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Leisure-time physical activity and mortality from influenza and pneumonia: a cohort study of 577 909 US adults

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ABSTRACT

Objective To examine the association of leisure-time physical activity with mortality from influenza and pneumonia.

Methods A nationally representative sample of US adults (aged ≥18 years) who participated in the National Health Interview Survey from 1998 to 2018 were followed for mortality through 2019. Participants were classified as meeting both physical activity guidelines if they reported ≥150 min/week of moderate-intensity equivalent aerobic physical activity and ≥2 episodes/week of muscle-strengthening activity. Participants were also classified into five volume-based categories of self-reported aerobic and muscle-strengthening activity. Influenza and pneumonia mortality was defined as having an underlying cause of death with an International Classification of Diseases, 10th Revision code of J09–J18 recorded in the National Death Index. Mortality risk was assessed using Cox proportional hazards, adjusting for sociodemographic and lifestyle factors, health conditions and influenza and pneumococcal vaccination status. Data were analysed in 2022.

Results Among 577 909 participants followed for a median of 9.23 years, 1516 influenza and pneumonia deaths were recorded. Compared with participants meeting neither guideline, those meeting both guidelines had 48% lower adjusted risk of influenza and pneumonia mortality. Relative to no aerobic activity, 10–149, 150–300, 301–600 and >600 min/week were associated with lower risk (by 21%, 41%, 50% and 41%). Relative to <2 episodes/week of muscle-strengthening activity, 2 episodes/week was associated with 47% lower risk and ≥7 episodes/week with 41% higher risk.

Conclusions Aerobic physical activity, even at quantities below the recommended level, may be associated with lower influenza and pneumonia mortality while muscle-strengthening activity demonstrated a J-shaped relationship.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The WHO and US Department of Health and Human Services recommend that adults perform ≥150 min/week of moderate-intensity equivalent aerobic physical activity and ≥2 episodes/week of muscle-strengthening activities.

⇒ Physical inactivity is a risk factor for severe COVID-19 illness and potentially for influenza and pneumonia mortality.

WHAT THIS STUDY ADDS

⇒ Among US adults, leisure-time aerobic physical activity was associated with significantly lower risk of influenza and pneumonia mortality, even at an amount below the recommended level.

⇒ Two episodes/week of muscle-strengthening activity was associated with lower risk of influenza and pneumonia mortality, whereas ≥7 episodes/week was associated with higher risk.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Efforts to reduce influenza and pneumonia mortality among adults might focus on decreasing the prevalence of aerobic inactivity and increasing the prevalence of achieving 2 episodes/week of muscle-strengthening activity.

INTRODUCTION

Guidelines from the WHO and US Department of Health and Human Services recommend that adults perform moderate-intensity aerobic physical activity for at least 150 min/week, or vigorous-intensity aerobic physical activity for at least 75 min/week, or an equivalent combination, plus muscle-strengthening activity (MSA) of moderate or greater intensity at least twice per week, to achieve substantial health benefits. According to the guidelines, these benefits include prevention of dementia, cardiovascular disease and some cancers; improved physical function and mental health; and greater longevity.[1 2]

Regular physical activity may also protect against infection and mortality from infectious diseases.[3] In their study of leisure-time physical activity and cause-specific mortality among National Health Interview Survey (NHIS) participants from 1997 through 2014, Zhao and colleagues reported that US adults who met the aerobic and muscle-strengthening guidelines had a 54% lower adjusted hazard of influenza and pneumonia mortality, relative to those who met neither guideline.[4] Influenza and pneumonia—which often present concomitantly and are typically grouped by the US National Vital Statistics System[5]—rank in the top 10 causes of death in the USA, before[6] and after[7 8] the emergence of COVID-19.

The objective of this study was to expand on the influenza and pneumonia findings presented by Zhao and colleagues. With a larger population, additional follow-up time, the inclusion of vaccination status and more granular categories of aerobic

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activity and MSA, we aimed to elucidate the association between the types and amounts of physical activity with influenza and pneumonia mortality risk.

