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Comparative adherence and quality of life studies to measure the impact of a novel patient education program for patients with chronic obstructive pulmonary disease

PhD thesis

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List of abbreviations

AB	antibiotic
ACOS	asthma-COPD overlap syndrome
BA	β_2-agonist
CAT	COPD assessment tool
CF	cystic fibrosis
COPD	chronic obstructive pulmonary disease
DPI	dry powder inhaler
FEV_1	forced expiratory volume in 1 sec
FEV_1/FVC	Tiffeneau-index, the quotient of FEV_1 and the forced vital capacity
FDC	fixed-dose combination
GOLD	Global Initiative for Obstructive Lung Disease
GP	general practitioner
(HR)QoL	(health related) quality of life
ICS+LABA	the combination of an inhalative corticosteroid and a β_2 agonist
LABA	long acting β_2 agonist
LAMA	long acting muscarinergic antagonist
MA	muscarinergic antagonist
MAQ	Medication Adherence Scale
MMAS-8	Morisky Medication Adherence Scale (8 questions)
mMRC	modified Medical Research Council Questionnaire
PA	*Pseudomonas aeruginosa*
PDE_4	phosphodiesterase-4 (enzyme)
pMDI	pressurized metered dose inhaler
PRO	patient reported outcome
RCT	randomized controlled trial
SABA	short acting β_2 agonist
SAMA	short acting muscarinergic antagonist
SGRQ	Saint George's Respiratory Questionnaire
SMI	soft mist inhaler
STROBE	Strengthening the Reporting of Observational studies in Epidemiology

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TGFβ	transforming growth factor, receptor β
TIP	tobramycin inhalation powder
TIS	tobramycin inhalation solution

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1. Introduction

1.1. Background and conceptualization

Chronic obstructive pulmonary disease (COPD) is a severe respiratory disorder that poses a tremendous burden on healthcare and economic resources. The prevalence of COPD has been steadily rising globally (1) and COPD-associated mortality is predicted to be the third-leading cause of death by 2020 (2). While smoking is one of the major risk factors for developing COPD, other triggers include age, genetic predisposition, and a history of bronchial asthma and recurrent respiratory infections (3). Age and COPD prevalence appear to have a positive correlation and approximately 9.0-10.0% of the >40-years population present with COPD (4).

The main goal in COPD management is to maintain stable lung function and prevent acute exacerbations. The pharmacotherapy of COPD includes bronchodilators such as β_2-adrenergic agonists (BAs) and muscarinic antagonists (MAs), and inhaled corticosteroids (5). The preferred route of administration of these agents is via the inhalation due to its advantages – smaller dose, rapid onset of action, and lower incidence of side-effects (6) numerous inhaler devices are available to COPD patients for use in maintenance therapy. However, similar to other chronic conditions, successful disease management relies intrinsically on treatment adherence, and poor adherence to inhaler therapies has been shown to be associated with an increase in mortality rates, hospitalization, and disease burden in COPD patients (7; 8).

Chronic health-related conditions such as COPD have an enormous impact on the patient's quality-of-life (QoL) and result in increased utilization of health services. Patients who are unable to self-manage their chronic condition also score low on health literacy, a modifiable risk factor that can be rectified through effective patient communication (9). Patient education programs improve patients' health awareness and knowledge, symptom management, self-care practices and overall health status (10; 11; 12) thereby reducing the propensity for negative outcomes and associated treatment costs (13; 14). Similar programs designed for patients with COPD have been implemented, especially around exacerbations (15; 16; 17), in community pharmacy settings (18; 19), or during rehabilitation (20; 21). In recent years, there have been

studies looking at the impact of patient education programs on QoL or adherence or both (22; 23; 24; 25; 26) in patients with COPD.

Despite an enormous wealth of information on the effectiveness of patient education in the management of COPD in other parts of the world, there is a noticeable paucity of data from Hungary. Hence, the main goal of our study was to address these shortcomings and our primary objective was to assess the effect of patient education on medication adherence and QoL in COPD patients. We also sought to analyze whether demographic and subgroup parameters influenced adherence and QoL. The available resources and facilities enabled us to pick this challenging, but so far less studied and promising scientific area.

Compliance expresses the extent to which a patient is loyal to the duration of the recommended medication, to the dose of the recommended drug(s), and to administration frequency (27). It is an important feature of the therapy, though it does not reflect any collaboration from the patient's side. According to the WHO, adherence is "the behavior of an individual in accordance with recommendations agreed with a health care professional in the field of medication, diet and lifestyle change" (28), while another source refers to adherence when an individual is taking medication and collaborates with change according to health care recommendations (29). While compliance is primarily a matter of following medical instructions, adherence is a feature of patient collaboration. The term "adherence" will be used throughout this dissertation, which also demonstrates my dedicated to patient-centered therapy. I believe that the therapeutic experience can only be achieved if the patient is actively involved in it.

Patient education will act as an umbrella term to refer to any action that the patient implements to increase their acceptance, improve their attitudes, as well as the same on the educator's side. I will apply "quality of life" in an extended meaning referring to the environment, income and household of the COPD patient, considering that this body of research was implemented in the healthcare context. Thus, the mental, physical, self-role (work, parent, and career) dimensions and social function (relationship, fitness, health perception, satisfaction and well-being) are also included – as opposed to the concept that these are usually referred to as health related quality of life (30).

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1.2. COPD: a current snapshot

This chapter has the aim to provide an insight into COPD care, its impact on the society and the patient. It highlights the major pathophysiology aspects, comorbidities and extensively discusses current therapeutic options. This background is important to understand the world of the patient with stable COPD, who will be in focus in the further chapters.

1.2.1. Epidemiology and social burden

The prevalence of COPD varies from country to country but represents a significant health and economic burden (1). The most important predisposing factor for the development of the disease is smoking (31), besides inhalation of environmental hazards, dust, contaminated air, occupational hazards, and infections (32).

According to the Rotterdam Study (33), the overall prevalence in the population should be around 5%. Prevalence changed significantly between 1990 and 2020, moving from the sixth to the third place as a leading death cause (2). This is supported by that the proportion of the elderly increases in aging societies, so the condition is expected to soar in absolute, as well as in relative numbers (1). By the age of 40, the prevalence of COPD rises to 9-10% (4).

The intrinsic deterioration of quality of life due to COPD, which frequently goes in pair with low medication rate, can be measured by quality of life questionnaires (34). The more symptomatic is the patient, the lower is their quality of life, and the greater is the social burden (1). This burden can be alleviated by effective measures to foster early diagnosis and to keep the patient engaged (35).

Between 1987 and 2009, a summary of 11 studies found that COPD patients were in the range of 56-69% vs. 65-77% non-COPD patients to be able to perform their work (36). Besides, directly incurred health costs, we should take into consideration the financial loss late diagnosis, lost working hours and loss of productivity can generate. Comorbidities present beside COPD increase this social burden (37).

1.2.2. Patient flow and infrastructure of COPD care and implications to Hungary

Patients with COPD are often diagnosed late (38) , so patients are referred to a physician only when symptoms get more prevalent (an important note to patient referral: outside Hungary, COPD patients are usually treated by GPs – the description below primarily considers the context of this study, so I limit the scope to Hungary). The first encounter for the patient in the healthcare sytems are the GP and nurse. Patients mainly report coughing, sputum and breathlessness; however, GPs do not always feel competent to treat COPD patients (39; 40). Pulmonologists report that even the condition may remain undiagnosed even after multiple exacerbations, since patients are only taking multiple antibiotic and expectorant treatment; thus, they support that patient care should be reinforced in the GP office (41).

The GP is a gatekeeper in the healthcare system: they can decide to treat a condition in their office; or to direct the patient to specialist care (or primary care, as referred to more often by international articles) (42). In order to facilitate the healthcare access process, patients can participate in COPD screening on a voluntary basis, and the GP can also refer their patients here, and an early diagnosis of the disease could be made with the participation of a pulmonologist (40). This is often not the case because of the lack of awareness of the disease or the patient's unwillingness to cooperate (43). In general, patients do not have a direct access to the pulmonologist, and they should be referred by the GP (44).

With the GP referral, the first pulmonologist consultation appointment is given to the patient within 1-6 weeks of time, depending on the actual workload of the pulmonology outpatient center. Here, the usual diagnostic procedures are made: lung function and the bronchodilator tests (39; 45), which is supplemented by health status assessment tools, supported by the GOLD guidelines (46).

Cormorbidities, if present, are usually treated by another specialist (47; 48) may that be a cardiology or oncology. Following the resolution of the comorbidity, the patient returned to the lung care provider for specialist advice and will be treated for COPD here in the long term.

After medication is prescribed, the pulmonologist, or the nurse provides some training, which normally includes inhaler use (49), especially if the patient has questions, finds it difficult to use, is uncertain about the therapy (50). The therapy can only be successful on the long-term, if the device is chosen according to the patient's needs and they are able to use it (51).

The lung specialist will usually return the patient to a two-week (in the case of therapy initiation) up to twelve-month check-up (in case of well-established maintenance therapy). The pulmonologist can issue a license to the GP, so that they can prescribe pulmonology medication with high reimbursement rate; thus, the pulmonologist-patient relationship becomes much less frequent than that of the GP and the patient (52).

Studying the process reveals that patient information can be obtained from the pulmonary therapist, the respiratory assistant, and the pharmacy (53). The intervention points of the PhD study were designed accordingly: quality of life and the adherence of the patients were monitored in the pulmonary outpatient center and the pharmacy. Exploratory and in-depth interviews were conducted with participants and pulmonologists, to gather information at the most major intervention points of care. *Figure 1* summarizes the patient flow of the study.

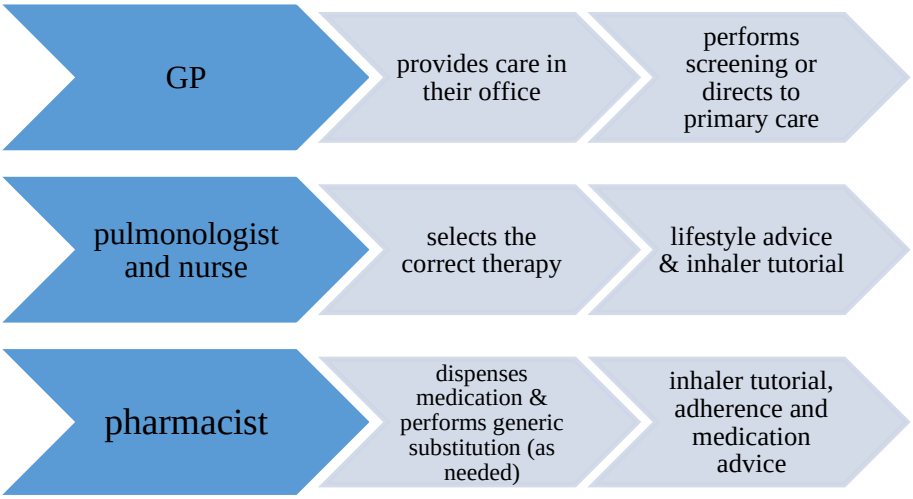

Figure 1: Intervention points in the patient flow in Hungary

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1.2.3. Pathophysiology & biochemistry. Phenotypes

The clinical appearance of COPD is chronic inflammation of the respiratory tract, of the lung parenchyma, and the vasculature (54). Irritant agents, often deriving from smoking, elicit an inflammatory immune response, which becomes permanent and causes tissue destruction. The result of the TGFβ pathway (55) is fibrotic lesion formation, first presents as small airway obstruction, and gradually expand to the bronchi (this makes it understandable that COPD can show a certain reversibility if diagnosed early. The macrophage pathway (56) creates the two phenotypes of COPD (*Table 1*). In patients with emphysema, T-cell inflammation or protease activity predominate, and the walls of the alveoli become ruptured, consequently the effective respiratory surface is reduced, and the surrounding vasculature is damaged. Reduced active respiratory surface develops adaptive hyperventilation; however, gas exchange is damaged. The result of the neutrophil/monocyte and protease pathway is the mucus hypersecretion, which yields bronchitis and colonization of bacteria. If the airways of the patient are blocked by mucus, clinical symptoms will include coughing, spitting and hawking, but no tissue destruction occurs. Finally, this process leads to the appearance of hypoventilation, which results a plummeting rate of gas exchange (56). *Figure 2* provides an overview of the inflammatory pathways.

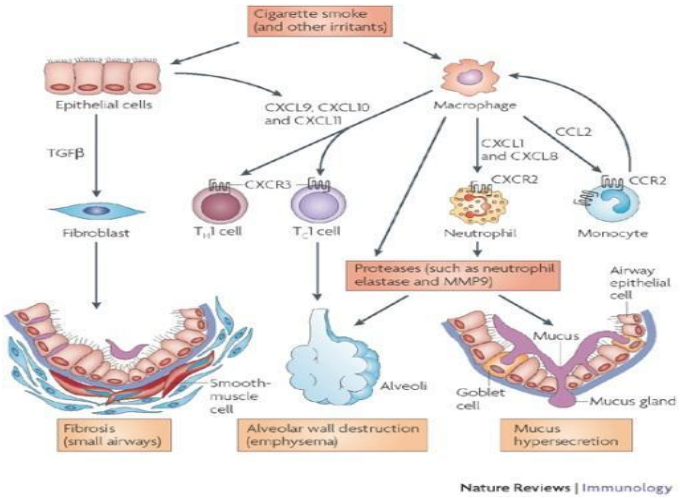

Figure 2: Inflammatory processes in COPD[1]

[1] This image is taken from (55).

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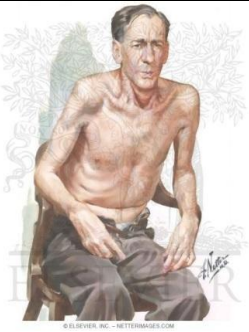
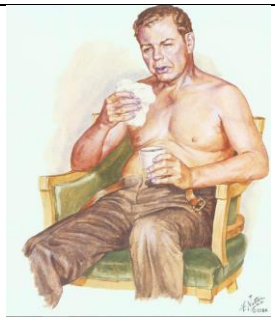
The most common symptoms are dyspnea, cough and/or sputum production, which worsen in the morning and are often accompanied by the suffocating feeling due to inability to get rid of the mucus (GOLD 2019). Irritating agents increase the number and size of mucinous cells, which produce more and more mucus; furthermore, the hair follicles are unable to self-cleanse, causing stagnant secretions to cause coughing and purging. Chest pain and shortness of breath may occur; usually these are the symptoms that bring the patient to a lung care provider. Exacerbations caused by colonized bacteria in mucus are common. Hyperinflation of the chest makes it hard for the patient to exhale; this is a process that develops gradually, and patients often get used to it, as well as to the decreased ability to perform physical activities and to become breathless rapidly (57).

Table 1: COPD phenotypes: the „pink puffer" and the „blue bloater"[2]

Emphysema		Bronchitis
 cachexic	patient profile	 corpulent
later, after 60 years of age (effort dyspnea)	manifestation	earlier, after 40 years of age
no coughing or cracking	symptoms	cough, purulent, copious secretion
breathing by pursed lips & breathing muscles	breathing	extensive use of accessory breathing muscles
whistling, barely audible heartbeat („barrel chest")	characteristics	breathing noises and beeps
„pink puffer" – hyperventilated, pink skin, no cyanosis		„blue bloater" – cardiac complaints, cyanosis, cor pulmonale, oedema

[2] Images were taken from: https://www.netterimages.com/images/vpv/000/000/013/13539-0550x0475.jpg [accessed: 15/9/2019] http://classconnection.s3.amazonaws.com/106/flashcards/1125106/jpg/blue_bloater1332976578322.jpg [accessed: 15/9/2019]

In chronic inflammation, the lungs are unable to get rid of the irritant, resulting in persistent mild inflammation, which impairs blood supply to the surrounding tissues and increases the risk of exacerbations (58). In the long run, this leads to tissue remodeling, and this is the moment where the process becomes irreversible. Secretion increases, which aggravates the symptoms and increases airway obstruction; additional cytokines, growth factors and proteases are produced (59). However, squamous cell metaplasia and goblet cell hyperplasia can be slowed by long-term (>3.5 years) nicotine abstinence (60), ie, if the patient stops smoking, inflammation would not disappear, mucus production and tissue remodeling would decrease.

1.2.4. Comorbidities

The majority of COPD patients suffer from multimorbid conditions, ie they have other diseases than COPD (55; 61). According to current guidelines, comorbidities should be treated as if they were present alone (62).

However, due to drug interactions, it is important to understand the background of these diseases and to select the drug for the patient that does not adversely affect the comorbid status, or make such a therapeutic choice for COPD, which has benefit on the other condition (63). The most common comorbidities are osteoporosis, anxiety / panic attack, heart problems, heart attack, diabetes (64), and 97.7% had at least one comorbidity and 53.5% had four (65). The number of comorbidities increases with age (61; 48).

Recently, the asthma-COPD overlap syndrome (ACOS) has gained increasing interest (66). It is estimated that 15-20% of COPD patients are affected by the overlap syndrome (67), which means that their condition have features resembling both COPD and asthma. These patients are generally younger, they are mostly in GOLD groups A or B, and no difference was found in exacerbation rate vs. patients with only one diagnosis (68). The bronchodilator test and exhaled NO levels can be used to discover the asthmatic component to be present, because these patients show incomplete reversibility with variable symptoms (67). The risk of exacerbations and the cost of treatment is higher than the one for only one condition being present, and mortality has been shown to be higher (69). Since the asthmatic eosinophilic inflammation responds well to steroids, treatment for ACOS patients should obligatorily contain it (70). ACOS patients were

not excluded from our research, so it should be considered as the comorbidity of the highest prevalence (with a ca. 20% rate).

1.2.5. Treatment

1.2.5.1. Non-pharmacological options

Smoking is a major cause and a massively aggravating factor in COPD, so the first step to any result should be smoking cessation (71). Continuing smoking not only enhances morning symptoms and mucus production, but also accelerates functional changes in the bronchi and contributes to the development of irreversible obstruction (60). In case of early diagnosis of COPD, smoking cessation can have some visible effects; otherwise, it is desired in any phase of the condition (71). The patient should be directed to a group or personal withdrawal program according to their preferences (72).

Referral to rehabilitation normally takes place after hospitalization or a major contact with the pulmonologist. Sessions include individualized care, and the methodology is as follows: the patient meets with a physiotherapist 2-3 times a week for 6 weeks, then again with the doctor after 6 weeks. This framework enables them to fill in quality of life, physical and depression tests to assess the effectiveness of rehabilitation (73).

Rehabilitation is also an option in Hungary, though patients are less willing to participate – this might be due to dropout from work and confrontation with working hours. Rehabilitation effectiveness is documented in literature and recommended from GOLD stage B (74). The physical activity component should be highlighted, because it improves the patient's life expectancy and quality of life (73); certainly, in such a form that is implemented according to the age and health status of the patient (75).

Pneumococcal vaccination is recommended (57), taking into consideration that the weakened immune system of COPD patients and their limited lung function make them more susceptible to infection, especially the *S. pneumoniae* strains.

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1.2.5.2. Pharmacological options

1.2.5.2.1. Diagnosis and GOLD classification

International guidelines of GOLD 2019 (57) describe diagnostic and classification tool, which is based on three pillars. These should be evaluated for each patient individually, and should be the primary factor to drive therapeutic decisions. *Figure 3* summarizes the factors driving therapeutic decisions.

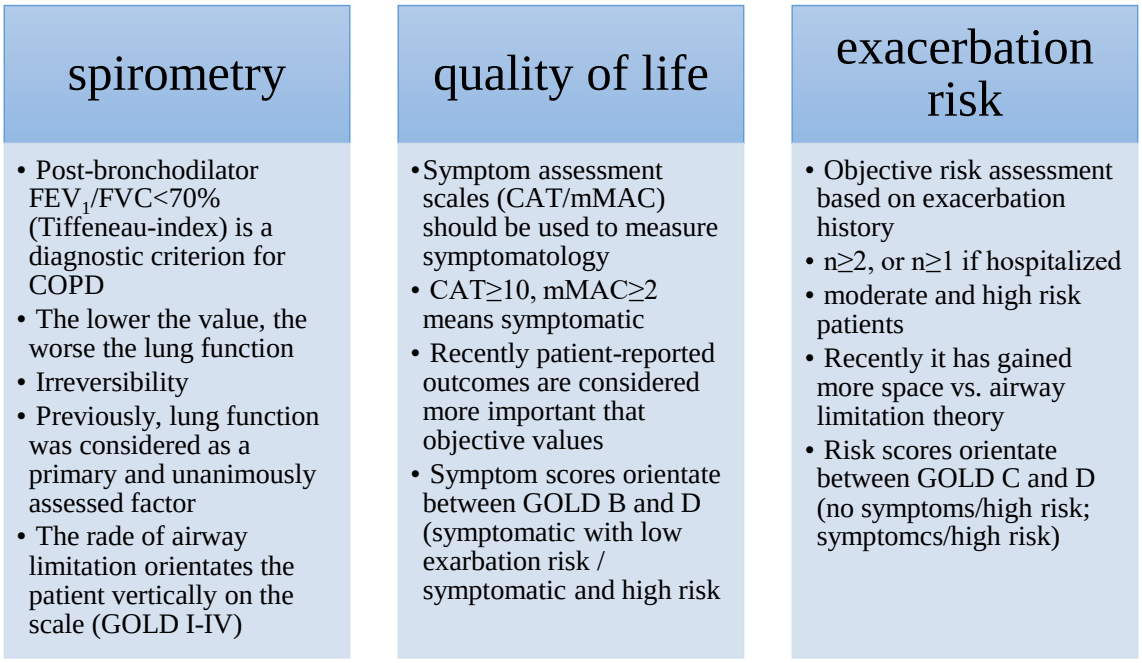

Figure 3: Pillars of COPD diagnosis and status assessment

The diagnosis of COPD can be established, if the patient is unable to exhale at least 70% of their vital capacity in one second (or 70% ≥FEV_1/FVC) (45). This step is called the spirometrically confirmed diagnosis (57).

In order to select the right treatment, patients should be classified in GOLD A, B, C, D groups, based on their symptoms and exacerbation risk – this implies that the assessment of FEV_1 is no longer the golden standard of COPD care (76), because what is important is how the patient feels about their condition. GOLD I-IV groups are still used to assess airflow limitation, but risk and symptoms are assessed in a square-shape system (the more symptomatic is the patient, the more to the right, and the higher the exacerbation risk, more upwards). *Figure 4* is a modified image from GOLD 2019, and clearly resumes the above.

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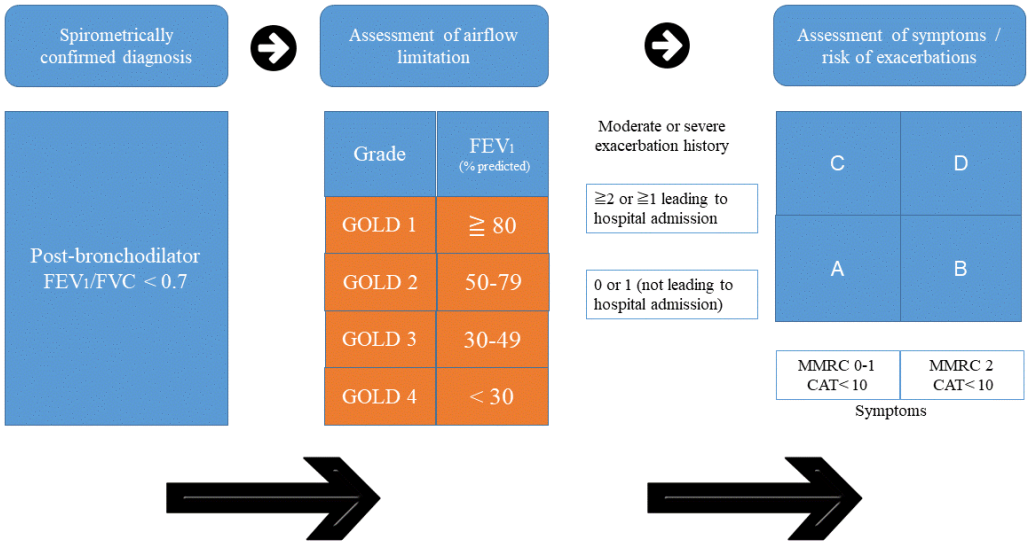

Figure 4: Diagnosis of COPD according to GOLD 2019

Symptomatology and exacerbation risk are equally important in assessing the status of COPD patients. Since exacerbators are excluded from the study, I will only focus on stable state in any part of the dissertation.

According to GOLD 2019, the overall aim of to reduce symptoms (relieve symptoms, improve exercise tolerance, and improve health status) and to reduce risk (prevent disease progression, prevent and treat exacerbations and reduce mortality).

1.2.5.2.2. Management of stable COPD

Since the study focusses on patients with stable COPD, and excludes patients with an exacerbation history in the last 6 months, this theoretical overview will be limited to the treatment of stable COPD. GOLD recommendations provide the official opinion of pulmonologists, though local regulations might slightly differ. Currently, in Hungary, the main stakeholder in COPD medication selection is the pulmonologist. The majority of the medication have high reimbursement, so prescribers should also obey the rules of eligibility stipulated by the Institute of Health Insurance Fund Management (NEAK).

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Table 2: Treatment options in COPD (unavailable solutions for Hungary are marked in grey)

Patient group	First line	Alternative	Optional
A	SAMA *or* SABA	LAMA *or* LABA *or* SAMA+SABA	theophylline
B	LAMA *or* LABA	LAMA+LABA	SABA *and/or* SAMA; theophylline
C	ICS+LABA *or* LAMA	LAMA+LABA *or* LAMA+PDE_4-inhibitor *or* LABA+PDE_4-inhibitor	SABA *and/or* SAMA; theophylline
D	ICS+LABA *and/or* LAMA	ICS+LABA and LAMA *or* ICS+LABA és PDE_4-inhibitor *or* LAMA+LABA *or* LAMA+PDE_4-inhibitor	carbocysteine; N-acetyl-cysteine; SABA *and/or* SAMA; theophylline

Table 2 provides an insight into the therapeutic options. Generally, long-acting bronchodilators are preferred over short-acting bronchodilators (77; 78), and combined inhalers yield greater results than monotherapy (79). Therapies are normally built up in a consecutive augmentation fashion: starting by one component of a fixed-dose combination, and adding the second (third) later (80).

In very mild forms of COPD, SAMA and SABA can be used. These are normally the part of an adjunctive therapy besides the long-acting agents, since COPD is barely diagnosed at this stage. From GOLD B onwards, LAMA is the most frequent choice in Hungary, although LABA can be used in monotherapy, too. LAMA seems to have therapeutic benefits over LABA in terms of rehabilitation and in reducing exacerbation risk (57). In case of contraindication, consultation with an ophthalmologist, urologist, and cardiologist is needed (81), and the other agent should be preferred. In case of worsening of the disease, this therapy is supplemented with LABA or LAMA. Cardiac effects of LABAs have caused certain difficulties in adding it to the therapy (82). It is important to note; however, that hypoxia that develops as a consequence of COPD, impairs blood oxygenation (42), which, by increasing heart rate, produces tachycardia, which can lead to unwanted fibrillation (which also increases the risk of stroke). Thus, the delivery of LABA is Janus-faced: it is worth bearing in mind cardiac comorbidities, but it is not necessary to vacillate with advancement, since it is in the patient's interest to provide the maximum amount of air (83). Continuing this line, the concomitant use

of both agents seems to be a reasonable option to counteract the downward spiral of COPD. As of the international guidelines, the combination therapy can be initiated from the beginning (84).

ICS+LABA is a base therapy for COPD from GOLD C, and the reasons behind it go completely aligned with the pathophysiology: local steroid treatment is an effective way to alleviate inflammatory processes. Recently, their previous supremacy in exacerbation risk reduction has been questioned, since it has been demonstrated that they have no superior effect in this regards compared to LAMA treatment (57). Consequently, a therapeutic need for triple combinations arises: this is a recently available option. This contains all standard pharmaceutical agents (LAMA+LABA+ICS).

