

DIETARY FACTORS ASSOCIATED WITH THE DEVELOPMENT OF PHYSICAL FRAILTY IN COMMUNITY-DWELLING OLDER ADULTS

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Abstract: *Objectives:* Nutrition plays an important role in the development of frailty, and the present study examined the association between energy, macronutrient, and food intake and the development of physical frailty. *Design:* Prospective cohort study. *Setting:* The National Institute for Longevity Sciences — Longitudinal Study of Aging (NILS-LSA), a community-based study. *Participants:* Participants included 166 men and 117 women aged 65–86 years without frailty components at baseline who participated in both the sixth (2008–2010) and seventh (2010–2012) waves of the NILS-LSA. *Measurements:* Physical frailty was assessed using the modified criteria established by the Cardiovascular Health Study (2001). All participants were classified as “robust (number of frailty components: 0),” “prefrail (1–2),” or “frail (3–5).” Energy, macronutrient, and food intake was calculated based on 3-day dietary records during the sixth wave. Associations between dietary intake per day and the development of frailty 2 years later (from robust at the sixth wave to prefrail/frail at the seventh wave) were examined using multiple logistic regression analysis after adjusting for sex, baseline age, and other covariables. *Results:* Among the participants included, 36% were classified as prefrail/frail 2 years later. Higher energy [1 standard deviation (SD), odds ratio (95% confidence interval): 362 kcal, 0.68 (0.49–0.94)], protein [16 g, 0.72 (0.53–0.97)], and fat [15 g, 0.69 (0.52–0.92)] intake was negatively associated with frailty development. Higher meat [38 g, 0.68 (0.51–0.92)] and dairy [114 g, 0.73 (0.55–0.96)] intake was negatively associated with frailty development. Higher energy intake was negatively associated with the development of weakness (low grip strength) and low activity, while higher protein intake was negatively associated with the development of low activity. *Conclusion:* Increased consumption of meat and dairy products may provide sufficient protein and fat necessary for achieving higher energy intake, thereby effectively preventing physical frailty among older Japanese individuals.

Key words: Physical frailty, dietary intake, longitudinal study, Japanese.

Introduction

Frailty is highly prevalent among older individuals and confers high risks for adverse health outcomes, including mortality, institutionalization, falls, and hospitalization (1). Given the increasing elderly population, preventive strategies against frailty have become imperative.

Nutrition plays a key role in the pathogenesis of frailty. Recent systematic reviews of epidemiological studies related to frailty and nutrition have identified various nutritional factors associated with frailty, including micronutrients, macronutrients, dietary patterns, diet quality, antioxidant capacity, and undernutrition (2, 3). Lorenzo-Lopez et al. had concluded that the appropriate nutritional quantity (adequate energy intake) and quality (nutritionally favorable contents) are important in the prevention of frailty (2). Few nutritional studies, however, have targeted frailty in Asians, with evidence among Japanese populations being particularly limited (4–6). The Japanese diet is characterized by its use of a wide variety of seasonal ingredients, as well as abundant aquaculture products (7) and high salt intake (8). Moreover, considering that Japanese individuals have the longest life expectancy

worldwide (9), the unique Japanese diet might have contributed in some way to such an extended, healthy life expectancy.

Three-generation studies on older Japanese women have shown that high protein intake, regardless of the source (fish, meat, eggs, dairy products, grains, potatoes, etc.) or amino acid composition, high amino acid intake (4), and antioxidant capacity of dietary origin (5) were negatively associated with frailty. This negative association was stronger when dietary antioxidant capacity was combined with high protein intake (6). Nevertheless, all aforementioned studies were cross-sectional in design, and the causal directions of such relationships had not been confirmed.

The present study focuses on the diet of community-dwelling older individuals to clarify how energy and macronutrient intake was associated with the development of physical frailty while determining food categories related to frailty prevention.

Methods

Study cohort

Data for this survey were collected as part of the National Institute for Longevity Sciences — Longitudinal Study of

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Aging (NILS-LSA). This project assessed the normal aging process over time using detailed questionnaires and medical checkups, anthropometric measurements, physical fitness tests, and nutritional examinations. The NILS-LSA included randomly selected age- and sex-stratified individuals from a pool of non-institutionalized residents in the National Center for Geriatrics and Gerontology neighboring Obu City and Higashiura Town in Aichi Prefecture. The first wave of the NILS-LSA was conducted from November 1997 to April 2000 and included 2267 participants (1139 men, 1128 women; age range, 40–79 years). Details regarding the NILS-LSA are reported elsewhere (10).

