COPD Evidence Tables

The evidence tables are presented in section order.

The methodological quality of each paper was rated using the Scottish Intercollegiate Guidelines Network (SIGN) system (Scottish Intercollegiate Guidelines Network. SIGN 50 Guideline Developers Handbook, 2001; ID 19457):

++	All or most of the SIGN methodology checklist criteria were fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought very unlikely to alter.
+	Some of the criteria were fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions.
-	Few or no criteria were fulfilled. The conclusions of the study are thought likely or very likely to alter.

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Chronic Obstructive Pulmonary Disease: Management of adults with Chronic Obstructive Pulmonary Disease in Primary and Secondary Care		
Managing Stable COPD Nutritional factors Index		
Author	**Publication Date**	**ID**
Ferreira IM, Brooks D, Lacasse Y, Goldstein RS, White J. Nutritional supplementation for stable chronic obstructive pulmonary disease. (Cochrane Review). *The Cochrane Library.Oxford: Update Software* 2003;**Issue 3**.	2003	1503
Baarends, E. M., Schols, A. M., MOSTERT, R., & Wouters, E. F. 1997, "Peak exercise response in relation to tissue depletion in patients with chronic obstructive pulmonary disease", *European Respiratory Journal*. vol. 10, no. 12, pp. 2807-2813.	1997	1587
Engelen, M. P., Schols, A. M., Baken, W. C., Wesseling, G. J., & Wouters, E. F. 1994, "Nutritional depletion in relation to respiratory and peripheral skeletal muscle function in out-patients with COPD", *European Respiratory Journal*. vol. 7, no. 10, pp. 1793-1797.	1994	1591
Gray-Donald, K., Gibbons, L., Shapiro, S. H., & Martin, J. G. 1989, "Effect of nutritional status on exercise performance in patients with chronic obstructive pulmonary disease", *American Review of Respiratory Disease*. vol. 140, no. 6, pp. 1544-1548.	1989	1613
Landbo, C., Prescott, E., Lange, P., Vestbo, J., & Almdal, T. P. 1999, "Prognostic value of nutritional status in chronic obstructive pulmonary disease", *American Journal of Respiratory & Critical Care Medicine*. vol. 160, no. 6, pp. 1856-1861.	1999	1596 (Same patient set as 1603).

Prescott, E., Almdal, T., Mikkelsen, K. L., Tofteng, C. L., Vestbo, J., & Lange, P. 2002, "Prognostic value of weight change in chronic obstructive pulmonary disease: results from the Copenhagen City Heart Study", *European Respiratory Journal.* vol. 20, no. 3, pp. 539-544.	2002	1603
Marquis, K., Debigare, R., Lacasse, Y., LeBlanc, P., Jobin, J., Carrier, G., & Maltais, F. 2002, "Midthigh muscle cross-sectional area is a better predictor of mortality than body mass index in patients with chronic obstructive pulmonary disease. [comment]", *American Journal of Respiratory & Critical Care Medicine.*, vol. 166, no. 6, pp. 809-813.	2002	1598
Palange, P., Forte, S., Felli, A., Galassetti, P., Serra, P., & Carlone, S. 1995, "Nutritional state and exercise tolerance in patients with COPD", *Chest*, vol. 107, no. 5, pp. 1206-1212.	1999	1601
Rogers, R. M., Donahoe, M., & Costantino, J. 1992, "Physiologic effects of oral supplemental feeding in malnourished patients with chronic obstructive pulmonary disease. A randomized control study", *American Review of Respiratory Disease.*, vol. 146, no. 6, pp. 1511-1517.	1992	1612
Schols, A. M. W. J., Slangen, J., Volovics, L., & Wouters, E. F. M. 1998, "Weight loss is a reversible factor in the prognosis of chronic obstructive pulmonary disease", *American Journal of Respiratory and Critical Care Medicine*, vol. 157, no. 6, pp. 1791-1797.	1998	8
Schols, A. M. W. J., Soeters, P. B., Dingemans, A. M. C., Mostert, R., Frantzen, P. J., & Wouters, E. F. M. 1993, "Prevalence and characteristics of nutritional depletion in patients with stable COPD eligible for pulmonary rehabilitation", *American Review of Respiratory Disease*, vol. 147, no. 5, pp. 1151-1156.	1993	1614
Schols, A. M. W. J., Mostert, R., Soeters, P. B., Greve, L. H., & Wouters, E. F. M. 1989, "Nutritional	1989	281

state and exercise performance in patients with chronic obstructive lung disease", *Thorax*, vol. 44, no. 11, pp. 937-941.		
Slinde, F., Gronberg, A. M., Engstrom, C. R., Rossander-Hulthen, L., & Larsson, S. 2002, "Individual dietary intervention in patients with COPD during multidisciplinary rehabilitation", *Respiratory Medicine.* vol. 96, no. 5, pp. 330-336.	2002	1514
Wilson, D. O., Rogers, R. M., Wright, E. C., & Anthonisen, N. R. 1989, "Body weight in chronic obstructive pulmonary disease. The National Institutes of Health Intermittent Positive-Pressure Breathing Trial", *American Review of Respiratory Disease.* vol. 139, no. 6, pp. 1435-1438.	1989	1610
Sahebjami, H. & Sathianpitayakul, E. 2000, "Influence of body weight on the severity of dyspnoea in chronic obstructive pulmonary disease", *American Journal of Respiratory & Critical Care Medicine*, vol. 161, no. 3 I, pp. 886-890.	2000	1616
Otte, K. E., Ahlburg, P., D'Amore, F., & Stellfeld, M. 1989, "Nutritional repletion in malnourished patients with emphysema", *Journal of Parenteral & Enteral Nutrition*, vol. 13, no. 2, pp. 152-156.	1989	289
Sahebjami, H., Doers, J. T., Render, M. L., & Bond, T. L. 1993, "Anthropometric and pulmonary function test profiles of outpatients with stable chronic obstructive pulmonary disease", *American Journal of Medicine*, vol. 94, no. 5, pp. 469-474.	1993	1605

Author / Title / Reference / Yr	Ferreira IM, Brooks D, Lacasse Y, Goldstein RS, White J. Nutritional supplementation for stable chronic obstructive pulmonary disease. (Cochrane Review). *The Cochrane Library.Oxford: Update Software* 2003;**Issue 3**. Ref ID: 1503
N=	RCT=9 N=277 (144 study and 133 control)
Research Design	Meta analysis of RCTs

Aim	To conduct a systematic review of randomised controlled trials to clarify whether nutritional supplementation (caloric supplementation for 2 weeks) improved anthropometric measures, pulmonary function, respiratory muscle strength and functional exercise capacity in patients with stable COPD.
Operational Definition	COPD characterised by a forced expiratory volume in 1 second (FEV1) less than 70%, and less than 15% reversibility after bronchodilator
Population	Patients with stable COPD
Intervention	Oral, enteral or parenteral nutritional support Nutritional support was defined as any caloric supplementation given for more than two weeks.
Comparison	Placebo or usual diet or other treatment regimens such as anabolic substances.
Outcome	Body weight, lean body mass, body mass index Timed walk test, submaximal or graded exercise Lung volumes, respiratory muscle function, peripheral muscle function Quality of life.
Characteristics	**Population** Excluded asthma Excluded patients with COPD undergoing treatment in the intensive care unit. 7 studies were in-patient, 2 studies were outpatient. 7 studies included only undernourished, whereas two included undernourished and nourished subjects. All except one study used oral supplementation.
Results	For each of the outcomes studied, the effect of nutritional support was small. The confidence intervals around the pooled effect sizes all included zero (i.e. were not significant) **Weight** Number of studies = 9 Patients treated/control = 144/133 Effect size natural [95% CI] = 1.65 kg [0.00/3.29] **Arm muscle circumference** Number of studies = 6 Patients treated/control = 66/66 Effect size natural [95% CI] = 0.3 cm [-0.5/1.0] **Triceps skin fold** Number of studies = 5 Patients treated/control] = 48/49 Effect size natural [95% CI] = 1.44 mm [-0.2/2.9] **6 minute walk** Number of studies = 3

	Patients treated/control = 38/39 Effect size natural [95% CI] = 3.4m [-46.1/52.9] **FEV1** Number of studies = 5 Patients treated/control = 60/59 Effect size natural [95% CI] = 0.5% [-5.4/6.4] **Pimax** Number of studies = 4 Patients treated/control = 36/34 Effect size natural [95% CI] = 0.1cm H_2O [-8.1/8.5] **PE max** Number of studies = 4 Patients treated/control = 36/34 Effect size natural [95% CI] = -3.0cm [-16.6/10.8] **Conclusion** There is no evidence from the meta-analysis that simple nutritional supplementation confers benefit to patients with COPD
SIGN Quality Rating	+
Hierarchy of Evidence Grading	1a
NCC CC ID	1503
Studies Included	DeLetter 1991, Efthimiou 1988, Fuenzalida 1990, Knowles 1988, Lewis 1987, Otte 1989, Schols 1995a, Schols 1995b, Whittaker 1990

Author / Title / Reference / Yr	Baarends, E. M., Schols, A. M., Mostert, R., & Wouters, E. F. 1997, "Peak exercise response in relation to tissue depletion in patients with chronic obstructive pulmonary disease", *European Respiratory Journal.* vol. 10, no. 12, pp. 2807-2813.Ref ID: 1587
N=	N=62 Location=The Netherlands
Research Design	Cross-sectional cohort study
Aim	To examine the relationship between body composition and peak exercise performance
Operational Definition	American Thoracic Society definition
Population	moderate to severe COPD Exclusions: patients exhibiting increase in FEV1 >10% after inhalation of B2-agnoists, patients suffering from respiratory tract infection or showing clinically visible signs of oedema, cardiovascular, neurological, endocrine or locomotor diseases.
Intervention	Body composition vs peak exercise performance

Comparison	NA
Outcome	Pulmonary function FEV1, FVC and IVC, total lung capacity, intrathoracic gas volume (ITGV) and airways resistance (Raw), transfer factor for carbon monoxide (TLCO), carbon monoxide transfer coefficient (KCO), Pimax, Pemax, PaO2 Body composition Total body water (TBW), fat free mass (FFM) Exercise testing VO2
Characteristics	Age 63 ± 9 FEV1 %pred 39 ± 13 Females 44 males 18 BMI kg/m2 23.2 ± 4.1 Females were significantly younger than males. Inspiratory vital capacity (IVC) and FEV1 in the female group was significantly superior, although respiratory muscle strength (Pimax and Pemax) was inferior. Body composition of the group varied widely: BMI ranged 15.3-34.3kg/m2 – females had a significantly higher fat mass (FM) than males, and a significantly lower FFM index.
Results	**Correlation between lung function and peak VO2** Peak VO_2 correlated best with TLCO (transfer factor for carbon monoxide) (% pred: r = 0.55, p<0.001) and to a lesser degree with KCO (carbon monoxide transfer coefficient) (% pred: r = 0.49, p <0.001) Subsequently ITGV (intrathoracic gas volume) (r = 0.47, p<0.001), residual volume (RV) (r = 0.45, p<0.01) and Pemax (cmH2O: r = 0.46, p<0.001) all correlated best with peak VO2. PImax (cmH2O: r = 0.43, p<0.01) and FEV1 (r = 0.35, p<0.01) correlated significantly with peak VO2. **Correlation between body composition and peak VO2** Peak VO2 correlated significantly with the FFM index (kg/m2; r = 0.57, p<0.001) BMI (kg/m2; r= 0.56, p<0.001) and ICW (kg/m2; r = 0.54, p<0.001) **Prediction variables for peak VO2** Using step-wise regression analysis fat free mass index (FFM) accounted for 31% of variation in peak VO2. Together FFM (fat free mass) and TLCO (transfer factor for carbon monoxide) explained 53% of the variation of peak VO2. **Exercise response in patients with or without FFM depletion** 26 patients had depletion of FFM 36 patients had no depletion of FFM FEV1 was not significantly different between patients with or without depletion of FFM

