Published in final edited form as:
Am J Geriatr Psychiatry. 2014 November ; 22(11): 1316–1324. doi:10.1016/j.jagp.2013.05.006.

Untangling Therapeutic Ingredients of a Personalized Intervention for Patients with Depression and Severe COPD (PID-C)

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Abstract

Objective—We developed a Personalized Intervention for Depressed Patients with COPD (PID-C) focused on mobilizing the patient to participate in the care of both conditions. We showed that PID-C reduced depressive symptoms and dyspnea-related disability more than usual care over 28 weeks. This study focused on untangling key therapeutic ingredients of PID-C.

Design—Randomized controlled trial

Setting—Community

Participants—138 who received the diagnoses of COPD and major depression after screening 898 consecutive admissions for acute inpatient pulmonary rehabilitation.

Intervention—9 sessions of PID-C vs. usual care over 28 weeks.

Measurements—Primary outcomes: 17-item Hamilton Depression Rating Scale, Pulmonary Functional Status and Dyspnea Questionnaire–Modified. Other measures: adherence to rehabilitation exercise (≥2 hours/week), adherence to adequate antidepressant prescriptions.

Results—Low severity of dyspnea-related disability and adherence to antidepressants predicted subsequent improvement of depression. Exercise and low depression severity predicted improvement of dyspnea-related disability.

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ClinicalTrials.gov Identifier: NCT00151372

Dr. Alexopoulos affirms that everyone who contributed significantly to this work has been included.

Conflicts of Interest: Dr. Alexopoulos has received grant support from Forest Pharmaceuticals; has consulted to Hoffman-LaRoche, Lilly, Pfizer, and Otsuka; and has served at the speakers' bureaus of Astra Zeneca, Avanir, Forest, Merck, Novartis, and Sunovion. No other authors report conflicts of interest.

Conclusions—PID-C led to an interacting spiral of improvement in both depression and disability in a gravely medically ill population with a 17% mortality rate over 28 weeks and an expected deterioration in disability. The inter-relationship of the course of depression and dyspnea-related disability underscores the need to target adherence to both antidepressants and COPD rehabilitation. PID-C may serve as a care management model for depressed persons suffering from medical illnesses with a deteriorating course.

Keywords

Geriatric depression; COPD; Personalized intervention; clinical trial; dyspnea; disability

INTRODUCTION

Greater longevity has increased the number of persons living with chronic deteriorating illnesses and progressive disability. About 80% of older adults live with one chronic condition, and 50% have at least two illnesses (1). Learning to live with and manage a chronic disease and remain independent and active are the goals for increasing numbers of older adults. Many older adults with debilitating chronic illnesses suffer from depression which worsens their outcomes (2) and limits their participation in activities that would promote disease stabilization and independent functioning. At a time in which healthcare is shifting towards reimbursement incentivizing health maintenance and improved outcomes (3), depressed patients with deteriorating illnesses pose a challenge. Chronic obstructive pulmonary disease (COPD) with co-occurring depression exemplifies the treatment challenges posed by aging adults with chronic illnesses requiring active patient participation in care (4).

COPD afflicts 10 million Americans (5). COPD mortality has continued to increase over the past 30 years (6). Currently, COPD is the fourth most frequent cause of death in the US, and its prevalence is increasing in women and minorities (7). Twenty-four percent of COPD patients have major depression (8, 9). In COPD patients, depression is associated with increased all-cause mortality, worse general and pulmonary health, and greater disability (10, 11).

Depression magnifies the experience of the demands of COPD treatment. Pulmonary rehabilitation, the cornerstone of COPD care, consists of strengthening, breathing, and endurance exercises requiring active and consistent participation by patients. These are demands that even non-depressed COPD patients often neglect. Only 50% of COPD patients engage in walking exercises and use oxygen adequately (12). Comorbid depression adds hopelessness and lack of energy to disability stemming from COPD and makes every task seem impossible to accomplish. Although antidepressants may reduce depression in COPD patients (13), one study showed that 72% of depressed COPD patients refused antidepressants (14).

