative outcomes instrument.³² The construct validity of the WURSS has been supported by measures of reliability, responsiveness, importance to patients and convergence.²² The WURSS-21 (short version used in this study) includes 10 items assessing symptoms, 9 items assessing functional impairments and 1 item assessing global severity and global change. Subjects filled in the one-page WURSS-21 at the end of each day in the study. From the responses recorded during the 84-day study, an URTI severity score was calculated by summing the daily URTI global severity score (0=not sick, 1=very mild URTI to 7=severe), with total days with URTI counted when subjects scored 1 or higher on a particular day. An URTI symptom score for the 84-day period was calculated by summing all 10 symptom scores for each day’s entry (0=do not have this symptom, 1=very mild to 7=severe).

Statistical methods

Subject characteristics (reported as mean \pm SD) were contrasted between physical fitness tertiles using one-way analysis of variance for age, BMI and education, and for all other variables (categorical) using χ^2 analysis (table 1). The general linear model (GLM) was used to examine the effect of self-reported fitness or exercise frequency on each of the three URTI measures (total days, severity score, symptom score). The GLMSELECT procedure in SAS (Statistical Analysis Systems, version 9.1.3; SAS Institute, Cary, North Carolina, USA) was used to identify confounding variables. The candidate confounders, that the GLMSELECT procedure selected from, were age, sex, education (total years), marital status, mental stress level, BMI and fruit intake. For each URTI measure (total days, severity score, symptoms score), the model with the smallest Akaike’s information corrected criterion was selected, and then a trend test was performed to study the effect of fitness or exercise frequency on the URTI measure after adjusting for confounders. The Benjamini–Hochberg method for false discovery rate (FDR) correction in the MULTTEST procedure in SAS was used to correct for multiple tests. Pairwise comparison

Table 1 Subject characteristics across physical fitness tertiles (N=1002) (mean±SD)

	Physical fitness tertiles			p Value
	Low (N=341)	Medium (N=311)	High (N=350)	
Age (years)	45.0±14.3	45.3±16.0	47.4±18.4	0.111
Body mass index (BMI) (kg/m ²)	29.7±6.5	26.3±4.8*	24.5±3.8*	<0.001
Education (total years)	14.9±3.7	15.9±2.6*	16.0±2.7*	<0.001
Smoking habit (% in tertile)	14.1%	9.6%	5.7%	0.001
Sex (% in tertile)				
Males	27.3%	43.1%	48.0%	<0.001
Females	72.7%	56.9%	52.0%	
Marital status (% in tertile)				
Married	59.2%	58.2%	53.7%	0.058
Single	24.9%	31.8%	31.7%	
Other	15.8%	10.0%	14.6%	
Stress level (% in tertile)				
Low	26.4%	38.9%	45.1%	<0.001
Medium	51.6%	49.8%	45.4%	
High	22.0%	11.3%	9.4%	
Exercise frequency (% in tertile)				
<1 day/week	44.9%	15.1%	4.3%	<0.001
1–4 days/week	49.3%	70.4%	53.1%	
≥5 days/week	5.9%	14.5%	42.6%	
Exercise habits, duration (% in tertile)				
<1 year or no Exercise	66.3%	24.4%	9.4%	<0.001
1–5 years	14.4%	18.0%	11.1%	
≥5 years	19.4%	57.5%	79.4%	
Fruit intake (% in tertile)				
≤1 serving/day	34.9%	26.7%	20.6%	<0.001
2 serving/day	34.9%	41.5%	34.3%	
≥3 serving/day	30.2%	31.8%	45.1%	

p-Values for age, BMI and education are from a one-way analysis of variance analysis (with '*' denoting $p < 0.05$ vs the low tertile), and for all other variables from a χ^2 analysis.

