

# COPD – Chronic Obstructive Pulmonary Disease

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### **1** Physiology of respiration

The primary goal is to provide the body with an  $O_2$  supply and remove  $CO_2$ . There is an exchange of gases between atmospheric air and blood. There are four basic mechanisms – (1) lung ventilation, (2) intrapulmonary distribution, (3) perfusion and (4) diffusion. Neural mechanisms of the brainstem regulate respiration, the so-called respiratory centre, and chemical detection mechanisms (central and peripheral chemoreceptors). The driving force of the gas movement is the difference between the pressures in the alveoli and the external environment. Pressure differences are generated by the activity of the respiratory muscles (diaphragm and chest muscles) and by external forces.

Lung volumes are the spaces occupied by air in the lungs during breathing. The summation of different lung volumes gives rise to lung capacities (*Appendix 1*). Ventilation is measured by a lung function test (spirometry), which examines lung volumes, capacities and flow rates (*Appendix 2*). The parameters measured are divided into static and dynamic. The static parameters – or volumes and capacities of the respiratory system (tidal volume, vital capacity, etc.) – inform about possible restrictive disorders, while the dynamic ones – or flow rates or volumes at maximum breathing effort (minute ventilation, maximum minute ventilation, etc.) – inform about obstructive disorders.

The inability of the respiratory system to provide the necessary gas exchange in the lungs is termed respiratory insufficiency. It can be of the 1st type - hypoxemic (normal PaCO2, hypoxemia ( $\downarrow$  PaO2)) or the 2nd type – hypoxemic-hypercapnic (hypercapnia ( $\uparrow$  PaCO2), hypoxemia ( $\downarrow$  PaO2)). It is categorized into (i) acute, a sudden uncompensated onset disorder, or (ii) chronic, i.e. with already developed compensatory and adaptive mechanisms.

### 2 COPD Definition

COPD is a preventable and treatable disease characterised by persistent respiratory symptoms, bronchial obstruction and abnormalities of the lower airways and alveoli, usually due to exposure to inhaled noxious substances. Other factors, such as genetics or altered prenatal development, are also involved. The most common symptoms are dyspnoea, cough, and expectoration of sputum.

### 3 COPD Epidemiology, Pathophysiology and Risk Factors

The prevalence of COPD is steadily increasing, currently estimated at 11.7 % of the world population and 6.7 % in the Czech Republic, which is about 710,000 patients, with only about 230,000 patients registered with pneumologists. It is reported that COPD is the cause of death in approximately 3,200 to 3,500 patients per year, and therefore COPD diagnosis should be made as early as possible.

The primary risk factor is active and passive smoking and persistent exposure to harmful influences such as environmental or workplace pollution (dust, gases, fumes, etc.). Other factors include asthma, frequent respiratory tract infections, history of pulmonary tuberculosis or HIV infection, use of selected medications, or genetic factors such as alpha-1-antitrypsin (A1AT) deficiency.

COPD is a heterogeneous disease with many extrapulmonary characteristics and comorbidities. It is caused by long-term inflammatory processes due to exposure to various inhaled noxious substances. Processes of oxidative stress, imbalance of proteases and antiproteases, and increased activation of pro-inflammatory cells, predominantly neutrophils and T-lymphocytes, are involved. In some patients, an eosinophilic type of inflammation is also present. Chronic inflammation leads to progressive elastic fibre breakdown, peribronchial fibrosis, destruction of alveolar walls, microvasculature and small bronchi, airway remodelling and chronic mucus hypersecretion. The functional consequences are



airway obstruction, hyperinflation, impaired gas exchange and reduced functional capacity. Among the systemic effects, a higher risk of cardiovascular disease, osteoporosis, depression, cachexia, diabetes mellitus or sleep apnoea syndrome, as well as lung cancer etc., are observed.

These mechanisms vary with the patient and lead to different disease manifestations, allowing us to categorise the clinical phenotypes and features of the disease.

#### 4 COPD Diagnosis

The fundamental diagnosis of COPD should encompass: 1. Clinical examination (history taking, assessment of inhalation risks, evaluation of symptom severity, and physical examination), 2. Pulmonary function testing and blood gas analysis (Appendix 2), 3. Imaging studies (chest X-ray to exclude comorbidities; a chest CT scan is not routinely recommended.), and 4. Laboratory testing (biochemistry, blood count, A1AT deficiency).

