

Mortality Risk Reductions for Replacing Sedentary Time With Physical Activities



Erika Rees-Punia, PhD,^{1,2} Ellen M. Evans, PhD,² Michael D. Schmidt, PhD,² Jennifer L. Gay, PhD,³ Charles E. Matthews, PhD,⁴ Susan M. Gapstur, PhD,¹ Alpa V. Patel, PhD¹

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Introduction: Excess sitting is a risk factor for early mortality. This may be resulting, at least in part, from the displacement of physical activity with sedentary behaviors. The purpose of this observational study was to examine the mortality risk reductions associated with replacing 30 minutes/day sitting for an equivalent duration of light or moderate to vigorous physical activity (MVPA).

Methods: Participants included 37,924 men and 54,617 women in the Cancer Prevention Study-II Nutrition Cohort, of which 14,415 men and 13,358 women died during follow-up (1999–2014). An isotemporal substitution approach to the Cox proportional hazards regression model was used to estimate adjusted hazard ratios and 95% CIs for mortality associated with the substitution of 30 minutes/-day self-reported sitting for light physical activity or MVPA. Analyses were conducted in 2018.

Results: Among the least active participants (≤ 17 minutes/day MVPA), the replacement of 30 minutes/day sitting with light physical activity (≤ 17 minutes/day MVPA) was associated with a 14% mortality risk reduction (hazard ratio=0.86, 95% CI=0.81, 0.89) and replacement with MVPA was associated with a 45% mortality risk reduction (hazard ratio=0.55, 95% CI=0.47, 0.62). Similar associations were seen among moderately active participants (light physical activity replacement, hazard ratio=0.94, 95% CI=0.91, 0.97; MVPA replacement, hazard ratio=0.83, 95% CI=0.76, 0.88). However, for the most active (MVPA >38 minutes/day), substitution of sitting time with light physical activity or MVPA was not associated with a reduction in mortality risk (hazard ratio=1.00, 95% CI=0.97, 1.03, and hazard ratio=0.99, 95% CI=0.95, 1.02, respectively).

Conclusions: These findings suggest that the replacement of modest amounts of sitting time with even light physical activity may have the potential to reduce the risk of premature death among less active adults.

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INTRODUCTION

Regular moderate to vigorous physical activity (MVPA) is associated with a lower risk of cardiovascular disease (CVD); certain cancers; and premature death.^{1–3} Distinct from physical inactivity, the amount of time spent sedentary is also associated with a higher risk of morbidity and mortality.^{4–9} This may be resulting, at least in part, from the displacement of physical activities (PAs) with sedentary behaviors.

There is a finite amount of time in a day, so it is necessary to consider how time spent on one behavior displaces time spent on another.¹⁰ Most previous studies explored associations with sedentary time without

considering the PA it displaces, leaving a gap in the understanding of healthful time use. Using isotemporal substitution models (ISM), it is possible to estimate the mortality risk reductions associated with replacing sedentary time with an equivalent amount of PA.^{11,12}

From the ¹American Cancer Society, Atlanta, Georgia; ²Department of Kinesiology, University of Georgia, Athens, Georgia; ³Department of Health Promotion and Behavior, University of Georgia, Athens, Georgia; and ⁴Metabolic Epidemiology Branch, National Cancer Institute, Bethesda, Maryland

Address correspondence to: Erika Rees-Punia, PhD, 250 Williams St. NW, Atlanta GA 30303. E-mail: erika.rees-punia@cancer.org
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Table 1. Baseline Characteristics of CPS-II, 1999 Survey (n=92,541)

