Better diet quality is associated with healthier aging among urban elderly

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Abstract.

BACKGROUND: Diet quality is suggested to be an important element in a healthy aging experience among elderly population.

OBJECTIVE: We investigated the association of diet quality and parameters related to healthy aging in elderly living in urban areas.

METHODS: A cross-sectional study was carried out on 1,355 older adults aged 60 years or older living in big cities in Indonesia from April 2016 until June 2017. Diet quality was assessed using the healthy eating index (HEI-2015) while healthy aging was determined using the healthy aging index (HAI) consisting of 5 physiological indicators: systolic blood pressure, forced vital capacity, random blood glucose, serum cystatin C, and digit symbol substitution test. The correlation among study variables was analyzed using Spearman's correlation test and linear regression test.

RESULTS: The HEI-2015 and HAI scores obtained in this study were (48.8 \pm 3.5) and (5.2 \pm 0.3) respectively, thus demonstrating a slightly poor diet quality and health status. The HEI-2015 score was strongly associated with the HAI (ρ =-0.85, p<0.05; β =-0.08, 95% CI: -0.13-(-0.02), p<0.05). Four components of the HEI-2015 were found to be strongly associated with the HAI score: whole fruits, total vegetables, sodium, and added sugars. The physiological parameters of the HAI correlating strongly with the HEI-2015 score were systolic blood pressure and random blood glucose.

CONCLUSIONS: Our study is the first to establish the strong correlation between the HEI-2015 and HAI. Our findings suggest that improving diet quality would help urban elderly support their healthy aging experience.

Keywords: Diet quality, healthy aging, elderly, healthy eating index

1. Introduction

Increases in the quality of life and improvements in public health over the past decades have led people worldwide to live longer today. The World Health Organization (WHO) estimated that the share of the world population aged 60 years and older would double from 1 billion in 2020 to 2.1 billion in 2050, thus outnumbering the share of children below 5 years old [1]. In Indonesia, there are currently more than 29.3 million elderly aged 60 years and over, or 10.8% of the total population [2]. This number is expected to increase by 20% in 2024 and reach 74 million or around 25% of the total population in 2050 [3].

Population aging poses considerable concerns and challenges for countries' economies. Older populations with poor health conditions could impose an economic burden on society and therefore, their health should be of concern [4]. In Indonesia, about 43% of the elderly people come from the lowerincome class [5]. They are vulnerable to poverty and

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are not enjoying a decent level of welfare. In 2019, 51.1% of Indonesian elderly experienced health complaints and illness conditions [3] while about 25% of them were frail [6]. It appears therefore primordial to seek for strategies to ensure healthy aging among the elderly population.

According to the WHO, healthy aging is defined as the process of developing and maintaining functional ability that enables well-being in older age [7]. Healthy aging is indeed a complex multidimensional concept that involves numerous life aspects, including social and psychological well-being, selfperceived health, health behaviors, absence of illness and disability, cognitive function, and security [8, 9]. The impact of diet on health has been well established. Healthy diet has been demonstrated to be an important element in aging and support a healthy aging process [10, 11]. Promoting a healthy diet in elderly would be vital to help them prevent agerelated diseases and preserve their overall good health status during aging.

This study aimed to investigate the association between diet quality and parameters related to healthy aging in Indonesian elderly living in urban areas. Diet quality was assessed using the healthy eating index (HEI-2015), a scoring metric designed to measure individual diet quality by assessing its compliance with the U.S. Dietary Guidelines for Americans (DGAs) [12]. The healthy aging index (HAI) is an index of physiological aging built upon indicators for different physiological parameters indicating organ structure and function [13]. In this study, we also analyzed the cross-correlation between the components of the HEI-2015 and HAI to determine which food groups played major roles in a healthy aging process and which particular physiological parameters are influenced by such food groups. The findings of this study would provide novel insights into the importance of good diet quality in supporting the healthy aging experience of older urban population in Indonesia.

