Effect of nonmeat, high-protein supplementation on quality of life and clinical outcomes in older residents of care homes: a systematic review and meta-analysis

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Context: *Care home residents are at risk of malnutrition owing to reduced food intake, anabolic resistance in aging muscle, and a high prevalence of medical morbidity and functional dependency. There has been limited consensus regarding the effectiveness of a high-protein diet on quality of life or clinical outcomes in care home residents.* ***Objective:*** *The aim of this review was to evaluate the effectiveness of nonmeat, high-protein supplementation on health-related quality of life (HRQOL) and relevant clinical and nutritional outcomes in older people in a care home setting.* ***Data Sources:*** *The following databases were searched (to February 2018) for randomized controlled trials: Embase, AMED, CINAHL, MEDLINE, the Cochrane Central Registry of Controlled Trials, OpenGrey, clinicaltrials.gov, the WHO International Clinical Trials Registry Platform, the ISRCTN registry, and the NIHR Clinical Research Network Portfolio.* ***Study Selection:*** *Trials were selected if they assessed a nonmeat, high-protein dietary intervention provided to care home residents who were aged 65 years or older.* ***Data Extraction:*** *Data from included trials were extracted if they assessed care home residents aged 65 years or older and compared those residents who received protein supplementation with those who did not. Trial quality was assessed using the Cochrane risk-of-bias tool. Meta-analysis was undertaken when appropriate.* ***Results:*** *Seventeen studies with 1246 participants fulfilled the inclusion criteria. All studies were of low or moderate quality. There was no evidence of improved HRQOL when the Short Form 36 (SF-36) was used to assess outcomes (standardized mean difference [SMD] = −0.10; 95%CI, −0.51 to 0.31;* $P = 0.62$*), although significant improvement was seen in the 1 trial that used the EQ-5D instrument (SMD = 2.58; 95%CI, 2.05–3.10;* $P < 0.00001$*).* ***Conclusions:*** *Nonmeat, high-protein oral supplements can improve markers of nutritional status in care home residents. However, there is insufficient high-quality evidence to determine the effect of such supplements on HRQOL in older adults in care homes.* ***Systematic Review Registration:*** *PROSPERO registration number: CRD42015029313.*

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INTRODUCTION

In the United Kingdom, 425 000 individuals live in care homes for older people. Such homes are long-term care facilities that may or may not have specialist nursing input but universally provide care for people with multiple morbidities and advanced functional dependency who can no longer be supported in their own home.[1] The number of beds in care homes is about 3 times that in acute-care hospitals, and care outcomes in care home residents are increasingly recognized to impact all of health and social care.[2] An important source of morbidity for care home residents is malnutrition, defined as a state of nutrition in which a deficiency, an excess, or an imbalance of energy, protein, and other nutrients causes measurable adverse effects on tissue/body form, function, and clinical outcome.[3] Malnutrition affects approximately 30% of older people living in care homes, who are at particular risk of protein energy malnutrition.[4] The multitude of poor outcomes attributable to inadequate nutrition includes an increased risk of infections, dehydration, and falls; an inability to perform activities of daily living; and a reduced health-related quality of life (HRQOL).[5] While malnutrition does not have to be an inevitability of aging, several factors put older adults at risk, including reduced appetite, poor dentition, swallowing difficulty, and altered taste and smell.[5] All of these may be addressed by the use of high-protein oral nutritional supplements, which may be particularly useful in care homes because both dietary intake and administration of medicines/supplements are supervised by care home staff.[6,7]

The most commonly administered oral nutritional supplements are protein-enriched drinks, which are easy to administer, require no mastication, and are less satiating than solids.[8] Supplementation with dietary protein from a nonmeat source avoids matters of cultural beliefs around food choices, as several religions and cultures prohibit consumption of particular meats. Moreover, the use of protein from nonmeat sources can be more sustainable from an environmental perspective.[9,10] While animal sources of protein deliver all the essential amino acids, the environmental impact of producing livestock for meat is almost double that associated with supporting a lacto-ovo-vegetarian diet.[11]

While many older people are affected by multiple chronic diseases, most regard the presence or absence of disease as less important than their overall quality of life.[12] Numerous systematic reviews have reported the prevalence of malnutrition among older adults. However, there is little evidence from systematic reviews to establish the best nutritional support for older adults in care homes.[13] Older adults are at particular risk of protein energy malnutrition, which results from reduced overall food intake and anabolic resistance in aging muscle.[6,7] Additionally, few studies have assessed the evidence regarding the effectiveness of a high-protein diet on quality of life or clinical outcomes in care home residents.[14,15] The primary purpose of this study was to gather the available evidence and perform a systematic review to assess the effect of nonmeat protein supplementation on quality of life in older people living in care homes.

METHODS

Protocol

The protocol for this review was registered in PROSPERO (registration no. CRD42015029313).

Reporting

This systematic review has been conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (see Table S1 in the Supporting Information online).[16]

Search strategy

A primary literature search was performed using the following databases of published literature: Embase, AMED (Allied and Complementary Medicine), CINAHL (Cumulative Index to Nursing and Allied Health Literature), MEDLINE, and the Cochrane Central Registry of Controlled Trials. In addition, the following databases of unpublished literature were also searched: OpenGrey, clinicaltrials.gov, the WHO International Clinical Trials Registry Platform, and the ISRCTN and NIHR Clinical Research Network portfolio. Databases were searched from their inception to February 1, 2018. The MEDLINE search strategy is presented in Table S2 in the Supporting Information online and was modified for each database. The reference lists of eligible studies were reviewed and the corresponding authors from each included paper contacted, where contact details were available, to identify any previously omitted trials. Three replies out of 13 inquiries were received.

