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Randomized Control Trials

MEDPass versus conventional administration of oral nutritional supplements – A randomized controlled trial comparing coverage of energy and protein requirements

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SUMMARY

Background & aims: The use of oral nutritional supplements (ONS) in the hospital setting is important to reach individual protein and energy goals in patients at risk for malnutrition. Compliance with ONS can be challenging but may be improved by prescribing ONS in smaller portions with medication rounds (MEDPass). We compared the likelihood of meeting energy and protein requirements in patients receiving ONS with MEDPass versus conventional ONS administration.

Methods: The MEDPass Trial is a randomized, controlled, open-label superiority trial conducted on medical and geriatric wards in a University Hospital in Switzerland. The MEDPass group was allocated to receive 50 ml of ONS four times per day with the medication rounds. The control group received ONS per conventional care between the meals. The primary outcome was the percentage of energy in relation to the individual requirement. Secondary outcomes included the coverage of protein intake in relation to the individual requirement, the amount of daily consumed ONS, the course of handgrip strength (HGS), body weight appetite and nausea. Furthermore, we compared 30-day mortality and hospital length of stay (LOS) was studied in medical patients.

Results: From November 22nd, 2018 until November 30th, 2021, 204 patients were included in the trial (MEDPass group n = 100, control group n = 104). A total of 203 patients at nutritional risk were analyzed in the intention-to-treat analysis (ITT). Regarding the primary endpoint, there was no difference in the coverage of energy requirement between the MEDPass and control group (82 vs. 85% (Δ −3%, 95%CI -11 to 4%), p = 0.38). Similarly, no differences were found for the secondary outcomes including coverage of protein requirement (101 vs. 104% (Δ −3%, 95% CI -12 -7%), p = 0.57, average daily intake of ONS (170 vs 173 ml (Δ − 3 ml, 95% CI -14 to 8 ml), p = 0.58) and 30-day mortality (3 vs. 8 patients, OR 0.4 (95% CI 0.1 −1.4), p = 0.15). The course of HGS, body weight, appetite and nausea did not differ between the groups (p = 0.29, p = 0.14, p = 0.65 and p = 0.94, respectively). The per protocol analysis including 178 patients showed similar results.

Conclusion: Within this controlled trial setting, we found a high compliance for ONS intake and high coverage of protein requirements but no further improvement when ONS was administered using

Abbreviations: BMI, Body Mass Index; EHR, Electronic Health Record; ESPEN, European Society for Clinical Nutrition and Metabolism; HGS, Handgrip Strength; ITT, Intention-To-Treat Analysis; LOS, Length of stay; MEDPass, Medication Pass Nutritional Supplement Program; MD, Medical Doctor; NRS 2002, Nutritional Risk Screening 2002; ONS, Oral nutritional supplements; REDCap®, Research Electronic Data Capture; RCT, Randomized Controlled Trial; RD, Registered Dietitian; RN, Registered Nurse; SAE, Serious Adverse Event; VAS, Visual Analogue Scale.

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MEDPass compared to conventional care. MEDPass administration may provide an alternative that is easy to integrate into nursing routines, which may lead to lower workload with cost benefits and reduction of food waste.
Trial registration: ClinicalTrials.gov: NCT03761680.

1. Introduction

The burden of malnutrition in hospitals is a main determinant of functional decline, poorer quality of life and higher morbidity and mortality rates [1]. Yet, recent trials found individualized nutritional therapy to be effective in inpatients at nutritional risk in reducing severe complications and 30-day mortality [2,3]. The use of ONS is efficient and cost-effective [4–6]. Nutritional therapy with ONS may reduce complications and mortality, prevent, or attenuate muscle loss, and improve nutritional status and function [5,7–9]. The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends the use of ONS for medical and geriatric patients at nutritional risk as part of a multimodal treatment concept [5,10]. These patients often suffer from chronic illness, which may be associated with appetite, weight loss and increased risk of disease related malnutrition due to inflammation and catabolism [5,10].

Compliance with ONS is often low which poses a barrier to adequate oral nutrition therapy [10,11]. There are no standards on ONS administration in terms of timing throughout the day which leads to unsystematic approaches. In hospital settings, ONS are conventionally served between main meals. The Medication Pass Nutritional Supplement Program (MEDPass) offers a systematic approach. In the MEDPass administration mode, ONS are distributed with medication rounds three or four times per day in smaller portions (50–120 ml) [12–19]. Preliminary trials suggest that using the MEDPass administration mode improves compliance with ONS prescription [13,14,16,18,20–22].

