

Nutritional status of frail elderly

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ABSTRACT

Introduction: Growing population of elderly requires effective medical diagnostics and help. Criteria developed by Fried et al. are most often used for the diagnosis of the frailty syndrome. An inherent element of frailty syndrome is malnutrition. Malnutrition results from inadequate food supply, coexistence of acute and chronic diseases. Effective nutritional interventions conducted on frail older persons can prevent them from developing the frailty syndrome.

Review: The prevalence of frailty in elders is 17% moreover 42.3% are prefrail. There are many scales designed to identify frailty syndrome, but the most common is the classification of Fried et al. Malnutrition is a common state in frail elderly. Basic questionnaire, which is used to diagnose malnutrition, is MNA (Mini-Nutritional Assessment). Mini-Nutritional Assessment Short-Form (MNA-SF) and Malnutrition Universal Screening Tool (MUST) also can be used.

Sarcopenia, which is defined as reduced muscle mass and strength and impaired muscle performance, significantly contribute to the development of frailty. Many studies have shown that an effective method in the preventing of sarcopenia is protein supplementation. Other beneficial lifestyle and diet changes, which can help prevent the development of frailty syndrome, are adherence to the Mediterranean diet, appropriate intake of carotenoids, vitamin E, selenium and zinc. Another important protective factor is vitamin D levels. Low serum 25(OH)D is strongly associated with frailty.

Conclusions: From a nutritional point of view adherence to a Mediterranean-style diet, sufficient intake of protein, micronutrients and vitamin D, as well as regular moderate physical activity, can be crucial in the preventing of the frailty syndrome.

Keywords: Frail elderly, nutritional status, diet, malnutrition, vitamin D

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INTRODUCTION

According to data from The World Factbook, people aged 65 years and older represent 8.32% of the world population (data estimated for year 2014) [1]. Along with growing population of the elderly the need to overcome negative effects of aging is becoming more urgent. Frailty syndrome, defined by Fried et al., includes five variables: unintentional weight loss, exhaustion, loss of grip strength, slowness and low physical activity. Coexistence of at least three out of five mentioned variables classify a person as frail [2]. Malnutrition is one of the symptoms of the frailty syndrome. It is considered a risk factor for ill-health and increased mortality. Additionally it contributes to impaired function of the body, prolonged hospitalization and deterioration of the quality of life [3]. Lack of gold standard for diagnosing malnutrition in the elderly hinders treatment. Only combination of various methods (anthropometry, laboratory tests, subjective global assessment, Mini-Nutritional Assessment, SCALES test) can be effective in determination of nutritional status [4]. By effective nutritional interventions conducted on frail older persons improvement of their risk profile is possible. Adhering to the principles of a balanced diet reduces the risk of two factors of the frailty syndrome- unintentional weight loss and loss of grip strength [5]. Main aim of this review is to demonstrate that improvement of the nutritional status in older people may help overcome the frailty syndrome.

Literature search

A Medline literature search included combination of following terms: "frail," "frailty," "nutrition," "nutritional status," "malnutrition," "diet," "older people," "elderly." Publications written in English and Polish were included, which gave the total number of thirty-two publications. Papers before year 2004 have been rejected.

Frailty syndrome

Based on the data from the Frailty Instrument for Primary Care of the Survey of Health, Ageing and Retirement in Europe (SHARE-FI) it has been shown that the prevalence of frailty in persons older than 65 years is 17%. Moreover, 42.3% are prefrail [6]. Scientists agree that frailty is a geriatric syndrome characterized by the reduction of physiological reserves and resistance to stressors. These changes make the elderly vulnerable for adverse health outcomes, including disability, dependency, falls; need for long-term care and mortality [2,7-9]. Due to its multidimensional nature, there are multiple criteria for diagnosing the frailty syndrome. Most commonly used frailty scale in research is the Cardiovascular Health Study (CHS) frailty scale. Previously mentioned scale consists of five factors. In the presence of three to