As an adjunctive therapy, it is possible to administer expectorant agents (carbocysteine and N-acetylcysteine), which may play a role in sputum removal, but no long-term effects have been shown on patient health status. At these phase, roborants and nutritional solutions might be needed to counteract cachexia. Due to narrow therapeutic window of theophylline derivatives, they are only recommended in adjunctive therapy, especially if the patient is unable to cooperate with inhalative therapy. Oxygen therapy is deployed at later phases of COPD – this is the *ultima ratio* to ensure O_2 saturation (57).

SAMA and SABA use as “relievers” is excessive. Underlying reasons can be low price, high availability (they can be prescribed by GPs), and fast onset of action; and these decrease patient adherence to long-acting medication. They indeed have a definite role in COPD therapy, though it should be noted that correctly built-up maintenance therapy requires no or minimal reliever use.

Table 3 provides an insight into the myriad of the therapeutic options to each aforementioned pharmacological group.

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Table 3: Overview of inhalative medication indicated for COPD treatment in Hungary

mechanism of action	active agent	inhaler	brand name
Muscarinergic antagonists (MAs)			
SAMA	ipratropium bromide	pMDI	Atrovent N
LAMA	tiotropium bromide	DPI, SMI	Spiriva Handihaler & Respimat
	glycopyrronium bromide	DPI	Seebri Breezhaler
	aclidinium bromide	DPI	Bretaris Genuair
	umeclidinium bromide	DPI	Incruse Ellipta
Fixed dose combinations (FDC)			
SAMA+SABA	ipratropium bromide+fenoterol	MDI, solution for inhalation	Berodual N
LAMA+LABA	tiotropium bromide+olodaterol	SMI	Spiolto Respimat
	glycopyrronium bromide+indacaterol	DPI	Ultibro Breezhaler
	aclidinium bromide+formoterol	DPI	Brimica Genuair
ICS+LABA+LAMA	umeclidinium+fluticasone furoate +vilanterol	DPI	Trilegy Ellipta
	glycopyrronium bromide + formoterol + beclometasone	pMDI	Trimbow spray
β_2-agonists (BAs)			
SABA	salbutamol	pMDI	Ventolin Evohaler, Buventol Easyhaler
	terbutaline	DPI, injection	Bricanyl
LABA	clenbuterol	tablet, solution for internal use	Spiropent
	formoterol	pMDI/DPI	Atimos spray, Foradil Aerolizer, Reviform Axahaler
	indacaterol	DPI	Onbrez Breezhaler
	olodaterol	SMI	Striverdi Respimat
	salmeterol	pMDI/DPI	Serevent Evohaler
Inhalative corticosteroids (ICS)			
ICS+LABA	beclometason+formoterol	pMDI	Foster spray
	budesonide+formoterol	DPI	Symbicort Turbuhaler, Bufomix Easyhaler

	fluticasone propionate +salmeterol	DPI	Seretide/Thoreus Diskus, Dimenio Elpenhaler, Fullhalle spray, Airflusol Forspiro
	fluticasone furoate +vilanterol	DPI	Relvar Ellipta

1.2.5.2.3. Specific considerations of inhalation therapy

Inhalers and inhalative treatment are preferred in current COPD therapy (85), whose selection requires special attention. It provides an opportunity to tailor-make the therapy to the patient's needs (51). The patient's symptoms, intelligence, expected degree of adherence should be taken into account in the selection process (77).

Pulmonologist interviews reveal that the use of pMDI / DPIs is considered simpler and may be chosen due to lack of time. Concerning the use of the SMI tool (Respimat), there is a consensus that the therapeutic benefits outweigh the DPIs, but there is not always time to teach this tool, but it is considered to be the most advanced. One-time daily administration seems to go in line with higher adherence rate (86), though there are patients who feel safer to sniff for the second time in the evening. From the therapeutic effect point if view, twice daily administration can be beneficial for less adherent people, since by forgetting one shot, they still reach 50% of their daily recommended dose.

Muscarinic antagonists act on acetylcholine receptors, and the specificity of the newer agents is expressed at the M_3 receptor (leading to a lower rate of adverse effects). Cholinergic tone produces *ab ovo* bronchoconstriction and mucosal secretion, so its antagonists are physiologically bronchodilator (which implies that they elicit bronchodilation under physiological conditions, too). M_3 receptors are located in the bronchi; thus, the introduction of MAs do not necessarily needs to reach the deeper airways. This is opposite for the BAs, since β_2 receptors lie in the small airways, which do require that the active agent contains such particles that are able to reach high deposition there. Corticosteroids act on almost all components of inflammation and reduce airway hyperreactivity, although they have no direct bronchodilator role. They are believed to inhibit the decline of respiratory function (87). *Table 4* is a pharmacological overview of mechanisms of action, and also provides and insight into the potential adverse effects (88), as well as contains comments of use, especially in the Hungarian practice.

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Table 4: The pharmacology of COPD medications and adverse effects

Pharma-cological group	Mechanism of action	Comments for use	Adverse effect profile
M_3 antagonists	reduction of the cholinergic bronchial constriction	basic therapy for COPD, first choice from GOLD B upwards	glaucoma, urinary retention, dry mouth
β_2 agonists	intracellular cAMP levels increase, smooth muscles relax, bronchoconstriction decreases	basic therapy for COPD, administered from a separate device B or in FDC with LAMA or as monotherapy	cardiovascular, tremor, hypokalemia
ICS (+LABA)	ICS affects all components of inflammation (intracellularly, it connects to a nucleus receptor, which, after connecting to a heat shock protein, induces a conformational change that sets the DNA binding domain free. After dimerization, in the nucleolus, it connects to the DNA responsive element, and affects transcription)	baseline COPD therapy in severe cases, in patients with increased risk of exacerbation	systemically absent, oral candidiasis, hoarseness, diabetes deterioration, depression
theophylline derivates	bronchodilation (mechanism unknown), inhibits the release of inflammatory mediators (primarily PDE_4)	adjunctive therapy if the patient is unable to use the inhaler for financial or intellectual reasons	cardiovascular, heart rate and contractility increase, diuretic effect
roflumilast	inhibitors of bronchial phosphodiesterase (PDE_4)	rarely used, though included in GOLD 2019	

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1.3. Appraisal of international good practice

This chapter has the aim to provide an overview of the current research trends in the key areas related to my research focus: patient attitudes and perceptions, quality of life and adherence. Wherever possible, I considered the education aspect, and gather input to the development of the content.

1.3.1. Systematic literature review

Seeking to better understand the theoretical background of current body of research related to the topics of the thesis, I performed a systematic literature review. As an general rule, literature review was performed for each research area according to the PRISMA recommendations (89), see *Figure 5*. As an example, for the perception chapter, the following key words were applied: (COPD AND patient education), then narrowed my results ((COPD NOT asthma) AND patient education) and finally evaluated the most specific results (((COPD NOT asthma) AND patient education) AND (percept* OR literacy)).

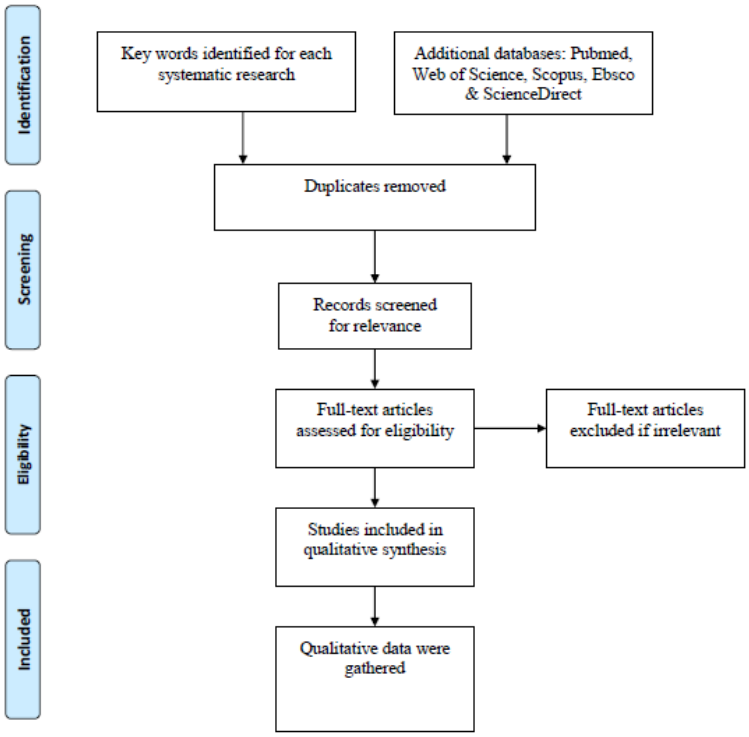

Figure 5: Literature review according to the PRISMA principles

1.3.2. Perceptions, attitudes and patient knowledge

In order to assess patient knowledge and to build relevant educational content, we should recognize what the patient needs and what information they already have (90). In the long run, only interventions that bring about changes in the patient's daily life can be successful (44). The patient should be empowered to be willing to make lifestyle changes in their own daily rhythm that allow for better disease management.

A further success factor of patient education that is should be tailored to existing needs, and should be country, population and disease specific (90). This means that before developing content, we should understand patients' capabilities, current knowledge, perceptions and attitudes at a given location. During our studies, we assumed that the Hungarian population is homogenous, and the *pilot* studies were performed in Budapest. The explorative interviews targeted the above objectives.

Initially, I wanted to observe the options of telemedicine to perform the education, though the current level of patient literacy turned down this ambition in the very beginning. It has been an interesting to see that attempts are made to educate COPD patients via the Internet or electronic devices, either in person or through smart devices (91). Further solutions include short messages, applications and other electronic means (92).

The first concept for development included coping skills training, which aims at inducing a change in the patients' life, starting from acceptance towards a health self-management of the disease. Coping skills training has proven to improve emotional balance and quality of life (93). The strength of the study is that n=326 patients were followed for a total of 4.4 years, while a telemedicine study demonstrated the beneficial effect on mortality (91). Healthcare systems may be less available for personal consultation in the future (78), so patients are likely to be driven towards higher acceptance of telemedicine solutions (94). This opens another interesting question: this direct contact enables a more direct connection between educator and patient. The future direction of attitudes slightly is to expand the effects of personal meetings by electronic interaction, and a higher rate of learning and putting into practice the information needed to self-manage the disease (95; 96). Patients with a better perceptions and coping strategies have achieved higher scores on quality of life questionnaires (n=100, Brief

Illness Perception Questionnaire (B-IPQ) and Utrecht Proactive Coping Competence Scale (UPCC)), and patients with an overly emotional response to the disease impaired their ability to cope with it. Patients that are more educated found more delicate and effective coping strategies.

In order to optimize patient outcomes, disease awareness, as well as patient perception should be evaluated (97; 98). Decreased acceptance or even neglecting their condition will yield marginal adherence. Improving these inherent characteristics of the therapeutic setting, and providing the patients with targeted information improves their quality of life (99; 100). This is not an easy path, since the patient's ability to report symptoms, or to verbalize medical history can also be difficult, that underlines the importance that patients and caregivers should speak the same language and be on the same page related to understanding the disease.

1.3.3. Patient education and self-management

While designing the education content, I identified similar body of research which describes an educational project with n = 62 patients with moderate to mild COPD (<70 years of age), who participated 2x2 hour weekly session, with 1 week gap fashion. Success factors were met if the number of GP consultations and reliever use decreased and patient satisfaction increased (101). Education was performed through a 19-page booklet with information on self-assessment and disease management. Oral sessions included education on the respiratory obstruction, anti-obstructive medication, exacerbation prevention, self-assessment and self-management, and physiotherapy. Twenty-one patients (84%) completed the study with one year follow-up. In the treated group, absenteeism at work was reduced by 95% (not significant), and patient satisfaction was 87%; and the relationship with the GP has improved (GPs are treating COPD patients in this setting). Overall, the study showed no improvement in quality of life parameters. Limiting factors include increased participation in asthma patients, and the experiments were performed almost 20 years ago, which is a fair timeframe to change paradigms of treatment and patient attitudes.

Concerning pulmonology rehabilitation, it is highlighted that asking as many stakeholders in the care flow as possible brings more input; and asking the patient and the caregiver at the same time can draw our attention to new discoveries (102). For the

conceptual perception assessment, it is worth including patient and caregiver interviews to map the needs of the two most important stakeholders of COPD care in Hungary.

A systematic analysis of 14 studies demonstrates that self-management reduces hospital admissions without deteriorating quality of life parameters (103). An important methodological point is highlighted: due to the heterogeneity of the studies, it is very hard to set up the optimal education, based on the publications reviewed, but it may be tailor-made (104). Finding the right balance between fixed content to keep measurements intercomparable is a methodological prerequisite, whilst personalization seems to bring the most benefits to the patient.

Taking the matter of standardization of education content to a national level, data providers in Germany present such diversity that prefer not to compare (105). The study confirms that these education projects should be either aligned individually or require a higher level of coordination for initiation. The most common errors that were found in 46 of the 95 programs are as follows: evaluation of program success, inadequate transparency of cost data and the lack of the same in quality of life interventions. It seems clear that success rates should be defined, although there are no consensus or an established method (106). A prerequisite for the achievement of success indicators is that the patient is actively involved in the therapeutic process and has an individual action plan for the self-management of the disease (107).

Although very softly, (108; 109) also affirm that a caring environment, nice and competent words initiate the self-management process in the COPD patient. Once they meet such condition, they become more aware of their disease and they are willing to do more in their homes. I should highlight the importance of “trial and error” effect in patient care: the more patients try, and get conscious about the disease, the more positively they think about the future and disease outcomes.

A holistic summary of patient education opportunities (110) include printed brochures, recorded videos and audio-visual materials, self-education, self-monitoring, self-directed therapy, patient involvement in therapy, patient interviews on side effects, organization of self-help and therapy groups, telemedicine, computer and internet patient information, targeted interventions to improve health literacy in disadvantaged groups, and targeted media campaigns. The methods mentioned here depict another

process: media and telemedicine should be the future direction, since it also corresponds with the limited availability of healthcare providers.

Another Canadian patient education project (111) covered adherence, inhalation techniques, health-related quality of life, and the use of health resources such as drug therapy and COPD exacerbations. Content included explanation of the current therapy, dosage, administration, patient expectations, duration of therapy, and potential outcomes, and follow-ups and improved inhaler use. By the "teach it back" strategy, understanding the components of adherence caused by a lack of knowledge and the patient's perceptions of the disease have helped to enhance adherence.

An analog of this study (112) examined COPD self-management on n=176 patients, with the following education content: COPD status, medication, and respiratory training. The Morisky questionnaire was used to measure adherence, and COPD Knowledge and SGRQ were used to measure quality of life (6 and 12 months follow-up). The article states that the success of COPD therapy depends on m education by 10% and by 90% on education.

Education should be structured to ensure that the measurements are inter-comparable. The education should consider the patients' capabilities, so that the content can be acquired, and it has cost-effective long-term effects: less frequent exacerbations result in decreased use of healthcare resources (113).

The following studies were implemented in the community pharmacy setting. For the role of the pharmacist, the following key areas have been identified (114):

(1) primary prevention: campaigns, lifestyle counseling, awareness raising;
(2) early diagnosis;
(3) management and ongoing support: pharmacist care, information on inhalation device use, disease outlook, dosage, self-management of the disease;
(4) overview and follow-up: monitoring adherence and device use. This connects to the content of the community pharmacy pillar of our education, and we considered these points to define the potential role of the pharmacist in our education project.

Inhaler use and follow-up in the community pharmacy setting were studied in 55 community pharmacies, with n=747 patients (115), using a 21-item questionnaire. 78.9% of patients made at least one mistake while using the inhaler, and dropped to 28.3% in the 4-6 week follow-up after education. This has the implication that the effects of education last for 6 weeks, so it is advisable that the follow-ups are planned at least for 3 months in a study.

The Belgian PHARMACOP study (116) shares the methodology of (115) and it is very similar to the final study design of our investigations. Altogether, n = 734 patients were enrolled and followed for 3 months between December 2010 and April 2011. Adherence to maintenance therapy and the use of inhalation devices were the focus of the study, and education was provided to patients at baseline and after 1 month. Both variables were significantly better in the intervention group, and a significantly lower number of hospitalizations were reported.

Using the in-depth interview method, n=173 patients were reported that the absence of depression, comorbidities, and patient perception of the disease have a much greater impact on adherence than demographics or disease severity (112). HBM (Health Belief Model) is a validated scale to evaluate patient beliefs and perceptions. Doctor's perceptions were examined, where the mention the following major symptoms: shortness of breath, fatigue and cough (117).

Another interesting insight, with a final research design similar to the one presented in this study affirms that according to semi-structured interviews with a representative sample of 34 patients of varying COPD severity, the four topics that were mostly mentioned by patients are the effects of symptoms, coping strategies and challenges, and areas needing support (118). The biggest challenges are the psychological impact, mental rejection of diagnosis and / or progression, impact of comorbidities and inadequate self-management skills. Patients demonstrated a need for assistance, and preferred non-pharmacological interventions.

The role of the relatives, especially the one of the spouse has been described (119), and it may be worth considering involving them in patient education. In the Hungarian context, it seems realistic approach that accompanying relatives are keen to learn about the conditions of the COPD patient, so delivering education to both targets is an

interesting idea. The same person could help a lot in constructing the inhaler (111), which may create a more favorable environment for adherence, too.

1.3.4. Quality of life, social context and coping strategies

A very interesting approach is that the COPD patient is asked about their expectations about the therapy, which is a modern way to self-determined PROs. The following main needs were accentuated by n=144 patients: breathlessness (64.6%) cough (13.9%), sputum production (11%), and exacerbation (8.3%). Self-improvement in PROs did not correlate with CAT score, but was significantly significant with FEV_1 (77). Based on how patients relate to their condition, it seems to be a conclusion they are more symptomatic than exacerbating, and this is reflected by their perceptions, too.

The effects of patient education demonstrated benefits the following parameters (n=941): frequency of referrals to rehabilitation, quality of life, psychological and individual parameters such as FEV_1, inhalation technique, smoking status (120). It should be noted that a non-validated quality of life scale and more qualitative individual parameters were used to evaluate the impact of education. Patient education with a one-year follow-up shows an inconsistent effect on HRQoL score (121), with one-third of patients significantly improving by the time of repeated patient education, although the effect on the population as a whole was small. The implication it has is that subgroup analyses might reveal further insight into the benefits to the patient, since different subgroups may show altered susceptibility to education.

The description of the methodology of Swiss national QualiCCare program was an interesting input to designing my research (122). Prior to the program, the Swiss population was estimated to have bad parameters in COPD care in international comparison. The study was conducted between 2013-14, and randomization was performed at the level of the GP. The selection criteria for the study were left loose: COPD diagnosis, former or current smoker, no other lung disease, no asthma and no hay fever, good German. The primary endpoint was to improve the quality of "treatment", but the secondary endpoint included a number of other aspects: referral to and participation in rehabilitation, written action plan, proactive follow-up, CAT score, and assessment of treatment quality by the GP. Overall, it seems that the study focused more on the quality of service than patient benefits.

For methodological reasons, it is worth looking into the CEGEDIM study (123), which uses SF12 as a general quality of life questionnaire and SGRQ as disease-specific one, and includes seven countries. The French subgroup analysis highlights the role of physical activity: it is worth paying special attention to this aspect, as reduced function may lead to further impairment and the effect of movement on the airways may improve COPD symptoms. The same idea is supported by (124), which adds a further recommendation that these activities should be supervised.

1.3.5. Adherence

The relationship between COPD and social stratification is examined in a Danish study (125), with data from n=13,369 patients, using proportion of days covered (PDC) to quantify adherence. Interestingly, only 32% of patients were found to have poor adherence (PDC = 0.8) and 5% did not use any medication (PDC = 0). The analysis showed lower adherence among lower income earners, the unemployed, immigrants and single people, and a positive association between low education and exacerbation and hospital admissions. The unemployed and those living alone were less likely to have exacerbation but higher death rates. The study introduces the concept of "health equity" as a priority in the healthcare system; and wishes to identify socioeconomic inequalities in the treatment of COPD. Besides this, the major reasons of non-adherence are identified (126): inhaler not used (20%), forgot to use (19%) and cost (15%).

A relationship between adherence and demographic characteristics was found in (127), where older age, lower levels of education, and lack of instruction in use were found to be the most important errors regardless of device. Malpractice can be observed at all levels of care and, but the above groups are especially at exposure of low adherence.

An interesting series analysis between 2008 and 2012 is the Italian SIRIO study (128), which aimed to demonstrate the economic burden of COPD. Economic issues are closely related to adherence indicators, as non-use of the drug increases the risk of exacerbation, which proportionally increases direct health costs, where one third in volume is spent on hospitalization (129), besides the hardly quantifiable additional burden on the society (number of lost working hours, salary of hospital worker, unpaid tax). In n=275, predominantly male patients it found that approximate treatment costs are as follows (2012, Italy): hospitalization EUR 1970, outpatient care EUR 463,

pharmaceutical costs EUR 499, indirect costs EUR 358, the total direct costs accounted for EUR 2,932 euros and the social costs 3291 euros. The following three actions can be made to reduce social burden (129):

(1) organizing national prevention campaigns and disseminating information on the disease;
(2) continuous training and education on obstructive pulmonary disease, dissemination of recommendations;
(3) ensuring access to basic services.

Considering the cost, the severity of the disease must also be taken into account, since the more severe the patient's condition; the more it will cost (130). Consequently, early detection and continuously available care is an important task of the health system.

Non-adherence rate in COPD is described in completely different ranges: 34% of patients did not use all of their prescribed medications at admission and 53% did not use the correct dose (131), which implies that adherence rate can be vastly in different geographical settings. As of education content, the study supports the idea that patients should be taught about the correct dosage and the types of medication (maintenance therapy, reliever).

Patient beliefs and perceptions should be evaluated when designing a study (132), which connects to (133), which describes a progressive and complex patient education and adherence monitor system. The first step was disease-specific education and it was followed by drug prescription control at the pharmacy. Primarily, I wanted to include monitoring dispensing data as an additional method to double check adherence, I could not finally find the necessary community pharmacy capacities to go this extent.

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1.4. Overview of scales and aspects of selection

During the study, I measured the patient reported outcomes (PRO), which I interpreted in accordance with relevant literature (134). Both single and multi-item questionnaires were used in the study to accurately measure and understand test parameters. The examined data were chosen to have both qualitative and quantitative parameters, thus recording the patient's subjective complaints and, where the patient reported such, comorbidities. As our sample is not representative in this respect, I left this analysis on a qualitative level (there are certain limitations which did not enable me to quantify this part of the research). However, when filling in the questionnaires, we put emphasis full completion of the tests to get quantitative data.

The study applies the following four types of scales:

(1) The nominal scale was used in the demographic questionnaire (eg. gender, smoking status). The data was coded in numeric form to facilitate processing (eg. active smoker 1, no smoker 0), this is called binary or dichotomous classification (134).
(2) I used an ordinal scale to evaluate the level of education in three groups (primary 1, secondary 2, upper 3), which can be used to set up an "order" related to the educational status of the patients.
(3) The interval scale does not have a fixed starting point; it evaluates differences and intervals in relation to each other. Although the symptomatic score (CAT) of a given patient would initially be an ordinal scale, the change in it that is monitored by follow-up can be considered as interval (eg, 2 points to 3, over 3 months).
(4) Absolute scales have an initial (zero) point, and they give a definite numerical value (like the absolute value of CAT symptom scores). Overall, interval and proportional scales can be classified as qualitative, while the nominal and ordinal scales are the qualitative measures (134).

In the quality of life tests, we measured utility, which is a commonly measured health economics parameter. Given the desire to get quantifiable data besides the qualitative ones, I had to select between direct and indirect modalities. The direct modalities of

utility measurements are the standard game, the time bet and the proportion scale, and all scales we used belong to the indirect group.

Validated scales are available for both quality of life and adherence, so I had to consider which one to select for this study. Below I review the aspects of this choice and the options available.

1.4.1. Demography

The demographic scale in this study is not validated; I created it in order to enable the creation of major demographic subgroups. The questions were chosen so that the sample is sufficiently separated, that is, to have a sufficient number of groups, but not too many, because there would be too few patients in each group to reach statistical significance (taking the overall n=118 patients enrolled in the study, this means 3-4 categories for each). After completing the informed consent form, patients were allocated a unique identifier to keep their personal data safe and to render the study anonymous. Each response was numerically coded, thus numerical values were used to record information about place of residence, age, gender, (previous) occupation, education, self-reported social status, smoking status, pulmonologist and GP satisfaction.

1.4.2. Quality of life and symptomatology

The literature offers a wide range of quality of life questionnaires, so there is no reason to develop new ones. To make the study comprehensive, the scales should meet the following criteria (ie. the questionnaire was chosen if it met the below categories, otherwise I kept searching for a new solution):

(1) general and a disease specific (by disease specificity I looked beyond other respiratory diseases, and wanted to have one that is specific to COPD);
(2) scientifically recognized and methodologically supported (demonstrated by literature data);
(3) cost-effective or free for academic use;
(4) easy to fill for the patient;
(5) should not exceed 20 minutes of administration time.

Certainly, there is no such as an “ideal” scale, the standards should be set by study design and determined to meet the requirements of the study objectives (135). Disease-specific

questionnaires have the greatest positive evidence (136), which underlines the importance to use such a questionnaire.

General quality of life scales measure the general condition, physical and mental status of the patients. Based on the five requirements stated above, I have considered the following scales:

(1) Sickness Impact Profile and Quality of Well Being questionnaires contain the most questions and take more than 20 minutes to complete, so I have excluded them. Since these exceed 20 minutes of administration, they would not be preferred neither by patients, nor educators, because so much time cannot be spent on
(2) The Nottingham Health Profile and the Medical Outcomes Study 36-Item Short Form Health Survey appeared to be more favorable at the beginning, though the abundance of questions (36 and 38, respectively) would have been confusing for the patient, so I excluded them.
(3) SF-36 could have been a very appealing choice, because visual analog scales are very easy to fill in and to understand. This feature is offered by the EQ-5D, which comprises the general scale and the visual analog scale in itself.
(4) Finally, EQ-5D-5L questionnaire was chosen due to the widespread use in other studies, and it is easy to administer due to the Likert scale (indicate on an ascending scale of four how they feel), and has the benefit to offer the visual analog scale (0-100 unit “thermometer”), too.

For disease specific questionnaires, the golden standard Saint George’s Respiratory Questionnaire (SGRQ) is so extensively used in the literature (137) that even though it is very extensive, and time consuming to (self-)administer, I decided to use it. Furthermore, the IP owner granted the license with no charge for this study. In addition to SGRQ, the Seattle Obstructive Lung Disease Questionnaire was considered; although one disease specific scale already covers the areas I wished to investigate.

For symptom assessment, the consecutive educations of GOLD propose two types of scales: modified Medical Research Council Questionnaire (mMRC) and the COPD Assessment Test (CAT). The mMRC is much shorter but it does not provide any specificity of the type of symptom: it only examines breathlessness related to motion

and physical activity. Although breathlessness in indeed a leading symptom, the patient may be symptomatic for other reasons (cough, expectoration, insomnia), which are incorporated in CAT. CAT examines symptomatology on eight questions, where patients put their level of exposure on an ascending Likert scale of five. Additionally, CAT is reported to yield the same results, no matter if self-administered, or assisted (138).

1.4.3. Adherence

The following methods have been identified to measure adherence in general (139):

(1) Indirect methods: mass measurement of inhaler, drug use on a self-declaration basis, *questionnaire*, electronic monitoring, assessment of inhalation technique, reading a drug counter or counting pills, monitoring pharmacy dispensation data, patient diary, interview with the patient
(2) Direct methods: biological test

Given the non-interventional nature of the study, I found it best to include a questionnaire to monitor adherence at all measurement points. The advantage of this is that the patient administers the questionnaire alone or assisted, which ensures that all questions are answered based on the immediate viewpoint of the patient, assistance is available if there are any points to clarify, and we have a written document for each measurement point.

