**Bronchoscopic lung volume reduction coil treatment for severe emphysema: systematic review and individual patient data meta-analysis**

**Supplementary appendix**

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# Search strategy

PubMed:

("Pulmonary Disease, Chronic Obstructive"[Mesh] OR COPD[tiab] OR "Chronic Obstructive Pulmonary Disease\*"[tiab] OR COAD[tiab] OR "Chronic Obstructive Airway Disease\*"[tiab] OR "Chronic Obstruct\*"[tiab] OR emphysema[tiab] OR hyperinflation[tiab]) AND (coil\*[tiab] OR repneu[tiab])

Web of Science:

ALL = ("Chronic Obstructive Pulmonary Disease\*" OR COPD OR COAD OR "Chronic obstructive airway disease\*" OR emphysema OR hyperinflation OR "Chronic obstructive lung disease\*")

Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years

ALL = (coil\* OR repneu)

Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years

#2 AND #1

Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years

Embase:

#1 'chronic obstructive lung disease':ti,ab,kw OR copd:ti,ab,kw OR 'chronic obstructive pulmonary disease\*':af OR 'chronic obstructive airway' OR (chronic AND obstructive AND ('airway'/exp OR airway) AND disease\*) OR coad OR 'emphysema'/exp OR emphysema OR 'hyperinflation'/exp OR hyperinflation

#2 coil:ti,ab,kw OR repneu:ti,ab,kw

#1 AND #2

# record selection

Total records retrieved: 814

Total records removed after title and abstract screening: 407 (88% agreement, Cohen’s κ: 0.50).

Total records excluded after full text screening: 35 (98% agreement, Cohen;s κ: 0.93)

* No full text available: 1
* Conference abstract: 22
* No registered clinical trial: 10
* Wrong study duration: 1
* Trial protocol: 1

