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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Subjective fatigue: Effects of pulmonary rehabilitation and its relationship with other variables in patients with COPD

Astrid Bams
Eliene Beckers

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij neurologische aandoeningen

PROMOTOR :

Prof. dr. Martijn SPRUIT

BEGELEIDER :

De heer Maarten VAN HERCK

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Furthermore, we also wish to thank the University Lung Centre Dekkerswald of Radboudumc for providing our data and all those who directly and indirectly participated in the patient recruitment and data acquisition, for making this thesis possible. We also want to give our thanks to the *FAntasTIGUE* consortium, for making this research topic possible. In addition, we would like to thank the University of Hasselt, Belgium and specialized rehabilitation centre, CIRO, the Netherlands, for providing the chance to conduct our thesis in their facilities.

Finally, we are sincerely grateful to each other for the kind cooperation and guidance through this master's thesis. We thank each other for working together through all deadlines in time, for motivating each other, support, and being able to be great partners.

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RESEARCH CONTEXT

This master's thesis was conducted by two master students in rehabilitation sciences and physiotherapy of the University of Hasselt (UHasselt), in Diepenbeek, Belgium. It was commissioned by the Hasselt university and is a part of a bigger research project of the FAntasTIGUE consortium.

This master's thesis situates within the research domain of rehabilitation of internal diseases and more specific chronic obstructive pulmonary disease (COPD). COPD is a chronic lung disease characterized by both respiratory and non-respiratory symptoms (https://goldcopd.org/). In this study, the importance of a common, but often forgotten non-respiratory symptom is highlighted (Kinsman, Fernandez, Schocket, Dirks, & Covino, 1983; Spruit et al., 2017). This non-respiratory symptom, subjective fatigue, is a complex and multidimensional phenomenon (Doyle et al., 2013; Kentson et al., 2016; Peters et al., 2011; Spruit et al., 2017). It can be defined as a constant, subjective and unpleasant whole body feeling of tiredness and exhaustion existing of multiple dimensions (Ream & Richardson, 1997; Small & Lamb, 1999). Almost half of the patients with COPD suffer from subjective fatigue and it impacts their daily living (Kouijzer, Brusse-Keizer, & Bode, 2018; Lewko, Bidgood, Jewell & Garrod, 2012; Spruit et al., 2017). Since symptoms of subjective fatigue worsen over time, even after receiving usual care, a more intense and multidisciplinary approach is necessary (Peters et al., 2011; Walke et al., 2007). This master's thesis focused on the effects of an individualized multidisciplinary inpatient pulmonary rehabilitation (PR) program on subjective fatigue, the relationship between a change in subjective fatigue and a change in secondary outcome measures, and to what extent a change in secondary outcome measures can predict a change in subjective fatigue following PR.

The master's thesis is conducted under the supervision of Professor Dr. Martijn A. Spruit and in co-operation with Drs. Maarten Van Herck. The master's thesis is a retrospective analysis, containing data of a recently published study by Peters et al. (2017). Therefore, the recruitment, methodology and data acquisition were not controlled by the two master students. On the contrary, data processing and data analysis were conducted by the two

master students, under the supervision of Drs. Maarten Van Herck. Similarly, academic writing, using a central format, was independently done by the two master students, and was guided by Drs. Maarten Van Herck when necessary.

Furthermore, the master students participated in two other studies of the FAntasTIGUE consortium, at the center of expertise for chronic organ failure (CIRO; Horn, the Netherlands) and Maastricht university medical center (MUMC+; Maastricht, the Netherlands). They helped with the data collection and data processing of both studies. Nor data nor results of these studies are included in this master's thesis.

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1. ABSTRACT

Background: A frequent symptom in chronic obstructive pulmonary disease (COPD) is subjective fatigue, a complex and multidimensional phenomenon. Since subjective fatigue is nonresponsive to usual care, the implementation of pulmonary rehabilitation (PR) is indicated.

Objectives: To analyze the effects of PR on subjective fatigue in COPD patients, to determine the relationship between a change in subjective fatigue and change in secondary outcome measures, and to determine if these changes are independent determinants of change in subjective fatigue following PR.

Participants: This is a retrospective analysis of patients recruited at University Lung Centre Dekkerswald of the Radboud University Medical Center who completed an individualized 12-week multidisciplinary inpatient PR program. From 459 COPD patients, a total of 446 patients met the inclusion criteria.

Measurements: Pre- and post-PR measurements were conducted of the primary (subjective fatigue, CIS-fatigue) and secondary outcome measures including health status (NCSI), body composition (BMI and FFMI), quadriceps muscle force (MicroFET), functional exercise capacity (6MWD), lung function (FEV1), and mood status (depression (BDI-PC) and anxiety (SCL-90 anxiety subscale)) in addition to demographical features.

Results: Subjective fatigue decreased significant and clinically relevant (Δ -10.4 ± 11.7 points, $p < 0.001$) following PR. Change in subjective fatigue was correlated with changes in all subdomains of health status, anxiety, FFMI, 6MWD % predicted, and age ($p < 0.05$). Changes in health-related quality of life (HRQoL), subjective complaints, and functional exercise capacity were independent predictors of change in subjective fatigue following PR and explained 26.9 % of the variance.

Conclusion: PR reduces subjective fatigue in COPD patients. Change in subjective fatigue is related with change in multiple variables. Important predictors of change in subjective fatigue are HRQoL, subjective complaints, and functional exercise capacity. However, further research is needed to determine contributing factors of subjective fatigue.

2. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a common chronic lung disease, which is characterized by airflow limitation, due to airway abnormalities and/or alveolar destruction (also known as pulmonary emphysema). COPD is usually caused by significant exposure to noxious particles or gases, such as tobacco smoking, and air pollution (https://goldcopd.org/). The prevalence of COPD is estimated at 210 million people worldwide and it is the fourth leading cause of death. Moreover, the disease burden is high with 63.9 million disease-adjusted life years (DALY's) in 2015 (GBD 2015 Chronic Respiratory Disease Collaborators, 2017; "WHO Guidelines Approved by the Guidelines Review Committee," 2008). Common respiratory symptoms are dyspnea, coughing, and sputum production, of which dyspnea is the most featured symptom (https://goldcopd.org/; Spruit, Vercoulen, Sprangers, & Wouters, 2017). Another common, but often forgotten (non-respiratory) symptom is subjective fatigue, which can be defined as a constant, subjective and unpleasant whole body feeling of tiredness and exhaustion existing of multiple dimensions (Kinsman, Fernandez, Schocket, Dirks, & Covino, 1983; Ream & Richardson, 1997; Small & Lamb, 1999; Spruit et al., 2017). It is the second most reported symptom, after dyspnea, and the most common extrapulmonary symptom (Blinderman, Homel, Billings, Tennstedt, & Portenoy, 2009; Walke et al., 2007). About half of the patients with COPD suffer from fatigue, and it has a major impact on patient's lives (Kouijzer, Brusse-Keizer, & Bode, 2018; Lewko, Bidgood, Jewell & Garrod, 2012; Spruit et al., 2017). Besides that, fatigue is also a prognostic factor for mortality in patients with COPD (Lewko et al., 2012; Stridsman, Skar, Hedman, Ronmark, & Lindberg, 2015).

