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# Spicy food consumption and biological aging across multiple organ systems: a longitudinal analysis from the China Multi-Ethnic cohort

Ning Zhang<sup>1</sup>, Feng Hong<sup>2</sup>, Yi Xiang<sup>1</sup>, Yuan Zhang<sup>1</sup>, Wen Qian<sup>3</sup>, Xuehui Zhang<sup>4</sup>, Liling Chen<sup>5</sup>, Zhuoma Duoji<sup>6</sup>, Xiong Xiao<sup>1</sup>\* and Xing Zhao<sup>1</sup>

#### **Abstract**

**Background** Biological aging is a common starting point for many chronic diseases and multimorbidity. Spicy food consumption is showing a growing trend worldwide. However, the association of spicy food consumption with the comprehensive biological age (BA) and organ-specific BAs remains unclear.

**Methods** This study included 7874 participants from the China Multi-Ethnic Cohort (CMEC), all participating in baseline and follow-up surveys. The CMEC was located in Southwest China, which has become one of the most prominent and typical regions regarding spicy food consumption in China and the world. We constructed comprehensive BA and organ-specific BAs based on composite indicators using the widely validated Klemera-Doubal method. The frequency of intake of spicy food was obtained by an electronic questionnaire. Follow-up analyses adjusted for baseline data were then employed to assess the longitudinal associations of spicy food consumption at baseline with both the comprehensive BA and the organ-specific BAs at follow-up.

**Results** Compared with non-spicy consumers, spicy consumers showed a decrease in comprehensive BA acceleration, with adjusted  $\beta = -0.23$  (-0.60 to 0.13) for 1-2 days/week,  $\beta = -0.69$  (-1.10 to -0.29) for 3-5 days/week and -0.32 (-0.63 to -0.01) years for 6-7 days/week, respectively. Higher estimates were observed for metabolic and kidney BA accelerations than for cardiopulmonary and liver BA accelerations. Compared to non-spicy consumers, spicy consumers showed a decrease in metabolic BA acceleration (3-5 days/week:  $\beta = -0.76$  (-1.28 to -0.24) years) and kidney BA acceleration (3-5 days/week:  $\beta = -1.89$  (-2.76 to -1.02) years).

**Conclusion** Spicy foods may have potential benefits for biological aging. Our findings highlight that spicy foods may slow comprehensive and organ-specific biological aging, especially metabolic and kidney biological aging.

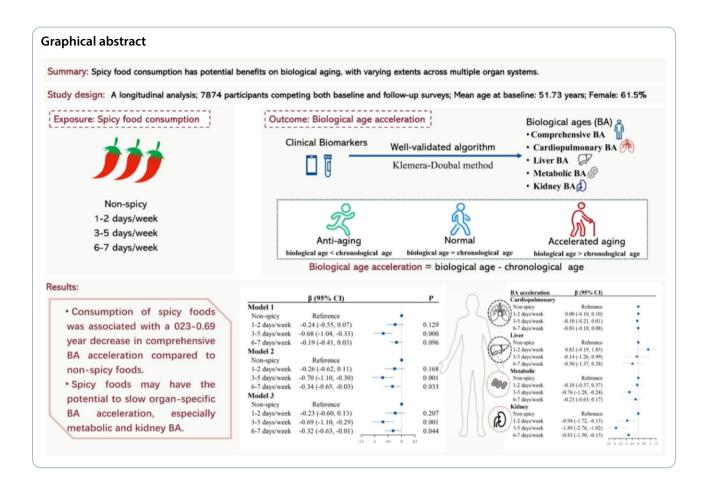
**Keywords** Spicy food, Biological aging, Biological age of multiple organ systems, Follow-up analyses adjusted for baseline

\*Correspondence: Xiong Xiao xiaoxiong.scu@scu.edu.cn

Full list of author information is available at the end of the article



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# Introduction

Aging is a common starting point for many chronic diseases and multimorbidity, which is a complicated multisystem process [1-6]. The aging process does not always approach steadily and chronologically, although chronological age (time since birth) is a widely used indicator of aging [1-6]. Individuals of the same chronological age always age at different rates (accelerated aging or decelerated aging), and there are even differences in the rate of aging of different organ systems within an individual [3, 4, 7]. Biological age (BA) is a more accurate descriptor of aging and a better predictor of aging-related morbidity and mortality than chronological age [3-5]. More importantly, in contrast to chronological age (a fixed course), BA is influenced by genetic and environmental exposures and can be modified through medications, lifestyle, etc [3, 4]. Consequently, in the context of a rapidly aging population, searching for effective modifiable factors to slow down or prevent biological aging and aging acceleration would hold significant potential for clinical and public health applications.

