LUNG HEALTH;
A NOVEL APPROACH TO COPD & EMPHYSEMA TREATMENT WITH INTERVENTIONAL BRONCHOSCOPY

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with assistance from

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OUTLINE

- Burden of chronic respiratory diseases (CRD) in adults and associated modifiable risk factors globally
  - COPD (chronic bronchitis and emphysema)
  - Lung Cancer
- Global and regional economic burden of COPD
- Novel diagnostic and treatment approaches and the role of interventional bronchoscopy
- An innovative corporate solution
- The Way Forward

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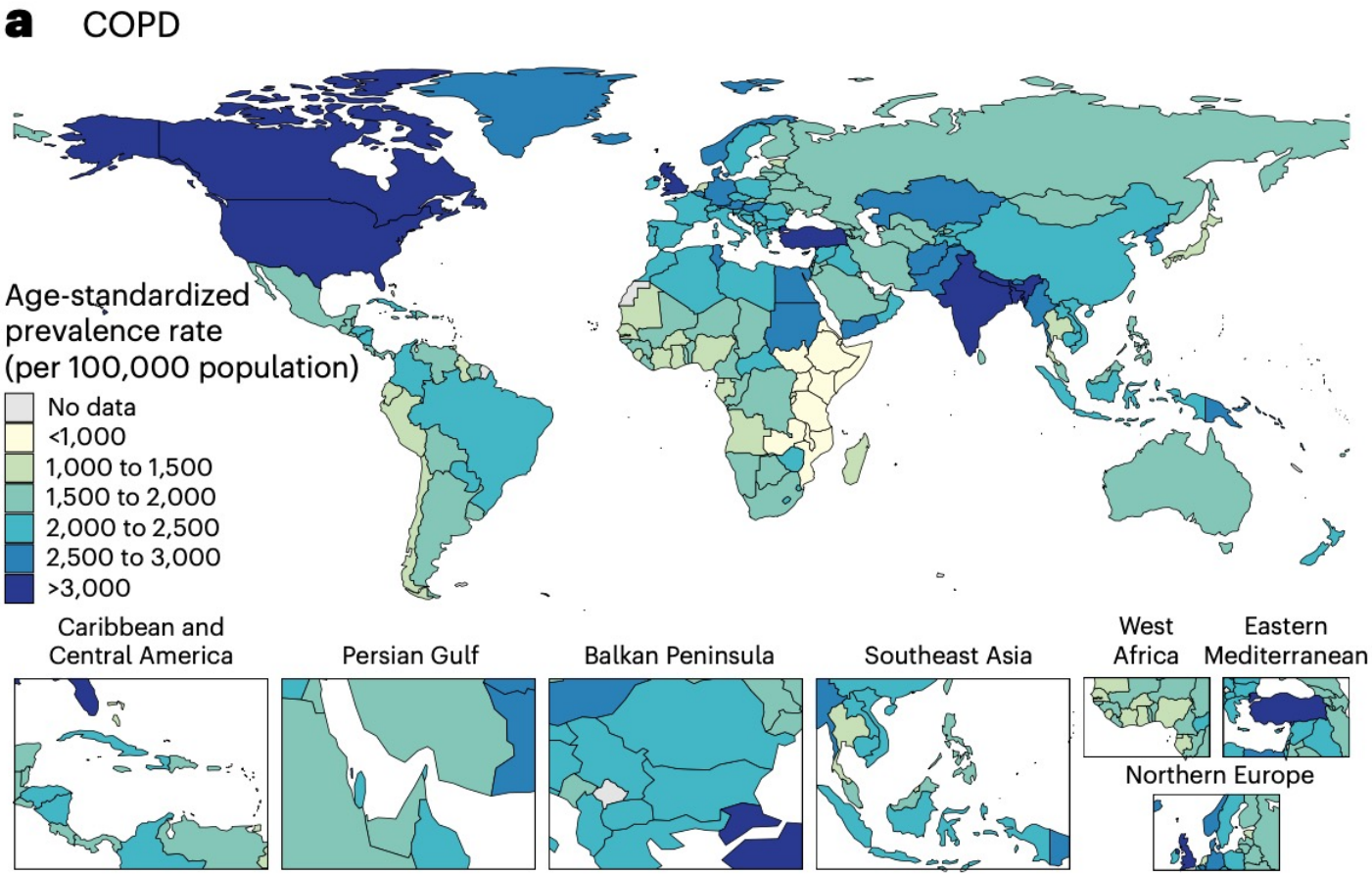
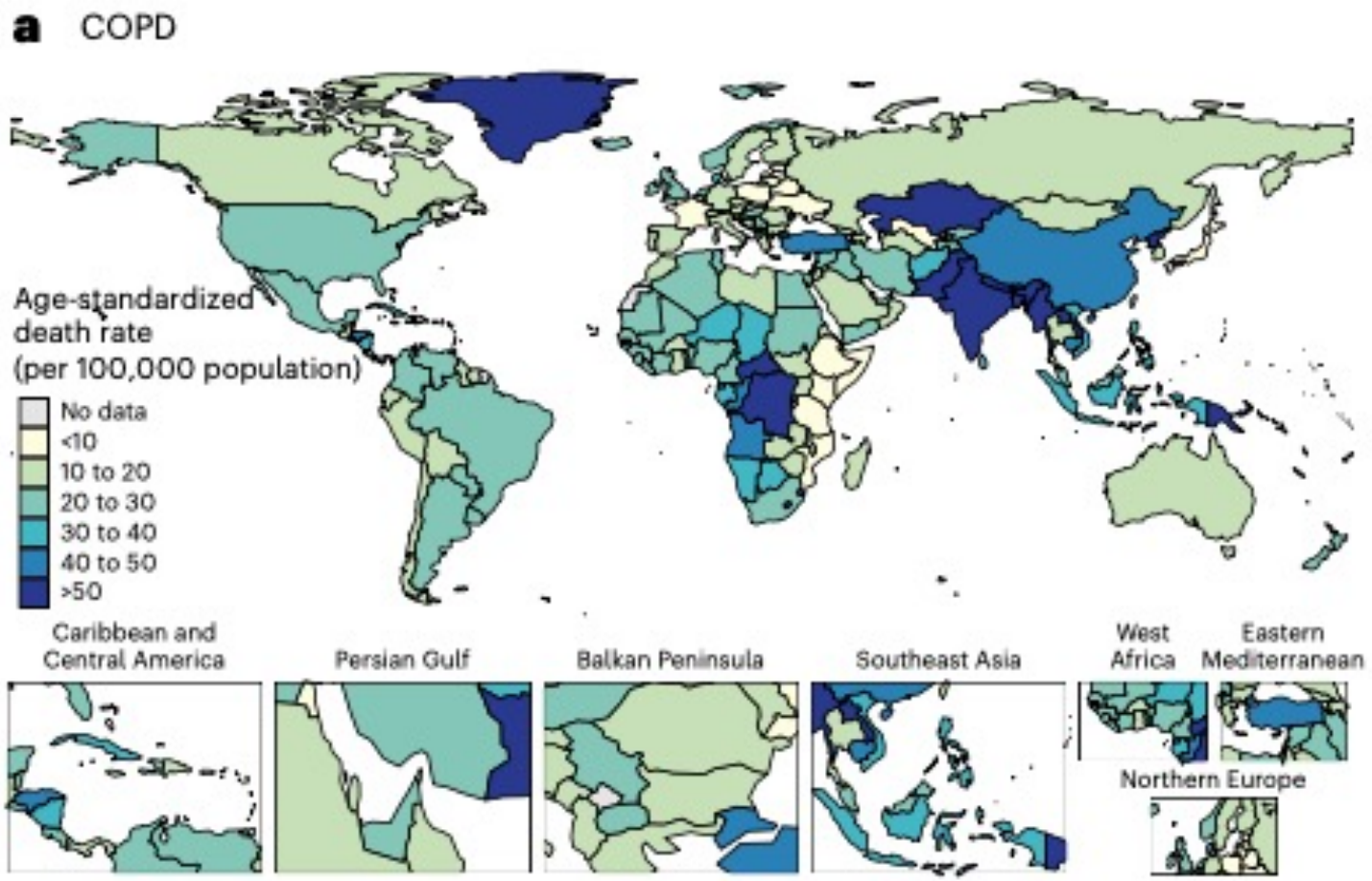


GLOBAL AGE SPECIFIC PREVALENCE OF CHRONIC RESPIRATORY DISEASES (CRD) IN 2023

Oh J, Kim S, Yim Y et al. Global regional and national burden od chronic respiratory diseases and impact of COVID-19 pandemic, 1990-2023: a Global burden of disease study. Nature Medicine, Vol. 32;197-223, 2026.

https://doi.org/10.1038/s41591-025-04077-9



GLOBAL AGE STANDARDIZED DEATH RATES OF CHRONIC RESPIRATORY DISEASES (CRD) IN 2023

Oh J, Kim S, Yim Y et al. Global regional and national burden od chronic respiratory diseases and impact of COVID-19 pandemic, 1990-2023: a Global burden of disease study. Nature Medicine, Vol. 32;197-223, 2026.

