

## **Online supplement**

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Kerstjens, Dirk-Jan Slebos. The effects of lung volume reduction treatment on diffusing capacity and gas exchange.

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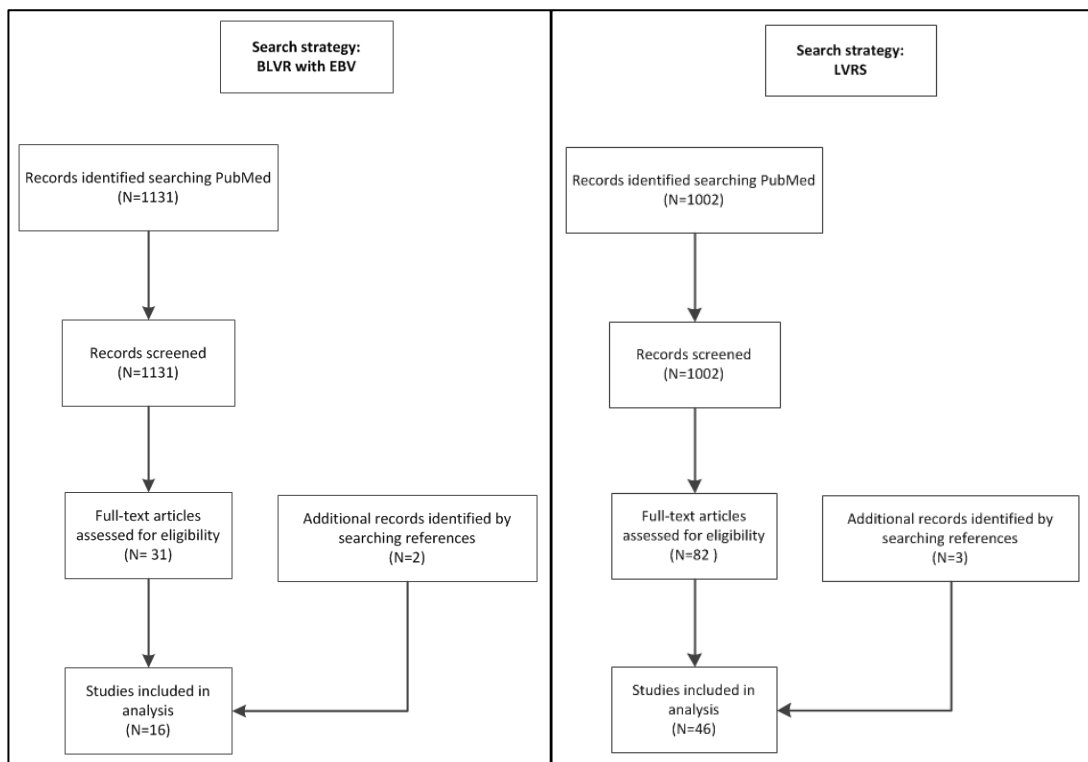
## Search Strategy

We performed a search for studies concerning lung volume reduction surgery and bronchoscopic lung volume reduction with endobronchial valves. If information on DL<sub>CO</sub>, p(A-a)O<sub>2</sub> gradient, PaO<sub>2</sub> combined with PaCO<sub>2</sub> before and after treatment was given, the article was included in the analysis

Suitability of the articles was screened by title and abstract. Clinical trials, observational studies and retrospective analyses were included. Other selection criteria were full text availability and text published in the English language.

The following search terms were used for bronchoscopic lung volume reduction with endobronchial valves: 'Endobronchial Valves'; 'Endobronchial Valve'; 'Lung Volume Reduction Valve'; Bronchial Valve'.

For studies concerning LVRS the search term 'Lung Volume Reduction Surgery' in title or abstract was used.