Spices are widely used for flavoring, coloring, preserving food, and medicinal purposes [8]. Spicy food (defined mainly by chili pepper content) is an integral part of culinary culture, and its consumption is growing worldwide

[8–10]. Previous population and animal studies have demonstrated the beneficial effects of spicy foods and their bioactive substances, such as capsaicin, in obesity, gastrointestinal disorders, cardiovascular disease, Alzheimer's disease, and cancer [8, 11–13]. In addition, existing studies suggest that capsaicin in spicy foods improves chronic inflammation, dysbiosis, and other hallmarks of aging [14–17]. Therefore, it is plausible to hypothesize that spicy food intake may slow down the biological aging process in humans.

BA measures based on composite biomarkers that reflect the landscape of aging in multiple organs and systems are already available [18, 19]. Compared to other measures (e.g., telomere length and epigenetic clocks), composite biomarker BA (e.g., Klemera-Doubal Method BA) is cost-effective while ensuring measurement accuracy, making them feasible for large population research and daily practice [20, 21]. However, there is still a lack of population-based evidence linking the consumption of spicy foods with accelerated BA. In addition, given that different organ systems within an individual age at different rates [7], there is also a lack of studies that examine the association between spicy food consumption and BAs across multiple organ systems, which could inform

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targeted interventions for aging-related diseases in each organ system.

The China Multi-Ethnic Cohort (CMEC) study, a large epidemiological study conducted in southwest China [22], provides a unique opportunity to investigate the association between spicy food and biological aging. More than half of the residents of Southwest China consume spicy food daily, and the region has become one of the most prominent and typical regions in China and the world concerning spicy food consumption [10, 22]. Therefore, we conducted a longitudinal study based on baseline and follow-up data from the CMEC. We first constructed comprehensive BA and organ-specific BAs based on composite indicators using the widely validated Klemera-Doubal method [19–21]. Follow-up analyses adjusted for baseline data were then employed to assess the longitudinal associations of spicy food consumption at baseline with both the comprehensive BA and the organ-specific BAs at follow-up.

# Methods

# **Study participants**

The CMEC is a prospective cohort study conducted in Southwest China. The baseline survey was conducted between May 2018 and September 2019 and included 99,556 participants aged 18 to 79 years [22]. The first follow-up survey was conducted between August 2020

and July 2021 and involved approximately 10% of the baseline participants, drawn from a cluster random sample of the baseline participants [20, 21]. In both surveys, participants were required to complete a touch-screen questionnaire (including spicy food consumption, etc.) based on face-to-face interviews, medical examinations, and clinical laboratory tests. All participants gave written informed consent before data collection. The CMEC was approved by the Sichuan University Medical Ethical Review Board and local ethics committees at each participating site.

Participants who participated in baseline and repeat surveys (n = 11,301) were included in the present study. We focused on adults aged 30-80 years. Tibetans have unique and substantially different dietary habits compared to Han and other ethnic minority groups, including high consumption of butter tea, and Zanba. Moreover, Tibetans predominantly reside in high-altitude regions (typically > 3,500 m above sea level), characterized by hypoxia, low atmospheric pressure, and extreme cold. These environmental factors may independently affect biological aging and interact with spicy food in ways. Thus, Tibetan participants were excluded from the study. We excluded participants who lacked complete data for BA construction in either survey and who missed data on spicy food and selected covariates at baseline. Finally, the current analysis included 7,874 participants. See Fig. 1

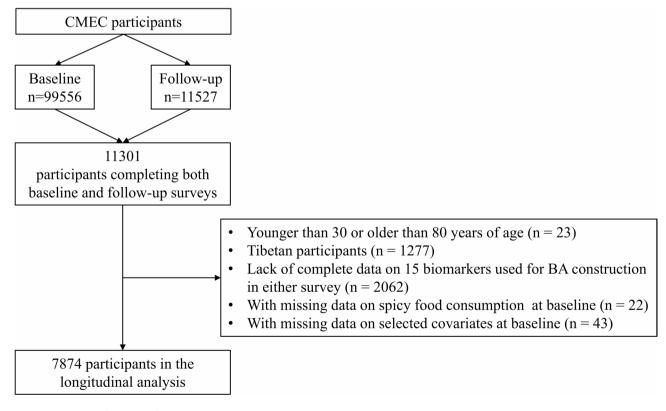


Fig. 1 The selection flow chart of the participants in this study

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for the flowchart of participants. Missing information on covariates is shown in Appendix Table S1.

# Construction of comprehensive and organ-specific BA accelerations

We constructed comprehensive BA and organ-specific BAs based on composite indicators in the baseline and follow-up survey of CMEC using the Klemera-Doubal method (KDM), which has been validated in Chinese and European populations [19-21, 23]. Our previous studies have described in detail the construction of comprehensive and organ-specific BAs based on the CMEC data [20, 21, 24]. We have performed validation analyses of constructed composite and organ-specific BAs in previous studies, and the results indicated that the composite and organ-specific BAs constructed in the CMEC had been validated to reflect frailty and age-related disease well. More details can be found in our previous studies [20, 21, 24]. As previously reported [20, 21, 24, 25], we calculated BA acceleration by subtracting chronological age (CA) from BA to account for the effect of CA. A positive value indicates faster aging and a negative value suggests slower aging. The BA accelerations were the primary target exposures for analysis.

