Development and Validation of the new McGill COPD Quality of Life Questionnaire

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Abstract:

Introduction: There is a need for a health-related quality of life questionnaire in COPD that fulfills the advantages of both, generic and disease-specific questionnaires. Objective: To finalize the development of a new, hybrid questionnaire (disease-specific items supplemented with items from the SF-36), the McGill COPD Quality of Life Questionnaire and to evaluate its psychometric properties (reliability, validity, responsiveness) in COPD subjects. Method: With pre-defined criteria, we selected items from the SF-36 to complement the previously developed COPD-specific module. Exploratory factor analysis was performed on these items (combined SF-36 items and those from the COPD-specific module) to identify domains of the new hybrid questionnaire. A prospective cohort, involving 4 hospitals in Québec with COPD subjects who underwent pulmonary rehabilitation, participated in the validation of the new questionnaire. Evaluation included the St. Georges Respiratory Questionnaire, SF-36 & COPD-specific module, and pulmonary function at baseline (pre-), post-rehabilitation, & yearly thereafter for 3 years. Results: The McGill COPD Quality of Life Questionnaire is available in English and French; it assesses three domains: symptoms, physical function and feelings and has 29 items. For the validation, we evaluated 246 COPD subjects (111 females). Subjects had a mean age of 66 years; 87% were ex- and 8% current smokers (mean: 61 pack-years); mean FEV_1 was 1.12 L (GOLD stages: II-27%, III-33% and IV-37%). There was less than 2% missing data and the floor and ceiling effects were less than 5%. The internal consistency (Cronbach's α) of the new scale was 0.68-0.82. Intraclass correlation coefficient for reliability was 0.74-0.96 for the sub-scales and 0.95 for the total score. Correlation of the new scale with the SGRQ, was moderately high (r=-0.88, 95% CI: -0.91 to -0.84), consistent with the a priori hypothesis for convergent validity. We evaluated responsiveness by the extent to which the new scale could detect the change in health status after rehabilitation. The effect size was 0.33 (pre-post rehabilitation mean score difference of 6), suggesting a moderate change. Conclusions: The new McGill COPD Quality of Life Questionnaire showed high internal consistency, reliability, convergent validity, and moderate responsiveness in COPD subjects.

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Abrégé:

Introduction: Il y a nécessité d'avoir accès à un questionnaire de qualité de vie qui pourrait offrir les avantages d'un questionnaire générique et ceux d'un questionnaire spécifique à la MPOC. Objectif: Finaliser l'élaboration d'un nouveau questionnaire hybride le 'McGill COPD Quality of Life Questionnaire' (éléments spécifiques à la maladie complémentés d'éléments génériques issus du SF-36) et évaluer ses propriétés psychométriques (fiabilité, validité, réponse au changement) chez les sujets atteint d'une MPOC. Méthodologie: Des items du SF-36 ont été sélectionnés à partir de critères prédéfinis. Une analyse factorielle préparatoire fut effectuée à partir des items sélectionnés du SF-36 et de tous les items du module spécifique à la MPOC développé antérieurement pour identifier les domaines du nouveau questionnaire hybride. Une cohorte prospective de patients ayant participé à un programme de réadaptation, impliquant 4 hôpitaux du Québec, ont été utilisée pour la validation du nouveau questionnaire. L'évaluation a inclus plusieurs questionnaires (St. Georges Respiratory Questionnaire, SF-36 et module spécifique à la MPOC), des tests de fonction pulmonaire en pré et post réadaptation, et annuellement pour 3 ans. Résultats: Le 'McGill COPD Quality of Life Questionnaire' est disponible en français et en anglais; il évalue trois domaines : symptômes, fonction physique et émotionnelle et contient 29 items. Pour sa validation, 255 sujets avec MPOC ont été évalués (111 femmes). L'âge moyen était de 66 ans; 87% étaient des anciens fumeurs et 8% des fumeurs courants (moyenne: 61 paquets-année); le VEMs moyen était de 1.12 L (échelle de sévérité: GOLD II-27%, III-33% et IV-37%). Moins de 2% des données étaient manquantes et les effets « plancher et plafond » étaient de moins de 5%. La cohérence interne (Cronbach's α) était de 0.68-0.82 ; la corrélation intra classe pour la fiabilité était de 0.74-0.96 pour les sous-échelles et 0.95 pour le score total. La corrélation du nouveau questionnaire avec le SGRQ était modérément élevée (r=-0.88, 95% CI: -0.91 to -0.84), correspondant à notre hypothèse à priori concernant la validité concourante. La réponse au changement fut évaluée en mesurant jusqu'à quel point la nouvelle échelle pouvait détecter les changements de l'état de santé après réadaptation. L'ampleur de l'effet était de 0.33 (différence moyenne de 6), suggérant un changement modéré. Conclusions: Le nouveau questionnaire 'McGill

COPD Quality of Life' a démontré un haut niveau de cohérence interne, de fiabilité, de validité concourante et de réponse au changement chez les sujets atteints d'une MPOC.

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Preface

Quality of life and health related quality of life (HRQL) is gaining more importance day-by-day in the clinicians', researchers' and policy makers' minds. HRQL is an important outcome measure in Chronic Obstructive Pulmonary Disease (COPD), for which there currently is no known cure. COPD has tremendous impact on the day-to-day lives of the patients however; measuring this impact is a tedious task. The physiological and functional measures available today are not sensitive enough to capture the impact of COPD on one's life. Thus, the measurement tools like quality of life questionnaires become even more important. Commonly two or more HRQL questionnaires are administered concurrently to capture the impact of COPD, its co-morbidities and treatment side-effects. Generic questionnaires capture general health issues as well as co-morbid conditions and side effects of treatment. Although the generic questionnaire allows for comparison across different diseases, it may be insensitive in detecting small changes in the patients' condition {Guyatt, 1999 84 /id} {Mahler, 2000 63 /id}. On the other hand, the disease-specific questionnaires focus on relevant aspects of disease specific issues and hence, are responsive to small changes in the patients' condition. Thus, both types of questionnaires, generic and disease-specific, have strengths and weaknesses.

Administration of many questionnaires to the already debilitated patients of COPD is tiresome, expensive and could potentially reduce participation rate. Thus, there is a need of having a tool which is short, self-administered, easily understood and most importantly self sufficient, so that there is no need of administration of any supplementary questionnaires. This study was thus envisioned a few years ago to design such a novel questionnaire. Thus far, our group has completed the development and validation of a COPD-specific module {Spahija, 2000 253 /id}. This COPD-specific module needs to be co-administered with Medical Outcomes Study Short Form-36 (SF-36). This study is a continuation of this development process. We have designed a novel questionnaire which is self-sufficient, short, self-administered, easily understood and available in English and French. We hope this novel tool stands the test of the time and serves the purpose for which it was envisioned.

Contribution of Authors

Many steps were involved in development of this project. A protocol was written by Dr. Smita Pakhale with the help of Dr. Jean Bourbeau and Dr. Sharon Wood-Dauphinee. Development of the new McGill questionnaire was done by Dr. Smita Pakhale, Dr. Adriana Spahija, Dr. Jean Bourbeau and Dr. Sharon Wood-Dauphinee. Dr. Jean Paul Collet had envisioned and designed the study early on. Ethics approval, recruitment of subjects was done under supervision of Dr. Jean Bourbeau, Dr. Francois Maltais, Dr. Marc Baltzan and Dr. Michel Rouleau as part of the Respiratory Health Network of the FRSQ. The study was centrally coordinated by Sarah Bernard (provincial coordinator of the COPD axis of the RHN of the FRSQ), which involved data base development and management. Statistical analysis was done by Dr. Smita Pakhale. Dr. Smita Pakhale wrote the manuscript with editing done by Dr. Jean Bourbeau, Dr. Sharon Wood-Dauphinee and Dr. Jadranka Spahija.

Organization of the thesis:

This manuscript based thesis is organized in five chapters. The first chapter covers the introduction of COPD and importance of health related quality of life in COPD.

Chapter 2 provides a literature review on chronic obstructive lung disease epidemiology and comprehensive assessment, what is quality of life, health-related quality of life, why and how we should measure quality of life in COPD, and the steps in developing and validating a measure.

Chapter 3 focuses on study rational, research question, general and specific objectives, and hypotheses of the study.

Chapter 4 presents the manuscript within this thesis. It is formatted according to the requirements of the "American Journal of Respiratory and Critical Care Medicine". It includes an introduction with the general and specific objectives of the study, a description of the methods in development and validation process of the new questionnaire and analysis. Then the manuscript summarizes the results obtained and

discuses them. This chapter ends with the limitations of the study and main conclusions. Acknowledgements are finally given, followed by the results table.

Chapter 5 summarizes the findings and conclusions of the project, describes the limitations and suggests areas of future research.

The appendices contain information of interest.

Due to the manuscript format and in order to follow the regulations of the Graduate and Postdoctoral Studies of McGill University, there is some duplication of material throughout the thesis.

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Chapter I

Introduction:

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality worldwide. Chronic symptoms like gradually progressing dyspnea on exertion, cough and phlegm have a debilitating impact on quality of life as it relates to health. It is a fourth leading cause of death in North America. The most important risk factors for COPD are smoking, environmental and occupational pollution. Though COPD is preventable and treatable, it is still not curable.

Assessing the impact of the disease is of great importance to guide the management of COPD, to evaluate the quality of various clinical programs and the benefit of a new treatment as part of a clinical trial. Traditionally this has been done using physiologic measurements. Although physiologic measurements provide information to clinicians, they are of limited interest to the patients; furthermore, they often correlate poorly with functional capacity and patient well-being. Hence, measuring quality of life with the help of a patient reported questionnaire is of immense importance in COPD. Moreover, COPD subjects' perception of disease severity does not necessarily match with the physicians' intuitive assessment.

Patient reported health status outcomes are measured with the help of two types of instruments: generic and disease-specific questionnaires. Generic questionnaires capture general health issues, co-morbidities, treatment side-effects etc. Being generic, they allow cross-condition comparison and comparison across different populations. However, because of their generic nature, they are less sensitive to small changes in a patient's condition due to the specific disease. Hence, disease-specific questionnaires are needed to capture small changes. The disease-specific questionnaires, however, have specific, focused questions pertaining to the disease, and hence, do not allow comparisons across

different diseases. As generic and disease-specific questionnaires have strengths and weaknesses, they are often administered together.

COPD subjects often have co-morbid conditions, and also may suffer from side-effects of the treatment. Hence, commonly generic and disease-specific questionnaires are administered together. However, administration of two questionnaires is time consuming, tedious to the patient, expensive and can increase non-participation. Moreover, the most commonly used disease-specific questionnaires in COPD have limitations such as a time consuming administration process requiring expert staff personnel, too many items, the possibility of reduced sensitivity due to yes/no questions, a lack of predictive power etc. Hence, it would be of great value if we had a novel questionnaire of health-related quality of life (HRQL) which would be sensitive to small change, easily administered, easily understood, short and most importantly combines the advantages of generic and disease-specific questionnaires.

Thus the global objective of this research is to finalize the development of a hybrid questionnaire (disease-specific items supplemented with generic items of the SF-36), the McGill COPD quality of life questionnaire, and to evaluate its psychometric properties (reliability, validity, responsiveness) in patients with moderate to severe COPD.

Chapter II: Literature Review

2.1 Chronic Obstructive Pulmonary Disease (COPD)

2.1.1 Definition and diagnosis of COPD

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines COPD as follows[1]: "COPD is a preventable and treatable disease with some significant extra pulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases." COPD is caused by exposure to cigarette smoke, or occupational and environmental dusts and gases[2].

Subjects with COPD present with exertional dyspnea, the most common early symptom, and chronic cough and sputum. As the dyspnea progresses subjects often unknowingly avoid activities causing dyspnea and eventually become sedentary. The chronic cough is characterized by insidious onset of mucoid sputum production[3]. COPD subjects may experience acute exacerbations with increased cough, purulent sputum, wheezing with or without fever. Thus, COPD being a chronic disease causes physical impairment, debility, reduced quality of life and death.

According to the American Thoracic Society and the European Respiratory Society (ATS/ERS) task force, objective demonstration of air flow obstruction by spirometry is mandatory for the diagnosis of COPD[2]. Though spirometry is useful, it does not substitute clinical judgment in the evaluation of the severity of disease in individual patients.

2.1.2 Epidemiology of COPD

The worldwide prevalence of COPD is 10.1± SE=4.8% overall (11.8±7.9% for men and 8.5±5.8% for women)[4]. COPD is also the fourth leading cause of death, following heart disease, cancer and stroke. Mortality due to heart disease and stroke, however, has decreased significantly between 1970 and 2002(32% and 52% respectively), while COPD mortality has increased exponentially (102.8%)[5]. In the United States alone, the estimate of the total (direct and indirect) annual cost of COPD is $38.9 billion in 2005 US dollars, according to the National Heart, Lung and Blood Institute (NHLBI)[6]. A fairly recent survey showed that the annual per patient cost of COPD in Canada is CA$3195.97 [7]. Similarly, it is a major cost to the health care systems in other western developed countries; Spain reports €3238 [8], Italy €1261.25[9], UK £1639.08 [10], and the Netherlands €1024[11]. Also in Japan, the estimated total cost of COPD is $6.8 billion US dollars annually[12;12]. COPD is, thus a predominant cause of morbidity and mortality and hence health care utilization across the globe.

2.1.3 Comprehensive assessment of COPD

Stratification of disease severity is usually done with the help of post-bronchodilator FEV_1. Though FEV_1 measurement is necessary for diagnostic purposes and for follow-up of the disease, FEV_1 correlates poorly with symptom intensity, exercise capacity and health related quality of life[3;13;14].

Thus, evaluation within the domains of impairment, activity limitation and participation restriction [15] captured by HRQL is essential for characterization of COPD. Moreover, physicians rarely rely on FEV_1 thresholds to make therapeutic decisions. It is very well accepted and recommended from guidelines that treatment effectiveness should be based on assessment of patient-perceived outcomes rather than on spirometry alone[2]. Therefore, measurement of HRQL is important, both in clinical practice and in a research setting. Moreover, exposure to long term smoking and pollution increases the prevalence of COPD in middle-aged individuals. COPD patients often exhibit other co-morbid conditions related to lifestyle activities, natural aging or systemic effects of COPD [16;17]. HRQL questionnaires are often used to capture the impact of both the co-morbidities and

systemic effects of COPD. Given the incurable nature of COPD, HRQL scores can be used as a measure of treatment outcome. .

2.2 Health Related Quality of Life

2.2.1 Health status vs. health related quality of life:

The World Health Organization has defined health as[18], " a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity." This definition has not been amended since 1948. Moreover, this definition has been criticized for its limitations as it does not differentiate between health and happiness[19]. Although happiness and quality of life have an inherent meaning to most people, they are subjective and difficult to define. Quality of life (QOL) is comprised of broad concepts that affect global life satisfaction, including good health, adequate housing, employment, personal and family safety, education, and leisure pursuits[20].

The concept of quality of life, when applied to matters related to health care, specifically to those life concerns that are most affected by health or illness, is referred to as "health related quality of life" (HRQL)[20]. The term health-related quality of life is widely used because, the widely valued aspects of life exist that are not generally considered as "health", including income, freedom, and quality of the environment[21]. Moreover, in the presence of illness or disease, almost all aspects of life can become health related.

Health-related quality of life is an important outcome of clinical care and of many research studies. Clinicians and policy makers have recognized the importance of measuring health-related quality of life, in order to make informed patient management and policy decisions[21]. The Food and Drug Administration (FDA) of USA has published guidelines in February 2006 for patient reported outcomes (PRO) [22]. The three main reasons for using PRO as stated by the FDA are as follows: *some treatment effects are known only to the patient, patients provide a unique perspective on treatment*

effectiveness, and formal assessment may be more reliable than informal interview. Health-related quality of life questionnaires thus are important in measuring outcomes such as treatment effects, prognosis, and predicting mortality and morbidity. Moreover, using PRO integrates the traditional "biomedical model" of health with the "social science or quality of life model."

2.2.2 Measurement of health-related quality of life in COPD:

As noted earlier, there are two types of health-related quality of life questionnaires: generic and disease-specific. Generic questionnaires capture general health issues as well as co-morbid conditions and side effects of treatment. Although the generic questionnaire allows for comparison across different diseases, it may be insensitive in detecting small changes in the patients' condition[23;24]. On the other hand, the disease -specific questionnaires, focus on relevant aspects of disease specific issues and hence, are more responsive to small changes in the patients' condition. Thus, both types of questionnaires, generic and disease-specific, have strengths and weaknesses. In recent years, it has been advocated that at least one of each type should be used in research studies.

Generic health-related quality of life:

The most commonly used generic health-related quality of life questionnaire is the Medical Outcomes Study Short Form-36 (SF-36). This evaluative measurement scale has been translated into more than 60 languages and the results obtained can be easily compared between studies and with existing population norms [25-27]. It can be self- or interviewer-administered in less than 15 minutes, and assesses the following eight health domains: physical functioning, social functioning, role limitation - physical and emotional, pain, mental health, vitality, and general health perceptions. The scale consists of 36 items, with number of items per domain varying between 2 and 8. Item scaling is on a yes/no, or 2-, 3-, 5-, or 6-point scale. Domain scores are transformed to a scale ranging from 0 (worst) to 100 (best). Total scores are reported as physical and mental health component scores, standardized to have a mean of 50 and a standard deviation of 10 in healthy U.S. population. For both, the domain and the total scores, patient values

can be compared to age and sex-matched norms generated from a healthy sample of the general Canadian[28] or U.S. population[29].

The psychometric properties of the SF-36 have been extensively studied in non-pulmonary populations. Although fewer studies have been done in COPD patients, the SF-36 appears psychometrically sound in this population. Internal consistency, test-retest reliability, and construct validity were acceptable[30]. In patients reporting a self-perceived health change over time, the responsiveness of the SF-36 was moderate for the domains of physical and social functioning. For a given domain, a 5-point difference between groups or a 5-point change over time is considered significant[31]; however, the Minimal Clinically Important Difference (MCID) for COPD patients has not been determined.