Characteristics	Total sitting time level ^a			Physical activity level ^b		
	High (n=31,248)	Moderate (n=29,566)	Low (n=31,727)	Low (n=24,169)	Moderate (n=36,785)	High (n=31,587)
Total sit minutes/day	342 ± 113	159 ± 33	60 ± 24	163 ± 140	185 ± 131	206 ± 137
TV	132 ± 87	64 ± 37	22 ± 15	67 ± 75	72 ± 70	78 ± 71
Work	68 ± 97	16 ± 30	6 ± 11	29 ± 67	32 ± 68	30 ± 63
Transportation	47 ± 52	27 ± 20	13 ± 10	24 ± 34	28 ± 33	34 ± 39
Home	62 ± 56	36 ± 26	14 ± 11	30 ± 40	37 ± 40	44 ± 43
Other	43 ± 55	21 ± 22	9 ± 10	21 ± 38	24 ± 36	28 ± 39
LPA minutes/day	21 ± 26	21 ± 24	16 ± 21	14 ± 20	18 ± 21	25 ± 28
MVPA minutes/day	41 ± 35	40 ± 33	30 ± 29	7 ± 4	26 ± 8	73 ± 30
Average minutes/day reported	404 ± 124	219 ± 56	107 ± 49	185 ± 143	228 ± 134	304 ± 149
Sex, %						
Male	46.9	39.7	36.4	37.3	38.0	47.3
Female	53.1	60.3	63.6	62.7	62.0	52.7
Age, years	68.1 ± 6.2	68.8 ± 5.9	69.6 ± 6.0	69.3 ± 6.4	68.8 ± 6.1	68.5 ± 5.9
Race/ethnicity, %						
White	97.6	97.8	96.8	97.0	97.6	97.6
Other	2.4	2.2	3.2	3.0	2.4	2.4
BMI	26.7 ± 4.6	26.0 ± 4.2	26.0 ± 4.3	27.2 ± 4.9	26.2 ± 4.3	25.7 ± 3.9
Education, %						
Less than college graduate	54.2	57.3	65.9	66.9	59.7	52.7
College and beyond	45.2	42.0	33.4	32.4	39.7	46.7
Missing	0.6	0.7	0.7	0.7	0.6	0.6
Alcoholic drinks/day, %						
Non-drinker	33.7	36.2	39.3	42.5	37.5	30.5
<1	30.3	31.1	28.8	25.7	31.0	32.2
1	11.1	11.1	9.2	7.2	10.1	13.4
>1	9.2	8.0	7.1	6.3	7.5	10.1
Missing	15.7	13.6	15.6	18.3	13.9	13.8
Smoke status, %						
Never	46.8	50.2	51.0	50.5	50.2	47.4
Former	45.7	43.6	41.4	40.0	43.3	46.6
Current	7.5	6.2	7.6	9.5	6.5	6.0
Diet score ^c	4.3 ± 1.9	4.5 ± 1.9	4.4 ± 1.9	3.9 ± 1.9	4.3 ± 1.9	4.7 ± 1.9
Comorbidity score ^d	0.7 ± 0.8	0.7 ± 0.8	0.7 ± 0.8	0.7 ± 0.8	0.7 ± 0.8	0.7 ± 0.7

Note: Values are presented as mean ± SD, unless otherwise noted.

^aSitting time categories split into approximate tertiles: high sitting >219 minutes/day, medium sitting ≤219 minutes/day to >103 minutes/day, low sitting ≤103 minutes/day.

^bPhysical activity level categories split into approximate tertiles: low active ≤17 MVPA minutes/day, moderate active >17 to ≤38 MVPA minutes/day, high active >38 MVPA minutes/day.

^cACS dietary guidelines adherence score.¹⁶

^dComorbidity score reflects the number of comorbidities, including high blood pressure, diabetes, and high cholesterol (0, 1, ≥2 comorbidities). ACS, American Cancer Society; CPS-II, Cancer Prevention Study-II; LPA, light physical activity; MVPA, moderate to vigorous physical activity.

The primary aim of this study is to estimate the mortality risks associated with replacing 30 minutes/day of sitting time with 30 minutes/day of either light PA (LPA) or MVPA in a large prospective cohort of U.S. adults over 14 years of follow-up. Secondary aims included estimating these mortality risks: (1) among low, moderate, and high active participants separately; (2) for cancer, CVD, and other causes of death; and (3) stratified by sex, age, and BMI.

METHODS

Study Population

The Cancer Prevention Study-II Nutrition Cohort (CPS-II NC) is a prospective study initiated by the American Cancer Society in 1992 and is described elsewhere.¹³ CPS-II NC was approved by the Emory University IRB.