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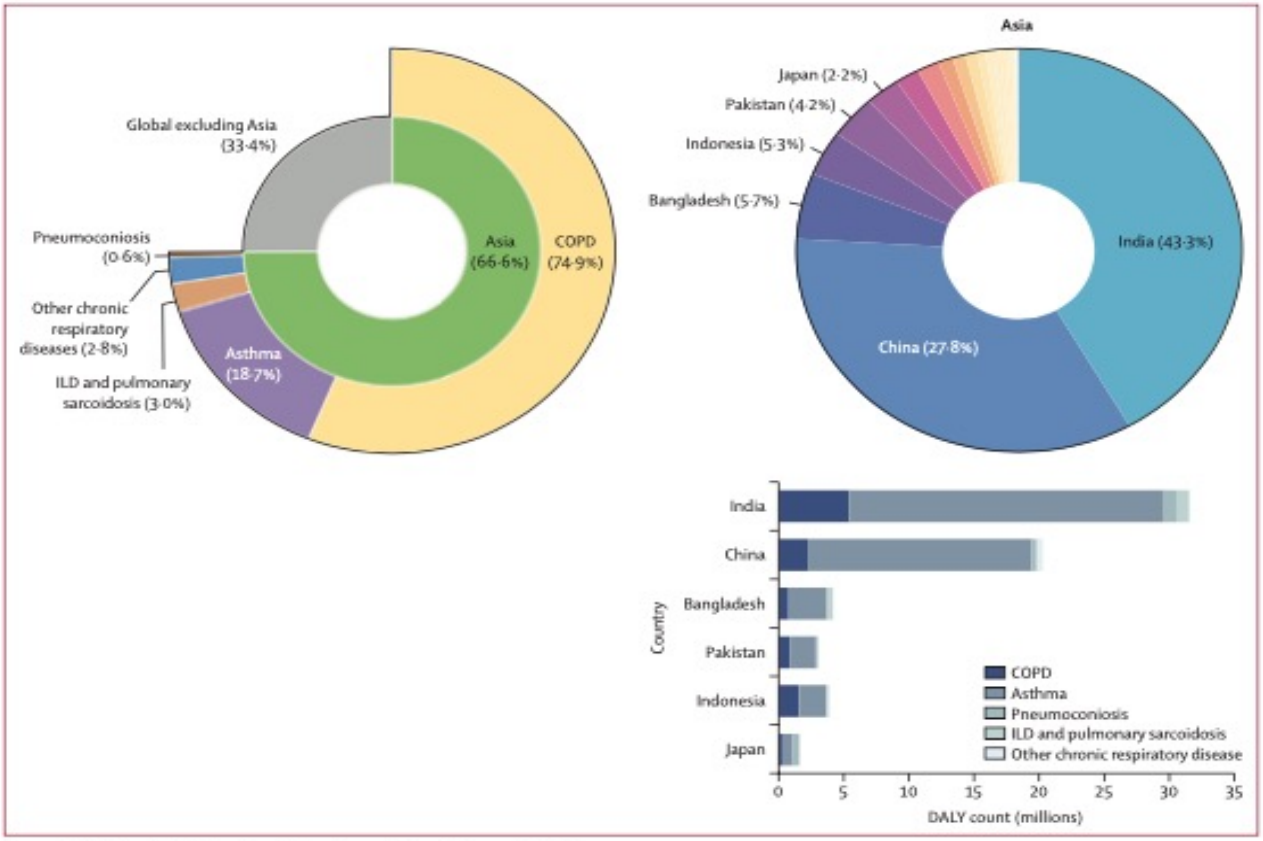
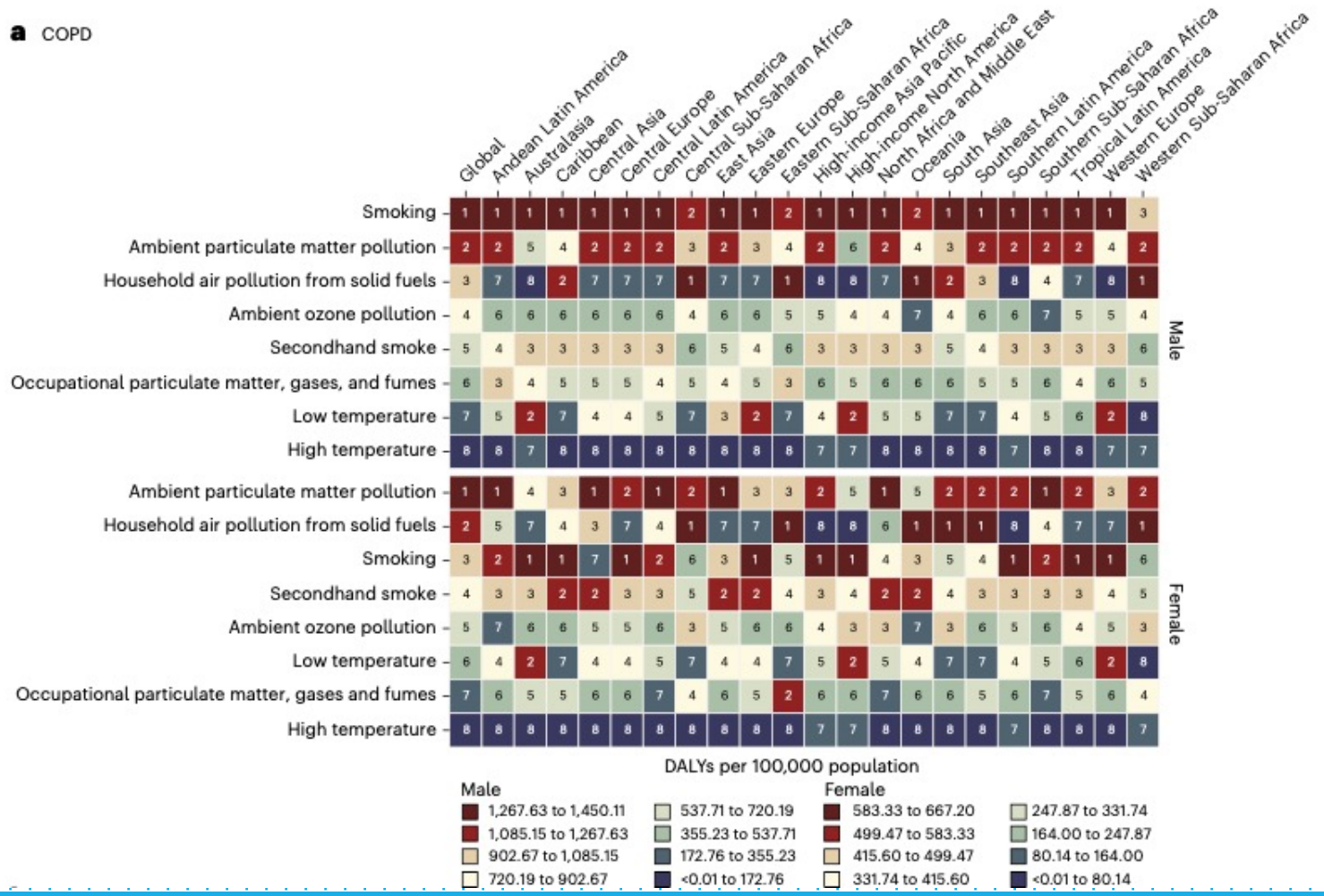


Figure 1: **Global and Asian burden of chronic respiratory diseases in 2023**
Values are GBD 2023 global estimates of disease burden based on DALY counts. COPD=chronic obstructive pulmonary disease. DALY=disability-adjusted life-year. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study. ILD=interstitial lung disease.

www.thelancet.com/respiratory **Published online January 21, 2026** **https://doi.org/10.1016/S2213-2600(25)00404-7**

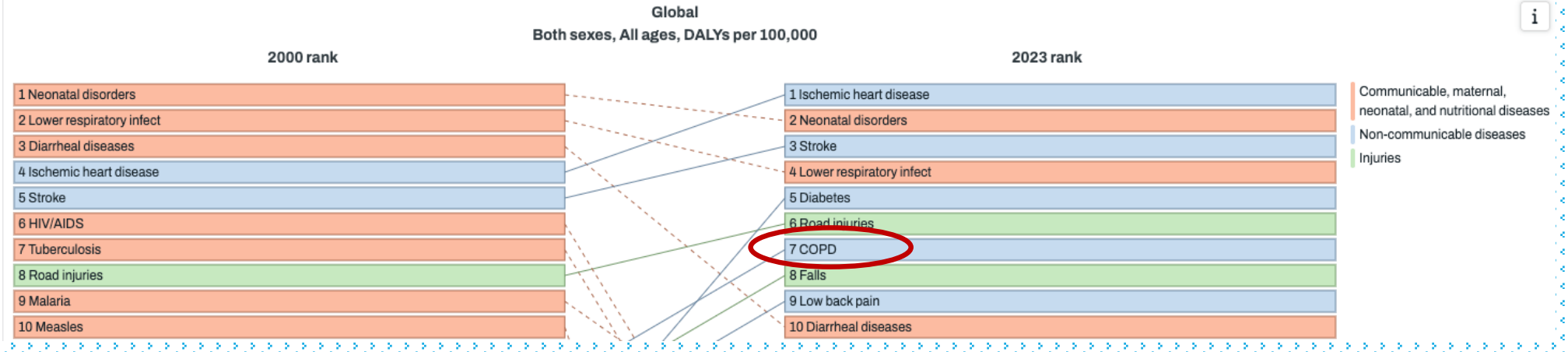
GLOBAL AND ASIAN BURDEN OF CHRONIC RESPIRATORY DISEASES IN 2023

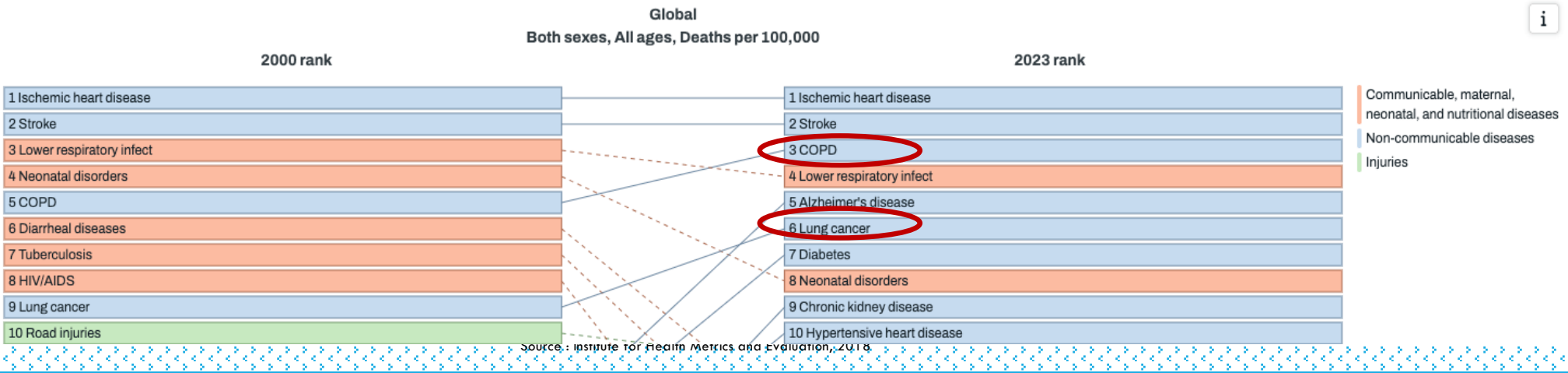


GLOBAL AND REGIONAL DISTRIBUTION OF AGE-STANDARDIZED DALY RATES FOR COPD BY RISK FACTOR IN MALES AND FEMALES, 2023

Oh J, Kim S, Yim Y et al. Global regional and national burden od chronic respiratory diseases and impact of COVID-19 pandemic, 1990-2023: a Global burden of disease study. Nature Medicine, Vol. 32;197-223, 2026.

