Supplemental Table S4: GRADE evidence rating: Nutritional interventions compared to usual care for older adults living with frailty or pre-frailty

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Nutrition	usual care	Absolute (95% CI)		
1. Physical ***(follow up: range 4 weeks to 24 weeks; assessed with: Activities of daily living (ADL), Muscle strength (handgrip & non-handgrip), Appendicular Lean mass (ALM))***											
7 [a]	randomised trials	serious [b]	not serious [c]	not serious	not serious [d]	none	373	321	SMD **0.16 SD higher** (0.02 higher to 0.29 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
2. Mobility ***(follow up: range 4 weeks to 24 weeks; assessed with: Performance measures (Gait speed, Timed up & go, chair sit & stand, balance, short physical performance battery))***											
7 [a]	randomised trials	serious [b]	not serious [e]	not serious	not serious	none	373	321	SMD **0.15 SD higher** (0.001 higher to 0.3 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
3. Health ***(follow up: range 12 weeks to 24 weeks; assessed with: Body weight & Body mass index)***											
4 [f]	randomised trials	serious [g]	not serious [c]	not serious	serious [h]	none	150	134	SMD **0.18 SD lower** (0.51 lower to 0.16 higher)	⊕⊕◯◯ LOW	CRITICAL
4. Frailty ***(follow up: range 12 weeks to 24 weeks; assessed with: Frailty criteria (Cardiovascular Health Study, Korean Longitudinal Study, Modified Fried))***											
3 [i]	randomised trials	serious [j]	not serious [c]	not serious	not serious [k]	none	155	100	SMD **0.22 SD lower** (0.44 lower to 0.01 lower)	⊕⊕⊕◯ MODERATE	CRITICAL

Appendix 6, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248.

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Nutrition	usual care	Absolute (95% CI)		
5. Diet quality ***(follow up: range 12 weeks to 24 weeks; assessed with: Kcal / day, MJ / day)***											
5 [l]	randomised trials	serious [m]	serious [n]	not serious	serious [o]	none	222	161	SMD **0.1 SD higher** (0.47 lower to 0.67 higher)	⨁◯◯◯ VERY LOW	CRITICAL
6. Quality of life ***(follow up: mean 24 weeks; assessed with: SF-36 Physical and Mental component score)***											
1 [p]	randomised trials	not serious	not serious	not serious	serious [o]	none	121	122	SMD **0.12 SD lower** (1.39 lower to 1.15 higher)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **SMD:** Standardized mean difference

Note: There was no data in the included studies for the following outcomes; Mortality, Health Service Use, and Social/Caregiver **GRADE – Nutrition-only Studies**

Explanations

a. Latham, 2003; Kim, 2012; Tieland, 2012; Pin Ng, 2015; Niccoli, 2017; Park, 2018; Wu, 2018

b. 2 out of 7 studies rated as unclear risk with concerns regarding incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

c. The confidence intervals overlap with low statistical heterogeneity observed across studies.

d. The sample size is adequate (=>300) in both intervention and control arms and effect estimate is precise (Confidence intervals do not include the no effect value "0").

e. The confidence intervals overlap with moderate level of statistical heterogeneity observed across studies.f. Kim, 2012; Tieland, 2012; Pin Ng, 2015; Wu, 2018

g. 1 out of 4 studies rated as unclear risk with concerns regarding incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

h. The sample size is not adequate (<300) in each arm and effect estimate is imprecise with confidence intervals including the no effect value of "0". i. Pin Ng, 2015; Park, 2018; Wu, 2018

j. 1 out of 3 studies rated as unclear risk with concerns regarding selective outcome reporting and other risk of bias (such as baseline imbalance across groups).

k.The sample size is not adequate (<300) in each arm, however, effect estimate is precise with confidence intervals not including the no effect value of "0". l. de Jong, 2000; Kim, 2012; Tieland, 2012; Park, 2018; Wu, 2018

m. 2 out of 5 studies rated as unclear risk with concerns regarding allocation concealment, blinding, incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

n. The confidence intervals do not overlap with substantial level of statistical heterogeneity observed across studies.

o. The sample size is not adequate (<300) in each arm and effect estimate is imprecise with confidence intervals including the no effect value of "0". p. Latham, 2003

Supplemental Table S5: GRADE evidence rating: Protein supplementation interventions compared to usual care for older adults living with frailty or pre-frailty

