

Online supplement

Therapeutic Advances in Respiratory Disease

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Fatigue is highly prevalent in patients with COPD and correlates poorly with the degree of airflow limitation

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Table S1 Female (n=506) versus male (n=784) patients with COPD

Characteristics - COPD	n	Female COPD (n=506)	n	Male COPD (n=784)	P-value
Age, years	506	62.6±9	784	66.1±9.5	<0.001
Current smoker, n (%)	476 ^a	171(35.9)	756 ^m	209(27.6)	0.002
Pack years	89 ^b	36.5±17.1	105 ⁿ	43.4±21.7	0.062
Long term oxygen therapy, n (%)	89 ^c	22(24.7)	105 ^o	32(30.5)	0.373
Charlson comorbidity index, points	232 ^d	2(1-3)	311 ^p	3(1-4)	0.001
COPD Assessment Test, points	313 ^e	19(14-25)	383 ^q	19(13-24)	0.255
Partner, n (%)	486 ^f	335(68.9)	764 ^r	616(80.6)	<0.001
Education, n (%)	474 ^g		752 ^s		0.138
Intermediate vocational education or lower		355(74.9)		534(71.0)	
Secondary general education or higher		119(25.1)		218(29.0)	
Working situation, n (%)	481 ^h		756 ^t		0.836
Paid work		119(24.7)		191(25.3)	
No Paid work		362(75.3)		565(74.7)	
Body composition					
BMI (kg/m ²)	506	25.6±5.5	784	26.3±4.7	<0.001
Underweight, n (%)	506	109(21.5)	784	94(12.0)	<0.001
Normal weight, n (%)		153(30.2)		231(29.5)	
Overweight, n (%)		147(29.1)		308(39.3)	
Obese, n (%)		97(19.2)		151(19.3)	
Spirometry					
FEV 1 (% predicted)	506	56.3±18.4	784	55±19.2	0.182
FEV 1 (Litres)	506	1.3±0.5	784	1.7±0.7	<0.001
FVC (Litres)	506	2.8±0.7	784	3.9±0.9	<0.001
GOLD, n (%)	506		784		0.121
I		51(10.1)		80(10.2)	
II		265(52.4)		366(46.7)	
III		160(31.6)		270(34.4)	
IV		30(5.9)		68(8.7)	
Medications in use, n	89 ⁱ	6(4-9.5)	105 ^u	8(5-13)	0.006
Dyspnoea					
mMRC, points	355 ^j	2(1-3)	409 ^v	2(1-3)	0.131
<2 mild dyspnoea, n (%)	355 ^k	144(43.0)	409 ^w	202(49.4)	0.081
≥2 severe dyspnoea, n (%)		191(57.0)		207(50.6)	
Fatigue					
CIS-Fatigue, points	506	37(29-46)	784	34(25-43)	<0.001
Normal fatigue, n (%)	506	104(20.6)	784	225(28.7)	0.001
Mild fatigue, n (%)		127(25.1)		208(26.5)	
Severe fatigue, n (%)		275(54.3)		351(44.8)	
Exacerbations last 12 months, r	327 ^l	1(0-2)	386 ^x	1(0-2)	0.653

Data are shown as mean±SD, median (IQR) or n(%). COPD, Chronic Obstructive Pulmonary Disease; BMI, Body Mass Index; FEV1 (% predicted), forced expiratory volume over 1 second of predicted; FVC, forced volume capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified Medical Research Council dyspnoea scale; CIS-Fatigue, Checklist Individual Strength subscale fatigue. ^a30 missing values; ^b417 missing values; ^c417 missing values; ^d274 missing values; ^e193 missing values; ^f20 missing values; ^g32 missing values; ^h25 missing values; ⁱ407 missing values; ^j151 missing values; ^k151 missing values; ^l179 missing values; ^m28 missing values; ⁿ679 missing values; ^o679 missing values; ^p473 missing values; ^q401 missing values; ^r20 missing values; ^s32 missing values; ^t28 missing values; ^u679 missing values; ^v375 missing values; ^w375 missing values; ^x398 missing values.

