



Review Article

Distribution of oral nutritional supplements with medication: Is there a benefit? A systematic review



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ABSTRACT

Objectives: Disease-related malnutrition remains a major burden for patients and health care systems. The Medication Pass Nutritional Supplement Program (MEDPass) involves providing patients with oral nutritional supplements (ONS) in unusually small amounts three to four times per day during medication rounds. This systematic review aims to evaluate the impact of MEDPass ONS administration on compliance, total energy and protein intake, food intake, body weight and handgrip strength in hospitalized adults and nursing-home residents.

Methods: We conducted a systematic literature search in the databases MEDLINE, Embase, ScienceDirect, and the Cochrane Library and included randomized controlled trials (RCTs), non-RCTs, and before–after studies. Validated tools specific to the study design were used to assess the included studies.

Results: Ten studies were identified, including two RCTs, three non-RCTs, and five before–after trials. Compliance increased by 23.4% to 66% with MEDPass administration, resulting in compliance rates of 72.7% to 96%. With MEDPass administration, body weight increased by 1% to 6.8% or remained stable. The assessed evidence on total energy intake is ambiguous for protein, with a trend toward an increased intake. Trials on energy intake from food show mixed results as well. One study suggested a slight increase in handgrip strength. The included studies predominantly raise concerns for bias.

Conclusions: We conclude that MEDPass ONS administration increases compliance in hospitalized adults and nursing-home residents. For all other outcomes, robust and well-powered trials are necessary.

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Introduction

Disease-related malnutrition (DRM) remains a major burden for patients and health care systems. The prevalence of DRM ranges from 18% to 60% at hospital admission [1–6]. DRM is associated with impairments on functional ability and quality of life, longer hospital stays, higher readmission rates, as well as increased morbidity and mortality [7,8], which leads to a significant economic impact on health care systems [9]. Oral nutritional supplements (ONS) are often used in nutrition therapy as a simple and effective intervention to treat DRM. The administration of ONS has been shown to have potential positive impacts on handgrip strength (HGS) [10,11], length of hospital stay, morbidity and mortality [12–14].

To date, there are no guidelines on how ONS should be administered, and there is general concern about compliance. In hospital settings, compliance with ONS reaches only around 67% [15].

Another concern is a potential reduction in appetite and consequently a reduction in food intake [16]. To increase compliance and appetite, different approaches to ONS administration are used. The distribution of ONS during medication rounds has gained interest in recent years [17]. The so-called Medication Pass Nutritional Supplement Program (MEDPass) involves providing patients with ONS three to four times per day during medication rounds. The volume of ONS provided with MEDPass ranges from 50 to 120 mL per round in small cups [17,18]. Thus, MEDPass administration is a standardized way of providing ONS compared with the conventional, unstandardized administration.

MEDPass administration may increase ONS compliance [19,20]. Furthermore, the administration of small portions may affect appetite positively and could lead to a higher total intake of energy and protein compared with conventional administration. As an indicator for energy intake, body weight (BW) is usually monitored in nutrition therapy. A well-established, sensitive indicator for catabolic metabolism is HGS [21].

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Table 1
Eligibility criteria for the included studies

Population	Intervention	Comparator	Outcomes	Study types
Included: Hospitalized adults (age >18 y), nursing-home residents Excluded: Patients receiving enteral/parenteral nutrition	Medication Pass Nutritional Supplement Program administration of ONS (1.5–3.2 kcal/mL), 3–4 times per day, 50–120 mL per administration	None or all other forms of ONS administration	Compliance, total energy and protein intake, food intake, body weight, hand-grip strength	Included: Randomized and non-randomized controlled trials, before–after studies Excluded: Observational studies, reviews, case reports, personal opinions, any other study types, studies without full text, qualitative studies

ONS, oral nutritional supplements

This systematic review assesses the evidence of MEDPass on clinical outcome parameters. To our knowledge, this is the first systematic review to evaluate the impact of MEDPass ONS administration on compliance, total energy and protein intake, food intake, BW and HGS.

Methods

The details of the method for this systematic review have been registered in the international prospective register of systematic reviews under the registration number CRD42021229949. This review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [22].

Eligibility criteria

To establish the eligibility criteria, the population, intervention, comparison, and outcomes model was used [23]. The following studies were eligible for inclusion: Papers published between 1980 and February 2021 in the German or English language. A preliminary search was conducted to assess the outcomes usually monitored. Thereafter, the outcomes listed in Table 1 were included.

Search strategies

The literature search was conducted from January 21, 2021 to February 5, 2021. The databases MEDLINE (PubMed), Embase, ScienceDirect, and the Cochrane Library were used to identify relevant trials. Additionally, reference lists of relevant publications were screened.