This study used the sixth wave of the NILS-LSA as the baseline study given that the first to fifth waves had a lower number of older participants (aged 65 and over) than the sixth to seventh waves. The sixth wave of the NILS-LSA was conducted from July 2008 to July 2010 and included 1173 men and 1129 women (age range, 40–89 years), among whom were newly recruited participants after the first wave of the study.

The exclusion criteria included the following: 1) age <65 years in the sixth wave ($n = 1,331$) given that these individuals were not considered older adults; 2) those who did not participate in the seventh wave ($n = 184$), which was conducted from July 2010 to July 2012, given that these individuals were not available for follow-up; 3) those whose body weight had not been measured during the fifth wave ($n = 42$), which was conducted from July 2006 to July 2008, given that shrinking could not be assessed in such individuals ($\geq 5\%$ unintentional weight loss within the prior 2 years); 4) presence of any frailty components during the sixth wave ($n = 430$; component number: 1 ($n = 240$), 2 ($n = 139$), and 3–5 ($n = 51$)); and 5) incomplete data on nutritional assessments or self-report questionnaire ($n = 32$) during the sixth wave. Ultimately, data from 283 Japanese individuals (166 men and 117 women, aged 65–86 years) during the sixth wave of the NILS-LSA were available for analysis.

The mean [\pm standard deviation (SD)] intervals between the fifth and sixth and sixth and seventh waves for each participant were 2.0 [± 0.1] and 2.0 [± 0.1] years, respectively. The study protocol was approved by the Ethics Committee on Human Research of the National Center for Geriatrics and Gerontology (No. 899-2), and written informed consent was obtained from all subjects.

Diagnosis of physical frailty

Physical frailty was assessed using five components, including slowness, weakness, exhaustion, low activity, and shrinking, based on a modified set of criteria (11) established by Cardiovascular Health Study (1). Details regarding the modified criteria are reported elsewhere (11).

Slowness was defined as gait disturbance or a gait speed of <1.0 m/s using a comfortable gait. Weakness was defined as a maximum grip strength of <26 and <18 kg in men and women, respectively. Exhaustion was assessed through self-

reports based on responses to two statements in the Center for Epidemiologic Studies of Depression scale: “I felt that everything I did was an effort” and “I could not get going.” Responses included “Rarely or none of the time (less than 1 day during the past week),” “Some or a little of the time (1–2 days),” “Occasionally or a moderate amount of time (3–4 days),” and “Most or all of the time (5–7 days).” Participants who did not answer “Rarely or none of the time” on two questionnaires were identified as showing exhaustion. Low activity was defined as the lowest 20% of leisure-time physical activity by gender. Shrinking was defined as $\geq 5\%$ unintentional weight loss within the prior 2 years (during the fifth to sixth and sixth to seventh waves).

All participants were classified into either “robust (n of component: 0),” “prefrail (1–2),” or “frail (3–5).”

Nutritional assessments

Nutritional intake was assessed during the sixth wave using a 3-day dietary record. The dietary record was completed over three continuous days (2 weekdays and 1 weekend day) (12), and most participants completed their records at home and returned them within 1 month. Food was either weighed separately on a scale (1-kg kitchen scales; Sekisui Jushi, Tokyo, Japan) prior to cooking or estimated according to portion sizes. Participants used a disposable camera (27 shots; Fuji Film, Tokyo, Japan) to photograph meals before and after eating. Dietitians used such photos to complete missing data and telephoned participants to resolve any discrepancies or obtain further information as necessary. Averages for 3-day food and nutrient intake (including alcohol intake) were calculated according to the Standard Tables of Food Composition in Japan 2010 and other sources (12, 13).

