ONLINE SUPPLEMENT/APPENDIX

Patient Preferences for Endobronchial Valve Treatment of Severe Emphysema

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METHODS

Definition of clinical benefit

The benefit attribute had three levels defined by specific items in St George's Respiratory Questionnaire (SGRQ) activity domain (questions 11 and 15) that were revised for brevity and language. These two questions ask the patient to provide an assessment of the activities that are difficult because of breathing. Question 11 is about which activities make the patient feel breathless; question 15 is about which activities the patient has more difficulty performing (see Figure A-1).

Figure A-1. Activities Domain Questions from the St George's Respiratory Questionnaire Used to Determine the Benefit Attribute and Levels

These are questions about what activities usually make you feel short of breath these days. For each statement, please check the box that applies to you these days.

I usually feel short of breath when I am…	True	False
Sitting or lying still	☐	☐
Washing or dressing yourself	☐	☐
Walking around the home	☐	☐
Walking outside on level ground	☐	☐
Walking up a flight of stairs	☐	☐
Walking up hills	☐	☐

These are questions about how your activities might be affected by your breathing problems. <u>For each statement</u>, please check the box that applies to you <u>because of your breathing problems</u>:

Because of my breathing…	True	False
I take a long time to get washed or dressed	☐	☐
I cannot take a bath or shower, or I take a long time to do it	☐	☐
I walk slower than other people my age, or I stop to rest	☐	☐
Jobs such as household chores take a long time, or I have to stop to rest	☐	☐
If I walk up one flight of stairs, I have to go slowly or stop	☐	☐
If I hurry or walk fast, I have to stop or slow down	☐	☐
My breathing makes it difficult to do things such as walk up hills, carry things upstairs, light gardening such as weeding, dance, bowl, or play golf	☐	☐
My breathing makes it difficult to do things such as carry heavy loads, dig in the garden, jog or walk briskly (5 miles per hour), play tennis or swim	☐	☐

Survey respondents were offered customized benefits derived from their individual baseline clinical status, identified by responses to these two questions at baseline. Three levels of the benefit were defined for each respondent:

- Level 1 (1-activity benefit): determined by the first box that the respondent checked as "true" in question 11

- Level 2 (2-activity benefit): determined by the first box that the respondent checked as "true" in question 11 and the first box that the respondent checked as "true" in question 15

- Level 3 (3-activity benefit): determined by the first and second boxes that the respondent checked as "true" in question 11 and the first box that the respondent checked as "true" in question 15

The phrasing of each benefit is presented in Table A-1. Figure 1, the example discrete-choice experiment (DCE) question, presents an example of how the benefit was described for a respondent who selected "washing or dressing yourself" as the first true response to question 11 in the SGRQ, "I cannot take a bath or shower, or I take a long time to do it" as the first true response to question 15 in the SGRQ, and "walk outside on level ground" as the second true response to question 11 in the SGRQ. For this respondent, three levels of the benefit are defined:

- Level 1 (1-activity benefit): get washed or dressed without shortness of breath

- Level 2 (2-activity benefit): get washed or dressed without shortness of breath AND take a bath or shower more easily

- Level 3 (3-activity benefit): get washed or dressed without shortness of breath AND take a bath or shower more easily AND walk outside on level ground without shortness of breath

There is some overlap in the items presented for SGRQ questions 1 and 15, in particular the items related to washing and dressing. If a respondent selected true for "washing or dressing yourself" in SGRQ question 11 and "I take a long time to get washed or dressed" in SGRQ question 15, the description for the 1-activity benefit is replaced with "walk around the home without shortness of breath" or the next item marked as "true" by the respondent.

Table A-1. Phrasing of Activity Benefit Based on St. George's Respiratory Questionnaire (SGRQ) Questions 11 and 15

SGRQ Question	Benefit
In SGRQ question 11, if the respondent checked true for: **I usually feel short of breath when I am…**	**The benefit was presented as:**
Sitting or lying still	Sit still without shortness of breath
Washing or dressing yourself	Get washed or dressed without shortness of breath
Walking around the home	Walk around home without shortness of breath
Walking outside on level ground	Walk outside on level ground without shortness of breath
Walking up a flight of stairs	Walk up a flight of stairs without shortness of breath
Walking up hills	Walk up hills without shortness of breath
In SGRQ question 15, if the respondent checked true for: **Because of my breathing…**	**The benefit was presented as:**
I take a long time to get washed or dressed	Get washed or dressed more easily
I cannot take a bath or shower, or I take a long time to do it	Take a bath or shower more easily
I walk slower than other people my age, or I stop to rest	Walk farther without stopping