With respect to the established population, intervention, comparison, and outcomes model, the following keywords were used as single terms or in combination with the Boolean operators AND and OR: “hospitalized adults”, “nursing home residents”, “MEDPass”, “medication pass”, “medication pass supplement program”, “medication pass nutritional supplement program”, “ONS”, “oral nutritional supplement”, “energy intake”, “protein intake”, “ONS intake”, “hand grip strength”, “body weight”, “fat-free mass”, “lean body weight”, “compliance”, and “adherence”. If a more general keyword (ie, “oral nutritional supplement”) was used, limitations were applied to specify the search, such as in PubMed for example: “Clinical study”, “clinical trial”, “controlled clinical trial”, “randomized controlled trial”, “humans”, and “adult: 19+ years”. The limitations were slightly adapted depending on the database. The search strategies were discussed and approved by all authors.

Study selection and data extraction

The primary reviewer screened the title and abstract of the studies that were obtained from the databases and removed duplicates using Citavi (version 6.4; Swiss Academic Software GmbH). Thereafter, the full text was assessed to apply the eligibility criteria. The eligibility of studies was discussed with the research team. After identifying all relevant records, relevant data points were extracted from the publications by the first author, and validated by KU. Questions were discussed with the review team. The following data were extracted from the studies: Author, year, study type, population, sample size, characteristics of intervention (mL, amount of kcal/mL ONS, frequency of administration) and comparator (if applicable), duration of intervention, outcomes (compliance, energy/protein intake, food intake, BW, HGS). All data were recorded in a Microsoft Excel (version 2008; Microsoft Corporation, Redmond, WA) spreadsheet. For relevant missing data, the study authors were contacted.

Evaluation of studies

The evaluation of the included studies was carried out descriptively. Different validated tools specific to the study design were used to assess the risk of bias (RoB). Depending on the study design, the following quality assessment tools were applied: Randomized controlled trials (RCTs; RoB 2.0 by Cochrane

Collaboration [24]; non-RCTs (ROBINS-I) [25]; and before–after studies (National Institutes of Health quality assessment tool for before–after studies without control group) [26]. The first and second authors evaluated the studies independently and compared their results. The other team members were consulted for discussions and clarifications.

Results

Study selection

Through the electronic database search, 3190 studies were identified. Six additional publications were identified by reference list screening and through contact with experts. After the removal of duplicates and irrelevant records through title and abstract screening, 117 articles remained. Of these, 107 were excluded, primarily because ONS was not administered with medication (n = 52) or the population did not fit the inclusion criteria (n = 29). Finally, 10 studies remained and were included in this review. Figure 1 shows the preferred reporting items for systematic reviews and meta-analyses flow diagram of the study selection process.

Study characteristics

The characteristics of included studies are presented in Table 2, 3, and 4. Two studies were RCTs [27,28], three were non-RCTs [29–31], and five studies were before–after studies without control groups [32–36]. Study duration varied from 6 d to 18 mo, and the number of study participants ranged from 11 to 495 patients. Five studies included hospitalized adults [27–31], four included nursing home residents [32,34–36], and one study included both populations [33]. The mean or median age of the study participants ranged from 68 to 88 y or was not specified. Six of 10 included studies specified the type of ONS [27,28,31–33,36], and two [28,31] of the publications reported that different ONS flavors were available.

Four studies were conducted in Europe [27–29,33], three studies were conducted in the United States [34–36], two in Australia [30,31], and one in Canada [32]. In eight studies, the clinical conditions of patients were not clearly stated [27–31,34–36]. The population in the study of Garcia-Gollarte [33] included primarily nervous system disorders (56%), metabolic disorders (23.6%), vascular disorders (22.2%), and psychiatric disorders (18.4%). The population of Doll-Shankaruk were primarily patients with dementia (81%) [32].

Results of included studies

An overview of the results of the RCTs, non-RCTs, and before–after studies is given in Tables 2 through 4.