five factors, a person is considered as frail, two to one as prefrail, or when none of the factors are present as robust [2]. Another method, also using the CHS frailty scale, is an innovative Platform for Evaluation of Frailty and Prevention of Disability. Innovative character of this study is based on focusing on the prevention of the frailty syndrome. Researchers developed a questionnaire to be used by general practitioners for screening frailty. Questionnaire consists of six questions, which relate to the patient's frailty status together with functional, social, cognitive, nutritional factor. After screening, a multidisciplinary team provides for each patient a personalized preventive plan of intervention against disability [8]. The main assumption of the Frailty Risk Index (FRI) is the use of Multisystem Risk Factors, which include 13 significant clinical risk indicators of prefrailty and frailty. The variables are as follows: older age, no education, heart failure, obstructive respiratory disorders, stroke, depressive symptoms, hearing impairment, visual impairment, chronic airflow obstruction, chronic kidney failure, low hemoglobin, high nutritional risk, and increased WCCs. During validation, the summary risks score (FRI) was related to the prevalence of prefrailty and frailty. Increasing number of present risk indicators enhanced this prevalence [10]. There are many other scales, which are used to assess the occurrence of the frailty syndrome, e.g. Frailty Index Comprehensive Geriatric Assessment (FI-CGA), the Multidimensional Prognostic Index (MPI) Index, the Short Emergency Geriatric Assessment (SEGAm) [10-13]. Each scale is related to nutritional status, differing only in the analyzed parameters.

Frail older adults are more often females, live alone, have a lower educational level [15], higher BMI, history of chronic disease and depression symptoms; smoke cigarettes [16,17]. According to NHANES III they are also at lower income levels and less likely to be white. From the nutritional approach frail elderly have lowest energy intake and are more likely to be food insufficient. In fact, people who were frail were 4.69 (95% CI 1.73-12.67) times more likely to report food insufficiency than people who were not frail [17].

Nutritional status of frail patients

Malnutrition is a common state connected to the senile period itself, as well as the frailty syndrome. It is associated with increased morbidity and mortality. Due to changes in body composition of the elderly, e.g. loss of lean body mass, loss of muscle strength and sarcopenia, increase in body fat, this group is at risk of malnutrition [3,14,15]. Also, coexisting acute and chronic diseases predispose to the formation of eating disorders,

reduction of appetite, which contributes to the occurrence of malnutrition. Anorexia itself can be regarded as an early risk factor of frailty [15]. Other factors responsible for the development of malnutrition are: weight loss of > 5% in previous month or > 10% in previous 6 months, significant under- or overweight (\pm 20% desirable body weight), increased catabolism (fever, trauma, burns), increased loss of nutrients (diarrhea, malabsorption), previous surgery of the GI tract, radiotherapy, medications debilitating hunger (steroids, antibiotics, cytostatics), alcohol dependence, reduction in serum albumin and decreased number of lymphocytes in peripheral blood [4,7]. Basic, validated for older people, questionnaire, which is used to diagnose malnutrition, is MNA (Mini Nutritional Assessment). Its full version contains eighteen questions, while a short-form screening version- the Mini-Nutritional Assessment Short-Form (MNA-SF) only six. Questions in the MNA relate to the anthropometric assessment (weight loss, mid-arm circumference, calf circumference, BMI), general assessment (patient's mobility, medications, neuropsychological problems), dietary and self assessment. Scoring for the MNA is as follows: \geq 24 well nourished, 17-23,5 at risk of malnutrition, <17 malnourished [18]. For the MNA-SF scoring works in the opposite direction- a lower score indicates a higher risk of malnutrition [14]. Studies examining the size of malnutrition vary between populations. Polish WOBASZ study, conducted on a sample of 1,013 elderly, showed that by short-form MNA questionnaire 13% of seniors were malnourished, and 57% at risk of malnutrition [19]. In the French study Gérontopôle, using the MNA, 34% of people aged 65 years and older were malnourished, and 9% at risk of malnutrition [8]. During analysis of the MNA and frailty in community dwelling older, significant statistical differences were found between risk of malnutrition and development of the frailty syndrome. Risk of malnutrition was found in 2.2% of the non-frail, in 12.2% of the pre-frail and in 46.9% of the frail participants ($p < 0.001$) [15]. Another screening tool for malnutrition is MUST (malnutrition universal screening tool). It consists of following variables: current BMI (as WHO defines it), known weight loss, the presence of acute disease/no nutritional intake for 5 days. A study among frail older hospital inpatients comparing MUST and MNA-SF showed that the MUST scored patients within a low risk category (77% low risk, 9% medium risk, 14% high risk), whereas the MNA-SF scored most within 'at risk' and 'malnourished' categories (46% malnourished, 45% at risk, 9% normal) [14].

