RESEARCH PAPER

Association between ultra-processed food intake and biological ageing in US adults: findings from National Health and Nutrition Examination Survey (NHANES) 2003–2010

Barbara Rita Cardoso[1,2], Junxiu Liu[3], Priscila Machado[4], Dayoon Kwon[5], Daniel W. Belsky[6], Euridice Martinez Steele[7]

[1]Department of Nutrition, Dietetics and Food, Monash University, Notting Hill, VIC 3168, Australia
[2]Victorian Heart Institute, Monash University, Clayton, VIC 3168, Australia
[3]Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[4]Institute for Physical Activity and Nutrition, Deakin University, Geelong, VIC, Australia
[5]Fielding School of Public Health, University of California Los Angeles, Los Angeles, CA, USA
[6]Robert N Butler Columbia Aging Center, Columbia University Mailman School of Public Health, New York, NY, USA
[7]Center for Epidemiological Studies in Health and Nutrition, University of Sao Paulo, Sao Paulo, Brazil

Address correspondence to: Barbara Rita Cardoso, Department of Nutrition, Dietetics and Food, Level 1 264 Ferntree Gully
Road, Notting Hill, VIC 3168, Australia. Email: barbara.cardoso@monash.edu

Abstract

Background: The association between ultra-processed food (UPF) intake and markers of biological ageing has been scarcely investigated, despite the evident adverse health effects associated with UPF. This study aimed to test the association between UPF intake and biological ageing, and evaluate how much of this association is accounted for by overall diet quality.
Methods: This cross-sectional study assessed 16 055 participants aged 20–79 years (51% women, 46 ± 0.3 years) from the National Health and Nutrition Examination Survey (NHANES) 2003–2010. Dietary UPF intake was assessed using the Nova system. Values were expressed as % of total energy intake and were denominated as a continuous variable and in quintiles. Diet quality was assessed with the American Heart Association 2020 and the Healthy Eating Index 2015. Biological ageing was assessed **using the PhenoAge algorithm**.
Results: For each 10% of energy intake accounted for by UPF, participants were 0.21 (95%CI 0.16–0.26) years biologically older in terms of PhenoAge. As compared to participants in the lowest UPF quintile (≤39%), those in the highest UPF quintile (68–100%) were 0.86 (95% CI 0.55, 1.16) years older (P-for-trend across quintiles ≤0.001). Adherence to a healthy diet moderately attenuated the relationship between UPF and PhenoAge (adjusted $\beta = 0.14$ per 10% increment of UPF).
Conclusions: Adults with higher UPF tended to be biologically older. This association is partly independent of diet quality, suggesting that food processing may contribute to biological ageing acceleration. Our findings point to a compelling reason to target UPF consumption to promote healthier ageing.

Keywords: ultra-processed food; ageing; diets; biological ageing; older people

Key Points

- Ultra-processed food (UPF) consumption is associated with signs of accelerated biological ageing.
- Adherence to a healthy diet explained only part of the association of UPF intake with older biological age.
- Other properties of UPF related to processing may contribute to an acceleration of biological processes of ageing.

Introduction

Life expectancy is increasing globally, with the population above 60 years projected to double from 2015 to 2050, reaching nearly 2.1 billion [1]. The global demographic shift towards an ageing population poses economic and societal challenges [2], in part because gains in lifespan are not being matched by gains in healthy years of life [3]. Understanding how dietary choices impact the ageing process may pave the way to promoting longevity and reducing the burden of age-related illnesses.

The emerging field of geroscience proposes that one strategy to increase healthy years of life or 'healthspan' is to intervene in the biological processes of ageing [4]. Biological ageing refers to the gradual accumulation of molecular and cellular damage over time, which leads to the decline in physiological function and increased vulnerability to diseases. The Geroscience Hypothesis is premised on evidence that a number of molecular changes (called 'hallmarks') are characteristic of ageing across mammalian species and mediate ageing-related risk for many different chronic diseases [5, 6]. In laboratory animals, interventions to slow or reverse the accumulation of ageing hallmarks can extend healthspan [7]. Translation of these therapies to treat human ageing is a key frontier in geroscience [8, 9]. In parallel, it may be possible to identify environments and behaviours that affect ageing biology, offering more immediate opportunities for intervention [10].

Diet is a key environmental/behavioural pathway with potential to affect healthy ageing [11]. People with healthier dietary patterns tend to exhibit a slower pace of biological ageing as compared to those with less healthy diets [12–15]. Healthy diet indices used in previous research mostly focus on the consumption of whole, plant-based foods, which results in high intake of fibre, and limited consumption of saturated fat, sodium and added sugar [16]. Although the importance of specific nutrients and food groups for health outcomes is indisputable, the impact of food processing on health is emerging as a dietary feature potentially relevant to healthy longevity.