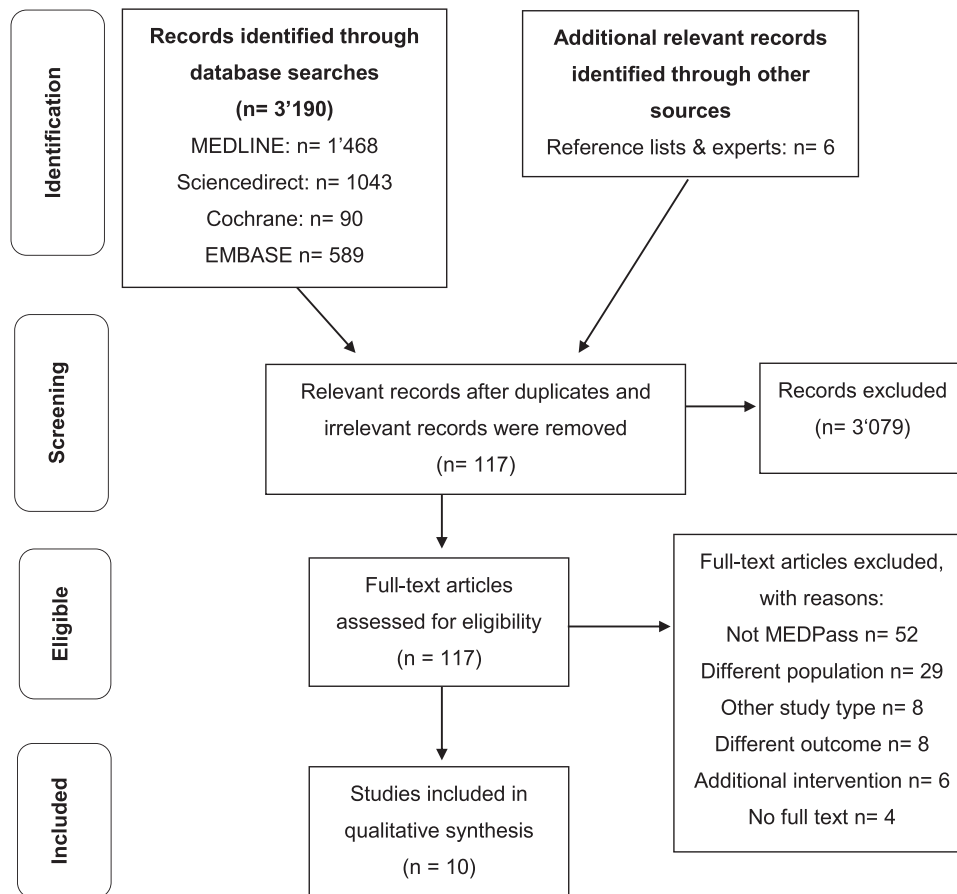


Fig. 1. PRISMA flow diagram.

Compliance

Compliance was assessed in one RCT [28], three non-RCTs [29–31], and three before–after studies [32–34]. ONS intake was monitored daily [28–33] and the amount of ONS consumed was recorded in the medication chart [28–33]. Measurement of the consumed amount was described in two studies [28,29]. In one study, there was no information on the frequency and documentation of ONS monitoring [34].

Van den Berg et al. reported that ONS intake of at least 75% of the prescribed volume was 23.4% higher in the MEDPass group than the control group (72.7% vs 49.3%; $P = 0.005$) [28]. All non-RCTs defined compliance as percentage of the ONS intake prescribed. Jukkola et al. reported 95% compliance with the MEDPass program compared with 48% in the control group [31]. In another non-RCT, compliance was reported to be 17.3% higher in the intervention group than the control group (90.3% vs 63%) [29]. Campbell et al. showed no significant increase in compliance (73.8% standard deviation [SD]: 34.7) vs 80.0% [SD: 34]) [30].

In one before–after study, an increase of 66% in compliance was observed. However, the method of compliance assessment was not specified [34]. Two other studies reported a high compliance to the MEDPass program of 96% (percentage of portions prescribed) [32] and 95.8% (SD: 19.6) (percentage of ONS intake prescribed) during the first 4 wk and 86.6% (SD: 18.8) during the second 4 wk [33].

Total energy/protein intake (food and oral nutritional supplements)

Total energy/protein intake from food and ONS was assessed in one RCT [27], one non-RCT [30], and one before–after study [35]. Potter et al. reported an increase of total energy intake of 319 kcal in the MEDPass group (22.7%), with 1409 kcal (SD: 483 kcal) versus 1090 kcal (SD: 417 kcal) in the control group ($P = 0.001$) [27].

The only non-RCT assessing total energy and protein intake reported a nonsignificant difference in total energy and protein intake through food and ONS in the MEDPass versus control groups [30]. The before–after study assessing total energy and protein intake reported a 17% decrease in energy intake after the implementation of MEDPass, but protein intake remained unchanged [35].

Food intake (without oral nutritional supplements)

Energy/protein intake from food without oral nutritional supplements was assessed in one RCT [27], one non-RCT [30], and two before–after studies [35,36]. Potter et al. did not observe a significant difference in food intake in the MEDPass group (1078 kcal [SD: 440 kcal] vs 1090 kcal [SD: 417 kcal] in the control group) [27]. The only non-RCT [30] assessing food intake observed no significant increase in energy or protein intake from food.