	TLCO was not significantly different between patients with or without depletion of FFM Total lung capacity (TLC) was significantly higher in FFM depleted patients compared with non-depleted patients ($p<0.05$) Peak VE (minute ventilation) and the increase in VT (tidal volume) were still significantly different between the patients with or without FFM depletion ($p<0.05$) when a relationship between FEV1 (% pred) and the increase in VT ($p<0.05$) and VE ($p<0.001$) was considered. Peak oxygen pulse (peak VO2/peak FC (cardiac frequency)) was significantly different ($p<0.01$) between the patients with or without FFM depletion when the contribution of TLCO (% pred, $p<0.01$) to the variation of the oxygen pulse was taken into account. **Conclusion** Depletion of FFM significantly contributes to disturbed exercise capacity in COPD patients. FFM index correlated better with peak exercise capacity than BMI and ICW (intracellular water) index Depletion of FFM contributes to a blunted VT (tidal volume) and decreased peak oxygen pulse in response to peak exercise.
SIGN Quality Rating	+
Hierarchy of Evidence Grading	11b
NCC CC ID	1587

Author / Title / Reference / Yr	Engelen, M. P., Schols, A. M., Baken, W. C., Wesseling, G. J., & Wouters, E. F. 1994, "Nutritional depletion in relation to respiratory and peripheral skeletal muscle function in out-patients with COPD", *European Respiratory Journal.* vol. 7, no. 10, pp. 1793-1797.Ref ID: 1591
N=	N=72 Location=The Netherlands Site=Outpatients
Research Design	Prospective cohort study
Aim	To investigate tissue depletion in relation to physiological function measured by lung function, respiratory and peripheral skeletal muscle function, in a random outpatient population with COPD.
Operational Definition	Breathlessness, and chronic airflow limitation defined as FEV1 lower than the 95% CI of FEV1 reference and no significant improvement after inhalation of a B2 agonist.
Population	COPD Exclusions: malignant disease, recent surgery, severe endocrine disorders or sarcoidosis, or if suspected abnormal fluid balance manifested by presence of oedema or regular use of diuretics. Bronchiectasis or other chronic pulmonary diseases were also

	excluded.
Intervention	Nutritional status vs physiological factors
Comparison	NA
Outcome	Fat free mass (FFM), body weight expressed as percentage of ideal body weight (PIBW), fat-free mass expressed as percentage of ideal body weight (FFMPIBW), Pimax, Pemax, IVC, Kco, intrathoracic gas volume (ITGV), TV, total lung capacity (TLC)
Characteristics	Body weight expressed as percentage of ideal body weight PIBW <90% was taken as being threshold for nutritional depletion Subjects divided into two groups: depleted (n = 15) and non-depleted (n = 57) Mean age 62 ± 13 years 55 men and 17 women Medication included theophyllines, bronchodilators, anticholinergics and corticosteroids. 21% patients had nutritional depletion according to above definition
Results	**Weight loss and depletion of fat-free mass** 47% of depleted patients (n = 15) and 13% of nondepleted patients (n =57) exhibited recent (within 6 months) involuntary weight loss 14% of the patients were characterised by weight loss and depletion of fat-free mass, whereas 7% had either weight loss or a depleted fat-free mass. **Carbon dioxide transfer (KCO)** When expressed as a percentage of the reference value, a significantly lower KCO (transfer factor for carbon dioxide) was found in the depleted group (depleted KCO % pred = 64.9 vs normal KCO % pred = 81.9) p = 0.008 **Muscle strength** Measures of muscle strength were lower in the depleted group, but only the difference in handgrip strength reached statistical significance (p<0.01) Analysis of covariance revealed a significant effect of the KCO on peripheral skeletal muscle strength (p<0.01) **Difference between emphysematous (KCO <60%) and bronchitic (KCO >80%) patients** 38% of patients with a KCO <60% predicted were considered depleted compared with only 5% of the patients with KCO > 80% predicted (p = 0.009) Stratification by KCO revealed significantly higher values for intrathoracic gas volume (ITGV), inspiratory vital capacity (IVC), total lung capacity (TLC) and residual volume (RV) in the group with a KCO <60%, whereas the degree of airway obstruction and the airway resistance were not significantly different between the groups. **Conclusion** Depleted patients are more likely to exhibit lower values for respiratory and peripheral skeletal muscle strength than nondepleted patients. Depleted patients do not show a pronounced difference in spirometry or intrathoracic gas volumes compared with nondepleted patients. Carbon dioxide transfer coefficient is significantly lower in depleted patients. Stratification by KCO, which may discriminate between emphysema and bronchitis, also appeared to discriminate the prevalence of

	tissue depletion.
SIGN Quality Rating	+
Hierarchy of Evidence Grading	11b
NCC CC ID	1591

Author / Title / Reference / Yr	Gray-Donald, K., Gibbons, L., Shapiro, S. H., & Martin, J. G. 1989, "Effect of nutritional status on exercise performance in patients with chronic obstructive pulmonary disease", *American Review of Respiratory Disease.* vol. 140, no. 6, pp. 1544-1548.Ref ID: 1613
N=	N=135 Location=Canada
Research Design	Cohort study
Aim	To examine the relationship between nutritional status of patients with severe COPD and functional capacity.
Operational Definition	American Thoracic Society criteria
Population	Stable COPD Exclusions: FEV1 greater than 50% of predicted, ratio of FEV1/FVC > 60% predicted or FEV1 after salbutamol was greater than 60% predicted. Serious medical condition including morbid obesity, asthma, severe psychological problems or recent exacerbation of COPD excluded.
Intervention	Nutritional status vs functional capacity
Comparison	NA
Outcome	Nutrition, respiratory function, exercise performance, dyspnoea and quality of life.
Characteristics	Age 63.6 yrs Men 74% women 26% Further characteristics in table
Results	**Nutrition** 24.4% of subjects had %IBW of <90% 86% of those with a weight of <80% IBW and 60% of those with weight < 90% had an abnormally low triceps skin fold thickness (TSF) (< 60% standard) Among underweight subjects (IBW <90% predicted), 32% reported weight loss of > 5% in the last year. When compared with their usual weight, 81% of underweight subjects had lost > 10% body weight, with self-reported weight losses of as much as 43%. The mean weight loss from usual weight in the underweight group was 17% (± 13%)

Results continued	

Results continued

Comparison of nutritional and anthropometric characteristics by % ideal body weight

The mean % IBW for the three groups were 80.2 ± 1.3, 104.8 ± 8.6 and 130.6 ± 8.9
TSF and mid arm circumference were reduced in the underweight group
Mean haemoglobin values were high in all groups, with slightly lower values in the underweight group.
A comparison of IBW < 90% with IBW > 90% indicates a statistically significant difference in haemoglobin (14.9 vs 15.9; $p<0.01$), haematocrit (46.2 vs 48.6; $p<0.01$) and albumin (4 vs 4.1; $p<0.05$)

	% IBW < 90% (n = 33)	**% IBW 90-119% (n = 72)**	**% IBW > 120% (n = 30)**
Age, yr	65 ± 1.37	63.2 ± 0.93	62.9 ± 0.97
Height, cm	162.5 ± 1.47	166.2 ± 0.86	165.7 ± 1.44 ($p<0.05$ difference between the three groups)
Weight, kg	48 ± 1.31	65.6 ± 0.97	81.2 ± 1.85 ($p<0.05$ difference between the three groups)
Triceps skin fold	8.3 ± 0.66	12.2 ± 0.59	16.5 ± 1.38 ($p<0.05$ difference between the three groups)
Arm muscle circumference	21.8 ± 0.43	25.7 ± 0.35	28.7 ± 0.57 ($p<0.05$ difference between the three groups)
Haemoglobin, g/dl	14.9 ± 0.27	15.8 ± 0.2	16.2 ± 0.24 ($p<0.05$ difference between the three groups)
Haematocrit, %	46.1 ± 0.77	49.1 ± 0.59	49.8 ± 0.88 ($p<0.05$ difference between the three groups)
Serum albumin, g/dl	4 ± 0.049	4.1 ± 0.033	4.2 ± 0.052
Total lymphocyte count, 10^9/ L	1802 ± 114.8	1847 ± 91	2160 ± 314.3

Results continued	Respiratory Function FEV1 values were low because of entry criteria requiring Grade 4 or Grade 5 dyspnoea; 52.6% patients had an FEV1 < 30% predicted. % FEV1 was not different among the 3 groups, despite small but significant differences in absolute values of FEV1 Diffusing capacity was reduced in the underweight group ($p<0.01$); however, upon adjustment for age, sex and haemoglobin level, the differences between groups disappeared. % IBW was a predictor of both expiratory muscle strength and inspiratory muscle strength in regression analysis.

	% IBW < 90% (n = 33)	% IBW 90-119% (n = 72)	% IBW > 120% (n = 30)
FEV, L	0.65 ± 0.04	0.83 ± 0.04	0.85 ± 0.06 ($p<0.05$ difference between the three groups)
FEV1, % predicted	26.8 ± 1.66	31.2 ± 1.37	31.2 ± 1.77
FEV1, FVC, %	30 ± 6.9	33.2 ± 7.4	35.1 ± 10.8 ($p<0.05$ difference between the three groups)
PaCO2, mmHg	45 ± 1.2	43.3 ± 0.83	44.5 ± 1.0
PaO2, mmHg	72.2 ± 1.7	69.6 ± 1.1	70.2 ± 1.4
DLCO ml/min mmHg	10.1 ± 0.31	12.5 ± 0.52	15.6 ± 0.95 ($p<0.01$ difference between the three groups)
DLCO % pred	68.1 ± 5.2	70.5 ± 4.9	80.5 ± 6
TLC, L	7.2 ± 0.17	7.5 ± 0.13	7.3 ± 0.23
Functional residual capacity	5.9 ± 0.22	5.7 ± 0.12	5.5 ± 0.21
PI max, cm H2O	38.6 ± 2.61	40.5 ± 1.79	47.7 ± 2.59 ($p<0.05$ difference between the three groups)
PE max, cm H2O	71.7 ± 5.16	80.7 ± 4.28	102.4 ± 7.2

Results	Exercise performance, dyspnoea and quality of life VO2 max absolute expressed as percent predicted was significantly lower in the underweight group com pared with the other two groups combined ($p<0.001$) Regression analysis demonstrated that %VO2 max was associated with FEV1 ($R^2 = 0.23$; $p<0.01$) and after controlling for FEV1, %IBW explained a further 8% ($p<0.001$) of the variance in %VO2 max. No significant differences were observed between groups in the 6-minute walk, oxygen cost score or quality of life score.

