HHS Public Access

Author manuscript

Am J Geriatr Psychiatry. Author manuscript; available in PMC 2017 November 01.

Published in final edited form as:

Am J Geriatr Psychiatry. 2016 November ; 24(11): 964–974. doi:10.1016/j.jagp.2016.07.014.

Two Behavioral Interventions for Patients with Major Depression and Severe COPD

George S. Alexopoulos, MD[1], **Jo Anne Sirey, PhD**[1], **Samprit Banerjee, PhD**[1], **Dimitris N. Kiosses, PhD**[1], **Cristina Pollari, MPH**[1], **Richard S. Novitch, MD**[2], **Amanda Artis, MS, MPH**[1], and **Patrick J. Raue, PhD**[1]

[1]Weill Cornell Medicine, Institute for Geriatric Psychiatry

[2]Burke Rehabilitation Hospital

Abstract

Objective—Personalized Intervention for Depressed Patients with COPD (PID-C), a treatment mobilizing patients to participate in their care, was found more effective than usual care. To further improve its efficacy, we developed a Problem Solving-Adherence (PSA) intervention integrating problem solving into adherence enhancement procedures. We tested the hypothesis that PSA is more effective than PID-C in reducing depressive symptoms. Exploratory analyses sought to identify patients with distinct depressive symptom trajectories and compare their clinical profiles.

Design—Randomized controlled trial.

Setting—Acute inpatient rehabilitation and community.

Participants—101 diagnosed with COPD and major depression after screening 633 consecutive admissions for acute inpatient rehabilitation.

Intervention—14 sessions of PID-C vs. PSA over 26 weeks.

Measurements—24-item Hamilton Depression Rating Scale (HAM-D).

Results—PSA was not more efficacious than PID-C in reducing depressive symptoms. Exploratory latent class growth modeling identified two distinct depressive symptoms trajectories. Unlike patients with unfavorable course (28%) who remained symptomatic, patients with favorable course (72%) had a decline of symptoms during the hospitalization followed by a milder decline after discharge. Patients with unfavorable course were younger, had greater scores in disability, anxiety, neuroticism, and dyspnea related limitation in activities and lower self-efficacy scores.

Corresponding Author: George S. Alexopoulos, MD; Weill Cornell Institute of Geriatric Psychiatry; 21 Bloomingdale Road; White Plains, NY 10605. Phone: (914) 997-5767. Fax: (914) 997-5926. gsalexop@med.cornell.edu.

Conflicts of Interest: Dr. Alexopoulos serves at the speakers' bureaus of Takeda, Lundbeck, Otsuka, and Sunovion. No other authors report conflicts of interest.

Conclusions—Both interventions led to sustained improvement depressive symptoms. PID-C matches the skills of clinicians employed by community rehabilitation programs and can be integrated in the care of depressed COPD patients. Patients with severe disability, anxiety, neuroticism, and low self-efficacy are at risk for poor outcomes and in need of close follow-up and targeted interventions.

Keywords

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

INTRODUCTION

COPD afflicts 17% of older men and 13% of older women.(1) Despite reduced cigarette smoking, the number of COPD patients continues to rise because the illness onset occurs many years after the insult of smoking.(2) COPD has been the only major chronic disease for which death rates have increased over the past 30 years.(1) It is projected that, by 2020, COPD will be the third leading cause of death worldwide.

At least 24% of COPD patients have had one or more episodes of major depression, frequently of long duration.(3) Depressive symptoms are associated with disability, high medical burden and mortality.(4, 5) Antidepressants have modest efficacy in COPD patients.(6) Along with limited efficacy, patients' reluctance to receive antidepressants further reduces the impact of antidepressants on the care of patients with major depression and COPD.(7)

Pulmonary rehabilitation consisting of strengthening, breathing, and endurance exercises is the cornerstone of COPD treatment (8) and has been shown to improve major depression in COPD patients.(9) Despite its clinical benefit, adherence to rehabilitation remains a problem among COPD patients.(3) Depression further worsens treatment adherence. Compared to non-depressed patients, the odds are 3 times greater that depressed medical patients will be noncompliant with prescribed medications, exercise, diet, health related behavior, vaccination, and appointments.(10)

In response to concerns about treatment adherence, we developed the Personalized Intervention for Depressed patients with COPD (PID-C) and documented that it reduced depressive symptoms and dyspnea-related disability more than usual care.(9) PID-C is administered by care managers who identify patient specific treatment barriers, and through support and targeted interventions (i.e. correction of misconceptions, misunderstanding of recommendations, misattribution of symptoms, hopelessness, dissatisfaction with treatment, logistic barriers), help them to work both on their exercise regimens and encourage them to adhere to medication prescribed by their own physicians. Care managers also work with the patients' physicians in monitoring the patients' treatment and progress.

To further improve the efficacy of PID-C, we developed Problem Solving-Adherence (PSA), an intervention integrating problem solving techniques into the adherence enhancement procedures of PID-C. We reasoned that, in addition to low motivation and energy, depressed COPD patients lack problem solving skills required for adhering to rehabilitation and

treatment. We selected problem solving because it is effective in reducing depression and disability in older adults, including patients with executive dysfunction (11, 12), a common impairment in COPD patients (13) interfering with planning, initiating, and sequencing behavior, thus complicating treatment adherence. This report tests the primary hypothesis of this study, which postulates that PSA is more effective than PID-C in reducing depressive symptoms over a period of 26 weeks. Exploratory analyses were conducted to identify groups of patients with distinct depressive symptom trajectories and compare their clinical profiles.