Furthermore, subjective fatigue is a complex, multifactorial phenomenon. It is rarely an isolated symptom. Behavioral, systemic, physical, psychological and situational factors can contribute to the experience of subjective fatigue (Doyle et al., 2013; Kentson et al., 2016; Peters et al., 2011; Spruit et al., 2017). The degree of airflow limitation, on the other hand, does not influence the impact of subjective fatigue in patients with COPD (Kentson et al., 2016; Peters et al., 2011; Spruit et al., 2017). Symptoms of subjective fatigue worsen over time, despite optimal usual care. So, it appears that usual care is not satisfactory and there is a need for a different, more intensive and multidimensional approach (Peters et al., 2011; Walke et al., 2007).

Pulmonary rehabilitation (PR) is a cornerstone of the management of COPD and can be defined as *"a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with a chronic respiratory disease and to promote the long term adherence to health-enhancing behaviors"* (Spruit et al., 2013). The effects of PR in patients with COPD are extensive, clinically relevant and dispersed over several domains such as exercise capacity, symptom burden, and quality of life (QoL) (Cote & Celli, 2005; McCarthy et al., 2015; Ries, Kaplan, Limberg, & Prewitt, 1995; Spruit, Troosters, Trappenburg, Decramer, & Gosselink, 2004). Furthermore, PR has statistically significant effects on muscle strength, muscle fatigue, mood status, hospital utilization, and duration of hospital stay (Cote & Celli, 2005; Garuti et al., 2003; Lacasse, Martin, Lasserson, & Goldstein, 2007; Paz-Diaz, Montes de Oca, Lopez, & Celli, 2007; Pitta et al., 2008; Ries et al., 1995; Spruit et al., 2013). To increase its efficacy for an individual, it is important to target the specific needs of each patient (Spruit & Wouters, 2019).

Yet, there is insufficient high-quality literature on the impact of PR on subjective fatigue since insufficient research has been performed with subjective fatigue as a primary outcome measure. Therefore, many questions remain unanswered. Against this background, the following research questions are formulated: (1) 'What is the effect of PR on subjective fatigue in patients with COPD?', (2) 'Whether and to what extent is a change in subjective fatigue in patients with COPD following PR related to a change in one of the secondary outcome measures?' and (3) 'Whether and to what extent are change in secondary outcome measures independent determinants of change in subjective fatigue in patients with COPD following PR?'

3. METHODS

3.1. Study design

Data from a recently published study of Peters and colleagues were used in the current study (Peters et al., 2017). Patients were recruited between July 2002 and July 2013 and completed the pulmonary rehabilitation (PR) program at the University Lung Centre Dekkerswald of the Radboud University Nijmegen Medical Centre (Radboudumc) (Nijmegen, the Netherlands). This retrospective analysis of data collected before and after an individualized 12-week inpatient multidisciplinary PR program, was approved by the Research Ethics Committee of the Radboudumc (Radboudumc; CMO 2018-4994) on 10 December 2018. This study is part of a broader project regarding subjective fatigue in chronic lung diseases conducted by the *FAntasTIGUE* consortium.

Eligibility criteria in the current study were (1) a diagnosis of chronic obstructive pulmonary disease (COPD) ($FEV_1/FVC < 0.7$) according to the global initiative for chronic obstructive lung disease criteria (GOLD-criteria) (https://goldcopd.org/), (2) the completion of an individualized 12-week inpatient multidisciplinary PR program at the University Lung Centre Dekkerswald of Radboudumc, (3) the availability of pre-PR data regarding age, sex, height, weight and lung function (to determine predicted values), and (4) the availability of pre- and post-PR data regarding subjective fatigue. Patients who did not meet these criteria were not included in this study.

3.2 Pulmonary rehabilitation

Before the start of the PR program, patients underwent a broad health status assessment and were interviewed by a pulmonologist, psychologist, physiotherapist, nurse, dietician, psychomotor therapist, and creative therapist, to adapt the PR program to the patient's needs. The baseline assessment was followed by an individualized 12-week inpatient multidisciplinary PR program consisting of physical training, education, group- and individual therapy sessions, according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) recommendations (Spruit et al., 2013). Treatment progress was assessed every

three weeks, discussed with the patient and adapted if necessary. After completion of the PR program, the patients were reassessed.

3.3 Outcome measures

Subjective fatigue was the primary outcome measure of this study. Secondary outcome measures were health status, body composition, quadriceps muscle force, functional exercise capacity, lung function, and mood status. Also, patients demographics like age and sex were considered.

3.3.1 Primary outcome measure

Subjective fatigue was measured by the Checklist Individual Strength fatigue severity subscale (CIS-fatigue), a multidimensional fatigue-specific measure. The CIS-fatigue consists of eight items, each scored on a seven-point Likert scale (Vercoulen et al., 1994). The total score ranges from eight to 56 points. A higher score indicates a more severe experience of subjective fatigue. Based upon the total score patients can be classified upon their level of subjective fatigue into three categories. A score of ≤ 26 points indicates normal fatigue, a score between 27 and 35 points indicates mild fatigue, and a score of ≥ 36 indicates clinically relevant fatigue. A correction between normal and abnormal fatigue was made, which is necessary because of the natural course of subjective fatigue. (Peters et al., 2011; Servaes, Gielissen, Verhagen, & Bleijenberg, 2007). The CIS-fatigue has a high internal consistency and test-retest reliability and is also a valid measure of subjective fatigue. Its reliability and validity have been tested in healthy subjects, and in various chronic conditions (Beurskens et al., 2000; Servaes et al., 2007; Vercoulen et al., 1994; Worm-Smeitink et al., 2017). The minimal clinically important difference (MCID) of the CIS-fatigue is ten points (Peters et al., 2011). The original Dutch version of the CIS-fatigue was administered as a part of the Nijmegen Clinical Screening Instrument (NCSI) (Peters et al., 2009). The CIS-fatigue is represented in the appendix.

3.3.2 Secondary outcome measures

The Nijmegen Clinical Screening Instrument is a composition of existing instruments to give a complete and detailed view on the health status of patients with COPD. Health status can be divided into eight subdomains: quality of life (QoL), health-related QoL (HRQoL, i.e. physical satisfaction and satisfaction of the future), satisfaction with relations, subjective impairment, behavioral impairment, subjective complaints (i.e. dyspnea severity and hindrance), dyspnea (emotions), and subjective fatigue. More in-depth information regarding the NCSI is reported by Peters et al. (2009).

Body composition consists of Body Mass Index (BMI) and Fat-Free Mass Index (FFMI). BMI was calculated as the ratio weight/height² (Kg/m²) (Ischaki et al., 2007; "Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee.," 1995). Based upon their BMI score, patients were classified into four groups: underweight (BMI < 21), normal weight (21 ≤ BMI ≤ 25), overweight (BMI > 25), and obesity (BMI > 30) (Vanfleteren et al., 2016). The FFMI was measured with bioelectric impedance analysis (BIA) and was calculated as the ratio of fat-free weight/height² (Kg/m²) (Ischaki et al., 2007).