Eligibility

Studies included were randomized controlled trials involving a nonmeat, high-protein dietary intervention conducted in residents of care homes who were aged 65 years or older. High-protein supplements were defined as supplements containing more than 20 g of protein and more than 20% of the total caloric value from

protein. Moderate-protein supplements were defined as containing more than 10 g of protein or more than 10% of the total caloric value from protein. Trials in which participants were recruited during acute admissions to hospitals or rehabilitation units were excluded, as were those conducted in sheltered housing settings. Studies were eligible for inclusion irrespective of country of origin or language or year of publication. All comparison arms, including those comprising controls assigned to a standard diet or a placebo product, were included, although trials using co-interventions combined with a dietary intervention, such as a dietary intervention plus physical activity, were excluded. When trials presented data on multiple intervention arms, eg, a dietary intervention vs a dietary intervention and physical activity vs physical activity alone, data from the group that received the dietary intervention alone were extracted.

Study identification

Two authors (A.I.C.D. and S.A.) independently screened all titles and abstracts against the predefined eligibility criteria described above. The full text of each paper that met the eligibility criteria was then obtained and reviewed independently by the same authors (A.I.C.D. and S.A.). Those papers that met the criteria were included in the final analysis. Disagreements about study eligibility were discussed between the 2 authors and adjudicated by 2 senior authors (T.O.S. and P.K.M.).

Outcomes and data extraction

The primary outcome was HRQOL, as assessed by the SF-36, the EQ-5D instrument, and the dementia quality of life questionnaire. Secondary outcomes included adverse events (including admissions to hospital, gastrointestinal symptoms), falls, functional assessments, body weight, body mass index (BMI), mid upper arm circumference (MUAC), and grip strength. Data were extracted by 1 author (A.I.C.D.) and verified by a second author (S.A.). Disagreement was resolved by discussion and review of the source paper and adjudicated by a senior author (T.O.S.). The following data were extracted: participant characteristics, details of the dietary intervention, trial design features, and the outcomes of interest.

For body weight, BMI, and MUAC, the change in each value for each group was recorded, and if this value was not presented in the data, a value was estimated using the difference in mean values for these outcomes from before and after the intervention and an estimated standard deviation using a correlation coefficient of 0.5.[17]

Quality assessment

The quality of all included studies was assessed independently by 2 authors (A.I.C.D. and S.A.) using the Cochrane risk-of-bias tool.[18] Any disagreement in appraisal score was satisfied through discussion and adjudication by a third author (T.O.S.).

Data analysis

All included studies were randomized controlled trials. The effect size of such trials depends on how the control was defined. The heterogeneity of each study was assessed through examination of the data extraction table and assessment of between-study variability with respect to participants, recruitment, intervention, and any co-interventions. When there was study heterogeneity or insufficient data (fewer than two datasets presenting mean and standard deviations or event count data for a specific outcome) to pool results, a narrative analysis was conducted in which the trends in results (descriptive and statistical) were reported instead of pooling the data into a meta-analysis. A meta-analysis was performed when there was low risk of study heterogeneity. Statistical heterogeneity was assessed using the inconsistency value (I^2) and the χ^2 test. Where I^2 was 30% or less and χ^2 $P > 0.10$, a fixed-effects model analysis was conducted. When these criteria were not met, a random-effects model analysis was performed. All continuous outcomes of HRQOL, functional assessment, body weight, BMI, MUAC, and grip strength were evaluated using the mean difference (MD) for individual studies or the standardized mean difference (SMD) for trials that used different measurements to capture the same domain. Results were presented in forest plots. Categorical outcomes such as adverse events and falls were assessed using a risk ratio (RR).

All analyses were presented as forest plots with 95%CIs. Predefined subgroup analyses of study outcomes by duration of intervention (> 12 weeks or ≤ 12 weeks) and total protein content were performed. Protein content was classified as high (> 20 g of protein), moderate (10–20 g of protein), or low (< 10 g of protein). Calorie content was classified as high ($> 20\%$ calories from protein), moderate (10%–20% calories from protein), or low ($< 10\%$ calories from protein). Follow-up intervals were up to 2 years post randomization. To assess publication bias resulting from small sample size, a funnel plot was planned for the primary outcome analyzed and/or any analysis for which there was a minimum of 10 datasets.[18] The intention was to examine the clustering effect if the original studies reporting the data accounted for clustering within a care home. All analyses were conducted in collaboration

for verification by 2 authors (A.I.C.D. and T.O.S.) using Review Manager (RevMan) software.[19] For all analyses, $P \leq 0.05$ was deemed statistically significant.

The GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) approach was used to analyze the weight of the evidence for each individual outcome.[20,21] Through this, the strength of evidence underpinning each analysis was categorized as high, moderate, low, or very low, with evidence graded on the basis of study design, study quality, consistency, directness of evidence, precision, and reporting bias.[20,21]

RESULTS

Study selection

The results of the literature search are shown in Figure 1. The search identified 431 potentially relevant papers, of which 17 fulfilled the inclusion criteria.[6,22–37] Two of the included studies reported on the same trial, but participants were counted only once.[25,34] When trials were stratified by the protein content of the intervention, 5 fulfilled the criteria of high protein (> 20 g of protein and > 20% of total calories from protein)[6,25,26,32,34,36] and 12 fulfilled the criteria of moderate protein (> 10 g of protein or >10% of total calories from protein).[22–24,27–33,35,37]

Study characteristics

Study characteristics are summarized in Table 1.[6,22–37] A total of 1246 participants from 16 trials (range, 34 to 175 participants) were identified.[22,31] This included 271 males and 934 females; the sex of 41 participants was not documented in 1 trial.[28] The mean age in the studies ranged from 78.7 to 89.6 years.[29,33] The presence of dementia or cognitive impairment, as indicated by the Mini-Mental State Examination (MMSE) score, was described in 13 trials.[22–31,34,35,37] In this systematic review, an MMSE score of 9 or below indicated severe cognitive impairment, 10 to 18 moderate cognitive impairment, 19 to 23 mild cognitive impairment, and 24 to 30 normal cognition, in accordance with Mungas.[38] The mean baseline MMSE in the included trials ranged from 18 to 26.[22,28] In 3 trials, 100% of participants had a diagnosis of dementia.[29–31] There was no consistent measure of frailty, but several trials provided information on the prevalence of chronic illness,[24,27,31,33,34,36,37] which ranged from a mean of 1.8 to 5 comorbid diseases.[24,27]

The standard diet for participants prior to intervention contained a mean of 1560 kcal and 56 g of protein daily. Most interventions used a liquid supplement: 10 used a milk-based supplement,[6,23–26,29,30,34–37] 1 used a soya drink,[27] 3 used an enriched diet or a choice of supplement,[31–33] 1 used high-protein cookies,[22] and 1 used an amino acid supplement.[28] The protein content of intervention supplements ranged from 8 g[28] to 40 g,[32] with total calories ranging from 32 kcal[28] to 600 kcal.[25,32–37] The duration of the intervention ranged from 4 weeks[6] to 9 months.[36] Ten trials used a standard diet as a comparison,[6,22,23,25,26,29–32,34,35] while 4 used a placebo noncalorie drink,[24,29,36,37] 1 used a snack of unspecified content,[27] 1 used a placebo maltodextrin tablet,[28] and 1 provided dietary advice.[33]

Risk of bias

The risk-of-bias quality assessment is summarized in Figure S1 in the Supporting Information online and the GRADE assessment of outcomes in Table 2. There was a strong risk of selection and performance bias owing to the lack of blinding of participants and/or personnel in 14 trials[6,22,24–27,29,30,32–37] and to unclear blinding in 2 further trials.[23,29] A placebo supplement was employed in 6 trials,[24,27–29,36,37] and blinding of the outcome assessor was described in 5 trials.[24,28,35–37] The risk of reporting bias was largely unclear,[6,22–36] while the risk of attrition bias was high, with the attrition rate exceeding 15% in 7 trials[29,32–37] and not described in 3 trials.[6,22,23]

Health-related quality of life

Health-related quality of life was assessed by the SF-36 in 2 trials[28,32] and the EQ-5D instrument in 1 trial.[33] Heterogeneity was too high to draw conclusions from meta-analysis of these 3 trials, although the results are shown in Figure 2[28,32,33] for interest only. In subgroup analysis, there was no evidence of improved HRQOL when the multidimensional assessment tool SF-36 was used (SMD = −0.10; 95%CI, −0.51 to 0.31; $P = 0.62$; 2 trials), although significant improvement was seen in the single trial that used the EQ-5D, whose intervention was classed as having moderate protein content (SMD = 2.58; 95%CI, 2.05–3.10; $P < 0.00001$; 1 trial). The evidence was graded as low quality because of the significant heterogeneity between the trials ($I^2 = 96\%$) and the results of the GRADE assessment.

Adverse events, deaths, and falls

Four trials reported data on death[24,33,34,37] and 8 reported data on adverse events.[23–26,29,35,37] There was no significant difference in the number of adverse events (RR=1.11; 95%CI, 0.70–1.76; Figure 3[23–26,29,35,37]) or deaths (RR=0.53; 95%CI, 0.22–1.25; see Figure S2 in the Supporting Information online) reported. There was no available data on the incidence of falls in any of the trials.