Stress testing, such as spiroergometry or the Six Minute Walk Test (6MWT), is a practical and simple test to assess a patient's fitness and exercise tolerance. The principle of the test is to walk a certain number of metres in 6 minutes. According to the studies carried out so far, a distance of more than 500 metres for women and more than 600 metres for men is considered normal.

According to the World Health Organization (WHO) recommendations, patients should be screened for alpha-1-antitrypsin deficiency.

The CAT = COPD Assessment Test (*Appendix 3*) or the modified dyspnoea scale - mMRC (*Appendix 4*) - are recommended to assess the severity of symptoms. The BODE index (*Appendix 5*) assesses prognostic factors in patients with COPD.

The diagnosis of COPD is based on spirometry, demonstrating evidence of post-bronchodilator airway obstruction. Indications for spirometry include chronic dyspnea, cough, and expectoration of sputum. Among other pulmonary function tests, it is appropriate to conduct body plethysmography and an examination of the lungs' diffusing capacity for carbon monoxide. These tests provide information on potential hyperinflation of the lung parenchyma, restrictive ventilatory defect, or diffusion impairment (reduction in cases of emphysema, fibrosis, or heart failure).

Concerning the final diagnosis, differential diagnosis is necessary, especially the exclusion of bronchial asthma, bronchiolitis, bronchiectasis, cystic fibrosis, gastroesophageal reflux, tracheobronchomalacia, tracheal stenosis, primary ciliary dyskinesia, pulmonary embolism, cor pulmonale, and heart failure.

#### **5 COPD Classification**

A combined assessment of COPD uses the ABCD tool, which divides patients into four categories (*Appendix 6*). To correctly categorise patients, it is necessary to perform the GOLD (Global Initiative for Chronic Obstructive Lung Disease) classification with stages I–IV based on lung function, assess the level of symptoms using the CAT questionnaire or the mMRC scale, and know the number of exacerbations in the last 12 months. Based on clinical manifestations, imaging studies, functional changes, and other parameters, patients are classified into six COPD phenotypes (*Appendix 7*), which allow for a personalised treatment approach for each patient.



#### 6 COPD Management

COPD cannot yet be cured or stopped completely. The aim is to control symptoms, reduce the number and severity of exacerbations, improve quality of life, and treat complications and comorbidities. Management of COPD is divided into (i) generalised, which is the same for all symptomatic patients regardless of their clinical phenotype, and (ii) personalised, targeting specific features in an individual patient.

Generalised management (*Appendix 8*) includes non-pharmacological approaches such as risk elimination, especially smoking cessation, physical activity (daily aerobic physical exercise, preferably regular walking – the optimal number of steps for COPD patients is approximately 5,000 to 6,000 per day), pulmonary rehabilitation, education on inhalation techniques, and a healthy diet. Pharmacological approaches include influenza and pneumococcal vaccination and bronchodilator therapy (*Annex 9*). The pharmacological approach to complications and comorbidities, both internal and psychological, is an integral part of generalised management.

The basis of personalised management is treatment specific to individual COPD phenotypes (Annex 10).

For every patient with severe A1AT deficiency, alpha-1-antitrypsin replacement therapy (augmentation therapy) is available at the National Centre of the Thomayer University Hospital, Prague.

In the terminal phase of the disease, when patients develop respiratory failure, long-term home oxygen therapy (LTOT), home non-invasive ventilatory support (NIVP), and supportive, nutritional and palliative treatment are indicated. Palliative treatment mainly aims to eliminate severe and otherwise uncontrollable dyspnoea and includes, but is not limited to, the administration of low-dose opioids, hydration, or pain management.

Surgical management of COPD includes bullectomy, lung volume reduction surgery (LVRS), bronchoscopic lung volume reduction (BLVR), or lung transplantation.

#### 7 COPD Exacerbation

Exacerbation of COPD is an acute event characterised by worsening the patient's difficulties that goes beyond daily fluctuations and leads to a change in treatment.

COPD exacerbations can be triggered by a variety of factors. The most common cause is respiratory infections.

The treatment of exacerbation aims to minimise the adverse effects and prevent subsequent side effects. In order to initiate treatment, short-acting inhaled beta<sub>2</sub> agonists (SABA) alone or with the addition of anticholinergics are recommended. After an exacerbation, long-acting bronchodilators should be started immediately. Systemic corticosteroids (CS) may relieve obstruction (FEV<sub>1</sub>), improve oxygenation, accelerate recovery, and reduce hospitalisation time. However, their administration should not be longer than 5–7 days. Antibiotics, if indicated, can speed recovery and reduce the risk of early relapse and treatment failure. They also reduce the length of hospital stays. Treatment should not last longer than 5–7 days. In cases of acute respiratory failure, low-flow oxygen therapy is often necessary. When there's significant hypercapnia or respiratory acidosis, non-invasive mechanical ventilation should be employed. It improves gas exchange, reduces the strain on respiratory muscles, and the need for intubation. Consequently, it shortens the duration of hospitalization and enhances the patient's survival.