SGRQ Question	Benefit
Jobs such as household chores take a long time, or I have to stop to rest	Do jobs such as chores without stopping
If I walk up one flight of stairs, I have to go slowly or stop	Walk up a flight of stairs without stopping
If I hurry or walk fast, I have to stop or slow down	Hurry or walk faster without stopping
My breathing makes it difficult to do things such as walk up hills, carry things upstairs, light gardening such as weeding, dance, bowl, or play golf	Walk up hills and other similar activities more easily
My breathing makes it difficult to do things such as carry heavy loads, dig in the garden, jog or walk briskly (5 miles per hour), play tennis or swim	Carry heavy loads and other similar activities more easily

Assuming no other change in outcomes for the other two domains in the SGRQ tool (symptoms and impact), the three levels of benefit presented in the DCE questions represent a minimum of a 2-, 4-, or 6-point improvement in the total SGRQ score. This was considered a conservative estimate of the true benefit that a patient would receive from the treatment. Previous research demonstrates that improvements in SGRQ domain-level scores were associated with improvements in other endpoints, such as lung function, exercise capacity, and dyspnea (https://www.thoracic.org/members/assemblies/assemblies/srn/questionaires/sgrq.php).

Data Analysis

The random-parameters logit (RPL) model contained effects-coded variables for each attribute level for improvement in ability to breathe and type of treatment. Frequency of hospitalizations and the two risks were modeled as continuous linear variables. A constant term captured the joint effect of the attribute levels "current treatment" and "no improvement in breathlessness" associated with the current treatment alternative, while the frequency of hospitalizations and risks associated with current treatment were modeled as part of the continuous variables. In the

survey instrument, respondents were told that current treatment had a risk of less than 1% for pneumothorax and death, so current treatment was modeled as having 0% risk of death and pneumothorax in the RPL model. A Wald χ^2 test was used to determine the statistical significance of differences between adjacent attribute levels ($P < 0.05$).

To calculate the preference shares, individual conditional posterior parameters were computed using the observed sequence of choices for each respondent and the estimated distribution around the parameter estimates for each attribute level from the RPL model.[1-5] The individual parameters were combined with a specific vector of attribute levels, presented in Table 2 and Figure 4 in the manuscript to compute the probability that each respondent in the sample would select a specific treatment profile over another. Finally, the average of the individual probabilities was used to calculate the probability of selection for each profile.

The RPL results were used to calculate the maximum acceptable risk of a pneumothorax and death for improvements in the efficacy attributes (improvements in ability to breathe and frequency of hospitalizations for exacerbations). Risk equivalence for improvement in treatment attribute k from level 2 to level 1 =

$$\frac{\beta_{k,l=1} - \beta_{k,l=2}}{\beta \text{risk}},$$

where βrisk is the change in the level of risk, either risk of death or risk of pneumothorax. The ratio provides the number of average units of risk required to induce a level of disutility equal to improvement in treatment attribute k from a worse level to a better level (level 2 to level 1).

RESULTS

Sample Demographics

Additional sample demographics are contained in Table A-2.

Table A-2. Demographic Characteristics of Survey Respondents

|	All Respondents N = 294
Highest level of education completed	
Less than high school	2 (0.7%)
Some high school	6 (2.0%)
High school or equivalent (e.g., GED)	65 (22.1%)
Some college but no degree	88 (29.9%)
Technical school	21 (7.1%)
Associate's degree (2-year college degree)	31 (10.5%)
4-year college degree (e.g., BA, BS)	35 (11.9%)
Some graduate school but no degree	16 (5.4%)
Graduate or professional degree (e.g., MBA, MS, MD, PhD)	30 (10.2%)
Employment status	
Employed full-time	17 (5.8%)
Employed part-time	5 (1.7%)
Self-employed	6 (2.0%)
Homemaker or student	8 (2.7%)
Retired	135 (45.9%)
Disabled/unable to work	120 (40.8%)
Unemployed	3 (1.0%)
Race (check all that apply)	
White	277 (94.2%)
Other	12 (4.1%)
Prefer not to share	5 (1.7%)

Discrete-Choice Experiment

The RPL model produced preference weights (coefficients) for each attribute level and the constant representing the choice of current treatment (a combination of the effects of "current treatment" as the level for treatment type and "no improvement in breathlessness" for the benefit attribute). Across the 9 DCE questions, 19% of respondents always selected the current treatment option, while 51% never chose current treatment.

