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Two Interventions for Patients with Major Depression and Severe COPD: Impact on Quality of Life

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Abstract

Objective: Clinically significant depression occurs in approximately 40% of COPD patients and both illnesses severely impair quality of life. This study tests the hypothesis that problem solving integrated with a treatment adherence intervention (PSA) is superior to a personalized treatment adherence intervention alone (PID-C) in improving quality of life in depressed COPD patients.

Methods: After screening 633 admissions for acute rehabilitation, we studied quality of life in 87 participants with major depression (by DSM-IV) and severe COPD randomly assigned to 14 sessions of PID-C or PSA over 26 weeks. Quality of life was assessed with the Word Health Organization Quality of Life-BREF (WHOQOL-BREF) at baseline, and week 10, 14 and 26.

Results: The hypothesis was not supported. Exploratory latent class growth modeling identified two quality of life trajectories. In 80.5% of participants, quality of life remained unchanged and improved in the remainder 19.5% during the first 14 weeks. Patients with a stable quality trajectory had higher quality of life at baseline and a stronger sense of personal agency.

Limitations: Absence of an “inert treatment” arm, small sample size, and high number of participants who exited prior to randomization.

Conclusion: Maintaining quality of life is a favorable outcome in depressed patients with COPD whose course is one of deterioration. These findings highlight the usefulness of PID-C, a simple to learn, personalized adherence enhancement intervention that after further testing, may be integrated in the rehabilitation and care of depressed COPD patients.

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Keywords

Depression; COPD; Quality of Life; Personalized Intervention; Clinical Trial

INTRODUCTION

The prevalence of most chronic diseases is declining(1). Chronic obstructive pulmonary disease (COPD) afflicts 11.6% of older adults (2) and is the only common chronic disease whose prevalence continues to rise despite reduction in smoking (3). Approximately 40% of COPD patients suffer from clinically significant depression at some point of their illness (4). Both COPD (5) and depression(6) worsen quality of life. In COPD patients, depression increases the risk of mortality more than in other chronic medical illnesses (7), elevates the risk of COPD exacerbations (8) and predicts worsening of quality of life at 1 year follow-up(9)

We developed two interventions aimed to improve depression, disability, and quality of life in depressed, COPD patients. Both interventions target adherence of COPD patients to treatment prescribed by their own physicians. The focus on adherence has been based on findings indicating that antidepressant drugs and pulmonary rehabilitation may improve depression of COPD patients to varying degrees but adherence to treatment of this population has been problematic(10). Fewer than 30% of depressed COPD patients agree to receive antidepressant drugs(11). Pulmonary rehabilitation can reduce symptoms of major depression in COPD patients independently of antidepressant use (12). Nonetheless, adherence to pulmonary rehabilitation has been poor in non-depressed COPD patients (13) and depression further may reduce adherence(12).

What is distinct in both of our interventions is that they are personalized based on a systematic review of reasons for non-adherence in individual patients. One intervention, the Personalized Intervention for Depressed Patients with COPD (PID-C) provides individualized treatment adherence strategies. The other intervention, the Problem Solving-Adherence (PSA), integrates problem solving into adherence enhancement procedures. We introduced problem solving because COPD patients often have executive, attention, and memory deficits (14) likely to impair problem solving skills needed for adhering to clinical recommendations; problem solving therapy has been found effective in reducing both depression(15) and disability (16) in depressed elders with executive dysfunction.

This analysis used data of a randomized clinical trial whose aim was to compare the impact of PID-C with that of PSA on depression and dyspnea related disability (17), (18). Although both PID-C and PSA reduce depression (17) and dyspnea related disability (18), it is important to examine the impact of these interventions on quality of life separately. Quality of life is affected in complex ways by depression (6) and dyspnea of COPD (5), but itself represents a distinct dimension of health reflecting the individual's perception and personal beliefs of their position in life in the context of the culture and value systems and in relation to their goals, expectations, standards, and concerns (19). This report, tests the hypothesis that PSA is more effective than PID-C in improving the quality of life of patients with major depression and COPD over a period of 26 weeks. Its rationale is that PSA, a treatment

intended to strengthen problem solving skills, can increase the participants' sense of mastery and have a more positive effect than PID-C, which only addresses treatment adherence. Exploratory analyses sought to identify groups of patients with distinct quality of life trajectories and compare their clinical profiles.

