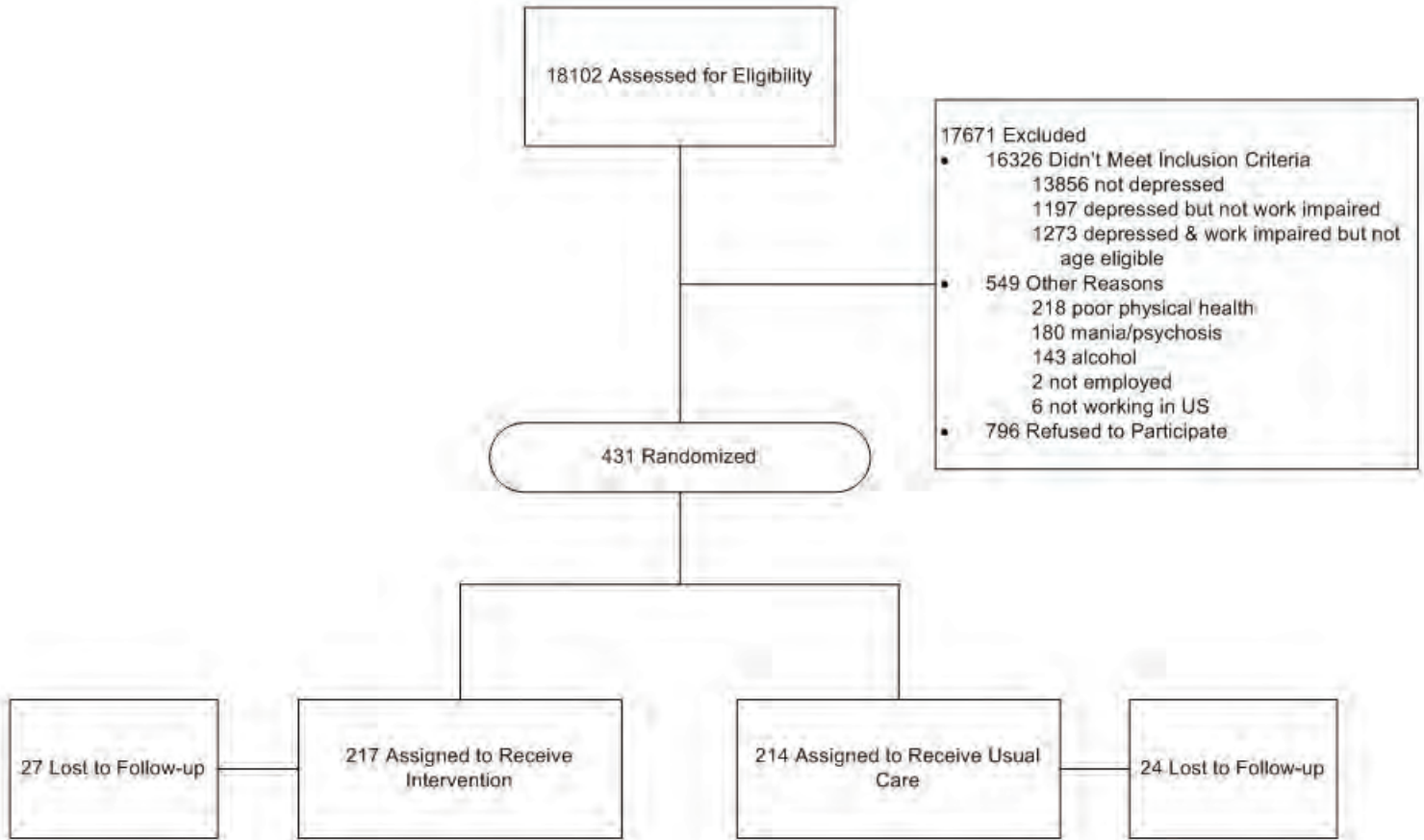


Figure 1: CONSORT Diagram for Randomized Controlled Trial (RCT) of an Experimental Work-Focused Intervention for Employed Adults with Depression and Work Limitations



Sensitivity Analyses of Results Obtained from Mixed Effects Models Testing Outcomes of Work-Focused Intervention (WFI) vs. Usual Care for Employees with Depression

Sensitivity analysis 1: In this sensitivity analysis, the last observation carried forward (LOCF) method was used to impute the missing outcome values at follow-up due to drop-out. The LOCF model results were compared to those obtained from the original mixed effects models. These analyses tested the robustness of the mixed effects model results because LOCF is considered in clinical trial research to be a more conservative approach. This model was estimated using analysis of covariance with main effects for treatment replacing treatment-by-time interactions. Compared to the original models, LOCF analyses yielded similar results without changing the significance of the WFI and usual care comparison. For at-work productivity loss, the change in effect size from the original model to the new model was -.72 to -.60. For depression symptom severity, the change in effect size from the original model to the new model was -.60 to -.48.