Table S2 Female (n=97) versus male (n=102) patients without COPD

Characteristics – non-COPD	n	Female non-COPD	n	Male non-COPD	P-value
		(n=97)		(n=102)	
Age, years	97	62.2±9.8	102	63.8±9	0.216
Current smoker, n (%)	97	20(20.6)	102	25(24.5)	0.512
Pack years	77 ^a	13.4±20.6	56 ^e	21.4±19.9	0.002
Long term oxygen therapy, n (%)	-	-	-	-	-
Charlson comorbidity index, points	77 ^b	1(0-2)	56 ^f	0(0-2)	0.647
COPD Assessment Test, points	-	-	-	-	-
Partner, n (%)	97	84(86.6)	102	85(83.3)	0.520
Education, n (%)	97		102		0.210
Intermediate vocational education or lower		76(78.4)		72(70.6)	
Secondary general education or higher		21(21.6)		30(29.4)	
Working situation, n (%)	96 ^c		102		0.672
Paid work		28(29.2)		27(26.5)	
No Paid work		68(70.8)		75(73.5)	
Body composition					
BMI (kg/m ²)	97	27.1±5.2	102	27.9±3.8	0.053
Underweight, n (%)	97	8(8.2)	102	1(1.0)	0.020
Normal weight, n (%)		33(34.0)		25(24.5)	
Overweight, n (%)		33(34.0)		49(48.0)	
Obese, n (%)		23(23.7)		27(26.5)	
Spirometry					
FEV 1 (% predicted)	97	112.4±20.9	102	110.6±20.8	0.239
FEV 1 (Litres)	97	2.5±0.5	102	3.5±0.8	<0.001
FVC (Litres)	97	3.3±0.7	102	4.6±1	<0.001
GOLD, n (%)	-		-		-
I		-		-	
II		-		-	
III		-		-	
IV		-		-	
Medications in use, n	77 ^d	2(1-5)	56 ^g	2(1-5)	0.523
Dyspnoea					
mMRC, points	-	-	-	-	-
<2 mild dyspnoea, n (%)	-	-	-	-	-
≥2 severe dyspnoea, n (%)	-	-	-	-	-
Fatigue					
CIS-Fatigue, points	97	22(13-28)	102	19(11-26.3)	0.394
Normal fatigue, n (%)	97	69(71.1)	102	77(75.5)	0.303
Mild fatigue, n (%)		15(15.5)		18(17.6)	
Severe fatigue, n (%)		13(13.4)		7(6.9)	
Exacerbations last 12 months, n	-	-	-	-	-

Data are shown as mean±SD, median (IQR) or n(%). COPD, Chronic Obstructive Pulmonary Disease; BMI, Body Mass Index; FEV1 (% predicted), forced expiratory volume over 1 second of predicted; FVC, forced volume capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified Medical Research Council dyspnoea scale; CIS-Fatigue, Checklist Individual Strength subscale fatigue. ^a20 missing values; ^b20 missing values; ^c1 missing values; ^d20 missing values; ^e46 missing values; ^f46 missing values; ^g46 missing values.

Table S3 Non-COPD control groups from the Home Sweet Home study (*n*=133) and the Adaptation study (*n*=66)