Exacerbations are classified according to their severity:

• mild (treated with SABA only)

- moderate (treated with SABA + ATB or oral corticosteroids)
- severe (hospitalisation or emergency department visit is required); usually associated with acute respiratory failure

#### 8 Pulmonary Rehabilitation

Pulmonary rehabilitation in patients with COPD is always part of complex interdisciplinary care. It is an essential part of treatment during and after exacerbation and in the stable phase of the disease, where it helps to solve most of the difficulties. Concerning patients with COPD, it may be indicated during hospitalisation, outpatient treatment, or spa treatment or therapy in specialised treatment centres *(Annex 11).* 

During pulmonary rehabilitation, newly diagnosed COPD patients are informed about the nature of their disease, their regimen and how to behave during an acute exacerbation.

Pulmonary rehabilitation in patients with COPD improves the quality of life, exercise tolerance, and physical fitness, reduces the incidence of dyspnoea, improves muscle strength, including respiratory muscles, and facilitates the performance of activities of daily living (ADLs), including increased levels of physical activity. Thus, pulmonary rehabilitation helps to slow the progression of the overall deterioration of the condition.

#### 9 Oxygen Therapy

Home long-term oxygen therapy (LTOT) in patients with COPD has been shown to reduce symptoms and improve cognitive function, exercise tolerance and quality of life. The criteria for LTOT in the Czech Republic are resting  $PaO_2 < 7.3$  kPa or resting  $PaO_2 7.3$ –8.0 kPa, together with one of the following criteria: pulmonary hypertension, polycythaemia, saturation < 90 % during at least 30 % of sleep time, or exertion-induced desaturation. A 6-month abstinence from smoking is required. Use an oxygen concentrator or portable liquid oxygen for at least 16 hours per day.

In stable COPD patients with chronic hypercapnic respiratory failure, home non-invasive ventilatory support (NIVP) is indicated. Treatment improves lung function, blood gas values and quality of life. In the case of concomitant hypoxemia, concurrent LTOT is indicated.

#### **10 Smoking Cessation**

Tobacco dependence is the most important preventable cause of morbidity and mortality. More than 70 % of smokers in the Czech Republic would like to quit, and up to 40 % try to do so each year. However, only around 3 % of those who try it unassisted succeed each year. The success rate with professional help can be up to ten times higher.

Smoking prevalence in the Czech Republic has been mildly declining over the past decade. According to NAUTA (National Research on Tobacco and Alcohol Use in the Czech Republic), in 2022, 24.4% of the population aged 15 and over smoked regularly (with 16.2% being daily smokers) compared to 31.3% in 2012. Men smoke more than women (30.5% vs. 18.7%). The number of underage smokers is also decreasing. However, it remains true that the vast majority of smokers have their first cigarette before their 18th birthday. On average, daily smokers consume 12 cigarettes per day. E-cigarettes are used by 10.2% of the population aged over 15; 36.2% of users cite less harm to health as a reason for switching, while 26.8% point to greater acceptance by their surroundings. Heated tobacco is used by 6.6% of the



population, and smokeless tobacco by 5%. Passive smoking continues to be a significant concern, with 14.7% of the population exposed to cigarette smoke at home and 21.1% at work.

Tobacco dependence is (i) psycho-socio-behavioural, involving the attachment of smoking to specific situations, society, and activities, and (ii) physical, which is classic drug dependence present in the majority of smokers (80–90 %). It involves the multiplication of acetylcholine-nicotine receptors and, above all, withdrawal symptoms when nicotine is excluded. Withdrawal symptoms can be suppressed by first-line drugs: varenicline, nicotine, bupropion and, more recently, cytisine. However, pharmacotherapy must always be combined with intervention – the smoker must actively change their daily stereotypes and address their psycho-socio-behavioural addiction, which medication cannot help. Many addicts also use nicotine replacement therapy (nicotine patches, gum, lozenges, sachets, etc.), which delivers nicotine to the body without the several thousand harmful substances of tobacco smoke. Smokers who, despite their best efforts, have not been able to quit in the last few years also use nicotine in the form of electronic cigarettes or heated tobacco, an alternative to smoking that has the potential to reduce the health risks of cigarette smoking.