To address the needs of depressed patients with severe COPD, we developed a patient-centered intervention. Unlike earlier trials in COPD that targeted principally depression and anxiety symptoms (15, 16), our Personalized Intervention for Depression and COPD (PID-C) focused on mobilizing the patient to participate in the care of both conditions. Care

managers offering PID-C help depressed COPD patients to identify obstacles to participation in treatment. They then offer support and interventions (i.e., correcting misconceptions about their conditions, misunderstanding of recommendations, misattribution of symptoms, hopelessness, dissatisfaction with treatment experience, and logistic barriers) targeting treatment obstacles specific to individual patients and help them to work both on their exercise regimens and to take antidepressants as prescribed by their own physicians. The care managers also informed the patients' physicians by telephone of the patients' status and adherence to treatment and rehabilitation. We studied 138 patients with major depression and severe COPD and reported that PID-C offered in the community led to greater improvement than usual care in the trial's primary outcomes, i.e., depressive symptoms and signs and in dyspnea-related disability than usual care over 28 weeks, with benefits sustained 6 months after the last session (17). PID-C also led to higher remission rate of depression than usual care over 28 weeks.

This analysis focused on untangling key therapeutic ingredients of PIC-D. Its dual targets of promoting rehabilitation exercise critical to COPD management and adherence to antidepressant treatment was based on the assumption that depression and dyspnea-related disability are intertwined and influence each other's courses. We also anticipated that adherence to antidepressants would be followed by improvement of depression while engagements in rehabilitation exercises would improve dyspnea-related disability. Accordingly, we tested the hypothesis that improvement of dyspnea-related disability and adherence to adequate antidepressant treatment would be followed by reduction of depressive symptoms. A related hypothesis was that reduction in depression severity and performing rehabilitation exercises would be followed by improvement in dyspnea-related disability.

METHODS

Setting and Participants

To maximize inclusion of patients with severe COPD, participants were recruited from consecutive admissions to an acute inpatient pulmonary rehabilitation unit. They signed consent approved by the Weill-Cornell IRB. COPD participants were selected who met DSM-IV criteria (18) for unipolar major depression and had a score of 14 or greater on the 17-item Hamilton Depression Rating Scale (HAM-D) (19). COPD diagnosis was made by a pulmonologist (RSN) according to the American Thoracic Society Guidelines (20) after examination, spirometry, and other tests. DSM-IV diagnosis was assigned after a SCID-R (18) interview. Patients with other DSM-IV psychiatric diagnoses (except anxiety disorders) or severe cognitive impairment (i.e., Mini Mental State Examination (21) score ≤20) were excluded. Patients with milder cognitive impairment were included, because it is common in patients with severe COPD.

Randomization and Interventions

At the end of hospitalization, participants were randomized (1:1) into PID-C or usual care (UC) in blocks of 5 using random numbers provided by our Biostatistics Unit. Assessments were conducted by trained assistants blind to the nature of the intervention, study goals, and

randomization. One of the authors (PJR), also blind to treatment assignment, provided training, conducted rating reliability studies every 3 months, and reviewed all assessments prior to assigning final ratings.

PID-C—PID-C care managers were social workers. Training consisted of didactics on COPD, depression, and the PID-C Manual (Table 1) and three supervised practice cases. The first session (30 minutes) with patients occurred prior to discharge. The remaining sessions (30 minutes) were conducted in the patients' homes at weeks 3, 4, 8, 12, 16, 20, 24, and 26. The first session focused on alliance and evaluation of risks to treatment engagement in individual patients. Subsequent sessions consisted of clinical state review and reinforcement of plans to address treatment engagement. The care managers telephoned the patients' physicians and informed them of the patients' status and adherence to treatment and rehabilitation. Physicians' recommendations for depression and COPD were given according to clinical indication and not influenced by PID-C managers.

Usual Care (UC)—The only intervention provided in the UC arm was a letter to the patients' own physicians sent on discharge from the rehabilitation hospital informing the physicians of the diagnosis of depression.