Industrial food processing involves physical, chemical and biological processes used by food manufacturers to alter foods from their natural state before consumption or meal preparation. Based on the extent and purpose of these processes, the Nova classification system categorises foods and beverages into four groups: unprocessed or minimally foods, processed culinary ingredients, processed foods and ultra-processed foods (UPFs) [17]. UPFs are defined as industrial formulations of several ingredients including oils, fats and starch that typically contain cosmetic additives and/or substances of rare culinary use opposed to little (if any) whole foods [17]. UPFs account for >50% of energy intake in the usual diet of US and British populations [18], with a steady increase observed in Asian, African Middle Eastern and Latin-American countries [19]. Multiple studies found strong associations between UPF intake and cardiovascular diseases, type 2 diabetes, obesity, mental disorders, all-cause

and heart-disease-related mortality [20]. In this study, we aimed to test if higher UPF consumption was associated with signs of accelerated biological ageing. Furthermore, we assessed how much of this association is accounted for by total energy intake and overall diet quality, assessed with the American Heart Association (AHA) 2020 continuous diet score [21] and the Healthy Eating Index 2015 (HEI-2015) [22, 23]. Our analysis from the US National Health and Nutrition Examination Surveys (NHANES) sheds new light on how dietary intake may contribute to healthy longevity.

Methods

Study population

This cross-sectional study included data from the 2003–2010 NHANES, given that only these sequenced cycles collected all data required for calculation of PhenoAge for ≥18-year-old participants (e.g. C-reactive protein (CRP) is not available for cycles 2011–12, 2013–14). The NHANES protocol was approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board. All the NHANES participants provided informed consent. Given that questions about the history of CVD and diabetes, which are important factors to be accounted for because of potential reverse causation, were only asked to individuals aged 20 years and over, we excluded 18- and 19-year-olds from our analysis. Furthermore, individuals aged 85 and over were topcoded at 85 years of age in cycles 2003–04 and 2005–06; and individuals aged 80 and over were topcoded at 80 years of age in cycles 2007–08 and 2009–10. Thus, we limited our analysis to people aged between 20 and 79 years old with reliable data for at least the first of two 24-hour dietary recalls. We excluded all participants with missing data necessary for the PhenoAge calculation (*n* = 2096), pregnant women (*n* = 539) and people with missing data for physical activity, a continuous variable used as covariate (*n* = 3). From the 18 693 participants within the eligible age range in the 2003–2010 NHANES cycles and reliable data for at least the first of two 24 h dietary recalls, 16 055 also met the remaining eligibility criteria and were included in our analysis (Fig. S1).

Dietary intake

All NHANES participants were eligible for two 24-hour dietary recall interviews: the first in-person at the Mobile Examination Center (MEC) and the second by phone 3–10 days later [24, 25]. We utilised all available dietary intake data for each participant, using means of both recall days when available and one day otherwise.

Based on food code and SR code descriptions, all food items were assigned to one of the four Nova groups: unprocessed/minimally processed foods, processed culinary ingredients, processed foods and UPFs (Supplementary Methods 1) [17, 26]. The contribution (%) of each Nova

group to total daily energy intake was calculated for each participant.

The overall diet quality was assessed using the AHA 2020 continuous diet score [21] and the HEI-2015 [22, 23]. The AHA diet score assigns points to 'beneficial' dietary components (fruits and vegetables; whole grains; fish and shellfish; nuts, seeds and legumes) while "harmful" components (sugar-sweetened beverages; sodium; processed meat; saturated fat) score inversely. HEI-2015, ranging 0–100, reflects 13 dietary components from 2015–2020 Dietary Guidelines for Americans [22] classified as "adequacy" (e.g. fruits, vegetables, whole grains) or "moderation" (e.g. refined grains, sodium). In both diet quality indices, higher scores represent a higher diet quality.

Biological ageing

In lack of a gold standard for the measurement of biological ageing [27], we used PhenoAge as this method can be applied to routinely collected clinical data with the best validation evidence for prediction of healthspan [28–32]. The PhenoAge was developed by modelling survival probabilities from blood chemistry data among participants in NHANES III [28] using an algorithm that includes chronological age and nine blood analytes. Importantly, prior studies established that PhenoAge is sensitive to lifestyle exposures, including nutrition [13, 33–35], and revealed slowed ageing in response to calorie restriction [36], an intervention established to slow biological ageing [37]. Values of the PhenoAge can be interpreted as the age at which an individual's mortality risk would match the average in the NHANES III training sample.

We implemented a modified version of PhenoAge algorithm adapted for use in a randomised trial of calorie restriction [36] using the 'BioAge' R package (Table S1). We computed PhenoAge gap as the difference between predicted biological age and chronological age. A higher PhenoAge gap value indicates an advanced state of biological ageing and increased risk of diseases and mortality.

Covariates

Demographics (age, sex, ethnicity, education, poverty-income ratio) and smoking status were collected using a Computer-Assisted Personal Interviewing system by trained interviewers. Body measures (height and weight) were collected by trained health technicians. Physical activity was assessed with the Global Physical Activity Questionnaire. History of CVD was noted if participants reported a physician's diagnosis of heart failure, coronary heart disease, angina, heart attack or stroke. History of diabetes was identified if participants reported a doctor's diagnosis, use of hypoglycemic agents or insulin, or HbA1c levels ≥6.5% (Hb1Ac was measured in blood with Tosoh Automated Hb1Ac Analyser HLC-723G8). Further details

of the covariates are presented in the Supplementary Methods 2.

Statistical analysis

Demographic and clinical characteristics were presented as mean with standard deviation (SD) for continuous variables, or % weighted (SD) for categorical variables. Data were compared across the population-stratified quintiles of the dietary contribution of UPF (% of total energy intake) using P-for-trend for continuous variables or Pearson's chi-square for categorical variables.