### **11 Conclusion**

The diagnosis and treatment of COPD have undergone significant changes in recent years. While pharmacotherapy is an essential component of the disease's comprehensive treatment, it is becoming increasingly personalized.

The cornerstone of pharmacotherapy is bronchodilation treatment. Monotherapy with long-acting anticholinergics (LAMA), or dual therapy in a fixed combination with  $\beta_2$  agonists (LAMA + LABA), is typically employed. For specific phenotypes (ACOS, frequent exacerbations), the inclusion of inhaled corticosteroids (ICS) in the treatment regimen is appropriate. Currently, fixed triple combinations (ICS + LABA + LAMA) are also consolidating their position in the therapeutic scheme for COPD.

Drugs are inhaled and available in different inhalation systems; therefore, continuous and repeated patient education in inhalation techniques is essential.

Non-pharmacological treatment has also significantly developed. The emphasis is mainly on the physical activity of patients and complex pulmonary rehabilitation.

Maximum efforts should be made in prevention, especially not smoking cigarettes or inhaling other fumes.

### Resources

- 1. Doporučený postup ČPFS pro diagnostiku a léčbu stabilní CHOPN: <u>file:///C:/Users/AZ/Downloads/1\_1\_DP\_CPFS\_pro\_diagnostiku\_lecbu\_stabilni\_CHOPN.pdf</u>
- GOLD aktuální doporučení pro diagnostiku a klasifikaci CHOPN: <u>https://goldcopd.org/2022-gold-reports-2/</u>
- Brat K a kol. CHOPN diagnóza a léčba stabilní fáze onemocnění; personalizovaný přístup k léčbě s využitím fenotypických rysů nemoci. Vnitř lék 2021; 67(4): 230-239. <u>https://casopisvnitrnilekarstvi.cz/pdfs/vnl/2021/04/07.pdf</u>
- 4. Koblížek V a kol. Doporučené diagnostické a terapeutické postupy pro všeobecné praktické lékaře 2019: <u>www.svl.cz/files/files/Doporucene-postupy/2017/DP-CHOPN-2019.pdf</u>
- 5. Pauk N. Diagnostika a léčba CHOPN. Medical Tribune 2020: https://www.tribune.cz/archiv/diagnostika-a-lecba-chopn/



#### **COPD – Chronic Obstructive Pulmonary Disease**

- 6. Musil J a kol. Doporučený postup pro diagnostiku a léčbu exacerbace CHOPN 2019: <u>http://www.pneumologie.cz/guidelines/</u>
- 7. Chlumský J a kol. Doporučený postup pro interpretaci základních vyšetření plicních funkcí 2019: http://www.pneumologie.cz/guidelines/
- 8. Neumannová K a kol. Doporučený postup plicní rehabilitace 2019: <u>http://www.pneumologie.cz/guidelines/</u>
- 9. Chlumský J a kol. Doporučení pro indikaci a provádění DDOT 2019: http://www.pneumologie.cz/guidelines/
- Šťastný B a kol. Doporučené postupy pro praktické lékaře Léčba závislosti na tabáku v ordinaci všeobecného praktického lékaře 2022: <u>https://www.svl.cz/files/files/Doporucene-postupy/2020/DP-Tabak.pdf</u>

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## **Appendix 1: Lung volumes**

-	Inspirační kapacita (IC)	Inspiratory Capacity (IC)
-	Exspirační rezervní objem (ERV)	Expiratory Reserve Volume (ERV)
-	Reziduální objem (RV)	Residual Volume (RV)
-	Vitální kapacita (VC)	Vital Capacity (VC)
-	Inspirační rezervní objem (IRV)	Inspiratory Reserve Volume (IRV)
-	Dechový objem (TV)	Tidal Volume (TV)
-	Funkční reziduální kapacita (FRC)	Functional Residual Capacity (FRC)
-	Celková plicní kapacita (TLC)	Total Lung Capacity (TLC)

### **Appendix 2: Pulmonary Function Testing (Spirometry)**

Pulmonary function testing is a laboratory method, the results of which have a significant impact on the correct diagnosis and treatment. It is one of the primary internal examination methods, similar to blood pressure measurement or ECG. Concerning the patient, the examination is easy, simple, and infinitely repeatable. It must be performed by trained personnel and standardised procedures.

