

# Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: National Emphysema Treatment Trial Research Group. A Randomized Trial Comparing Lung-Volume-Reduction Surgery with Medical Therapy for Severe Emphysema. *N Engl J Med* 2003; 348:2059-73.

**Supplementary Appendix 1. Criteria for Inclusion and Exclusion.\*****Inclusion criteria**

History and physical exam consistent with emphysema

CT scan evidence of bilateral emphysema

Prerehabilitation postbronchodilator TLC  $\geq 100\%$  predicted

Prerehabilitation postbronchodilator RV  $\geq 150\%$  predicted

Prerehabilitation FEV<sub>1</sub> (maximum of pre- and postbronchodilator values)  $\leq 45\%$  of predicted and, if age  $\geq 70$  years prerehabilitation, FEV<sub>1</sub> (maximum of pre- and postbronchodilator values)  $\geq 15\%$  of predicted

Prerehabilitation room air, resting PaCO<sub>2</sub>  $\leq 60$  mm Hg ( $\leq 55$  mm Hg in Denver)

Prerehabilitation room air, resting PaO<sub>2</sub>  $\geq 45$  mm Hg ( $\geq 30$  mm Hg in Denver)

Prerehabilitation plasma cotinine  $\leq 13.7$  ng/ml (if not using nicotine products) or prerehabilitation arterial carboxyhemoglobin  $\leq 2.5\%$  (if using nicotine products)

Body-mass index  $\leq 31.1$  (males) or  $\leq 32.3$  (females) as of randomization

Nonsmoker (tobacco products) for 4 months prior to initial interview and patient remains a nonsmoker throughout screening (by history)

Approval for surgery by cardiologist if any of the following findings are noted prior to randomization (approval must be obtained prior to randomization):

- Unstable angina
- Left ventricular ejection fraction cannot be estimated from the echocardiogram
- Left ventricular ejection fraction  $< 45\%$
- Dobutamine-radionuclide cardiac scan indicates coronary artery disease or ventricular dysfunction
- $> 5$  premature ventricular beats/minute (does not apply during exercise testing)
- Cardiac rhythm other than sinus or premature atrial contractions noted during resting EKG
- S<sub>3</sub> gallop on physical examination

Completion of all prerehabilitation assessments

Judgment by study physician that patient is likely to be approved for surgery upon completion of the rehabilitation program

Completion of NETT rehabilitation program

Completion of all postrehabilitation and all randomization assessments

Approval for surgery by pulmonary physician and thoracic surgeon in consultation with the anesthesiologist, postrehabilitation and just prior to randomization

Consent

**Supplementary Appendix 1. (Continued.)****Exclusion criteria**

Postrehabilitation, postbronchodilator FEV<sub>1</sub>  $\leq 20\%$  predicted and either non-heterogeneous emphysema on CT scan or D<sub>L</sub>CO  $\leq 20\%$  predicted (enacted May 2001)

Inability to provide a valid D<sub>L</sub>CO measurement (enacted May 2001)

CT scan evidence of diffuse emphysema judged unsuitable for LVRS

Previous lung volume reduction surgery (laser or excision)

Pleural or interstitial disease which precludes surgery

Giant bulla ( $\geq 1/3$  of the volume of the lung in which the bulla is located)

Clinically significant bronchiectasis

Pulmonary nodule requiring surgery

Previous sternotomy or lobectomy

Myocardial infarction within 6 months of interview and ejection fraction  $< 45\%$

Congestive heart failure within 6 months of interview and ejection fraction  $< 45\%$

Uncontrolled hypertension (systolic  $> 200$  mm Hg or diastolic  $> 110$  mm Hg)

Pulmonary hypertension: mean P<sub>PA</sub> on right heart catheterization  $\geq 35$  mm Hg ( $\geq 38$  mm Hg in Denver) or peak systolic P<sub>PA</sub> on right heart catheterization  $\geq 45$  mm Hg ( $\geq 50$  mm Hg in Denver); right heart catheterization is required to rule out pulmonary hypertension if peak systolic P<sub>PA</sub> on echocardiogram  $> 45$  mm Hg

Unplanned, unexplained weight loss  $> 10\%$  usual weight in 90 days prior to interview or unplanned, explained weight loss  $> 10\%$  usual weight in 90 days prior to interview that is judged likely to interfere with completion of the trial

History of recurrent infections with daily sputum production judged clinically significant

Daily use of more than 20 mg of prednisone or its equivalent as of randomization

History of exercise-related syncope

Resting bradycardia ( $< 50$  beats/min), frequent multifocal PVCs, or complex ventricular arrhythmia or sustained SVT

Other cardiac dysrhythmia which, in the judgment of the supervising physician, might pose a risk to the patient during exercise testing or training

Oxygen requirement during resting or Part 1 oxygen titration exceeding 6 L/min to keep saturation  $\geq 90\%$