Sensitivity Analysis 1^a : Intention-to-Treat Analysis with Last Observation Carried Forward^b

	Work-Focused Intervention						Usual Care						Difference in Change Scores				
	Baseline (N=217)		Follow-Up (N=217)		Change Mean	Effect Size	Baseline (N=214)		Follow-Up (N=214)		Change Mean	Effect Size	Change	95% CI	Effect Size	p	
	Mean	SD	Mean	SD			Mean	SD	Mean	SD							
Presenteeism^c																	
Percent at-work productivity loss	10.2	4.3	6.7	4.8	-3.5	-.81	10.4	4.5	9.2	5.0	-1.2	-.27	-2.5	-3.2 to -1.7	-.60	<.001	
Depression^d																	
Symptom severity	14.4	5.2	8.4	6.8	-6.1	-1.17	14.3	4.9	11.1	5.7	-3.2	-.65	-2.9	-4.0 to -1.8	-.48	<.001	

^a Models were adjusted for study site, baseline mean age, percent male, percent White, percent married, percent white collar occupation, mean number of comorbidities, percent full-time employed, and mean scores of model dependent variable.

^b The missing values on the outcome variables at follow-up were imputed from the baseline value.

^c Based on the Work Limitations Questionnaire (WLQ). Scale scores indicate the percent of time limited in the past two weeks in ability to perform job tasks (e.g., time management). The percent at-work productivity loss variable is the mean percent difference in productivity compared to an external healthy benchmark employee norm. Possible scale scores range from 0 to 100, with higher scores indicating greater percentage of time limited in the past two weeks in ability to perform job tasks. Possible productivity loss scores range from 0 to 25, with higher scores indicating greater productivity loss.

^d Depression symptom severity is the mean Patient Health Questionnaire (PHQ-9) score. Possible scores range from 0 to 27. Higher scores indicate more severe depressive symptoms.

Sensitivity analysis 2: This sensitivity analysis examined the effect on at-work productivity loss of including study participants who were either employed or unemployed at follow-up. In the original mixed effects models, non-employment at follow-up was treated as missing. In these models, the maximum possible at-work productivity loss was assigned to unemployed participants. For at-work productivity loss, the change in effect size from the original model to the new model was $-.72$ to $-.62$ and statistical significance of the group differences did not change.

Sensitivity Analysis 2^a. Mixed Effects Model Including both Employed and Non-Employed at Follow-up^b

	Work-Focused Intervention						Usual Care				Difference in Change Scores					
	Baseline (N=217)		Follow-up (N=217)		Change		Baseline (N=214)		Follow-Up (N=214)		Change		95% CI	Effect Size	p	
	Mean	SD	Mean	SD	Mean	Effect Size	Mean	SD	Mean	SD	Mean	Effect Size				
Presenteeism^c																
Percent at-work productivity loss	10.2	4.3	6.1	5.2	-4.1	-.95	10.4	4.5	9.2	5.4	-1.1	-.24	-3.1	-4.1 to -2.2	-.62	<.001

^a Mixed effects models were adjusted for study site, baseline mean age, percent male, percent White, percent married, percent white collar occupation, mean number of comorbidities, percent full-time employed, and mean scores of model dependent variable.

^b Analysis assumes maximum attainable at-work productivity loss (27%) for individuals who were no longer employed at follow-up.

^c Based on the Work Limitations Questionnaire (WLQ). Scale scores indicate the percent of time limited in the past two weeks in ability to perform job tasks (e.g., time management). The percent at-work productivity loss variable is the mean percent difference in productivity compared to an external healthy benchmark employee norm. Possible scale scores range from 0 to 100, with higher scores indicating greater percentage of time limited in the past two weeks in ability to perform job tasks. Possible productivity loss scores range from 0 to 25, with higher scores indicating greater productivity loss.

