

University of Groningen

Adoption Patterns of Bronchoscopic Lung Volume Reduction Procedures in Germany and Predicted Procedure Volumes for Other European Countries

Pietzsch, Jan B.; Busca, Rachele; Rott, Christina; Geisler, Benjamin P.; Weber, Simon A.; Slebos, Dirk-Jan; Deslee, Gaetan; Herth, Felix J. F.

Published in:
Respiration

DOI:
[10.1159/000491677](https://doi.org/10.1159/000491677)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2019

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Pietzsch, J. B., Busca, R., Rott, C., Geisler, B. P., Weber, S. A., Slebos, D.-J., Deslee, G., & Herth, F. J. F. (2019). Adoption Patterns of Bronchoscopic Lung Volume Reduction Procedures in Germany and Predicted Procedure Volumes for Other European Countries. *Respiration*, 97(1), 34-41. <https://doi.org/10.1159/000491677>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Adoption Patterns of Bronchoscopic Lung Volume Reduction Procedures in Germany and Predicted Procedure Volumes for Other European Countries

Jan B. Pietzsch^a Rachele Busca^b Christina Rott^c Benjamin P. Geisler^{a, d}
Simon A. Weber^e Dirk-Jan Slebos^f Gaëtan Deslee^g Felix J.F. Herth^h

^aWing Tech Inc., Menlo Park, CA, USA; ^bPneumRx Ltd., a BTG International Group Company, London, UK; ^cPneumRx GmbH, a BTG International Group Company, Düsseldorf, Germany; ^dDepartment of Medicine, Massachusetts General Hospital/Harvard Medical School, Boston, MA, USA; ^eCellogic GmbH, Berlin, Germany; ^fDepartment of Pulmonary Diseases, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; ^gDepartment of Pulmonary Diseases, INSERM Unit 1250, University Hospital of Reims, Reims, France; ^hPneumology and Critical Care Medicine, Thoraxklinik, University of Heidelberg and Translational Lung Research Center Heidelberg, Member of the German Lung Research Network, Heidelberg, Germany

Keywords

Pulmonary disease · Chronic obstructive pulmonary disease · Emphysema · Lung volume reduction · Bronchoscopy · Germany · Europe

Abstract

Background: Bronchoscopic lung volume reduction (BLVR) using valves and coils has been approved for use since 2003 and 2010, respectively. **Objective(s):** To study adoption patterns of BLVR in an early-adopting country, and to estimate potential treatment volumes in other European countries. **Methods:** Therapy- and age-specific volumes for endobronchial valve and coil procedures were obtained from German federal statistics for 2007–2016. Therapy-specific and total BLVR procedure volumes and growth were computed, and

patterns in treatment age and device utilization analyzed. Patient volumes for other European countries were predicted using mean German patient volumes of the last 3 data years and age-specific population and emphysema incidences. **Results:** Over the study period, annual BLVR procedure volumes grew from 91 to 2,053 (+2,256%), reaching a peak of 2,556 procedures in 2013. Coil procedures constituted 36% of the total volume in 2016. Treatment age was stable over time, with highest procedure counts in age group 60–64 years for valves and 65–69 years for coils. A limited increase in device use per procedure was observed. For Germany, 1,655 newly treated BLVR patients were estimated per year, approximating about 5% of the annual newly diagnosed severe emphysema cases. Predicted volume estimates for other European countries ranged from 1 for Liechtenstein to 1,226 for France. **Conclusions:** Analysis of German

procedure data show pronounced BLVR therapy uptake in the early years of adoption, with the more recently introduced coil therapy used in about one-third of patients. Estimated patient volumes to date constitute only a small fraction of the severe emphysema population.

© 2018 S. Karger AG, Basel

Introduction

Emphysema is a debilitating condition that constitutes a substantial subset of chronic obstructive pulmonary disease (COPD) [1, 2]. It is associated with significantly reduced quality of life and life expectancy, as well as increased healthcare resource utilization [1, 3].

Bronchoscopic lung volume reduction (BLVR) offers a minimally invasive treatment approach for selected subsets of patients and provides benefits comparable to those previously demonstrated for lung volume reduction surgery [4, 5]. While BLVR approaches comprise a wide range of technology, ranging from placement of implantable devices to vapor-based treatment, endobronchial valve therapy (EBV) and endobronchial coil therapy have become the mainstay BLVR approaches to date [5]. Further, BLVR techniques serve a much wider emphysema patient population than can be treated by lung volume reduction surgery, like lower lobe predominant disease, homogeneous emphysema distribution, and patients who are not fit enough or unwilling to undergo surgery.