Figure A-3 presents the normalized mean preference weight estimates and the 95% confidence interval for each attribute level. Preferences for attribute levels were ordered as expected, with more levels of benefit being preferred to fewer levels of benefit and lower levels of risk being preferred over higher levels of risk. All levels within each attribute were statistically significantly different from each other at $p < 0.05$. Table A-3 presents the estimated preference weights.

Respondents demonstrated a strong preference for a new treatment over current treatment, as evidenced by the large negative preference weight on the constant term for the combination of "current treatment" as treatment type and "no improvement in breathlessness" associated with the current treatment option. Over the ranges presented in the survey, the most important change to respondents was moving from the constant term representing the combination of "current treatment" and "no improvement in breathlessness" to the overall mean value for a hypothetical treatment and improvement in breathlessness (the mean value was normalized to zero). The next most important change was a reduction in the risk of pneumothorax from 90% to 0%, followed by an improvement in the benefit (breathlessness and the ability to do more activities) from the one activity to three categories. The change from one hospitalization every 6 months to one

hospitalization every 3 years was least important relative to the other attributes. A 1% increase in the risk of death was approximately four times more important than a 1% increase in the risk of pneumothorax.

Figure A-3. Preference Weights (N = 294)
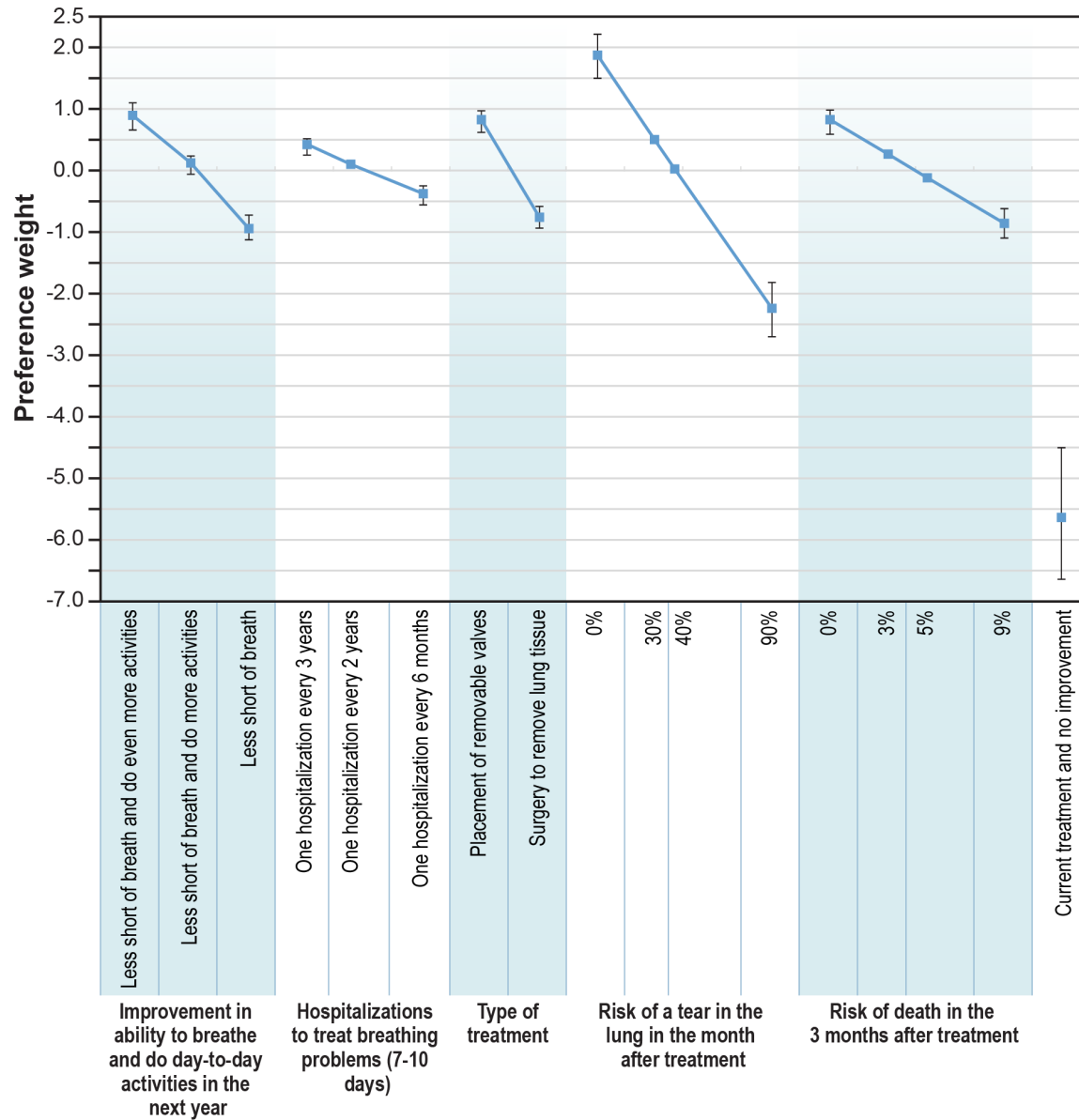
Note: The vertical bars surrounding each mean preference weight denote the 95% confidence interval of the point estimate. The preference weights indicate the ranking of levels within each attribute (i.e., a higher preference weight indicates that a level is more preferred). The scale of the preference weights is arbitrary, but differences between preference weights for an attribute can be interpreted as a measure of expected change in well-being associated with changes in attribute levels. Larger differences between preference weights indicate that respondents viewed the change as relatively more important. For a single attribute, the vertical distance between the most-preferred level to the least-preferred level indicates the overall importance of that attribute.