METHODS

Study design and data source

This was a longitudinal study of US adults aged ≥18 years who participated in NHIS from 1998 through 2018. NHIS is an ongoing, cross-sectional household interview survey that captures health information on a representative sample of the civilian, non-institutionalised population of the USA. Using stratified sensitivity analyses and adjustments, we explored the influence of these characteristics, as well as health-related behaviours and baseline health status, on the association between physical activity and influenza and pneumonia mortality. Sample design, interview methodology and data availability details are provided elsewhere.[9]

Physical activity measurements

To ascertain aerobic leisure-time physical activity, participants were asked how frequently they participated for ≥10 min in vigorous-intensity activities that caused heavy sweating or large increases in breathing or heart rate and light-intensity or moderate-intensity activities that caused only light sweating or slight to moderate increases in breathing or heart rate. During the study period, NHIS did not distinguish between light-intensity and moderate-intensity aerobic activities. Respondents provided the frequency and duration of each session. MSA was assessed by one question that asked how often the respondent participated in leisure-time physical activities specifically designed to strengthen their muscles, such as lifting weights or performing calisthenics.

Using the customary methodology,[1 2] we calculated moderate-to-vigorous physical activity (MVPA) min/week as the sum of light-intensity or moderate-intensity aerobic activity min/week plus twice vigorous-intensity aerobic activity min/week. We also calculated MSA episodes/week. We classified participants into four groups based on their adherence to the guidelines: meeting neither guideline (<150 min/week of MVPA and <2 episodes/week of MSA); meeting only the aerobic guideline (≥150 min/week of MVPA and <2 episodes/week of MSA); meeting only the muscle-strengthening guideline (<150 min/week of MVPA and ≥2 episodes/week of MSA) and meeting both guidelines (≥150 min/week of MVPA and ≥2 episodes/week of MSA).

We also classified participants in more detailed physical activity levels. To maximally equalise the distribution of participants while resembling physical activity guideline categories, we defined five levels of aerobic physical activity (<10, 10–149, 150–300, 301–600 and >600 min/week of MVPA) and muscle-strengthening physical activity (<2, 2, 3, 4–6 and ≥7 episodes/week of MSA).

Covariates

We used the following variables from NHIS: sex; age; race/ethnicity; education; marital status; smoking; alcohol consumption; body mass index (BMI); presence of diagnosed heart disease, stroke, hypertension, diabetes, cancer, chronic obstructive pulmonary disease (COPD) and asthma; and influenza and pneumococcal vaccination status.

We classified age as 18–34, 35–49, 50–64, 65–74 and ≥75 years, and race/ethnicity as non-Hispanic white, non-Hispanic black, Hispanic and non-Hispanic other. We classified education as less than high school, high school graduate or equivalent, some college or associate's degree and college graduate or higher. We classified marital status as married; divorced, separated or widowed; never married and other. We classified smoking as never (<100 lifetime cigarettes), former (≥100 lifetime cigarettes but not currently smoking) and current. We classified alcohol consumption as never (<12 lifetime drinks), former (≥12 lifetime drinks but none in previous year), current but not heavy (previous year average <8 drinks/week for women and <15 drinks/week for men) and current heavy (≥8 for women and ≥15 for men). We classified BMI as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), obesity (≥30.0 kg/m^2) and unknown. We dichotomised underlying health conditions as present or absent. Heart disease included coronary heart disease, myocardial infarction, angina and other heart diseases; diabetes included frank diabetes, borderline diabetes and pre-diabetes; COPD included emphysema and chronic bronchitis (COPD was added to NHIS in 2012) and asthma included those with current and previous asthma. We excluded participants with missing data.

NHIS asked participants if they had received an influenza vaccine in the previous 12 months and had ever received a pneumococcal vaccination. We classified participants as yes, no and unknown. We did not distinguish between intramuscular and intranasal influenza vaccination, the latter of which was ascertained from 2004 through 2015.

Mortality

We obtained mortality outcomes from the 2019 NHIS-National Death Index public-use linked mortality files. We merged survey responses with mortality outcomes using the unique public identification number assigned by National Center for Health Statistics (NCHS). Detailed methodology regarding NHIS linkage to the National Death Index is available elsewhere.[10] For those assumed dead, we attributed mortality to influenza or pneumonia if the underlying cause of death had an *International Classification of Diseases, Injuries, and Causes of Death, 10th Revision* code between J09 and J18. For those assumed alive, we assigned a censoring date of 31 December 2019.[11]

Population and follow-up time

A total of 611 505 adult NHIS participants were eligible for linkage to the National Death Index.[11] After excluding those with missing physical activity data (n=19 175) or covariate data (n=14 421), the final analytic sample was 577 909. For all decedents, we calculated follow-up time as the duration between quarter and year of interview and quarter and year of death. For those assumed alive, we calculated follow-up time as the duration between quarter and year of interview and censoring, per NCHS recommendations.[11]

Equity, diversity and inclusion statement

Our study sample is designed to be nationally representative, reflecting the demographic, geographic and socioeconomic diversity of the US population. Although small, our author team includes a diversity of disciplines (preventive medicine, infectious diseases and epidemiology) and sex (two men and one woman).

