Introduction

e world is currently facing the challenge of a continuously aging population. People aged 60 and over will represent 22% of the world's population by 2050 [1].

is demographic shift is primarily attributed to declining fertility rates and increased life expectancy. While advancements in living standards and healthcare have contributed to prolonged lifespans, they have also been accompanied by a rising prevalence of chronic diseases and disabilities among older adults. Consequently, the increase in healthy life expectancy has lagged significantly behind the overall growth in lifespan [2, 3].

erefore, investigating the factors contributing to accelerated aging is necessary, as it is closely associated with increased susceptibility to chronic diseases and an increased mortality risk [4].

Phenotypic age (PhenoAge) and PhenoAgeAccel are emerging biomarkers of biological aging that integrate multiple physiological and biochemical indicators to e ectively assess an individual's biological aging status. ese metrics not only reflect an individual's relative aging level compared with their peers and provide an evaluation of current health status, but also serve as predictive tools for future disease risk and mortality. As such, they o er a valuable foundation for developing personalized prevention strategies [4, 5].

e continuous increase in SSB consumption has made SSB intake a major global public health issue. In 2020, the

Characteristics	Total (*N* = 3,925)		Accelerated aging (*N* = 923)		Delayed aging (*N* = 3,002)		*P*-value
	Mean	SD	Mean	SD	Mean	SD	
Chronological age (year)	45.95	15.40	49.62	15.36	45.08	15.28	< 0.0001
PhenoAge (year)	41.91	17.76	56.30	18.88	38.51	15.66	< 0.0001
PhenoAgeAccel (year)	-4.03	7.47	6.67	9.78	-6.57	3.57	< 0.0001
Body roundness index	5.14	2.15	6.58	2.56	4.80	1.89	< 0.0001
Body mass index (kg/m^2)	28.59	6.33	32.49	7.60	27.66	5.61	< 0.0001
Weight (kg)	82.57	20.38	93.69	23.26	79.94	18.69	< 0.0001
Height (cm)	169.71	9.96	169.73	9.96	169.71	9.96	0.9552
Waist circumference (cm)	98.19	15.82	108.45	17.03	95.76	14.49	< 0.0001
SSB intake (kcal/d)	146.01	234.02	174.29	264.30	139.32	225.75	0.0002
Total energy intake (kcal/d)	2206.13	1000.44	2161.00	1085.30	2216.81	978.98	0.1692
Protein intake (gm)	85.71	43.67	83.47	44.08	86.24	43.55	0.1190
Carbohydrate intake (gm)	262.70	127.56	255.39	141.13	264.45	124.07	0.0802
Total fat intake (gm)	84.72	47.47	84.22	50.30	84.84	46.78	0.7457
Ca□eine intake (mg)	186.97	224.29	179.74	215.15	188.68	226.36	0.3258
Moisture intake (mg)							

sweetened beverage (LNCSB) may be associated with weight reduction [45]. Obesity further disrupts the metabolism, decreasing insulin sensitivity and increasing di culty adapting to the demand for energy supply [46]. Obesity not only accelerates the progression of age-related diseases but also may directly impact the aging process [47, 48]. e deterioration of nutritional signaling pathways is one of the important metabolic e ects of aging, with mechanistic target of rapamycin (mTOR) and sirtuins being the most classical examples [49]. e intricate interactions among obesity, metabolic dysregulation, and these nutrient-sensing pathways provide insights into how obesity accelerates aging [48]. Overall, these findings support our conclusion that SSB intake is significantly associated with PhenoAgeAccel, a relationship that may be partially mediated by obesity. Notably, both BRI and BMI were used as measures of obesity in this study. It has

associated with higher BMI, potentially increasing the risk of chronic obesity-related diseases [56]. e intake of SSB late at night may exacerbate metabolic dysregulation and lead to more severe obesity, contributing to related conditions such as accelerated aging, which aligns with our findings. On the other hand, sugar can enter the human body through the gastrointestinal tract. Intestinal epithelial cells throughout the gut contain a molecular clock synchronized by signals generated from food intake [57]. For example, brush border disaccharidases have been found to exhibit circadian rhythmic activity [58].

is may partially explain why the intake of SSB at di er-

Fig. 5 Mediation e□ects of obesity on the association between the energy of SSB intake and PhenoAgeAccel. Note: exposure: SSB intake, outcome: PhenoAgeAccel, mediator: BRI (**A**); BMI (**B**). Adjusted for Model 2 (adjusted covariates: gender, age, race/ethnicity, education level, marital status, PIR, smoking

whereas subjective well-being has been shown to positively impact physical and mental health, particularly in older adults [64]. In the interaction analyses, we considered downstream factors, including smoking, alcohol consumption, and physical activity, that may have a moderating e ect on the relationship between SSB intake timing and PhenoAgeAccel. Another interesting finding was that smoking is a moderating variable in this association. Recently, a cohort study based on the UK Biobank reported that a shorter time from waking up to smoking the first cigarette is associated with an increased risk of developing type 2 diabetes [65]. Similarly, Tang et al. reported that the duration from waking up to smoking the first cigarette is related to chronic kidney disease (CKD), and further research indicated that unhealthy dietary habits exacerbate this association [66]. Collectively, these health factors, along with biological age, PhenoAge, and age-related diseases, form a complex and interconnected network.