	% IBW < 90% (n = 33)	% IBW 90-119% (n = 72)	% IBW > 120% (n = 30)
VO2 max, L/min	0.54 ± 0.18	0.74 ± 0.22	0.91 ± 0.26 (p<0.01

				difference between the three groups)
	VO2 max, % predicted	37.2 ± 2.09	47 ± 2.19	53.7 ± 2.45 (p<0.01 difference between the three groups)
	6 minute walk, m	313.3 ± 18.2	305.3 ± 13.9	342.8 ± 2.3
	Oxygen cost score, mm	49.2 ± 2.22	50.4 ±1.82	49.4 ± 2.8
	Quality of life score	6.2 ± 0.27	6.5 ± 0.24	6.9 ± 0.34
	Current smokers %	24	20	14
	Conclusion In underweight COPD subjects peak exercise performance and ventilatory muscle strength are decreased; however submaximal exercise performance, dyspnoea and overall quality of life are not affected.			
SIGN Quality Rating	+			
Hierarchy of Evidence Grading	11b			
NCC CC ID	1613			

Author / Title / Reference / Yr	Landbo, C., Prescott, E., Lange, P., Vestbo, J., & Almdal, T. P. 1999, "Prognostic value of nutritional status in chronic obstructive pulmonary disease", *American Journal of Respiratory & Critical Care Medicine*. vol. 160, no. 6, pp. 1856-1861. Ref ID: 1596 (same patient set as 1603).
N=	N=2132 Location=Denmark Duration=17 years
Research Design	Cohort study
Aim	To examine the prevalence and prognostic importance of body mass index in patients with COPD
Operational Definition	Ratio of FEV1 to FVC of <0.7
Population	COPD
Intervention	BMI categorised into four groups 1) Underweight (less than 20 kg/m2) 2) Normal weight (20-24.9 kg/m2) 3) Overweight (25-29.9 kg/m2) 4) Obese (30kg/m2 and above)

Comparison	NA
Outcome	Ventilatory function
Characteristics	**2132 subjects available for analysis** **Females (n = 914)** Age (y) = 55.8 ± 10.8 FEV1 % predicted = 66.1 ± 16.6 BMI, kg/m2 = 24.1 ± 4.6 Underweight (<20kg/m2) = 142 (15.5%) **Males (n = 1218)** Age (y) = 57.7 ± 11.0 FEV1 % predicted = 64.7 ± 18.1 BMI, kg/m2 = 22.5 ± 3.8 Underweight (<20kg/m2) = 62 (5.1%)
Results	**Baseline characteristics** At initial examination, the men were significantly older and had a higher mean BMI than the women. **All cause mortality** There was an independent effect of BMI on survival, with significantly higher mortality seen in underweight subjects than in those of normal weight. This was present independently of sex. **All cause mortality in relation to BMI. Estimated rate ratios RR (95% confidence interval)** **Males n = 1218** BMI <20 kg/m2 = 48 deaths: RR (95% CI) = 1.64 (1.2 – 2.23) 20-24.9 kg/m2 = 301 deaths RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = 295 deaths: RR (95% CI) = 1.01 (0.86 – 1.19) > 30kg/m2 = 87 deaths: RR (95% CI) = 1.06 (0.83 – 1.35) Test for linear trend = NS **All cause mortality in relation to BMI. Estimated rate ratios RR (95% confidence interval)** **Females n = 914** BMI <20 kg/m2 = 72 deaths: RR (95% CI) = 1.42 (1.07 – 1.89) 20-24.9 kg/m2 = 172 deaths RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = 83 deaths: RR (95% CI) = 0.85 (0.64 – 1.11) > 30kg/m2 = 36 deaths: RR (95% CI) = 1.10 (0.75 – 1.60) Test for linear trend = NS **All cause mortality in relation to BMI in patients stratified according to %FEV1. Estimated rate ratios (95% confidence interval)**

	The effect of BMI on all-cause mortality is dependent on the stage of COPD. A significant effect of BMI on all-cause mortality was present only in subjects with severe COPD (FEV1%pred <50) in whom mortality was lowest in the obese and increased with decreasing BMI (p<0.001). **FEV1 < 50% pred (severe COPD) n = 275 deaths** BMI <20 kg/m2 = RR (95% CI) = 1.63 (1.15 – 2.31) 20-24.9 kg/m2 = RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = RR (95% CI) = 0.66 (0.49 – 0.87) > 30kg/m2 = 36 deaths: RR (95% CI) = 0.62 (0.41 – 0.94) Test for linear trend = p<0.001 **FEV1 50-69% pred (moderate COPD) n = 478 deaths** BMI <20 kg/m2 = RR (95% CI) = 1.24 (0.89 – 1.72) 20-24.9 kg/m2 = RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = RR (95% CI) = 0.96 (0.77 – 1.19) > 30kg/m2 = 36 deaths: RR (95% CI) = 1.22 (0.92 – 1.61) Test for linear trend = NS **FEV1 >70% pred (mild COPD) n = 341 deaths** BMI <20 kg/m2 = RR (95% CI) = 1.50 (0.99 – 2.28) 20-24.9 kg/m2 = RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = RR (95% CI) = 1.24 (0.98 – 1.56) > 30kg/m2 = 36 deaths: RR (95% CI) = 1.34 (0.88 – 2.06) Test for linear trend = NS **Mortality from COPD** COPD Mortality was highest in underweight subjects and decreased for increasing BMI in both men and women (p<0.001) The impact of BMI on COPD mortality was stronger than that on all-cause mortality, with RRs between the lowest and highest BMI of 5.56 (range 2.47 to 12.54) and 7.17 (range 2.45 to 21) in men and women respectively. **Mortality from COPD in relation to BMI. Estimated rate ratios RR (95% confidence interval)** **Males n = 1218** BMI <20 kg/m2 = 20 deaths: RR (95% CI) = 3.34 (1.94 – 5.83) 20-24.9 kg/m2 = 50 deaths RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = 425 deaths: RR (95% CI) = 0.72 (0.47 – 1.11) > 30kg/m2 = 87 deaths: RR (95% CI) = 0.60 (0.29 – 1.25) Test for linear trend = p<0.001 **Mortality from COPD in relation to BMI. Estimated rate ratios RR (95% confidence interval)**

	Females n = 914 BMI <20 kg/m2 = 25 deaths: RR (95% CI) = 2.45 (1.42 – 4.22) 20-24.9 kg/m2 = 38 deaths RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = 9 deaths: RR (95% CI) = 0.48 (0.22 – 1.07) > 30kg/m2 = 5 deaths: RR (95% CI) = 0.34 (0.12 – 0.97) Test for linear trend = p<0.001 **COPD mortality in relation to BMI in patients stratified according to %FEV1. Estimated rate ratios (95% confidence interval)** In all three stages of COPD the highest mortality was found in underweight subjects. In subjects with severe COPD mortality continued to decrease with increasing BMI, with an RR of 7.11 (range 2.97 to 17.05) in underweight compared with obese subjects. A similar but weaker association was found in subjects with mild and moderate COPD. **FEV1 < 50% pred (severe COPD) n = 103 deaths** BMI <20 kg/m2 = RR (95% CI) = 2.20 (1.31 – 3.68) 20-24.9 kg/m2 = RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = RR (95% CI) = 0.55 (0.33 – 0.90) > 30kg/m2 = 36 deaths: RR (95% CI) = 0.31 (0.13 – 0.71) Test for linear trend = p<0.001 **FEV1 50-69% pred (moderate COPD) n = 65 deaths** BMI <20 kg/m2 = RR (95% CI) = 1.96 (0.95 – 4.03) 20-24.9 kg/m2 = RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = RR (95% CI) = 0.78 (0.42 – 1.44) > 30kg/m2 = 36 deaths: RR (95% CI) = 0.93 (0.38 – 2.27) Test for linear trend = p = 0.06 **FEV1 >70% pred (mild COPD) n = 31 deaths** BMI <20 kg/m2 = RR (95% CI) = 3.38 (1.4 – 8.18) 20-24.9 kg/m2 = RR (95% CI) = 1.00 reference 25-29.9 kg/m2 = RR (95% CI) = 0.93 (0.69 – 2.24) > 30kg/m2 = 36 deaths: RR (95% CI) = 0.71 (0.09 – 5.45) Test for linear trend = p = 0.05 **Conclusion** There is an independent effect of BMI on both all-cause mortality and COPD mortality in both men and women; poor prognosis is related to being underweight.

	The association between BMI and survival differs according to stage of ventilatory impairment; in subjects with severe COPD, mortality continues to decrease with increasing BMI.
SIGN Quality Rating	++
Hierarchy of Evidence Grading	11a
NCC CC ID	1596

Author / Title / Reference / Yr	Prescott, E., Almdal, T., Mikkelsen, K. L., Tofteng, C. L., Vestbo, J., & Lange, P. 2002, "Prognostic value of weight change in chronic obstructive pulmonary disease: results from the Copenhagen City Heart Study", *European Respiratory Journal*. vol. 20, no. 3, pp. 539-544. Ref ID: 1603
N=	N=1612 Location=Denmark Duration=14 years
Research Design	Cohort study
Aim	To examine the prevalence and prognostic importance of weight change in unselected patients with COPD
Operational Definition	Ratio of FEV1 to FVC of <0.7
Population	COPD
Intervention	BMI
Comparison	-
Outcome	Ventilatory function
Characteristics	10.424 subjects available for analysis **Females with COPD (n = 736) vs Females without COPD (n = 5096)** Age (y) = 55.8 ± 9.0 vs 51.8 ± 11.2 FEV1 % predicted = 67.3 ± 21.7 vs 90 ± 18.1 Never smokers (%) = 131 (17.8) vs 1539 (30.2) Heavy smokers (%) = 274 (52.3) vs 1235 (44.4) **Males with COPD (n = 876) vs Males without COPD (n = 3716)** Age (y) = 56.6 ± 9.7 vs 50.9 ± 11.9 FEV1 % predicted = 66.3 ± 20.6 vs 89.6 ± 17.9 Never smokers (%) = 34 (3.9) vs 490 (13.2) Heavy smokers (%) = 506 (72.1) vs 1555 (64)
Results	Baseline characteristics In both males and females subjects with COPD were older, more were smokers and the proportion of heavy smokers was higher. 57.3% of females with COPD died during 19 years follow-up, 68.5% of males.

	A total of 263 subjects died from COPD-related causes, 165 of these occurred in subjects with COPD at baseline. Baseline weight and subsequent weight changes by severity of COPD In females, baseline BMI was lower in subjects with impaired lung function (p = 0.009) whereas no difference was found in males. <u>Females BMI (kg/m2)</u> FEV1/FVC <50% pred – 23.8 ± 4.3 FEV1/FVC 50-70% pred – 24.1 ± 4.2 FEV1/FVC > 70% pred – 24.3 ± 4.2 No COPD - 24.7 ± 4.2 In both females and males, weight changes differed with lung function with mean weight loss seen in subjects with poorest lung function and mean weight gain seen in subjects without airways obstruction (p<0.001). <u>Females BMI increase (kg/m2)</u> FEV1/FVC <50% pred = -0.2 ± 2.11 FEV1/FVC 50-70% pred = 0.08 ± 2.37 FEV1/FVC > 70% pred = 0.17 ± 1.92 No COPD = 0.4 ± 2.21 <u>Males BMI increase (kg/m2)</u> FEV1/FVC <50% pred = -0.16 ± 2.03 FEV1/FVC 50-70% pred = 0.29 ± 1.70 FEV1/FVC > 70% pred = 0.00 ± 1.49 No COPD = 0.35 ± 1.76 The proportion of subjects that lost > 1 unit BMI (~3.8kg) increased with decreasing lung function reaching 35.3% and 27.4%, respectively in females and males with severe COPD. (p<0.001) <u>Females weight loss >-1 kg/m2 (%)</u> FEV1/FVC <50% pred = 35.3 FEV1/FVC 50-70% pred = 26.9 FEV1/FVC > 70% pred = 19.7 No COPD = 17 <u>Males weight loss >-1 kg/m2 (%)</u> FEV1/FVC <50% pred = 27.4 FEV1/FVC 50-70% pred = 19.9 FEV1/FVC > 70% pred = 22.4 No COPD = 15.7 Mortality Among subjects with COPD, all-cause mortality was increased in subjects who lost > 1 BMI unit. An excess mortality was seen in subjects who lost >3 units BMI (~10 kg). Mortality in subjects who gained weight did not differ significantly from those with a stable weight.