In their before–after study, Remsburg et al. found an increase of 19% (energy and protein intake) [35]. Welch et al. found an increase of 7.3% (SD: 13.4%; $P < 0.005$) in percentage of meal intake

Table 2
Characteristics and results of randomized controlled trials

Author and year	Population	n	Intervention	Comparator	Duration	Results				
						Compliance	TEI, kcal (food and ONS)	Food intake (without ONS) energy intake, kcal	Body weight, % change	Handgrip strength, kg
Potter et al., 2001 [27]	Hospitalized elderly	381	3 × 120 mL (1.5 kcal/mL), ready-made ONS (Entera)	No ONS	18 mo	n.a.	I: 1409 (SD: 483); C: 1090 (SD: 417); P = 0.001	I: 1078 (SD: 440); C: 1090 (SD: 417); n.s.	I: +1 (SD: 5.6) vs C: -1 (SD: 6.1; P = 0.003). Adjusted for confounders I: +2 (SD: 4.5), C: -0.8 (SD: 5.3), n.s.	n.a.
Van den Berg et al., 2015 [28]	Malnourished inpatients	234	4 × 62 mL (2.4 kcal/mL), ready-made ONS (Nutridrink Compact)	2 × 125 mL (between meals, 2.4 kcal/mL), ready-made ONS (Nutridrink Compact)	maximum 30 d	Consumption ≥ 75% of ONS prescribed; I: 72.7%, C: 49.3% (P = 0.005)	n.a.	n.a.	n.a.	n.a.

C, control group; I, intervention group; n.a., not assessed; n.s., not significant; ONS, oral nutritional supplements; SD, standard deviation; TEI, total energy intake

Table 3
Characteristics and results of nonrandomized controlled trials

Author and year	Population	n	Intervention	Comparator	Duration	Results				
						Compliance (% ONS prescribed)	Total energy/protein intake (food and ONS)	Food intake (without ONS); energy intake, kcal; protein intake, g	BW	Handgrip strength, kg
Jukkola et al., 2005 [31]	Acute care geriatric patients	200	4 × 60 mL (2 kcal/mL); ready-made ONS (Two-Cal HN)	2 × 150–250 mL (1.2–2.0 kcal/mL), between meals, ready-made ONS (Ensure Plus, Resource Fruit Beverage)	23–36 d	I: 95; C: 48; n.s.a.	n.a.	n.a.	n.a.	n.a.
Baumann et al., 2012 [29]	Hospitalized adults at nutritional risk	10	4 × 50 mL (2 kcal/mL); type of ONS not stated	Standard care (ONS between meals/request; 2 kcal/mL), type of ONS not stated	6–8 d	I: 90.3; C: 63; n.s.a.	n.a.	n.a.	I: -0.5 to 4.6 kg; C: -0.1 to 2.9 kg; n.s.a.	I: n = 3 +0, 2 -3, n = 1 -3; C: n = 1 +2.5, n = 2 -2.5, n = 1 -11; n.s.a.
Campbell et al., 2013 [30]	Malnourished geriatric inpatients	98	4 × 60 mL (2 kcal/mL); type of ONS not stated	2 × 250 mL (1 or 1.5 kcal/mL); type of ONS not stated	2 wk	I: 80.0 (SD: 34.0); C: 73.8 (SD: 34.7); n.s.	Energy (kcal/kg BW): I: 30.0 (SD: 7.0), C: 28.8 (SD: 7.7); n.s.; protein (g/kg ideal BW), I: 1.34 (SD: 0.34), C: 1.29 (SD: 0.3); n.s.	Energy: I: 1347 (SD: 357), C: 1299 (SD: 409), n.s.; protein: I: 61 (SD: 17), C: 61 (SD: 17); n.s.	I: 1.5% (SD: 5.8), C: 0.4% (SD: 3.8); n.s.	n.a.

BW, body weight; C, control group; I, intervention group; n.a., not assessed; n.s., not significant; n.s.a., no statistical analysis; ONS, oral nutritional supplements; SD, standard deviation; TEI, total energy intake