Assessment and Outcomes

The targets of PID-C were two clinical outcomes that influence the function and quality of life of COPD patients: 1) Depressive symptoms. 2) Dyspnea-related disability quantified with the Pulmonary Functional Status and Dyspnea Questionnaire–Modified (PFSDQ-M), an interviewer-administered scale consisting of questions on degree of performance and frequency of activities in 10 different activities influenced by dyspnea. The PFSDQ-M has good psychometric properties and significant correlations with FEV_1, FEV_1 (% predicted), FVC (% predicted), FEV_1/FVC (%) and PO_2 (22, 23). Medical burden was assessed with the Charlson Comorbidity Index (CCI) (24). Adherence to exercise was quantified using the COPD Rehabilitation and Activity Follow-up Talley (CRAFT), a structured interviewer-rated instrument, to quantify the length of time participants devoted to each recommended exercise. Anxiety was rated with the sum of psychic anxiety and somatic anxiety scores of HAM-D. Executive dysfunction was assessed with the Stroop Color-Word Test (25) and the Initiation/Perseveration Domain of the Dementia Rating Scale (26). Neuroticism was rated with the NEO-PI (27). Social network and support were rated with the Duke Social Support Index (28).

Depression, adequacy of antidepressant prescription (daily dosages: bupropion≥200 mg, nortriptyline≥50 mg, sertraline≥50 mg, paroxetine ≥20 mg, fluoxetine≥20 mg, citalopram≥20 mg, venlafaxine≥76 mg, escitalopram≥10 mg, mirtazapine≥30 mg, or duloxetine≥60 mg) and adherence (taking>80% of dosages) were assessed at hospital admission, discharge, 14, 22, 28 and 52 weeks from discharge. PFSDQ-M and exercise were assessed at admission, and at 14, 28, and 52 weeks from discharge.

Statistical Analysis

All participants who completed baseline assessments were included in intent-to-treat analyses. Cox's proportional hazards survival analysis was used to compare time to remission of depression between the two arms between discharge and 28 weeks. To study the course of depression, profiles of baseline and weekly HAM-D scores between discharge and 28 weeks (intervention phase), and 28 to 52 weeks were compared between PID-C and UC using mixed-effects models. A similar approach was used to study dyspnea-related disability (PFSDQ-M) from admission to 28 weeks and from 28 weeks to 52 weeks. The models included time-trend parameter(s), intervention group, and time-intervention interaction. Time dependent predictors were assessed by examining the effects of lagged predictor scores on subsequent HAM-D or PFSDQ-M scores in the next assessment session using mixed-effects regression models. Exploratory moderation analysis examined: 1) the interaction of baseline variables with treatment; and 2) the three-way interaction of baseline variables with treatment and with time in the model described above.

RESULTS

Consecutively admitted pulmonary patients (N=898) were screened. Of these, 138 met criteria and signed consent; the flow of participants is described elsewhere (CONSORT Table in Appendix) (17). Their inpatient stay (mean=17.6 days, SD=8.0) was higher than that of non-depressed patients (mean=14.5, SD=6.0; Mann-Whitney U=31768, z=4.0, P<0.001). With the exception of education, there were no significant differences among participants assigned to PID-C or UC (Table 2).

Attrition—Eighteen percent of PID-C and 17% of UC participants died during the intervention phase (discharge to 28 weeks). Other attrition was 25% in the PID-C and 17% in the UC arm. Mortality was lower during follow-up (28–52 weeks) (CONSORT Table in Appendix). Attrition from other causes was 24% vs. 26%. There were no differences in overall rates of attrition between the two arms at 28 weeks (χ^2=0.394, df=1, p=0.53) or 52 weeks (χ^2=0.449, df=1, p=0.50). There were no significant differences in age, education, severity of depression or dyspnea-related disability between those who dropped-out for reasons other than death and those who remained in the study.

Course of Depression

A mixed effects model showed comparable reduction in depression scores (HAM-D) between PID-C and UC (treatment arm X time: $F_{[1, 175]=}0.27$, p=0.787) during the participants' stay in the rehabilitation hospital.

