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DIETARY INFLAMMATORY INDEX, PRE-FRAILTY AND FRAILTY AMONG OLDER US ADULTS: EVIDENCE FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2007-2014

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Abstract: *Objective:* This study aimed to investigate the association between dietary inflammation, pre-frailty and frailty among older US adults. Additionally, effect modification of gender on the association between dietary inflammation and frailty was assessed. *Design:* Study data came from the National Health and Nutrition Examination Survey (2007-2014) – a nationally representative, cross-sectional study of adults. *Participants:* The analytic sample included adults ≥60 years (n=7,182). *Measurements:* Dietary Inflammatory Index (DII®) scores were calculated from 24-hour dietary recalls; DII was categorized into quintiles from Quintile 1 (Q1) (least inflammatory) to Q5 (most inflammatory). Frailty was assessed by four criteria: exhaustion, weakness, low body mass, and low physical activity. Individuals were then categorized into robust (0 criteria), pre-frail (1-2 criteria), or frail (3-4 criteria). Multinomial logistic regression was used to examine the odds of frailty categories (pre-frail vs. robust; frail vs. robust). *Results:* After adjusting for potential confounders, individuals in DII quintile 5 (vs Q1) were more likely to be pre-frail (OR = 1.71; 95% CI: 1.36-2.15) and frail (OR = 1.70; 95% CI: 1.02-2.85). Individuals in Q4 had greater odds of frailty only (OR = 1.82; 95% CI: 1.13, 2.93). No evidence of effect modification by gender on the association of DII and frailty was found. *Conclusion:* This study expands upon previous evidence of a relationship between dietary inflammation and frailty. When designing nutrition-based frailty interventions, inflammatory properties of diets should be considered.

Key words: Nutrition, NHANES, Dietary Inflammatory Index, frailty, pre-frailty.

Introduction

Frailty is an age-related syndrome of physiologic decline that affects approximately 10% of community-dwelling older adults (1). Another 41.6% of older adults are considered to be pre-frail, a condition thought to be a precursor of frailty development (2). In research practice, frailty is typically defined as a syndrome of unintentional weight loss, slow walking speed, low grip strength, low energy, and/or low physical activity (1). The frailty syndrome increases vulnerability to adverse health outcomes through underlying physical changes (3), and is associated with worsening mobility (1), acute illness, falls (4), injuries, disability (5), hospitalization, dementia and Alzheimer's (6), institutionalization (7), and mortality (8).

Despite increasing interest in frailty, the pathophysiological mechanisms contributing to frailty are not well understood. Previous studies have demonstrated that systemic inflammation is a potential mechanism influencing frailty development. For example, prior findings show that when compared to robust individuals, pre-frail and frail individuals have higher levels of inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), and fibrinogen (9). Higher levels of CRP and IL-6 also are associated with poor physical performance (10) and with loss of muscle strength (11). Higher levels of IL-6 have been linked with slower gait speed and gait speed decline (12). Relatively few studies have investigated potential sources of systemic inflammation in relation to frailty development; however, such information may be key to strategies aimed at addressing and preventing frailty and its consequences.

Diet, as an important potential source of pro-inflammatory or anti-inflammatory compounds, is an important modulator of inflammation (13). Several studies suggest that individuals' diets are related to either greater or lesser levels of systemic inflammatory markers such as C-reactive protein (CRP) and fibrinogen (14, 15). Researchers from the University of South Carolina developed a tool in 2014 called the Dietary Inflammatory Index (DII®) to measure the inflammatory potential of diet (16). Pro-inflammatory diets, as indicated by higher DII scores, have been shown to be associated with greater incidence of frailty (17) and chronic inflammatory-related health outcomes, such as cardiovascular disease (18), diabetes (19), and cancer (20). However, evidence regarding the potential association between dietary inflammation and frailty is limited (17). Additionally, compared to robust individuals, pre-frailty has been found to be associated with inflammation (9), cardiovascular disease (21), and greater mortality (8). One study by Shivappa and colleagues among older adults in the US with arthritis found that more pro-inflammatory DII scores were associated with greater incidence of frailty; however, that study did not examine the association between DII and pre-frailty (17). Shivappa and colleagues also found differences in the association between frailty and obesity by sex; however,

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generalizability of these results was limited by the selective nature of the sample.