Other generic measures used in COPD are Sickness Impact Profile (SIP), Nottingham Health Profile (NHP), Hospital Anxiety and Depression Scale and Mood Adjective Check List, utility measures like the Standard Gamble and the Quality of Well-Being index (QWB) [23;32;33].

Disease specific health-related quality of life:

Disease specific quality of life questionnaires commonly used in COPD are Chronic Respiratory Questionnaire[34-36] (CRQ) and St. George's Respiratory Questionnaire[37] (SGRQ), though there are many others available [38].

The CRQ consists of 20 questions divided into four domains: dyspnea, fatigue, emotional function, and mastery (feeling of being in control). The dyspnea domain measures shortness of breath on five activities chosen by individual patients as being important in their daily lives. Thus, CRQ is an individualized, labor-intensive instrument requiring 20-30 minutes of staff time for each administration. Clinically, the CRQ is usually scored by converting domain scores to a 7-point scale, permitting uniform comparison between domains. Converted scores are obtained by dividing the raw score by the number of items in each domain. For research purposes, the 7-point scale or the raw score can be used. Raw scores allow a greater numerical range, an advantage for statistical analyses, and

allow consideration of overall health-related quality of life (out of 140). For both converted and raw scores, a higher score represents better health-related quality of life. This approach produces a questionnaire that is very sensitive to change but is not standardized. Consequently, it can be used neither to compare the patients at one point in time nor to compare patients from two different clinical trials. Even then the CRQ is presently widely used North America, especially in clinical trials and rehabilitation programs[14;38]. However, the typical distribution of changes in scores following rehabilitation is usually wider with the SGRQ than with the CRQ[38]. As a result, the sample size needed to detect small but clinically important changes in scores is usually larger when the SGRQ is used as a primary outcome than the CRQ. Studies to date have provided strong evidence of the test-retest reliability[30;36;39;40], internal consistency, and construct validity[30;36;40] of the CRQ. Evidence of the responsiveness of the CRQ has been demonstrated by studies evaluating the effects of pulmonary rehabilitation[36;41;42] as well as other interventions. A change in score of 0.5 represents a MCID for a given domain of the CRQ[43;44]. Similarly, a change in score of 1.0 represents moderate change, while 1.5 or more represents a large change[43]. In summary, there exists strong evidence of the psychometric properties of the CRQ, thereby supporting its use as an outcome measure in COPD.

The SGRQ has 76 items divided into three sub-scales: symptoms (problems caused by specific respiratory symptoms), activity (restriction of activity by dyspnea) and impact (impact on everyday social functioning and psychological disturbances in life caused by the disease). Every item has a pre-determined weight; both sub-scale scores and the total score are usually reported. The majority (80%) of items in SGRQ are dichotomous (yes/no). It is self-administered and takes 20 minutes to complete[38]. Individual questionnaire items are rated either by choosing the most applicable response from four or five choices, or by a true/false answer. Responses are then scored using weights, which 0 to 100, with higher scores indicating a lower quality of life. The scoring process is tedious, and is therefore a practical limitation to using this questionnaire in a clinical environment. For research purposes, scoring of the SGRQ is performed with the help of the computer using statistical or database applications. The SGRQ shows good test-retest

reliability and construct validity. Also, the SGRQ was sensitive to change over time in a randomized controlled trial of nasal positive pressure ventilation in hypercapnic COPD patients[45], and in studies investigating the effects of medication[46]. Demographic and disease related factors account for very little of the variance in weights between patients. There was no significant difference between the questionnaire item weights obtained from asthmatic or COPD patients[37], nor in the weights obtained in six different countries. The SGRQ also appears to be responsive to clinically important change, as 4 points represents a small change or MCID, 8 points represents moderate change, and 12 points represents a large change[47]. Therefore, the SGRQ demonstrates strong psychometric properties in a COPD population.

Measurement strategy based on the choice of a generic and specific health-related quality of life questionnaires:

The most common strategy to overcome the individual limitations of the generic and disease specific questionnaires is to use both types of questionnaires in a given study. However, this approach can represent a significant burden on the patient given the time-consuming nature of such questionnaires. Moreover, though the generic and disease-specific questionnaires are co-administered, both these questionnaires are independently developed and validated.

The measurement strategy based on the choice of a generic questionnaire supplemented by a specific module offers the advantage of using a widely accepted generic tool along with a disease-specific module. The benefit is that there are fewer questions for the patient to answer. This strategy has been widely used for other disorders: prostatic cancer[48;49], multiple sclerosis[49] and osteoporosis[50]. Our team developed a COPD-specific module[51] to be administered with SF-36.

2.3 Development and validation of a measurement Tool:

Any measure of quality of life should measure health with good accuracy and repeatability. Validity and responsiveness are essential attributes for a questionnaire to be of value in clinical trials. The steps in developing and validating such a measure are presented in the following sections.

2.3.1 Development of a measurement tool:

The following steps should be followed in the process of development of a measure according to the FDA document: 1) identification of concepts and domains that are to be measured; 2) identification of the intended application of the PRO instrument and identification of the intended population[22] .

Such development should be guided by a conceptual definition or framework. This is important to be able to determine whether the measure is conceptually consistent with its intended application, i.e. as a measure of quality of life for a given population. In an effort to capture the impact of COPD, a new questionnaire of health-related quality of life should be able to regard the interplay between psychological and physical factors but also the systemic effects of the disease and related co-morbidities.

Once the conceptual framework has been developed, generation of items should be done using focus groups, interviews with the patients, clinicians, family members, caregivers, researchers, expert panels and other sources[52].

Item generation for the measure is incomplete without patient involvement. Hence, item generation should incorporate input from a wide range of patients with the condition of interest to represent appropriate variations in severity and in population characteristics such as age or sex. Moreover, input from their family members and care providers are also important.

The choice of data collection method (self-administered, administered by a staff, or supervised self-administered) and mode of administration (interview, paper-based, electronic, web-based and interactive voice response formats) should be considered.

The choice of recall period that is most suitable depends on the purpose and intended use of the instrument, the characteristics of the disease/condition, and the treatment to be tested.

2.3.2 Development of COPD-specific module:

In phase I of our project, a COPD-specific module was developed[51].

A comprehensive pool of items was generated from literature review and from focus groups. Discussions held with small groups of individuals allowed the identification of items related to COPD and treatment affecting health-related quality of life. As a result, a list of 90 items was generated. Items were scaled on a 5-point Likert scale. From a list of patients undergoing pulmonary rehabilitation, 128 patients who fulfilled certain eligibility criteria, were mailed a set of questionnaires and were asked to provide basic demographic and clinical information, complete a questionnaire enquiring about the extent to which the scaled items limited their quality of life, complete the SGRQ and the SF-36. A subset of 64 patients was asked to complete the new items and the SF-36 a second time within one week. Finally, items were selected based upon the pre-defined criteria from responses of 105 COPD patients. The pre-defined criteria were as follows: item not in SF-36, < 5% missing responses, quasi-normal frequency distribution, reasonable test-retest reliability, item to item correlation with SF-36 and preliminary items between 0.3 and 0.7, no differences between French and English and acceptable face validity.

Thus, a COPD-specific module with 17 items was generated. It has three domains: Symptoms (6 items), Physical Function (6 items) and Feelings (5 items). This process of validation was initiated using a cross-sectional data of COPD patients for reliability (internal consistency) and validity. Test-rest reliability was assessed with a longitudinal

data where the COPD-specific module was administered twice at 1-2 week interval in stable COPD subjects.

2.3.3 Steps in validating a measurement tool:

The process of validation is long and complex. Indeed, it is never ending. Each study in which a health related quality of life questionnaire is used contributes to the body of knowledge concerning its performance, and thereby to its validity.

Psychometric properties (Reliability, Validity, Responsiveness)

Tests designed to measure an underlying domain may have different purposes. They may attempt to distinguish between subjects on a given domain (discriminative property), to predict the results of a concurrent or future outcome (predictive property) and to measure change within subjects over time (evaluative property). The COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) questionnaire final round proposed a checklist based on the consensus for assessing the methodological quality of studies of measurement properties[53].

In addition to assessing the reliability, validity and responsiveness, evaluation of missing data, floor and ceiling effect is essential in the validation process. If the missing data is non-ignorable, analyzing only the observed data generates serious bias[54]. Hence, missing data should be imputed if more than 50% of the items are scored in a given sub-scale. Though there are different methods suggested for imputation[54;55] of missing data in questionnaires, one method often used is to impute the values based on the mean scores in the given subscale if more than 50% items were answered in that sub-scale; the same method advised for SF-36 [56;57].

The floor effect is the percentage of subjects with the lowest possible score and the ceiling effect is the percentage of subjects with the highest possible score. It is desirable

to have the floor and ceiling effects less than 15%[58]. If there is a high ceiling or floor effect, subjects cannot be distinguished from each other as they all have the same score. Moreover, these effects reduce reliability as between subject variability is decreased amongst those subjects with the highest or the lowest scores. In addition, responsiveness is limited as positive or negative changes cannot be measured in these subjects with the highest or the lowest scores.

Reliability: Reliability is defined as the degree to which the instrument is free from measurement error. Internal consistency, often considered a form of reliability, is the extent to which items on a scale correlate with each other and with the scale's total score. The Cronbach's α coefficient, calculated to evaluate internal consistency, ranges from 0 to 1, with higher values representing higher levels of internal consistency. The Cronbach's α is generally considered acceptable if greater than 0.7, good if greater than 0.8, and excellent if above 0.9 [59]. However, a Cronbach's α over 0.9 may suggest redundancy of items. Since the Cronbach's α is influenced by the total number of items in an instrument, and increases in value if related items are added, alpha coefficient must be interpreted accordingly. Alpha is an increasing function of test length as well as the test homogeneity. Alpha is a poor estimate of the general factor saturation of a test [60] for it can seriously overestimate the size of a general factor, and a better but not perfect estimate of total test reliability because it underestimates total reliability. For the questionnaires, the Cronbach's α between 0.7 and 0.9 is considered acceptable by the experts in the field of quality of life research[52;59].

Test-retest reliability is the likelihood that an instrument will give the same reading when used to measure the same thing in a different setting. This presumes that the patient's health will not have changed between assessments. The usual approach is to recruit patients and make assessments within 1-2 weeks. Pearson's correlation coefficient (rho) can be used to quantify reliability but it fails to take into account variability in results attributable to systematic, as opposed to random, differences in test scores with multiple applications. Reliability is better evaluated using Intraclass Correlation Coefficient (ICC) which reflects both systematic and random differences in test scores (judged excellent if

higher than 0.75)[61]. Thus rather than measuring the correlation between two sets of scores, the ICC tells us about the concordance, the extent to which repetition of the test yields the same values under the same conditions in the same individuals. Generally test-retest estimates are lower in value than those for internal consistency because they involve measuring at different times.

Validity: Validity is defined as the degree to which the instrument truly measures the construct(s) it purports to measure. There are many different types of validity described in the literature; the most commonly used validity is the convergent and divergent validity which refer to construct validity. Other areas of validity concern the criterion validity, concurrent and predictive capacity of the questionnaire. Convergent and divergent validity are concepts that are well accepted by the experts in the field, whereas other types of validity are not yet universally accepted [53].The argument based approach to validity offers several advantages[62] and makes the concept of validity more fluid. Validity is associated with the interpretation assigned to test scores rather than with the test scores or the test[62].

Convergent validity refers to the extent to which a new measure agrees with the results from other instruments believed to be assessing the same attribute. In contrast, divergent validity refers to the extent to which a new measure agrees with the results of other instruments believed to be assessing dissimilar attributes. Convergent and divergent construct validity is assessed by Pearson product-moment correlations. We defined correlation as weak if $r < 0.3$, moderate if $0.3 \leq r \leq 0.6$ and strong if $r > 0.6$[52].

Responsiveness- Responsiveness has been defined as the ability of a questionnaire to detect clinically important changes over time, even if these changes are small[63]. A lack of clarity exists about the definition and adequate approach for evaluating responsiveness. There are 25 definitions and 31 measures of responsiveness in the literature, which leads to variable results[64]. [64]. Definitions differ in the kind of change that a responsive instrument should be able to detect, e.g. (clinically) important changes over time [65;66] or

changes due to treatment effects [52;67], or changes in the true value of the underlying construct [68].

Responsiveness is a measure of longitudinal validity [58]. It should be assessed (like construct validity) by testing predefined hypothesis e.g. expected correlations between changes in measures, or expected differences in changes between "known" groups [64]. This shows the ability of a questionnaire to measure changes if they really have happened. Moreover, the instrument should be able to distinguish clinically important change from measurement error [58].

The most commonly used responsiveness statistics are the Cohen's Effect Size[69], the standard error of measurement (SEM) [70;71] -based criteria for identifying meaningful intra-individual changes and the approximate value of half a standard deviation [72].
The SEM is the standard error in an observed score related to measuring with a particular test that obscures the true score[70;71]. As SEM is expressed in the original metric of measure, it is easy to interpret.

Thus, Cohen's effect size and SEM are the two most appropriate statistical measures of responsiveness, as both provide unique information and each captures an important relation between treatment effect and variability in response[70]. Cohen's effect size is calculated by dividing the mean difference between the baseline score and the post-treatment score of the total group by the standard deviation of the baseline score of the total group. Whereas SEM is calculated as $\sigma_x\sqrt{1-r_{xx}}$, where σ_x is standard deviation of the instrument and r is reliability coefficient. SEM should be interpreted with caution, as under some circumstances, any measure based on variability in change scores can give misleading information[70].

Minimally Important Difference (MID):

The interpretation of responsiveness is incomplete without knowing the value of MID for the instrument. Many have challenged the concept of responsiveness as a separate psychometric property. Moreover, responsiveness has many definitions and formulas in

the literature[64]. The MID is defined as 'the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate in the absence of troublesome side-effects and excessive cost, a change in the patient's management'[43]. To estimate the MID it is necessary to have the information such as judgments by patients about different amounts of change. One-SEM change has been validated as equivalent to minimal clinically important difference[71]. Half a standard deviation of baseline score appears to hold in a wide variety of situations, with some exceptions[72]. Use of half a standard deviation as MID however has been heavily criticized in the literature[73-75].

2.3.4 Validation of COPD-specific module:

The first phase of this project completed the preliminary validation of the COPD-specific module using a cross-sectional data base of moderate COPD subjects[51]. The COPD-specific module has high reliability (internal consistency and test-retest reliability) and validity.

2.4 Summary of the Literature Review:

The importance of measurement of health-related quality of life in COPD is increasing day by day. HRQL is used as a treatment outcome in many intervention trials and its use is been recognized by the FDA[22]. Currently, generic and COPD disease-specific questionnaires are administered together in order to assess the impact of the disease and co-morbidities in patients from different populations and various disease severity, and also to capture the impact of various intervention to COPD. Most commonly used generic questionnaire is SF-36[25;57] and disease-specific questionnaire is SGRQ[37].
The SF-36 and SGRQ are widely used and validated in COPD population[33;38;76-79].

Today, the generic and disease-specific questionnaires are often administered together[24] because there are no instruments that incorporate both generic and disease specific constructs for use with COPD patients. However, administration of two separate questionnaires to chronically debilitated COPD subjects is unwise. In addition to being expensive and time consuming, it is taxing to the patients. Moreover, administration of many lengthy questionnaires may deter subjects from participating in research studies.

Chapter III:

Study rationale, research questions, objectives and hypotheses:

3.1 Study rationale:

The measure of health-related quality of life (HRQL) is a critical aspect of patient evaluation and management. Because disturbances of health in COPD are multidimensional, the instrument used has to take into account the several aspects of the health of the patients. There are two types of HRQL questionnaires: generic and disease-specific.

Generic health questionnaires are widely available and have been subjected to careful development. They can be used in any population and are adequate for cross-condition comparisons. Further, patients with COPD commonly have co-morbid conditions and may have adverse effects from their treatments, which could be missed by a disease specific questionnaire. These are more likely to be captured by a generic health instrument. However, they do not focus on the areas of HRQL which are most commonly affected in COPD patients; they contain irrelevant items, and are less sensitive to changes. Unlike generic questionnaires, disease-specific questionnaires have greater sensitivity for disease changes and hence have increased responsiveness as they focus on relevant aspects of HRQL.

There are only two disease-specific questionnaires commonly used in chronic respiratory conditions such as chronic obstructive pulmonary disease (COPD), the Chronic Respiratory Questionnaire (CRQ) and the St. Georges Respiratory Questionnaire (SGRQ). The CRQ needs to be administered by an experienced staff member and is quite labor-intensive; hence it is not commonly preferred by clinicians and researchers. The SGRQ is, thus, the most commonly used instrument. The majority of the questions in SGRQ have dichotomous (yes/no) responses, however, and this may lead to problems with sensitivity to change. The current best approach to HRQL assessment is to supplement a disease-specific questionnaire with a generic quality of life questionnaire,

but the administration of two separate questionnaires is time consuming, expensive, may be irritating to the patients, and could increase the non-participation rate.

In order to overcome the shortcoming of the current approach, and to gain the advantages of both, generic and disease specific questionnaires, we have designed a new model for a questionnaire. The new model, the McGill COPD quality of life questionnaire, is made up of a combination of disease-specific and generic questions (SF-36). This bilingual (English & French) "hybrid" measurement scale will be easy to understand and is self-administered.

In the next section of the thesis we will review our recent efforts in developing the COPD-specific module and finalize the development of the McGill COPD quality of life questionnaire. Before using this new questionnaire in clinical programs or in trials, we need to further study the instrument's psychometric properties with respect to reliability, validity and responsiveness.

3.2 Research question:

In light of the study rationale, our study question was as follows:

Does a hybrid questionnaire (disease-specific items supplemented with generic items from the SF-36), the McGill COPD quality of life questionnaire, have measurement properties (reliability, validity and responsiveness) at least as strong as those of the SGRQ in assessing health related quality of life in subjects with moderate to severe COPD?

3.3 General objective:

To finalize the development of a hybrid questionnaire (disease-specific items supplemented with generic items of the SF-36), the McGill COPD quality of life questionnaire, and to evaluate its psychometric properties (reliability, validity, responsiveness) in patients with moderate to severe COPD

3.4 Specific objectives and Hypotheses:

Phase 1 of the thesis:

Recently our team[51] developed a COPD-specific module to be used with the SF-36. In addition to this development (as a continuation of this development process,) we have designed a new, hybrid McGill COPD Quality of Life Questionnaire.