Among the 151,343 men and women who completed the 1999 CPS-II NC survey, participants were excluded for history of cancer (n=27,515), CVD (n=15,258), or lung disease (n=3,179); missing

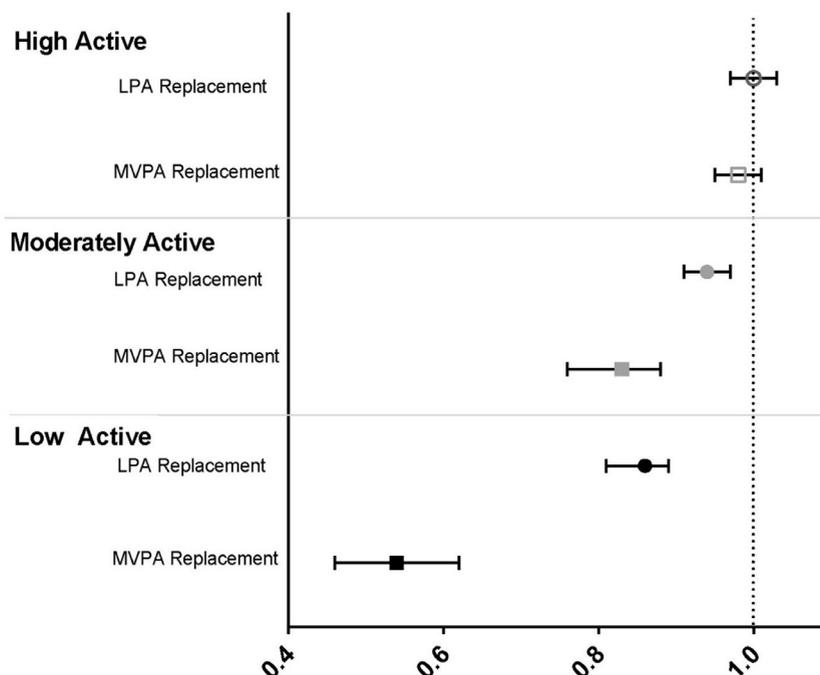


Figure 1. Estimated risk (HR) for all-cause mortality associated with replacement of 30 minutes of sitting time with physical activity. Note: Models adjust for age (continuous); sex; race (white, other); alcohol use (non-drinker, <1, 1, ≥ 2 drinks/day, unknown); smoking status (never, current, former); years since quitting among former smokers (<10, 10–19, ≥ 20 years); cigarette frequency and smoking duration among current smokers (<20 cigarettes/day for ≤ 35 years, <20 cigarettes/day for >35 years, ≥ 20 cigarettes/day for ≤ 35 years, ≥ 20 cigarettes/day for >35 years); aspirin use (non-user, <15, 15–29, ≥ 30 pills/month, unknown); education (high school or some college, college graduate or higher, unknown); occupational status (employed, not employed/retired); ACS dietary guidelines adherence score (0–<3, 3–<6, ≥ 6 , unknown)¹⁶; comorbidity score (0, 1, ≥ 2 comorbidities, including high blood pressure, diabetes, and high cholesterol); and BMI (continuous). MVPA categories split into approximate tertiles: low active ≤ 17 MVPA minutes/day, moderate active >17 to ≤ 38 MVPA minutes/day, high active >38 MVPA minutes/day. ACS, American Cancer Society; HR, hazard ratio; LPA, light physical activity; MVPA, moderate to vigorous physical activity.

information on PA ($n=3,370$) or sitting time ($n=2,210$); reporting zero minutes of sitting time ($n=147$); missing/extreme (top and bottom 0.1%) BMI ($n=4,445$); or missing smoking status ($n=113$). To reduce the possibility of reverse causality resulting from undiagnosed illness at baseline, participants dying within the first year of follow-up ($n=673$) or reporting no MVPA or activities of daily living were also excluded ($n=1,892$). The remaining 92,541 participants were included in this analysis.

Measures

Average daily sitting time, LPA, and MVPA were assessed using the 1999 CPS-II NC self-administered questionnaire, which can be found on the American Cancer Society website: www.cancer.org/research/we-conduct-cancer-research/epidemiology/cancer-prevention-questionnaires.html.

The primary outcome was all-cause mortality ascertained through biennial linkage of the cohort with the National Death Index.¹⁴ Causes of death were classified using the ICD-10 as cancer, CVD, and all other causes combined.¹⁵

Statistical Analysis

Cox proportional hazards regression modeling with an ISM framework was used to compute hazard ratios (HRs) and 95% CIs for the replacement of 30 minutes/day sitting with LPA or MVPA in two models: (1) adjusted for age, sex, and total time (sitting,

LPA, MVPA); and (2) adjusted for age, sex, total time, and other potential confounders. Potential confounders included race, alcohol use, smoking, aspirin use, education, occupational status, American Cancer Society dietary guidelines adherence score,¹⁶ comorbidity score, and BMI.