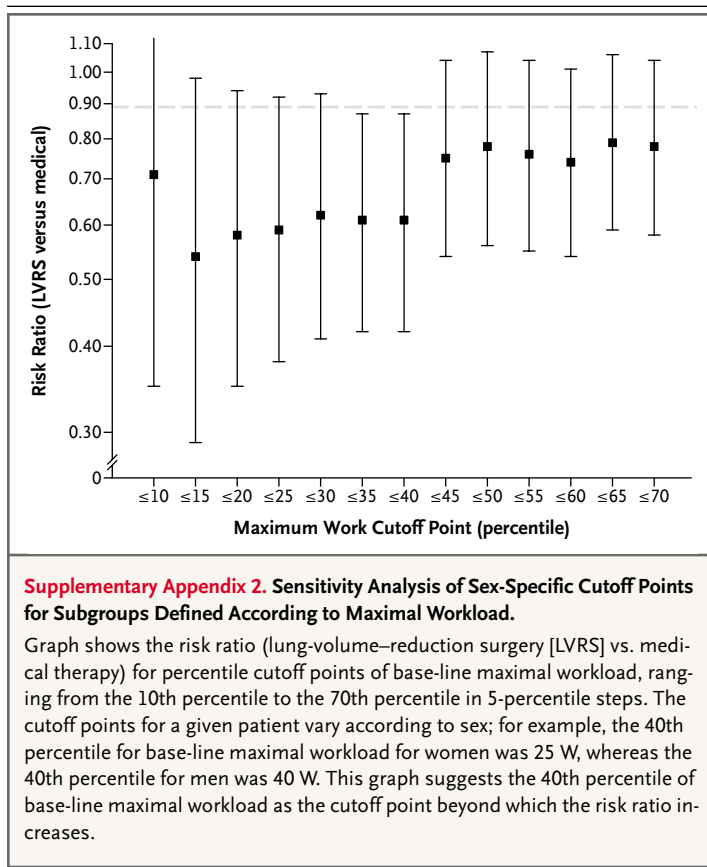
Evidence of systemic disease or neoplasia that is expected to compromise survival over the duration of the trial

Any disease or condition which may interfere with completion of tests, therapy, or follow-up

Six-minute walk distance  $\leq 140$  m postrehabilitation

Inability to complete successfully any of the screening or base-line data collection procedures (e.g., hypoxemia to SpO<sub>2</sub>  $< 80\%$  within 2 minutes of unloaded pedaling despite supplemental oxygen, inability to coordinate a regular cadence of  $> 40$  cpm, inability to complete 3 minutes unloaded pedaling, claudication, lower extremity or back orthopedic problems that prohibit sustained pedaling)

\* CT denotes computed tomography, TLC total lung capacity, FEV<sub>1</sub> forced expiratory volume in one second, PaCO<sub>2</sub> partial pressure of arterial carbon dioxide, PaO<sub>2</sub> partial pressure of arterial oxygen, EKG electrocardiogram, D<sub>L</sub>CO carbon monoxide diffusing capacity, LVRS lung-volume-reduction surgery, P<sub>PA</sub> pulmonary-artery pressure, PVC premature ventricular contraction, SVT supraventricular tachycardia, and SpO<sub>2</sub> oxygen saturation by pulse oximetry. The body-mass index is the weight in kilograms divided by the square of the height in meters.