Sarcopenia, which is defined as reduced muscle mass and strength and impaired muscle performance, significantly contribute to the development of frailty [7]. Reduced lean body mass

leads to decrease in total body protein and contributes to increased frailty [16-18,20]. Many studies have shown the positive impact of protein supplementation on muscle mass, strength and physical performance. In a randomized controlled double blind study the impact of 24 weeks of dietary protein supplementation on muscle mass, strength and physical performance has been assessed. Subjects (65 frail elderly) were randomly assigned to either a placebo or protein supplementation group. Daily protein intake was 15 g for breakfast and another 15 g for lunch. After 24 weeks lean body mass increased from 47.2 kg (95% CI, 43.5-50.9) to 48.5 kg (95% CI, 44.8-52.1) in the protein group and did not change in the placebo group. Strength and physical performance improved significantly in both groups ($P=0.000$) with no interaction effect of dietary protein supplementation [21]. Another study, with the intervention period also lasting for 24 weeks, determined the effect of protein supplementation (15g protein in a beverage) on cognitive performance in frail elderly. Among the 65 respondents protein supplementation did not improve any of the cognitive domain scores [22]. Researchers who investigated protein consumption with risk of incident frailty obtained more favorable results. In the Women's Health Initiative Observational Study 24,417 women were involved, aged 65-79 years, who were free of frailty at baseline. A 20% increase in protein intake (as a percentage of total energy) was associated with a strong, dose-responsive lower risk (of 32%) of incident frailty after a 3 years follow-up [23,24]. A new approach to protective impact of protein consumption on the development of the frailty syndrome concerns comparison of dietary protein source (animal or plant) and quality (amino acid components). Among the group of 2108 Japanese women (aged 65-94 years), 22.8% were frail. Mean intake of total protein was 74.0 g/d (43.5 g/d animal, 30.5 g/d plant). Protein (both animal and plant) and amino acid intakes in the frail group were significantly lower than those in the non-frail group. Results may indicate that the source of protein or kind of amino acid might not be particularly important in preventing frailty [16]. Improving muscle mass and strength, gait and balance, as well as reducing the rate of falls in elderly, thus preventing sarcopenia and frailty syndrome, should be accomplished by a multi-component exercise intervention program that consists of strength, endurance, and balance training [25].

The Mediterranean diet is known for its beneficial health properties and declining overall mortality [26]. Adherence to the diet can be summarized with 2 instruments: the Mediterranean Diet Adherence Screener (MEDAS) and the Mediterranean Diet Score (MDS). Based on data from the senior-ENRICA cohort (1815 participants,

60 years and older), the effect of the Mediterranean diet (MD) on the development of the frailty syndrome was investigated. After a 3,5 year follow-up, researches found that an increasing adherence to the MD was associated with a decreasing risk of frailty, referring to the global dietary pattern, not single foods [27]. By using the Mediterranean Diet Score (MDS), data from the InCHIANTI study (690 community-living persons, ≥ 65 years old) was used to define adherence to a Mediterranean-style diet. MDS was categorized into 3 categories: low adherence (MDS ≤ 3), medium adherence (MDS 4–5), and high adherence (MDS ≥ 6). Individuals were followed for 6 years to identify incident frailty. Higher adherence to a Mediterranean-style diet was associated with lower odds of developing frailty (OR 0.30; 95% CI 0.14-0.66) compared with those with lower adherence [28].

Some studies had shown that increased number of micronutrient deficiencies and low serum beta-carotenoids were significant risk factors for frailty [10,17]. It is certain that during the process of ageing micronutrient deficiencies are becoming more often. An inappropriate intake of specific nutrient likes vitamin D, A, E, B₆, B₁₂, folate, zinc, and selenium contributes to formation of deficiencies. In 766 women, of who 250 were frail and 516 not frail at baseline, serum micronutrients were measured. Significant differences between frail and non-frail women were found in serum concentrations of total carotenoids ($p=.006$), α -tocopherol ($p=.06$), 25-hydroxyvitamin D ($p < .0001$), selenium ($p < .0001$), and zinc ($p = .001$). Older women who had one or more indicators of poor micronutrient status had significantly higher risk of becoming frail [29].