Previous investigations have shown that replacing SSB with healthy beverages like plain water, low-fat milk, and unsweetened co ee can help reduce the incidence of diabetes and CKD [32, 67]. ese substitutes are simple, a ordable, safe and e ective. Some have even suggested

Published online: 08 January 2025

References

1. Newgard CB, Sharpless NE. Coming of age: molecular drivers of aging and therapeutic opportunities. J Clin Invest. 2013;123(3):946–50.
2. Gonzalez-Freire M, Diaz-Ruiz A, Hauser D, Martinez-Romero J, Ferrucci L, Bernier M, et al. The road ahead for health and lifespan interventions. Ageing Res Rev. 2020;59:101037.
3. Kuo PL, Schrack JA, Levine ME, Shardell MD, Simonsick EM, Chia CW, et al. Longitudinal phenotypic aging metrics in the Baltimore Longitudinal Study of Aging. Nat Aging. 2022;2(7):635–43.
4. Liu Z, Kuo PL, Horvath S, Crimmins E, Ferrucci L, Levine M. A new aging measure captures morbidity and mortality risk across diverse subpopulations from NHANES IV: a cohort study. PLoS Med. 2018;15(12):e1002718.
5. Levine ME, Lu AT, Quach A, Chen BH, Assimes TL, Bandinelli S, et al. An epigenetic biomarker of aging for lifespan and healthspan. Aging. 2018;10(4):573–91.
6. Tseng TS, Lin WT, Ting PS, Huang CK, Chen PH, Gonzalez GV, et al. Sugar-Sweetened beverages and arti□cially sweetened beverages Consumption and the risk of nonalcoholic fatty liver (NAFLD) and Nonalcoholic Steato-hepatitis (NASH). Nutrients. 2023;15(18):3997.
7. Meng Y, Li S, Khan J, Dai Z, Li C, Hu X, et al. Sugar- and arti□cially sweetened beverages Consumption Linked to type 2 diabetes, Cardiovascular diseases, and all-cause mortality: a systematic review and dose-response Meta-analysis of prospective cohort studies. Nutrients. 2021;13(8):2636.
8. US Department of Agriculture and US Department of Health and Human Services. Dietary Guidelines for Americans, 2020–2025. 9th edition. December 2020.
9. Marriott BP, Hunt KJ, Malek AM, Newman JC. Trends in Intake of Energy and Total Sugar from Sugar-Sweetened beverages in the United States among children and adults, NHANES 2003–2016. Nutrients. 2019;11(9):2004.
10. Kit BK, Fakhouri TH, Park S, Nielsen SJ, Ogden CL. Trends in sugar-sweetened beverage consumption among youth and adults in the United States: 1999–2010. Am J Clin Nutr. 2013;98(1):180–8.
11. Chhimwal J, Patial V, Padwad Y. Beverages and non-alcoholic fatty liver disease (NAFLD): think before you drink. Clin Nutr. 2021;40(5):2508–19.
12. Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. Am J Clin Nutr. 2013;98(4):1084–102.
13. Qin P, Li Q, Zhao Y, Chen Q, Sun X, Liu Y, et al. Sugar and arti□cially sweetened beverages and risk of obesity, type 2 diabetes mellitus, hypertension, and all-cause mortality: a dose-response meta-analysis of prospective cohort studies. Eur J Epidemiol. 2020;35(7):655–71.
14. Bo S, Fadda M, Castiglione A, Ciccone G, De Francesco A, Fedele D, et al. Is the timing of caloric intake associated with variation in diet-induced thermogenesis and in the metabolic pattern? A randomized cross-over study. Int J Obes (Lond). 2015;39(12):1689–95.
15. Dietary Guidelines Advisory Committee. Scienti□c report of the 2015 dietary guidelines advisory committee. Washington (DC): USDA and US Department of Health and Human Services; 2015.
16. Yang G, Cao X, Li X, Zhang J, Ma C, Zhang N, et al. Association of Unhealthy Lifestyle and Childhood Adversity with Acceleration of Aging among UK Biobank Participants. JAMA Netw Open. 2022;5(9):e2230690.
17. Thomas DM, Bredlau C, Bosy-Westphal A, Mueller M, Shen W, Gallagher D, et al. Relationships between body roundness with body fat and visceral adipose tissue emerging from a new geometrical model. Obes (Silver Spring). 2013;21(11):2264–71.
18. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. Hallmarks of aging: an expanding universe. Cell. 2023;186(2):243–78.
19. Kuo PL, Schrack JA, Shardell MD, Levine M, Moore AZ, An Y, et al. A roadmap to build a phenotypic metric of ageing: insights from the Baltimore Longitudinal Study of Aging. J Intern Med. 2020;287(4):373–94.
20. Li Q, Wang S, Milot E, Bergeron P, Ferrucci L, Fried LP, et al. Homeostatic dysregulation proceeds in parallel in multiple physiological systems. Aging Cell. 2015;14(6):1103–12.
21. Malik VS, Willett WC, Hu FB. Global obesity: trends, risk factors and policy implications. Nat Rev Endocrinol. 2013;9(1):13–27.
22. Welsh JA, Sharma AJ, Grellinger L, Vos MB. Consumption of added sugars is decreasing in the United States. Am J Clin Nutr. 2011;94(3):726–34.
23.

47. Santos AL, Sinha S. Obesity and aging: molecular mechanisms and therapeu-