The safety and effectiveness of EBV and coil therapy have been demonstrated in a number of national and multinational trials [6–12]. Further research is being conducted to characterize the therapies' performance in specific subsets of patients, and to reduce remaining uncertainty about the medium- and long-term performance of these therapies (e.g., clinicaltrials.gov identifiers NCT02022683 (TRANSFORM), NCT01796392 (LIBERATE), NCT01812447 (EMPROVE), NCT02823223 (valves in heterogeneous patients), NCT01682018 (valves in single lung transplant patients) for valves, and NCT02879331 (CYCLONE), NCT03360396 (ELEVATE) for coils).

EBV and coil therapy have received regulatory clearance in the European Union in 2003 and 2010, respectively. Pivotal trials for regulatory approval in the United States have been completed for EBV (clinicaltrials.gov identifier NCT01796392) and a pre-market approval application has been submitted to the United States Food and Drug Administration as of January 2018. For coils, Food and Drug Administration approval is ongoing.

In the German healthcare system, which was among the first in the world to adopt BLVR in regular clinical practice, EBV and coil therapy have been commercially used since 2007 and 2012, respectively, with a total of more than 12,000 procedures performed through the end of 2016. The detailed procedure coding information collected in Germany's hospital statistics provides an opportunity to study real-world adoption patterns and procedure characteristics of BLVR.

Our aim was to analyze these data in detail to provide useful insight for clinicians and healthcare administrators, and to estimate BLVR procedure volumes that might be expected in other European countries.

Materials and Methods

Study Data

Study data were obtained from procedure-specific data reported in annual diagnosis-related group hospital statistics (Fallpauschalenbezogene Krankenhausstatistik [diagnosis-related group-Statistik]) published by the German Federal Statistics Office. All BLVR procedure codes were identified from listings of the German "Operationen und Prozedurenschlüssel" (OPS) surgical and procedural codes. The respective codes for valves and coils, with definitions and information about their introduction, are shown in the appendix (online suppl. Table A1; for all online suppl. material, see www.karger.com/doi/10.1159/000491677).

For the current analysis, only valve and coil procedure codes were considered, as other BLVR approaches, including polymer-based foam instillation and vapor ablation, are more or less used in clinical trials only.

Analyses

Procedure Volume Collection and Analysis

For EBV, procedure volumes were collected for the 10-year period 2007–2016, and for endobronchial coil therapy for the 5-year period 2012–2016, after the therapy's commercial introduction. These data coincide with the availability of therapy-specific OPS codes. For both valves and coils, the available codes provide granular information about the use of devices, with valve codes specifying use of 1, 2, 3, 4, or 5 and more valves, and coil codes specifying usage levels between 1–2 coils for the lowest volume code and 17 or more coils for the highest volume code. See online supplementary Table A1.

For each analyzed year, utilization by code was collected in total and by age bracket, with age brackets defined in 5-year increments between "5 years and under" to "85 years and older." All valve code volumes were subsequently added up to provide the annual total procedure volume and the same was performed for the coil code volumes.

Treatment age was analyzed by plotting the age bracket-specific proportion of treatments as part of total and comparing the resulting distributions for valves (years 2007, 2012, and 2016) and coils (years 2012 and 2016).

Estimation of Treated Patients per Year, Germany

In addition to reporting of procedure volumes, we aimed to estimate the corresponding number of newly treated patients, that is, initial implants. This estimation took into account that procedures in which only one valve is implanted are predominantly repeat treatments, for example, for replacement of a dislodged or inadvertently exhaled valve. Further, for coils, it considered the fact that coil procedures are predominantly performed as bilateral, staged procedures, that is, index treatment requires 2 separate episodes of care, each of which is encoded as a separate procedure in the procedure statistics. Additionally, implantation of 1 to 2 or 3 to 4 coils is, in most cases, related to retreatment with coils [13]. Specifically, for estimation of patient volumes, we considered 15% of 1-valve procedures as new procedures, and 100% of procedures that used 2 or more valves. For coils, 5% of 1- to 2- and of 3- to 4-coil procedures were counted and 50% of the procedures involving 5 and more coils, reflecting the staged, bilateral implantation.

