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A randomised trial of dietary counselling and food fortification in stable chronic obstructive pulmonary disease

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ABSTRACT

Background: Malnutrition in chronic obstructive pulmonary disease (COPD) is associated with poor prognosis yet evidence to support the role of dietary counselling and food fortification is lacking.

Objective: To assess the impact of dietary counselling and food fortification on outcome in outpatients with COPD who are at risk of malnutrition.

Methods: Randomised, controlled trial (unblinded) in 59 outpatients with COPD (6 months intervention: 6 months follow-up). Intervention group received dietary counselling and advice on food fortification; controls received a dietary advice leaflet. Outcome measures: nutritional status, respiratory and skeletal muscle strength, respiratory function, perceived dyspnoea, activities of daily living (ADL) and quality of life.

Results: Intervention group consumed more energy (Difference 194 kcal/day; $p = 0.02$) and protein (Difference 11.8 g/day; $p < 0.001$) than controls. Intervention group gained weight during the intervention period and maintained weight during follow-up. Controls lost weight throughout the study. Significant differences were observed between groups in St. George's Respiratory Questionnaire Total Score (Difference 10.1; $p = 0.02$), Short Form-36 Health Change Score (Difference 19.2; $p = 0.029$) and Medical Research Council dyspnoea score (Difference 1.0; $p = 0.03$); difference in ADL score approached statistical significance (Difference 1.5; $p = 0.06$). No differences were observed between groups in respiratory function or skeletal and respiratory muscle strength. Improvements in some variables persisted for 6 months beyond the intervention period.

Conclusion: Dietary counselling and food fortification resulted in weight gain and improvements in outcome in nutritionally at risk outpatients with COPD, both during and beyond the intervention period.

INTRODUCTION

In patients with chronic obstructive pulmonary disease (COPD) weight loss and being underweight are associated with poor prognosis and increased mortality, independent of disease severity (1). Recent reviews of nutritional intervention in COPD suggest the effects on weight change, body composition and functional measures are minimal (2; 3), in part due to the small numbers of subjects and short-term interventions. Both reviews concluded that larger, randomised controlled trials (RCT) are required.

In the management of malnutrition the main aims of nutritional intervention are to maximise nutrient intake and, through minimising weight loss and/or promoting weight gain, to improve clinical and functional outcomes. To achieve these goals dietitians may use one or any combination of the following strategies; dietary counselling to increase the frequency and/or alter the types of food and fluid consumed; food fortification to increase nutrient density of food and/or drink; provision of prescribable oral nutritional supplements (ONS). Evidence suggests that ONS are invaluable to some patients when used appropriately (3) yet, while dietitians are uniquely trained to provide dietary counselling and advice on food fortification, surprisingly little evidence exists to support these strategies (4).

ONS are used routinely both in hospital and the community yet alone they may be insufficient or inappropriate for some patients. Reported compliance rates are as low as 50 %, especially in the elderly (5; 6) and may be affected by taste fatigue (7) gastro-intestinal symptoms (8), individual preferences and lifestyle (9). For some patients dietary counselling and advice on food fortification may have advantages over ONS by offering greater variety and flexibility. Furthermore, intervention may result in changes in dietary habits that persist beyond the intervention period and thus result in maintenance of any weight gain and/or clinical and functional benefits achieved.

The aim of this study was to assess the specific impact of dietary counselling and food fortification on patient-centred outcomes in outpatients with COPD identified as at risk of malnutrition.

METHODS

Recruitment and randomisation
Subjects were recruited in chest clinic at St. Thomas', Guy's and Lewisham Hospitals from August 2001 to May 2003. All patients with a clinical diagnosis of COPD and identified as at risk of malnutrition (Score 3 – 5) using a validated nutrition screening tool (10) (online supplement 1) were invited to participate in the study if aged 18 years or more and able to give informed consent. Those with conditions likely to compromise nutritional status further were excluded i.e. unstable diabetes mellitus, current disseminated malignancy, congestive cardiac failure and untreated thyroid disease. Informed, written consent was obtained and randomisation occurred in a standard way using sealed opaque envelopes containing randomised codes.

Intervention
Intervention lasted for the first 6 months of the study, the following 6 months being used to measure the effects of cessation. All subjects received a leaflet providing advice on nourishing snacks and drinks and encouraging food fortification (11). Controls were handed the leaflet during the baseline assessment but its contents were never discussed. Intervention subjects were offered a package of treatment incorporating dietary counselling by an experienced dietitian (CEW) and a supply of milk powder (MP) for use in food fortification. The aim was to increase energy intake by up to 600 kcal/day while ensuring an adequate balance of macro and micronutrients (online supplement 2).

Outcome measures
All assessments were conducted by the investigator (CEW) during seven home visits (baseline, months 1, 3, 6, 7, 9 and 12). Dietary intake was assessed at baseline using the diet history method and prior to all subsequent assessments using 5-day dietary diaries (12). The amount of MP consumed was recorded during each assessment. Dietary intake data were analysed using Microdiet Version 1.1 (University of Salford, UK). Weight was measured without shoes, in light clothing, using portable scales (Soehnle, Germany). Height was measured, without shoes, using a wall-fixed stadiometer (Holtain Ltd., Crymych, Wales). To assess changes in muscle mass mid arm circumference (MAC) and triceps skinfold thickness (TSF) were measured and mid arm muscle circumference (MAMC) was calculated. To assess changes in fat mass skinfold thickness was measured at four sites (biceps, triceps, sub-scapular and supra-iliac) using Harpenden skinfold calipers (Holtain Ltd, Crymych, Wales), according to standard methodology (13). The St. George's Respiratory Questionnaire (14) provided an assessment of respiratory health status and a generic tool, the SF-36 (15) provided an indication of health change. Dyspnoea was assessed using the Medical Research Council Dyspnoea Scale (16), a five-point scale where a score of 1 indicates physical activity is not limited by dyspnoea and a score of 5 indicates the patient is too dyspnoeic to leave the house. Activities of daily living (ADL) were assessed using the amended Townsend score (17) which consists of 11 questions. Scores range from 0 to 22, higher scores indicating more difficulty performing daily activities. Skeletal muscle strength was assessed on the non-dominant arm (18) using a hand-grip dynamometer (Takei, Japan). Respiratory and diaphragmatic muscle strength were assessed using maximal sniff and mouth pressure measurements according to standard protocol (19) using a Morgan Pmax monitor (P.K. Morgan Ltd, Rainham, Kent).