**eTable 1.** Records excluded after full text screening including exclusion reason

|  |  |  |
| --- | --- | --- |
| **Authors (year of publication)** | **Title** | **Exclusion reason** |
| No authors listed (2015) | Endobronchial coils for better quality of life | No full text found |
| Achenbach, H. J.; Juech, M. (2014) | First experiences of a regional lung center offering coil treatment for severe emphysema | Abstract only |
| Bezzi, M.; Novali, M.; Bonifazi, M.; Failla, G.; Zuccatosta, L.; Foccoli, P.; Gasparini, S. (2013) | Lung volume reduction coils (LVR-coils) for pulmonary emphysema: Results of the Italian National registry | Abstract only |
| Bezzi, M.; Novali, M.; Bonifazi, M.; Failla, G.; Zuccatosta, L.; Giustolisi, M.; Foccoli, P.; Gasparini, S. (2013) | First results of the Italian national registry for the endoscopic treatment of pulmonary emphysema by lung volume reduction coils | Abstract only |
| Biener, L.; Skowasch, D.; Hollmann, S.; Schreiber, T.; ickenig, G.; Fimmers, R.; Pizarro, C. (2020) | Endoscopic Lung Volume Reduction in COPD: The Impact of Coil Implantation on Patients' Physical Activity | Wrong study design |
| Bostancı, K.; Bilgi, Z.; Ömercikoğlu, H.; Çetinkaya, Ç.; Olgun Yıldızeli, Ş.; Yüksel, M.; Stamenovic, D. (2019) | Endobronchial coils in treatment of advanced emphysema: A single center experience | Wrong study design |
| Bostanci, K.; Bilgi, Z.; Omercikoglu, H.; Olgun, S.; Stamenovic, D.; Yuksel, M. (2015) | Endobronchial coils for COPD palliation: A single institution experience | Abstract only |
| Connolly, T. A. (2016) | Lung Volume Reduction Coils as a Novel Bronchoscopic Treatment for Emphysema | Wrong study design |
| Deslée, G.; Leroy, S.; Perotin, J. M.; Mal, H.; Dutau, H.; Bourdin, A.; Vergnon, J. M.; Pison, C.; Kessler, R.; Jounieaux, V.; Salaün, M.; Marceau, A.; Dury, S.; Benzaquen, J.; Bonnaire, M.; Dukic, S.; Barbe, C.; Marquette, C. H. (2017) | Two-year follow-up after endobronchial coil treatment in emphysema: results from the REVOLENS study | Wrong study duration |
| Fellrath, J. M.; Plojoux, J.; Scherer, T.; Franzen, D.; Lovis, A.; Brutsche, M.; Soccal, P. M. (2017) | Endobronchial coil therapy: First results from the Swiss registry | Abstract only |
| Grosse, U.; Hetzel, J.; Gündel, L.; Gatidis, S.; Syha, R.; Schabel, C.; Springer, F.; Horger, M. (2014) | Impact of endobronchial coiling for lung volume reduction on pulmonary volume and attenuation: Preinterventional and postinterventional computed tomography-quantification using separate lobe measurements | Wrong study design |
| Hartman, J. E.; Klooster, K.; Augustijn, S.; Van Geffen, W. H.; Garner, J.; Shah, P. L.; Ten Hacken, N. H. T.; Slebos, D. J. (2019) | Mechanisms of action of endobronchial coil treatment | Abstract only |
| Herth, F. J.; Eberhard, R.; Gompelmann, D.; Slebos, D. J.; Ernst, A. (2010) | Bronchoscopic lung volume reduction with a dedicated coil: a clinical pilot study | Wrong study design |
| Herth, F.J.; Slebos, D.J.; Shah, P.L.; Hetzel, M.; Schmid-Bindert, G.; LaPrad, A.S.; Deslée, G.; Valipour, A. (2019) | Protocol of a Randomized Controlled Study of the PneumRx Endobronchial Coil System versus Standard-of-Care Medical Management in the Treatment of Subjects with Severe Emphysema (ELEVATE) | Trial protocol and published results included |
| Hetzel, M.; Merk, T.; Philipp, A.; Veitshans, S.; Willmes, P. (2013) | Six months outcomes from patients treated with lung volume reduction coils in a commercial setting: The RKK Stuttgart experience | Abstract only |
| Jabuonski, T. A.; Lazarus, D. R. (2016) | Lung Volume Reduction Coils for Severe Emphysema | Wrong study design |
| Jüch, M.; Achenbach, H. J. (2015) | Endoscopic lung volume reduction with nitinol coils in very severe emphysema: Mid-term effectiveness vs. disease related continuous loss of lung function | Abstract only |
| Kayikçi, H.; Çimen, P.; Katgi, N.; Tuksavul, F. F. (2019) | Efficacy and safety of the brochial volum reduction treatment for emphysema | Abstract only |
| Kemp, S. V.; Zoumot, Z.; Caneja, C.; Singh, S.; Ross, E.; Bicknell, S.; Chaudry, R.; Hopkinson, N. S.; Polkey, M. I.; Shah, P. L. (2012) | Randomised controlled trial of repneu endobronchial coils for the treatment of severe emphysema with hyperinflation (reset study) | Abstract only |
| Klose, H.; Harbaum, L.; Oqueka, T.; Baumann, H. J.; Trautmann, H.; er, U.; Gläser, S.; Bollmann, T. (2014) | ELVR - Coil treatment for severe emphysema: Program experience from Northern Germany | Abstract only |
| Lepper, P. M.; Hetzel, J.; Bals, R.; Hetzel, M. (2013) | Safety and short term results of 152 lung volume reduction (LVR) procedures using repneu LVR-coils | Abstract only |
| Mang, S.; Huss, N.; Schäfers, H. J.; Wehrfritz, H.; Massmann, A.; Lensch, C.; Langer, F.; Seiler, F.; Bals, R.; Lepper, P. M. | Endoscopic lung volume reduction coils for patients with severe emphysema-a single-centre retrospective analysis | Wrong study design |
| Marchetti, N.; Kaufman, T.; Chra, D.; Herth, F. J.; Shah, P. L.; Slebos, D. J.; Dass, C.; Bicknell, S.; Blaas, S. H.; Pfeifer, M.; Stanzell, F.; Witt, C.; Deslee, G.; Gesierich, W.; Hetzel, M.; Kessler, R.; Leroy, S.; Hetzel, J.; Sciurba, F. C.; Criner, G. J. (2018) | Endobronchial Coils Versus Lung Volume Reduction Surgery or Medical Therapy for Treatment of Advanced Homogenous Emphysema | Wrong study design |
| Pizarro, C.; Hollmann, S.; Tuleta, I.; Nickenig, G.; Skowasch, D. (2017) | Impact of lung volume reduction coils on patient's physical activity | Abstract only |
| Schwick, B. (2014) | Repneu lung volume reduction coils (LVRC) for severe emphysema | Abstract only |
| Shah, P. L.; Kemp, S. V. (2015) | Springing forward to medium-term results for endobronchial coils for emphysema | Wrong study design |
| Slebos, D.; Kerstjens, H. A. M.; Ernst, A.; Eberhardt, R.; Herth, F. J. (2010) | Lung Volume Reduction Coil Treatment Of Severe Heterogeneous Emphysema. A Pilot Study | Abstract only |
| Slebos, D. J.; Bicknell, S.; Gesierich, W.; Herth, F.; Hetzel, J.; Hetzel, M.; Kessler, R.; Marquette, C. H.; Pfeifer, M.; Shah, P.; Stanzel, F.; Witt, C.; Deslee, G. (2013) | Lung volume reduction coil sustained treatment effectiveness in heterogeneous and homogeneous emphysema | Abstract only |
| Slebos, D. J.; Blaas, S.; Deslee, G.; Geseirich, W.; Herth, F. J.; Hetzel, J.; Hetzel, M.; Kessler, R.; Marquette, C. H.; Pfeifer, M.; Stanzel, F.; Witt, C. (2012) | Lung volume reduction coil treatment for patients with severe heterogeneous emphysema, a multicenter feasibility trial | Abstract only |
| Slebos, D. J.; Ernst, A. Blaas, S.; Gesierich, W.; Herth, F. (2010) | Bronchoscopic Lung Volume Reduction Coil treatment of severe heterogeneous emphysema | Abstract only |
| Stanzel, F.; Gesierich, W.; Hetzel, M.; Deslee, G.; Kessler, R.; Witt, C.; Marquette, C. H.; Pfeifer, M.; Blaas, S.; Hetzel, J.; Herth, F.; Slebos, D. J. (2012) | 12-Month effectiveness data in 85 patients treated bilaterally with LVRC | Abstract only |
| Trautmann, H. (2013) | Unilateral treatment with lung volume reduction coils in patients with severe emphysema | Abstract only |
| Wise, J. (2016) | Coils implanted into lungs show promise for emphysema | Wrong study design |
| Zoumot, Z.; Kemp, S.; Chaudhuri, R.; Caneja, C.; Bicknell, S.; Hopkinson, N. (2012) | Outcomes of the RePneu Endobronchial Coils for the treatment of severe emphysema with hyperinflation (RESET) trial | Abstract only |
| Zoumot, Z.; Kemp, S. V.; Caneja, C.; Hopkinson, N. S.; Singh, S.; Shah, P. L (2013) | Preliminary medium-term follow-up data from a single centre experience of a randomised controlled crossover study of the lung volume reduction coils | Abstract only |