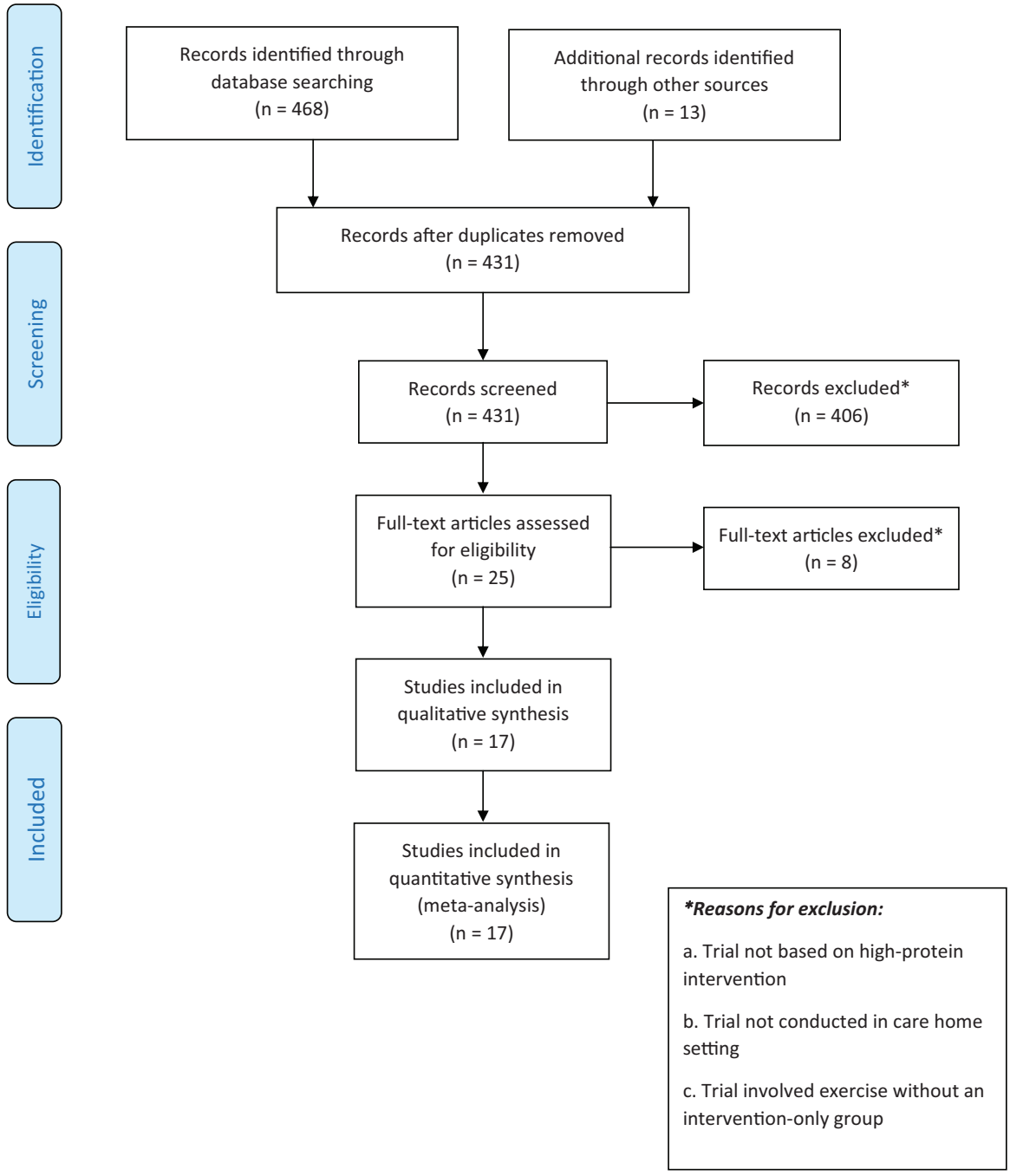

Figure 1 **Flow diagram of the literature search process.**

Study heterogeneity was not significant for the analysis of adverse events ($I^2 = 20\%$) or deaths ($I^2 = 0\%$). The results of GRADE assessment showed the evidence underpinning the assessment of adverse events, deaths, and falls to be of low quality.

Functional assessment

Data on functional outcomes was assessed using the Barthel Index in 2 trials[32,34] and an alternative score based on activities of daily living in 2 other trials.[23,29] Study heterogeneity was not significant ($I^2 = 0\%$). There were no significant differences between the control and intervention groups (SMD = −0.04; 95%CI, −0.29 to 0.22; $P = 0.57$; see Figure S3 in the Supporting Information online), even when limiting assessment to the studies that used high-protein supplementation[32,34] (SMD = −0.11; 95%CI, −0.44 to 0.23; $P = 0.41$). On the basis of GRADE assessment, the evidence was graded as low quality.