Sample size calculation and statistical analysis
In malnourished patients, weight gain in excess of 2.0 kg is associated with improved functional and clinical outcomes {3}. Mean weight loss over the previous year in 198 weight-losing and thin patients with COPD seen in chest clinics at Guy's and St. Thomas' Hospitals was 5.4 ($\pm$ 3.7) kg i.e. 10 ($\pm$ 8.6) %. A reduction in weight loss of 3.0 kg would be a 55 % improvement (0.8 of standard deviation). To detect such a difference at the 5 % level with 80 % power would require 26 patients in each group.

All patients who completed at least two assessments (baseline and one other) were included in an intention-to-treat analysis, to provide an unbiased assessment of the treatment effect. For continuous data, the final measurement for each patient (when they withdrew, died or completed the study) was recorded and for ordinal data, the median score was calculated for each patient from baseline until they withdrew, died or completed the study. Further analysis was conducted on all patients who completed the study, to analyse changes during the intervention and post-intervention periods separately. For continuous data, one-way analysis of covariance (ANCOVA) was conducted to compare groups, controlling for baseline measurements. For non-parametric data, Rank ANCOVA tests were conducted to compare groups, controlling for baseline measurements (20). All tests were two-tailed and $p < 0.05$ was considered statistically significant. All data were analysed on completion of the study using SPSS Version 11.5 (SPSS Inc., Chicago, Illinois, USA). All results are reported after controlling for baseline measurements unless otherwise stated.

Ethical approval was obtained from the Guy's and St. Thomas' Hospital NHS Trust Ethics Committee (EC97/363) and the University Hospital Lewisham Ethics Committee (03/08/12).

RESULTS

Sixty-six patients were recruited. Fifty-nine (89 %) completed the baseline assessment and 37 (56 %) completed the study (Figure 1). The main reason patients failed to complete the study was deterioration in their clinical condition (online supplement 3).

At baseline, no significant differences were observed between patients who completed the study (n = 37) and those who did not (n = 22) (Table 1).

Table 1 – Baseline data comparing patients who completed the study with those who did not (n = 59)

	Completed (n = 37)	Withdrew or died (n = 22)	p
Demographics			
Males: Females	18:19	12:10	-
Age (years)	69.0 (47 - 85)	69.1 (46 – 89)	0.97
Weight (kg)	53.9 (8.2)	54.4 (7.4)	0.82
Body Mass Index (kg/m^2)	19.9 (1.6)	19.5 (1.6)	0.38
Unintentional change from usual weight (kg)	- 8.7 (6.0)	- 8.6 (5.6)	0.93
% fat mass	23.3 (6.2)†	21.5 (7.7)	0.35
Smoking status and respiratory function			
Ex-smokers	20 (54 %)	12 (55 %)	)
Smokers	14 (38 %)	10 (45 %)	) 0.37
Non-smokers	3 (8 %)	0 (0 %)	)
FEV_1 (% predicted)	31.9 (12.5)	31.7 (14.4)	0.95
FEV_1/FVC	0.44 (0.14)	0.44 (0.13)	0.91
MRC dyspnoea score	3 (1 – 5)	4 (1 – 5)	0.16
Nutrient intake (Diet history method)			
Energy (kcal/day)	2015 (406)	1850 (360)	0.11
Protein (g/day)	68.3 (11.9)	65.9 (11.1)	0.44
Quality of life and functional status			
St George's Respiratory Questionnaire Total Score	57.1 (3.2)	60.8 (3.8)	0.68
Activities of Daily Living (ADL) score	12 (7 – 18)	12 (8 – 18)	0.93

Values are mean (range) for age, mean (SD) for weight, body mass index, unintentional weight change, % fat mass, FEV_1 (% predicted), FEV_1/FVC, nutrient intake, SGRQ Total score and ADL score and number (%) patients for smoking status; p values for unpaired t-tests for age, weight, body mass index, FEV_1, FEV_1/FVC, nutrient intake and SGRQ Total score, χ^2 test for smoking status and Mann-Whitney test for MRC dyspnoea and ADL scores; † *n = 36 as one patient did not consent to measurement*

At baseline the intervention and control groups were comparable (Table 2). No subjects attended a pulmonary rehabilitation programme while participating in the study.

Table 2 - Patient characteristics at baseline (n = 59)

	Intervention (n = 31)	Control (n = 28)
Demographics		
Males: Females	16:15	14:14
Age (years)	68.9 (48 - 89)	69.2 (46 - 85)
Weight (kg)	54.5 (7.3)	53.5 (8.5)
Height (m)	1.65 (0.1)	1.66 (0.1)
Body mass index (kg/m^2)	19.9 (1.4)	19.5 (1.9)
Unintentional change from usual weight (kg)	-8.0 (5.2)	- 9.2 (6.2)
% fat mass	23.2 (7.2)†	22.0 (6.4)
Smoking status		
Ex-smokers	18 (58 %)	14 (50 %)
Smokers	11 (36 %)	13 (46 %)
Non-smokers	2 (6 %)	1 (4 %)
Disease severity and respiratory function		
FEV_1 (% predicted)	30.9 (12.8)	32.7 (14.6)
FEV_1/FVC	0.44 (0.14)	0.45 (0.13)
MRC dyspnoea score	3 (1 – 5)	4 (1 – 5)
Social circumstances		
Lived with spouse/partner/family members	20 (65 %)	18 (64 %)
Lived alone	11 (35 %)	10 (36 %)
Co-morbidities		
Depression	8 (26 %)	10 (36 %)
Hypertension	11 (35 %)	6 (21 %)
Cardio-vascular disease	9 (29 %)	7 (25 %)
Gastro-oesophageal reflux	3 (10 %)	8 (29 %)
Respiratory therapy		
Oral steroids	3 (10 %)	1 (4 %)
β_2-stimulants	22 (71 %)	19 (68 %)
Broncho-dilators	19 (51 %)	18 (64 %)
Adreno-stimulants	10 (32 %)	6 (21 %)
Inhaled steroids	23 (74 %)	19 (68 %)
Theophylline	6 (19 %)	5 (18 %)
Long term oxygen therapy	7 (23 %)	3 (11 %)
Nutrient intake (Diet history method)		
Energy (kcal/day)	1974 (371)	1931 (425)
Protein (g/day)	68.5 (11.6)	66.1 (11.6)
Quality of life and functional status		
St George's Respiratory Questionnaire Total Score	55.5 (19.6)	61.9 (17.1)
Activities of Daily Living (ADL) score	12 (7 – 18)	12 (8 – 18)

Values are mean (SD) for weight, height, BMI, unintentional weight change, % fat mass, FEV_1 (% predicted), FEV_1/FVC, nutrient intake and SGRQ Total Score; mean (range) for age; median (range) for MRC dyspnoea and ADL scores; number (%) patients for smoking status, respiratory therapy, social circumstances and co-morbidities; † n = 30 as one patient did not consent to measurement

Fifty patients completed at least one dietary diary. The intervention group consumed significantly more energy and protein than the control group (Table 3). In those who completed the study the intervention group consumed significantly more energy (p = 0.02) and protein (p < 0.001) than the control group during the intervention period although no differences were observed between the groups during follow-up (Figure 2). In the intervention group four subjects failed to comply with any advice. Of the 24 (77 %) who used MP for more than 14 days, mean use was 26.8 g MP/day (130 kcal/day; 4.8 g protein/day). None of the control group used MP during the study.