Statistical analysis

We assessed participant characteristics across strata of physical activity guideline adherence, and we compared the four groups with the Wald χ^2 test. To determine the association of guideline adherence with influenza and pneumonia mortality—and the association by aerobic and muscle-strengthening levels—we used weighted Cox proportional hazards regression to calculate HRs with 95% CIs.

Using a directed acyclic graph (online supplemental figure S1), we selected potentially confounding variables and developed two adjusted models. The first model included sex, age, race/ethnicity, education and marital status. The second model added BMI category, smoking status, alcohol consumption, presence or absence of underlying conditions (ie, heart disease, stroke, hypertension, diabetes, cancer, COPD and asthma) and receipt of influenza or pneumococcal vaccine. Age was assessed continuously in both models. To explore the independent effect of aerobic and muscle-strengthening physical activity, we adjusted each activity type for the other.

We performed several sensitivity analyses. First, given the strong correlation between age and mortality, we stratified by select age categories (50–64, 65–74 and ≥75 years). Second, to address potential reverse causality and confounding by indication, we excluded participants who (1) had an underlying condition at baseline, (2) ever smoked, (3) had an abnormal BMI and (4) died within 2 years of their NHIS interview. Third, to explore the impact of physical activity intensity, we assessed the association of vigorous-intensity aerobic activity with mortality, not doubling the minutes and additionally adjusting for light-intensity and moderate-intensity aerobic physical activity min/week. Finally, we re-analysed MSA using 0 episodes/week as the referent group.

For all analyses, we established significance at a two-sided α of 0.05, and we verified the proportional hazards assumption using Kaplan-Meier curves and Schoenfeld residuals. To account for the complex survey design and sample weights, we used survey procedures in SAS V.9.4 (SAS Institute). The public was not involved in the design, conduct, reporting or dissemination plans of our research.

RESULTS

Population characteristics

Of the 577 909 participants, most were women (52.2%) and non-Hispanic white (69.2%). Roughly half (50.5%) did not meet either the aerobic or muscle-strengthening guidelines. Guideline adherence was significantly different by sex, age category, race/ethnicity, education, marital status, smoking status, alcohol consumption, BMI category, presence of each underlying health condition and receipt of influenza or pneumococcal vaccine (p<0.001 for all) (table 1).

Physical activity levels and influenza and pneumonia mortality

During a median (SE) of 9.23 (0.01) years of follow-up, 81 431 deaths were recorded, including 1516 deaths attributed to influenza and pneumonia. Compared with participants who met neither physical activity guideline, those who met both guidelines had 48% lower adjusted risk of influenza and pneumonia mortality (HR=0.52; 95% CI: 0.39 to 0.68), and those who met only the aerobic guideline had 36% lower adjusted risk (HR=0.64; 95% CI: 0.54 to 0.76). Meeting only the muscle-strengthening guideline was not associated with a significant difference in mortality (HR=1.16; 95% CI: 0.88 to 1.54) (table 2).

Adjusting for muscle-strengthening category (in addition to sociodemographic and lifestyle factors, underlying conditions and vaccination status), persons who reported MVPA in any category (10–149, 150–300, 301–600 and >600 min/week) had lower risk of influenza and pneumonia mortality compared with those who did not report any MVPA, ranging from 21% lower risk for those reporting 10–149 min/week to 50% for those reporting 301–600 min/week (figure 1). Adjusting instead for the aerobic category, persons who reported 2 MSA episodes/week had 47% lower risk of influenza and pneumonia mortality compared with those who reported <2 episodes/week. The risk was 41% higher among those who reported ≥7 episodes/week (figure 2).

Sensitivity analyses

Findings largely held across subpopulations, although some categories lost statistical significance when restricted to select age categories (online supplemental table S1), those without an underlying condition (online supplemental table S2), those who never smoked (online supplemental table S3) and participants with normal BMI (online supplemental table S4). Outcomes remained consistent after excluding the 11 138 participants who died within 2 years of the interview (online supplemental table S5). Compared with participants who reported no vigorous-intensity aerobic physical activity, those who reported 75–150 min/week had 56% lower adjusted mortality risk (online supplemental table S6). Compared with participants who reported no MSA, those with 1 episode/week had a similar adjusted mortality risk (HR=1.09; 95% CI: 0.58 to 2.05) (online supplemental table S7).