Spirometry is a physiological test measuring the volume of inhaled or exhaled air as a function of time. The primary examination includes measuring resting (static) and dynamic volume parameters. The basic parameters monitored include: resting expiratory (EVC) or inspiratory (IVC) vital capacity, forced vital capacity (FVC), forced expiratory volume in 1 second (FEV<sub>1</sub>), peak expiratory flow (PEF), and maximum expiratory flows at different levels of forced vital capacity (MEF<sub>25</sub>, MEF<sub>50</sub>, MEF<sub>75</sub>). The FEV<sub>1</sub>/FVC ratio is called the Tiffeneau index, the physiological value of which is 80 % (0.8). It helps in the diagnosis of obstructive and restrictive lung disease. If the value is 0.7 or less, COPD is suspected.

Either volume or flow is measured. The volume measurement is expressed on a volume/time curve, while the flow measurement is shown on a flow/volume loop:



MEF – maximální výdechové průtoky na různých úrovních FVC MIF<sub>so</sub> – střední nádechový průtok v úrovni 50 % nadechnuté FVC

-	čas nádech průtok	Time Inspiration Flow
-	výdech objem MEF – maximální výdechové	Expiration Volume MEF – maximum expiratory flow rates
prů -	itoky na různých úrovních FVC MIF50 – střední nádechový průtok	at different FVC levels $MIF_{50}$ – mean inspiratory flow
<mark>v ú</mark>	rovni 50 % nadechnuté FVC	at 50 % of inspired FVC

**Forced Expiratory Flow Rates:** 





A g – plocha pod výdechovou částí křivky průtok-objem FVC – usilovná vitální kapacita FEF 25-75 – usilovný výdechový průtok MEF 25-75 – maximální výdechový průtok MIF 50 % nadechnuté FVC PIF – maximální průtok dosažený na vrcholu usilovného nádechu VCin – nádechová vitální kapacita

- -	průtok síla A <sub>ex</sub> – plocha pod výdechovou částí	Flow Power A <sub>ex</sub> – area under the exhalation section
křiv - - -	vky průtok-objem FVC FVC – usilovná vitální kapacita FEF <sub>25-75</sub> – usilovný výdechový průtok MEF <sub>25-75</sub> – maximální výdechový průtok MIF <sub>50</sub> – střední nádechový průtok	of the flow-volume curve FVC – forced vital capacity FEF <sub>25-75</sub> – forced expiratory flow MEF <sub>25-75</sub> – maximum expiratory flow MIF <sub>50</sub> – mean inspiratory flow at 50 % of
V Ú - na	rovni 50 % nadechnuté FVC PIF – maximální průtok dosažený vrcholu usilovného nádechu	inspired FVC PIF – peak inspiratory flow
-	VCin – nádechová vitální kapacita	VCin – inspiratory vital capacity

#### Spirometry interpretation:

The highest values of FVC and  $FEV_1$  are evaluated in the dynamic ventilation parameter readings. The other parameters are read from the trial in which the highest sum of FVC and  $FEV_1$  was achieved. The higher of at least two reproducible values of VC and IC is used for the resting ventilation parameters.



1 – přijatelné úsilí 2 – předčasné ukončení manévru či uzávěr glottis
3 – nedostatečné úsilí 4 – kašel 5 – pomalý start výdechu 6 – nedostatečný nádech 7 – uzávěr náustku jazykem

- - -	průtok objem 1 – přijatelné úsilí 2 – předčasné ukončení manévru	Flow Volume 1 – Acceptable effort 2 – premature termination of the manoeuvre
či u. - - - -	závěr glottis 3 – nedostatečné úsilí 4 – kašel 5 – pomalý start výdechu 6 – nedostatečný nádech 7 – uzávěr náustku jazykem	or glottis closure 3 – insufficient effort 4 – cough 5 – slow start of expiration 6 – poor inspiration 7 – obstruction of the mouthpiece by tongue





(PVD – pulmonary vascular diseases, CWD – chest wall diseases, NMD – neuromuscular diseases, IIP – idiopathic interstitial pneumonitis)

-	ano	Yes
-	ne	No
-	v normě	Normal
-	restrikce	Restriction
-	obstrukce	<b>Obstruction</b>
-	smíšená	Mixed
-	OPC	PVD
-	OHS, NMO	CWD, NMD
-	IIP	IIP
-	astma	asthma
-	CHOPN	COPD

#### Bronchodilator test (BDT):

It is indicated in the differential diagnosis of dyspnoea, cough, and chest pressure, in monitoring the condition of patients and the effect of treatment, to evaluate the effect of individual bronchodilator drugs, as part of the preoperative examination, and for assessment purposes. The test is also performed if the values are within the appropriate limits, but the subject presents clinical difficulties.