Other measurements

Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, under a fasted state (fasting for at least 12 h) with participants wearing light clothing and no shoes. Body mass index (BMI) was calculated by dividing the body weight in kilograms by the square of the height in meters. Information regarding a history of hypertension, heart disease, hyperlipidemia, and diabetes (past and current), current smoking status (yes/no), education (≤ 9 or ≥ 10 years of school), and annual family income (<3,500,000 or $\geq 3,500,000$ yen per year) were obtained using self-report questionnaires and confirmed by medical doctors or trained staff. Physical activity was assessed using the MET score (a multiple of the resting metabolic rate), which was obtained from participant interviews conducted by trained interviewers using a semi-quantitative assessment method to assess the participant’s level of habitual physical activity during leisure-time and work, as well as their sleeping hours (14).

Table 1
 Baseline characteristics according to physical frailty status after 2 years in older Japanese adults

| | Physical frailty | | P ^a |
|---|------------------|--------------------------|----------------|
| | Robust (n = 181) | Prefrail/frail (n = 102) | |
| Men (%) | 65.2 | 47.1 | 0.003 |
| Age (years) ^b | 71.6 ± 4.9 | 72.4 ± 5.0 | 0.181 |
| BMI (kg/m ²) ^b | 22.9 ± 2.8 | 23.1 ± 2.7 | 0.447 |
| Alcohol intake (g/day) ^b | 11.4 ± 17.0 | 6.5 ± 12.1 | 0.011 |
| Current smoker (%) | 5.5 | 3.9 | 0.550 |
| Education, ≤9 years (%) | 23.2 | 31.4 | 0.133 |
| Family income, <3,500,000 JPY/year (%) | 30.4 | 39.2 | 0.130 |
| Hypertension (%) | 39.8 | 51.0 | 0.068 |
| Heart disease (%) | 5.0 | 6.9 | 0.509 |
| Hyperlipidemia (%) | 23.8 | 28.4 | 0.386 |
| Diabetes (%) | 9.9 | 11.8 | 0.633 |
| Energy intake, kcal/day ^b | 2082.5 ± 360.0 | 1907.3 ± 338.3 | <0.001 |
| Macronutrient intake, g/day ^b | | | |
| Protein | 80.1 ± 15.8 | 74.3 ± 14.0 | <0.001 |
| Fat | 55.9 ± 14.7 | 49.5 ± 14.0 | <0.001 |
| Carbohydrate | 290.0 ± 54.0 | 277.5 ± 51.4 | 0.058 |
| Food intake, g/day ^b | | | |
| Cereals | 440.7 ± 114.1 | 415.3 ± 112.7 | 0.072 |
| Potatoes | 42.1 ± 30.7 | 45.0 ± 47.6 | 0.528 |
| Beans | 76.6 ± 54.8 | 70.4 ± 54.0 | 0.358 |
| Nuts and seeds | 3.0 ± 5.1 | 2.5 ± 3.0 | 0.373 |
| Non-green yellow vegetables | 206.9 ± 94.4 | 210.8 ± 89.8 | 0.732 |
| Green yellow vegetables | 136.6 ± 78.7 | 136.0 ± 86.6 | 0.957 |
| Fruit | 165.2 ± 119.9 | 185.5 ± 134.5 | 0.191 |
| Mushrooms | 13.0 ± 14.3 | 12.1 ± 11.8 | 0.628 |
| Seaweed | 19.6 ± 20.6 | 23.8 ± 22.4 | 0.113 |
| Fish and shellfish | 99.6 ± 48.9 | 92.0 ± 48.7 | 0.211 |
| Meat | 67.5 ± 38.9 | 51.1 ± 34.5 | <0.001 |
| Eggs | 42.5 ± 24.9 | 45.3 ± 25.1 | 0.364 |
| Milk and dairy products | 178.7 ± 116.4 | 153.5 ± 109.1 | 0.075 |

BMI, body mass index; JPY, Japanese yen; a. Differences in proportions and means were assessed using the chi-square test and independent t-test, respectively; b. Mean ± standard deviation.

Statistical analysis

All statistical analyses were performed using Statistical Analysis System software version 9.3 (SAS Institute, Cary, NC, USA). Participants were categorized into two groups according to the number of physical frailty components (0 as robust, 1–5 as prefrail/frail) given the small number of cases in components “2 (n = 17),” “3 (n = 3),” “4 (n = 0),” and “5 (n = 0).”

Differences in proportions and means of baseline characteristics according to physical frailty status after 2 years were assessed using the chi-square test and independent t-test, respectively. Comparisons between baseline dietary intakes according to the number of physical frailty components after 2 years were performed using a general linear model adjusted for sex and baseline age.