Briefly, we first selected the indicators for constructing BA by considering a combination of the following aspects, including the function of the indicator in the aging process, reporting of previous literature, accessibility of CMEC data, and correlation with CA. Then, 43 biomarkers were selected. For each selected biomarker, we performed a Box-Cox transformation for data normalization and then retained biomarkers with a correlation coefficient|r|>0.1 with CA. For biomarkers reflecting the same health information, only one was retained based on the available knowledge and the correlation between them. Finally, the comprehensive BA incorporated 15 biomarkers: systolic blood pressure, waist-to-hip ratio, peak expiratory flow, gamma-glutamyl transpeptidase, albumin, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, aspartate aminotransferase, creatinine, alkaline phosphatase, urea, mean corpuscular volume, glycosylated hemoglobin, and platelet count. For organ-specific BAs, these selected biomarkers were further categorized into four systems based on the organ/system function they represent [24]. The cardiopulmonary BA included systolic blood pressure and peak expiratory flow; the metabolic BA included low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, glycosylated hemoglobin, triglyceride, and waist-to-hip ratio; the liver BA included aspartate aminotransferase, gamma-glutamyl transpeptidase, alkaline phosphatase, albumin; and the kidney BA included creatinine and urea.

Comprehensive BA and organ-specific BAs were calculated separately according to the established function, which models a series of regressions of these selected biomarkers on CA and indicates the predicted physiologic age at the individual level [19–21, 24]. Given the recognized differences in the aging process, we implemented sex stratification and computed BAs separately [19–21, 24]. See Appendix Text S1 for details on constructing comprehensive and organ-specific BA accelerations.

# Assessment of spicy food consumption

As with the China Kadoorie Biobank study [8], spicy food intake refers to the consumption of any "hot" spices while cooking or eating, including fresh/dried chili peppers, chili sauce, chili oil, or other chili-containing spices. Other pungent spices not derived from chili-such as Sichuan pepper, black pepper, and turmeric—were not included in this definition. In the baseline questionnaire, we asked the participants, "During the past month, how often did you eat hot, spicy foods?": never or rarely, only occasionally, 1-2 days/week, 3-5 days/week, or 6-7 days/week. Participants who consumed spicy food at least once per week (regular consumers) were asked to provide additional information on the strength of the spice preferred (weak, moderate, strong). Non-spicy consumers (never or rarely, only occasionally) were the reference group in this study.

#### Assessment of covariates

Covariate information was obtained through the baseline questionnaire, including sociodemographic characteristics (age, sex, ethnic group, urbanicity, highest education attained, and marital status), lifestyle behaviors (regular smoking, frequency of alcohol consumption, physical activity in metabolic equivalent tasks per day (METs-h/ day), healthy diet, and strength of the spice preferred), and self-reported physician-diagnosed chronic diseases (cancer, cardiovascular disease (CVD), diabetes and chronic obstructive pulmonary disease (COPD)). Habitual dietary intake in the past year was assessed using a qualitative food frequency questionnaire. A healthy diet was assessed using the Dietary Approaches to Stop Hypertension (DASH) score, which has been reported to reduce cardiometabolic risk in our previous studies [10, 24].

#### Statistical analysis

We used means (standard deviations) or frequencies (proportions) for continuous or categorical variables, respectively, to describe the characteristics of participants across the four frequency levels of spicy food consumption. In addition, we described the baseline characteristics of the participants in this study versus the

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CMEC overall participants to assess the representativeness of this study population.

First, to examine the association between baseline spicy food consumption and the follow-up comprehensive BA acceleration, we constructed follow-up adjusted for baseline analysis using multiple linear regression model, with non-spicy as the reference group. Model 1 was adjusted for age, sex, ethnic group, and baseline comprehensive BA acceleration. Model 2 was additionally adjusted for other sociodemographic characteristics (urbanicity, highest education attained, and marital status) and lifestyle behaviors (regular smoking, frequency of alcohol consumption, physical activity, healthy diet, and strength of the spice preferred). Model 3 was further adjusted for self-reported physician-diagnosed chronic diseases (cancer, CVD, diabetes, and COPD). In addition, we performed the same analyses to assess the association of spicy consumption at baseline with each organ-specific BA acceleration at follow-up (i.e., cardiopulmonary, metabolic, liver, and kidney).

