

**CHARACTERISTICS, STABILITY AND OUTCOMES OF THE GOLD 2011
COPD GROUPS IN THE ECLIPSE COHORT**

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Table 1E: Distribution and outcomes during follow-up of the four GOLD 2011 groups by gender.

	MALES					FEMALES				
Distribution	Group A	Group B	Group C	Group D	Overall p value MALES	Group A	Group B	Group C	Group D	Overall p value FEMALES
N	304	187	334	550		191	106	149	280	
Percent	22%	14%	24%	40%		26%	15%	21%	39%	
Outcomes during follow-up (3 yrs)										
Mortality rate (%)	17 (6%)	19 (10%)	29 (9%)	78 (14%)	<0.001	5 (3%)	9 (8%)	12 (8%)	36 (13%)	0.002
ECOPD (per year)	0.5 (0.7)	0.7 (1.0)	1.2 (1.4)	1.6 (1.7)	<0.001	0.6 (0.8)	1.1 (1.0)	1.5 (1.4)	1.9 (1.6)	<0.001
≥1 Hospitalization (%)	30 (10%)	42 (23%)	106 (32%)	244 (45%)	<0.001	26 (14%)	29 (28%)	37 (25%)	134 (48%)	<0.001

Table 2E. Self-reported comorbidities, concomitant medication use and markers of systemic inflammation (median [IQR]) in the four GOLD 2011 groups.

	Group A	Group B	Group C	Group D	P value
Self-reported comorbidities					
Hypertension, %	213 (44%)	150 (53%)	153 (33%)	324 (41%)	<0.001
Angina, %	40 (9%)	45 (17%)	38 (8%)	90 (12%)	0.001
Heart attack, %	43 (9%)	35 (12%)	22 (5%)	80 (10%)	0.001
Stroke, %	15 (3%)	19 (7%)	16 (3%)	29 (4%)	0.053
Heart failure, %	24 (5%)	30 (11%)	19 (4%)	68 (9%)	<0.001
Arrhythmia, %	53 (11%)	35 (13%)	48 (10%)	103 (13%)	0.408
Osteoporosis, %	57 (12%)	42 (16%)	60 (13%)	118 (15%)	0.344
Osteoarthritis, %	66 (14%)	48 (18%)	54 (12%)	112 (14%)	0.144
Rheumatoid arthritis, %	10 (2%)	11 (4%)	17 (4%)	22 (3%)	0.374
Inflammatory bowel disorder, %	21 (4%)	20 (7%)	17 (4%)	42 (5%)	0.146
Diabetes, %	50 (10%)	44 (15%)	27 (6%)	92 (11%)	<0.001
Peptic ulcer, %	45 (10%)	37 (14%)	50 (11%)	83 (10%)	0.379
Reflux/heartburn, %	129 (27%)	96 (34%)	101 (21%)	215 (27%)	0.002
Depression requiring treatment,	62 (13%)	57 (20%)	68 (14%)	154 (19%)	0.005
Anxiety/panic attacks, %	57 (12%)	58 (20%)	56 (12%)	178 (22%)	<0.001
Concomitant Medications					
LABA use, %	250 (51%)	181 (62%)	347 (72%)	649 (78%)	<0.001
LABA Only, %	33 (7%)	20 (7%)	22 (5%)	30 (4%)	0.037
ICS use, %	256 (52%)	187 (64%)	364 (75%)	702 (85%)	<0.001
ICS Only, %	39 (8%)	26 (9%)	39 (8%)	83 (10%)	0.516
ICS+LABA, %	217 (44%)	161 (55%)	325 (67%)	619 (75%)	<0.001
Tiotropium use, %	159 (32%)	140 (48%)	219 (45%)	449 (54%)	<0.001
Statin use, %	112 (23%)	91 (31%)	96 (20%)	187 (23%)	0.004
Systemic Inflammation					
WBC, 10/L	7.1 [2.6]	7.8 [3.0]	7.5 [2.5]	7.9 [2.6]	<0.001
Neutrophils, %	62.5 [11.8]	65.4 [11.3]	65.0 [11.0]	66.8 [11.1]	<0.001
hsCRP, mg/L	2.5 [3.8]	4.0 [5.7]	2.7 [5.1]	4.0 [7.5]	<0.001
IL-6, pg/mL	1.1 [1.5]	1.9 [3.1]	1.4 [2.0]	1.8 [2.7]	<0.001
IL-8, pg/mL	6.7 [7.8]	9.6 [12.7]	6.4 [9.2]	7.4 [10.2]	<0.001
Fibrinogen, mg/dL	420.8 [113.0]	442.5	443.0	474.0	<0.001
TNF α , ng/mL	2.4 [33.7]	2.4 [20.0]	2.4 [3.7]	2.4 [2.5]	<0.001
CC-16, ng/mL	4.9 [3.6]	5.3 [4.2]	5.1 [3.3]	4.9 [3.4]	0.337
CCL-18, ng/mL	100.4 [49.1]	113.1 [60.7]	100.8 [48.6]	110.5 [58.6]	<0.001
SPD, ng/mL	118.9 [82.6]	111.2 [87.0]	121.2 [89.4]	120.2 [87.1]	0.381

LABA, long-acting β 2 agonist; ICS, Inhaled corticosteroids; WBC, white blood cells count; hsCRP, high sensitivity C-reactive protein, IL, interleukin; TNF α , tumor necrosis factor alpha; CC-16, clara cell 16 protein; CCL-18 Chemokine Ligand 18; SPD, surfactant protein D.