Table 4

Characteristics and results of before–after studies without control group

Author and year	Population	n	Before	Intervention	Duration	Results				
						Compliance	Total energy/protein intake (food and ONS)	Food intake (without ONS)	BW	Handgrip strength, kg
Lewis et al., 1998 [34]	Transitional care unit patients at nutritional risk	34	1 × 270 mL (1.5 kcal/mL); type of ONS not stated	3 × 90mL (1.5 kcal/mL); type of ONS not stated	3.5 mo	+66% n.s.a.; method of assessment not specified	n.a.	n.a.	>5% BW loss: I: 6%, B: 18%; n.s.a.	n.a.
Rensburg et al., 2001 [35]	Nursing-home residents	20	n.s.	3–4 × 60mL (2 kcal/mL); type of ONS not stated	4 wk	n.a.	Energy: –17%; TPI: no change; n.s.a.	Energy intake: +19%; protein intake: +19%; n.s.a.	Stable weight: 89% of residents; weight decrease: 11% of residents; n.s.a.	n.a.
Welch et al., 2003 [36]	Nursing-home residents	30	2 × 120 mL (1.05 kcal/mL); type of ONS not stated	4 × 60 mL (2 kcal/mL); ready-made ONS (TwoCal HN)	4 wk	n.a.	n.a.	% of meal intake: Breakfast + 10% lunch + 6%, dinner +16%; total meals +7.3% (SD: 13.4; <i>P</i> < 0.005)	I (kg): 101.2 (SD: 18.8); B (kg): 98.75 (SD: 17.1; <i>P</i> < 0.01)	n.a.
Doll-Shankaruk et al., 2008 [32]	Nursing-home residents at nutritional risk	11	3 × 125 mL (1.06 kcal/mL) between meals; type of ONS not stated	4 × 60 mL (2 kcal/mL); ready-made ONS (Ressource 2.0)	6 mo	96% portions prescribed; n.s.a.	n.a.	n.a.	Average weight increase: 2.6 kg (6.4%); n.s.a.	n.a.
Garcia-Gollarte et al., 2011 [33]	Institutionalized patients (hospital/nursing home) who are malnourished or at nutritional risk	495	200–240 mL with or between meals (type and kcal/mL not stated)	50–60 mL (2 kcal/mL); ready-made ONS (TwoCal HN); frequency not stated	8 wk	% ONS prescribed: 95.8% (SD: 19.6) during first half, 86.6% (SD: 18.8) during second half of study; n.s.a.	n.a.	n.a.	Intent to treat: +1.8 kg (SD: 2; +3.5%); per protocol: +2 kg (SD: 2; +3.9%)	n.a.

BW, body weight; C, control group; I, intervention group; n.a., not assessed; n.s., not significant; n.s.a., no statistical analysis; ONS, oral nutritional supplements; SD, standard deviation; TEI, total energy intake

after the intervention [36]. Which unit was used for this evaluation is unclear [36].

Body weight

BW was assessed in one RCT [27], two non-RCTs [29,30], and all before–after studies [32–36]. Potter et al. observed an increase of 1% in BW in the MEDPass group compared with a decrease of 1% in the control group ($P = 0.003$) in their RCT [27]. Campbell et al. and Baumann et al. found no significant difference in BW change in their non-RCTs [29,30].

In the before–after studies, the observed increases in BW were +2.4% ($P < 0.01$) in the study by Welch et al., +3.5% ($P < 0.05$) in the study by Garcia-Gollarte et al., and +6.4% (no P -value) in the study by Doll-Shankaruk et al. [32,33,36]. In their before–after study, Lewis et al. found that 6% of patients lost >5% of their initial BW compared with 18% of patients before the intervention. Remsburg et al. observed that 89% of participants maintained or increased their BW and 12% decreased their BW after MEDPass implementation [35].

Handgrip strength

There was only one study assessing HGS [29]. The authors of this non-RCT found an increase of 0.2 to 3 kg in three patients and decrease of 1 kg in one patient in the intervention group. In the control group, the researchers found a decrease of 2.5 to 11 kg in three patients and increase of 2.5 kg in one patient.

Risk of bias within studies

The overall evaluated RoB in the included studies is shown in Table 5. In the RCTs, there is some concern regarding bias, but the non-RCTs are evaluated as critical-to-serious, and the judgment of RoB in the before–after studies ranges from poor to good.

The aim of this systematic review was to assess the evidence on the MEDPass ONS administration mode in terms of clinical effectiveness. A total of 10 studies were identified, with only two studies designed as RCTs [27,28], three non-RCTs [29–31], and five before–after studies without a control group [32–36].

With regard to compliance, the evidence suggests that the administration of ONS with medication rounds increases adherence by 23.4% to 66%, resulting in high compliance rates of 72.7%

to 96%. These rates are higher than overall ONS compliance in hospital settings at 67% [15]. However, a statistical analysis of compliance was only conducted in one RCT [28] and one non-RCT [30], and the non-RCT showed no statistical difference [30]. A possible explanation for this improved compliance may be the attitude toward ONS administered in the MEDPass mode and the small volume [31]. ONS might be perceived as medication rather than food [37]. Additionally, nurses can encourage patients to drink their ONS more often when delivered four times per day [37]. However, compliance of ONS intake may be influenced by several other factors [38].