## Supplementary Appendix 3. Postrehabilitation Base-Line Characteristics of Non-High-Risk Patients.\*

Characteristic	All Non-High-Risk Patients		Patients with Upper-Lobe Predominance				Patients with Non-Upper-Lobe Predominance			
	Surgery (N=538)	Medical Therapy (N=540)	Surgery, Low Exercise Capacity (N=139)	Medical Therapy, Low Exercise Capacity (N=151)	Surgery, High Exercise Capacity (N=206)	Medical Therapy, High Exercise Capacity (N=213)	Surgery, Low Exercise Capacity (N=84)	Medical Therapy, Low Exercise Capacity (N=65)	Surgery, High Exercise Capacity (N=109)	Medical Therapy, High Exercise Capacity (N=111)
Age at randomization — yr	67.0±6.2	67.1±5.8	67.2±5.2	67.6±5.4	66.6±6.4	66.5±5.6	67.4±6.7	69.0±5.5	67.3±6.4	66.4±6.6
Race or ethnic group — no. (%)										
Non-Hispanic white	513 (95)	511 (95)	130 (94)	142 (94)	199 (97)	201 (94)	77 (92)	61 (94)	107 (98)	107 (96)
Non-Hispanic black	17 (3)	18 (3)	7 (5)	5 (3)	2 (1)	7 (3)	7 (8)	4 (6)	1 (1)	2 (2)
Other	8 (1)	11 (2)	2 (1)	4 (3)	5 (2)	5 (2)	0 (0)	0 (0)	1 (1)	2 (2)
Sex — no. (%)†										
Female	235 (44)	200 (37)	63 (45)	51 (34)	88 (43)	85 (40)	38 (45)	25 (38)	46 (42)	39 (35)
Male	303 (56)	340 (63)	76 (55)	100 (66)	118 (57)	128 (60)	46 (55)	40 (62)	63 (58)	72 (65)
Distribution of emphysema on CT — no. (%)‡										
Upper-lobe predominance	345 (64)	364 (67)	139 (100)	151 (100)	206 (100)	213 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Non-upper-lobe predominance	193 (36)	176 (33)	0 (0)	0 (0)	0 (0)	0 (0)	84 (100)	65 (100)	109 (100)	111 (100)
Heterogeneous	306 (57)	314 (58)	103 (74)	110 (73)	147 (71)	144 (68)	27 (32)	21 (32)	29 (27)	39 (35)
Homogeneous	232 (43)	226 (42)	36 (26)	41 (27)	59 (29)	69 (32)	57 (68)	44 (68)	80 (73)	72 (65)
Perfusion ratio§	0.30±0.22	0.29±0.23	0.23±0.13	0.20±0.11	0.23±0.14	0.22±0.12	0.48±0.34	0.40±0.20	0.40±0.19	0.47±0.37
Maximal workload — W	40.0±21.1	41.3±22.3	22.4±11.5	22.8±11.8	51.2±17.8	52.5±19.1	25.0±9.7	23.3±9.4	53.2±19.9	56.2±19.3
Distance walked in 6 min — ft	1239.4±307.5	1247.8±309.9	1075.2±277.1	1058.4±244.0	1352.9±280.9	1346.0±289.1	1112.7±275.7	1075.8±272.4	1332.1±288.9	1417.7±265.7
FEV <sub>1</sub> after bronchodilator use — % of predicted value	28.1±6.8	27.9±6.5	25.4±6.8	25.2±6.1	29.5±6.5	29.1±6.6	25.9±5.9	26.6±6.0	30.7±6.4	30.0±5.7
Total lung capacity after bronchodilator use — % of predicted value	127.4±15.0	127.6±14.1	128.0±14.1	127.2±15.3	125.1±14.3	126.6±13.5	130.7±17.8	131.6±15.9	128.4±14.8	127.6±12.1
Residual volume after bronchodilator use — % of predicted value	214.4±45.6	216.7±43.8	223.5±43.3	226.0±48.2	206.6±42.0	210.2±39.2	227.9±57.4	226.3±45.7	207.2±40.5	211.1±42.0
Carbon monoxide diffusing capacity — % of predicted value	29.2±9.3	29.4±9.5	26.0±8.5	26.0±8.4	31.2±8.4	31.0±9.3	27.0±9.3	26.8±9.0	31.3±10.5	32.7±9.7
PaO <sub>2</sub> — mm Hg	65.0±10.6	64.8±10.1	63.8±10.0	63.6±10.5	66.1±10.7	66.2±9.7	63.6±11.7	63.3±10.0	65.7±10.1	64.7±10.2
PaCO <sub>2</sub> — mm Hg	42.8±5.7	42.4±5.5	43.9±6.2	43.2±5.7	42.6±5.8	42.5±5.6	42.6±5.8	42.8±5.2	42.1±4.6	41.1±5.1
St. George's Respiratory total score¶	52.2±12.8	53.2±12.8	54.3±12.1	57.0±12.4	51.2±12.5	50.8±12.5	56.2±13.2	55.5±12.8	48.1±12.6	51.4±12.8
Quality of Well-Being average daily score	0.58±0.12	0.57±0.11	0.57±0.12	0.54±0.12	0.59±0.12	0.58±0.11	0.56±0.11	0.55±0.11	0.60±0.11	0.59±0.11
UCSD Shortness of Breath total score**	60.7±18.3	62.3±18.8	64.5±16.9	71.0±15.9	59.0±17.7	57.1±18.6	68.3±17.7	68.5±17.2	53.3±18.2	56.8±18.1

\* Base-line measurements were obtained after rehabilitation but before randomization, except for carbon monoxide diffusing capacity, which was obtained before rehabilitation. Plus-minus values are means ±SD. High-risk patients were defined as those with a forced expiratory volume in one second (FEV<sub>1</sub>) that was 20 percent or less of the predicted value and either homogeneous emphysema or a carbon monoxide diffusing capacity that was 20 percent or less of the predicted value. CT denotes computed tomography, PaO<sub>2</sub> the partial pressure of arterial oxygen, and PaCO<sub>2</sub> the partial pressure of arterial carbon dioxide.

† Among non-high-risk patients, P for homogeneity=0.03. Among patients with upper-lobe predominance and low exercise capacity, P for homogeneity=0.04.