https://doi.org/10.1038/s41591-025-04077-9

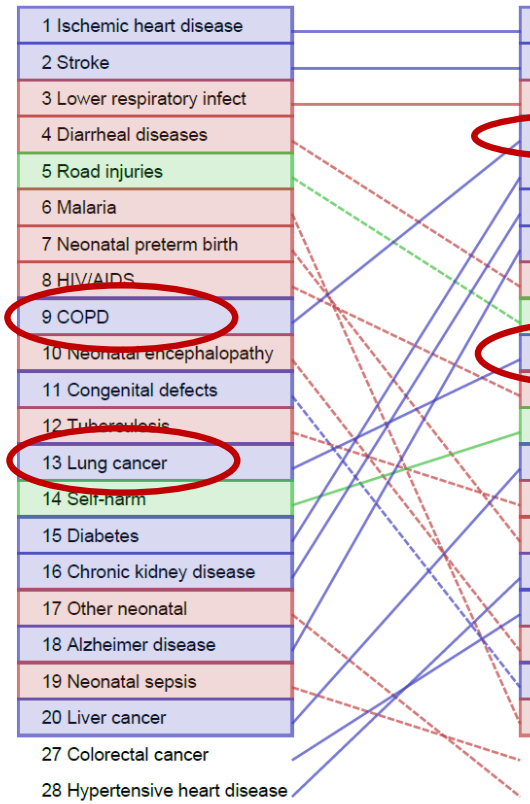




Source: Institute for Health Metrics and Evaluation, 2018

LEADING CAUSES OF DISEASE BURDEN BY DALYS IN 2000 VERSUS 2023

https://vizhub.healthdata.org/gbd-compare/



Leading Causes 2040	Mean % change number of YLLs	Mean % change all-age YLL rate	Mean % change age-standardized YLL rate
1 Ischemic heart disease	25.9 (-30.0 to 118.3)	5.8 (-41.8 to 86.9)	-26.0 (-60.4 to 35.9)
2 Stroke	3.7 (-33.6 to 69.4)	-12.9 (-45.2 to 41.2)	**-39.7 (-63.9 to -2.5)**
3 Lower respiratory infect	-18.4 (-47.6 to 13.3)	**-31.5 (-55.8 to -4.4)**	-35.3 (-59.5 to 0.4)
4 COPD	30.0 (-15.7 to 92.2)	9.2 (-28.5 to 60.7)	-29.5 (-56.8 to 4.1)
5 Diabetes	**89.9 (31.7 to 164.9)**	**59.4 (8.8 to 126.5)**	12.2 (-22.1 to 63.0)
6 Chronic kidney disease	96.2 (-4.9 to 275.9)	64.7 (-20.5 to 212.2)	22.3 (-39.9 to 127.5)
7 Alzheimer disease	**128.1 (57.7 to 211.3)**	**91.4 (30.7 to 162.0)**	-0.9 (-24.5 to 37.5)
8 Diarrheal diseases	-34.5 (-77.0 to 49.1)	-45.0 (-80.9 to 24.7)	-45.4 (-74.7 to 11.4)
9 Road injuries	**-31.4 (-45.4 to -8.7)**	**-42.4 (-53.9 to -21.4)**	**-40.4 (-51.2 to -19.8)**
10 Lung cancer	15.8 (-13.0 to 49.2)	-2.8 (-26.2 to 26.8)	**-30.5 (-48.2 to -8.3)**
11 HIV/AIDS	**-27.6 (-37.0 to -15.8)**	**-39.2 (-47.4 to -29.4)**	**-34.4 (-43.8 to -25.2)**
12 Self-harm	5.6 (-18.0 to 39.1)	-11.4 (-30.9 to 17.6)	-15.3 (-30.7 to 9.7)
13 Liver cancer	**60.2 (24.6 to 125.5)**	**34.4 (5.2 to 91.7)**	4.3 (-20.6 to 46.7)
14 Tuberculosis	-31.2 (-48.9 to 1.3)	**-42.3 (-57.2 to -14.8)**	**-47.0 (-61.3 to -19.7)**
15 Neonatal preterm birth	**-49.0 (-63.3 to -31.1)**	**-57.3 (-68.4 to -43.2)**	**-47.2 (-59.1 to -34.3)**
16 Hypertensive heart disease	**80.4 (5.3 to 225.0)**	51.5 (-12.5 to 175.0)	-3.9 (-42.2 to 73.3)
17 Colorectal cancer	**54.0 (14.1 to 106.1)**	29.3 (-5.1 to 72.7)	-10.8 (-32.5 to 21.7)
18 Neonatal encephalopathy	**-45.0 (-67.4 to -11.4)**	**-53.9 (-72.0 to -26.1)**	**-44.3 (-66.8 to -13.5)**
19 Congenital defects	**-39.4 (-58.5 to -17.2)**	**-49.2 (-65.1 to -30.8)**	**-32.1 (-47.7 to -15.8)**
20 Malaria	**-57.4 (-66.5 to -47.4)**	**-64.2 (-71.7 to -56.1)**	**-58.5 (-69.8 to -48.9)**
21 Neonatal sepsis			
29 Other neonatal			

Source : Institute for Health Metrics and Evaluation, 2018

LEADING CAUSES OF DISEASE BURDEN BY DALYS IN 2040 VERSUS 2016

What causes the most deaths?

Non-communicable diseases

Cause	2013 rank	2023 rank	Change in deaths per 100k, 2013-2023
Ischemic heart disease	1	1	↓ −6.6
Alzheimer's disease	4	2	↑ +6.8
Stroke	5	3	↑ +5.6
COPD	3	4	↑ +0.7
Lung cancer	2	5	↓ −9.3
Chronic kidney disease	6	6	↑ +13.1
Drug use disorders	15	7	↑ +15.8
Hypertensive heart disease	11	8	↑ +8.9
Diabetes	9	9	↑ +3.1
Colorectal cancer	7	10	↑ +0.2

Top 10 causes of deaths per 100k in 2023 and rate change 2013–2023, all ages combined

See related publication: Global burden of 292 causes of death in 204 countries and territories and 660 subnational locations, 1990–2023: a systematic analysis for the Global Burden of Disease Study 2023

LEADING CAUSES OF DEATHS IN THE USA, 2013 VERSUS 2023

What causes the most deaths?

- Communicable, maternal, neonatal, and nutritional diseases
- Non-communicable diseases
- Injuries

Cause	2013 rank	2023 rank	Change in deaths per 100k, 2013-2023
Ischemic heart disease	1	1	↑ +14.4
Nature disaster	121	2	↑ +61.8
Stroke	2	3	↓ −5.5
COPD	3	4	↑ +6.4
Lung cancer	4	5	↑ +6.5
Chronic kidney disease	6	6	↑ +8.7
Lower respiratory infect	9	7	↑ +15.2
Diabetes	5	8	↑ +6.3
Alzheimer's disease	8	9	↑ +8.9
Hypertensive heart disease	7	10	↑ +2.5

Top 10 causes of deaths per 100k in 2023 and rate change 2013–2023, all ages combined

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LEADING CAUSES OF DEATHS IN TÜRKIYE, 2013 VERSUS 2023

RECAP – GLOBAL CRD AND COPD BURDEN

- Chronic Respiratory Diseases (CRD) is one of the most prevalent medical conditions, constituting a major burden of illness worldwide, with about 600 million prevalent cases and 4 million deaths worldwide.
- COPD constitutes the largest proportion of CRDs worldwide, estimated at around 90% of all CRD cases. The numbers are likely to increase with ageing of the population and increasing prevalence of COPD from cohorts of smokers reaching later decades of life, especially in the developing world.
- COPD is the third leading cause of death globally.
- COPD is projected to remain as one of the top 3 leading causes of premature death and disability, resulting in considerable loss of longevity, life quality, productivity and welfare, and major increase in healthcare spending.
- Almost all risk factors for COPD are avertable; yet they face the well-known obstacles to behavioral change (e.g., smoking), particularly in low and high middle-income countries/emerging economies.

OUTLINE

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ECONOMIC BURDEN OF COPD

Source : Agarwal, D.
www.thelancet.com/lancetgh
Vol 11 August 2023

COPD generates substantial cost for health systems

See Articles page e1183

hronic obstructive pulmonary disease (COPD) is a substantial public health concern worldwide. The economic cost of COPD includes the expenses incurred for COPD screening, diagnosis, and management, the direct and indirect costs of which add a burden to health systems, directly impacting countries' health budgets. The economic cost of COPD in the USA is substantial and is increasing—COPD had a projected cost of US$49 billion in 2020.[1] The estimated direct cost of COPD in Europe was reported to range from €1963 to €10 701 per patient per year.[2] In India, COPD incurs 2–4-fold higher costs compared with asthma and ischaemic heart disease[3] and studies have shown that the costs of managing acute exacerbations of COPD contribute 45–70% to the total expenses of COPD management. COPD causes an economic loss of more than 100 000 crore rupees (US$13·4 billion) per annum in India,[4] which is forecast to increase in the coming years due to the increased prevalence of COPD and poor awareness of COPD among the community and health-professionals.[5]

In *The Lancet Global Health*, Simiao Chen and colleagues[6] provide a comprehensive picture of the economic burden of COPD in countries and territories globally, which will help organisations such as WHO, the European Respiratory Society, and the American Thoracic Society to design policy at the country level (if needed). Chen and colleagues' findings could help individual countries to plan strategies to reduce the burden of COPD and inform updates of the COPD screening, diagnosis, and management guidelines, led by the *Global Initiative for Chronic Obstructive Lung Disease*. Chen and colleagues' study contributes substantially to the current literature, and researchers could use the findings to develop future implementation research in countries with a high burden of COPD, helping to design solutions to reduce the economic burden of COPD. The local context for screening, diagnosis, and management of COPD differs from country to country due to variations in health system infrastructure and services provided. Within a country such as India, there are a lot of variations at the state level when it comes to health system infrastructure, services, and policies. These are crucial factors that researchers and policy makers need to nsider when planning interventions to reduce the onomic burden of COPD. In low-income and middle-come countries (LMICs) such as India, the private alth sector also plays a central role in the health onomy, and its involvement as a key stakeholder eds to be considered. Research with integrated proaches is warranted, involving all relevant akeholders to combat the increasing burden of PD. Most data on the cost of COPD have come from udies in the USA and Europe, with little work being ne in Asian countries despite Asia having a higher PD burden.[7]

To fully understand the implications of the burden COPD, it needs to be described in terms of societal d individual or household financial consequences.[8] here is a considerable out-of-pocket health-care st for patients with COPD, particularly among those th severe COPD because they have exacerbations d frequent hospitalisations. Patients with COPD ed support in dealing with their disease, as many ce emotional as well as physical challenges. Further research is needed to better understand the emotional challenges faced by people with COPD.

Increasing awareness of COPD is essential to educate society. Researchers and policy makers could plan some cost-effective interventions highlighting the need to adopt different cost-related policy approaches according to the course of the disease burden. Community-based screening with the help of community health workers could make a real difference in reducing economic loss from COPD if individuals are diagnosed at an early disease stage. Awareness among the community and involvement of all stakeholders are also crucial. Research is needed to study current challenges with use of spirometry in the field for confirming diagnosis, so that simplified spirometry might be developed as an alternative. Screening and diagnosing COPD at an early stage can help save substantial direct and indirect costs for both patients and the public health system. Interventions using innovative and locally made technology will allow every patient, even in rural and remote areas, to be diagnosed early in their disease course and attain a better health-related quality of life with regular interventions provided by the existing primary health system.

Chronic obstructive pulmonary disease (COPD) is a substantial public health concern worldwide. The economic cost of COPD includes the expenses incurred for COPD screening, diagnosis, and management, the direct and indirect costs of which add a burden to health systems, directly impacting countries' health budgets. The economic cost of COPD in the USA is substantial and is increasing—COPD had a projected cost of US$49 billion in 2020.[1] The estimated direct cost of COPD in Europe was reported to range from €1963 to €10 701 per patient per year.[2] In India, COPD incurs 2–4-fold higher costs compared with asthma and ischaemic heart disease[3] and studies have shown that the costs of managing acute exacerbations of COPD contribute 45–70% to the total expenses of COPD management. COPD causes an economic loss of more than 100 000 crore rupees (US$13·4 billion) per annum in India,[4] which is forecast to increase in the coming years due to the increased prevalence of COPD and poor awareness of COPD among the community and health-care professionals.[5]

Country	Est. Annual Direct Cost per Patient (USD)	Total Annual Economic Burden (National)	Primary Cost Driver
USA	~$9,981 – $10,367	~$49 Billion	Hospitalizations & ER visits
Germany	~$8,644	~€15–20 Billion	Long-term care & Rehabilitation
France	~$5,200 – $6,000	~€10–12 Billion	Medication & Specialist visits
UK	~$2,100 – $4,500	~£1.9 Billion (Direct)	Emergency admissions
Türkiye	~$1,031 – $1,500	~$2.5–3 Billion	Hospitalization & exacerbations

A COMPARATIVE BREAKDOWN OF ANNUAL DIRECT COSTS AND TOTAL ECONOMIC BURDEN OF COPD IN SELECTED OECD COUNTRIES

ECONOMIC BURDEN OF COPD IN EU

Source : Rehman A, Hassali MAA et al: The conomic burden of chronic obstructive pulmonary disease (COPD) in Europe: results from a systemic review of the literature. The European journal of Health Economics. (2020) 21:181-194. https://doi.org/10.1007/s10198-019-01119-1

