

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

# Nutritional Interventions for the Delayed Progression or Reversal of Frailty: Clinical Effectiveness

Service Line: Rapid Response Service  
Version: 1.0  
Publication Date: May 28, 2018  
Report Length: 7 Pages

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**Cite As:** Nutritional interventions for the delayed progression or reversal of frailty: clinical effectiveness. Ottawa: CADTH; 2018 May. (CADTH rapid response report: summary of abstracts).

**Acknowledgments:**

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## Research Question

What is the effectiveness of nutritional interventions for delaying or reversing the progression of frailty in those with frailty?

## Key Findings

One systematic review and five randomized controlled trials were identified regarding the effectiveness of nutrition interventions to reverse or delay the progression of frailty in those with frailty.

## Methods

A limited literature search was conducted on key resources PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit the retrieval to health technology assessments, systematic reviews, and meta-analyses, and randomized controlled trials. The search was limited to English language documents published between January 1, 2011 and May 14, 2018. Internet links were provided, where available.

## Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

**Table 1: Selection Criteria**

<b>Population</b>	Patients with frailty (living in the community, living in long term care, or in acute care)
<b>Intervention</b>	Nutritional interventions
<b>Comparator</b>	Usual Care
<b>Outcomes</b>	Effectiveness and clinical benefit from the patient standpoint, patient-centred outcomes; e.g. <ul style="list-style-type: none"> <li>• Quality of life improvements</li> <li>• Improvements on a frailty scale</li> <li>• Improvements in functional status</li> <li>• Increased muscle strength or stamina</li> <li>• Healthcare utilization/need for interventions (need for a trip to the ER, length of stay)</li> </ul>
<b>Study Designs</b>	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies

## Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

One systematic review and five randomized controlled trials were identified regarding the effectiveness of nutritional interventions to reverse or delay the progression of frailty in those with frailty. No relevant health technology assessments, meta-analyses, or non-randomized studies were identified.

Additional references of potential interest are provided in the appendix.

## Overall Summary of Findings

One systematic review<sup>1</sup> and five randomized controlled trials<sup>2-6</sup> were identified regarding the effectiveness of nutritional interventions to reverse or delay the progression of frailty in those with frailty.

According to one systematic review, supplementation of vitamin D and proper nutrition were effective measures to reduce frailty.<sup>1</sup>

Three randomized studies (RCTs) examined improvements in functional status.<sup>3-5</sup> In one study, older adults with frailty taking a nutrient supplement (l-leucine and cholecalciferol enriched supplement with medium-chain triglycerides) for three months increased their walking speed.<sup>3</sup> No improvements were observed in a second group given the same nutrient supplement plus long-chain triglycerides, or in a control group.<sup>3</sup> The authors of two other RCTs examined protein supplementation and functional status, with both studies showing an overall greater effect of protein supplementation relative to a control group.<sup>4-5</sup> One RCT showed that twelve weeks of protein supplementation generally increased physical functioning versus a control group.<sup>4</sup> Specifically, mobility/static and dynamic balance improved and physical performance remained stable in the protein supplement intervention group, while both decreased in controls.<sup>4</sup> Paradoxically, there was a greater decrease in usual gait speed in the protein supplement intervention group versus the control group.<sup>4</sup> The second RCT showed that, after six weeks of a traditional weight loss regimen control condition or a high-protein weight loss regimen in frail adults with obesity, the protein group experienced comparatively greater improvements in function.<sup>5</sup>

Three randomized studies examined increased muscle strength or stamina.<sup>2-3,6</sup> In one RCT, older adults with frailty in a high intensity resistance training program were randomized to a protein supplement intervention or no-supplement control.<sup>2</sup> The intervention group experienced greater improvements in grip strength and knee extensor force versus the control group.<sup>2</sup> In a second RCT, older adults with frailty who were randomized to take a nutrient supplement (l-leucine and cholecalciferol enriched supplement with medium-chain triglycerides) for three months increased their right-hand grip strength, improved their 10-second leg open-and-close test performance, and increased peak expiratory flow.<sup>3</sup> No improvements in strength were observed in a second group given the same nutrient supplement plus long-chain triglycerides, or in a control group.<sup>3</sup>