To examine potential effect modifiers, we conducted stratification analysis among predefined subgroups, including age, sex, ethnic group, healthy diet score, and strength of the spice preferred among regular spicy consumers. To assess the robustness of our findings, we also performed several sensitivity analyses. First, we used a more stringent exclusion criterion by excluding selfreported physicians diagnosed with chronic diseases. Second, we adjusted for a healthy diet by replacing the DASH with the Mediterranean diet for the assessment. Third, we alternatively adjusted for BMI as a covariate. Fourth, we additionally adjusted chronic kidney disease, as well as chronic hepatitis and liver cirrhosis in the sensitivity analysis to further verify the robustness of our results, although our main analysis has adjusted the most common self-reported health conditions in the study participants. Finally, to reduce the risk of bias and model misspecification, we used targeted learning [26] to estimate the association between spicy food consumption at baseline and BA acceleration at follow-up. Targeted learning is a causal inference methodology that incorporates the benefits of machine learning with statistical inference and can provide consistent, doubly robust estimates [26, 27]. All statistical analyses were conducted using R version 4.4.1.

#### Results

# Characteristics of the participants

Table 1 shows the baseline characteristics of the CMEC participants according to the level of spicy food consumption. Among 7874 participants, the mean age was 51.73 (SD 10.80) years, 4844 (61.5%) participants were male, and 5115 (65.0%) were Han Chinese. Consumers of spicy food were more likely to be young. Consumers of

spicy food, but less frequently than 6–7 days/week, were more likely to be Han Chinese, urban residents, highly educated, to have a healthier diet, and to have a high level of BA acceleration. In addition, the participants in this study had similar baseline characteristics to the CMEC baseline participants (see Appendix Table S2).

# Associations of spicy food consumption with comprehensive BA acceleration

Figure 2 shows the estimated associations of baseline spicy food consumption with comprehensive BA acceleration. Similar results were observed across the three models. Compared with non-spicy consumers, spicy consumers showed a decrease in comprehensive BA acceleration. Compared with non-spicy consumers, 1–2 days/week spicy consumers showed a trend towards a decrease in comprehensive BA acceleration, with  $\beta$  = –0.23 (95% CI: –0.60 to 0.13) years. Compared with non-spicy consumers, 3–5 days/week spicy consumers showed a decrease in comprehensive BA acceleration, with  $\beta$  = –0.32 (95% CI: –1.10 to –0.29) years. Compared with non-spicy consumers, 6–7 days/week spicy consumers showed a decrease in comprehensive BA acceleration, with  $\beta$  = –0.32 (95% CI: –0.63 to –0.01) years.

# Associations of spicy food consumption with organspecific BA accelerations

Figure 3 shows the estimated associations of spicy food consumption with each organ-specific BA acceleration. Spicy food intake showed varying degrees of associations with organ-specific BA accelerations, although some results were not statistically significant. Model 1, Model 2, and Model 3 showed similar results. The results for Models 1 and 2 are shown in Appendix Table S3. Higher estimates were observed for metabolic BA acceleration and kidney BA acceleration than for cardiopulmonary BA acceleration and liver BA acceleration. Compared with non-spicy consumers, spicy consumers showed a decrease in metabolic BA acceleration (3–5 days/week:  $\beta = -0.76$ , 95% CI -1.28 to -0.24; 6-7 days/week:  $\beta$ = -0.23, 95% CI -0.63 to 0.17 years) and in kidney BA acceleration (3–5 days/week:  $\beta$  = –1.89, 95% CI –2.76 to -1.02; 6-7 days/week: -0.83, 95% CI -1.50 to -0.15 years). Compared with non-spicy consumers, spicy consumers showed a trend towards a decrease in cardiopulmonary BA acceleration (3–5 days/week:  $\beta$  = –0.10, 95% CI – 0.21 to 0.01; 6–7 days/week: –0.01, 95% CI – 0.10 to 0.08 years) and in liver BA acceleration (3–5 days/week: β = -0.14,95% CI -1.26 to 0.99; 6-7 days/week: -0.50,95%CI – 1.37 to 0.38 years).

# Results of subgroup analysis and sensitivity analysis

Table 2 shows the results of the subgroup analyses of spicy food consumption and the comprehensive BA

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**Table 1** Baseline characteristics of study participants in the CMEC