Table 1 **Summary of the characteristics of the included studies**

Reference	Country/setting	No. (control group/ intervention group)	Mean age (y)	Percent female	Baseline cognition (% with dementia)	Mean baseline BMI	Baseline diet	Dietary intervention	Protein content of intervention (g)	Energy content of intervention (kcal)	Placebo	Duration of intervention and follow-up
Smoliner et al (2008)[32]	Germany/nursing homes	52 (30/22)	85.2	73	ND	CG: 22.5±3.4 IG: 21.6±3.6	2000 kcal 80 g protein	Enriched diet (using cream/ oil)+300 ml snacks	40 (from snacks alone)	600 (from snacks alone)	None	12 wk
Bonnefoy et al (2003)[36]	France/retirement home	57 (27/30)	83.0	88	0	CG: 27.32±0.8 IG: 27.13±0.9	2000 kcal	400 ml supplement drink	30	400	400 ml noncalorie/ protein drink	9 mo
Iuliano et al (2013)[6]	Australia/low-level care home	130 (62/68)	86.5	78	ND	CG: 25.4±4.9 IG: 23.7±5.0	1497±307 kcal 56±15 g protein	2 servings of dairy foods (liquid/solid)	25±12	215±299	None	4 wk
Josbe et al (2015)[25]; Stange et al (2013)[34]	Germany/nursing homes	87 (42/45)	87.0	91	CG: 66 IG: 80	CG: 22.5±3.1 IG: 23.0±3.4	1263±374 kcal 41.3±15.1 g protein	250 ml Fortimel Compact	24 (1 study reported as 48 g but same intervention)	600	None	12 wk
Lauque et al (2000)[26]	France/nursing homes	35 in comparable groups of same BMI status (22/13)	85.4 (estimated)	84	CG: 68 IG: 86	CG: 21.8±0.9 IG: 22.3±0.7	1573 kcal 60 g protein	300–400 ml nutritional supplement drink	24	393±23	None	60 d
Stow et al (2015)[35]	United Kingdom/ care and nursing homes	93 (32/32 & 29)	ND	82	CG: 78 IG (A): 78 IG (B): 69	CG: 19 (17–0.5) IG (A): 20.1 (18.7–24.8) IG (B): 18.4 (17.6–21.6)	1553 kcal 41 g protein	(A) 250–400 ml food-based liquid supplement (B) 250–400 ml liquid nutritional supplement	(A) 20–25 (B) 24	(A) 600 (B) 600	None	6 mo
Kwok et al (2001)[23]	Hong Kong/nursing home	51 (24/28)	CG: 79.7 IG: 81.2	60	CG: 9 IG: 32	CG: 20.1±3.1 IG: 19.1±3.1	1198±403 kcal 61.6±21.2 g protein	2 cups low-lactose milk	18.8	175	None	7 wk
Parsons et al (2017)[33]	United Kingdom/ care home	104 (51/53)	CG: 87.3 IG: 89.6	86	0	39% BMI <18.5 41% BMI 18.5–20	1360 kcal 51.8 g protein	Voluntary intake of range of supplements	Target: 16	Target: 600	Dietary advice	12 wk
Fiatarone et al (1994)[24]	United States/care home	50 (26/24)	CG: 89.2 IG: 85.7	62	Mean MMSE CG: 22.2±1.0 IG: 22.7±1.3	CG: 25.8±0.5 IG: 25.4±0.7	1485±58 kcal	240 ml supplement drink	15.3	360	240 ml noncalorie/protein drink	10 wk
Pouyssegur et al (2015)[22]	France/nursing home	175 (87/88)	CG: 86.8 IG: 85.4	80	Mean MMSE 18±8.3	19.2±2.9	ND	8 high-protein cookies	11.5	244	None	6 wk with 18 wk follow-up
Young et al (2004)[31]	Canada/care home	34 (34/34); crossover study	88.2	79	100	23.8±3.6	1514 kcal 54.7±17.4 g protein	Various (mainly 75% of a supplement bar and a glass of juice)	10.6	250	None	12 wk

(continued)

Table 1 **Continued**

Reference	Country/setting	No. (control group/ intervention group)	Mean age (y)	Percent female	Baseline cognition (% with dementia)	Mean baseline BMI	Baseline diet	Dietary intervention	Protein content of intervention (g)	Energy content of intervention (kcal)	Placebo	Duration of intervention and follow-up
Wouters-Wesseling et al (2002)[29]	The Netherlands/ psychogeriatric nursing home	34 (16/18)	82.7	85	100	24.5±4.2	1543±377 kcal 53.7±18.3 g protein	200 ml supplement drink	11.2	300	None	5 wk
Lee et al (2013)[27]	Taiwan/nursing home	92 (45/47)	CG: 80.2 IG: 78.9	58	Mean MMSE score CG: 14.1±6.1 IG: 15.0±5.5	CG: 20.31±2.61 IG: 20.43±2.50	ND	50 g soy protein–based drink	9.5	250	Afternoon snack (content ND)	24 wk
Wouters-Wesseling et al (2006)[30]	The Netherlands/ psychogeriatric nursing home	35 (16/19)	CG: 78.7 IG: 85.3	89	100	CG: 20.7±2.7 IG: 20.7±3.2	1496±415 kcal 55±16 g	250 ml supplement drink	8.5	273	250 ml noncalorie, no protein drink	3 mo
Manders et al (2009)[37]	The Netherlands/ care and nursing homes	176 (57/119)	CG: 81.0 IG: 81.0	74	Mean MMSE score CG: 24.0 (11.2–27.8) IG: 23.0 (9.6–27.4)	CG: 25.0±3.5 IG: 26.1±3.7	1793±332 kcal 58.8±15.4 g protein	250 ml nutrient drink	8.75	250	250 ml noncalorie, no protein drink	24 wk
Rondanelli et al (2011)[28]	Italy/nursing home	41 (21/20)	CG: 79.9 IG: 83.5	ND	Mean MMSE score CG: 21.1±2.04 IG: 26.05±2.09	CG: 22.1±2.6 IG: 21.8±2.3	59±8 g protein	8 g essential amino acid supplement	8	32	Maltodextrin tablet	8 wk

Abbreviations: BMI, body mass index; CG, control group; IG, intervention group; MMSE, Mini-Mental State Exam; ND, not described.

Body weight

The mean change in mean body weight was reported in 13 trials.[22–27,29,30,32–35,37] Meta-analysis showed a significant increase in mean body weight with intervention across all included trials (MD = 1.11; 95%CI, 0.97–1.24; $P < 0.0001$; see Figure S4 in the Supporting Information online). This effect was also evident in the high-protein group[25,26,32] (MD = 2.12; 95%CI, 1.34–2.91; $P < 0.00001$; see Figure S4 in the Supporting Information online) and, by a smaller magnitude, in the moderate-protein group (MD = 1.08; 95%CI, 0.94–1.21; $P < 0.00001$; see Figure S4 in the Supporting Information online).[22–24,27,29,30,33–35,37] On the basis of GRADE assessment, the evidence was graded as moderate quality with overall substantial study heterogeneity ($I^2 = 75\%$).