	Effect of weight change on mortality did not differ with severity of COPD. The effect of baseline BMI was U shaped with excess mortality associated with both under and overweight In subjects with mild or moderate COPD and in subjects without COPD, no modification of the effect of baseline BMI was found; however, among patients with severe COPD (FEV1 % pred <50), effect of weight change differed with baseline weight. In all groups, weight loss was associated with increased mortality; however, normal and underweight subjects (BMI <25) with severe COPD differed from the remaining in experiencing increased survival after weight gain. The reverse was found in the overweight and obese (BMI > 25), among whom the best survival was seen in subjects who had stable weight or who had decreased their weight. <ins>All cause mortality in relation to weight change. Estimated rate ratios RR (95% confidence interval)</ins> <ins>Subjects with COPD vs subjects with no COPD</ins> Subjects with COPD n = 1612 vs subjects with no COPD n = 8812 Deaths = Subjects with COPD = 1022 vs subjects with no COPD = 3287 Weight change in BMI units > - 3kg/m2 = Subjects with COPD RR (95% CI) 1.71 (1.32-2.23) vs subjects with no COPD RR (95% CI) 1.63 (1.38 – 1.92) - 1-3 kg/m2 = Subjects with COPD RR (95% CI) 1.18 (1.00-1.39) vs subjects with no COPD RR (95% CI) 1.20 (1.08 – 1.32) -1 - +1 kg/m2 = reference + 1-3 kg/m2 = Subjects with COPD RR (95% CI) 1.07 (0.91-1.26) vs subjects with no COPD RR (95% CI) 0.99 (0.9 – 1.08) >+ 3 kg/m2 = Subjects with COPD RR (95% CI) 1.26 (0.93-1.72) vs subjects with no COPD RR (95% CI) 1.39 (1.19 – 1.61) Initial BMI <20 kg/m2 = Subjects with COPD RR (95% CI) 1.24 (0.98-.1.57) vs subjects with no COPD RR (95% CI) 1.31 (1.11 – 1.54) 20-24.9 kg/m2 = reference 25-29.9 kg/m2 = Subjects with COPD RR (95% CI) 1.04 (0.91-1.21) vs subjects with no COPD RR (95% CI) 1.08 (1.00 – 1.17) > 30kg/m2 = Subjects with COPD RR (95% CI) 1.23 (0.99-1.54) vs subjects with no COPD RR (95% CI) 1.28 (1.14 – 1.43) <ins>Mortality from COPD in relation to weight change. Estimated rate ratios RR (95% confidence interval)</ins> The highest risks were found in subjects who lost weight between examinations, whereas weight increase did not seem to increase risk of COPD-related death. Unlike all-cause mortality, the risk function for baseline BMI was linear with the lowest risk seen in patients who increased their weight. <ins>Weight change in BMI units</ins> > - 3kg/m2 = Subjects with COPD RR (95% CI) 2.14 (1.18-3.89) - 1-3 kg/m2 = Subjects with COPD RR (95% CI) 1.31 (0.89-1.92) -1 - +1 kg/m2 = reference + 1-3 kg/m2 = Subjects with COPD RR (95% CI) 0.83 (0.53-1.32) >+ 3 kg/m2 = Subjects with COPD RR (95% CI) 0.95 (0.43-2.08) <ins>Initial BMI</ins> <20kg/m2 = Subjects with COPD RR (95% CI) 1.68(1.06-2.66) 20-24.9 kg/m2 = reference

	25-29.9 kg/m2 = Subjects with COPD RR (95% CI) 0.66 (0.44-0.98) > 30kg/m2 = Subjects with COPD RR (95% CI) 0.72 (0.38-1.35) Conclusion A high proportion of subjects with COPD experienced significant weight loss, which is associated with increased mortality. Weight gain seems to have a protective effect in under and normal-weight subjects with severe COPD.
SIGN Quality Rating	++
Hierarchy of Evidence Grading	11b
NCC CC ID	1603

Author / Title / Reference / Yr	Marquis, K., Debigare, R., Lacasse, Y., LeBlanc, P., Jobin, J., Carrier, G., & Maltais, F. 2002, "Midthigh muscle cross-sectional area is a better predictor of mortality than body mass index in patients with chronic obstructive pulmonary disease.", *American Journal of Respiratory & Critical Care Medicine.*, vol. 166, no. 6, pp. 809-813. Ref ID: 1598
N=	N=142 Location=Canada Duration= mean follow-up 41 months Site=Outpatient
Research Design	Retrospective cohort study
Aim	To test the hypothesis that a reduction in mid thigh muscle cross-sectional area obtained by CT scan (MTCSA) is a better predictor of mortality in COPD than low body mass index.
Operational Definition	Diagnosis based on current and past smoking history, clinical evaluation and pulmonary function tests. No definition given.
Population	Stable COPD
Intervention	Mid thigh cross-sectional area vs mortality
Comparison	NA
Outcome	Mortality
Characteristics	Age 65 ± 9 years N = 26 females n = 116 males BMI 26 ± 6 FEV1 % pred 64 ± 16
Results	**Prediction of Mortality** Univariate analysis indicated that age, sex, FEV1 % pred, BMI, thigh circumference, MTCSA ct, Wpeak and PaCO2 were related to mortality with p<0.15. It was found that MTCSAct was the variable with the strongest inverse relationship with mortality (p = 0.0008) FEV1% predicted was the only other variable with a statistically significant relationship to mortality (p = 0.01)

	Hazard Ratio	95% CI	p Value
Age, years	1.04	0.99-1.10	0.1151

	<table><tr><td>Age, years</td><td>1.04</td><td>0.99-1.10</td><td>0.1151</td></tr><tr><td>Sex, F/M</td><td>2.06</td><td>0.86-4.95</td><td>0.1047</td></tr><tr><td>FEV1, % predicted</td><td>0.96</td><td>0.93-0.99</td><td>0.0050</td></tr><tr><td>BMI, kg/m2</td><td>0.92</td><td>0.84-1.00</td><td>0.0577</td></tr><tr><td>Thigh circumference, cm</td><td>0.94</td><td>0.9-0.98</td><td>0.0084</td></tr><tr><td>MTCSAct, cm2</td><td>0.96</td><td>0.94-0.98</td><td>0.0003</td></tr><tr><td>Peak work rate, % predicted</td><td>0.98</td><td>0.96-1</td><td>0.0801</td></tr><tr><td>PaCO2, mmHg</td><td>1.09</td><td>1.01-1.16</td><td>0.0214</td></tr></table>A MTCSAct <70 cm2 was associated with a fourfold increase (95% CI, 1.52-8.09) in mortality rate, independently of any other variables (p = 0.004) **Interaction between MTCSAct and FEV1** Patients were divided into four subgroups based on FEV1 (< or > 50% predicted) and MTCSAct (< or > 70 cm2)<table><tr><td></td><td>Number of deaths/n of patients</td><td>Hazard Ratio</td><td>95% CI</td></tr><tr><td>FEV1 > 50% and MTCSAct > 70 cm2</td><td>1/29</td><td>1 (reference)</td><td>-</td></tr><tr><td>FEV1 > 50% and MTCSAct < 70 cm2</td><td>1/16</td><td>2.14</td><td>0.13-34.4</td></tr><tr><td>FEV1 < 50% and MTCSAct > 70 cm2</td><td>6/51</td><td>3.37</td><td>0.41-28.00</td></tr><tr><td>FEV1 < 50% and MTCSAct < 70 cm2</td><td>17/46</td><td>13.16</td><td>1.74-99.20</td></tr></table>**Conclusion** MTCSAct was a better predictor of mortality than BMI and MTCSA had a strong impact on mortality in patients with an FEV1 < 50% predicted.
SIGN Quality Rating	+
Hierarchy of Evidence Grading	11b
NCC CC ID	1598

Author / Title / Reference / Yr	Palange, P., Forte, S., Felli, A., Galassetti, P., Serra, P., & Carlone, S. 1995, "Nutritional state and exercise tolerance in patients with COPD", *Chest*, vol. 107, no. 5, pp. 1206-1212. Ref ID: 1601
N=	N=28 Location=Italy

Research Design	Prospective cohort study
Aim	To investigate possible relationship between nutritional state and exercise tolerance in patients with COPD.
Operational Definition	Exertional dyspnoea, FEV 1 <60% predicted and room air PaO2 > 55 mmHg.
Population	COPD Exclusions: sacral or ankle oedema, cor pulmonale, metabolic, renal, hepatic, neuromuscular disorders.
Intervention	Nutritional status vs exercise tolerance
Comparison	NA
Outcome	Nutritional assessment, ideal body weight, body mass index, triceps skin fold thickness, heart rate, minute ventilation, oxygen uptake, CO2, PaO2 and Pa CO2.
Characteristics	Patients receiving standard medications. Age 66 ± 7 years FEV1, L/s 1.2 ± 0.5 FEV1, % pred 38 ± 15 ** very low? FVC, L/s 2.7 ± 0.5 FVC, % pred 63 ± 13 PaO2, mmHg 73 ± 11 PaCO2 mm Hg 42 ± 5
Results	Subjects were divided into three groups according to % ideal body weight (%IBW): Group 1 n = 8 % IBW <90 Group 2 n = 13, % IBW >90<110 Group 3 n = 7, % IBW > 110

	Group 1 % IBW <90	**Group 2 % IBW >90<110**	**Group 3 %IBW >110**
% IBW	82 ± 2 (p<0.05 vs GP 3 & GP2)	100 ± 2 (p<0.05 vs GP 3)	115 ± 1
BMI kg/m2	18.9 ± 0.5 (p<0.05 vs GP 3 & GP2)	23 ± 0.4 (p<0.05 vs GP 3)	26.5 ± 0.3
TSF, mm	8.1 ± 0.5 (p<0.05 vs GP 3 & GP2)	13.1 ± 0.5 (p<0.05 vs GP 3)	16.2 ± 0.3
FEV1 % pred	25 ± 2	40 ± 5	40 ± 4
FRC % pred	126 ± 4	118 ± 5	109 ± 3
PaO2, mm Hg	68 ± 3	72 ± 3	75 ± 3
PaCO2, mm Hg	42 ± 2	41 ± 1	40 ± 1
VD/VT rest	0.54 ± 0.03 (p<0.05 vs GP 3)	0.5 ± 0.02	0.43 ± 0.03

SaO2	91 ± 1	93 ± 1	94 ± 1
Exercise indices			
Max workload, W	33 ± 4 (p<0.05 vs GP 3)	48 ± 4	64 ± 7
VO2 peak, L/min	0.77 ± 0.06 (p<0.05 vs GP 3 & GP2)	1.09 ± 0.07 ((p<0.05 vs GP 3)	1.43 ± 0.07
AT, % pred VO2 max	31 ± 3	40 ± 2	46 ± 6
Change VO2/ change W	13.4 ± 0.4 (p<0.05 vs GP 3 & GP2)	11.6 ± 0.4	10.8 ± 0.2
VO2/W/Ve, mL/W/L	0.96 ± 0.14 (p<0.05 vs GP 3)	0.71 ± 0.06	0.51 ± 0.06
Ve/VCO2	43 ± 0.82	38.4 ± 2.33	39.4 ± 1.32
SaO2 (%)	90 ± 2	92 ± 1	93 ± 1