The purpose of this study was to examine whether there is an association between DII, pre-frailty and frailty among a nationally representative sample of older US adults. We hypothesized that greater DII scores, indicating a more pro-inflammatory diet, would be associated with greater odds of pre-frailty and frailty. Gender was examined as a potential effect modifier of the association between DII and frailty.

Methods

Data Source

This study used data from the National Health and Nutrition Examination Survey (NHANES). NHANES is a nationally representative cross-sectional study conducted yearly and released in two-year cycles by the Centers for Disease Control and Prevention. NHANES respondents are selected through a complex, multistage, probability sampling design. Participants are first interviewed in their home and asked to report demographic, dietary, and health-related information. In addition, participants undergo detailed medical examination by trained survey personnel in a mobile survey center, including measures of height, weight, and blood pressure. More detailed explanation of NHANES survey procedures and sampling design are available elsewhere (22).

We used NHANES data from waves 2007-2014 (N=40,610). Participants aged ≥60 years with complete data from a one-day 24-hour dietary recall and responses to frailty questions were considered eligible for analysis, yielding a final analytic sample of 7,182.

Outcome: Pre-Frailty and Frailty

Frailty and pre-frailty were defined using a modified four-criteria version of phenotypic frailty (1), adapted and validated in previous NHANES studies (8, 23). Criteria included weakness, exhaustion, low physical activity, and low body mass. Weakness was defined as having some difficulty, much difficulty, or being unable to lift or carry 10 pounds. Exhaustion was defined as having some difficulty, much difficulty, or being unable to walk from one room to the other on the same floor. Low physical activity was defined as being in the lowest 20% of the weighted sum of the average minutes of moderate and vigorous recreational activity per day; the weights used were according to NHANES suggested Metabolic Equivalency of Task (MET) scores – vigorous activities = 8 MET and moderate activities = 4 MET (22). Low body mass index (BMI) was defined as having BMI < 18.5 kg/m^2. Frailty criteria were summed and categorized into three levels: robust, defined as having 0 criteria; pre-frail, defined as having 1-2 criteria; and frail, defined as having 3-4 criteria.

Exposure: Dietary Inflammatory index

The Dietary Inflammatory Index (DII®) is a measure developed to help estimate the level by which individuals' diets increase or decrease systemic inflammatory processes. DII is based on inflammatory effect scores assigned to forty-five food parameters, including macro- and micronutrients, flavonoids, spices and food items. Inflammatory effect score for each food parameter was derived by Shivappa and colleagues (16), where 1,943 qualifying articles that assessed the relationships between each food parameter and inflammatory biomarkers (e.g., C-reactive protein (CRP), interleukin (IL)-1b, IL-4, IL-6, IL-10, and tumor necrosis factor a) were scored. After weighting articles based on study design, inflammatory effect scores were assigned to food parameters that were associated with pro- or anti-inflammation. Negative effect scores mean anti-inflammation, while positive scores mean pro-inflammation.

DII was calculated using dietary recall interview. The first of two 24-hour assessments was used to determine dietary intake, a procedure which has been validated (24). Dietary recall was collected in person at a mobile examination center by a trained dietary interviewer. Based on this interview, 26 food parameters were utilized to calculate individual consumption value. The food parameters used in the calculation were: carbohydrate, protein, fat, alcohol, fiber, cholesterol, saturated fatty acids, monosaturated fatty acids, polysaturated fatty acids, niacin, thiamin, riboflavin, vitamin B12, vitamin B6, Fe, Mg, Zn, Se, vitamin A, vitamin C, vitamin D, vitamin E, folic acid, β-carotene, omega 6 and omega 3. Individuals' intake of each of these food parameters was standardized to obtain z scores by subtracting the individualized consumption value by the global mean then dividing this by the global standard deviation. To minimize an effect of positive skewing, z scores were then converted to proportions (i.e., with values from 0 to 1). These proportions were then doubled, and one was subtracted in order to center the score around zero. The centered proportions were then multiplied by their respective inflammatory effect score (16). Finally, the DII score was calculated by summing each food score per individual. The DII score was used as a continuous variable and categorized into quintiles using scores from the total sample population (all ages). Analysis was limited to individuals ≥ 60. More positive DII scores indicate pro-inflammatory diets, while negative DII scores indicate anti-inflammatory diets. Energy-adjusted DII (E-DII) scores were calculated by dividing the food parameters by energy intake and then multiplying by 1000. The DII has been validated with a range of inflammatory markers – including c-reactive protein and interleukin - in various populations (25–28).