It can be argued that ONS are dense in both energy and protein and may therefore negatively impact appetite [23]. Consequently, enhancing compliance using the MEDPass administration mode may not automatically lead to improved total nutritional intake because conventional food intake may decline. Preliminary studies on this subject reported ambiguous results [14,17,24,25]. None of them assessed intake systematically but rather in a subsample of participants or for part of their study duration. Furthermore, most of these trials had risk of bias as evaluated in a systematic review [19]. The aim of the MEDPass Trial was to compare the difference in total energy and protein coverage in patients using MEDPass versus conventional administration of ONS. In addition, the course of handgrip strength (HGS), body weight, appetite, nausea as well as length of stay (LOS) and 30-day mortality were studied as secondary outcomes.

2. Material & methods

2.1. Study design & participants

The MEDPass Trial is a randomized, controlled, open-label clinical superiority trial (RCT) conducted with parallel groups. The design details are published elsewhere [26]. The MEDPass Trial included medical as well as geriatric inpatients at the Tiefenau facility of the University Hospital of Bern. We included patients >18 years of age with a positive risk screening for malnutrition (total score ≥3 points) according to the Nutritional Risk Screening 2002 (NRS 2002) [27]. Screening had to be performed within 72 h of admission. Further inclusion criteria were an expected hospital LOS ≥3 days after nutritional screening, patients who qualified for and approved ONS prescription. We excluded patients with acute disease metabolism such as an initial admission to the intensive care unit or an intermediate postoperative state and patients with diseases causing severe malassimilation such as short bowel syndrome. Furthermore, patients unable to eat orally or supplemented with or scheduled for enteral or parenteral nutrition were excluded. Lastly, patients with mini mental state examination <16 points, poor German skills or with terminal medical conditions were also excluded [26]. Informed consent for participation in this trial was obtained from all patients by a registered dietitians (RD) [28]. The MEDPass Trial was approved by the Competent Ethics Committee of the Canton Bern of Switzerland on October 15th, 2018 (Project-ID 2018-01512) and registered on ClinicalTrials.gov, NCT03761680.

2.2. Randomization and procedures

Patients were randomly assigned 1:1 by the RDs to receive ONS by either the MEDPass intervention or in the unstandardized conventional administration mode between meals. Randomization was stratified according to the NRS 2002 total score and the energy content of the ONS. The randomization list was prespecified by the Clinical Trial Unit of the University of Bern and electronically integrated into the Research Electronic Data Capture (REDCap®) program (Vanderbilt University, Nashville, TN, USA, 2020, version 9.1.15) [29]. The RDs were blinded to the randomization sequence.

Treatment with ONS according to the assigned group was prescribed as soon as possible after randomization. Patients in the MEDPass group received 50 ml of ONS four times per day distributed by the registered nurses (RN) on the ward during medication rounds. Patients in the control group were provided with ONS in the conventional administration mode (unstandardized clinical practice of ONS administration). This regimen's prescriptions could have ranged from one to four bottles of ONS per day and were served between the meals and/or after the evening meal. The staff were instructed not to make any changes to their conventional administration mode. ONS was prescribed by the attending medical doctor (MD) and listed in the medication chart of the electronic health record (EHR). All ONS used in the MEDPass Trial were selected according to patients' nutritional needs and flavor preferences. Patients were allowed to choose from a wide range of available products at University Hospital of Bern with an energy density of 1.5 kcal/ml and 2 kcal/ml from different providers (Abbott Nutrition, Fresenius Kabi, Nestlé Health Science).

2.3. Outcomes

2.3.1. Energy, protein, ONS intake & coverage of energy and protein requirements

Energy, protein and ONS intake were assessed continuously until discharge or for a maximum of 30 days. At baseline, the RDs

calculated daily energy and protein requirements according to relevant current clinical nutrition guidelines for the patients in the MEDPass Trial published before the trial started [5,10,30,31]. Oral food intake was assessed after every meal by the personnel collecting the trays. Consumption of each component of every meal was evaluated separately (100%, 75%, 50%, 25% or 0%) and a patient-reported diet history was collected for food intake between the main meals. All food items on site were prepared according to recipes of the Bern University Hospital database. Energy and protein intakes were primarily calculated within the electronic menu system LogiMen® (Kretschmer-Keller Leonberg, Germany, 2016, version 5.4). Energy and protein intake from food items that were consumed and not registered in LogiMen® were calculated by the RDs using nut.s nutritional software® (dato Denkwerkzeuge, Vienna, Austria, 2008, version 1.32.74). All calculations were recalculated by one of the co-investigators blinded to patient allocation. The amount of ONS consumed was monitored by the RNs by measuring the amount consumed and documenting it in the EHR with an accuracy of ±5 ml. The RDs calculated energy and protein intake from ONS according to intake and specific ONS consumed. For coverage of energy and protein requirements, the total daily energy and protein intakes were compared with the patients' individual requirements (percentage intake of predicted energy and protein requirements). The average coverage of energy and protein throughout the study period was calculated per patient.

