

Table 1: Tests Using Only the Last Assessment

Model <sup>2</sup>	Treatment Effect Estimates <sup>1</sup>					
	6-Minute Walk Test			Forced Vital Capacity		
	Mean	SE	Z-Score	Mean	SE	Z-Score
1. T-Test	0.41	0.19	2.14	0.27	0.10	2.81
2. Wilcoxon	0.28	0.14	2.03	0.25	0.11	2.26
3. ANOVA	0.41	0.19	2.14	0.27	0.10	2.79
4. ANCOVA <sup>3</sup>	0.40	0.20	2.04	0.24	0.09	2.54
5. ANCOVA <sup>4</sup>	0.41	0.19	2.16	0.25	0.09	2.76
6. ANCOVA <sup>5</sup>	0.40	0.18	2.16	0.25	0.08	2.98
7. ANCOVA <sup>6</sup>	0.36	0.20	1.85	0.20	0.08	2.63
8. Augmentation (1) <sup>7</sup>	0.44	0.19	2.28	0.23	0.09	2.52
9. Augmentation (2) <sup>7</sup>	0.43	0.19	2.23	0.23	0.09	2.56

Notes:

1. Treatment effect estimates and standard errors were pooled across trials, after standardizing by the baseline standard deviation of the outcome measure within each trial. The reported mean treatment effect and SE are therefore expressed as proportions of the baseline variation.
2. The outcome measure is change from baseline to endpoint in all models.
3. Adjusted for baseline score for the outcome measure.
4. Adjusted for baseline score for the outcome measure and study center.
5. Adjusted for baseline score for the outcome measure, age and gender.
6. Adjusted for baseline score for the outcome measure, age, gender, weight, height, 6- and 12-minute walk test, forced vital capacity, apnea/hypopnea index and shoulder flexion (as available in each trial).
7. All baseline variables listed above were considered as auxiliary covariates. Augmentation in each arm used either the single best predictor of the outcome (1) or a model based on forward stepwise selection (2) chosen to optimize Mallows's Cp. Tsiatis, A.A., Davidian, M., Zhang, M., and Lu, X. (2008). Covariate adjustment for two-sample treatment comparisons in randomized clinical trials: A principled yet flexible approach. *Statistics in Medicine* 27, 4658–4677.

Table 2: Longitudinal Models

Model	Specification				Treatment Effect Estimates <sup>5</sup>					
	Working Correlation <sup>1</sup>	Model for Effect of Time <sup>2</sup>	Time of Treatment Effect Assessment <sup>3</sup>	Included Visits <sup>4</sup>	6-Minute Walk Test			Forced Vital Capacity		
					Mean	SE	Z-Score	Mean	SE	Z-Score
<i>No baseline adjustment</i>										
10. Unstructured	Unstructured	None	Average	All	0.28	0.14	1.97	0.17	0.08	2.18
11. Toeplitz	Toeplitz	None	Average	All	0.28	0.15	1.91	0.18	0.07	2.45
12. CS	Compound Symmetry	None	Average	All	0.28	0.14	2.04	0.17	0.08	2.17
13. CS, Categorical	Compound Symmetry	Categorical	Last Visit	All	0.41	0.19	2.15	0.27	0.09	2.84
14. CS, Linear	Compound Symmetry	Linear	Last Visit	All	0.32	0.18	1.75	0.16	0.08	1.98
15. CS, Quadratic	Compound Symmetry	Quadratic	Last Visit	All	0.32	0.18	1.79	0.16	0.07	2.15
<i>Adjusted for baseline score for the outcome measure</i>										
16. Unstructured	Unstructured	None	Average	All	0.29	0.13	2.14	0.18	0.06	3.16
17. Toeplitz	Toeplitz	None	Average	All	0.29	0.14	2.10	0.17	0.06	2.99
18. CS	Compound Symmetry	None	Average	All	0.29	0.13	2.23	0.17	0.06	3.06
19. CS, Categorical	Compound Symmetry	Categorical	Last Visit	All	0.42	0.18	2.33	0.26	0.08	3.12
20. CS, Linear	Compound Symmetry	Linear	Last Visit	All	0.32	0.17	1.92	0.15	0.06	2.31
21. CS, Quadratic	Compound Symmetry	Quadratic	Last Visit	All	0.33	0.16	1.98	0.17	0.07	2.45
22. Unstructured, Last Two	Unstructured	None	Average	Last Two	0.37	0.16	2.35	0.18	0.08	2.32
23. CS, Last Two	Compound Symmetry	None	Average	Last Two	0.37	0.16	2.29	0.18	0.08	2.34
<i>Adjusted for baseline score for the outcome measure, age and gender</i>										
24. Unstructured	Unstructured	None	Average	All	0.28	0.14	2.03	0.16	0.06	2.73
25. Toeplitz	Toeplitz	None	Average	All	0.28	0.14	1.98	0.17	0.06	2.93
26. CS	Compound Symmetry	None	Average	All	0.27	0.14	1.92	0.16	0.06	2.72
27. CS, Categorical	Compound Symmetry	Categorical	Last Visit	All	0.41	0.19	2.10	0.25	0.08	3.00
28. CS, Linear	Compound Symmetry	Linear	Last Visit	All	0.32	0.17	1.86	0.15	0.06	2.29
29. CS, Quadratic	Compound Symmetry	Quadratic	Last Visit	All	0.32	0.17	1.88	0.14	0.06	2.21
<i>Adjusted for baseline score for the outcome measure, age, gender, weight, height, 6- and 12-minute walk test, forced vital capacity, apnea/hypopnea index and shoulder flexion<sup>6</sup></i>										
30. Unstructured	Unstructured	None	Average	All	0.27	0.14	1.97	0.12	0.06	1.98
31. Toeplitz	Toeplitz	None	Average	All	0.27	0.14	1.86	0.13	0.06	2.15
32. CS	Compound Symmetry	None	Average	All	0.27	0.14	1.98	0.12	0.06	1.99
33. CS, Categorical	Compound Symmetry	Categorical	Last Visit	All	0.39	0.18	2.13	0.22	0.06	3.44
34. CS, Linear	Compound Symmetry	Linear	Last Visit	All	0.31	0.17	1.86	0.11	0.06	1.97
35. CS, Quadratic	Compound Symmetry	Quadratic	Last Visit	All	0.31	0.17	1.77	0.11	0.07	1.76