A significant difference in final body weight was observed between the intervention and control groups (Table 3). In those who completed the study, intervention patients gained weight during the intervention period and maintained weight during follow-up whereas control patients lost weight throughout the study (Figure 3).

Table 3 – Energy and protein intake and measures of body composition, skeletal and respiratory muscle strength and respiratory function

	Baseline	Intervention	Control	Difference	95 % Confidence Interval	*p*
Dietary intake		(n = 28)	(n = 22)			
Energy (kcal/d)	1996	1979 (54)	1785 (61)	194	+ 31 to + 357	0.02
Protein (g/d)	67.8	72.7 (1.8)	60.9 (2.0)	11.8	+ 6.3 to + 17.3	<0.001
Body composition		(n = 30)	(n = 25)			
Weight (kg)	54.6	55.7 (0.9)	52.6 (1.0)	3.1	+ 0.5 to + 5.7	0.02
MAC (cm)	25.9	26.2 (0.3)	25.3 (0.4)	0.9	0.0 to + 1.9	0.05
MAMC (cm)	23.0	22.9 (0.2)	22.4 (0.2)	0.5	- 0.2 to + 1.2	0.13
S4SF (mm)	32.1	36.3 (1.8)*	29.7 (1.9)	6.6	+ 1.4 to + 11.8	0.01
Muscle strength and respiratory function						
Handgrip strength (kg)	23.0	22.2 (0.4)	21.9 (0.5)	0.3	- 0.9 to + 1.6	0.58
Pmax Expiratory (cm H_2O)	72.1	80.8 (4.2)	71.6 (4.4)	9.2	- 2.9 to + 21.4	0.13
Pmax Inspiratory (cm H_2O)	47.2	54.5 (2.5)	54.6 (2.6)	0.1	- 7.4 to + 7.2	0.98
Sniff pressure (cm H_2O)	48.7	55.2 (2.7)	55.3 (2.9)	0.1	- 8.1 to + 7.9	0.98
FEV_1 (L)	0.83	0.78 (0.03)	0.81 (0.04)	0.03	- 0.13 to + 0.07	0.56
FVC (L)	1.97	1.80 (0.06)	1.98 (0.07)	0.18	- 0.36 to + 0.01	0.06

*Values are adjusted for baseline measurements and expressed as means (SE); Difference = difference in measurements between intervention and control groups; 95 % confidence interval for the difference between intervention and control groups; p values for ANCOVA tests between intervention and control groups. Intention to treat analysis. MAC = mid arm circumference; MAMC = mid arm muscle circumference; S4SF = sum of four skinfold thickness measurements. * n = 29 (1 patient did not consent to measurement).*

Intervention patients gained fat mass and maintained muscle mass whereas control patients lost both fat and muscle mass. The observed difference between the groups in the sum of four skinfold thickness measurements was statistically significant in both the intention-to-treat analysis (Table 3) and in those who completed the study (6 months: Difference = 6.6 mm; p = 0.02; 12 months: Difference = 9.7 mm; p = 0.01). The difference observed in MAMC was not statistically significant when analysed on an intention to treat basis. In those who completed the study, however, a significant difference in MAMC was observed between the groups at twelve months (Difference = 0.9 cm: p = 0.04) though not at six months (Difference = 0.5 cm; p = 0.15).

Table 4 – Quality of life

	Baseline	Intervention	Control	Difference	95% Confidence Interval	p
St George's Respiratory Questionnaire						
Intention-to-treat (n = 41)	73.4	(n = 23)	(n = 18)			
Activity	43.5	70.4	78.7	8.3	-17.3 to + 0.5	0.06
Impacts	60.6	35.4	52.8	17.4	- 28.8 to –- 6.1	0.004
Symptoms	55.3	59.5	61.6	2.1	- 14.4 to + 10.3	0.73
Total		51.2	61.3	10.1	- 18.5 to – 1.7	0.02
Completed study (n = 37)						
Six months	74.8	(n = 20)	(n = 17)			
Activity	46.1	67.0 (3.3)	80.4 (3.5)	13.4	- 23.3 to – 3.6	0.009
Impacts	62.8	42.3 (2.8)	48.5 (3.0)	6.2	- 14.5 to + 2.2	0.14
Symptoms	57.6	63.2 (2.4)	66.6 (2.5)	3.4	- 10.4 to + 3.7	0.34
Total		53.4 (2.2)	61.1 (2.4)	7.7	- 14.4 to – 1.1	0.02
Twelve months	75.4					
Activity	47.0	69.3 (2.9)[†]	80.5 (3.0)	11.2	- 19.8 to – 2.7	0.01
Impacts	62.8	35.8 (3.3)[†]	53.7 (3.5)[‡]	17.9	- 27.6 to – 8.2	0.001
Symptoms	58.2	63.4 (4.4)[†]	63.8 (4.5)	0.4	- 13.3 to + 12.5	0.95
Total		50.6 (2.7)[†]	63.9 (2.8)[‡]	13.3	- 21.3 to – 5.4	0.002
Short Form-36						
Intention-to-treat (n = 41)	34.8	(n = 23)	(n = 18)			
Health Change		51.7 (5.6)	32.5 (6.4)	19.2	+ 2.0 to + 36.4	0.029
Completed study (n = 37)						
Six months	35.4	(n = 19) [†]	(n = 17)			
Health Change		53.8 (4.8)	29.6 (5.0)	24.2	+ 10.1 to + 38.3	0.001
Twelve months	33.8	(n = 18)[‡]	(n = 16) [‡]			
Health Change		55.2 (5.7)	28.5 (6.1)	26.7	+ 9.7 to + 43.7	0.003

Values are adjusted for baseline measurements and expressed as means (SE); Difference = difference in measurements between intervention and control groups; 95 % confidence interval for the difference between intervention and control groups; p values for ANCOVA tests between intervention and control groups. St George's Respiratory Questionnaire: scores range from 0 (perfect health) to 100 (worst possible health); [†] n = 18 (2 patients refused to complete SGRQ at 12 months); [‡] n = 16 (1 patient failed to complete the Impacts section of SGRQ at 12 months). SF-36: Scores range from 0 (worst possible health) to 100 (perfect heath); [†]*1 patient refused to complete SF-36 at 6 months and another at 12 months;* [‡]*2 patients refused to complete SF-36 at 12 months*

Forty-one patients completed the SGRQ and the SF-36 on at least two occasions (baseline plus one other). In the intention-to-treat analysis the intervention group reported significantly better SGRQ Impacts and Total scores than the control group although there was no difference in the Symptoms score. The difference in the Activity scores approached significance. In those who completed the study, improvements in SGRQ Impacts and Total scores continued after the cessation of nutritional intervention (Table 4). The observed differences in scores were likely to be clinically significant since they exceeded the minimum clinically important difference of 4 points (21).