A general characteristic of the adherence scales I examined is that they are much less complicated than quality of life scales. Since they do not contain many questions, an internal benchmark I set that the selected one should meet the following criteria:

(1) less than 10 questions, consequently, easy to administer (>10 minutes);
(2) scientifically recognized and widely used;
(3) available free of charge for academic use or a license is granted in a cost-effective way (except for MMAS-8, which was not completely free, though a significant waiver was granted);
(4) COPD focused, or at least validated for it (other chronic diseases or only respiratory excluded)

Looking into a review on the adherence tools (140), there is an abundance of available scales, though their use is not that standardized as the one of quality of life scales. MAQ (Medication Adherence Scale) is a relatively often used scale, which identifies (non-)adherence dimensions (140): medication habits, adherence limitations, and medication beliefs. Interestingly, it states that non-adherence as a fact is much more studied that underlying behavior and factors that trigger non-adherent attitudes. This study suggest that before selecting the scale, patient characteristics of the sample should be considered.

A broad list of adherence scales is available in the literature (141). Contrary to the name of the Brief Medication Questionnaire, its administration cannot be implemented too fast, since medication should be administered in each case (this is an information the patients themselves might not be aware of); and the range of patients it was validated for included subjects suffering from diabetes and depression.

I also dropped the Hill-Bone Compliance Scale because of the inadequate disease profile (validated for subjects with hypertension). From the design point of view, the Self-Efficacy for Appropriate Medication Use Scale seemed lengthy as it provides 13 questions and 3 Likert-scale answers. Due to its methodology and its desire to include disease-related beliefs, the Medication Adherence Report Scale (MARS) scale was an appealing option; however, internal consistency data are not yet available, and the scale itself was originally designed for schizophrenia patients, so its use in chronic diseases is still questionable.

Finally, thanks to its comprehensive and widely accepted literature, I chose the MMAS-8 scale for the study. The license was granted at available price for this study, and the scale itself is easy to administer (eight yes/no questions with one inverse question), and easy to process and evaluate. By definition, good adherence is 8 points, medium adherence between 6-8, and low adherence below 6. A limitation of this scale is that it focuses on drug intake, which is associated with MPR (medication possession ratio), and does not consider beliefs and perceptions extensively. However, despite these relative shortcomings, I found this scale to be the most suitable for participating in the study. The 8-question version is the latest, most sensitive and specific version of the questionnaire, and the addition of 4 additional questions allowed for further refinement of the method compared to the previous measurement arrangement in place since 1986

(142). Please consult *Table 5* for a complete overview.

Table 5: Overview of the selected questionnaires

Questionnaire	Meets eligibility criteria	Interpretation	Administration time	Outcome
MMAS-8	yes [license granted with discount]	good adherence: 8 points, medium: 6-8 points, low: <6 points	ca. 10 min	8 questions to measure medication adherence
EQ-5D + VAS	yes	utility is calculated based on patient input on a Likert scale, the higher the value the higher the utility	ca. 10 min	generic quality of life and snapshot on current health status
CAT	yes	asymptomatic: <10 points symptomatic: >10 points	ca. 8 min	8 questions to assess symptoms on a scale of 0-5
SGRQ	yes [though somewhat lengthy to administer]	based on patient input, impact, activity and total scores are calculated, the higher the value, the worse health status (inverse relationship)	ca. 25 min	comprehensive appraisal of disease specific quality of life

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2. Objectives

2.1. Mission statement

The main goal of the dissertation is to provide guidance on the ideal patient education content, validate it in a real-life setting, and to elucidate its effect on patient-related outcomes. As for adherence, an adherence appraisal cystic fibrosis was also targeted.

In a stepwise approach, the following objectives were set (*Figure 6* is a graphic overview of the objectives scheme):

2.1.1. to assess the attitudes of two key players (patient, physician) in COPD patient care. This new methodology should be reproducible, widely applicable, and personalized & understandable to patients.

For the pulmonologist interviews, I set the following project specific objectives:

- to develop a patient education program that is based on the expert opinion of pulmonology therapists who play a key role in the care of COPD patients;
- to understand the perceptions and attitudes of the pulmonary therapist, and to gain a comprehensive landscape of patient and condition, the success of the treatment, and their relation to adherence;
- to assess the potential of improving patient adherence in outpatient care, rehabilitation and hospital settings.

For the patient interviews, I set the following project specific objectives:

- to assess the opportunities of COPD disease management in the community pharmacy setting;
- to understand patient attitudes, perceptions, fears, beliefs that affect the everyday life of patients;
- to create a local good practice and to investigate how the community pharmacy pillar of integrated care can work in the context of Hungary.

2.1.2. to conduct *pilot* studies to determine the optimal scenario to *go live* with the education project;

2.1.3. to investigate the effect of education on quality of life and adherence of COPD patients at different study sites (Budapest and the countryside) by a different set of validated scales; and to investigate the longitudinal effects of education;

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2.1.4. to propose the ideal conditions of education (pharmacist care in the community pharmacy setting or pulmonologist care in the outpatient setting, assisted by a nurse);

2.1.5. to understand the background of adherence in a wider context of pulmonary conditions, including the different setting of cystic fibrosis.

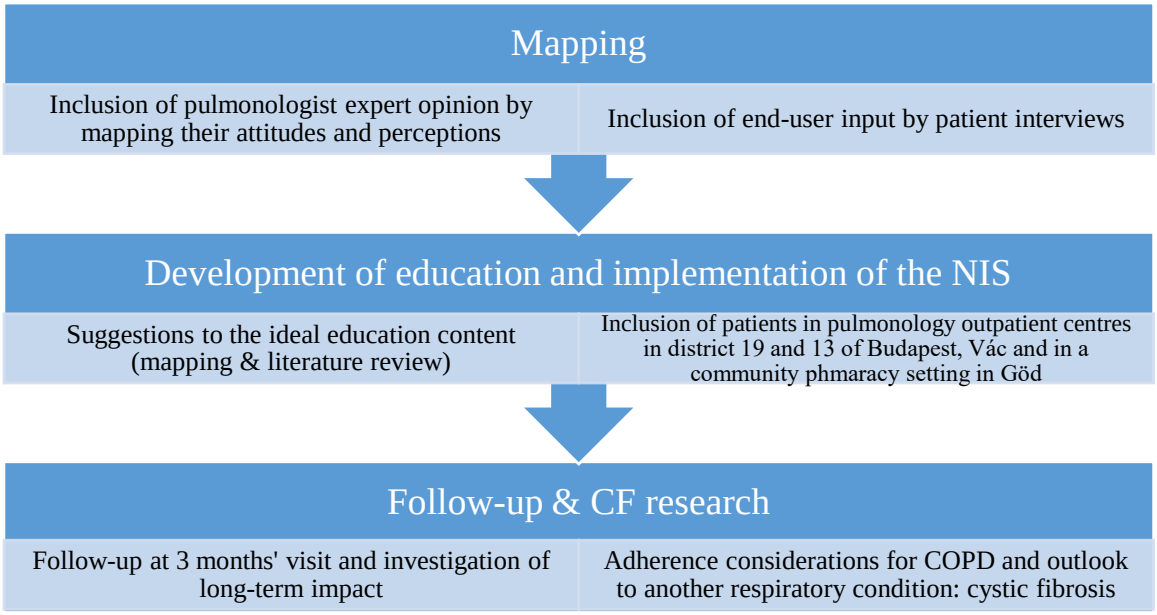

Figure 6: Overview of the research objectives

2.2. Hypotheses

2.2.1. Patient-centered education content can be developed based on the attitudes and perceptions of pulmonologists and patients.

2.2.2. This education content has a positive impact on medication adherence and quality of life, and this demonstrated by validated scales.

2.2.3. A methodological overview to broaden the scope with CF medication adherence will help me reveal more about adherence patterns and patient attitudes in respiratory conditions.

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3. Methods

3.1. Attitudes and perceptions

3.1.1. Pulmonologists

We interviewed 20 pulmonologists who are involved in the care of COPD patients; they work in outpatient centers, hospitals and rehabilitation centers. An interview lasted 30 minutes and we examined three clusters of questions. *Table 5* details the topics of the methodological blocks. It is important to underline that the order of these is in line with the objectives of the study but may differ from the one of the interview blocks.

The interviews were prepared by a mixed method and recorded in writing. In addition to the semi-structured groups of questions, I tried to allow more space to physicians' views to develop, resulting in an overall shift towards in-depth interviewing methodology (143). We focused primarily on developing their own thoughts and perceptions, and in each case, we also recorded the specific terms used by the pulmonary therapists.

Table 5: Pulmonologist interview methodology

Aim	Topic	Sample questions
1	Educational program	How do patients experience COPD? What bothers them the most?
		What does an ideal training program look like for your patients?
		What key elements would you mention to teach the patient anyway?
		What does doctor-patient collaboration mean to you?
		What can pulmonologist, a GP, a pharmacist and an educator do? How?
2	Patient characteristics and pulmonologist perceptions	What are your experiences with COPD patients in the outpatient centers? How many of 10 patients have already been diagnosed with COPD?
		What condition do your patients have?
		What is your main motivation for treatment?
		How would you describe a typical COPD patient?
		What is a good treatment?
3	Adherence & its improvements in the pulmonology outpatient centers	What do you think most influences the patient's cooperation?
		How to choose an inhaler for the patient?
		Who can decide on the inhaler? What are the aspects of pharmacy generic substitution?
		What methods do you use in pulmonary practice to promote patient adherence?
		What can a lung care provider do to improve patient adherence?

3.1.2. Patients

3.1.2.1. Study context

Göd is a medium-size city with around 19,800 inhabitants (144). According to the Rotterdam Study (33), COPD prevalence is 4.6%, so 5% seems to be a rationale approximation in a European setting (2). This means that the overall COPD population of Göd should be around 95 people, out of which, N=6 were included in our study (7%). Inczeffy Pharmacy is a central and well-known community pharmacy in the city, and it has gained an innovative reputation due to their commitment to patient education programs.

3.1.2.2. Inclusion of study participants

During dispensing medication, patients with the J44 ICD classification code were offered to participate in the *pilot* project. Altogether, patients were screened for 5 working days; 25 showed their interest and eight were willing to participate in the education session, and finally six patients showed up.

3.1.2.3. Interview methodology

We performed exploratory in-depth interviews with the patients (145). The structure of the interview has been designed to determine the key elements of a patient education program based on patient input and needs; so the major aim of the interviews was to explore their needs as of education content (146). *Table 6* provides an overview of this structure and an insight into the explorative questions. One interview lasted ca. 30 minutes. The methodology showed some mixed features with a loose semi-structured interview, since we had previously set the major topics we wanted to direct patients to. Altogether, we interviewed them by using the active listening technique, which means that we concentrated on their thoughts and let them relatively freely talk about their condition. At the end of the interviews, patients participated in an educational session (prototype education) where they could ask freely about their doubts related to their disease. Their reactions were assessed before and after the prototype session.

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Table 6: Interview methodology guide corresponding to the objectives of the study

Aim	Topic	Sample questions
1	In-depth interviews to understand patient attitudes, perceptions	How do you feel about your disease?
		What disturbs you most in COPD?
		What would you like to do if you could breathe freely?
		Do you think your condition will get any better?
		What does a regular day of yours look like?
2	Explorative interviews for educational content & insights to adherence	Do you have any questions related to your condition? / What would you like to know about it?
		What have you heard about it?
		Can you tell us how to use these inhalers?
		What would you like to change about the condition?
		Do you believe that you / the doctor / your educator can make a change? How?
3	Creating local good practice in Göd	How can the pharmacy staff be engaged?
		How can we engage local stakeholders to keep up with the project?

3.1.2.4. Symptom assessment

We invited the patients to self-administer the COPD Assessment Tool (CAT),[3] which is a standard method to assess symptomatology in pulmonology practice (147). CAT is an 8-item questionnaire to assess their symptoms on an ascending scale until 5, and scores range 0-40. Patients are considered symptomatic above 10 scores.

[3] We fully complied with the guidelines at https://www.catestonline.org, and we solely used the licence for academic research purposes.

3.2. Impact of education on quality of life and adherence

3.2.1. Study design

This non-interventional, multicenter, longitudinal study was conducted between March 2016 and February 2017 at three pulmonology outpatient centers in and around Budapest, Hungary (district 13 and 19 in Budapest and Vác). Study subjects were patients visiting the center, having an established diagnosis of COPD by a pulmonologist, and providing an informed consent to participate in the study. Subject recruitment was random in the sense that every tenth patient visiting the center for consultation was invited to participate in the study and if eligible and providing consent, enrolled. In case the tenth patient was ineligible or refused consent, the next patient was invited and so on until a subject was recruited. Study subjects underwent two study visits – one at baseline and the other at follow-up approximately three months later. At baseline, subjects' sociodemographic and medical data was collected, subjects were asked to fill in the adherence, symptom perception, and QoL questionnaires (described below), and patient education was provided (described below). At the follow-up visit, subjects were asked to fill in the same questionnaires again. Subjects' education level was assessed on a scale of three, ranging from basic to university level. Social status of the subjects as well as their perception on certain outcomes were self-reported as given in *Table 9*.

The study was conducted in accordance with the principles stated in the Declaration of Helsinki (1961) and its subsequent revisions, Good Clinical Practice guidelines, as well as national laws. Prior approval of the study was obtained from the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (241/2015).

3.2.2. Inclusion criteria

Patients who had a diagnosis of COPD and signed a patient consent statement were selected for the study (see *Figure 7* for a summary). Patients with the below conditions were excluded from the study:

(1) barriers to completing the questionnaires (dyslexia, mental retardation, severe psychosis);

(2) other untreated chronic conditions that affect quality of life (heart failure, pulmonary fibrosis, ischemic heart disease);
(3) exacerbation within less than 3 months;
(4) acute respiratory disease or tumor at the time of screening.

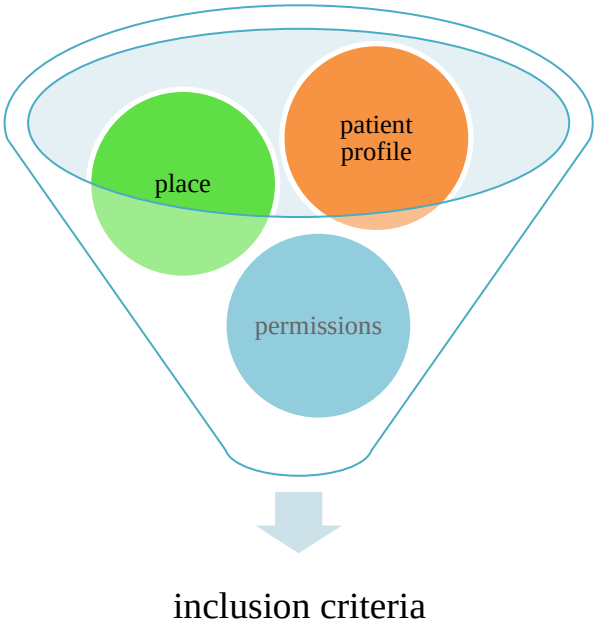

Figure 7: The study enrollment process

3.2.3. Patient education

Nurses or pulmonology assistants who had been previously trained to instruct subjects using the standardized content conducted patient education, based on a fixed content, face-to-face on an individual basis. Subjects were encouraged to ask questions and provided with take-home lessons at the end of the session. By keeping the content same for all study subjects, we ensured uniform patient education, although by answering subjects' questions we also allowed for an individualized approach (please consult *Figure 8* for more details in patient education).

Education provided during personal meetings were reiterated through a short leaflet, which subjects took with them (please see its content in attachment). Information contained in the leaflets was based on that provided by pulmonologists in a previous in-depth interview as well as systematic reviews (97; 148; 149). The leaflet contained the following key blocks: disease, treatment, and self-management. The disease block

provided information on COPD and symptomatic alterations in the lungs and identified the present type and state of the subject's COPD. The treatment block contained information about use and medications such as short-acting BAs and MAs to prevent exacerbations, correct technique for inhaler use, and symptoms of and actions to be taken in case of exacerbations. The third block informed subjects about smoking cessation, breathing techniques in case of shortness of breath, physical exercise, and lifestyle modifications (please consult *Figure 9* for more details on the study flow).

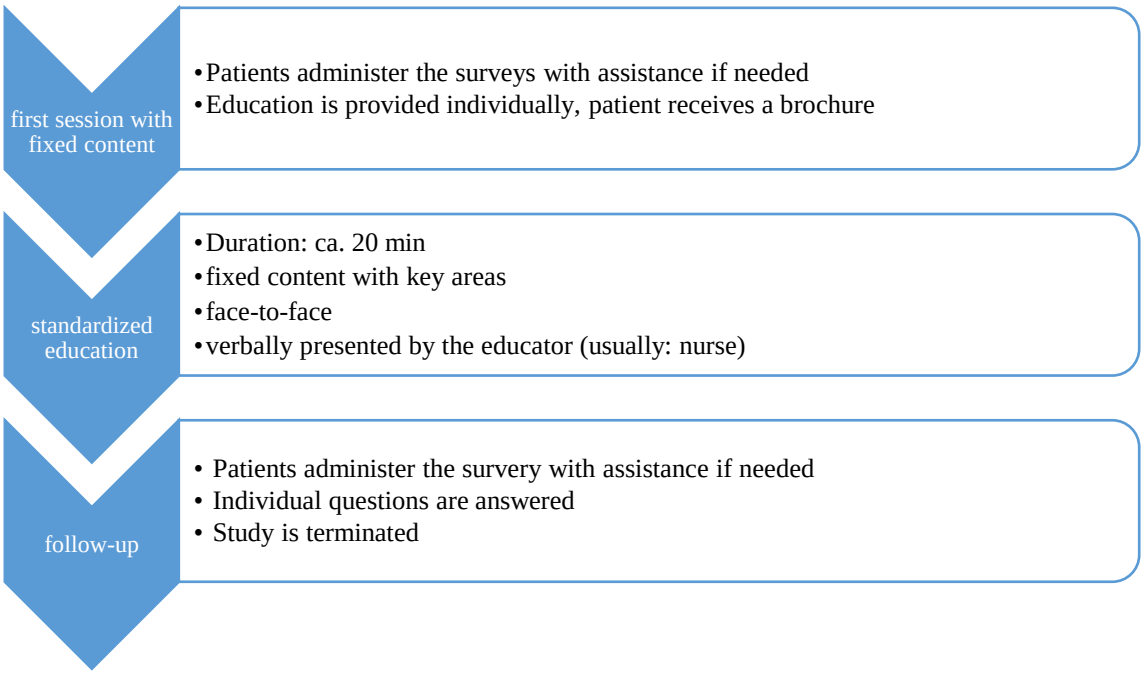

Figure 8: The patient education methodology

3.2.4. Assessment questionnaires

Quality-of-life scales were selected in accordance with currently employed general and disease-specific algorithms (15; 148; 150). For adherence, we used the Morisky Medication Adherence Scale (MMAS-8) which has been validated for chronic disease conditions as well as COPD (22; 151).

Each study subject was provided with a standardized questionnaire at enrolment and at follow-up. The questionnaire included three QoL algorithms designed to assess general and disease-specific QoL and one adherence algorithm. Wherever possible, validated Hungarian versions of these algorithms were procured and used with the written permission of the holders of the intellectual property of the same.

3.2.5. QoL algorithm

3.2.5.1.1. Generic measurement tools: EQ-5D-5L and EQ-5D-VAS

The EuroQoL-5D-5L measures five parameters related to health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each on an ascending scale peaking at 5 (152). The visual analog scale (VAS) allows the patient to indicate their current wellbeing on a scale of 0-100. Values on these scales range from 0.281 to 1.000, with higher values indicating better QoL (153; 154).

3.2.5.1.2. Disease-specific measurement tools: SGRQ and CAT

The St. George's Respiratory Questionnaire (SGRQ) is a comprehensive scale that measures symptoms, activity, and impact scores (155). Questions 1-8 relate to patient recollection of their symptoms in the preceding period while questions 9-16 inquire about the patient's current state on which activity and impact scores are calculated. The SGRQ scores range from 0 to 100, with lower values indicating better QoL and a reduction of four units is generally taken as a clinically significant improvement (74).

The COPD Assessment Tool (CAT) is an 8-item questionnaire for assessment of symptoms. Patients rate their symptoms (cough, phlegm, tightness in the chest, etc.) on an ascending scale until five. Scores range from 0 to 40 and higher scores indicate higher severity and debilitation in patients (156).

3.2.6. Adherence algorithm

The eight-item MMAS-8 (157; 158; 159) has been widely used and recently validated through a meta-analysis for evaluation of adherence. Higher scores indicate higher adherence.

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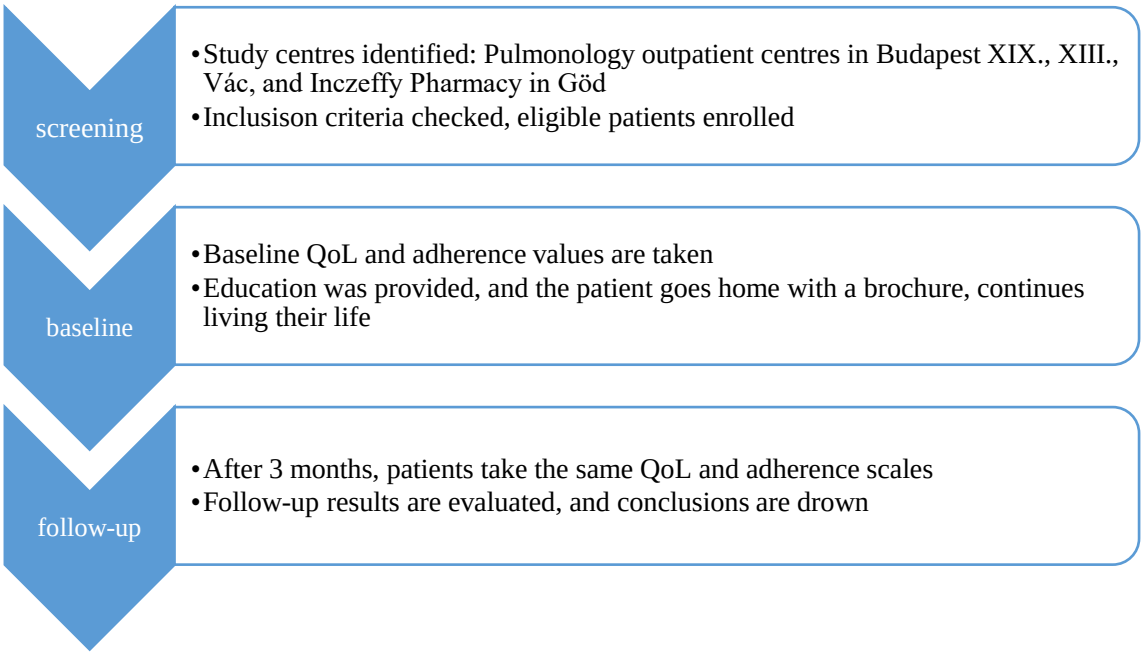

Figure 9: The study flow chart

3.2.7. Sample size calculation and data analysis

While calculating sample size we operated on the assumption that at least 10 subjects per variable would be required in order to achieve the primary objective and impart enough power to the study (160). Practically, this was performed in such a manner that every tenth patient in the pulmonology outpatient centers was offered to participate in the study, once they met the eligibility criteria. This helped us randomize the patients who participated in the study, and we provided equal access to education vs. standard procedures.

Moreover, we also considered adherence (MMAS-8) and COPD symptomatology (CAT) scores to be important markers for us to be able to distinguish the effects of patient education, because these are presumably able to detect changes in patient status besides the known correlation between education and adherence. At the same time, the other questionnaires were handled with the same care, though initially we assumed that these are primarily for detecting minute changes.

Bearing these requirements in mind, we estimated that a sample size of approximately 100 subjects would be sufficiently large to yield statistically significant results and achieve the research objective, and finally n=118 questionnaires were sufficiently

recorded and checked to be included in the study. Altogether, eight questionnaires should be excluded from our analysis; because the missing answers would have made it impossible to provide the desired accuracy to be considered as valid, whilst the exact number of missing questions was determined in accordance with the evaluation guides.

Based on the results of the *pilot* study, patients are more keen to fulfill paper-based questionnaire, so all of them were printed, allocated, and administered by the patient, and where possible, with assistance. Data were digitalized in Excel; numerical transformations took place to enable SPSS analysis. Then, we analyzed data using IBM SPSS Statistics version 22.0. Serialization of data enabled us to quantitatively analyze them, so quantitative variables were evaluated by paired-samples *t*-tests and mixed-measures ANOVA (demographics, all single input data, like quality of life and adherence scores), and ANCOVA to study temporal effect (ie. the 3 months longitude of the study). For study the effect of independent variables such as age, education, etc., we used the *t*-test, one-way ANOVA, and mixed-measures ANCOVA. Furthermore, we employed correlation analysis to compare baseline data to the follow-up data, as well as for multiple comparisons of the changes of a single value vs the change of another value. Results were considered significant at $P < .05$, and we also noted the tendencies, wherever relevant.

3.3. Background of adherence in a wider context

A systematic literature search of English-language articles was conducted in April 2015 using Medline and Embase (via Scopus) with the following search terms: (adheren* OR persisten* OR complian*) AND ("cystic fibrosis" OR muscoviscidosis) AND ("Pseudomonas aeruginosa") AND (antibiotic*). No publication date limits were defined. The search results were processed in two steps: first, the titles and abstracts were screened; next, all the full text of all the potentially relevant articles were analyzed. The references of the included articles were screened for additional eligible studies. The literature screening was conducted by two independent reviewers; disagreements between reviewers were resolved by consensus (*Figure 10* summarizes the steps of screening). The reasons for exclusion in both steps were the following:

(1) the article reported no new evidence (ie, editorial, letter, case report, or review),
(2) the article was a case study,
(3) the article was not related to CF, and
(4) the article had not assessed adherence to inhaled ABs for the treatment of chronic PA infection in CF. This review included only publications in which data on adherence to inhaled ABs were clearly separated from adherence data of other medications.

The data extraction was limited to findings relevant to the research topic. The following information was extracted from each included study:

(1) the first author and year of publication,
(2) the country,
(3) the study design,
(4) the study year,
(5) study exclusion and inclusion criteria,
(6) the study population characteristics,
(7) the medication therapy,
(8) the method of measuring and defining adherence,
(9) adherence data, and
(10) predictors and consequences of non-adherence to inhaled ABs in CF.

In case of studies in which adherence rates were presented graphically only, WebPlotDigitizer 3.8 was used to extract numerical data accurately out of figures. The scope of this review was to give a systematic overview on the adherence to inhaled ABs in CF; therefore, results of adherence measures that were not applied to assess adherence to inhaled ABs were not abstracted from the included studies.

For the quality assessment of the included studies, the strengthening the reporting of observational studies in epidemiology (STROBE) checklist (161) was used. Two review authors independently assessed all the studies; disagreements were resolved by consensus. The results of the quality assessment were summarized as the percentage of the fulfilled criteria for each study (criteria that were not applicable to a study were excluded from the quality assessment), ranging from 0% (none of the applicable STROBE criteria fulfilled) to 100% (all applicable STROBE criteria fulfilled).

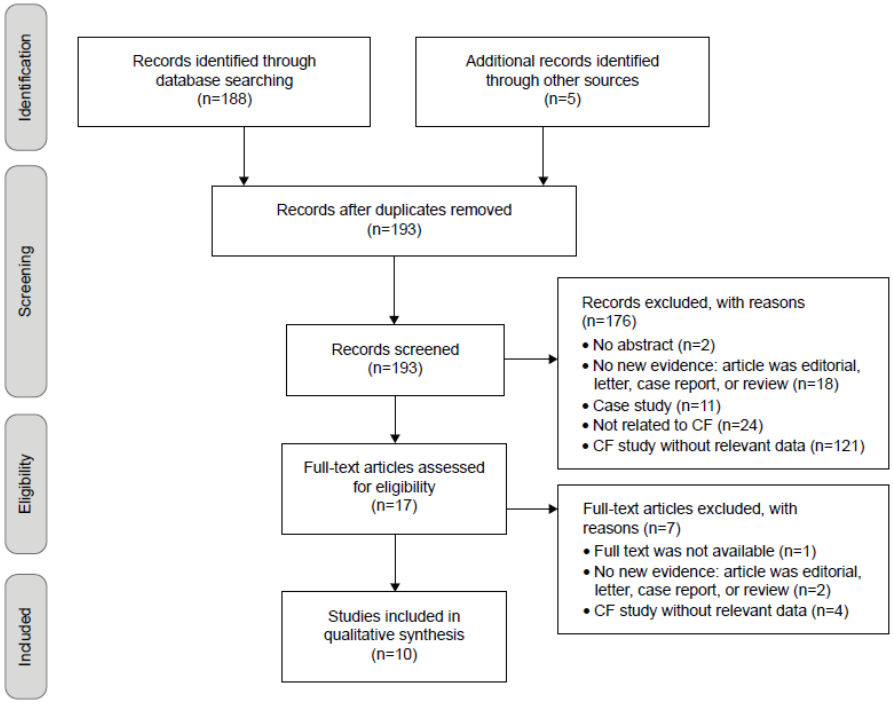

Figure 10: Screening methodology

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4. Results

4.1. Attitudes and perceptions

4.1.1. Pulmonologists

4.1.1.1. The study population

The in-depth interview was conducted with 20 pulmonologists. The majority of those working in the profession are over 50, most of them working in an outpatient center (*Table 7*). According to the Hungarian Society of Pulmonologists (162), there are 540 active pulmonary physicians in the country, almost 50% of whom are over 55 years old. The interviewees were selected so that their distribution by gender, age, and workplace corresponded to that of Hungarian pulmonologists. About 4% of the total sample stated during our interviews (see *Table 7* for further details).