2. Methods

2.1. Subjects and data collection

A cross-sectional study was carried out on 1,355 older adults of both sexes aged 60 years or older living in 3 big cities in Indonesia: Jakarta, Bandung (West Java), and Bogor (West Java) from April 2016

until June 2017. The study design was approved by the Ethics Committee of Universitas Indonesia (KET-159/UN2.F12.D1.21/PPM.00.02/2016) and all participants provided informed consent. Potential participants were contacted and asked for their participation in the study. To be eligible, the participants should be at least 60 years old at the time of the study, in an overall good health conditions, and not be cared in nursing homes. The screening was conducted for each participant by asking for recommendations of overall good health conditions from general practitioners. The participants also should not under regular medication for diabetes, cardiovascular diseases, or cancer. In return, the interested participants were offered a free medical check up screening at our partner laboratories (equivalent to USD60). All the measurements for this study (anthropometry, blood pressure, blood extraction, etc) were done once by professional clinicians during the medical check up visit. The blood pressure was measured using a sfigmomanometer. Participants also attended interview sessions with a dietician who tried to obtain information about the participants' sociodemographic profile, lifestyle, and dietary intake in the last 24 hours (24hour dietary recall/24HR). The information regarding the 24HR was collected by querying the participants about the type and the intake estimation quantity of their meals in the past 24 hour prior to the medical check up or interview with a dietetician. All the 24HR data were collected for a further analysis.

2.2. Healthy eating index (HEI-2015)

The HEI-2015 was the latest version of HEI developed by the United States Department of Agriculture (USDA) in collaboration with the National Cancer Institute (NCI). Participants' individual HEI-2015 score was analyzed using the 24HR data obtained from the interview session with a dietician. To translate the list and the quantity of foods consumed by the participants into different components in the HEI-2015 scoring system, we used the online food data bank available at Fatsecret Indonesia (open source). The HEI-2015 consisted of 13 components: total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, added sugars, and saturated fats [12]. Depending on how much each component was consumed (Table 1), the individual HEI-2015 score was calculated by adding up all the scores of the 13 components. The HEI-2015 score ranges from 0 to 100, with a higher score representing a better diet quality (scores>80 good, 51–80 needs improvement, and <51 poor). It is noteworthy that although the HEI has not been validated in Indonesia and its implementation to measure individual diet quality is still not common, recent Indonesian studies have succeeded in obtaining valid findings using the HEI [14][15].

2.3. Healthy aging index (HAI)

In this study, the HAI score was analyzed according to Wu et al. in 2017 [16] that proposed a modified version of the original HAI developed by Sanders et al. in 2014 [13]. The HAI comprised 5 indicators: systolic blood pressure (SBP), forced vital capacity (FVC), random blood glucose (RBG), serum cystatin C (CysC), and digit symbol substitution test (DSST). Each indicator was given score 0–2 according to the outcome: 0 for the 'healthiest', 1 for 'intermediate', and 2 for the 'least healthy' outcome. The HAI score was calculated by adding up all the scores of the 5 indicators, thus resulting in an integer ranging between 0 and 10. Therefore, lower HAI scores indicate better health conditions. Cut-off points were applied according to the previous studies (Table 1).

The SBP and FVC were measured using an automatic blood pressure monitor (M6 Comfort, Omron Healthcare) and an electronic spirometer (SP80B, Contec) respectively. From the participants' blood samples collected during the medical check up, the RBG was measured using a glucometer (Accu-Chek, Roche) while the serum CysC was analyzed using an immunoturbidimetry assay (Cystatin C kit, Shanghai Jingyuan Company, China). The DSST, conceived to measure cognitive function, consisted of 9 digitsymbol pairs followed by a list of digits. The test was performed by asking each respondent to write down the corresponding symbol to each digit given as fast as possible within the time limit (90 s). The number of correct answers/symbols for each participant was then calculated as score.

Table 1
Cut-off points used to categorize each component of the healthy aging index (HAI) and healthy eating index (HEI-2015)