**Table S1: DL<sub>CO</sub> before and after Lung Volume Reduction Surgery**

Study	Year	N (treated)	Interval (months)	Baseline DL <sub>CO</sub> (%pred)	Follow Up DL <sub>CO</sub> (%pred)	ΔDL <sub>CO</sub> (% absolute)	P-value
Sciurba <sup>1</sup>	1996	20	3	44	47	3	0.15
Brenner <sup>2</sup>	1997	145	Unknown	28.5	46.1	17.6	<0.001
Martinez <sup>3</sup>	1997	17	3 to 6	43.3	48.2	4.9	0.13
Gelb <sup>4</sup>	1998	12	12	18	47	29	0.004
Norman <sup>5</sup>	1998	14	3	20.8	21.9	1.1	NS
Stammberger <sup>6</sup>	1998	40	3	44	46	2	NS
Oswald <sup>7</sup>	1998	9	3 to 6	46	50	4	NS
Gelb <sup>8</sup>	1999	6	27	35	59	24	Unknown
O'Brien <sup>9</sup>	1999	41	3 to 6	33	40	7	0.07
Geddes <sup>10</sup>	2000	24	12	36	45	9	0.11
Homan <sup>11</sup>	2001	36	6	38.7	43.1	4.4	0.0046
Bloch <sup>12</sup>	2002	115	3	40	43	3	<0.01
Goldstein <sup>13</sup>	2003	28	12	35	37	2	NS
Ciccone <sup>14</sup>	2003	250	6	34	39	5	<0.001
Tutic <sup>15</sup>	2004	21	6	37	40	3	NS
Meyers <sup>16</sup>	2004	20	6	16	27	11	Unknown
Hardoff <sup>17</sup>	2005	35	12	44.2	52.7	8.5	NS
Mineo <sup>18</sup>	2006	30	12	50.1	59.3	9.2	<0.01
Weder <sup>19</sup>	2009	250	6	39.4	44.9	5.5	NS
Cremona <sup>20</sup>	2011	14	Unknown	27	37	10	0.08
Layton <sup>21</sup>	2015	10	7	31	33	2	0.29
Ginsburg <sup>22</sup>	2015	91	12	28.6	33.8	5.2	<0.001
Clarenbach <sup>23</sup>	2015	14	3	35	40	5	0.061
Sievi <sup>24</sup>	2016	12	3	34	37.7	3.7	Unknown
Caviezel <sup>25</sup>	2018	30	3	31.3	26.7	-4.6	0.686
Caviezel <sup>26</sup>	2018	33	3	15	24	9	<0.001

DL<sub>CO</sub> = Diffusing Capacity of the Lung for Carbon Monoxide, NS = not significant. Baseline and follow up DL<sub>CO</sub> is given in percentage of predicted. Due to variable reporting of confidence intervals (i.e. standard deviation, interquartile range, minimum-maximum) these values are not reported in this table.

**Table S2: DL<sub>CO</sub> before and after Endoscopic Lung Volume Reduction with Endobronchial Valves**

Study	Year	N (Treated)	Interval (months)	Baseline DLco (%pred)	Follow Up DLco (%pred)	ΔDL <sub>CO</sub> (absolute %)	P-value
Toma <sup>27</sup>	2003	8	1	35.6	45.8	10.2	0.02
Snell <sup>28</sup>	2003	10	1	31	34.3	3.3	0.04
Yim <sup>29</sup>	2004	21	3	50.8	60.6	9.8	0.43
Hopkinson <sup>30</sup>	2005	19	1	35.9	40.9	5	0.02
Venuta <sup>31</sup>	2005	13	3	33	50	17	0.01
Wan <sup>32</sup>	2006	98	3	32.7	36.8	4.1	0.06
Chung <sup>33</sup>	2010	7	3	38	38	0	0.34
Kotecha <sup>34</sup>	2011	16	1	34.7	39.5	4.8	0.02
Hillerdal <sup>35</sup>	2014	15	6	28	38	10	Unknown
Klooster <sup>36</sup>	2015	22	6	40.9	44.2	3.3	0.021
Park <sup>37</sup>	2015	43	6	31.6	34.3	2.7	<0.05
Fiorelli <sup>38</sup>	2016	49	6	52	54.7	2.7	0.7
Fiorelli <sup>39</sup>	2017	33	3	58	59	1	0.91
Kemp <sup>40</sup>	2017	65	6	32.3	33.6	1.3	0.004
Criner <sup>41</sup>	2018	128	12	34.6	36.4	1.8	0.013

DL<sub>CO</sub> = Diffusing Capacity of the Lung for Carbon Monoxide. Baseline and follow up DL<sub>CO</sub> is given in percentage of predicted. Due to variable reporting of confidence intervals (i.e. standard deviation, interquartile range, minimum-maximum) these values are not reported in this table.