2.3.2. Handgrip strength, body weight, appetite, and nausea

HGS, body weight, appetite and nausea were assessed at baseline and on weekly study visits (7 ± 2 days) until discharge or for a maximum of 30 days. HGS was evaluated by the RDs using the JAMAR® Hydraulic Hand Dynamometer (Patterson Medical, Warrenville, IL, USA) with an accuracy of ±0.5 kg. The measurement was always conducted in a standardized manner and if possible, on the dominant hand. Measurements were performed three times with a break of at least 30 s and the highest value was noted [32]. Body weight was monitored by the nursing staff with an accuracy of ±0.1 kg. Immobile patients were weighed on the seca® wheelchair scale (Vogel & Halke, Germany, model 665) and mobile patients on the sitting scale seca® (Vogel & Halke, Germany, model 959). Body weight measurements were prescribed by the MDs according to the study schedule. RDs evaluated if body weight measurements were valid according to the patient's clinical status and medications and discussed the validity with the MDs in case of uncertainties. Data on body weight measurements which was considered invalid was excluded from the analysis of the secondary outcome course of body weight. Appetite and nausea were recorded by the RDs using a visual analogue scale (VAS). The scale visible to the patient only showed smileys. Measurements were converted to a scale ranging from 0 to 10 cm with an accuracy of ±0.1 cm placed on the backside of the VAS tool.

2.3.3. Hospital LOS, 30-day mortality and safety outcomes

Hospital LOS and 30-day mortality were assessed after the participants were discharged or after 30 days of trial inclusion. Hospital LOS was assessed from the EHR as number of days and only in medical inpatients since the geriatric inpatients in the facility have a prefixed duration of stay (two weeks for most patients, one or three weeks for a minor proportion of the patients). Assessment of 30-day mortality was performed per telephone call to the patients' home or the institution the patient was referred to. If patients were still hospitalized, the information was available in the EHR. Serious adverse events (SAE) were monitored continuously according to Good Clinical Practice [33].

2.4. Statistical methods

For the power-analysis, we assumed that administration of ONS using the MEDPass mode would increase energy intake by at least 10% (i.e. by 200 kcal/d from an average energy requirement of 2000 kcal/d for a patient that weights 75 kg). Therefore, to demonstrate that intervention group patients have an increased average daily energy intake of 200 kcal/day (from 2000 ± 500 kcal to 2200 ± 500 kcal), 200 patients were needed to achieve 80% power (alpha error of 0.05). The sampsi command in STATA® (Stata Corp, USA, 2017, version 15.3) was used for the power analysis.

The primary analysis was an intention-to-treat analysis (ITT) analysis. For the coverage energy and protein requirements and for the evaluation of average intake of ONS/day, linear regression analysis adjusted for stratification factors was used to compare differences between the groups. This method was also planned for evaluation of LOS. Logistic regression analysis adjusted for stratification factors was used for difference in 30-day mortality between the groups. Repeated measure linear mixed effects models were used for the evaluation of differences in course of HGS throughout the hospitalization, weight changes throughout the hospitalization, and course of appetite and nausea throughout the hospitalization.

After assessment of the distribution of the variables using quantile–quantile plots, procedural parameters were analyzed with Mann-Withney-U tests (two-sided, unpaired, not continuity corrected), and chi-square tests (not continuity corrected) for continuous and categorical variables respectively.

A per protocol analysis was conducted excluding patients that did not comply with the study protocol (ONS-prescription for <80% of the study duration), patients of which >10% of meals could not be assessed during the time of intake monitoring, patients that were nil per os for >10% of their meals during the time of intake monitoring, patients that did not receive the randomized intervention throughout the entire study period and patients violating eligibility criteria at discharge. The same parameters and tests as in the primary analysis were assessed and conducted on the per protocol dataset.

ITT and per protocol analyses were performed with R, version 4.1.3 [34]. using the packages nnet [35], lmerTest [36], and modelbased [37].

3. Results

3.1. Trial population

From November 22nd, 2018 until November 30th, 2021, patients were recruited until 80% power was achieved. A total of 204 patients at nutritional risk according to the NRS 2002 screening tool were recruited to the trial (MEDPass group n = 100, control group n = 104). One patient in the control group was excluded post randomization and therefore lost to follow-up because ONS was never prescribed. The per protocol analysis included 178 patients (MEDPass group n = 86, control group n = 92). Details are shown in the consort flow diagram (Fig. 1). Most patients were recruited from the geriatric wards (MEDPass group n = 98, control group n = 97). The MEDPass and control group included two and six patients from the medical wards, respectively. The mean age in the MEDPass and control group was 82 years (SD 6 and 7, respectively) and had a mean body mass index (BMI) of 24.5 and 24.1 kg/m2 (SD 4.7 and 4.5, respectively). Most patients had a NRS 2002 total score of 3 or 4 (n = 154) and an NRS 2002 subscore for impaired nutritional status of 1 or 2 (n = 171). The main disease categories at inclusion were cardiovascular and infectious diseases. Patient baseline characteristics did not differ between the groups (Table 1).