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| **eTable 2.** Adjusting follow-up to be calculated from final treatment | | | | |
| **Trial** | **Original follow up** | **Time between original follow-up endpoint and second coil treatment** | **Adjusted follow-up**† | **Follow-up categorisation**\* |
| Slebos4 | 6 months  after *final treatment* | - | 6 months | 6 months |
| Deslée6 | 6 and 12 months  after *final treatment* | - | 6 and 12 months | 6 and 12 months |
| Klooster7 | 6 months  after *1st treatment* | 2 months | 4 months | 3 months |
| RESET5,8 | 3, 6 and 12 months after *final treatment* | - | 3, 6 and 12 months | 3, 6 and 12 months |
| RENEW10 | 12 months  after *1st treatment* | 4 months | 8 months | 6 months |
| REVOLENS9 | 6 and 12 months  after *randomization* | 1 – 3 months | 4 (3-5) and 10 (9 – 11) months | 3 and 12 months |
| REACTION11 | 3 months  after *final treatment* | - | 3 months | 3 months |
| ELEVATE12 | 6 months  after *1st treatment* | 2 months | 4 months | 3 months |
| † original follow-up minus time between original follow-up and second coil treatment  \* Follow-up categories:  - 3 months (0-4 months after final treatment)  - 6 months (5 – 8 months after final treatment)  - 12 months (9 – 12 months after final treatment) | | | | |