Assessed evidence on total energy intake is ambiguous, with a reported increase of 22.7% [27], a decrease of 17% [35], or no significant difference [30]. For total protein intake, no significant differences were observed [30,35]. Food intake without oral nutritional supplements increased in the before–after study by Welch et al by 7.3% [36]. Energy and protein intake from food also increased by 19% in the study by Remsburg et al. [35], but did not change significantly in the RCT and non-RCT [27,30]. Remsburg et al. [35], who found a decrease in total energy intake, also found a trend toward an increase in food intake. Hence, supplement intake may not have a detrimental effect on appetite and food intake [15].

Of note, in all studies, intake was assessed either in a sample of study participants or not for the entire length of stay. This procedure is prone to errors, which reduces the strength of evidence, and could be an explanation that 89% of participants were weight stable and only 11% lost weight, even though the total energy intake decreased overall [35]. There has never been a study in which total energy and protein intake were studied consistently and systematically throughout the hospitalization period. These outcomes are clinically more relevant than ONS compliance [28].

BW increases with MEDPass intervention ranged from 1% to 6.8% [27,32,33,36]. In some studies, BW remained unchanged [29,30]; however, in hospital settings or nursing homes, patients often receive medications that have an impact on BW (ie, diuretics) [39,40]. This was only controlled for in one study [27], which makes drawing reliable conclusions impossible.

The only study assessing HGS suggested a slight increase in HGS with MEDPass compared with the tendency of decrease in the control group. The small number of participants, the lack of statistical analysis, and the serious RoB obviously limit the strength of the evidence. No clear conclusion regarding HGS is possible. Since HGS has recently been proposed as a prognostic marker of mortality and morbidity [21], ways to improve HGS are certainly called for. Therefore, additional studies assessing the effect of MEDPass administration on HGS are needed.

Our population of interest was patients in institutionalized settings. The participants in the included studies represent a geriatric population. Hence, our findings cannot be extrapolated to patients in a different setting or a younger age group. Furthermore, the clinical conditions were not stated in most studies. The difference in clinical conditions might explain the inconsistent findings, at least to some degree. Additionally, heterogeneity in study design, amount of ONS prescribed, ONS energy density, and the absence of a statistical analysis in most studies limits interpretation.

The strongest evidence found in this systematic review is for an advantage in ONS compliance, which is due to the quantity of trials that investigated compliance, as well as the almost consistent results. However, evidence quality is rather low overall, with few randomized and/or controlled studies and a majority of before–after studies. The definition of compliance varied between the studies, limiting the comparability of the results. Additionally, in both RCTs, there is some concern for bias. The

Table 5
Risk of bias for included studies

Study	Design	RoB tool	Judgment
Potter et al., 2001 [27]	RCT	Cochrane RoB 2	Some concern
Van den Berg et al., 2015 [28]	RCT	Cochrane RoB 2	Some concern
Jukkola et al., 2005 [31]	Non-RCT	Cochrane ROBINS-I	Critical
Baumann et al., 2012 [29]	Non-RCT	Cochrane ROBINS-I	Serious
Campbell et al., 2013 [30]	Non-RCT	Cochrane ROBINS-I	Serious
Lewis et al., 1998 [34]	Before–after	NIH Assessment Tool	Poor
Remsburg et al., 2001 [35]	Before–after	NIH Assessment Tool	Fair
Welch et al., 2003 [36]	Before–after	NIH Assessment Tool	Good
Doll-Shankaruk et al., 2008 [32]	Before–after	NIH Assessment Tool	Fair
Garcia-Gollarte et al., 2011 [33]	Before–after	NIH Assessment Tool	Good

NIH, National Institutes of Health; RCT, randomized controlled trial; RoB, risk of bias

other included studies equally raise concern for bias, and are predominantly of low sample size. Only three studies [27,28,30] performed a power analysis.

We screened our systematic review for internal validity. No analysis of publication bias (ie, funnel plot) was performed to determine the impact of a potential publication bias [41]. Additionally, clinicaltrials.gov was not sought out to identify unpublished trials. Although we reduced this bias by contacting experts on the topic, the potential bias still exists. Search bias was reduced by the utilization of four databases and by searching for grey literature. A search in the Cumulative Index to Nursing and Allied Health Literature database was not included in the review because this search might not improve the search strategy for this clinical question [42]. By thoroughly screening the reference lists, the risk of search bias was minimized. However, ruling out the possibility of having missed eligible publications is impossible. Furthermore, only papers in the German or English language were included, which poses some risk of selection bias.