The SF-36 Health Change score was significantly different in the intention to treat analysis and at both six and twelve months in those who completed the study, reflecting improvement in the intervention group and deterioration in the control group (Table 4).

Perceived dyspnoea was less of a problem for the intervention group since median dyspnoea score was significantly lower in the intervention group in the intention-to-treat analysis (Intervention = 3 (range 1 – 5); Control = 4 (range 1 – 5; p = 0.03). In those who completed the study, a significant difference was observed in dyspnoea scores at 6 (Intervention = 3 (range 1 - 5); Control = 4 (range 2 - 5); p = 0.002) but not at 12 months (Intervention = 3 (range 1 - 5); Control = 4 (range 2 - 5); p = 0.24). The observed differences in dyspnoea score were likely to be clinically significant, reflecting the difference between being able to walk less than 100 yards before being limited by dyspnoea and being able to walk further e.g. to the local shops.

The intervention group found it easier to perform everyday activities than the control group since the median ADL score in the intervention patients was lower than in controls. This approached statistical significance in the intention-to-treat analysis (Intervention = 11 (range 7 - 15); Control = 13 (range 9 – 18); p = 0.06) and in those who completed the study, the difference in scores between the groups was statistically significant at 6 months (Intervention = 11 (range 7 -

17); Control = 13 (range 8 - 18); $p = 0.02$) and approached significance at 12 months (Intervention = 10 (range 7 - 16); Control = 13 (range 9 - 19); $p = 0.06$).

In contrast to the subjective functional measures, no differences were observed between the groups in objective functional measures or respiratory function in either the intention-to-treat analysis (Table 3) or in those who completed the study (data not shown).

DISCUSSION

This is one of the first RCTs to evaluate the specific impact of dietary counselling on outcome in any patient group (4). The study is unusual in that it measured the effect of intervention not only on nutritional outcomes but also on objective and subjective measures of functional status. Furthermore this study measured the effects of cessation of intervention, an area that is rarely investigated.

In the current study dietary counselling resulted in significant benefits in dietary intake, body composition, quality of life and subjective measures of functional status. Intervention patients gained approximately 2 kg body weight during the intervention period and maintained weight during follow-up. This study therefore confirms the conclusions of a recent review that in order to observe any benefits from nutritional intervention in outpatients with COPD, weight gain of at least 2 kg is required (3).

Only two other studies have reported the effects of dietary counselling on body composition (22) or patient-centred outcomes (23) in any patient group and similar to the current study, the results showed that dietary counselling was beneficial. Possible reasons for these benefits include the fact that in both studies, similar to the current study, counselling was individualised to each patient's needs and intervention lasted for at least six months. Similar to the current study, one of the studies found some beneficial effects persisted for at least six months beyond the intervention period (23). This persistence of the beneficial effects of dietary counselling beyond the intervention period contrasts with studies measuring the effects of cessation of ONS in general (3) and in outpatients with COPD in particular (24, 25). In studies using ONS, cessation resulted in decreased nutritional intake and body weight towards baseline and some loss of functional benefits. Dietary counselling may result in changes in dietary habits which persist beyond the intervention period, a potential benefit of this strategy over the use of ONS. Furthermore, by tailoring advice to an individual's preferences, symptoms and lifestyle it may be possible to achieve good compliance since using food and drink is likely to offer greater variety and flexibility than using ONS alone. In the current study compliance was good with only four (14 %) intervention patients failing to comply with any advice or food fortification. No control patients made any significant improvements to their diet or bought MP even though they received a leaflet recommending these strategies. More research is required comparing ONS with dietary counselling, including the specific effects of each strategy on dietary intake and behaviour, both during and after intervention. Since MP is not available on prescription a cost analysis should be conducted and supply issues will need to be addressed if such products are to be used in routine clinical practice.

In the current study the intervention group showed improvements in psycho-social function, reflected in changes in quality of life scores. This may have beneficially influenced their motivation to undertake daily activities or their ability to cope with activity-related dyspnoea. The mechanism for these effects has yet to be elucidated and further research is required in this area.

In the current study, the observed differences between the groups in weight change, body composition, quality of life and subjective functional measures occurred in the absence of changes in objective functional measures. These results concur with those reported in a recent review (2) where nutritional support had no significant effect on lung function or respiratory muscle strength in patients with stable COPD. The majority of patients in the current study were sedentary and more than one quarter were effectively housebound. The role of nutritional intervention (dietary counselling and/or ONS) in conjunction with pulmonary rehabilitation and/or exercise training therefore requires evaluation.

There are a number of limitations to this study, a major one being the potential for bias arising from inadequate blinding to treatment allocation and outcome assessment. To minimise bias all results were analysed at the end of the study and no interim analyses were conducted. Furthermore the dietary diaries were analysed by two independent dietitians, both of whom were blind to the treatment group and outcome assessment. Future studies evaluating the impact of dietary counselling and food fortification should be adequately blinded to determine if the observed treatment effect in the current study can be replicated.

The observed differences between the groups in weight change are not fully accounted for by the differences in recorded dietary intake, particularly in the six months following cessation of intervention. Two different methods were used to assess intake i.e. diet history method at baseline and 5-day dietary diaries at all subsequent assessments. Results from the two methods are not directly comparable since diet history tends to over-estimate intake and, due to under-reporting, dietary diaries tend to under-estimate (12). While changes in dietary behaviour may account for some of the observed differences in weight change and dietary intake in the current study, other factors may have contributed, in particular differences in physical activity level, energy expenditure or inflammatory status. Since data on physical activity and energy expenditure were not collected in the current study it is not possible to determine the relative contributions of these potential confounding factors. Some patients with COPD exhibit a low-level inflammatory response (26; 27) the consequences of which may result in a poor response to nutritional intervention (26). Inflammatory markers were not measured in the current study so it is not possible to determine whether any patients who failed to respond to dietary counselling had a low-level inflammatory response.