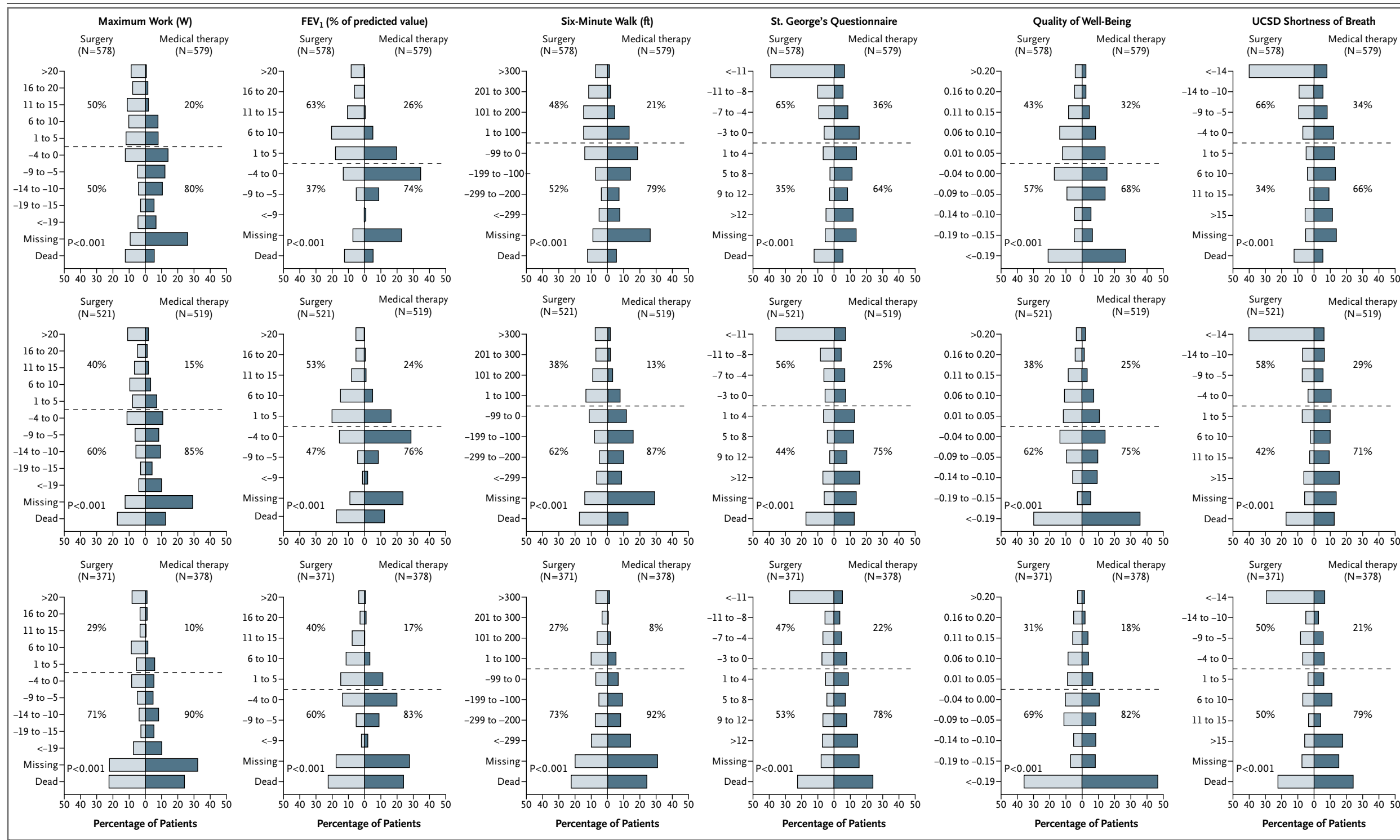
‡ Upper-lobe predominance of emphysema was judged subjectively by each center's radiologist; choices were upper-lobe predominance, lower-lobe predominance, diffuse, or superior segments of lower lobes predominantly involved; the latter three choices were grouped as non-upper-lobe predominance. The heterogeneity of the emphysema was based on subjective scores assigned by each center's radiologist to each of three zones in each lung.

§ The perfusion ratio was derived from the radionuclide perfusion scan. Each lung is divided into three zones; a percentage of total perfusion is assigned to each zone. The ratio is calculated as the sum of the percentages assigned to the two upper zones divided by the sum of the percentages assigned to the four middle and lower zones.

¶ The St. George's Respiratory Questionnaire is a 51-item health-related quality-of-life questionnaire about respiratory symptoms that is completed by the patient; the total score ranges from 0 to 100, and lower scores indicate better health-related quality of life.

|| The Quality of Well-Being scale is a 77-item questionnaire on quality of life that is completed by the patient. The average daily total score ranges from 0 to 1, with higher scores indicating better quality of life.

\*\* The UCSD Shortness of Breath Questionnaire is a 24-item questionnaire on shortness of breath (dyspnea) that is completed by the patient; the total score ranges from 0 to 120, and lower scores indicate less shortness of breath.