The PID-C intervention phase began at discharge from the rehabilitation hospital and extended over 26 weeks while the patients lived in the community. From the time of discharge to the 28 week assessment, PID-C participants had greater decline in depression than UC participants (treatment X time: $F_{[1,396]}$=5.40; p=0.021). At 28 weeks, the effect size of the HAM-D difference was 0.53 (95% CI: 0.09–0.97). PID-C participants had a higher remission rate (HAM-D≤7) than UC participants (Wald χ^2=5.78, df=1, p=0.016, hazard ratio=2.18; NNT=3.83) (17).

Effect of Adherence to Antidepressants—We divided participants into adherent (>80% adherence) to adequate antidepressant treatment vs. non-adherent, i.e., either less adherent (<80%) or on inadequate dosages. Then, we assessed the relationship of adherence status (i.e., at 6 and 22 weeks after discharge) to depression severity assessed at later time points (i.e., at 14 and 28 weeks respectively). Mixed effects analysis showed that adherence to adequate antidepressant treatment contributed to the advantage of PID-C over UC in reducing depressive symptoms and signs later in the course of treatment (Table 3). In the whole group, adherent patients had an average of 1.69 HAM-D points greater reduction of depression than non-adherent patients.

Effect of Dyspnea-Related Disability—We assessed the relationship of PFSDQ-M (i.e., at discharge and at 14 weeks) to depression severity at later assessment points (i.e., at 14 and at 28 weeks respectively). A mixed effects model demonstrated that dyspnea-related disability contributed to the advantage of PID-C over UC in reducing depressive symptoms and signs at later time points (Table 3). In the whole group, for every 10 point decrease in disability (PFSDQ-M), there was an average of 0.10 point reduction in depressive symptoms and signs (HAM-D).

Moderators' Analyses—Mixed effects models were constructed consisting of intervention, time, intervention X time, a moderator variable (i.e., age, education, dyspnea-related disability, anxiety, overall cognitive impairment, response inhibition, initiation-perseveration, neuroticism, social support, network, and social interaction at baseline), moderator X intervention, moderator X time, and moderator X intervention X time. None of the variables moderated the difference in depression decline between PID-C and UC.

Course of Dyspnea-Related Disability

PID-C participants experienced greater reduction in dyspnea-related disability (PFSDQ-M) than UC patients over the period of 28 weeks (PID-C X time = −0.1193: $F_{[1,197]}$=4.11; p=0.044). Post-hoc two-sided comparisons of LS means after Bonferroni's adjustment compared dyspnea related disability in PID-C participants vs. UC participants at 22 weeks (131.80 vs. 154.36; t_{172}=−2.19; p=0.060), and 28 weeks (126.81 vs. 154.39; t_{227}=−2.35; p=0.039). At 28 weeks, the effect size of the PFSDQ-M difference was 0.40 (95% CI: −0.01–0.87).

Effect of Exercise—We assessed the relationship of adequate rehabilitation exercise (>2 hours/week) at 6 and 22 weeks to dyspnea-related disability at subsequent times, i.e., at 14 and 28 weeks respectively. Mixed effects model analysis showed that adequate exercising contributed to the advantage of PID-C over UC in reducing dyspnea-related disability (Table 4). In the whole group, patients who exercised longer than 2 hours/week had an average of 18 points greater reduction in PFSDQ-M scores than those who exercised less.

Effect of Depression—A similar analysis examined the relationship of severity depression at 6 and 22 weeks to PFSDQ-M scored during subsequent assessments, i.e., over time. Mixed effects model analysis showed that reduction in depression severity (HAM-D) contributed to the advantage of PID-C over UC in reducing dyspnea-related disability at

later assessments (Table 4). In the whole group, for every point decrease in depression, there was an average 2.34 point reduction in PFSDQ-M.

Moderators' Analyses—We used the same mixed effects models analyses as those for depression to identify moderators of dyspnea-related disability. PID-C was associated with greater reduction of PFSDQ-M than UC in patients with less cognitive impairment (MMSE x Treatment: $F_{[1,82.9]}=4.45$; p=0.038). No other variable significantly moderated the difference in PFSDQ-M between PID-C and UC arms.