| Characteristic   | Overall       | Non-spicy     | 1-2 days/week | 3-5 days/week | 6-7 days/week |
|--|---------------|---------------|---------------|---------------|---------------|
|  | n=7874        | n=1338        | n=849         | n=591         | n=5096        |
| Age (years)  | 51.73 (10.80) | 55.00 (11.17) | 50.12 (11.25) | 48.67 (11.08) | 51.50 (10.38) |
| Female (%)   | 4844 (61.5)   | 839 (62.7)    | 520 (61.2)    | 360 (60.9)    | 3125 (61.3)   |
| Han ethnic group (%)                                   | 5115 (65.0)   | 907 (67.8)    | 729 (85.9)    | 514 (87.0)    | 2965 (58.2)   |
| Urban residence (%)                                    | 3006 (38.2)   | 616 (46.0)    | 547 (64.4)    | 347 (58.7)    | 1496 (29.4)   |
| Highest education (%)                                  |               |               |               |               |               |
| No formal school                                       | 1705 (21.7)   | 316 (23.6)    | 92 (10.8)     | 64 (10.8)     | 1233 (24.2)   |
| Primary school   | 1943 (24.7)   | 399 (29.8)    | 184 (21.7)    | 96 (16.2)     | 1264 (24.8)   |
| Middle and high school                                 | 3296 (41.9)   | 515 (38.5)    | 399 (47.0)    | 308 (52.1)    | 2074 (40.7)   |
| College or university                                  | 930 (11.8)    | 108 (8.1)     | 174 (20.5)    | 123 (20.8)    | 525 (10.3)    |
| Married (%)  | 7075 (89.9)   | 1157 (86.5)   | 764 (90.0)    | 534 (90.4)    | 4620 (90.7)   |
| Healthy diet (%) <sup>a</sup>                          | 3409 (43.3)   | 534 (39.9)    | 476 (56.1)    | 339 (57.4)    | 2060 (40.4)   |
| Regular smoking (%)                                    |               |               |               |               |               |
| Never  | 5981 (76.0)   | 1097 (82.0)   | 659 (77.6)    | 448 (75.8)    | 3777 (74.1)   |
| Current  | 1508 (19.2)   | 183 (13.7)    | 133 (15.7)    | 114 (19.3)    | 1078 (21.2)   |
| Previous   | 385 (4.9)     | 58 (4.3)      | 57 (6.7)      | 29 (4.9)      | 241 (4.7)     |
| Physical activity (METs-h/day)                         | 26.63 (18.19) | 24.23 (18.45) | 23.13 (15.61) | 24.20 (16.03) | 28.12 (18.58) |
| Frequency of alcohol consumption (%)                   |               |               |               |               |               |
| Never/rarely   | 6462 (82.1)   | 1209 (90.4)   | 716 (84.3)    | 465 (78.7)    | 4072 (79.9)   |
| Monthly  | 364 (4.6)     | 26 (1.9)      | 37 (4.4)      | 39 (6.6)      | 262 (5.1)     |
| 1–2 days/week  | 242 (3.1)     | 18 (1.3)      | 31 (3.7)      | 27 (4.6)      | 166 (3.3)     |
| 3–5 days/week  | 213 (2.7)     | 22 (1.6)      | 21 (2.5)      | 26 (4.4)      | 144 (2.8)     |
| 6–7 days/week  | 593 (7.5)     | 63 (4.7)      | 44 (5.2)      | 34 (5.8)      | 452 (8.9)     |
| Moderate or strong of spice strength (%)               | 1884 (24.0)   | 0 (0.0)       | 116 (13.7)    | 120 (20.3)    | 1648 (32.3)   |
| Self-reported physician-diagnosed chronic diseases (%) |               |               |               |               |               |
| Diabetes   | 401 (5.1)     | 96 (7.2)      | 42 (4.9)      | 30 (5.1)      | 233 (4.6)     |
| CVD  | 684 (8.7)     | 142 (10.6)    | 63 (7.4)      | 56 (9.5)      | 423 (8.3)     |
| COPD   | 480 (6.1)     | 108 (8.1)     | 38 (4.5)      | 34 (5.8)      | 300 (5.9)     |
| Cancer   | 67 (0.9)      | 15 (1.1)      | 4 (0.5)       | 7 (1.2)       | 41 (0.8)      |
| BA accelerations (years)                               |               |               |               |               |               |
| Comprehensive BA acceleration                          | -0.35 (4.76)  | -0.05 (4.84)  | -1.03 (4.61)  | -0.97 (4.69)  | -0.24 (4.75)  |
| Cardiopulmonary BA acceleration                        | 0.00 (1.16)   | 0.08 (1.21)   | 0.06 (1.13)   | -0.01 (1.16)  | -0.03 (1.15)  |
| Liver BA acceleration                                  | -1.20 (12.67) | -1.79 (12.45) | -2.40 (12.84) | -1.39 (12.84) | -0.83 (12.66) |
| Kidney BA acceleration                                 | 0.17 (9.15)   | 0.20 (9.24)   | 0.27 (9.35)   | 0.76 (8.55)   | 0.07 (9.17)   |
| Metabolic BA acceleration                              | 0.08 (6.78)   | 0.32 (6.75)   | -0.85 (6.51)  | -0.69 (6.42)  | 0.27 (6.86)   |

Abbreviation: BA: biological age; CVD: cardiovascular disease; COPD: chronic obstructive pulmonary disease

Data are expressed as mean (standard deviation) or numbers (percentage)

