Few Pharmacologic Interventions Prevent or Mitigate Frailty: A Systematic Review

Leah Bolles, BS[1], **Michael DeGloria**, BS[1], **Hailey Cray**, MPH[1], **Rebekah Harris**, PT DPT PhD[1,2], **Saadia Qazi**, DO MPH MSc[1,2], **Ariela Orkaby**, MD MPH[1,3]

[1]New England Geriatric Research Education and Clinical Center (GRECC), VA Boston Healthcare System, Jamaica Plain, MA, USA [2]Harvard Medical School, Boston, MA, USA [3]Division of Aging, Brigham & Women's Hospital, Harvard Medical School, Boston, MA, USA

Introduction

- Frailty is a multidimensional clinical syndrome which limits the ability of older adults to cope with both everyday and acute stressors
- Most interventions for frailty target lifestyle improvements
- Uncertainty remains as to whether pharmacologic interventions may prevent or mitigate this syndrome

Aim

- This systematic review aims to explore the efficacy of existing pharmacologic options for the treatment of frailty

Methods

- Librarian guided search: PubMed, CINAHL, Embase, Clinicaltrials.gov, and ProQuest from article inception to 10 June 2025
- Two authors independently screened articles and extracted data (LB, MD), disagreements were resolved by a third author (HC)

Inclusion Criteria:

- Human adults, randomized controlled trial, pharmacologic intervention

Frailty definition:

- Validated frailty measure (Fried, Rockwood, Gait Speed, etc.)

Outcome:

- Change in frailty

Results

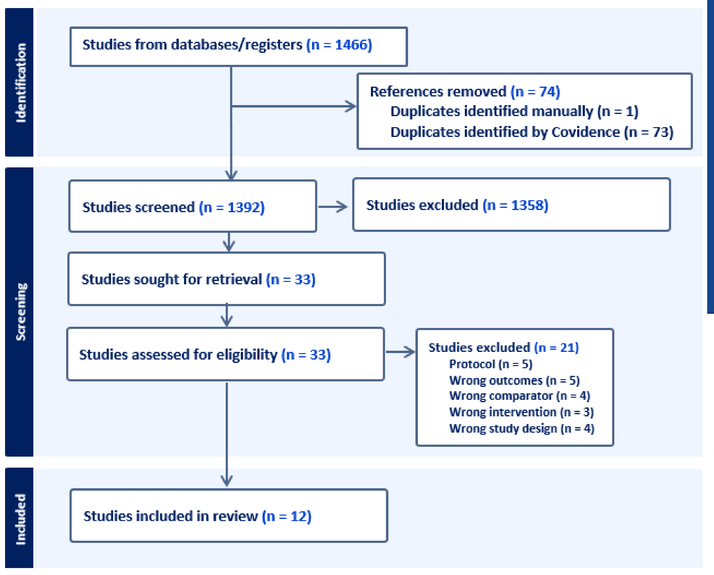

Figure 1. PRISMA diagram of selection of studies.