Conclusions

We conclude that the MEDPass administration of ONS can be recommended to increase compliance in hospitalized adults and nursing-home residents. The exact effects on total energy and protein intake, as well as BW have yet to be determined, because our findings deliver ambiguous or nonsignificant results. The effect on HGS is also unclear, considering only one small study examined this effect. The overall quality of the assessed evidence is rather low; thus, well-designed and well-powered studies are needed to shed light on the question of which ONS administration mode may be advantageous for clinical practice. Further research should assess the influence of compliance on quantitative outcomes (ie, BW, body composition, HGS) and the effect of MEDPass on energy and protein intake. A well-powered RCT, monitoring energy and protein intake throughout the hospitalization period, is currently underway, and will add valuable evidence on this topic [39].

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References

- [1] Löser C. Malnutrition in hospital: The clinical and economic implications. *Dtsch Arztebl Int* 2010;107:911–7.
- [2] Khalatbari-Soltani S, Marques-Vidal P. Impact of nutritional risk screening in hospitalized patients on management, outcome and costs: A retrospective study. *Clin Nutr* 2016;35:1340–6.
- [3] Correia MITD, Perman MI, Waitzberg DL. Hospital malnutrition in Latin America: A systematic review. *Clin Nutr* 2017;36:958–67.
- [4] Souza TT, Sturion CJ, Faintuch J. Is the skeleton still in the hospital closet? A review of hospital malnutrition emphasizing health economic aspects. *Clin Nutr* 2015;34:1088–92.
- [5] Imoberdorf R, Meier R, Krebs P, Hangartner PJ, Hess B, Stäubli M, et al. Prevalence of undernutrition on admission to Swiss hospitals. *Clin Nutr* 2010;29:38–41.
- [6] Schuetz P, Fehr R, Baechli V, Geiser M, Deiss M, Gomes F, et al. Individualised nutritional support in medical inpatients at nutritional risk: A randomised clinical trial. *Lancet* 2019;393:2312–21.
- [7] Zhang X, Tang T, Pang L, Sharma SV, Li R, Nyitray AG, et al. Malnutrition and overall survival in older adults with cancer: A systematic review and meta-analysis. *J Geriatr Oncol* 2019;874–83.
- [8] Felder S, Lechtenboehmer C, Bally M, Fehr R, Deiss M, Faessler L, et al. Association of nutritional risk and adverse medical outcomes across different medical inpatient populations. *Nutrition* 2015;31:1385–93.
- [9] Khalatbari-Soltani S, Marques-Vidal P. The economic cost of hospital malnutrition in Europe; a narrative review. *Clin Nutr* 2015;10:e89–94.
- [10] Matheson EM, Nelson JL, Baggs GE, Luo M, Deutz NE. Specialized oral nutritional supplement (ONS) improves handgrip strength in hospitalized, malnourished older patients with cardiovascular and pulmonary disease: A randomized clinical trial. *Clin Nutr* 2021;40:844–9.
- [11] Cawood AL, Elia M, Stratton RJ. Systematic review and meta-analysis of the effects of high protein oral nutritional supplements. *Ageing Res Rev* 2012;11:278–96.
- [12] Gomes F, Schuetz P, Bounoure L, Austin P, Ballesteros-Pomar M, Cederholm T, et al. ESPEN guidelines on nutritional support for polymorbid internal medicine patients. *Clin Nutr* 2018;37:336–53.
- [13] Stratton RJ, Elia M. A review of reviews: A new look at the evidence for oral nutritional supplements in clinical practice. *Clin Nutr* 2007;2:5–23. Suppl.
- [14] Elia M, Normand C, Norman K, Laviano A. A systematic review of the cost and cost effectiveness of using standard oral nutritional supplements in the hospital setting. *Clin Nutr* 2016;35:370–80.
- [15] Hubbard GP, Elia M, Holdaway A, Stratton RJ. A systematic review of compliance to oral nutritional supplements. *Clin Nutr* 2012;31:293–312.
- [16] Cox NJ, Ibrahim K, Sayer AA, Robinson SM, Roberts HC. Assessment and treatment of the anorexia of aging: A systematic review. *Nutrients* 2019;11:144.
- [17] Dillabough A, Mammel J, Yee J. Improving nutritional intake in post-operative hip fracture patients: A quality improvement project. *Int J Ortho Trauma Nurs* 2011;15:196–201.
- [18] Bender S, Pusateri M, Cook A, Ferguson M, Hall JC. Malnutrition: Role of the TwoCal HN Med Pass program. *Medsurg Nurs* 2000;9:284–95.
- [19] Canadian Agency for Drugs and Technologies in Health. The Medication Pass Nutritional Supplement Program in patients receiving medication: A review of clinical effectiveness and guidelines. Canadian Agency for Drugs and Technologies in Health: Ottawa, Ontario; 2015.
- [20] Roberts M, Potter J, McColl J, Reilly J. Can prescription of sip-feed supplements increase energy intake in hospitalised older people with medical problems? *Br J Nutr* 2003;90:425–9.
- [21] Kaegi-Braun N, Tribollet P, Baumgartner A, Fehr R, Baechli V, Geiser M, et al. Value of handgrip strength to predict clinical outcomes and therapeutic response in malnourished medical inpatients: Secondary analysis of a randomized controlled trial. *Am J Clin Nutr* 2021;114:731–40.
- [22] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med* 2009;6:e1000097.
- [23] Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: A key to evidence-based decisions. *ACP J Club* 1995;123:A12–3.
- [24] Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. Rob 2: A revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898.
- [25] Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;355:i4919.
- [26] National Institutes of Health. Quality assessment tool for before–after (pre–post) studies with no control group. Available at: <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>. Accessed September 20th, 2021.
- [27] Potter JM, Roberts MA, McColl JH, Reilly JJ. Protein energy supplements in unwell elderly patients—A randomized controlled trial. *JPEN. J Parenter Enteral Nutr* 2001;25:323–9.
- [28] van den Berg GH, Lindeboom R, van der Zwet WC. The effects of the administration of oral nutritional supplementation with medication rounds on the achievement of nutritional goals: A randomized controlled trial. *Clin Nutr* 2015;34:15–9.
- [29] Baumann A, Dolder A, Stanga Z, Joray M, Kurmann S. Einhaltung von Therapieempfehlungen - Eine prospektive Studie mit zwei Verabreichungsmodi für Trinknahrungen. *Aktuel Ernährungsmed* 2013;38.
- [30] Campbell KL, Webb L, Vivanti A, Varghese P, Ferguson M. Comparison of three interventions in the treatment of malnutrition in hospitalised older adults: A clinical trial. *Nutr Dietet* 2013;70:325–31.
- [31] Jukkola K, MacLennan P. Improving the efficacy of nutritional supplementation in the hospitalised elderly. *Australas J Ageing* 2005;24:119–24.
- [32] Doll-Shankaruk M, Yau W, Oelke C. Implementation and effects of a medication pass nutritional supplement program in a long-term care facility: A pilot study. *J Gerontol Nurs* 2008;34:45–51.
- [33] García-Gollarte F, Muñoz-Fernández R, Coucheiro-Vilar S, Herrando-Sanchis V, Turro-Ribalta T, Enrich-Polat G, et al. MEDPASS is an effective approach to oral nutritional supplementation to increase elderly malnourished patients intake and compliance and improve nutrition status and outcomes. *J Aging Res Clin Pract* 2012;1:156–61.
- [34] Lewis D, Boyle KD. Gaining strength. *Nurs Manage* 1998;29:37–8.

