

# **Medication adherence, quality of life and health burden in chronic obstructive pulmonary disease**

**Ph.D. THESIS OUTLINES**  
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## **Summary**

Chronic obstructive pulmonary disease (COPD) is considered to be a major public health problem worldwide.

In the course of my researches, I measured the health related quality of life and the medication adherence in patients with COPD, identified the relationship between these two factors and estimated the overall health burden of COPD in Hungary.

My study reinforced that COPD impairs the patients' quality of life markedly and that non-adherence to medication regimens is a significant problem in the management of COPD.

My results suggest that the quality of life measurement could help the early diagnosis of COPD, the long-term management of COPD and the improvement of medication adherence. In my study, adherence was associated with age, current smoking status, quality of life, number of respiratory drugs, number of daily respiratory drug doses. Better quality of life may be considered a trigger for non-adherence. Therefore, quality of life monitoring within routine clinical practice would aid in the improvement of adherence. My study confirms that beside SGRQ, EQ-5D is also a reliable and valid method to assess the quality of life in patients with COPD. Practical significance of my results is that due to the simplicity of EQ-5D questionnaire; this instrument can be used more easily than the disease-specific SGRQ within routine clinical practice.

COPD results in considerable health burden for the Hungarian society. In the background of the health burden of COPD, beside the quality of life decrement, high prevalence and mortality of COPD also play a considerable role.

In summary, consideration of quality of life and medication adherence within routine clinical practice could optimize the management of COPD patients, which would lead to the decrease of disease burden of COPD in the long run.

## **1. Introduction**

Chronic obstructive pulmonary disease (COPD) is considered to be a major health problem in industrialized and developing countries.

COPD impairs the patients' quality of life markedly; limits patients' physical efficiency, workplace-, social- and free-time activities.

Poor adherence in patients with COPD is common, which significantly reduces the clinical benefit of the therapy. Non-adherence is a multidimensional phenomenon; it frequently occurs because of a variety of reasons. These include factors that are related to the characteristics of the patient, the disease, characteristics of the therapies, as well as the doctor-patient relationship. It is necessary to identify factors impacting adherence to improve patient's drug taking behaviour.

Although quality of life and medication taking behaviour have both been studied intensively, less is known about the association between these factors. Only a few trials have so far investigated the association of adherence with quality of life, therefore further studies are needed to identify the relationship between these two factors.

## **2. Objectives**

The aims of this research were to assess the quality of life and medication adherence in COPD patients, to identify the relationship between these two factors and to estimate the overall health burden of COPD in Hungary.

- 1.** Assessment of the quality of life and medication adherence in COPD patients.
  - a.** Measurement of the quality of life and identification factors related to the quality of life in patients with COPD.

I analyzed:

- i.** the relation between the general and disease-specific quality of life and disease severity,
- ii.** the effect of age, gender, lung function and medication adherence on the quality of life,
- iii.** the correlation between the general and disease-specific quality of life measurement methods.

- b.** Evaluation of the medication adherence and assessment of factors with possible impact on adherence in COPD patients.
  - i.** I analyzed the effect of gender, age, disease severity, lung function, current smoking status, number of respiratory drugs, number of daily respiratory drug doses, cost of COPD medication and quality of life on medication adherence.
- 2.** Defining the health burden of COPD in Hungary and comparing it with the health burden of other chronic illnesses.

I analyzed:

- i.** the quality of life decrement in patients with COPD, asthma and rheumatoid arthritis (RA) compared to the quality of life's data of general Hungarian population,
- ii.** the health burden of COPD, asthma and RA in Hungary.

### **3. Methods**

1. This was an observational, cross-sectional study carried out in the Pulmonary Unit of the St. Borbála Hospital and Outpatient Clinic (Dorog). Four general practitioners and one pulmonologist participated in the study. The study was approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics.

Subjects included were diagnosed with COPD at least one year prior, were over 40 years of age and received ongoing COPD medication. Patients were excluded if they had a history of asthma, allergic rhinitis, lung operation or other respiratory disease; a serious concomitant diseases, such as serious heart failure, serious liver or renal failure; an acute coronary syndrome or acute cerebrovascular disease in the last 3 months; or if there has been any modification to their COPD drug treatment during the last 3-month period. The enrolment period occurred between March and November of 2009, and the planned number of subjects was 250.