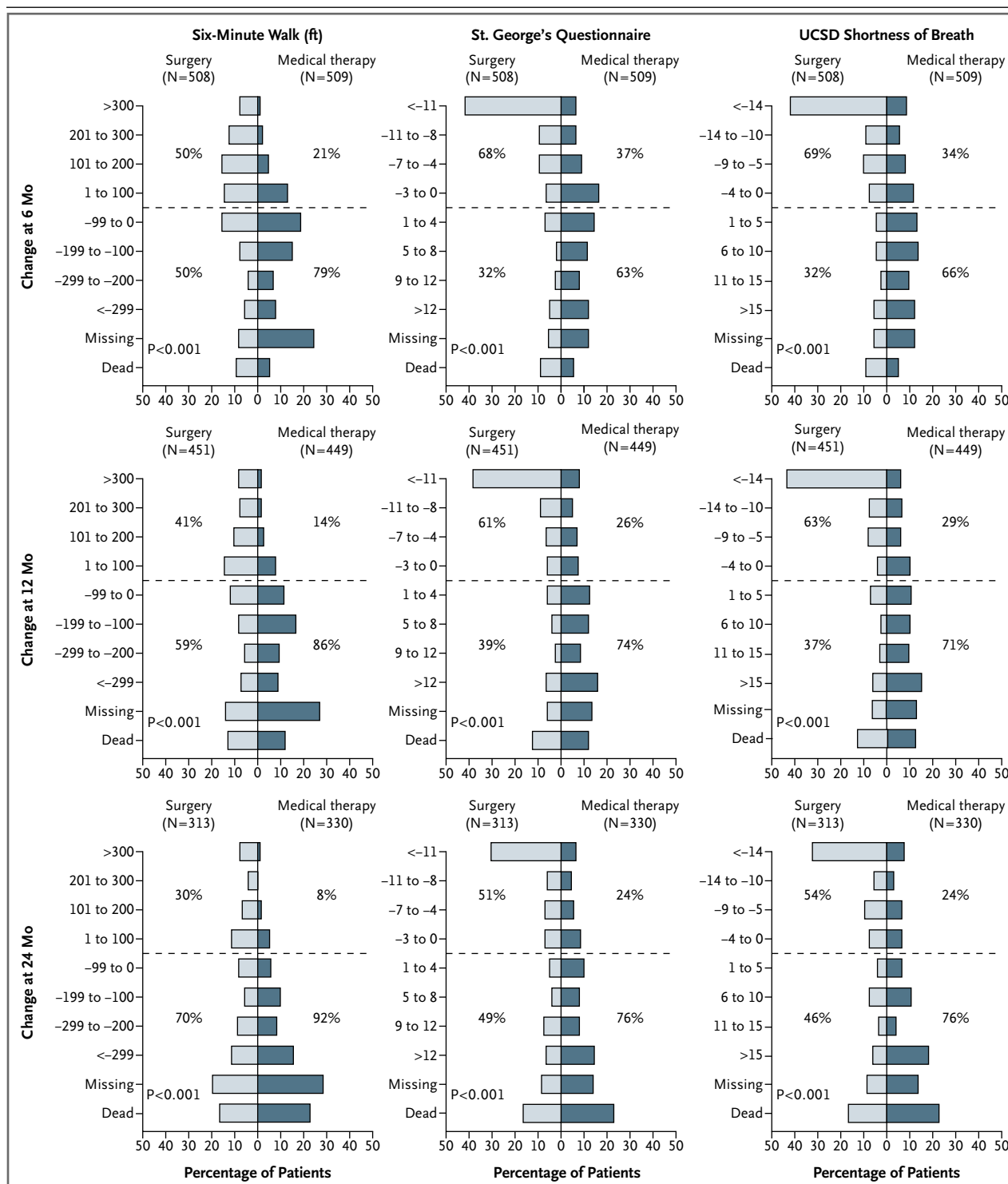
**Supplementary Appendix 4. Histograms of Changes from Postrehabilitation Base Line in Exercise Capacity (Maximal Workload), Percentage of Predicted Value for Forced Expiratory Volume in One Second (FEV<sub>1</sub>), Distance Walked in Six Minutes, Health-Related Quality of Life (St. George's Respiratory Questionnaire), Quality of Life (Quality of Well-Being Scale), and Dyspnea (UCSD Shortness of Breath Questionnaire) after 6, 12, and 24 Months of Follow-up.**

The category "missing" includes patients who were too ill to complete the procedure or who declined to complete the procedure but did not explain why. For the Quality of Well-Being scale, patients who died were assigned a score of 0 on the questionnaire for the visit, and patients who did not complete the questionnaire were assigned a score equal to half of the lowest score observed for the visit. P values were determined by the Wilcoxon rank-sum test. The degree to which the bars are shifted to the upper left of the chart indicates the degree of a relative benefit of lung-volume-reduction surgery (LVRS) over medical treatment. The percentage shown in each quadrant is the percentage of patients in the specified treatment group with a change in the outcome falling into that quadrant. This was an intention-to-treat analysis.

Supplementary Appendix 5. Patient's Place of Residence According to the Time since Randomization.*												
Variable	All Patients		Non-High-Risk Patients		Upper-Lobe Predominance, Low Exercise Capacity		Upper-Lobe Predominance, High Exercise Capacity		Non-Upper-Lobe Predominance, Low Exercise Capacity		Non-Upper-Lobe Predominance, High Exercise Capacity	