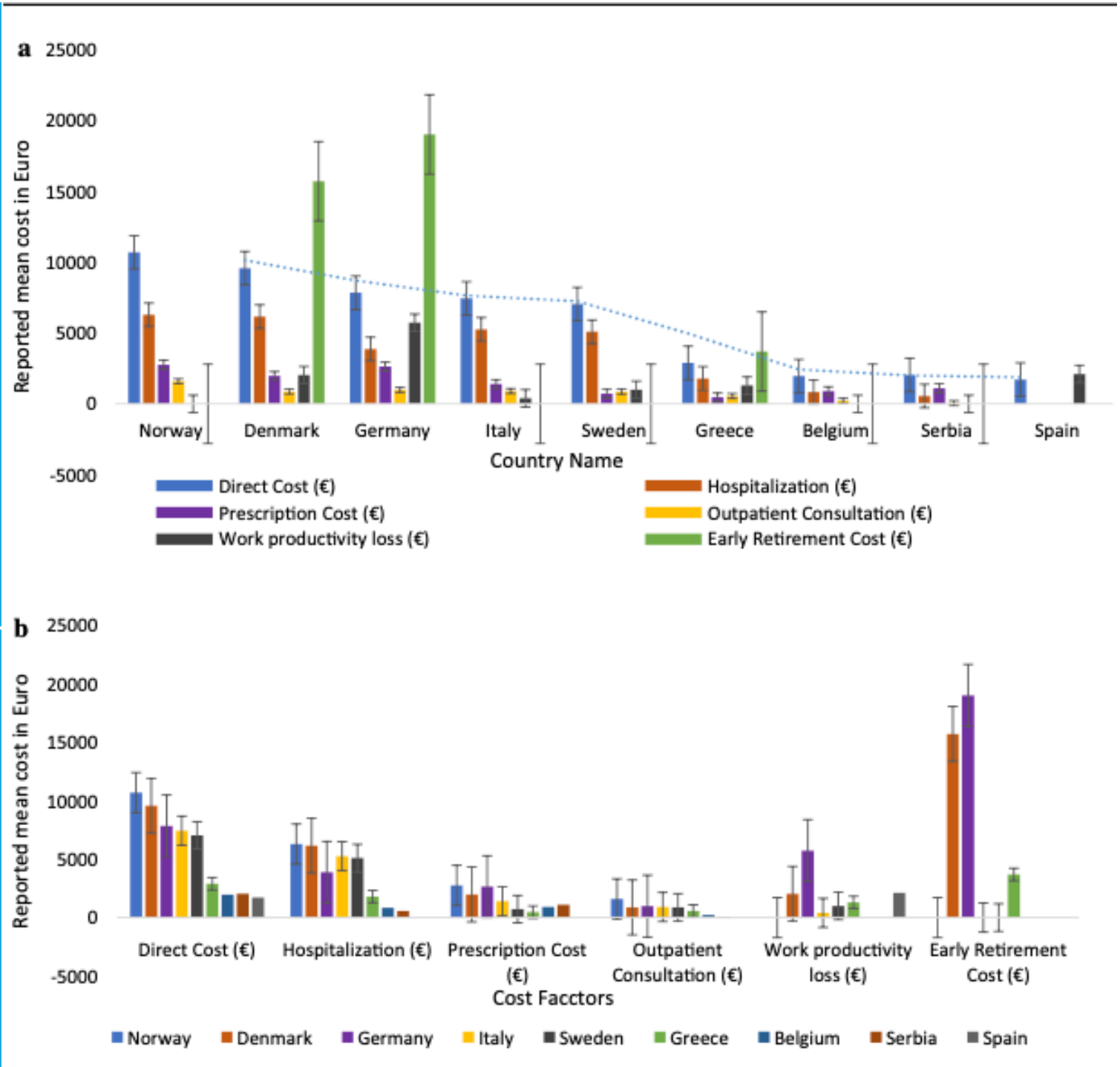


Fig. 2 **a** Cost of management of COPD in nine different European Countries. **b** Comparison of different cost factors in management of COPD in nine different European Countries

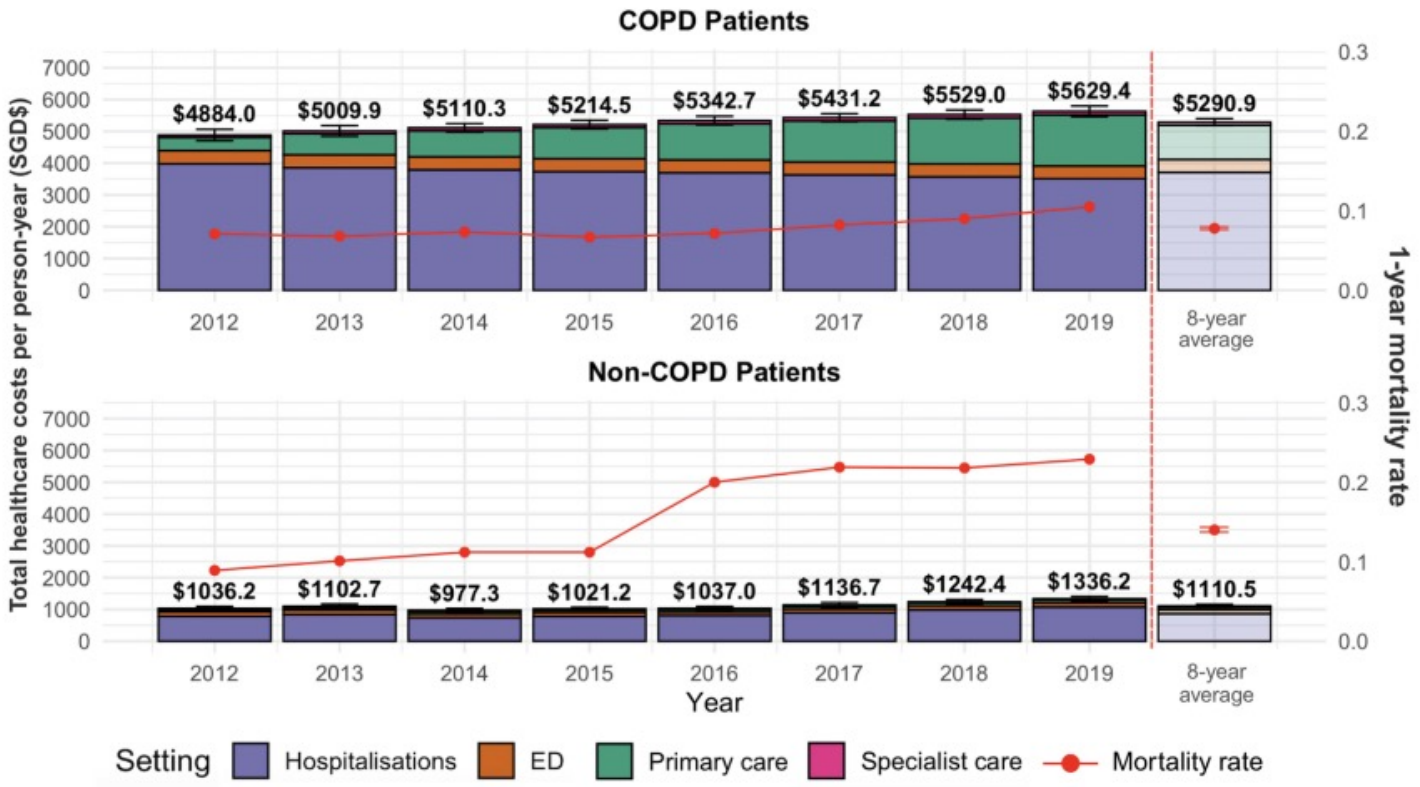
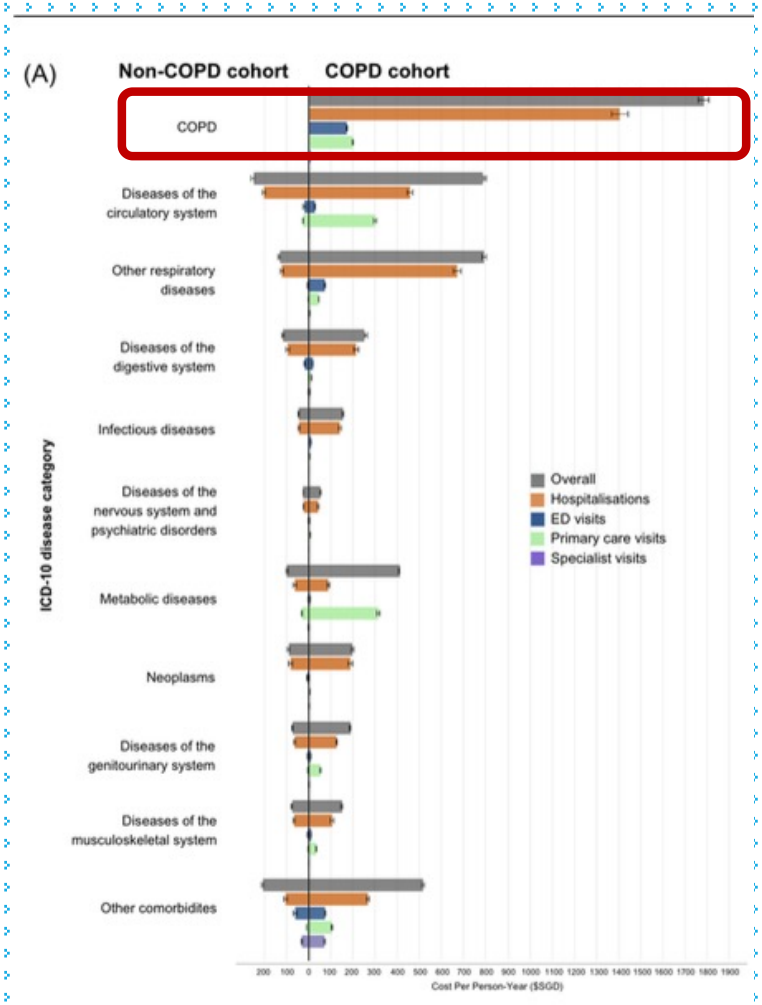


Figure 1 Time trends of total healthcare costs and 1-year mortality rates for COPD and non-COPD cohorts by setting from 2012 to 2019. The translucent column represents the 8-year average costs in each cohort. The error bars indicate the 95% confidence intervals of the total cost estimates and 1-year median mortality rates. All costs were measured in 2023 Singaporean dollars (SGD$1=US$0.76=£0.60=€0.69).
Abbreviations: COPD, chronic obstructive pulmonary disease; ED, emergency department; SGD, Singapore dollar.