Healthy aging index (HAI)	Score 0	Score 1	Score 2
Systolic blood pressure (SBP)*, mmHg			
Men	SBP≤125	125 <sbp<139< td=""><td>SBP≥139</td></sbp<139<>	SBP≥139
Women	SBP<130	130 <sbp<150< td=""><td>$SBP \ge 150$</td></sbp<150<>	$SBP \ge 150$
Forced vital capacity (FVC) [#] , L			
Men	FVC≥3.8	3.2 <fvc<3.8< td=""><td>FVC≤3.2</td></fvc<3.8<>	FVC≤3.2
Women	FVC≥2.6	2.1 <sbp<2.6< td=""><td>FVC≤2.6</td></sbp<2.6<>	FVC≤2.6
Random blood glucose (RBG)*, mg/dL	RBG≤100	100 <rbg<125< td=""><td>RBG≥125</td></rbg<125<>	RBG≥125
Cystatin C (CysC)*, mg/dL			
Men	CysC≤0.93	0.93 <cysc<1.11< td=""><td>CysC≥1.11</td></cysc<1.11<>	CysC≥1.11
Women	CysC≤0.90	0.90 <cysc<1.09< td=""><td>CysC≥1.09</td></cysc<1.09<>	CysC≥1.09
Digit symbol substitution test (DSST)*			
Men	DSST≥53	38 <dsst<53< td=""><td>DSST≤38</td></dsst<53<>	DSST≤38
Women	DSST≥56	39 <dsst<56< td=""><td>$DSST \leq 39$</td></dsst<56<>	$DSST \leq 39$
Healthy eating index (HEI-2015) ^{\$}	Score 0	Score 5	Score 10
Total fruits (TF), cup/1,000 kcal	TF=0	TF≥0.8	-
Whole fruits (WF), cup/1,000 kcal	WF=0	WF≥0.4	-
Total vegetables (TV), cup/1,000 kcal	TV=0	TV≥1.1	-
Greens and beans (GB), cup/1,000 kcal	GB=0	GB≥0.2	-
Whole grains (WG), ounce/1,000 kcal	WG=0	_	WG≥1.5
Dairy (D), cup/1,000 kcal	D=0	_	D≥1.3
Total protein foods (TPF)	TPF=0	$TPF \ge 2.5$	-
Seafood and plant proteins (SPP)	SPP=0	$SPP \ge 0.8$	-
Fatty acids (FA)^	FA≤1.2	_	FA≥2.5
Refined grains (RG), ounce/1,000 kcal	RG≥4.3	_	RG≤1.8
Sodium (S), mg/1000 kcal	S≥2,000	_	S≤1,100
Added sugars (AS), g/1000 kcal	AS≥65	_	AS≤16.25
Saturated fats (SF), g/1000 kcal	SF≥17.8	_	SF≤8.9

*) Wu et al., 2017 [16]. ^{#)} Dieteren et al., 2020 [21]. ^{\$)} Krebs-Smith et al., 2018 [12] with some modifications. ⁾ Calculated using the following equation: ((PUFAs+MUFAs)/SFAs), where PUFAs: polyunsaturated fatty acids, MUFAs: monounsaturated fatty acids, and SFAs: saturated fatty acids.

2.4. Statistical analysis

Data analysis was performed using SPSS version 20.0 (IBM). Mean and standard deviation values were used as descriptive statistics. The Shapiro-Wilk test was applied to determine data normality prior to further analyses. The mean difference of the HEI-2015 and HAI scores within each variable was analyzed using the student's *t*-test or one-way ANOVA. If ANOVA showed a statistically significant effect (p < 0.05), the mean within subgroups was compared using the Tukey's post-hoc test. Correlation tests were performed on ordinal and continuous variables using the Spearman's rho correlation test. Firstly, the correlation was investigated between the independent variables (age, education level, and monthly expense) and the dependent variables (HEI-2015 and

HAI scores). The significance limit used for statistical analyses in this study was set to be p < 0.05. Afterwards, the subgroups of the HEI-2015 and HAI were also tested for potential correlations with HEI-2015 components as independent variables and HAI components as dependent variables. To adjust the multiple testings performed in the comparison, the Bonferroni correction was used by dividing the p value with the number of tested hypotheses. Furthermore, the association between the HEI-2015 and HAI scores was tested using linear regression analysis with CI 95%.

3. Results

As shown in Table 2, the older adult population involved in this study consisted mainly of female

Table 2

The healthy eating index (HEI-2015) and healthy aging index (HAI) scores according to the sociodemographic, lifestyle, and weight status of the participants