The specific objective of this final phase of development:

To finalize the development of the McGill COPD quality of life questionnaire that has both disease-specific and generic components i.e. to combine the COPD-specific module developed earlier and some items from SF-36.

Phase 2 of the thesis:

The second phase of the thesis project is made up of the evaluation of the psychometric properties of the McGill COPD quality of life questionnaire:

To evaluate the following psychometric properties of the McGill COPD quality of life questionnaire:

a.In terms of reliability the specific objectives were:

a1. To estimate the internal consistency of the McGill COPD quality of life questionnaire when used with moderate to severe COPD patients;

a2. To estimate the test-retest reliability (i.e., reproducibility) of the McGill COPD quality of life questionnaire

For reliability we hypothesized that the reliability indexes of the McGill COPD quality of life questionnaire will be within acceptable thresholds (0.7-0.95: Cronbach's alpha, intraclass correlation coefficient or weighted Kappa). For weighted Kappa the threshold is always lower than ICCs, though there are no specific published guidelines for questionnaires.

b. In terms of validity the specific objectives were:

b1. To determine the convergent construct validity (against the SGRQ)

b2. To determine divergent construct validity (against the pain sub-scale of SF-36)

Though there are other types of validity such as known group construct validity and predictive criterion validity described in the literature, we decided to describe convergent and divergent validity for the purposes of this thesis. Moreover, convergent and divergent validity are well accepted concepts by all the experts in the filed, where as other types of validity are not yet universally accepted[53].

For convergent construct validity, we hypothesized that the McGill COPD quality of life questionnaire scores (total and sub-scale), will correlate moderately to strongly with SGRQ scores (total and sub-scale) (moderate if $0.3 \leq r \leq 0.6$ and strong if $r > 0.6$).

For divergent construct validity, we hypothesized that the correlations between the McGill COPD quality of life questionnaire scores and scales from SF-36 measuring dissimilar constructs such as bodily pain should be weak ($r<0.3$) and lower than that with other sub-scales measured physical and social functioning in SF-36.

c. In estimating responsiveness the specific objectives were:

c1. To determine if the McGill COPD quality of life questionnaire scores could detect expected changes in COPD patients after 6-8 weeks of a pulmonary rehabilitation program.

c2. To determine if changes in the McGill COPD quality of life questionnaire scores over time are of similar direction and magnitude as changes in the SGRQ

Many have challenged the concept of responsiveness as a separate psychometric property. Moreover, responsiveness has many definitions and formulas in the literature[64].

We decided to describe one of the most accepted versions of responsiveness, Cohen's effect size, for the purpose of this thesis.

For the responsiveness, we hypothesized that the McGill COPD quality of life questionnaire scores will change similarly to the SGRQ scores after pulmonary rehabilitation and in turn will have similar effect size.

d. **To describe the floor & ceiling effects of all the items**

e. **To report the non-response rate of individual items and across all items**

Chapter IV: Manuscript

4.1 Preface to the manuscript

In the first and the third chapter, we highlighted the importance of measuring health related quality of life and the current practice in COPD. A COPD-specific module for use with the SF-36 was developed[51] by our group and is in the process of publication.

Currently there is no instrument sufficient in itself to measure health related quality of life (HRQL) in people with COPD. There is a need for a questionnaire giving the possibility of using both generic and disease-specific items, in order to capture the impact of COPD on subjects' lives, not only the impact of the lung disease but the systemic components, the related co-morbidities and the treatment adverse events.

The manuscript summarizes the development of the new, hybrid "McGill COPD Quality of Life Questionnaire" as well as its validation in moderate to severe COPD subjects who were part of a provincial pulmonary rehabilitation cohort. Of the 246 subjects recruited for the provincial cohort, data for the McGill COPD Quality of Life Questionnaire were collected on 141 subjects.

Subjects were, thus, a convenience sample of COPD patients with moderate to severe disease, who were taking part in a pulmonary rehabilitation program of supervised exercise. They were evaluated pre- and post-pulmonary rehabilitation within 2 months, 1, 2 and 3 years. For the present study, we used the data collected pre- and post-rehabilitation.

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Development and Validation of the new McGill COPD Quality of Life Questionnaire

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KeyWords: HRQL, psychometric property, hybrid, generic, disease-specific

Abstract:

Introduction: There is a need for a health-related quality of life questionnaire in COPD that fulfills the advantages of both, generic and disease-specific questionnaires. Objective: To finalize the development of a new, hybrid questionnaire (disease-specific items supplemented with items from the SF-36), the McGill COPD Quality of Life Questionnaire and to evaluate its psychometric properties (reliability, validity, responsiveness) in COPD subjects. Method: With pre-defined criteria, we selected items from the SF-36 to complement the previously developed COPD-specific module. Exploratory factor analysis was performed on these items (combined SF-36 items and those from the COPD-specific module) to identify domains of the new hybrid questionnaire. A prospective cohort, involving 4 hospitals in Québec with COPD subjects who underwent pulmonary rehabilitation, participated in the validation of the new questionnaire. Evaluation included the St. Georges Respiratory Questionnaire, SF-36 & COPD-specific module, and pulmonary function at baseline (pre-), post-rehabilitation, & yearly thereafter for 3 years. Results: The McGill COPD Quality of Life Questionnaire is available in English and French; it assesses three domains: symptoms, physical function and feelings and has 29 items. For the validation, we evaluated 246 COPD subjects (111 females). Subjects had a mean age of 66 years; 87% were ex- and 8% current smokers (mean: 61 pack-years); mean FEV_1 was 1.12 L (GOLD stages: II-27%, III-33% and IV-37%). There was less than 2% missing data and the floor and ceiling effects were less than 5%. The internal consistency (Cronbach's α) of the new scale was 0.68-0.82. Intraclass correlation coefficient for reliability was 0.74-0.96 for the sub-scales and 0.95 for the total score. Correlation of the new scale with the SGRQ, was moderately high (r=-0.88, 95% CI: -0.91 to -0.84), consistent with the a priori hypothesis for convergent validity. We evaluated responsiveness by the extent to which the new scale could detect the change in health status after rehabilitation. The effect size was 0.33 (pre-post rehabilitation mean score difference of 6), suggesting a moderate change. Conclusions: The new McGill COPD Quality of Life Questionnaire showed high internal consistency, reliability, convergent validity, and moderate responsiveness in COPD subjects.
Funding: Respiratory Health Network of the Fonds de la recherche en santé du Québec (FRSQ) and GlaxoSmithKline.

Introduction:

Chronic obstructive pulmonary disease (COPD), although preventable and treatable, is still not curable. The worldwide prevalence of COPD is 10.1± SE=4.8% overall (11.8±7.9% for men and 8.5±5.8% for women)[4]. COPD is also the fourth leading cause of death, following heart disease, cancer and stroke. Moreover, while mortality due to heart disease and stroke has reduced significantly between 1970 and 2002 (32% and 52% respectively), COPD mortality has increased (102.8%) [5]. COPD is, thus is a predominant cause of morbidity and mortality and, hence, health care utilization across the globe.

Severity of COPD is graded into four stages according the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [1] criteria. However, physiological severity of COPD as described by the GOLD categories does not necessarily translate into subjects' perceptions of severity of their disease[13;14;32]. An ideal measure would have to reflect not only the physiological function, but also be closely related to the bio-psychosocial consequences of the disease and patient's ability to cope with the demands of daily living. Thus, measuring health related quality of life (HRQL) is important in clinical practice and in research. Moreover, exposure to long term smoking and pollution increases the prevalence of COPD in middle-aged individuals. In addition, COPD patients often exhibit other co-morbid conditions related to lifestyle activities, natural aging or systemic effects of COPD [16;17]. Clinicians and policy makers have recognized the importance of measuring this construct, in order to inform patient management and policy decisions[21]. A cure for COPD is still not in sight, and hence, improvement in HRQL is the major goal of pharmacological and non-pharmacological treatments. Recognizing the importance of HRQL, the Food and Drug Administration (FDA) of USA published guidelines, in February 2006, for the development of patient reported outcomes (PROs) [22].

Rationale for another type of HRQL questionnaire for COPD:

There are two types of health related quality of life questionnaires: generic and disease-specific. Generic questionnaires capture general health issues such as co-morbid

conditions and side effects of treatment. Although the generic questionnaire allows cross-condition comparison, it may be insensitive in detecting small changes [23]. On the other hand, the disease-specific questionnaires focus on relevant aspects of the disease and can thus detect small changes in the subjects' condition. Both types of questionnaires, generic and disease-specific, have strengths and weaknesses[32]. Today, they are often administered together[24] because there are no instruments that incorporate both generic and disease specific constructs for use with COPD patients. The administration of two separate questionnaires is, however, time consuming, expensive, may be irritating to the patients, and can increase the non-participation rate.

The most commonly used generic quality of life questionnaire is the Medical Outcomes Study Short Form-36 (SF-36). It has been translated into more than 60 languages, takes 10 minutes to complete, and results obtained can be easily compared with existing population norms [25-27]. It is a self administered or interviewer-administered, evaluative instrument that allows comparison of different diseases. Disease specific quality of life questionnaires commonly used in COPD are the Chronic Respiratory Questionnaire (CRQ) [34-36] and the St. George's Respiratory Questionnaire (SGRQ) [37] though there are many others available [38]. The CRQ has 20 questions divided in four domains: dyspnea, fatigue, emotional function, and mastery (feeling of being in control). The dyspnea domain measures shortness of breath on five activities chosen by individual subjects as being important in their daily lives. Thus, the CRQ is an individualized, labor-intensive instrument requiring 20-30 minutes of staff time for each administration. Perhaps for this reason clinicians and researchers do not commonly use it. The SGRQ is, therefore, the most commonly used instrument. However, the majority (80%) of the questions in SGRQ have dichotomous (yes/no) responses and, hence, the instrument may have problems with sensitivity to change. Importantly, the two-point scale is less reliable, less interesting and more ambiguous to respondents [80-82] than the scales with more categories. Moreover, the SGRQ is long, having 76 items divided into three sub-scales: symptoms (problems caused by specific respiratory symptoms), activity (restriction of activity by dyspnea) and impact (impact on everyday social functioning and psychological disturbances in life

caused by the disease); every item has a pre-determined weight. Finally, both the SGRQ and the CRQ fail to predict future outcomes, including mortality, in COPD subjects [83].

It follows that the ideal questionnaire for COPD should have the strengths of generic and disease-specific questionnaires to capture the co-morbidities of COPD, the treatment side effects and the small changes due to the disease itself. Hence, this new, hybrid and unique instrument was designed by combining items from a generic questionnaire, the SF-36, and a respiratory disease specific module [51]. The decision to utilize the SF-36 was due to its brevity, relevance, availability in many languages and cultures (permitting its utilization in international trials). The resulting tool has the ability to detect changes in quality of life related to COPD, while retaining the ability to compare this population with other subject groups. To the best of our knowledge, this approach to developing a quality life questionnaire has never been done before.

The current study is part of a larger research initiative that has been on-going for some years. Our team has already developed a COPD-specific module[51] to be used in conjunction with the SF-36. Multiple sources of information, including COPD subjects and their significant others, as well as experts in the fields of COPD and quality of life research participated in item generation for the module. The COPD-specific module has 17 items divided into three sub-scales: Symptoms – 6 items, Physical Function – 5 items and Feelings – 5 items. Testing of the psychometric properties of this COPD-specific measure used a cross-sectional data base of COPD subjects[51]. The COPD-specific module was developed by a bilingual team in English and French at the same time. Our current work is a continuation of this project.

The objectives of the present study were to finalize the development of a new, hybrid questionnaire (disease-specific items supplemented with generic items from the SF-36), the McGill COPD quality of life questionnaire, and to evaluate its psychometric properties (reliability, validity, responsiveness) in subjects with moderate to severe COPD. It was hypothesized that the McGill COPD quality of life questionnaire will behave similarly to the SGRQ, a disease specific questionnaire.

Methods

This study was part of a pulmonary rehabilitation cohort in COPD patients from 4 hospitals in the province of Québec. All subjects in the cohort took part in a pulmonary rehabilitation program of 6-8 weeks duration at the respective center. The Research Ethics Board of all participating hospitals approved the study protocol, and written informed consent was obtained from all participants. The present study has two distinct components: 1) Final phase of development of the new hybrid questionnaire and 2) Validation of the new questionnaire.

Final phase of the Development of the new McGill COPD Quality of Life Questionnaire:

The McGill COPD quality of life questionnaire is a hybrid questionnaire which combines all the items from the COPD-specific module[51] and selected items from the SF-36. This new questionnaire was developed by a bilingual team in English and French at the same time. The question format is the same as that of the SF-36 in order to maintain a consistent style and appearance; a higher score on the new hybrid questionnaire indicates a better quality of life. This final phase of development determined which items from the SF-36 should be combined with the questions of the earlier developed COPD-specific module; the new McGill COPD Quality of Life Questionnaire was, thus, created from this combination.

In order to select items from the SF-36, we established pre-defined criteria. The first two questions of the SF-36 (self-assessed general health question and health transition question) were excluded. The question one was too general and the health transition question, requiring patients to assess change from the previous year, was not appropriate. A correlation matrix with the remaining items from the SF-36 and all the items from the COPD-specific module was then created. Those items from the SF-36 with a correlation greater than 0.6 with any item in the COPD-specific module were excluded, to avoid redundancy.

As the aim was to create a responsive instrument, change in the remaining items (after excluding items with correlation greater than 0.6) (from pre to post pulmonary rehabilitation) was examined in two small subsets of subjects. One was a randomly selected sample of subjects (n=20) and another was a sample of subjects who showed a good improvement in their functional capacity (improvement equivalent to minimal clinically important difference on either the 6-minute walk test or the constant work rate cycle endurance test[CET])[84] after completing a pulmonary rehabilitation program (n=22). If there was no change or only a very insignificant improvement (change score less than 0.25) in the mean change score after undergoing pulmonary rehabilitation, that item was removed.

Once the final selection of items from the SF-36 was complete, these items were combined with all the items from the COPD-specific module to form a new, hybrid McGill COPD quality of life questionnaire.

Lastly, to identify the health domains in the hybrid questionnaire, exploratory factor analysis was done using all the items in the new hybrid questionnaire. Eigenvalue-one procedure with varimax rotation was employed to rotate the factors to a simple structure. The fit was done by optimizing the log likelihood assuming multivariate normality over the uniquenesses [85]. Items with a loading of greater than 0.4 were assigned to a specific factor[86].

Psychometric Evaluation of the McGill COPD Quality of Life Questionnaire:

Selection of Subjects- The inclusion criteria were: a clinical diagnosis of COPD; older than 40 years; currently or previously smoking with a smoking history of at least 10 pack-years; forced expiratory volume in one second (FEV_1) after the use of a bronchodilator less than 80 percent of the predicted normal value, and FEV_1 to forced vital capacity (FVC) ratio less than 70 percent; no asthma, heart failure, dementia or unstable psychological condition; no acute medical condition that contraindicated the patient taking part in an exercise program; French or English speaking, and agreed to

consent to participate in the study. Patients were required to have completed the baseline evaluation (before rehabilitation) and at least one evaluation immediately after rehabilitation (within 1-2 months).

Measures- Patients' assessments included a complete medical history, pulmonary function tests at rest, CET, 6MW and quality of life measured by the SF-36, SGRQ, and the new McGill COPD quality of life questionnaire. The data collected at each respective center were centralized in one place.

Complete Medical History:

Each new patient enrolled in the study provided his/her name, sex, age, marital status, education, occupation, language, address and the Régie de l'assurance maladie du Québec (RAMQ) identification. Personal information of all patients was stored separately for follow up purposes. Study database identified the patients with a unique identification code. The clinical evaluation included measurements of weight, height and respiratory functions. The medical profile contained information about the primary and secondary diagnoses, surgeries, various diagnostic examinations, medications, allergies, vaccines, smoking history, and oxygen therapy.

Pulmonary Function Test:

Spirometry and lung volumes were measured at rest according to the American Thoracic Society guidelines[87;88]. The results were compared with predicted normal values from the European Community for Coal and Steel/European Respiratory Society[89].

Cycle Endurance Test:

The CET was performed on an electromagnetically braked cycle ergometer and the workload was set at 80% of peak work capacity achieved during incremental cycle ergometry. Patients were asked to cycle for as long as possible and no encouragement was provided during the tests to avoid any potential confounding effect on exercise performance[90].

6-Minute Walk Test:

The 6MW test was used to measure functional exercise capacity. The 6MW test has been studied in several different populations, with different diseases and is a valid and reliable measure[91-96]. The 6MW test was administered in a standardized manner [97]using an elliptical walking course at each participating center. Two tests were performed with sufficient rest periods between the tests (at least 20 minutes). The result was reported in meters as the best of the two trials.

SF -36:

The SF-36 was self-administered. The SF-36 has 36 items within eight domains; it took 10 minutes to complete. The raw scores were converted to standardized scores as per the users' manual[57]. The final scores were reported as eight domain scores and two summary scores: Physical Health and Mental health. The final scores ranged from 0 to 100, with higher scores indicating a better quality of life. The final scores could be easily compared with existing population norms [25-27].

SGRQ:

The SGRQ[37] was self-administered. It consists of 76 weighted items within three domains: symptoms, activity and impact. The SGRQ is a valid and reliable measure of HRQL in COPD patients [38]. They took approximately 20 minutes to complete. Items were rated either by choosing the most applicable response from four or five choices, or by a true/false answer. Responses were then scored using weights and scores were converted to a percentage ranging from 0 to 100, with higher scores indicating a lower quality of life.

Statistical analysis:

Descriptive statistics: To describe the socio-demographic characteristics of the subjects, medians, standard deviations, counts and percentages were calculated. Floor and ceiling

effects of the items and non-response rates were evaluated as percentages. Statistical analysis was done using R (2.7.1)[98].

Imputation of missing data: Though there are different methods suggested for imputation[54;55] of missing data in questionnaires, we imputed the values of the missing items based on the mean scores in the given subscale if more than 50% items were answered in that sub-scale; the same method advised for SF-36 [56;57]. Subjects were excluded, if more than 50% items were missing.