Analysis of Number of Devices Used, per Procedure

To obtain a perspective on the relative utilization of devices per procedure, we computed the relative proportion each code contributed toward the total procedure volume in a given year. Changes in device utilization were analyzed via Cuzick's test, a nonparametric test for trend across ordered groups (an extension of the Wilcoxon rank-sum test with correction for ties). For coils, for which utilization is reported in increments of 2 coils, we used the mean of each increment for analysis.

Approximation of BLVR Patient Volumes in Other European Countries

Predictions of potential BLVR patient volumes that might be expected in other European countries were derived from the German data as follows. First, the 3-year average for procedure volumes observed in period 2014–2016 was computed to provide a more stable procedure volume input. Subsequently, age bracket-specific procedure incidences were computed, using age bracket-specific population data for Germany. Countries identified for analysis included those European countries for which the European Statistics Agency (EuroStat) publishes detailed population data. For each of these countries, corresponding age bracket-specific population data were used to calculate the estimated procedure volumes, by code and in total, based on data reported for year 2016. To account for potential difference in emphysema prevalence and hence treatment incidence, we used data from a recent meta-analysis of COPD prevalence [14] that provides region-specific prevalence rates to calculate an adjustment factor. This adjustment factor (1.0 for other Western European countries, 0.810 for Northern European countries, 0.993 for Central European countries, and 0.761 for Southern European countries) was multiplied on the crude country-specific procedure volume estimate to obtain estimated total volumes.

Estimation of Relative BLVR Treatment Incidence

Finally, an approximation of the percent of patients, relative to all annually newly diagnosed severe emphysema patients, was computed. For this calculation, we divided the computed patient volume by the estimated incidence of severe emphysema. This incidence was derived as follows: data for Germany from the BOLD study suggest a prevalence of GOLD III/IV of 0.8% [15]. Further,

prior data suggest approximately 33.5% of GOLD III/IV COPD patients suffer from emphysema [16], a subset of which might be candidates for BLVR treatment. Based on current German population data, this yielded an estimate of the GOLD III/IV emphysema prevalence. An annual incidence of newly diagnosed GOLD III/IV patients was computed from the prevalence estimate by dividing prevalence by projected mean survival in this patient group of 7 years [17].

Results

Procedure and Patient Volumes in Germany

BLVR procedure volumes, for the period 2007–2011, were contributed by EBV only, and increased more than 6-fold in the 5-year period from 2007 to 2011, reaching a volume of 646 procedures prior to the introduction of coil therapy. Valve procedure volumes continued to grow through 2013 (peak at 1,673 procedures), and then showed a more stable volume (1,318 reported procedures in 2016). Coil procedures grew from 388 procedures in 2012 to 1,081 procedures in 2014, and – similar to valves – showed stable volume to gradual decline in 2015 and 2016, reaching a volume of 735 procedures in 2016, for total combined BLVR procedure volume of 2,053 procedures in 2016 (Fig. 1).

Using the specified calculation approach to account for repeat procedures that cannot be considered new BLVR patient treatments, a total newly treated patient volume of 1,465 is estimated for 2016, with coils contributing 359 of these patients (24.5%). The highest total number of annually treated BLVR patients was reached in 2013 (1,904; Fig. 1b). Relative to a computed annual incidence of newly diagnosed severe emphysema patients (GOLD III/IV) in Germany of 31,594, this suggests that approximately 4.6% of severe emphysema patients received BLVR treatment in 2016.

Treatment Patterns: Age and Numbers of Devices

The relative proportion of procedures in the different age brackets is shown in Figure 2, and shows widely consistent treatment age throughout. In the latest data year, 2016, the highest numbers of valve procedures were performed in age bracket 60–64 years, and in age bracket 65–69 years for coils.