Table 3E: Mean (SD), median [IQR], or proportion of the main anthropometric, clinical, functional, radiological and systemic inflammatory variables, as well as outcomes at 3-years follow-up, of the three different C subgroups explored here (patients in C1 qualified because FEV₁<50% ref, patients in C2 qualified because they had more than 2 exacerbations in the previous year, and patients in C3 qualified based of both). For further explanations, see text. NS = non-significant

	C subgroups			p values
	C1	C2	C3	Overall
N	336	62	85	
Percent	70	13	18	
GOLD 2011 assessment variables				
mMRC dyspnoea score	0.8 (0.4)	0.8 (0.4)	0.8 (0.4)	NS
FEV ₁ % predicted post-	39.7 (7.6)	63.7 (8.7)	36.3 (8.5)	<0.001
ECOPD 12 months	0.3 (0.5)	2.5 (1.0)	2.8 (1.5)	<0.001
Demographics				
Age, years	63.2 (7.2)	61.8 (7.7)	62.3 (6.9)	NS
Female, %	28	44	32	NS
BMI, kg/m ²	25.1 (5.0)	25.9 (4.7)	25.2 (5.0)	NS
FFMI, kg/m ²	16.7 (2.5)	17.1 (2.6)	16.6 (2.4)	NS
Smoking, pack-years	45.3 (22.7)	46.1 (24.1)	44.2 (24.6)	NS
Current smoker, %	43	52	38	NS
Symptoms				
Chronic Bronchitis, %	38	45	33	NS
SGRQ-C Total Score	43.2 (17.0)	41.8 (14.9)	51.9 (15.2)	<0.001
CESD Total score	9.2 (8.2)	10.1 (7.4)	10.0 (8.9)	NS
Self-reported comorbidities				
Hypertension, %	35	30	29	NS
Angina, %	8	8	10	NS
Heart attack, %	5	0	7	NS
Stroke, %	3	7	4	NS
Heart failure, %	4	2	6	NS
Arrhythmia, %	10	8	12	NS
Osteoporosis, %	12	16	16	NS
Osteoarthritis, %	9	22	17	0.009
Rheumatoid arthritis, %	3	4	5	NS
Inflammatory bowel	3	3	6	NS
Diabetes, %	7	0	6	NS
Peptic ulcer, %	11	16	6	NS
Reflux/heartburn, %	20	32	20	NS
Depression requiring	14	15	15	NS
Anxiety/panic attacks,	11	14	13	NS
Concomitant medications				
LABA use, %	68	71	86	0.006

Tiotropium use, %	43	37	59	0.015
ICS use, %	72	71	93	<0.001
Statin use, %	21	19	18	NS
Physiology				
FEV ₁ % reversibility	10.1 (13.5)	8.7 (9.7)	12.1 (15.7)	NS
SaO ₂ , %	94.4 (3.0)	95.6 (2.2)	93.7 (4.4)	<0.001
6MWD, m	405 (108)	446 (97)	394 (97)	0.029
BODE Index	2.8 (1.0)	0.8 (0.8)	3.0 (1.0)	<0.001
Imaging				
%LAA, -950HU	19.9 (11.1)	10.7 (8.2)	21.3 (13.0)	<0.001
Systemic inflammation				
WBC, 10 ⁹ /l	7.6 [2.5]	7.6 [2.3]	7.4 [2.6]	NS
Neutrophils, %	65.5 [11.2]	62.1 [11.4]	66.3 [11.2]	0.002
hsCRP, mg/l	2.5 [4.2]	2.7 [5.7]	4.0 [5.9]	0.043
IL-6, pg/ml	1.4 [2.1]	1.2 [1.7]	1.4 [2.1]	NS
IL-8, pg/ml	6.4 [9.5]	6.6 [9.3]	6.7 [8.6]	NS
Fibrinogen, mg/dl	442.0	436.5	466.0	NS
TNFA, ng/ml	2.4 [0.0]	2.4 [51.4]	2.4 [4.8]	0.005
CC-16, ng/ml	5.1 [3.0]	4.6 [3.5]	5.4 [4.2]	NS
CCL-18, ng/ml	100.0 [48.8]	103.1 [48.2]	98.9 [49.6]	NS
SPD, ng/ml	118.4 [91.2]	120.4 [58.9]	133.1 [95.0]	NS
Outcomes during follow-up (3 years)				
Mortality rate, %	29 (9)	0	12 (14)	0.01
ECOPD, per year	1.1 (1.2)	1.6 (1.2)	2.1 (1.8)	<0.001
Rate of FEV ₁ decline,	-28.0 (47.6)	-38.1 (44.3)	-33.5 (36.8)	NS