Source: Juang YR, Lim, LHM et al. Healthcare costs and trends of Multimorbidity in COPD patients: a population-based study in Singapore. Intl. J. Chronic Obstructive Pulmonary Disease. 2026:21. https://doi.org/10.2147/COPD.S563620

HEALTHCARE SPENDING FOR COPD AND NON-COPD PATIENTS IN SINGAPORE



Source: Juang YR, Lim, LHM et al. Healthcare costs and trends of Multimorbidity in COPD patients: a population-based study in Singapore. Intl. J. Chronic Obstructive Pulmonary Disease. 2026:21. https://doi.org/10.2147/COPD.S563620

HEALTHCARE SPENDING PER PATIENT FOR COPD AND NON-COPD PATIENTS IN SINGAPORE

Table 2 Estimated Annualised Total Costs of Multimorbidity by Age-Sex Subgroup for COPD Patients

Disease Category	Females Aged 40–64	Males Aged 40–64	Females Aged 65 or Above	Males Aged 65 or Above	p-value
Cost (SGD$), mean (95% CI)					
Total	4287.9 (4156.9–4497.9)	4958.6 (4831.8–4986.2)	5339.7 (5199.2–5461.7)	5658.8 (5613.3–5798.6)	<0.001
COPD	1213.3 (1137.2–1241.3)	1771.7 (1716.4–1816.4)	1747.5 (1710.2–1791.9)	1859.2 (1835.3–1892.0)	<0.001
Diseases of the circulatory system	475.5 (403.5–556.8)	755.4 (768.0–789.1)	787.4 (787.6–845.3)	844.7 (820.4–836.9)	<0.001
Other respiratory diseases	794.7 (735.6–848.8)	645.9 (622.8–668.6)	874.8 (820.0–914.7)	901.2 (887.9–911.7)	<0.001
Diseases of the digestive system	207.6 (198.4–247.5)	222.6 (221.0–246.0)	301.4 (279.7–343.7)	265.5 (253.5–280.9)	<0.001
Infectious diseases	143.6 (118.0–161.6)	148.2 (141.2–155.4)	146.2 (141.7–153.0)	165.6 (159.6–167.1)	0.26
Diseases of the nervous system and psychiatric disorders	47.4 (37.2–52.1)	51.6 (49.8–53.1)	50.0 (47.8–58.5)	55.5 (48.1–60.0)	0.93
Metabolic diseases	388.1 (360.6–440.9)	400.9 (392.1–402.0)	382.2 (359.2–392.5)	433.5 (426.1–436.1)	0.55
Neoplasms	146.4 (101.5–174.3)	193.3 (189.7–209.7)	139.1 (114.3–134.2)	221.5 (206.6–244.7)	<0.001
Diseases of the genitourinary system	194.4 (137.8–212.9)	133.5 (130.0–139.4)	224.7 (219.1–244.8)	228.9 (217.2–226.6)	<0.001
Diseases of the musculoskeletal system	199.5 (123.3–222.6)	156.1 (151.1–163.0)	194.9 (167.3–207.6)	130.6 (125.4–135.7)	<0.001
Other comorbidities	485.0 (446.5–506.8)	483.5 (467.2–504.7)	494.9 (485.7–529.2)	555.0 (546.6–559.7)	0.15

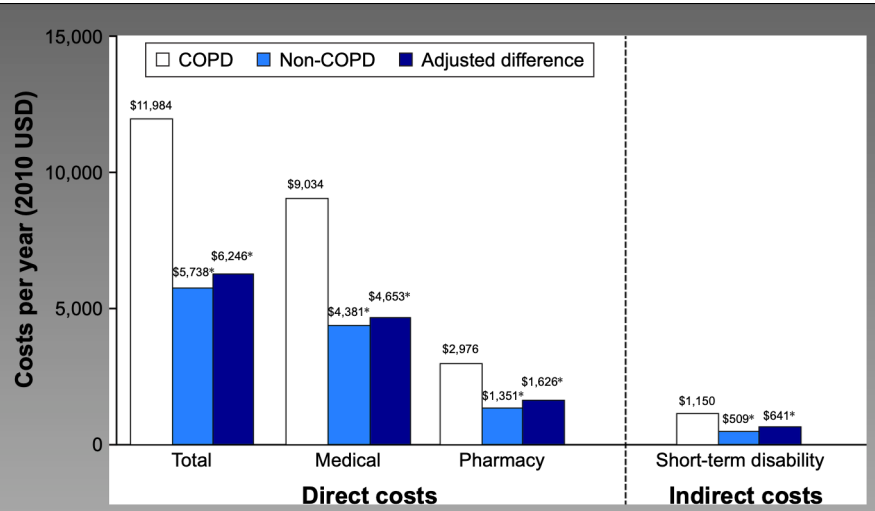
Note: All costs were measured in 2023 Singaporean dollars (SGD$1=US$0.76=£0.60=€0.69).
Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; SGD, Singapore dollars.

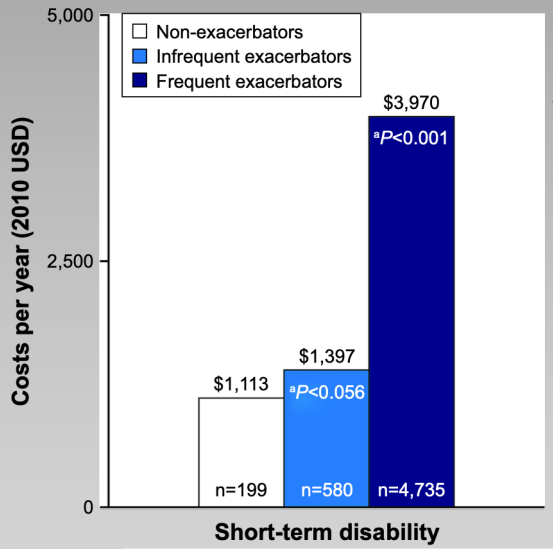
Source: Juang YR, Lim, LHM et al. Healthcare costs and trends of Multimorbidity in COPD patients: a population-based study in Singapore. Intl. J. Chronic Obstructive Pulmonary Disease. 2026:21. https://doi.org/10.2147/COPD.S563620

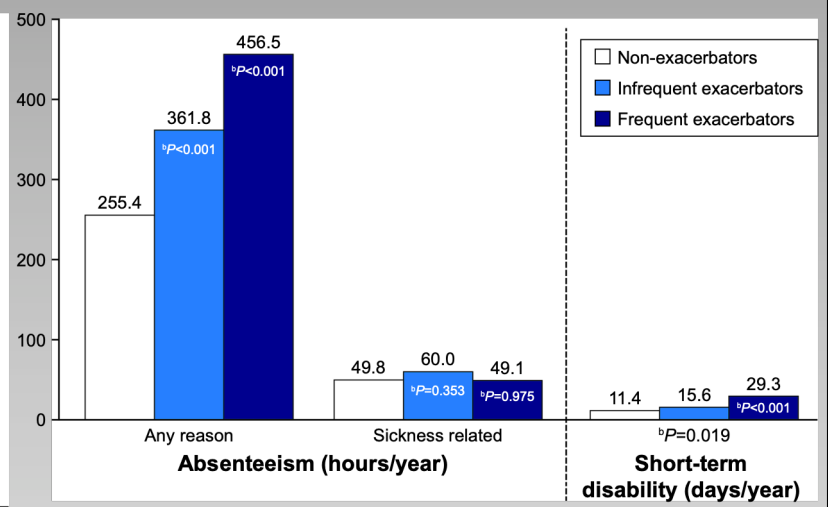
HEALTHCARE SPENDING PER PATIENT FOR COPD AND NON-COPD PATIENTS IN SINGAPORE

COPD: DIRECT AND INDIRECT COSTS AND LOSS OF PRODUCTIVITY

Patel JG, et al: COPD Affects Worker Productivity and Healthcare Costs. Intl J of COPD, 2018;13: 2301-2311.







Plain language summary

Working-age patients with COPD are costly to employers and incur approximately twice as high costs as those without COPD. Productivity claims associated with COPD were responsible for 10% of the overall cost burden. This retrospective, observational, matched cohort study aimed to measure the true burden of COPD in insured, working individuals by calculating incremental direct and indirect costs. Direct costs for patients with frequent exacerbations were 22% higher than for patients with infrequent exacerbations and 55% higher than for those classified as non-exacerbators. This study reveals a number of statistically significant predictors of high incremental costs associated with COPD, for example, the frequency of exacerbations.

Impact of COPD on Health Care Costs

COPD FOUNDATION

WHAT ARE THE COSTS OF COPD?

While COPD receives less attention among employers compared to other chronic diseases, it is the third leading cause of death in the U.S. and seventy percent of the 24 million individuals with COPD are under age 65. COPD is one of the most burdensome diseases for employers but with half of the 24 million not properly diagnosed, the cost burden may be greater than the data reveals.

- In 2010, COPD resulted in $49.9 billion in direct and indirect costs . [2]
- Commercially-insured COPD patients cost more per patient annually than those with Medicare.[3]
- Total costs incurred by COPD patients are approximately $6000 higher than non-COPD patients. [4]
- 13-14% of COPD patients had a hospital readmission; 41-49% had a readmission within 60 days.[3]
- The average direct per patient costs for commercially insured increased 6% per year between 2006 and 2009.[3]
- Treatments that reduce frequency of COPD-related exacerbations are associated with lower COPD-related medical costs.[3]
- 40% of COPD costs could be avoided by preventing complications and hospitalizations.[5]
- Individuals with COPD had more days of lost productivity than any other chronic condition. [10]

The majority of COPD expenditures are due to complications and hospitalizations, many of which are preventable. As with other chronic diseases, improved health care management can reduce poor outcomes and decrease costs related to COPD. [6] Better care and staying on treatment can lower the avoidable costs and make patients feel better, which increases productivity and decreases absenteeism. Thus, effective management of COPD patients can result in decreased costs, increased productivity, and decreased absenteeism.

AN (OUTDATED) SUMMARY OF THE IMPACT OF COPD ON HEALTHCARE COSTS IN THE USA(*)

(*) Added here to highlight USA specific details of the cost domains

RECAP – ECONOMIC BURDEN OF COPD BURDEN

- **Direct Costs and Hospitalization:** Hospitalization is the primary cost driver, often exceeding $3,500 per admission, with intensive care usage significantly raising costs. In Europe, direct costs range from roughly €2,000 to over €10,000 per patient annually.

- **Regional Variations:** The USA and Europe face substantial, rising costs. In 2020, US costs were estimated at $49 billion, and in Europe, the economic burden was roughly $56 billion.

- **Indirect Costs:** Productivity losses are significant, with an estimated 16.9 work-loss days per patient annually in some studies, totaling nearly €1,000 per patient in productivity loss.

- **Key factors driving these costs** include late diagnosis, disease severity, and the high rate of exacerbations

- The **economic burden** is increasing due to aging populations and high comorbidity risks.

- **Total Economic Impact:** By 2030, the cost of COPD in developed countries is projected to reach over **$2 trillion, with per-patient costs potentially reaching $4,800.**

OUTLINE

- Burden of chronic respiratory diseases (CRD) in adults and associated modifiable risk factors globally
  - COPD (chronic bronchitis and emphysema)
  - Lung Cancer
- Global and regional economic burden of COPD
- Novel diagnostic and treatment approaches and the role of interventional bronchoscopy
- An innovative corporate solution
- The Way Forward

COPD DEFINITION:

THE GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE (GOLD)

"Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. The chronic airflow limitation that characterizes COPD is caused by a mixture of small airways disease (e.g., obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person. Chronic inflammation causes ***structural changes****, small airways narrowing and destruction of lung parenchyma. A loss of small airways may contribute to airflow limitation and muco-ciliary dysfunction, a characteristic feature of the disease."*

COPD PATHOLOGY

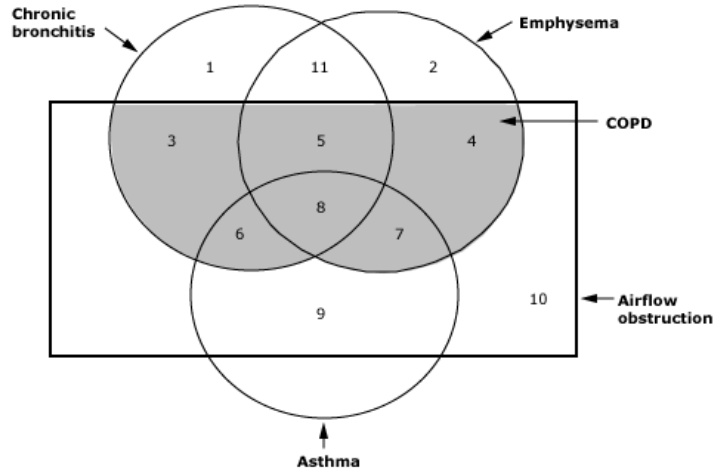
- Predominantly affecting airways, but also the alveoli (lung parenchyma)
  - **Airways**
    - chronic inflammation, including T-lymphocytes, neutrophils, monocytes, macrophages
    - goblet cell hyperplasia and hypertrophy
    - mucus gland hyperplasia
    - fibrosis
    - narrowing and collapse of small airways
  - **Lung parenchyma**
    - dilation and destruction of acinus (respiratory bronchiole, and alveolar ducts, sacs and alveoli)

COPD: MORE THAN ONE DISEASE

"COPD is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. The chronic airflow limitation that characterizes COPD is caused by a mixture of small airways disease (e.g., obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person. Chronic inflammation causes structural changes, small airways narrowing, and destruction of lung parenchyma. A loss of small airways may contribute to airflow limitation and muco-ciliary dysfunction, a characteristic feature of the disease."