METHODS

Participants:

The study methods have been reported elsewhere (17). Briefly, participants were recruited from consecutive admissions to the inpatient, pulmonary unit of an acute rehabilitation hospital from February 2008 to October 2014. There was no change in admission policies or treatment during this period. All participants signed consent approved by the Weill Cornell Medicine Institutional Review Board. The selection criteria were: 1) COPD diagnosed by a pulmonologist according to the American Thoracic Society Guidelines (20); 2) unipolar major depression by SCID-R and DSM-IV (21), (22); 3) a score of 20 or greater on the 24-item Hamilton Depression Rating Scale (HAM-D) (23); 4) absence of DSM-IV diagnoses other than unipolar major depression; 5) Mini Mental State Examination (24) score of 24 or higher; and 3) absence of intent or plan to attempt suicide in the near future. Depressed patients with anxiety disorders other than obsessive compulsive disorder were included.

Assessment:

Participants were assessed by trained research assistants, blind to treatment assignment. The outcome variable was the World Health Organization Quality of Life-BREF (WHOQOL-BREF) composite score. The WHOQOL-BREF is a 26-item quality of life scale, which includes one item from each of the 24 facets of WHOQOL-100 plus two items from the Overall Quality of Life and the General Health facet(25). The composite WHOQOL-BREF score offers information on the individual's perception of own physical health, psychological wellbeing, social relationships, and environment (6, 26). The WHOQOL-BREF has high test-retest reliability(19) and has been validated in diverse populations with a variety of medical conditions in many countries (19). The WHOQOL-BREF was completed at baseline, and week 10 (end of weekly session phase), 14 (after the first monthly session) and 26 (after last session). We selected this schedule of WHOQOL-BREF administration because it permits an intent-to-treat analysis that makes optimal use of data in a very sick population with a predictably high attrition and missed data.

At entry, medical burden was quantified with the Charlson Comorbidity Index (CCI) (27). Severity of depression was assessed with the HAM-D, and neuroticism with the NEO-PI (28). Dyspnea-related disability was rated with the Pulmonary Functional Status and Dyspnea Questionnaire-Modified (PFSDQ-M), a scale that assesses dyspnea during ten activities (29) (30). Overall disability was quantified with the World Health Organization Disability Assessment Schedule (WHODAS) (31). Overall cognitive impairment was quantified with the Mini-Mental State Examination (24) and executive dysfunction with the Stroop Color Word Scale (32), and the Initiation/Perseveration Domain of Dementia Rating Scale (33). Self-efficacy was assessed with the Liverpool Self-Efficacy Scale, which consists

of two subscales, i.e. personal control and personal agency (34). Blood gases values were obtained from the participants' medical record.

Randomization:

Participants were randomized to PID-C or PSA in 5-subject blocks using random numbers. The clinical team was blind to randomization.

Interventions:

Care managers (master's level social workers) conducted 14 sessions of PID-C or PSA over 26 weeks. The first 2 sessions occurred during the hospitalization and 8 sessions were offered weekly after discharge at the participants' homes or the therapists' offices depending on ability to travel. Four additional monthly booster sessions reinforced the positive behaviors developed during the first 10 weekly sessions. All sessions were audiotaped and 10% of randomly selected sessions were evaluated for adherence to manuals with the PID-C and PSA Adherence Scales (Composite scores range: 1-5). Treatment fidelity ratings were performed by an experienced clinical psychologist, not a member of the research team, trained in PID-C and PSA. PID-C and PSA have been described elsewhere (17, 18) (Manuals in Appendix). Below is a brief outline of these two interventions.

PID-C:

Guided by the PID-C Manual, care managers worked with each patient to identify barriers to this patient's adherence to recommendations of his/her own physicians. Then, care managers targeted these barriers with interventions such as correction of misunderstanding of recommendations, misattribution of symptoms, hopelessness, dissatisfaction with treatment, and management of logistic obstacles. Care managers also interacted with the patients' physicians and office personnel on how to reinforce treatment adherence. When appropriate, caregivers participated in the patients' care. The care managers informed the participants' physicians of any changes in the patients' status and of any problems with adherence and discussed plans for addressing them.

PSA:

PSA integrates the personalized approach to treatment adherence of PID-C with development of problem solving skills likely to improve treatment adherence. Treatment adherence problems related to misunderstanding or limited information are approached with psychoeducation and direct instruction. Hopelessness, helplessness and fatigue interfering with prescribed exercise and activities, social isolation and neglect of important relationships are addressed with problem solving skill development using the following steps: 1. Problem definition; 2. Establishment of achievable goals; 3. Generation of alternative solutions; 4. Application of the decision making process; 5. Evaluation and selection of solutions; 6. Implementation of the preferred solution; and 7. Evaluation of outcome. Care managers encourage patients to focus on the process of addressing the problem at hand, so that they could use the same approach in subsequent problems.