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| **eTable 3.** Included trials per follow-up category and number of patients | | | | |
| **Follow-up category** | **Trials** | **Total number of patients** | **Number of patients in standard-of-care group** | **Number of patients in coil treatment group** |
| 3 month | Klooster7  RESET5  REVOLENS9  REACTION11  ELEVATE12 | 292 | 112 | 180 |
| 6 month | Slebos4  Deslée6  RESET8  RENEW10 | 411 | 157 | 254 |
| 12 month | Deslée6  RESET8  REVOLENS9 | 183 | 50 | 133 |

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| **eTable 4**. Inclusion and exclusion criteria of all included trials | | | | | | | |
| **MAJOR INCLUSION CRITERIA** | | | | | | | |
|  | **Age (years)** | **FEV1 (% predicted)** | **RV (% predicted)** | **TLC (% predicted)** | **MMRC** | **Smoking cessation** | **Emphysema distribution** |
| **Slebos**4 | > 35 | < 45 | - | > 100 | ≥ 2 | > 8 weeks | Heterogeneous |
| **RESET**5,8 | ≥ 35 | ≤ 45 | - | > 100 | ≥ 2 | > 8 weeks | Hetero- or homogeneous |
| **Klooster**7 | > 35 | ≤ 35 | > 225 | > 120 | ≥ 2 | > 6 months | Homogeneous |
| **Deslée**6 | > 35 | < 45 | > 175 | > 100 | > 2 | > 8 weeks | Heterogeneous |
| **REVOLENS**9 | - | < 50% | > 220 | > 100 | ≥ 2 | > 8 weeks | Hetero- or homogeneous |
| **RENEW**10 | ≥ 35 | ≤ 45 | > 175 | > 100 | ≥ 2 | > 8 weeks | Heterogeneous |
| **REACTION**11 | - | < 45% | > 175 | > 100 | ≥ 2 | > 6 months | Hetero- or homogeneous |
| **ELEVATE**12 | - | 15 – 45 | ≥ 200 | > 100 | ≥ 2 | Yes, no specific duration | Hetero- or homogeneous |
| **MAJOR EXCLUSION CRITERIA** (similar for all trials) | | | | | | | |
| Change in FEV1 > 20% postbronchodilator | | | | | | | |
| DLCO < 20% of predicted | | | | | | | |
| Severe gas exchange abnormalities defined as PaCO2 > 8.0 kPa and/or PaO2 < 6.0 kPa on room air | | | | | | | |
| Uncontrolled pulmonary hypertension defined by right ventricular pressure > 50 mmHg and/or evidenced by echocardiogram | | | | | | | |
| History of recurrent clinically significant respiratory infections and/or COPD exacerbations | | | | | | | |
| Clinically significant bronchiectasis | | | | | | | |
| Previous lung surgery or lung transplant | | | | | | | |
| Giant bulla (>1/3 of the lung volume) | | | | | | | |
| 6-minute walk test < 140 meter | | | | | | | |
| Use of antiplatelet therapy (e.g. clopidogrel) or anticoagulant therapy | | | | | | | |
| Use of > 20 mg prednisone (or equivalent) daily | | | | | | | |
| Any other disease that might compromise survival or is likely to interfere with completion of study or follow-up assessments or would adversely affect outcomes | | | | | | | |
| Abbreviations: FEV1, forced expiratory volume in 1 second; RV, residual volume; TLC, total lung capacity; MMRC, modified medical research council; DLCO, diffusion capacity of the lung for carbon monoxide; PaCO2, partial pressure of carbon dioxide; PaO2, partial pressure of oxygen; COPD, chronic obstructive pulmonary disease. | | | | | | | |