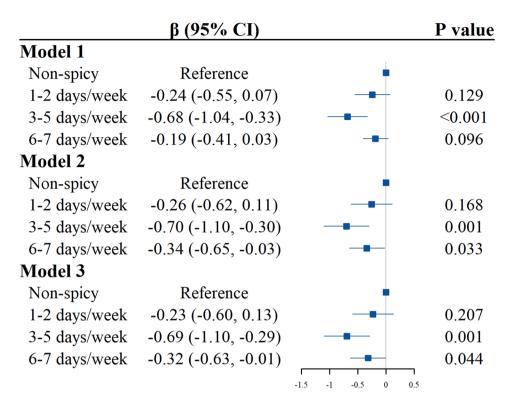
acceleration. Spicy food consumption showed stronger associations with comprehensive BA acceleration among female, Han Chinese, and healthy diet participants than male, non-Han, and unhealthy diet participants. In sensitivity analyses, our results did not materially change when we used a stricter exclusion criterion (Appendix Table S4), adjusted for a healthy diet score according to the Mediterranean diet (Appendix Table S5), additionally adjusted for BMI (Appendix Table S6), additionally adjusted for chronic kidney disease, chronic hepatitis and liver cirrhosis (Appendix Table S7), and used the targeted learning approach (Appendix Table S8).

#### Discussion

Our study, set against the backdrop of accelerated aging and the widespread consumption of spicy foods, was the first to estimate the association of spicy food consumption with comprehensive BA acceleration and organ-specific BA acceleration. This estimation is based on the CMEC longitudinal data from populations with a strong preference for spicy foods. Notably, over 60% of our participants reported consuming spicy foods almost daily. Our results revealed a decrease in comprehensive BA acceleration for spicy food consumers compared to non-spicy food consumers. For organ-specific BA accelerations, we observed higher estimates for metabolic

<sup>&</sup>lt;sup>a</sup> Healthy diets were assessed based on the DASH score, which included fruits, vegetables, legumes, dairy, whole grains, red and processed meats, and sodium, ranging from 7 to 35. The median DASH score was taken as the cut-off value. A healthy diet was defined as a DASH score greater than 21

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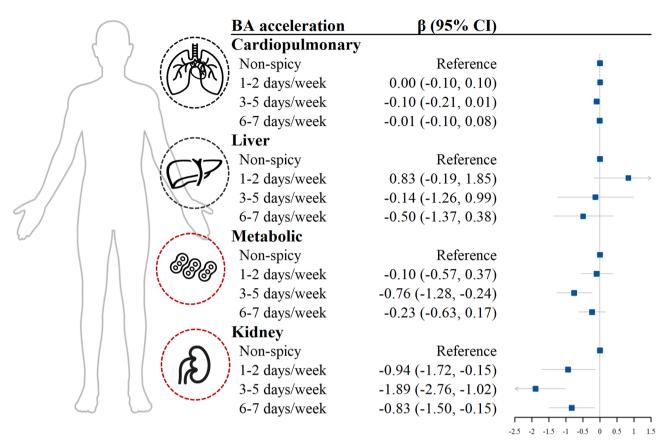
**Fig. 2** Association between spicy food consumption and comprehensive BA acceleration. Model 1 was adjusted for baseline comprehensive BA acceleration, age, sex and ethnic group. Model 2 was additionally adjusted for urbanicity, education, marital status, healthy diet, smoking status, alcohol consumption, physical activity, and spice strength. Model 3 was additionally adjusted for self-reported diseases (diabetes, CVD, COPD, and cancer)

BA acceleration and kidney BA acceleration than for cardiopulmonary BA acceleration and liver BA acceleration, although some results were not statistically significant. Importantly, we found that spicy food consumption showed stronger associations with comprehensive BA acceleration among female, Han Chinese, and healthy diet participants than male, non-Han, and unhealthy diet participants.

To the best of our knowledge, there are no studies that have estimated the association between spicy food intake and biological aging. Our finding suggests that consuming spicy foods has potential benefits for comprehensive BA. Although there is limited research on the direct mechanisms of spicy food intake and biological aging, there is evidence that capsaicin, the main active component of chili peppers, may improve some of the hallmarks of aging. After capsaicin ingestion, it is predominantly distributed to organs such as the kidney, heart, and liver, where it activates TRPV1. This activation in these organs has been shown to improve endothelial function, antiinflammatory, and glucose and lipid metabolism [10, 11, 28]. These have been linked to chronic inflammation, altered intercellular communication, and nutrient-sensing disorders, which are hallmarks of aging [14]. Dietary capsaicin modulates intestinal flora and improves ecological dysbiosis, another hallmark of aging [8, 14]. In addition, chili fruits contain high levels of antioxidants such as ascorbic acid and glutathione, and capsaicin is capable of exerting antioxidant effects through non-receptormediated mechanisms [28]. In addition, our study found that in the CMEC, the threshold for spicy food intake was approximately 3-5 days/week, beyond which there was no further reduction in BA. Similar to our findings, previous studies have also found a threshold for spicy food intake. Several plausible explanations may account for the threshold. First, frequent and continuous exposure to spicy food has been shown to induce the desensitization of the TRPV1 receptor, which may diminish the physiological responses to capsaicin and reduce the strength of the association beyond a certain consumption frequency [29, 30]. Second, the bioaccessibility and bioavailability of bioactive compounds may reach a saturation point, beyond which additional intake does not confer further biological advantages [8, 9], Furthermore, participants in our study were drawn from the southwestern region of China, where spicy food is a culturally ingrained and widely accepted dietary habit [10, 22]. Many individuals in this region report high habitual intake, and those consuming spicy food more than 5 days/week may have already reached an exposure ceiling, limiting the potential for further benefits.