Training and Fidelity—Care managers attended a one-day workshop, which consisted of a presentation and discussion of the principles of each therapy and role-play of typical sessions. Care managers treated 3 practice cases of each treatment, which were audiotaped and rated. Certification requires an average score of 4 in the PID-C Adherence Scale and the PSA Adherence for each case, in 3 consecutive cases. Clinician investigators offered weekly supervision during the trial. The average composite score of 10% of randomly selected audiotaped sessions in the PID-C Adherence Scale was 4.67 (SD: 0.55) and in the PSA Adherence Scale was 4.29 (SD: 0.69), both in the “good” to “excellent” range.

Data Analysis:

We used mixed effects models to compare the profiles of quality of life (WHOQOL-BREF) scores of PID-C vs. PSA measured at baseline, weeks 10, 14 and 26. This analysis accounted for repeated measurements and included time-trend parameter(s), treatment group, and time by treatment interaction as fixed effect and participant-specific random intercept. The p-values for within treatment group post-hoc tests of WHOQOL-BREF change from baseline to week 10, 14 and 26 were adjusted for multiple comparisons by Holms step-down procedure (35). We used latent class growth modeling (LCGM) to identify subgroups with distinct quality of life trajectories and examined up to five trajectory solutions employing censored normal distribution (36). First, we estimated the trajectory coefficients, calculated their 95% Bootstrap-*t* confidence interval in 1000 bootstrap samples, and selected the order (constant, linear, or non-linear, i.e. quadratic, cubic or quartic) of each trajectory using significance of $\alpha=0.05$. We, then, tested the derived model against a model with one less trajectory using the change in Bayesian Information Criterion (BIC) as an approximation to the log Bayes factor ($2 \text{ BIC} > 2$)(37). We used the average posterior probabilities of group membership as a measure of internal reliability for each trajectory. Values greater than 0.70 to 0.80 suggest that the trajectories classify groups with similar patterns of change separately from groups with different patterns of change. This analysis showed that a two-trajectory model fit the data best. We tested baseline clinical and demographic characteristics between the two groups of participants belonging to each trajectory to identify their clinical profile of participants. Finally, we built logistic regression models to predict trajectory membership with depression severity (HAM-D), disability (WHODAS), Charlson’s comorbidity index, total Dyspnea, MMSE, Liverpool Self-Efficacy’s Personal Agency and Control subscales as predictors. The missing values in covariates were imputed fifteen times using multiple imputation with chained equations via predictive mean matching. The estimates and their confidence intervals of regression models were pooled over fifteen imputed datasets (38). To test the predictive ability of this regression model, each imputed dataset was split randomly into two parts – training (N=60) and test (N=27) – the model parameters were estimated with the training data and prediction metrics (Area Under the Receiver Operator Characteristic curve or AUROC) evaluated on the test data using model estimates from the training data.

RESULTS

This study screened 633 patients, consecutively admitted to the pulmonary service of a rehabilitation hospital. Of the 633 patients, 147 met selection criteria (17), and signed

informed consent and 101 were randomized to either the PID-C or the PSA intervention at a ratio of 1:1. Their flow into the study (CONSORT diagram) can be found in the Appendix. Among randomized participants, the mean inpatient stay was 19.6 days (SD: 17.1). There were no significant differences in demographics and clinical characteristics among participants assigned to PID-C or PSA at baseline, including age, race, education, and severity of depression or disability. There were no differences in overall rate of attrition between the two intervention arms at 26 weeks ($\chi^2=0.0714$, $df=1$, $p=0.7893$). During the 26 weeks of the study 14% (7/50) of PID-C and 13.7% (7/51) of PSA participants died ($\chi^2=0.0016$, $df=1$, $p=0.9682$). This paper reports on the subset of participants ($N=87$) who had at least one follow up assessment of quality of life (WHOQOL-BREF) after the baseline assessment.