Sensitivity Analysis 3: This sensitivity analysis addressed potential confounding due to variation in the number of days from baseline to follow-up survey completion. A "number of days" covariate was added to the original mixed effects. Compared to the original models, adding the number of days from baseline to follow-up as a covariate did not change the results.

Sensitivity Analysis 3^a. Mixed Effects Model Including Covariate of Time to Follow-up^b

	Work-Focused Intervention						Usual Care				Difference in Change Scores						
	Baseline (N=217)		Follow-Up (N=217)		Change		Baseline (N=214)		Follow-Up (N=214)		Change		Change	95% CI	Effect Size	p	
	Mean	SD	Mean	SD	Mean	Effect Size	Mean	SD	Mean	SD	Mean	Effect Size					
Presenteeism^c																	
Percent at-work productivity loss	10.2	4.3	6.1	5.2	-4.1	-.95	10.4	4.5	9.2	5.4	-1.1	-.24	-3.1	-4.1 to -2.1	-.62	<.001	
Depression^d																	
Symptom severity	14.4	5.2	7.1	6.1	-7.3	-1.40	14.3	4.9	10.6	5.6	-3.7	-.76	-3.8	-5.0 to -2.7	-.61	<.001	

^a Mixed effects models were adjusted for study site, baseline mean age, percent male, percent White, percent married, percent white collar occupation, mean number of comorbidities, percent full-time employed, and mean scores of model dependent variable.

^b The length of follow-up (mean time between baseline to follow-up in days) was included as a covariate.

^c Based on the Work Limitations Questionnaire (WLQ). Scale scores indicate the percent of time limited in the past two weeks in ability to perform job tasks (e.g., time management). The percent at-work productivity loss variable is the mean percent difference in productivity compared to an external healthy benchmark employee norm. Possible scale scores range from 0 to 100, with higher scores indicating greater percentage of time limited in the past two weeks in ability to perform job tasks. Possible productivity loss scores range from 0 to 25, with higher scores indicating greater productivity loss.

^d Depression symptom severity is the mean Patient Health Questionnaire (PHQ-9) score. Possible scores range from 0 to 27. Higher scores indicate more severe depressive symptoms.

Sensitivity Analysis 4: This analysis tested the sensitivity of original results to number of WFI counselor sessions that participants attended (mean 6.5 sessions \pm 2.9). The original mixed effects models were supplemented to include variables quantifying the number of counselor sessions attended and the interaction of sessions attended with a time indicator (representing follow-up). Since the number of sessions attended might depend on participant baseline characteristics not experimentally-determined, a propensity score was included. It was developed by regressing the number of sessions on age, gender, race, marital status, white collar occupation, number of baseline comorbidities, full-time employment and study site. This propensity score, along with its interaction with the time indicator, were also included in the mixed effects models. This analysis showed that a greater number of WFI sessions attended resulted in less (better) at-work productivity loss and depression symptom severity at follow-up ($p < .05$). Therefore, the study demonstrated a WFI dose-response relationship.

Sensitivity Analysis 4: Number of Counselor Sessions Provided

	Percent At-Work Productivity Loss			Depression Symptom Severity		
	Coefficient	p	95% CI	Coefficient	p	95% CI
Treatment indicator	-.55	.50	-2.16 to 1.06	1.97	.03	.21 to 3.73
Follow-up indicator	-1.96	.01	-3.43 to -.49	-4.09	<.001	-5.87 to -2.31
Follow-up by treatment	.25	.81	-1.79 to 2.29	-1.33	.28	-3.74 to 1.08
Number of sessions	.06	.56	-.16 to .28	-.28	.02	-.52 to -.04
Follow-up by number of sessions	-.49	<.001	-.76 to -.22	-.32	.05	-.63 to -.01
Propensity score ^a	.00	.99	-.41 to .41	-.12	.60	-.57 to .33
Propensity score by follow-up	.27	.24	-.18 to .72	.15	.59	-.40 to .70

^a The propensity score is the predicted value of number of sessions based on study site, age, gender, race, marital status, occupation, number of comorbidities, full-time employment status. Missing values for race and marital status were replaced by mean values and missing indicators in the propensity score model.