Covariates

Self-reported age, sex, race and ethnicity, education, smoking status, and summed score of 10 common co-morbidities (arthritis, cancer, congestive heart failure, coronary heart disease, diabetes, heart attack, high blood pressure, osteoporosis, stroke, and weak or failing kidneys;

Table 1
Weighted sample characteristics (n=7,182) by DII categories, NHANES 2007-2014

	Q1: Most AI	Q2: Some AI	Q3: Some PI	Q4: More PI	Q5: Most PI
			% or Mean (se)		
Age (Years), mean (se)	70.49 (0.23)	69.69 (0.24)	69.14 (0.28)	69.33 (0.25)	68.72 (0.31)
Female	60.7	53.8	51.6	51.5	49.6
Less than high school education	17.3	19.8	21.3	23.6	26.2
Race/Ethnicity					
White Non-Hispanic	53.2	51	52.1	53	50.8
Black Non-Hispanic	17.1	19.7	21.2	22.4	30
Hispanic	20.3	24	21.4	21	16.3
Other	9.4	5.3	5.3	3.6	2.8
Frailty status					
Robust	49.4	45.1	44	43.5	36.1
Pre-frail	44.7	49.6	50	49.6	57.5
Frail	5.9	5.3	6	6.9	6.4
Smoking status					
Never	55.6	50.2	46.2	45.3	41.2
Former	38	40.6	40.7	38.2	37.3
Current	6.4	9.1	13.4	16.5	21.5
Chronic conditions, mean (se)	2.02 (0.05)	2.08 (0.06)	2.02 (0.6)	2.10 (0.06)	2.07 (0.06)

Note. DII: Dietary inflammatory index; Q: Quintile; AI: Anti-inflammatory; PI: Proinflammatory; chi square test for categorical variables, t-test for continuous

range: 0-10) were considered as potential confounders. Age and the summed co-morbidity score were analyzed as continuous variables, while sex (male/female), education (less than 9th grade, some high school, high school graduate or GED equivalent, some college or AA degree, or college graduate or above), race and ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic, and other race), and smoking status (current, former, or non) were considered as categorical variables.

Statistical Analyses

All analyses were completed using SAS® 9.4 software. To determine an appropriate model and covariates, model selection was utilized based on change in estimate and not p-values. In short, each covariate was added one at a time to a crude model including only DII; if the variable produced at least a 10% change in estimate compared to the crude association, it was kept in the final model. This was done until no added variable produced a change ≥10%.

Descriptive statistics were calculated for demographic and health-related sample characteristics by frailty categories. We used logistic regression to estimate the odds of frailty as a binary outcome (frail vs. non-frail). In separate analyses, we used multinomial logistic regression to examine the odds of frailty categories (pre-frail vs. robust; frail vs. robust). DII was operationalized as a continuous variable and then divided into quintiles, to examine potential for non-linear associations between DII and frailty occurrence. The fully adjusted model included age, gender, race and ethnicity, education, summed co-morbidities score, and smoking status. Gender was examined as a possible effect modifier of the association between DII and frailty, by including an interaction term between DII and gender in logistic regression models and by stratifying analysis by gender. Logistic regression was used to estimate the odds of each frailty component associated with different levels of dietary inflammation. All models were estimated using appropriate SAS survey procedures and NHANES strata, cluster, and sampling probability weights to account for the NHANES complex survey design and to produce unbiased national estimates. Sampling probability weights were appropriately constructed based on NHANES guidance (29).

Results

Of the 7,182 analytic sample respondents, 2,185 (30.4%) were in the most anti-inflammatory diet group, 1,359 (19.9%) in some anti-inflammatory, 1,262 (17.6%) in some pro-inflammatory, 1,146 (16.0%) in more pro-inflammatory,

and 962 (13.4%) in most pro-inflammatory. Table 1 presents weighted descriptive statistics for sample characteristics across DII categories. Individuals in quintile 5 (Q5) – most pro-inflammatory group – tended to be younger, male, less educated, more minority race, smokers, and have higher co-morbidities. Compared to individuals with the most anti-inflammatory diets, those who had the most pro-inflammatory diets were more pre-frail and frail.