We used regression models to test the association between UPF intake (as both a continuous variable and quintiles of intake) with biological ageing, including a progressively more comprehensive set of covariates in our models to account for potential confounding, reverse causality or test potential mediation. Tests of linear trend were carried out by treating quintiles as a single continuous ordinal variable. The models were adjusted as follows: Model 1: NHANES cycle, chronological age and gender; Model 2: additionally adjusted for ethnicity, education and poverty-income ratio; Model 3: additionally adjusted for physical activity and smoking status; and Model 4: additionally adjusted for body mass index (BMI) and history of CVD and diabetes. These latter covariates in model 4 were included to account for potential reverse causality that could dilute the studied associations towards the null when assessed through cross-sectional studies. We constructed three other models that were adjusted for total energy intake (Model 5), AHA diet score (Model 6) and HEI-15 diet score (Model 7) in addition to the covariates used in Model 4 to test the hypothesis that UPF intake affects biological ageing over and above total energy intake and overall diet quality.

We used a weighed restricted cubic spline in model 4 with five knots (5th, 27.5th, 50th, 72.5th, and 95th) as per Harrell's recommendations [38] to examine the shape of the dose–response relationship curve between %kcal UPF (as a continuous variable) and PhenoAge gap.

To examine potential differences in the association between UPF and PhenoAge gap by gender, chronological age (continuous), BMI (continuous), smoking status, physical activity (continuous), history of CVD and diabetes, total energy intake and diet quality indices (AHA and HEI-15, continuous), Wald F tests were used to evaluate interaction terms in Model 4 using UPF as a continuous variable. Analyses were stratified according to statistically significant interaction variables. We further performed a sensitivity analysis where we ran all seven models (using UPF as both continuous and quintiles of intake) excluding participants with implausible energy intake (defined as consumption of <800 kcal/d or >4200 kcal/d in men and <500 kcal/d or >3500 kcal/d in women) for either day 1 or 2 as suggested by Banna et al. [39].

Statistical analysis was performed with STATA/SE 16.0 for Windows (StataCorp LLC) using the survey design (svy) and considering the sample weights provided by NHANES

Table 1. Characteristics and measured data from NHANES 2003–2010 participants across quintiles of UPFs intake (*n* = 16 055)