- Notes:
1. Within-patient correlation structure for generalized estimating equations.
  2. Main effects of time and interactions with treatment were included in the model.
  3. The treatment effect was estimated either by averaging across all included visits or by using the model-based estimate at the last visit.
  4. Outcomes were included either from all post-baseline visits or from the last two visits.
  5. Treatment effect estimates and standard errors were pooled across trials, after standardizing by the baseline standard deviation of the outcome measure within each trial. The reported mean treatment effect and SE are therefore expressed as proportions of the baseline variation.
  6. Some variables were not available from all trials.

**Table 3: Tests Using Only the Last Assessment - Subgroup With Baseline 6-Minute Walk Test < Median**

Model <sup>2</sup>	Treatment Effect Estimates <sup>1</sup>					
	6-Minute Walk Test			Forced Vital Capacity		
	Mean	SE	Z-Score	Mean	SE	Z-Score
1. T-Test	0.41	0.31	1.33	0.08	0.12	0.65
2. Wilcoxon	0.32	0.23	1.40	0.04	-0.03	-1.29
3. ANOVA	0.41	0.29	1.39	0.07	0.11	0.66
4. ANCOVA <sup>3</sup>	0.37	0.30	1.26	0.07	0.11	0.66
5. ANCOVA <sup>4</sup>	0.48	0.36	1.34	0.09	0.13	0.69
6. ANCOVA <sup>5</sup>	0.49	0.26	1.87	0.07	0.11	0.68
7. ANCOVA <sup>6</sup>	0.69	0.27	2.51	0.04	0.08	0.42
8. Augmentation (1) <sup>7</sup>	0.59	0.31	1.89	0.11	0.12	0.93
9. Augmentation (2) <sup>7</sup>	0.64	0.32	1.99	0.13	0.11	1.13

Notes:

1. Treatment effect estimates and standard errors were pooled across trials, after standardizing by the baseline standard deviation of the outcome measure within each trial. The reported mean treatment effect and SE are therefore expressed as proportions of the baseline variation.
2. The outcome measure is change from baseline to endpoint in all models.
3. Adjusted for baseline score for the outcome measure.
4. Adjusted for baseline score for the outcome measure and study center.
5. Adjusted for baseline score for the outcome measure, age and gender.
6. Adjusted for baseline score for the outcome measure, age, gender, weight, height, 6- and 12-minute walk test, forced vital capacity, apnea/hypopnea index and shoulder flexion (as available in each trial).
7. All baseline variables listed above were considered as auxiliary covariates. Augmentation in each arm used either the single best predictor of the outcome (1) or a model based on forward stepwise selection (2) chosen to optimize Mallows' Cp. Tsiatis, A.A., Davidian, M., Zhang, M., and Lu, X. (2008). Covariate adjustment for two-sample treatment comparisons in randomized clinical trials: A principled yet flexible approach. *Statistics in Medicine* 27, 4658–4677.