Table 2 Total days, severity score and symptom score for URTI over 12 weeks across physical fitness and exercise frequency tertiles

	Physical fitness tertile			p For trend; FDR p value
	Low (N=341)	Medium (N=311)	High (N=350)	
URTIs, total days	8.18 (6.81 to 9.67)	4.95* (3.89 to 6.13)	4.41* (3.44 to 5.49)	<0.001; <0.001
URTIs severity score	16.1 (13.2 to 19.4)	11.2* (8.6 to 14.0)	11.0* (8.7 to 13.7)	0.006; 0.006
URTIs symptom score	88.2 (71.0 to 107)	59.4* (44.9 to 76.0)	58.2* (44.7 to 73.4)	0.005; 0.006
	Exercise frequency tertile			p For trend; FDR p value
	Low <1 day/week (N=214)	Medium 1–4 days/week (N=573)	High ≥5 days/week (N=215)	
URTIs, total days	8.60 (6.91 to 10.5)	5.46* (4.52 to 6.50)	4.89* (3.62 to 6.35)	<0.001; 0.002
URTIs severity score	18.2 (14.5 to 22.3)	11.5* (9.47 to 13.8)	10.7* (7.91 to 13.9)	0.001; 0.003
URTIs symptom score	93.9 (72.8 to 118)	63.7* (51.6 to 77.1)	55.0* (39.4 to 73.2)	0.003; 0.006

Data are presented as least square means (95% CIs) after adjustment for age, education level marital status, sex, stress level, body mass index and fruit intake.

* $p < 0.05$ compared to the low fitness or exercise frequency tertile.

FDR, false discovery rate; URTI, upper respiratory tract infection.

was performed among the three fitness or exercise frequency levels. The normality of the residuals from each model was examined. When the normality assumption was violated, outliers with studentised residue > 3.0 or < -3.0 were excluded, and when needed, square root transformation on the response variable was performed. In table 2, p for trend values represents adjusted fitness and exercise frequency data for the outcome measures, and in the legend for figure 1A,B, p values are listed separately for factors selected by the model.

RESULTS

The mean number of days with URTI (unadjusted) during the 12-week study periods differed significantly between the

winter and fall cohorts (13.0±15.4 and 8.17±11.9 days, respectively, $p < 0.001$). The relationship between perceived physical fitness level and URTI measures was nearly identical, however, between cohorts (both $p = 0.004$) and data were combined to improve statistical power when adjusting for the influence of potential confounding factors.

Table 1 summarises subject characteristics across low, medium and high fitness tertiles, with an emphasis on factors that were tested for inclusion in the statistical model. Mean ages and marital status were comparable across fitness tertiles. BMI and the proportion with smoking habit and high stress decreased across low-to-high fitness tertiles, while years of education, the proportion of males, high