Sensitivity Analysis 5: This analysis addressed the possible heterogeneity of the WFI treatment effects based on which WFI counselor provided the care. Based on the WFI group only, the standard deviation of the WFI counselor random effect was evaluated for changes in the at-work productivity loss score and depression symptom severity score, and these changes were compared to the main treatment effect from the respective original mixed effects model. Eleven counselors provided WFI care. The mean number of completed WFI sessions per participant was 6.5 ± 2.9 during the study. For at-work productivity loss, the main effect for the WFI intervention was 3.5 times the size of the standard deviation of the counselor effect. For depression symptom severity, the main effect for the WFI intervention was 1.9 times the size of the standard deviation of the counselor effect. These results suggested that gains in at-work productivity loss were achieved by 100% of the WFI counselors and gains in depression symptom severity were achieved by 95%. Therefore, outcome gains were achieved by all, or nearly all, of the counselors.

Sensitivity Analysis 5: WFI Counselor Effect

	Percent At-Work Productivity Loss			Depression Symptom Severity		
	Coefficient	p	95% CI	Coefficient	p	95% CI
Treatment indicator	-3.02	<.001	-4.02 to -2.02	-3.38	<.001	-4.69 to -2.07
SD of counselor effect	.87			1.78		

Sensitivity Analysis 6: Each usual-care group enrollee was advised to contact a healthcare provider (e.g., primary care physician, psychiatrist and behavioral health specialist) and/or, if available, the employer-sponsored Employee Assistance Program (EAP). There were 21 usual-care group participants who received EAP counseling as of follow-up. This analysis investigated if the outcomes for these individuals differed from the WFI group outcomes. The mixed effects model method was used for this analysis replacing data from the entire usual-care group with data from the portion that used EAP services. The WFI group outcomes were superior to those of the usual-care group accessing EAP, with little change in the effect sizes in either direction.

Sensitivity Analysis 6: Experimental Intervention vs. Usual Care w/EAP: Presenteeism, Absenteeism and Depression Symptom Severity Outcomes: Mixed Effects Modeling^a

	Work-Focused Intervention						Usual Care who Visited EAP at Follow-up						Difference in Change Scores				
	Baseline (N=217)		Follow-up (N=190)		Change	Effect Size	Baseline (N=21)		Follow-up (N=21)		Change	Effect Size	Change	95% CI	Effect Size ^e	p	
	Mean	SD	Mean	SD			Mean	SD	Mean	SD							
Presenteeism^b																	
Percent at-work productivity loss	10.2	4.3	5.7	4.3	-4.5	-1.05	11.1	5.0	8.8	5.6	-2.3	-.46	-3.6	-5.8 to -1.5	-.81	.001	
Depression^c																	
Symptom severity	14.4	5.2	7.1	6.1	-7.3	-1.40	15.8	4.7	11.2	6.6	-4.6	-.98	-4.7	-7.3 to -2.2	-.79	<.001	

^a Models were adjusted for study site, baseline mean age, percent male, percent White, percent married, percent white collar occupation, mean number of comorbidities, percent full-time employed, and mean scores of model dependent variable. All significance tests were conducted using the chi-square test with a degree of freedom of 1.

^b Based on the Work Limitations Questionnaire (WLQ). Scale scores indicate the percent of time limited in the past two weeks in ability to perform job tasks (e.g., time management). The percent at-work productivity loss variable is the mean percent difference in productivity compared to an external healthy benchmark employee norm. Possible scale scores range from 0 to 100, with higher scores indicating greater percentage of time limited in the past two weeks in ability to perform job tasks. Possible productivity loss scores range from 0 to 27, with higher scores indicating greater productivity loss.

^c Depression symptom severity is the mean Patient Health Questionnaire (PHQ-9) score. Possible scores range from 0 to 27. Higher scores indicate more severe depressive symptoms

^e Effect size was computed as the ratio of the difference of change score and the pooled standard deviation of baseline scores for both groups.

Patient Perspective

Dr. C is 46-year old physician and associate professor for an academic medical center, where he has worked for the past three years. On average, he works 60 hours per week. Dr. C is divorced, has no children and lives alone in his own home. He responded to an announcement on his employer's website offering online, private mental health screening, with the possibility of eligibility for a new depression intervention program. After completing the screening, Dr. C received immediate results indicating that he had depression symptoms consistent with dysthymia (persistent depressive disorder) and work activity limitations resulting in a moderate at-work productivity loss.

Based on screening, Dr. C's PHQ-9 severity score of 11 indicated mild symptom severity characterized by dysphoria, anhedonia, fatigue and difficulty concentrating. He also reported carpal tunnel syndrome, lower back pain and allergies. According to responses on the Work Limitations Questionnaire (WLQ), he had lost 15% in work productivity during the prior two weeks. Work activity limitations included difficulty thinking clearly at work, concentrating on work, finishing work tasks, handling the workload and maintaining a routine or schedule.