Hypothesis Testing: Comparison of Quality of Life of PID-C vs. PSA

The mean (SD) of WHOQOL-BREF among PID-C participants was 42.19 (22.96) at baseline, 50.74 (18.99) at week 10, 52.21 (23.48) at week 14, and 43.75 (21.96) at week 26 of the treatment period. The corresponding figures for PSA participants were 34.82 (21.61) at baseline, 39.71 (20.37) at week 10, 40.97 (13.43) at week 14, and 45.00 (21.55) at week 26. Longitudinal mixed model analysis of QOL assessments at baseline, week 10, week 14 and week 26 showed that the two treatment groups did not differ significantly in their QOL trajectories (treatment x time interaction: $F(3,78)=1$, $p=0.4$) (Figure 1). The two treatment arms had a difference in effect size (Cohen's d) of 0.33 at baseline, 0.56 at week 10, 0.59 at week 14 and 0.06 at week 26.

Exploratory Analysis: Trajectories of Quality of Life

Exploratory latent class growth analysis sought to identify distinct quality of life (WHOQOL-BREF) trajectories of all participants ($N=87$), who were treated with either PID-C or PSA. After reviewing up to five trajectories of various shapes (linear, quadratic, cubic, quartic), a two-trajectory solution best fit the data (2 BIC = 123.2) (Figure 2). The first was a “stable QOL trajectory” of participants with high QOL at baseline that remained unchanged throughout the intervention. The second trajectory was an “improving QOL trajectory” of participants who started with a low quality of life that improved in the first 14 weeks, when they received frequent sessions, and slightly declined after the intense intervention phase (14-26 weeks). The mean (SD) posterior probabilities for membership in the “stable” and the “improving” trajectories were 0.96 (0.13) and 0.88 (0.13) respectively. The “stable QOL trajectory” encompassed 70 participants (estimate of intercept: 7.9 points, 95% Bootstrap CI: 2.59, 9.39). The “improving QOL trajectory” encompassed 17 participants (linear slope: 1.82, 95% Bootstrap CI: 1.71, 2.31; quadratic slope: -0.04, 95% Bootstrap CI: -0.05, -0.03).

There was no significant difference in the distribution of interventions (PSA vs. PID-C) in each of the two QOL trajectories ($\chi^2=0.0$, $df=1$, $p=1$). Specifically, 52.9% (37/70) of participants with a “stable QOL trajectory” received PSA and 47.1% (33/70) received PID-C. In the “improving QOL trajectory”, 52.9% (9/17) received PSA and 47.1% (8/17) received PID-C. There were no significant differences between the stable and the improving trajectories in demographics, severity of depression, dyspnea, medical burden, disability,

overall cognitive impairment, executive dysfunction, neuroticism, and blood gases (Table 1). Regression analysis used to predict trajectory membership showed that personal agency was a significant predictor of trajectory membership after accounting for personal control, depression severity, dyspnea, disability, cognitive impairment, and medical burden (Table 2). One unit increase in Personal Agency score increased the odds of belonging to the “stable QOL trajectory” by 1.94 (95% CI: 1.16, 3.23; $t=2.58$, $df=75.2$, $p = 0.0119$). The AUROC of the regression model evaluated on the test data portion ($N=27$) of each imputed dataset ranged from 0.88 to 0.96, which demonstrates the regression model’s ability to predict trajectory membership.

Quality of Life versus Dyspnea

In an earlier report on the same sample, we identified two groups of depressed COPD participants with distinct trajectories of dyspnea (PFSDQ-M) (18). One group had a stable dyspnea trajectory throughout the intervention period and another had an improving trajectory. Since dyspnea may influence quality of life, we examined whether the trajectories of quality of life and dyspnea included the same participants. Among the 87 participants, 45 (51.7%) belonged to the “stable” trajectories of both dyspnea and QOL; 10 (11.5%) belonged to the “improving” trajectory of both outcomes; 7 (8%) belonged to the improving trajectory QOL and stable trajectory of dyspnea; and 25 (28.7%) belonged to the improving trajectory of dyspnea and the stable trajectory of QOL. Membership to stable or improving trajectories for QOL was not significantly associated with the corresponding trajectories of dyspnea ($\chi^2=3.04$; $df = 1$; $p = 0.10$).

DISCUSSION

This study did not support the hypothesis that an intervention integrating adherence enhancement procedures with problem solving (PSA) benefits quality of life more than a personalized adherence enhancement intervention (PID-C) in depressed patients with severe COPD. It is unclear why problem solving skills imparted by PSA failed to improve the trajectory of quality of life in COPD patients more than treatment adherence procedures. A plausible explanation is that personalized targeting of barriers to adherence pertinent to each individual patient offered by PID-C is sufficient to maintain or improve quality of life, since many of COPD patients fail to adhere to their rehabilitation regimens (13) and depression further worsens treatment adherence (12).