The quadriceps muscle force was assessed with the microFET, an electric hand-held dynamometer. To determine the maximal exertion, patients performed three trials with the left and right leg. If there was a difference of ten percent between each of the three trials, a fourth trial was conducted. Only the highest value of the left or right leg expressed as Newton-meter (Nm), was used for analysis. To detect a clinical change, the difference between pre- and post-PR values must exceed the MCID of 7.5 Nm (Vaidya et al., 2018). Sex, age, and weight are correlated to muscle force and were used to create normative data. The expected force was compared with the observed force to calculate the percentage of the predicted quadriceps muscle force (quadriceps muscle force % predicted) (Andrews, Thomas, & Bohannon, 1996).

Functional exercise capacity was measured with the six-minute walking distance test (6MWD). The walking distance was expressed in meters. A change in distance was found clinically relevant in patients with COPD when it exceeded the MCID of 30 meters, compared to baseline

(Polkey et al., 2013). The reference values for healthy elderly subjects, established by Troosters and colleagues, were used to express the distance as a percentage of the predicted value (6MWD % predicted) (Troosters, Gosselink, & Decramer, 1999). The 6MWD was executed according to the ATS/ERS statement (Holland et al., 2014).

A post-bronchodilator spirometry test according to ATS/ERS guidelines was used to determine lung function (FEV_1) (Culver et al., 2017; Miller et al., 2005). A change in FEV_1-values was found clinically relevant when the difference between pre- and post-PR-values exceeded the MCID of 0.1 liters (Jones et al., 2014). Also, the percentage of the predicted value is used (FEV_1 % predicted), which is based on a calculation of the predicted value and the real value (Coates et al., 2013; Culver et al., 2017; Miller et al., 2005).

Mood status was measured in the form of anxiety and depression. Clinical symptoms of anxiety were measured with the anxiety subscale of the symptom checklist-90 (SCL-90), a comprehensive self-rating scale consisting of ten items. This subscale covers feelings of restlessness, nervousness, tension, and panic attacks. Each item was scored on a 5-point Likert scale. The total score for the anxiety subscale ranges from ten to 50, with a higher score indicating a higher level of anxiety. The SCL-90 anxiety subscale is a valid and suitable scale for detecting anxious disorders but can also be used as a screening tool for anxiety in a general population. In addition, the internal consistency of this subscale was found to be good (Derogatis & Cleary, 1977; Lundin, Hallgren, & Forsell, 2015; Schauenburg, & Strack, 1999). For identifying clinically problematic anxiety, a cut-off score of 23 was used (Kloens, Barelds, Luteijn, & Schaap, 2005). Meanwhile, clinical symptoms of depression were measured with the Beck Depression Inventory for Primary Care (BDI-PC), a self-reported questionnaire consisting of seven items. This questionnaire was a part of the subdomain QoL of the NCSI. Each item was scored on a 4-point Likert scale, with a maximum score of 21 points. A higher score indicates a higher level of depression. This is a reliable and valid tool to detect depressive symptoms. A cut-off score of 4 points was used to detect symptoms of minor depression (Beck, Guth, Steer, & Ball, 1997).

3.4. Data-analysis

Data is presented as mean ± standard deviation (SD). Changes in outcome measures, following an individualized 12-week inpatient multidisciplinary PR program, were assessed using a paired t-test. The relationship between a change in subjective fatigue and change in secondary outcome measures was evaluated by a Pearson correlation coefficient. Reasoning from the fact that the absolute value and the % predicted value would be highly correlated, only the % predicted values were reported for quadriceps muscle force, functional exercise capacity, and lung function. Also, only QoL was reported because of the overlap with depression. To investigate which changes in secondary outcome measures predict a change in subjective fatigue, a stepwise multiple linear regression analysis was performed. Variables that significantly correlated with a change in subjective fatigue (Pearson correlation coefficient) were included in the stepwise multiple linear regression analysis. Again, no absolute values for quadriceps muscle force, functional exercise capacity, and lung function were included in the analysis to prevent multicollinearity. To correct for missing values, cases were excluded pairwise.

All the analyses used a 95% confidence interval (CI). Results were statistically significant if the p-value was below 0.05 (two-tailed). Statistics were conducted using IBM SPSS Statistics 25 for Windows.

4. RESULTS

4.1 Baseline patient characteristics

Of the 459 patients of the study by Peters et al. (2017), 446 patients met the inclusion criteria and were included in the analysis. Of them, 53.4% were male. Patients had a mean age of 60.5 ± 8.8 years. Most patients had moderate to very severe COPD (GOLD 2: 23.1%, GOLD 3: 48.2%, and GOLD 4: 24.7%), and were former smokers (85.3%). Thirty-three percent had their lung disease for more than ten years. Underweight was seen in 15.5% of the patients, while 31.4% and 17.9%, respectively, had overweight and were obese. Patient's mean anxiety and depression scores were below the cutoff point of clinical relevance. Three-quarter of all patients reported one or more comorbidities. These comorbidities included back pain, joint complaints, psychiatric complaints, diabetes mellitus, cancer, cardiac disease, and other complaints. The mean subjective fatigue score, measured by the CIS-fatigue, was 41.9 ± 9.3 points. Clinically relevant subjective fatigue was found in 334 patients (74.9%).

The baseline characteristics of the study participants are shown in Table 1.

4.2. Effect of PR on subjective fatigue and other outcome measures

Compared to the baseline score, the mean subjective fatigue score decreased from 41.9 ± 9.3 points to 31.5 ± 10.4 points after the PR program. The change in subjective fatigue (Δ -10.4 ± 11.7 points) following PR was found statistically significant ($p < 0.001$) and clinically relevant, since the change in subjective fatigue score exceeded the MCID (Table 2). The prevalence of clinically relevant fatigue decreased following PR from 74.9% pre-PR to 33.0% post-PR (Figure 1).

Changes in other subdomains of the NCSI all reached statistical significance (QoL: $p < 0.001$; HRQoL: $p < 0.001$; satisfaction with relations: $p < 0.001$; subjective impairment: $p < 0.001$; behavioral impairment: $p = 0.005$; subjective complaints: $p < 0.001$; and dyspnea (emotions): $p < 0.001$). Also, significant differences were seen in the FEV_1 ($p < 0.001$), FEV_1 % predicted ($p < 0.001$), quadriceps muscle force ($p < 0.001$), quadriceps muscle force % predicted ($p < 0.001$),

6MWD ($p < 0.001$), 6MWD % predicted ($p < 0.001$), anxiety ($p < 0.001$), depression ($p < 0.001$), and FFMI ($p = 0.026$) after the 12-week PR program. The change in FEV_1 (Δ 0.1 ± 0.3 l/s) reached the MCID, while the change in quadriceps muscle force (Δ 26.0 ± 64.1 Nm) and the change in 6MWD (Δ 57.6 ± 73.2 m) exceeded the MCID. BMI, on the other hand, did not improve ($p = 0.636$). More details can be found in Table 2.

4.3. Relationship between a change in subjective fatigue and a change in secondary outcome measures

Table 3 shows a significant correlation between a change in subjective fatigue and change in FFMI ($r = -0.126$, $p = 0.026$), anxiety ($r = 0.243$, $p < 0.001$), QoL ($r = 0.300$, $p < 0.001$), HRQoL ($r = 0.424$, $p < 0.001$), satisfaction with relations ($r = 0.142$, $p = 0.003$), subjective impairment ($r = 0.306$, $p < 0.001$), behavioral impairment ($r = 0.131$, $p = 0.005$), subjective complaints ($r = 0.369$, $p < 0.001$), dyspnea (emotions) ($r = 0.245$, $p < 0.001$), 6MWD % predicted ($r = -0.323$, $p < 0.001$), and age ($r = 0.111$, $p = 0.020$). Correlations between change in subjective fatigue and changes in BMI, FEV_1 % predicted, quadriceps muscle force % predicted, and sex did not reach statistical significance.