**eTable 5.** Baseline characteristics according to group. Results are reported as frequency (percentage), mean (SD) or median (IQR). Univariate analysis was performed using Fisher’s exact test, independent sample T-test or Mann-Whitney U-test, where appropriate.

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| --- | --- | --- | --- |
|  | **Usual care (n = 269)** | **Coil treatment (n = 411)** | ***P*-value** |
| Gender (female) | 124 (46%) | 216 (53%) | .12 |
| Age (years) | 64 (58 – 69) | 63 (57 – 68) | .07 |
| BMI | 23.5 (20.7 –27.1) | 23.8 (21.1 – 27.0) | .86 |
| Smoking (pack-years) | 41.0 (30.0 –59.5) | 40.0 (29.8 – 50.0) | .07 |
| FEV1 (L) | 0.69 (0.59 – 0.84) | 0.68 (0.58 – 0.84) | .58 |
| FEV1 (% predicted) | 25.5 (21.0 – 30.5) | 25.3 (20.8 – 29.8) | .54 |
| FVC (L) | 2.39 (1.96 –2.91) | 2.45 (1.95 – 2.90) | .98 |
| RV (L) | 5.31 (4.55 – 6.13) | 5.26 (4.45 – 6.06) | .35 |
| RV (% predicted) | 241 (225 –268) | 241 (217 –276) | .98 |
| RV/TLC ratio | 67.0 (6.82) | 66.9 (6.95) | .77 |
| DLCO (% predicted) | 32.2 (26.2 – 40.2) | 31.5 (25.7 – 38.7) | .32 |
| SGRQ (total score) | 56.5 (14.6) | 60.1 (12.3) | < .001 |
| 6MWD (m) | 311 (247 – 366) | 314 (245 – 374) | .67 |
| MMRC |  |  | .55 |
| 1 | 1 (0.4%) | 0 (0.0) |  |
| 2 | 83 (36.2%) | 113 (27.5) |  |
| 3 | 103 (45.0%) | 155 (37.7) |  |
| 4 | 42 (18.3%) | 70 (17.0) |  |

BMI, body mass index; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity; DLCO, diffusing capacity of the lung for carbon monoxide; SGRQ, St. George respiratory questionnaire; 6MWD, 6-minute walk distance; MMRC, modified medical research council.

**Afbeelding met tafel

Automatisch gegenereerde beschrijving**

**eFigure 1.** Risk of Bias assessment using the revised Cochrane Risk of Bias tool for randomized trials (above) and the risk of bias in non-randomized studies of interventions tool (below).