Table 2
Odds of frailty by continuous DII score and DII category, NHANES 2007-2014

	Crude	Adjusted[a]
	OR (95% CI)	OR (95% CI)
DII Continuous	1.07 (1.00-1.14)*	1.06 (0.99-1.15)
DII Quintiles		
Q1: Most AI	Ref	Ref
Q2: Some AI	1.03 (0.71-1.49)	1.02 (0.70-1.48)
Q3: Some PI	1.03 (0.66-1.61)	1.05 (0.66-1.67)
Q4: More PI	1.61 (1.08-2.39)*	1.63 (1.03-2.59)*
Q5: Most PI	1.27 (0.85-1.89)	1.22 (0.76-1.96)

Note. OR: odds ratio; DII: Dietary inflammatory index; Q: Quintile; AI: Anti-inflammatory; PI: Proinflammatory; a Adjusted for age, gender, race, education, summed co-morbidities score, and smoking status; * p<0.05

Table 2 displays crude and adjusted logistic regression results describing odds of being frail compared to non-frail (the combined pre-frail or robust groups). When examining DII as a continuous variable, a one-unit increase in DII (more pro-inflammatory) was associated with significantly greater odds of frailty in crude model (OR = 1.07, 95% CI: 1.00, 1.14). Adjusted model estimates suggested a similar increase in odds of frailty with increasing DII scores, (OR = 1.06, 95% CI: 0.99, 1.15). In categorical analysis, compared to individuals with anti-inflammatory diets (Q1), only individuals with moderately pro-inflammatory diets (Q4) had greater odds of frailty in fully adjusted (OR = 1.63, 95% CI: 1.03, 2.59) and crude (OR = 1.61, 95% CI: 1.08, 2.39) models.

Results from crude and adjusted multinomial logistic regression models estimating the odds of pre-frailty and frailty are displayed in Table 3. When DII was considered as a continuous variable, a one-unit increase in DII score was associated with greater odds of pre-frailty (OR = 1.09; 95% CI: 1.06, 1.12) and frailty (OR = 1.12; 95% CI: 1.03, 1.22). Compared to those with most anti-inflammatory diet (Q1), those with the highest pro-inflammatory diet (Q5) were 1.70 times as likely to be frail (OR = 1.70; 95% CI: 1.02-2.85) and 1.71 times as likely to be pre-frail (OR = 1.71; 95% CI: 1.36-2.15). Individuals with moderately pro-inflammatory diets (Q4) had 1.21 greater odds of pre-frailty (OR= 1.21; 95% CI: 0.99-1.48) and 1.82 greater odds of being frail (OR = 1.82; 95% CI: 1.13, 2.93) compared to individuals with anti-inflammatory diets (Q1); however, secondary analysis indicated that odds of frailty were not significantly different between individuals with moderately pro-inflammatory diets (Q4) and most pro-inflammatory diets (contrast p=0.14).

Table 4 displays adjusted logistic regression results for the odds of individual frailty components, comparing each quintile of DII to the most anti-inflammatory quintile. All levels of pro-inflammatory diet (Q3, Q4, Q5), when compared to the most anti-inflammatory (Q1) diet, were associated with increased odds of low physical activity, weakness, and exhaustion. Comparing those in Q1, those in any pro-inflammatory group (Q3, Q4, Q5) had lower odds of low BMI.

In sensitivity analysis, we recategorized DII into four groups. Results from the quartile analysis had a similar trend to the quintile analysis presented for pre-frail and frail individuals. When DII was categorized into quartiles, compared to those in Q1, those in Q4 had 1.51 greater odds of being frail (OR = 1.51; 95% CI: 0.90-2.57) and 1.59 greater odds of being pre-frail (OR = 1.59; 95% CI: 1.30-1.93).