Intervention Program

A study counselor, Ms. B was assigned to Dr. C. Prior to the first scheduled telephone visit (of eight total), she mailed an introductory letter to his home and a workbook, which supports psycho-education and cognitive behavioral therapy (CBT). During this initial telephone session, Dr. C reported that his first episode of depression occurred during medical school and since then he has had three more episodes meeting DSM criteria for major depression. Dr. C has been on therapeutic doses of an antidepressant for the past 10 years since his divorce. He has seen several psychotherapists intermittently during the past decade. Overall, his treatment has provided some, but not full, depression symptom relief.

Care Coordination. According to Ms. B, Dr. C was aware of depression's symptoms but he did not fully understand that his difficulties at work were common to depression. He was reluctant to make changes to his current antidepressant regimen. Ms. B encouraged Dr. C to make a PCP appointment specifically to discuss his current depression symptoms, work limitations and disappointment with the relief obtained from prior antidepressant treatment. To support the upcoming primary care visit, Ms. B faxed the PCP a report of Dr. C's PHQ-9 and WLQ and an accompanying explanation of results. This report was updated every four weeks for the duration of the intervention.

At a follow-up session with Ms. B, Dr. C reported that he met with his PCP. They discussed Dr. C's concentration difficulties, which persisted despite taking antidepressants. While his PCP was willing to increase the dosage, Dr. C, with his PCP's support, preferred to give the study intervention a try. He agreed to check-in with his PCP again to discuss antidepressant treatment. He did not resume an antidepressant during the course of the intervention.

Work Coaching and Modification. Dr. C. indicated that he hadn't mentioned his work problems to anyone and had no idea how to resolve them, other than to try and work harder, which he found difficult to do. Dr. C reported he was falling behind in multiple aspects of his work. An important grant deadline had been missed, clinical documentation was overdue by weeks and a lecture series scheduled to begin was not completed. Dr. C frequently found his mind wandering, felt mentally "foggy" and had no organized work routine.

In subsequent sessions, several strategies were identified to address difficulty thinking clearly and concentrating at work, planning and organizing work and completing work on time. Probing more deeply into Dr. C's work behaviors, he reported that he frequently would "surf the net" during work hours when he found himself unable to think clearly or concentrate on work. As a result, he used up valuable time and found it difficult to recover his focus. Ms. B and Dr. C developed an experiment: when he felt he was losing mental focus he would take a brief break, walking outside. Together they identified the early signs that his mind was wandering and agreed on a response (the walks). They also set a limit on the number of breaks to be taken and their duration. Second, Ms. B recommended that Dr. C try to use his Outlook Calendar to set priorities each day and allocate time consistent with the level of priority. At the end of each day, he would review his progress, which helped him to evaluate the next day's "to do" list. Each morning, the first 15 minutes were devoted to establishing the day's plan. To help Dr. C further improve his organizational skills and efficiency, he would try to meet with colleagues for grant-writing advice and assistance. Together, Ms. B and Dr. C did some role-playing so he could practice his request and manage his feelings of incompetence, which he experienced in such situations.

CBT Strategies. Ms. B and Dr. C developed several behavioral strategies to address fatigue and dysphoria. Dr. C agreed to using an activity calendar to help him identify and experiment with activities he found pleasurable and to integrate them into his routine. Eventually he restarted a lapsed exercise regimen, which he found made him feel less depressed. In addition, Dr. C pushed himself to reconnect with and meet friends twice a week and schedule a weekly meeting with several colleagues who had shared research interests. Within several weeks he noted that his energy level and mood improved. Dr. C worked on an activity sheet recording his success in undertaking these activities and how they made him feel, which reinforced their importance.

To address frequent self-critical thoughts while working, Dr. C learned several specific cognitive strategies (thought stopping, changing the subject, exaggeration) for interrupting, challenging, and distancing from his negative thinking. Also Dr. C added a pop-up message displaying positively reinforcing statements and simple strategies to counteract these thoughts.

Outcome. By the final session, Dr. C's WLQ productivity loss score improved from 15% to 3% (consistent with no major illness) and his PHQ-9 severity score declined from 11 to 3. With Ms. B's assistance, she and Dr. C co-created a self-care plan to sustain his use of the strategies he found to be most effective.