Characteristics	All participants	Quintiles of UPF (% of total energy intake)					*P*-value
		Q1 (0–39.1%)	Q2 (39.2–49.5%)	Q3 (49.6–57.9%)	Q4 (60.0–67.5%)	Q5 (67.6–100%)	
NHANES cycle, *n* (%)							
2003–04	3398 (24.2)	618 (16.2)	760 (22.0)	750 (21.9)	674 (20.5)	596 (19.4)	
2005–06	3446 (24.5)	678 (19.2)	760 (21.8)	703 (20.5)	699 (20.1)	606 (18.4)	
2007–08	4459 (25.4)	888 (17.5)	847 (19.0)	880 (19.7)	892 (20.5)	952 (23.3)	
2009–10	4752 (25.9)	1027 (19.5)	844 (16.6)	878 (18.7)	946 (21.2)	1057 (24.0)	
Chronological age (years)[a]	45.6 (0.3)	47.6 (0.4)	47.2 (0.4)	46.6 (0.4)	45.4 (0.4)	41.7 (0.4)	<0.001
Female, % (SD)[b]	50.7 (0)	48.2 (1.1)	51.2 (1.1)	50.3 (1.0)	51.6 (1.0)	52.0 (1.1)	0.116
Race/Ethnicity, % (SD)[b]							<0.001
Mexican American	8.2 (0.9)	8.4 (1.0)	9.6 (1.1)	9.0 (1.0)	7.9 (0.9)	6.2 (1.0)	
Non-Hispanic White	72.0 (1.6)	63.3 (2.4)	71.9 (1.8)	73.4 (1.6)	74.3 (1.8)	75.8 (1.8)	
Non-Hispanic Black	10.5 (0.8)	9.5 (0.8)	9.1 (0.8)	10.1 (0.9)	11.3 (1.1)	12.5 (1.2)	
Other/Multiracial	9.3 (0.7)	18.8 (1.7)	9.4 (0.9)	7.5 (0.8)	6.5 (0.7)	5.5 (0.6)	
Education, % (SD)[b]							<0.001
Incomplete high school	17.3 (0.7)	20.0 (1.0)	17.2 (1.1)	16.4 (0.9)	16.8 (1.1)	16.5 (0.9)	
High school graduate	24.7 (0.7)	18.8 (1.1)	22.5 (1.4)	24.0 (1.0)	25.9 (0.9)	31.2 (1.4)	
Incomplete college	31.3 (0.5)	28.7 (1.1)	30.0 (1.3)	30.3 (1.1)	34.4 (1.0)	32.7 (1.1)	
College graduate	26.6 (1.0)	32.6 (1.4)	30.2 (1.6)	29.2 (1.4)	22.8 (1.3)	19.5 (1.4)	
Missing	0.1 (0)	0	0.1 (0)	0.1 (0)	0.1 (0)	0.1 (0)	
Poverty-income ratio, % (SD)[b]							<0.001
<1.30	18.7 (0.8)	18.8 (1.0)	15.6 (0.8)	16.6 (0.9)	18.1 (1.1)	23.8 (1.6)	
≥1.30	75.9 (0.9)	75.0 (1.4)	78.8 (0.9)	78.6 (1.1)	75.8 (1.2)	71.6 (1.5)	
Missing	5.4 (0.4)	6.2 (0.7)	5.6 (0.5)	4.8 (0.5)	6.1 (0.7)	4.6 (0.8)	
BMI category, % (SD)[b]							<0.001
≤24.9 kg/m^2	31.2 (0.7)	35.1 (1.4)	31.4 (1.2)	29.0 (1.0)	30.1 (1.2)	30.9 (1.4)	
25–29.9 kg/m^2	32.9 (0.6)	34.0 (1.2)	32.6 (1.1)	35.5 (0.9)	32.5 (1.2)	30.2 (1.5)	
>30 kg/m^2	34.2 (0.7)	29.1 (1.2)	34.1 (1.4)	33.8 (1.3)	35.1 (1.1)	37.9 (1.2)	
Missing	1.7 (0.1)	1.8 (0.4)	1.9 (0.3)	1.7 (0.3)	2.3 (0.3)	1.0 (0.2)	
Smoking status, % (SD)[b]							<0.001
Current smoker	24.5 (0.6)	21.6 (1.2)	22.1 (1.2)	21.9 (1.2)	25.7 (1.1)	30.4 (1.1)	
Non-smoker	50.8 (0.8)	51.2 (1.7)	51.6 (1.3)	52.8 (1.5)	50.2 (1.4)	48.3 (1.3)	
Former smoker	24.7 (0.6)	27.2 (1.3)	26.2 (1.1)	25.2 (1.4)	24.1 (1.1)	21.3 (0.9)	
Missing	0.01 (0.01)	0.02 (0.02)	0.01 (0.01)	0.04 (0.04)	0.04 (0.04)	0	
Physical activity (z-score, min/day)[a]	0.09 (0.01)	0.21 (0.03)	0.10 (0.02)	0.09 (0.03)	0.05 (0.03)	0.03 (0.03)	<0.001
History of CVD, % (SD)[b]	7.3 (0.4)	7.9 (0.7)	7.3 (0.5)	7.2 (0.6)	7.2 (0.6)	7.0 (0.7)	0.964
Missing	0.4 (0.01)	0.4 (0)	0.3 (0.1)	0.3 (0.1)	0.4 (0.2)	0.4 (0.1)	
History of diabetes, % (SD)[b]	9.2 (0.3)	9.1 (0.7)	10.2 (0.6)	9.9 (0.7)	8.9 (0.5)	8.0 (0.6)	0.076
Total energy intake (kcal/day)[a]	2160 (11)	2052 (24)	2159 (22)	2163 (20)	2201 (22)	2211 (20)	<0.001
HEI score[a]	52.7 (0.3)	60.4 (0.4)	56.8 (0.3)	53.4 (0.3)	49.8 (0.3)	44.7 (0.3)	<0.001
AHA score[a]	35.4 (0.3)	42.5 (0.4)	38.5 (0.3)	35.9 (0.4)	32.4 (0.3)	29.0 (0.3)	<0.001
PhenoAge gap (years)[a]	−5.80 (0.07)	−6.50 (0.10)	−6.03 (0.11)	−5.88 (0.10)	−5.54 (0.10)	−5.19 (0.11)	<0.001
Dietary %kcal UPF[a]	54.3 (53.6, 55.1)	30.0 (0.2)	44.5 (0.0)	53.7 (0.0)	62.5 (0.0)	76.7 (0.0)	<0.001

BMI, body mass index; HEI, Healthy Eating Index; AHA, American Heart Association index; UPF, ultra-processed food. Values presented as mean (SD), unless stated otherwise. Comparisons across quintiles were performed using. [a]Linear regression (P-for-trend). [b]Pearson chi-square.

for the first day 24-h recall. A *P*-value at or below 0.05 was considered statistically significant.

Results

Table 1 shows characteristics of the study sample (n = 16 055) and their distribution across quintiles of UPF intake. On average, the participants in this study were 46 years old, and 51% were females. The mean %kcal UPF was 54.3% for the overall study population, ranging from 30.0% in the first quintile of intake (Q1) to 76.7% in the fifth quintile (Q5). Younger, Non-Hispanic White and Non-Hispanic Black, non-college graduates, lower income, current smokers, less-physically active participants tended to be concentrated among the highest quintiles of UPF intake. Overall, 34% of the study population was classified as having obesity, with increasing rates across the UPF intake quintiles. The study population presented similar demographic characteristics when compared with the 2003–2010 NHANES population at the same age bracket who completed at least the first of two 24 h dietary recalls (Table S2).