The number of devices used per procedure for valves shows a fairly broad distribution between 1 and 5 or more valves, with the largest number of procedures using 3 valves. Over the years, a slight change can be observed toward the use of more devices (the proportion of procedures using 5 or more valves increased significantly over

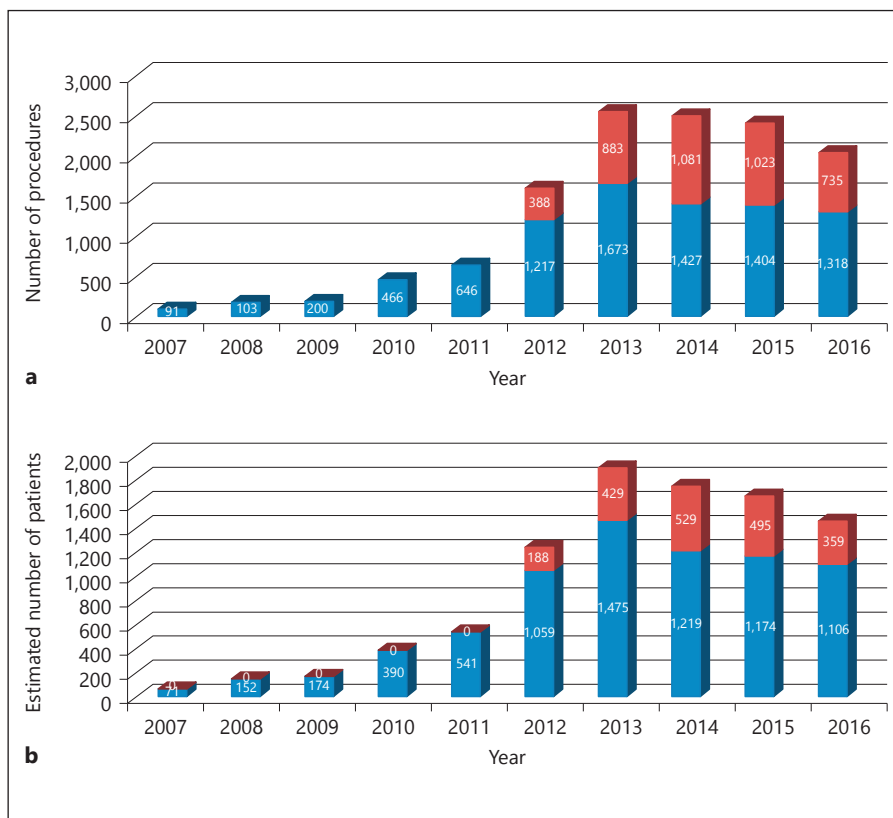


Fig. 1. BLVR procedure counts for valves and coils, Germany 2007–2016 (a); Estimated number of patients treated with valves and coils, Germany 2007–2016 (b).