Table 4E: Mean (SD), median [IQR], or proportion of the main anthropometric, clinical, functional, radiological and systemic inflammatory variables, as well as outcomes at 3-years follow-up, of the three different D subgroups explored here (patients in D1 qualified because FEV1<50% ref, patients in D2 qualified because they had more than 2 exacerbations in the previous year, and patients in D3 qualified based of both). For further explanations, see text. NS = non-significant.

	D subgroups			p values
	D1	D2	D3	Overall
N	522	72	236	
Percent	63	9	28	
GOLD 2011 assessment variables				
mMRC dyspnoea	2.5 (0.7)	2.5 (0.7)	2.7 (0.8)	NS
FEV ₁ % predicted	35.1 (8.7)	60.2 (9.3)	35.1 (8.5)	<0.001
ECOPD 12 months	0.4 (0.5)	2.8 (1.1)	2.9 (1.2)	<0.001
Demographics				
Age, years	63.7 (7.0)	63.5 (7.1)	63.5 (6.6)	NS
Female, %	28	57	39	<0.001
BMI, kg/m ²	26.3 (6.0)	29.0 (7.3)	26.3 (5.7)	0.012
FFMI, kg/m ²	17.0 (2.8)	17.9 (3.3)	17.0 (2.9)	NS
Smoking, pack-	51.5 (26.7)	50.3 (33.8)	50.6 (27.9)	NS
Current smoker, %	32	36	31	NS
Symptoms				
Chronic bronchitis,	37	39	40	NS
SGRQ-C Total	60.2 (15.8)	65.3 (15.3)	65.5 (14.4)	<0.001
CESD Total score	12.5 (9.2)	15.3 (10.5)	15.3 (10.0)	<0.001
Self-reported comorbidities				
Hypertension, %	41	42	41	NS
Angina, %	10	16	14	NS
Heart attack, %	9	15	10	NS
Stroke, %	3	7	3	NS
Heart failure, %	10	8	7	NS
Arrhythmia, %	12	19	14	NS
Osteoporosis, %	12	17	23	<0.001
Osteoarthritis, %	11	36	16	<0.001
Rheumatoid	2	5	3	NS
Inflammatory	5	12	4	0.046
Diabetes, %	12	15	9	NS
Peptic ulcer, %	9	11	12	NS
Reflux/heartburn,	23	49	30	<0.001
Depression	16	27	22	0.035
Anxiety/panic	19	32	26	0.015
Concomitant medications				
LABA use, %	73	81	88	<0.001

Tiotropium use, %	52	60	57	NS
ICS use, %	81	88	92	<0.001
Statin use, %	24	24	19	NS
Physiology				
FEV ₁ %	10.3 (14.7)	9.6 (10.9)	10.4 (15.2)	NS
SaO ₂ , %	93.6 (3.2)	95.1 (2.0)	93.7 (3.3)	<0.001
6MWD, m	313 (117)	320 (92)	289 (111)	0.015
BODE Index	5.1 (1.5)	3.3 (1.2)	5.5 (1.6)	<0.001
Imaging				
%LAA, -950HU	22.9 (13.2)	15.2 (9.8)	24.0 (11.9)	<0.001
Systemic inflammation				
WBC, 10 ⁹ /l	7.8 [2.6]	7.7 [2.7]	8.0 [2.6]	NS
Neutrophils, %	66.9 [11.3]	65.1 [12.7]	67.0 [10.5]	NS
hsCRP, mg/l	3.7 [7.5]	3.9 [6.3]	4.5 [7.8]	NS
IL-6, pg/ml	1.8 [2.7]	2.1 [2.4]	1.8 [2.9]	NS
IL-8, pg/ml	7.0 [10.6]	8.8 [10.4]	7.5 [9.1]	NS
Fibrinogen, mg/dl	470.0 [147.5]	457.3	483.0	0.042
TNFA, ng/ml	2.4 [2.7]	2.4 [7.4]	2.4 [0.0]	NS
CC-16, ng/ml	4.8 [3.4]	4.7 [3.4]	4.9 [3.4]	NS
CCL-18, ng/ml	107.1 [59.0]	109.9	114.0	NS
SPD, ng/ml	121.3 [85.0]	122.8	115.8	NS
Outcomes during follow-up (3 years)				
Mortality rate, %	72 (14)	8 (11)	34 (14)	NS
ECOPD, per year	1.2 (1.4)	2.1 (1.7)	2.6 (1.8)	<0.001
Rate of FEV ₁	-32.8	-31.0 (42.6)	-30.1	NS