Secondary analyses tested for effect modification by MVPA tertiles, sex, age, and BMI. All statistical tests were two-sided. Analyses were conducted in 2018 using SAS, version 9.4.

RESULTS

During 14 years of follow-up, 14,415 men and 13,358 women died. Participants reporting more MVPA were leaner, had a higher educational attainment, and were less likely to be current smokers (Table 1). Sitting time largely included watching TV (39%) and reading (20%).

Overall, reallocation of 30 minutes/day of sitting to LPA (HR=0.94, 95% CI=0.92, 0.96) or MVPA (HR=0.92, 95% CI=0.90, 0.93) was associated with significant reductions in mortality risk. However, there was significant variation by underlying MVPA level (Figure 1). In the stratified analysis, replacement of sitting with LPA was associated with a reduced mortality risk for only low (HR=0.86, 95% CI=0.81, 0.89) and moderately (HR=0.94, 95% CI=0.91,

Table 2. Multivariable Adjusted HR (95% CI) of Mortality Associated With Replacement of Sitting Time

Cause of death	Activity level, HR (95% CI) ^a			<i>p</i> _{int} ^b
	Low active	Moderate active	High active	
Cancer				
Deaths, <i>n</i>	2,085	2,904	2,528	
Model 1				
Replace with LPA	0.90 (0.83, 0.97)	0.91 (0.88, 0.97)	1.01 (0.99, 1.07)	
Replace with MVPA	0.53 (0.39, 0.70)	0.81 (0.70, 0.93)	1.00 (0.97, 1.06)	
Model 2				
Replace with LPA	0.91 (0.85, 0.97)	0.94 (0.89, 0.98)	1.03 (0.98, 1.06)	0.0026 LPA
Replace with MVPA	0.69 (0.51, 0.94)	0.83 (0.74, 0.96)	1.00 (0.97, 1.05)	0.0004 MVPA
CVD				
Deaths, <i>n</i>	3,009	3,548	2,678	
Model 1				
Replace with LPA	0.81 (0.76, 0.86)	0.91 (0.86, 0.95)	1.00 (0.96, 1.06)	
Replace with MVPA	0.44 (0.34, 0.56)	0.76 (0.67, 0.86)	0.99 (0.95, 1.03)	
Model 2				
Replace with LPA	0.83 (0.79, 0.89)	0.91 (0.88, 0.96)	1.00 (0.97, 1.07)	<0.0001 LPA
Replace with MVPA	0.53 (0.41, 0.68)	0.83 (0.72, 0.94)	0.99 (0.95, 1.04)	<0.0001 MVPA
All other causes				
Deaths, <i>n</i>	3,722	4,227	3,072	
Model 1				
Replace with LPA	0.83 (0.78, 0.89)	0.94 (0.90, 1.00)	0.97 (0.94, 1.01)	
Replace with MVPA	0.40 (0.32, 0.49)	0.79 (0.70, 0.88)	0.96 (0.93, 0.99)	
Model 2				
Replace with LPA	0.83 (0.79, 0.89)	0.94 (0.90, 0.98)	0.97 (0.94, 1.01)	<0.0001 LPA
Replace with MVPA	0.48 (0.37, 0.59)	0.80 (0.72, 0.91)	0.96 (0.93, 1.00)	<0.0001 MVPA

Note: Model 1 adjusts for age (continuous) and sex. Model 2 adjusts for age; sex; race (white, other); alcohol use (non-drinker, <1, 1, ≥2 drinks/day, unknown); smoking status (never, current, former); years since quitting among former smokers (<10, 10–19, ≥20 years); cigarette frequency and smoking duration among current smokers (<20 cigarettes/day for ≤35 years, <20 cigarettes/day for >35 years, ≥20 cigarettes/day for ≤35 years, ≥20 cigarettes/day for >35 years); aspirin use (non-user, <15, 15–29, ≥30 pills/month, unknown); education (high school or some college, college graduate or higher, unknown); occupational status (employed, not employed/retired); ACS dietary guidelines adherence score (0–<3, 3–<6, ≥6, unknown)¹⁷; comorbidity score (0, 1, ≥2 comorbidities, including high blood pressure, diabetes, and high cholesterol); and BMI (continuous).

^aPhysical activity level categories split into approximate tertiles: low active ≤17 MVPA minutes/day, moderate active >17 to ≤38 MVPA minutes/day, high active >38 MVPA minutes/day.