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease: 2020 Report.

Chronic obstructive pulmonary disease



This nonproportional Venn diagram shows subsets of patients with chronic bronchitis, emphysema, and asthma (black circles). The subsets defined as COPD are shaded gray. Subset areas are not proportional to actual relative subset sizes. Asthma is, by definition, associated with reversible airflow obstruction; in variant asthma, special maneuvers may be necessary to make the obstruction evident. Patients with asthma whose airflow obstruction is completely reversible (subset 9) are not considered to have COPD. In many cases it is virtually impossible to differentiate patients with asthma whose airflow obstruction does not remit completely from persons with chronic bronchitis and emphysema who have partially reversible airflow obstruction with airway hyperreactivity. Thus, patients with unremitting asthma are classified as having COPD (subsets 6, 7 and 8). Chronic bronchitis and emphysema with airflow obstruction usually occur together (subset 5), and some patients may have asthma associated with these two disorders (subset 8). Individuals with asthma exposed to chronic irritation, as from cigarette smoke, may develop chronic productive cough, a feature of chronic bronchitis (subset 6). Such patients are often referred to in the United States as having asthmatic bronchitis or the asthmatic form of COPD. Persons with chronic bronchitis or emphysema without airflow obstruction (subsets 1, 2 and 11) are not classified as having COPD. In order to emphasize that cough and sputum are abnormal, individuals with these symptoms and normal lung function were classified as GOLD Stage 0, at risk, in the original GOLD classification [1]. This stage was deleted in the 2006 revision because of uncertainties about whether it is progressive [2]. Patients with airway obstruction due to diseases with known etiology or specific pathology, such as cystic fibrosis or obliterative bronchiolitis (subset 10), are not generally included in the definition of COPD.

1. Data from: Global initiative for chronic obstructive lung disease (GOLD). Workshop report: Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: Update 2005.
2. Data from: Global initiative for chronic obstructive lung disease (GOLD). Workshop report: Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: Update 2006.

COPD DIAGNOSIS & STAGING

- Diagnosis
  - Relatively easy, with well-established criteria for Diagnosis and Differential Diagnosis (Chronic obstructive asthma, bronchiectasis, etc.
    - Lung Function Tests (LFT) - Spirometry
    - Chest X-Ray
    - CT Scan, as needed
  - Significant overlap with Emphysema and Chronic bronchitis
- Staging
  - GOLD, based on symptoms and exacerbation
  - BODE Index (six-minute walking)
  - COPD Foundation
- Universal Access to Diagnostics

COPD STAGING

Multidimensional assessment of COPD

GOLD "ABCD" grading: Assessment of symptoms and risk of exacerbations for initiation of COPD therapy		
Assess exacerbation risk: Exacerbations/Hospitalizations	**Assess symptoms**	
	mMRC* 0 to 1; CAT <10¶	**mMRC ≥2; CAT ≥10**
0 or 1 exacerbations without hospitalization	A	B
≥2 exacerbations or ≥1 hospitalization	C	D

GOLD: Severity of airflow limitation (based on postbronchodilator FEV_1)		
Stage	**Severity**	**FEV_1 (percent predicted)**
In patients with FEV_1/FVC <0.7:Δ		
GOLD 1	Mild	≥80
GOLD 2	Moderate	50 to 79
GOLD 3	Severe	30 to 49
GOLD 4	Very severe	<30

COPD: chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC: modified Medical Research Council dyspnea scale; CAT: COPD Assessment Test; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity.

* mMRC dyspnea scale: Refer to UpToDate graphic.

¶ http://www.catestonline.org.

Δ The GOLD guidelines (www.goldcopd.org) prefer the threshold of <0.7 to the alternative of the fifth percentile lower limit of normal (LLN) for FEV_1/FVC.

From the Global Strategy for the Diagnosis, Management and Prevention of COPD 2017, © Global Initiative for Chronic Obstructive Lung Disease (GOLD), www.goldcopd.org. Adapted with permission. The content within this table is still current as of the 2019 GOLD report.

CONVENTIONAL COPD TREATMENT AND CASE MANAGEMENT

- **Aim**
  - **There is no cure, only palliation**
    - Symptoms
    - Quality of Life
    - Functionality
    - Prevention of exacerbations
- **Case management options**
  - **Pharmacological (bronchodilators &glucocorticoids)**
    - **A**nti-inflammatory and smooth muscle relaxant
    - Both inhaled therapy
    - Considerable follow up and dose adjustment
    - Side effects of multidrug therapy
  - Antibiotics
  - Vaccines
  - **Non-pharmacological**
    - posture, aid to expectoration
    - smoking cessation
  - **Oxygen Therapy**
  - **Bronchoscopic and Surgical Interventions**
    - Mostly for emphysema (lung volume reduction)
  - **Lung Transplantation**

A NOVEL APPROACH TO COPD TREATMENT AND CASE MANAGEMENT: YKK RESECTOR BALLOON

- **Long lasting and sustainable improvement in**
  - Symptoms
  - Quality of Life
  - Functionality
  - Prevention of exacerbations
- **Significant reduction in need for pharmacological therapy**
- **Prospects of phasing out of oxygen therapy**
- **Prospects for reduced lung cancer risk**
- **Bronchoscopic (non-surgical) Intervention**

Observational Study

Medicine®

OPEN

Follow-up outcomes of chronic obstructive pulmonary disease patients who underwent dilatation and curettage with the Karakoca resector balloon

A 188-case series over 5 years

Yalcin Karakoca, MD[a,*], Guler Gogus, MD[a], Seha Akduman, MD[b], Baykal Erturk, MD[c]

Abstract

We previously reported satisfactory results with the Karakoca resector balloon in 10 patients with stage IV chronic obstructive pulmonary disease (COPD) who did not respond to medical treatment. In this article, we present the outcomes of the Karakoca resector balloon dilatation and curettage technique in a larger case series (n = 188).

A total of 188 COPD patients [mean age (SD): 69.2 (8.0) years; 46 females] classified as stage III to IV by the Global Initiative for Obstructive Lung Disease criteria underwent balloon desobstruction for segmental and subsegmental bronchi by therapeutic bronchoscopy. None of the patients could have achieved symptom relief even under high-dose inhaled bronchodilators and corticosteroids, oral corticosteroids, or oxygen and noninvasive mechanical ventilation therapy before the intervention. Forced expiratory volume in 1 s (FEV_1) and oxygen saturation (SpO_2) were measured, and modified Borg dyspnea scale (MBS) scores were determined before and 1 week and 1 month after the intervention.

All patients were active smokers and 80% had concomitant chronic diseases. After the intervention, there was a notable reduction in the oxygen need of the patients. Comparison of lung function tests 1 week after the procedure with results before the procedure showed significant improvements in FEV_1, MBS, and SpO_2 levels ($P < 0.001$ for each), and the improvements were maintained for the entire postprocedural month ($P < 0.001$ for each). Except for 4 males, all patients were free of symptoms.

These results confirmed our early observations that balloon dilatation and curettage is a safe and successful technique for medical treatment-resistant COPD.

Abbreviations: COPD = chronic obstructive pulmonary disease, DC = dilatation and curettage, FEF = forced expiratory flow, FEV_1 = forced expiratory volume in 1 s, FVC = forced vital capacity, GOLD = Global Initiative for Obstructive Lung Disease, MBS = modified Borg scale, SpO_2 = oxygen saturation, VQ = ventilation/perfusion lung scan.

Keywords: chronic obstructive pulmonary disease, Karakoca resector balloon desobstruction, stage III to IV

YKK RESECTOR BALLOON TREATMENT PROTOCOL

- Selection Criteria
  - COPD staging according to GOLD (Stages III and IV)
  - Any additional criteria, i.e., severity, frequency of attacks, AntiB and other medications, Lung Function Tests, Oxygen saturation, home-based oxygenotherapy, anesthesia etc.)
  - Clear documentations of symptoms and signs for interventional therapy
- Treatment protocol
  - Pre intervention preparation
  - Intervention
  - Post-intervention/rehabilitation
- Post intervention follow up
  - Duration
  - Standard testing, (LFTs, SpO2, Quality of life assessment, patient experience, satisfaction, etc.)

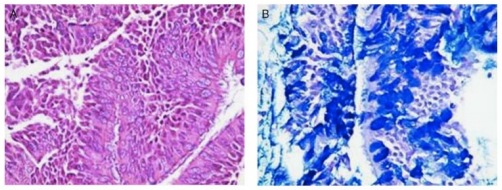


FIGURE 3. Histopathologic results of biopsies obtained before the procedure. A, H&E staining (×400), showing goblet cell hyperplasia. B, PAS/AB pH 2.5 staining (×400), showing increased acidic mucin contents of hyperplastic goblet cells.

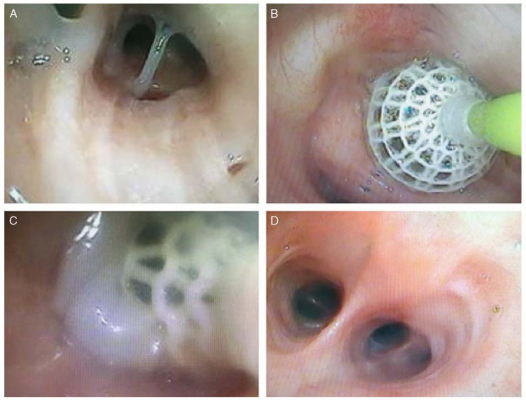


TABLE 2. FEV_1 Results Before and 1 Week and 1 Month After the Procedure

		FEV_1 (L)		
			After	
Patient	Procedure Date	Before	1 wk	1 mo
A.Y.	15.4.2014	0.69	1.19	1.52
V.P.	11.6.2013	1.17	1.33	1.31
R.O.	18.11.2013	0.55	0.61	0.78
I.M.	22.10.2013	0.71	0.74	1.06
K.O.	8.5.2014	0.99	1.06	1.21
O.E.	17.5.2013	1.16	1.41	1.59
K.O.	11.11.2013	0.98	1.19	1.21
A.Y.	17.5.2013	0.91	1.06	1.05
N.N.G.	2.10.2012	0.99	1.00	1.37
F.O.	22.5.2013	0.70	1.06	1.00

TABLE 3. Borg Dyspnea Scale and SpO_2 Levels Before and 1 Week and 1 Month After the Procedure

	Modified Borg Dyspnea Scale			Resting Oxygen Saturation (%)		
		After			After	
Patient	Before	1 wk	1 mo	Before	1 wk	1 mo
A.Y.	9	3	3	85	93	94
V.P.	7	3	3	90	95	94
R.O.	10	7	7	82	90	91
I.M.	10	3	3	89	95	97
K.O.	7	4	3	89	96	95
O.E.	7	3	3	91	96	96
K.O.	9	9	9	88	92	91
A.Y.	10	3	3	87	93	93
N.N.G.	7	3	3	88	94	93
F.O.	10	3	3	88	94	96

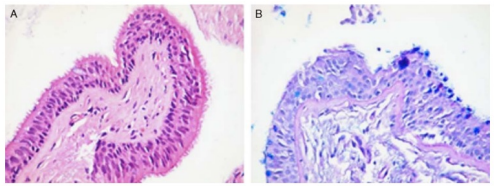


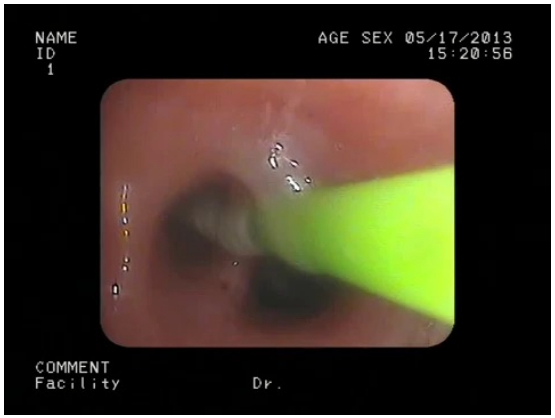
FIGURE 4. Histopathologic results of biopsies obtained after the procedure. A, H&E staining (×400), showing a marked reduction in the number of goblet cells. B, PAS/AB pH 2.5 staining (×400), showing scattered goblet cells and a reduction in their acidic mucin content.