METHOD

Participants

The participants were consecutively admitted patients to the acute inpatient pulmonary rehabilitation unit of a rehabilitation hospital. All participants signed consent approved by the Weill Cornell Medicine Institutional Review Board (IRB). The hospital accepts patients with impairment in ambulation and other functions due to respiratory diseases and patients requiring respiratory support.

Participants were required to have the diagnosis of COPD, meet DSM-IV criteria (14) for unipolar major depression, and have a score of 20 or greater on 24-item Hamilton Depression Rating Scale (HAM-D).(15) Patients were excluded if they had DSM-IV diagnoses other than unipolar major depression, significant cognitive impairment (i.e. Mini Mental State Examination (16) score of 23 or lower), or were unable to complete research interviews. Depressed patients with anxiety disorders were included.

Assessment

The diagnosis of COPD was made by a pulmonologist (RSN) according to the American Thoracic Society Guidelines(17). Psychiatric diagnosis was assigned according to DSM-IV criteria after a SCID-R(18) interview conducted within the first 2 days after admission.

Further assessment was conducted by trained research assistants, unaware of treatment assignment and hypotheses. Depressive symptoms were rated with the HAM-D. Dyspnea-related disability was quantified with the Pulmonary Functional Status and Dyspnea Questionnaire–Modified (PFSDQ-M), an interviewer-administered scale for COPD patients assessing dyspnea during the performance of ten activities.(19–21) Global disability was assessed with the World Health Organization Disability Assessment Schedule II 12-item (WHODAS-II-12).(22) Medical burden was quantified with the Charlson Comorbidity Index (CCI).(23) Anxiety [Generalized Anxiety Disorder 7-item Scale (24)], neuroticism [NEO-PI.(25)], and self-efficacy [Liverpool Scale.(26)] were assessed at entry because they are often associated with poor outcomes of depression.(27–33)

Treatment at the Rehabilitation Hospital

Treatment included respiratory, physical, occupational, and speech therapy, and social work planning of post-discharge support services. The average length of stay was two weeks.

Subjects were randomized to PID-C or PSA in 5-subject blocks using random numbers. The clinical team was unaware of the randomization status.

Treatment and Assessment Protocol

Fourteen sessions of either PID-C or PSA were offered over 26 weeks. The first 2 sessions were administered during hospitalization. They introduced the treatment rationale, assessed the participants' needs, and formed a personalized plan. The subsequent 8 sessions were administered weekly after discharge at the participants' homes or the therapists' offices depending on the participants' ability to travel. Four additional monthly sessions intended to reinforce the skills and behaviors imparted during the first 10 weekly sessions. Sessions were audiotaped and 10% of randomly selected sessions were evaluated for treatment fidelity with the PID-C and PSA Adherence Scales (Composite scores: 1: very poor, 2: poor: 3: satisfactory, 4: good, 5: excellent). Treatment fidelity ratings were performed by an experienced psychologist, who was not a member of the research team and who had been trained in problem solving therapy, PID-C and PSA.

Interviews by research assistants were conducted prior to therapy sessions. Severity of depression (HAM-D), was assessed at baseline, discharge and at 10^{th}, 14^{th}, and 26^{th} week.

PID-C

PID-C consisted of in-person approximately 45 min in-person sessions with patients and interaction with their physicians by telephone when needed. A manual guided care managers in evaluating barriers to adherence to physicians' recommendations in individual patients and plans to address them.(34, 35) When caregivers participated in the patients' care, the care managers interacted with them using the same guidelines with those for patients. The care managers remained in telephone contact with the patients' physicians and informed them of any changes in the patients' status and any problems with adherence.

The PID-C care managers were master's level social workers. They received the PID-C Manual and readings on COPD and depression. They also attended a one-day workshop conducted by PJR (clinical psychologist) in which they role played typical sessions. Therapists, then, treated 3 practice cases, which were audiotaped and rated by PJR. More practice cases were used as needed until therapists received an average PID-C Treatment Adherence Scale score of 4 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), i.e. "good" to "excellent" range.

PSA

PSA integrates the personalized approach to adherence barriers of PID-C with development of problem solving skills. As in PID-C, the first targeted problems were related to adherence to treatment recommendations. Some adherence problems (e.g. misunderstanding, limited information) were addressed with education and direct instruction. However, hopelessness, helplessness and fatigue interfering with exercise and activities, social isolation and neglect of important relationships were addressed with problem solving skill development using the

following steps: 1. Selection and problem definition; 2. Establishment of realistic and 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 introduced learning exercises that made use of multi-modal presentation of material, and within session repetition of the taught material, i.e. "Say-it, show-it, do-it".(36) They encouraged patients to focus on the process of addressing the problem at hand, so that they could use the same approach in subsequent problems.

Training in PSA started with a one-day workshop offered by PJR. Care managers received references on COPD and depression and the PSA manual (Appendix) and role-played administration of PSA. After the workshop, care managers treated 3 practice cases, and the sessions were audiotaped and reviewed using the PSA Treatment Adherence Scale. More practice cases were used as needed until therapists received an average PSA Treatment Adherence Scale score of 4 for each case in 3 consecutive cases. During the trial, the average PSA Adherence Scale composite score of audiotaped sessions was 4.29 (SD: 0.69), i.e. within the "good" and "excellent" range.