In the current study, the control group received a leaflet encouraging food fortification and providing advice for increasing nutritional intake. In clinical practice, this may be the extent of nutritional intervention for outpatients with COPD and this study suggests that, compared with dietary counselling and advice on food fortification, it is ineffective in achieving weight gain and functional benefits in this patient group. Further studies are required to establish which patients are most likely to respond to, and potentially benefit from, dietary counselling and advice on food fortification. The possible effects of inflammatory status, psycho-social function, coping strategies, exercise training and pulmonary rehabilitation also require evaluation.

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COMPETING INTERESTS

The authors have no competing interests to declare.

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FIGURE LEGENDS

Figure 1 - Trial profile
Figure 2 - a) Total energy and b) total protein intake/day
Figure 3 - Weight change from baseline in patients who completed the study (n = 37)

REFERENCES

(1) Landbo C., Prescott E., Lange P., Vestbo J., Almdal T.P. Prognostic value of nutritional status in chronic obstructive pulmonary disease. American Journal of Respiratory and Critical Care Medicine 1999; 160:1856-1861.

(2) Ferreira I.M., Brooks D., Lacasse Y., Goldstein R.S., White J. Nutritional supplementation for stable chronic obstructive pulmonary disease (Cochrane Review). The Cochrane Database of Systematic Reviews 2000.

(3) Stratton R.J., Green C.J., Elia M. Disease-related malnutrition: an evidence-based approach to treatment. Wallingford, Oxon. OX10 8DE UK: CAB International, 2003.

(4) Baldwin C., Parsons T., Logan S. Dietary advice for illness-related malnutrition in adults (Review). The Cochrane Database of Systematic Reviews 2001; (2):1-67.

(5) Payette H., Boutier V., Coulombe C., Gray-Donald K. Benefits of nutritional supplementation in free-living, frail, undernourished elderly people: A prospective randomized community trial. Journal of the American Dietetic Association 2002; 102(8):1088-1095.

(6) Bonnefoy M., Cornu C., Normand S., Boutitie F., Bugnard F., Rahmani A. et al. The effects of exercise and protein-energy supplements on body composition and muscle function in frail elderly individuals: a long-term controlled randomised study. British Journal of Nutrition 2003; 89:731-738.

(7) Bolton J., Shannon V., Smith V., Abbott R., Bell S.J., Stubbs L. et al. Comparison of short-term and long-term palatability of six commercially available oral supplements. Journal of Human Nutrition and Dietetics 1990; 3:317-321.

(8) Keele A.M., Bray M.J., Emery P.W., Duncan H.D., Silk D.B.A. Two phase randomised controlled clinical trial of postoperative oral dietary supplements in surgical patients. Gut 1997; 40(3):393-399.

(9) Lad H., Gott M., Gariballa S.E. Health professionals' and elderly patients' views, attitudes and compliance with prescribed oral nutritional supplements. Proceedings of the Nutrition Society 2004; 63:43A.

(10) Weekes C.E., Elia M., Emery P.W. The development, validation and reliability of a nutrition screening tool based on the recommendations of the British Association for Parenteral and Enteral Nutrition (BAPEN). Clinical Nutrition 2004; 23:1104-1112.

(11) National Advisory Group for Elderly People. "Have you got a small appetite?" 2001. British Dietetic Association, Birmingham, UK

(12) Bingham S.A. The dietary assessment of individuals; methods, accuracy, new techniques and recommendations. Nutrition Abstracts and Reviews (Series A) 1987; 57 (10): 705-742

(13) Durnin J.V.G.A., Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. British Journal of Nutrition 1974; 32:77-97.

(14) Jones P.W., Quirk F.H., Baveystock C.M., Littlejohns P. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. American Review of Respiratory Diseases 1992; 145:1321-1327.

(15) Ware J.E., Sherbourne C.D. The MOS 36-Item Short-Form Health Survey (SF-36) I: Conceptual framework and item selection. Medical Care 1992; 30(6):473-483.

(16) Medical Research Council. Questionnaire on respiratory symptoms: instructions to interviewers. 1986. London, MRC Committee on Environmental and Occupational Health.

(17) Bond J., Carstairs V. Services for the elderly: a survey of the characteristics and needs of a population of 5,000,000 old people. 42. 1982. Edinburgh, Scottish Home and Health Department.

(18) Griffith C.D.M., Clark R.G. A comparison of the "Sheffield" prognostic index with forearm muscle dynamometry in patients from Sheffield undergoing major abdominal and urological surgery. Clinical Nutrition 1984; 3:147-151.

(19) Kolouris N., Mulvey D.A., Laroche C.M., Sawicka E.M., Green M., Moxham J. The measurement of inspiratory muscle strength by sniff esophageal, nasopharyngeal and mouth pressures. American Review of Respiratory Diseases 1989; 139:641-646.

(20) Vickers A.J., Altman D.G. Analysing controlled trials with baseline and follow up measurements. British Medical Journal 2001; 323:1123-1124.

(21) Jones P.W. Interpreting thresholds for a clinically significant change in health status in asthma and COPD. European Respiratory Journal 2002; 19(3):398-404.

(22) Campbell K.L., Ash S., Davies P.S.W., Bauer J.D. Randomised controlled trial of nutritional counselling on body composition and dietary intake in severe CKD. American Journal of Kidney Disease 2008; 51: 748-758

(23) Imes S., Pinchbeck B., Thomson A.B.R. Diet counselling improves the clinical course of patients with Crohn's disease. Digestion 1988; 39: 7-19

(24) Efthimiou J., Fleming J., Gomes C., Spiro S.G. The effect of supplementary oral nutrition in poorly nourished patients with chronic obstructive pulmonary disease. American Review of Respiratory Diseases 1988; 137:1075-1082.