DISCUSSION

In this large US cohort, adults who met the aerobic and muscle-strengthening physical activity guidelines were about half as likely to die from influenza and pneumonia as their peers who met neither guideline. Relative to those who were aerobically inactive, mortality was lower in participants who performed leisure-time aerobic physical activity—even at a level below the recommended minimum of 150 MVPA min/week. Independent of achieving the aerobic guideline, adults who performed 2 MSA episodes/week had lower mortality than those who performed <2 episodes, while mortality was higher among those who performed ≥7 episodes.

Our findings largely correspond to and extend those of prior investigations by analysing more detailed categories of aerobic and muscle-strengthening physical activity and by including important confounding variables, such as vaccination status. In an early study, Paffenbarger and colleagues dichotomised 3686 San Francisco longshoremen in 1951 as 'low energy workers' (4750–8250 kcal/week of occupational physical activity) or 'high energy workers' (8500–10 750 kcal/week). In the following 22 years, the latter group experienced 74% lower adjusted risk of pneumonia mortality (p=0.087).[12] Among 24 656 adults who died of natural causes in Hong Kong during the 1998 influenza epidemic (predominantly influenza A subtype H3N2), respiratory and cardiovascular mortality was lower among those who had reported moderate levels of exercise during a baseline health assessment in 1988, compared with those who had reported no exercise.[13] A longitudinal study of 83 165 US women found a 25% lower age-adjusted incidence of community-acquired pneumonia among those in the highest quintile of walking, compared with those in the lowest quintile,[14] and walking appeared protective against pneumonia mortality in a longitudinal study of 110 792 Japanese adults.[15] Zhao and colleagues reported a 54% lower adjusted hazard of influenza and pneumonia mortality among US adults who met both aerobic and muscle-strengthening guidelines, compared with neither.[4]

Table 1 Baseline characteristics of participants, by physical activity guideline level

