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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

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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		Quintiles of UPF (% of total energy intake)					
	All participants	Q1 (0–39.1%)	Q2 (39.2–49.5%)	Q3 (49.6–57.9%)	Q4 (60.0–67.5%)	Q5 (67.6–100%)	*P*-value
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 $\leq$ 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 $\geq$60 years) indicates a somewhat stronger association between UPF intake and PhenoAge gap among the $\geq$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.

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Supplementary Data: Supplementary data are available at *Age and Ageing* online.

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