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Protein suppl.	usual care	Absolute (95% CI)		
1. Physical ***(follow up: range 4 weeks to 24 weeks; assessed with: Activities of daily living (ADL), Muscle strength (handgrip & non-handgrip), Appendicular Lean mass (ALM))***											
5 [a]	randomised trials	serious [b]	not serious [c]	not serious	not serious [d]	none	195	149	SMD **0.16 SD higher** (0.01 higher to 0.31 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
2. Mobility ***(follow up: range 4 weeks to 24 weeks; assessed with: Performance measures (Gait speed, Timed up & go, chair sit & stand, balance, short physical performance battery))***											
5 [a]	randomised trials	serious [b]	not serious [e]	not serious	not serious [d]	none	195	149	SMD **0.2 SD higher** (0.02 higher to 0.39 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
3. Health ***(follow up: range 12 weeks to 24 weeks; assessed with: Body weight & Body mass index)***											
3 [f]	randomised trials	serious [g]	not serious [c]	not serious	serious [h]	none	93	84	SMD **0.12 SD lower** (0.58 lower to 0.34 higher)	⊕⊕◯◯ LOW	CRITICAL
4. Frailty ***(follow up: mean 12 weeks; assessed with: Frailty criteria (Cardiovascular Health Study, Korean Longitudinal Study, Modified Fried))***											
2 [i]	randomised trials	serious [j]	not serious [c]	not serious	serious [h]	none	98	50	SMD **0.18 SD lower** (0.45 lower to 0.09 higher)	⊕⊕◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Protein suppl.	usual care	Absolute (95% CI)		
5. Diet quality ***(follow up: range 12 weeks to 24 weeks; assessed with: Kcal / day, MJ / day)***											
4 [k]	randomised trials	serious [l]	serious [m]	not serious	serious [h]	none	173	124	SMD **0.01 SD lower** (0.69 lower to 0.67 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **SMD:** Standardized mean difference

Note: There was no data in the included studies for the following outcomes; Mortality, Quality of Life, Health Service Use, and Social/Caregiver

Explanations

a. Kim, 2012; Tieland, 2012; Niccoli, 2017; Park, 2018; Wu, 2018

b. 2 out of 5 studies rated as unclear risk with concerns regarding incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

c. The confidence intervals overlap with low statistical heterogeneity observed across studies.

d. The sample size is not adequate (<300) in each arm, however, effect estimate is precise with confidence intervals not including the no effect value of "0". e. The confidence intervals overlap with moderate level of statistical heterogeneity observed across studies. f. Kim, 2012; Tieland, 2012; Wu, 2018

g. 1 out of 3 studies rated as unclear risk with concerns regarding selective outcome reporting and other risk of bias (such as baseline imbalance across groups).

h. The sample size is not adequate (<300) in each arm and effect estimate is imprecise with confidence intervals including the no effect value of "0". i. Park, 2018; Wu, 2018

j. 1 out of 2 studies rated as unclear risk with concerns regarding selective outcome reporting and other risk of bias (such as baseline imbalance across groups).

k. Kim, 2012; Tieland, 2012; Park, 2018; Wu, 2018

l. 1 out of 4 studies rated as unclear risk with concerns regarding incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

m. The confidence intervals do not overlap with substantial level of statistical heterogeneity observed across studies.

Appendix 6, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248.

Supplemental Table S6: GRADE evidence rating: Combined Approach interventions compared to usual care for older adults living with frailty or pre-frailty

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Nutrition & physical activity	Usual care	Relative / Absolute (95% CI)		
1. Physical ***(follow up: range 12 weeks to 52 weeks; assessed with: Activities of daily living (ADL), Muscle strength (handgrip & non-handgrip), Appendicular Lean mass (ALM))***											
6 [a]	randomised and non-randomised trials	serious [b]	not serious [c]	not serious	not serious [d]	none	258	256	SMD **0.19 SD higher** (0.06 higher to 0.32 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
2. Mobility ***(follow up: range 12 weeks to 52 weeks; assessed with: Performance measures (Gait speed, Timed up & go, chair sit & stand, balance, short physical performance battery))***											
6 [a]	randomised and non-randomised trials	serious [b]	not serious [e]	not serious	not serious [d]	none	258	256	SMD **0.25 SD higher** (0.02 higher to 0.48 higher)	⊕⊕⊕◯ MODERATE	CRITICAL
3. Health ***(follow up: range 12 weeks to 52 weeks; assessed with: Body weight & Body mass index)***											
3 [f]	randomised and non-randomised trials	serious [g]	not serious [c]	not serious	serious [h]	none	158	152	SMD **0.05 SD lower** (0.42 lower to 0.33 higher)	⊕⊕◯◯ LOW	CRITICAL
4. Frailty ***(follow up: range 12 weeks to 52 weeks; assessed with: Modified Fried criteria)***											
2 [i]	randomised trials	serious [j]	not serious [c]	not serious	not serious [d]	none	100	113	SMD **0.41 SD lower** (0.68 lower to 0.14 lower)	⊕⊕⊕◯ MODERATE	CRITICAL