Ventilatory parameters are measured 30 minutes after bronchodilator administration. If a beta<sub>2</sub> mimetic bronchodilator with a rapid onset of action (salbutamol) is used, measurements can be made earlier (but after at least 15 minutes). In the event of a questionable or negative salbutamol test result, the measurement may be repeated in a further 15 minutes and then in an additional 30 minutes, or the amount of salbutamol administered by nebulisation may be increased up to a total dose of 5 mg under medical supervision.

A change in FEV<sub>1</sub>  $\ge$  12 % and 200 ml in absolute value indicates a positive test.

#### Diagnosis of COPD based on spirometry:

In patients with  $FEV_1/FVC < 0.70$ , the severity of bronchial obstruction is determined by the  $FEV_1$  value – GOLD classification, stages 1–4.

GOLD 1	lehká	FEV <sub>1</sub> ≥ 80 % n. h. (náležitých hodnot)
GOLD 2	středně těžká	50 % ≤ FEV <sub>1</sub> < 80 % n. h.
GOLD 3	těžká	30 % ≤ FEV <sub>1</sub> < 50 % n. h.
GOLD 4	velmi těžká	FEV <sub>1</sub> < 30 % n. h.

-	lehká	mild
-	střední těžká	moderate
-	těžká	severe
-	velmi těžká	very severe
-	n. h. (náležitých hodnot)	r.v. (reference values)

#### Appendix 3: CAT = COPD Assessment Test

The CAT questionnaire, covering eight quality-of-life domains, assesses COPD symptoms' severity.

The score ranges from 0–40 points (0–5 for each area) and depends entirely on the patient's subjective assessment.

It focuses on shortness of breath and other symptoms of COPD – cough, expectoration, chest tightness, limitation of daily activity, sleep disturbances, and fatigue.

It is advisable to complete the CAT questionnaire at each patient follow-up and to monitor the effect of the chosen treatment on COPD symptoms based on the results obtained on an ongoing basis.

Your name:				Today's date:	COPD Assessment Test
How is you	Ir COP	D? Take th	ne COPD A	ssessment Te	st™ (CAT)
This questionnaire v Pulmonary Disease) your healthcare profe	vill help you a is having on y ssional to help	nd your healthcar your wellbeing and p improve the mana	e professional mease I daily life.Your answ gement of your COF	ure the impact COPD (C rers, and test score, can b D and get the greatest ber	hronic Obstructive e used by you and nefit from treatment.
For each item below for each question. <b>Example:</b> I am	place a mark very happy	(X) in the box that $0 \times 2$	t best describes you	currently. Be sure to only s I am very sad	elect one response
I never cough		012	345	I cough all the tim	e SCORE

-		I cough all the time
I have no phlegm (mucus) In my chest at all	002345	My chest is completely full of phlegm (mucus)
My chest does not feel tight at all	012345	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	002345	When I walk up a hill or one flight of stairs I am very breathless
l am not limited doing any activities at home	012345	I am very limited doing activities at home
l am confident leaving my home despite my lung condition	012345	l am not at all confident leaving my home because of my lung condition
I sleep soundly	012345	I don't sleep soundly because of my lung condition
I have lots of energy	002345	I have no energy at all

## Appendix 4: mMRC (Modified Medical Research Council) Dyspnoea Scale

The mMRC scale is used to assess the severity of symptoms, where grades 0-4 are defined.

The physician determines the grades based on the patient's level of exertional dyspnoea, similar to the NYHA classification used in cardiology.

mMRC Grade 0		
mMRCGrade 1		
mMRC Grade 2On level ground, I walk slower than people of the same age.		
mMRC Grade 3	I stop for breath after walking about 100 yards or after a few minutes on level ground.	
mMRC Grade 4	I am too breathless to leave the house, or I am breathless when dressing.	

### **Appendix 5: BODE Index**

With its four categories, the BODE Index is used to assess prognostic factors of COPD:

- B: Body Mass Index (BMI)
- O: Obstruction degree of bronchial obstruction according to postbronchodilator FEV1
- D: Dyspnoea level of exertional dyspnoea according to the mMRC scale
- E: Exercise load tolerance using the 6MWT

The evaluation of the BODE index is simple – the higher the score, the worse the long-term prognosis of patients and the higher the risk of death.

The BODE index ranges from 0–10. Patients with a BODE score of around "5" require specialist care. A score of "7" or more is an indicator for consideration of lung transplantation.