**eTable 6.** Summary of mixed model results.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Follow-up** | **N (patients・trials**) | **Estimated effect of coil treatment (95%CI)** |
| **FEV1 (L)** | 3-month | 264・5 | 0.09 (0.06 to 0.12) |
| 6-month | 367・4 | 0.07 (0.03 to 0.10) |
| 12-month | 144・3 | 0.07 (0.00 to 0.14) |
| **RV (L)** | 3-month | 261・5 | -0.45 (-0.62 to -0.28) |
| 6-month | 368・4 | -0.33 (-0.52 to -0.14) |
| 12-month | 140・3 | -0.36 (-0.64 to -0.08) |
| **SGRQ (Points)** | 3-month | 258・5 | -12.3 (-15.8 to -8.8) |
| 6-month | 371・4 | -10.1 (-12.8 to -7.3) |
| 12-month | 140・3 | -9.8 (-15.0 to -4.7) |
| **6MWD (m)** | 3-month | 164・4† | 38 (18 to 58) |
| 6-month | 369・4 | 10 (-7 to 26) |
| 12-month | 140・3 | 27 (-5 to 58) |

† The ELEVATE trial did not report 6MWD outcomes and therefore 6MWD data was only available for 164 patients at 3-month follow-up (56%).

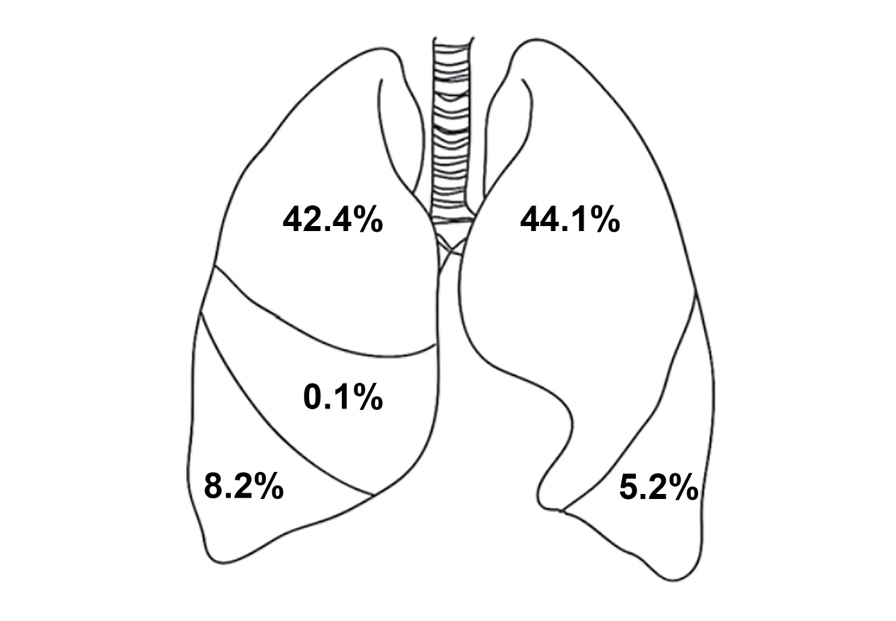
95%CI, 95% confidence interval; FEV1, forced expiratory volume in 1 second; RV, residual volume; SGRQ, St. George Respiratory Questionnaire; 6MWD, 6-minute walk distance.

**eTable 7.** Summary of procedure and coil details of 411 patients. Data are presented as frequency (percentage) or median (range).