Body mass index

The mean change in BMI was reported in 8 trials.[23,26,27,29,32,34–36] Meta-analysis showed significant increase in mean BMI across all included trials (MD = 0.86; 95%CI, 0.61–1.10; $P < 0.00001$; see Figure S5 in the Supporting Information online). This effect was seen in both the high-protein group[26,32,36] (MD = 1.05; 95%CI, 0.68–1.41; $P = 0.0004$; see Figure S5 in the Supporting Information online) and the moderate-protein group[23,27,29,34,35] (MD = 0.70; 95%CI, 0.37–1.03; $P < 0.00001$; see Figure S5 in the Supporting Information online). Using the GRADE approach, the analyses on BMI were graded as moderate-quality evidence with low overall study heterogeneity ($I^2 = 0\%$).

Mid upper arm circumference

The mean change in MUAC was reported in 6 trials.[23,25,27,29,34,35] The MUAC was maintained better in the intervention group than in the control group (MD=0.51; 95%CI, 0.23–0.79; $P = 0.0004$; see Figure S6 in the Supporting Information online). Evidence of change in MUAC measures, as assessed by GRADE, was graded as moderate quality with substantial overall study heterogeneity ($I^2 = 73\%$).

Grip strength

Grip strength was assessed in 5 trials[23,26,31,32,34] that demonstrated substantial statistical heterogeneity ($I^2 = 60\%$). There was a significant change in grip strength in the subgroup that received moderate-protein supplementation (MD=1.29; 95%CI, 0.45–2.14; $P = 0.003$; see Figure S7 in the Supporting Information

Table 2 **GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) assessment of outcomes**

Outcome measure	Quality assessment				No. of participants		Effect			Evidence grade
	Design	Quality	Consistency	Directness	High-protein intervention	Standard diet/placebo	MD/ SMD/RR (95%CI)	*P* value	I^2	
QOL (SF-36)	RCT	Low	Low	Moderate	42	51	SMD −0.10 (−0.51 to 0.31)	0.62	0%	Low
QOL (EQ-5D instrument)	RCT	Low	Low	Moderate	53	51	SMD 2.58 (2.05–3.10)	<0.00001	N/A	Low
Adverse effects (group total)	RCT	Low	Low	High	335	268	RR 1.11 (0.70–1.76)	0.67	20%	Low
Adverse effects (>20%/>20 g protein group)	RCT	Low	Low	High	82	83	RR 1.28 (0.64–2.55)	0.48	62%	Low
Deaths (group total)	RCT	Moderate	Moderate	High	167	140	RR 0.53 (0.22–1.25)	0.15	0%	Low
Deaths (>20%/>20 g protein group)	RCT	Moderate	Moderate	High	45	42	RR 0.40 (0.11–1.45)	0.16	N/A	Low
Functional assessment (group total)	RCT	Low	Low	High	115	117	SMD −0.04 (−0.29 to 0.22)	0.79	0%	Low
Functional assessment (>20%/>20 g protein group)	RCT	Low	Low	High	67	72	SMD −0.11 (−0.44 to 0.23)	0.53	0%	Low
Change in mean BW (group total)	RCT	High	High	High	446	440	MD 1.11 (0.97–1.24-)	<0.00001	75%	Moderate
Change in mean BW (>20%/>20 g protein group)	RCT	High	Moderate	High	50	87	MD 2.12 (1.34–2.91)	<0.00001	81%	Moderate
Change in mean BMI (group total)	RCT	High	High	High	242	228	MD 0.86 (0.61–1.10)	<0.00001	0%	High
Change in mean BMI (>20%/>20 g protein group)	RCT	High	High	High	65	79	MD 1.05 (0.68–1.41)	0.0004	0%	High
Change in mean MUAC (group total)	RCT	Moderate	Low	High	163	172	MD 0.51 (0.23–0.79)	0.0004	73%	Low
Change in mean MUAC (>20%/>20 g protein group)	RCT	Moderate	Low	High	57	70	MD 0.64 (0.11–1.18)	0.02	83%	Low
Change in grip strength (group total)	RCT	Low	Low	High	122	128	MD 0.63 (−0.05 to 1.32)	0.07	60%	Low
Change in grip strength (>20%/>20 g protein group	RCT	Low	Low	High	77	87	MD −0.63 (−1.80 to 0.53)	0.29	33%	Low

Abbreviations: BMI, body mass index; BW, body weight; CI, confidence interval; MD, mean difference; MUAC, mid upper arm circumference; QOL, quality of life; RCT, randomized controlled trial; RR, risk ratio; SF, short form; SMD, standardized mean difference.