Table 3
Crude and adjusted multinomial logistic regression of frailty status, NHANES 2007-2014

	Crude		Adjusted[a]	
	Pre-frail (95% CI)	Frail (95% CI)	Pre-frail (95% CI)	Frail (95% CI)
DII continuous	1.09 (1.05-1.13)*	1.11 (1.04-1.19)*	1.09 (1.06-1.13)*	1.12 (1.03-1.22)*
DII Quintiles				
Q1: Most AI	Ref	Ref	Ref	Ref
Q2: Some AI	1.12 (0.93-1.34)	1.08 (0.74-1.58)	1.12 (0.94-1.35)	1.09 (0.73-1.62)
Q3: Some PI	1.27 (1.05-1.53)*	1.15 (0.73-1.82)	1.32* (1.10-1.59)	1.23 (0.76-2.00)
Q4: More PI	1.22 (0.99-1.50)	1.75 (1.16-2.65)*	1.21 (0.99-1.48)	1.82 (1.13-2.93)*
Q5: Most PI	1.70 (1.37-2.10)*	1.64 (1.08-2.50)*	1.71 (1.36-2.15)*	1.70 (1.02-2.85)*

Note. DII: Dietary inflammatory index; Q: Quintile; AI: Anti-inflammatory; PI: Proinflammatory; a Adjusted for age, gender, race, education, summed co-morbidities score, and smoking status; * p<0.05

Table 4
Adjusted logistic regression of frailty components, NHANES 2007-2014

	Low BMI	Low Physical Activity	Weakness	Exhaustion
DII Continuous	0.86 (0.75 - 0.99)*	1.09 (1.05 - 1.14)*	1.05 (1.00 - 1.10)*	1.06 (1.00 - 1.11)*
DII Quintiles				
Q1: Most AI	Ref	Ref	Ref	Ref
Q2: Some AI	0.79 (0.34 - 1.85)	1.07 (0.90 - 1.29)	0.96 (0.73 - 1.27)	0.81 (0.61 - 1.08)
Q3: Some PI	0.36 (0.16 - 0.81)*	1.37 (1.12 - 1.66)*	1.10 (0.89 - 1.36)	1.32 (0.90 - 1.92)
Q4: More PI	0.78 (0.43. 1.40)	1.34 (1.09 - 1.66)*	1.14 (0.88 - 1.47)	1.52 (1.13 - 1.59)*
Q5: Most PI	0.45 (0.22 - 0.93)*	1.67 (1.33 - 2.10)*	1.19 (0.90 - 1.58)	1.11 (0.79 - 1.59)

Note. DII: Dietary inflammatory index; Q: Quintile; AI: Anti-inflammatory; PI: Proinflammatory; a. Adjusted for age, gender, race, education, summed co-morbidities score, and smoking status; * $p<0.05$

Interaction terms between gender and DII were not statistically significant in either multinomial (p=0.27) or logistic regression models (p=0.15). In separate analyses by gender, estimates of the association between DII and frailty were similar to overall results, indicating no multiplicative effect modification by gender (results not shown).

Discussion

Using data from the NHANES, a large, nationally representative survey, this study examined the association between dietary inflammatory potential and the geriatric syndrome of frailty. The results show that individuals with more pro-inflammatory diets, as indicated by higher DII scores, were more likely to be both pre-frail and frail after adjusting for health-related and demographic covariates. Categorical analyses further suggest that increased likelihood of frailty is similar among those with moderately and very pro-inflammatory diets when compared to those with anti-inflammatory diets. Although previous studies found an association between dietary inflammation and frailty only among men (17), we found no significant differences in this association by gender.

Our findings are consistent with a previous study by Shivappa and colleagues that examined the relationship between dietary inflammation and incident frailty over eight years of follow-up (17). Similar to our results, those individuals in the highest DII category had higher frailty incidence. Shivappa and colleagues also found that DII level was only associated with greater incidence of frailty among men, suggesting potential interaction between gender and dietary inflammation. In contrast, our results were similar when stratified by gender. Differences in results between this and the previous study may reflect different methodological approaches. For example, NHANES data are nationally representative, while the previous study by Shivappa and colleagues used data only from individuals with arthritis. Evidence of interaction may therefore reflect differences in the severity or rate of arthritis between frail and non-frail individuals, between men and women, or both.

Although previous studies indicate that pre-frail individuals may indeed have higher levels of inflammatory biomarkers compared to robust individuals (8), the association between DII and pre-frailty has not been evaluated. Our study found that more pro-inflammatory diets were associated with a greater likelihood of pre-frailty while controlling for key confounders. While it is not clear to what extent pre-frailty may be seen as a precursor of frailty, these results suggest that dietary inflammation may be an important factor in the development of frailty components individually, even in individuals not considered to be frail by standard cutoff criteria. Additionally, pre-frailty has been shown to be a risk facrtor of death (8), cardiovascular diseases (21), and disability (30), independent of frailty. The identification of factors that distinguish between robust and pre-frail individuals may therefore have clinical and public health implications, as the latter group may have distinctly greater risk of poor health outcomes and of becoming frail. Addressing dietary inflammation may be an important consideration, not only in treating frailty but also in developing strategies to help prevent frailty from developing in the first place.