**Table S3: DL<sub>CO</sub> before and after LVRS (in ml/min/mmHg)**

<b>Study</b>	<b>Year</b>	<b>N (treated)</b>	<b>Interval (months)</b>	<b>Baseline DLco (ml/min/mmHg)</b>	<b>Follow Up DLco (ml/min/mmHg)</b>	<b>ΔDL<sub>CO</sub> (absolute)</b>	<b>P-value</b>
<b>Ferguson<sup>42</sup></b>	1998	18	3-6	10.59	10.19	-0.40	NS
<b>Albert<sup>43</sup></b>	1998	46	3	7.44	9.44	2	<0.05
<b>Fujimoto<sup>44</sup></b>	1999	12	6	11.2	14.5	3.3	<0.05
<b>Kuwahira<sup>45</sup></b>	2000	20	6	9.03	8.96	-0.07	NS
<b>Miller<sup>46</sup></b>	2005	54	6	7.58	8.69	1.11	0.144

**NS = Not significant**

**Table S4: Variation in change in DL<sub>CO</sub> before and after Lung Volume Reduction Treatment**

**2a. Absolute change in DL<sub>CO</sub> (%pred)**

Study	Year	Treatment	n (Treated)	ΔDL <sub>CO</sub> (Abs. change in %pred)
Oswald <sup>7</sup>	1998	LVRS	9	4 (-9 to +34)
Gelb <sup>8</sup>	1999	LVRS	6	23 (-6.0 to +29)
Wan <sup>32</sup>	2006	BLVR	98	17.2±52
Clarenbach <sup>23</sup>	2015	LVRS	14	5.0 [1.0 to 7.0]
Kemp <sup>40</sup>	2017	BLVR	65	2.78±8.84
Criner <sup>41</sup>	2018	BLVR	128	1.8±8.44

**2b. Relative change in DL<sub>CO</sub> (%pred)**

Study	Year	Treatment	n (Treated)	ΔDL <sub>CO</sub> (%)
Albert <sup>43</sup>	1998	LVRS	46	24±54
O'Brien <sup>9</sup>	1999	LVRS	41	8.5±45
Meyers <sup>16</sup>	2004	LVRS	20	70±82

**2c. Absolute change in DL<sub>CO</sub> (ml/min/mmHg)**

Study	Year	Treatment	n (Treated)	ΔDL <sub>CO</sub> (ml/min/mmHg)
Homan <sup>11</sup>	2001	LVRS	36	0.96±1.831
Snell <sup>28</sup>	2003	BLVR	10	0.45 (-0.6 to 2.2)

Table S4. 2a: Change in DL<sub>CO</sub> represented as absolute change in percentage of predicted. S4b: Change in DL<sub>CO</sub> represented as relative change in percentage of predicted. S4c: Change in DL<sub>CO</sub> represented as absolute change in ml/min/mmHg. Data represented as either mean±SD; median (min-max) or median [IQR]. LVRS=Lung Volume Reduction Surgery, BLVR=Bronchoscopic lung volume reduction.