Appendix 6, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Nutrition & physical activity	Usual care	Relative / Absolute (95% CI)			
5. Frailty *(follow up: range 12 weeks to 52 weeks; assessed with: Prevalence of frailty at post-intervention)*												
3 [k]	randomised and non-randomised trials	serious [l]	not serious [c]	not serious	not serious [m]	none	39 / 174 (22.4%)	59 / 185 (31.9 %)	**RR 0.720** (0.520 to 0.999)	**89 fewer per 1,000** (from 153 fewer to 0 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
6. Diet quality (follow up: range 18 weeks to 24 weeks; assessed with: MJ / day)												
2 [n]	randomised trials	serious [o]	serious [p]	not serious	serious [h]	none	73	68	SMD **0.53 SD higher** (0.98 lower to 2.04 higher)		⊕◯◯◯ VERY LOW	CRITICAL
7. Quality of life (follow up: range 12 weeks to 52 weeks; assessed with: SF-36 Physical & Mental component, EQ5D-VAS, WHOQOL-BREF score)												
3 [q]	randomised trials	serious [l]	not serious [c]	not serious	serious [h]	none	126	141	SMD **0.31 SD higher** (0.05 lower to 0.67 higher)		⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; **SMD:** Standardized mean difference; **RR:** Risk ratio

Note: There was no data in the included studies for the following outcomes; Mortality, Health Service Use, and Social/Caregiver

Explanations

a. Tieland, 2012; Yamada, 2012; Kwon, 2015; Luger, 2016; Serra-Prat, 2017; Kang, 2019

b. 4 out of 7 studies rated as unclear risk (2 studies) and high risk (2 studies) with concerns regarding randomization, allocation concealment, blinding, incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups). c. The confidence intervals overlap with low statistical heterogeneity observed across studies.

d. The sample size is not adequate (<300) in each arm, however, effect estimate is precise with confidence intervals not including the no effect value of "0".

e. The confidence intervals overlap with moderate level of statistical heterogeneity observed across studies. f. Tieland, 2012; Serra-Prat, 2017; Kang, 2019

g. 1 out of 3 studies rated as high risk with concerns regarding randomization, allocation concealment, blinding, incomplete and selective outcome reporting, and other risk of bias (such as baseline imbalance across groups).

h. The sample size is not adequate (<300) in each arm and effect estimate is imprecise with confidence intervals including the no effect value of "0". i. Luger, 2016; Serra-Prat, 2017

j. 1 out of 2 studies rated as unclear risk with concerns regarding blinding and other risk of bias (such as baseline imbalance across groups).

k. Nykänen, 2012, Luger, 2016; Serra-Prat, 2017

l. 2 out of 3 studies rated as unclear risk with concerns regarding blinding and other risk of bias (such as baseline imbalance across groups).

m. The sample size is not adequate (<300) in each arm, however, effect estimate is precise with confidence intervals not including the no effect value of "1"

n. de Jong, 2000; Tieland, 2012

o. 1 out of 2 studies rated as unclear risk with concerns regarding blinding and other risk of bias (such as baseline imbalance across groups).

p. The confidence intervals do not overlap with substantial level of statistical heterogeneity observed across studies.q. Kwon, 2015; Luger, 2016; Serra-Prat, 2017

Appendix 6, as supplied by the authors. Appendix to: Racey M, Ali MU, Sherifali D, et al. Effectiveness of nutrition and combined nutrition and physical activity interventions in older adults with frailty or prefrailty: a systematic review and meta-analysis. *CMAJ Open* 2021. DOI:10.9778/cmajo.20200248.