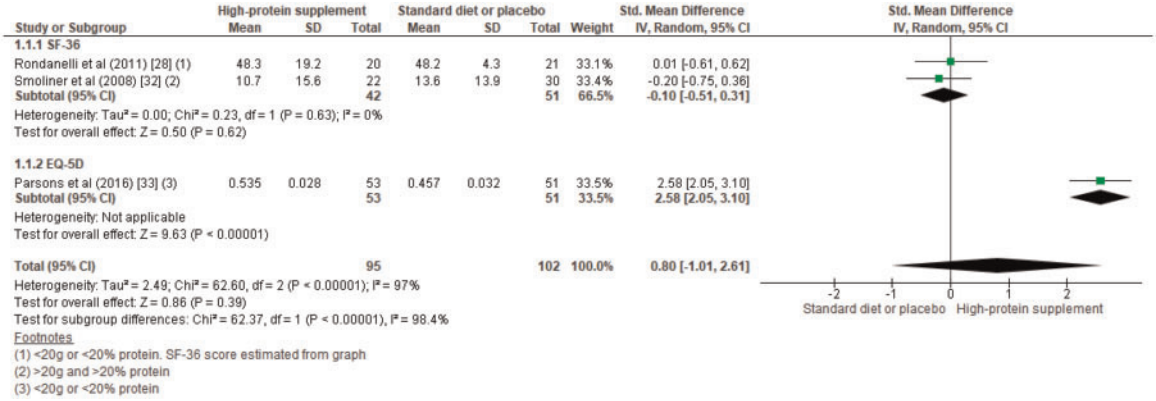

Figure 2 **Forest plot assessing quality-of-life assessments between the interventions in meta-analysis.** Abbreviation: IV, inverse variation.

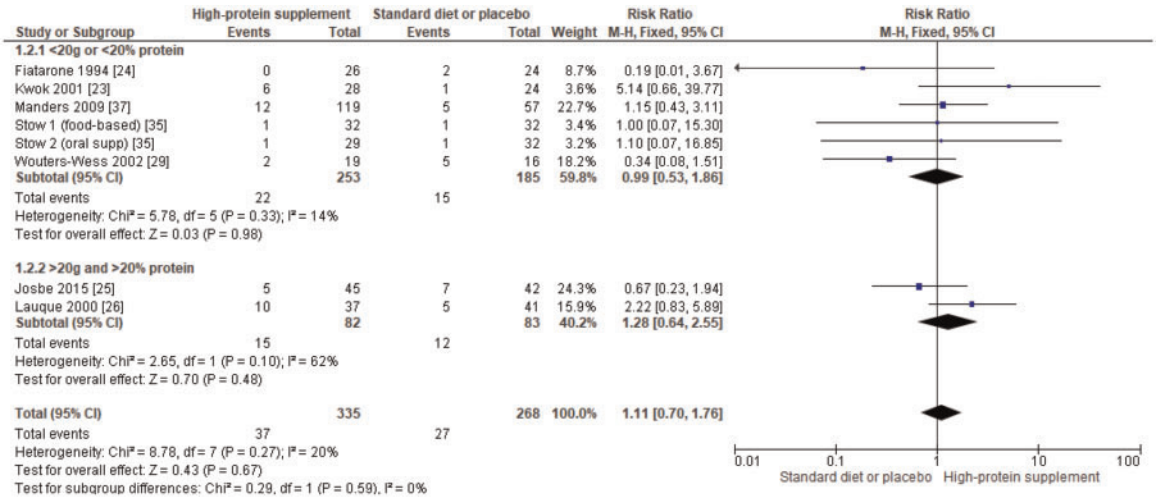

Figure 3 **Forest plot assessing adverse events reported between the interventions in meta-analysis.** Abbreviation: M-H, Mantel-Haenszel.

online), and although the change in the high-protein subgroup was not statistically significant, there does appear to be a tendency of an effect (MD=0.63; 95%CI, −0.05 to 1.32; $P = 0.07$; see Figure S7 in the Supporting Information online). As assessed by the GRADE approach, the evidence was graded as low quality.

Duration of interventions

There were 12 trials (reported in 13 articles) with an intervention duration of 12 weeks or less[6,22–26,28–34] and 4 trials with an intervention of more than 12 weeks.[27,35–37] The minimum length of intervention was 4 weeks[6] and the maximum length 9 months.[36] Subgroup analysis by duration of intervention ($>$ 12 weeks or $\leq$ 12 weeks) was not significant for adverse events ($P = 0.84$), deaths ($P = 0.61$), change in body weight ($P = 0.12$), or change in BMI ($P = 0.16$). However, there were significant subgroup differences for MUAC ($P = 0.005$), with a stronger effect observed for more than 12 weeks of intervention (MD=0.95; 95%CI, 0.53–1.37; $P < 0.00001$) compared with 12 or fewer weeks of intervention (MD=0.14; 95%CI: −0.24 to 0.52; $P = 0.47$). There was insufficient data to examine the effect of duration of intervention on grip strength.

DISCUSSION

The key finding of this systematic review is that a non-meat, high-protein enriched dietary intervention appears to be effective for surrogate markers of clinical outcomes, but high-quality evidence of the effect on HRQOL, an important health outcome in old age, is lacking.