Table 7: Gender, working affiliation and age of pulmonologists

			%
	total number	**20**	
gender	male	3	15%
	female	17	85%
main affiliation	hospital	7	35%
	outpatient center	12	60%
	rehabilitation	1	5%
age	under 40	3	15%
	40-50	8	40%
	over 50	9	45%

4.1.1.2. Patient characteristics and pulmonary physician perceptions

We asked the doctors to characterize the COPD patients they care for, to mention signs and observations from which they can immediately determine that they are dealing with a COPD patient. Many similar elements appeared “smoker”, “under-socialized”, “coughing”, “breathless”, “slow”, “older”, “and male”. Separation according to the textbook types of emphysema / bronchitis was also observed. One of the two types of lung therapist figuratively described this as "the thin, lean and smoking”, the “dry” type, and the “sputumy, corpulent, puffy” who is more “sputulent”. One of the interview subjects said that the proportion of women could be growing due to the massive smoking

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promotion in the previous decades. This emancipation focuses primarily on Budapest and its surrounding area, where COPD patients are evenly distributed gender wise. The disease is also associated with a socioeconomic gradient: patients are less socialized, with more men than women in the countryside, as women are more likely to get with the more “chic” diagnosis of asthma (see *Table 8* for more patient characteristics).

Table 8: Major characteristics of the COPD patient

(values are created as of their occurence in the pulmonologist interviews)

Coughing, breathless, sputum, slow	68,4%
Smoking	63,2%
Lower social status	31,6%
Male	26,3%
Over 50 years	26,3%
Lean, thin and improductive cough	21,1%
Cyanosis	15,8%
All of them are different / depends on stage	10,5%
Limited movement, choking feeling upon movement	10,5%
Judging and obstinate	10,5%
Obese	5,3%
Pensioner	5,3%
Female	5,3%
Comorbidities	5,3%
Procrastinating	5,3%

Figure 11 gives an insight how pulmonologists think about the diagnostical status of COPD. The results showed an average of 4.2 patients are diagnosed (standard deviation = 1.7) out of 10 patients, with values ranging from 2 to 10.

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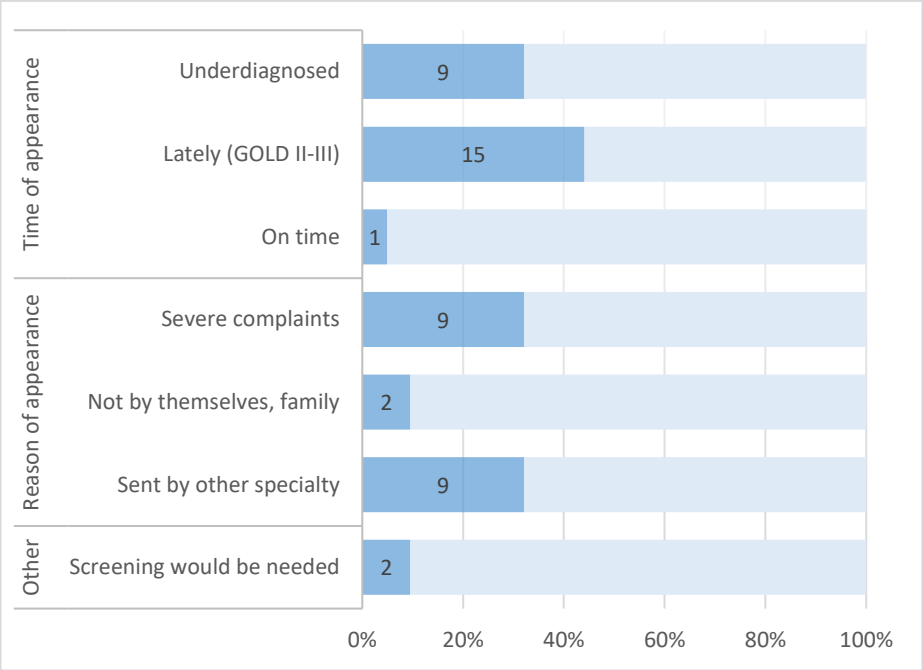

Figure 11: The extent of diagnosedness of COPD and its circumstances (axis y: time and reason of appearance in the pulmonology outpatient center, axis x: numbers of answers and percentage)

Pulmonary therapists consider awareness raising important, as there are many undiagnosed patients. Patients appear for consultation at a later stage, and only serious complaints call their attention to the presence of the disease (see *Figure 11*). Often, the patient comes from a co-order, that is, COPD is found to be comorbid (*Figure 11*). Opinions include the words "complaint", "respiratory infection", "FEV_1 <50%" and "family member bothered (by fatigue / cough)". Thus, it is the symptom that primarily disturbs the patient or a family member and directs them toward diagnosis. "Hard to guide", "needs multiple follow-ups", has the "worst" adherence – these are the most commonly noted expressions. Unlike cardiovascular and psychiatric diseases (163), COPD patients have low level of disease knowledge. It contributes to bagatellizing their disease, and leads to low motivation to stop smoking or to take the recommended therapy seriously.

Disease acceptance is inadequate: lung diseases are seen as a kind of temporary "infection". Most of the patient also have financial problems, so the therapy focuses on the cheapest component, which is reliever medication. There was only one positive opinion: which related to the positive effects of patient depression popping up at the

time of the diagnosis on adherence, but when he was satisfied with the drug at the second encounter, he was more receptive to the therapy. These initially hesitant patients usually do not consider their inhaler as a medicine, but refer to it as a "curative pipe".

4.1.1.3. Adherence and its improvement

The perception of adherence in COPD is worse than average: patients are considered to have low or medium low adherence. Symptomatic patients are more adherent, but this effect is temporary: they take the drug only while they are feeling ill (*Figure 12*).

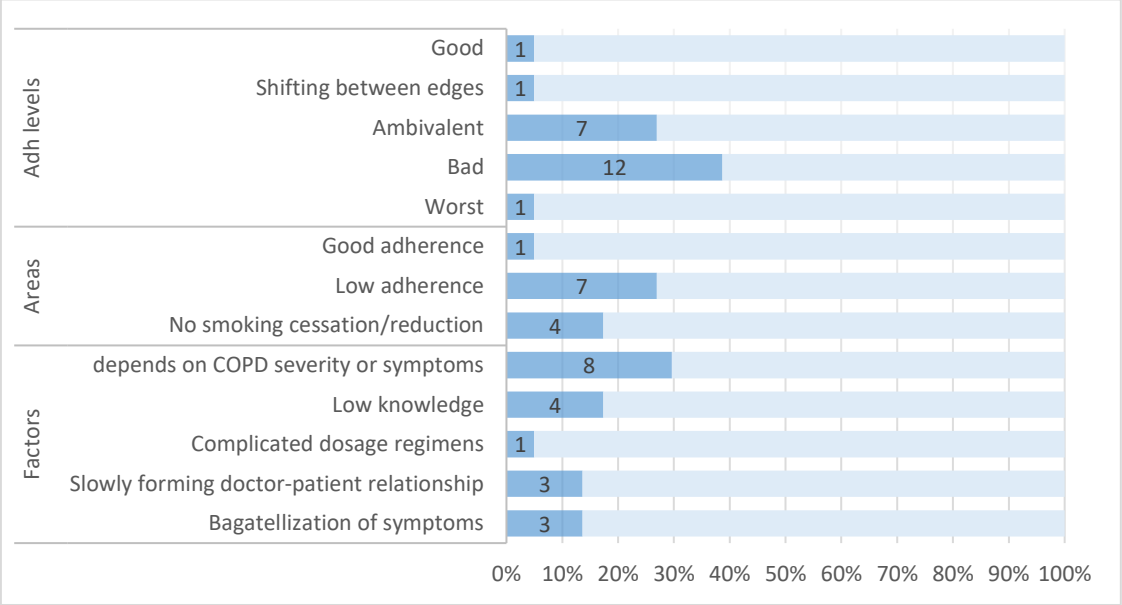

Figure 12: Adherence levels of patients, characteristics of each group and factors affecting adherence, according to pulmonologist expert opinion (numbers and percentages of answers on axis x)

Subjects interviewed repeatedly returned to disease perception, emphasizing that the asymptomatic patient “does not take their disease seriously”, the symptomatic “wants some medication”, but they do not feel the connection between smoking and COPD. Patients tend to say that they prefer to take the medicine, but refuse to quit smoking. Often the environment and air pollution are cited as the cause of the disease. The doctors interviewed said, “it is very difficult to start therapy”, “it is easier for patients with severe conditions.”

One view is that it is worth classifying COPD patients according to adherence: there are those with minimal adherence (about 60%), with whom no or very limited results can be achieved. “Good” adherence is approx. 30-40% (up to 6 total medication purchases

per year). There is a very narrow group of people who belong to the “perfect” adherence group (over 10 medication purchases per year, 10%). Another view is that adherence to COPD is around 20% and highlights the role of patient education programs that promote adherence to the inhaler and its proper use.

With respect to generic formulations and devices, we have assessed the openness of pulmonary physicians to permit the replacement the prescription (with the same active ingredient) with a cheaper drug at the pharmacy. Opinions are in consensus: the choice of the active ingredient and the route of administration should be kept entirely within the competences of the physician, and there is no particular need for a pharmacy inhaler substitution. Two interviewees have taken a different view: at the patient’s request, they consider switching to another brand if the price is less than two thousand forints. Thus, this amount may be a psychological limit that the patient is willing to spend on their COPD medication. Another opinion is that pharmacists should have the opportunity to do the generic substitution, once the new inhaler technique is taught to the patient. In this case, monthly monitoring of patients is needed, and pulmonary therapy should be implemented in the pharmacist-GP-pulmonologist triangle (164). *Figure 13* provides a deeper insight into factors affecting patient adherence.

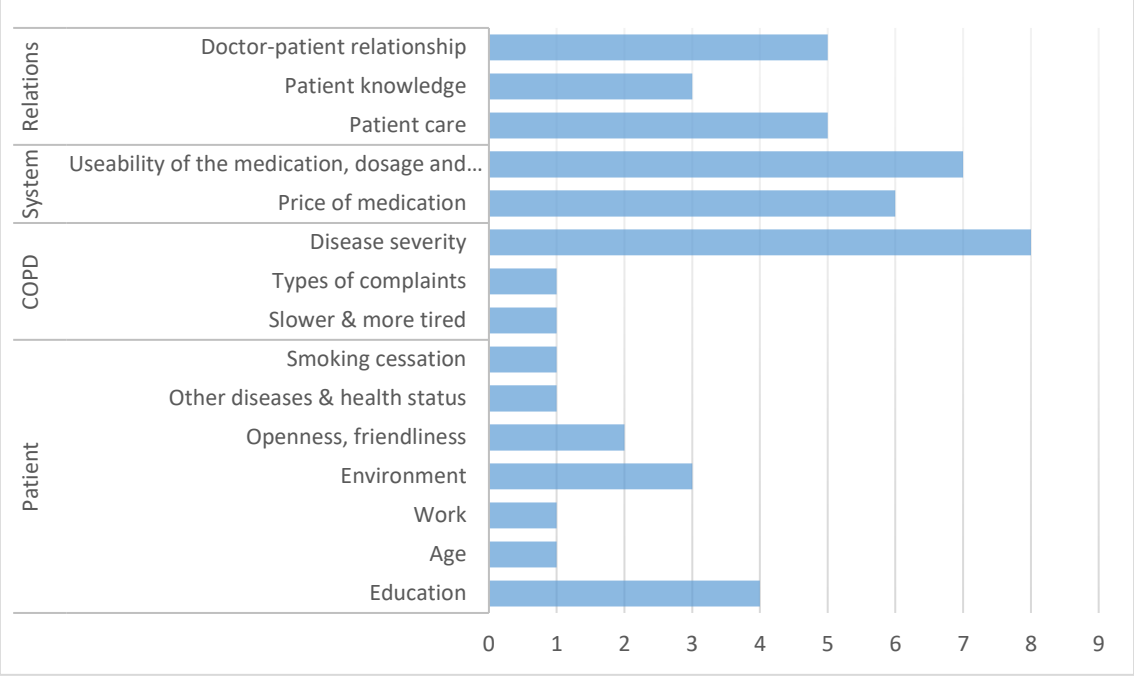

Figure 13: Doctor-patient relationship, features of the system and the disease and patient characteristics to determine adherence (number of answers on axis x)

Leading factors affecting adherence are the severity of the disease, the “usability” of the inhaler, its cost, disease severity and the physician-patient relationship (communication). Two of these are non-variable parameters of the patient (education is unalterable, albeit its projection of disease consciousness is alterable; COPD status is given, whilst symptom and exacerbation control can be improved), while patient contact and communication, and perceptions related to the “usability” of the drug are important inputs to the patient education content (*Figure 13*). Among the factors influencing adherence the price of medication and the financial situation of the patient appear; however, interviewees less frequently reported this. Interestingly, only one case is reported, where the type of the inhaler comes on the first place among the leading factors of adherence.

Understanding the relationship between COPD and smoking also plays an important role in the development of disease awareness (35). In education, we have to expect that patients are expected to be coming from a lower social scale, less educated, and the majority will be men. Symptoms, exacerbation, and family disturbance factor will be the cause of the application for pulmonology care. Screening programs will play an important role in following up previous smokers or getting new patients to be more interested in self-management of the disease (57).

4.1.1.4. Aspects of the education content

Interviews describe the following points that I have observed to develop the education content.

(1) Fostering smoking cessation is a priority and should be a priority in the program (165; 57);
(2) Personal education (lung care, hospital or rehabilitation center) is preferred to education on the phone (166);
(3) Content can be repetitive; should include a definition of the disease, symptoms, and information on the use of the drug (167);
(4) It is necessary that the patient be familiar with the language of the education, so we have to use simple and easy-to-remember words (168);

(5) Elements should be like a “fairy-tale”, like a short story to keep the patient focused and to let them fully internalize content.

(6) Pulmonary interviews mention the following content, in order of appearance frequency: symptoms & causes, development of the disease, understanding therapy, inhaler use, assessment of status, especially exacerbation, rehabilitation (the latter includes gymnastics, swimming and relaxation in the form of a one-week course).

(7) Relationship with patients and communication paradigms play an important role in the success of the program (169), so we need to gain the patient’s commitment from the beginning. During development, this issue is worth consideration from both sides: besides patient education, it may be worthwhile to initiate a training course where we improve the communication of the doctor and thus improve patient acceptance for the disease. One interview particularly emphasizes that quality time with the patient is important and equal treatment (“partnership”) is needed with the patient (169).

(8) Patience empowerment and lifestyle have been reported to be included in the education – besides patient support emphasizing that the disease did not develop shortly, so results can be expected if the therapy is applied chronically. Improving patient attitudes is also important for long-term effects (170). This aspect was highlighted in all interviews, but along different lines: smoking cessation, breathing exercises, control and medication replacement, and exercise and weight management.

(9) Two interviews switch back to medical communication: the doctor should send positive feedback, and “celebrate the patient.” If patients accept their illness and believe that the inhaler can help, this is the first step on the road to healing (171).

(10) Participation in rehabilitation and the day-to-day implementation of results are key to its long-term success (172).

(11) The inhaler is expected to be easy and quick to learn. It seems important to introduce the use of the inhaler in small steps, but both patients and physicians are open to new solutions when they see the benefits of the technique (173). Powder inhalers require the best possible inspiratory force, and many find this

method easier to accomplish (168). Patients also like to see the effect visually. With regard to sprays, lung doctors have noted coordination as a concern, where adherence is currently considered the lowest.

(12) It has also been mentioned that once-daily active agents, although easier to administer, if the daily dose is missed, the whole dose is omitted, whereas twice-daily agents offer the secure feeling for patients who want to take drugs twice a day, and even if one of the doses is missed, the other one can exert the effect. Adherence is higher for inexpensive formulations, particularly short-acting β-agonists, muscarinic antagonists, and their combination formulations. In this case, it is supported by their fast onset of action, too.

4.1.2. Patients

The community pharmacy setting is a challenging venue for patient education. Originally, we intended to incorporate a comparative aspect to a longitudinal study which assesses the impact of education on quality of life and adherence; however, pharmacy patients turned out to be more willing to be educated in a one-time occasion than in a follow-up intervention. Consequently, the community pharmacy pillar to this study was halted, whilst the interviews provided patient insight to the education content we developed for the further course of the aforementioned study. The patients' desire to get pharmacist advice fast (174), seems to also appear in a German setting, which verifies the need for pharmacy disease management projects (patients who attended such sessions were enabled to use their inhaler significantly better, although this means 29% overall) (175). This idea has been further developed in Japan, where pharmacist-led clinics were proven to improve quality of life (176).

4.1.2.1. Self-perception and patient related quality of life

Patients did not mention the textbook like symptoms (sputum secretion, dyspnea and coughing) on the first instance; however, they always relate to real-life actions they would like to perform: to play tennis, to play with the grandchildren and to paint. Falsely, they identify their illness as asthma, and they see no relation to smoking (but one patient). They get used to the symptoms, and they mostly perceive them as "they come by age", "they are natural"; thus, they accept their conditions. *These activities*

should be used when developing the patient profile for the education content; additionally, we should use the patients' own words to help them memorize its content. Figure 14 summarizes the implications for the education content.

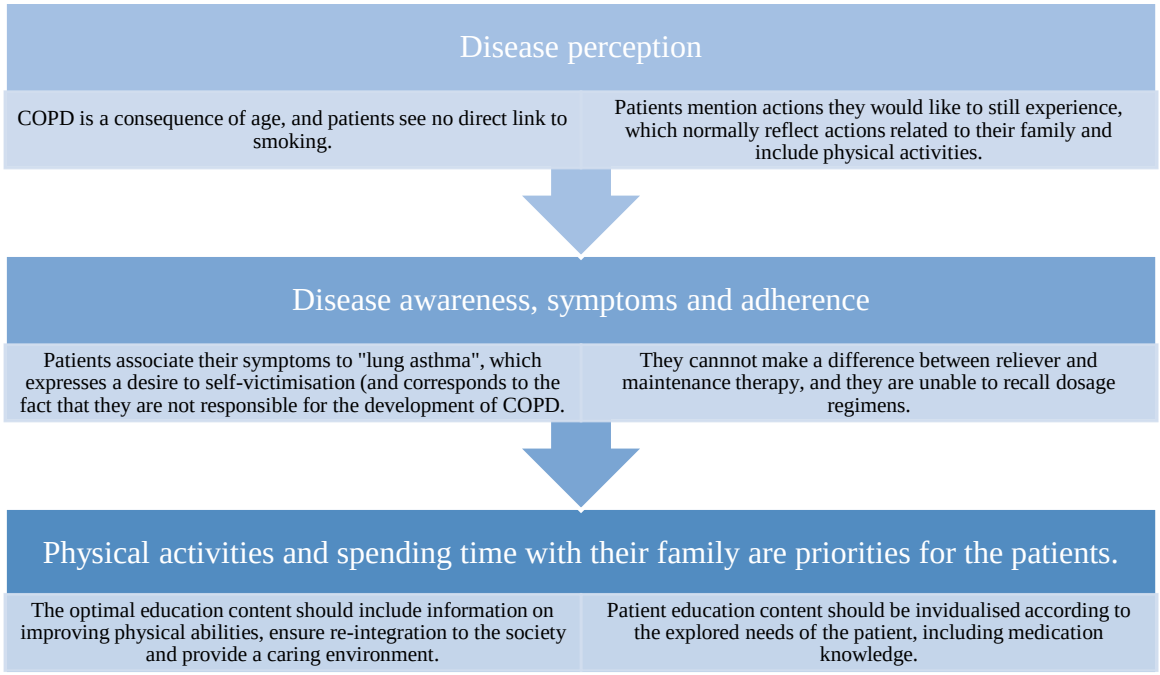

Figure 14: Major patient perceptions & attitudes and their implications for the development of education content

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4.1.2.2. Medication use and symptoms

None of the patients was able to identify the reliever drug; even the most asymptomatic patient used it every morning, in an inadequate dose. Once-daily inhalers were preferred, since one occasion is the frequency everyone declared as adequate for the treatment of the disease. One patient reported a willingness to apply alternative methods, namely she was interested in herbal drinks as a possible treatment option. The patients were unaware of the inhalation therapy they used; hence, there was no apparent fear of steroids. Based on their CAT scores, all patients were symptomatic, which implies that they are either not compliant, or do not have the right medication. *This implies that the patient education program should focus on basis elements of medication (reliever and maintenance therapy), dosage regimens – and the impact could be evaluated by repeated CAT assessment.*

4.1.2.3. Patient attitudes and adherence

The interviews reveal a truly diverse image of COPD attitudes. The main symptoms are feeling powerless and the lack of physical performance. Two patients mentioned repeatedly their disability in moving and taking the stairs, and one patient was completely confined to oxygen therapy. *An important implication of these is that the education program should reinforce physical activities, tailor-made to the current condition of the patient; furthermore, breathing techniques should be incorporated to avoid the abrupt appearance of breathlessness.*

The lack of adherence is a variant, which was challenging to get the patient talk about. Finally, they all confessed that they do not either take their medication in the prescribed manner, or make changes to treatment regimens upon self-judgement. The better they feel, the less they take the medication. *The implication of this is that we should make sure that patients understand that COPD is a chronic condition, and medications should be taken; also in case, they feel right. Interestingly, SMART dosage is available in the case of certain drugs, so this is another aspect that should be included in the education content (please consult Figure 15 for more adherence insight).*

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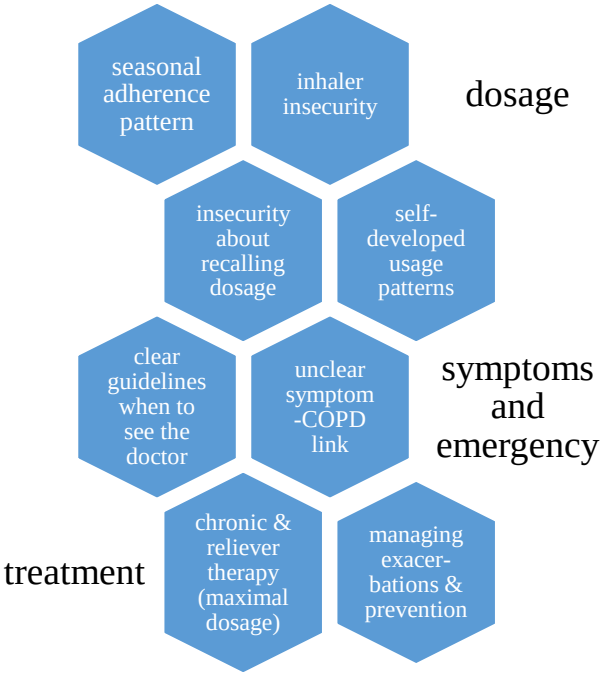

Figure 15: Mapping patient insight to adherence patterns

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4.2. Impact of education on quality of life and adherence

4.1.3. Subject characteristics

We enrolled a total of 118 subjects in our study. The study cohort had a predominance of women (n = 70, 59.3%) and an average [± standard deviation (SD)] age of 67.3 (± 9.4) years (*Table 9*). A total of 39.8% (n = 47) of our subjects were current smokers. A substantial majority of the cohort were urban residents (n = 88, 74.6%) with university or high school education (n = 96; 81.4%), and good or above average social status (n = 103; 87.3%). The self-reported responses of >90.0% of the subjects to questions on adherence, the quality of received education, regular check-ups, and trust in their pulmonologist were positive. At the follow-up visit, subject adherence to treatment was self-reported to be good (n = 49, 41.5%) or moderate (n = 51, 43.2%).

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Table 9. Sociodemographic characteristics of and self-reported perceptions of outcomes in study patients.

		n (%)
Gender	Male	48 (40.68)
	Female	70 (59.32)
Age in years, mean (SD)	Male	68.83 (8.39)
	Female	66.16 (9.91)
	Total	67.25 (9.38)
Smoking status	Yes	47 (39.83)
Daily cigarette consumption, mean (SD)		11.15 (5.94)
Residential location	Urban	88 (74.58)
	Semi-urban	20 (16.95)
	Rural	10 (8.47)
Education	University	28 (23.73)
	High School	68 (57.63)
	Basic	22 (18.64)
Social status	Good	4 (3.39)
	Above average	99 (83.90)
	Below average	14 (11.86)
	Poor	1 (0.85)
Adherence to COPD medication vs. other medication	Same or better	113 (95.76)
	Worse	5 (4.24)
Quality of received education	Comfortable	113 (95.76)
	Less or more comfortable	5 (4.24)
Importance of COPD check-ups vs. other check-ups	Same or more	117 (99.15)
	Less	1 (0.85)
Trust in pulmonologist vs. general practitioner	Better	109 (92.37)
	Worse	9 (7.63)

Abbreviations: SD–standard deviation; COPD–chronic obstructive pulmonary disease

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4.1.4. Assessment questionnaire performance scores

Table 10 shows the comparison between baseline and follow-up scores for CAT, MMAS-8, EQ5D and SGRQ scales using the paired samples *t*-test. We noticed an overall increase in adherence with mean (± SD) MMAS-8 total scores increasing from 6.72 (± 1.46) at baseline to 7.01 (± 1.15) at follow-up (t = -2.073; P = .040). With respect to severity of COPD symptoms the improvement in CAT scores proved to be non-significant (t = -0.441; P = .660). There was no significant difference in the QoL (EQ5D; t = -0.784; P = .435) and general symptoms (SGRQ; t = -0.063; P = .950) scores between baseline and follow-up. Mean scores and comparisons of subscales are also shown in *Table 10*.

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Table 10. Comparison of baseline and follow-up scores on self-reporting of COPD symptom, QoL, and treatment adherence.