All of the patients gave written consent to participate in the study after receiving a detailed description of the study. For each patient, who was enrolled, the physician recorded the age, gender, current smoking status and the currently prescribed respiratory therapy. The examination included a post-bronchodilator spirometry and completion of the self-reported postal questionnaire. The questionnaire consisted of three parts: the Morisky Medication Adherence Scale (MMAS – medication adherence questionnaire), the St. George’s Respiratory Questionnaire (SGRQ – disease-specific quality of life questionnaire) and the EuroQol (EQ-5D – general quality of life questionnaire). The above-listed instruments were used with previous authorisation of their owners. The deadline for the submission of the postal questionnaires was January 31, 2010.

**2.** The quality of life data (EQ-5D index), for the health burden calculation, came from previous observational, cross-sectional clinical studies of the University Pharmacy Department of Pharmacy Administration, Semmelweis University (Department of Pulmonology, Semmelweis University, Budapest (asthma, COPD);

Pulmonary Unit of the St. Borbala Hospital and Outpatient Clinic, Dorog (COPD); and the Rheumatology Unit of Polyclinic of the Hospitaller Brothers of St. John of God, Budapest (RA)). The data of 869 patients were analyzed (402 with asthma, 214 with COPD and 253 with RA). All of the studies were approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics.

The health burden of the disease, expressed in QALYs (Quality Adjusted Life Years), was calculated by adding the health loss due to decreased quality of life (overall health loss) and health loss due to disease specific mortality (overall years of life lost). Overall health loss due to decreased quality of life was estimated by multiplying the number of patients with the EQ-5D index decrement. Overall years of life lost was calculated by multiplying age/disease/gender specific crude mortality with age/gender specific life expectancy, age/disease/gender specific EQ-5D index and the number of inhabitants in the age cohort. The health burden calculation was limited to the Hungarian population aged between 45 and 84. EQ-5D index values for the general



population were obtained from a Hungarian health interview survey (OLEF 2000); age and gender specific prevalence and other demographic inputs came from the database of Hungarian Central Statistical Office; age and gender specific from World Health Organization (2009).

#### **4. Results**

**1.** A total of 250 patients were asked to participate in the cross-sectional study described above. Of the 250 patients, 23 refused to participate. The remaining 227 patients were included at the baseline. A total of 176 participants completed the study and sent back the self-reported postal questionnaire (77,5% response rate). Of these responses, 170 were usable, as 6 had to be excluded because of one or more unanswered items.

There were more female (58,2%) than male patients among the respondents. The mean age of the group was 63,83 (SD 11,24) years. Three-quarters of the patients were current smokers (72,9%). The prevalence of GOLD Stage II was more than 50% in the study population, the average FEV<sub>1</sub> of the patients was 64,21% (SD 17,34). The mean number of daily respiratory drugs was 2,03

(SD 0,99), the mean number of daily respiratory drug doses was 5,58 (SD 3,18) and the average COPD medication costs per month paid by the patient was 1427,71 Ft (SD 1062,34). The mean EQ-5D index score of the patients was 0,55 (SD 0,21), the mean SGRQ total score was 56,22 (SD 16,19). Taken together, 58,2% of the participants reported themselves to be adherent to respiratory therapy.

**a. i.** The quality of life decrement of COPD patients increased proportionally with the progression of the disease.

**ii.** Based on univariate (Pearson's correlation analysis, ANOVA) and multivariate (ANCOVA) statistical analyzes quality of life was significantly associated with age and lung function. Quality of life was strongly correlated with age; relation between quality of life and lung function was only moderate. Medication adherence was not an independent predictor of quality of life.

**iii.** My result showed strong correlation between EQ-5D index and SGRQ total score.

**b.** Based on univariate (Pearson's  $\chi^2$  test, ANOVA) and multivariate (logistic regression) statistical analyzes age, current smoking status, number of respiratory drugs, number of daily respiratory drug doses and quality of life (EQ-5D index) were found to be independent predictors of adherence in COPD patients.

**2. i.** Measured with EQ-5D, asthma, COPD and RA patients tend to have worse quality of life than Hungarian population in the same age cohort. Comparing the examined diseases, between the age of 45 to 74 RA was associated with the highest decrease in the quality of life, between the age of 75 to 84 asthma and COPD impaired the patient's quality of life the most. My results did not show significant differences between the two respiratory disorders regarding the quality of life.

**ii.** Based on my estimates, in 2009 COPD, asthma and RA had a total health burden of 66 911, 20 905 and 10 660 QALYs concerning the total patient population in Hungary aged between 45 to 84, respectively. QALY loss was primarily due to the decrement of quality of life in the case of asthma and RA; while in COPD, QALY loss was mainly due to disease specific mortality.

## **5. Conclusions**

**1. a.** COPD impairs the patient's quality of life markedly. Quality of life measurement may be used as a non-invasive patient-centered monitoring system in the management of COPD. My results suggest that quality of life measurement could help the early diagnosis of COPD and the long-term management of COPD.