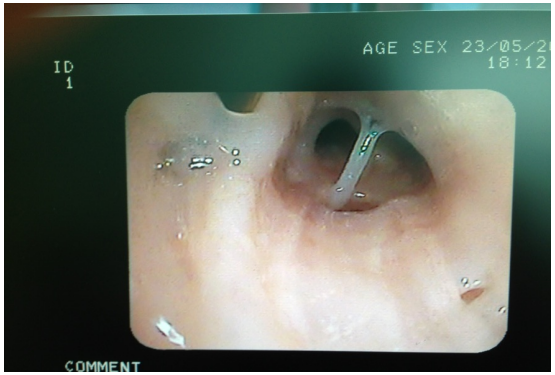
ORIGINAL INVESTIGATION

Use of Resector Balloon Desobstruction in Patients With Severe Chronic Obstructive Pulmonary Disease

A Pilot Feasibility Study on a Novel Desobstruction Technique

Yalcin Karakoca, MD, Guler Karaagac Gogus, MD,† and Ozlem Yapicier, MD‡*





Click on the Link Below for the Video display

YKK Resector Balloon Demonstration

A VISUAL DISPLAY OF YKK RESECTOR BALLOON DEMONSTRATION

Abstract

Background: Previously, we have reported satisfactory results with Karakoca resector balloon in 10 patients in 2015, 188 patients in 2018 with stage IV chronic obstructive pulmonary disease (COPD) who did not respond to medical treatment. In this article, we present the outcomes of Karakoca resector balloon dilatation and curettage technique in a big case series (n=1032).

Methods: A total of 1032 COPD patients [mean age (standard deviation): 69.8 (8.0) years; 83 females] classified as stage III-IV by Global Initiative for Obstructive Lung Disease criteria underwent balloon curettage starts from distal trachea and continues with main carina, main, lobar, segmental and subsegmental bronchi up to 3 mm diameter distally, where there are not much goblet cells remain in airway mucosa, by Karakoca Resector Balloon therapeutic bronchoscopy. None of the patients could have achieved symptom relief even under high dose inhaled bronchodilators and corticosteroids, oral corticosteroids, oxygen and noninvasive mechanical ventilation therapy before the intervention. Six-minute walking test, pulmonary function test performed, oxygen saturation (SpO_2) were measured, and modified Borg dyspnea scale (MBS) scores were determined before and one week, one month and six month after the intervention.

68.0 % patients were active smokers, 31.2 % were ex-smokers, 0.8 % were nonsmoker (severe asthma) patients. 88.6 % had concomitant chronic diseases. After the intervention, there was a notable reduction in the oxygen need of the patients. Comparison of lung function tests before and after the procedure showed significant improvements in pulmonary function, modified Borg dyspnea scale scores and SpO_2 levels ($p<0.001$ for each); and the improvements were maintained for the entire post-procedure month ($p<0.001$ for each) and post procedure six month ($p<0.001$ for each). Except 7 males, all patients were free of symptoms, the 7 patients all of them were mixed COPD highly emphysematous. These results confirmed our 10 years of observations that balloon dilatation and curettage is safe and successful technique for treatment-resistant COPD and severe asthmatics, balloon dilatation ad curettage decrease the mortality rate and improves quality of life in COPD patients also thought us Karakoca resector balloon curettage may decrease or prevent central bronchial carcinoma in smokers.

Respiratory parameters prior to and 1 week, 1 month and 6 month after the operation (n=1032).

		Preoperative	Postoperative 1 week		Postoperative 1 month		Postoperative 6 month	
		(n=1014)	(n=1020)	P value	(n=1020)	P* value	(n=1025)	P* value
FEV1, L	Mean (SD)	0,72 (0.22)	1.10 (0.36)	<0.001	1.31 (0.45)	<0.001	1.34 (0.39)	<0.001
	Median (min-max)	0.64 (0.38-2.28)	1.06 (0.44-2.73)		1.24 (0.51-4.40)		1.31 (0.58-4.68)	
FVC,L	Mean (SD)	1.71 (0.42)	2.18 (0.45)	<0.001	2.38 (0.51)	<0.001	2.44 (0.52)	<0.001
	Median (min-max)	1.72 (0.68-3.51)	2.23 (0.92-3.78)		2.30 (0.88-4.60)		2.36 (0.87-4.70)	
FEV1/FVC	Mean (SD)	43.2 (9.4)	52.1 (10.4)	<0.001	57.4 (11.2)	<0.001	58.2 (10.8)	<0.001
	Median (min-max)	41.0 (26-76)	52.8 (29-83)		55.8 (30-86)		56.1 (32-84)	
FEF 25-75 (L/s)	Mean (SD)	0.46 (2.72)	0.49 (0.18)	<0.001	0.57 (0.29)	<0.001	0.62 (0.19)	<0.001
	Median (min-max)	0.27 (0.13-0.36)	0.42 (0.12-1.12)		0.56 (0.11-1.17)		0.55 (0.12-1.20)	
MBS score	Mean (SD)	8.71 (0.66)	5.10 (0.64)	<0.001	4.9 (0.68)	<0.001	4.2 (0.67)	<0.001
	Median (min-max)	9 (8-10)	5.0 (4-8)		5 (3-7)		4.5 (3-6)	
SpO2 %	Mean (SD)	86.8 (4.2)	92.6 (1.6)	<0.001	94.5 (2.2)	<0.001	94.6 (2.2)	<0.001
	Median (min-max)	87 (68-93)	93 (88-95)		94.8 (91-98)		95.0 (92-98)	
6MWT (m)	Mean (SD)	66.4 (40.6)	244.8 (74.2)	<0.001	382.6 (112.2)	<0.001	440.8 (96.4)	<0.001
	Median (min-max)	58 (8-210)	226 (46-410)		393.4 (72-860)		498.4 (86-970)	

FEF=forced expiratory flow, FEV1= forced expiratory volume in 1 s, FVC= forced vital capacity, MBS= modified Borg scale, SpO2= oxygen saturation, 6MWT= 6 min walking test

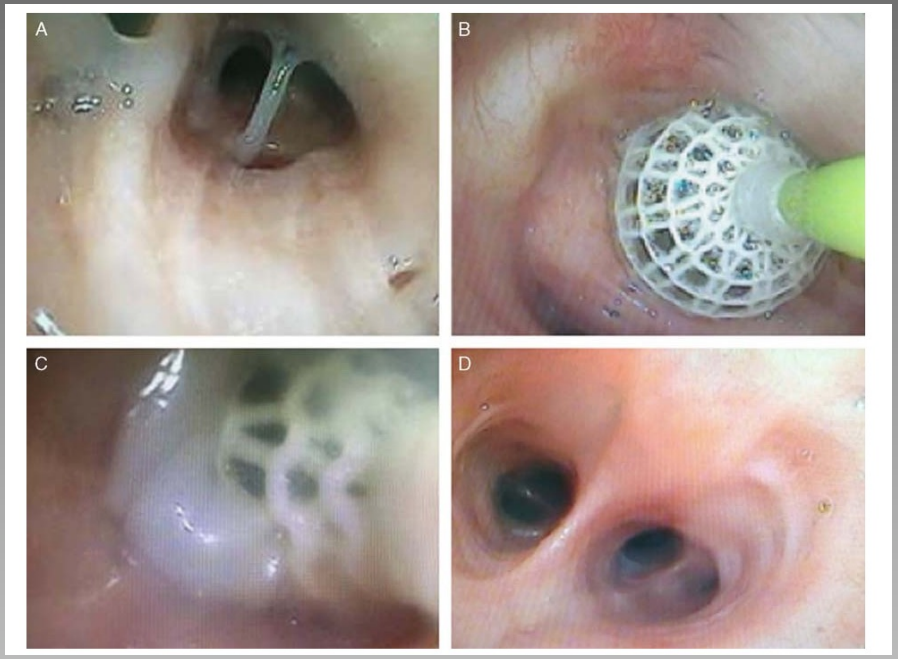
*Postoperative 1 week vs. postoperative 1 month, 6 month

Comparisons were performed by using Wilcoxon signed-rank test.

Patient Entubated in ICU n=11, Patient Tracheostomised n=7

EXCERPT FROM "HEALTH AND ECONOMIC OUTCOMES OF 1032 PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE WHO UNDERWENT BRONCHOSCOPIC INTERVENTION WITH KARAKOCA DILATATION AND CURETTAGE BALLOON"

[UNDER PREPARATION]


A
B
C
D

OUTLINE

- Burden of chronic respiratory diseases (CRD) in adults and associated modifiable risk factors globally
  - COPD (chronic bronchitis and emphysema)
  - Lung Cancer
- Global and regional economic burden of COPD
- Novel diagnostic and treatment approaches and the role of interventional bronchoscopy
- An innovative corporate solution
- The Way Forward

1. VISION AND MISSION STATEMENT

- Our vision: All COPD patients benefit from interventional bronchoscopy to lead healthier and fully functional lives of minimal dependence on pharmacological treatment.
- Our mission: Build an innovative medical care platform for interventional bronchoscopy as the new global standard for COPD treatment.
- Our Motto: "***an effortless breath of fresh air***"

2. WHERE DO WE STAND- CURRENT STATE

- Almost two decades of practical experience with interventional bronchoscopy
  - First with end stage lung cancer (des-obstruction of bronchi in terminal lung cancer cases)
  - A decade long experience in interventional bronchoscopic treatment of Stage III and IV COPD cases with chronic bronchitis
  - And now, bronchoscopic treatment of emphysema with valve implants.
- Several publications, more in preparation
  - A very large collection of cases in database, ready to be exploited for more up-to-date scientific publications
- Established business and manufacturing facility for mass production of YKK resector balloons and emphysema valves of different gauge, both patented in Türkiye, and the USA (YKK resector balloon only).
- Name recognition in Türkiye and Europe for interventional bronchoscopy in COPD
- Steady flow of patients to YKK practice willing to pay large sums out of pocket

3. MARKET OVERVIEW – DEMAND [GLOBAL]

- Chronic Respiratory Diseases (CRD) is one of the most prevalent medical conditions worldwide.
- COPD constitutes the largest proportion of CRDs worldwide, estimated at around 600 million cases. The numbers are likely to increase with ageing of the population and increasing prevalence of COPD from cohorts of smokers reaching later decades of life, especially in the developing world.
- COPD is projected to remain as one of the top 3 leading causes of premature death and disability, resulting in considerable loss of longevity, life quality, economic productivity and welfare.
- About 20% of COPD patients, or 120 million cases, are in Stages III and IV, for whom interventional bronchoscopic treatment with the YKK resector balloon and valves is medically indicated.
- We estimate that globally only 25% of the targeted patient group, or 30 million cases, could afford to pay for the treatments costs out of pocket.
- Reimbursement by health insurance (public or private) is envisaged to kick in in high- and middle-income countries once the intervention has been approved by the regulatory authorities.