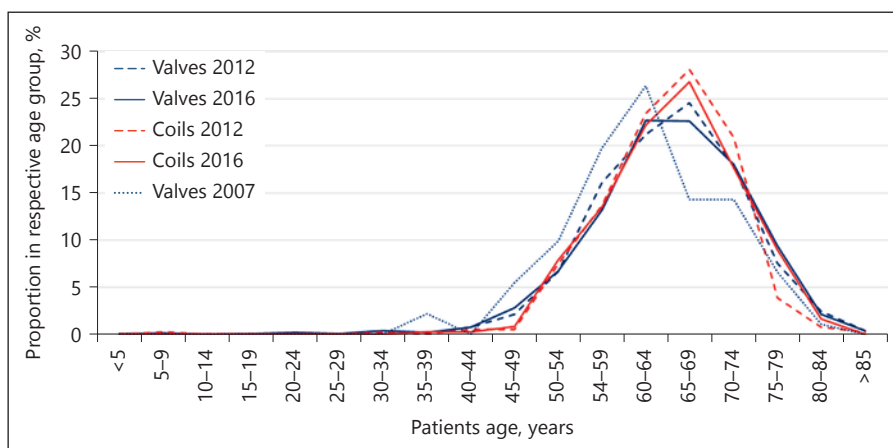


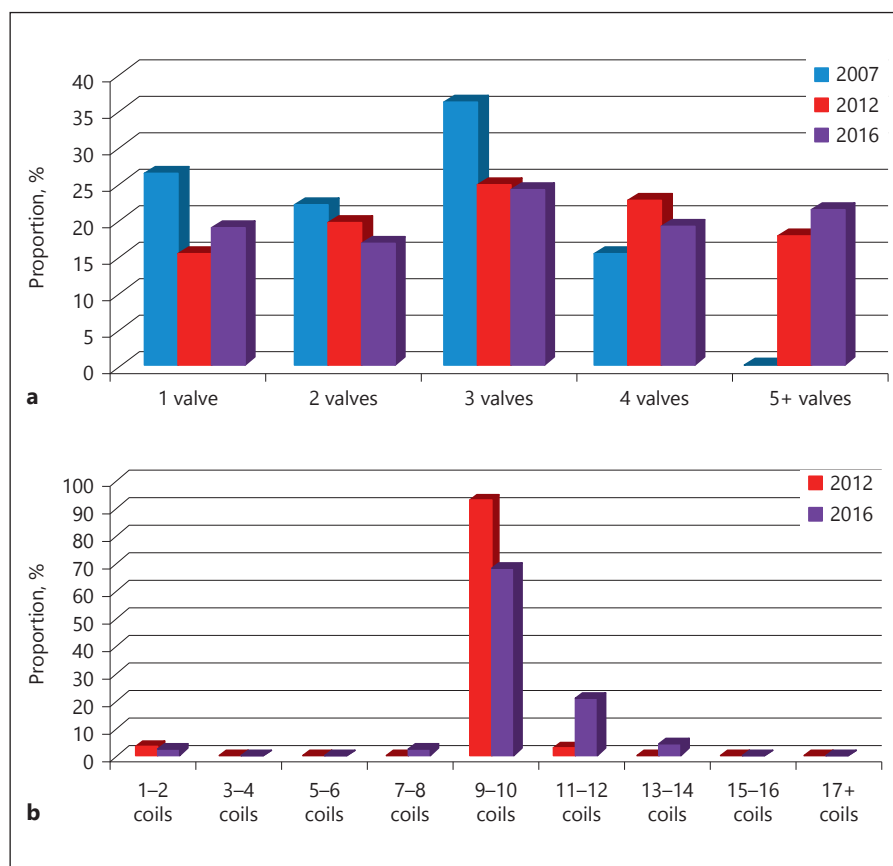
Fig. 2. Age distribution of valve and coil procedures years 2007, 2012, 2016 and 2012, 2016, respectively. Detailed procedure volumes by age brackets are provided in the online appendix.

time [p for trend: 0.011], and the proportion of procedures using 2 and 3 valves decreased significantly over time [p for trend: 0.010 and 0.014, respectively]). The majority of coil procedures used 9 or 10 coils (per side), with a trend toward the use of more coils between 2012 and 2016 (p for trend: 0.072) – a result that aligns with the instructions for use which suggest the use of 10–12 coils per upper lobe treated and of 10–14 per lower lobe treated Figure 3.

Predictions of Annual Treatment Volumes for Other European Countries

Taking the 3-year average 2014–2016 for purposes of extrapolation to Europe, yielded 1,627 BLVR patients treated per year in Germany. Using this 3-year patient volume estimate 2014–2016 and converting it taking into account age bracket-specific treatment incidence rates, age-specific population in each country, and the relative estimated emphysema incidence compared to

Fig. 3. Numbers of valves per procedure, 2007, 2012, and 2016 (a); Number of coils per procedure 2012 and 2016 (b). The majority of procedures involving one valve or less than 5 coils can be expected to be related to re-interventions.



Germany/Western Europe, BLVR treatment volumes in other European countries with available data from the European Statistics Agency ranged from 1 patient per year in Liechtenstein to 1,216 patients per year in France (Fig. 4).

Discussion

Our analysis of administrative data from the German healthcare system provides detailed insight into the adoption of BLVR therapies, with 10 years of data available for valve therapy and 5 years for coils. The data suggest a gradual uptake in procedure volumes over the years, with most substantial increase in the total number of BLVR procedures after introduction of coil therapy in 2012 and 2013, and a plateauing and potential decrease in procedure volumes in the period 2014–2016.

The highest number of BLVR procedures was performed in patients aged 60–69 years old, and the age distribution proved stable over the study period, with some

deviation toward slightly younger patient population observed in the early years of valve adoption.

Our data suggest further that the number of devices used per procedure has gradually increased over the course of the study period. However, these changes in device utilization were limited overall.

This paper also provides perspective on potential treatment volumes that might be expected after market introduction of valves and coils in other European countries. While these extrapolations are based on several assumptions – including the primary assumption that German adoption patterns for BLVR are representative for other European healthcare systems – they provide useful directional information about the potential volumes that might be expected in these countries. The data could be used as a starting point for budget impact analyses and other means to plan for the market utilization and reimbursement of BLVR therapy in other European countries.