Vitamin d levels

Vitamin D, besides its widely described effects on the skeletal system, affects the central nervous system, muscles (e.g. reduces muscle strength) and balance, which is especially important in preventing falls and fractures [30]. In addition, vitamin D deficiency usually occurs in the form of latent hypovitaminosis and causes secondary hyperparathyroidism. It causes high bone turnover and, consequently, the loss of bone mass. The prevalence of vitamin D deficiency in the elderly ranges from 5% to 25% of people living alone and from 60% to even 80% of those living in nursing homes. These values vary mainly depending on latitude, lifestyle, exposure to light, and supplementation of the diet of vitamin D and calcium [31,32]. In an Italian study, concerning association of low vitamin D levels with the frailty syndrome, 561 women (mean age 75.6) and 444 (mean age 74.2) men were examined. Concentration of 25(OH)D lower than 50 nmol/L was defined as insufficient. The median of 25(OH)D for women and men were 33.4 (22.7–

49.4) nmol/L and 48.5 (34.1–73.1) nmol/L, respectively. 11.8% of women and 8.9% of men had the prevalence of frailty, while 43.6% of women and 35.6% of men were intermediate frail. A strong, independent association of low 25(OH)D with frailty in men was found [30]. Data from the third NHANES gave information about impact of serum 25(OH)D on frailty. Low 25(OH)D concentrations (< 37.4 nmol/L) were associated with a 3.7-fold increase in the odds of frailty among whites and a 4-fold increase in the odds of frailty among non-whites [33]. On the other hand, in a study conducted among African American population no association between 25(OH)D levels and occurrence of either frailty or prefrailty was found. The lack of association may be explained by very low levels of 25(OH)D in this population [34]. Effective diet and training program can result in significant improvement of geriatric frailty. Three-month exercise and nutritional program resulted in short-term (3-month) frailty status improvement and long-term effect on bone mineral density and serum 25(OH)D among 117 older adults [35]. Investigations aiming vitamin D focused not only on its influence on frailty syndrome, but also on cognitive executive function. The ProMuscle Study examined the association between vitamin D and cognitive performance in a prefrail and frail elderly population. 127 participants (mean age 79 years old) had mean serum 25(OH)D of 54nmol/L. 17% of the population had serum 25(OH)D levels below 30 nmol/L, 53% below 50 nmol/L and 23% 75 nmol/L or higher. Serum 25(OH)D levels decreased with age ($p=.03$). Strong association was found between serum 25(OH)D and executive functioning, less significant association was observed for serum 25(OH)D with information-processing speed [36].

CONCLUSIONS

Nutrition is one of the major determinants of successful aging. A proper way of eating is consistent with genetic, social and psychological aspects of life as well as an overall well-being. Disorders of nutritional status, resulting in the development of malnutrition, sarcopenia, and consequently, the frailty syndrome, should be compensated by the appropriate diagnostic, treatment and consumption of food. Improvement of quality of life in older adults can be achieved by a diet consistent with current guidelines (high amounts of vegetables, fruits, whole grains, poultry, fish, low-fat dairy products). Furthermore, some studies have shown that proper intake of vitamins (especially vitamin D) may influence cognitive performance. Regular physical activity, adherence to a Mediterranean-style diet, sufficient intake of protein, micronutrients and vitamin D can be

crucial to the prevention of the frailty syndrome, which should be confirmed by further research.