	Met neither guideline,* n (weighted %)	Met aerobic only,† n (weighted %)	Met strength only,‡ n (weighted %)	Met both guidelines,§ n (weighted %)	P value
Total	303 227 (50.5)	153 156 (27.2)	20 742 (3.6)	100 784 (18.7)	
Sex					
Male	119 427 (43.4)	70 367 (49.4)	9737 (50.7)	54 454 (57.0)	<0.001
Female	183 800 (56.6)	82 789 (50.6)	11 005 (49.3)	46 330 (43.0)	
Age, years					
18–34	70 709 (26.0)	45 894 (32.1)	5201 (28.9)	40 150 (42.3)	<0.001
35–49	78 319 (27.4)	43 260 (29.2)	5114 (25.9)	29 455 (29.2)	
50–64	74 985 (25.2)	36 448 (23.9)	4919 (24.0)	19 864 (19.5)	
65–74	38 817 (10.9)	17 369 (9.5)	2826 (11.4)	7697 (6.3)	
≥75	40 397 (10.5)	10 185 (5.2)	2682 (9.8)	3618 (2.7)	
Race/ethnicity					
NH white	181 279 (65.9)	104 520 (72.8)	13 498 (69.0)	70 600 (73.2)	<0.001
NH black	48 836 (13.3)	17 273 (9.4)	3154 (13.3)	11 991 (10.7)	
Hispanic	57 357 (15.4)	22 227 (12.1)	2959 (12.0)	12 599 (10.9)	
NH other¶	15 755 (5.5)	9136 (5.7)	1131 (5.7)	5594 (5.2)	
Education					
<High school	71 773 (20.7)	18 765 (11.1)	2873 (12.2)	6090 (6.2)	<0.001
High school	94 818 (32.2)	38 275 (25.4)	5401 (26.6)	17 419 (17.7)	
Some college	82 125 (27.7)	47 868 (31.2)	6801 (32.9)	33 953 (33.5)	
College graduate	54 511 (19.4)	48 248 (32.3)	5667 (28.4)	43 322 (42.7)	
Marital status					
Married	137 388 (55.4)	75 446 (58.3)	8860 (52.7)	44 259 (52.1)	<0.001
DSW	92 318 (20.4)	34 198 (14.1)	6281 (19.7)	19 046 (11.8)	
Never married	57 415 (17.7)	34 487 (20.6)	4586 (21.3)	31 432 (29.0)	
Other**	16 106 (6.5)	9025 (7.0)	1015 (6.3)	6047 (7.1)	
Smoking status					
Never	170 051 (56.3)	88 039 (58.3)	11 705 (58.0)	64 268 (65.2)	<0.001
Former	66 571 (21.7)	35 614 (23.0)	5357 (24.8)	22 424 (21.4)	
Current	66 605 (21.9)	29 503 (18.7)	3680 (17.3)	14 092 (13.3)	
Alcohol consumption					
Never	86 435 (27.3)	27 383 (17.7)	3744 (18.3)	12 034 (12.8)	<0.001
Former	56 804 (17.7)	20 339 (12.4)	3483 (14.9)	9371 (8.6)	
Current, non-heavy	146 567 (50.5)	96 643 (64.3)	12 518 (62.1)	72 899 (72.5)	
Current, heavy	13 421 (4.4)	8791 (5.6)	997 (4.7)	6480 (6.1)	
BMI, kg/m^2					
<18.5	6523 (2.2)	2331 (1.5)	397 (2.0)	1314 (1.3)	<0.001
18.5–24.9	96 524 (31.8)	56 080 (36.7)	7725 (37.9)	43 442 (42.8)	
25.0–29.9	98 485 (32.5)	53 821 (35.1)	7168 (34.3)	36 310 (36.1)	
≥30.0	91 382 (30.1)	37 472 (24.3)	5074 (24.1)	18 348 (18.4)	
Unknown	10 313 (3.4)	3452 (2.3)	378 (1.7)	1370 (1.3)	
Underlying condition					
Heart disease	46 199 (14.0)	15 770 (9.7)	3153 (13.6)	7896 (7.3)	<0.001
Stroke	12 819 (3.7)	2775 (1.6)	865 (3.4)	1123 (1.0)	<0.001
Hypertension	108 765 (33.2)	41 164 (25.1)	6939 (29.9)	19 456 (17.9)	<0.001
Diabetes	35 262 (10.7)	10 928 (6.6)	2012 (8.6)	3915 (3.6)	<0.001
Cancer	24 901 (7.5)	9910 (6.0)	1826 (7.7)	5016 (4.6)	<0.001
COPD	22 220 (6.8)	6575 (3.9)	1255 (5.4)	2939 (2.7)	<0.001
Asthma	35 853 (11.8)	17 126 (11.2)	2674 (12.5)	12 155 (12.2)	<0.001
Vaccination					
Influenza††	107 012 (34.1)	54 001 (34.3)	8221 (37.4)	34 812 (33.8)	<0.001
Pneumococcal‡‡	68 919 (20.8)	28 695 (17.0)	5489 (23.5)	16 102 (14.6)	<0.001

Sample adults who participated in the National Health Interview Survey from 1998 to 2018 and were eligible for linkage to the National Death Index through 2019 (n=577 909).
*Reported <150 min/week of moderate-intensity equivalent physical activity and <2 episodes/week of muscle-strengthening activity.
†Reported ≥150 min/week of moderate-intensity equivalent physical activity and <2 episodes/week of muscle-strengthening activity.
‡Reported ≥2 episodes/week of muscle-strengthening activity and <150 min/week of moderate-intensity equivalent physical activity.
§Reported ≥150 min/week of moderate-intensity equivalent physical activity and ≥2 episodes/week of muscle-strengthening activity.
¶Includes persons who identify as non-Hispanic and any of American Indian or Alaska Native, Asian, Native Hawaiian or Pacific Islander or multiracial.
**Living with partner, refused and do not know.
††Reported receiving an influenza vaccination in the prior 12 months.
‡‡Reported ever receiving a pneumococcal vaccine.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; DSW, divorced, separated or widowed; NH, non-Hispanic.