Table A-3. Estimated Preference Weights for RPL Model (N = 294)

Attribute	Levels	Estimated Preference Weight (95% CI)
Improvement in ability to breathe and do day-to-day activities in the next year	Less short of breath	−0.950* (−1.166 to −0.734)
	Less short of breath and do more activities	0.082 (−0.052 to 0.217)
	Less short of breath and do even more activities	0.868* (0.659 to 1.077)
Hospitalizations to treat breathing problems (7-10 days)	One hospitalization every 6 months	−0.431* (−0.584 to −0.279)
	One hospitalization every 2 years	0.054* (0.035 to 0.073)
	One hospitalization every 3 years	0.378* (0.244 to 0.511)
Type of treatment	Surgery to remove lung tissue	−0.791* (−0.962 to −0.620)
	Placement of removable valves	0.791* (0.620 to 0.962)
Risk of a tear in the lung in the month after treatment	0% risk of tear	1.839* (1.489 to 2.189)
	30% risk of tear	0.460* (0.372 to 0.547)
	40% risk of tear	0.00 (0 to 0)
	90% risk of tear	−2.299* (−2.737 to −1.862)
Risk of death in the 3 months after treatment	0% risk of death	0.789* (0.582 to 0.995)
	3% risk of death	0.232* (0.171 to 0.293)
	5% risk of death	−0.139* (−0.176 to −0.103)
	9% risk of death	−0.881* (−1.112 to −0.650)
Current treatment and no improvement		−5.641* (−6.742 to −4.540)

* $P < 0.01$ for difference from mean (zero).

CI = confidence interval; RPL = random-parameters logit.

Maximum Acceptable Risk

Table A-4 presents the maximum acceptable risks for pneumothorax for improvements in breathlessness, and reductions in the frequency of hospitalizations for exacerbations (the results for risk of death are presented in the body of the article). The maximum acceptable risk of pneumothorax for a change from a one-activity improvement in breathlessness to a three-activity improvement was 39.5%. The maximum acceptable risk of pneumothorax for a reduction in frequency of a hospitalization for COPD exacerbation of once every 6 months to once every 3 years was 17.6%. On average, respondents were willing to tolerate a risk of pneumothorax beyond the upper range of 90% tested in the survey for a treatment that delivered at least a one-activity improvement in breathlessness compared to current management with no improvement in breathlessness.

Table E-2. Maximum Acceptable Risk of Tear in the Lung Calculations for Improvement in Ability to Breathe and Do Day-to-Day Activities and Frequency of Hospitalizations

Benefit	From	To	Maximum Acceptable Risk for Change (95% CI)
Improvement in ability to breathe and do day-to-day activities in the next year	No treatment and no improvement in breathlessness	Less short of breath (one-activity improvement)	>90%
	Less short of breath (one-activity improvement)	Less short of breath and do more activities (two-activity improvement)	22.5% (15.7%-29.2%)
	Less short of breath and do more activities (two-activity improvement)	Less short of breath and do even more activities (three-activity improvement)	17.1% (10.9%-23.2%)
	Less short of breath (one-activity improvement)	Less short of breath and do even more activities (three-activity improvement)	39.5% (30.1%-49.0%)
Hospitalizations to treat breathing problems	Every 6 months	Every 2 years	10.6% (6.6%-14.5%)
	Every 2 years	Every 3 years	7.0% (4.4%-9.6%)
	Every 6 months	Every 3 years	17.6% (11.1%-24.1%)

CI = confidence interval.

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