Non-response rate- The total percentages of missing values per question and per subject were calculated. We hypothesized that there would be less than 5% missing data in our study population.

Floor and ceiling Effects- Floor and ceiling effect was evaluated by calculating the percentage of subjects with the lowest possible and highest possible scores respectively. We calculated the percentage of subjects with maximum and minimum scores on the COPD McGill questionnaire at baseline. We hypothesized that the floor and ceiling effects will be less than 15% in our study population.

Reliability- Two types of reliability, internal consistency and test-retest reliability have been estimated. Internal consistency is the extent to which multiple items in a questionnaire subscale are measuring the same concept (construct). Internal consistency was estimated using Cronbach's alpha coefficients [99]. Cronbach's alpha ranges from 0 to 1, with higher values representing higher levels of internal consistency. Cronbach's alpha is generally considered acceptable if greater than 0.7, good if greater than 0.8, and excellent if above 0.9 [59]. However, Cronbach's alpha over 0.9 may suggest redundancy of items. For the questionnaires, the Cronbach's α between 0.7 and 0.9 is considered acceptable by the experts in the field of quality of life research[52;59].

Test-retest reliability is the likelihood that an instrument will give the same reading when used repeatedly to measure the same thing. Test-retest reliability was calculated by

comparing the consistency of scoring of the new McGill COPD questionnaire administered on two occasions using one-way analysis of variance (ANOVA) with subjects as a random factor to obtain variance estimates and an estimator of the Intraclass Correlation Coefficient (ICC) [61;100]. The ICC ranges from 0 to 1, with values closer to 1 representing stronger reliability. Interpretation of ICC scores is difficult and varies according to the use of the instrument. Generally speaking, ICC should always be higher than 0.7 to make decisions at group level [59]. An ICC of 0.9 is considered appropriate at the individual level [59]. We hypothesized that the ICC for our new questionnaire will be greater than 0.75.

Validity- Although there are many different types of validity described in the literature, we decided to describe convergent and divergent validity for the purposes of this study. Moreover, convergent and divergent validity are well accepted concepts by all the experts in the field, where as other types of validity are not yet universally accepted [53].The argument based approach to validity offers several advantages[62] and makes the concept of validity more fluid. Validity is associated with the interpretation assigned to test scores rather than with the test scores or the test[62].

Convergent validity refers to the extent to which the new McGill COPD questionnaire scores agree with the result of other instruments that is believed to be assessing the same attribute. Whereas divergent validity refers to the extent to which the new McGill questionnaire scores agree with the result of other instruments that is believed to be assessing dissimilar attribute.

Convergent construct validity was assessed by Pearson product-moment correlations between baseline McGill COPD questionnaire scores and baseline SGRQ scores. It was hypothesized that the McGill COPD quality of life questionnaire sub-scale and total scores will be strongly correlated with SGRQ sub-scale and total scores We defined correlation as weak if $r < 0.3$, moderate if $0.3 \leq r \leq 0.6$ and strong if $r > 0.6$. The divergent construct validity was assessed by Pearson product-moment correlations between baseline McGill scores and SF-36 subscales. It was hypothesized that the correlations

between McGill COPD quality of life questionnaire scores and unrelated scales from SF-36 with dissimilar constructs such as bodily pain subscale will be weak ($r<0.3$) and lower than that with other subscales measured physical and social functioning in SF-36.

Responsiveness- We evaluated the responsiveness of the McGill COPD Questionnaire. Responsiveness has been defined as the ability of a questionnaire to detect clinically important changes over time, even if these changes are small[63]. A lack of clarity exists about the definition and adequate approach for evaluating responsiveness. There are 25 definitions and 31 measures of responsiveness in the literature, which leads to variable results[64].

Responsiveness was assessed by measuring the Cohen's Effect Size[69]:

$$\text{Effect Size} = \frac{\text{Mean (Baseline score} - \text{Post-rehab score)}_{\text{total group}}}{\text{SD Baseline score}_{\text{total group}}}$$

Cohen's effect size is considered one of the most appropriate measures of responsiveness, as it provides unique information and captures an important relation between treatment effect and variability in response[70].

In addition, we assessed the responsiveness by comparing the magnitude and the direction of the change in the total McGill COPD questionnaire score with the change in the total scores of SGRQ after pulmonary rehabilitation. We hypothesized that the magnitude and the direction of the change in the total McGill COPD questionnaire scores will be similar to the change in the total SGRQ scores.

Results:

Development of the new McGill COPD Quality of Life Questionnaire:

Twenty five items were left from the SF-36 questionnaire, after removing the first two items and the items with correlations >0.6 with any item in the COPD-specific module. Based on the mean change score, items were further removed if there was no or very insignificant response after pulmonary-rehabilitation in a group of COPD patients who showed improvement in their functional capacity (as described in the methods) and thus, 12 items were finally selected from the SF-36. The 17 items from the COPD-specific module and 12 items from SF-36 thus created the new hybrid McGill COPD questionnaire with 29 items.

The exploratory factor analysis performed using the baseline data yielded three domains. All the items from the COPD-specific module were grouped under a single domain. However, based on face validity of these items we decided to split them in three separate sub-scales. The items from the SF-36 were grouped under two separate domains other than the COPD-specific module items. Hence, we created sub-scales with suffix A and B to differentiate items from COPD- specific module in sub-scale A and items from the SF-36 in sub-scale B. Figure 4.1 shows the composition of the new questionnaire after performing the exploratory factor analysis.

The final score of the new McGill COPD quality of life questionnaire is designed to be similar to the SF-36 i.e. higher score indicates better quality of life. Some items in which a higher score reflected lower quality of life needed recoding as per the SF-36 manual. Thus these items were recoded such that the response number 1 meant that subjects were most affected by the disease and 5 meant that the subjects were least affected by the disease. The recoding for the items from the SF-36 is described in the table 4.1.

Validation of the new McGill COPD Quality of Life Questionnaire:

There were 246 subjects in the cohort; 141 had completed the COPD-specific module and could be included in the validation study of the McGill COPD questionnaire. The baseline sociodemographic and clinical characteristics of the validation study population

are given in the table 4.2. However, the baseline sociodemographic and clinical characteristics of the cohort were similar to the study population (table in the appendix).

Missing data, floor and ceiling effect:

The total percentages of missing values per question and per subject were between 0 and 2%. For each item, the non-missing data were normally distributed; the mean score imputation strategy was utilized.

The percentage of subjects with maximum (ceiling effect) and minimum (floor effect) scores on COPD McGill questionnaire at baseline for the sub-scales and the total score is presented in table 4.3.

Reliabilty:

Internal Consistency: Cronbach's alpha for the sub-scales ranged from 0.68 to 0.82. The individual values are presented in table 4.3.

Test-retest Reliability: Fifty stable COPD subjects completed the new McGill COPD questionnaire twice, 1-2 weeks apart before they entered the pulmonary rehabilitation program. However, two subjects reported having exacerbation within 4 weeks of administration of the questionnaire and were excluded from the analysis. Thus, a total of 48 subjects provided data for the ICCs (table 4.3) The $ICC_{Consistency}$ and $ICC_{Agreement}$ yielded exactly the same values for all the sub-scales.

Validity and Responsiveness:

Validity:

Convergent Construct Validity:

Convergent construct validity was examined by comparing the McGill COPD questionnaire with SGRQ scores at baseline. The individual values for the sub-scale

scores are presented in table 4.4. The correlation coefficient of the total scores was -0.88 (95% CI: -0.91 to -0.84) (Figure 4.2).

Divergent Construct Validity:

Divergent construct validity was examined by comparing the total McGill COPD questionnaire score with the pain sub-scale of the SF-36. The correlation coefficient was 0.17 (95% CI: 0.00 to 0.32). However, the correlation with physical function sub-scale of the SF-36 was 0.66 (95% CI: 0.56 to 0.74) and with social function sub-scale of the SF-36 was 0.61 (95% CI: 0.50 to 0.70).

Responsiveness:

After undergoing 6-8 weeks of pulmonary rehabilitation there was improvement in the total mean score of the McGill COPD questionnaire by 6 points and that of SGRQ by 7 points. The Cohen's effect size for the McGill COPD questionnaire was 0.33 and for SGRQ was 0.44.

Discussion:

This prospective, multi-center study has developed and validated a new health-related quality of life questionnaire for COPD. This new hybrid questionnaire, the McGill COPD quality of life questionnaire, was based on a novel concept of combining questions from the SF-36 and from a COPD-specific module, aiming at measuring health-related quality of life in COPD patients. The strategy of administering a disease-specific module along with a generic questionnaire is widely used especially in the field of cancer[101]. Our group earlier developed a COPD-specific module to be administered along with the SF-36[51]. However, the strategy of combining items from a generic questionnaire with a disease-specific module to the best of our knowledge has not been used before. With the addition of 17 disease-specific questions to selected core questions from the SF-36, it is possible to tap both generic and disease specific components of health-related quality of life. However, it remains to be evaluated if we still can use the new questionnaire and compare across diseases similar to the existing generic questionnaires.

Another original feature of this study was the simultaneous development of an English and French version by a bilingual team avoiding issues related to direct item translation. Furthermore, this study demonstrated that the new questionnaire has high internal consistency, reliability, convergent and divergent validity, and moderate responsiveness in COPD subjects with moderate to severe disease. The responsiveness was similar between the new questionnaire and the SGRQ. The prospective pulmonary rehabilitation cohort allowed us to estimate the responsiveness of this new questionnaire using an intervention that is very well known to benefit HRQL in COPD patients[102].

Questionnaire development:

The initial phase of the questionnaire development [51] included an in-depth literature review, interviews with health professionals and patients, focus group discussions involving COPD subjects, their partners and care givers. For the final phase of the questionnaire development, we combined items from the SF-36 and the items from the earlier developed COPD-specific module; we reduced the questionnaire to a minimum number of items to yield the new McGill COPD Quality of Life questionnaire. We used pre-defined criteria to reduce items; however, there was no concrete science behind the process of item reduction. As we were aiming to develop an evaluative scale, we decided to use item responsiveness in small samples of COPD patients. This strategy of creating small samples to estimate item responsiveness was arbitrary; however, there are no guidelines to choose items in order to create a responsive scale. The face validity of the items and their importance as stated by the focus groups participating in the first phase of this study was used extensively in addition to the pre-defined criteria.

Finally, we chose to proceed with an exploratory factor analysis to identify the domains. Though most all items from the COPD-specific module fell in a single domain, we decided to divide them in three sub-scales based upon their face validity and content validity. Even if we called the questions related to dyspnea and fatigue as 'symptoms';

they, in fact, involve physical functioning. Moreover the 'feelings' sub-scale items involve breathing problems. The population in this study was quite homogeneous. It comprised of subjects with moderate to severe COPD, the majority of whom reported having dyspnea on exertion, a chronic cough and sputum production. Consequently, for subjects with moderate to severe COPD, symptoms, physical activities, social activities, and emotional reactions all are intertwined. Though we refer to the domains being separate, all arise from the common symptom of COPD: exertional dyspnea and limitations in physical function due to dyspnea.

Validation of the questionnaire:

The McGill COPD Quality of Life Questionnaire has been developed to offer the advantages, of both a generic and disease specific health-related quality of life questionnaires with a minimum of additional questions to a few core questions from the SF-36. This avoids the problem of redundancy which is often found between independently developed generic and specific questionnaires. The present study used a Quebec provincial pulmonary rehabilitation cohort for validation of the new questionnaire. Preliminary evidence for reliability, validity and responsiveness suggested that the questionnaire can be used as an evaluative instrument in future studies. Use of this questionnaire has only been validated in moderate to severe COPD group of subjects. If this questionnaire is to be used for mild COPD subjects or for other pulmonary diseases e.g. sarcoidosis, idiopathic pulmonary fibrosis etc., it needs to be validated in subjects with those respiratory disorders.

Missing-data, Floor and ceiling effects- The minimal amount of missing-data in our study is quite impressive as compared to up to 23% of missing data in SGRQ[103]. Brevity, clarity of the language and the 5-point Likert scale for reducing ambiguity could be the reasons for minimal non-response. In the literature, the floor and ceiling effects for individual SF-36 sub-scales are reported to be quite high in COPD subjects, but our questionnaire did not have this problem[33;104]. This could be because of our rigorous process to select items. If there is a high ceiling or floor effect, subjects cannot be

distinguished from each other as they have the same score. Moreover, these effects reduce reliability as between subject variability is decreased amongst those subjects with the highest or the lowest scores. In addition, responsiveness is limited as positive or negative changes cannot be measured in these subjects with the highest or the lowest scores.

Reliability- As hypothesized, Cronbach's alpha was between 0.7 and 0.9 except for the symptom sub-scale. Though a lower alpha means lower item to item correlations, we decided to include all the items in the symptom sub-scale due to high face validity and content validity for the COPD subjects.

The group of moderate to severe COPD subjects in our study was quite homogeneous. Hence, the Cronbach's alpha and the ICCs obtained, despite using such a homogeneous cohort, are quite impressive. Though all the ICCs are above 0.9, the symptom, physical function A and feeling A sub-scales ICCs are less than 0.9. The low ICC in our study could be due to lack of variability amongst the subjects, though it could also be due to lack of agreement.

Validity- The SGRQ is the most commonly used COPD-disease specific questionnaire thus far. We used SGRQ scores to validate our new questionnaire. As was hypothesized, the convergent validity was strong (r= -0.88) when total McGill COPD questionnaire score was compared with the SGRQ total score.

The divergent validity for our new questionnaire was showing as hypothesized, lower correlation (r=0.17) with the scale measuring different construct than our new questionnaire. The Pain sub-scale of the SF-36, which measures presence and severity of pain, was used to compare with the new questionnaire, which measures disease severity of COPD. The correlation coefficient of the total McGill score with the pain sub-scale was substantially lower than that of physical function and social function sub-scales of SF-36. Having obtained these values of convergent and divergent validity, we can be quite confident about interpretations based on the scores of the new questionnaire.

Responsiveness- As was hypothesized, we have demonstrated that the new questionnaire has similar responsiveness as the SGRQ. The difference between pre- and post-rehabilitation scores of our questionnaire and that of SGRQ were similar in direction and magnitude, as was hypothesized. Unfortunately we did not have estimates of the minimal important difference to further interpret responsiveness. However, as our questionnaire has items with a 5-point Likert scale as opposed to SGRQ, with 80% of items as yes/no, we believe that our questionnaire will be more sensitive to small changes. This needs further testing.

Strengths and limitations of the study:

The novel concept of developing a hybrid questionnaire using the well established tool like the SF-36 is the major strength of this study. The originality of this approach in development of the new questionnaire is also important. Use of a 5-point Likert scale in a HRQL questionnaire is favored by experts in the field[59;81]. However, the most commonly used disease-specific questionnaire for COPD, the SGRQ, has primarily dichotomous items. The new questionnaire has all the items anchored on 5-point Likert scale.

The validation of the new questionnaire was performed using a prospective cohort which had standardized evaluation. Though there are many schools of thoughts, the validation techniques used the most accepted formulae and concepts in the field of quality of life research.

The COPD population in this study is comprised of a typical sample of COPD patients commonly encountered in the routine clinical practice in North America. The study results are probably generalizable across North America. Pulmonary rehabilitation is a very effective treatment in moderate to severe COPD patients and has been shown to improve HRQL[102]. Making use of a treatment strategy which has already been proven to be effective adds strength to this study. Moreover, SGRQ has been extensively validated in COPD patients[38] and using such a tool adds strength to our results. However, this is a

single validation study for the new questionnaire and further validation studies are essential in North American and worldwide populations.

There are limitations to our study. The sample was relatively homogenous, with all subjects having moderate to severe COPD, being ex-smokers with a significant smoking history and median age 66 years. However this is a typical population of COPD who come to the attention of health care personnel as they require treatment. This questionnaire will be of immense use in this typical COPD population often encountered in clinics and in hospitals. None the less, this questionnaire needs to be validated if it is to be used in other populations including mild COPD subjects. Of course, this is a rule for using any measurement instrument, though it is not always strictly followed.

Though Cronbach's alpha in our symptom sub-scale was somewhat lower than recommended, we believe that, it is still better than having very high alpha. Higher than 0.9 alpha means presence of redundant items in the scale and Cronbach's alpha for two of the three sub-scales of SGRQ was more than 0.95 in study by Hajiro et al [14] and lower than 0.9 for all three sub-scales by Barr et al[103]. Moreover, lower alpha in symptom subscale could be due to homogeneity of the population in this study as Cronbach's alpha is proportional to the part of the variance of the sum.

There are many psychometric measurement properties available today. However, we decided to report only a few here. The analysis of the present study could be expanded to incorporate other types of validity and other types of responsiveness measures. We only described the convergent and divergent construct validity here for the sake of this thesis. We did not estimate Known-group and predictive validity.

Moreover, we do not have data on any anchor-based measure to estimate the Minimal Clinically Important Difference (MCID). The MCID should be known to interpret the effect size. The MCID can be estimated by using patient based anchors like hospitalization or acute exacerbation in COPD patients[43]. The Minimally Important Difference (MID) is defined as 'the smallest difference in score in the domain of interest

which patients perceive as beneficial and which would mandate in the absence of troublesome side-effects and excessive cost, a change in the patient's management'[43]. We did not have data on patient based anchors; hence only the distribution method of assessing responsiveness was estimated in this thesis.

The concept of quality of life and its implications on the daily life are different for males and females. Though we recognize the differences in perception of quality of life for males and females[105-107] we could not validate the new questionnaire separately for males and females due to smaller sample size. Moreover, our study population comprised mainly of white race. Thus, this new questionnaire needs to be studied in other races and cultures for cross-cultural validity.

Conclusion:

In conclusion, the new McGill COPD quality of life questionnaire is highly reliable, valid and is responsive to change in moderate to severe COPD subjects. It is available in English and French. It is very easy to understand, short and has all items on 5-point Likert scale. Most importantly, the convergent construct validity against SGRQ is very strong (r=-0.88) and the changes in the McGill COPD quality of life questionnaire scores over time were of similar direction and magnitude as changes in the SGRQ. The new questionnaire needs to be validated in other populations and situations. Further studies will be needed to be done to refine and complete the evaluation of the measurement properties of the questionnaire for various COPD populations (mild disease, aging, different races and female) and settings (language, interview or self-administered). Finally, another important issue to be addressed in future studies is the meaning of the McGill COPD questionnaire scores (clinical interpretation) or clinically important difference (CID); this is important as it is commonly used to judge therapy effectiveness.