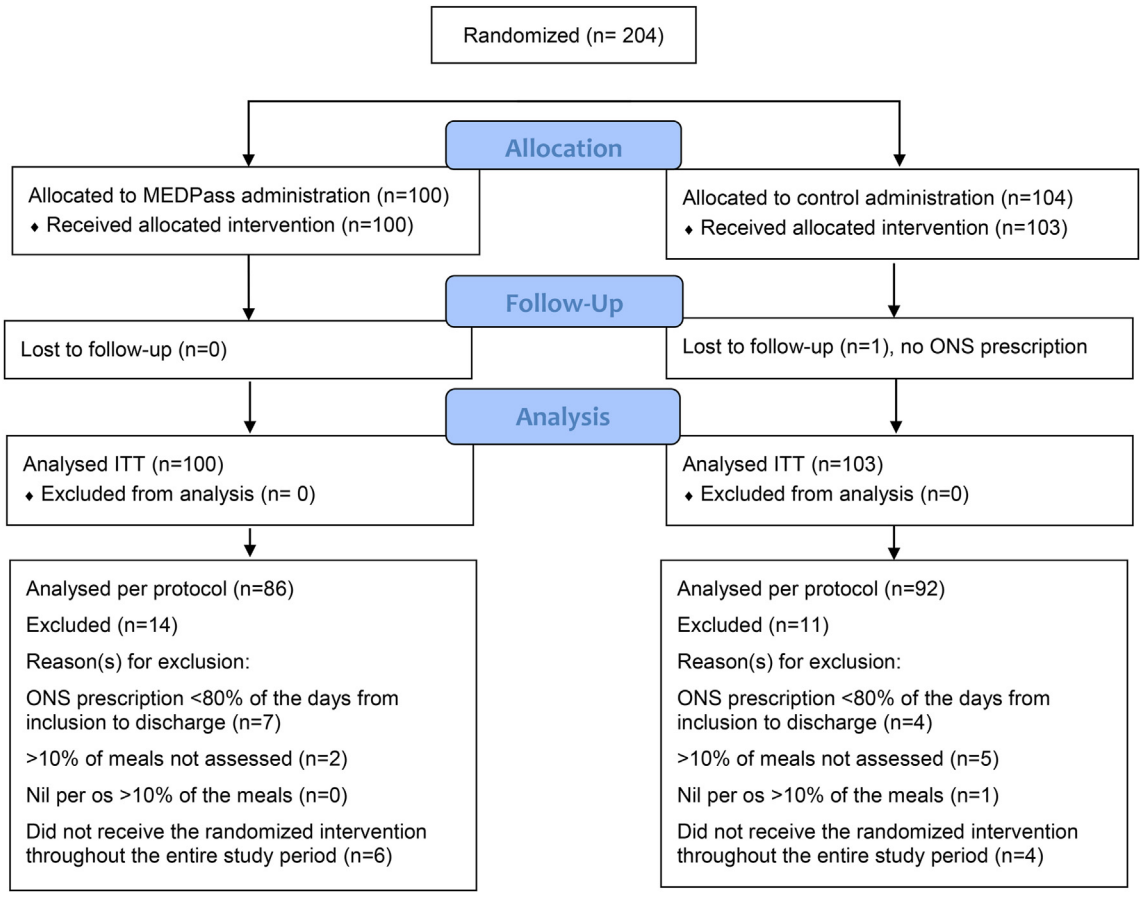

Fig. 1. Consort flow diagram of the MEDPass Trial.

3.2. Intention to treat analysis

We analyzed 203 patients in the ITT. The mean compliance to ONS prescription (percentage of ONS consumed compared to the prescription) was 93% (SD 13) in MEDPass versus 89% (SD 12) in conventional administration ($p = 0.002$). In the ITT analysis 55% of the patients (52% MEDPass and 59% control group) reached ≥75% coverage of energy requirements and 81% (80% and 83%, respectively) reached ≥75% coverage of protein requirements. Coverage of energy requirements did not differ between the MEDPass and control group (82 vs. 85% (Δ −3%, 95% CI -11 to 4%), $p = 0.38$) (Fig. 2 & Table 2). This also applies for coverage of protein requirements (101 vs. 104% (Δ −3%, 95% CI -12 to 7%), $p = 0.57$) (Fig. 3 & Table 2), the average amount of daily ONS intake (170 vs. 173 ml (Δ −3 ml, 95% CI -14 to 8 ml), $p = 0.58$) and 30-day mortality (3 vs. 8 patients, OR 0.4 (95%CI 0.1 to 1.4), $p = 0.15$) (Table 2). Furthermore, the course of HGS, appetite and nausea did not differ between the groups ($p = 0.29$, $p = 0.65$ and $p = 0.94$, respectively) (Supplementary Figs. 1, 3 and 4). Mean patient body weight decreased over time ($p < 0.001$) with no significant difference between the groups ($p = 0.14$) (Supplementary Fig. 2). Hospital LOS was not analyzed due to the small number of patients recruited from the medical wards ($n = 8$). There were no SAEs in either group.