Anthropometric indices
Mean %IBW and mean BMI were statistically different among the three groups.
The triceps skin fold thickness (TSF), a marker of body fat mass, was markedly reduced in GP1 vs GP2 as well as vs GP3
Exercise indices
The lowest values of maximal workload were observed in the malnourished group (workload GP1 33 ± 4; GP2, 48 ± 4 and GP3 64 ± 7 W)
The lowest values of VO2 were also observed in the malnourished group (VO2 peak GP1, 0.77 ± 0.06; GP2 1.09 ± 0.07 and GP3 1.43 ± 0.07 L/min)
The highest values of ΔVO2/ΔW and VO2/W/Ve were observed in group 1.
Conclusion
In patients with stable COPD, malnutrition significantly affects muscle aerobic capacity and exercise tolerance

SIGN Quality Rating	-
Hierarchy of Evidence Grading	11a
NCC CC ID	1601

Author / Title / Reference / Yr	Rogers, R. M., Donahoe, M., & Costantino, J. 1992, "Physiologic effects of oral supplemental feeding in malnourished patients with chronic obstructive pulmonary disease. A randomized control study", *American Review of Respiratory Disease.*, vol. 146, no. 6, pp. 1511-1517. Ref ID: 1612
N=	N=28 Location=USA Site=Inpatient and outpatient

Research Design	Randomised controlled trial
Aim	To determine whether nutritional support, adequate to provide weight gain in malnourished patients with emphysema in an inpatient setting, could be sustained in an outpatients setting. In addition, to determine whether weight gain resulted in measurable physiologic improvement.
Operational Definition	FEV1/FVC <0.60, single breath diffusing capacity of carbon monoxide (DLCO) <60% predicted and body weight < 90% of ideal body weight (IBW)
Population	Malnourished patients with emphysema. Exclusions - those with recent COPD exacerbation, diseases that affect metabolism and weight maintenance such as diabetes, thyroid dysfunction, mal absorption, alcoholism, myopathic disease, or neoplastic disease. Patients who had received nutritional supplements in the 3 months prior to enrolment were also excluded.
Intervention	Inpatient nutritional support + standard care for 4 weeks to initiate return to ideal body weight – nutritionally balanced meal plan with caloric intake of 1.7 times resting energy expenditure with approximately 1.5g/kg protein
Comparison	Standard care alone. Control patients were hospitalised for 2 weeks (non continuous). No attempt was made to provide diet intervention or aggressive feeding.
Outcome	Pulmonary function Resting energy expenditure Exercise testing Ventilatory and Non ventilatory Muscle Testing Quality of Life Measure of Dyspnoea
Characteristics	Control Group vs Intervention Group Age, yr = 64 ± 2.0 vs 64 ± 2.0 Weight, kg = 54.9 ± 2.9 vs 52.1 ± 1.6 Ideal Body Weight (%) = 78.6 ± 2.0 vs 77.8 ± 1.6 FEV1 L = 1.0 ± 0.1 vs 1.0 ± 0.1 Further characteristics included in table No significant differences between groups
Results	**Weight change** The nutritional support regimen resulted in a significantly greater weight change in the intervention population at 4 months post enrolment than in the control population (p = 0.04). A mean weight gain of 2.4kg was noted in the intervention group compared with a 0.5kg weight loss in the control group. Baseline – Control 54.9 kg vs Intervention 52.1 kg 4 weeks – Control 55.3 kg vs Intervention 53.8 kg 4 months – Control 54.5 kg vs Intervention 54.5 kg <u>Triceps skin fold and mid arm circumference</u>

	Differences between groups did not reach statistical significance **Muscle function** Handgrip strength and maximal expiratory muscle pressure increased significantly in the intervention population. Handgrip improved 5.5kg-force for the intervention group, with a reduction of 6kg-force in the control group (p = 0.01) ** baseline difference p=0.21. Pemax improved 14.9 cm H2O for the intervention group and dropped 9.2cm H2O in the control group (p = 0.03) <u>Handgrip strength</u> Baseline – Control 67.5 kg-force vs Intervention 57.7 kg-force ** 4 weeks – Control 66.8 kg-force vs Intervention 59.8 kg-force 4 months – Control 61.5 kg-force vs Intervention 63.2 kg-force <u>Maximal expiratory pressure</u> Baseline – Control 108 cm H2O vs Intervention 89.7 cm H2O 4 weeks – Control 114.9 cm H2O vs Intervention 104.6 cm H2O 4 months – Control 98.9 cm H2O vs Intervention 104.5 cm H20 <u>Maximal Inspiratory Pressure</u> Differences between groups did not reach statistical significance **Exercise performance** Exercise performance demonstrated a mean increase in the 12-minute walk of 429 feet for the intervention population compared with a decline of 1 foot for the control population (p<0.05). **Caloric Intake** There was a statistically significant increase in the mean total energy intake in the intervention population during the 3-month outpatient follow-up (control = 1.43 vs 1.73 in the intervention population; p<0.05) **Weight Gain** The intervention subjects gained weight during the initial phase of the investigation, which included an inpatient period of education, caloric monitoring (mean increase = 1.7 kg). During the subsequent 3-month outpatient phase, the intervention population demonstrated an additional weight gain. **Quality of Life and Measures of Dyspnoea** There were no statistically significant differences in the SIP scores between the control and the intervention groups at enrolment and 4 months. Measures of dyspnoea also did not differ significantly between the control and intervention groups.
SIGN Quality Rating	-
Hierarchy of Evidence Grading	1b
NCC CC ID	1612

Author / Title / Reference / Yr	Schols, A. M. W. J., Slangen, J., Volovics, L., & Wouters, E. F. M. 1998, "Weight loss is a reversible factor in the prognosis of chronic obstructive pulmonary disease", *American Journal of Respiratory and Critical Care Medicine*, vol. 157, no. 6, pp. 1791-1797.Ref ID: 8
N=	**<u>Study 1 (retrospective)</u>** n = 400 Location= The Netherlands Duration – 10 wk Site – inpatient pulmonary rehabilitation centre <u>Study 2 (prospective)</u> n = 203 Location = The Netherlands Duration = 8 weeks
Research Design	Survival analyses on two studies
Aim	Study 1 To investigate retrospectively the relationship between body weight and survival, adjusting for the influence of age, sex, lung function, recent weight loss, and smoking. Study 2 To investigate prospectively the effects of treatment and treatment response (i.e. weight gain and improvement of maximal inspiratory mouth pressure) on survival.
Operational Definition	**<u>Study 1</u>** According to American Thoracic Society Guidelines FEV1 <70% predicted with increased in FEV1 <15% after salbutamol **<u>Study 2</u>** According to American Thoracic Society Guidelines FEV1 <70% predicted with increased in FEV1 <15% after salbutamol
Population	**<u>Study 1</u>** Moderate to severe COPD Exclusions: unstable disease or other confounding disorders such as malignancies, insulin dependent diabetes mellitus, and thyroid or cardiovascular disease. <u>Study 2</u> COPD Exclusions: As above + patients with BMI > 29 kg/m2 were excluded.
Intervention	**<u>Study 1)</u>** Retrospective study, including 400 (72% male) patients with COPD none of whom had received nutritional therapy **<u>Study 2)</u>** A post hoc analysis of a prospective study, including 203 patients with COPD who had participated in an RCT Physiological effects of nutritional therapy alone (n = 71) or in combination with anabolic steroid treatment (n = 67) after 8 week studied in patients prestratified into depleted group and nondepleted group. Nutritional support consisted of high caloric liquid supplement.
Comparison	NA
Outcome	Mortality

Characteristics

	Retrospective study 1 (n = 400)		Prospective study 2 (n = 203)	
	Mean	SEM	Mean	SEM
Age, yr	65	0.5	65	0.6
FEV, pre % pred	37	0.7	34	1.1
FEV1, post % pred	40	0.6	46	1.0
FEV1, post/pre %	109	0.5	108	0.6
IVC, % pred	74	0.9	68	1.3
PaO2, kPa	9	0.07	8.7	0.1
PaCO2, kPa	5.4	0.05	5.4	0.05
BMI, kg/m2	24	0.2	21.5	0.2

Results

Study 1

Survival was significantly decreased in both underweight and normal weight patients as compared with overweight and obese patients ($p<0.0001$)

A history of weight loss was also significantly related to decreased survival ($p<0.005$)

The group with severe airflow obstruction (FEV1 < 45%) showed decreased survival compared with those FEV1 >45% ($p = 0.0072$)

Chronic hypoxemia (PaO2 <7.3 kPa) and chronic hypercapnia (PaCO2 >6 kPa) were also associated with decreased survival ($p<0.0018$ and $p<0.001$ respectively)

Smoking behaviour in this group of patients did not significantly influence survival rates

Multivariate analysis of predictors of mortality: Retrospective study 1

BMI as a continuous variable was a significant predictor of survival in addition to age and PaO2.

After stratification of the group into BMI quintiles a threshold value of 25 kg/m2 was identified below which the mortality risk was clearly increased.

Variables		**RR**	**95%CI**	**p value**
BMI, kg/m2	linear	0.928	0.894-0.963	<0.0001
Age, yr	linear	1.041	1.002-1.062	<0.0001
PaO2, kPa	linear	0.862	0.752-0.975	<0.005
PaCO2, kPa	linear	1.129	0.929-1.372	NS
FEV1 %	linear	0.999	0.983-1.008	NS
IVC %	linear	1.000	0.989-1.011	NS
Men vs women		1.220	0.999-1.490	NS

smoking vs non smoking		1.160	0.886-1.528	NS

Study 2
Nutritional intervention resulted in a significant increase in weight, fat-free mass and fat-mass whereas no significant changes in any of these parameters were seen in the placebo group.
Relative to a similar body weight gain as the group receiving nutritional support only, the anabolic steroids group showed a larger increase in fat-free mass and maximal inspiratory mouth pressure without causing adverse side effects.
On the basis of weight change > 2kg/8wk, 50% of the treated patients were characterised as responders, including 24% of placebo group.
In 62%of the patients an improvement in Pimax was shown.
Weight gain in depleted and non-depleted patients with COPD was significantly associated with decreased mortality risk
Improvement in Pimax during rehabilitation was also associated with decreased mortality risk.

Multivariate analysis of predictors of mortality: Prospective study 2
No significant difference between the treatments on survival was shown.
On multivariate analysis weight gain in depleted and non-depleted patients with COPD was an independent predictor of survival in addition to BMI and age.

Variables		**RR**	**95%CI**	**p value**
Change in weight	linear	0.996	0.992-0.999	<0.01
Change in Pimax	linear	0.990	0.976-1.004	NS
Treatment	P vs A	0.753	0.447-1.267	NS
	N vs A	0.872	0.530-1.432	NS
BMI	linear	0.868	0.803-0.939	<0.001
FEV1	linear	0.983	0.962-1.003	NS
IVC	linear	0.995	0.982-1.008	NS
PaO2	linear	0.877	0.751-1.024	NS
PaCO2	linear	0.977	0.707-1.352	NS
Age, yr	linear	1.056	1.022-1.090	<0.001

Conclusion
The combined results of two survival analyses provide evidence to support the hypothesis that body weight has an independent effect on survival in COPD.
Moreover the negative effect of low body weight can be reversed by appropriate therapy in some patients with COPD.

