Supplementary Information

Additional file 1: Table S1-S23. Table S1 - Summary of each genome-wide association study. **Table S2** - Exposure harmonization. **Table S3** - Outcome standardization and compliance report. **Table S4** - Prediction intervals of meta-analyses. **Table S5** - RCS fitting curve model details. **Table S6** - Sensitivity analyses of RCS curve. **Table S7** - Risk of bias assessments (RoB2). **Table S8** - Trim-and-fill analysis. **Table S9** - Instrument SNPs for MVPA. **Table S10** - Results for TSMRs (MVPA-aging). **Table S11** - Pleiotropy analyses (MVPA-aging). **Table S12** - Heterogeneity analyses (MVPA-aging). **Table S13** - MR Steiger test of directionality (MVPA-aging). **Table S14** - MRlap-corrected MR estimates (MVPA-aging). **Table S15** - Results for potential mediators. **Table S16** - Significant enriched biological pathways. **Table S17** - Results for Mediation analyses. **Table S18** - Genetic colocalization of mediators and aging outcomes. **Table S19** - Results for TSMRs (MVPA-human organ BAG). **Table S20** - Pleiotropy analyses (MVPA-human organ BAG). **Table S21** - Heterogeneity analyses (MVPA-human organ BAG). **Table S22** - MR Steiger test of directionality (MVPA-human organ BAG). **Table S23** - MRlap-corrected MR estimates (MVPA-human organ BAG).

Additional file 2: Figure S1. Subgroup analyses. (A-C) Forest plots display effect size estimates within subgroups defined by: participant demographics (age, BMI, sex, ethnicity); intervention parameters (physical activity modality, mMET-volume, intervention duration); and technical methodologies (source of biospecimen and method for outcome measurement). Analyses were performed for outcomes where between-study heterogeneity (I^2) was detected.

Additional file 3: Figure S2-S6. Meta-regression analyses of continuous moderators. Bubble plots with fitted regression lines illustrate the results of univariate meta-regression, evaluating the association between the standardized mean difference (SMD) in aging-related outcomes and the following continuous variables: participant mean age, mean BMI, physical activity volume (mMET), study sample size and intervention duration (months).

Additional file 4: Figure S7-S8. Sensitivity analyses. Forest plots from sensitivity analyses assessing the robustness of the primary meta-analysis estimates. Analyses were conducted by excluding studies based on detection methodology and study-level risk-of-bias ratings. Data are showed as standardized mean difference (SMD) [95% confidence intervals (CI)]. Fixed-effect and random-effects models were employed to pool effect sizes. Heterogeneity was assessed by Q-test and I^2 statistics.

Additional file 5: Figure S9. Non-linear dose‑response analyses. (A) RCS curve of the association between PA and Telomerase. Changes in telomerase reached the peak (0.79 [-0.039, 1.5862]) at PA level of 11.5 [10.54, 15] mMET h/week. (B) RCS curve of the association between PA and FI. The vertical axis denotes the standardized mean differences (SMD) in corresponding aging indicators between meta-analytical intervention and control groups. Independent variable PA converted to mMET h/week. The bold line represents the estimated dose-response curve. The shaded area and area between the colored dashed lines indicates 95% confidence-band boundaries.

Additional file 6: Figure S10. Assessment of Publication Biases. (A) Contour-enhanced funnel plot of meta-analysis on PA and Telomerase. (B) Funnel plot of meta-analysis on PA and global DNA methylation. (C) Contour-enhanced funnel plot of meta-analysis on PA and Frailty index. Egger's test could not be implemented due to insufficient sample size. Distinct color-coded regions denote different levels of literature result statistical significance, including white ($P>0.05$), dark gray ($0.05<P<0.1$), gray ($0.01<P<0.05$), light gray ($P<0.01$). Solid dots represent included studies, while hollow dots indicate missing studies imputed by Trim-and-fill analysis.

Additional file 7: Figure S11. MR leave−one−out sensitivity analysis for MVPA and aging indicators.

Additional file 8: Figure S12. Colocalization analysis of pQTL with aging-related outcomes. Regional association plots (left) for the lead pQTL variant (lead SNP) of NCAN and its corresponding locus for the aging outcomes (IEAA, ALM). Each point represents a SNP, colored by its linkage disequilibrium (R^2) with the lead colocalized variant (purple diamond). Locus Compare plot (right) showing the correlation between pQTL and outcome association statistics across the shared locus. The dashed line indicates the diagonal ($y = x$). All analyses were performed with a ±500 kb window

around the NCAN gene coordinates. The legend, positioned at the bottom center, indicates R^2 bins relative to the lead variant.

Additional file 9: Figure S13. Manhattan plots of genome-wide association studies (GWAS) for biological age gaps (BAGs) across nine organ systems. (A-I) Each plot displays $-\log_{10}(p)$ of association against chromosomal position. Points are colored alternately by chromosome, and each point represents a SNP. The solid red horizontal line indicates the genome-wide significance threshold ($p = 5\times10^{-8}$). The blue dashed line indicates the suggestive threshold ($p = 1\times10^{-5}$). Top associated SNPs surpassing the genome-wide significance threshold are labeled with their rs ID.

Additional file 10: Search Strategy.