My study confirms that SGRQ and EQ-5D are both reliable and valid methods for the assessment of quality of life in patients with COPD; there was a strong correlation between EQ-5D index and SGRQ total score. The practical significance of my results is that due to the simplicity of EQ-5D questionnaire; this instrument can be used more easily than the disease-specific SGRQ within routine clinical practice.

**b.** The present study indicates that the level of adherence to respiratory therapy is quite low. The adherence rate of 58.2% identified in this sample is consistent with the results of previous studies that evaluated self-reported adherence in COPD.

Understanding factors associated with adherence to medication could help in enhancing health outcomes in

COPD. In our study, adherence was associated with age, current smoking status, number of respiratory drugs, number of daily respiratory drug doses and quality of life and was not related to gender, cost of COPD medication per month paid by the patient, GOLD stages or FEV<sub>1</sub>.

Middle-aged and/or smoking patients should be given special attention by their physicians, as the non-adherence rate is high in these populations. Our findings suggest that using less frequent dosing regimens could be an effective method for enhancing adherence to respiratory therapy.

Higher EQ-5D scores were negatively correlated with adherence. Patients may neglect taking their medication when feeling well. This neglect can lead to a higher quality of life, which could be a predictor of non-adherence. In the short-term, the improvement in the quality of life should be greater than what would be expected from the optimal adherence. Therefore, quality of life monitoring within routine clinical practice would aid in the improvement of medication adherence and the health outcomes in COPD patients.

2. COPD, asthma and RA impair the patients' quality of life markedly. The relative quality of life decrement is, however, different in each observed disease. In the study, RA was associated with significantly lower quality of life compared to the respiratory diseases.

The health burden of COPD was much higher than the QALY loss caused by asthma and RA. In the background of the health burden of COPD, beside the quality of life decrement, high prevalence and mortality of COPD also play a considerable role.

Age and quality of life (EQ-5D index) data related to specific diseases are essential inputs for health economic models.

In summary, consideration of the quality of life and medication adherence within routine clinical practice could optimize the management of COPD patients, which would lead to the decrease of disease burden of COPD in the long run.

## **6. Publications by the Ph.D candidate**

### **Scientific books and chapters related to the thesis**

1. Ágh T, Mészáros Á. Adherence to therapy in chronic obstructive pulmonary disease. In: Kian-Chung Ong (szerk.). Chronic Obstructive Pulmonary Disease - Current Concepts and Practice. InTech, Rijeka, 2012: 275-290. ISBN:978-953-51-0163-5

### **Peer-reviewed scientific publications related to the thesis**

1. Inotai A, Ágh T, Mészáros Á. (2012) Quality of life, utility and health burden in asthma, chronic obstructive pulmonary disease and rheumatoid arthritis. Int J Pers Cent Med, 2:505-510.
2. Inotai A, Rojkovich B, Fülöp A, Jászay E, Ágh T, Mészáros Á. (2012) Health related quality of life and utility in patients receiving biological and non-biological treatments in rheumatoid arthritis. Rheumatol Int, 32:963-969. **IF: 1,431**
3. Ágh T, Inotai A, Mészáros Á. (2011) Factors associated with medication adherence in patients with chronic obstructive pulmonary disease. Respiration, 82: 328-334. **IF: 2,543**

4. Ágh T, Mészáros Á. (2010) Compliance and persistence with medications for chronic obstructive pulmonary disease. Clin Exp Med J, 4: 15-22.
5. Ágh T, Bodnár R, Ágh L. (2010) Az életminőség-mérés szerepe asztmás betegek gondozásában. Med Univ, 43: 179-181.
6. Orosz M, Gálffy G, Kovács D, Ágh T, Mészáros Á. (2010) Az asthmás és COPD-s betegek életminőségét befolyásoló tényezők [Quality of life, possible influential factors of asthmatics and COPD patients]. Med Thorac, 63: 277-283.
7. Ágh T, Mészáros Á. (2010) A terápiahűség egészség-gazdaságtani szempontjai [Pharmacoeconomic impact of compliance]. Acta Pharm Hung, 80: 75-80.
8. Ágh T, Mészáros Á. (2009) Terápiás compliance és perzisztencia a krónikus obstruktív tüdőbetegség gyógyszeres kezelésében [Compliance and persistence with medication in chronic obstructive pulmonary disease]. Orv Hetil, 150: 1497-1502.



9. Ágh T, Ágh L. (2009) A beteg-együtműködés jelentősége hypertonia, diabetes mellitus, dyslipidaemia gyógyszeres kezelésében. Med Univ, 42: 3-6.

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