A particular strength of the present study is that detailed utilization data were available for the German healthcare system starting from the first year of respective

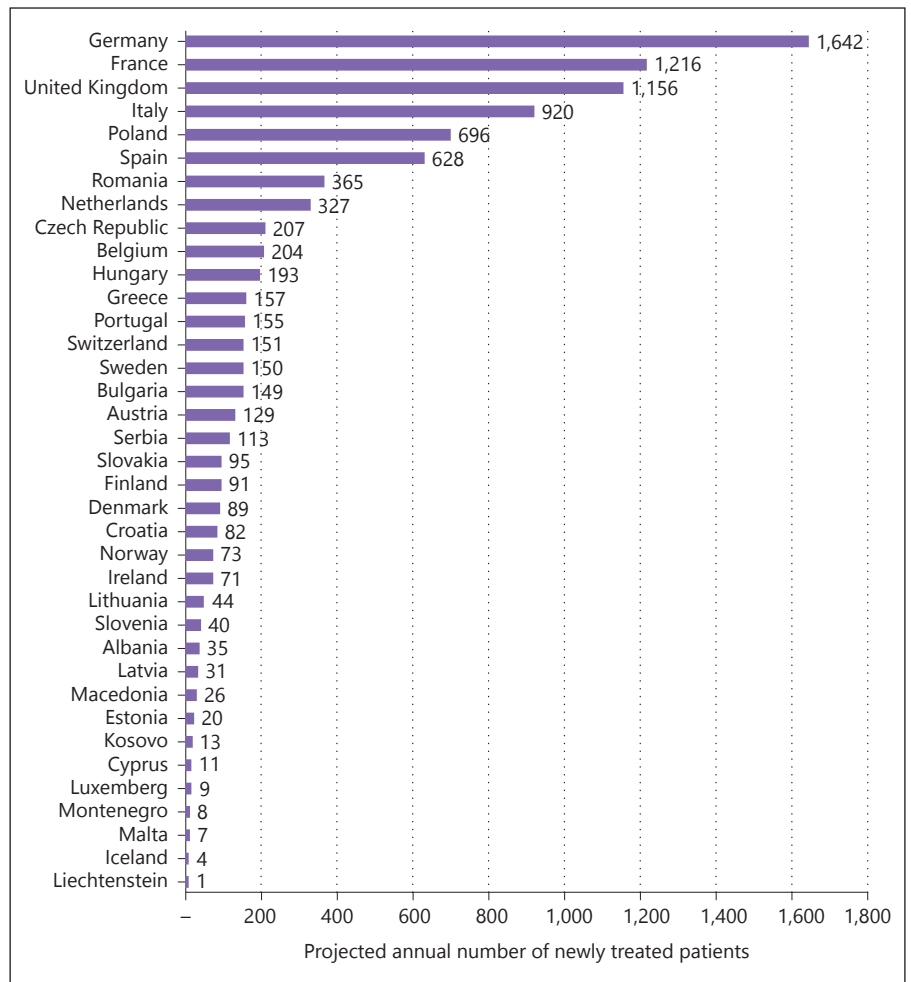


Fig. 4. Projected annual number of newly treated BLVR patients in European countries, based on German BLVR adoption experience to-date.

therapy adoption for valves and coils in 2007 and 2012. These data not only provide procedure volumes, but also information about treatment age and specific levels of procedural device utilization.

At the same time, our study is subject to several limitations. First, our estimation of patient volumes is based on assumptions about index treatments versus re-intervention treatments. While our estimates are supported by information from clinical studies, they are ultimately based on expert opinion. The estimated number of patients might vary somewhat if differing assumptions are made. However, our estimate should – directionally – provide an estimate that is very close to actual patient volumes. Second, data about the incidence of severe emphysema are sparse. As such, our estimation of the percent of newly diagnosed severe emphysema patients treated with BLVR therapy can, again, only provide directional information. However, even if the estimated incidence was twice as high, our finding that BLVR is cur-