These findings have important implications for frailty intervention development. Previous nutrition-based interventions for frailty have generally focused on protein-energy supplementation (31), micronutrient supplementation (32), and nutritional counseling (33). These interventions demonstrated limited improvements in individual frailty components such as physical activity level, grip strength, body weight, and/or walking speed; however, as nutrition-based frailty interventions are usually combined with exercise, it is difficult to assess the independent influence of specific nutrients on frailty. Although, certain micronutrients have been found to be associated with frailty (31, 32), results of the present study suggest that considering the inflammatory properties of overall diet may also be relevant to frailty prevention. Determining the average inflammatory potential of overall diet, for instance, helps distill an important feature of nutrient and food intake,

independent of any particular nutrient or food. From a practical standpoint, a focus on reducing dietary inflammation, on average, rather than on supplementation of specific nutrients, may help simplify and improve adherence to current nutrition-based interventions for frailty.

Despite this study's strengths, there are some limitations worth noting. First, NHANES data are cross-sectional and thus we were unable to assess the temporality of frailty and dietary inflammation scores. Frailty may lead to poorer nutrition (more pro-inflammatory diets) due to lack of access or decreases in mobility. However, as noted before, previous studies have found similar associations between dietary inflammation and incident frailty (17). Furthermore, individuals with prevalent frailty, as measured by cross-sectional data, may be less severely frail and more likely to participate in research interviews. Second, dietary intakes were measured through a 24-hour recall interview. As such, diet at the time of interview may not reflect long-term, habitual dietary patterns; however, prior work has demonstrated the validity and utility of this approach to assess associations between diet and health outcomes (34, 35). Additionally, the diets of older adults have been found to be relatively stable for at least five to seven years (36, 37), suggesting that 24-hour recall may be an accurate reflection of diet over a longer period of time. Finally, due to lack of availability of certain measures, this study used a modified version of the frailty phenotype model, which could lead to misclassification of frailty status. However, previous studies have found similar rates of frailty and pre-frailty using this modified measure (8).

Weighing its strengths and limitations, the current study contributes important information to current knowledge regarding the potential association of dietary inflammation in frailty. Whereas previous studies have been restricted to individuals with specific medical conditions, the NHANES complex sampling design allowed us to evaluate this association in a nationally representative sample. Additionally, this study is one of the first to evaluate the association between dietary inflammation and likelihood of pre-frailty. This is important because it suggests that frailty may be prevented or ameliorated by interventions focusing on inflammatory potential of individual diets, independent of other intervention approaches.

Conflicts of Interest: None

Disclosure: The Dietary Inflammatory Index (DII®) is a registered trademark of the University of South Carolina. Dr. James R. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company planning to license the right to his invention of the DII® from the University of South Carolina in order to develop computer and smart phone applications for patient counseling and dietary intervention in clinical settings. Drs. Michael D. Wirth and Nitin Shivappa are employees of CHI. These activities have no direct bearing on the use of the DII® as a research tool.

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Ethical standards: This study used retrospective survey data and did not include any animal or human experiments.