One RCT examined the effect of caloric restriction on strength in older adults with frailty and obesity and showed that there was no difference in knee extension and flexion between

those patients randomized to a year-long caloric restriction to induce and maintain a weight loss of 10% from baseline body weight versus a control condition.<sup>6</sup>

No included studies examined quality of life improvements in relation to nutritional interventions. No included studies examined healthcare utilization or the need for interventions in relation to nutritional interventions.

## References Summarized

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-analyses

1. Veninsek G, Gabrovec B. Management of frailty at individual level - clinical management: systematic literature review. *Zdr Varst*. 2018 Jun;57(2):106-115. [PubMed: PM29651322](#)

### Randomized Controlled Trials

2. Niccoli S, Kolobov A, Bon T, Rafilovich S, Munro H, Tanner K, et al. Whey protein supplementation improves rehabilitation outcomes in hospitalized geriatric patients: a double blinded, randomized controlled trial. *J Nutr Gerontol Geriatr*. 2017 Oct-Dec;36(4):149-165. [PubMed: PM29252150](#)
3. Abe S, Ezaki O, Suzuki M. Medium-chain triglycerides in combination with leucine and vitamin d increase muscle strength and function in frail elderly adults in a randomized controlled trial. *J Nutr*. 2016 May;146(5):1017-26. [PubMed: PM27075909](#)
4. Kim CO, Lee KR. 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 Mar;68(3):309-16. [PubMed: PM22879453](#)

### *Frail with Obesity*

5. Porter Starr KN, Pieper CF, Orenduff MC, McDonald SR, McClure LB, Zhou R, et al. Improved function with enhanced protein intake per meal: a pilot study of weight reduction in frail, obese older adults. *J Gerontol A Biol Sci Med Sci*. 2016 Oct;71(10):1369-75. [PubMed: PM26786203](#)
6. Armamento-Villareal R, Aguirre L, Napoli N, Shah K, Hilton T, Sinacore DR, et al. Changes in thigh muscle volume predict bone mineral density response to lifestyle therapy in frail, obese older adults. *Osteoporos Int*. 2014 Feb;25(2):551-8. [PubMed: PM23892583](#)

### Non-Randomized Studies

No literature identified.

## Appendix — Further Information

### Systematic Reviews and Meta-Analyses

#### *Alternative Population – Mixed (Frail and Pre-Frail Population)*

7. Cheng H, Kong J, Underwood C, Petocz P, Hirani V, Dawson B, et al. Systematic review and meta-analysis of the effect of protein and amino acid supplements in older adults with acute or chronic conditions. *Br J Nutr*. 2018 Mar;119(5):527-542.

[PubMed: PM29508691](#)

8. Dewansingh P, Melse-Boonstra A, Krijnen WP, van der Schans CP, Jager-Wittenaar H, van den Heuvel E. Supplemental protein from dairy products increases bodyweight and vitamin d improves physical performance in older adults: a systematic review and meta-analysis. *Nutr Res*. 2018 Jan;49:1-22.

[PubMed: PM29420989](#)

#### *Alternative Intervention – Combined (Nutrition and Physical Activity)*

9. Lozano-Montoya I, Correa-Perez A, Abraha I, Soiza RL, Cherubini A, O'Mahony D, et al. Nonpharmacological interventions to treat physical frailty and sarcopenia in older patients: a systematic overview - the senator project ONTOP series. *Clin Interv Aging*. 2017;12:721-740.

[PubMed: PM28490866](#)

10. Thomas DK, Quinn MA, Saunders DH, Greig CA. Protein supplementation does not significantly augment the effects of resistance exercise training in older adults: a systematic review. *J Am Med Dir Assoc*. 2016 Oct 1;17(10):959.e1-9.