**Table S5: p(A-a)O<sub>2</sub> gradient before and after Lung Volume Reduction Treatment**

Study	Year	Type LVR	N treat	Baseline p(A-a)O <sub>2</sub> gr (kPa)	Follow up p(A-a)O <sub>2</sub> gr (kPa)	Δ p(A-a)O <sub>2</sub> gr
Snell <sup>28</sup>	2003	BLVR	10	3.2	3.2	0.0
Venuta <sup>31</sup>	2005	BLVR	13	2.5	3.3	0.8
Venuta <sup>47</sup>	2012	BLVR	40	3.4	3.4	0.0
Fiorelli <sup>38</sup>	2016	BLVR	49	4.2	3.3	-0.9
Fiorelli <sup>39</sup>	2017	BLVR	33	3.9	4.1	0.2
Cooper <sup>48</sup>	1995	LVRS	20	4.8	4.2	-0.6
Cooper <sup>49</sup>	1996	LVRS	150	4.7	4.2	-0.5
Sciurba <sup>1</sup>	1196	LVRS	20	4.2	4.5	0.3
Roue <sup>50</sup>	1996	LVRS	13	5.3	5.0	-0.3
Ferguson <sup>42</sup>	1998	LVRS	18	6.7	7.1	0.4
Date <sup>51</sup>	1998	LVRS	39	3.4	3.1	-0.3
Cassina <sup>52</sup>	1998	LVRS	30	5.0	4.4	-0.6
Albert <sup>43</sup>	1998	LVRS	46	4.0	4.1	0.1
Gelb <sup>4</sup>	1998	LVRS	12	3.9	3.6	-0.3
Norman <sup>5</sup>	1998	LVRS	14	4.8	3.7	-1.1
Stammberger <sup>6</sup>	1998	LVRS	40	4.1	3.9	-0.2
Oswald <sup>7</sup>	1998	LVRS	9	3.2	3.4	0.2
Shade <sup>53</sup>	1999	LVRS	33	3.6	3.2	-0.4
Fujimoto <sup>44</sup>	1999	LVRS	12	4.2	3.6	-0.6
Leyenson <sup>54</sup>	2000	LVRS	42	3.0	4.6	1.6
Malthaner <sup>55</sup>	2000	LVRS	24	3.9	4.7	0.8
Geddes <sup>10</sup>	2000	LVRS	24	3.9	2.8	-1.1
Pompeo <sup>56</sup>	2000	LVRS	30	4.1	3.8	-0.3
Kuwahira <sup>45</sup>	2000	LVRS	20	4.1	3.8	-0.3
Cassart <sup>57</sup>	2001	LVRS	11	5.0	4.4	-0.6
Bloch <sup>12</sup>	2002	LVRS	115	5.0	4.9	-0.1
Ciccione <sup>14</sup>	2003	LVRS	250	4.5	3.9	-0.6
Takayama <sup>58</sup>	2003	LVRS	23	3.8	3.2	-0.6
Tutic <sup>15</sup>	2004	LVRS	21	5.8	4.9	-0.9
Meyers <sup>16</sup>	2004	LVRS	20	4.8	4.7	-0.1
Hillerdal <sup>35</sup>	2005	LVRS	53	4.5	4.5	0
Cremona <sup>20</sup>	2011	LVRS	14	4.3	4.2	-0.1
Pompeo <sup>59</sup>	2012	LVRS	63	4.1	4.0	-0.1
Dauriat <sup>60</sup>	2016	LVRS	52	4.4	4.0	-0.4
Caviezel <sup>25</sup>	2018	LVRS	30	5.2	4.7	-0.5
You <sup>61</sup>	2018	LVRS	15	0.3	0.6	0.3

LVRS=Lung Volume Reduction Surgery. BLVR = Bronchoscopic Lung Volume Reduction.



**Table S6: Change in DL<sub>CO</sub>, PaO<sub>2</sub> and p(A-a)O<sub>2</sub> gradient before and after LVRT**

Study	Year	Type LVR	N treat	ΔDL <sub>CO</sub> (%pred)	Δ PaO <sub>2</sub> (kPa)	Baseline p(A-a)O <sub>2</sub> gradient (kPa)	Follow up p(A-a)O <sub>2</sub> gradient (kPa)	Δ p(A-a)O <sub>2</sub> gradient
Snell <sup>28</sup>	2003	BLVR	10	3.3	0.15	3.2	3.2	0
Venuta <sup>31</sup>	2005	BLVR	13	17	-0.4	2.5	3.3	0.8
Fiorelli <sup>38</sup>	2016	BLVR	49	2.7	1	4.2	3.3	-0.9
Fiorelli <sup>39</sup>	2017	BLVR	33	1	0	3.9	4.1	0.2
Scirba <sup>1</sup>	1996	LVRS	20	3	0.3	4.2	4.5	0.3
Gelb <sup>4</sup>	1998	LVRS	12	29	1.3	3.9	3.6	-0.3
Norman <sup>5</sup>	1998	LVRS	14	1.1	1.1	4.8	3.7	-1.1
Stamberger <sup>6</sup>	1998	LVRS	40	2.0	0.8	4.1	3.9	-0.2
Oswald <sup>7</sup>	1998	LVRS	9	4.0	0	3.2	3.4	0.2
Geddes <sup>10</sup>	2000	LVRS	24	9	0.4	3.9	2.8	-1.1
Bloch <sup>12</sup>	2002	LVRS	115	3	0.3	5	4.9	-0.1
Ciccione <sup>14</sup>	2003	LVRS	250	5	1.1	4.5	3.9	-0.6
Tutic <sup>15</sup>	2004	LVRS	21	3	0.5	5.8	4.9	-0.9
Meyers <sup>16</sup>	2004	LVRS	20	11	1.2	4.8	4.7	-0.1
Cremona <sup>20</sup>	2011	LVRS	14	10	0.7	4.3	4.2	-0.1
Caviezel <sup>25</sup>	2018	LVRS	30	-4.6	0.4	5.2	4.7	-0.5

LVRS=Lung Volume Reduction Surgery. BLVR = Bronchoscopic Lung Volume Reduction.

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