No population-based study has investigated the association of spicy food intake with BAs across multiple organ systems. Our results showed that spicy food intake had

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**Fig. 3** Association between spicy food consumption and biological aging across multiple organ systems. Model was adjusted for baseline organ-specific BA acceleration, age, sex, ethnic group, urbanicity, education, marital status, healthy diet score, smoking status, alcohol consumption, physical activity, spice strength and self-reported diseases

a stronger association with metabolic BA and kidney BA than other organ system BAs. This may be related to the different aging rates in different organ systems and the different distribution of TPRV1 in different organ systems [7, 31, 32]. Metabolism and the kidneys (a metabolically active organ), which are primarily responsible for the homeostasis of the organisms, maybe the first to be disrupted and further accelerate other aging-related diseases [7, 33]. Previous studies have similarly demonstrated the potentially beneficial effects of spicy food intake on metabolic and kidney disease [31, 34]. Expression of TRPV1 was detected in kidney, adipose tissue, endothelium, and other organ tissues [31, 32]. TPRV1 activation by spicy food increases urinary sodium excretion, reduces lipid accumulation, and improves endothelium-dependent vasodilatation. This may be a possible mechanism for the association between spicy food consumption and metabolic and kidney biological aging [7, 14, 31, 34]. Future research could involve population intervention trials or randomized controlled trials to strengthen causal inference, or experimental studies to further investigate the potential mechanisms and threshold effects of bioactive substances in spicy foods on biological aging.

Similar to another study on spicy food consumption [35], our results suggest a stronger association between spicy food consumption and comprehensive BA in females than in males. This may be related to the fact that females do not respond to TPRV1 to the same extent as males [35]. We found that the association between spicy food consumption and BA was stronger in the Han Chinese compared to the non-Han Chinese, which may be related to the differences in genetic background between the Han Chinese and the non-Han Chinese. This is the first study investigating the association between spicy food consumption and BA acceleration in different ethnic subgroups, and further studies are needed. In addition, a stronger association between spicy foods and BA was found in participants with higher dietary quality, suggesting that dietary flavor, in addition to dietary quality, could be considered when specifying strategies to slow aging.

We incorporated 15 biomarkers to construct comprehensive BA and organ-specific BAs based on the widely validated KDM method. These biomarkers, such as waist-to-hip ratio, blood pressure, and lipids, have been widely and widely used in primary care, which ensures that BA measures are straightforward, cost-effective, and feasible for clinical implementation [7]. Composite BA measures

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**Table 2** Stratified analysis of estimated associations between spicy food consumption and biological aging according to predefined characteristics

| Subgroups                                     | β (95% CI) |                        |                            |  |  |  |  |
|---|------------|------------------------|----------------------------|--|--|--|--|
|   | Non-spicy  | 1–2 days/week          | 3–5<br>days/<br>week       | 6–7<br>days/<br>week                   |  |  |  |
| Age   |            |                        |                            |  |  |  |  |
| ≤50 years<br>(n=3649)                         | Reference  | -0.21<br>(-0.78, 0.36) | -0.73<br>(-1.34,<br>-0.12) | -0.24<br>(-<br>0.75,<br>0.28)          |  |  |  |
| >50 years<br>(n=4225)                         | Reference  | -0.23<br>(-0.71, 0.24) | -0.52<br>(-1.07,<br>0.03)  | -0.40<br>(-<br>0.78,<br>-0.01)         |  |  |  |
| Sex<br>Man<br>(n=3030)                        | Reference  | 0.09<br>(-0.39, 0.57)  | 0.06<br>(-0.47,<br>0.58)   | -0.19<br>(-<br>0.60,                   |  |  |  |
| Woman<br>(n=4844)                             | Reference  | -0.38<br>(-0.89, 0.12) | -1.14<br>(-1.70,<br>-0.57) | 0.21)<br>-0.37<br>(-<br>0.81,<br>0.07) |  |  |  |
| Ethnic group                                  |            |                        |                            | 0.07)                                  |  |  |  |
| Han<br>(n=5115)                               | Reference  | -0.41<br>(-0.84, 0.03) | -0.79<br>(-1.26,<br>-0.31) | -0.43<br>(-<br>0.82,<br>-0.03)         |  |  |  |
| Non-Han<br>(n=2759)                           | Reference  | 0.55<br>(-0.20, 1.30)  | -0.39<br>(-1.27,<br>0.49)  | -0.02<br>(-<br>0.53,<br>0.49)          |  |  |  |
| Diet  |            |                        |                            | 0.15)                                  |  |  |  |
| Unhealthy<br>(n=4809)                         | Reference  | -0.26<br>(-0.76, 0.24) | -0.51<br>(-1.07,<br>0.06)  | -0.38<br>(-<br>0.78,<br>0.02)          |  |  |  |
| Healthy<br>(n = 3715)                         | Reference  | -0.15<br>(-0.69, 0.39) | -0.80<br>(-1.39,<br>-0.21) | -0.22<br>(-<br>0.71,<br>0.28)          |  |  |  |
| Spice<br>strength<br>among spicy<br>consumers |            |                        |                            | ,                                      |  |  |  |
| Weak<br>(n=4652)                              | -          | Reference              | -0.41<br>(-0.83,<br>0.01)  | -0.05<br>(-<br>0.35,<br>0.25)          |  |  |  |
| Moderate and strong $(n=1884)$                | -          | Reference              | -0.69<br>(-1.57,<br>0.20)  | -0.35<br>(-<br>1.01,<br>0.32)          |  |  |  |