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Table 4.1: Items from SF-36 needing recoding as per the SF-36 manual and/or needed to change direction for the McGill Q: Highest score=best score (1- most affected by the disease & 5- least affected by the disease):

No.	Item£	Question	Recoding$ needed as per SF-36 manual	Needed to change direction for McGill Q¥	Linear* or non-linear
1	SFpf5	One flight	No	No	
2	SFpf6	Bending	No	No	
3	SFpf7	More than one km	No	No	
4	SFrp1	Cut down on amount of time	No	No	
5	SFrp2	Accomplished less	No	No	
6	SFrp4	Difficulty in performing…	No	No	
7	SFsf1	…interfered with normal social activities…	Yes	Yes	Linear
8	SFvt1	Full of life	Yes	Yes	Linear
9	Sfmh1	Been nervous	No	No	
10	SFmh4	Down hearted & blue	No	No	
11	SFvt3	Warn out	No	No	
12	SFgh5	Health is excellent	Yes	Yes	Linear

£ - Items from SF-36 in their standard short forms (e.g. SFpf4 –4th item from physical function sub-scale of SF-36 etc)

$ - SF-36 scoring: Highest score is best in SF-36 scoring system, some questions have reverse direction and hence need recoding

¥ - The McGill Q scoring: Highest score is worst score in the McGill Q, some questions from SF-36 hence needed re-coding

* - Linear recoding: 1=5, 2=4, 3=3, 4=2 and 5=1

Table 4.2: Baseline Sociodemographic and Clinical characteristics of the study population (n=141)

	Mean(sd)	Range
Age (years)	65.6 (8.1)	36-83
Sex(F/M)	62/80	
Race	130- White 1-Other 11-Missing	
BMI (kg/M^2)	26.7 (5.4)	16.2-43.6
Pack*years	58.7 (26.8)	7.2 -168
MRC Dyspnea score	2.9 (0.96)	1-5
FEV_1 (L)	1.18 (0.41)	0.49 -2.43
FEV_1%	48.0% (15.6)	18-89
FEV1/FVC	48.1 (13.7)	17 -84
SGRQ symptom	49.3 (19.5)	8.9 -90.5
SGRQ Activity	64.5 (19.1)	5.6 - 100
SGRQ Impact	31.3 (17.6)	0 -76.2
SGRQ Total	44.3 (15.6)	11.2 -76.6

BMI -body mass index; MRC-Medical Research Council; FEV1-post-bronchodialator forced expiratory volume in 1 second; FEV1% - percent predicted FEV1; FVC-forced vital capacity; SGRQ-St. George Respiratory Questionnaire.

Table 4.3: Non-response Rate, Floor and Ceiling Effect, Internal Consistency and Test-retest Reliability of the McGill COPD Questionnaire:

	Symptoms	Physical Function		Feelings		Total Score
		A	B	A	B	
Total Non-response Rate (%)	3.5	2.1	0.7	0.7	0	2.8
Floor Effect (%)	0	0	0	0	0	0
Ceiling Effect (%)	0	0.7	1.4	5	0	0
Internal Consistency	0.68	0.78	0.82	0.80	0.76	-
Test-retest Reliability (ICC: Consistency and Agreement)	0.79	0.87	0.92	0.74	0.96	0.95

Table 4.4: Pearson product-moment correlation coefficients between baseline McGill COPD Questionnaire and SGRQ scores depicting Convergent Construct Validity

	SGRQ Symptom	SGRQ Activity	SGRQ Impact	SGRQ Total
McGill Symptom	-0.56(-0.66 to -0.44)			
McGill Physical Function A		-0.68(-0.76 to -0.58		
McGill Physical Function B		-0.66(-0.75 to -0.56)		
McGill Feelings A			-0.78(-0.84 to -0.71)	
McGill Feelings B			-0.67(-0.75 to -0.57	
McGill Total				-0.88(-0.91 to -0.84)

Figure 4.1: Composition of the new McGill COPD Quality of Life Questionnaire

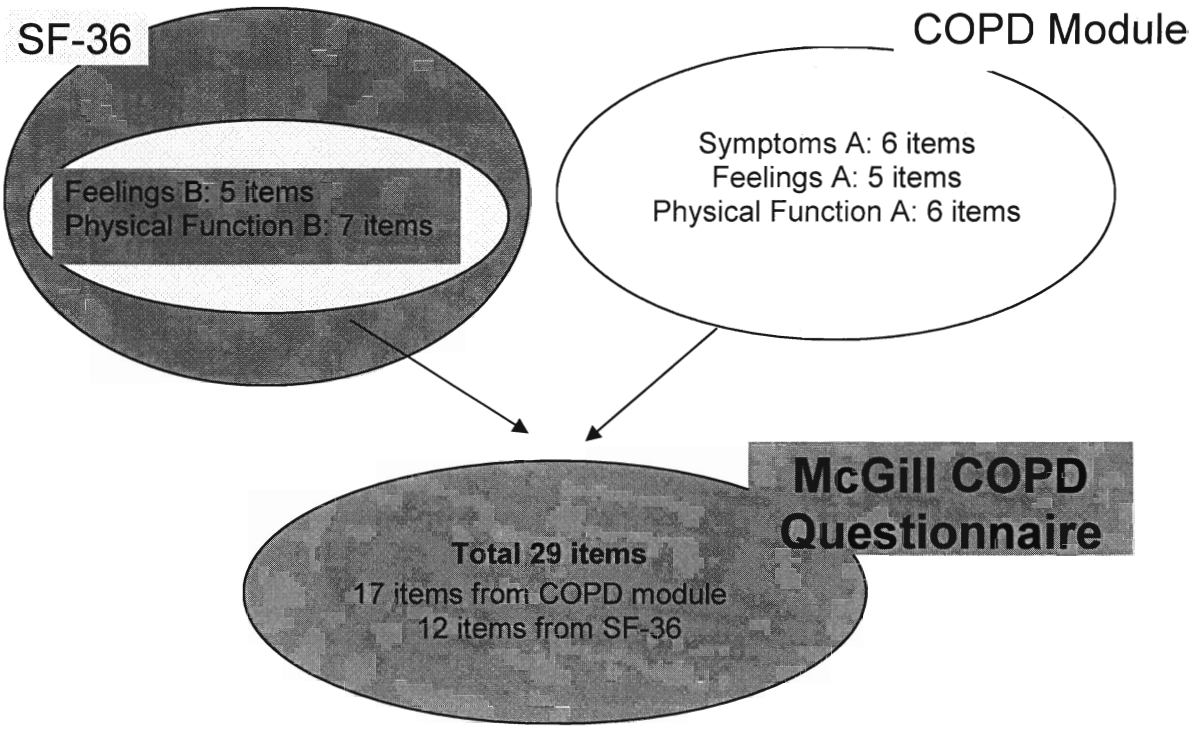
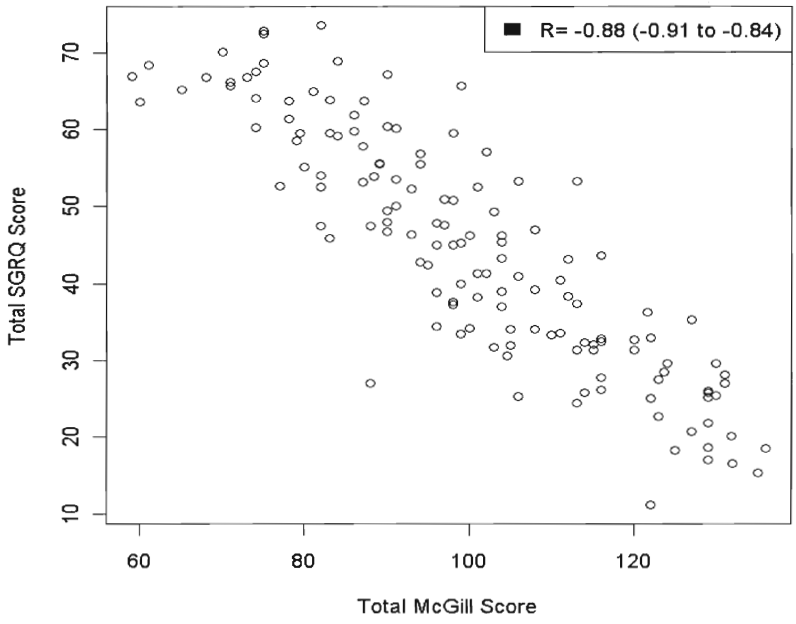


Figure 4.2: Correlation of the total McGill COPD questionnaire score with the total SGRQ score:



Chapter V: Conclusion

5.1 Summary and Conclusion:

COPD is a major cause of morbidity and mortality worldwide. It is caused by exposure to cigarette smoke, or occupational and environmental dusts and gases[2]. Though COPD is preventable and treatable, it is still not curable. Chronic and progressive symptoms of COPD such as cough, phlegm and dyspnea on exertion cause a debilitating impact on quality of life as it relates to health. Thus, COPD is responsible for physical impairment, debility and reduced quality of life; however, its severity cannot be well measured with objective parameters like lung function or exercise tests. Measuring health related quality of life and patient reported outcomes is thus of immense importance in clinical practice, research and policy making.

Current best practice to measure HRQL in COPD is with the administration of two types of instruments: generic and disease-specific questionnaires. The generic questionnaires are useful as they capture the co-morbidities and treatment side effects in COPD patients. In addition, generic questionnaire data can be compared amongst different populations with different diseases. However, the generic questionnaires are less sensitive to small changes due to the disease. Disease-specific questionnaires are sensitive to these small changes, but their much focused questions pertaining to the disease do not allow cross condition comparisons. The generic and disease-specific questionnaires are often administered together due to their weaknesses and strengths[21;32].

Administration of many questionnaires is time consuming, taxing to the patient, expensive and may increase non-participation rate. A novel questionnaire which is short, self-administered, easily understood and most importantly captures the benefits of both, the generic and the disease-specific questionnaires, thus becomes a necessity.

This study, thus, had the objective of developing such a novel questionnaire and evaluating its psychometric properties (reliability, validity, responsiveness) in patients with moderate to severe COPD.

Recently our team [51] developed a COPD-specific module to be used with the SF-36. In addition to this development, and as a continuation of this developmental process, we designed a new, hybrid questionnaire using a novel approach. This approach of developing a questionnaire, to the best of our knowledge, has never been used before. With pre-defined criteria we selected items from the SF-36 and combined them with all the items from the COPD-specific module developed earlier by our team. Using exploratory factor analysis and input from the experts in the field, we divided them in to three domains: Symptoms, Physical Function and Feelings. There are 29 items in this new, hybrid McGill COPD quality of life questionnaire.

The psychometric evaluation of this new questionnaire used data from a prospective-cohort study. The longitudinal pulmonary rehabilitation cohort of Quebec, Canada formed a database for the study. This cohort has 255 subjects and 141 of them provided data on the McGill COPD quality of life questionnaire. Subjects were, thus, a convenience sample of COPD patients with moderate to severe disease, who were taking part in a pulmonary rehabilitation program of supervised exercise. They were evaluated pre- and post-pulmonary rehabilitation at less than 2 months, 1, 2 and 3 years. The validation study thus used a prospective cohort which had standardized evaluations.

Two types of reliability, internal consistency and test-retest, were estimated. Internal consistency calculated Cronbach's alpha as a test statistic. It ranged from 0.68 to 0.82. Though the acceptable range for Cronbach's alpha for a questionnaire is 0.7 to 0.9, alphas obtained in this study are quite impressive considering the homogeneity of the sample. The correlation between any two items originates from the fact that they have some true score variance in common. Moreover, Cronbach's alpha is indeed proportional to the part of the variance of the sum {Bravo, 1991 307 /id}. In addition, the most commonly used

disease-specific questionnaire in COPD, SGRQ, has yielded wide range of alphas in different studies[14;103]. Thus, this new questionnaire can be considered to be internally reliable.

Forty eight stable COPD subjects provided data for the test-retest reliability on two occasions, 1-2 weeks apart. Intra Class Correlation coefficients (ICCs) were 0.74 to 0.96 for the sub-scales and the total score. For decision making for groups, ICCs should be more than 0.7 and for individuals it should be more than 0.9. The ICCs obtained in this study demonstrate acceptable test-retest reliability of this new questionnaire.

The convergent construct validity was examined by correlating the sub-scale and total scores of the new questionnaire and the SGRQ. As hypothesized, we found strong correlations amongst the new questionnaire and the SGRQ scores. The correlation coefficient, rho, for the total score was -0.88 (95% CI: -0.91 to -0.84). The value of rho is negative since the scoring of the SGRQ and the McGill COPD questionnaire are in opposite direction (1-most affected by disease and 5-least affected by disease in the new questionnaire and vice versa in the SGRQ). Divergent construct validity was investigated by correlating the new questionnaire total score with the Pain sub-scale of the SF-36. These dissimilar constructs (COPD disease severity and the Pain sub-scale of SF-36 measuring presence and impact of pain) had a very low correlation, rho = 0.17 (95% CI: 0.00 to 0.32). As hypothesized, the correlation with the Pain sub-scale was less than that of the correlations with other sub-scales of SF-36. The correlation with the Physical Function sub-scale was 0.66 (95% CI: 0.56 to 0.74) and with Social Function it was 0.61 (95% CI: 0.50 to 0.70. Having obtained these values, we can be quite confident about interpretations based on the scores of the new questionnaire. We did not estimate other types of validities e.g. known-group and predictive.

Responsiveness was estimated using the Cohen's effect size. Cohen's effect size for the new questionnaire was 0.33. This is interpreted as a small to moderate effect size[69]. In other words, a value of 0.33 indicates a change of 33% of one standard deviation of the baseline score. The pre- to post-rehabilitation improvement in the total mean score was 6

points on the new questionnaire. As hypothesized, this change in the mean score of the new questionnaire was in the same direction and magnitude as the SGRQ which improved by 7 points. It is important to note that this study used a sample of the COPD population typically encountered in clinics and hospitals in North America. Moreover, the intervention, supervised pulmonary rehabilitation, used in this study to estimate responsiveness is the most commonly used intervention in validation studies in COPD and has shown to improve quality of life in COPD patients[102]. Though we did not estimate all the available psychometric properties, the validation techniques used the most accepted formulae and concepts in the field of quality of life research.

5.2 Future Research:

The new hybrid questionnaire, the McGill COPD Quality of Life Questionnaire, was not developed to reinvent the measurement of HRQL in patients with COPD, but to create a measure that will offer the best of the both worlds, generic and disease specific measurement of quality of life. The present study gives several indications of the relative merits of this new instrument of measure for COPD patient. However, this new questionnaire has its strengths and weaknesses, as is true with any instrument. Information on the performance of an instrument in a given disease and population is of immense importance to the investigators and clinicians; therefore, proper choice of the instrument can be made for the required properties of that instrument.

Limited number of studies and lack of experience in using it are the major difficulties encountered in comparing a new questionnaire with an old, widely used one. This new questionnaire is a new-kid-on-the-block. The size of the validation is limited to one study whilst other questionnaire such as the SGRQ has been widely tested. As favorable as the results may seem to be with this new questionnaire, these results will need to be repeated in other studies.

There is need for future studies to continue assessing the validity of this new questionnaire in COPD patients and other chronic respiratory diseases. The new questionnaire has only been validated once for patients with COPD with moderate to severe disease. However, even in COPD patients, this questionnaire has limitations and studies will be needed to determine if it can be used with different types of COPD patients, and with different time-frames e.g., can the new questionnaire assess mild to moderate to severe types of COPD; can the new questionnaire be used in acute settings like acute exacerbations of COPD or long-term intervals like long term outcome of COPD.

While we had a homogeneous sample of COPD subjects available for the validation study, this is the typical COPD population encountered in North American health care system. In consequence, the results of our study should be generalized at least to North America. However, this is a single validation study for the new questionnaire and further validation studies are essential in North American population. In addition, it would be reassuring to see that the questionnaire perform as well in other countries, in different cultures and languages. Sex differences may also be an area that needs future research with this new questionnaire. Differences in perception of quality of life are well known[105;106]. As we did not have sufficient numbers to analyze males and females separately, we did not study the psychometric properties by gender. Thus, males and females need to be studied separately to further analyze the psychometric properties of this new tool.

Some of the psychometric properties of the questionnaire need to be assessed or revisited. Cronbach's alpha for the Symptom sub-scale was less than optimal. This could be due to lack of internal consistency, but also could be due to homogeneity of the study population. Thus, this psychometric property needs to be studied further in a different COPD population. There are other types of validity described in the literature; we have tested convergent and divergent validities. Another area of validity that might be important to assess is the predictive validity, the predictive capacity of the questionnaire.

Finally, more research is needed concerning the responsiveness of this new questionnaire. The interpretation of responsiveness is incomplete without knowing the value of Minimally Important Difference (MID) for the instrument. However, to estimate the MID we would have needed other types of information such as judgments by patients about different amounts of change with or without an intervention. Thus, MID for this new questionnaire still needs to be assessed.

Despite the limitations listed above, the new questionnaire has demonstrated that it has minimal missing data, floor and ceiling effects and good internal consistency, reliability, convergent and divergent validity and responsiveness. This new questionnaire offers a great potential and it has several merits to justify its use in future studies.

Reference List

1. Rabe, K. F., S. Hurd, A. Anzueto, P. J. Barnes, S. A. Buist, P. Calverley, Y. Fukuchi, C. Jenkins, R. Rodriguez-Roisin, C. van Weel, and J. Zielinski. 2007. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: GOLD Executive Summary. *Am J Respir Crit Care Med* 176:532-555.

2. Celli, B. R., W. MacNee, A. Agusti, A. Anzueto, B. Berg, A. S. Buist, P. M. A. Calverley, N. Chavannes, T. Dillard, B. Fahy, A. Fein, J. Heffner, S. Lareau, P. Meek, F. Martinez, W. McNicholas, J. Muris, E. Austegard, R. Pauwels, S. Rennard, A. Rossi, N. Siafakas, B. Tiep, J. Vestbo, E. Wouters, and R. ZuWallack. 2004. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J* 23:932-946.