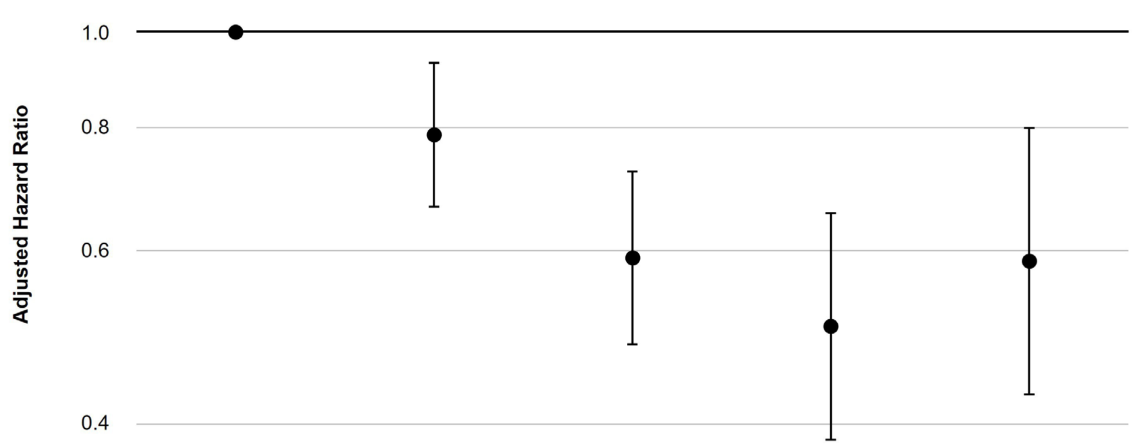
Table 2 HRs for influenza and pneumonia deaths, by meeting physical activity guidelines

Guideline met	Deaths	Person-years	Unadjusted HR (95% CI)	Adjusted HR* (95% CI)	Adjusted HR† (95% CI)
Neither‡	1128	3 133 418	1.00 (ref)	1.00 (ref)	1.00 (ref)
Aerobic only§	239	1 571 944	0.43 (0.36 to 0.50)	0.60 (0.50 to 0.71)	0.64 (0.54 to 0.76)
Strength only¶	71	208 731	1.00 (0.75 to 1.33)	1.12 (0.85 to 1.49)	1.16 (0.88 to 1.54)
Both**	78	1 016 632	0.20 (0.15 to 0.26)	0.46 (0.35 to 0.61)	0.52 (0.39 to 0.68)

Sample adults who participated in the National Health Interview Survey from 1998 to 2018 and were eligible for linkage to the National Death Index through 2019 (n=577 909).
*Adjusted for sex, age, race/ethnicity, education and marital status.
†Adjusted for sex; age; race/ethnicity; education; marital status; smoking status; alcohol consumption; body mass index; presence of heart disease, stroke, hypertension, diabetes, cancer, chronic obstructive pulmonary disease and asthma and influenza and pneumococcal vaccination status.
‡Reported <150 min/week of moderate-intensity equivalent physical activity and <2 episodes/week of muscle-strengthening activity.
§Reported ≥150 min/week of moderate-intensity equivalent physical activity and <2 episodes/week of muscle-strengthening activity.
¶Reported ≥2 episodes/week of muscle-strengthening activity and <150 min/week of moderate-intensity equivalent physical activity.
**Reported ≥150 min/week of moderate-intensity equivalent physical activity and ≥2 episodes/week of muscle-strengthening activity.

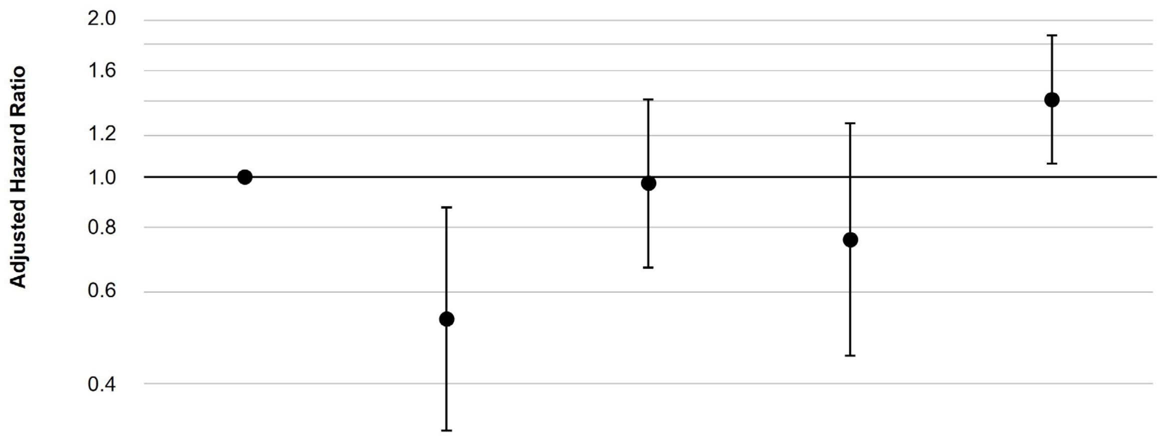
By analysing aerobic activity and MSA in more granular categories, our study provides important insights for the prevention of influenza and pneumonia mortality. First, the risk was significantly lower among participants who performed 10–150 min/week of leisure-time MVPA, compared with those who performed none. Although this level is often labelled 'insufficient' because it falls below the recommended duration, it may confer health benefits relative to physical inactivity. Previous studies have demonstrated that insufficient aerobic activity, compared with inactivity, is associated with lower overall mortality[16–18] and lower infectious disease mortality,[19 20] including from COVID-19.[21] Second, independent of aerobic activity, mortality risk was significantly lower among participants who performed 2 MSA episodes/week, compared with those who performed <2 episodes/week. At the opposite end, we found that ≥7 MSA episodes/week was associated with an increased risk. A J-shaped dose-response between MSA and all-cause mortality has been observed elsewhere.[22] While beyond the scope of this study, plausible explanations range from inaccurate responses (such as reporting occupational physical activity, which may not confer the same protective effect as leisure-time physical activity[23]) to haemodynamic ramifications of frequent, high-intensity MSA.[24–26]