	Surgery	Medical Therapy	Surgery	Medical Therapy	Surgery	Medical Therapy	Surgery	Medical Therapy	Surgery	Medical Therapy	Surgery	Medical Therapy
<b>1 Mo</b>												
Private home (%)	66.8	97.5	69.7	97.6	65.5	97.4	74.3	96.7	66.7	100	68.8	98.2
Nursing home or rehabilitation facility (%)	0.7	0	0.6	0	0.7	0	0.5	0	1.2	0	0	0
Acute care hospital (%)	24.0	0.3	23.1	0.4	29.5	0.7	19.4	0.5	21.4	0	22.9	0
Living, no data (%)	4.9	2.0	4.5	1.9	2.9	2.0	3.9	2.8	7.1	0	5.5	0.9
Dead (%)	3.6	0.2	2.2	0.2	1.4	0	1.9	0	3.6	0	2.8	0.9
No. of patients	608	610	538	540	139	151	206	213	84	65	109	111
P value	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Median time since surgery (mo)	0.7		0.7		0.8		0.7		0.8		0.7	
<b>2 Mo</b>												
Private home (%)	78.3	96.1	80.9	95.9	77.0	93.4	83.0	96.2	78.6	98.5	83.5	97.3
Nursing home or rehabilitation facility (%)	0.7	0.2	0.7	0.2	2.2	0	0	0.5	1.2	0	0	0
Acute care hospital (%)	8.4	0.3	8.6	0.2	13.0	0	8.7	0	7.1	1.5	3.7	0
Living, no data (%)	5.8	2.8	5.0	3.0	5.0	4.6	5.8	3.3	6.0	0	2.8	1.8
Dead (%)	6.9	0.7	4.8	0.7	2.9	2.0	2.4	0	7.1	0	10.1	0.9
No. of patients	608	610	538	540	139	151	206	213	84	65	109	111
P value	<0.001		<0.001		<0.001		<0.001		<0.001		0.001	
Median time since surgery (mo)	1.7		1.7		1.8		1.7		1.7		1.7	
<b>4 Mo</b>												
Private home (%)	84.5	94.3	87.7	94.6	90.7	91.4	90.3	95.3	79.8	98.5	85.3	95.5
Nursing home or rehabilitation facility (%)	0.8	0.2	0.9	0.2	1.4	0.7	0.5	0	2.4	0	0	0
Acute care hospital (%)	1.8	0.5	2.0	0.6	2.9	0	1.5	0.5	3.6	0	0.9	1.8
Living, no data (%)	4.4	2.8	3.7	2.4	2.2	4.0	3.9	2.4	6.0	0	3.7	1.8
Dead (%)	8.4	2.3	5.6	2.2	2.9	4.0	3.9	1.9	8.3	1.5	10.1	0.9
No. of patients	608	610	538	540	139	151	206	213	84	65	109	111
P value	<0.001		<0.001		0.89		0.05		0.001		0.008	
Median time since surgery (mo)	3.7		3.7		3.7		3.6		3.6		3.7	