Characteristics – non-COPD	<i>n</i>	Home Sweet Home (<i>n</i>=133)	<i>n</i>	Adaptation (<i>n</i>=66)	P- value
Male, <i>n</i> (%)	133	56 (42.1)	66	46 (69.7)	<0.001
Age, years	133	63.5±10.2	66	62.2±7.5	0.188
Current smoker, <i>n</i> (%)	133	34 (25.6)	66	11 (16.7)	0.158
Pack years	133	16.8±20.6	-	-	-
Charlson comorbidity index, points	133	1 (0-2)	-	-	-
Partner, <i>n</i> (%)	133	119 (89.5)	60 ^a	50 (75.8)	0.011
Education, <i>n</i> (%)	133		66		
Intermediate vocational education or lower		112 (84.2)		36 (54.5)	<0.001
Secondary general education or higher		21 (15.8)		30 (45.5)	
Working situation, <i>n</i> (%)	133				0.183
Paid work		33 (24.8)		22 (33.8)	
No Paid work		100 (75.2)		43 (66.2)	
Body composition					
BMI (kg/m ²)	133	27.9±4.7	66	26.6±4.0	0.050
Underweight, <i>n</i> (%)		6 (4.5)		3 (4.5)	0.202
Normal weight, <i>n</i> (%)		34 (25.6)		24 (36.4)	
Overweight, <i>n</i> (%)		54 (40.6)		28 (42.4)	
Obese, <i>n</i> (%)		39 (29.3)		11 (16.7)	
Spirometry					
FEV 1 (% predicted)	133	111.2±23.4	66	112.1±14.6	0.290
FEV 1 (Litres)		2.9±0.9		3.4±0.6	<0.001
FVC (Litres)		3.7±1.1		4.4±0.8	<0.001
Medications in use, <i>n</i>	133	2 (1-5)	-	-	-
Fatigue					
CIS-Fatigue, points	133	24 (14.5-31.0)	66	14 (9.8-21.3)	<0.001
Normal fatigue, <i>n</i> (%)		87 (65.4)		59 (89.4)	0.001
Mild fatigue, <i>n</i> (%)		27 (20.3)		6 (9.1)	
Severe fatigue, <i>n</i> (%)		19 (14.3)		1 (1.5)	

Data are shown as mean±SD, median (IQR) or *n*(%). COPD, Chronic Obstructive Pulmonary Disease; BMI, Body Mass Index; FEV1 (% predicted), forced expiratory volume over 1 second of predicted; FVC, forced volume capacity; CIS-Fatigue, Checklist Individual Strength subscale fatigue. ^a6 missing values.

Table S4 Summary of multiple regression analysis

			95% CI for B	
	Beta	p-value	Lower Bound	Upper Bound
Gender	-0.208	0.017	-7.788	-0.788
Age	-0.270	<0.001	-0.496	-0.147
Marital status	0.021	0.735	-3.779	5.349
Smoking status	0.082	0.214	-1.295	5.732
Pack-years	0.012	0.853	-0.059	0.071
LTOT	-0.082	0.268	-5.254	1.471
Charlson	0.052	0.448	-0.601	1.353
Exacerbations	0.133	0.051	-0.003	1.402
FEV1%pred	0.136	0.084	-0.011	0.169
FVC	-0.267	0.003	-4.349	-0.934
Nr. of medications	0.258	0.002	0.226	0.947
mMRC	0.324	<0.001	1.409	3.993

Beta = standardized coefficient

Table S5 COPD populations from the Adaptation study (*n*=165), Home Sweet Home study (*n*=194), Paloma study (*n*=293) and the outpatient population from the Amphia hospital (*n*=638)