The findings of this study are biologically plausible. Physical activity is associated with lower incidence of several comorbidities, including stroke and coronary heart disease,[2] which increase the mortality risk among adults hospitalised with community-acquired pneumonia.[27] Clinical trials have demonstrated that aerobic training programmes improve expectoration in persons with cystic fibrosis[28] and peak oxygen uptake in persons with COPD.[29] In addition to these salutary cardiovascular and pulmonary effects, physical activity has been associated in meta-analyses with a healthier immune profile: increased CD4 cell count (n=24 studies), which may speed the immunologic



Aerobic physical activity	<10 min/wk	10–149 min/wk	150–300 min/wk	301–600 min/wk	>600 min/wk
No. participants (weighted %)	210 358 (34.1)	113 611 (20.0)	86 095 (15.5)	87 243 (15.8)	80 602 (14.7)
Influenza and pneumonia deaths	926	273	139	92	86
Person-years	2 181 939	1 160 211	886 899	886 438	815 239
Adjusted hazard ratio (95% CI)	1.00 [reference]	0.79 (0.67 to 0.93)	0.59 (0.48 to 0.72)	0.50 (0.39 to 0.66)	0.59 (0.43 to 0.80)

Figure 1 Adjusted HRs (95% CI) for influenza and pneumonia mortality based on weekly min of moderate-intensity equivalent aerobic physical activity. Adjusted for sex; age; race/ethnicity; education; marital status; smoking status; alcohol consumption; body mass index; presence of heart disease, stroke, hypertension, diabetes, cancer, chronic obstructive pulmonary disease and asthma; influenza and pneumococcal vaccination status and muscle-strengthening activity category. Based on sample adults who participated in the National Health Interview Survey from 1998 to 2018 and were eligible for linkage to the National Death Index through 2019 (n=577 909).



Muscle-strengthening activity	<2 episodes/wk	2 episodes/wk	3 episodes/wk	4–6 episodes/wk	≥7 episodes/wk
No. participants (weighted %)	456 383 (77.7)	28 519 (5.2)	40 996 (7.6)	27 528 (5.2)	24 483 (4.3)
Influenza and pneumonia deaths	1367	18	40	20	71
Person-years	4 705 362	285 906	426 890	273 241	239 327
Adjusted hazard ratio (95% CI)	1.00 [reference]	0.53 (0.32 to 0.87)	0.97 (0.67 to 1.41)	0.76 (0.45 to 1.27)	1.41 (1.06 to 1.87)

Figure 2 Adjusted HRs (95% CI) for influenza and pneumonia mortality based on weekly episodes of muscle-strengthening activity. Adjusted for sex; age; race/ethnicity; education; marital status; smoking status; alcohol consumption; body mass index; presence of heart disease, stroke, hypertension, diabetes, cancer, chronic obstructive pulmonary disease and asthma; influenza and pneumococcal vaccination status and aerobic physical activity category. Based on sample adults who participated in the National Health Interview Survey from 1998 to 2018 and were eligible for linkage to the National Death Index through 2019 (n=577 909).