Parameter	0 points	1 point	2 points	3 points
BMI (kg/m²)	> 21		<u>&lt;</u> 21	
FEV <sub>1</sub> (% r.v.)	<u>&gt;</u> 65	50–64	36–49	<u>&lt;</u> 35
mMRC (0–4)	0–1	2	3	4
6MWT (m)	<u>&gt;</u> 350	250–349	150–249	< 150

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#### **Appendix 6: COPD Categories according to ABCD**

Concerning the classification of COPD, we use the GOLD – ABCD scale to categorise patients according to their spirometric parameters, symptoms (mMRC, CAT), and the occurrence of acute exacerbations in the previous 12 months.

A and B are categories for patients with mild (grade 1:  $FEV_1 \ge 80 \% r.v.$ ) or moderate (grade 2:  $FEV_1 50-80 \% r.v.$ ) bronchial obstruction and without frequent acute exacerbations. Category A has minimal subjective symptoms, whereas B is associated with more pronounced clinical manifestations. In categories C and D, patients suffer from severe (grade 3:  $FEV_1 30-50\% r.v.$ ) or very severe (grade 4:  $FEV_1 < 30 \% r.v.$ ) bronchial obstruction and have frequent acute exacerbations. Category C is associated with minimal and category D with more severe symptoms.

Patients in category A can be followed in a general practitioner's practice without risk, their main therapeutic component being eliminating risk factors.

Patients in category C represent a group with minimal symptoms but more severe lung function impairment and repeated exacerbations. Their treatment does not necessarily include all costly inhaled medications, but they should be followed up by a pulmonologist.

On the other hand, patients in category B require a lot of attention. These are those with a less marked decline in lung function and fewer exacerbations but a high mortality risk.

Category D patients are at extreme risk of respiratory and cardiovascular morbidity and mortality; their treatment must be maximal in all aspects.

A specific phenotype should always be sought in COPD patients falling into categories B and D, and their treatment should be generalised and personalised.

Assessment of symptoms/risk of exacerbations		Number of exacerbations
C	D	$\geq$ 2, possibly $\geq$ 1 with hospitalisation required
А	В	0 or 1 (unless it leads to acute hospitalisation)
mMRC 0–1 CAT < 10	mMRC <u>&gt; 2</u> CAT <u>&gt;</u> 10	

### **Appendix 7: COPD Phenotypes**

There are six clinical phenotypes of COPD, which can be defined based on clinical manifestations, imaging examinations, functional changes, and other parameters.

Some patients may have more than one of these phenotypes.

According to the phenotype, the management of these patients is not only generalised but also personalised.

#### **BRONCHITIS PHENOTYPE** productive cough (> 3 months/year in the last two years or more) **EMPHYSEMA PHENOTYPE** lifelong absence of productive cough dry cough may be present simultaneous signs of pulmonary emphysema (according to chest HRCT and functional examination) COPD BRONCHIECTASIS PHENOTYPE accentuated daily expectoration younger age non-smokers or less intense smokers prolonged or repeated infections of the lungs or lower respiratory tract haemoptysis, or the presence of blood in the mucus HRCT signs of bronchiectasis COPD OVERLAP WITH BRONCHIAL ASTHMA Two major or one major + two minor criteria must be met Major criteria: (a) significantly positive BDT (rise of $FEV_1 \ge 15 \% a \ge 400 \text{ ml}$ ) (b) positive bronchoconstriction testing (c) - FENO (> 45–50 ppb) or - eosinophils in sputum (> 3 %) (d) history of bronchial asthma Minor criteria: (a) positive BDT (rise of $FEV_1 \ge 12 \% a \ge 200 \text{ ml}$ ) (b) - in total IgE (c) history of atopy FREQUENT EXACERBATION PHENOTYPE frequent acute exacerbations (> 2/year) treated with ATB or systemic steroids PULMONARY CACHEXIA PHENOTYPE reduced FFMI (men < 16 kg/m<sup>2</sup>, women < 15 kg/m<sup>2</sup>), or BMI < 21 kg/m<sup>2</sup> (irrespective of gender) – with no other apparent cause

#### **COPD – Chronic Obstructive Pulmonary Disease**

#### Basic clinical manifestations of the defined phenotypes:

occasional expectoration	$\rightarrow$	bronchitis phenotype of COPD
repeated exacerbations	$\rightarrow$	frequent exacerbation phenotype
clinical features of both COPD and AB	$\rightarrow$	COPD overlap with AB
daily purulent expectoration	$\rightarrow$	COPD overlap with bronchiectasis
dyspnoea without expectoration	$\rightarrow$	emphysema phenotype
cachexia without other cause	$\rightarrow$	pulmonary cachexia phenotype