4.4. Determinants of change in subjective fatigue

A stepwise multiple linear regression analysis was used to predict changes in subjective fatigue based on changes in secondary outcome measures. Three models were produced and are represented in Table 4. Significant predictors of change in subjective fatigue were a change in HRQoL ($p < 0.001$), subjective complaints ($p = 0.001$), and 6MWD % predicted ($p = 0.004$), as shown by the third model. This model explained 26.9% of the variance in change in subjective fatigue, $F(3, 191) = 23.413$, $p < 0.001$, $R^2 = 0.269$.

5. DISCUSSION

5.1 The effect of PR on subjective fatigue

In this retrospective analysis, a statistically significant and clinically relevant improvement of subjective fatigue was found after completing an individualized 12-week inpatient multidisciplinary PR program. Similar improvements in subjective fatigue after PR were also shown by several meta-analyses (Lacasse et al., 2007; McCarthy et al., 2015; Yang, Lin, Xu, & Zhang, 2019). However, these meta-analyses used a QoL measurement tool of which subjective fatigue is a component, in comparison to the multidimensional fatigue tool used in this study.

Few studies have assessed subjective fatigue as a primary outcome measure, with a fatigue-specific measurement tool. One study found no statistically significant change in frequency, duration, and severity of subjective fatigue, and no statistically significant change in functional limitations due to fatigue, following a PR program. These results were probably caused by underpowering of that study, due to a small sample size (Theander, Jakobsson, Jorgensen, & Unosson, 2009). Two other studies reported statistically significant improvements in the reduced activity, general fatigue, and physical fatigue components of the Multidimensional Fatigue Inventory (MFI-20). No statistically significant differences were found in the motivational and mental fatigue components of the MFI-20 (Lewko, Bidgood, Jewell, & Garrod, 2014; Mkacher, Mekki, Chaieb, Tabka, & Trabelsi, 2015). These results can be ascribed to several possible explanations. The PR programs might be too short or not intense enough to change the motivational and mental fatigue components of the MFI-20. Also, these studies might be underpowered to detect changes in all domains of the MFI-20. Furthermore, the PR programs might not be sufficiently individualized. However, Mkacher et al. (2015) used a 24-week inpatient PR program. This suggests that the duration of a PR program might not be an important explanatory factor, leaving insufficient power and lack of an intense, individualized, multidisciplinary approach as important determinants of these results. This explanation agreed with the findings of van Ranst and colleagues (2011). An intense, individualized, multidisciplinary inpatient PR program was used, similar to the current study's PR program. A

statistically significant and clinically relevant improvement in subjective fatigue, as part of a QoL measurement, was reported (van Ranst, Otten, Meijer, & van 't Hul, 2011).

5.2 Relationship between change in subjective fatigue and change in other variables

The present study indicates a relationship between change in subjective fatigue and change in secondary outcome measures like health status (QoL, HRQoL, satisfaction with relations, subjective impairment, behavioral impairment, subjective complaints, and dyspnea (emotions)), anxiety, functional exercise capacity (6MWD % predicted), FFMI, and age, after the completion of a 12-week PR program.

Most studies investigated the relationship between subjective fatigue and other variables in a cross-sectional way, i.e. not following a PR program. Only one other study aimed to investigate the relationship between a change in subjective fatigue and other variables in patients with COPD following a PR program (Lewko et al., 2014). The PR program duration was considerably shorter (seven weeks) compared to that of the current study and consisted of individual exercise training and multidisciplinary education sessions. Similar to the current study's results, a positive correlation was found between a change in subjective fatigue and change in HRQoL, which indicates that an improvement in HRQoL is related with an improvement in subjective fatigue following PR. In addition, Lewko et al. (2014) found a negative relationship between a change in subjective fatigue and functional exercise capacity, which is indicative that an improvement in functional exercise capacity is related to a decrease in subjective fatigue. This finding is also in accordance with that of the current study. Furthermore, no correlations were reported between a change in subjective fatigue and a change in BMI or quadriceps muscle force, which agrees to the current study's results. In contrast to the current study's findings, no correlation was found between change in subjective fatigue and change in anxiety following PR. This might be due to the non-significant change in anxiety following PR. The current study, on the other hand, did report a statistically significant change of anxiety after PR and found a significant positive correlation between change in anxiety and change in subjective fatigue.

5.3 Prediction model for change in subjective fatigue

The current study also aimed to analyze possible determinants to predict a change in subjective fatigue. A small amount (26.9%) of the variance in change of subjective fatigue could be explained by change in HRQoL, subjective complaints and functional exercise capacity.

Some cross-sectional studies also tried to identify predictive determinants of subjective fatigue. The variance in these prediction models explained 36-62% of subjective fatigue. Subjective fatigue was in one study predicted by the combination of depression, muscle strength, lung function, exercise capacity, age, BMI, perceived exertion, and blood oxygenation (Lewko, Bidgood, & Garrod, 2009). Another prediction model ascribed the variance of subjective fatigue to dyspnea, depressed mood, and sleep quality (Kapella, Larson, Patel, Covey, & Berry, 2006). Likewise, in Korean subjects with COPD, also dyspnea and depressed mood could explain almost half of the variance of subjective fatigue (Oh, Kim, Lee, & Kim, 2004). Meanwhile, the study of Baghai-Ravary et al. (2009) found depression, dyspnea, exacerbation frequency and a reduction in time spent outdoors important predictors. Lastly, one study found dyspnea and physical symptoms important predictors of subjective fatigue (Gift & Shepard, 1999).

Based on these results, we can conclude that there is a variety of predicting variables that can explain subjective fatigue. However, the current study's prediction model only explained one-fourth of the variance in change in subjective fatigue following PR. This limited amount of variance could be ascribed to the fact that some possibly important contributors were not measured in the current study, such as physical activity, sleep quality, blood oxygenation, and so on (Spruit et al., 2017). Another possible explanation is that inappropriate measurement tools were used for some of the secondary outcome measures, which may distort the changes in these outcome measures obtained from the PR program. Furthermore, this study is the first study to investigate which changes in secondary outcome measures can predict a change in subjective fatigue following a PR program. This means that the predictive variables found in the current study are probably the ones that need to be addressed with PR to reduce subjective fatigue.

5.4 Strengths and limitations

This study has several strengths. The 12-week individualized inpatient multidisciplinary PR program was conducted according to the ATS/ERS recommendations and the improvement of subjective fatigue exceeded the MCID, which indicates the importance of an individualized inpatient multidisciplinary PR program to reduce subjective fatigue. The measurement of subjective fatigue was performed by a well-validated fatigue-specific questionnaire with high internal consistency and reliability. This questionnaire was a proven method to rate and classify subjective fatigue into severity categories (Beurskens et al., 2000; Servaes et al., 2007; Vercoulen et al., 1994; Worm-Smeitink et al., 2017). Furthermore, the study had a large sample size of 446 included patients. This, and the fact that this study included a versatile population, makes that the results give a better representation of the general COPD population. Moreover, because of the implication of a prediction model in this study, it is possible to predict a reduction in subjective fatigue by improving the contributing factors with PR. Therefore, improvements in these contributors can be partially generalized to improvements in subjective fatigue. In this study, a stepwise multiple linear regression analysis was performed instead of direct multiple linear regression analysis to become a prediction model. This provides a model with only the most considerable predictors of subjective fatigue, so it becomes clear which outcome measures should be targeted.