(25) Knowles J.B., Fairbarn M.S., Wiggs B.J., Chan-Yan C., Pardy R.L. Dietary supplementation and respiratory muscle performance in patients with COPD. Chest 1988; 93(5):977-983

(26) Creutzberg E.C., Schols A.M.W.J., Weling-Scheepers C.A.P.M., Buurman W.A., Wouters E.F.M. Characterization of non-response to high caloric oral nutritional therapy in depleted patients with chronic obstructive pulmonary disease. American Journal of Respiratory and Critical Care Medicine 2000; 161: 745-752
(27) Eid A.A., Ionescu A.A., Nixon L.S., Lewis-Jenkins V., Matthews S.B., Griffiths T.L., Shale D.J. Inflammatory response and body composition in chronic obstructive pulmonary disease 2001; 164: 1414-1418

Figure 1 - Trial profile

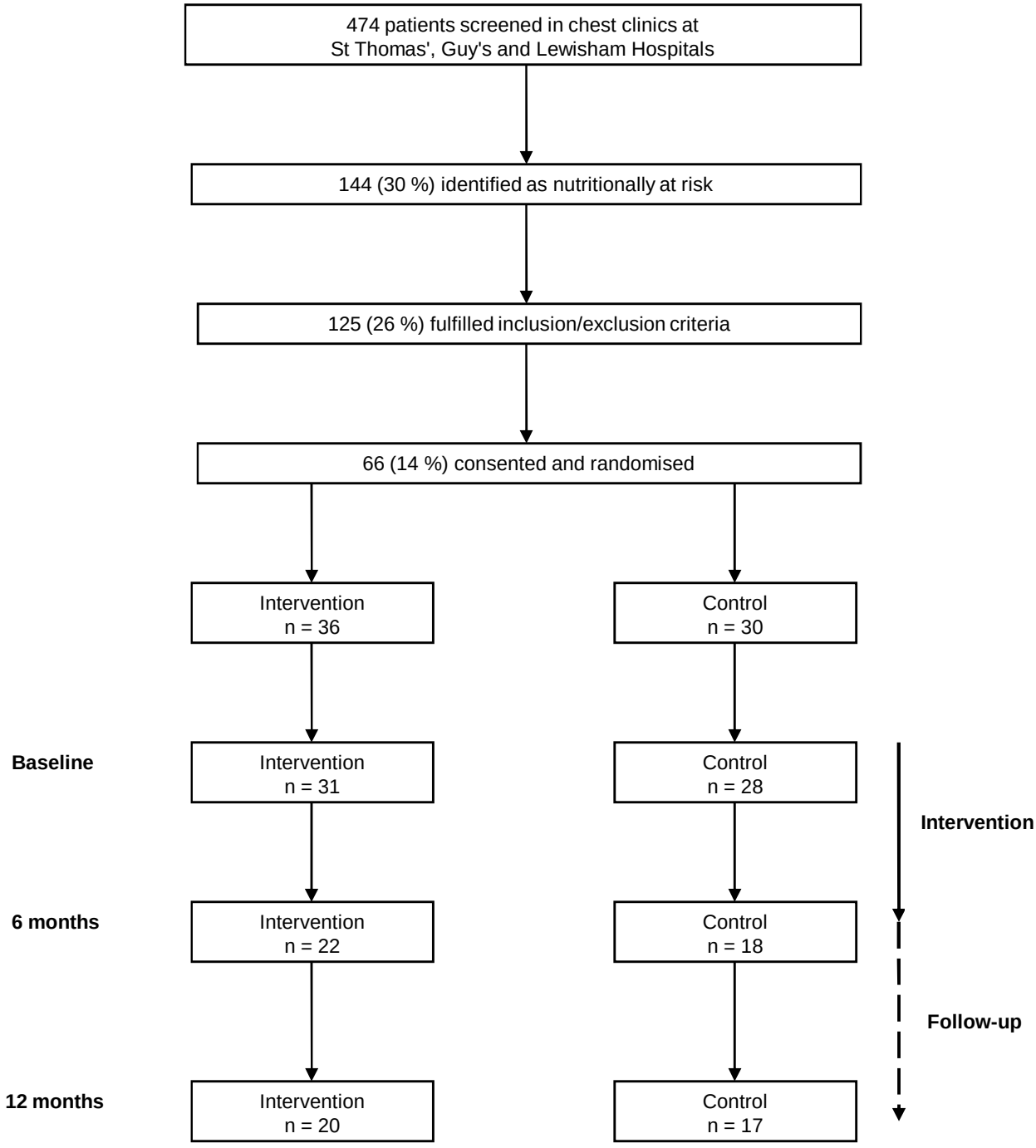
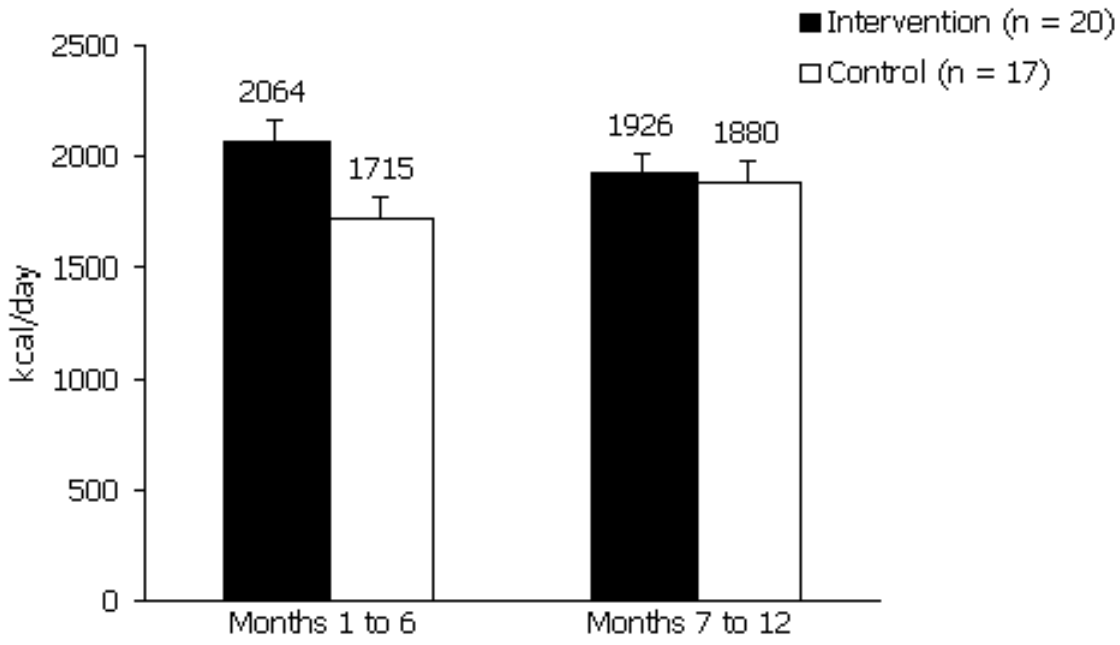


Figure 2 – a) Total energy and b) total protein intake/day

Values are adjusted means for total energy (kcal/day) and protein (g/day) intake during the intervention (Months 1 to 6) and follow-up (Months 7 to 12) periods in the intervention and control groups; error bars are standard error of the adjusted mean; p = 0.02 for months 1 to 6 and p = 0.74 for months 7 to 12 for energy intake; p < 0.001 for months 1 to 6 and p = 0.39 for months 7 to 12 for protein intake

a)



b)