3.3. Per protocol analysis

We included 178 patients in the per protocol analysis. Due to incompliance with the study protocol, 14 patients were excluded from the ITT data set in the MEDPass group and 11 patients were excluded from the control group. The criteria used to test compliance to the study protocol did not differ between groups (Fig. 1). In the per protocol population, mean compliance to ONS prescription was 94% (SD 9) in MEDPass versus 89% (SD 12) in conventional administration ($p = 0.002$). 60% of the patients reached ≥75% coverage of energy requirements (56% MEDPass and 63% control group) and 84% (83% and 86%, respectively) reached ≥75% coverage of protein requirements. The per protocol analysis showed similar results with no statistically significant differences for any of the endpoints. Coverage of energy requirements did not differ between groups (84 vs. 87% (Δ −2%, 95% CI -10 to 5%), $p = 0.54$) (Table 3). The same applied for coverage of protein requirements (104 vs. 106% (Δ −2%, 95% CI -12 to 7%), $p = 0.64$) and the average amount of daily total ONS intake (176 ml in both groups (Δ 0 ml, 95% CI -11 to 10 ml), $p = 0.93$) (Table 3). Thirty-day mortality showed a trend towards to higher mortality in the control group but was not statistically different (1 vs. 8 patients, OR 0.12 (95% CI 0.01–1.01), $p = 0.051$) (Table 3). As in the ITT, the course of HGS and nausea did not differ between the groups ($p = 0.23$ and $p = 0.92$, respectively) (Supplementary Figs. 5 and 8). Weight decreased over time ($p < 0.001$) with no significant difference between the groups ($p = 0.14$) (Supplementary Fig. 6) and appetite increased over time ($p = 0.047$) with no difference between the groups ($p = 0.78$) (Supplementary Fig. 7).

4. Discussion

This study investigated the MEDPass versus conventional ONS administration mode in geriatric and medical inpatients at

Table 1
Baseline patient characteristics.

	MEDPass (n = 100)	Control (n = 103)
Sociodemographics		
Age, years, mean (SD)	82 (6)	82 (7)
Male, n (%)	49 (49)	51 (50)
Geriatric ward, n (%)	98 (98)	97 (94)
Nutritional assessment and therapy		
Weight, kg, mean (SD)	70 (16)	67 (15)
BMI, kg/m^2, mean (SD)	24.5 (4.7)	24.1 (4.5)
NRS 2002 total score, n (%)		
3	32 (32)	34 (33)
4	43 (43)	45 (44)
5–7	25 (25)	24 (23)
NRS 2002 subscore impaired nutritional status, n (%)		
0	8 (8)	5 (5)
1	46 (46)	51 (50)
2	41 (41)	33 (32)
3	5 (5)	14 (14)
Energy content of ONS, n (%)		
1.5 kcal/mL	54 (54)	55 (53)
2.0 kcal/mL	46 (46)	48 (47)
Number of days with ONS prescription, days, mean (SD)	8.6 (4.3)	8.6 (3.8)
Involvement of the dietician, n (%)		
No individual nutritional therapy	5 (5)	3 (3)
Individualized nutritional therapy w/o food orders	85 (85)	94 (91)
Individualized nutritional therapy with individualized food orders	10 (10)	6 (6)
Disease category		
Gastrointestinal disease	7 (7)	11 (11)
Infectious disease	24 (24)	20 (19)
Cardiovascular disease	24 (24)	21 (20)
Neurological disease	8 (8)	6 (6)
Oncologic disease	5 (5)	8 (8)
Other disease	32 (32)	37 (36)

BMI: body mass index; NRS 2002: nutritional risk screening 2002; ONS: oral nutritional supplement.
If the percentages do not add up exactly to 100%, it is due to rounding differences.