However, some methodological considerations need to be made. Because this study is a retrospective analysis, no control was exercised over data-extraction and the applied methods. Patients were recruited by convenience sampling, so no control group could be included. Also, the validity of some measurement tools could be questioned. For instance, the use of BMI can be misinterpreted since it does not account the proportions of fat tissue, muscle mass, bone mass, and fluids in body weight (Ischaki et al., 2007). The FFMI was measured to give additional information of the body composition. However, FFMI was not measured with a gold standard tool. There is a tendency to overestimate the FFMI with the BIA which can influence the results (Buckinx et al., 2015). Also, quadriceps muscle force was not measured using a gold standard tool. The quadriceps muscle force was measured with a hand-held dynamometer, in which the outcome is limited by the assessors' force. This also

implies a measurement error due to the variance of force between assessors (O'Shea, Taylor, & Paratz, 2007; Roebroeck, Harlaar, & Lankhorst, 1998). Furthermore, due to the individualized approach of the PR program, the most interfering types of interventions with subjective fatigue could not be identified. Either way, we did address the importance of an individualized, inpatient multidisciplinary PR program to improve subjective fatigue in COPD-patients.

In addition, the current study used a 95% CI with a p-value below 0.05 indicating a statistically significant result. With the use of a 95% CI, it is easier to find a statistically significant result, compared to the use of a 99% CI. Because of this decision, there were more significant results found in the current study, but not all were clinically relevant. This choice was made to correct for the (possible) large proportion of missing data, which reduces the available data to conduct analyses. This was especially applicable for the stepwise multiple linear regression analysis. Also, another correction was made in advance to correct for missing data, by excluding cases pairwise. This was possible because of the large sample size. However, this could have led to possible invalid conclusions and data misinterpretation, especially in the stepwise multiple linear regression analysis where the sample size was almost halved.

5.5 Recommendations

5.5.1 Research considerations

This study emphasized the importance of an intense, multidisciplinary and individual treatment approach to reduce subjective fatigue in patients with COPD. However, future studies are needed to determine the optimal duration and frequency of an individualized inpatient multidisciplinary PR program, and to investigate which type of interventions are needed to provide the most favorable reduction of subjective fatigue in COPD. Studies with prolonged follow-up are needed as well to determine the long-term effects of PR on subjective fatigue. Furthermore, few studies evaluated the relationship between a change in subjective fatigue and change in other outcome measures. There is a lack of studies that investigate which changes in outcome measures, following PR, predict a change in subjective fatigue. So, future research should focus on the contributing factors of subjective fatigue. Studies should

provide large datasets with a clear and united description of their definition of subjective fatigue. Also, researchers need to use valid and fatigue-specific measurement tools to evaluate subjective fatigue.

5.5.2 Clinical implications

The results of this study demonstrated the importance of an individualized inpatient multidisciplinary PR program for the reduction of subjective fatigue in patients with COPD. All patients with COPD should be assessed for subjective fatigue because of its high prevalence and invalidating character, and when indicated, an appropriate PR program should be composed.

The experience of subjective fatigue appears to be related to many physical and psychological factors. Patients who suffer from clinically relevant subjective fatigue should be further assessed to determine the presence of these contributing factors to provide an enhanced, patient-tailored, and more fatigue-specific PR program. Furthermore, despite the limited prediction of a change in subjective fatigue by the stepwise multiple linear regression analysis, interventions should be tailored to improve HRQoL (i.e. physical satisfaction and satisfaction of the future), subjective complaints (i.e. dyspnea severity and hindrance), and functional exercise capacity in order to decrease subjective fatigue.

6. CONCLUSION

This study clearly illustrates the importance of an individualized multidisciplinary inpatient PR program to decrease subjective fatigue in patients with COPD. Also, this study gave more insight in the different variables that are related to a change in subjective fatigue after PR. Relationships were found between change in subjective fatigue and change in all subdomains of health status, anxiety, FFMI, 6MWD % predicted, and age. This study is the first that tried to identify the independent predictors of change in subjective fatigue after PR. Independent predictors included HRQoL (i.e. physical satisfaction and satisfaction of the future), subjective complaints (i.e. dyspnea severity and hindrance), and functional exercise capacity. Improvements in these variables following PR explained 26.9 % of the improvements found in subjective fatigue. However, since this prediction model only predicted a small amount of the variance in change of subjective fatigue, further research is needed to determine contributing factors of subjective fatigue.

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8. APPENDIX

CIS-fatigue: original Dutch version; CIS-fatigue: translation in English

Table 1: Baseline patient characteristics (n = 446)

Table 2: Baseline values and changes following pulmonary rehabilitation

Figure 1: Prevalence (%) of normal, mild and clinically relevant subjective fatigue before and after pulmonary rehabilitation

Table 3: Correlation between a change in subjective fatigue and a change in secondary outcome measures

Table 4: Results of a stepwise multiple linear regression analysis: determinants of a change in subjective fatigue

Declaration of intent (in Dutch: verklaring op eer)

Inventory form (in Dutch: inventarisatieformulier)

CIS-fatigue: original Dutch version

De volgende 8 uitspraken gaan over moeheid in de afgelopen twee weken. Het antwoord dat u geeft, geeft aan in welke mate u vindt dat de uitspraak op u van toepassing is. U kunt ook de tussenliggende hokjes gebruiken, om uw antwoord te nuanceren.							
	Ja, dat klopt ↓			Geen ja, geen nee ↓			Nee, dat klopt niet ↓
1. Ik voel me moe.	7	6	5	4	3	2	1
2. Lichamelijk voel ik me uitgeput.	7	6	5	4	3	2	1
3. Ik voel me fit.	1	2	3	4	5	6	7
4. Ik voel me slap.	7	6	5	4	3	2	1
5. Ik voel me uitgerust.	1	2	3	4	5	6	7
6. Lichamelijk voel ik me in een slechte conditie.	7	6	5	4	3	2	1
7. Ik ben gauw moe.	7	6	5	4	3	2	1
8. Lichamelijk voel ik me in een uitstekende conditie.	1	2	3	4	5	6	7

CIS-fatigue: translation in English

The following 8 statements are about fatigue in the past two weeks. The answer you give indicates the extent to which you think the statement applies to you. You can also use the intervening boxes to nuance your answer.							
	Yes, that's right ↓			Not yes, not no ↓			No, that is not right ↓
1. I'm feeling tired.	7	6	5	4	3	2	1
2. Physically, I feel exhausted.	7	6	5	4	3	2	1
3. I feel fit.	1	2	3	4	5	6	7
4. I feel weak.	7	6	5	4	3	2	1
5. I feel rested.	1	2	3	4	5	6	7
6. Physically, I feel in a bad condition.	7	6	5	4	3	2	1
7. I get tired quickly.	7	6	5	4	3	2	1
8. Physically, I feel in an excellent condition.	1	2	3	4	5	6	7