^b*p*-value for interaction by PA category; boldface indicates statistical significance (*p*<0.01).

ACS, American Cancer Society; CVD, cardiovascular disease; HR, hazard ratio; LPA, light physical activity; MVPA, moderate to vigorous physical activity.

0.97) active participants, but not highly active participants. Benefits were greater when replacing sitting time with MVPA (low active, HR=0.55, 95% CI=0.47, 0.62; moderately active, HR=0.83, 95% CI=0.76, 0.88). Results for grouped causes of death were similar (Table 2).

Given the significant interaction by underlying MVPA, analyses by sex, age, and BMI were restricted to the low and moderately active groups (Table 3). Results were similar when stratified by sex and BMI. However, significant interactions by age revealed larger mortality benefits for older adults when sitting was replaced with LPA.

DISCUSSION

In this large prospective study, replacement of 30 minutes/day of sitting with LPA or MVPA was

associated with lower mortality risk, but results varied substantially by underlying MVPA level. Among low to moderately active adults (MVPA 38 minutes/day or less), replacing sitting with LPA was associated with a reduction in cancer, CVD, and all-cause mortality. Additionally, replacement of sitting with MVPA resulted in larger mortality benefits. However, among the highly active participants, the same reallocation of sitting to LPA or MVPA was not associated with additional mortality benefits.

Application of the ISM in this study revealed a significant association of reallocation of sitting time to LPA with mortality in low and moderately active participants. This finding is relevant to public health as LPA may be more attainable for certain groups failing to meet PA guidelines (e.g., older adults), and suggests an important strategy for gaining further health benefits from PA for

Table 3. Stratified Multivariable Adjusted HR (95% CI) of Mortality Associated With Replacement of Sitting Time

Variable	All-cause, HR (95% CI)	Cancer, HR (95% CI)	CVD, HR (95% CI)	Other, HR (95% CI)
Male (n=22,978)				
Deaths, n	9,469	2,409	3,282	3,778
Replace with LPA	0.91 (0.89, 0.93)	0.91 (0.88, 0.98)	0.88 (0.83, 0.91)	0.93 (0.88, 0.97)
Replace with MVPA	0.74 (0.70, 0.78)	0.88 (0.77, 0.97)	0.73 (0.67, 0.81)	0.66 (0.60, 0.71)
Female (n=37,976)				
Deaths, n	10,026	2,580	3,275	4,171
Replace with LPA	0.89 (0.85, 0.92)	0.92 (0.86, 1.00)	0.89 (0.82, 0.94)	0.84 (0.81, 0.89)
Replace with MVPA	0.76 (0.71, 0.81)	0.86 (0.78, 0.96)	0.76 (0.68, 0.82)	0.69 (0.63, 0.76)
p_{int}^a for sex	0.13 LPA, 0.55 MVPA	0.89 LPA, 0.86 MVPA	0.76 LPA, 0.81 MVPA	0.01 LPA , 0.34 MVPA
Age <65 years (n=15,375)				
Deaths, n	1,742	793	396	553
Replace with LPA	0.94 (0.88, 1.01)	0.94 (0.83, 1.04)	0.97 (0.83, 1.13)	0.91 (0.79, 1.06)
Replace with MVPA	0.73 (0.66, 0.86)	0.80 (0.66, 0.97)	0.81 (0.62, 1.06)	0.64 (0.50, 0.80)
Age 65–<75 years (n=33,152)				
Deaths, n	9,825	2,838	3,033	3,954
Replace with LPA	0.90 (0.88, 0.94)	0.91 (0.86, 0.97)	0.89 (0.83, 0.94)	0.91 (0.88, 0.97)
Replace with MVPA	0.74 (0.70, 0.79)	0.86 (0.76, 0.94)	0.74 (0.65, 0.81)	0.69 (0.64, 0.76)
Age ≥75 years (n=12,427)				
Deaths, n	7,928	1,358	3,128	3,442
Replace with LPA	0.88 (0.85, 0.92)	1.00 (0.83, 1.11)	0.86 (0.81, 0.92)	0.86 (0.80, 0.91)
Replace with MVPA	0.74 (0.70, 0.79)	0.97 (0.88, 1.06)	0.76 (0.68, 0.83)	0.65 (0.60, 0.72)
p_{int} for age group	0.04 LPA , 0.19 MVPA	0.50 LPA, 0.15 MVPA	0.11 LPA, 0.41 MVPA	0.04 LPA , 0.26 MVPA
Normal weight BMI (n=24,663)				
Deaths, n	8,173	1,907	2,678	3,588
Replace with LPA	0.89 (0.86, 0.94)	0.91 (0.86, 1.01)	0.88 (0.82, 0.94)	0.88 (0.86, 0.94)
Replace with MVPA	0.70 (0.66, 0.74)	0.89 (0.79, 0.99)	0.68 (0.61, 0.76)	0.62 (0.56, 0.68)
Overweight BMI (n=24,575)				
Deaths, n	7,645	2,113	2,562	2,970
Replace with LPA	0.91 (0.88, 0.94)	0.94 (0.88, 0.98)	0.88 (0.83, 0.94)	0.91 (0.86, 0.97)
Replace with MVPA	0.78 (0.74, 0.86)	0.86 (0.76, 0.97)	0.81 (0.72, 0.89)	0.74 (0.68, 0.83)
Obese BMI (n=11,716)				
Deaths, n	3,677	969	1,317	1,391
Replace with LPA	0.89 (0.83, 0.94)	0.91 (0.81, 1.00)	0.86 (0.79, 0.97)	0.89 (0.81, 0.97)
Replace with MVPA	0.74 (0.67, 0.81)	0.83 (0.70, 0.99)	0.74 (0.64, 0.86)	0.70 (0.60, 0.80)
p_{int} for BMI	0.68 LPA, 0.05 MVPA	0.98 LPA, 0.57 MVPA	0.57 LPA, 0.23 MVPA	0.83 LPA, 0.04 MVPA