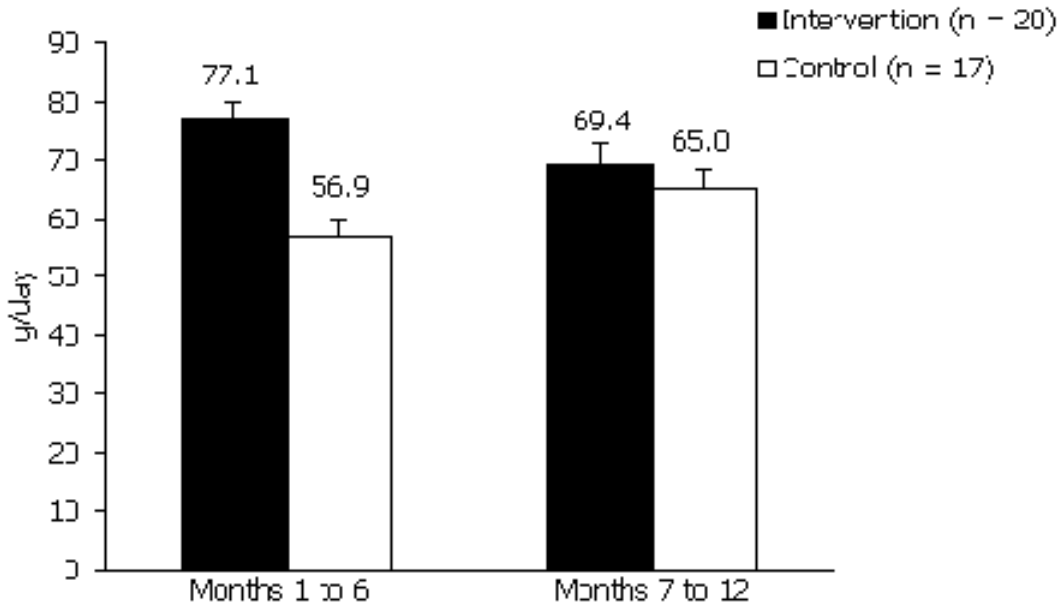
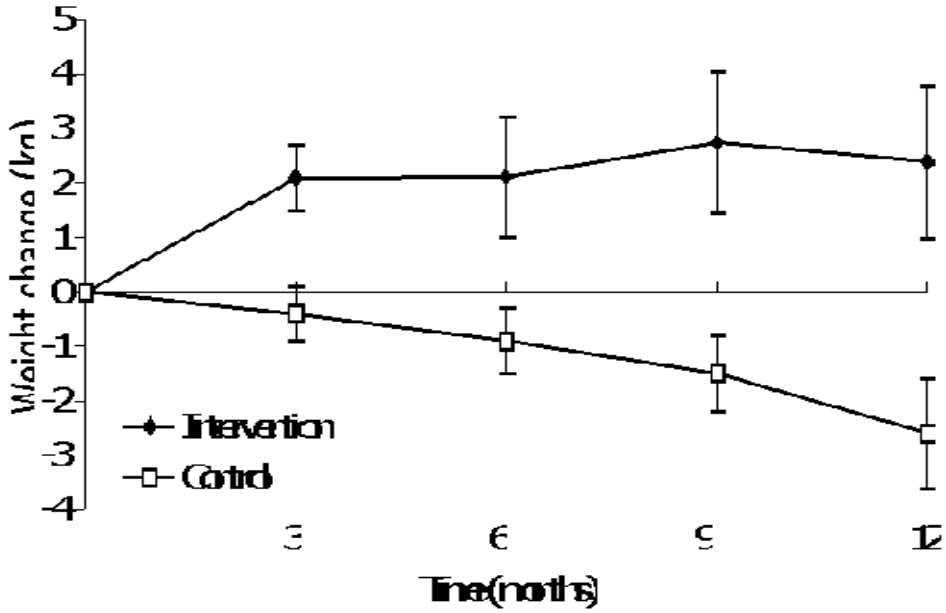


Figure 3 - Weight change from baseline in patients who completed the study (n = 37)
Mean weight change (kg) for the intervention and control groups at 3, 6 (intervention period), 9 and 12 months (follow-up period); error bars are standard error of the mean; difference in body weight at 6 months = 3.0 kg (p = 0.03) and at 12 months = 4.8 kg (p = 0.01)



Nutrition Screening Tool

Guy's and St Thomas' Hospital NHS Trust

Patient ..... **Hospital No.** .....

COMPLETE THIS FORM DURING EACH OUT-PATIENT APPOINTMENT OR HOME VISIT

Date of assessment						
Has the patient unintentionally lost weight in the last 3 - 6 months or since the last assessment?						
NO		**0**	**0**	**0**	**0**	**0**
YES		**2**	**2**	**2**	**2**	**2**
Has the patient unintentionally been eating less in the last 3 - 6 months or since the last assessment?						
NO		**0**	**0**	**0**	**0**	**0**
YES		**2**	**2**	**2**	**2**	**2**
NBM/unable to eat for ≥ 5 days		**3**	**3**	**3**	**3**	**3**
TOTAL SCORE						
Usual weight (kg): **Recalled height (m):**	**Actual weight (kg)**					
Arm: R / L **Mid-point (cm):** **MAC (cm):**	**Body mass index (kg/m^2)**					
Is the Body Mass Index (BMI) in the pale green category? Please circle appropriate response.		**YES/NO**	**YES/NO**	**YES/NO**	**YES/NO**	**YES/NO**
CLINICIAN'S OR NURSE'S SIGNATURE						
Date patient referred to dietitian						

ACTION PLAN

Score 0 - 2	**Re-assess patient during every out-patient appointment or home visit**
Score 3 - 5	**or BMI in pale green category** **or MAC < 23.2 cm (females); MAC < 26.4 cm (males)** **or patient on tube feed (NG/PEG/jejunostomy) or parenteral nutrition** **or patient has Grade 3 – 4 pressure sore** **Refer to dietitian for full nutritional assessment**

Intervention

Intervention lasted for the first 6 months of the study, the following 6 months being used to measure the effects of cessation.

All subjects (intervention and control) received a leaflet providing advice on nourishing snacks and drinks and encouraging food fortification i.e. "Have you got a small appetite?" National Advisory Group for Elderly People, British Dietetic Association (NAGE leaflet).

Control subjects were handed the leaflet during the baseline assessment but its contents were never discussed. Control subjects received no dietary counselling and were offered no nutritional products during the study.