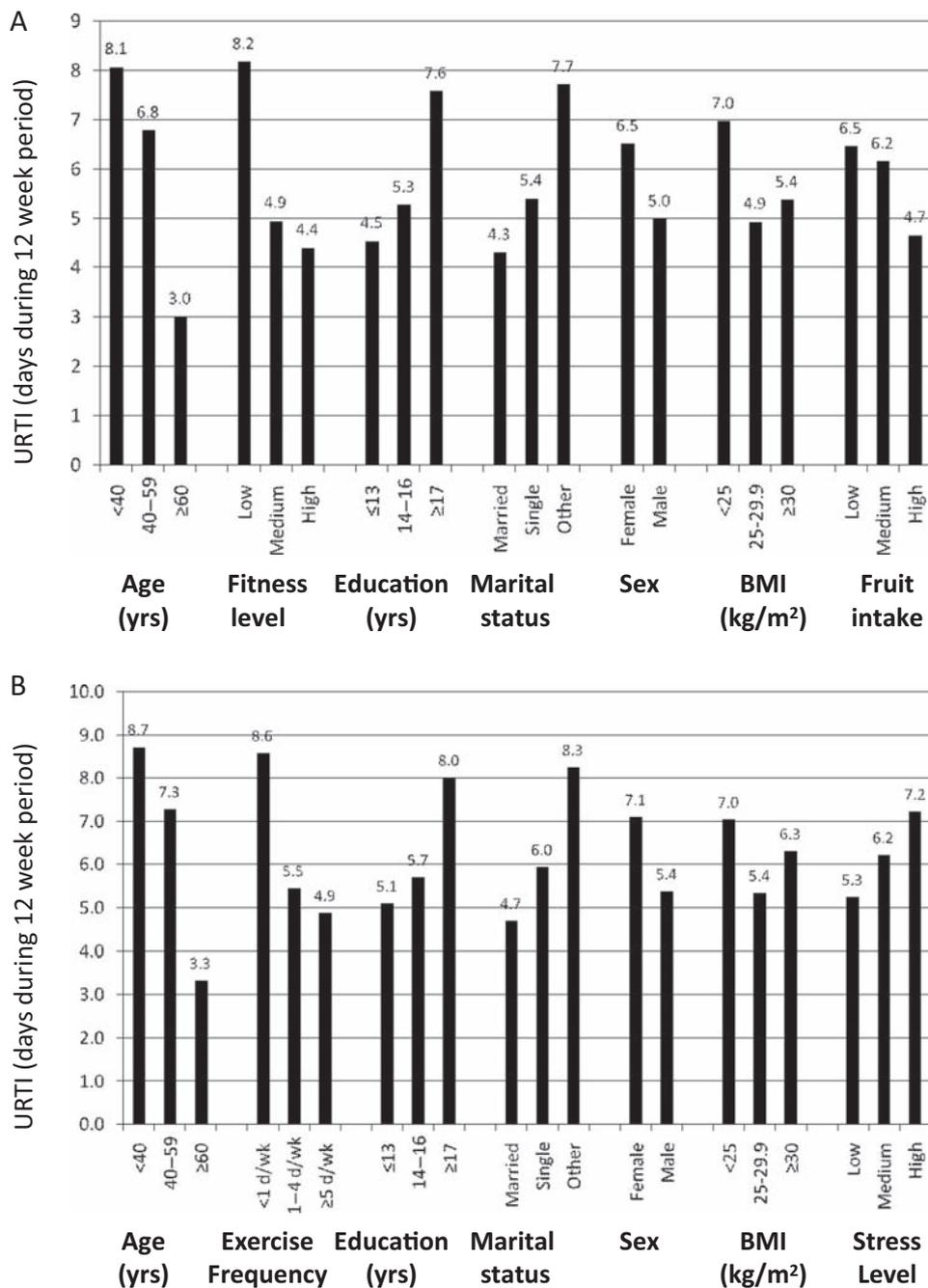


Figure 1 The effect of fitness (A) or exercise frequency (B) and factors selected into the model on total days with upper respiratory tract infection (URTI) (means squares) during the 12-week study period measure. For (A), false discovery rate (FDR) adjusted p values are <0.001 for age, fitness level and education, and $p < 0.05$ for all other factors. For (B), p for trend (FDR values) is <0.001 for age, $p < 0.002$ for exercise frequency, education and marital status, $p = 0.02$ for sex, and $p = 0.12$ for body mass index (BMI) and $p = 0.13$ for stress level.

exercise frequency (≥ 5 days/week) and high fruit intake (≥ 3 servings/day) increased. About 8 in 10 subjects in the high fitness tertile had been following their exercise routine for at least 5 years.

Table 2 compares the adjusted least square means for total days with URTI, severity scores and symptom scores across physical fitness and exercise frequency tertiles. Of the factors listed in table 1, only smoking habit was found to have no significant influence on the URTI measures (and exercise habit duration was listed only as a subject characteristic and not tested for inclusion). Total days with URTI during the 12-week study were 46% lower in the high versus low physical fitness

tertile, and 43% lower in those reporting 5 or more days of aerobic activity per week versus less than 1 day per week.

Figure 1 compares least square means for total days with URTI across all factors selected into the fitness (A) and exercise frequency (B) models. FDR adjusted p values are listed in the legend. In the fitness model (figure 1A), the highest adjusted means for total days with URTI during the 12-week study were measured for younger adults and those with low perceived fitness. Older age, high or medium fitness level, lower education, being married or male, and eating 3 or more servings of fruit per day were each associated with an adjusted mean of 5 or fewer days with URTI during the study. A low

versus higher BMI was linked to increased days with URTI. These patterns were reflected in the exercise frequency model (figure 1B), with the exception that mental stress level was selected in the place of fruit intake.