Table 1

Baseline patient characteristics (n = 446)

Variables	Patients (*n* = 446)
Male	238 (53.4)
Age (years)	60.5 ± 8.8
Subjective fatigue	41.9 ± 9.3
Normal	29 (6.5)
Mild	83 (18.6)
Clinically relevant	334 (74.9)
Anxiety	17.6 ± 7.2
Depression	3.4 ± 3.0
GOLD-stage: (FEV_1 % predicted)	
1. mild	17 (4.0)
2. moderate	98 (23.1)
3. severe	205 (48.2)
4. very severe	105 (24.7)
Duration of lung disease:	
< 1 year	49 (11.2)
2-5 years	127 (28.9)
6-10 years	81 (18.5)
> 10 years	145 (33.0)
Smoking status:	
Smoker	47 (10.7)
Quit smoking	376 (85.3)
Never smoked	18 (4.1)
Nutritional status: BMI (kg/m^2):	25.9 ± 5.5
Underweight	69 (15.5)
Normal weight	157 (35.2)
Overweight	140 (31.4)
Obese	80 (17.9)
Self-reported comorbidities (yes)	336 (76.2)
Back pain	111 (25.2)
Joint complaints	91 (20.6)
Psychiatric complaints	72 (16.3)
Diabetes mellitus	41 (9.3)
Cancer	6 (1.4)
Cardiac disease	70 (15.9)
Other complaints	90 (20.4)

Data are expressed as N (%) or mean ± SD

N = number; SD = standard deviation; BMI = body mass index; GOLD = Global Initiative for Chronic Obstructive Lung Disease; FEV_1 % predicted = percentage of the predicted post-bronchodilator Forced Expiratory Volume in one second.

Table 2

Baseline values and changes following pulmonary rehabilitation

Outcome measure	Pre-PR Mean ± SD	Post-PR Mean ± SD	Δ	p-value (95% CI)
BMI (kg/m²)	25.9 ± 5.5	25.9 ± 5.0	-0.0 ± 1.3	0.636
FFMI (kg/m²)	16.5 ± 2.2	16.7 ± 2.1	0.1 ± 1.1	**0.026***
Anxiety	17.6 ± 7.2	14.7 ± 6.4	-3.0 ± 5.7	**< 0.001***
Depression	3.4 ± 3.0	1.9 ± 2.2	-1.5 ± 2.6	**< 0.001***
NCSI				
QoL	26.8 ± 14.8	19.3 ± 12.3	-7.4 ± 12.5	**< 0.001***
HRQoL	5.8 ± 1.7	4.0 ± 1.7	-1.8 ± 2.0	**< 0.001***
Satisfaction with relations	3.8 ± 1.8	3.3 ± 1.6	-0.6 ± 2.1	**< 0.001***
Subjective impairment	16.4 ± 5.2	12.9 ± 5.1	-3.5 ± 5.5	**< 0.001***
Behavioral impairment	27.2 ± 14.0	25.3 ± 14.5	-1.9 ± 14.6	**0.005***
Subjective complaints	13.0 ± 3.8	9.8 ± 4.2	-3.2 ± 4.4	**< 0.001***
Dyspnea (emotions)	12.9 ± 4.0	11.0 ± 3.9	-1.9 ± 3.8	**< 0.001***
Subjective fatigue	41.9 ± 9.3	31.5 ± 10.4	-10.4 ± 11.7	**< 0.001***
FEV_1 (l/s)	1.2 ± 0.5	1.3 ± 0.7	0.1 ± 0.3	**< 0.001***
FEV_1 % predicted	42.6 ± 17.8	44.3 ± 20.0	1.7 ± 8.7	**< 0.001***
Quadriceps muscle force (Nm)	296.2 ± 105.4	322.2 ± 106.8	26.0 ± 64.1	**< 0.001***
Quadriceps muscle force % predicted	84.6 ± 21.9	91.3 ± 24.0	6.7 ± 20.7	**< 0.001***
6MWD (m)	379.3 ± 102.6	436.9 ± 97.6	57.6 ± 73.2	**< 0.001***
6MWD % predicted	58.0 ± 15.3	66.0 ± 14.9	7.9 ± 11.6	**< 0.001***

*: $p < 0.05$ (significant)

PR = pulmonary rehabilitation; SD = standard deviation; Δ = post-pre-PR difference; CI = confidence interval; BMI = body mass index; FFMI = fat-free mass index; NCSI = Nijmegen Clinical Screening Instrument; QoL = quality of life, HRQoL = health-related quality of life; FEV_1 (l/s); post-bronchodilator Forced Expiratory Volume in one second expressed in liters; FEV_1 % predicted = percentage of the predicted post-bronchodilator Forced Expiratory Volume in one second; Nm = Newton meter; quadriceps muscle force % predicted = percentage of the predicted quadriceps muscle force; 6MWD (m) = 6-minute walking distance expressed in meters; 6MWD % predicted = percentage of the predicted 6-minute walking distance.

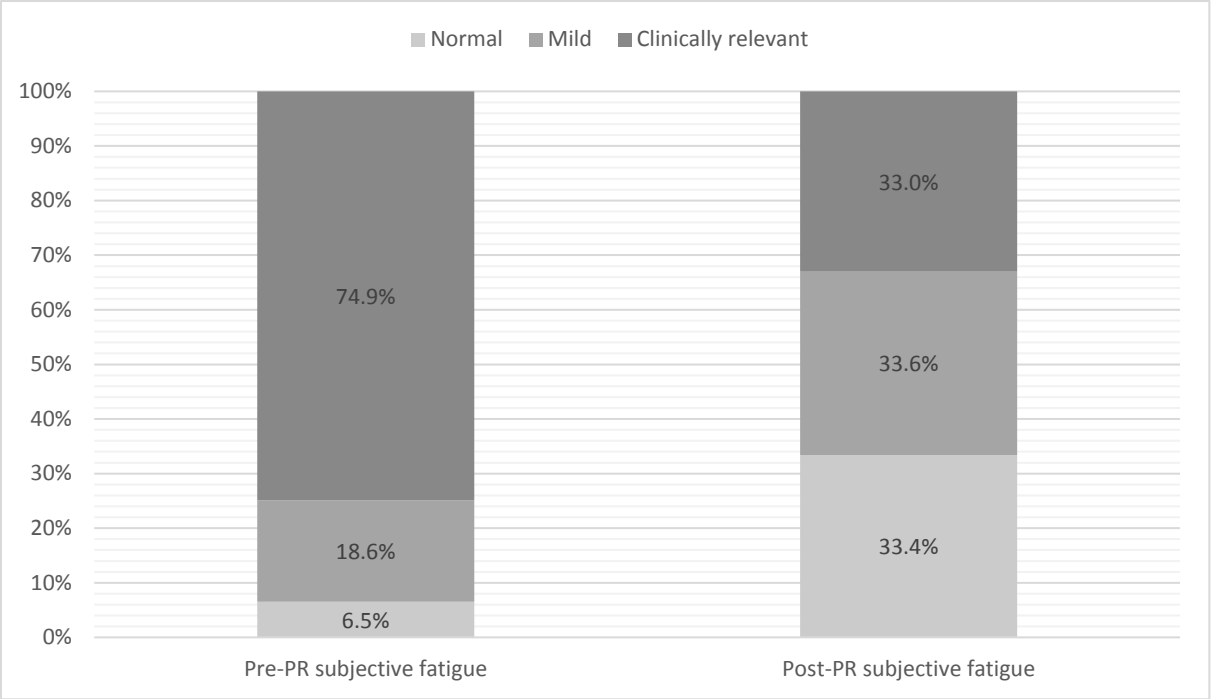

Figure 1: Prevalence (%) of normal, mild and clinically relevant subjective fatigue before and after pulmonary rehabilitation