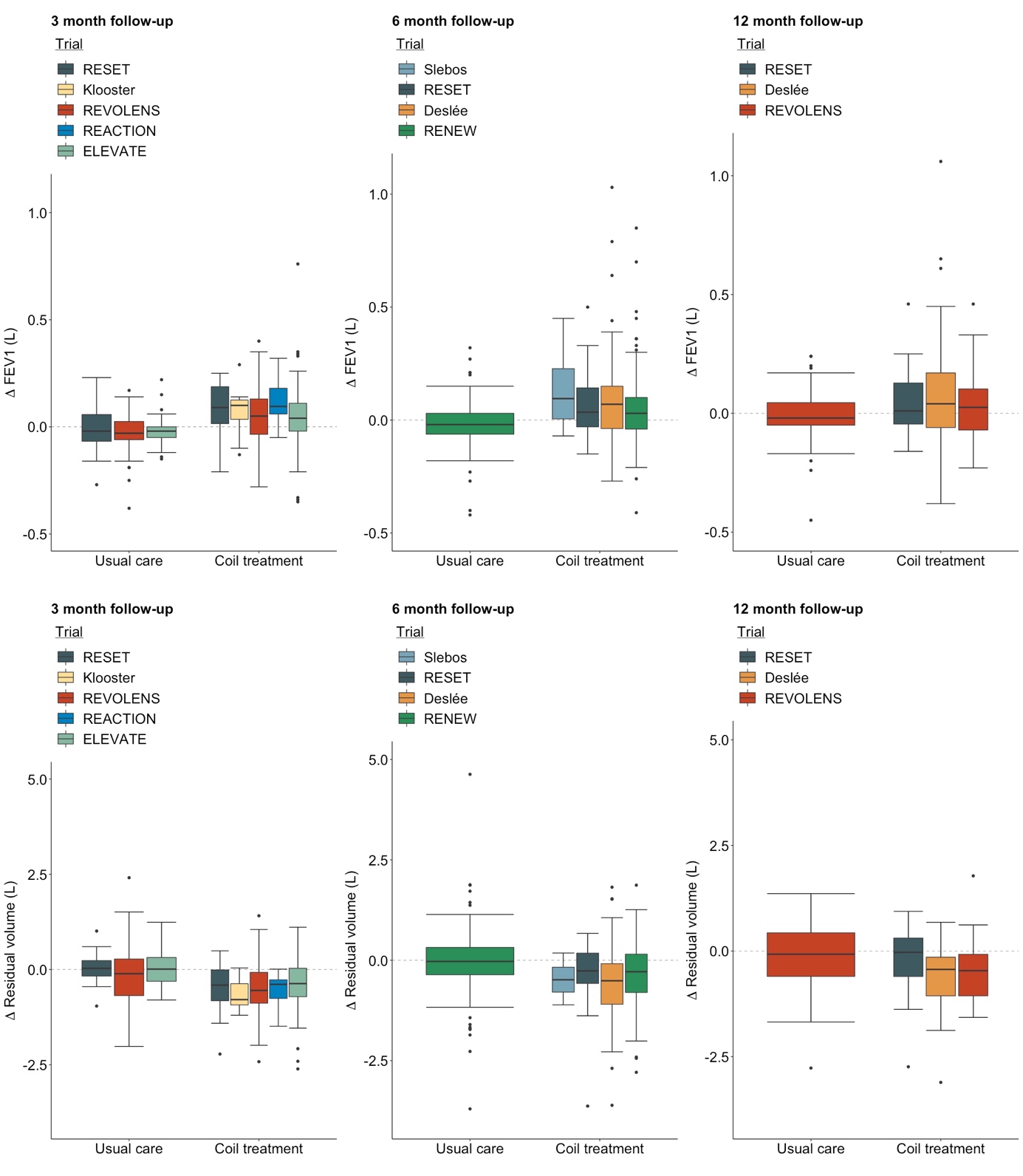
|  |  |  |
| --- | --- | --- |
| **Variable** | **No. procedures** | **Outcome** |
| **Treatment**  Unilateral  Bilateral | 788 | 34 (8%)  377 (92%) |
| **Procedure time (min)**† | 484 | 41 (15 – 140) |
| **Coils per treatment**\* | 651 | 10 (2 – 20) |
| **Coil sizes**\*  70 mm  85 mm  100 mm  125 mm  150 mm  175 mm  200 mm | 651 | 5 (0.1%)  21 (0.3%)  2908 (43.8%)  3200 (48.2%)  445 (6.7%)  58 (0.9%)  2 (0.03%) |
|  | | |