tend to capture physiological alterations earlier than specific phenotypes [36]. By 2050, the people aged 60 and over will reach 2.1 billion, representing 22% of the world's population [20]. Biological aging can be intervened

through lifestyle interventions, and our findings provide additional references for intervening in biological aging, especially kidney and metabolic biological aging.

# Strengths and limitations

The present study estimated the longitudinal association between spicy food consumption and comprehensive BA and explored the associations between spicy food consumption and organ-specific BAs. However, there are several limitations of this study that are worth noting. First, spicy food intake was based on self-reported information, and inter-individual differences in spice perception may lead to potential measurement error. Additionally, the lack of detailed intake data on spicy food limits our ability to quantify exact exposure levels. However, in Chinese culinary traditions, the intake of spicy foods is often derived from cooking practices using chili peppers and chili-based condiments (e.g., chili oil, chili sauce), rather than being tied to specific, easily quantifiable food items. As a result, this makes it challenging to quantify spicy food intake based on serving sizes, especially in underdeveloped, multi-ethnic regions with diverse local cuisines and language barriers. We used a questionnaire similar to the China Kadoorie Biobank, which has been shown to provide valid estimates of spicy food consumption in the Chinese population [8, 9, 37]. Second, the KDM-BAs we constructed were limited by the accessibility of biochemical markers, which prevented us from constructing BAs for certain organ systems, such as the brain. In addition, we are unable to fully capture the specific aging processes of the immune system due to the paucity of critical indicators related to immunity. However, the constructed BA based on markers that are widely used and economical in primary care ensures that this measure is suitable for large population surveys and clinical implementation. In addition, our previous studies have validated the constructed composite BA and organ-specific BAs in the CMEC participants, showing that the BA measurements can predict aging-related symptoms and diseases [20, 21, 24]. Third, this study only included participants who attended the baseline and follow-up surveys (approximately 10% of the CMEC baseline participants). Although we found that the baseline characteristics of the participants included in the study were similar to the whole CMEC participants (Appendix Table S2), caution is warranted in generalizing the findings of this study to other populations. Fourth, despite reasonable controls on confounders, the potential for residual confounding remains. Finally, this exploratory study identified the association between spicy food consumption and biological aging at the population level, which may be partially driven by bioactive compounds such as capsaicin. Further studies are needed to elucidate

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the underlying mechanisms linking these bioactive components of spicy food to biological aging.

#### Conclusion

The consumption of spicy foods may have potential benefits for biological aging. Our findings highlight that spicy foods may slow comprehensive and organ-specific biological aging, especially metabolic and kidney biological aging.

# **Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12937-025-01147-z.

Supplementary Material 1

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#### **Author contributions**

NZ, XX, and FH contributed to the design of the present study. NZ and XX wrote the analysis plan and the first and final draft of the paper. XZ and FH reviewed and commented on the data analysis, all drafts, and the final paper. All other authors were involved in the conduct of the study, analysis of data, interpretation of results, and provided critical comments on all drafts of the report.

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#### Data availability

The CMEC data are available on request to the authors.

#### **Declarations**

### **Ethical approval**

Ethical approvals were obtained by the Sichuan University Medical Ethical Review Board for the CMEC study.

#### Informed consent

Informed consent was obtained from all individual participants included in the study.

# Competing interests

The authors declare no competing interests.

# Conflict of interest

None declared.

#### **Disclosure Summary**

The authors have nothing to disclose.

# **Author details**

<sup>1</sup>West China School of Public Health and West China Fourth Hospital, Sichuan University, Chengdu, China

<sup>2</sup>School of Public Health, the Key Laboratory of Environmental Pollution Monitoring and Disease Control, Ministry of Education, Guizhou Medical University, Guiyang, China

<sup>3</sup>Chengdu Center for Disease Control and Prevention, Chengdu, China <sup>4</sup>School of Public Health, Kunming Medical University, Kunming, China <sup>5</sup>Chongqing Municipal Center for Disease Control and Prevention, Chongqing, China

<sup>6</sup>Tibet University Medical College, Lhasa, China

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