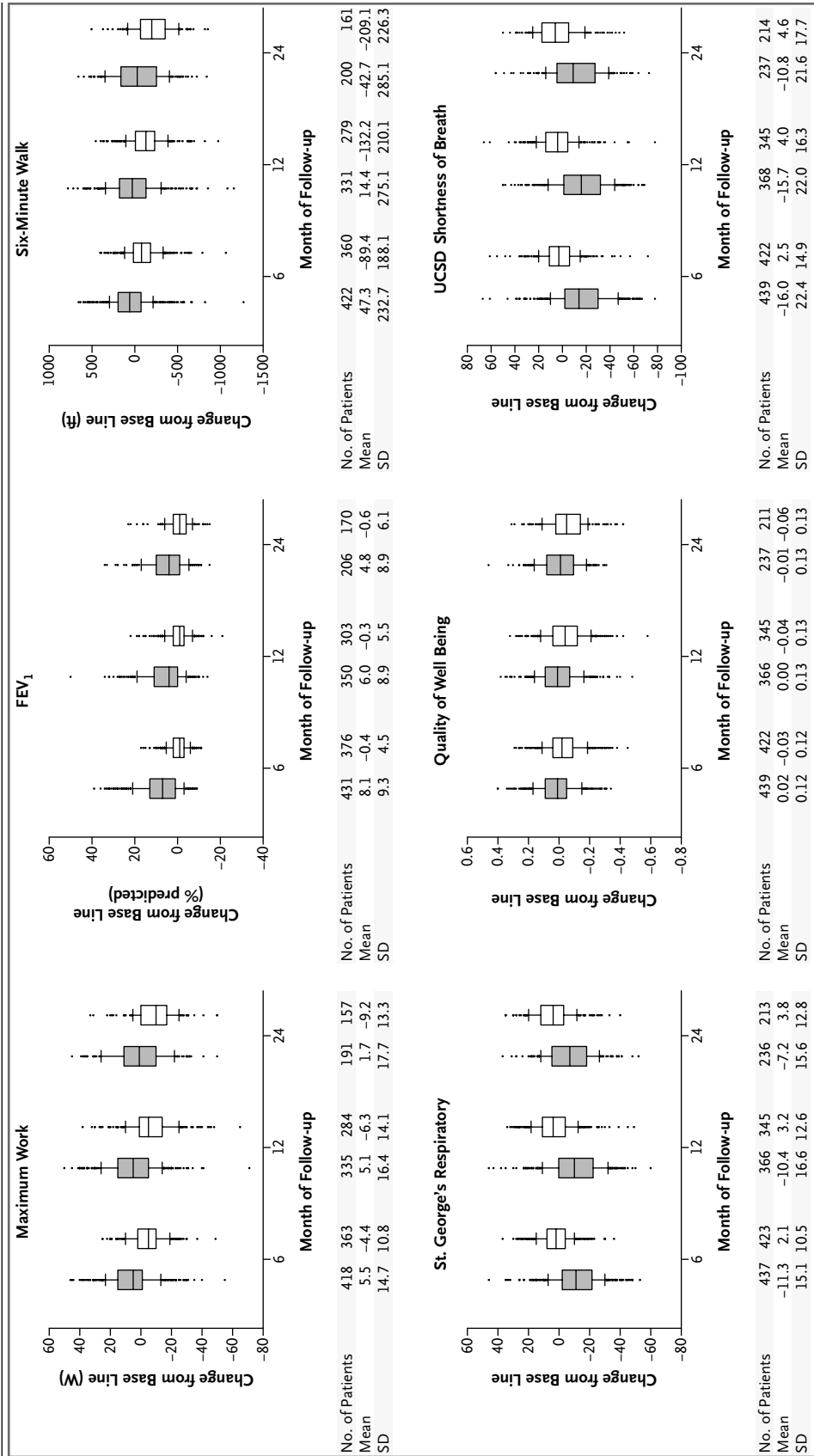
Supplementary Appendix 5. (Continued.)												
Variable	All Patients		Non-High-Risk Patients		Upper-Lobe Predominance, Low Exercise Capacity		Upper-Lobe Predominance, High Exercise Capacity		Non-Upper-Lobe Predominance, Low Exercise Capacity		Non-Upper-Lobe Predominance, High Exercise Capacity	
	Surgery	Medical Therapy	Surgery	Medical Therapy	Surgery	Medical Therapy	Surgery	Medical Therapy	Surgery	Medical Therapy	Surgery	Medical Therapy
<b>8 Mo</b>												
Private home (%)	85.3	90.9	88.6	91.2	89.5	84.8	91.2	94.0	86.4	89.2	84.5	96.0
Nursing home or rehabilitation facility (%)	0.5	0.2	0.6	0.2	1.5	0.7	0	0	1.2	0	0	0
Acute care hospital (%)	0.7	0.5	0.8	0.4	0.8	0	0.5	1.0	1.2	0	1.0	0
Living, no data (%)	2.2	3.1	2.0	3.1	3.0	4.8	2.6	2.5	0	3.1	1.0	2.0
Dead (%)	11.2	5.3	8.0	5.1	5.3	9.7	5.7	2.5	11.1	7.7	13.6	2.0
No. of patients	580	582	510	512	133	145	193	201	81	65	103	101
P value	0.002		0.16		0.22		0.26		0.60		0.005	
Median time since surgery (mo)	7.7		7.8		7.7		7.8		7.7		7.7	
<b>18 Mo</b>												
Private home (%)	78.4	83.8	83.0	84.3	87.3	77.2	84.4	90.9	76.7	74.1	80.0	87.5
Nursing home or rehabilitation facility (%)	0.2	0.6	0.2	0.7	0.9	1.6	0	0.5	0	0	0	0
Acute care hospital (%)	0.6	0.8	0.7	0.7	0	0.8	1.2	0.5	1.4	0	0	1.3
Living, no data (%)	3.3	2.1	2.9	2.0	2.5	0.8	3.0	1.6	2.7	1.7	3.3	5.0
Dead (%)	17.6	12.8	13.2	12.3	9.3	19.5	11.4	6.5	19.2	24.1	16.7	6.3
No. of patients	518	517	448	447	118	123	167	186	73	58	90	80
P value	0.02		0.60		0.04		0.06		0.67		0.14	
Median time since surgery (mo)	17.7		17.7		17.7		17.7		17.7		17.8	
<b>27 Mo</b>												
Private home (%)	73.8	72.8	79.1	74.9	81.1	61.2	79.0	83.1	75.9	61.9	78.9	85.5
Nursing home or rehabilitation facility (%)	0.3	0.8	0.3	0.6	1.1	1.0	0	0.7	0	0	0	0
Acute care hospital (%)	0.8	0.5	0.6	0.6	1.1	1.0	0	0.7	1.9	0	0	0
Living, no data (%)	4.2	4.0	4.4	3.7	4.4	4.1	7.3	3.4	1.9	0	1.4	6.5
Dead (%)	21.0	22.0	15.6	20.3	12.2	32.7	13.7	12.2	20.4	38.1	19.7	8.1
No. of patients	401	401	339	350	90	98	124	148	54	42	71	62
P value	0.74		0.16		0.002		0.41		0.11		0.25	
Median time since surgery (mo)	26.7		26.8		26.7		26.8		26.6		26.9	