- [35] Rensburg RE, Sobel T, Cohen A, Koch C, Radu C. Does a liquid supplement improve energy and protein consumption in nursing home residents? *Geriatr Nurs* 2001;22:331–5.
- [36] Welch P, Porter J, Endres J. Efficacy of a medication pass supplement program in long-term care compared to a traditional system. *J Nutr Elderly* 2003;22:19–28.
- [37] Lambert K, Potter J, Lonergan M, Tapsell L, Charlton KE. Qualitative study of patients and health-care professionals' views on the efficacy of the nutrition as medication oral nutrition supplement program. *Nutr Dietet* 2017;74:341–8.
- [38] den Uijl LC, Kremer S, Jager G, van der Stelt AJ, de Graaf C, Gibson P, et al. That's why I take my ONS. Means-end chain as a novel approach to elucidate the personally relevant factors driving ONS consumption in nutritionally frail elderly users. *Appetite* 2015;89:33–40.
- [39] Traves KP, Studdiford JS, Pickle S, Tully AS. Edema: Diagnosis and management. *Am Fam Phys* 2013;88:102–10.
- [40] Wang FW, Shi J, Yang JW, Wang ZH, Ye JH, Ye Y, et al. The impact of weight management and related diuretic medication intervention based on body weight changes on cardiac function and re-hospitalization rate in patients with chronic congestive heart failure. *Zhonghua Xin Xue Guan Bing Za Zhi* 2017;45:874–9.
- [41] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;339:b2700.
- [42] Beckles Z, Glover S, Ashe J, Stockton S, Boynton J, Lai R, et al. Searching CINAHL did not add value to clinical questions posed in NICE guidelines. *J Clin Epidemiol* 2013;66:1051–7.