	Score, mean (SD)		*t*(df=117)	*P*
	Baseline	Follow-up		
CAT_Total	16.65 (7.61)	16.9 (7.93)	-0.441	0.660
CAT1	2.45 (1.22)	2.44 (1.13)	0.101	0.920
CAT2	**2.21 (1.38)**	**2.04 (1.30)**	**1.860**	**0.065**$^{+}$
CAT3	1.35 (1.26)	1.41 (1.39)	-0.531	0.597
CAT4	3.17 (1.50)	3.08 (1.48)	0.716	0.475
CAT5	1.90 (1.49)	2.05 (1.58)	-1.233	0.220
CAT6	1.25 (1.51)	1.41 (1.66)	-1.149	0.253
CAT7	1.92 (1.35)	1.86 (1.44)	0.377	0.707
CAT8	**2.41 (1.26)**	**2.6 (1.13)**	**-1.714**	**0.089**$^{+}$
MMAS-8_Total	**6.72 (1.46)**	**7.01 (1.15)**	**-2.073**	**0.040***
MMAS-8_1	0.73 (0.45)	0.75 (0.43)	-0.598	0.551
MMAS-8_2	**0.84 (0.37)**	**0.91 (0.29)**	**-1.806**	**0.074**$^{+}$
MMAS-8_3	0.85 (0.36)	0.89 (0.31)	-1.295	0.198
MMAS-8_4	**0.81 (0.40)**	**0.89 (0.31)**	**-2.404**	**0.018***
MMAS-8_5	0.20 (0.40)	0.19 (0.41)	0.323	0.747
MMAS-8_6	0.92 (0.28)	0.92 (0.28)	0.000	1.000
MMAS-8_7	**0.86 (0.35)**	**0.92 (0.27)**	**-1.907**	**0.059**$^{+}$
MMAS-8_8	0.74 (0.12)	0.72 (0.14)	1.274	0.205
EQ5D_VAS	67.41 (16.91)	68.62 (17.42)	-0.784	0.435
EQ5D1	2.08 (1.03)	2.19 (1.04)	-1.416	0.159
EQ5D2	1.27 (0.62)	1.29 (0.67)	-0.342	0.733
EQ5D3	1.72 (0.84)	1.83 (0.95)	-1.470	0.144
EQ5D4	1.87 (0.79)	1.89 (0.87)	-0.232	0.817
EQ5D5	1.54 (0.75)	1.57 (0.84)	-0.403	0.688
SGRQ_Total	37.86 (15.83)	37.79 (17.67)	0.063	0.950
SGRQ_symp	38.66 (23.85)	37.17 (25.71)	0.825	0.411
SGRQ_act	52.58 (18.41)	52.34 (18.89)	0.149	0.882
SGRQ_imp	29.22 (16.26)	29.68 (18.94)	-0.332	0.740

$^{+}$p<0.1; *p<0.05

Abbreviations: COPD–chronic obstructive pulmonary disease; QoL–quality-of-life; CAT–COPD Assessment Tool; MMAS-8–Morisky Medication Adherence Scale-8; EQ5D–EuroQoL-5D-5L; SGRQ–St. George Respiratory Questionnaire; symp–symptoms component; act–activity component; imp–impact component.

Highlighted rows indicate covariables that either demonstrate a statistically significant association or a trend towards it.

4.1.5. Effect of gender, occupation, and education on performance scores

We also evaluated our data to identify the effects of gender, occupation, and education as inter-subject variables on the change in assessment scores. Due to smaller sizes of subgroups, we investigated only the main effects while controlling for other independent variables as covariates.

Table 11: Comparison of results for scales (t- and F-values given) for adherence, COPD symptoms, and QoL by time, gender, occupation, and education with mixed measures (ANOVA and ANCOVA).

Effect	*t*	*F*	df		*P*
			Hypothesis	Error	
Adherence					
TIME(2) ∞ MMAS(8) ∞ GENDER(2)	0.103	1.630	7	99	0.136
TIME(2) ∞ MMAS(8) ∞ OCCUPATION(2)	0.043	0.632	7	99	0.728
TIME(2) ∞ MMAS(8) ∞ EDUCATION(3)	**0.284**	**2.364**	**14**	**200**	**0.005***
MMAS_Total(2) ∞ GENDER(2)	0.017	2.013	1	114	0.103
MMAS_Total(2) ∞ OCCUPATION(2)	0.001	0.074	1	114	0.787
MMAS_Total(2) ∞ EDUCATION(3)	0.019	1.066	2	113	0.348
COPD symptoms					
TIME(2) ∞ CAT(8) ∞ GENDER(2)	**0.182**	**3.138**	**7**	**99**	**0.005***
TIME(2) ∞ CAT(8) ∞ OCCUPATION(2)	0.074	1.135	7	99	0.348
TIME(2) ∞ CAT(8) ∞ EDUCATION(3)	0.189	1.492	14	200	0.117
CAT_Total(2) ∞ GENDER(2)	0.002	0.245	1	114	0.622
CAT_Total(2) ∞ OCCUPATION(2)	0.004	0.372	1	114	0.543
CAT_Total(2) ∞ EDUCATION(3)	0.034	1.821	2	113	0.167
Quality of life					
TIME(2) ∞ EQ5D(5) ∞ GENDER(2)	0.024	0.616	4	101	0.652
TIME(2) ∞ EQ5D(5) ∞ OCCUPATION(2)	0.018	0.461	4	101	0.764
TIME(2) ∞ EQ5D(5) ∞ EDUCATION(3)	0.062	0.817	8	204	0.589
EQ5D_Total(2) ∞ GENDER(2)	0.002	0.240	1	114	0.625
EQ5D_Total(2) ∞ OCCUPATION(2)	0.003	0.306	1	114	0.581
EQ5D_Total(2) ∞ EDUCATION(3)	0.002	0.121	2	113	0.886

*p<0.05

Abbreviations: COPD–chronic obstructive pulmonary disease; QoL–quality-of-life; ANOVA–analysis of variance; ANCOVA–analysis of covariance; MMAS–Morisky Medication Adherence Scale-8; CAT–COPD Assessment Tool; EQ5D–EuroQoL-5D-5L.

Numbers in brackets indicate the number of the given variable. Time: 1–Baseline, 2–Follow-up; Gender: 1–Male, 2–Female; Education: 1–Basic, 2–High School, 3–University; MMAS/CAT/EQ5D_Total: total scores of scales at 1–Baseline, 2–Follow-up; Occupation: 1–active working status, 2–pensioner; MMAS/CAT/EQ5D (X)–where 'X' is the number of questions in the specific questionnaire

Overall, we could not discern any significant association between gender and occupation on the change in total scores (*Table 11*). Besides examining total scores, we

looked at the pattern of individual questions of the questionnaires, and we identified a significant difference in two cases. Thus, we discovered that there is a difference between subjects based on their education level on the pattern of MMAS-8 scores by time [TIME(2) ∞ MMAS(8) ∞ EDUCATION(3)] (F = 2.364; P = .005)., *Post hoc t*-tests showed a significant improvement in MMAS-8 scores in patients with basic education for questions M4 [t = -2.485; P = .021] and M8 [t = -1.766; P = .046]. Differences in pattern of adherence (MMAS-8) by education and time are shown in *Figure 16A.*

We also observed a statistically significant difference between genders in CAT score patterns [TIME(2) ∞ CAT(8) ∞ GENDER(2)] (F = 3.138, P = .005) (*Table 11***)**. There was no significant difference in scores for any item on the CAT questionnaire in female subjects. In contrast, on *post hoc* analysis we noticed that in male patients, CAT6 (difficulties in leaving home) scores had increased significantly by the time of follow-up [t = -1.543; P =.049] (*Figure 16B*). On comparing the two groups (male vs. female) by independent sample *t*-test, the significant difference in CAT6 scores in between the genders was found to be only at baseline. This implies that male patients found their symptoms preventing them from leaving their home much less disturbing than female patients (t = -2.267; P = .025) at baseline, but by the time of follow-up this difference was not detectable (t = -0.159; P = .312). Differences in pattern of COPD symptomatology (CAT) by gender and time are shown in *Figure 16B.*

To measure the relationship between the changes in the different assessment algorithms we used, we created one variable per scale using the ratio of baseline to follow-up scores. In most cases, we found the interaction between the changes to be negligible or not statistically significant (*Table 11*). However, there was a weak interaction between the changes in CAT and the SRGQ scores.

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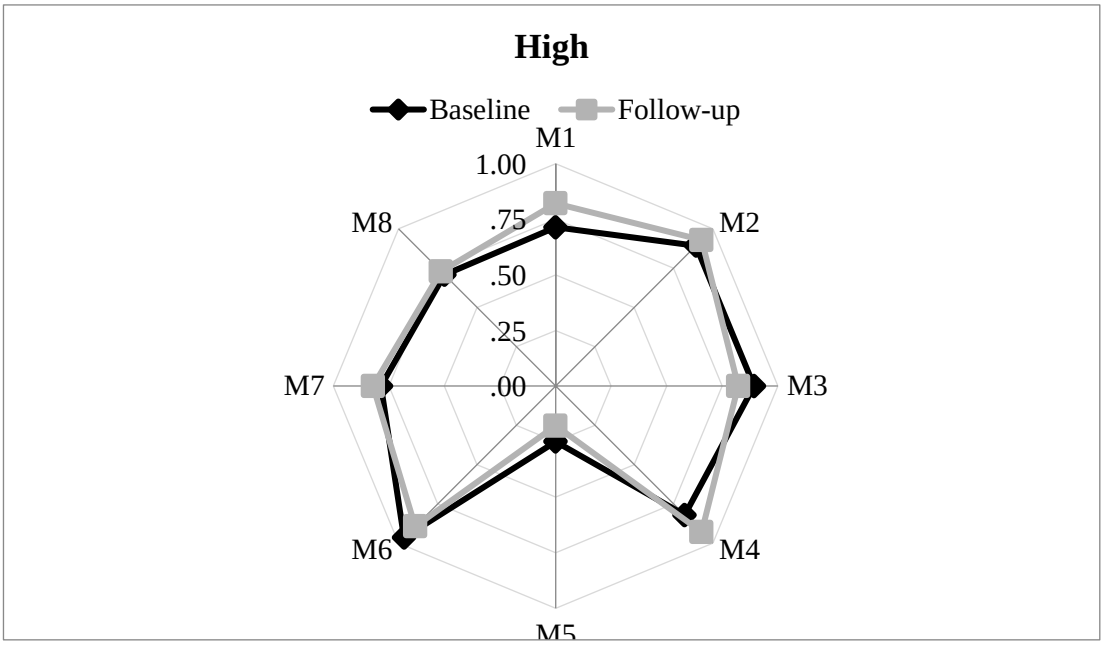
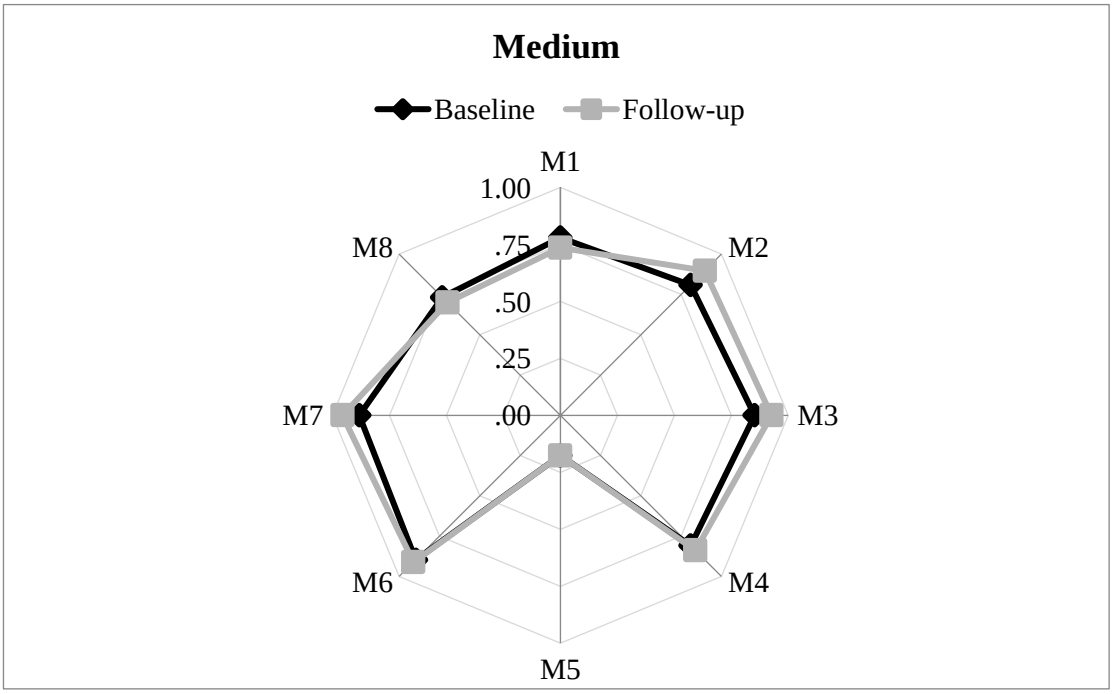
Figure 17: Difference in pattern of adherence (A) and COPD symptomatology (B) at baseline and follow-up.

(A) Differences in pattern of adherence (MMAS-8) by education and time ("basic" refers to elementary education, "medium" to high school, and "high" to university graduates)





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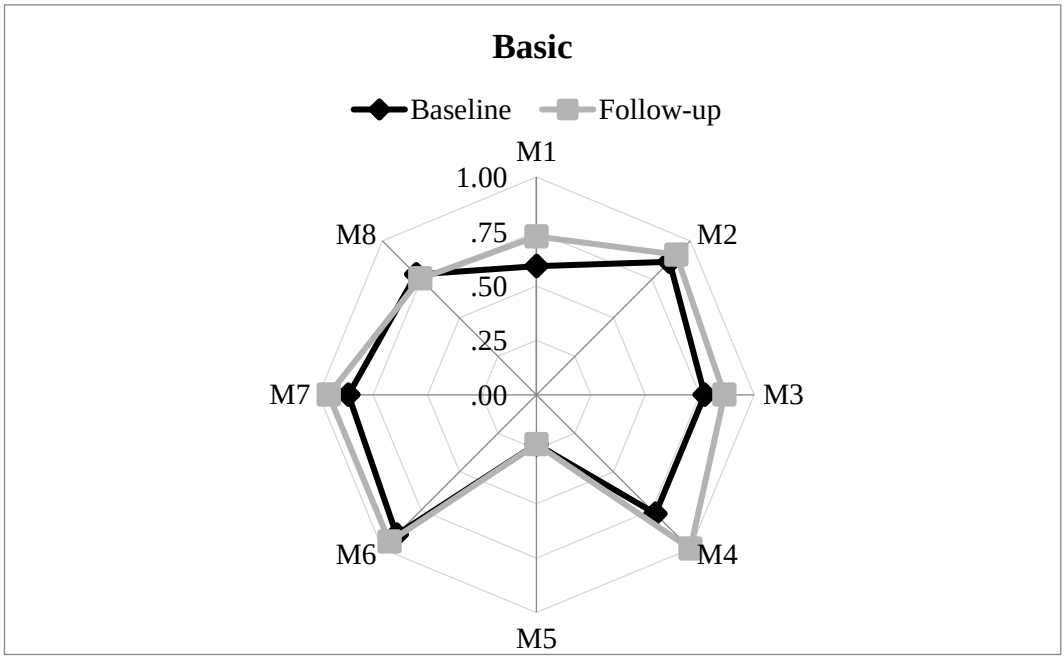

(B) Differences in pattern of symptomatology (CAT) by gender and time with mixed measures (ANOVA)

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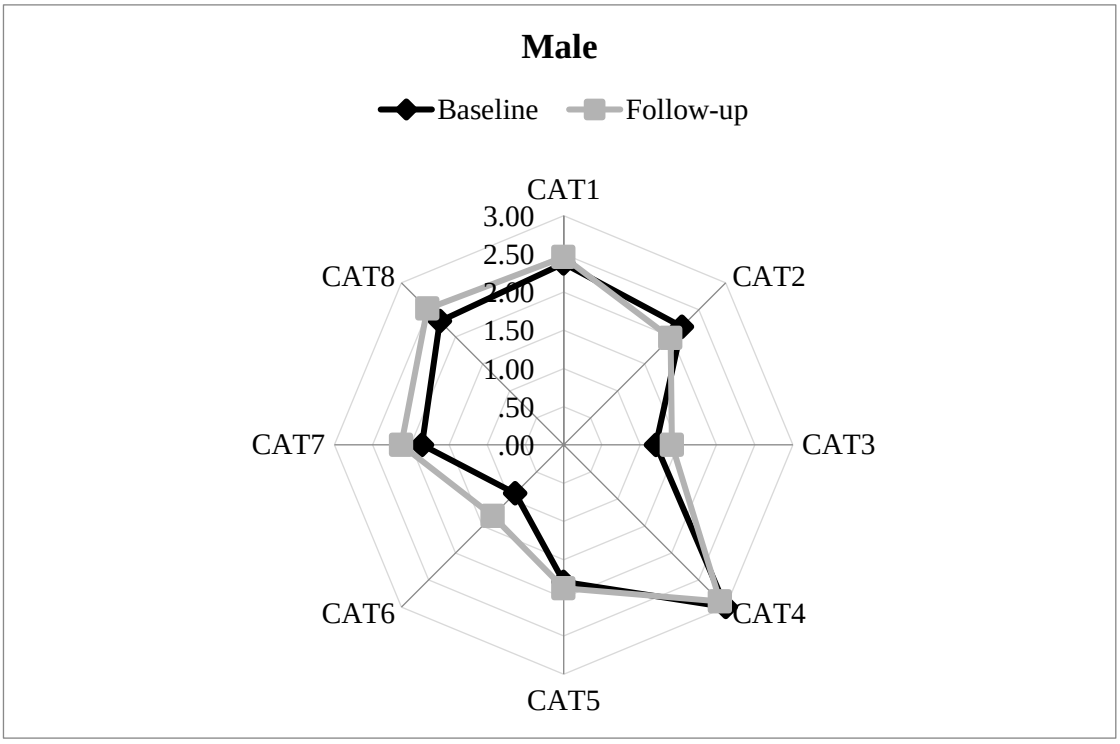

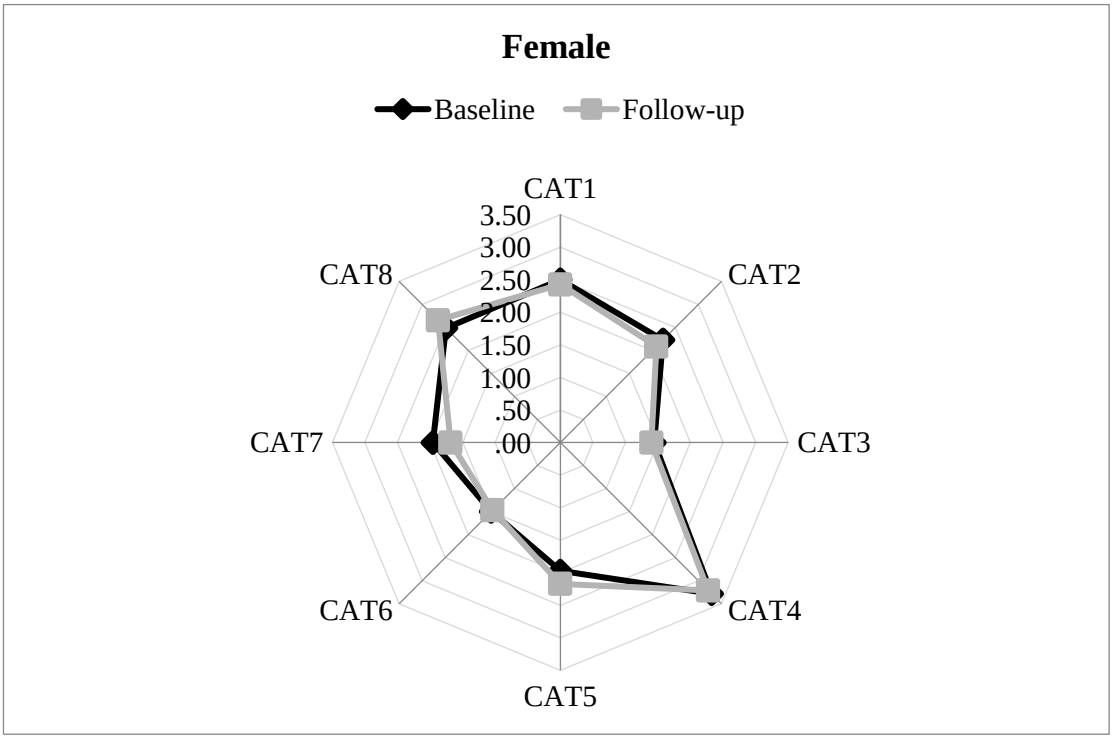

Abbreviations: COPD–chronic obstructive pulmonary disease; MMAS-8–Morisky Medication Adherence Scale-8; CAT–COPD Assessment Tool; ANOVA–analysis of variance

4.2. Learnings from the *pilot* studies

In each setting, we started an exploratory study with the participation in 6-8 patients. The objective of these studies was to get a *proof of concept* how to go big with the project. Finally, I did not manage to scale up the community pharmacy pillar of the investigation; the outpatient setting seemed more feasible to reach the desired number of patients.

The scope of these studies were the following:

(1) what kind of education they would welcome? when and how long are they willing to participate?
(2) what content they would benefit from?
(3) what is needed so they collaborate for the initial study, as well as during follow-up?

For the pharmacy setting, I considered the patient interviews the *pilot* studies, and finally made the decision that due to reduced availability of the patients, I will suspend recruitment in this setting. Community pharmacy patients appeared to have more inclination towards short interactions and interviews, but they seemed reluctant to take part in educational sessions in their free time, especially if they had to come back to the pharmacy for the sessions.

For the outpatient setting, this was performed in district 19 of Budapest. It turned out to be a clear benefit for the patients to implement this project while they were waiting for the pulmonologist. These exploratory sessions revealed that patients are willing to spend 20-25 min on questionnaire administration, and more or less, they can concentrate for the same amount of time to the education content. Personal meetings were always preferred, and the above benefit should be used to ensure their participation. Patients were willing to participate voluntarily, and they welcomed more information about their disease, so they considered this as necessary benefit to compensate their efforts.

4.3. Background of adherence in a wider context

The literature search resulted in 188 hits, and five additional records were identified through hand search of the references of relevant articles. The screening of the titles and abstracts identified 17 potentially eligible studies. After the review of the relevant full texts, ten studies were finally included in the systematic review. The flow diagram of the systematic literature review process is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) template (89).

Three studies were randomized controlled trials (RCTs) (177; 178; 179) three were prospective cohort studies (180; 181; 182), and four retrospective studies (183; 184; 185; 186) were also included. The population size varied between 28 and 832 subjects (185; 186), with a mean age of 9.1 to 28.7 years (177; 185). Seven studies focused on measuring adherence to inhaled tobramycin (178; 179; 180; 181; 183; 184; 186), one on inhaled colistimethate (185), one on inhaled levofloxacin (177), and one on inhaled aztreonam lysine (182). The general characteristics of the reviewed studies are summarized in *Table 12*.

Medication adherence to inhaled ABs was analyzed by pharmacy refill history (30%) (183; 184; 186), daily phone diary 10%) (181), parent and/or child self-reports (20%) (180; 181), vials counting (30%) (177; 178; 182), or electronic monitoring (10%) (185).

(179) did not describe the method for measuring adherence, while (181; 182) did not report how adherence was defined in their studies. Six studies (177; 179; 178; 180) determined adherence as categorical variable only, four studies (181; 182; 184; 185) as continuous only, and one study as both (179). Measurement methods, results, and predictors/consequences of adherence to inhaled ABs are presented in *Table 12*.

Except for the studies conducted by (184; 181) most studies assessed adherence to inhaled ABs only and did not evaluate adherence to other medications simultaneously (*Table 13*).

The included studies fulfilled the STROBE criteria between 52% (185) and 73% (179; 186). The majority of the studies described their scope, study design, settings, participants, variables, measurements, and main results adequately. All but one (185)

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of the reviewed studies described their statistical methods in detail; however, none of them undertook a sensitivity analysis to examine the robustness of the results. Furthermore, no study provided information on missing data and how they dealt with the same.

Table 12: Summarized adherence data from randomized control trials and real world studies (taken from the Bodnár (2016) article, co-authored by Mate Olah)

Study characteristics	Randomized controlled trials			Real-world studies	
				Prospective cohort studies	
	Geller et al[20]	Ramsey et al[22]	Regnault et al[21]	Harrison et al[23]	Modi et al[24]
Study length	28 days[a]	24 weeks	24 weeks	12 months	3 months
No of subjects, total (on inhaled ABs)	151 (114)	520 (258)	454 (454)	78 (TIP: 51, TIS: 78)	37 (10)
Age, years	28.7 (9.0)[b]	• Tobramycin group: 20.8 (9.5)[b] • Placebo group: 20.6 (10.0)[b]	25.6 (10.8)[b]	26.3 (16–56)[c]	10.1 (2.5)[b]
Male, %	56.3	• Tobramycin group: 58 • Placebo group: 50	56.2	59	51
FEV_1, % predicted	52.3 (15.3)[b]	• Tobramycin group: 49.9 (15.5)[b] • Placebo group: 51.2 (16.8)[b]	52.8 (14.5)[b]	63.5[f]	79.6 (20.8)[b]
Inhaled ABs	Inhaled levofloxacin	Inhaled tobramycin	TIP, TIS	TIP, TIS	Inhaled tobramycin
Adherence					
Measurement	Vials counting	Vials counting	NR	Self-report adherence	Parent/child self-report, daily phone diary
Variable type	Categorical	Categorical	Continuous, categorical	Categorical	Continuous
Definition	Adherent patients: ≥80% of the required doses taken	Adherent patients: ≥75% of the ampoule dispensed	• Adherence: % of doses taken • Adherent patients: ≥80% of the required doses taken	• Excellent: >80% adherence • Moderate: 50%–80% adherence • Poor: <50% adherence	NR
Results, %/mean (SD) %[h]	% of adherent subjects: 92.3%–97.3%	% of adherent subjects: 88%	• Adherence: ▪ Cycle 1: 96.5 (10)%[b,e] ▪ Cycle 2: 93.9 (15)%[b,e] ▪ Cycle 3: 93.6 (14.5)%[b,e] • % of adherent subjects: ▪ Cycle 1: 93.4%[e] ▪ Cycle 2: 88.1%[e] ▪ Cycle 3: 86.4%[e]	• TIS at baseline: ▪ Excellent: 44.9% ▪ Moderate: 30.6% ▪ Poor: 24.5% • TIP at 12-month: ▪ Excellent: 77.5% ▪ Moderate: 17.5% ▪ Poor: 5.0%	• Parent self-report: 85.0 (33.7)%[b] • Child self-report: 83.3 (25.8)%[b] • Diary: 36.1 (35.6)%[b]
Predictors/ consequences	NR	NR	Higher patient satisfaction and lower perceived impact of side effects were found to be statistically significantly associated with better adherence	Adherence increased after transition from TIS to TIP	NR

Notes: [a]Treatment period; [b]mean (SD); [c]median (range); [d]mean (range); [e]mean; [f]median; [g]one cycle: 28 days on therapy followed by 28 days off therapy; [h]only adherence results for inhaled ABs are presented; [i]adherence rate was presented graphically only; [j]difference was not assessed with statistical methods.
Abbreviations: ABs, antibiotics; FEV_1, forced expiratory volume in 1 second; BID, two times daily; CF, cystic fibrosis; CFQ-R, cystic fibrosis questionnaire-revised; TID, three times daily; NR, not reported; MPR, medication possession ratio; SD, standard deviation; TIP, tobramycin inhalation powder; TIS, tobramycin inhalation solution.

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Table 13: Overview of retrospective trials
(taken from the Bodnár (2016) article, co-authored by Mate Olah)

	Retrospective studies			
Oermann et al[25]	**Briesacher et al[26]**	**Eakin et al[27]**	**McNamara et al[28]**	**Wertz et al[29]**
18 months	12 months	12 months	12 months	12 months
274 (BID: 89, TID: 189)	804 (804)	95 (65)	28 (28)	832 (388)
28.5 (12.5)[b]	<6: 13.2% 6–10: 12.2% 11–17: 31.5% 18–25: 22.0% ≥26: 21.1%	20.9 (11.9)[b]	9.1 (3–15)[d]	TIS user group: 19* Nonuser group: 30*
55.1	52.7	48.9	57	TIS user group: 52* Nonuser group: 46*
55.6 (11.6)[b]	NR	80.1 (24.8)[b]	75 (54–99)[c]	NR
Inhaled aztreonam lysine (BID, TID)	TIS	Inhaled tobramycin	Inhaled colistimethate	TIS
Vials counting	Pharmacy refill records	Pharmacy refill records	Electronic monitoring	Pharmacy refill records
Continuous NR	Categorical • High: ≥4 cycles per 12 months[e] • Medium: >2 to <4 cycles per 12 months[e] • Low: ≤2 cycles per 12 months[e]	Continuous MPR: defined as the sum of all days of medication supply received, divided by the number of days the medication was prescribed for chronic use during the study period	Continuous The number of treatments taken divided by numbers of prescribed treatments ×100%	Categorical • High: >4 fills per 12 months • Medium: 2–3 fills per 12 months • Low: 1 fill per 12 months
• BID: 92% • TID: 88%	• High: 7% • Medium: 22% • Low: 71%	MPR: 65%[i]	• Adherence at 6 months: 64 (35)%[b] • Overall monthly adherence at 12 months: 60%–70%	• High: 29.64% • Medium: 34.54% • Low: 35.82%
• Dosing regimen was not statistically significantly associated with adherence • CFQ-R scores were comparable between BID and TID groups	• High adherence was significantly associated with a decreased risk of hospitalization, but inpatient costs were similar between the three adherence groups • Outpatient costs were lower in high adherence group[j] • Drug costs were higher among high users[j]	• Adherence was not correlated with number of medications prescribed • No statistically significantly difference in age was found in adherence • Adherence to inhaled ABs was not associated with the occurrence of pulmonary exacerbation, and change in FEV_1% predicted slope	• Evening adherence (75%) was significantly better than morning adherence (58%) • Tendency for better overall adherence in children <12 years (71%) than in teenagers (50%)[j] • Changing the treatment regimens from twice daily to once daily improved adherence significantly (in the month pre- and post-change from 26% to 54%)	• CF-related medication use was generally greater for the high adherence group compared with the medium and low adherence groups ($P<0.0001$) • Increase in adherence was associated with decreased health care resource utilization, increased drug costs, and decreased inpatient costs ($P<0.05$)

5. Discussion

5.1. Attitudes and perception of pulmonologists and patients

High awareness levels are needed for the programme to be successful (172; 57), so we ensured this continuous contact by providing a leaflet that summarizes education content, and patients can recap on it whenever they wish.