Data Analysis

Profiles of repeated HAM-D scores were compared (PID-C vs. PSA) using mixed-effects models to account for repeated measurements over time. They included time-trend parameter(s), treatment group, and time by treatment interaction as fixed effect and subject-specific random intercept. We then tested the one-sided post-hoc hypothesis that PID-C is as effective as PSA within δ points at weeks 14 and 26 by constructing 95% one-sided confidence intervals (CI). We determined δ as the largest upper limit of the two CIs at weeks 14 and 26. We used latent class growth modeling (LCGM) to identify subgroups, with distinct depression trajectories. Using the censored normal distribution in the SAS PROC TRAJ program,(37) we tested separate models with one, two, and three distinct trajectories to identify subgroups with distinct depression trajectories within the whole sample, the PID-C arm only, and the PSA arm only. 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 a significance level of α=0.05. The so derived model was tested against a model with one less trajectory using the change in Bayesian Information Criterion (BIC) as an approximation to the log Bayes factor(37) ($2\Delta BIC > 2$). The average posterior probabilities of group membership was used as a measure of internal reliability for each trajectory. Values greater than .70 to .80 suggest that the trajectories classify groups with similar patterns of change separately from groups with different patterns of change.(38)

RESULTS

Consecutively admitted pulmonary patients (N=633) were screened and 147 met criteria and signed consent (Figure 1). Among randomized subjects (N=101), the mean inpatient stay was 19.6 days (SD=17.1). There were no significant differences in demographic and clinical characteristics among participants assigned to PID-C or PSA.

Attrition

Fourteen percent of PID-C and 13.7% of PSA participants died during the intervention phase (discharge to 26 weeks). There were no differences in overall rates of attrition between the two arms at 26 weeks (χ^2=0.0714, df=1, p=0.7893). There were no significant differences in age, education, severity of depression, or disability between those who dropped-out for reasons other than death and those who remained in the study.

Course of Depressive Symptoms

PID-C participants had a similar course of depression with PSA participants. (treatment × time: $F_{[1,146]}$=0.71; p=0.4015). We conducted a *post-hoc* one-sided hypothesis test which indicated that PID-C was as good as PSA within 2.1 points based on HAM-D difference between the two groups both at week 14 (0.129, 95% one sided CI:−∞, 1.87) and at week 26 (0.4752, 95% one sided CI:−∞, 2.06). Exploratory LCGM analysis sought to identify distinct trajectories of HAM-D.

Whole sample analysis

Subjects who had at least one follow-up assessment (N=87) had two distinct depression (HAM-D) trajectories (2Δ*BIC*=21.16) (Figure 2). The average posterior probabilities for membership in the favorable and unfavorable depression trajectories were 0.85 and 0.90 respectively. Seventy two percent of patients (63/87) had a favorable trajectory with a non-linear, cubic trend [-3×10^{-4}, 95%CI: (-4.03×10^{-4}, -1.97×10^{-4})], while 28% (24/87) had an unfavorable trajectory with a nonlinear, quartic trend over the course of the study [3×10^{-5}, 95%CI: (2×10^{-6}, 5.80×10^{-5})]. While both trajectories had a decline of depression by discharge, the favorable trajectory continued this downward trend until week 14. In contrast, the unfavorable trajectory had a slight increase in depression by the 10th week (end of weekly sessions), followed by a sharper increase by the 14th week, and persistence of depressive symptoms until the 26th week.

There was neither an association between treatment group and depression trajectory (χ^2 = 0.02, df=1, p=0.88) nor significant differences in depression severity at baseline (Table 1). However, patients with an unfavorable depression trajectory were younger and had greater overall disability at baseline compared to patients with a favorable trajectory. Moreover, patients with an unfavorable trajectory had greater scores in anxiety, neuroticism, and dyspnea related limitation in activities and lower scores on self-efficacy at baseline.

PID-C only analysis

The PID-C arm had two distinct depression (HAM-D) trajectories (2Δ*BIC*=29.78) (Figure 3). The average posterior probabilities of trajectory membership for favorable and unfavorable trajectories were 0.96 and 0.86 respectively. The favorable depression trajectory (N=33) was non-linear, quadratic (9.60×10^{-3}, 95%CI: (7.06×10^{-3}, 0.01)) with a steep decline in depression during hospitalization, followed by a gradual decline until the end of the study. The unfavorable trajectory (N=8) had no significant change in depression over the course of the study (estimated HAM-D: 23.54 ± 2.00). Patients with unfavorable trajectory had greater scores in anxiety and neuroticism and lower scores in self-efficacy and in subjective support (Table 2).

PSA only analysis

The PSA group had two distinct depression (HAM-D) trajectories ($2\Delta BIC = 7.14$) (Figure 3). The average posterior probabilities of membership to favorable and unfavorable trajectories were 0.94 and 0.82, respectively. The favorable trajectory (N=34) was non-linear (quartic) [6.00×10^{-5}, 95%CI: (5.63×10^{-5}, 6.37×10^{-5})] with a sharp depression decline by discharge. This improvement was sustained until the end of weekly PSA sessions (week 10) followed by an increase in depression in the ensuing 4 weeks, and a HAM-D decline between week 14 and 26. In the unfavorable trajectory (N=12), depression remained unchanged throughout the study (estimated HAM-D: 20.90±1.08). There were no significant differences between the two trajectories in demographic and clinical variables at baseline.

DISCUSSION

The principal finding of this study is that PSA is not more efficacious than PID-C in reducing symptoms of major depression in patients with severe COPD. Personalized treatment adherence procedures with and without PST led to a sustained, clinically significant improvement of depression in more than 70% of patients with major depression and severe COPD. These outcomes are quite favorable for depressed patients with severe medical burden evidenced by a mortality rate of 14% over 26 weeks and considering that depressed COPD patients both resist taking antidepressants and have a rather low response rate when they receive them.(6, 7)

The study hypotheses were not supported. It is unclear why integration of problem solving techniques with adherence enhancement procedures did not significantly improve the trajectory of depressive symptoms. Arguably, problems related to adherence to rehabilitation are the main problems of this very sick COPD population during the post-discharge period. Therefore, addressing these problems directly may be adequate for improving depression at that time. It is reasonable to hypothesize that problem solving skills imparted by PSA are most useful during remission of depression when patients attempt to enrich their social and other functions and needs skills beyond those required for adherence to rehabilitation. This hypothesis can be tested by a recurrence prevention study.