rently only used in a small portion of severe emphysema patients would still hold. To this end, it should be noted that prior studies [6, 7] have suggested that around 20% of severe emphysema patients diagnosed and screened for treatment are expected to be candidates for BLVR treatment. Our estimated patient incidence is likely larger than the subset of patients considered in these prior studies, which suggests that our estimates are generally in agreement with these earlier findings. Third, while our extrapolation to other European countries takes into account age-specific procedure incidence and provides for an incidence adjustment based on differences in emphysema prevalence, other factors might influence potential BLVR treatment volumes in these countries. Different approaches to patient identification, availability of experts trained in bronchoscopic procedures and of reference centers, different disease management pathways, and funding mechanisms might all contribute to some level of variation from our projected levels. Further, our

data are based on the German procedural volumes several years after introduction of BLVR therapies in Germany. In early years of adoption, volumes in other countries could be expected to be lower. Similarly, BLVR adoption in Germany might further increase in future years, which would in turn increase the observed BLVR treatment volumes, and hence the projections for other countries. Parameters potentially supporting volume growth might include aging populations, comprehensive coverage and proper reimbursement, improved identification and recruitment of BLVR candidates by increased awareness among general practitioners and better health education for emphysema patients, broader therapy acceptance by pulmonologists on the basis of more targeted patient selection, new and further improved safety and effectiveness data from ongoing trials, and broader access to newer BLVR technologies. Vice versa, reasons for potential decrease of BLVR procedure volumes might include a reduction of smoking habits in the population, less environmental pollution, negative coverage decisions and lack of dedicated funds for bronchoscopic approaches, and limited acceptance of BLVR by referring practitioners.

In conclusion, pronounced therapy uptake was observed during the early years of BLVR adoption, with the more recently introduced endobronchial coil therapy used in around one-third of patients. Observed procedure volumes only correspond to a small fraction of the patients with severe emphysema and may vary in different countries, depending on the different approaches and

thus warranting further specific assessments in each country. This might suggest that patients, at present, are carefully selected. Future market entry of BLVR devices should be accompanied by post-marketing registries or other means of collecting real-world data on device utilization and performance in each country.

Financial Disclosure and Conflicts of Interest

Jan B. Pietzsch, PhD, is President, CEO, and shareholder of Wing Tech Inc., a technology consulting firm focusing on early-stage assessment of medical technologies. Wing Tech Inc. received consulting fees from BTG/PneumRx Ltd to conduct the analyses underlying this study and supporting publication development. Rachele Busca, MBA, M.Sc., is Director of Access and Value Strategy at PneumRx Ltd, a BTG International Group Company. Christina Rott is Market Access Manager at PneumRx GmbH. Benjamin P. Geisler, MD, MPH, is a senior consultant for Wing Tech Inc. Simon Weber is a health economist at Cellogic GmbH, and in this role provided consulting services to Wing Tech Inc., which received consulting fees from BTG/PneumRx Ltd to conduct the analyses underlying this study and supporting publication development. Gaëtan Deslee, MD, PhD, Deslée has been involved as investigator in previous studies sponsored by BTG/PneumRx, and received travel reimbursements and speaker fees for educational sessions and consulting from BTG/PneumRx. Dirk J. Slebos, MD, PhD, is an advisor and consultant to PneumRx/BTG UK/USA, and PulmonX Inc. USA and reports grants, and non-financial support from both companies. Felix J.F. Herth, MD, is an advisor and consultant to PneumRx/BTG UK/USA, PulmonX Inc. USA, Uptake Inc. USA and Olympus Medical Tokyo and reports grants, and non-financial support from both companies. He has been involved as investigator in previous studies sponsored by these companies.