References

1. Fried LP, Tangen CM, Walston J, et al. Frailty in Older Adults: Evidence for a Phenotype. J Gerontol Med Sci Am. 2001;56(3):146-156. doi:10.1093/gerona/56.3.M146.
2. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. J Am Geriatr Soc. 2012;60(8):1487-1492. doi:10.1111/j.1532-5415.2012.04054.x.
3. Xue Q-L. The frailty syndrome: definition and natural history. Clin Geriatr Med. 2011;27(1):1-15. doi:10.1016/j.cger.2010.08.009.
4. Cheng M-H, Chang S-F. Frailty as a Risk Factor for Falls Among Community Dwelling People: Evidence From a Meta-Analysis. J Nurs Scholarsh an Off Publ Sigma Theta Tau Int Honor Soc Nurs. 2017;49(5):529-536. doi:10.1111/jnu.12322.
5. Gale CR, Cooper C, Sayer AA. Prevalence of frailty and disability: findings from the English Longitudinal Study of Ageing. Age Ageing. 2015;44(1):162-165. doi:10.1093/ageing/afu148.
6. Searle SD, Rockwood K. Frailty and the risk of cognitive impairment. Alzheimers Res Ther. 2015;7(1):54. doi:10.1186/s13195-015-0140-3.
7. Bongue B, Buisson A, Dupre C, Beland F, Gonthier R, Crawford-Achour E. Predictive performance of four frailty screening tools in community-dwelling elderly. BMC Geriatr. 2017;17(1):262. doi:10.1186/s12877-017-0633-y.
8. Crow RS, Lohman MC, Titus AJ, et al. Mortality Risk Along the Frailty Spectrum: Data from the National Health and Nutrition Examination Survey 1999 to 2004. J Am Geriatr Soc. 2018;66(3):496-502. doi:10.1111/jgs.15220.
9. Soysal P, Stubbs B, Lucato P, et al. Inflammation and frailty in the elderly: A systematic review and meta-analysis. Ageing Res Rev. 2016;31:1-8. doi:10.1016/j.arr.2016.08.006.
10. Puzianowska-Kuznicka M, Owczarz M, Wieczorowska-Tobis K, et al. Interleukin-6 and C-reactive protein, successful aging, and mortality: the PolSenior study. Immun Ageing. 2016;13:21. doi:10.1186/s12979-016-0076-x.
11. Schaap LA, Pluijm SMF, Deeg DJH, Visser M. Inflammatory markers and loss of muscle mass (sarcopenia) and strength. Am J Med. 2006;119(6):526.e9-17. doi:10.1016/j.amjmed.2005.10.049.
12. Verghese J, Holtzer R, Oh-Park M, Derby CA, Lipton RB, Wang C. Inflammatory markers and gait speed decline in older adults. J Gerontol A Biol Sci Med Sci. 2011;66(10):1083-1089. doi:10.1093/gerona/glr099.
13. Galland L. Diet and Inflammation. Nutr Clin Pract. 2010;25(6):634-640. doi:10.1177/0884533610385703.
14. Corley J, Kyle JAM, Starr JM, McNeill G, Deary IJ. Dietary factors and biomarkers of systemic inflammation in older people: the Lothian Birth Cohort 1936. Br J Nutr. 2015;114(7):1088-1098. doi:10.1017/S000711451500210X.
15. Xu H, Sjogren P, Arnlov J, et al. A proinflammatory diet is associated with systemic inflammation and reduced kidney function in elderly adults. J Nutr. 2015;145(4):729-735. doi:10.3945/jn.114.205187.
16. Shivappa N, Steck SE, Hurley TG, Hussey JR, Hebert JR. Designing and developing a literature-derived, population-based dietary inflammatory index. Public Health Nutr. 2014;17(8):1689-1696. doi:10.1017/S1368980013002115.
17. Shivappa N, Stubbs B, Hebert JR, et al. The Relationship Between the Dietary Inflammatory Index and Incident Frailty: A Longitudinal Cohort Study. J Am Med Dir Assoc. 2018;19(1):77-82. doi:10.1016/j.jamda.2017.08.006.
18. Namazi N, Larijani B, Azadbakht L. Dietary Inflammatory Index and its Association with the Risk of Cardiovascular Diseases, Metabolic Syndrome, and Mortality: A Systematic Review and Meta-Analysis. Horm Metab Res = Horm und Stoffwechselforsch = Horm Metab. May 2018. doi:10.1055/a-0596-8204.
19. Denova-Gutierrez E, Munoz-Aguirre P, Shivappa N, et al. Dietary Inflammatory Index and Type 2 Diabetes Mellitus in Adults: The Diabetes Mellitus Survey of Mexico City. Nutrients. 2018;10(4). doi:10.3390/nu10040385.
20. Fowler ME, Akinyemiju TF. Meta-analysis of the association between dietary inflammatory index (DII) and cancer outcomes. Int J Cancer. 2017;141(11):2215-2227. doi:10.1002/ijc.30922.
21. Sergi G, Veronese N, Fontana L, et al. Pre-frailty and risk of cardiovascular disease in elderly men and women: the Pro.V.A. study. J Am Coll Cardiol. 2015;65(10):976-983. doi:10.1016/j.jacc.2014.12.040.
22. National Center for Health Statistics. National Health and Nutrition Examination Survey, 2013–2014 Overview. Natl Heal Nutr Exam Surv. 2013:1-6. https://www.cdc.gov/nchs/data/nhanes/nhanes_13_14/2013-14_overview_brochure.pdf.
23. Blodgett J, Theou O, Kirkland S, Andreou P, Rockwood K. Frailty in NHANES: Comparing the frailty index and phenotype. Arch Gerontol Geriatr. 2015;60(3):464-470. doi:10.1016/j.archger.2015.01.016.
24. Statistics NC for H. Plan and operation of the Third National Health and Nutrition Examination Survey, 1988-94. Vital Heal Stat. 1994;32:1-407. http://ci.nii.ac.jp/naid/10011434759/en/. Accessed April 14, 2018.
25. Boden S, Wennberg M, Van Guelpen B, et al. Dietary inflammatory index and risk of first myocardial infarction; a prospective population-based study. Nutr J. 2017;16(1):21. doi:10.1186/s12937-017-0243-8.
26. Shivappa N, Wirth MD, Hurley TG, Hebert JR. Association between the dietary inflammatory index (DII) and telomere length and C-reactive protein from the National Health and Nutrition Examination Survey-1999-2002. Mol Nutr Food Res.