Variable	n (%)	HEI-2015, mean (SD)	HAI, mean (SD)
Sex			
Male	638 (47)	46.0 (3.1) ^a	5.5 (0.3)°
Female	717 (53)	51.2 (3.2) ^b	$5.0(0.3)^{n}$
Age (years)			
60–69	845 (62)	49.5 (3.4) ^d	5.2 (0.4) ^p
70–79	384 (28)	$48.6(3.7)^{d}$	5.2 (0.3) ^p
80 or older	126 (9)	44.7 (3.8) ^c	5.6 (0.4) ^q
Marital status			
Married	913 (67)	48.5 (3.5) ^e	5.3 (0.4) ^s
Never married	12 (1)	50.7 (3.3) ^e	5.0 (0.3) ^{rs}
Widowed	362 (27)	49.7 (3.2) ^e	5.2 (0.4) ^s
Separated/divorce	68 (5)	47.2 (3.0) ^e	4.8 (0.2) ^r
Education level			
No formal education	168 (12)	45.8 (3.0) ^f	$5.5(0.3)^{v}$
Primary education	526 (39)	47.4 (3.5) ^{fg}	5.5 (0.3) ^v
Secondary education	487 (36)	50.4 (3.6) ^{fg}	$5.1 (0.4)^{u}$
Higher education	174 (13)	51.2 (3.2) ^g	4.6 (0.3) ^t
Monthly expense			
USD200 or less	417 (31)	47.7 (3.6) ^h	$5.5(0.2)^{W}$
USD201-USD400	733 (54)	48.7 (3.5) ^h	5.1 (0.4) ^w
USD401-USD650	183 (14)	51.2 (3.6) ^h	$5.2 (0.3)^{\text{w}}$
USD651 or more	22 (2)	49.4 (3.3) ^h	$5.0(0.3)^{\rm w}$
Regular physical activity			
Yes	590 (44)	49.1 (3.6) ⁱ	$4.9 (0.3)^{x}$
No	765 (56)	48.6 (3.9) ⁱ	5.4 (0.3) ^y
Smoker or ever smoke			
Yes	518 (38)	47.9 (3.4) ^j	5.6 (0.2) ^a
No	837 (62)	49.3 (3.8) ^j	5.0 (0.3) ^z
Weight status (BMI)			
Underweight (<18.5 kg/m ²)	85 (6)	$42.2 (4.1)^k$	5.2 (0.3) ^b
Normal (18.5–24.9 kg/m ²)	835 (62)	50.1 (3.3) ^m	5.2 (0.4) ^b
Overweight (25.0–29.9 kg/m ²)	262 (19)	48.9 (3.2) ^{lm}	5.3 (0.4) ^b
Obese (\geq 30.0 kg/m ²)	173 (13)	45.4 (3.4) ¹	5.8 (0.2) ^c
Total	1,355 (100)	48.8 (3.5)	5.2 (0.3)

Note: Different letters within a variable indicate a significant difference (p < 0.05). Data were analyzed using student's *t*-test or one-way ANOVA followed by Tukey's post-hoc test.

Variable	Mean (SD)	Association with HEI-2015 (ρ)	Association with HAI (ρ)
Age		-0.68*	0.70*
Education level		0.74*	-0.72*
Monthly expense		0.15	-0.18
BMI		0.38	-0.45
Healthy eating index (HEI-2015)	48.8 (3.5)	1.00	-0.85*
Total fruits (max. score 5)	3.6 (0.6)		-0.35
Whole fruits (max. score 5)	2.8 (0.4)		-0.61#
Total vegetables (max. score 5)	4.1 (0.5)		-0.72#
Greens and beans (max. score 5)	3.0 (0.6)		-0.24
Whole grains (max. score 10)	2.5 (1.0)		-0.32
Dairy (max. score 10)	6.9 (0.5)		-0.25
Total protein foods (max. score 5)	4.6 (0.4)		-0.08
Seafood and plant proteins (max. score 5)	3.8 (0.7)		-0.18
Fatty acids (max. score 10)	4.8 (0.6)		-0.48
Refined grains (max. score 10)	1.9 (0.8)		0.31
Sodium (max. score 10)	1.6 (0.8)		0.86#
Added sugars (max. score 10)	5.8 (1.0)		0.88#
Saturated fats (max. score 10)	4.8 (0.6)		0.59
Healthy aging index (HAI, max. score 10)	5.2 (0.3)	-0.85*	1.00
Systolic blood pressure (max. score 2)	1.24 (0.3)	$-0.90^{\$}$	
Forced vital capacity (max. score 2)	0.89 (0.2)	-0.14	
Random blood glucose (max. score 2)	1.15 (0.3)	$-0.82^{\$}$	
Serum cystatin C (max. score 2)	1.21 (0.2)	-0.33	
Digit symbol substitution test (max. score 2)	0.55 (0.2)	-0.45	

Table 3

Correlation between sociodemographic profile, the healthy eating index (HEI-2015) score, and the healthy aging index (HAI) score

*) p < 0.05, #) p < 0.00385, \$) p < 0.01 (following Bonferroni correction for multiple comparisons). Data were statistically analyzed using Spearman's rho correlation test.