Table 2. Association between UPF intake (% of total energy intake) and PhenoAge gap and in US adults from NHANES 2003–2010 (*n* = 16 055)

	Quintiles of UPF (% of total energy intake)						UPF (% of total energy intake)	
	β (95% CI)					P-trend	β (95% CI)[a]	P-value
	Q1	**Q2**	**Q3**	**Q4**	**Q5**			
Model 1	-	0.48 (0.23, 0.73)	0.63 (0.33, 0.90)	1.03 (0.76, 1.30)	1.44 (1.14, 1.75)	<0.001	0.33 (0.27, 0.38)	<0.001
Model 2	-	0.47 (0.23, 0.72)	0.60 (0.34, 0.86)	0.90 (0.64, 1.16)	1.21 (0.91, 1.51)	<0.001	0.28 (0.22, 0.33)	<0.001
Model 3	-	0.46 (0.22, 0.70)	0.60 (0.34, 0.85)	0.86 (0.58, 1.13)	1.14 (0.84, 1.44)	<0.001	0.26 (0.20, 0.31)	<0.001
Model 4		0.32 (0.07, 0.56)	0.44 (0.21, 0.67)	0.71 (0.44, 0.98)	0.90 (0.60, 1.20)	<0.001	0.21 (0.16, 0.26)	<0.001
Model 5	-	0.31 (0.07, 0.56)	0.44 (0.21, 0.67)	0.70 (0.43, 0.98)	0.90 (0.60, 1.20)	<0.001	0.21 (0.16, 0.26)	<0.001
Model 6	-	0.21 (−0.04, 0.46)	0.26 (0.03, 0.50)	0.45 (0.18, 0.71)	0.57 (0.26, 0.88)	<0.001	0.14 (0.09, 0.20)	<0.001
Model 7	-	0.24 (−0.01, 0.49)	0.28 (0.05, 0.52)	0.48 (0.20, 0.75)	0.57 (0.24, 0.89)	<0.001	0.14 (0.09, 0.20)	<0.001

Model 1: adjusted for NHANES cycle, chronological age and gender Model 2: adjusted for NHANES cycle, chronological age, gender, ethnicity, education and poverty-income ratio Model 3: adjusted for NHANES cycle, chronological age, gender, ethnicity, education, poverty-income ratio, physical activity and smoking status Model 4: adjusted for NHANES cycle, chronological age, gender, ethnicity, education, poverty-income ratio, physical activity, smoking status, BMI, history of CVD and diabetes Model 5: adjusted for NHANES cycle, chronological age, gender, ethnicity, education, poverty-income ratio, physical activity, smoking status, BMI, history of CVD and diabetes, and energy intake Model 6: adjusted for NHANES cycle, chronological age, gender, ethnicity, education, poverty-income ratio, physical activity, smoking status, BMI, history of CVD and diabetes, and AHA diet score Model 7: adjusted for NHANES cycle, chronological age, gender, ethnicity, education, poverty-income ratio, physical activity, smoking status, BMI, history of CVD and diabetes, and HEI-15 diet score. [a]Presented for 10% increase in UPF intake (as % kcal).

There was a significant linear decrease in diet quality (assessed as HEI-15 and AHA scores) across the UPF intake quintiles. On the other hand, there was a significant linear increase in total energy intake and PhenoAge gap across the UPF intake quintiles. No differences regarding gender, history of CVD or diabetes were observed across UPF intake quintiles (Table 1).

The analysis revealed little evidence of non-linearity in the restricted cubic spline model (coefficient for linear term = 0.02 (95% CI 0.00, 0.04); Wald test for linear term *P*-value = 0.046; Wald test for all non-linear terms *P*-value = 0.550). Quintiles of UPF intake were positively associated with PhenoAge gap in all the adjusted models (P-for-trend ≤ 0.001), indicating accelerated biological ageing as UPF intake increased (Table 2). Based on the fully adjusted model (model 4), we observed that the highest UPF quintile presented a 0.9 (95% CI 0.60, 1.20) higher absolute PhenoAge gap compared to the lowest quintile, while a 0.21 (95% CI 0.16, 0.26) increase in PhenoAge gap was observed for every 10% increase in UPF intake (Table 2).

We further identified that adherence to a healthy diet, as indicated by higher AHA and HEI-15 scores, was associated with lower PhenoAge gap, while total energy intake had no association with PhenoAge gap (Table S3). Further adjustment for energy intake (model 5) resulted in no differences in the effect sizes between UPF and PhenoAge gap. Adherence to a healthy diet, assessed by both AHA and HEI-15 scores, attenuated the relationship between UPF and PhenoAge gap (from 0.21 to 0.14 years, models 6 and 7), although the association remained significant after adjusting for each of these two indicators of diet quality (Table 2).

Our analysis revealed no interaction of UPF intake with gender, BMI, physical activity, smoking status, history of CVD, diabetes, total energy intake and the two diet quality scores (HEI-15 and AHA) (Table S4).

However, we observed an interaction between UPF intake and chronological age. Our stratified analysis by age group (20–39, 40–59 and ≥60 years) indicates a somewhat stronger association between UPF intake and PhenoAge gap among the ≥60-year-old group (Table 3). We further performed a sensitivity analysis excluding those with potential implausible energy intake. The results were based on data from 13 881 participants and did not meaningfully differ from those observed in the main analyses (Table S5).

Discussion

In this analysis of a representative sample of US adults, we identified that UPF intake is associated with older biological age assessed by PhenoAge. Although lower diet quality, as assessed by standard indices, may partly explain the association between UPF intake and biological ageing, other mechanisms associated with food processing are also likely involved. Our results support earlier research linking UPF consumption to ageing markers such as telomere length [40], frailty [41], cognitive decline [42] and dementia [43]. Given the global demographic shift towards an ageing population, demonstrating UPF's adverse effects reinforces the need for dietary-focused public health strategies to prolong a healthy life span.