3. Rennard, S., M. Decramer, P. M. A. Calverley, N. B. Pride, J. B. Soriano, P. A. Vermeire, and J. Vestbo. 2002. Impact of COPD in North America and Europe in 2000: subjects' perspective of Confronting COPD International Survey. *Eur Respir J* 20:799-805.

4. Buist, A. S., W. M. Vollmer, and M. A. McBurnie. 2008. Worldwide burden of COPD in high- and low-income countries. Part I. The Burden of Obstructive Lung Disease (BOLD) Initiative. *Int J Tuberc.Lung Dis* 12:703-708.

5. Jemal, A., E. Ward, Y. Hao, and M. Thun. 2005. Trends in the Leading Causes of Death in the United States, 1970-2002. *JAMA* 294:1255-1259.

6. Foster, T. S., J. D. Miller, J. P. Marton, J. P. Caloyeras, M. W. Russell, and J. Menzin. 2006. Assessment of the economic burden of COPD in the U.S.: a review and synthesis of the literature. *COPD* 3:211-218.

7. Chapman, K. R., J. Bourbeau, and L. Rance. 2003. The burden of COPD in Canada: results from the confronting COPD survey. *Respiratory Medicine* 97:S23-S31.

8. Izquierdo, J. L. 2003. The burden of COPD in Spain: results from the confronting COPD survey. *Respir Med* 97:S61-S69.

9. Dal Negro, R., A. Rossi, and I. Cerveri. 2003. The burden of COPD in Italy: results from the confronting COPD survey. *Respiratory Medicine* 97:S43-S50.

10. Britton, M. 2003. The burden of COPD in the U.K.: results from the confronting COPD survey. *Respir Med* 97:S71-S79.

11. Wouters, E. F. M. 2003. The burden of COPD in the Netherlands: results from the confronting COPD survey. *Respir Med* 97:S51-S59.

12. Nishimura, S. and C. Zaher. 2004. Cost impact of COPD in Japan: Opportunities and challenges? *Respirology* 9:466-473.

13. Weiss, S. T., D. L. DeMeo, and D. S. Postma. 2003. COPD: problems in diagnosis and measurement. *Eur Respir J* 21:4S-12.

14. Hajiro, T., K. Nishimura, M. Tsukino, A. Ikeda, H. Koyama, and T. Izumi. 1998. Comparison of Discriminative Properties among Disease-specific Questionnaires

for Measuring Health-related Quality of Life in Patients with Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med* 157:785-790.

15. World Health Organization : *International Classification of Functioning, Disability and Health:* ICF. 2001. Geneva, WHO.

16. Maclay, J. D., D. A. McAllister, and W. MacNee. 2007. Cardiovascular risk in chronic obstructive pulmonary disease. *Respirology* 12:634-641.

17. Wouters, E. F. M., E. C. Creutzberg, and A. M. W. J. Schols. 2002. Systemic Effects in COPD*. *Chest* 121:127S-130.

18. Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19 June - 22 July 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) and entered into force on 7 April 1948. The definition has not been amended since 1948. http://www.who.int/suggestions/faq/en/ accessed June 12, 2008. 2008.

19. Saracci, R. 1997. The world health organisation needs to reconsider its definition of health. *BMJ* 314:1409.

20. Bergner. 1989. Quality of Life, Health Status, and Clinical Research. *Med Care* 27:S148-S156.

21. Guyatt, G. H., D. H. Feeny, and D. L. Patrick. 1993. Measuring Health-related Quality of Life. *Ann Int Med* 118:622-629.

22. http://www.fda.gov/cber/gdlns/prolbl.htm Last acessed on 15th Jan 2008. http://www.fda.gov/cber/gdlns/prolbl.htm Last acessed on 15th Jan 2008 . 2008.

23. Guyatt, G. H., D. R. King, D. H. Feeny, D. Stubbing, and R. S. Goldstein. 1999. Generic and Specific Measurement of Health-Related Quality of Life in a Clinical Trial of Respiratory Rehabilitation. *J Clin Epidemiol* 52:187-192.

24. Mahler, D. A. 2000. How Should Health-Related Quality of Life Be Assessed in Patients With COPD? *Chest* 117:54S-557.

25. Ware, J. E., Jr. and C. D. Sherbourne. 1992. The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual Framework and Item Selection. *Med Care* 30:473-483.

26. Martin, M., M. Kosinski, J. B. Bjorner, J. E. J. Ware, R. MacLean, and T. Li. 2007. Item Response Theory Methods can Improve the Measurement of Physical Function by Combining the Modified Health Assessment Questionnaire and the SF-36 Physical Function Scale. [Article]. *Qual Life Res* 16:647-660.

27. McHorney, C. A., J. E. Ware, Jr., and A. E. Raczek. 1993. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and Clinical Tests of Validity in Measuring Physical and Mental Health Constructs. *Med Care* 31:247-263.

28. Hopman, W. M., T. Towheed, T. Anastassiades, A. Tenenhouse, S. Poliquin, C. Berger, L. Joseph, J. P. Brown, T. M. Murray, J. D. Adachi, D. A. Hanley, E. Papadimitropoulos, and The Canadian Multicentre Osteoporosis Study Research Group. 2000. Canadian normative data for the SF-36 health survey. *Can Med Assoc J* 163:265-271.

29. Ware, J. E., Jr., M. Kosinski, and T. Kennedy-Martin. 1994. SF-36 Physical and Mental Summary Scales: A User's Manual.

30. Harper, R., J. E. Brazier, J. C. Waterhouse, S. J. Walters, N. M. B. Jones, and P. Howard. 1997. Comparison of outcome measures for patients with chronic obstructive pulmonary disease (COPD) in an outpatient setting. *Thorax* 52:879-887.

31. Ware, J. E., Jr., Snow, K. K., Kosinski, M., and Gandek, B. SF-36 Health Survey manual and interpretation guide. 1993. Boston, MA, USA, New England Medical Center, Health Institute.

32. Engstrom, C. P., L. O. Persson, S. Larsson, and M. Sullivan. 2001. Health-related quality of life in COPD: why both disease-specific and generic measures should be used. *Eur Respir J* 18:69-76.

33. Prieto, L., J. Alonso, M. Ferrer, and J. M. Anto. 1997. Are results of the SF-36 health survey and the nottingham health profile similar?: A comparison in COPD patients. *J Clin Epidemiol* 50:463-473.

34. Guyatt, G. H., L. B. Berman, M. Townsend, S. O. Pugsley, and L. W. Chambers. 1987. A measure of quality of life for clinical trials in chronic lung disease. *Thorax* 42:773-778.

35. Guyatt, G. H., M. Townsend, J. Keller, J. Singer, and S. Nogradi. 1989. Measuring functional status in chronic lung disease: Conclusions from a randomized control trial. *Respir Med* 83:293-297.

36. Wijkstra, P. J., E. M. TenVergert, R. Van Altena, V. Otten, D. S. Postma, J. Kraan, and G. H. Koeter. 1994. Reliability and validity of the chronic respiratory questionnaire (CRQ). *Thorax* 49:465-467.

37. Jones, P. W., F. H. Quirk, C. M. Baveystock, and P. Littlejohns. 1992. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. *Am.Rev.Respir Dis* 145:1321-1327.

38. Lacasse Y, Wong E, Guyatt GH, and R. S. Goldstein. 1997. Health status measurement instruments in chronic obstructive pulmonary disease. *Can.Respir J* 4:152-164.

39. Martin, L. L. 1994. Validity and Reliability of a Quality-of-Life Instrument: The Chronic Respiratory Disease Questionnaire. *Clin Nurs Res* 3:146-156.

40. Guyatt, G. H., S. Walter, and G. R. Norman. 1987. Measuring change over time: Assessing the usefulness of evaluative instruments. *J Chron Dis* 40:171-178.

41. Goldstein, R. S., E. H. Gort, M. A. Avendano, D. Stubbing, and G. H. Guyatt. 1994. Randomised controlled trial of respiratory rehabilitation. *The Lancet* 344:1394-1397.

42. Guell, R., P. Casan, M. Sangenis, F. Morante, J. Belda, and G. H. Guyatt. 1998. Quality of life in patients with chronic respiratory disease: the Spanish version of the Chronic Respiratory Questionnaire (CRQ). *Eur Respir J* 11:55-60.

43. Jaeschke, R., J. Singer, and G. H. Guyatt. 1989. Measurement of health status : Ascertaining the minimal clinically important difference. *Control Clin Trials* 10:407-415.

44. Redelmeier, D. A., G. H. Guyatt, and R. S. Goldstein. 1996. Assessing the minimal important difference in symptoms: A comparison of two techniques. *J Clin Epidemiol* 49:1215-1219.

45. Jones, R. L., J. M. Neary, G. C. Man, and T. G. Ryan. 1995. Hypercapnic ventilation response in patients with lung disease: improved accuracy by correcting for ventilation ability. *Respiration* 62:70-75.

46. Aaron, S. D., K. L. Vandemheen, D. Fergusson, F. Maltais, J. Bourbeau, R. Goldstein, M. Balter, D. O'Donnell, A. McIvor, S. Sharma, G. Bishop, J. Anthony, R. Cowie, S. Field, A. Hirsch, P. Hernandez, R. Rivington, J. Road, V. Hoffstein, R. Hodder, D. Marciniuk, D. McCormack, G. Fox, G. Cox, H. B. Prins, G. Ford, D. Bleskie, S. Doucette, I. Mayers, K. Chapman, N. Zamel, M. FitzGerald, and for the Canadian Thoracic Society/Canadian Respiratory Clinical

Research Consortium. 2007. Tiotropium in Combination with Placebo, Salmeterol, or Fluticasone Salmeterol for Treatment of Chronic Obstructive Pulmonary Disease: A Randomized Trial. *Ann Intern Med* 146:545-555.

47. Jones, P. W. 1995. Issues concerning health-related quality of life in COPD. *Chest* 107:187S-193.

48. Litwin, M. S., R. D. P. Hays, A. Fink, P. A. M. Ganz, B. Leake, and R. H. M. Brook. 1998. The UCLA Prostate Cancer Index: Development, Reliability, and Validity of a Health-Related Quality of Life Measure. [Article]. *Med Care* 36:1002-1012.

49. Fischer, J. S., N. G. LaRocca, D. M. Miller, P. G. Ritvo, H. Andrews, and D. Paty. 1999. Recent developments in the assessment of quality of life in Multiple Sclerosis (MS). *Multi Sclero* 5:251-259.

50. Marquis, P., P. Cialdella, and C. De la Loge. 2001. Development and validation of a specific quality of life module in post-menopausal women with osteoporosis: The QUALIOSTΓäó. *Qual Life Res* 10:555-566.

51. Spahija, J., J.-P. Collet, J. Bourbeau, T. Ducruet, A. Robinson, and S. Wood-Dauphinee. 2000. A new module for measuring quality of life in COPD patients. *Am J Respir Crit Care Med*A823.

52. Streiner, D. L. and G. R. Norman. 2002. Health Measurment Scales. A Practical Guide to Their Development and Use., Third Ediition ed. Oxford University Press, New York, USA.

53. Mokkink, L. B., C. B. Terwee, D. L. Knol, P. W. Stratford, J. Alonso, D. L. Patrick, L. M. Bouter, and H. C. W. de Vet. 2006. Protocol of the COSMIN study: COnsensus-based Standards for the selection of health Measurement INstruments. *BMC Medical Research Methodology* 6:2.

54. Morita, S., K. Kobayashi, K. Eguchi, T. Matsumoto, M. Shibuya, Y. Yamaji, and Y. Ohashi. 2005. Analysis of incomplete quality of life data in advanced stage cancer: A practical application of multiple imputation. *Qual Life Res* 14:1533-1544.

55. Van, J. R. 2007. Two-way imputation: A Bayesian method for estimating missing scores in tests and questionnaires, and an accurate approximation. *Compu Stat Data Analy* 51:4013-4027.

56. Cheung, Y. B., R. Daniel, and G. Y. Ng. 2006. Response and non-response to a quality-of-life question on sexual life: a case study of the simple mean imputation method. *Qual Life Res* 15:1493-1501.

57. Ware, J. E., Jr. 2007. User's Manual for the SF-36v2™ Health Survey – Second Edition. SF-36.org, 640 George Washington Highway Lincoln, RI 02865 USA.

58. Terwee, C. B., S. D. M. Bot, M. R. De Boer, D. A. W. M. van der Windt, D. L. Knol, J. Dekker, L. M. Bouter, and H. C. W. de Vet. 2007. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol* 60:34-42.

59. Nunnally, J. C. 1994. Psychometric theory McGraw-Hill, New York.

60. Zinbarg, R. E., W. Revelle, I. Yovel, and W. Li. 2005. Cronbach's alpha, Revelle's beta, and Mcdonald's wH: their relations with each other and two alternative conceptualizations of reliability. *Psychometrika* 70:123-133.

61. Fleiss JL. 1986. Reliability of measurment. *The design and analysis of clinical experiments*1-32.

62. Kane, M. T. 1992. An argument-based approach to validity. *Psychol Bull* 112:527-537.

63. Guyatt, G. H., R. A. Deyo, M. Charlson, M. N. Levine, and A. Mitchell. 1989. Responsiveness and validity in health status measurement: A clarification. *J Clin Epidemiol* 42:403-408.

64. Terwee, C. B., F. W. Dekker, W. M. Wiersinga, M. F. Prummel, and P. M. Bossuyt. 2003. On assessing responsiveness of health-related quality of life instruments: guidelines for instrument evaluation. *Qual Life Res* 12:349-362.

65. Fitzpatrick, R., S. Ziebland, C. Jenkinson, and A. Mowat. 1992. Importance of sensitivity to change as a criterion for selecting health status measures. *Qual Health Care* 1:89-93.

66. Beaton, D. E., S. Hogg-Johnson, and C. Bombardier. 1997. Evaluating changes in health status: Reliability and responsiveness of five generic health status measures in workers with musculoskeletal disorders. *J Clin Epidemiol* 50:79-93.

67. Tuley, M. R., C. D. Mulrow, and C. A. McMahan. 1991. Estimating and testing an index of responsiveness and the relationship of the index to power. *J Clin Epidemiol* 44:417-421.

68. Testa, M. A. and D. Sin. 1996. Assessment of quality of life outcomes. *N Engl J Med* 334:835-840.

69. Cohen, J. 1988. Statistical power analysis for the behavioral sciences. .

70. Norman, G. R., K. W. Wyrwich, and D. L. Patrick. 2008. The mathematical relationship among different forms of responsiveness coefficients. *Qual Life Res* 16:815-822.

71. Wyrwich, K. W., N. A. Nienaber, W. M. Tierney, and F. D. Wolinsky. 1999. Linking Clinical Relevance and Statistical Significance in Evaluating Intra-Individual Changes in Health-Related Quality of Life. *Med Care* 37:469-478.

72. Norman, G. R. 2003. Interpretation of Changes in Health-related Quality of Life: The Remarkable Universality of Half a Standard Deviation. *Med Care* 41:582-592.

73. Beaton, D. E. 2003. Simple as possible? Or too simple? Possible limits to the universality of the one half standard deviation. *Med Care* 41:593-596.

74. Norman, G. R. 2003. Is It Simple or Simplistic? *Med Care* 41:599-600.

75. Wright. 2003. Interpreting Health-Related Quality of Life Scores: The Simple Rule of Seven May not be so Simple. *Med Care* 41:597-598.

76. Anthonisen, N. R., J. Manfreda, C. P. W. Warren, E. S. Hersfield, G. K. M. Harding, and N. A. Nelson. 1987. Antibiotic Therapy in Exacerbations of Chronic Obstructive Pulmonary Disease. *Ann Int Med* 106:196.

77. Boueri, F. M. V., B. L. Bucher-Bartelson, K. A. Glenn, and B. J. Make. 2001. Quality of Life Measured With a Generic Instrument (Short Form-36) Improves Following Pulmonary Rehabilitation in Patients With COPD. *Chest* 119:77-84.

78. Schlenk, E. A., J. A. Erlen, J. Dunbar-Jacob, J. McDowell, S. Engberg, S. M. Sereika, J. M. Rohay, and M. J. Bernier. 1998. Health-related quality of life in chronic disorders: a comparison across studies using the MOS SF-36. *Qual Life Res* 7:57-65.

79. Molken, M. R., B. Roos, and J. A. Van Noord. 1999. An empirical comparison of the St George's Respiratory Questionnaire (SGRQ) and the Chronic Respiratory Disease Questionnaire (CRQ) in a clinical trial setting. *Thorax* 54:995-1003.

80. Preston, C. C. and A. M. Colman. 2000. Optimal number of response categories in rating scales: reliability, validity, discriminating power, and respondent preferences. *Acta Psychologica* 104:1-15.

81. Miller, G. A. 1956. The magical number seven, plus or minus two: some limits on our capacity for processing information. *Psycho Rev* 63:81-97.

82. Jones RR. Differences in response consistency and subjects' preferences for three personality inventory response formats. In Proceedings of the 76th Annual

Convention of the American Psychological Association , 247-248. 1968. Washington.

83. Oga, T., K. Nishimura, M. Tsukino, S. Sato, T. Hajiro, A. Ikeda, and M. Mishima. 2002. Health status measured with the CRQ does not predict mortality in COPD. *Eur Respir J* 20:1147-1151.

84. Laviolette, L., J. Bourbeau, S. Bernard, Y. Lacasse, V. Pepin, M. J. Breton, M. Baltzan, M. Rouleau, and F. Maltais. 2008. Assessing the impact of pulmonary rehabilitation on functional status in COPD. *Thorax* 63:115-121.

85. Lawley, D. N. and A. E. Maxwell. 1971. Factor Analysis as a Statistical Method, Second edition ed. Butterworths, 27-32.

86. Kim, J. O. and C. W. Mueller. 1978. Factor analysis: Statistical methods and practical issues Sage Publications Inc., London.

87. Miller, M. R., J. Hankinson, V. Brusasco, F. Burgos, R. Casaburi, A. Coates, R. Crapo, P. Enright, C. P. M. van der Grinten, P. Gustafsson, R. Jensen, D. C. Johnson, N. MacIntyre, R. McKay, D. Navajas, O. F. Pedersen, R. Pellegrino, G. Viegi, and J. Wanger. 2005. Standardisation of spirometry. *Eur Respir J* 26:319-338.