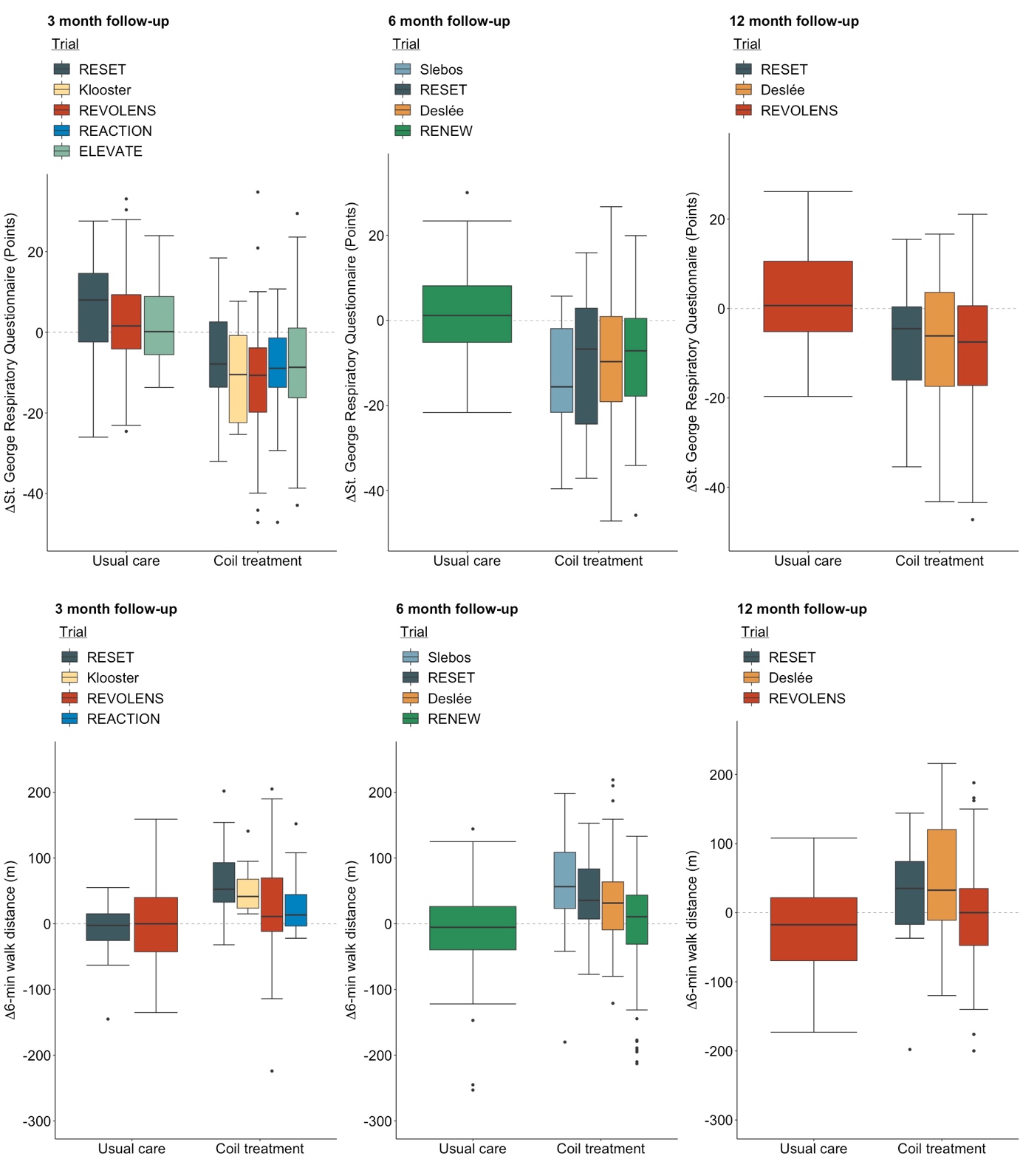
† No data supplied by RENEW trial

\*No data supplied by ELEVATE trial



**eFigure 2.** Distribution per lobe of 6639 coils used in 651 procedures.





**eFigure 3.** Boxplots of outcome variables per trial. FEV1, forced expiratory volume in 1 second.