Regardless of intervention, quality of life did not worsen in 80.5% of patients and even improved in the remaining 19.5% at least during the intense phase of the intervention. Maintaining quality of life for 26 weeks is a favorable outcome in a population with major depression, disability, severe COPD, high overall medical burden, and a death rate of 14% over 26 weeks. Documenting that PID-C was followed by no worsening or improvement of quality of life is encouraging. PID-C was originally designed for use by masters-level clinicians (39) and matches the skills of clinicians in rehabilitation and home health care services. Therefore, it can be integrated in the care of COPD patients offered by such programs across the nation.

Exploratory latent class growth modeling of the entire sample identified two groups with distinct courses of quality of life. Approximately 80.5% of patients had a stable quality of life trajectory through both phases of the intervention. In 19.5% of participants, quality of life improved in the first 14 weeks, when they received frequent sessions of either intervention, and slightly declined during the booster session phase (Figure 2).

Depression severity and dyspnea were statistically indistinguishable in the two quality of life trajectories at baseline. Moreover, the groups of the two trajectories of quality of life were different than the groups with the corresponding trajectories of dyspnea. Thus, quality of life appears to be a distinct dimension of health, whose trajectory of response to PID-C and PSA is not fully accounted by dyspnea.

Patients with a stable quality of life trajectory started with better quality of life than patients with the improving trajectory. Personal agency was the only baseline variable that distinguished individuals with a stable quality of life trajectory from those with an improving trajectory; the effect size was rather small but clinically significant. In our participants, personal agency may reflect the patients' confidence that they can cope with their illness and meet the demands of treatment and rehabilitation. Integration of interventions aiming to improve personal agency may increase the impact of PID-C on quality of life, since self-management programs targeting self-efficacy have been shown to improve health outcomes in patients with chronic diseases (40).

Limitations of this study include the absence of a usual care arm, the small sample, the administration of both interventions by the same therapists, and the high number of participants who exited prior to randomization. A usual care arm could have revealed if the interventions were superior to usual care in improving the outcomes of depressed COPD patients. In another sample, we have shown that PID-C led to greater decline in depressive symptoms, and to lower disability than usual care during the 28 weeks of PID-C administration and 6 month follow-up after the last session (39); the participants of this study were recruited from the same rehabilitation center as the present study using similar selection criteria. The sample of our study was small. For this reason, we used the same therapists to administer both interventions. This strategy reduced the need to introduce the impact of therapists in group comparisons and increased the power to detect differences in this small sample of a difficult to enroll population. Administration of both interventions by the same therapists may have contaminated the interventions. However, the high fidelity of therapists to the interventions' manuals suggests that the effect of contamination was very small. A high number of participants who met selection criteria and signed informed consent exited before randomization, mainly because of increased medical burden or mortality. Thus, this study's findings may be generalized to less severely ill populations.

In conclusion, adding problem solving skills to a treatment adherence enhancement intervention failed to improve the trajectory of quality of life in COPD patients more than a treatment adherence intervention alone. Both personalized interventions (PID-C and PSA) targeting adherence to rehabilitation and treatment prescribed by the patients' own physicians prevented worsening of quality of life in most patients with major depression and severe COPD over 26 weeks. Those with stable quality of life trajectory had better quality of

life and a stronger personal agency at baseline. Integrating problem solving strategies with adherence enhancement procedures of PID-C did not further improve quality of life. These findings highlight the clinical usefulness of PID-C, a simple to administer, personalized adherence enhancement intervention. The effectiveness of PID-C requires further testing in community settings. If demonstrated that community clinicians can administer PID-C with fidelity and improve patient outcomes, PID-C can become an important addition to the rehabilitation and care of depressed COPD patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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- Compared the impact of problem solving integrated with a treatment adherence intervention (PSA) to that of a personalized treatment adherence (PID-C) alone in improving quality of life in depressed COPD patients over 26 weeks.
- Regardless of treatment assignment, quality of life remained unchanged in 80.5% of patients and improved in the remainder 19.5%.
- These findings highlight the usefulness of PID-C, a simple to learn intervention, suitable for dissemination.

Figure 1.