response to microbes and sustain the memory thereof[3]; increased salivary immunoglobulin A concentration (n=7 studies), which may strengthen mucosal defenses[3]; and decreased levels of C reactive protein (n=7 studies) and interleukin-6 (n=5 studies), which may reduce chronic inflammation and its negative immunomodulatory effects.[30] Acute bouts of moderate-intensity physical activity are also associated with transient improvements in innate and adaptive immune cells, including natural killer and highly cytotoxic T lymphocytes and immature B cells. These transient immunologic benefits may accumulate over time[31] and acquire a magnified importance at older ages, perhaps through the mediating impact of physical activity on telomere shortening and immunosenescent processes.[32]

Regular physical activity may also enhance the immune response to vaccination. In a recent meta-analysis, habitual aerobic physical activity level was positively correlated with antibody titers following influenza vaccination, but not pneumococcal vaccination.[33] Evidence for physical activity as an acute vaccine adjuvant is more tenuous, although this may reflect intervention heterogeneity in clinical trials. For example, older adults randomised to a 10-month aerobic activity programme prior to influenza vaccination sustained seroprotection for a longer duration than those randomised to a flexibility and balance programme.[34] In another trial, a brisk 45-minute walk before influenza and pneumococcal vaccine did not affect antibody response.[35] Analysed collectively, trial data suggest that single-session physical activity interventions have no impact on vaccine response, whereas those exceeding 2 weeks enhance post-vaccination influenza titers.[33]

Strengths and limitations

This study benefits from a large and nationally representative sample, granular leisure-time physical activity data and prolonged follow-up, but it has some limitations. First, exposure data were self-reported at a single time point. These data are susceptible to recall and social desirability biases.[36 37] Exposure status may have also changed during the follow-up period, although some health behaviours, including annual influenza vaccination,[38] are often consistent over time. Second, NHIS inquired about leisure-time physical activity in bouts of ≥10 min; it did not capture other domains or shorter episodes of physical activity, despite these counting toward the aerobic guideline, and it did not distinguish between light-intensity and moderate-intensity activity.[1 2] Third, dichotomous classification of underlying conditions in NHIS prevents analysis of disease severity, which may be associated with physical activity participation and mortality. Fourth, we obtained outcomes from the public-use linked mortality files, which are less complete than the restricted-use files to protect participant privacy.[11] However, the public-use and restricted-use files generate similar HRs for influenza and pneumonia mortality by several sociodemographic factors.[39] Finally, individuals may alter their physical activity based on underlying conditions. Although we cannot dismiss reverse causality and confounding by indication, we are reassured by the consistency of our findings across primary and sensitivity analyses.

Clinical and public health implications

This study has at least two clinical implications. First, the mortality benefit associated with 'insufficient' aerobic physical activity and with 2 MSA episodes/week might provide additional justification for healthcare providers to promote physical activity among their inactive patients. These potentially achievable targets are relevant to large segments of the population: 34.1% of the weighted sample were aerobically inactive, and 77.7% reported <2 MSA episodes/week. Second, given the increased mortality risk among those reporting ≥7 MSA episodes/week, clinical decision tools related to physical activity screening may want to flag very high levels of MSA, in addition to levels below guidelines.

Although the outcome was influenza and pneumonia mortality, the pathophysiologic principles may apply to COVID-19 and other infectious respiratory diseases. Consistent with this finding, the Centers for Disease Control and Prevention, based on a review of 25 studies, concluded that physical inactivity is an independent risk factor for severe COVID-19 illness.[40] In one of the largest studies, patients who were physically inactive before COVID-19 diagnosis had greater odds of hospitalisation (OR=2.26) and death (OR=2.49) than their peers who consistently met the aerobic guideline—ORs exceeding those of smoking, severe obesity and metastatic cancer history.[41]

Current physical activity guidelines emphasise prevention of non-communicable diseases.[1 2] When updated, these guidelines may wish to reflect the emerging body of evidence demonstrating an association between physical activity and lower mortality from infectious diseases.

CONCLUSION

Among 577K US adults followed for a median of 9.2 years, meeting both the aerobic and muscle-strengthening guidelines was associated with nearly half the risk of influenza and pneumonia mortality, compared with meeting neither guideline. Aerobic physical activity was associated with lower risk of influenza and pneumonia mortality, even at amounts below the guideline recommendation, whereas MSA displayed a J-shaped dose–response. Considering the plausible biological mechanisms and the consistency with previous studies, this protective association may warrant additional clinical and public health efforts to decrease the prevalence of aerobic inactivity and inadequate MSA.

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