Table 3

Correlation between a change in subjective fatigue and a change in secondary outcome measures

Variable	Pearson correlation coefficient	P-value (95% CI)
Δ BMI (kg/m²)	0.012	0.812
Δ FFMI (kg/m²)	**-0.126**	**0.026***
Δ Anxiety	**0.243**	**< 0.001***
Δ QoL	**0.300**	**< 0.001***
Δ HRQoL	**0.424**	**< 0.001***
Δ Satisfaction with relations	**0.142**	**0.003***
Δ Subjective impairment	**0.306**	**< 0.001***
Δ Behavioral impairment	**0.131**	**0.005***
Δ Subjective complaints	**0.369**	**< 0.001***
Δ Dyspnea (emotions)	**0.245**	**< 0.001***
Δ FEV_1 % predicted	-0.053	0.303
Δ quadriceps muscle force % predicted	-0.070	0.218
Δ 6MWD % predicted	**-0.323**	**< 0.001***
Sex	0.038	0.419
Age	**0.111**	**0.020**

*: $p < 0.05$ (significant)

CI = confidence interval; Δ = post-pre PR difference; BMI = body mass index; FFMI = fat-free mass index; QoL = quality of life; HRQoL = health-related quality of life; FEV_1 % predicted = percentage of the predicted post-bronchodilator Forced Expiratory Volume in one second; quadriceps muscle force % predicted = percentage of the predicted quadriceps muscle force; 6MWD % predicted = percentage of the predicted 6-minute walking distance.

Table 4

Results of a stepwise multiple linear regression analysis: determinants of a change in subjective fatigue

Model	Variables	B	Standard error	β	t-value	p-value (95% CI)
1	(Constant)	-5.864	1.029	-	-5.696	**< 0.001***
	Δ HRQoL	2.497	0.384	0.424	6.506	**< 0.001***
2	(Constant)	-4.668	1.046	-	-4.461	**< 0.001***
	Δ HRQOL	1.982	0.396	0.337	5.003	**< 0.001***
	Δ Subjective complaints	0.665	0.178	0.252	3.741	**< 0.001***
3	(Constant)	-3.836	1.064	-	-3.605	**< 0.001***
	Δ HRQoL	1.727	0.398	0.293	4.341	**< 0.001***
	Δ Subjective complaints	0.590	0.176	0.224	3.353	**0.001***
	Δ 6MWD % predicted	-0.193	0.066	-0.192	-2.948	**0.004***

*: $p < 0.05$ (significant)

Model 1:

R: 0.424; R^2: 0.180; adjusted R^2: 0.176; standard error of the estimate: 10.59277

$F(1, 193) = 42.333$ ($p < 0.001$)

Model 2:

R: 0.485; R^2: 0.236; adjusted R^2: 0.228; standard error of the estimate: 10.25317

$F(2, 192) = 29.590$ ($p < 0.001$)

Model 3:

R: 0.519; R^2: 0.269; adjusted R^2: 0.257; standard error of the estimate: 10.05381

$F(3, 191) = 23.413$ ($p < 0.001$)

B = unstandardized regression coefficient; β = standardized regression coefficient; CI = confidence interval; Δ = post-pre PR difference; HRQoL = health-related quality of life; 6MWD % predicted = percentage of the predicted 6-minute walking distance.

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit Revalidatiewetenschappen aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

1. Ik ben ingeschreven als student aan de UHasselt in de opleiding 2e master Revalidatiewetenschappen en kinesitherapie, waarbij ik de kans krijg om in het kader van mijn opleiding mee te werken aan onderzoek van de faculteit Revalidatiewetenschappen aan de UHasselt. Dit onderzoek wordt begeleid door Prof. Dr. Martijn A. Spruit en kadert binnen het opleidingsonderdeel 'Wetenschappelijke stage/masterproef deel 2'. Ik zal in het kader van dit onderzoek creaties, schetsen, ontwerpen, prototypes en/of onderzoeksresultaten tot stand brengen in het domein van 'Revalidatie van inwendige aandoeningen' (hierna: "De Onderzoeksresultaten").

2. Bij de creatie van De Onderzoeksresultaten doe ik beroep op de achtergrondkennis, vertrouwelijke informatie[1], universitaire middelen en faciliteiten van UHasselt (hierna: de "Expertise").

3. Ik zal de Expertise, met inbegrip van vertrouwelijke informatie, uitsluitend aanwenden voor het uitvoeren van hogergenoemd onderzoek binnen UHasselt. Ik zal hierbij steeds de toepasselijke regelgeving, in het bijzonder de Algemene Verordening Gegevensbescherming (EU 2016-679), in acht nemen.

4. Ik zal de Expertise (i) voor geen enkele andere doelstelling gebruiken, en (ii) niet zonder voorafgaande schriftelijke toestemming van UHasselt op directe of indirecte wijze publiek maken.

5. Aangezien ik in het kader van mijn onderzoek beroep doe op de Expertise van de UHasselt, draag ik hierbij alle bestaande en toekomstige intellectuele eigendomsrechten op De Onderzoeksresultaten over aan de UHasselt. Deze overdracht omvat alle vormen van intellectuele eigendomsrechten, zoals onder meer – zonder daartoe beperkt te zijn – het auteursrecht, octrooirecht, merkenrecht, modellenrecht en knowhow. De overdracht geschiedt in de meest volledige omvang, voor de gehele wereld en voor de gehele beschermingsduur van de betrokken rechten.

6. In zoverre De Onderzoeksresultaten auteursrechtelijk beschermd zijn, omvat bovenstaande overdracht onder meer de volgende exploitatiewijzen, en dit steeds voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding:

   - het recht om De Onderzoeksresultaten vast te (laten) leggen door alle technieken en op alle dragers;

[1] Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo snel mogelijk op de hoogte brengt.

- het recht om De Onderzoeksresultaten geheel of gedeeltelijk te (laten) reproduceren, openbaar te (laten) maken, uit te (laten) geven, te (laten) exploiteren en te (laten) verspreiden in eender welke vorm, in een onbeperkt aantal exemplaren;
- het recht om De Onderzoeksresultaten te (laten) verspreiden en mee te (laten) delen aan het publiek door alle technieken met inbegrip van de kabel, de satelliet, het internet en alle vormen van computernetwerken;
- het recht De Onderzoeksresultaten geheel of gedeeltelijk te (laten) bewerken of te (laten) vertalen en het (laten) reproduceren van die bewerkingen of vertalingen;
- het recht De Onderzoeksresultaten te (laten) bewerken of (laten) wijzigen, onder meer door het reproduceren van bepaalde elementen door alle technieken en/of door het wijzigen van bepaalde parameters (zoals de kleuren en de afmetingen).