DISCUSSION

URTI is caused by multiple and diverse pathogens, impeding prevention strategies and making it unlikely that a unifying vaccine will be developed.^{3 33 34} Various demographic characteristics predict lower URTI rates including older age, male gender and being married, as confirmed in this study and others.³ Few lifestyle strategies for URTI prevention other than proper hygiene have received consistent scientific support. Limited data support a moderate reduction in URTI risk with higher fruit intake and low levels of mental stress,^{4 35} as confirmed in this study. Our data indicate that near-daily aerobic activity and the perception of being physically fit have a strong influence on URTI frequency and symptomatology, consistent with other epidemiologic and randomised exercise training trials.^{11–19}

We combined data from two cohorts of approximately 500 subjects each that were studied during the winter and fall seasons. After controlling for important confounders, total days with URTI during the 12-week study were 43–46% lower in the high versus low tertiles for aerobic activity and perceived physical fitness level, respectively, and URTI severity and symptomatology were reduced 32–41%. Limitations in this study include lack of adjustment for all potential confounders including exposure to URTI pathogens at work and from children in the home.

Although methodology varies widely, other epidemiologic and randomised exercise training studies consistently report a reduction in URTI incidence or risk of 18–67%.^{11–19} Within certain subgroups such as the elderly or those with high mental stress, the reduction in URTI with aerobic exercise training may have more significance. Fondell *et al*,¹⁵ eg, reported an 18% reduction in URTI risk between high and low physical activity quartiles, but this risk reduction improved to 42% among those with high perceived mental stress. A randomised study of elderly women (mean age, 73 years) showed that walking 30–40 min, 5 days/week, for 12 weeks at 60% heart rate reserve, reduced URTI rates to 20% as compared with 50% among sedentary controls.¹⁸ A 1-year randomised study of 115 overweight, postmenopausal women showed that regular moderate exercise (166 min/week, ~4 days/week) lowered URTI risk compared to controls modestly during the first half year, but then more strongly during the final months.¹⁹

The underlying mechanisms for the reduction in URTI risk with aerobic exercise training are still being explored and debated. Each aerobic exercise bout causes a transient increase in the recirculation of immunoglobulins, and neutrophils and natural killer cells, two cells involved in innate immune defenses.^{16 17} Animal data indicate that lung macrophages play an important role in mediating the beneficial effects of moderate exercise on lowered susceptibility to infection.³⁶ Stress hormones, which can suppress immunity, and pro- and anti-inflammatory cytokines, indicative of intense metabolic activity, are not elevated during moderate aerobic exercise.^{16 17} Although the immune system returns to pre-exercise levels within a few hours after the exercise session is over, each session may improve immunosurveillance against pathogens that reduce overall URTI incidence and symptomatology.

What is already known

- ▶ A few epidemiologic reports support reduced upper respiratory tract infection (URTI) rates in physically active or fit individuals.
- ▶ The primary criticism has been that the incidence of URTI and related symptoms were not measured with validated methods.

What this study adds

- ▶ After controlling for important confounders, total days with upper respiratory tract infection (URTI) using validated methods during the 12-week study were 43–46% lower in the high versus low tertiles for aerobic activity and perceived physical fitness level, respectively.
- ▶ URTI severity and symptomatology were reduced 32–41%.

CONCLUSIONS

These data indicate that high perceived physical fitness and near-daily aerobic activity are important correlates of reduced URTI frequency (43% and 46%, respectively), severity (32%, 41%) and symptomatology (34%, 41%). These data are consistent with government guidelines urging the general public to include exercise within their daily routines to improve health.³⁷ Among the various demographic and lifestyle factors evaluated in this study of 1002 men and women, perceived fitness and exercise frequency ranked second only to older age in the magnitude of reduction of days with URTI during the winter and fall seasons.

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Competing interests None.

Ethics approval This study was conducted with the approval of the Appalachian State University.

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