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Table 2
Baseline dietary intake and odds ratios for developing physical frailty^a after 2 years in older Japanese adults

| | Mean | 1SD | Model 1 ^b OR (95%CI) | P | Model 2 ^c OR (95%CI) | P |
|-----------------------------|--------|-------|------------------------------------|-------|------------------------------------|-------|
| Energy intake, kcal/day | 2019.4 | 361.7 | 0.68 (0.49–0.94) | 0.019 | - | - |
| Macronutrient intake, g/day | | | | | | |
| Protein | 78.6 | 15.5 | 0.72 (0.53–0.97) | 0.029 | 0.86 (0.56–1.33) | 0.491 |
| Fat | 53.6 | 14.8 | 0.69 (0.52–0.92) | 0.011 | 0.77 (0.52–1.14) | 0.193 |
| Carbohydrate | 285.5 | 53.3 | 0.85 (0.64–1.12) | 0.241 | 1.50 (0.89–2.55) | 0.130 |
| Food intake, g/day | | | | | | |
| Cereals | 431.6 | 114.1 | 0.91 (0.68–1.21) | 0.508 | 1.08 (0.78–1.51) | 0.635 |
| Potatoes | 43.1 | 37.6 | 1.11 (0.87–1.43) | 0.373 | 1.18 (0.91–1.53) | 0.218 |
| Beans | 74.4 | 54.5 | 0.93 (0.71–1.21) | 0.574 | 0.97 (0.74–1.27) | 0.808 |
| Nuts and seeds | 2.8 | 4.5 | 0.86 (0.65–1.14) | 0.293 | 0.91 (0.68–1.21) | 0.503 |
| Non-green yellow vegetables | 208.3 | 92.6 | 1.09 (0.84–1.42) | 0.499 | 1.16 (0.89–1.51) | 0.275 |
| Green yellow vegetables | 136.4 | 81.5 | 0.99 (0.77–1.27) | 0.911 | 1.03 (0.80–1.33) | 0.834 |
| Fruit | 172.5 | 125.5 | 1.07 (0.83–1.39) | 0.585 | 1.24 (0.93–1.64) | 0.138 |
| Mushrooms | 12.7 | 13.5 | 1.00 (0.78–1.30) | 0.987 | 1.02 (0.79–1.33) | 0.860 |
| Seaweed | 21.2 | 21.3 | 1.19 (0.93–1.53) | 0.162 | 1.20 (0.93–1.54) | 0.164 |
| Fish and shellfish | 96.9 | 48.9 | 0.97 (0.74–1.28) | 0.833 | 1.10 (0.82–1.48) | 0.527 |
| Meat | 61.6 | 38.1 | 0.68 (0.51–0.92) | 0.011 | 0.73 (0.54–0.99) | 0.040 |
| Eggs | 43.5 | 25.0 | 1.20 (0.93–1.56) | 0.166 | 1.30 (0.99–1.71) | 0.062 |
| Milk and dairy products | 169.6 | 114.3 | 0.73 (0.55–0.96) | 0.024 | 0.78 (0.59–1.03) | 0.081 |

SD, standard deviation; OR, odds ratio; CI, confidence interval; BMI, body mass index; a. Development of physical frailty was defined as prefrailty or frailty after 2 years; b. Model 1: adjusted for sex, baseline age, education, family income, smoking status, alcohol intake, BMI, and medical history; c. Model 2: further adjusted for energy intake.

To determine linear associations between dietary intakes and frailty development, 1 SD of each dietary intake was treated as a measure of amount. Moreover, associations between baseline energy, macronutrient, or food intake (1 SD) increase and frailty development after 2 years were examined using multiple logistic regression analysis after adjusting for sex, baseline age, education, family income, smoking status, alcohol intake, BMI, and medical history (Model 1). Model 2 further adjusted for energy intake concerning for macronutrient and food intake. All reported P values were two-sided, and P values < 0.05 were considered significant.

Results

Of the total number of participants, 36% (n = 102) were classified as prefrail/frail during the seventh wave. Among the prefrail/frail group, 82, 17, 3 and none had 1, 2, 3 and 4 or 5 physical frailty components, respectively. The prefrail/frail group had a lower proportion of men and lower alcohol, macronutrient, and meat intake than the robust group (Table 1).