The depression outcomes of the PID-C treated group were similar to those of an earlier study of a similar population, which documented the superiority of PID-C over usual care in patients with major depression and severe COPD.(9) PID-C is rather easy to teach and was designed for use by bachelor and masters-level clinicians. Therefore, it can become part of comprehensive care for COPD patients offered by home healthcare and pulmonary rehabilitation programs, many of which employ clinicians with similar background.

Exploratory latent class growth modeling of the entire sample identified two groups with distinct course of depression. The group with a favorable course (72.4% of patients) had a precipitous reduction of depressive symptoms and signs during the hospitalization. Improvement of depression during this phase was likely an effect of the COPD comprehensive intense rehabilitation program rather than the two intervention sessions administered during the hospitalization. This view is consistent with literature demonstrating that inpatient rehabilitation for COPD leads to improvement of major depression regardless

of use of antidepressants.(6) There was further improvement after discharge when most of the intervention sessions were administered. By contrast, the unfavorable course group had a less prominent improvement of depression during the hospitalization, a worsening of symptoms during the transition from weekly to monthly sessions, and overall remained depressed throughout the study period.

At baseline, medical burden, overall cognitive impairment and initiation/perseveration scores did not distinguish patients with favorable from those with unfavorable depression trajectories. However, patients with unfavorable course of depression were younger and had greater overall disability, anxiety, neuroticism, and dyspnea related limitation in activities and lower scores on self-efficacy. A similar clinical profile identified patients with unfavorable depression course in the PID-C arm. There were no statistically significant differences in baseline clinical characteristics between patients with favorable and unfavorable course of depression.

The observation that disability, anxiety, neuroticism, and low self-efficacy were associated with unfavorable course of depression in COPD patients is consistent with earlier literature. Specifically, overall disability and dyspnea related disability are closely associated with depressive symptoms in COPD patients.(9, 39) In the Collaborative Depression Study, anxiety symptoms during depressive episodes correlated strongly with the persistence of depressive symptoms and this relationship was stable over decades.(27) It has been proposed that anxious depression may have a biosignature distinct from non-anxious depression or pure anxiety.(28) Similarly, neuroticism has been associated with treatment resistance of depression(29), pain catastrophizing and pain related anxiety independently of depression or pain severity(30). Self-efficacy, an individual's sense of personal control and mastery, plays an important role in improving overall functioning and illness management.(31) In patients with COPD, those with low self-efficacy had more functional limitations than those with equally severe disease but higher self-efficacy for carrying out activities.(32) These observations are consistent with our findings in another sample indicating that self-efficacy is associated with overall functioning in patients with major depression and severe COPD after controlling for age, medical burden, and depression severity.(33)

This study has several limitations including the rather small sample, the absent of a no-intervention comparison group, and the administration of both interventions by the same therapists. The sample size did not permit meaningful moderation analysis to identify patients who may have preferentially benefited by one of the two interventions. A no-intervention comparison group may have shown to what extent either intervention is superior to usual care. However, an earlier study of depressed COPD patients recruited from the same rehabilitation hospital and using the same selection criteria showed that PID-C led to greater decline in depressive symptoms, and less disability than usual care over 28 weeks and 6 months after the last session.(9) Use of the same therapists for both interventions of our study reduces the need to introduce the impact of different therapists in group comparisons and increases power, much needed in a study of a difficult to recruit population. Therapists' preference of one intervention vs. the other may have introduced bias. However, the high fidelity of therapists to both treatment manuals suggests that therapist preference had a minimal, if any, impact on the results. PID-C was as effective as PSA within 2.1 HAM-D

points. Although not pre-determined, this difference is clinically meaningful as it is and more conservative than that of the National Institute for Clinical Excellence (NICE), which defines as clinically significant a drug-placebo difference of 3 HAM-D points (40). One third of qualified patients exited before randomization, many because of serious medical illnesses or mortality. Thus, this study's findings are pertinent to less severely ill populations. Finally, the analyses of subgroups with different trajectories were conducted *post hoc* and the resulting predictors of outcome should be viewed as preliminary.

In conclusion, two personalized interventions targeting adherence to rehabilitation and treatment prescribed by the patients' own physicians improved depression in 72% of patients with major depression and severe COPD over 26 weeks. Integration of PST into adherence procedures did not significantly improved outcomes of depression. PID-C matches the skill set of bachelor and masters-level clinicians employed by home healthcare and pulmonary rehabilitation programs and can be integrated in comprehensive care programs for COPD patients. Severe disability, anxiety, neuroticism, and low self-efficacy were associated with an unfavorable course of depression. This profile may identify depressed COPD patients at risk for poor outcomes and in need of close follow-up and targeted interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding/Support: NIMH grants R01 MH076829 and P30 MH085943, and by the Sanchez Foundation. Dr. Novitch is partially supported by a grant from the Will Rogers Institute.