Least-square estimates (from mixed model analysis) of quality of life (WHOQOL-BREF) in 87 participants with major depression and severe COPD randomly assigned to Personalized Intervention for Depression and COPD (PID-C) or to Problem Solving Adherence Intervention (PSA)

Figure 2. Latent growth curve model of quality of life (WHOQOL-BREF) trajectories in the combined group of 87 participants with major depression and severe COPD identifying two distinct trajectories – a “stable” trajectory (N=70) in red and an “improving” trajectory (N=17) in blue.

Table 1.

Demographic and Clinical Characteristics of 87 Older Patients with Major Depression and COPD followed for 26 weeks after discharge from an Inpatient Rehabilitation Service.

QOL Trajectory							
	Improving N=17		Stable N=70				
Variable	N	%	N	%	χ^2	df	Holm's Adjusted p-value
Female	11	64.7	47	67.1	0.0366	1	1
PSA Group	9	52.9	37	52.9	0	1	1
	Mean	SD	Mean	SD	t*	df	Holm's Adjusted p-value
Age (years)	73.1	8.7	71.8	9.4	0.5	85	1
Education (years)	14.8	2.5	13.6	3.4	1.4	85	1
WHOQOL-BREF	13.3	12.0	49.7	15.1	−8.3	49	<.0001
HAM-D	25.0	3.5	24.0	4.0	1.0	84	1
Dyspnea (PFSDQ-M)							
TOTAL	159.2	85.7	114.1	69.1	2.3	80	0.5327
Change in Activities	55.2	26.1	38.9	23.5	2.5	80	0.3391
Fatigue with Activities	49.6	34.8	36.8	25.2	1.7	80	1
Dyspnea with Activities	54.5	29.4	38.4	24.4	2.3	80	0.5148
CCI	4.7	4.0	3.3	2.1	2.0	82	0.9235
MMSE	28.4	1.3	27.4	2.0	1.9	81	1
DRS-IP	33.9	3.0	32.4	4.2	1.3	76	1
Stroop Color-Word	23.6	10.8	22.4	9.2	0.4	64	1
NEO	14.1	5.2	11.2	4.9	2.1	84	0.7053
Liverpool Self-Efficacy							
Control	12.3	2.6	14.8	2.6	−3.6	84	0.015
Personal Agency	10.2	1.5	12.5	1.9	−4.6	84	0.0004
WHODAS	37.7	8.0	31.6	7.3	3.1	83	0.0746
Blood Gases							
FIO2	23.0	4.5	21.3	3.4	1.5	61	1
PCO2	51.3	18.8	47.1	8.9	1.1	60	1
PH	7.5	0.0	7.5	0.0	−0.1	60	1
PO2	57.8	12.7	60.1	14.0	−0.5	60	1

* Two Independent Sample t-test

Note: WHOQOL-BREF: World Health Organization Quality of Life/abbreviated 26-item version; HAM-D: Hamilton Depression Rating Scale; PFSDQ-M: Pulmonary Functional Status & Dyspnea Questionnaire-Modified; CCI: Charlson Comorbidity Index; MMSE: Mini Mental State Examination; DRS-IP: Dementia Rating Scale-Initiation/Perseveration; NEO: Neuroticism; WHODAS: World Health Organization Disability Assessment Schedule II 12-item.

Table 2.

Multivariate Regression Analysis with Trajectory Membership as Outcome and Baseline Characteristics as Independent Variables.

VARIABLES	Odds Ratio*	95% CI	P
Control	1.012	(0.719-1.43)	0.9428
Personal Agency	1.938	(1.163-3.23)	0.0119
Dyspnea	0.997	(0.987-1.01)	0.5355
Cognitive Impairment	0.762	(0.474-1.23)	0.2579
Medical Burden	0.814	(0.653-1.02)	0.0673
Severity of Depression	1.037	(0.872-1.23)	0.6771
Disability	0.788	(0.516-1.21)	0.2685

* Odds Ratio Estimates; their 95% CI and p-values are calculated based on pooled estimates over 15 imputed datasets using Rubin's formula. The reference group is the Improving Trajectory.

Note: Control and Personal Agency: Liverpool Self-Efficacy Scale; Dyspnea: Pulmonary Functional Status & Dyspnea Questionnaire-Modified (PFSDQ-M); Cognitive Impairment: Mini Mental State Examination; Medical Burden: Charlson Comorbidity Index; Severity of Depression: Flamliton Depression Rating Scale-24 Item; Disability: World Health Organization Disability Assessment Schedule II 12-item.