De overdracht van rechten voor deze exploitatiewijzen heeft ook betrekking op toekomstige onderzoeksresultaten tot stand gekomen tijdens het onderzoek aan UHasselt, eveneens voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding.

Ik behoud daarbij steeds het recht op naamvermelding als (mede)auteur van de betreffende Onderzoeksresultaten.

7. Ik zal alle onderzoeksdata, ideeën en uitvoeringen neerschrijven in een "laboratory notebook" en deze gegevens niet vrijgeven, tenzij met uitdrukkelijke toestemming van mijn UHasseltbegeleider Prof. Dr. Martijn A. Spruit.

8. Na de eindevaluatie van mijn onderzoek aan de UHasselt zal ik alle verkregen vertrouwelijke informatie, materialen, en kopieën daarvan, die nog in mijn bezit zouden zijn, aan UHasselt terugbezorgen.

Gelezen voor akkoord en goedgekeurd,

Naam: Astrid Boms

Adres: Anjelierenstraat 32, 3530 Houthalen-Oost

Geboortedatum en -plaats : 23/08/1996 te Gent

Datum: 12/09/2018

Handtekening: Boms

Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit Revalidatiewetenschappen aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

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4. Ik zal de Expertise (i) voor geen enkele andere doelstelling gebruiken, en (ii) niet zonder voorafgaande schriftelijke toestemming van UHasselt op directe of indirecte wijze publiek maken.

5. Aangezien ik in het kader van mijn onderzoek beroep doe op de Expertise van de UHasselt, draag ik hierbij alle bestaande en toekomstige intellectuele eigendomsrechten op De Onderzoeksresultaten over aan de UHasselt. Deze overdracht omvat alle vormen van intellectuele eigendomsrechten, zoals onder meer – zonder daartoe beperkt te zijn – het auteursrecht, octrooirecht, merkenrecht, modellenrecht en knowhow. De overdracht geschiedt in de meest volledige omvang, voor de gehele wereld en voor de gehele beschermingsduur van de betrokken rechten.

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---

[1] Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo snel mogelijk op de hoogte brengt.

- het recht om De Onderzoeksresultaten te (laten) verspreiden en mee te (laten) delen aan het publiek door alle technieken met inbegrip van de kabel, de satelliet, het internet en alle vormen van computernetwerken;
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8. Na de eindevaluatie van mijn onderzoek aan de UHasselt zal ik alle verkregen vertrouwelijke informatie, materialen, en kopieën daarvan, die nog in mijn bezit zouden zijn, aan UHasselt terugbezorgen.

Gelezen voor akkoord en goedgekeurd,

Naam: Eliene Beckers

Adres: Grote Baan 459 3530 Houthalen-Helchteren

Geboortedatum en –plaats : 03/04/1996 te Heusden

Datum: 12/09/2018

Handtekening:

Beckers E.

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UHASSELT
KNOWLEDGE IN ACTION

INVENTARISATIEFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
12/09/2018	Afspraken over verloop MP2.	Promotor: Copromotor/Begeleider: Student(e): Student(e): Bechers E.
02/01/2019 16/02/2019	Feedback inleiding via mail	Promotor: Copromotor/Begeleider: Student(e): Student(e): Bechers E.
01/02/2019	Dataset in ontvangst genomen en bespreking	Promotor: Copromotor/Begeleider: Student(e): Student(e): Bechers E.
09/02/2019 08/05/2019	Vragen dataset en methode doorgestuurd en beantwoord via mail	Promotor: Copromotor/Begeleider: Student(e): Student(e): Bechers E.
07/03/2019 23/03/2019	Data-analyse (en appendix) doorgestuurd via mail	Promotor: Copromotor/Begeleider: Student(e): Student(e): Bechers E.
14/04/2019	Inleiding, methode en resultaten doorgestuurd via mail	Promotor: Copromotor/Begeleider: Student(e): Student(e): Bechers E.
13/05/2019 19/05/2019	Volledige MP2 doorgestuurd naar Maarten Van Herck en feedback ontvangen	Promotor: Copromotor/Begeleider: Student(e): Student(e): Bechers E.
23/05/2019	Volledige MP2 doorgestuurd naar Martijn Spruit	Promotor: Copromotor/Begeleider: Student(e): Student(e): Bechers E.
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): Astrid Bams **Datum:** 2/6/2019

Titel Masterproef: Subjective fatigue: Effects of pulmonary rehabilitation and its relationship with other variables in patients with COPD

1) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:
   - NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
   - 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
   - 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
   - 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering
   - 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.
   - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag	O	O	O	O	O	O
Methodologische uitwerking	O	O	O	O	O	O
Data acquisitie	O	O	O	O	O	O
Data management	O	O	O	O	O	O
Dataverwerking/Statistiek	O	O	O	O	O	O
Rapportage	O	O	O	O	O	O

in andere studie v Fantastique Consortium

2) Niet-bindend advies: Student(e) krijgt toelating/~~geen toelating~~ (schrappen wat niet past) om bovenvermelde Wetenschappelijke stage/masterproef deel 2 te verdedigen in bovenvermelde periode. Deze eventuele toelating houdt geen garantie in dat de student geslaagd is voor dit opleidingsonderdeel.

3) Deze wetenschappelijke stage/masterproef deel 2 mag wel/~~niet~~ (schrappen wat niet past) openbaar verdedigd worden.

4) Deze wetenschappelijke stage/masterproef deel 2 mag wel/~~niet~~ (schrappen wat niet past) opgenomen worden in de bibliotheek en docserver van de UHasselt.

Datum en handtekening Student(e)	Datum en handtekening promotor(en)	Datum en handtekening ~~Co-promotor(en)~~ Begeleider(s)
2/6/2019	ingesprongt	
~~Bams~~	27/05/2019	27/5/2019

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): Eliene Beckers **Datum:** 2/6/2019

Titel Masterproef: Subjective fatigue : Effects of pulmonary rehabilitation and its relationship with other variables in patients with COPD

1) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:
   - NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
   - 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
   - 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
   - 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering
   - 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.
   - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag	X	O	O	O	O	O
Methodologische uitwerking	X	O	O	O	O	O
Data acquisitie	O	O	O	O	X	O
Data management	O	O	O	O	O	X
Dataverwerking/Statistiek	O	O	O	O	X	O
Rapportage	O	O	O	O	X	O

in andere studie v Fantastique consortium

2) Niet-bindend advies: Student(e) krijgt toelating/~~geen toelating~~ (schrappen wat niet past) om bovenvermelde Wetenschappelijke stage/masterproef deel 2 te verdedigen in bovenvermelde periode. Deze eventuele toelating houdt geen garantie in dat de student geslaagd is voor dit opleidingsonderdeel.

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4) Deze wetenschappelijke stage/masterproef deel 2 mag wel/~~niet~~ (schrappen wat niet past) opgenomen worden in de bibliotheek en docserver van de UHasselt.

Datum en handtekening Student(e)	Datum en handtekening promotor(en)	Datum en handtekening Co-promotor(en)
Beckers E.	Masprijt	
03/06/2019	27/05/2019	27/05/2019