References

1. Raherison C, Girodet P-O. Epidemiology of COPD. European Respiratory Review. 2009; 18:213–221. [PubMed: 20956146]
2. NHLBI. Morbidity, Mortality: 2004 Chart Book on Cardiovascular, Lung, and Blood Diseases. May. 2004 NIH Webpage.
3. Alexopoulos GS, Latoussakis V. Depression comorbidity with COPD. Psychiatr Ann. 2004; 34:289–295.
4. Jennings JH, Digiovine B, Obeid D, et al. The association between depressive symptoms and acute exacerbations of COPD. Lung. 2009; 187:128–135. [PubMed: 19198940]
5. de Voogd JN, Wempe JB, Koeter GH, et al. Depressive symptoms as predictors of mortality in patients with COPD. Chest. 2009; 135:619–625. [PubMed: 19029432]
6. Alexopoulos GS, Sirey JA, Raue PJ, et al. Outcomes of depressed patients undergoing inpatient pulmonary rehabilitation. The American journal of geriatric psychiatry: official journal of the American Association for Geriatric Psychiatry. 2006; 14:466–475. [PubMed: 16670251]
7. Yohannes AM, Connolly MJ, Baldwin RC. A feasibility study of antidepressant drug therapy in depressed elderly patients with chronic obstructive pulmonary disease. International journal of geriatric psychiatry. 2001; 16:451–454. [PubMed: 11376459]
8. ACCP/AACVPR. Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based guidelines. American College of Chest Physicians American Association of Cardiovascular and Pulmonary Rehabilitation Pulmonary Rehabilitation Guidelines Panel. Chest. 1997; 112:1363–1396. [PubMed: 9367481]

9. Alexopoulos GS, Kiosses DN, Sirey JA, et al. Personalised intervention for people with depression and severe COPD. The British journal of psychiatry: the journal of mental science. 2013; 202:235–236. [PubMed: 23391728]
10. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Med. 2000; 160:2101–2107. [PubMed: 10904452]
11. Arean PA, Raue P, Mackin RS, et al. Problem-solving therapy and supportive therapy in older adults with major depression and executive dysfunction. The American journal of psychiatry. 2010; 167:1391–1398. [PubMed: 20516155]
12. Alexopoulos GS, Raue PJ, Kiosses DN, et al. Problem-solving therapy and supportive therapy in older adults with major depression and executive dysfunction: effect on disability. Archives of general psychiatry. 2011; 68:33–41. [PubMed: 21199963]
13. Stuss DT, Peterkin I, Guzman DA, et al. Chronic obstructive pulmonary disease: effects of hypoxia on neurological and neuropsychological measures. Journal of clinical and experimental neuropsychology. 1997; 19:515–524. [PubMed: 9342687]
14. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR (Text Revision). 4th. Washington, DC: American Psychiatric Association; 2000.
15. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960; 23:56–62. [PubMed: 14399272]
16. Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12:189–198. [PubMed: 1202204]
17. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 1995; 152:S77–121. [PubMed: 7582322]
18. First, MB.; Spitzer, RL.; Williams, JBW.; Gibbon, M. Structured clinical interview for DSM-IV - patient version (SCID-P). Washington: American Psychiatric Press; 1995.
19. Lareau SC, Breslin EH, Meek PM. Functional status instruments: outcome measure in the evaluation of patients with chronic obstructive pulmonary disease. Heart Lung. 1996; 25:212–224. [PubMed: 8635922]
20. Lareau SC, Meek PM, Roos PJ. Severe COPD: Effects on activites of daily living and dyspnea. Am J Crit Care Med. 1996; 153:A421.
21. Lareau SC, Meek PM, Roos PJ. Additional testing of the modified pulmonary functional status and dyspnea questionnaire (PFSDQ-M): ease of use, stability, reliability, and validity. Am J Crit Care Med. 1997; 155:A722.
22. Epping-Jordan JA, Ustun TB. The WHODAS-II: leveling the playing field for all disorders. WHO Mental Health Bulletin. 2000; 6:5–6.
23. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40:373–383. [PubMed: 3558716]
24. Spitzer RL, Kroenke K, Williams JW, et al. A brief measure for assessing generalized anxiety disorder: The gad-7. Archives of Internal Medicine. 2006; 166:1092–1097. [PubMed: 16717171]
25. Costa PT, McCrae RR. The NEO personality inventory. Manual, Odessa, FL, Psychological Assessment Resources. 1985
26. Airlie J, Baker GA, Smith SJ, et al. Measuring the impact of multiple sclerosis on psychosocial functioning: the development of a new self-efficacy scale. Clinical rehabilitation. 2001; 15:259–265. [PubMed: 11386395]
27. Coryell W, Fiedorowicz JG, Solomon D, et al. Effects of anxiety on the long-term course of depressive disorders. The British Journal of Psychiatry. 2012; 200:210–215. [PubMed: 21984801]
28. Andreescu C, Lenze EJ. Anxiety – depression comorbidity – bête noire or quick fix? The British journal of psychiatry: the journal of mental science. 2012; 200:179–181. [PubMed: 22383763]
29. Takahashi M, Shirayama Y, Muneoka K, et al. Low Openness on the Revised NEO Personality Inventory as a Risk Factor for Treatment-Resistant Depression. PLoS ONE. 2013; 8:e71964. [PubMed: 24019864]