(53%), married (67%), and non-smoking (62%) individuals who have completed their primary education (39%). Young elderly aged 60-69 years composed the majority of the population studied (62%). Since the subjects in this study were at least 60 years of age and the retirement age in Indonesia was set to 57 years old, almost all subjects did not work anymore during the time this study was held. Therefore, we asked them about their monthly expense, instead of their income, to obtain information regarding their economic status. In terms of weight status derived from the body mass index (BMI), the majority of the subjects were considered as normal (62%) with a relatively high proportion of overweight and obese individuals (19% and 13% respectively). Only 29% of the subjects reported regular physical activities. Significant difference within groups regarding the HEI-2015 and HAI scores was found on the following variables: sex, age, education level, and weight status.

Table 3 demonstrates a strong and significant association between the HEI-2015 and HAI scores (ρ =-0.85, p<0.05). Such a correlation was further confirmed using a linear regression analysis with the HEI-2015 score as predictor and the HAI score as

response variable (β =-0.08, 95% CI: -0.13-(-0.02), p < 0.05). Age and education level were also significantly correlated with the HEI-2015 and HAI scores. A further correlation analysis has led us to identify some components of the HEI-2015 with strong correlations with the HAI score, including whole fruits, total vegetables, sodium, and added sugars. The physiological parameters of the HAI that correlated strongly with the HEI-2015 score were systolic blood pressure and random blood glucose.

4. Discussion

One of the main objectives of this study was to assess the association of diet quality and health aging in urban elderly population. A similar study conducted by Fauziyana in 2020 [17] failed to establish such an association. In the study, the HEI-2015 was used to assess diet quality while healthy aging was defined by parameters that differed from our study, including active daily living (ADL) to measure physical function, mini mental state examination (MMSE) to measure cognitive function, geriartic depressive screening scale (GDSS) to measure psychological health, and social engagement index. The diet quality found in the study was considered to be poor with the HEI-2015 score of (46.1 ± 8.5) that did not differ much from the HEI-2015 score concluded in our study (48.8 ± 3.5) (Table 2). However, in the same study [18], significant correlations were found between the elderly's nutritional status measured by Mini Nutritional Assessment short form (MNA-SF) and all the healthy aging-related parameters mentioned previously [17], except for physical functionality measured by ADL. In our study, we could establish a positive association between diet quality and parameters related to healthy aging.

In this study, we observed that female elderly exhibited a better diet quality and health status compared to male elderly, as demonstrated by a higher HEI-2015 score and a lower HAI score (Table 2). This phenomenon was due to male subjects tending to adopt a less healthy lifestyle compared to female subjects. The proportion of smokers and people reporting no regular physical activities was higher in male (76% and 64% respectively) than in female subjects (5% and 49% respectively). Moreover, among the total of 435 overweight and obese participants involved in this study, 72% appeared to be male. Older subjects aged 80 years or older, along with subjects with lower education level also demonstrated overall lower diet quality and health status within their respective groups. Previous studies have confirmed that highlyeducated individuals had better diet quality and health while smoking was associated with lower diet quality and health [13, 16, 19, 20].

The HAI score generated from this study was (5.2 ± 0.3) , relatively higher from the score generated in previous studies ranging from 1.5 to 4.3 [16, 21]. A higher HAI score represents a lower health status. Therefore, the health status of our subjects were considered to be lower compared to other subjects in the previous studies. Smoking and physically inactive subjects exhibit significantly higher HAI scores, but not HEI-2015 scores, compared to non-smoking and physically active subjects. A recent meta-analysis study revealed that physical activity was positively associated with healthy aging (ES: 1.39, 95% CI = 1.23-1.57) [22]. Another metaanalysis study reported that non-smokers had more than double the odds of experiencing healthy aging (OR: 2.36, 95% CI: 2.03-2.75) compared with current smokers [23].