## **Appendix 8: Generalized Management of Stable COPD**

pro každé	ho pacienta		4. krok
		3. krok	léčba
1. krok eliminace rizik	2. krok paušální léčba	fenotypicky cílená terapie	respiračního selhávání péče o terminální CHOPN
pro každého pacie	enta	for every patient	1
1. Krok		Step 1	
2. KrOK		Step 2	
J. KIOK 4 krok		Step 3	
eliminace rizik		risk elimination	
paušální léčba		generalized mar	nagement
fenotypicky cílená	terapie	targeted phenot	ypic therapy
léčba respiračního	o selhávání	respiratory failur	<mark>e management</mark>
péče o terminální	CHOPN	terminal COPD of	<mark>care</mark>

In patients with a clear clinical phenotype, step 3 - targeted phenotypic therapy - is added to the treatment.

In the presence of hypoxaemia/hypercapnia or progression of the disease to the terminal phase, the fourth therapeutic step is added.

### **Appendix 9: Selected Inhaled Bronchodilators**



- 3-	-4xdenně	3–4x per day	
- 2>	denně	2x per day	
- 1	denně	1x per day	

Principles of bronchodilator treatment:

- Bronchodilator drugs are the basis for treating COPD symptoms.
- Inhalation administration is preferred.
- The choice between beta<sub>2</sub>-agonists, anticholinergics and theophylline or combination therapy depends on the availability of products and the individual patient's response to treatment, both in terms of relief of discomfort and side effects.
- Bronchodilators are given as needed or as a regular treatment to prevent or relieve symptoms.
- Long-acting bronchodilators are more convenient for patients. They are more suitable and effective for achieving lasting relief than short-acting bronchodilators.
- Compared with increasing the dose of a single bronchodilator, combinations of bronchodilators from different pharmacological classes may increase the effectiveness of treatment and reduce the risk of adverse effects.



#### Appendix 10: Management Recommendations for COPD Phenotypes



## MUNI SIMU MED

- - -	fenotyp bronchitický PDE4 inhibitor (roflumilast) mukoaktivní medikace	bronchitis phenotype PDE4 inhibitor (roflumilast) mucoactive medication
(N- cai - - - - -	acetylcystein, erdostein, carbocystein) bocysteine) ATB (azitromycin, moxifloxacin) fyzioterapie fenotyp emfyzematický LVRS (horní laloky) bulektomie substituce A1AT (FEV1 30 až 60 % n.l	(N-acetylcysteine, erdosteine, ATB (azithromycin, moxifloxacin) physiotherapy emphysema phenotype LVRS (upper lobes) bullectomy (bullae > 30 % hemitor.) h., A1AT substitution (FEV <sub>1</sub> 30–60 % r.v.,
A1. - - - - - - - -	AT < 0,5 g/L) BVR (heterogenní) fenotyp exacerbační PDE4 inhibitor (roflumilast) IKS + LABA mukoaktivní medikace ATB overlap CHOPN + AB IKS + LABA IKS + LABA IKS + LABA + LAMA (antileukotrieny) fenotyp kachexie rehabilitace aerobní + silová nutriční podpora	A1AT < 0.5 g/L) BVR (heterogeneous) exacerbation phenotype PDE4 inhibitor (roflumilast) ICS + LABA mucoactive medication ATB overlap COPD + AB ICS + LABA ICS + LABA ICS + LABA ICS + LABA + LAMA (antileukotrienes) cachexia phenotype rehabilitation aerobic + strength nutritional support
(ar) - -	nabolická substituce) CHOPN + bronchiektazie fyzioterapie mukoaktivní medikace	(anabolic substitution) COPD + bronchiectasis physiotherapy mucoactive medication
(N· cai -	acetylcystein, erdostein, carbocystein) bocysteine) ATB (azitromycin, moxifloxacin)	(N-acetylcysteine, erdosteine, ATB (azithromycin, moxifloxacin)

### **Appendix 11: Pulmonary Rehabilitation**

Pulmonary rehabilitation includes patient examination, education, medical rehabilitation, occupational therapy, and nutritional and psychosocial support. It is based on the cooperation between the patient, their family, and all professionals involved in the treatment.



Indications for pulmonary rehabilitation





### Resources

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