Surprisingly, few trials objectively measured HRQOL. It was interesting to note that, even within the high-protein subgroups, there was no evidence of improved HRQOL on a multidimensional SF-36

assessment ($P = 0.62$). Nonetheless, the single trial that reported the results of assessment by EQ-5D demonstrated a significant improvement in HRQOL, even in groups meeting the criteria for moderate-protein supplementation ($P < 0.00001$).[33] Since this was only a single study that presented a number of methodological limitations, the evidence for assessment by EQ-5D remains limited, but it does provide a signal that should be further investigated. Notably, of those studies that included HRQOL as an outcome measure, the inclusion of participants with a diagnosis of dementia was lacking. This absence of data on the effect of a high-protein diet on HRQOL in care homes for those with cognitive impairment or dementia must be addressed in future research, given that this population comprises a significant proportion of care home residents. Perhaps this paucity of data reflects the difficulties in assessing self-reported measures like HRQOL in populations with a high prevalence of dementia using validated tools without relying on a proxy. Even in relatively simple HRQOL measures with validated proxy versions, most notably the EQ-5D, there are acknowledged issues with relying on proxy respondents in the care home setting.[39] However, dementia-specific HRQOL measures, such as the questionnaire for HRQOL for people with dementia,[40] should be considered for future studies.

Only 4 trials incorporated an objective measure of change in function[23,28,32,34] (Barthel Index or activities of daily living score), and it is possible that the duration of the included trials was too short to show any significant variation. Similarly, while there was a tendency toward a difference, the study interventions did not result in significant changes in grip strength ($P = 0.07$). However, grip strength has previously been noted to be very low among care home residents[41] and may be affected by both a floor effect and poor sensitivity to change. It could be that the relatively invasive nature of the investigations to measure such outcomes, such as muscle biopsy and dual-energy X-ray absorptiometry scanning, in cohorts of older, frailer individuals has proved off-putting for researchers working in the care home setting. Recent innovations in measuring muscle turnover, including microbiopsy, ultrasonography, and excreted amino acid–derived indices of muscle turnover, could potentially allow more-sensitive outcome measures to be employed in this very frail cohort.[42]

While no significant change in adverse effects or deaths were noted among participants receiving a protein-rich nutritional intervention, a previous meta-analysis of protein and energy supplementation in older people reported that there was a reduction in the mortality rate for those malnourished at baseline.[14,43] In the trials included in this review, generally only those participants within the BMI range defined as normal were randomized, and therefore changes may have been apparent if those with low BMI, who were likely more malnourished, were also included.

It is important to consider that the population included in the studies may have been a subcohort of the care home population and was not representative of the population as a whole. Certainly the incidence of reported comorbidities in the trials that described this was significantly lower than that reported in most cohort studies of care home residents, suggesting this may have been a less comorbid and less frail subpopulation. Of note, those studies that were conducted in groups without dementia were almost certainly a subset, given that the estimated prevalence of dementia in cohort studies of care home residents is between 69% and 80%.[44,45]

Meta-analysis found small but statistically significant gains in both body weight (MD = 1.11 kg) and BMI (MD = 0.86 kg/m^2), with a more significant effect noted in the high-protein group on subanalysis (MD = 2.12 kg). Likewise, other meta-analyses also found significant increases in body weight following protein supplementation in older adults.[43,46] However, an increase in skeletal muscle mass specifically, rather than an increase in body weight, would be the desired outcome for improved function and HRQOL. While a meta-analysis by Dewansingh et al[46], showed a tendency toward increased lean body mass following supplementation with more than 20 g of protein per day, a trial of long-term leucine supplementation in healthy older men did not improve skeletal muscle mass or strength.[47] Lean body mass is an important surrogate marker of nutritional status, and should be included in future studies. It was omitted from the current meta-analysis because there were no results available for any of the included studies.

It has been previously suggested that nutritional status can be improved by protein supplementation.[15,43,48] This review indicates that the macronutrient composition of nutritional supplements, in terms of the protein content, may have a direct influence on the extent of nutritional gains observed in older adults in residential care. Similarly, a study of protein intake for more than 2000 elderly participants demonstrated that those in the highest quintile of protein intake lost significantly less lean body mass over 3 years than those in the lowest quintile.[49] This is particularly interesting, given that protein-rich diets have gained huge popularity as a weight-loss strategy, in part by relying on the satiating effect of protein to prevent excess calorie ingestion.[50]

The strengths of this study are related to the systematic manner in which the literature was searched. The main limitation is the narrow focus of the research question, which focused on nonmeat protein

supplementation and HRQOL-related outcomes in a care home setting. The paucity of data in this arena, while an important catalyst for further research, should not be seen as representative of the broader literature on nutrition and patient outcomes.

CONCLUSION

High-protein oral supplements can improve markers of nutritional status (body weight and BMI) in care home residents, but there is insufficient high-quality evidence to determine the effect of nonmeat, high-protein interventions on HRQOL in older residents of care homes.

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Supporting Information

The following Supporting Information is available through the online version of this article at the publisher's website.

Table S1 **PRISMA checklist**

Table S2 **Search strategy for MEDLINE**

Figure S1 **Results of the risk-of-bias assessment**

Figure S2 **Forest plot comparing the assessment of mortality between the interventions in meta-analysis**

Figure S3 **Forest plot assessing the functional assessment scores between the intervention groups in meta-analysis**

Figure S4 **Forest plot assessing the change in mean body weight in meta-analysis**

Figure S5 **Forest plot assessing the change in mean body mass index (BMI) in meta-analysis**

Figure S6 **Forest plot assessing the change in mean mid upper arm circumference (MUAC) in meta-analysis**

Figure S7 **Forest plot assessing the outcome of grip strength measurement in meta-analysis**

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