88. Wanger, J., J. L. Clausen, A. Coates, O. F. Pedersen, V. Brusasco, F. Burgos, R. Casaburi, R. Crapo, P. Enright, C. P. M. van der Grinten, P. Gustafsson, J. Hankinson, R. Jensen, D. Johnson, N. MacIntyre, R. McKay, M. R. Miller, D.

Navajas, R. Pellegrino, and G. Viegi. 2005. Standardisation of the measurement of lung volumes. *Eur Respir J* 26:511-522.

89. Quanjer, P. H., Tammeling G.J., and Cotes J.E. 1993. Lung Volumes and forced ventilatory flows. *Eur Respir J* 6 (Suppl 16):5-40.

90. Guyatt, G. H., S. O. Pugsley, M. J. Sullivan, P. J. Thompson, L. Berman, N. L. Jones, E. L. Fallen, and D. W. Taylor. 1984. Effect of encouragement on walking test performance. *Thorax* 39:818-822.

91. Reesink, H. J., M. N. van der Plas, N. E. Verhey, R. P. van Steenwijk, J. J. Kloek, and P. Bresser. 2007. Six-minute walk distance as parameter of functional outcome after pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension. *J Thorac Cardiovas Surg* 133:510-516.

92. Ingle, L., K. Goode, A. S. R. Rigby, J. G. F. Cleland, and A. L. Clark. 2006. Predicting peak oxygen uptake from 6-min walk test performance in male patients with left ventricular systolic dysfunction. *Eur J Heart Failure* 8:198-202.

93. Deboeck, G., G. Niset, J. L. Vachiery, J. J. Moraine, and R. Naeije. 2005. Physiological response to the six-minute walk test in pulmonary arterial hypertension. *Eur Respir J* 26:667-672.

94. Flaherty, K. R., A. C. Andrei, S. Murray, C. Fraley, T. V. Colby, W. D. Travis, V. Lama, E. A. Kazerooni, B. H. Gross, G. B. Toews, and F. J. Martinez. 2006. Idiopathic Pulmonary Fibrosis: Prognostic Value of Changes in Physiology and Six-Minute-Walk Test. *Am J Respir Crit Care Med* 174:803-809.

95. Cunha, M. T., T. Rozov, R. C. de Oliveira, and J. R. Jardim. 2006. Six-minute walk test in children and adolescents with cystic fibrosis. *Pediatr Pulmonol* 41:618-622.

96. Bourbonnais, J. M. and L. Samavati. 2008. Clinical predictors of pulmonary hypertension in sarcoidosis. *Eur Respir J* 32:296-302.

97. 2002. ATS Statement: Guidelines for the Six-Minute Walk Test. *Am J Respir Crit Care Med* 166:111-117.

98. R Development Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing . 2008. Vienna, Austria.

99. Cronbach LJ. 1951. Coefficient and the internal structure of tests. *Psychometrika* 16:297-334.

100. Shrout, P. and J. L. Fleiss. 1979. Intraclass correlations: Uses in assessing rater reliability. *Psychol Bull* 36:420-428.

101. Sprangers, M. A., A. Cull, K. Bjordal, M. Grovenvold, and N. K. Aaronson. 1993. The European Organization for Research and Treatment of Cancer approach to quality of life assessment: Guidelines for developing questionnaire modules. *Qual Life Res* 2:287-295.

102. Griffiths, T. L., M. L. Burr, I. A. Campbell, V. Lewis-Jenkins, J. Mullins, K. Shiels, P. J. Turner-Lawlor, N. Payne, R. G. Newcombe, A. A. Lonescu, J.

Thomas, and J. Tunbridge. 2000. Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. *The Lancet* 355:362-368.

103. Barr, J. T., G. E. Schumacher, S. Freeman, M. LeMoine, A. W. Bakst, and P. W. Jones. 2000. American translation, modification, and validation of the St. George's Respiratory Questionnaire. *Clin Therape* 22:1121-1145.

104. Alonso, J., L. Prieto, M. Ferrer, G. Vilagut, J. M. Broquetas, J. Roca, J. S. Batlle, and J. M. Anto. 1998. Testing the Measurement Properties of the Spanish Version of the SF-36 Health Survey Among Male Patients with Chronic Obstructive Pulmonary Disease. *J Clin Epidemiol* 51:1087-1094.

105. French, C. T., K. E. Fletcher, and R. S. Irwin. 2005. A Comparison of Gender Differences in Health-Related Quality of Life in Acute and Chronic Coughers. *Chest* 127:1991-1998.

106. Kastura, H., K. Yamada, R. Wakabayashi, and K. Kida. 2007. Gender-associated differences in dyspnoea and health-related quality of life in patients with chronic obstructive pulmonary disease. *Respirology* 12:427-432.

107. Zahran, H. S., Kobau, R., Moriarty, D. G., Zack, M. M., Holt, J., and Donehoo, R. Health-Related Quality of Life Surveillance --- United States, 1993--2002. MMWR Surveillance Summaries 54[SS04], 1-35. 2005.

Chapter VI: Appendices

Table with Baseline characteristics of the cohort:

Baseline Sociodemographic and Clinical characteristics for all subjects (N=246):

Parameters	Mean (sd)	Range
Age (years)	65.7 (8.3)	36 -84
Sex(F/M)	103/143	
Race	215 –White 1-Other 30 -Missing	
BMI	27.1 (5.4)	16.2 -43.6
Pack*years	59.8 (30.3)	0 -183.8
MRC Dyspnea score	3 (0.93)	1-5
FEV1	1.13 (0.39)	0.43 -2.5
FEV!%	45.9 (15.1)	16 - 89
FEV1/FVC	45.7 (14.3)	17 -84

McGill COPD Quality of Life Questionnaire:

HRN Health Respiratory Network of the FRSQ

Pulmonary Rehabilitation Research Infrastructure
COPD Research Axis

McGill COPD Quality of Life Questionnaire

Centre |_|_|_| Project |_|_|_| Subject Visit |_|_|_| |_|_|_| |_|

Pre-rehabilitation evaluation (visit 1) ☐ Post-rehabilitation evaluation < 1 month (visit 2) ☐

Post-rehabilitation evaluation : 1 yr (visit 3) ☐ 2 yrs (visit 4) ☐ 3 yrs (visit 5) ☐

Date |_|_|_| yyyy-mmm-dd Time at the beginning of the questionnaire |_|_|:|_|_| on 24:00

Current or recent exacerbation

The subject currently has or had an exacerbation in the past 4 weeks? No ☐ Yes ☐

Symptoms

1- How much fatique have you experienced in <u>the last four weeks</u> ? ☐

1- No fatigue at all
2- Some fatigue
3- Moderate fatigue
4- A lot of fatigue
5- Extreme fatigue

2- On an average day during <u>the past four weeks</u>,

1- Nerver
2- A few times
3- Some times
4- Many times
5- All the time

a. How often have you **coughed** ? ☐

b. How often did you bring up **phlegm** ? ☐

3- On an average day during the past four weeks, how much shortness of breath did you have while :

1- No shortness of breath
2- Very little shortness of breath
3- Moderate shortness of breath
4- A lot of shortness of breath
5- Extreme shortness of breath

a. Doing you **normal daily activities**. ☐
b. Performed activities that required you to raise your **arms overhead**. ☐
c. Walking on the level **at your own pace**. ☐

Feeling A

4- During the last four weeks, how often did the fear of becoming short of breath limit you in your activities of daily life ? ☐

1- All of the time
2- Many times
3- Some of the times
4- A few times
5- None of the time

5- On an average day in the past four weeks how often have you felt :

	All of the time	Many of the times	Some of the times	A few times	None of the time
a. **Fringhtened or worried** about not being able to breathe.	1	2	3	4	5
b. **Frustrated** or impatient.	1	2	3	4	5
c. That everything seems **too much of an effort**.	1	2	3	4	5
d. **Unable to accept** your pulmonary condition.	1	2	3	4	5

Feeling B

These questions are about how you feel and how things have been with you during the past 4 weeks.
6 ***For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...***

	All the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	1	2	3	4	5
b. Have you been very nervous?	1	2	3	4	5

c. Have you felt downhearted and depressed?	1	2	3	4	5
d. Did you feel worn out?	1	2	3	4	5

7 ***How TRUE or FALSE is each of the following statements for you***

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. My health is excellent.	1	2	3	4	5

Physical Function A

8 ***Compared to a person your own age, how much more time does it take <u>you to perform your daily activities</u> ?***

1- Not at all longer
2- Somewhat longer
3- Moderately longer
4- Quite a bit longer
5- A lot longer

9 ***The following items are about activities you might do <u>during a typical day</u>. To what extend do your breathing problems now limit you in your ability to perform these activities ?***

	Not limited at all	Limited a little	Moderately limited	Limited a lot	Extremely limited
a. **Climbing a slope** or hill.	1	2	3	4	5
b. Getting **outside** the house.	1	2	3	4	5
c. **Going outside** on days which are hot/sunny, cold/damp or windy, or have elevated dust/pollution levels.	1	2	3	4	5
d. Being **autonomous** in your own home ie. not requiring any assistance.	1	2	3	4	5
e. Being able to **function sexually** (If sexual activity is not an issue for you, answer « not limited at all »)	1	2	3	4	5

Physical Function B

10 ***The following items are about activities you might do <u>during a typical day</u>. Does your <u>health now limit you</u> in these activities ? If so, how much ?***

		Not limited at all	Limited a little	Moderately limited	Limited a lot	Extremely limited
a.	Climbing **one** flight of stairs.	1	2	3	4	5
b.	Bending, kneeling, or stooping.	1	2	3	4	5
c.	Walking **more than a kilometer**.	1	2	3	4	5

11 ***During the <u>past 4 weeks</u>, how much of the time have you had any of the following problems with your work or other daily activities <u>as a result of you physical health</u>?***

		All the time	Most of the time	Some of the time	A little of the time	None of the time
a.	Cut down the **amount of time** you spent on work or other activities	1	2	3	4	5
b.	**Accomplished less** than you would like	1	2	3	4	5
c.	Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2	3	4	5

12 ***During the <u>past 4 weeks</u>, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?***

1- Not at all
2- Slightly
3- Moderately
4- Quite a bit
5- Extremely

Time at the end of the questionnaire. : on 24:00

SF-36 Health Survey Questionnaire – V2

Pulmonary Rehabilitation Research Infrastructure
COPD Research Axis

SF-36 HEALTH SURVEY QUESTIONNAIRE - V2

Centre |__|__| Project |__|__|__| Subject Visit |__|__|__| |__|__|__| |__|

Pre-rehabilitation evaluation (visit 1) ☐ Post-rehabilitation evaluation < 1 month (visit 2) ☐

Post-rehabilitation evaluation : 1 yr (visit 3) ☐ 2 yrs (visit 4) ☐ 3 yrs (visit 5) ☐

Date |__|__|__|__|__|__|__|__| yyyy-mmm-dd Time at the beginning of the questionnaire |__|__| : |__|__| on 24:00

Current or recent exacerbation

The subject currently has or had an exacerbation in the past 4 weeks? No ☐ Yes ☐

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

For each of the following questions, please mark and check in the one box that best describes your answer.

Questionnaire

1- In general, would you say your health is : ☐

1- Excellent
2- Very good
3- Good
4- Fair
5- Poor

2- <u>Compared to one year ago</u>, how would you rate your health in general <u>now</u>? ☐

1- Much better now than one year ago
2- Somewhat better now than one year ago
3- About the same as one year ago

4- Somewhat worse now than one year ago
5- Much worse now than one year ago

3- The following items are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

1- Yes, limited a lot
2- Yes, limited a little
3- No, not limited at all

a.	**Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	
b.	**Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	
c.	Lifting or carrying groceries	
d.	Climbing **several** flights of stairs	
e.	Climbing **one** flight of stairs	
f.	Bending, kneeling, or stooping	
g.	Walking **more than a kilometre**	
h.	Walking **several hundred meters**	
I.	Walking **one hundred meters**	
j.	Bathing or dressing yourself	

4- During the <u>past 4 weeks</u>, how much of the time have you had any of the following problems with your work or other daily activities <u>as a result of you physical health</u>?

	All the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Were limited in the **kind** of work or other activities	1	2	3	4	5
d. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2	3	4	5

5- During the <u>past 4 weeks</u>, how much of the time have you had any of the following problems with you work or other regular daily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Did work or other activities **less carefully as usual**	1	2	3	4	5

6- ***During the <u>past 4 weeks</u>, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?***

1- Not at all
2- Slightly
3- Moderately
4- Quite a bit
5- Extremely

7- ***How much <u>bodily</u> pain have you had during the <u>past 4 weeks</u>?***

1- None
2- Very mild
3- Mild
4- Moderate
5- Severe
6- Very severe

8- ***During the <u>past 4 weeks</u>, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?***

1- Not at all
2- A little bit
3- Moderately
4- Quite a bit
5- Extremely

9- ***These questions are about how you feel and how things have been with you <u>during the past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the <u>past 4 weeks</u>...***

	All the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	1	2	3	4	5
b. Have you been very nervous?	1	2	3	4	5
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5
d. Have you felt calm and peaceful?	1	2	3	4	5
e. Did you have a lot of energy?	1	2	3	4	5
f. Have you felt downhearted and depressed?	1	2	3	4	5
g. Did you feel worn out?	1	2	3	4	5
h. Have you been happy?	1	2	3	4	5
i. Did you feel tired?	1	2	3	4	5

10- During the <u>past 4 weeks</u>, how much of the time has your <u>physical health or emotional</u> problems interfered with your social activities (like visiting with friends, relatives, etc.)? ☐

1- All the time
2- Most of the time
3- Some of the time
4- A little of the time
5- None of the time

11- How TRUE or FALSE is each of the following statements for you

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people.	1	2	3	4	5
b. I am as healthy as anybody I know.	1	2	3	4	5
c. I expect my health to get worse.	1	2	3	4	5
d. My health is excellent.	1	2	3	4	5

Time at the end of the questionnaire ____ : ____ on 24:00

INFORMATION AU PATIENT

RÉSEAU EN SANTÉ RESPIRATOIRE DU FRSQ – AXE MPOC

Infrastructure de recherche en réadaptation respiratoire

French Consent:

Étude Provinciale d'une Cohorte de Patients en Réadaptation Respiratoire

Dr Jean Bourbeau, Investigateur principal

1. Introduction

La maladie pulmonaire obstructive chronique (MPOC) est une maladie chronique qui, entre autres, atteint la capacité respiratoire. Vous êtes donc limité dans vos activités par une sensation d'essoufflement plus ou moins prononcée. Plusieurs traitements sont disponibles pour améliorer vos symptômes tels que les médicaments bronchodilatateurs et la réadaptation respiratoire.

Pour bien comprendre l'impact de cette maladie nous devons continuer à faire de la recherche sur les effets de différents traitements dont la réadaptation respiratoire.

Actuellement, nous désirons mettre en place, à travers la province, un groupe d'individus atteints de MPOC qui participent à un programme de réadaptation pulmonaire, et étudier les caractéristiques des patients et des programmes qui sont les plus favorables à une amélioration de leur situation. C'est ce que nous appelons une étude de cohorte. Nous voulons recueillir l'ensemble des informations des individus de la cohorte et constituer une banque de données provinciale é partir de cette cohorte.

Nous vous demandons d'accepter de faire partie de la banque de données de cette étude de cohorte que nous voulons constituer à travers la province de Québec.

2. Procédures de l'étude

INFORMATION AU PATIENT

RÉSEAU EN SANTÉ RESPIRATOIRE DU FRSQ – AXE MPOC

Infrastructure de recherche en réadaptation respiratoire

Dans le cadre de votre programme de réadaptation, le personnel de votre hôpital fera des évaluations de vos symptômes de votre condition au repos et à l'exercice, de votre condition psychosociale, et de la qualité de votre vie. Ils vous questionneront sur vos antécédents médicaux et vous aurez à passer un examen physique. Cette évaluation de votre état de santé sera faite avant le début du programme, après le programme et à chaque année pour trois ans. Tous ces tests d'évaluation font partie de l'évaluation habituellement effectuée avant et après le programme de réadaptation. Ces tests nous permettrons de s'assurer que le programme d'exercice sera fait en toute sécurité ainsi que de suivre votre état de santé suite au programme et de faire les ajustements nécessaires à votre traitement. Nous demanderons aussi une série de questions concernant vos attitudes et votre comportement face à l'exercice. Ces questions seront répétées par téléphone à chaque 2 mois pour un an.

RÉSEAU EN SANTÉ RESPIRATOIRE DU FRSQ – AXE MPOC

Infrastructure de recherche en réadaptation respiratoire

Procédures de l'étude (suite)

Toutes les informations relatives à votre état de santé et recueillies lors de ces tests d'évaluation seront entrées dans une banque des données informatisée provinciale. Nous pourrons ainsi utiliser vos données pour juger de votre condition personnelle et aussi répondre aux questions de recherche qui se rapportent aux répercussions qu'un programme de réadaptation a sur la santé des gens atteints de MPOC et sur le système de santé.

Nous voudrions aussi avoir votre permission pour conserver vos données et les utiliser pour d'autres projets de recherche dans le futur. Pour utiliser vos données dans d'autres projets de recherche, ces nouveaux projets devront préalablement faire l'objet d'une évaluation par le comité d'éthique de l'hôpital.

Les tests qui suivent font partis de l'évaluation clinique habituelle en pré et post-réadaptation. Ces tests seront effectués dans le cadre de votre évaluation clinique que vous acceptiez de prendre part ou non à l'étude.

Tests avant de débuter votre programme de réadaptation	• **Évaluation clinique :** Rencontre avec le pneumologue et l'infirmière ou autre professionnel en MPOC à la clinique de l'hôpital. • **Formule sanguine complète, gaz artériel, électrocardiogramme, radiographie pulmonaire et spirométrie.** • **Tests de fonction respiratoire :** au repos. • **Test d'effort** : maximal et sous maximal (en endurance) sur bicyclette stationnaire. • **Test de marche de 6 minutes** • **Mesure de perception de la fatigue et de l'essoufflement (échelle de BORG)**
Tests après avoir complété votre programme de réadaptation et à	• **Évaluation clinique** • **Spirométrie** • **Test d'endurance**

tous les ans pour 3 ans	• **Test de marche de 6 minutes**

Les tests qui suivent sont les tests additionnels qui s'ajouteront à l'évaluation dans le cadre de l'étude.