By recognizing the information level they already had (90), we provided an opportunity to ask questions they were interested in. This was implemented only after the education sessions, in order to avoid that education sessions are not formalized and ubiquitous, which is the pre-requisite to make the sessions intercomparable.

In the long run, we have to trigger a change in the patient's life (44; 167), and that the patient is willing to intervene in his or her daily rhythm that is better enables disease management (167). Ideally, this is done in an integrated approach, meaning that the lung therapist is primarily involved in patient care, and secondly the GP and pharmacist are involved in the care (164). In our setting, we initiated this lifestyle changes by incorporating breathing techniques in the education sessions; and integrated care was investigated by the incorporation of the two key actors in COPD care in Hungary: the pulmonologist and the pharmacist.

In terms of adherence, our data are consistent consistent international literature, particularly in terms of combination therapy (values of inadequate adherence vary between 50-70% (169). The high standard deviation is also characteristic of the summary studies (1), and the similar study from Hungary (24) shows the number of COPDs with optimal adherence are at around 60%, this is a much more positive value than what is outlined in the interviews. Higher adherence can be expected under supervision and in clinical trials (1), so education is expected to positively influence on adherence (44; 172).

5.2.Impact of education on quality of life and adherence

In this first of its kind study to determine the effect of patient education on treatment adherence and QoL in subjects with COPD in Hungary, we noticed a clear association in between patient education and adherence at the time of follow up. In the parameters tested using the MMAS-8 scale, there were statistically significant changes in total score and for M4 and positive trends in M2, and M7 (*Table 10*). This implies that adherence improved in relation to:

(1) taking medication in the two weeks preceding the follow-up visit,
(2) remembering to take medications when travelling or leaving home, and
(3) being more comfortable with the treatments.

Furthermore, a substantial proportion of our subjects reported either good (41.5%) or moderate (43.2%) adherence by the end of the study.

It should be noted that this study captures the data related to slightly more women than men. Event though pulmonologists identified men among the basic characteristics of the COPD patient, our target population included ca. 10% more women than men. This implies that women might be more disease conscious, or may take follow-up visits more seriously (since every tenth patient was offered the opportunity to take part in this study, men and women should have been represented in the same proportion in line with the natural gender distribution).

In comparison with another study from our research group (187), baseline SGRQ quality of life status seems to be higher (scores are lower, but this indicates and inverse relationship with quality of life status). This implies that our subjects could have reported been in better health status; consequently, demonstrating an improvement on the already higher values might be less likely than in the case of starting from quality of life status. Altogether, our sample includes more women and subjects with lower SGRQ scores, which means that our results might be more focused on women with better disease specific life.

The assumption that patient education would result in improvement of patients' QoL has been well supported by numerous studies (19; 20; 26), including in a hospital setting (15). Although the change in our subjects' overall QoL scores at follow-up were not

statistically valid, we were able to discern noticeable trends in certain aspects of the QoL algorithms. Two of these were the CAT2 and CAT8 scores (*Table 10*) which imply that patient education improved subject perception of the amount of mucus in their respiratory system. With these algorithms, we also noted that our subjects reported feeling less energetic at follow-up although we speculate that this could be due to a change in patient attitudes for the lengthy follow-up procedure. We also observed certain gender-specific trends: our male subjects tended to show an improvement in CAT3 and CAT6-8 scores indicating that they felt less chest pain, were more confident when leaving their homes, were sleeping better, and felt more energetic due to the educational intervention. On the other hand, the changes in CAT6 scores in our female subjects suggest that they were more symptom-conscious at the time of follow-up. These findings suggest that perhaps patient education programs will have to be tailored by gender as well as the individual in order for patients to successfully manage their COPD. We must also note here that while we designed our education content in order to keep it simple and provide key messages to our subjects. Furthermore, in the interest of consistency, we provided the same content to all study subjects without any personalization or alteration.

Medication adherence has been shown to be associated with certain sociodemographic characteristics such as gender, age, affluence, and education (188). Higher education levels in patients are associated with better health literacy and medication knowledge (189; 190; 191). Consequently, these patients could be more proactive about seeking medical attention, adherent to prescribed treatments, and seek to make appropriate lifestyle changes. In our study, we noticed that subjects who had a university-level education scored better on question M8 on the MMAS-8 scale, which asked subjects if they had trouble remembering to take their medication. However, this finding also indicates that other appropriate measures will have to be developed to help improve adherence in patients who are not as educated.

One of the goals of our study was to identify any three-way correlation between patient education, adherence, and QoL. However, we could not discover any statistically valid correlation between adherence and QoL. Despite this, we did notice a loose association between changes in SGRQ and CAT scores implying that patient perception of

symptoms, as measured by CAT, correlate to decrease in QoL scores, as measured by SGRQ. In other words, the more symptoms a patient perceives, the worse they score on the QoL scale, especially on issues related to daily activities and societal impact. Additionally, the changes in SGRQ were paralleled by changes in the EQ-5D scores indicating that these trends move in the same direction. Larger studies will be required in the future in order to ascertain whether such patterns are a true effect or an aberration.

While our study provides a few insights on association between patient education and management of COPD in the outpatient scenario in Hungary, it was limited in scope. Since our study was a longitudinal cohort investigation, we did not have a control group, ie, subjects who received no professional counselling. While our sample size was adequate for our main objective, the results from our sub-group analysis cannot be reliably extrapolated to the general population with COPD. Furthermore, we did not classify our subjects according to the Global Initiative for Chronic Obstructive Lung Disease guidelines, which would have helped us; better understand their status, symptoms, and risk of exacerbation. Lastly, we did not analyze the data from our subjects for the effect of seasonal fluctuations, which are known to have an impact on severity of COPD symptoms.

It should be noted that our study focusses on hard endpoints and joins the mainstream direction of outcome based research. This certainly implies that intermediate effects of education was less measured than the value it captures at the level of therapy experience and adherence patterns. In order to assess the *ad interim* results of patient eduation, patient satisfaction or knowledge are assessed. In this study, we applied a single-item question to measure the impact of education on treatment regimens. The seventh question of MMAS-8 measures if patients are more able to adhere to daily treatment regimens, where endline scores show a positive trend (almost significant) in comparison with baseline scores. This implies that the education session positively influenced medication taking, and provides an intermediary link between education and the hard endpoint (patient reported outcome).

To provide a more holistic frame to our research, the factors potentially affecting the quality of life and adherence besides the education we provided, should be discussed. Quality of life should be analyzed in a multifactorial system. Factors affecting it can be

interpreted at the patient level: physical characteristics of the patient (age, weight, fitness), comorbidity (cardiological, psychiatric, asthma overlap), characteristics of therapy (fast effect, cheap effect), and psychic status.

The most widely used disease-specific quality of life questionnaire in COPD, SGRQ distinguishes three dimensions: symptoms (part 1), activities, and effects (part 2). Accordingly, these three main effects should be interpreted as the leading determinants of disease that affect quality of life.

Adherence is also multifactorial, here we suggest the following summarizing categories:

(1) Personality of the patient (age, personality traits, education, beliefs, relationship to alternative therapies, psychological status);
(2) Characteristics of the disease (severity, presence, progression, lifestyle impact, disease awareness, comorbidities);
(3) Characteristics of the therapy (mode of administration, frequency, duration and cost, side effects, previous therapies, fast onset, ergonomic considerations for the drug, success);
(4) Doctor-patient relationship (personality, intimate atmosphere, professionalism, concentration, “rituals”, messages);
(5) Features of the healthcare system (environment, waiting time, helpfulness of support staff, pharmacy availability, often changing prices or prescribing rules).

While designing the study, we sought to exclude other factors that influence patient quality of life. Consequently, patients with exacerbation within 3 months, other lung diseases, severe and uncontrolled cardiac disease, and uncontrolled mental problems were excluded, when designing the inclusion criteria. The 3-month control was defined as patients whose natural history did not require a change of medication, so external factors were considered unchanged except for education (including demographics). The internal consistency of the education was ensured by training the trainers, randomly checking them, and providing patient content with a fixed content for the formalized part of the education. Finally, this implies that the changes in the scores are attributable to the education we performed.

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To put our research in a further context, it should be considered what broader outcome measures exist (134). In this research, PROs were preferred as the most patient centric quantifier.

(1) Patient reported outcome: outputs that represent value to the patient in any forms (physical fitness, asymptomatic, quality of life parameters). For the sake of comparability, we use a validated questionnaire to ensure comparability with international research trends and results across sites.
(2) Clinical outcome: the patient's objective clinical parameters should be the primary consideration; this is lung function, especially the FEV_1. Previous clinical practice has examined this as a primary result, but insight that is more contemporary considers patient reported outcomes (too).
(3) Social and economic outcomes: at the societal level, we can broadly interpret the importance of education, as the positive impact on adherence reduces the social burden of the disease and reduces patients' sick leave. At the (health) economics level, the effectiveness of education can be interpreted as the QALY gain if there is such a spillover effect.

5.3. Background of adherence in a wider context

Ten studies were identified and included in this systematic review (177; 178; 179; 180; 181; 183; 184; 185; 186; 182). The majority of the studies focused on measuring adherence to inhaled tobramycin (n=7) (178; 179; 180; 181; 182; 183; 186). To our knowledge, this is the first systematic review of the adherence to inhaled ABs in CF. The results from the present study contribute to understanding the current status of adherence to inhaled ABs and for planning future research that can add to the global picture of adherence in CF.

5.3.1. Methodological issues: RCTs vs real-world studies

Most of the included publications were real-world studies (n=7) (180; 181; 182; 183; 184; 185; 186) contrary to RCTs (n=3) (177; 178; 179). From the viewpoint of health care professionals, real-world studies provide more reliable information about medication adherence in contrast with RCTs, which may overestimate adherence. As RCTs are mainly designed to assess safety and efficacy of pharmaceuticals, the study design emphasizes internal validity over generalizability. In these studies, because of protocol requirements, the data may not be applicable to the more heterogeneous patient group encountered in actual clinical practice. Effectiveness studies (eg, prospective cohort studies and retrospective studies), where treatment and/or disease management is studied under real-world conditions (eg, in unselected populations; patients are under routine care, taking open-label treatment, with no additional visits), remedy some of these limitations. This issue is especially relevant in case of adherence data. In RCTs, usually better treatment adherence is obtained due to the continuous, obligatory control visits or measurement of serum drug levels. Moreover, patients sometimes feel that they are in favored situation, because they are eligible to take part in the study and use a novel, not launched medication in CF. In addition, between regular visits, phone calls also remind patients to the use/ administration of the drug, or they are asked about their experiences related to the new drug.

In the included RCTs (177; 178; 179), the proportion of adherent patients (75%-80% of required doses taken) ranged between 86.4% (inhaled tobramycin, measurement method was not reported) (179), and 97.3% (inhaled levofloxacin,

measured by vials counting) (177). In contrast, in the prospective cohort study (180) only 44.9% of patients reported greater than 80% adherence to TIS (tobramycin inhalation solution) and 7.5% to tobramycin inhalation powder (TIP) (measured by patient self-report). In the included retrospective studies, the proportion of highly adherent patients (4 fills per 12 months) was found to be in the range of 7% (inhaled tobramycin, measured by pharmacy refill records) (183) to 29.6% (inhaled tobramycin, measured by pharmacy refill records) (186) (*Table 12*).

5.3.2. Adherence rates to inhaled antibiotics

Determining an overall rate for adherence to inhaled ABs in CF was difficult because different adherence definitions and measurement methods were applied in the reviewed studies; furthermore, two of the included studies (181; 182) did not declare a clear definition for adherence. In prospective cohort studies, adherence rates ranged between 36% (inhaled tobramycin, measured by daily phone diary), and 92% (inhaled aztreonam, measured by vials counting) (182), and in retrospective studies it ranged between 60% and 70% (inhaled colistimethate, measured by electronic monitoring) (185) (*Table 12*). Adherence to inhaled ABs did not differ significantly from adherence rates to other CF-related medications (*Table 13*) (184).

5.3.3. Predictors of adherence

In the reviewed studies, adherence to inhaled ABs was found to be associated with the age of patients, patient's satisfaction, treatment burden (ie, adverse events and taste), and time of drug administration (ie, morning vs evening inhalation) (179; 183; 185). Treatment adherence was better in those patients who were younger than 12 years of age (12 years of age: 71% vs $12 years of age: 50%) (185). A reasonable explanation may be the presence of parental supervision in this age group. This result is similar to the findings (181), who reported that parental supervision of CF medical treatments can improve children's treatment adherence. Furthermore, preadolescents and adolescents who spent more of their treatment time supervised by mothers had better adherence. Interestingly, (184) could not identify any relationships between age and treatment adherence. Patient satisfaction with inhalation AB therapy was linked to patient adherence, and side effects seemed to be the key drivers of patients' behavior regarding

their inhaled ABs in CF (179). Patients' self-perception about the efficacy of the drug (192), clinical response (192), cumulative toxicity (192), drug intolerance (183), treatment burden, and the time and frequency of administration[24] could determine adherence to therapy. Evening adherence (75%) was significantly better than morning adherence (58%) to inhaled colistimethate (185). A possible explanation of this phenomenon could be that children have to wake up early in the morning for complete airway clearance, chest physiotherapy, and inhalation before going to school. Unpleasant taste of the inhaled AB, delay in the improvement of lung function (FEV_1), and respiratory symptoms may also lead to non-adherence (177; 183; 193). Furthermore, adherence to a novel medication may be better than to an older one (177).

Real-world studies enable better understanding of the predictors of non-adherence from patients' viewpoint compared with RCTs. However, since measuring adherence to inhaled ABs as a phenomenon is relatively new, many of its potential predictors have not yet been evaluated, such as relationship between treatment adherence and health-related quality of life, relationship between clinical parameters (eg, FEV_1) and adherence, or direct comparison of adherence between various type of inhaled ABs in CF.

5.3.4. Consequences of non-adherence

In RCTs, high adherence was observed between artificial conditions compared to real-world studies. Therefore, this analysis made conclusions about consequences of non-adherence on the basis of results published by real-world studies (180; 181; 182; 183; 184; 185; 186). Most studies concentrated on the level of adherence, on the identification of non-adherence, and on how adherence can be improved. However, only few (n=4) researches dealt with the consequences (180; 183; 184; 186). Further studies are needed to understand the clinical consequences of non-adherence in CF.

Generally, the examination of financial impact, not the clinical impact, of poor adherence dominated in the reviewed articles. However, it was difficult to clarify the real effect of non-adherence on clinical outcomes because of the natural progression of the disease. There are many factors (eg, microbiological agents and CF-related complications), not only treatment adherence, in CF that may have an impact on the

progression of the disease. Our analysis suggests that better adherence to inhaled ABs in patients with CF is significantly associated with decreased health care utilization, median outpatient costs, excluding drug costs, and decreased risk of hospitalization (183; 186). Moreover, reductions in CF-related hospitalizations translated to significant reductions in CF-related inpatient costs. That could mean that low-adherence users may have more frequent pulmonary exacerbations and CF-related complications (186). However, that adherence to inhaled tobramycin was not significantly associated with the occurrence of pulmonary exacerbation and change in FEV_1% predicted slope (184).

5.3.5. Enhancing adherence

Only few of the authors of the reviewed articles developed suggestions on how adherence to inhaled ABs can be improved. Changing treatment regimen from twice daily to once daily significantly improved adherence (26% vs 54%, in 1 month) (185). In a real-world, prospective cohort study, the use of a more rapid delivery system could result in increased adherence to inhaled ABs (180). In their research, TIP was associated with better adherence compared with TIS (*Table 12*).

In the recent years, some useful tools have been developed to improve medication adherence in patients with CF. Internet-based adherence interventions and mobile phone applications became more and more popular (194). Besides telemedical patient management, it still seems important to improve patient education programs to provide home service programs in collaboration with social workers. However, the most important issue is to recognize the necessity of routine adherence monitoring during CF care. It is also important that physicians do not expect adherence to be the sole responsibility of patients, because improving treatment adherence is teamwork. Clinicians should understand their patients' problems in relation to side effects or with time of administration and help patients to choose an inhaled AB that is the best for the patient. If adherence is routinely monitored and results are discussed openly with patients, then treatment regimens can be individualized for patients. This kind of interaction can result in sustainable levels of adherence during the CF care.

5.4.Research objectives & hypotheses

The following research objectives and hypotheses were set for this research, and I can provide the following argumentation to discuss their accomplishment:

Objectives

(1) to assess the attitudes of two key players (patient, physician) in COPD patient care. This new methodology should be reproducible, widely applicable, and personalized & understandable to patients.

Patient and pulmonologist intervews were conducted, and they provided input to the education content that I have applied in three study centers (see Chapter 4.1). Patient knowledge on treatment regimens was evaluated, and the education has positively affected this parameters, whilst I demonstrated significant improvement of total adherence scores.

For the pulmonologist interviews, I set the following project specific objectives:

4.3.1.1. to develop a patient education program that is based on the expert opinion of pulmonology therapists who play a key role in the care of COPD patients;

The patient education program was successfully designed, implemented and reported, please see Chapter 4.2 that describes the impact the project created.

4.3.1.2. to understand the perceptions and attitudes of the pulmonary therapist, and to gain a comprehensive landscape of patient and condition, the success of the treatment, and their relation to adherence;

The COPD patient profile, therapeutic attitudes of pulmonary therapists were reported in Chapters 4.1 and discussed in 5.1.

4.3.1.3. to assess the potential of improving patient adherence in outpatient care, rehabilitation and hospital settings.

The adherence aspects of patient education are highlighted in the results section (4.1), and due to the patient population of the pulmonologist interviews, I have incorporated knowledge of specialists of all three affiliations mentioned above.

For the patient interviews, I set the following project specific objectives:

4.3.1.4. to assess the opportunities of COPD disease management in the community pharmacy setting;

Although our results highlight that the pharmacy setting is not an ideal place for education for our study, our pilot study conducted in the Inczeffy Pharmacy provided an insight to patient attitudes by in-depth interviews.

4.3.1.5. to understand patient attitudes, perceptions, fears, beliefs that affect the everyday life of patients;

Results of patient data are available in Chapter 4.1.2. This knowledge was used to compile a guide to the education content patients would welcome (see Chapter 6.1).

4.3.1.6. to create a local good practice and to investigate how the community pharmacy pillar of integrated care can work in the context of Hungary.

Integrated care is defined in this thesis as the collaboration between the GP, pharmacist and the medical specialist. The community pharmacy and the outpatient center opportunities have been explored, though it was implemented in different localities (district 13, 19 of Budapest, Vác and Göd for the pharmacy). We have created a local good practice in the city of Göd for the benefit of patients, which can be complemented in the future by further integration of pulmonologists from the same region and GPs.

(2) to conduct *pilot* studies to determine the optimal scenario to *go live* with the education project;

Pilot studies were implemented both in the pharmacy and in the outpatient center (the latter one was not sufficiently moderated to report systematically) with the participation of 6-20 in each location. The education project went live as assumed.

(3) to investigate the effect of education on quality of life and adherence of COPD patients at different study sites (Budapest and the countryside) by a different set of validated scales; and to investigate the longitudinal effects of education;

Validated scales were selected as described in Chapter 1.4, the study site scope was accomplished, and the longitudinal feature was assured by a 3-month follow-up. The impact we created is described in Chapters 4.2 and 5.2.

(4) to propose the ideal conditions of education (pharmacist care in the community pharmacy setting or pulmonologist care in the outpatient setting with nurses);

For this study, the pharmacy setting was excluded from follow-up due to the limited number of patients. Also, we had to consider the patients' desire to be primarily education in the pulmonology outpatient center, especially when they are waiting for examinations. Consequently, we have chosen the outpatient center setting to recruit the bulk of our participants.

(5) to understand the background of adherence in a wider context of pulmonary conditions, including the different setting of cystic fibrosis.

The review that our research group has published was written upon the request of the journal, which demonstrates the need from the scientific community for such a journal article. The detailed discussion section in Chapter 5.3 provides this wider context to inhalative therapy in CF.

Hypotheses

(1) Patient-centered education content can be developed based on the attitudes and perceptions of pulmonologists and patients.

I accept the first hypothesis, because my PhD research successfully developed this education content.

(2) This education content has a positive impact on medication adherence and quality of life, and this demonstrated by validated scales.

Total medication adherence scores and certain dimensions were proven to be significantly better due to education, whilst a positive tendency was demonstrated on certain elements of COPD symptomatology. I accept this hypothesis, since certain elements improved, though not all of them improved.

(3) A methodological overview to broaden the scope with CF medication adherence will help me reveal more about adherence patterns and patient attitudes in respiratory conditions.

I accept this hypothesis, since the appraisal is ready and it provides the desired insight.

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6. Conclusions

6.1.Attitudes and perceptions

The perception project has managed to meet the objectives that were observed previously. Conclusions to prepare the educational content, based on pulmonologist expert opinion, will be summarized in the following points and by *Figure 18A*:

(1) As for patient profile, pulmonologists generally meet male patients who are under socialized, breathless, coughing, smoking. If a patient brochure is created, it is recommended that we use such a sample patient so that they feel more attached to the material. Further implications include plain language, especially by including the words they use.

(2) Patients should be educated from the basics, since currently awareness and disease acceptance are missing. Consequently, it is necessary to explain the acronym COPD, laying stress on the chronic component of the disease (eg. medication cannot be stopped if symptoms are ameliorated); to make sure about the relationship between smoking and COPD, and to promote smoking cessation.

(3) The unambiguous symptoms of the disease, such are fatigue, coughing and breathlessness should be associated with it, and the education sessions should explain how the treatment resolves these symptoms (consistent with the lack of disease coverage). Patients should understand what is the role of each medication (at least if it is a reliever or maintenance therapy), and the supremacy of long-term treatment over the frequent administration of the fast onset relievers.

(4) Correct dosage, frequency, and proper inhaler use should be the part of everyday life. It should be clear that the lack of adherence is associated with more frequent GP visits and exacerbations, and the latter vastly deteriorates quality of life and long-term survival rates. Consequently, the patients has to know when to contact the doctor and when not to.

(5) Bidirectional and open communication between patient and healthcare provider, and the question of trust have also appeared in the interviews, which elevate this process to a higher level. Patient engagement and self-management are fostered if the above are created and the patient is willing to take responsibility of their actions and willing to take care of themselves.

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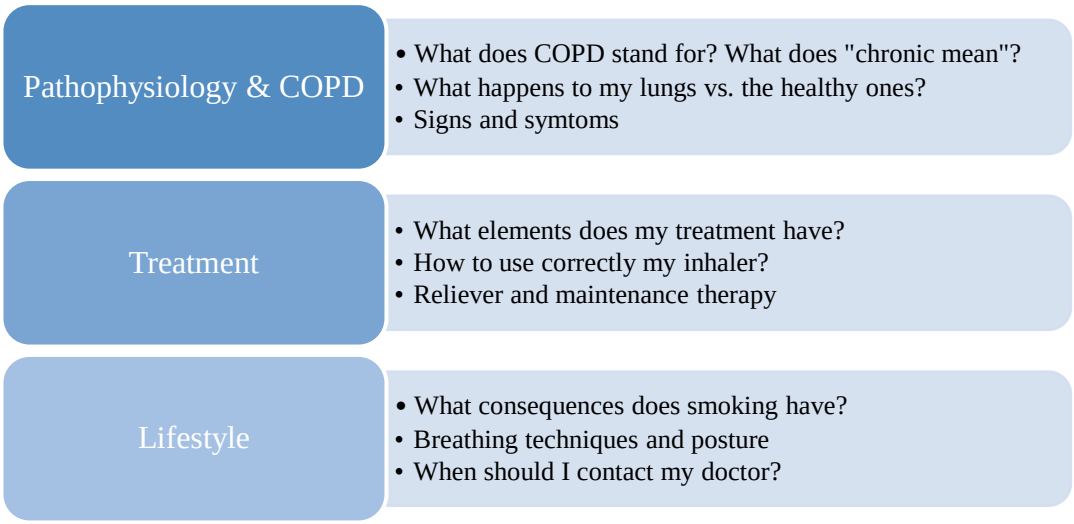

Figure 18A: Patient education content based on pulmonologist opinion

According to interviews, COPD patient education is badly needed. It is useful to do this in a structured way, using the experience of specialists, according to the patient's language and level of knowledge (195). Above we have presented attitudes regarding the diagnosis of COPD, the physician's patient picture, the patient's adherence, and the inhaler.

It would be interesting to further develop research: a higher number of subjects, conducting similar studies among patients, and extending the scope to the overlapping issues of quality of life and quality of life and adherence.

In conclusion, patient education is of paramount importance in the treatment of COPD. Considering the lessons of this article, it is worth developing a training program tailored to the local context that addresses the needs of stakeholders (196).

Patient interviews vastly reveal the missing concepts, lack of pragmatic knowledge and (non)-adherence data that should be tackled by in our education program. A patient education project was piloted in the community setting, and we will do our best to ensure the scientific support to its continuation (hopefully this means this initiative will continue on the long-term in Göd). Furthermore, this study has the benefit to envision the three key intervention areas that should be targeted by an education program.

(1) A relatively small number of COPD patients prefers the pharmacy to get education; however, those who come indeed, are motivated.

(2) Patients get used to COPD, and they accept “that this comes by age”, “I cannot do this”, though all of them mentioned an activity they still wish to pursue.

(3) Active listening to patient needs is an effective way to reveal important insight (146). Namely, asking semi-structured questions; and permitting them to talk about their issues helped us create the guidelines for such content they can benefit. Recording patients’ words and phrases also helps us to put together an easy-to-understand material with catchy content.

(4) There is a need to expand the project, since once the patients decided to open up, they share all their experience; furthermore, these patient clubs are also in favor of their social inclusion and provide an opportunity to meet their peers.

(5) *Figure 18B* seeks to incorporate the patient insight to an ideal education content. Since the project was well accepted, a local epitome has been created in the Inczeffy Pharmacy.