3. MARKET OVERVIEW – SUPPLY [GLOBAL]

- At present, our capacity as the sole provider of bronchoscopic treatment is maxed at a few hundred patients a year pointing out to a considerable, and ever increasing, unmet need.
- We estimate that globally there would be approximately 300,000 licensed chest physicians and/or thoracic surgeons who would theoretically be eligible for certification in bronchoscopic COPD treatment.
- We assume that up to 10% of the eligible licensed physicians would be interested in, and qualified for, certification following a one-month theoretical and practical training.
- We further assume that a very large proportion of these physicians will be in East Asia (China, Malaysia, Thailand and Vietnam) and Europe (Türkiye, Russia, Ukraine) regions where there is a mix of public and private healthcare with significant out-of-pocket spending as a proportion of total health spending, limited penetration of private health insurance, and a well-established or burgeoning medical tourism industry.
- The "supply" of bronchoscopists could be quickly increased by enhanced and accelerated training in robot assisted bronchoscopy.

3. MARKET OVERVIEW – SUPPLY [UNITED STATES]

- United States provides a particularly promising ecosystem for interventional bronchoscopic treatment of COPD because of high prevalence of COPD, Medicare coverage applicable to most older COPD patients, public private mix healthcare coverage, reliable regulatory environment with strict enforcement of IPR, and huge potential for savings relative to traditional pharmaceutical treatment options.

- Partnership with industry could accelerate regulatory approval, access to robotic bronchoscopy and enhance training of interventional bronchoscopists.

4. ASSESSMENT OF POTENTIAL COMPETITION (I)

- **Pharmaceutical treatment:**
  - Life long therapy, with potential drug side effects, particularly in patients with multiple morbidity and reliant on other drugs
  - No definitive cure, but rather maintenance therapy and secondary prevention of flare ups
  - Heavy financial and disability burden on patients for life-long adherence to treatment
  - May require supplementary treatment with such as oxygen therapy and physiotherapy, with additional costs and loss of functionality and quality of life
  - Significant and ever increasing direct and indirect healthcare costs, both out-of-pocket and insurance (premium, deductibles, co-payments) to the patient and the society.

4. ASSESSMENT OF POTENTIAL COMPETITION (II)

- **Lung Transplantation:**
  - Proven alternative treatment, albeit in a very limited number of sites globally
  - Long term survival is still short, only about 50% of cases surviving beyond 5 years
  - Very expensive, and unaffordable for most, particularly where there is no insurance coverage.
  - Very limited organ donor base and compatibility
  - Strict eligibility criteria and medical indication assessment

5. ASSESSMENT OF RISKS [GLOBAL]

- Risk of counterfeit device manufacturing and distribution in countries with lax regulatory enforcement and sanctions. PROBABILITY: HIGH
- Risk of opponents undermining the value of interventional bronchoscopic COPD treatment as a result of vested interest (Big Pharma), competitive pressure (from non-participating healthcare business), physician associations and lobby groups. PROBABILITY: HIGH
- Risk of hostile takeover, either legally or illegally, during the early adapter stage, by a large medical industry player with deep pocket to sustain legal cost pertaining to patent infringement and unilateral termination of existing contracts with providers. PROBABILITY: MEDIUM
- Risk of more efficacious and cheaper pharmaceutical treatment options. PROBABILITY: LOW/MEDIUM
- Risk of timely scale up of operations with training of trainers (PROBABILITY: MEDIUM/LOW)
- Risk of market shrinkage. PROBABILITY: VERY LOW (before 2050)

6. WHY START IN THE USA

- DEMAND:
  - Very high prevalence of COPD Burden with a sizeable Chronic Bronchitis component and affordability of interventional bronchoscopy.
- SUPPLY:
  - Existing patent registration of the YKK resector ballon and pending registration of the emphysema valve.
  - Interventional bronchoscopic treatment of COPD patients with the YKK balloon resector is non-existent.
  - High potential for rapid scale up of operations, especially with the adoption robotic bronchoscopy.
- DIRECT AND INDIRECT COST BURDEN:
  - The direct (medical) and indirect (lost of mobility, functionality and productivity as well as intangible costs) cost of lifelong care management of COPD patients to health insurers, patients and families and the broader society.
- VALUE FOR MONEY:
  - Bronchoscopic treatment of COPD patients with the YKK balloon resector is bound to be cost effective in the long run given the lifelong treatment and indirect costs, particularly in the USA where the main component of the costs are related to hospitalization due to exacerbations.

OUTLINE

- Burden of chronic respiratory diseases (CRD) in adults and associated modifiable risk factors globally
  - COPD (chronic bronchitis and emphysema)
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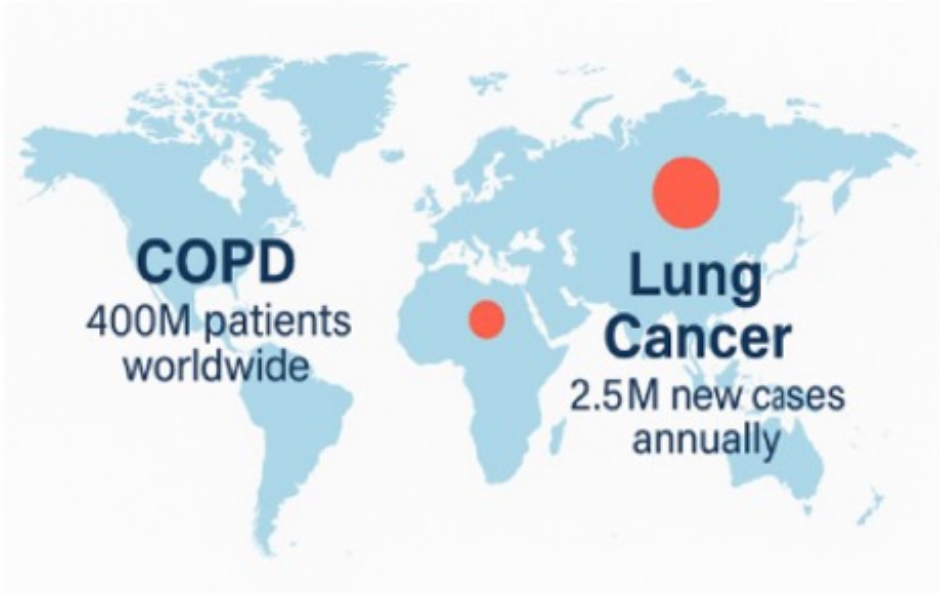
- The Way Forward

WHERE WE ARE AND THE WAY FORWARD [GLOBAL]

- Securing partnership with the industry (medical equipment), particularly for robotic bronchoscopy
- Accelerating the patenting approval (emphysema valve).
- Agreeing on the manufacturing base of the CE certified YKK resector balloon and the emphysema valve to expand manufacturing capacity to meet USA and global operational needs.
- Establishing training Hubs in the USA, Europe and Asia in robotic bronchoscopy for physicians (pulmonologists, interventional bronchoscopists)
- Standardization of robot assisted interventional bronchoscopy as the new medical care platform for COPD treatment
  - Accreditation of health care facilities of interest
  - Training and certification of interventional bronchoscopists
  - Formalization of the applicable medical procedures for quality control and assurance (i.e., standard treatment protocol (STP), Patenting and Good Manufacturing Process (GMP) standards for the balloon resector and other applicable devices

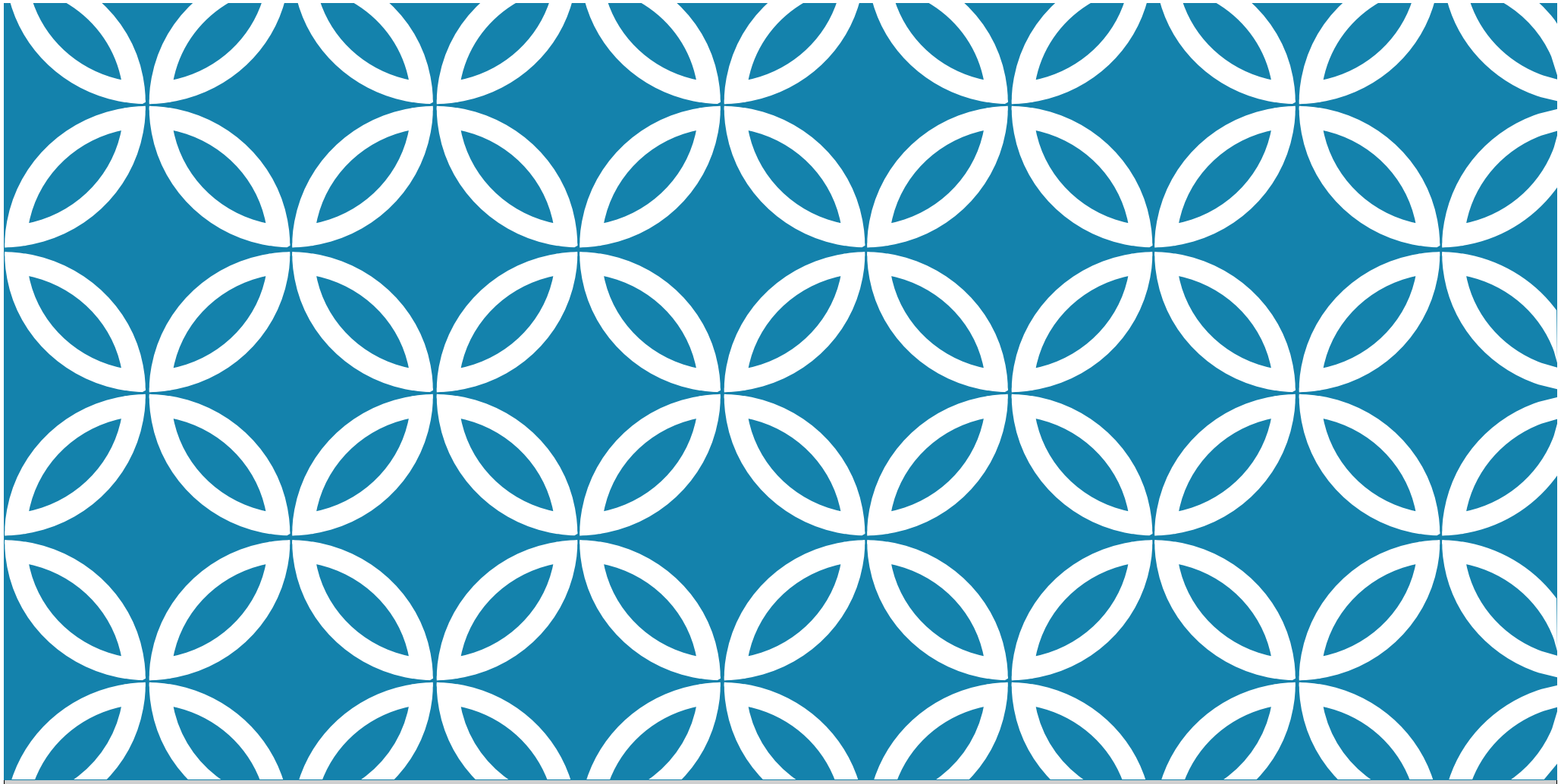
Two breakthrough products:

Resector Balloon & Emphysema Valve



- Targeting COPD (400M patients)
  & Lung Cancer (2.5M new cases/year)
- Till now 15,000+ interventions performed by Mr.Karakoca, no side effects
- Scalable, capital-light model

IN SUMMARY



THANK YOU