SIGN Quality Rating	+
Hierarchy of Evidence Grading	11b
NCC CC ID	8

Author / Title / Reference / Yr	Schols, A. M. W. J., Soeters, P. B., Dingemans, A. M. C., MOSTERT, R., Frantzen, P. J., & Wouters, E. F. M. 1993, "Prevalence and characteristics of nutritional depletion in patients with stable COPD eligible for pulmonary rehabilitation", *American Review of Respiratory Disease*, vol. 147, no. 5, pp. 1151-1156. Ref ID: 1614
N=	N=255 Location=The Netherlands Site=Inpatient pulmonary rehabilitation centre
Research Design	Cross-sectional study from cohort of COPD patients
Aim	To establish which measure of depletion, body weight or fat free mass best predicts physical impairment in COPD
Operational Definition	-
Population	Moderate to severe COPD consecutively admitted to an intensive pulmonary rehabilitation program Exclusions: unstable pulmonary or cardiac conditions, active gastrointestinal disorders, recent surgery, or severe endocrine disorders or patients exhibiting an increase in FEV1 > 10% of baseline after inhalation of B2-agonist.
Intervention	Nutritional status vs functional capacity
Comparison	NA
Outcome	Lung function, exercise performance
Characteristics	

	Males (n = 203)	**Females (n = 52)**
Age, yr	65 ± 8	62 ± 9
IVC, % pred	67 ± 18	71 ± 20
FEV1, % pred	33 ± 14	41 ± 17
PaO2 mmHg	66 ± 12.8	68.3 ± 12.0
PaCO2 mmHg	41.3 ± 6.8	39.8 ± 6
Pimax, kPa	5.3 ± 2.3	3.4 ± 1.5
Pemax, kPa	7.7 ± 3.3	4.4 ± 2
Walking Distance	666 ± 263	575 ± 274

Results	**Patients classified by PaO2** Hypoxaemic (PaO2< 55mmHg) Normoxaemic (paO2 >55mmHg) • Depletion of body mass was most pronounced in patients suffering from chronic hypoxemia (pAO2 < 55 mmHg n = 48), 40-50% of whom exhibited subnormal values for body composition measures and serum albumin concentration. **Patients classified by FEV1** FEV1 <35%, FEV1 35-50% and FEV1> 50% • In normoxaemic patients PIBW (p<0.001), FFMPIBW (p<0.01), PIMMC (p<0.001), CHI (p<0.001) and albumin (p<0.01) were positively associated with FEV1; however, no significant differences established between FEV1 35-50% and FEV > 50%. **Patients classified according to body weight** <u>Below normal body weight</u> 1) PIBW < 90% and FFMPIBW < 63% (females)/67% males (n = 66) 2) PIBW < 90% and FFMPIBW > 63/67% n = 23) • After adjusting for significantly lower PIBW in Group 1 (81.1 ± 6.6 vs 85.9 ± 3.9%), depletion of FFM in this group was reflected in lower values for PIMMC (p = 0.06), CHI (p<0.01), and 12 minute walking distance (p = 0.02) than in Group 2. <u>Normal body weight</u> 3) PIBW > 90% and FFMPIBW < 63/67% (n = 24) 4) PIBW > 90% and FFMPIBW > 63/67% (n = 138) • After adjusting for differences in gender and the significantly lower PIBW in Group 3 (95.8 ± 5.3% vs 107.6 ± 12.9%), depletion of FFM in this group was reflected in a lower CHI (p<0.001). • Depletion of FFM also coincided in theses normal-weight patients with a decreased respiratory muscle strength (maximal inspiratory muscle pressure, Pimax, p = 0.02) and decreased exercise performance (p = 0.05). <u>Below normal body weight or fat free mass</u> 2) PIBW < 90% and FFMPIBW > 63/67% n = 23) 3) PIBW > 90% and FFMPIBW < 63/67% (n = 24) Despite significantly lower values for PIBW, subcutaneous fat mass (p<0.001), and PIMMC (p<0.01) in Group 2, CHI (p = 0.02) and 12-min walking distance were significantly lower (p<0.04) in Group 3. <u>Total patients</u> After stepwise analysis on total group of patients it was established that the functional measures Pimax, maximal expiratory pressure (Pemax) and 12 minute walking distance were better predicted by FFMPIBW than PIBW. **Arterial blood gases and spirometry** No significant differences between groups. **Conclusion** Nutritional depletion commonly occurs in COPD patients, particularly in those with chronic hypoxemia.

	Fat free mass is a better predictor of body mass depletion than body weight. Depletion of fat free mass may occur in a substantial proportion of normal-weight COPD patients. CHI is lower in patients exhibiting depleted fat-free mass. Those with greater depletion of fat free mass show decrease in CHI and walking distance compared with those with less fat free mass depletion.
SIGN Quality Rating	+
Hierarchy of Evidence Grading	11b
NCC CC ID	1614

Author / Title / Reference / Yr	Schols, A. M. W. J., Mostert, R., Soeters, P. B., Greve, L. H., & Wouters, E. F. M. 1989, "Nutritional state and exercise performance in patients with chronic obstructive lung disease", *Thorax*, vol. 44, no. 11, pp. 937-941. Ref ID: 281
N=	N=83 Location=The Netherlands
Research Design	Prospective cohort study
Aim	To evaluate the relation between some measures commonly used for assessing nutritional state and exercise performance in patients with stable COPD.
Operational Definition	FEV1 <50% pred
Population	Stable COPD. Exclusions: cardiovascular, neurological, endocrine, and locomotor diseases and those with an arterial oxygen tension (pAO2) below 7.3 kPa were excluded.
Intervention	Nutritional state vs exercise capacity
Comparison	NA
Outcome	Lung function, exercise performance, nutritional state
Characteristics	71 males and 12 females Mean age 62 ± 8 yrs Mean inspiratory vital capacity (IVC) 2.7 ± 0.6 FEV1 0.9 ± 0.3 Signs of ventricular hypertrophy were found in 46 patients
Results	**All patients** <u>Partial Correlation coefficients r between nutritional measures and 12 minute walking distance</u> The 12 minute walking test showed a significant correlation with the serum albumin concentration and creatinine height index but no association with body weight or serum prealbumin or transferrin concentration

	Percentage ideal body weight r = 0.19 (NS) Creatinine height index r = 0.35 (p = 0.001) Serum concentration of albumin r = 0.44 (p = 0.001) Serum concentration of transferrin r = 0.09 (NS) Serum concentration of prealbumin r = 0.10 (NS) <u>Partial Correlation coefficients r between lung function and 12 minute walking distance</u> Inspiratory vital capacity r = 0.21 (p = 0.03) FEV1 r = 0.29 (p = 0.002) Arterial oxygen tension r = 0.42 (p = 0.001) Arterial carbon dioxide tension r = 0.21 (p = 0.03) **Patients divided according to walking performance (high, medium and low performance)** There was no significant correlation between walking performance and percentage ideal body weight, serum concentrations of transferring or prealbumin, IVC, FEV1, PaCO2. <u>PaO2 was significantly different between the three groups (p = 0.005)</u> <432 low walking performance PaO2 (kPa) = 9.0 ± (0.9) 432-940 medium walking performance PaO2 (kPa) = 9.7 ± (1.4) >940 high walking performance PaO2 (kPa) = 10.9 ± (2.0) <u>Serum albumin was significantly different between the three groups (p = 0.001)</u> <432 low walking performance Serum albumin (g/l) = 37.9 ± (4.7) 432-940 medium walking performance Serum albumin (g/l) = 41.6 ± (4.3) >940 high walking performance Serum albumin (g/l) = 44.3 ± (3.6) • Right ventricular hypertrophy was not associated with impaired exercise performance. • Weight loss was reported more often in the low (36%) and medium (67%) performance groups than in the high (7%) performance group. • The creatinine height index was below normal in the low performance group. • Serum albumin concentration was low in the low performance group and lower in the medium than in the high performance group. • Albumin was positively associated with PaO2 (r = 0.28, p<0.005) <u>Conclusion</u> – In patients with COPD, skeletal muscle mass and serum albumin concentration are positively associated with exercise performance as measured with a 12 minute walk.
SIGN Quality Rating	+
Hierarchy of Evidence Grading	11a
NCC CC ID	281

Author / Title / Reference / Yr	Slinde, F., Gronberg, A. M., Engstrom, C. R., Rossander-Hulthen, L., & Larsson, S. 2002, "Individual dietary intervention in patients with COPD during multidisciplinary rehabilitation", *Respiratory Medicine*. vol. 96, no. 5, pp. 330-336.Ref ID: 1514
N=	N=93 Location=Sweden Site= Supervised and home-based Duration=12 months
Research Design	Post hoc analysis of RCT
Aim	To evaluate the effect of a 1 year individual multifaceted dietary intervention during multidisciplinary rehabilitation.
Operational Definition	FEV1 <50% predicted
Population	COPD Exclusions: disabling or severe diseases and/or coexistence of other causes of impaired pulmonary function. History of asthma or acute exacerbation.
Intervention	Standard care and Dietary advice to achieve dietary balance and recommended weight group n = 69. Dietary advice given on the basis of results from diet history and socio-economic status. Intervention group divided into three groups; NW Normal weight (dietary advice given aiming at weight maintenance), OW; overweight (weight-reducing advice) and UW; underweight (dietary advice based on an energy-rich and protein-rich diet)
Comparison	Standard care. No dietary advice n = 24. Control subjects had no contact with the dietician or physiotherapist, but performed anthropometric assessment, bioelectrical impedance assessment, and measurement of lung health parameters at baseline and study end.
Outcome	Nutritional assessment at start and end (12 months) Anthropometric measurements, bioelectrical impedance assessment, measurements of FEV1, 6-min walking distance performed at start, after 3,6, 9 and 12 months.
Characteristics	No significant differences between groups at baseline. Age – Intervention group vs control group Men 65.8 (6.2) vs 67.2 (5.8) Women 63.4 (6.9) vs 66.3 (5.4) <u>Weight (kg) – Intervention group vs control group</u> Men 69.6 (12.7) vs 71.5 (14.6) Women 61.9 (9.9) vs 64 (12.5) <u>BMI (kg/m2) – Intervention group vs control group</u> Men 22.7 (3.5) vs 22.7 (4.2) Women 23.4 (3.9) vs 23.6 (4.5) <u>FEV1 (% pred) – Intervention group vs control group</u> Men 33.3 (11.0) vs 33.4 (10.6) Women 36.6 (14.9) vs 35 (10.3) <u>% Reference weight - Intervention vs control group</u> Men 89.3 (13.9) vs 89.8 (17.0)

Women 95 (15.6) vs 96.4 (18.1)
% Body fat – Intervention group vs control group
Men 20.3 (7.5) vs 18.8 (7.5)
Women 29.5 (8.1) vs 32.6 (8.8)