Conflicts of interest

None

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REFERENCES

1. Central Intelligence Agency. Washington: 2014. Available from: <https://www.cia.gov/library/publications/the-world-fact-book/geos/xx.htm> [Internet] [cited 2014 Oct 21]
2. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci*. 2004 Mar;59(3):255-63.
3. Özga E, Małgorzewicz S. Assessment of nutritional status of the elderly. *Geriatrics*. 2013; 7:98-103. (Polish)
4. Babiarczyk B. Monitoring of nutritional status in elderly short-and long-term care residents. *Gerontol. Pol*. 2008;16(1):18-24. (Polish)
5. Kelaiditi E, Abellan van Kan G, Cesari M. Frailty: role of nutrition and exercise. *Curr Opin Clin Nutr Metab Care*. 2014 Jan;17(1):32-9.
6. Romero-Ortuno R, Walsh C, Lawloe B, Kenny R. A Frailty Instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). *BMC Geriatr*. 2010 Aug 24;10:57.
7. Dorner T, Lackinger C, Haider S, Luger E, Kapan A, Luger M, Schindler K. Nutritional intervention and physical training in malnourished frail community-dwelling elderly persons carried out by trained lay "buddies": study protocol of a randomized controlled trial. *BMC Public Health*. 2013 Dec 27;13:1232.
8. Subra J, Gillette-Guyonnet S, Cesari M, Oustric S, Vellas B, the Platform Team. The integration of frailty into clinical practice: preliminary results from the Gérontopôle. *J Nutr Health Aging*. 2012 Aug;16(8):714-20.
9. Clegg A, Young J, Iliffe S, Rickett M, Rockwood K. Frailty in elderly people. *Lancet*. 2013 Mar;381(9868):752-62.
10. Pin Ng T, Feng L, Zin Nyunt M, Larbi A, Bee Yap K. Frailty in Older Persons: Multisystem Risk Factors and the Frailty Risk Index (FRI). *J Am Med Dir Assoc*. 2014 Sep;15(9):635-42.
11. Wou F, Conro S. The frailty syndrome. *Medicine*. 2013 Jan;41(1):13-5.
12. Oubaya N, Mahmoudi R, Jolly D, Zulfiqar A.A, Quignard E, Cunin C, Nazeyrollas P, Novella J.L, Dramé M. Screening for Frailty in Elderly Subjects Living at Home: Validation of the Modified Short Emergency Geriatric Assessment (SEGAm) Instrument. *J Nutr Health Aging*. 2014;18(8):757-64.
13. Bouillon K, Kivimaki M, Hamer M, Sabia S, Fransson E, Singh-Manoux A, Gale C, Batty G. Measures of frailty in population-based studies: an overview. *BMC Geriatr*. 2013 Jun 21;13:64.
14. Slee A, Birch D, Stokoe D. A comparison of the malnutrition screening tools, MUST, MNA and bioelectrical impedance assessment in frail older hospital patients. *Clin Nutr*. 2014 May;1-6.
15. Bollwein J, Volkert D, Diekmann R, Kaiser M.J, Uter W, Vidal K, Sieber C.C, Bauer J.M. Nutritional status according to the Mini Nutritional Assessment (MNA) and frailty in community dwelling older. *J Nutr Health Aging*. 2013 Apr;17(4):351-6.
16. Kobayashi S, Asakura K, Suga H, Sasaki S, Three-generation Study of Women on Diets and Health Study Group. High protein intake is associated with low prevalence of frailty among old Japanese women: a multicenter cross-sectional study. *Nutr J*. 2013 Dec 19;12:164.
17. Smit E, Winters-Stone K, Loprinzi P, Tang A, Crespo C. Lower Nutritional Status and Higher Food Insufficiency in Frail Older US Adults. *Br J Nutr*. 2013 Jul 14;110(1):172-8.
18. Dent E, Chapman I, Piantadosi C, Visvanathan R. Performance of nutritional screening tools in predicting poor six-month outcome in hospitalized older patients. *Asia Pac J Clin Nutr*. 2014;23(3):394-9.
19. Waśkiewicz A, Sygnowska E, Broda E. Ocena stanu zdrowia i odżywienia osób w wieku powyżej 75 lat w populacji polskiej badanie WOBASZ-SENIOR. *Bromat. Chem. Toksykol*. 2012;45(3):614-8. (Polish)
20. Melissa Bernstein M, Munoz N, Square K. Position of the Academy of Nutrition and Dietetics: Food and Nutrition for Older Adults: Promoting Health and Wellness. *J Acad Nutr Diet*. 2012 Aug;112(8):1255-77.
21. Tieland M, Dirks M, van der Zwaluw N, Verdijk L, van de Rest O, de Groot L, van Loon L. Protein Supplementation Increases Muscle Mass Gain During Prolonged Resistance-Type Exercise Training in Frail Elderly People: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Am Med Dir Assoc*. 2012 Oct;13(8):713-9.
22. Zwaluw N, van de Rest O, Tieland M, Adam J, Hiddink g, van Loon L, de Groot L. The impact of protein supplementation on cognitive performance in frail elderly. *Eur J Nutr*. 2014 Apr;53(3):803-12.
23. Boirie Y, Morio B, Caumon E, Cano N. Nutrition and protein energy homeostasis in elderly. *Mech Ageing Dev*. 2014 Mar-Apr;136-137:76-84.
24. Beasley J, LaCroix A, Neuhouser M, Huang Y, Tinker L, Woods N, Michael Y, Curb J,