Table 2 shows the baseline dietary intakes and odds ratios for developing physical frailty. In Model 1, the odds ratio (95%

confidence interval) for developing physical frailty was 0.68 (0.49–0.94) with a 1 SD increase in energy intake (SD; 361.7 kcal/day) after adjusting for sex, baseline age, education, family income, smoking status, alcohol intake, BMI, and medical history. The odds ratio for developing physical frailty was also significantly lower with greater protein and fat intake. With regard to food group, the odds ratio for developing physical frailty was significantly lower with greater intake of meat or milk and dairy products.

After adjusting for energy intake (Model 2), the odds ratio for developing physical frailty did not reach statistical significance for protein or fat intake. Moreover, the odds ratio for developing physical frailty with greater intake of milk and dairy products was weaker (P < 0.1).

Table 3 shows the association between energy and macronutrient intake and physical frailty components. Greater energy intake reduced the odds ratio for developing weakness (weak grip strength) and low activity after multivariate adjustment. Although greater protein and fat intake reduced the odds ratio for developing low activity, carbohydrate intake was not associated with the development of any physical frailty components.

Table 3

Baseline energy and macronutrient intake and odds ratios^a for physical frailty components after 2 years in older Japanese adults

| | n, % | Energy Intake | Macronutrient intake | | |
|--------------------|-----------|-------------------------------------|---|---|--|
| | | 1SD 361.7kcal/day OR (95% CI) | Protein 1SD 15.5 g/day OR (95% CI) | Fat 1SD 14.8 g/day OR (95% CI) | Carbohydrate 1SD 53.3 g/day OR (95% CI) |
| Frailty components | | | | | |
| Shrinking | 23, 8.1% | 0.98 (0.58–1.66) | 0.97 (0.61–1.55) | 0.95 (0.59–1.51) | 0.99 (0.61–1.60) |
| Weakness | 13, 4.6% | 0.32 (0.12–0.85) | 0.43 (0.18–1.03) | 0.55 (0.26–1.17) | 0.45 (0.19–1.05) |
| Exhaustion | 58, 20.5% | 0.77 (0.53–1.14) | 0.83 (0.59–1.19) | 0.80 (0.57–1.11) | 0.90 (0.64–1.26) |
| Slowness | 10, 3.5% | 0.56 (0.20–1.59) | 0.67 (0.22–2.00) | 0.49 (0.18–1.34) | 0.81 (0.34–1.96) |
| Low activity | 21, 7.4% | 0.44 (0.22–0.89) | 0.36 (0.18–0.73) | 0.53 (0.29–0.99) | 0.67 (0.38–1.19) |

SD, standard deviation; OR, odds ratio; CI, confidence interval; BMI, body mass index. a. Adjusted for sex, baseline age, education, family income, smoking status, alcohol intake, BMI, and medical history.

Discussion

The present study showed that higher energy, protein, and fat intake was associated with reduced development of physical frailty after 2 years among older Japanese adults. Moreover, higher intake of meat and dairy products were found to reduce the development of physical frailty after 2 years. To the best of our knowledge, the current study is the first longitudinal study on older Japanese adults to demonstrate the relevance of nutritional factors in the prevention of physical frailty.

Numerous prior studies have focused on the association between proteins and frailty from the perspective of skeletal muscle maintenance and physical strength. A three-city cohort study on community-dwelling older individuals in France demonstrated a negative association between a protein intake of 1 g/kg of body weight and frailty (15), while a three-generation study on older Japanese women reported that high protein intake, regardless of the source (fish, meat, eggs, dairy products, grains, potatoes, etc.) or amino acid composition, and high amino acid intake were negatively associated with physical frailty (4). The results presented herein support such findings given that higher protein and fat intake appeared to reduce the development of physical frailty.

Notably, the odds ratio for developing frailty was no longer significant for protein and fat intake after adjusting for energy intake. This indicates that increased energy intake mediated the contributions of protein and fat intake toward reducing frailty development. Despite the generally reduced energy intake during old age (16), maintaining high protein and fat intake may effectively reduce the development of frailty.