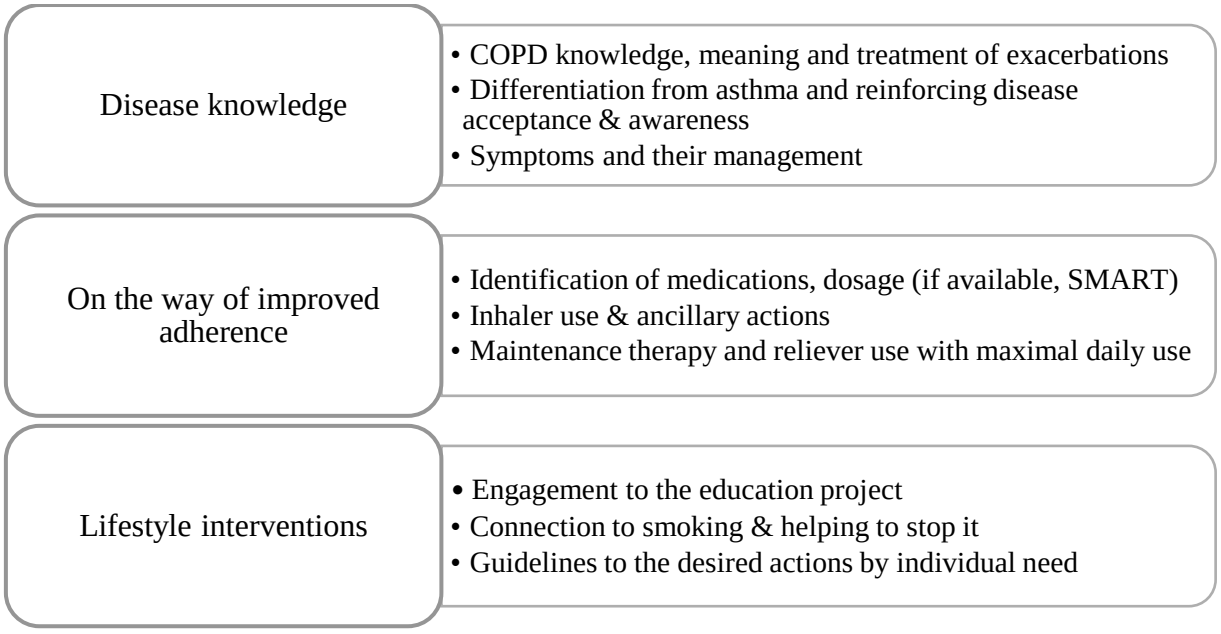

Figure 18B. Elements of the suggested education content by COPD patient interviews

It is worth comparing *Figure 18A and 18B*. Even though patients and pulmonologists communicate differently about COPD, the major elements turned out to be similar. All mentioned topics were grouped in three, and three major areas of interest could be identified. Education content was finally developed using these results, and internal bias was diminished by applying two independent evaluators for patient and pulmonologist interviews.

6.2.Impact of education on quality of life and adherence

In conclusion, although we did not establish a clear relationship between patient education and QoL, we were successful in demonstrating an association in between patient education and medication adherence. Our research highlights the groups that are receptive to education and parameters that affect adherence in the environment of an outpatient pulmonology center, where the context is fixed, internal consistency of the education ensured, and patients continue with their medications for a period of three months. Patient education results in an improvement in adherence, especially in unique situations such as being away from home. Larger studies will be required to assess the adequacy of current patient counselling strategies and implement newer and improved policies to ensure successful self-management of COPD in Hungary.

6.3.Background of adherence in a wider context

Different adherence definitions and measurement methods made it difficult to determine an overall rate for adherence to inhaled ABs in CF based upon the reviewed studies. Our analysis suggests that probably because of their highly controlled conditions, RCTs provide higher adherence rate to inhaled ABs than real-world studies. Adherence to inhaled ABs was found to be associated with the complexity of treatment, time of drug administration, age of patients, treatment burden (ie, adverse events and taste), and patient satisfaction. Further research is needed to better understand the predictors of adherence to inhaled ABs, which would be critically important to the development of effective adherence-enhancing interventions. Routine adherence monitoring, discussing the possible reasons of non-adherence with the patient, and changing treatment regimens on the basis of patient burden may optimize patient management and hence improve adherence in patients with CF.

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6.4. Novelties

This body of research had the objective to contribute to our existing knowledge of COPD patient education, quality of life and adherene, and CF adherence in the Hungarian context. This PhD thesis has managed to demonstrate the following novelties:

(1) It has envisioned The Hungarian COPD patient profile by pulmonology in-depth interviews;

(2) It has described the perceptions and attitudes of Hungarian pulmonologist related to COPD treatment and adherence;

(3) It has created a patient centered education content that is tailor-made to the needs of Hungarian patients;

(4) It has created the major guidelines, along which pulmonologists think that COPD patients can be educated (this provided a fix element to the education project);

(5) It has initiated a local good practice in the Inczeffy Pharmacy in Göd with a *pilot* community pharmacy project to gather patient insight and information of the implementation of such an educational project in the pharmacy setting;

(6) It has described attitudes and perceptions related of Hungarian COPD patients related to COPD treatment and adherence;

(7) It has performed impact studies in Hungary as a pioneer to demonstrate the impact of COPD patient education of a diverse set of quality of life and adherence questionnaires;

(8) It has demonstrated significant correlation with total adherence and positive or significant correlation with dimensions of adherence (especially in unique situations such as being away from home, being more treatment-conscious and taking medication at 2 weeks after the medical visit);

(9) It has provided a peer reviewed overview of challenges of CF treatment, along with an appraisal of adherence of respiratory conditions in a wider context.

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7. Summary

The PhD thesis have met three *pre-study* objectives; additionally, the advances to our current knowledge are highlighted.

Firstly, it had the objective to develop a patient-centered education content with the inclusion of pulmonologist expert opinion and patient needs for the first time in Hungary.

Secondly, it had the objective to measure the impact of this education program on the adherence quality of life of COPD patients, also considering the long-term benefits, pioneering with a complex set of dimensions with Hungarian patient data.

Thirdly, it had the objective to gather insight into adherence patterns in a wider range in pulmonology, by including cystic fibrosis as a model disease.

The study has shown that pulmonologist and patient attitudes are different, especially articulated differently. However, when they are summarized by two independent evaluators, needs can be unified by a tailor-made patient education program, which was structured for the study to ensure inter-comparability.

The structured education was performed n=118 times, and the same number of patients benefited of the long-term benefits. We used a various range of adherence and quality of life scales, which had been carefully selected for the target population, taking availability, cost-effectiveness and target willingness into account. Adherence was measured on the latest and most complete MMAS-8 scale; whilst symptomatology was measured by the standardized CAT test; disease-specific quality of life was measured by the SGRQ test, and general quality of life on the EQ-5D-5L and VAS scales.

Our results highlight that this educational program was successful, marked effects were registered especially related to adherence. Statistically significant improvement was achieved on the overall adherence scores, which are supported by the following dimensions: “pre-visit medication taking”, “taking medication when leaving home” and “overall comfortability with the treatment”. Our methodological overview summarizes the main factors determining adherence in CF, which helps this thesis broaden its perspectives in adherence in the domain of respiratory diseases.

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8. Összefoglaló

A doktori értekezés három előre meghatározott célt teljesített; valamint az alábbiak összefoglalják a munka tudományos értékét.

Először, egy betegközpontú oktatási program kidolgozását tűzte ki célul, a pulmonológus szakértői véleményének és a betegek szükségleteinek bevonásával elsőként Magyarországon.

Másodszor, a célom az volt, hogy ennek az oktatási programnak a COPD-s betegek életminőségére és adherenciájára gyakorolt kvalitatív és kvantitatív hatását leírjam, figyelembe véve a hosszú távú előnyöket és az egyes dimenziókat is.

Harmadszor, a célom az volt, hogy az adherencia kérdéseit szélesebb kontextusban, a cisztás fibrózist mint modellbetegséget is bevonva vizsgáljam.

A tanulmány kimutatta, hogy a pulmonológusok és a betegek attitűdje eltér, különösképpen másképp kommunikálnak ezekről. Két független értékelő bevonásával mindkét kulcsszereplő szempontjait figyelembe véve egy betegérdekekre szabott oktatóprogramot fejlesztettem ki (ezt a vizsgálat során fixesítettük, hogy a mérések összehasonlíthatóak legyenek).

Oktatásban n = 118 beteg részesült, őket longitudinális vizsgálatban 3 hónapos utánkövetéssel vizsgáltuk. Az adherenciát az MMAS-8 skálán mértük; míg a tüneteket a CAT-teszttel; a betegség-specifikus életminőséget az aranystandard SGRQ-teszttel, az általános életminőséget az EQ-5D-5L és a VAS-skálákon mértük.

Az eredmények rámutattak arra, hogy ez az oktatási program sikeres volt, különösen az adherencia tekintetében. Statisztikailag szignifikáns javulást írtam le a teljes adherencia-pontszámot illetően, valamint egyértelmű javulást az alábbi dimenziókban: „vizit előtti gyógyszeres kezelés”, „gyógyszer szedése otthonról távozáskor” és „általános kezeléssel való elégedettség”.

Módszertani áttekintésünk összefoglalja azokat a fő tényezőket, amelyek leírják a cisztás fibrózisban alkalmazott inhalatív terápiával kapcsolatos adherencia megfontolásait, ezáltal kitekintést adnak más, hasonló tüdőgyógyászati kórképben leírt terápiahűségre is.

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Additional sources used for the compilation of figures and tables, which are not my work. Mate Olah and Szilvia Kresznerits created all other diagrams.

Figure 2 has been taken from (55).

Table 1 contains the images taken from the following sources:

https://www.netterimages.com/images/vpv/000/000/013/13539-0550x0475.jpg [accessed: 15/9/2019]
http://classconnection.s3.amazonaws.com/106/flashcards/1125106/jpg/blue_bloater1332976578322.jpg [accessed: 15/9/2019]

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10. List of publications

10.1. Publications relevant to the dissertation

(1) **Oláh M**, Kresznerits Sz, Gonda X, Perczel-Forintos D, Szabó M, Csánky E, Mészáros Á (2020) Impact of education on dimensions of adherence in patients with chronic obstructive pulmonary disease. *Acta Poloniae Pharmaceutica* 77: 195-204. **IF_{2018}=0.447**

(2) **Oláh M**, Kresznerits Sz, Perczel-Forintos D, Kun Cs, Csánky E, Mészáros Á (2020) Egy oktatóprogram fejlesztésének lehetőségei tüdőgyógyász szakorvosok krónikus obstruktív tüdőbetegséggel kapcsolatos megítélése alapján [Aspects of developing an education programme based on pulmonologists' appraisal related to chronic obstructive pulmonary disease]. *Orvosi Hetilap* 161: 95-102. **IF_{2018}=0.564**

(3) **Oláh M**, Inczeffy-Ivicsics K, Mészáros Á (2019) How to design an education programme for patients with chronic obstructive pulmonary disease? – Learnings from a pilot community pharmacy based project to evaluate patient attitudes. *Acta Pharmaceutica Hungarica* 89: 109-115.

(4) **Oláh M**, Mészáros Á (2017) Added value of different healthcare professionals, with special regard to pharmacists to COPD therapy experience. *Acta Pharmaceutica Hungarica* 87: 3-4

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(6) Ágh T, Bodnár R, **Oláh M**, Mészáros Á (2015) Adherence to Inhaled Antibiotics for the Treatment of Chronic Pseudomonas Aeruginosa Infection in Patients with Cystic Fibrosis: A Systematic Literature Review. *Value in Health* 18:7 (ISPOR reprint)

DOI:10.14753/SE.2020.2399

10.2. Other publications, not relevant to the dissertation

(1) Kristof Z, Kresznerits S, **Olah M**, Gyollai A, Lukacs-Miszler K, Halmai T, Fountoulakis KN, Tenyi T, Dome P, Gonda X (2018) Mentalization and empathy as predictors of violence in schizophrenic patients: Comparison with nonviolent schizophrenic patients, violent controls and nonviolent controls. *Psychiatry Res*. 268: 198-205. **IF_{2018}=2.208**

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12. Attachments

12.1. Ethical permission

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Protokoll: -

Dr. Mészáros Ágnes
egyetemi docens
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Gyógyszerügyi Szervezési Intézet

Budapest

Tárgy: „Komparatív COPD életminőség és adherencia-vizsgálatok" című kutatás

Tisztelt Docens Asszony!

A Semmelweis Egyetem Regionális, Intézményi Tudományos és Kutatásetikai Bizottsága a 2015. október 26-án megtartott ülésén és a 2016. január 21-én pótlólag megküldött dokumentum alapján az alábbi döntést hozta:

A bizottság a kutatási tervet szakmai és etikai szempontból megfelelőnek, valamint az intézmény tárgyi és személyi feltételeit a kutatás végzésére alkalmasnak találta.

A bizottság fenti döntését az egészségügyről szóló 1997. évi CLIV. törvény és az emberen végzett orvostudományi kutatásokról szóló 23/2002. (V.9.) EüM rendelet alapján hozta.

Felhívjuk figyelmét az adatvédelemmel kapcsolatos jogszabályok szigorú betartására. (1997. évi XLVII. törvény 21. §: az egészségügyi és a hozzájuk kapcsolódó személyes adatok kezeléséről és védelméről.
2011. évi CXII. törvény: az információs önrendelkezési jogról és az információszabadságról.)

Tájékoztatásul közöljük, az IKEB bármikor ellenőrizheti, hogy a kutatást, vizsgálatot a kutatási tervben és az engedélyben előírtaknak megfelelően végzik-e [23/2002. (V.9.) EüM rendelet 18. §].

A vizsgálat befejezését követően kérjük a Bizottság részére a jelentés megküldését.

Budapest, 2016. január 22.

Dr. Sótonyi Péter
egyetemi tanár

Kérem, a fenti TUKEB számra minden esetben hivatkozni szíveskedjék.

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12.2. Informed consent form

A vizsgálat helyszíne: .....

Vizsgálatvezető neve és beosztása: Mészáros Ágnes PhD egyetemi docens, c. egyetemi tanár, Semmelweis Egyetem Egyetemi Gyógyszertár Gyógyszerügyi Szervezési Intézet

A tájékoztatást végző személy: neve: Dr. Oláh Máté
beosztása: gyógyszerész, PhD-hallgató

.....[beteg neve] tájékoztatást kaptam a fenti vizsgálatról és elolvastam a mellékelt Betegtájékoztatót. Lehetőségem volt a kapott információkat megbeszélni, kérdéseket feltenni. Beleegyezem a vizsgálatban való részvételbe és részvételem teljesen önkéntes. Megértettem, hogy beleegyezésemet bármikor, indoklás nélkül visszavonhatom, és ez nem befolyásolja ellátásomat.

Ezen Írásos Beleegyezési Nyilatkozat aláírásával hozzájárulok ahhoz, hogy személyes adataimat, beleértve a testi vagy lelki egészségi állapotommal kapcsolatos adatokat a Betegtájékoztatóban leírt módon használják fel.

Engedélyezem, hogy önkéntesen részt kívánok venni a vizsgálatban. Engedélyezem, hogy a vizsgálattal kapcsolatosan megadott adataimhoz való hozzáférést, és beleegyezem, hogy a kérdésekre adott válaszaimat a kutatás kapcsán közzétett kiadványhoz felhasználják a személyazonosságomra vonatkozó bármely adat nyilvánossá tétele nélkül.

Résztvevő személy adatai:

Név: .....

Születési idő: ..... kora:

Lakóhely: ..... [település neve]

Telefonszám: .....

E-mail: .....

…….…… ……
Tájékoztatást végző aláírása dátum

…….…… ……
Beteg dátum

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12.3. Questionnaires

12.3.1. CAT

Milyen az Ön COPD betegséggel kapcsolatos közérzete? Kérjük, végezze el a COPD Állapotfelmérő Teszt™-et (COPD Assessment Test, CAT)

Az alábbi kérdőív alapján Ön és az Önt ellátó egészségügyi szakember jobban fel tudja majd mérni, hogy a COPD (krónikus obstruktív tüdőbetegség) milyen hatást gyakorol az Ön közérzetére és mindennapi életére.A válaszok és a tesztpontszám segítségével Ön és az Ön orvosa a kezelés minél nagyobb sikere érdekében jobban tudja majd kezelni az Ön COPD betegségét.

Minden alábbi megállapításnál ahhoz a számhoz tegyen (X) jelet, amelyik legjobban jellemzi az Ön aktuális állapotát. Fontos, hogy minden megállapításnál csak egy számot jelöljön be.

Példa: Nagyon boldog vagyok	0 X 2 3 4 5	Nagyon szomorú vagyok	
			PONTSZÁM
Soha nem köhögök	0 1 2 3 4 5	**Állandóan köhögök**	
Egyáltalán nincs váladék (nyák) a légutaimban	0 1 2 3 4 5	**A légutaim teljesen tele vannak váladékkal (nyákkal)**	
Egyáltalán nem érzek mellkasi feszülést	0 1 2 3 4 5	**Nagyon erős mellkasi feszülést érzek**	
Emelkedőn felfelé vagy egy lépcsőfordulót megtéve nem fulladok	0 1 2 3 4 5	**Emelkedőn felfelé vagy egy lépcsőfordulót megtéve nagyon fulladok**	
A betegségem egyáltalán nem korlátoz az otthoni tevékenységeimben	0 1 2 3 4 5	**Otthoni tevékenységem nagy mértékben korlátozott**	
Tüdőbetegségem ellenére nyugodtan el merek menni otthonról	0 1 2 3 4 5	**Tüdőbetegségem miatt nem merek teljesen nyugodtan elmenni otthonról**	
Mélyen alszom	0 1 2 3 4 5	**Tüdőbetegségem miatt nem alszom mélyen**	
Rengeteg az energiám	0 1 2 3 4 5	**Teljesen erőtlen vagyok**	
			ÖSSZESÍTETT PONTSZÁM

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12.3.2. Demography

Orvos tölti ki!
A beteg tüdőgyógyászati gyógyszerei:
A beteg más BNO-kód alá tartozó gyógyszerei:

Kérem, az alábbi kérdésekre őszintén válaszoljon! Az erre adott válaszok nem befolyásolják a megítélést vagy a programban való részvételt!

Életkorom (év): férfi / nő

Jelenlegi foglalkozásom:

Legmagasabb iskolai végzettségem: alap / közép / felső

Társadalmilag ide sorolom a családom helyzetét (húzza alá a megfelelőt!):

kifejezetten jó körülmények között, az átlagosnál job körülmények között élünk

megfelelő körülmények között, átlagos szinten élünk

az átlag alatti életszínvonalon élünk

nagyon rossz körülmények között élünk

Dohányzom / nem dohányzom. Ha igen, napi hány szálat?

A tüdőgyógyászati szereimmel kapcsolatban

jobban betartom a terápiát / kevésbé tartom be a terápiát, mint más gyógyszereimnél.

elegendő / túl kevés / túl sok információval rendelkezem a használatról.

A tüdőgyógyászati kontrollra járást

fontosabbnak / ugyanolyan fontosnak / kevésbé fontosnak tartom, mint a többi betegségem kezelését.

A tüdőgyógyászomban bízok / nem bízok, jó a viszonyunk / lehetne jobb a viszonyunk.

A háziorvosommal jobb / rosszabb / ugyanolyan a viszonyom, mint a tüdőgyógyásszal.

Bármilyen egyéb hozzáfűznivaló:

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12.3.3. EQ-5D and VAS

Az egyes címsorok alatt kérjük, jelölje be azt az EGY négyzetet, amely a legjobban jellemzi az On MAI egészségi állapotát.

MOZGÉKONYSÁG

- Nincs problémám a járással ❑
- Enyhe problémám van a járással ❑
- Mérsékelt problémám van a járással ❑
- Súlyos problémám van a járással ❑
- Képtelen vagyok járni ❑

ÖNELLÁTÁS

- Nincs problémám a tisztálkodással vagy az öltözködéssel ❑
- Enyhe problémám van a tisztálkodással vagy az öltözködéssel ❑
- Mérsékelt problémám van a tisztálkodással vagy az öltözködéssel ❑
- Súlyos problémám van a tisztálkodással vagy az öltözködéssel ❑
- Képtelen vagyok önállóan tisztálkodni vagy öltözködni ❑

SZOKÁSOS TEVÉKENYSÉGEK *(pl. munka, tanulás, házimunka, családi vagy szabadidős tevékenységek)*

- Nincs problémám a szokásos tevékenységeim elvégzésével ❑
- Enyhe problémám van szokásos tevékenységeim elvégzésével ❑
- Mérsékelt problémám van szokásos tevékenységeim elvégzésével ❑
- Súlyos problémám van szokásos tevékenységeim elvégzésével ❑
- Képtelen vagyok elvégezni szokásos tevékenységeimet ❑

FÁJDALOM / ROSSZ KÖZÉRZET

- Nincs fájdalmam vagy rossz közérzetem ❑
- Enyhe fájdalmam vagy kissé rossz közérzetem van ❑
- Mérsékelt fájdalmam vagy közepesen rossz közérzetem van ❑
- Súlyos fájdalmam vagy nagyon rossz közérzetem van ❑
- Rendkívül erős fájdalmam vagy rendkívül rossz közérzetem van ❑

SZORONGÁS / DEPRESSZIÓ

- Nem szorongok vagy nem vagyok depressziós ❑
- Enyhén szorongok vagy enyhén depressziós vagyok ❑
- Mérsékelten szorongok vagy közepesen depressziós vagyok ❑
- Nagyon szorongok vagy súlyosan depressziós vagyok ❑
- Rendkívül erősen szorongok vagy rendkívül depressziós vagyok ❑

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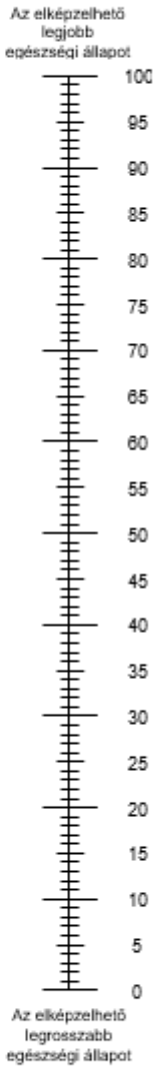
- Szeretnénk megtudni, hogy MA milyen jó vagy rossz az Ön egészségi állapota.
- Ez a skála 0-tól 100-ig számozott.
- Az elképzelhető legjobb egészségi állapotot „100", míg az elképzelhető legrosszabb egészségi állapotot „0" jelöli.
- Kérjük, jelölje X-szel a skálán azt a pontot, amely megmutatja, hogy milyen az Ön MAI egészségi állapota.
- Ezután az alábbi rubrikába írja be azt a számot, amelyet a skálán megjelölt.

AZ ÖN MAI EGÉSZSÉGI ÁLLAPOTA = ☐



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12.3.4. MMAS-8

©Morisky gyógyszer előírás pontos betartására vonatkozó skála (MMAS-8-Item). Ez egy általános pontos betartásra vonatkozó skála és az egészségi problémát be kell helyettesíteni az egyes kérdés elemeknél.

Jelezte, hogy gyógyszert szed (egészségi problémája, mint például "magas vérnyomás" megnevezése) kezelésére. Egyes személyek több problémát neveztek meg gyógyszer-szedési szokásaikkal kapcsolatban és kíváncsiak vagyunk az Ön tapasztalataira. Nincs jó vagy rossz válasz. Kérjük, válaszoljon minden egyes kérdésre az (egészségi probléma) gyógyszerelésével kapcsolatos személyes tapasztalata alapján.

(Kérjük, karikázza be a megfelelő számot)

	Nem=1	**Igen=0**
1. Előfordul-e néha, hogy elfelejti beszedni (egészségi probléma) tablettáit?		
2. Az emberek néha nem veszik be gyógyszereiket, nem azért mert elfelejtik, hanem egyéb okból kifolyólag. Az elmúlt két hetet átgondolva, volt-e olyan nap, amikor nem szedte be (egészségi probléma) gyógyszerét?		
3. Előfordult-e valaha is, hogy csökkentette vagy abbahagyta gyógyszere szedését anélkül, hogy orvosát arról tájékoztatta volna, mivel rosszabbul érezte magát, amikor azt beszedte?		
4. Amikor elutazik, vagy elmegy otthonról, előfordul-e néha, hogy elfelejti magával vinni a(z) (egészségi probléma) gyógyszerét?		
5. Beszedte-e (egészségi probléma) gyógyszerét tegnap?		
6. Amikor úgy érzi, hogy (egészségi problémája) jól be van állítva, előfordul-e néha, hogy abbahagyja gyógyszere szedését?		
7. Komoly kellemetlenséget okoz néhány ember számára a mindennapi gyógyszerszedés. Előfordul-e hogy gondot jelent Önnek az, hogy ragaszkodjon az Ön (egészségi problémájának) kezelési előírásához?		

8. Milyen gyakran okoz nehézséget az, hogy emlékezzen összes gyógyszere beszedésére? **(Kérjük, karikázza be a megfelelő választ)**

Soha/ritkán……..**4**

Alkalmanként……..**3**

Néha……..**2**

Rendszeresen……..**1**

Mindig ……**0**

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12.3.5. SGRQ

ST. GEORGE'S RESPIRATORY QUESTIONNAIRE
HUNGARY

A SZENT GYÖRGY KÓRHÁZ LÉGZÉSI PANASZOKKAL KAPCSOLATOS KÉRDŐÍVE (SGRQ)

Ez a kérdőív segít abban, hogy minél többet megtudjunk légzési problémáiról és arról, hogy problémái hogyan befolyásolják az Ön életét. Azt szeretnénk megtudni, hogy betegsége kapcsán Önnek milyen tényezők okozzák a legtöbb problémát, és nem azt, hogy orvosa vagy ápolója mit tekint problémának.

Kérjük, figyelmesen olvassa el az utasításokat és kérdezzen rá, ha valamit nem ért. Ne gondolkozzon túl sokat a válaszokon.

Mielőtt elkezdené a kérdőív kitöltését, kérjük, jelölje meg (✓) a megfelelő négyzetet, annak megfelelően, hogy milyennek tartja jelenlegi egészségi állapotát.	Nagyon jó	Jó	Közepes	Rossz	Nagyon rossz
	☐	☐	☐	☐	☐

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A Szent György Kórház Légzési Panaszokkal Kapcsolatos Kérdőíve
1. RÉSZ

A következő kérdések azzal kapcsolatosak, hogy az elmúlt 4 hétben milyen gyakran fordultak elő Önnek légzési panaszai.

Kérjük, minden kérdésnél jelöljön meg (✓) egy négyzetet.

	Hetente szinte minden nap	Hetente néhány nap	Havonta néhány nap	Csak légúti fertőzéseik alkalmával	Egyáltalán nem
1. Az elmúlt 4 hétben köhögtem:	☐	☐	☐	☐	☐
2. Az elmúlt 4 hétben váladékkal járó köhögésem volt:	☐	☐	☐	☐	☐
3. Az elmúlt 4 hétben légszomjam volt:	☐	☐	☐	☐	☐
4. Az elmúlt 4 hétben ziháló légzéssel járó rohamom volt:	☐	☐	☐	☐	☐

5. Az elmúlt 4 hétben hányszor volt súlyos, vagy nagyon kellemetlen légzési panaszokkal járó rohama?

Kérjük, jelöljön meg (✓) egy négyzetet.

- Több, mint három roham ☐
- Három roham ☐
- Két roham ☐
- Egy roham ☐
- Nem volt roham ☐

6. Mennyi ideig tartott a legsúlyosabb, légzési panaszokkal járó rohama?
(Ha Önnek nem volt súlyos rohama, térjen át a 7. kérdésre)

Kérjük, jelöljön meg (✓) egy négyzetet.

- Egy hétig vagy tovább ☐
- Három, vagy annál több napig ☐
- Egy vagy két napig ☐
- Egy napnál rövidebb ideig ☐

7. Az elmúlt 4 hét alatt hány jó (kevés légzési panasszal járó) napja volt egy átlagos hetet tekintve?

Kérjük, jelöljön meg (✓) egy négyzetet.

- Egy jó napom sem volt ☐
- 1 vagy 2 jó napom volt ☐
- 3 vagy 4 jó napom volt ☐
- Majdnem mindegyik napom jó volt ☐
- Mindegyik napom jó volt ☐

8. Amikor zihálló légzése van, reggelente súlyosabb a zihálás?

Kérjük, jelöljön meg (✓) egy négyzetet.

- Nem ☐
- Igen ☐

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A Szent György Kórház Légzési Panaszokkal Kapcsolatos Kérdőíve
2. RÉSZ

1 Szakasz

Hogyan jellemezné légzési panaszait?