DISCUSSION

The principal finding of this study is that adherence to adequately prescribed antidepressants and secondarily reduction of dyspnea-related disability were followed by greater improvement of depression in patients treated with PID-C than usual care patients. Similarly, exercising longer than 2 hours per week and secondarily reduction of depression severity were followed by greater improvement in dyspnea-related disability in PID-C than usual care patients.

The relationship of adherence to adequate antidepressant prescriptions to improvement of depression is hardly surprising (29). The salutary effect of exercise to subsequent improvement of dyspnea-related disability is consistent with literature documenting that exercise is the cornerstone of COPD rehabilitation (7). Further, these findings are consistent with studies showing that depression worsens the outcomes of COPD (8, 30) and increases dyspnea and the resultant disability (31). What is unique about this study is the demonstration that an intervention led to an interacting spiral of improvement in both depression and dyspnea-related disability in a gravely medically ill population with a 17% mortality rate over 28 weeks and an expected deterioration in disability.

The findings of this study challenge the view that depression occurring in the context of increasing discomfort, physical limitations and a bleak medical prognosis cannot be helped effectively. In this study, 63% of PID-C participants achieved remission by the end of 28 weeks, while 37% achieved remission among those receiving usual care. PID-C yielded one additional remission over UC for every 3.8th patient by the 28th week (17). Overall cognitive impairment or executive dysfunction did not influence the efficacy of PID-C in depression although executive dysfunction has been shown to compromise the efficacy of antidepressant drugs (32, 33).

Similarly challenged is the view that disability caused by a deteriorating severe medical disease can only minimally be addressed. In the PID-C arm, dyspnea-related disability improved by 15% by the end of the intervention. By contrast in UC patients, dyspnea-related disability remained unchanged by the end of the intervention. The improvement of the PID-C arm is considerable given the severity of the patients' COPD. Dyspnea-related disability is an important health indicator that predicts involvement in a range of activities (34) and affects health related quality of life (35). Thus it is not merely a proxy for physiologic measures of pulmonary function, although the PFSDQ-M has been validated against

pulmonary function tests (22, 23). Group differences in the course of dyspnea-related disability could not be attributed to baseline differences in FEV_1% values (Table 2).

Limitations of the study include infrequent assessments, high attrition, and usual care as the comparison condition. These limitations were, in part, due to the study's focus on severe COPD. While its clinical state justifies an intensive intervention, concerns about burden limited the number of assessments. Severely ill COPD patients have high mortality, are often unable to live in the community, and may refuse follow-up because of fatigue. Our models also assume that data were missing at random although we have inadequate information supporting this assumption. Nonetheless, the two arms had similar attrition and no significant baseline clinical differences between those who remained in the study and those who exited. Employing uncontrolled "usual care" as a comparison condition may be a limitation, but it is the modal treatment in the U.S. and reflects the ecology of treatment offered in the community. Finally our time-dependent predictor variables (i.e., adherence to antidepressants, exercise, severity of depression, dyspnea related disability) were not randomly assigned and may be confounded by other variables.

The beneficial effect of PID-C on the deleterious interaction of depression and disability can be used in health management models for the increasing numbers of depressed persons suffering from deteriorating medical illnesses requiring active patient participation in their care. PID-C was designed for use by bachelor and master-level clinicians in community-based service settings. While it was implemented by research social workers, PID-C requires only brief training. Therefore, it lends itself for use by nurses, rehabilitation therapists and social workers of home healthcare and aftercare rehabilitation programs treating COPD patients across the nation. However, training and appropriate administrative arrangements would be required for PID-C to become part of the practice of these health organizations.

In conclusion, a personalized intervention targeting barriers to treatment for both depression and COPD improved depressive symptoms, remission rate, and dyspnea more than usual care in patients with a bleak prognosis. The inter-relationship of depression and dyspnea-related disability underscores the need to target barriers to both antidepressant treatment and COPD rehabilitation. PID-C may serve as a care model for the increasing numbers of depressed older persons suffering from deteriorating medical illnesses who often assume that nothing can be done for them, give up their treatment, and accelerate their deterioration and demise.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding/Support: NIMH R01 HLB071992, P30 MH068638, P30 MH085943 and by the Sanchez Foundation. Dr. Novitch is partially supported by a grant from the Will Rogers Institute.