[PubMed: PM27670605](#)

#### *No Comparator*

11. Zhou J, Huang P, Liu P, Hao Q, Chen S, Dong B, et al. Association of vitamin D deficiency and frailty: a systematic review and meta-analysis. *Maturitas*. 2016 Dec;94:70-76.

[PubMed: PM27823748](#)

### Randomized Controlled Trials

#### *Alternative Intervention – Combined (Nutritional and Physical Activity)*

12. Collins J, Longhurst G, Roschel H, Gualano B. Resistance training and co-supplementation with creatine and protein in older subjects with frailty. *J Frailty Aging*. 2016;5(2):126-34.

[PubMed: PM27224505](#)

#### *Alternative Population (Pre-Frail and Frail) and Alternative Intervention (Combined - Nutritional and Physical Activity)*

13. Ng TP, Nyunt MSZ, Feng L, Feng L, Niti M, Tan BY, et al. Multi-domains lifestyle interventions reduces depressive symptoms among frail and pre-frail older persons: randomized controlled trial. *J Nutr Health Aging*. 2017;21(8):918-926.

[PubMed: PM28972245](#)

14. Ng TP, Feng L, Nyunt MS, Feng L, Niti M, Tan BY, et al. Nutritional, physical, cognitive, and combination interventions and frailty reversal among older adults: a randomized controlled trial. *Am J Med.* 2015 Nov;128(11):1225-1236.e1.

[PubMed: PM26159634](#)

#### *Alternative Intervention – Combined (Nutrition and Physical Activity)*

15. Kapan A, Luger E, Haider S, Titze S, Schindler K, Lackinger C, et al. Fear of falling reduced by a lay led home-based program in frail community-dwelling older adults: a randomised controlled trial. *Arch Gerontol Geriatr.* 2017 Jan - Feb;68:25-32.

[PubMed: PM27588891](#)

16. Kim H, Suzuki T, Kim M, Kojima N, Ota N, Shimotoyodome A, et al. Effects of exercise and milk fat globule membrane (mfgm) supplementation on body composition, physical function, and hematological parameters in community-dwelling frail Japanese women: a randomized double blind, placebo-controlled, follow-up trial. *PloS One.* 2015;10(2):e0116256.

[PubMed: PM25659147](#)

17. Chan DC, Tsou HH, Yang RS, Tsao JY, Chen CY, Hsiung CA, et al. A pilot randomized controlled trial to improve geriatric frailty. *BMC Geriatr.* 2012 Sep 25;12:58.

[PubMed: PM23009149](#)

#### Non-Randomized Studies

##### *Alternative Population – Mixed (Frail and Non-Frail)*

18. Ntanasi E, et al. Adherence to Mediterranean Diet and Frailty. *J Am Med Dir Assoc.* 2018 Apr;19(4):315-32.

[PubMed: PM29289542](#)

Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29289542>

##### *Alternative Outcome*

19. Garcia-Esquinas E, Rahi B, Peres K, Colpo M, Dartigues JF, Bandinelli S, et al. Consumption of fruit and vegetables and risk of frailty: a dose-response analysis of 3 prospective cohorts of community-dwelling older adults. *Am J Clin Nutr.* 2016 Jul;104(1):132-42.

[PubMed: PM27194305](#)

20. Talegawkar SA, Bandinelli S, Bandeen-Roche K, Chen P, Milanesechi Y, Tanaka T, et al. 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.

[PubMed: PM23096005](#)

##### *Alternative Intervention – Unspecified Nutritional Supplementation*

21. Waters DL, Vawter R, Qualls C, Chode S, Armamento-Villareal R, Villareal DT. Long-term maintenance of weight loss after lifestyle intervention in frail, obese older adults. *J Nutr Health Aging.* 2013 Jan;17(1):3-7.

[PubMed: PM23299370](#)