\* High-risk patients had a forced expiratory volume in one second that was 20 percent or less of the predicted value and either homogeneous emphysema or a carbon monoxide diffusing capacity that was 20 percent or less of the predicted value. Upper-lobe predominance of emphysema was judged subjectively by each center's radiologist; choices were upper-lobe predominance, lower-lobe predominance, diffuse, or superior segments of lower lobes predominantly involved; the latter three choices were grouped as non-upper-lobe predominance. A low base-line exercise capacity was defined as a postrehabilitation base-line maximal workload at or below the sex-specific 40th percentile (25 W for women and 40 W for men); a high exercise capacity was defined as a workload above this threshold. All subgroup analyses excluded high-risk patients. P values are for homogeneity.



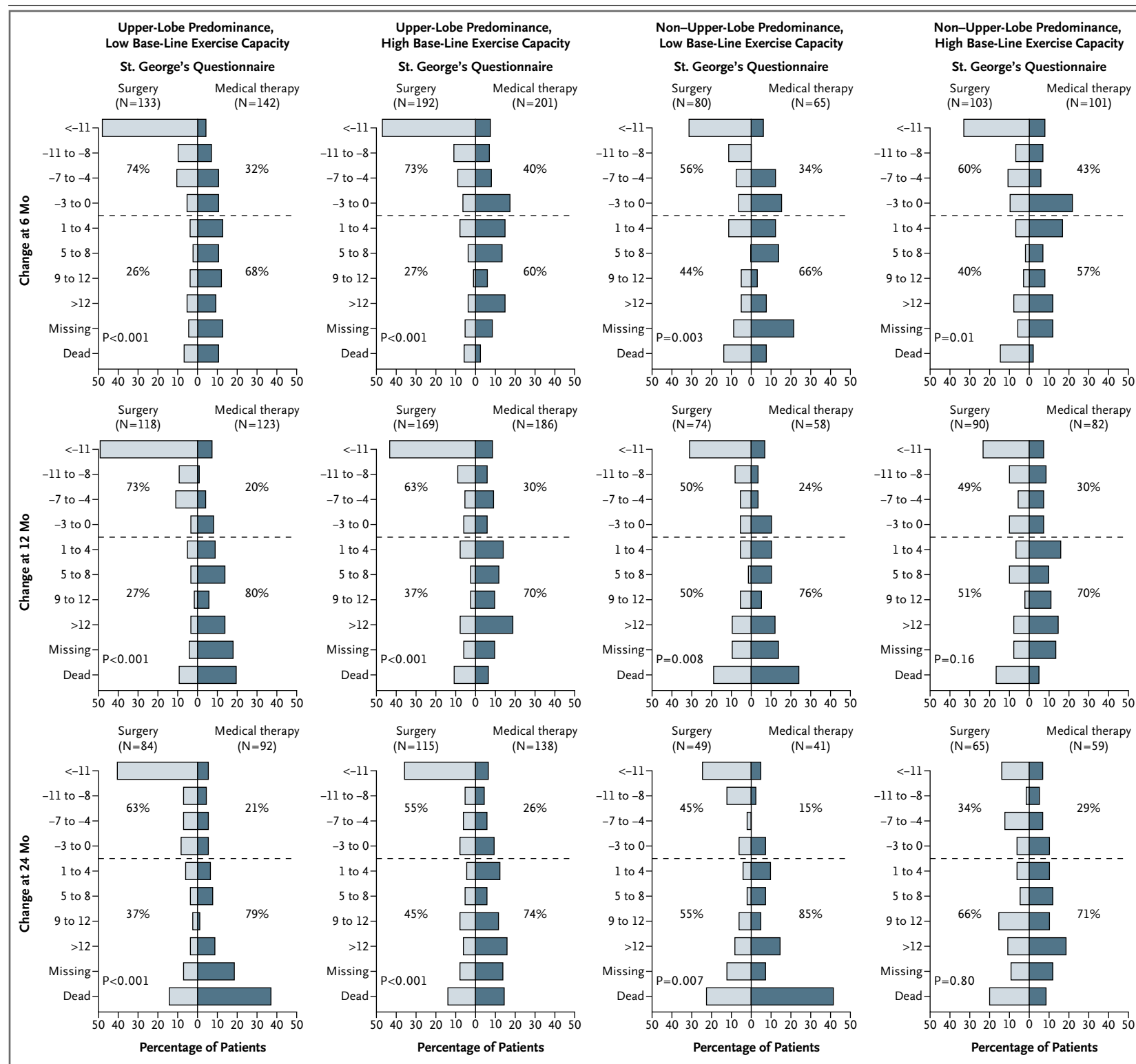
**Supplementary Appendix 6.** Histograms of Changes from Postrehabilitation Base Line in Distance Walked in Six Minutes, Health-Related Quality of Life (St. George's Respiratory Questionnaire), and Dyspnea (UCSD Shortness of Breath Questionnaire) after 6, 12, and 24 Months of Follow-up.

High-risk patients were excluded. The category "missing" includes patients who were too ill to complete the procedure or who declined to complete the procedure but did not explain why. P values were determined by the Wilcoxon rank-sum test. The degree to which the bars are shifted to the upper left of the chart indicates the degree of relative benefit of lung-volume-reduction surgery (LVRS) over medical treatment. The percentage shown in each quadrant is the percentage of patients in the specified treatment group with a change in the outcome falling into that quadrant. High-risk patients had an FEV<sub>1</sub> that was 20 percent or less of the predicted value and either homogeneous emphysema or a carbon monoxide diffusing capacity that was 20 percent or less of the predicted value. This was an intention-to-treat analysis.



**Supplementary Appendix 7. Box Plots of Changes from Postrehabilitation Base Line in Exercise Capacity (Maximal Workload), Percentage of the Predicted Value for Forced Expiratory Volume in One Second (FEV<sub>1</sub>), Distance Walked in Six Minutes, Health-Related Quality of Life (St. George's Respiratory Questionnaire), General Quality of Life (Quality of Well-Being Scale), and Dyspnea (UCSD Shortness of Breath Questionnaire), among Patients who Completed the Procedure after 6, 12, or 24 Months of Follow-up.**

High-risk patients were excluded. Solid boxes represent patients assigned to lung-volume–reduction surgery (LVRS); open boxes represent patients assigned to medical therapy. The line inside each box indicates the median value, the top and bottom of each box indicate the 1st and 3rd quartiles, and the tails of the boxes extend to the most extreme values not considered to be outliers. Values outside the tails of the box plot are considered to be outliers. High-risk patients had an FEV<sub>1</sub> that was 20 percent or less of the predicted value and either homogeneous emphysema or a carbon monoxide diffusing capacity that was 20 percent or less of the predicted value. This was not an intention-to-treat analysis, since it was limited to surviving patients.



**Supplementary Appendix 8. Histograms of Changes in Health-Related Quality of Life (St. George's Respiratory Questionnaire) after 6, 12, and 24 Months of Follow-up among Subgroups of Non-High-Risk Patients.**

The category "missing" includes patients who were too ill to complete the procedure or who declined to complete the procedure but did not explain why. P values were determined by the Wilcoxon rank-sum test; the degree to which the bars are shifted to the upper left of the chart indicates the degree of relative benefit of lung-volume-reduction surgery (LVRS) over medical treatment. The percentage shown in each quadrant is the percentage of patients in the specified treatment group with a change in outcome falling into that quadrant. High-risk patients had a forced expiratory volume in one second that was 20 percent or less of the predicted value and either homogeneous emphysema or a carbon monoxide diffusing capacity that was 20 percent or less of the predicted value. Low base-line exercise capacity was defined as a maximal workload at or below the sex-specific 40th percentile (25 W for women, 40 W for men); high exercise capacity was defined as a workload above this threshold. This was an intention-to-treat analysis.