Characteristic COPD	<i>n</i>	Adaptation study (<i>n</i> =165)	<i>n</i>	Home Sweet Home study (<i>n</i> =194)	<i>n</i>	Paloma study (<i>n</i> =293)	<i>n</i>	Outpatient population (<i>n</i> =638)	P-value
Male, <i>n</i> (%)	165	128 (77.6)	194	105 (54.1)	293	203 (69.3)	638	348 (54.5)	<0.001
Age, years	165	64.3±9.2	194	66.0±8.7	293	66.6±10.1	638	63.6±9.3	<0.001
Current smoker, <i>n</i> (%)	164	45 (27.4)	194	33 (17.0)	293	50 (17.1)	581	252 (43.3)	<0.001
Pack years	-		194	40.3±20.0	-		-		-
Long term oxygen therapy, <i>n</i> (%)	-		194	54 (27.8)	-		-		-
Charlson comorbidity index, points	-		194	2 (1-3)	-		349	3 (1-4)	0.363
COPD Assessment Test, points	-		193	21 (16-26)	-		503	17 (12-24)	<0.001
Partner, <i>n</i> (%)	161	127 (78.9)	194	177 (91.2)	291	213 (73.2)	604	434 (71.9)	<0.001
Level of education, <i>n</i> (%)	160		191		291		584		<0.001
Intermediate vocational education or lower		131 (81.9)		163 (85.3)		230 (79.0)		365 (62.5)	
Secondary general education or higher		29 (18.1)		28 (14.7)		61 (21.0)		219 (37.5)	
Working status, <i>n</i> (%)	159		194				594		<0.001
Paid work		39 (24.5)		17 (8.8)	290	60 (20.7)		194 (32.7)	
No Paid work		120 (75.5)		177 (91.2)		230 (79.3)		400 (67.3)	
Body composition									
BMI (kg/m ²)	165	25.5±4.0	194	26.3±5.3	293	26.6±4.5	638	25.8±5.4	0.018
Underweight, <i>n</i> (%)		23 (13.9)		32 (16.5)		26 (8.9)		122 (19.1)	0.006
Normal weight, <i>n</i> (%)		55 (33.3)		55 (28.4)		89 (30.4)		185 (29.0)	
Overweight, <i>n</i> (%)		63 (38.2)		65 (33.5)		122 (41.6)		205 (32.1)	
Obese, <i>n</i> (%)		24 (14.5)		42 (21.6)		56 (19.1)		126 (19.7)	
Spirometry									
FEV 1 (% predicted)	165	51.6±13.7	194	47.2±17.8	293	57.8±20.3	638	58.0±18.8	<0.001
FEV 1 (Litres)	165	1.5±0.5	194	1.2±0.6	293	1.6±0.6	638	1.7±0.7	<0.001
FVC (Litres)	165	3.6±0.9	194	3.1±1.0	293	3.5±1.0	638	3.5±1.0	<0.001
GOLD, <i>n</i> (%)	165		194		293		638		
I		4 (2.4)				42 (14.3)		85 (13.3)	<0.001
II		82 (49.7)		90 (46.4)		136 (46.4)		323 (50.6)	

III		71 (43.0)		65 (33.5)		93 (31.7)		201 (31.5)	
IV		8 (4.8)		39 (20.1)		22 (7.5)		29 (4.5)	
Medications in use, <i>n</i>	-		194	7 (5-11)	-		-		-
Dyspnoea									
mMRC, points	-		194	3 (2-4)		550		1 (1-2)	<0.001
<2 mild dyspnoea, <i>n</i> (%)				44 (22.7)				302 (54.9)	<0.001
≥2 severe dyspnoea, <i>n</i> (%)				150 (77.3)				248 (45.1)	
Fatigue									
CIS-Fatigue, points	CIS-Fatigue, points	26 (19-34)	194	36 (29-42)	293	35 (27-43)	638	37 (28-48)	<0.001
Normal fatigue, <i>n</i> (%)	Normal fatigue, <i>n</i> (%)	88 (53.3)		35 (18.0)		70 (23.9)		136 (21.3)	<0.001
Mild fatigue, <i>n</i> (%)	Mild fatigue, <i>n</i> (%)	37 (22.4)		57 (29.4)		85 (29.0)		156 (24.5)	
Severe fatigue, <i>n</i> (%)	Severe fatigue, <i>n</i> (%)	40 (24.2)		102 (52.6)		138 (47.1)		346 (54.2)	
Exacerbations last 12 months, <i>n</i>	0		189	1 (0-3)	0		524	0 (0-2)	<0.001

Data are shown as mean±SD, median (IQR) or n(%). COPD, Chronic Obstructive Pulmonary Disease; BMI, Body Mass Index; FEV1 (% predicted), forced expiratory volume over 1 second of predicted; FVC, forced volume capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified Medical Research Council dyspnoea scale; CIS-Fatigue, Checklist Individual Strength subscale fatigue.

File S1: Checklist Individual Strength (CIS-Fatigue score)

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Dept. of Medical Psychology

Instruction: On the next page you find 8 statements. With these statements we wish to get an impression of how you have felt during the last twee weeks.

Yes, that is
true



No, that is
not true



1. I feel tired.							
2. Physically I feel exhausted.							
3. I feel fit.							
4. I feel powerless.							
5. I am rested.							
6. Physically I feel I am in a bad condition.							
7. I tire easily.							
8. Physically I feel I am in an excellent condition.							