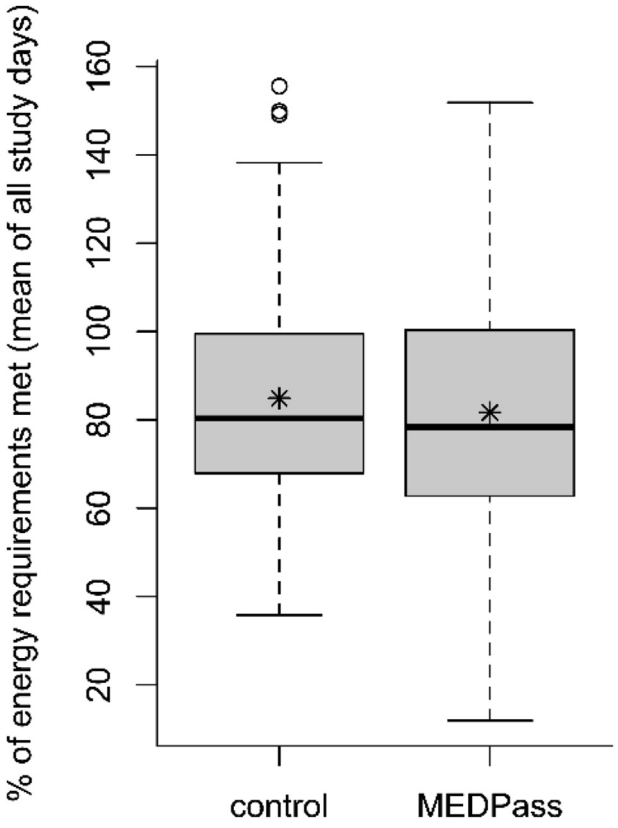

Fig. 2. Coverage of energy requirements ITT. *represents mean.

nutritional risk. In the ITT analysis 203 patients were included. There was no difference in the coverage of energy and protein requirement between the MEDPass and control group (82 vs. 85% and 101 vs. 104%, respectively). Furthermore, the course of HGS, body weight, appetite and nausea did not differ between the groups (p = 0.29, p = 0.14, p = 0.65 and p = 0.94, respectively). The per protocol analysis including 178 patients showed similar results.

4.1. Performance of the study groups

MEDPass and control group showed similarly high coverage of energy and protein requirements in medical and geriatric inpatients compared with conventional administration (ITT: 82 and 85% coverage of energy requirements and 101 and 104% of coverage of protein requirements) (Table 2). Unblinded designs are known to have potential effects on patients' behaviors and reactivity, and it is therefore plausible that patients in our control group enhanced their compliance [38–40]. However, in the MEDPass Trial, blinding of participants was not feasible due to the different times of ONS administration. When comparing ≥75% coverage of requirements with a recent large Swiss multicenter trial in medical inpatients, patients in the ITT of the MEDPass Trial performed lower regarding ≥75% coverage of energy requirements (55 vs. 79%) and similar for ≥75% coverage of protein requirements (81% vs. 79%) [3]. The difference in ≥75% coverage of energy requirements might have occurred because in the MEDPass Trial, only 10% of patients in the intervention group ordered meals with the RD whereas in the multicenter RCT, it was the case for all patients in the intervention group [3].

There was a statistically significant difference of compliance to ONS in MEDPass versus conventional administration in the ITT (93% MEDPass versus 89% conventional administration, p = 0.002) as well as in the per protocol analysis (94% MEDPass versus 89% conventional administration, p = 0.002). Higher compliance of

Table 2
Results Intention to treat analysis.

	MEDPass (n = 100)	Control (n = 103)	p-value[a]
Coverage of energy requirements (% of individual requirement)			
mean (SD)	82 (27)	85 (26)	
linear model[b]: estimate ± SE (95% CI)	−3 ±4 (-11-4)	N/A	0.38
Coverage of protein requirements (% of individual requirement)			
mean (SD)	101 (33)	104 (32)	
linear model[b]: estimate ± SE (95% CI)	−3 ±5 (-12-7)	N/A	0.57
Average intake of ONS/day (ml)			
mean (SD)	170 (30)	173 (48)	
linear model[b]: estimate ±SE (95% CI)	−3 ±6 (-14-8)	N/A	0.58
30- day mortality, n (%)	3 (3)	8 (8)	
logistic regression[b]: OR (95% CI)	0.36 (0.09–1.43)	1 (N/A)	0.15

[a] Mann-Withney-U Test for continuous variables (two-sided, unpaired, not continuity corrected), chi-squared test for categorical variables. N/A: not applicable.
[b] Adjusted for stratification factors NRS 2002 total score and the energy content of the ONS.