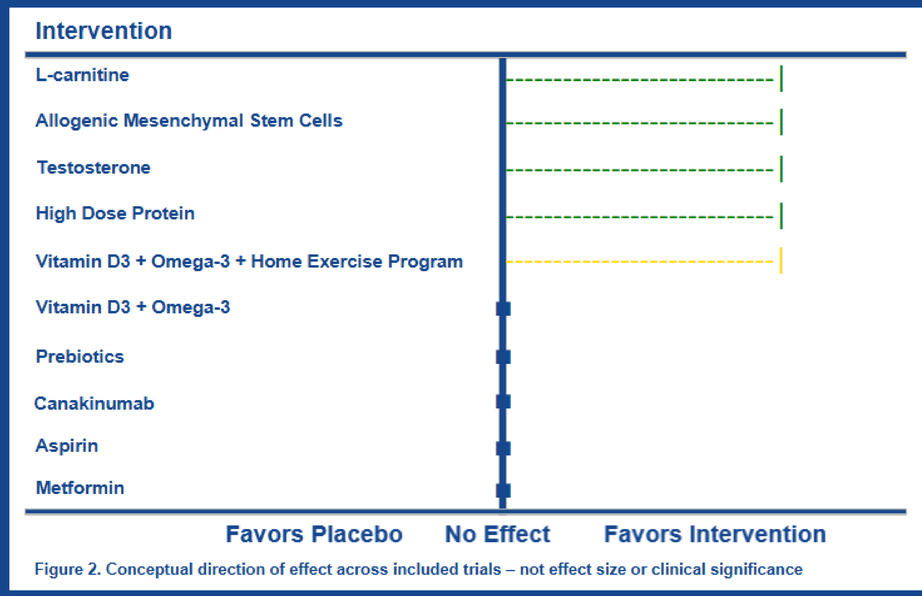

Figure 2. Conceptual direction of effect across included trials – not effect size or clinical significance

Further research is needed to identify effective pharmacologic interventions for frailty.

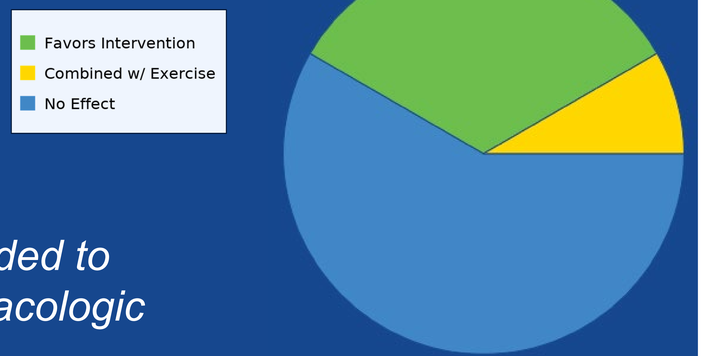

Figure 3. Descriptive distribution of trial findings

Limitations

- Data was insufficient to conduct a meta-analysis due to heterogeneity across trials

Conclusions

- Data remains limited to guide therapeutic approaches to prevent or mitigate frailty in older adults
- Future trials should continue to investigate pharmacologic interventions for frailty prevention

Table 1. Summary of Randomized Controlled Trials Evaluating Pharmacologic Interventions for Frailty

Authors	Intervention	Sample Size	Results
Badrasawi et al., 2016	L-carnitine supplement	50	• Significant improvement in mean FI score and hand grip test in L-carnitine group
Buigues et al., 2016	Darmocare Pre® (prebiotic)	50	• No significant improvement in mean FI score between groups
Espinoza et al., 2022	Aspirin	19,114	• No significant difference in risk of incident frailty between groups
Gagesch et al., 2023	Vitamin D3, Omega-3s, SHEP	1,137	• No significant difference in risk of pre-frail/frail for vitamin D3, omega 3-s, or SHEP individually • Combination of the three significantly decreased the risk of pre-frailty
Handono et al., 2025	Aspirin	6,595 in Fried analysis, 8,766 in Frailty Index	• No significant improvement or attenuation of frailty in prefrail or frail older adults
Hazuda et al., 2021	Metformin	2,385	• No significant difference in odds of frailty between groups
Orkaby et al., 2022	Vitamin D3, Omega-3s	25,057	• No significant difference in mean or incident frailty scores between groups
Orkaby et al., 2024	Canakinumab	9,942	• No significant difference in mean frailty scores between groups
Park et al., 2018	Protein	120	• Gait speed significantly improved in the 1.5 g protein · kg body weight^{-1} · d^{-1} group • No significant differences found in overall mean/incident frailty
Strollo et al., 2013	Testosterone	600	• Significant improvement in mean frailty score in all three treatment groups when compared to control
Tompkins et al., 2017	Allogenic Human Mesenchymal stem cells	30	• Significant improvement in physical markers of frailty in the 100-M dose
Witham et al., 2025	Metformin	72	• No significant improvement in physical markers of frailty

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