30. Kadimpati S, Zale EL, Hooten MW, et al. Associations between Neuroticism and Depression in Relation to Catastrophizing and Pain-Related Anxiety in Chronic Pain Patients. PLoS ONE. 2015; 10:e0126351. [PubMed: 25902153]
31. McCathie HC, Spence SH, Tate RL. Adjustment to chronic obstructive pulmonary disease: the importance of psychological factors. The European respiratory journal. 2002; 19:47–53. [PubMed: 11852894]
32. Kohler CL, Fish L, Greene PG. The relationship of perceived self-efficacy to quality of life in chronic obstructive pulmonary disease. Health psychology: official journal of the Division of Health Psychology, American Psychological Association. 2002; 21:610–614.
33. Marino P, Sirey JA, Raue PJ, et al. Impact of social support and self-efficacy on functioning in depressed older adults with chronic obstructive pulmonary disease. International Journal of Chronic Obstructive Pulmonary Disease. 2008; 3:713–718. [PubMed: 19281085]
34. Sirey JA, Raue PJ, Alexopoulos GS. An intervention to improve depression care in older adults with COPD. International journal of geriatric psychiatry. 2007; 22:154–159. [PubMed: 17173354]
35. Alexopoulos GS, Raue PJ, Sirey JA, et al. Developing an intervention for depressed, chronically medically ill elders: a model from COPD. International journal of geriatric psychiatry. 2008; 23:447–453. [PubMed: 17932995]
36. Thompson LW, Davies R, Gallagher D, et al. Cognitive therapy with older adults. Clinical Gerontologist. 1986; 5:245–279.
37. Jones BL, Nagin DS, Roeder K. A SAS procedure based on mixture models for estimating developmental trajectories. Sociological methods & research. 2001; 29:374–393.
38. Andruff H, Carraro N, Thompson A, et al. Latent class growth modelling: a tutorial. Tutorials in Quantitative Methods for Psychology. 2009; 5:11–24.
39. Alexopoulos GS, Kiosses DN, Sirey JA, et al. Untangling therapeutic ingredients of a personalized intervention for patients with depression and severe COPD. The American journal of geriatric psychiatry: official journal of the American Association for Geriatric Psychiatry. 2014; 22:1316–1324. [PubMed: 23954038]
40. National Institute for Clinical Excellence. Depression: Management of depression in primary and secondary care. London: National Institute for Clinical Excellence; 2004.

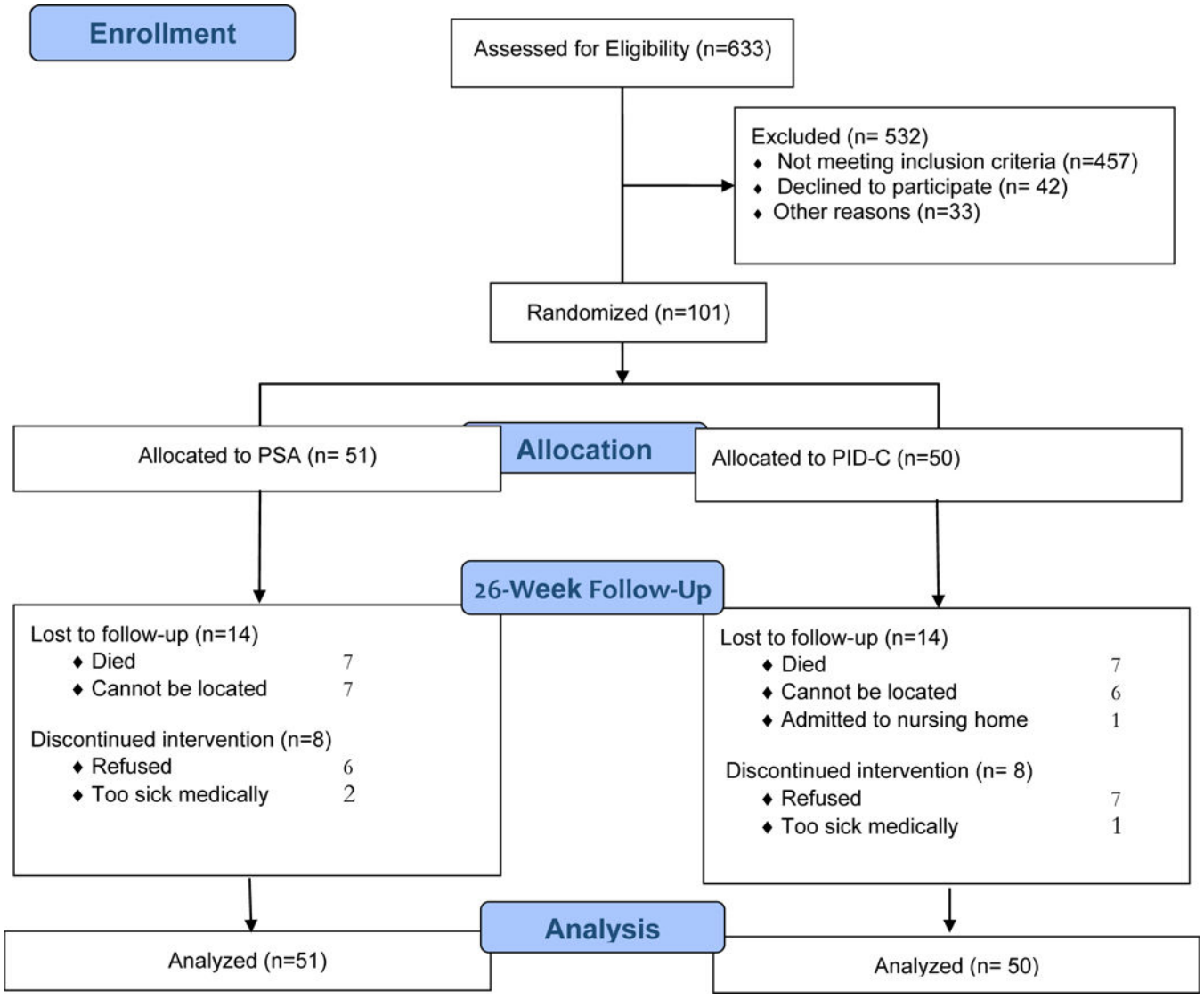

Figure 1.
Flow diagram of participant progress through the phases of the randomized trial.