- Prentice R. Protein Intake and Incident Frailty in the Women's Health Initiative Observational Study. *J Am Geriatr Soc.* 2010 Jun;58(6):1063–71.
25. Cadore E.L, Rodríguez-Mañas L, Sinclair A, Izquierdo M. Effects of Different Exercise Interventions on Risk of Falls, Gait Ability, and Balance in Physically Frail Older Adults: A Systematic Review. *Rejuvenation Res.* 2013 Apr;16(2):105-14.
26. Mitrou P, Kipnis V, Thiébaud A, Reedy J, Subar A, Wirfält E, Flood A, Mouw T, Hollenbeck A, Leitzmann M, Schatzkin A. Mediterranean dietary pattern and prediction of all-cause mortality in a US population: results from the NIH-AARP Diet and Health Study. *Arch Intern Med.* 2007 Dec;167(22):2461-8.
27. León-Muñoz L, Guallar-Castillón P, López-García E, Rodríguez-Artalejo F. Mediterranean Diet and Risk of Frailty in Community-Dwelling Older Adults. *J Am Med Dir Assoc.* 2014 Dec;15(12):899-903.
28. Talegawkar S, Bandinelli S, Bandeen-Roche K, Chen P, Milaneschi Y, Tanaka T, Semba R, Guralnik J, Ferrucci L. A Higher Adherence to a Mediterranean-Style Diet is Inversely Associated with the Development of Frailty in Community-Dwelling Elderly Men and Women. *J Nutr.* 2012 Dec;142(12):2161-6.
29. Semba R, Bartali B, Zhou J, Blaum C, Ko C.-W, Fried L. Low Serum Micronutrient Concentrations Predict Frailty Among Older Women Living in the Community. *J Gerontol A Biol Sci Med Sci.* 2006 Jun;61(6):594-9.
30. Shardell M, Hicks G, Miller R, Kritchevsky S, Andersen D, Bandinelli S, Cherubini A, Ferrucci L. Association of Low Vitamin D Levels with the Frailty Syndrome in Men and Women. *J Gerontol A Biol Sci Med Sci.* 2009 Jan;64(1):69-75.
31. Visser M, Deeg D, Puts M, Seidell J, Lips P. Low serum concentrations of 25-hydroxyvitamin D in older persons and the risk of nursing home admission. *Am J Clin Nutr.* 2006 Sep;84(3):616-22.
32. Kupisz-Urbańska M, Galus K. Epidemiology of vitamin D deficiency among elderly people - chosen aspects. *Gerontol. Pol.* 2011;19(1):1-6. (Polish)
33. Wilhelm-Leen E, Hall Y, deBoer I, Chertow G. Vitamin D deficiency and frailty in older Americans. *J Intern Med.* 2010 Aug;268(2):171-80.
34. Morley J.E, Malmstrom T.K, Miller D.K. A simple frailty questionnaire (Frail) predicts outcomes in middle aged african americans. *J Nutr Health Aging.* 2012 Jul;16(7):601-8.
35. Chan CD, Tsou H-H, Yang R-S, Tsauo J-Y, Chen C-Y, Hsiung C, Kuo K. A pilot randomized controlled trial to improve geriatric frailty. *BMC Geriatrics.* 2012 Sep 25;12:58.
36. Brouwer-Brolsma E, van de Rest O, Tieland M, van der Zwaluw N, Steegenga W, Adam J, van Loon L, Feskens E, de Groot L. Serum 25-Hydroxyvitamin D Is Associated With Cognitive Executive Function in Dutch Prefrail and Frail Elderly: A Cross-Sectional Study Exploring the Associations of 25-Hydroxyvitamin D With Glucose Metabolism, Cognitive Performance and Depression. *J Am Med Dir Assoc.* 2013 Nov;14(11):852.e9-17.