Results

Change in intake in selected nutrients from baseline to study end

Intervention Group	**Energy (kJ)**	**Fat (g)**	**Fat (E%)**	**Carbohydrate (g)**	**Carbohydrate (E%)**	**Protein (g)**	**Protein (E%)**
NW start	8251 (3887)	73.4 (31.3)	34.1 (6.5)	246.9 (149)	48.6 (7.1)	76.3 (27.7)	16 (2.7)
NW end	7531 (2377)	61.0 * (24.1)	30.3 (6.7)	231.8 (84.3)	51.4 (8)	75.7 (25.7)	16.9 (2.9)
UW start	7908 (2015)	76.8 (23.2)	36.7 (5.4)	220.7 (68.2)	46.2 (5.4)	71.2 (17.9)	15.3 (2.7)
UW end	8571 * (2420)	80 (27.3)	34.9 (4.7)	247.1 (77.7) *	48 (6.4)	82 * (19.3)	16.5 (3.6)
OW start	7782 (1707)	70.7 (29.2)	33.4 (10.6)	240.6 (53.4)	52.9 (13.3)	63.9 (26.5)	13.4 (3.9)
OW end	5343 * (1096)	39 * (15)	27.0 (6.3)	172.6 (32.2)	54.6 (6.1)	60.2 (17.3)	18.7 * (3.5)
	Ca (mg)	Fe (mg)	Vitamin D (ug)	Vitamin (mg)	Vitamin E (mg)	Vitamin C (mg)	
NW start	997 (446)	14.4 (6.6)	5.2 (4.4)	1.3 (0.7)	6.6 (3.9)	73.5 (63.2)	
NW end	1029 (414)	14.3 (6.7)	5.6 (4.8)	1.1 (0.6)	6.1 (3.2)	86.7 (58.9)	
UW start	974 (386)	12.4 (4.3)	4.5 (2.7)	1.0 (0.6)	6.4 (3.1)	50 (37.7)	
UW end	1175 (481)	14.8 (4.8)	5.1 (2.1)	1.1 (0.8)	6.6 (3.8)	79.1 (44.3)	
OW start	979 (430)	12.6 (2.4)	4.6 (1.7)	1.1 (0.8)	6.0 (2.3)	96.7 (120.8)	
OW end	889 (481)	10.1 (3.6)	2.7 (1.7)	0.6 (0.3)	3.4 (1.6)	78.9 (66.4)	

Normal weight
The intake of nutrients in the NW group was unchanged; however their fat intake decreased significantly.
Underweight
Mean energy intake increased significantly in the UW group and significantly reduced their fat energy percentage intake.
Patients in the UW group increased their intake of calcium, iron and vitamin C.
Overweight
The OW group showed a significant decrease in mean energy intake, a profound reduction in fat intake and reduced their intake of vitamins D and E.

	Body weight <u>Underweight Group</u> Body weight at 3 and 6 months was significantly higher than at baseline; however at 9 and 12 months no difference was observed from baseline values. <u>Overweight Group</u> There was no significant difference in body weight at any time point. <u>Normal weight Group</u> There was a statistically significant increase in bodyweight at 6 months compared with baseline. **Body Mass Index** BMI did not change significantly in any of the groups over the course of the study **% Body Fat** % Body Fat did not change significantly in any of the groups between start and end of study **6 minute walking distance** In the normal weight group a significant increase in 6-min walking distance was seen when comparing the start to the end of the study. No significant differences were seen in UW or OW groups.
SIGN Quality Rating	-
Hierarchy of Evidence Grading	1b
NCC CC ID	1514

Author / Title / Reference / Yr	Wilson, D. O., Rogers, R. M., Wright, E. C., & Anthonisen, N. R. 1989, "Body weight in chronic obstructive pulmonary disease. The National Institutes of Health Intermittent Positive-Pressure Breathing Trial", *American Review of Respiratory Disease.* vol. 139, no. 6, pp. 1435-1438.Ref ID: 1610
N=	N=779 Location= US Duration=3 years
Research Design	Retrospective cohort study
Aim	To examine the relationship between body weight, pulmonary function and survival.
Operational Definition	FEV1 <60% predicted and % TLC greater than 80.
Population	Stable COPD Exclusions: published elsewhere
Intervention	Body weight vs pulmonary function and survival
Comparison	NA
Outcome	Nutritional and anthropometric characteristics, respiratory function, exercise performance, dyspnoea, quality of life

Characteristics

Age 63.6 yrs
Men 74% women 26%
Further characteristics in table

Results

Nutrition

- 24.4% of subjects had %IBW of <90%
- 86% of those with a weight of <80% IBW and 60% of those with weight < 90% had an abnormally low triceps skin fold thickness (TSF) (< 60% standard)
- Among underweight subjects (IBW <90% predicted), 32% reported weight loss of > 5% in the last year.
- When compared with their usual weight, 81% of underweight subjects had lost > 10% body weight, with self-reported weight losses of as much as 43%.
- The mean weight loss from usual weight in the underweight group was 17% (± 13%)

Comparison of nutritional and anthropometric characteristics by % ideal body weight

- The mean % IBW for the three groups were 80.2 ± 1.3, 104.8 ± 8.6 and 130.6 ± 8.9
- TSF and mid arm circumference were reduced in the underweight group
- Mean haemoglobin values were high in all groups, with slightly lower values in the underweight group.
- A comparison of IBW < 90% with IBW > 90% indicates a statistically significant difference in haemoglobin (14.9 vs 15.9; p<0.01), haematocrit (46.2 vs 48.6; p<0.01) and albumin (4 vs 4.1; p<0.05)

	% IBW < 90% (n = 33)	**% IBW 90-119% (n = 72)**	**% IBW > 120% (n = 30)**
Age, yr	65 ± 1.37	63.2 ± 0.93	62.9 ± 0.97
Height, cm	162.5 ± 1.47	166.2 ± 0.86	165.7 ± 1.44 (p<0.05 difference between the three groups)
Weight, kg	48 ± 1.31	65.6 ± 0.97	81.2 ± 1.85 (p<0.05 difference between the three groups)
Triceps skin fold	8.3 ± 0.66	12.2 ± 0.59	16.5 ± 1.38 (p<0.05 difference between the three groups)
Arm muscle circumference	21.8 ± 0.43	25.7 ± 0.35	28.7 ± 0.57 (p<0.05 difference between the three groups)
Haemoglobin, g/dl	14.9 ± 0.27	15.8 ± 0.2	16.2 ± 0.24 (p<0.05 difference between the three groups)

Haematocrit, %	46.1 ± 0.77	49.1 ± 0.59	49.8 ± 0.88 ($p<0.05$ difference between the three groups)
Serum albumin, g/dl	4 ± 0.049	4.1 ± 0.033	4.2 ± 0.052
Total lymphocyte count, 10^9/ L	1802 ± 114.8	1847 ± 91	2160 ± 314.3

Respiratory Function

- FEV1 values were low because of entry criteria requiring Grade 4 or Grade 5 dyspnoea; 52.6% patients had an FEV1 < 30% predicted.
- % FEV1 was not different among the 3 groups, despite small but significant differences in absolute values of FEV1
- Diffusing capacity was reduced in the underweight group ($p<0.01$); however, upon adjustment for age, sex and haemoglobin level, the differences between groups disappeared.
- % IBW was a predictor of both expiratory muscle strength and inspiratory muscle strength in regression analysis.

	% IBW < 90% (n = 33)	**% IBW 90-119% (n = 72)**	**% IBW > 120% (n = 30)**
FEV, L	0.65 ± 0.04	0.83 ± 0.04	0.85 ± 0.06 ($p<0.05$ difference between the three groups)
FEV1, % predicted	26.8 ± 1.66	31.2 ± 1.37	31.2 ± 1.77
FEV1, FVC, %	30 ± 6.9	33.2 ± 7.4	35.1 ± 10.8 ($p<0.05$ difference between the three groups)
PaCO2, mmHg	45 ± 1.2	43.3 ± 0.83	44.5 ± 1.0
PaO2, mmHg	72.2 ± 1.7	69.6 ± 1.1	70.2 ± 1.4
DLCO ml/min mmHg	10.1 ± 0.31	12.5 ± 0.52	15.6 ± 0.95 ($p<0.01$ difference between the three groups)
DLCO % pred	68.1 ± 5.2	70.5 ± 4.9	80.5 ± 6
TLC, L	7.2 ± 0.17	7.5 ± 0.13	7.3 ± 0.23
Functional residual capacity	5.9 ± 0.22	5.7 ± 0.12	5.5 ± 0.21
PI max, cm H2O	38.6 ± 2.61	40.5 ± 1.79	47.7 ± 2.59 ($p<0.05$ difference between the three groups)
PE max, cm H2O	71.7 ± 5.16	80.7 ± 4.28	102.4 ± 7.2

Exercise performance, dyspnoea and quality of life

	• VO2 max absolute expressed as percent predicted was significantly lower in the underweight group compared with the other two groups combined (p<0.001) • Regression analysis demonstrated that %VO2 max was associated with FEV1 (R^2 = 0.23; p<0.01) and after controlling for FEV1, %IBW explained a further 8% (p<0.001) of the variance in %VO2 max. • No significant differences were observed between groups in the 6-minute walk, oxygen cost score or quality of life score.

	% IBW < 90% (n = 33)	**% IBW 90-119% (n = 72)**	**% IBW > 120% (n = 30)**
VO2 max, L/min	0.54 ± 0.18	0.74 ± 0.22	0.91 ± 0.26 (p<0.01 difference between the three groups)
VO2 max, % predicted	37.2 ± 2.09	47 ± 2.19	53.7 ± 2.45 (p<0.01 difference between the three groups)
6 minute walk, m	313.3 ± 18.2	305.3 ± 13.9	342.8 ± 2.3
oxygen cost score, mm	49.2 ± 2.22	50.4 ±1.82	49.4 ± 2.8
Quality of life score	6.2 ± 0.27	6.5 ± 0.24	6.9 ± 0.34
Current smokers %	24	20	14

Conclusion
In underweight COPD subjects peak exercise performance and ventilatory muscle strength are decreased; however submaximal exercise performance, dyspnoea and overall quality of life are not affected.

SIGN Quality Rating	+
Hierarchy of Evidence Grading	11b
NCC CC ID	1613

Author / Title / Reference / Yr	Sahebjami, H. & Sathianpitayakul, E. 2000, "Influence of body weight on the severity of dyspnoea in chronic obstructive pulmonary disease", *American Journal of Respiratory & Critical Care Medicine*, vol. 161, no. 3 I, pp. 886-890.Ref ID: 1616
N=	N=90 Location= US
Research Design	Cross-sectional cohort study
Aim	To assess the severity of dyspnoea in well defined groups of stable, normal weight and underweight patients with COPD with various degrees of airways obstruction; and to determine whether pulmonary function tests, gas exchange parameters, and respiratory muscle strength differed between the two groups and correlated with the severity of dyspnoea
Operational Definition	FEV1 less than 75% predicted

	FEV1/FVC ratio of less than 75% BMI less than 28kg/m2
Population	COPD patients divided into normal weight (BMI of 21-28 kg/m2) and underweight (BMI <21 kg/m2) Exclusions: obesity, patients with mixed obstructive and restrictive ventilatory defects, acute COPD exacerbations for any reason, other illnesses known to affect nutritional status or body weight, significant cardiac diseases, neuromuscular disorders and pre- or postoperative states.
Intervention	BMI vs dyspnoea
Comparison	NA
Outcome	FEVC, FEV1, FEV1/FVC, MVV, TLC, FRC, RV, RV/TLC, PaO2, PaCO2, pH, DCO , Pimax, Pemax, RMS
Characteristics	(see table below)
Results	**Dyspnoea** Severity of dyspnoea was significantly greater in the underweight (3.1 ± 0.9) compared with the normal weight 2.5 ± 1.2) patients with COPD (p = 0.0358) None of the underweight patients was free of dyspnoea, while 7.0% of the normal weight subjects were not troubled by breathlessness except with strenuous exercise. A larger percentage of normal weight patients (43.8 vs 27.2%) complained for slight to moderate dyspnoea (scale 1-2), whereas a larger percentage of underweight subjects (63.6 vs 40.3%) had moderately severe to severe dyspnoea (scale 3-4). The distribution of very severe dyspnoea (scale 5) was similar in the two groups

Characteristics:

	Normal weight	**Underweight**	**p value**
n	57	33	
Age, yr	66.1 ± 7.3	69.7 ± 4.8	NS
Height, cm	173.4 ± 5.1	172.6 ± 4.8	NS
Weight, kg	74.1 ± 6.4	56 ± 4.6	<0.0001
Body Mass Index, kg/m2	24.5 ± 1.8	18.7 ± 1.2	<0.0001
Oral prednisone			
patients, n	5 (8.7%)	2(6.1%)	
Range, mg/d	5-15	5-10	
Dyspnoea	2.5 ± 1.2	3.1 ± 0.9	0.0358

Pulmonary Function

	Normal weight	Underweight
FVC % pred	74.5 ± 13	76.8 ± 18
FEV1 % pred	48.9 ± 13	45.7 ± 13
FEV1/FVC	52.1 ± 11	47.6 ± 9
MVV % pred	52.4 ± 16	50 ± 15
TLC % pred	107.1 ± 12	112 ± 13
FRC % pred	120.5 ± 19	121.8 ± 18
RV % pred	148.1± 26	152.3 ±28
RV/TLC % pred	134.2 ± 18	132.7 ± 16

Gas exchange parameters

The mean values of PaO2, PaCO2 and pH were similar in the underweight and normal weight patients with COPD.
Diffusing capacity was reduced in both groups, but significantly more so in the underweight patients
In both groups of patients with COPD, Pimax, Pemax and RMS were lower than the predicted normal range.