Although Japan has lower obesity rates compared to other countries, obesity has recently become a much more important public health issue. Accordingly, citizens ≥ 40 years old had begun receiving specific health checkups and health guidance to prevent and improve metabolic syndrome during the fiscal

year 2008 (17), while obese individuals with a BMI ≥ 25 kg/m² and those with metabolic diseases had been provided weight loss guidance. Moreover, underweight status (low body weight) during old age carries poorer prognosis than obesity (18, 19). However, the older generation has been strongly advised to avoid obesity from early adulthood to middle age in order to prevent cardiovascular diseases and metabolic syndrome. Therefore, many individuals in this generation may have focused on avoiding obesity in their old age and consequently do not ingest sufficient amounts of proteins or fats, resulting in long-term low energy intake. However, maintaining high energy intake in older individuals may reduce the risk of reduced grip strength and leisure-time physical activity, which were frailty components used in the present study.

Although greater intake of meat and dairy products has been shown to particularly reduce the development of frailty, some older individuals may refrain from consuming meat and dairy products to prevent obesity. A recent study demonstrated that diet diversity decreased with age and that the intake of dairy products decreased in men and women with increasing age (20). Dairy products contain good proteins and fats and are rich in minerals, such as calcium, which are essential for bone metabolism. Moreover, a high intake of dairy products during old age is likely desirable. Meat is also rich in amino acids, such as branched chain amino acids, which are essential for maintaining muscle mass (21, 22). Although some older individuals may refrain from eating meat because of reduced bite strength, the proactive intake of meat is likely worth recommending.

As part of a sub-analysis, the present study examined how the increased intake of saturated or unsaturated fatty acids was related to the development of frailty after 2 years. The results demonstrated that the odds ratio for developing physical frailty was significantly reduced with increased intake of saturated fatty acids (1 SD, 12.9 g/day) (odds ratio, 0.68;

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95% confidence interval, 0.51–0.91). Concerning unsaturated fatty acid intake, the odds ratio was marginally significant [1 SD, 8.7 g/day, odds ratio, 0.76 (0.57–1.01)]. Moreover, no significant relationship had been observed between the intake of n-3 or n-6 polyunsaturated fatty acids and the development of frailty. These results suggest that increased intake of saturated fatty acids, which is not always recommended given the need to reduce cardiovascular disease risk (23), should be recommended to prevent frailty in old age.

The present study exhibits the following primary strengths. First, factors associated with frailty prevention had been clarified in a relatively healthy older population that was randomly selected from the community. Given that frailty is becoming a major public health issue in the aging Japanese society (24), epidemiological evidence for nutritional issues is sorely needed. Second, we assessed nutritional intake using 3-day dietary records and photographs, which is one of the best methods for assessing individual food intake (12). Finally, the average dietary intake for older participants in the present study was consistent with the National Nutrition Survey in Japan (25). Therefore, the present results could perhaps be more applicable to non-institutionalized, community-dwelling older participants.

Several limitations of the present study must also be considered. First, relatively fewer individuals had been categorized as frail given that subjects were randomly selected from the community and prefrail/frail was a principal outcome. The target population included relatively healthy older individuals who were able to participate in an institution-type survey. Therefore, nutritional risk factors for institutionalized individuals or those living at home and unable to participate in this type of survey had not been assessed. Second, the Japanese intake of meat and dairy products is considered low by global standards (26, 27). Therefore, the present findings may not be extrapolated to Western populations who consume relatively large amounts of meat and dairy products. Although the present study does not suggest that a greater intake of meat and dairy products is better, it does recommend increasing protein and fat intake from meat and dairy products in populations with relatively low intake. Given that poor nutrition is central to frailty (28), avoiding poor nutrition through an abundant intake of energy, proteins, and fats is important in non-obese older individuals.

Conclusions

This two-year prospective cohort study showed that increasing meat and dairy consumption to ensure sufficient protein and fat intake and achieve higher energy levels may be an appropriate option to help prevent the development of physical frailty among older Japanese individuals.

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Conflicts of interest: All authors declare no conflict of interest.

Ethics Statement: The NILS-LSA followed the principles of the Declaration of Helsinki and the Ethical Guidelines for Epidemiological Research in Japan. The study was approved by the Ethics Committee of the National Center for Geriatrics and Gerontology (No. 899-2). Written informed consent was obtained from all participants.

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