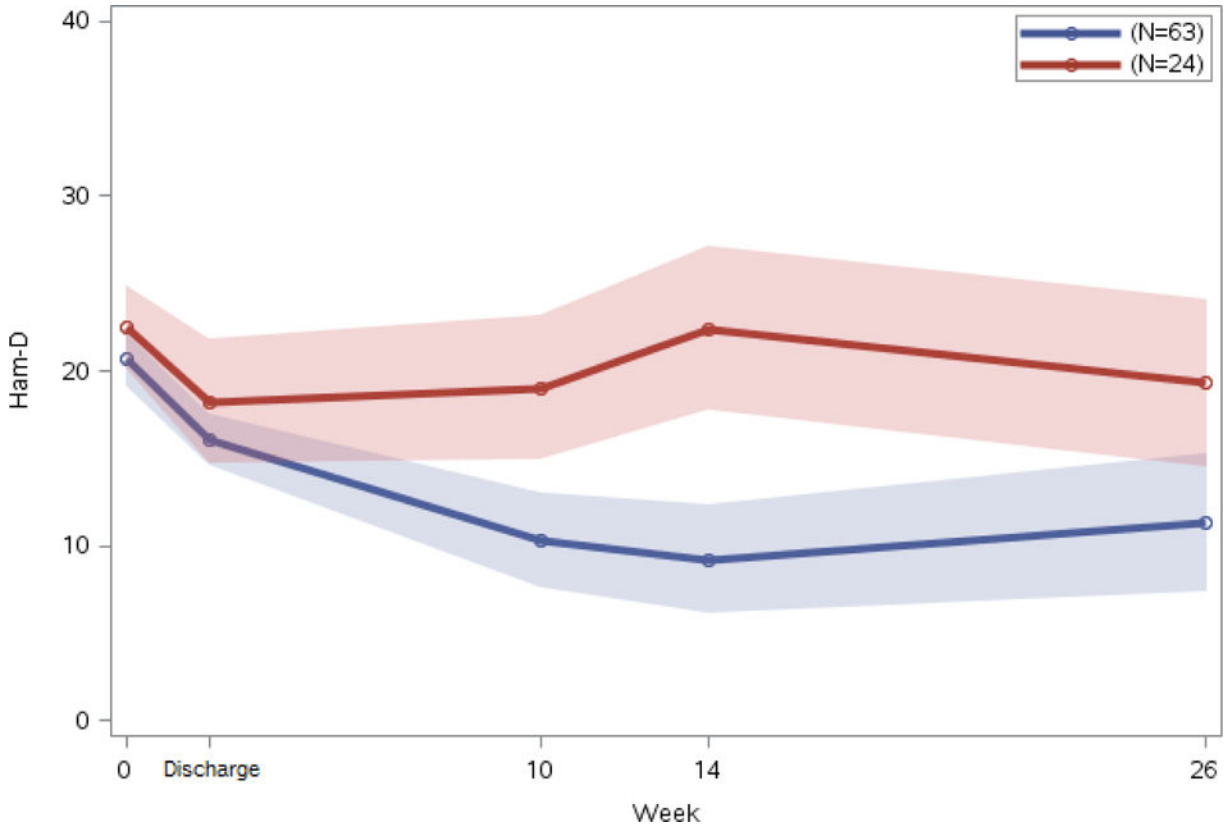

Figure 2. Distinct trajectories of depression severity of patients with major depression and severe COPD randomly assigned to receive PID-C or PSA

Legend to Figure 2: Latent class growth modeling (LCGM) identified two subgroups with distinct depression trajectories.