The intervention group were offered a package of treatment by the dietitian (CEW) incorporating dietary counselling for the subject, nutrition-related advice for his or her carers and a free 6-month supply of milk powder for use in food fortification. The aim was to increase energy intake by up to 600 kcal/day. The proportion to be provided by milk powder or dietary change was determined on an individual basis following discussion with the patient and/or carer.

Dietary counselling and advice on food fortification was provided by a dietitian with fifteen years clinical experience including formal, postgraduate training in counselling skills and behaviour modification techniques. An eclectic approach, using a variety of clinical skills, was used to encourage dietary change in the intervention group.

Advice was provided on five occasions during the intervention period i.e. baseline, week 2 and months 1, 3 and 6. At baseline, the dietitian spent 30 to 45 minutes providing advice and practical demonstrations. During each follow-up visit the dietitian spent 15 to 20 minutes reviewing recent dietary changes and discussing alternative strategies for intervention where necessary.

1. Dietary counselling

The goal of dietary counselling was to increase energy intake and to ensure an adequate balance of macro and micronutrients in accordance with national recommendations. Patients were advised to choose foods that would provide a diet that met their nutritional requirements without having to increase portion sizes to such an extent that they felt “overfaced” i.e. unable to eat a meal due to its quantity. Emphasis was therefore placed on energy dense foods and food fortification.

Baseline visit

The dietitian discussed the NAGE leaflet in detail with the subject. Subjects were encouraged to identify two or three realistic and achievable changes they would be willing to make to their diet and

were given a choice of several ways in which this could be achieved e.g. eat breakfast, snacks between meals, change from semi-skimmed to full cream milk, use sugar in drinks and on cereals in preference to artificial sweeteners.

Advice was tailored to take account of each subject's lifestyle, eating habits, symptoms, likes and dislikes and any religious or ethical restrictions. Limitations imposed by therapeutic diets e.g. diabetic or lipid-lowering, were also taken into account. If the subject was not responsible for food purchase or meal preparation, the advice was also discussed with those who were e.g. spouse, carer or friend. Emphasis was placed on presenting subjects with small, manageable portion sizes rather than large meals. In addition, relatives or carers were asked to offer favourite treats or meals. Carers were encouraged not to pressurise subjects to eat a meal but to congratulate them if they managed to do so. Subjects who regularly ate out were asked to describe typical menus and advised on suitable choices to help increase energy and protein intakes. Emphasis was placed on making the most of situations when subjects felt hungry e.g. particular time of day, and circumstances that were conducive to eating e.g. lunch clubs or sharing meals with family and friends.

To reinforce verbal advice, typed summary sheets were compiled and sent to the patients following the visit.

Week 2 and Months 1, 3 and 6 visits

During each follow-up visit, the dietitian reviewed changes the subject had made as a result of the dietary advice provided at baseline. If subjects had been unable to make the proposed changes, the possible reasons were discussed and alternatives were suggested. Subjects who had made changes and wished to make more were encouraged to do so. A maximum of two new changes were agreed for review at the next assessment.

At 6 months subjects were encouraged to continue with any dietary changes they had made already.

Months 7, 9 and 12 visits

No further dietary counselling was provided during these visits.

2. Food fortification using milk powder

All intervention subjects were offered a free supply of milk powder for the 6-month intervention period for use in food fortification. The product, PLUSPINTS (Kerry Foods, Eire) consists of dried skimmed milk powder with non milk fat and provides the following nutrients.

Table S1 – Nutritional content of PLUSPINTS (Kerry Foods, Eire)

	Nutritional content/100 g powder
Energy	486 kcal (2033 kJoules)
Protein	18.0 g
Carbohydrate	45.0 g
Fat	26.0 g
Vitamin C	25 mg
Vitamin A	450 µg
Vitamin D	8.7 µg

One heaped tablespoon of PLUSPINTS weighs approximately 10 g and subjects were advised to add 4 to 6 heaped tablespoons of the product to one pint of full cream milk and to use the "fortified milk" in drinks, on breakfast cereal, in soups and sauces, mashed potatoes and desserts. This would provide 200 to 300 kcal and 7 to 11 g protein per day.

A leaflet was designed to describe how to use the milk powder and was handed to all subjects who agreed to try the product. The recipe leaflet provided advice on how to add milk powder directly to a variety of savoury and sweet foods and the dietitian provided practical demonstrations during home visits. The information provided in the leaflet was based on recipe testing undertaken by the investigator prior to commencement of the study.

At 6 months, the free supply of milk powder ceased and subjects were advised to purchase milk powder from local shops if they wished. They were provided with a leaflet describing the product and where it could be bought locally.

Subjects were also advised to use milk powder following any infections or exacerbations and/or if their weight fell below a pre-determined level (i.e. 5 % below current weight).

Online supplement 3

Reasons why patients failed to complete the study (n = 22)

Group	Sex	Age (years)	Reason
B	Female	78	Moved out of area after baseline assessment
B	Female	78	Withdrew after baseline assessment (reason not given)
B	Female	74	Withdrew after baseline assessment (RIP)
A	Female	82	Withdrew after baseline assessment (reason not given)
B	Male	55	Withdrew after baseline assessment (social reasons)
B	Female	74	Withdrew at 1 month due to frequent hospitalisation for exacerbations of COPD
A	Female	63	Withdrew at 1 month due to frequent hospitalisation for multiple conditions
B	Female	69	Withdrew at 1 month due to diagnosis of cor pulmonale
A	Male	81	Withdrew following diagnosis of lung cancer at 2 months (RIP at 7 months)
B	Male	66	RIP at 2 months (complications of COPD)
B	Male	75	Withdrew following diagnosis of lung cancer at 3 months (RIP at 4 months)
A	Male	77	Withdrew following chest infection at 3 months (reason not given)
A	Male	69	Withdrew at 3 months for social reasons
B	Female	68	Withdrew at 3 months for investigation of unexplained weight loss
A	Male	57	RIP at 4 months (complications of COPD)
A	Female	78	RIP at 5 months (cardiac arrest)
B	Male	50	Moved out of area at 6 months
B	Male	46	Withdrew following diagnosis of cancer of the larynx at 6 months
A	Male	48	Failed to comply with any measurements therefore withdrawn at 6 months
A	Male	68	Lost to follow-up at 7 months (reason unknown)
A	Female	65	Withdrew following diagnosis of congestive cardiac failure at 7 months
A	Male	89	Withdrew following diagnosis of liver cancer at 9 months (RIP at 12 months)

A = Intervention; B = Control; RIP = died within 12 months of recruitment