Tests avant et après avoir complété votre programme de réadaptation et à tous les ans pour 3 ans	• **Questionnaires de qualité de vie et de dyspnée** : Ce sont des questionnaires de qualité de vie dont certains sont spécifiques pour les patients MPOC. • **ATS-DLD-78** : symptômes et tabagisme (environ 5 minutes) • **SF-36** : limitations physiques et psychologiques (15 minutes) • **SGRQ** : symptômes, activités et impact de la maladie (15 minutes) • **Geriatric Depression Scale**: dépression (environ 10 minutes) • **EQ-VAS** : perception de l'état de santé (<1 minute) • **London Chest Activity of Daily Living Scale (LCADL):** essoufflement avec activités quotidiennes (5 minutes) **Les questionnaires suivants évalueront votre niveau d'activité physique et vos attitudes relatives à l'exercice.** **CHAMPS :** activité physique régulière (15 minutes) **Auto-Efficacité :** confiance dans votre capacité à faire de l'exercice (10 minutes) **Profil de Comportement face à l'exercice :** comportement antérieur et actuel, attitudes, barrières à l'exercice, support pour l'exercice, adhérence au programme d'exercice (10 minutes). **Sommaire Hebdomadaire d'Exercices :** exercices effectués lors de la semaine dernière (10 minutes). (Notez que ce questionnaire ne sera pas administré avant ou immédiatement après le programme de réadaptation) **Problèmes de Santé / Utilisation des Services de Santé :** problèmes de

	santé et utilisation des médicaments et des services de santé (Notez que ce questionnaire ne sera pas administré avant ou immédiatement après le programme de réadaptation) On vous demandera aussi de répondre à un questionnaire le CHAMPS par téléphone 4 mois après la fin de votre programme de réadaptation, à un Questionnaire d'Auto-Efficacité, au Sommaire Hebdomadaire d'Exercices et Problèmes de Santé / Utilisation des Services de Santé 2, 4, 6 et 8 mois (par entrevue téléphonique) après la fin de votre programme de réadaptation.

1. Constitution de la banque de données

Comme plusieurs hôpitaux participent à ce projet, les données seront centralisées et tenues en toute confidentialité grâce au site Internet sécurisé du Réseau en Santé Respiratoire du FRSQ (Laboratoire de Télématique Biomédical de l'Université de Sherbrooke). Les données qui sont recueillies dans la banque centralisée sont non nominales (aucun nom ou information pouvant nous permettre de vous reconnaître personnellement). Il n'est donc pas possible de reconnaître votre identité personnelle dans la banque centralisée du Laboratoire de Télématique Biomédical de l'Université de Sherbrooke. Nous pourrons par contre consulter un grand nombre d'informations non nominales afin de mieux comprendre l'effet du programme de réadaptation respiratoire sur la maladie dont vous êtes atteint.

2. Autres renseignements

Nous aimerions aussi pouvoir consulter les renseignements sur votre santé en ayant accès à votre dossier de la RAMQ(Régie de l'Assurance Maladie du Québec) et de MED ECHO (base de données sur les hospitalisations), pour l'année qui précède et les 3 années suivant votre programme de réadaptation.

3. Confidentialité

Toute utilisation ou étude des données de la banque de données ne permettra pas, en aucun moment, de vous identifier. Vous serez identifié, dans la banque centralisée, par un numéro. Votre nom, date de naissance, adresse, code postal, numéro de téléphone, numéro de dossier, numéro d'assurance maladie et autres données nominatives qui pourraient permettre de vous

identifier ne pourront pas faire partie de la banque de données. Ces informations nominales ne seront accessibles qu'aux personnes responsables dans votre hôpital et seront conservées à l'hôpital seulement. La banque de données est gérée par les chercheurs de l'axe MPOC du Réseau en santé respiratoires du FRSQ en collaboration avec le Laboratoire de Télématique Biomédical (sous la responsabilité de l'Université de Sherbrooke). De plus, seulement les personnes autorisées par le Réseau en Santé Respiratoire ont accès à la base de données.

1. RISQUES

Il n'y a aucun risque à faire partie de la banque de données centralisée puisqu'elle est sécurisée et ne comporte aucun test autre que ceux déjà effectués dans le cadre du programme de réadaptation (à l'exception de quelques questionnaires). Toutes les informations permettant de vous identifier seront gardées à l'hôpital confidentiellement.

RÉSEAU EN SANTÉ RESPIRATOIRE DU FRSQ – AXE MPOC

Infrastructure de recherche en réadaptation respiratoire

2. BÉNÉFICES

Il n'y a aucun bénéfice additionnel pour vous à être sur une banque de données. Ceci n'est pas un outil de diagnostic ou de traitement.

3. COÛTS ET COMPENSATION

Nous n'offrons aucune compensation puisque vous n'encourrez aucuns frais supplémentaires. Les visites et les tests sont ceux déjà prescrits dans le cadre du programme en réadaptation respiratoire et de votre suivi clinique.

4. DROIT DE REFUS OU DE SE RETIRER DE L'ÉTUDE

Vous êtes absolument libre de refuser d'être inclus dans l'étude ou plus tard de vous en retirer sans que cela change quoi que ce soit à votre programme de réadaptation ou aux soins.

5. DROITS LÉGAUX

Il ne vous en coûtera rien pour participer à cette étude. Vous n'aurez pas à payer pour les examens ou les tests prévus. En signant ce formulaire de consentement, vous ne renoncez aucunement à vos droits légaux et vous ne libérez ni le chercheur ni le commanditaire de leurs responsabilités légales et professionnelles.

6. PERSONNES À CONTACTER

Si vous avez des questions ou désirez vous retirer de la banque de données de l'étude, vous pouvez contacter :
Dr Jean Bourbeau, Directeur du program de réadaptation pulmonaire à l'Institut Thoracique du Centre de Santé McGill au (514) 934-1934, poste 32185 ou téléavertisseur (514) 406-1946.
Hanen M'Kaouar, Coordinatrice de la cohorte en réadaptation pulmonaire à l'Institut Thoracique du Centre de Santé McGill au (514) 934-1934, poste 32601 ou téléavertisseur (514) 406-1928. .
Représentant des patients de l'hôpital : (514) 934-1934, poste 35655
Pour toutes questions au sujet de vos droits en tant que participant à un projet de recherche, vous pouvez contacter l'ombudsman de centre universitaire de santé McGill au (514) 934-1934 poste 35655. Si vous croyer avoir été blessé en participant à cette étude, vous pouvez contacter le Directeur des services professionnels **Dr Michel Marcil** au (514) 934-1934, poste 34329.

RÉSEAU EN SANTÉ RESPIRATOIRE DU FRSQ – AXE MPOC

Infrastructure de recherche en réadaptation respiratoire

ÉTUDE PROVINCIALE D'UNE COHORTE DE PATIENTS EN RÉADAPTATION RESPIRATOIRE

Investigateur Principal: Dr. Jean Bourbeau, M.D.

1. Je comprends qu'il s'agit d'un projet de recherche.
2. J'ai lu toutes les pages de ce formulaire de consentement. Le personnel de recherche m'a expliqué l'information ainsi que les procédures impliquées dans cette recherche. J'ai eu l'occasion de poser des questions auxquelles on a répondu de manière satisfaisante. On m'a donné le temps de considérer soigneusement l'information et de décider de participer ou non à cette recherche.
3. J'ai été informé que ma participation à cette recherche est entièrement volontaire et que je peux refuser d'y participer ou me retirer à n'importe quel moment, sans qu'il y ait de conséquences sur mon suivi médical.
4. J'autorise les investigateurs de la recherche ainsi que les autorités de réglementation et le comité d'éthique de cette institution à consulter mes dossiers médicaux pour les besoins de cette recherche seulement. Cette autorisation est valable pour une période de 5 ans.
5. Je comprends que je recevrai une copie de ce formulaire de consentement que je pourrai conserver pour ma propre information, une fois que je l'aurai signé.
6. Je comprends que je ne renonce à aucun de mes droits légaux en signant ce formulaire, ni ne libère les investigateurs, les commanditaires ou l'établissement de santé ou se déroule la recherche de leurs responsabilités civiles et professionnelles.
7. Ma signature ci-dessous confirme que j'accepte volontairement de participer à cette recherche.

_____ _____

Signature du sujet Nom (lettres moulées)

Date

RÉSEAU EN SANTÉ RESPIRATOIRE DU FRSQ – AXE MPOC

Infrastructure de recherche en réadaptation respiratoire

Signature de l'investigateur Date	Nom (lettres moulées)

Je suis d'accord pour que mon nom soit conservé dans un registre et que l'on communique avec moi pour m'offrir d'autres projets de recherche dans le futur.		
Oui je suis d'accord : ☐	ou	Non, je ne suis pas d'accord : ☐

Signature du sujet Date	Nom (lettres moulées)

PATIENT INFORMATION

FRSQ - RESPIRATORY HEALTH NETWORK – COPD AXIS

Infrastructure FOR RESEARCH IN respiratorY REHABILATATION

English Consent:

PROVINCIAL COHORT STUDY OF PATIENTS IN RESPIRATORY REHABILITATION

DR JEAN BOURBEAU, PRINCIPAL INVESTIGATOR

7. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a chronic illness that ultimately diminishes the respiratory capacity. You are therefore limited in your activities by a perceived shortness of breath which can range in severity. Several treatments are available to improve symptoms such as bronchodilator medication and respiratory rehabilitation.

To better understand the impact of this disease we must continue to study the effects of various treatments including respiratory rehabilitation.

Presently, we wish to put in place and follow up across the province, a group of individuals with COPD who are participating in a respiratory rehabilitation program, and study the patient characteristics and programs which most benefit their condition. This is what we call a cohort study. We would like to collect all this individual information from the cohort and create a provincial data bank that will include the entire cohort.

We ask that you accept to participate in the creation of this data bank as part of the cohort study across the province of Quebec.

8. STUDY PROCEDURES

Within your rehabilitation program the personnel of your hospital will evaluate your symptoms and your condition during rest and exercise, as well as your psychosocial condition, and quality of life. They will ask you questions concerning your medical history and you will have to have a physical examination. This evaluation of your state of health will be performed before the start of the program, after the program and once a year for three years. All of these evaluation tests are routinely done in clinic before and after the rehabilitation program. These tests will allow us to ensure that the exercise program can be done with complete safety as well as follow your level of health after the program and to make any necessary adjustments to your treatment. We will

also ask a series of questions on your attitudes and behaviour concerning exercise. These questions will be repeated by telephone every 2 months for one year.

All the information related to your state of health and collected from the evaluation tests will be entered into a provincial computerized data bank. We could then use your data to judge your personal condition, as well as answer research questions related to the repercussions of a rehabilitation program on the health of individuals with COPD and the health system. We would also like to have your permision to save your data and use it for future research projects. In order to use your data for other research projects, these projects would be subject to preliminary evaluation by the Research Ethics Board of the hospital.

The following tests are part of the routine clinical evaluation pre and post-rehabilatation. These tests will be performed as part of your clinical evaluation regardless of whether or not you accept to participate in this study.

Tests done before your rehabilatation program	• **Clinical evaluation :** Meet with the pulmonologist and nurse or other professionals at the COPD clinic. • **Complete blood work, arterial blood gas, electrocardiogram, chest x-ray and spirometry.** • **Respiratory function tests:** At rest. • **Exercise tests** : Maximal and sub-maximal (endurance) on a stationary bicycle. • **6 minute walk test** • **Measurement of perceived shortness of breath and leg fatigue (BORG scale)**
Tests done after having completed your rehabilatation and each year for 3 years	• **Clinical evaluation** • **Spirometry** • **Endurance test** • **6 minute walk test**

The following tests are the tests to be added to the evaluation as part of the study.

Tests done before and after having completed your rehabilitation and each year for 3 years	• **Quality of life questionnaires and dyspnea**: these are quality of life questionnaires, whereby some are specific to COPD patients. • **ATS-DLD-78 :** symptoms and smoking (5 minutes) • **SF-36** physical and psychological limitations (15 minutes) • **SGRQ :** symptoms, activities and disease impact (15 minutes) • **Geriatric Depression Scale:** depression (10 minutes) • **EQ-VAS:** perceived health status (<1 minute) • **London Chest Activity of Daily Living Scale (LCADL) :** shortness of breath with daily activities (5 minutes) The following questionnaires assess your level of physical activity and your attitudes towards exercise. • **CHAMPS :** usual physical activity (15 minutes) • **Self-Efficacy :** confidence in ability to do exercise (10 minutes) • **Exercise Behaviour Profile :** past and present behaviour, attitudes, barriers to exercise, support for exercise, adherence to exercise program (10 minutes) • **One-Week Exercise Log :** exercise carried out during the previous week (10 minutes) (Note that this questionnaire will not be administered before or immediately after the rehabilitation program). • **Health Problems / Health Services Utilization :** health problems and use of medications and health services (Note that this questionnaire will not be administered before or immediately after the rehabilitation program). You will also be asked to complete the CHAMPS by telephone 4 months after the end of your rehabilitation program, and to complete the Self-Efficacy Questionnaire, One-Week Exercise Log and Health Problems / Health Services Utilization questionnaire 2, 4, 6, and 8 months (telephone interview) after the end of your rehabilitation program.

9. DATA BANK IMPLEMENTATION

Considering that several hospitals will be participating in this project, the data will be centralised and kept in complete confidentiality within the secure internet site provided by the FRSQ Respiratory Network (Telematic Biomedical Laboratory, Sherbrooke University). The data collected within the centralised bank doesn't include your name or other information that could allow us to identify you personally. It is therefore impossible to identify you personally in the central bank of the Telematic Biomedical Laboratory at Sherbrooke University. We could however retrieve a large amount of information that could help us better understand the effects of respiratory rehabilitation program in COPD.

10. OTHER INFORMATION

We would also like to be able to consult the information on your state of health by having access to RAMQ (Régie de l'Assurance Maladie du Québec) and MED ECHO (data base of hospitalisations), for the year preceding your program and the 3 years following your rehabilitation program.

11. CONFIDENTIALITY

All use and study of the data from the data bank will not allow us at any time to identify you. You will be identified within the central data bank by a number. Your name, date of birth, address, postal code, telephone number, file number, medical health insurance number and other nominal data that could make it possible to identify you will not be part of the data bank. That nominal information will only be accessible to those responsible for your care in your hospital and will be conserved only in that hospital. The data bank will be managed by the researchers of the COPD axis of the FRSQ Respiratory Network in collaboration with the telematic Biomedical laboratory (under the responsibility of Sherbrooke University). In addition, only those authorised by Respiratory Network will have access to the data bank.

12. RISKS

There are no risks by taking part in this centralised data base because it is secure and does not involve any tests other than those already established as part of the rehabilatation program (except a few additional questionnaires). All the information that could identify you will be kept confidentially at the hospital.

13. BENEFITS

There is no additional benefit to you by being part of a data base. This is not a diagnostic or a treatment tool.

14. COST AND COMPENSATION

We are not offering any compensation because you will not incur any additional costs. The visits and tests are those already prescribed within the framework of your respiratory rehabilatation program and clinical visit.

15. RIGHT TO REFUSE OR WITHDRAW FROM THE STUDY

You are free to withdraw from this data bank of the cohort study at any time after telling the study investigator. Leaving the study will not affect your future medical care.

16. LEGAL RIGHTS

You are not waiving any of your legal rights by participating in this study or by signing this consent form, including, for example, the right to seek damages under civil law for any research related injury. This consent form does not free the researcher or sponsor of their legal and professional responsibilities.

17. PERSONS TO CONTACT

If you have any questions or would like to withdraw from the study, you can contact:
Dr Jean Bourbeau, Director of the Pulmonary Rehabilatation Program at the Montreal Chest Institut of the McGill University Health Centre, Montreal at (514) 934-1934, extension 32185 or pager (514) 406-1946.
Hanèn M'Kaouar, Coordinator of the Pulmonary Rehabilatation Cohort study/data bank at the Montreal Chest Institute of the McGill University Health Centre, Montreal at (514) 934-1934, extension 32601 or pager (514) 406-1928.
Patient representative of the hospital:
For all other questions concerning the subject of your rights regarding your participation in a research project, you can contact the ombudsman of the McGill University Health Centre at (514) 934-1934 local 35655. If you believe that you have been injured while participated in this study, you can contact the Director of Professional services **Dr Michel Marcil** at (514) 934-1934 local 34329.

PROVINCIAL COHORT STUDY OF PATIENTS IN RESPIRATORY REHABILITATION

Principal Investigator: Dr. Jean Bourbeau, M.D.

1. I understand that this is a research study.

2. I have read all the pages of the consent form. The research personnel have explained the information and procedures involved in the study. I have had the opportunity to ask questions and my questions have been answered satisfactorily. I have been given time to consider the information carefully and to decide whether or not to participate in this study.

3. I have been informed that my participation in this study is entirely voluntary and that I may refuse to participate, or withdraw at any time, without any consequences to my ongoing medical care.

4. I authorize the release of my medical records to study investigators, as well as the regulatory authorities and the ethics committee of this institution for purposes of this study only. This authorization will be valid for a period of 5 years.

5. I understand that I will be given a copy of this informed consent to keep for my own information, once it is signed.

6. I understand that I do not give up any of my legal rights by signing this form nor am I freeing the investigators, sponsors, or the health establishment where the study takes place from their civil and professional responsibilities.

7. My signature below indicates that I voluntarily agree to take part in this study.

_____	_____	
Subject's signature	Name (in block letters)	Date
_____	_____	
Investigator's signature	Name (in block letters)	Date

FRSQ - RESPIRATORY HEALTH NETWORK – COPD AXIS

Infrastructure FOR RESEARCH IN respiratorY REHABILATATION

I accept that my name be kept in a register so that I can be contacted for participation in other reasearch projects in the future.
Yes I accept : ☐ or No, I do not accept : ☐

_____ _____

Subject's signature Name (in block letters) Date