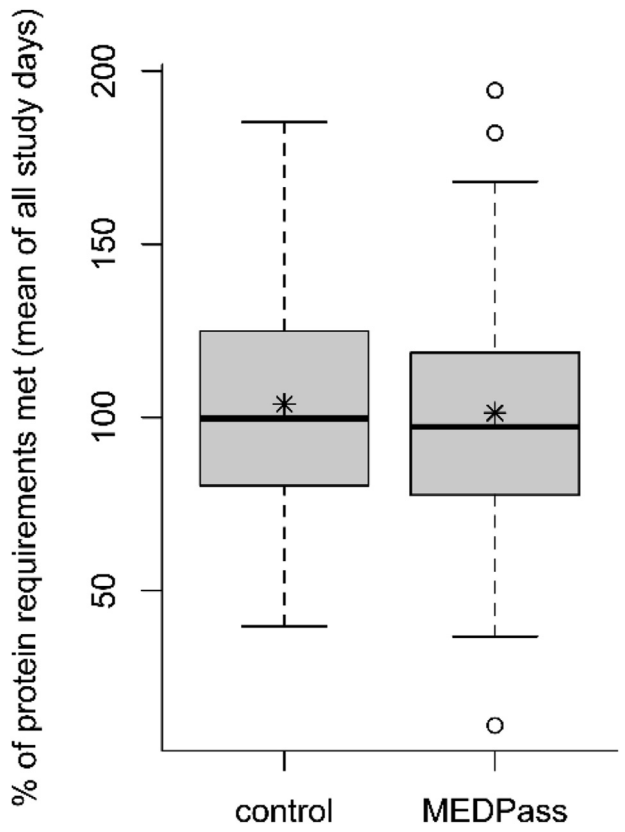

Fig. 3. Coverage of protein requirements ITT. *represents mean.

MEDPass versus conventional administration has been demonstrated in previous trials [13,14,16,18,20–22] and was the basis for our trial hypothesis. Even though statistical difference is given in the MEDPass Trial, the compliance to conventional ONS administration was surprisingly high compared to other studies. With conventional administration, compliance with ONS in hospital settings has been reported around 67% in previous trials [11]. In more recent RCTs, Deutz et al. found that one third of patients took ≥75% of prescribed ONS [41] and van den Berg et al. reported 49.3% of patients compliant with consumption of ≥75% of ONS prescription [18]. These results underline the unexpectedly high compliance to conventional administration in the MEDPass Trial. On the other hand, certain RCTs, found comparable compliance to conventional ONS prescription as in the MEDPass Trial (88–100%) [42–44]. The effect of being observed in a study setting is still not fully understood [39,45]. It is plausible, that the compliance of ONS in the control group of the MEDPass Trial does not reflect clinical reality and has influenced our main results.

Table 3
Results per protocol analysis.

	MEDPass (n = 86)	Control (n = 92)	p-value[a]
Coverage of energy requirements (% of individual requirement)			
mean (SD)	84 (26)]	87 (25)	
linear model[b]: estimate ± SE (95% CI)	−2 ±4 (-10-5)	N/A	0.54
Coverage of protein requirements (% of individual requirement)			
mean (SD)	104 (32)	106 (32)	
linear model[b]: estimate ±SE (95% CI)	−2 ±5 (-12-7)	N/A	0.64
Average intake of ONS/day (ml)			
mean (SD)	176 (20)	176(44)	
linear model[b]: estimate ±SE (95% CI)	0 ± 5 (-11-10)	N/A	0.93
30- day mortality, n (%)	1 (1)	8 (9)	
logistic regression[b]: OR (95% CI)	0.12 (0.01–1.01)	1 (N/A)	0.051

[a] Mann-Withney-U Test for continuous variables (two-sided, unpaired, not continuity corrected), chi-squared test for categorical variables. N/A: not applicable.
[b] Adjusted for stratification factors NRS 2002 total score and the energy content of the ONS.

4.2. Secondary outcomes

The MEDPass Trial investigated on the course of HGS, weight, appetite, nausea as well as 30-day mortality. None of these parameters showed significant differences. Body weight was increased in MEDPass versus conventional ONS administration in one previous RCT [24]. Other non-RCTs found no difference in body weight between groups [13,14]. HGS was only evaluated in one small non-RCT (n = 10) and found a trend to higher HGS with MEDPass administration [13]. Together with the results of the MEDPass Trial, it remains unclear if MEDPass administration improves the course weight or HGS. The course of appetite and nausea as well as mortality were not assessed in previous MEDPass studies so there is no data to compare our results to.

4.3. Advantages of MEDPass administration

The outcomes investigated by the MEDPass Trial are unambiguously important to nutritional therapy. However, as the evidence is not clear regarding the administration mode, other aspects must be taken into consideration to decide on an administration mode for daily clinical practice. These aspects – apart from better compliance to ONS - might include workload and management of ONS by nursing staff, economic aspects as well as patients' preferences.