The authors would like to thank Mr. Timothy E. Clark and Ms. Susan Friedman, LCSW for their contributions to this study.

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Table 1

Personalized Intervention for Depression and COPD (PID-C)*

Session 1 (Rehabilitation Hospital)
Introduction of the Role of Care Manager
Describe the adherence enhancement intervention and explain how it might help
Assessment of Causes of Non-Adherence
Use this guide to identify causes of non-adherence in each individual patient
Misconceptions about COPD and depression
Misunderstanding about treatment and about the actual regimen
Misattribution of depressive symptoms
Hopelessness
Overestimation of the energy needed to perform daily exercises
Dissatisfaction with prior treatment or after-care arrangements
Practical barriers to treatment, e.g. scheduling visits and access to care, transportation, finances.
Education
Brief discussion of facts about depression and its impact on the care of COPD
Sessions 2–9 (At Home)
Ongoing Assessment
Depressive symptoms, dyspnea-related disability
Treatment recommendations (rehabilitative, medical, psychiatric) and barriers to adherence
Address Barriers to Adherence
Focus on causes of non-adherence pertinent to the individual patient
Misconceptions about COPD and depression: Address incorrect facts about COPD and depression, recognize and address stigma
Misunderstanding about the actual regimen: Discuss the role of prescribed treatment and exercise in reducing dyspnea and disability and in preventing exacerbations
Misattribution of depressive symptoms: Identify likely contributors to symptoms and clarify the role of prescribed antidepressant treatment in reducing them
Hopelessness: Identify hopelessness as a symptom of depression that fuels poor expectations about treatment.
Discuss the role of antidepressant treatment and exercise in improving function and in conferring a feeling of empowerment. Offer support.
Overestimation of the energy needed to perform daily exercises: Describe in realistic terms what needs to be done, when, and how.
Dissatisfaction with after-care: Help patient develop a plan to address concerns (e.g., coach patient to express their concerns and ask question of health professionals)
Practical barriers: Help patients develop concrete strategies to address practical issues (e.g., identify ways to attend appointments; devise reminders for taking medications and conducting exercises; enlist help of family members and social services).
Collaboration with Physicians
Inform the physicians about any significant changes in the patients' status as well as any problems with adherence, and engage them in addressing them. Discuss depression treatment guidelines.

* The Manual is available on request (gsalexop@med.cornell.edu)

Table 2

Demographic and Clinical Characteristics of 138 Patients with Major Depression and COPD at Entry.

	Usual Care (N=71)		Intervention (N=67)			
					χ^2	p
Female *No, (%)*	**49 (69.0)**		**42 (62.7)**		**0.62**	**0.43**
	Mean (SD)	**Range**	**Mean (SD)**	**Range**	**z[1]**	**p**
Age	71.0 (7.7)	54–86	70.9 (8.5)	54–86	−0.10	0.92
Education (years)	14.0 (3.0)	4–20	12.7 (3.29)	4–20	−2.46	0.01
Length of COPD illness (months)	95.9 (79.0)	1–348	81.3 (85.5)	1–348	−1.59	0.11
Depression (HAM-D)[2]	19.1 (2.9)	14–27	19.0 (3.2)	14–26	−0.36	0.72
Dyspnea (PFSDQ-M Total)[3]	153.0 (61.2)	52–268	151.0 (58.5)	59–274	−0.21	0.84
MMSE[4]	27.5 (2.0)	21–30	27.3 (1.9)	24–30	−0.63	0.53
Stroop Color-Word[5]	23.2 (8.0)	7–51	25.3 (10.6)	3–56	1.18	0.24
DRS Initiation/Perseveration[6]	32.7 (4.2)	16–37	32.4 (4.3)	22–37	0.34	0.74
Disability (WHODAS-II)[7]	37.2 (5.8)	22–49	38.5 (7.3)	22–59	0.97	0.33
Social Network[8]	4.2 (3.9)	0–14	5.7 (4.7)	0–14	1.81	0.07
Subjective Social Support[8]	18.6 (2.4)	11–21	18.5 (2.5)	11–21	−0.24	0.82
Social Interaction[8]	6.7 (1.8)	3–11	6.2 (2.3)	0–13	−1.22	0.22
Instrumental Support[8]	9.0 (2.2)	2–13	9.3 (2.2)	3–13	0.70	0.48
Neo-PI Neuroticism[9]	14.0 (5.1)	4–25	14.4 (5.6)	1–26	0.55	0.59
FEV_1%[10]	37.8 (17.0)	17–81	35.2 (13.0)	16–64	−0.43	0.67