2017;61(4). doi:10.1002/mnfr.201600630.
27. Wirth MD, Shivappa N, Davis L, et al. Construct Validation of the Dietary Inflammatory Index among African Americans. J Nutr Health Aging. 2017;21(5):487-491. doi:10.1007/s12603-016-0775-1.
28. Shivappa N, Wirth MD, Murphy EA, Hurley TG, Hebert JR. Association between the Dietary Inflammatory Index (DII) and urinary enterolignans and C-reactive protein from the National Health and Nutrition Examination Survey-2003-2008. Eur J Nutr. April 2018. doi:10.1007/s00394-018-1690-5.
29. No Title. CDC National Health and Nutrition Examination Survey: Analytic Guidelines. http://www.cdc.gov/nchs/data/series/sr_02/sr02_161.pdf.
30. Acosta-Benito MA, Sevilla-Machuca I. Using prefrailty to detect early disability. J Family Community Med. 2016;23(3):140-144. doi:10.4103/2230-8229.189106.
31. Kim C-O, Lee K-R. Preventive effect of protein-energy supplementation on the functional decline of frail older adults with low socioeconomic status: a community-based randomized controlled study. J Gerontol A Biol Sci Med Sci. 2013;68(3):309-316. doi:10.1093/gerona/gls167.
32. Hutchins-Wiese HL, Kleppinger A, Annis K, et al. The impact of supplemental n-3 long chain polyunsaturated fatty acids and dietary antioxidants on physical performance in postmenopausal women. J Nutr Health Aging. 2013;17(1):76-80. doi:10.1007/s12603-012-0415-3.
33. Rydwik E, Frandin K, Akner G. Effects of a physical training and nutritional intervention program in frail elderly people regarding habitual physical activity level and activities of daily living--a randomized controlled pilot study. Arch Gerontol Geriatr. 2010;51(3):283-289. doi:10.1016/j.archger.2009.12.001.
34. Shivappa N, Steck SE, Hurley TG, et al. A population-based dietary inflammatory index predicts levels of C-reactive protein in the Seasonal Variation of Blood Cholesterol Study (SEASONS). Public Health Nutr. 2014;17(8):1825-1833. doi:10.1017/S1368980013002565.
35. Hebert JR, Hurley TG, Steck SE, et al. Considering the value of dietary assessment data in informing nutrition-related health policy. Adv Nutr. 2014;5(4):447-455. doi:10.3945/an.114.006189.
36. Weismayer C, Anderson JG, Wolk A. Changes in the stability of dietary patterns in a study of middle-aged Swedish women. J Nutr. 2006;136(6):1582-1587. doi:10.1093/jn/136.6.1582.
37. Jankovic N, Steppel MT, Kampman E, et al. Stability of dietary patterns assessed with reduced rank regression; the Zutphen Elderly Study. Nutr J. 2014;13:30. doi:10.1186/1475-2891-13-30.