4.3.1. Workload and management of ONS by nursing staff

In a qualitative focus group investigation, RNs described advantages regarding workflow. Patient motivation to take ONS was reported easier and monitoring of ONS more accurate as it is documented together with the medication [46]. Simpler monitoring was also stated by the vast majority of questioned nursing staff in the trial of Jukkola and MacLennan [21]. The preparation of the ONS shots for MEDPass administration accounts for additional work which is more than compensated for because patients perceive ONS as medication rather than food and therefore have to be motivated less to take it [46]. Furthermore, Dillabough et al. conducted 20 interviews with RNs and nursing students and stated that integrating the MEDPass mode was easier and more efficient for 80% of the participants because several responsibilities are managed at once [15]. In three more trials that questioned nursing staff, MEDPass administration was not perceived as more time consuming when compared to conventional administration [18,21,47]. Overall, workload was not higher and management of ONS was easily integrated in nursing routines with MEDPass administration. These are key findings for MEDPass administration because quality of care and patient outcomes are affected negatively in times of nursing shortage [48,49].

4.3.2. Economic aspects

RNs reported subjectively less perceived ONS waste with MEDPass administration in two trials [15,21]. These subjective reports are underlined by a quantitative analysis of ONS waste by Welch et al. which reported on a 2-week period for 30 participants.

ONS waste in the MEDPass group was two liters versus 30.8 L with conventional administration ($p < 0.001$) [25]. Baumann et al. calculated theoretical cost efficiency which was better with the MEDPass mode of administration [13].

4.3.3. Patient preferences

Campell et al. surveyed 25 patients each on MEDPass and conventional administration in their non-randomized trial with the European Quality of Life 5 Dimensions questionnaire and found higher overall QOL in patients on MEDPass admininistration ($p = 0.004$) [14]. During implementation of MEDPass administration in the study of Dillabough et al., 73% of the 22 participants reported to like consuming ONS administered with the medication rounds [15]. One of the reasons for liking the MEDPass administration was the fact that medication is easier to swallow with the ONS [15]. However, taking ONS directly with medication was not allowed in the MEDPass Trial to avoid possible food–medication interactions [26]. Overall, patient preferences trend towards MEDPass administration although individual preferences should be considered whenever possible in clinical practice [50].

4.4. Limitations

Participants of the MEDPass Trial were mainly recruited on the geriatric wards as patients on the medical wards were often hospitalized for a short period of time or refused to participate in the trial due to their unscheduled hospitalization and acute situation [51]. Therefore, analysis of hospital LOS was not possible as planned due to the small number of patients recruited from the medical wards ($n = 8$). Also, the mean age of our participants (82 years) limits the extrapolation of our results to a younger population. The ESPEN published a new ESPEN Guideline on clinical nutrition in hospitalized patients with acute or chronic kidney disease in 2021. According to this guideline, the protein requirement is 1 g/kg to 1.3 g/kg body weight for patients with acute or chronic kidney disease and acute/critical illness [52]. Applying this new guideline to the MEDPass Trial population may have led to a lower coverage of protein requirement in patients with acute or chronic kidney disease and acute illness. Furthermore, the occurrence of type II-error cannot be excluded with 80% power. Finally, we expected lower compliance to ONS in the control group, but the controlled trial may have increased compliance and thereby potentially masked positive effects of MEDPass administration.

5. Conclusion

Within this controlled trial setting, we found a high compliance for ONS intake and high coverage of protein requirements in both ONS administration modes. There was no difference in coverage of energy and protein requirements, course of HGS, body weight, appetite, and nausea when ONS was administered using MEDPass compared to conventional care. The ITT and per protocol analysis showed similar results. Further trials should investigate the integration of MEDPass administration mode into the nursing routine, as it may lead to improved care quality and economic savings within the healthcare system.

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Author contributions

SK: conceptualization, software, data curation, project administration, supervision, funding acquisition, writing – original draft.

ER: conceptualization, investigation, writing – review & editing.

KS: investigation, formal analysis, visualization, writing – review & editing.

PS: conceptualization, supervision of formal analysis, writing – review & editing.

KU: project administration (substitute of SK), investigation, writing – review & editing.

MV: conceptualization, validation of all energy and protein calculations, writing – review & editing.

ABS: conceptualization, funding acquisition, writing – review & editing.

AWS: primary investigator, supervision, conceptualization, writing – review & editing.

DB: supervision, writing – review & editing.

ZS: sponsor, conceptualization, funding acquisition, writing – review & editing.

Conflict of Interest

SK: SK has received honorariums from Abbott Nutrition and Fresenius Kabi and consulting fees from Omanda Medical Nutrition.

ER, KAS, KU, MV, AWS, DB and ABS: no conflicts of interest.

PS: The institution of PS has received grants unrelated to this project from Nestlé Health Science, Abbott Nutrition, Thermofisher and bioMerieux.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2022.11.015.

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