Physical activity, sedentary behavior with longevity and aging: observational and Mendelian randomization studies

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Physical activity showed protective effects on longevity and age acceleration (AA), with the effects being partly mediated through lipids, while sedentary behavior had a detrimental impact on AA. Moderate physical activity was associated with higher likelihood of longevity and lower AA, whereas vigorous physical activity showed opposite results.

BACKGROUND

- Aging is a multifaceted process involving physical, biological, and psychological changes, often measured by biological age or markers like age acceleration (AA).
- Low physical activity (PA) and high sedentary behavior (SB) are linked to higher mortality and morbidity risks. However, the association of PA and SB with longevity remains understudied, with inconsistent findings from observational studies on PA's impact on longevity, such as inverse U-shaped relationships, no associations, or sex-specific results.
- The impact of different PA intensities (e.g., walking vs. vigorous PA) needs further investigation to determine their distinct effects on aging.

METHODS

- Based on the GBCS, we conducted prospective analyses to examine the associations of total and specific PA in different intensities, SB with longevity, and cross-sectional analyses to assess the associations with AA.
- We also conducted mediation analyses to identify the mediating roles of lipids in these associations.
- Two-sample MR studies, with the associations between the genetic variants and exposure and between the variants and outcome are estimated from two sets of individuals, was used to confirm the causations of PA, SB with longevity and AA.
- Longevity was defined as participants whose age at follow-up or at death were at or above the 90th age percentile.
- AA was defined as the residual resulting from a linear model that regressed phenotypic age against chronological age.

RESULTS

- Of 20,924 participants aged 50+, during an average follow-up of 15.0 years, compared with low PA, moderate and high PA were associated with higher likelihood of longevity, and also cross-sectionally associated with lower AA.
- Higher levels of moderate PA (MPA) were associated with higher likelihood of longevity and lower AA, whereas vigorous PA (VPA) showed opposite effects.
- The association of PA with longevity observed in GBCS was mediated by low-density lipoprotein cholesterol (LDL-C) by 8.23%, while the association with AA was mediated through LDL-C, triglycerides and total cholesterol by 5.13%, 7.81%, and 3.37%, respectively. Additionally, in two-sample MR, SB was positively associated with AA (β (95% CI): 1.02 (0.67, 1.36) years).

RESULTS CONTINUED

<u>Table 1.</u> Associations of physical activity and sedentary behavior with age acceleration (AA)

	Crude model	Model 1 [a]	Model 2 [b]
PA level			
Low	0.00	0.00	0.00
Moderate	-1.65 (-2.67, -0.64) **	-1.65 (-2.67, -0.64) **	-1.43 (-2.41, -0.45) **
High	-2.59 (-3.60, -1.58) ***	-2.59 (-3.60, -1.58) ***	-2.09 (-3.06, -1.11) ***
PA frequency, d/w			
Walking	-0.13 (-0.29, 0.02)	-0.04 (-0.19, 0.12)	-0.02 (-0.17, 0.13)
MPA	-0.12 (-0.16, -0.09) ***	-0.07 (-0.11, -0.03) ***	-0.03 (-0.06, 0.01)
VPA	0.09 (-0.01, 0.18)	0.20 (0.10, 0.30) ***	0.04 (-0.06, 0.13)
PA duration, hr/d			
Walking	-0.25 (-0.33, -0.18) ***	-0.09 (-0.19, 0.0004)	-0.08 (-0.17, 0.01)
MPA	-0.42 (-0.56, -0.28) ***	-0.12 (-0.29, 0.04)	-0.0001 (-0.16, 0.16)
VPA	0.14 (-0.33, 0.62)	0.82 (0.32, 1.31) **	0.12 (-0.37, 0.60)
SB, hr/d	0.15 (0.09, 0.21) ***	0.12 (0.06, 0.18) ***	0.05 (-0.005, 0.11)

[a] Model 1: adjusted for metabolic equivalent score except for physical activity level. [b] Model 2: Model 1 additionally adjusted for sex, occupation, education, family income, smoking status, alcohol use, and self-rated health. [c] Cases were defined as participants with AA exceeding 5 years.
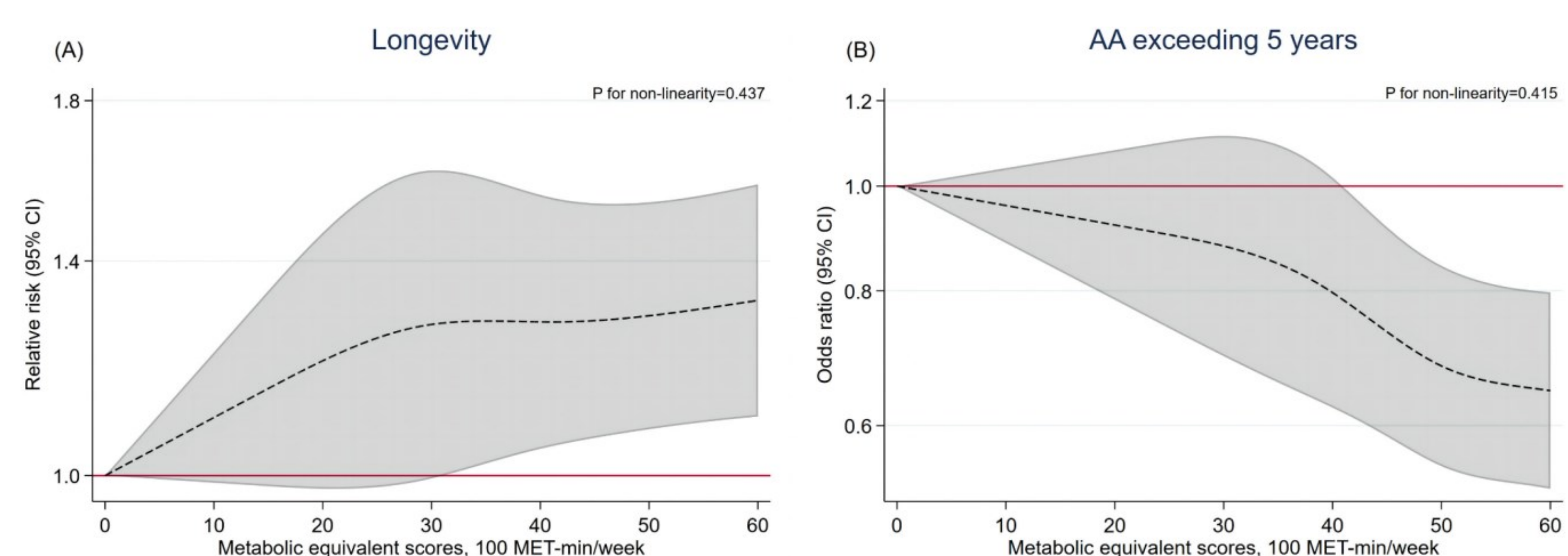*P<0.05, **P<0.01, ***P<0.001.

Fig 1 Associations of physical activity level (metabolic equivalent scores) with longevity and age acceleration (AA) exceeding 5 years in Guangzhou Biobank Cohort Study

CONCLUSIONS

- PA showed protective effects on longevity and AA, with the effects being partly mediated through lipids, while SB had a detrimental impact on AA.
- MPA was associated with higher likelihood of longevity and lower AA, whereas VPA showed opposite results.
- Our findings support current advocacy for "sit less and move more" in the context of healthy longevity and aging, and provide additional evidence on the potential detrimental effects of VPA in the elderly.
- Further MR studies with a sufficient number of SNPs are warranted to confirm the effects of both total and specific PA on longevity and AA.

ADDITIONAL KEY INFORMATION

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