	Normal weight	Underweight	p values
PaO2, mmHg	75 ± 0.4	71.9 ± 6.3	NS
PaCO2, mmHg	39.4± 4	38 ± 3.7	NS
pH	7.4 ± 0.02	7.41 ± 0.02	NS
DCO % pred	57 ± 17	36 ± 11	<0.001

	Respiratory Pressure Pimax was significantly more reduced in the underweight group compared with normal weight patients. Pemax was similar in the two groups.

	Normal weight	Underweight	p value
Pimax cmH20	66 ± 19	55 ± 18	0.0205
Pimax % pred	62 ± 17	52 ± 17	0.0343
Pemax cm H2O	116 ± 30	105 ± 29	NS
Pemax % pred	58 ± 15	53 ± 14	NS
RMS cmH2O	91 ± 22	79 ± 19	0.0320
RMS % pred	59 ± 14	52 ± 12	0.0537

Correlation between dyspnoea scale as dependent variable and other parameters in all patients

	r	p value
DCO, % pred	-0.512	<0.001
MVV, % pred	-0.439	<0.001
FEV1 % pred	-0.374	<0.001
RMS, % pred	-0.329	<0.001
Pimax, % pred	-0.306	<0.001
RV/TLC %	0.295	<0.01
FVC % pred	-0.272	<0.01
Pemax cm H2O	-0.268	<0.01
FEV1/FVC %	-0.263	<0.02
BMI kg/m2	-0.261	<0.02

Dyspnoea scale correlated significantly with %DCO ($r = -0.512$, $p<0.001$).
In stepwise multiple regression model with dyspnoea scale as the outcome, %DCO and %MVV combined were the strongest predictors of the severity of dyspnoea ($R2 = 0.3$, $p = 0.001$)

Conclusion
Underweight patients with COPD are more dyspnoeic than normal weight patients.

SIGN Quality Rating	+
Hierarchy of Evidence Grading	11b
NCC CC ID	1616

Author / Title / Reference / Yr	Otte, K. E., Ahlburg, P., D'Amore, F., & Stellfeld, M. 1989, "Nutritional repletion in malnourished patients with emphysema", *Journal of Parenteral & Enteral Nutrition*, vol. 13, no. 2, pp. 152-156.Ref ID: 289
N=	N=28 Location=Denmark Duration – 13 weeks
Research Design	Randomised controlled trial
Aim	To examine the effect of nutritional supplementation on indices of anthropometrics, pulmonary function, immunological status, and subjective well-being in malnourished patients with emphysema pulmonum (EP)
Operational Definition	FEV1 less than 70% predicted, residual volume of more than 40% of total lung capacity and body weight less than 80% ideal body weight.
Population	Malnourished ambulant patients with stable emphysema pulmonum Exclusion: thyroid disease, peptic ulcer, osteoarthritis, diabetes mellitus, malignant disease and symptoms of cardiac ischaemic.
Intervention	Fed group n = 13 supplemented with nutritional formula providing 1Kcal/ml, 20% energy protein 50% energy carbohydrate, 30% energy fat, ascorbic acid, calcium, phosphorus, magnesium, sodium, potassium and chloride.
Comparison	Control group supplemented with reference product of same consistency and taste providing 0.1Kcal/ml.
Outcome	Anthropometrics, pulmonary function tests, immunological tests, subjective well-being
Characteristics	**Fed group** 10 women and 3 men mean age 56.5 yr (34-69) **Control groups** 12 women and 3 men Mean age 53.9 yr (48-66)
Results	**Anthropometrics** Patients in the fed group gained significantly more weight than those in the control group. Mean sum of skin folds (triceps, biceps, sub scapular and suprailiac) increased significantly in the fed group compared with the control group

	Fed Group	**Control group**	
	Difference (before-after)	Difference (before-after)	p values
Weight (kg)	1.52 ± 0.39	0.16 ± 0.2	<0.01
IBW (%)	2.44 ± 0.62	0.22 ± 0.37	<0.01
MAMC (cm)	0.10 ± 0.15	-0.03 ± 0.15	NS
SFS (mm)	2.73 ± 0.87	-0.93 ± 0.81	<0.01

	Pulmonary Function Tests No significant differences between the groups were seen.

	Fed Group	**Control Group**	
	difference (before-after)	Difference (before-after)	p values
FEV1 (% pred)	-1.8 ± 1.74	-0.09 ± 1.27	NS
FVC % pred	-3.15 ± 2.88	1.57 ± 3.16	NS
MVV (% pred)	-2.52 ± 4.20	3.15 ± 2.07	NS
PaO2 (mmHg)	-1.6 ± 3.47	-1.51 ± 3.02	NS
PaCO2 (mm Hg)	-0.10 ± 2.01	1.30 ± 1.6	NS
12 minute walking distance (m)	-80.2 ± 74	50.1 ± 28.5	NS

Subjective well being
No significant differences were seen between groups
Immunological tests
No significant differences were seen between groups
Conclusion
Nutritional supplementation produces weight gain in malnourished patients with pulmonary emphysema, but it does not change other indices of well-being.

SIGN Quality Rating	+
Hierarchy of Evidence Grading	1b
NCC CC ID	289

Author / Title / Reference / Yr	Sahebjami, H., Doers, J. T., Render, M. L., & Bond, T. L. 1993, "Anthropometric and pulmonary function test profiles of outpatients with stable chronic obstructive pulmonary disease", *American Journal of Medicine*, vol. 94, no. 5, pp. 469-474. Ref ID: 1605
N=	N=126 Location=US Duration – 1 year (i.e. 1 year to take measurements from 126 patients) Site – Chest clinic outpatients
Research Design	Prospective cohort study
Aim	To determine the prevalence of nutritional status, and their correlation with pulmonary function test results (taken within previous 6 months), in a population of outpatients with stable COPD.
Operational Definition	FEV1/FVC <70% and total lung capacity greater than 80% predicted.
Population	Stable COPD. Exclusions: history of asthma, patients with mixed obstructive and restrictive ventilatory defects, acute exacerbations of COPD due to any cause, or other illnesses known to affect nutritional status or body weight.
Intervention	Nutritional status vs pulmonary function
Comparison	NA
Outcome	Triceps skin fold thickness, mid arm muscle circumference, arm muscle circumference, flow rates, lung volumes, single-breath carbon monoxide diffusing capacity (DLCO), residual capacity, arterial blood samples.
Characteristics	Groups divided according to weight. Normal weight (BMI 20-27) n = 67 (53.2%) / Underweight (BMI <20) n = 29 (23%) / Overweight (BMI > 27) n = 30 (23.8%)

	Underweight (n = 29)	**Normal weight 9n = 67)**	**Overweight (n = 30)**
Age, y	63.5 ± 1.4	64 ± 0.8	63.9 ± 1.2
Height (cm)	170.4 ± 1	172.4 ± 0.5	174.5 ± 2
Weight (kg)	51.8 ± 0.9	69.2 ± 0.8	93.6 ± 2.4 (p<0.0001) among the three groups
Body Mass Index, kg/m2	17.7 ± 0.2	23.2 ± 0.2	30.5 ± 0.5 (p<0.001 for differences among the three groups)
Arm muscle circumference, cm	21.5 ± 0.3	12.4 ± 0.5	18.9 ± 1.4 (p<0.001 for differences between the three groups)
Triceps skin fold, mm	6.2 ± 0.5	12.4 ± 0.5	18.9 ± 1.4 (p<0.001 for differences between the three groups)

No significant differences between age of groups; however anthropometric parameters significantly different between groups

Results	**Effect of body weight on pulmonary Function** A significant and positive correlation existed for all subjects between BMI as the independent variable and %FEV1 and FEV1/FVC ratio. A significant and negative correlation existed between the BMI as the independent variable and %RV and RV/TLC ratio. Spirometric values were not significantly different between groups. Lung volumes, expressed as % predicted, were not significantly different among the three groups.

	Underweight (n = 29)	Normal weight (n = 67)	Overweight (n = 30)
FVC1, % predicted	61.9 ± 4	66.2 ± 2.6	65.3 ± 3.3
FEV1, % predicted	32.7 ± 2.8	38 ± 2.2	38.7 ± 2.8
FEV1/FVC %	42.2 ± 1.9	45 ± 1.4	47.6 ± 2.3
TLC, % predicted	110.4 ± 2.7	116.9 2.7 (	109.1 ± 2.6
VC, % predicted	67 ± 4.1	77.1 ± 3.3	72 ± 3.4
RV, % predicted	182.4 ± 8.8	184.4 ± 6.1	170.5 ± 6.4
RV/TLC %	62 ± 2.3	59.5 ± 1.3	58 ± 1.6

Effect of body weight on Gas Exchange parameters

Diffusing capacity for carbon monoxide (DLCO) expressed in absolute values (or as % predicted) was significantly different among all groups ($p<0.001$) being lowest in the underweight and highest in the overweight patients.

A very high correlation existed between DLCO and BMI as the independent variable.

All 29 (100%) underweight patients had abnormally low %DLCO; whereas in 44/64 (68.7%) normal weight patients and in only 11 of 30 overweight patients (36.6%) this parameter was lower than normal.

	Underweight (n = 26)	Normal weight (n = 66)	Overweight (n = 27)
DLCO, ml/min mmHg	8.9 ± 0.9	15.1 ± 0.8	20.1 ± 1
DLCO % pred	35.4 ± 3.4	59.3 ± 3.3	79.1 ± 3.7
PaO2, mmHg	67.6 ± 2.1	69.4 ± 1.2	70.5 ± 1.8
PaCO2, mmHg	PaCO2 mmHg	39.2 ± 1	38.4 ± 0.8
38.7 ± 1.2	7.41 ± 0.006	7.41 ± 0.004	7.41 ± 0.005

No significant difference was observed between groups in PaO2, PaCO2 or pH.

Conclusion

A substantial number of stable COPD patients have nutritional abnormalities. BMI is a simple and accurate indicator of nutritional status in these patients. BMI correlates significantly with some tests of pulmonary function.

SIGN Quality Rating	+
Hierarchy of Evidence Grading	11b
NCC CC ID	1605