References

- 1 Kaplan RM, Ries AL: Health-related quality of life in emphysema. *Proc Am Thorac Soc* 2008; 5:561–566.
- 2 Rycroft CE, Heyes A, Lanza L, Becker K: Epidemiology of chronic obstructive pulmonary disease: a literature review. *Int J Chron Obstruct Pulmon Dis* 2012;7:457–494.
- 3 Martinez FJ, Foster G, Curtis JL, Criner G, Weinmann G, Fishman A, DeCamp MM, Benditt J, Sciruba F, Make B, Mohsenifar Z, Diaz P, Hoffman E, Wise R: Predictors of mortality in patients with emphysema and severe airflow obstruction. *Am J Respir Crit Care Med* 2006;173:1326–1334.
- 4 Shah PL, Herth FJ, van Geffen WH, Deslee G, Slebos DJ: Lung volume reduction for emphysema. *Lancet Respir Med* 2017;5:147–156.
- 5 Slebos DJ, Shah PL, Herth FJ, Valipour A: Endobronchial valves for endoscopic lung volume reduction: best practice recommendations from expert panel on endoscopic lung volume reduction. *Respiration* 2017;93:138–150.
- 6 Sciruba FC, Ernst A, Herth FJ, Strange C, Criner GJ, Marquette CH, Kovitz KL, Chiacchierini RP, Goldin J, McLennan G; VENT Study Research Group: A randomized study of endobronchial valves for advanced emphysema. *N Engl J Med* 2010;363:1233–1244.
- 7 Herth FJ, Noppen M, Valipour A, Leroy S, Vergnon JM, Ficker JH, Egan JJ, Gasparini S, Agusti C, Holmes-Higgin D, Ernst A; International VENT Study Group: Efficacy predictors of lung volume reduction with Zephyr valves in a European cohort. *Eur Respir J* 2012;39:1334–1342.
- 8 Sciruba FC, Criner GJ, Strange C, Shah PL, Michaud G, Connolly TA, Deslee G, Tillis WP, Delage A, Marquette CH, Krishna G, Kalhan R, Ferguson JS, Jantz M, Maldonado F, McKenna R, Majid A, Rai N, Gay S, Dransfield MT, Angel L, Maxfield R, Herth FJ, Wahidi MM, Mehta A, Slebos DJ; RENEW Study Research Group: Effect of endobronchial coils vs usual care on exercise tolerance in patients with severe emphysema: the RENEW Randomized Clinical Trial. *JAMA* 2016;315:2178–2189.
- 9 Deslee G, Mal H, Dutau H, Bourdin A, Vergnon JM, Pison C, Kessler R, Jounieaux V, Thiberville L, Leroy S, Marceau A, Laroumagne S, Mallet JP, Dukic S, Barbe C, Bulsei J, Jolly D, Durand-Zaleski I, Marquette CH; REVOLENS Study Group: Lung volume reduction coil treatment vs usual care in patients with severe emphysema: the REVOLENS Randomized Clinical Trial. *JAMA* 2016;315:175–184.
- 10 Wang Y, Lai TW, Xu F, Zhou JS, Li ZY, Xu XC, Chen HP, Ying SM, Li W, Shen HH, Chen ZH: Efficacy and safety of bronchoscopic lung volume reduction therapy in patients with severe emphysema: a meta-analysis of randomized controlled trials. *Oncotarget* 2017;8:78031–78043.

- 11 Klooster K, ten Hacken NH, Hartman JE, Kerstjens HA, van Rikxoort EM, Slebos DJ: Endobronchial valves for emphysema without interlobar collateral ventilation. *N Engl J Med* 2015;373:2325–2335.
- 12 Valipour A, Slebos DJ, Herth F, Darwiche K, Wagner M, Ficker JH, Petermann C, Hubner RH, Stanzel F, Eberhardt R, Team IS: Endobronchial valve therapy in patients with homogeneous emphysema. Results from the IMPACT Study. *Am J Respir Crit Care Med* 2016;194:1073–1082.
- 13 Hartman JE, Klooster K, Ten Hacken NHT, Slebos DJ: The safety and feasibility of re-treating patients with severe emphysema with endobronchial coils: a Pilot Study. *COPD* 2017;14:339–343.
- 14 Blanco I, Diego I, Bueno P, Fernandez E, Casas-Maldonado F, Esquinas C, Soriano JB, Miravittles M: Geographical distribution of COPD prevalence in Europe, estimated by an inverse distance weighting interpolation technique. *Int J Chron Obstruct Pulmon Dis* 2018;13:57–67.
- 15 Geldmacher H, Biller H, Herbst A, Urbanski K, Allison M, Buist AS, Hohlfeld JM, Welte T: (The prevalence of chronic obstructive pulmonary disease [COPD] in Germany. Results of the BOLD study). *Dtsch Med Wochenschr* 2008;133:2609–2614.
- 16 Methvin JN, Mannino DM, Casey BR: COPD prevalence in southeastern Kentucky: the burden of lung disease study. *Chest* 2009;135:102–107.
- 17 Pietzsch JB, Garner A, Herth FJ: Cost-effectiveness of endobronchial valve therapy for severe emphysema: a model-based projection based on the VENT study. *Respiration* 2014; 88:389–398.