This analysis showed that for every 10% increase in UPF consumption, there is a 2.4-month increase in the gap between biological and chronological age, evidence that UPF intake may accelerate biological ageing. If we assume a standard diet of 2000 kcal/day, adding an extra 200 calories of UPF daily (roughly equivalent to an 80 g serving of chicken bites or a small chocolate bar) could lead to the biological ageing process advancing by >2 months compared

Table 3. Association between quintiles of UPF intake (% of total energy intake) and PhenoAge gap by age group in US adults from NHANES 2003–2010 (n = 16 055)

| | Quintiles of UPF (% of total energy intake) | | | | | | UPF (% of total energy intake) | |
| | β (95% CI) | | | | | P-trend | β (95% CI)[a] | P-value |
	Q1	Q2	Q3	Q4	Q5			
20–39 years	-	0.46 (0.05, 0.88)	0.60 (0.21, 0.99)	0.69 (0.22, 1.16)	1.00 (0.55, 1.46)	<0.001	0.20 (0.12, 0.28)	<0.001
40–59 years	-	0.02 (−0.40, 0.43)	0.18 (−0.17, 0.52)	0.52 (0.14, 0.90)	0.64 (0.22, 1.07)	<0.001	0.19 (0.12, 0.27)	<0.001
≥ 60 years	-	0.64 (0.19, 1.10)	0.70 (0.25, 1.14)	0.97 (0.54, 1.40)	1.00 (0.52, 1.48)	<0.001	0.23 (0.14, 0.33)	<0.001

Models adjusted for NHANES cycle, chronological age, gender, ethnicity, education, poverty-income ratio, physical activity, smoking status, BMI, history of CVD and diabetes 20–39 years: n = 5632; 40–59 years: n = 5620; ≥ 60 years: n = 4803. [a]Presented for 10% increase in UPF intake (as % kcal).

to chronological ageing. Despite a seemingly small effect size, it holds significant public health implications. Based on previous research on PhenoAge's links to morbidity, disability and mortality [32], this rise predicts nearly 2% more mortality, 0.75% more incident disability and 0.5% more incident chronic disease over 2 years. The association between UPF and PhenoAge gap was to some extent stronger in older adults, which highlights the potential role of nutrition in promoting healthy ageing and preventing age-related diseases.

The association between UPF intake and biological ageing remained significant after adjusting for diet quality and total energy intake, suggesting that other factors such as lower flavonoid or phytoestrogen intake [44, 45], or higher content of package materials such as bisphenol or phthalates [46] or compounds formed during processing such as acrylamides [47] might also explain the association [16]. Previous research indicates that caloric restriction slows biological ageing [36] and increases healthy lifespan [48, 49]. While we found an association between UPF and energy intake (as reported in previous research [50], our findings indicate caloric intake does not affect the link between UPF intake and biological ageing.

Our results extend an earlier observation in a Spanish cohort linking high UPF intake with shorter leukocyte telomere length, a candidate biomarker of ageing [40]. Several dietary guidelines advocate for limiting UPF intake [51] due to their connection with over 30 adverse health outcomes [20], and our findings provide another reason to target UPF consumption to promote healthier ageing.

We acknowledge limitations. There is no gold standard for assessing biological ageing. We focused on PhenoAge based on its predictive value for ageing-related health outcomes and sensitivity to nutritional exposure [29, 30, 32, 52]. Dietary intake was assessed using self-reported 24-hour recalls, the least biased self-report instrument available [53]. We employed a standardised system to classify foods, but NHANES data may lack brand-specific details crucial for accurate classification, as it focuses on nutrient concentrations rather than food processing [26, 54]. Social desirability bias may lead to UPF underreporting, while food intake estimates may not reflect the usual diet, potentially biasing associations towards null. Furthermore, despite standardised NHANES methods [55–57], previous research indicates that over 25% of energy intake may be misreported [58]. However, our sensitivity analysis revealed no impact of misreporting on results, as effect sizes remained similar when excluding individuals with extreme energy intake. Our study focused on ages 20–79 due to NHANES design, limiting findings' extrapolation to younger and older populations. The cross-sectional design of this study limits causal inference due to the lack of event temporality and residual confounding. Thus longitudinal studies tracking diet and lifestyle changes are needed to solidify our findings. Additionally, given prior research linking UPF intake to mortality, investigating biological ageing as a potential mediator of the association is recommended.

Conclusions

Intake of UPF was associated with older biological age in US adults aged 20 to 79 years. Adherence to a healthy diet explained only part of the association of UPF intake with older biological age, suggesting that other properties of UPF related to processing may contribute to an acceleration of biological processes of ageing.

References

1. United Nations, Department of Economic and Social Affairs, Population Division. *World Population Prospects 2022: Ten Key Messages*. 2022, New York: United Nations. https://doi.org/10.18356/9789210014380.

2. Scott AJ. The longevity economy. *Lancet Healthy Longev*. 2021;**2**:e828–35.

3. World Health Organization. *Progress Report on the United Nations Decade of Healthy Ageing, 2021–2023*. Geneva: World Health Organization, 2023.

4. Kennedy BK, Berger SL, Brunet A *et al.* Geroscience: linking aging to chronic disease. *Cell*. 2014;**159**:709–13.

5. López-Otín C, Blasco MA, Partridge L *et al.* The hallmarks of aging. *Cell*. 2013;**153**:1194–217.

6. López-Otín C, Blasco MA, Partridge L *et al.* Hallmarks of aging: an expanding universe. *Cell*. 2023;**186**:243–78.

7. Campisi J, Kapahi P, Lithgow GJ *et al.* From discoveries in ageing research to therapeutics for healthy ageing. *Nature*. 2019;**571**:183–92.