Ham-D: 24-item Hamilton Depression Rating Scale

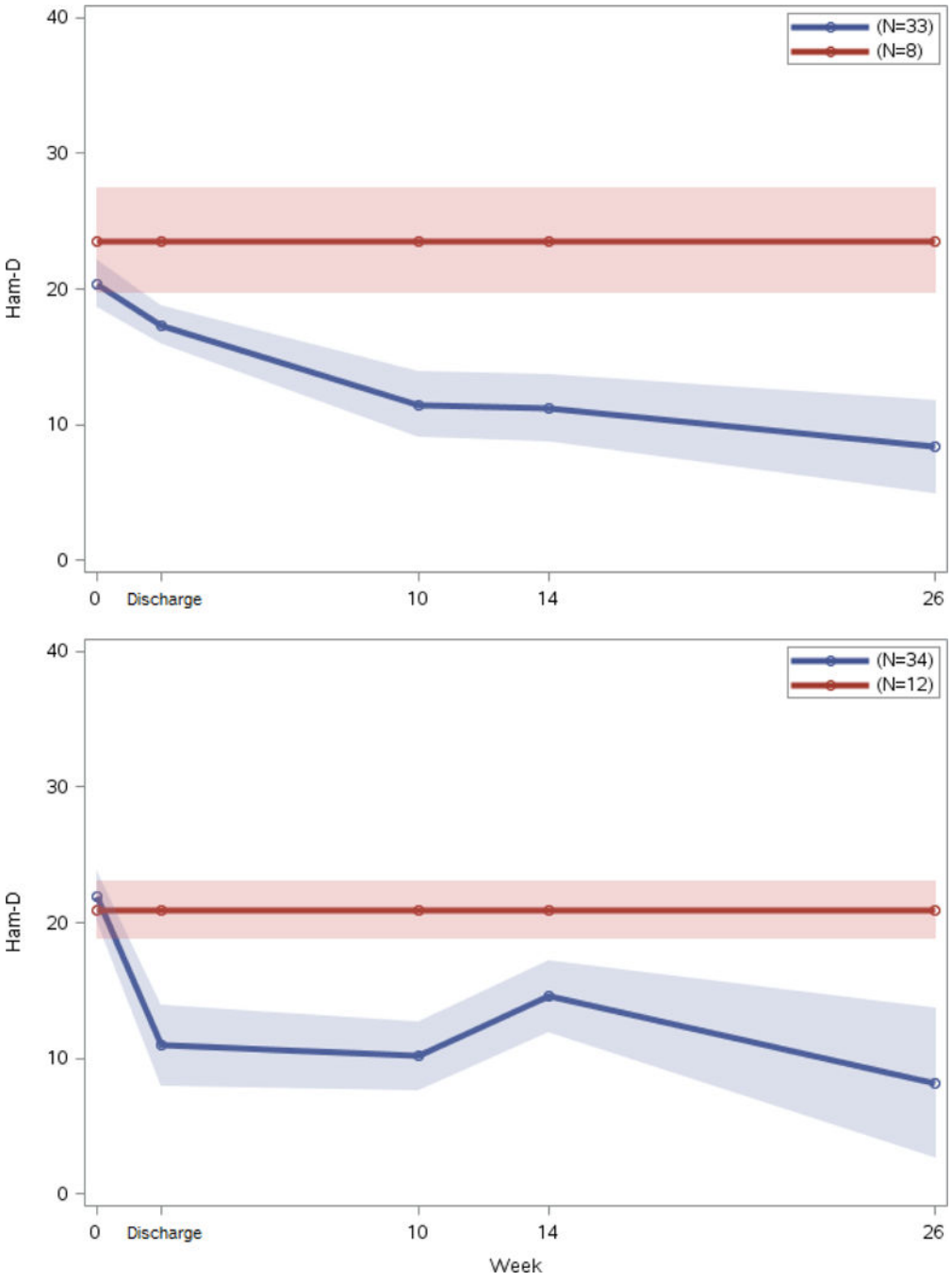

FIGURE 3. Distinct trajectories of depression severity of patients with major depression and severe COPD treated with PID-C (top) and PSA (bottom)

Legend to Figure 3: Latent class growth modeling (LCGM) identified subgroups with distinct depression trajectories in PID-C (top) and PSA (bottom) treated patients.

Ham-D: 24-item Hamilton Depression Rating Scale

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.

	Favorable Course (N=63)		Unfavorable Course (N=24)			
Variable					χ^2	**p**
Female, N (%)	43 (68.3)		15 (62.5)		0.2589	0.6109
	Median	**IQR**	**Median**	**IQR**	**Test Statistic**[a]	p
Age	75	13	67.5	15	816	0.0228
Education (years)	13	4	13.5	5	1161	0.3093
HAM-D	23	5	24	7.5	1167	0.2358
MADRS	22	8	23	9	1056.5	0.7209
PFSDQ-M						
Change in Activity	36	32	54	28	1092.5	0.0191
Shortness of Breath	32	40	44.5	24	1014	0.1313
CCI	3.5	3	2.5	3	995	0.8062
MMSE	28	3	28	2	1017	0.6019
DRS-IP	33	7	34	5.5	855	0.4576
GAD-7	5.5	7.5	10	7	1275.5	0.0114
NEO	11	7	15	9	1223	0.0298
Liverpool Self-Efficacy						
Control	15	3	13	3	809.5	0.0607
Personal Agency	12	2	11	2	703.5	0.0033
WHODAS II-12	30.5	9	35	10	1285.5	0.0034
Blood Gases						
FIO_2	21	0	21	0	513	0.9891
PCO_2	46	11	45.5	9.5	502	0.9807
PH	7.5	0.05	7.5	0.05	459	0.4719
PO_2	58	16	59	18	538	0.5896

[a]Wilcoxon Mann-Whitney U-Statistic

Note: HAM-D: Hamilton Depression Rating Scale; MADRS: Montgomery-Åsberg 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; GAD-7: Generalized Anxiety Disorder 7-item Scale; NEO: Neuroticism; WHODAS II-12:World Health Organization Disability Assessment Schedule II 12-item

Table 2

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

	Favorable Course (N=33)		Unfavorable Course (N=8)			
Variable						**Fisher's p**
Female, N (%)	22 (66.7)		4 (50.0)			0.4338
	Median	**IQR**	**Median**	**IQR**	**Test Statistic[a]**	p
Age	76	10	66.5	13	121.5	0.1299
Education	12	4	12	2.5	175.5	0.8076
HAM-D	23	5	26.5	9	207	0.2029
MADRS	22	8	23	12	176	0.5887
PFSDQ-M						
Change in Activity	32	32	55.5	29	220.5	0.0870
Shortness of Breath	28	33	55.5	28	227.5	0.0521
CCI	3	3	3	4.5	153	0.8186
MMSE	28	3	27	2	138.5	0.9704
DRS-IP	35	5	30.5	4	87.5	0.2799
GAD-7	6	6	12	7.5	242	0.0045
NEO	11	8	16	5.5	228.5	0.0478
Liverpool Self-Efficacy						
Control	14	2	12	1.5	73.5	0.0018
Personal Agency	12	2	10	2	75.5	0.0021
WHODAS II-12	31	12	37.5	9.5	219	0.0963
Blood Gases						
FIO_2	21	0	21	151	75	0.1431
PCO_2	44	12	55	35	81.5	0.2451
PH	7.5	0.05	7.5	0.05	44.5	0.2971
PO_2	56	15	55.5	27.5	62.5	1.0000

[a]Wilcoxon Mann Whitney U-Statistic

Note: HAM-D: Hamilton Depression Rating Scale; MADRS: Montgomery-Åsberg 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; GAD-7: Generalized Anxiety Disorder 7-item Scale; NEO: Neuroticism; WHODAS II-12:World Health Organization Disability Assessment Schedule II 12-item