Note: Models adjust for age (continuous); sex; race (white, other); alcohol use (non-drinker, <1, 1, ≥2 drinks/day, unknown); smoking status (never, current, former); years since quitting among former smokers (<10, 10–19, ≥20 years); cigarette frequency and smoking duration among current smokers (<20 cigarettes/day for ≤35 years, <20 cigarettes/day for >35 years, ≥20 cigarettes/day for ≤35 years, ≥20 cigarettes/day for >35 years); aspirin use (non-user, <15, 15–29, ≥30 pills/month, unknown); education (high school or some college, college graduate or higher, unknown); occupational status (employed, not employed/retired); ACS dietary guidelines adherence score (0–<3, 3–<6, ≥6, unknown); comorbidity score (0, 1, ≥2 comorbidities, including high blood pressure, diabetes, and high cholesterol); and BMI (continuous). Only moderate and low active participants were included (n=60,954).

^a p -value for interaction by sex/age group/BMI; boldface indicates statistical significance ($p<0.05$).

ACS, American Cancer Society; CVD, cardiovascular disease; HR, hazard ratio; LPA, light physical activity; MVPA, moderate to vigorous physical activity.

many already engaging in MVPA. This study was one of the first to explore the role of age on the replacement of sitting time and found that older adults may benefit more from the replacement of sitting time with LPA. However, it is possible that the assessed LPAs may be of higher relative intensity for adults older than age 65 years, resulting in larger than expected mortality risk

estimates. It is also possible that participation in purposeful, leisure-time PA later in life may represent better general health.

Strengths of this study include the prospective design with long follow-up, a large sample size, and the use of a statistical approach that allows for the consideration of displaced activities. Nonetheless, it is important to note

that these risk estimates are modeled using the ISM framework and are not describing associations of actual changes in behavior.

Limitations

This study relied on self-reported PA and sitting time, which may be over- or under-estimated and may not account for all waking hours. Another limitation is the lack of information on certain activities of daily living (e.g., cleaning, self-care, cooking) that are particularly common for older adults. Finally, participants are predominantly white and educated, and therefore may not represent the general U.S. population.

CONCLUSIONS

Among the least and moderately active, replacing 30 minutes/day of sitting with 30 minutes/day of LPA or MVPA was associated with longevity, and reallocating sitting time to MVPA provided the most benefit for time invested. As many adults do not engage in any MVPA, evidence of associated benefits for LPA highlights the potential for targeting lower-intensity PA behaviors to improve health.

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ERP performed the analysis and drafted the manuscript and takes responsibility for the integrity and accuracy of the results. AVP, SMG, CEM, MDS, JLG, and EME contributed to the concept and design of the study. All authors contributed to critical revision of the manuscript.

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