Using the Spearman's correlation test, we identified different independent variables associated with the HEI-2015 and HAI scores, among which age and education level appeared to be associated in a negative and positive manner respectively with diet quality and health status (Table 3). These findings confirmed the previous results presented in Table 2. A strong and significant correlation between the HEI-2015 and HAI scores (ρ =-0.85, p < 0.05) encouraged us to determine how different components of both parameters might correlate to each other. Among all the 13 components of the HEI-2015, 4 appeared to be strongly associated with the HAI score: whole fruits, total vegetables, sodium, and added sugars. With regard to the HAI, the systolic blood pressure (SBP) and random blood glucose (RBG) correlated strongly with diet quality (HEI-2015). Indeed, higher consumption of fruits and vegetables has been shown to reduce the risk of hypertension and type 2 diabetes [24, 25]. Conversely, excessive sodium and sugar consumption was associated with a higher risk of hypertension and type 2 diabetes [26-29].

The findings regarding the HEI-2015 score in this study would also allow to evaluate different components lacking in the elderly diet. The HEI-2015 score obtained in this study was considered as poor diet quality (Krebs-Smith). Other studies led by Indonesian researchers also showed poor diet quality (HEI-2015 score < 50) in healthy Indonesian women and preschool-age children living in the urban area [14, 15]. According to the 2020-2025 Dietary Guidelines for Americans [30], the HEI-2015 score of American citizens ranged from 51 (teenagers of 14-18 years) to 63 (elderly aged 60 or older). The cut-off for good diet quality is the HEI-2015 score of at least 80 [12]. By analyzing the consumption level of each HEI-2015 component in Table 3, we could propose some nutritional recommendations for urban elderly population in order to improve their diet quality. The 3 components that appeared to contribute the least partial scores for the integral HEI-2015 score were sodium (1.6/10), refined grains (1.9/10), and whole grains (2.5/10). Therefore, to improve the diet quality of the urban elderly population, we would recommend increasing the consumption of whole grains and reducing the consumption of salt and refined grains. Implementing this could be challenging. On one hand, consuming whole grains since is not part of Indonesian food culture. On the other hand, the elderly should consume less white rice (the major source of refined grains in Indonesian diet) and use less salt (the main source of sodium) in their daily diet. Some strategies could be proposed, such as replacing white rice with brown rice or choosing

whole-wheat bread over white bread to reduce the consumption of refined grains and increase the consumption of whole grains at the same time. Regarding the sodium intake, the concerned elderly people could opt for low sodium products in the market or get used to consuming less salty foods.

This study had some limitations. Firstly, the 24hour dietary recall was only done one time with the participants. It is recommended to use at least two recalls, on a weekday and on a weekend, to obtain a more representative individual diet habit. Secondly, the variables of smoking status and physical activity in this study were designed to be nominal (yes/no questions) while the association of these variables with the HEI-2015 or HAI scores could have been analyzed if such variables had been set to be ordinal or continuous (e.g. how many cigarettes do you usually smoke in a day? or how often do you practice sports ?). Finally, the HEI-2015 has not been validated in Indonesia. Adjusting the HEI-2015 with the Indonesian dietary guidelines and food habit would provide a better picture about the diet quality of Indonesian subjects. As recommendations, further studies could include a wider elderly population, including those living in rural area since their eating habit and lifestyle would be different from their urban counterparts. Follow-up studies after introducing certain diet recommendations to an elderly population could also be performed to look for improvements in some health status or overall well-being.

5. Conclusions

To conclude, our study highlights the importance of diet quality in maintaining the health status of the elderly as they grow older, a phenomenon known as healthy aging. The focus of studies on late adulthood should indeed be shifted from extending lifespan to extending healthspan: preserving overall good health status during aging to optimize individual's intrinsic capacity as they age. It is therefore important that the older adults in the population be willing to adopt a healthier lifestyle for a healthier aging experience. Our study suggested that the HEI-2015 could be used as a dietary standard to support healthy aging experience in the elderly. In addition, keeping a healthy body weight, quitting smoking, and being physically active would help maintain the health status of the elderly during aging.

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Conflict of interest

The authors declare no conflict of interest.

Ethical standards

The experiments in this study complied with the current laws of Indonesia and have been approved by the Ethics Committee of Universitas Indonesia (KET-159/UN2.F12.D1.21/PPM.00.02/2016).

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