Kérjük, jelöljön meg (✓) *egy négyzetet.*

- Ez a legfontosabb problémám ☐
- Meglehetősen sok problémát okoz számomra ☐
- Kevés problémát okoz számomra ☐
- Nem okoz problémát ☐

Amennyiben Ön valaha is fizetett munkaviszonyban állt, kérjük, válaszoljon:

Kérjük, jelöljön meg (✓) *egy négyzetet.*

- Légúti betegségem miatt abba kellett hagyni a munkámat ☐
- Légúti betegségem akadályoz munkámban, vagy állást kellett változtatnom ☐
- Légúti betegségem nem befolyásolja munkámat ☐

2 Szakasz

Az alábbi kérdés azzal kapcsolatos, hogy <u>mostanában</u> mely tevékenységek okoznak Önnek általában légszomjat.

Kérjük, minden állításnál jelöljön meg ***egy négyzetet*** annak megfelelően, hogy ***mostanában*** az Ön esetében az állítás igaz, vagy hamis.

	Igaz	Hamis
Ülés vagy fekvés nyugalomban	☐	☐
Mosakodás vagy öltözködés	☐	☐
Járkálás a lakásban	☐	☐
Séta sík terepen szabad levegőn	☐	☐
Lépcsőn felmenni egy emeletet	☐	☐
Séta emelkedőn felfelé	☐	☐
Sportolás vagy fizikai játékok a szabadban	☐	☐

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3 Szakasz

A következő kérdések a <u>mostanában</u> tapasztalt köhögésével és légszomjával kapcsolatosak.

Kérjük, minden állításnál jelöljön meg ***egy négyzetet*** annak megfelelően, hogy ***mostanában*** az Ön esetében az állítás igaz, vagy hamis.

	Igaz	Hamis
A köhögésem fájdalmat okoz	☐	☐
A köhögésem kifáraszt	☐	☐
A beszéd légszomjat okoz	☐	☐
Légszomjam van, ha lehajolok	☐	☐
Köhögésem, vagy légzésem miatt rosszul alszom	☐	☐
Könnyen kimerülök	☐	☐

4 Szakasz

A következő kérdések arra vonatkoznak, hogy légzési problémái <u>mostanában</u> milyen egyéb problémákat okoznak Önnek.

Kérjük, minden állításnál jelöljön meg ***egy négyzetet*** annak megfelelően, hogy ***mostanában*** az Ön esetében az állítás igaz, vagy hamis.

	Igaz	Hamis
Zavar, ha köhögésem, illetve légzési panaszaim más emberek előtt jelentkeznek	☐	☐
Légzőszervi betegségem zavaró a családomnak, barátaimnak, illetve szomszédaimnak	☐	☐
Félelem, vagy pánik lesz rajtam úrrá, ha nem kapok levegőt	☐	☐
Úgy érzem, nem tudom megfelelően kezelni légzőszervi problémáimat	☐	☐
Nem tartom valószínűnek, hogy betegségem javulni fog	☐	☐
Betegségem miatt legyengültem	☐	☐
A testmozgás számomra nem biztonságos	☐	☐
Számomra minden túlságosan megerőltetőnek tűnik	☐	☐

5 Szakasz

A következő kérdések az Ön gyógykezelésére vonatkoznak. Amennyiben nem kap gyógykezelést, térjen át a 6. szakasz kérdéseinek megválaszolására.

Kérjük, minden állításnál jelöljön meg ***egy négyzetet*** annak megfelelően, hogy ***mostanában*** az Ön esetében az állítás igaz, vagy hamis.

	Igaz	Hamis
Gyógykezelésem nem sokat segít rajtam	☐	☐
Zavar, ha nyilvános helyen kell használnom gyógyszereimet	☐	☐
Gyógykezelésem kellemetlen mellékhatásokat okoz	☐	☐
Gyógykezelésem nagymértékben zavarja életemet	☐	☐

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6 Szakasz

A következő kérdések arra vonatkoznak, hogy a napi tevékenységeit milyen mértékben zavarhatja légzése.

Kérjük, minden állításnál, amely **légzése miatt** Önre vonatkozik jelöljön meg (✓) **egy négyzetet**, annak megfelelően, hogy az állítás igaz vagy hamis.

	Igaz	Hamis
Sokáig tart a mosakodás vagy az öltözködés	☐	☐
Sokáig tart, vagy egyáltalán nem tudok fürödni, zuhanyozni	☐	☐
A többi emberhez képest lassabban megyek, vagy közben meg kell állnom pihenni	☐	☐
A háztartási munka vagy hasonló tevékenységek elvégzése sok időmbe telik, vagy közben meg kell állnom pihenni	☐	☐
Ha egy emeletnyit megyek felfelé, lassan kell mennem, vagy meg kell állnom	☐	☐
Ha sietek vagy gyorsan megyek, lassítanom kell vagy meg kell állnom	☐	☐
Légzési problémáim miatt bizonyos tevékenységeket nehezebben végzek, ilyen például a hegymászás, lépcsőn való cipekedés, könnyű kerti munka, mint például a gyomlálás, táncolás, teke, golf	☐	☐
Légzési problémáim miatt bizonyos tevékenységeket nehezebben végzek, ilyen például nehéz teher cipelése, kertásás, hólapátolás, gyors séta illetve kocogás (kb. 8 km/óra sebességgel), teniszezés, vagy úszás	☐	☐
Légzési problémáim miatt bizonyos tevékenységeket nehezebben végzek, ilyenek például a nehéz fizikai munka, futás, biciklizés, gyors úszás vagy kimerítő sport	☐	☐

7 Szakasz

Szeretnénk megtudni, hogy légzési problémái <u>általában</u> hogyan befolyásolják mindennapi életét.

Kérjük, minden állításnál, amely **légzési problémái miatt** Önre vonatkozik jelöljön meg (✓) **egy négyzetet**, annak megfelelően, hogy az állítás igaz vagy hamis.

	Igaz	Hamis
Nem tudok sportolni, vagy fizikai játékokat játszani a szabadban	☐	☐
Nem tudok elmenni szórakozni vagy kikapcsolódni	☐	☐
Nem tudok elmenni otthonról vásárolni	☐	☐
Nem tudom elvégezni a házimunkát	☐	☐
Nem tudok az ágyamtól vagy székemtől nagyobb távolságra elmozdulni	☐	☐

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A Szent György Kórház Légzési Panaszokkal Kapcsolatos Kérdőíve

Felsorolunk még további tevékenységeket, melyek végzésében légzőszervi problémái megakadályozhatják. (Önnek nem kell ezeket bejelölnie, csak emlékeztetik Önt, hogy miben akadályozhatja Önt légzési problémája)

Sétálás vagy kutyasétáltatás

Otthoni vagy kerti teendők végzése

Szexuális aktus

Templomba járás, vagy sörözők, klubok, szórakozóhelyek látogatása

Séta rossz időben, vagy füstös helyen történő tartózkodás

Rokon- vagy barátlátogatás, gyermekekkel való játék

Kérjük írjon le bármi más olyan fontos tevékenységet, melynek végzésében Önt betegsége megakadályozhatja:

. . . . . .

. . . . . .

. . . . . .

. . . . . .

Kérjük, jelölje meg azt a négyzetet (csak egyet), amely legjobban jellemzi, hogy légzési problémái milyen hatással van Önre.

Légzési problémám semmiben sem akadályoz, amit szeretnék csinálni ☐

Légzési problémám egy-két olyan dologban akadályoz, amit szeretnék csinálni ☐

Légzési problémám a legtöbb olyan dologban akadályoz, amit szeretnék csinálni ☐

Légzési problémám minden olyasmiben akadályoz, amit szeretnék csinálni ☐

Köszönjük, hogy kitöltötte ezt a kérdőívet. Kérjük, ellenőrizze, hogy minden kérdést megválaszolt-e.

Hungarian version 6

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12.4. Education content

This chapter demonstrates the education content in a textwise form in Hungarian language in order to provide a better insight into the fixed content conveyed to the patient in each session.[4]

Bevezetés

A legtöbb ember számára a könnyű légzés magától értetődő, természetesen életfunkció. Csak akkor tudatosul bennünk, hogy mennyire kincs a könnyű, szabad légzés, amikor már nehezen kapunk levegőt.

Ha Önnél már COPD-t diagnosztizáltak, akkor bizonyára jól tudja, hogy tudja, hogy nem csupán egy dolog, ami meghatározza a közérzetét, illetve azt, hogy mit és milyen intenzitással tud csinálni. A COPD olyasvalami, ami befolyásolja a környezetében lévő embereket is.

Mi a COPD?

A COPD a krónikus obstruktív tüdőbetegség angol elnevezésének a rövidítése (Chronic Obstructive Pulmonary Disease). A köztudatban dohányos tüdőként vagy dohányos mellkasként szerepel, mert a legtöbb COPD-s jelenleg is aktív dohányos, vagy korábban dohányzott.

C: krónikus vagy idült. Ha már egyszer a betegség kialakult, akkor az már nem múlik el, ezzel együtt kell élnie (angolul Chronic).

O: obstruktív = beszűkült. A tüdőkben lévő légutak beszűkülnek, ami nehezíti a légzést is, de különösen a kilégzést (angolul Obstructive).

P: Tüdővel kapcsolatos (angolul Pulmonary).

D: A betegség szó kifejezésének (Disease) szóból származik. A betegség alatt a speciális jelek és tünetek együttesét értjük (ebben az esetben a tüdő működése nem megfelelő).

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Hogyan működik az egészséges tüdő?

Amikor lélegzünk, a levegőt beszívjuk a tüdőnkbe. A levegő az orrunkon vagy a szánkon keresztül egy széles csőbe, a légcsőbe jut, amely a torkunk hátsó részétől a mellkasunk közepéig húzódik. A légcső ezután két, valamivel vékonyabb csőre oszlik, a jobb és bal főhörgőre, amelyek az elágazás után a jobb és bal tüdőbe lépnek be. Ezt követően mindkét főhörgő a faágakhoz hasonlóan oszlik kisebb és kisebb járatokra, amíg a levegő eljut egészen a tüdőszövetekig, ahol a gázcsere megtörténik.

Ezeken a területeken találhatók az úgynevezett alveolusok, magyarul léghólyagocskák, ezek olyanok, mint apró, levegővel telt zsebek, amelyek miatt a tüdők megjelenése a szivacshoz hasonló. Az alveolusokban tisztul meg a vér a szén-dioxidtól, és frissül fel a levegő friss oxigénjével. Ez a légzés folyamata.

Az egészséges légutak karbantartásáért egyrészt azok az izmok felelnek, amelyek kívülről pányvaszerűen tartják nyitva a légutakat, másrészt a hörgőket belülről bélelő nyákréteg, amely összegyűjti a belégzett porokat és apró részecskéket, majd kimossa azokat.

Mi történik a COPD-s tüdőben?

A COPD hosszú évek alatt alakul ki. Rendszerint a légutak nyálkahártyáját tartósan irritáló kémiai anyagok okozzák, melyeket a cigarettafüsttel vagy szennyezett levegőből lélegzünk be.

1. A por- és füstszemcsék folyamatos izgató hatása miatt a légutak nyálkahártyája károsodik és megduzzad, a beszűkülő légutakon keresztül nehezebben áramlik a levegő a tüdőbe.

[4] The education content was developed in cooperation with Boehringer Ingelheim Hungary, and implemented as an unfunded project. This presented educational content is the intellectual property of Boehringer Ingelheim Magyarországi Fióktelepe.

2. A légúti nyálkahártya nagy mennyiségű váladékot termel, amelyet köpet formájában köhögünk fel.
3. A légutakat körülvevő izmok összehúzódása tovább fokozza a légutak szűkületét, így a tüdőbe lélegzett levegő csapdába kerül, nehezedik annak a kilégzése. Egyre több elhasznált levegő reked a tüdőkben, ezért kevesebb friss levegőt leszünk képesek beszívni.

Mindezek együttes jelenléte miatt a COPD-ben szenvedő emberek gyakran érzik úgy, hogy szorít a mellkasuk, és nem jut elég levegő a tüdejükbe, ezen kívül a fokozott váladéktermelés miatt tartós köhögés is kínozza őket.

Súlyos esetekben a tüdő alveolusai pattanásig feszülnek és sérülnek a beszorult levegő nyomásától, így azok már nem képesek ellátni a feladatukat, a szén-dioxid cseréjét. Ezt az állapotot emfizémának (tüdőtágulatnak) nevezik, amelyhez a betegség súlyosságától függően különböző mértékű légszomj társul.

Jelek és tünetek

Nem minden COPD-s betegnél jelentkeznek ugyanazok a tünetek, de az alábbiakból legalább egy van:

- tartós, nem szűnő köhögés
- produktív köhögés – sűrű köpettel járó köhögés
- zihálás – mely lehet sípoló vagy hangosan hörgő az egyes légvételeknél
- légszomj és nehézlégzés – egyeseknél csak fizikai terhelésre, másoknál viszont már a házimunka során is jelentkezhet
- fáradtság, gyengeség, erőtlenség
- gyakori és nehezen kezelhető légúti fertőzések
- fogyás

Miért lettem COPD-s?

Az Egészségügyi Világszervezet (WHO) becslése alapján világszerte kb. 80 millió ember szenved COPD-ben, amely a negyedik vezető halálok a világon. Ez a szám tovább fog nőni, ha nem hozzák meg azokat a komoly intézkedéseket, amelyek csökkentik a kockázati tényezőket.

A COPD kialakulását fokozza:

- néhány foglalkozás, pl. a szénbányászat
- környezetszennyezés
- öröklődő betegségek

Mi súlyosbítja a COPD-t?

A COPD egy progresszív betegség, ami azt jelenti, hogy az idő előre haladtával folyamatosan romlik a beteg állapota. Bizonyos tényezők képesek felgyorsítani ezt a folyamatot, mint pl. a cigarettafüst gyakori belégzése, elsősorban az aktív dohányzás, de a passzív dohányzás vagy a légszennyezettség is. Amennyiben ezek a tényezők megszűnnek, akkor a betegség romlása is lassulhat. Más tényezők is okozhatnak exacerbációt, azaz a tünetek fellángolását. A súlyos állapotromlás gyakran megelőzhető az alábbi okok kerülésével:

- cigarettafüst (saját vagy másé)
- beltéri légszennyezettség, pl. por, tisztítószerek, hajlakk, erős szagú parfümök, légfrissítők, vagy illatosított gyertyák
- foglalkozási légyszennyezettség, pl. szénpor, kemikáliák, füst, gőz
- kültéri légszennyezettség, pl. szmog, füst, kipufogógáz
- fertőzések, különösen a megfázás, arcüreggyulladás, mellkasi fertőzések, tüdőgyulladás, influenza
- allergia, különösen a háziállatokra és a háziporra
- szorongás, stressz
- időváltozás, extrém hideg és meleg időszak, erős szél, magas páratartalom
- a napi gyógyszeradag használatának elmulasztása

Kezelés

Számos különböző gyógyszer áll rendelkezésünkre a COPD kezelésében. A választás attól függ, hogy milyen tünetek vannak jelen, hogy mennyire súlyos a betegség, illetve hogy az egy adott állapot szinten tartására (fenntartó kezelés) vagy egy hirtelen bekövetkezett állapotromlás (exacerbáció) kezelésére adjuk. Néha az orvos – az aktuális állapotának megfelelően – megváltoztathatja a gyógyszeres kezelést.

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Fenntartó kezelés

Hosszú hatású hörgőtágítók – segítenek nyitva tartani a légutakat azáltal, hogy a légutakat körülvevő izmok összehúzódásának szabályozásával tágítják azokat. A hörgőtágítókat a beteg belélegezheti (ez a leghatékonyabb módszer), vagy tablettaként szájon át is beveheti. A fenntartó kezelésre használt hörgőtágítók rendszerint hosszú hatásúak (4-24 óra), éppen ezért fontos, hogy ezeket rendszeresen kell használni, a kontrollált állapot megtartása érdekében.

Mukolitikumok (köptetők) – segítenek a váladék feloldásában, felszakadásában, ezáltal könnyebb felköhögni. A köptetők használatánál fontos a bő folyadékbevitel.

Szteroidok – belégzéssel vagy tabletta formájában adagolhatóak. A szteroid csökkenti a légúti nyálkahártya duzzanatát és általában hörgőtágítóval kombinálva adják súlyos COPD-ben. Nagyon fontos a szteroid rendszeres használata, még akkor is, ha a beteg jól érzi magát. Amennyiben a beteg abba szeretné hagyni a szteroid használatát, feltétlenül beszélje meg a kezelőorvosával, mert a szteroid hirtelen felfüggesztése súlyos következményekkel járhat.

Oxigén – általában csak azok a súlyos állapotú COPD-sek kapják, akiknek a vére nagyon kevés oxigént tartalmaz. Amennyiben szükséges, akkor az orvosa ellenőrzi a vér oxigéntartalmát, majd az oxigénkezelés megkezdése után megismétli a vizsgálatot, hogy meggyőződjön arról, hogy javított-e az állapotán.

Védőoltások – fontosak annak érdekében, hogy elkerüljük azokat a fertőző betegségeket, amelyek a COPD tüneteinek súlyos romlásához, exacerbációhoz vezethetnek. Általában ajánlott a COPD-s betegek számára az influenza vakcina évenként beadása.

Rövid hatású hörgőtárgítók – a gyors és rövid hatású inhalációs hörgőtágítókat rendszerint a COPD heveny fázisában adják a betegnek. A hatástartamuk 4-6 óra, a légzést könnyítik. Ha a tünetek súlyosak, akkor célszerűbb a hagyományos túlnyomásos aeroszol (spray) helyett gépi porlasztót (inhalátort) használni.

Teofillinek – ritkábban, általában tabletta formájában alkalmazzák a COPD-s tünetek enyhítésére. Lassan tágítják a légutakat, megkönnyítve ezáltal a légzést, és segíthetnek a légutak gyulladásának csökkentésében is. Mivel viszonylag gyakran okozhatnak mellékhatásokat, ezért szükséges a vér teofillin-szintjének rendszeres ellenőrzése.

Rohamoldó terápia

Szteroidok – gyakran adják rövid ideig a tünetek fellángolása esetén, a légúti nyálkahártya duzzanatának csökkentésére.

Oxigén – az akut fellángolás időszakában oxigénmaszkon keresztül adható, ha a vér oxigénszintje alacsony.

COPD-sként élni

Az orvos által előírt gyógyszerek alkalmazása mellett nagyon sok dolog létezik, amit önállóan megtehetünk a tüneteink javítása érdekében, hogy a mindennapi életben jobban érezzük magunkat.

Hagyja abba a dohányzást!

A dohányzás a legrosszabb dolog, amit egy COPD-s tehet. A dohányzás abbahagyásával csökkenthetők a tünetek, lassítható a betegség progressziója és megelőzhetőek a fellángolások. Soha nem késő letenni a cigarettát.

Kérje orvosa tanácsát a dohányzás abbahagyásával kapcsolatban. Néhány ember könnyedén le tudja tenni a cigarettát, ha megérti, hogy a dohányzás már mennyi kárt okozott neki. Másoknak (a többségnek) ez nehezebben megy és rosszul érzik magukat a leszokás kezdetén.

Minden füstmentes nappal könnyebb lesz!

Gondoljon arra, hogy miért dohányzik és azokra a pillanatokra, amikor úgy érzi, rá kell gyújtania – próbálja meg kitalálni, hogyan kezelheti ezeket a helyzeteket dohányzás nélkül! Néhány hasznos módszer másoknak is segített:

- nikotintapasz vagy rágógumi – segítenek csökkenteni a nikotin-megvonás tüneteit

- jutalmazási rendszer – jutalmazza meg saját magát, ha sikerült rágyújtás nélkül eltöltenie az előre kijelölt időt (nap, hét, hónap)
- leszokás saját erőből – jelöljön ki egy napot, amikor abba szeretné hagyni a dohányzást, és hagyja is abba!
- támogató csoport – azok az emberek, akik hasonló helyzetben vannak vagy voltak, segíthetnek a cigaretta letételében. Később Ön is segíthet majd másoknak…
- Kerülje a dohányfüstöt – mások dohányzása is káros hatással lehet az Ön COPD-s tüneteire, illetve arra, hogy meg tudja-e állni, hogy ne gyújtson rá! Kerülje a dohányzásra kijelölt helyeket, vagy kérje meg a dohányzókat, hogy kint dohányozzanak.

A kiváltó okok kerülése

Kerüljön minden olyan anyagot vagy helyzetet, amelyek előidézhetik a COPD-s tüneteinek romlását! Ilyenek a füst, az erős szagok, hajlakk, környezeti légszennyezettség és a stressz. Győződjön meg arról, hogy otthona jól szellőzik, és használjon párásítót, ha nagyon száraz a levegő!

Légzéstechnikák

A légzőgyakorlat a napi rutin része. Ha rendszeresen alkalmazza ezeket a gyakorlatokat, automatikussá válnak, így a későbbiekben képes lesz javítani a légzését a mindennapi tevékenységei vagy a szokásosnál megerőltetőbb feladatainak elvégzése közben. Különböző légzési technikákat ajánlanak a COPD-s betegek számára. A leginkább elfogadott technika az összehúzott ajakkal történő, úgynevezett ajakfékes légzés.

Az ajakfékes légzés alapjai

1. Tegye a kezét csípőre, majd lélegezzen be lassan és mélyen az orrán keresztül.
2. Várjon egy vagy két másodpercet, majd húzza össze ajkait, mint amikor szívószálon keresztül iszik vagy fütyül!
3. Fújja ki a levegőt szép lassan és teljesen összecsücsörített ajkain keresztül, de erőltesse, hogy az utolsó csepp levegőt is kifújja a tüdejéből!
4. Várjon néhány pillanatot, mielőtt újrakezdené a gyakorlatot!

5. Néhány embernek akkor is segít ez a légzéstechnika, amikor fulladnak vagy stresszes állapotban vannak.

Testtartás

Ülő vagy álló testhelyzet is segítheti a maximális tüdőkapacitás (a legnagyobb belélegezhető levegőmennyiség) elérését. Ha görnyedten ül, vagy hajlottan áll, akkor a tüdő befogadóképessége csökken, és így nehezebben tudja teleszívni a tüdejét levegővel. Helyes testtartás mellett javul a közérzete és légzése is könnyebbé válik. Fulladás esetén bizonyos testtartásokat használva javíthat a légzésén. Válassza azt a pozíciót, amelyik az Ön számára a legkényelmesebb!

Ülő testhelyzet

Helyezze a lábait a földre (telitalppal), és tartsa a hatát a legegyenesebben, pihentesse az állát a kezein, vagy tegyen egy párnát az asztalra és fektesse rá karjait és fejét! Figyeljen a légzésére, és próbálja minél hosszabbra nyújtani a légézését!

Álló testhelyzet

Próbáljon kissé előrehajolni, kapaszkodjon az asztalba, vagy a szék háttámlájába! Ha nincs semmi, amiben kapaszkodni tudna, akkor helyezze a kezét a combjára és dőljön egy kicsit előre! Majd ugyanúgy, mint az ülő testhelyzetben, próbálja meg kontrollálni a légzését!

Étrend

- Gondoskodjon a bő folyadékbevitelről, lehetőleg koffein- és alkoholmentes italokat fogyasszon, amelyek segítenek feloldani a váladékot!
- Az egészséges, kiegyensúlyozott étrend bővelkedik fehérjében (sovány húsok, halak), energiadús, így kevésbé érzi magát fáradtnak.
- Próbáljon többször kis adagban étkezni, így elkerülhető a puffadásérzés, illetve az étkezéskor jelentkező fulladás!

Testmozgás

- A testmozgás az egészséges életvitel része, amelyet be kell építenie a napi tevékenységei közé!

- Válassza ki az Önnek legmegfelelőbb mozgásgyakorlatokat, amelyek elvégzése élvezetet nyújt. Nem csak a hangos edzőtermekben lehet nagy hatásfokú zsírégető gyakorlatokat végezni!
- Tűzze ki célul, hogy minden nap tornázzon egy kicsit!
- A légzésrehabilitáció vagy edzésprogram nagyon hasznos a legtöbb COPD-s beteg számára és a gyakorlatok otthon is kivitelezhetőek.
- Próbálja úgy végezni a légzőgyakorlatokat, hogy ne fulladjon ki túlságosan!

Pihenés

- A relaxációs technikák segíthetnek megnyugtatni a légzést, tágítják a tüdőt és megelőzik a stressz által okozott tüneteket, illetve állapotromlásokat.
- Ajakfékes légzéssel is könnyítheti a légzését.
- Másik hasznos módszer, ha szemeit lecsukva elképzel egy pozitív, megnyugtató képet és közben fej-, nyak- és vállmozgásokat végez, amelyek csökkentik a feszültséget. Keressen egy csendes, nyugodt helyet, ahol leülhet és megpihenhet egy kicsit!

Fertőzések megelőzése

- Próbálja meg kerülni a megfázott embereket, vagy azokat, akik köhögnek! Sok fertőzést meg tud előzni azzal, ha rendszeresen kezet most szappannal és vízzel, vagy kézfertőtlenítő folyadékot tart magánál, ha elmegy otthonról!
- Figyeljen arra, hogy rendszeresen megkapja a szükséges védőoltásokat! Ha nem biztos abban, hogy megkapta azokat, kérdezze meg kezelőorvosát!

Maradjon pozitív

Jó élni. Ne feledje:

- Kérje és fogadja el orvosa segítségét a dohányzás elhagyásában, a védőoltások felvételében, előzze meg a fertőzéseket, ismerje föl és enyhítse a hirtelen fellángoló tüneteket!
- Szedje gyógyszereit az előírtaknak megfelelően!
- Válasszon egészséges terhelések és stresszhelyzetek kezelésére!

- Éljen jól! – COPD-sként is aktív maradhat. Működjön együtt az orvosával, együtt sikerülhet!

Gyakran feltett kérdések

Mit tehetek, ha hirtelen fulladni kezdek?

Próbálja meg alkalmazni az ajakfékes légzési technikát! Keresse meg az okát, mitől alakulhatott ki a hirtelen fulladás és próbálja megszüntetni azt! Például, ha testmozgást vagy más fizikai tevékenységet végez, akkor függessze fel azokat, amíg légzése helyreáll! Ha füstös helyen van, akkor hagyja el mielőbb!

Mikor kell orvoshoz fordulnom?

Ha Ön sokkal rosszabbul érzi magát a szokásosnál, felmerül a légúti fertőzés lehetősége. Ha megváltozott a légzése, esetleg erősödött a köhögése, akkor mielőbb keresse fel az orvosát!

Mikor kell kórházba mennem?

Ha légzése hirtelen rosszabbodik, vagy ha úgy érzi, nem kap elég levegőt, akkor sürgős kórházi kezelésre van szüksége. Fontos, hogy legyen valaki, aki elviszi Önt a kórházba vagy értesíti a mentőt. Ön próbálja meg megőrizni a nyugalmát, amennyire csak lehet. Ha pánikba esik, az csak tovább súlyosbítja a tüneteit.

Elmehetek nyaralni?

A nyaralás egy nagyszerű alkalom a kikapcsolódásra. Beszélje meg orvosával és ellenőrizze, hogy van-e elegendő gyógyszere a hazaérkezésig. Ha messzebbre utazik, kérdezzen rá, hogy kell-e másik védőoltást kapnia előtte! Ha Ön repülőgépen fog utazni, és oxigénre van szüksége, akkor ezt foglaláskor jelezze a légitársaság felé, és ellenőrizze a magával vitt oxigénpalackra vonatkozó előírásokat! Ne feledje repülés során magánál tartani a gyógyszereit, még ha csak rövid ideig utazik is, mert a poggyászok elveszhetnek! Gondoskodjon arról, hogy távolléte alatt egészségbiztosítása fedezze az esetleges orvosi ellátás költségeit, ha a tünetek fellángolása miatt rászorulna.

Élhetek normális szexuális életet?

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Csak azért, mert Ön beteg, nem kell feladni az élet örömeit. Ön nyugodtan folytathatja az eddigi szexuális életét, de bizonyos dolgokhoz alkalmazkodnia kell. Például használjon más testhelyzeteket, diszkréten végezzen légzésgyakorlatokat a szexuális aktus előtt vagy közben, megelőzvén ezzel a fulladást, tapasztalja ki a lehetőségeket, melyekkel energiáját, erőnlétét leginkább meg tudja őrizni! A legfontosabb, hogy beszélje meg partnerével, mennyiben korlátozza Önt a betegsége és ez milyen hatással lehet a viszonyukra!