Table 4: Longitudinal Models - Subgroup With Baseline 6-Minute Walk Test < Median

Model	Specification				Treatment Effect Estimates <sup>5</sup>					
	Working Correlation <sup>1</sup>	Model for Effect of Time <sup>2</sup>	Time of Treatment Effect Assessment <sup>3</sup>	Included Visits <sup>4</sup>	6-Minute Walk Test			Forced Vital Capacity		
					Mean	SE	Z-Score	Mean	SE	Z-Score
<i>No baseline adjustment</i>										
10. Unstructured	Unstructured	None	Average	All	0.33	0.22	1.52	0.04	0.07	0.65
11. Toeplitz	Toeplitz	None	Average	All	0.33	0.22	1.52	0.04	0.07	0.64
12. CS	Compound Symmetry	None	Average	All	0.32	0.22	1.51	0.04	0.07	0.64
13. CS, Categorical	Compound Symmetry	Categorical	Last Visit	All	0.41	0.28	1.43	0.07	0.11	0.64
14. CS, Linear	Compound Symmetry	Linear	Last Visit	All	0.40	0.28	1.43	0.05	0.08	0.63
15. CS, Quadratic	Compound Symmetry	Quadratic	Last Visit	All	0.41	0.28	1.47	0.05	0.08	0.58
<i>Adjusted for baseline score for the outcome measure</i>										
16. Unstructured	Unstructured	None	Average	All	0.43	0.19	2.25	0.06	0.07	0.82
17. Toeplitz	Toeplitz	None	Average	All	0.44	0.19	2.32	0.06	0.07	0.95
18. CS	Compound Symmetry	None	Average	All	0.43	0.19	2.20	0.05	0.07	0.78
19. CS, Categorical	Compound Symmetry	Categorical	Last Visit	All	0.50	0.26	1.91	0.09	0.10	0.90
20. CS, Linear	Compound Symmetry	Linear	Last Visit	All	0.49	0.25	1.99	0.06	0.08	0.79
21. CS, Quadratic	Compound Symmetry	Quadratic	Last Visit	All	0.51	0.24	2.08	0.07	0.08	0.87
22. Unstructured, Last Two	Unstructured	None	Average	Last Two	0.43	0.25	1.75	0.05	0.09	0.53
23. CS, Last Two	Compound Symmetry	None	Average	Last Two	0.43	0.25	1.73	0.05	0.09	0.57
<i>Adjusted for baseline score for the outcome measure, age and gender</i>										
24. Unstructured	Unstructured	None	Average	All	0.32	0.22	1.44	0.05	0.07	0.67
25. Toeplitz	Toeplitz	None	Average	All	0.32	0.22	1.48	0.04	0.06	0.66
26. CS	Compound Symmetry	None	Average	All	0.32	0.21	1.50	0.04	0.07	0.62
27. CS, Categorical	Compound Symmetry	Categorical	Last Visit	All	0.40	0.29	1.38	0.07	0.11	0.67
28. CS, Linear	Compound Symmetry	Linear	Last Visit	All	0.38	0.27	1.42	0.05	0.08	0.62
29. CS, Quadratic	Compound Symmetry	Quadratic	Last Visit	All	0.40	0.27	1.49	0.06	0.08	0.70

- Notes:
1. Within-patient correlation structure for generalized estimating equations.
  2. Main effects of time and interactions with treatment were included in the model.
  3. The treatment effect was estimated either by averaging across all included visits or by using the model-based estimate at the last visit.
  4. Outcomes were included either from all post-baseline visits or from the last two visits.
  5. Treatment effect estimates and standard errors were pooled across trials, after standardizing by the baseline standard deviation of the outcome measure within each trial. The reported mean treatment effect and SE are therefore expressed as proportions of the baseline variation.
  6. Some variables were not available from all trials.