8. Kaeberlein M, Rabinovitch PS, Martin GM. Healthy aging: the ultimate preventative medicine. *Science*. 2015;**350**:1191–3.

9. Barzilai N, Cuervo AM, Austad S. Aging as a biological target for prevention and therapy. *JAMA*. 2018;**320**:1321–2.

10. Belsky DW, Baccarelli AA. To promote healthy aging, focus on the environment. *Nat Aging*. 2023;**3**:1334–44.

11. Al-Naggar IM, Newman JC, Kuchel GA. Healthy eating patterns: a stealthy geroscience-guided approach to enhancing the human healthspan. *J Nutr Health Aging*. 2023;**27**:238–9.

12. Wang S, Li W, Li S *et al.* Association between plant-based dietary pattern and biological aging trajectory in a large prospective cohort. *BMC Med*. 2023;**21**:310.

13. Thomas A, Belsky DW, Gu Y. Healthy lifestyle behaviors and biological aging in the U.S. National Health and Nutrition Examination Surveys 1999-2018. *J Gerontol A Biol Sci Med Sci*. 2023;**78**:1535–42.

14. Thomas A, Ryan CP, Caspi A *et al.* Diet, pace of biological aging, and risk of dementia in the Framingham Heart Study. *Ann Neurol*. 2024;**95**:1069–79.

15. Gensous N, Garagnani P, Santoro A *et al.* One-year Mediterranean diet promotes epigenetic rejuvenation with country- and sex-specific effects: a pilot study from the NU-AGE project. *Geroscience*. 2020;**42**:687–701.

16. Dicken SJ, Batterham RL. The role of diet quality in mediating the association between ultra-processed food intake, obesity and health-related outcomes: a review of prospective cohort studies. *Nutrients*. 2022;**14**:23.

17. Monteiro CA, Cannon G, Levy RB *et al.* Ultra-processed foods: what they are and how to identify them. *Public Health Nutr*. 2019;**22**:936–41.

18. Srour B, Kordahi MC, Bonazzi E *et al.* Ultra-processed foods and human health: from epidemiological evidence to mechanistic insights. *Lancet Gastroenterol Hepatol*. 2022;**7**: 1128–40.

19. Baker P, Machado P, Santos T *et al.* Ultra-processed foods and the nutrition transition: global, regional and national trends, food systems transformations and political economy drivers. *Obes Rev*. 2020;**21**:e13126.

20. Lane MM, Gamage E, Du S *et al.* Ultra-processed food exposure and adverse health outcomes: umbrella review of epidemiological meta-analyses. *BMJ*. 2024;**384**:e077310.

21. Lloyd-Jones DM, Hong Y, Labarthe D *et al.* Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;**121**:586–613.

22. Krebs-Smith SM, Pannucci TE, Subar AF *et al.* Update of the Healthy Eating Index: HEI-2015. *J Acad Nutr Diet*. 2018;**118**:1591–602.

23. Reedy J, Lerman JL, Krebs-Smith SM *et al.* Evaluation of the Healthy Eating Index-2015. *J Acad Nutr Diet*. 2018;**118**:1622–33.

24. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). *National Health and Nutrition Examination Survey Questionnaire. MEC In-Person Dietary Interviewers Procedures Manual*. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. March, 2010.

25. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). *National Health and Nutrition Examination Survey (NHANES). Phone Follow-Up Dietary Interviewer Procedures Manual*. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. March, 2001.

26. Steele EM, O'Connor LE, Juul F *et al.* Identifying and estimating ultraprocessed food intake in the US NHANES according to the Nova classification system of food processing. *J Nutr*. 2023;**153**:225–41.

27. Ferrucci L, Gonzalez-Freire M, Fabbri E *et al.* Measuring biological aging in humans: a quest. *Aging Cell*. 2020;**19**:e13080.

28. Levine ME, Lu AT, Quach A *et al.* An epigenetic biomarker of aging for lifespan and healthspan. *Aging (Albany NY)*. 2018;**10**:573–91.

29. Liu Z, Kuo PL, Horvath S *et al.* A new aging measure captures morbidity and mortality risk across diverse subpopulations from NHANES IV: a cohort study. *PLoS Med*. 2018;**15**:e1002718.

30. Hastings WJ, Shalev I, Belsky DW. Comparability of biological aging measures in the National Health and Nutrition Examination Study, 1999-2002. *Psychoneuroendocrinology*. 2019;**106**:171–8.

31. Parker DC, Bartlett BN, Cohen HJ *et al.* Association of blood chemistry quantifications of biological aging with disability and mortality in older adults. *J Gerontol A Biol Sci Med Sci*. 2019;**75**:1671–9.

32. Graf GH, Crowe CL, Kothari M *et al.* Testing black-white disparities in biological aging among older adults in the United States: analysis of DNA-methylation and blood-chemistry methods. *Am J Epidemiol*. 2022;**191**: 613–25.

33. Graf GH, Zhang Y, Domingue BW *et al.* Social mobility and biological aging among older adults in the United States. *PNAS Nexus*. 2022;**1**:1–10.