[1] Mann Whitney Wilcoxon;

[2] 17-item Hamilton Depression Rating Scale;

[3] Pulmonary Functional Status and Dyspnea Questionnaire–Modified;

[4] Mini Mental State Exam;

[5] Stroop Color-Word Interference Test;

[6] Mattis Dementia Rating Scale – Initiation/Perseveration Subscale;

[7] WHODAS-II Total score;

[8] Duke Social Support Index;

[9] NEO-PI Neuroticism Subscale;

[10] Pulmonary Function Test- % of Predicted Forced Expiratory Volume

Table 3

TIME-DEPENDENT PREDICTORS OF DEPRESSION SEVERITY IN 138 OLDER ADULTS WITH MAJOR DEPRESSION AND SEVERE COPD RANDOMLY ASSIGNED TO PID-C OR USUAL CARE

Variables	F	df	p
Depression Severity *(HAM-D 17)*			
Model 1: Adherence to Antidepressants*			
Treatment[1]	0.50	1, 235	0.58
Time[2]	0.58	1, 156	0.45
Treatment[1] x time[2]	1.01	1, 156	0.32
Adherence to Antidepressants	5.21	1, 236	0.023
Model 2: Dyspnea-Related Disability**			
Treatment[1]	1.32	1, 132	0.253
Time[2]	0.02	1, 81.1	0.90
Treatment[1] x Time[2]	0.05	1, 80.3	0.83
Dyspnea Related Disability	4.64	1, 146	0.033

[1]Treatment: Personalized Intervention for Depression and COPD (PID-C) vs. Usual Care

[2]Time in days

*The model evaluates the relationship of adherence at 6 and 22 weeks after discharge to HAM-D at 14 and 28 weeks respectively

**The model evaluates the relationship of PFSDQ-M at discharge and 14 weeks to HAM-D at 14 and 28 weeks respectively

Table 4

TIME DEPENDENT PREDICTORS OF DYSPNEA-RELATED DISABILITY IN 138 OLDER ADULTS WITH MAJOR DEPRESSION AND SEVERE COPD RANDOMLY ASSIGNED TO PID-C OR USUAL CARE

Variables	F	df	p
Dyspnea-Related Disability *(PFSDQ-M)*			
Model 1: Exercise*			
Treatment[1]	0.13	1, 155	0.72
Time[2]	0.06	1, 74.9	0.81
Treatment[1] x time[2]	0.87	1, 73.9	0.35
Exercise[3]	5.46	1, 96.6	0.022
Model 2: Severity of Depression**			
Treatment[1]	0.09	1, 157	0.77
Time[2]	0.88	1, 75.5	0.35
Treatment[1] x Time[2]	0.65	1, 73.1	0.42
Severity of Depression	6.33	1, 146	0.013

[1] Treatment: Personalized Intervention for Depression and COPD (PID-C) vs. Usual Care

[2] Time in days

[3] Adequate (2 hrs/week) vs. Inadequate Rehabilitation Exercise (less than 2 hrs/week)

* The model evaluates the relationship of exercise at 6 and 22 weeks after discharge to PFSDQ-M at 14 and 28 weeks respectively

** The model evaluates the relationship of Ham-D at 6 and 22 weeks to PFSDQ-M at 14 and 28 weeks respectively