34. Cao X, Zhang J, Ma C *et al.* Life course traumas and cardiovascular disease-the mediating role of accelerated aging. *Ann N Y Acad Sci*. 2022;**1515**:208–18.

35. Yang G, Cao X, Li X *et al.* Association of unhealthy lifestyle and childhood adversity with acceleration of aging among UK biobank participants. *JAMA Netw Open*. 2022;**5**: e2230690.

36. Kwon D, Belsky DW. A toolkit for quantification of biological age from blood chemistry and organ function test data: BioAge. *Geroscience*. 2021;**43**:2795–808.

37. Flanagan EW, Most J, Mey JT *et al.* Calorie restriction and aging in humans. *Annu Rev Nutr*. 2020;**40**:105–33.

38. Harrell F. *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis*. New York: Springer, 2001. https://doi.org/10.1007/978-1-4757-3462-1.

39. Banna JC, McCrory MA, Fialkowski MK *et al.* Examining plausibility of self-reported energy intake data: considerations for method selection. *Front Nutr*. 2017;**4**:45.

40. Alonso-Pedrero L, Ojeda-Rodríguez A, Martínez-González MA *et al.* Ultra-processed food consumption and the risk of short telomeres in an elderly population of the Seguimiento Universidad de Navarra (SUN) project. *Am J Clin Nutr*. 2020;**111**:1259–66.

41. Sandoval-Insausti H, Blanco-Rojo R, Graciani A *et al.* Ultra-processed food consumption and incident frailty: a prospective cohort study of older adults. *J Gerontol A Biol Sci Med Sci*. 2020;**75**:1126–33.

42. Cardoso BR, Machado P, Steele EM. Association between ultra-processed food consumption and cognitive performance in US older adults: a cross-sectional analysis of the NHANES 2011-2014. *Eur J Nutr*. 2022;**61**:3975–85.

43. Li H, Li S, Yang H *et al.* Association of ultraprocessed food consumption with risk of dementia: a prospective cohort study. *Neurology*. 2022;**99**:e1056–66.

44. Leitão AE, Roschel H, Oliveira-Júnior G *et al.* Association between ultra-processed food and flavonoid intakes in a nationally representative sample of the US population. *Br J Nutr*. 2024;**131**:1074–83.

45. Martínez, Steele E, Monteiro CA. Association between dietary share of ultra-processed foods and urinary concentrations of phytoestrogens in the US. *Nutrients*. 2017;**9**:1–15.

46. Martínez Steele E, Khandpur N, da Costa Louzada ML *et al.* Association between dietary contribution of ultra-processed foods and urinary concentrations of phthalates and bisphenol in a nationally representative sample of the US population aged 6 years and older. *PloS One*. 2020;**15**:1–21.

47. Martínez Steele E, Buckley JP, Monteiro CA. Ultra-processed food consumption and exposure to acrylamide in a nationally representative sample of the US population aged 6 years and older. *Prev Med*. 2023;**174**:107598.

48. Waziry R, Ryan CP, Corcoran DL *et al.* Effect of long-term caloric restriction on DNA methylation measures of biological aging in healthy adults from the CALERIE trial. *Nature Aging*. 2023;**3**:248–57.

49. Kraus WE, Bhapkar M, Huffman KM *et al.* 2 years of calorie restriction and cardiometabolic risk (CALERIE): exploratory outcomes of a multicentre, phase 2, randomised controlled trial. *Lancet Diabetes Endocrinol*. 2019;**7**:673–83.

50. Hall KD, Ayuketah A, Brychta R *et al.* Ultra-processed diets cause excess calorie intake and weight gain: an inpatient randomized controlled trial of ad libitum food intake. *Cell Metab*. 2019;**30**:67–77.e3.

51. Koios D, Machado P, Lacy-Nichols J. Representations of ultra-processed foods: a global analysis of how dietary guidelines refer to levels of food processing. *Int J Health Policy Manag*. 2022;**11**:2588–99.

52. Belsky DW, Moffitt TE, Cohen AA *et al.* Eleven telomere, epigenetic clock, and biomarker-composite quantifications of biological aging: do they measure the same thing? *Am J Epidemiol*. 2018;**187**:1220–30.

53. Prentice RL, Mossavar-Rahmani Y, Huang Y *et al.* Evaluation and comparison of food records, recalls, and frequencies for energy and protein assessment by using recovery biomarkers. *Am J Epidemiol*. 2011;**174**:591–603.

54. Slining MM, Yoon EF, Davis J *et al.* An approach to monitor food and nutrition from "factory to fork". *J Acad Nutr Diet*. 2015;**115**:40–9.

55. Blanton CA, Moshfegh AJ, Baer DJ *et al.* The USDA automated multiple-pass method accurately estimates group total energy and nutrient intake. *J Nutr*. 2006;**136**:2594–9.

56. Moshfegh AJ, Rhodes DG, Baer DJ *et al.* The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *Am J Clin Nutr*. 2008;**88**:324–32.

57. Rumpler WV, Kramer M, Rhodes DG *et al.* Identifying sources of reporting error using measured food intake. *Eur J Clin Nutr*. 2008;**62**:544–52.

58. Murakami K, Livingstone MBE. Prevalence and characteristics of misreporting of energy intake in US adults: NHANES 2003–2012. *Br J Nutr*. 2015;**114**:1294–303.