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Trained lay coaches and self-care cognitive-behavioral tools improve depression outcomes

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Objectives: Identify the key effective components of a depression self-care intervention.

Methods: Secondary analysis of data from 3 studies that demonstrated effectiveness of a similar depression self-care intervention (n=275): 2 studies among patients with chronic physical conditions and 1 among cancer survivors. The studies used similar tools, and telephone-based lay coaching. Depression remission and reduction at 6 months were assessed with either PHQ-9 (chronic condition cohorts) or CES-D (cancer survivor cohort). Multiple logistic regression was used to analyze data when the interaction p-value with cohort was <0.10.

Results: The 3 coached cohorts achieved better depression outcomes than usual care. The combination of coaching and joint use of 2 tools based on cognitive-behavioral therapy (CBT) was associated with depression remission and reduction among chronic condition cohorts but not among cancer survivors. Neither the number nor the length of coach calls were associated with outcomes in pooled data.

Conclusions: Trained lay coaching and use of CBT-based self-care tools were associated with improved depression outcomes in patients with chronic conditions but not among cancer survivors.

Practice implications: Trained lay coaching and CBT tools are key components of depression self-care interventions. Further research is needed on the effective components in cancer survivors.

Keywords: Depression, self-care, cognitive-behavioral therapy, pooled analysis.

1. INTRODUCTION

The aging of the population and the increased prevalence of chronic disease have highlighted the need for accessible psychological support for mental health sequelae of physical illness [1,2]. Low intensity psychological interventions (e.g., self-care materials) have been proposed to meet the needs of the population, particularly those with less severe symptoms, often as the first step in a stepped care approach [3]. Self-guided self-care interventions tend to have small but significant effect sizes [4,5] , but guided self-care interventions have been found to be as effective as standard cognitive-behavioral treatment (CBT)[6].

One limitation of guided self-care is the availability of health care professionals to provide the guidance. To address this limitation and to increase patient autonomy, we developed an innovative depression self-care intervention, delivered by trained lay coaches. We evaluated the intervention in several trials for depression in different target populations [7-10]. The intervention comprises a toolkit of core self-care tools based on CBT principles, supplementary relaxation tools, and informational tools on healthy lifestyle adapted to the needs of the target populations. Coaching was delivered in short telephone calls, using standardized protocols. The results of this research indicated beneficial effects of the coached interventions in different target populations on depression at 6 months: adjusted effect sizes were 0.42 (95% CI 0.08, 0.77) for a coached vs self-guided intervention among patients with chronic physical conditions not receiving therapy at study entry [9], and 0.60 (95% CI 0.33, 0.87) for a coached intervention vs usual care among cancer survivors [10]. These effect sizes are consistent with those reported in meta-analyses [5,6,11].

Despite evidence of effectiveness, it is unknown which intervention components, tools or coaching, lead to better depression outcomes. Can CBT-based self-care tools, of the type used in psychotherapy, be used effectively when coaching is provided by trained lay coaches? There has been remarkably little research on adherence to self-care interventions; existing research has been inconsistent in how adherence is defined and measured, and on the impact of adherence on outcomes [12]. The similarities in the interventions and outcomes in our previous studies enable pooling the data to allow a more comprehensive investigation of the associations between adherence and outcomes. The objectives of our study were to describe: 1) Differences in depression outcomes across cohorts (treatment arms); 2) Differences in tool use and coach calls across cohorts; 3) Whether tool use and the amount of coaching received by participants (number or length of calls) is associated with better depression outcomes; 4) Whether the joint use of two self-care tools is associated with better outcomes; and 5) Whether target population (chronic physical conditions vs cancer survivors), baseline anxiety, or satisfaction with the intervention modify the associations of self-care tools used with depression outcomes.

2. METHODS

2.1 Design and sample

This is a secondary analysis of data derived from 3 studies that were part of the DIRECT (Depression Intervention via Referral, Education and Collaborative Treatment) research

program. Across these 3 studies, 5 patient cohorts (treatment arms) were defined (see Table 1 for key features of each cohort).

- Study 1 [7] : uncontrolled pilot study of the coached DIRECT self-care (DIRECTsc) intervention in patients with chronic physical conditions in primary care **(cohort 1)**.
- Study 2 [8,9] : randomized controlled trial (RCT) of DIRECTsc for any chronic physical condition in primary care with coached **(cohort 2)** and self-guided **(cohort 3)** arms.
- Study 3 [10] : RCT of CanDIRECT in cancer survivors: intervention group was coached self-care **(cohort 4)** versus usual care controls **(cohort 5)**. Note that cohort 5 was included for comparative purposes; it was not included in the adherence analysis, as no intervention was provided.

In the current analysis, for study 2 we excluded patients receiving counseling at study entry, because we found that the intervention was not effective in these patients [9]. In study 3, patients receiving counseling were excluded at the outset. In cohort 1, patients receiving counseling at least once a month were excluded. Methodological details of these studies can be found in the primary publications [7,8,10].

2.2 Interventions

In cohorts 1-4, participants received a paper Toolkit; cohort 4 also had access to a web-site containing the self-care tools. For cohorts 1-3, the core tools were: a Depression Workbook widely used in Canada [13] and a Mood Monitoring Tool (MMT) developed by our team. The Workbook was designed for self-guided use across different health conditions, allowing the user to focus on skills that are more relevant to them (e.g., activation, realistic thinking, and problem-solving), and contains many exercises. Because self-monitoring is an important component of self-care [14], the MMT was based on similar tools used in CBT [15]. This tool allowed users to record their mood multiple times each day, and to identify daily events that may be associated with mood. The piloting of the self-care intervention among cancer survivors revealed that anxiety was a prominent symptom [16]. As a result, cohort 4 participants were provided the same CBT-based core tools and an additional CBT-based Anxiety Workbook [17] (similar format to the Depression Workbook). Relaxation CDs and informational tools (e.g., on symptoms of depression, healthy eating, and exercise, tailored to the target population) were also provided. All tools were available in English and French.

In cohorts 1, 2, and 4, participants were offered coaching by trained lay coaches supervised by a clinical psychologist in short (10-15 minute) telephone calls, weekly for 3

months decreasing to monthly for up to 6 months. Using scripted agendas, coaches guided and encouraged participants in the selection of tools, they did not provide psychotherapy. Cancer survivors in cohort 4 had slightly longer calls on average: 15 minutes vs 11-12 minutes in the chronic condition cohorts (Table 1). Cohort 3 (self-guided) did not receive coaching. Cohort 5 (usual care) received neither a Toolkit nor coaching.

2.3 Measures

2.3.1 Baseline measures

All studies collected data on age, sex, years of education, the 12-item Short-Form (SF-12) [18] (with computation of Physical and Mental Component Summary scores, PCS and MCS), and the 13-item Patient Activation Measure (PAM) [19]. Anxiety at baseline was measured by the GAD-7 [20] in chronic condition cohorts 2 and 3; in the cancer survivor cohort (4) we used the HADS anxiety subscale [21]. We used psychometrically equivalent cut-points to define clinically significant anxiety: 5.9 for the GAD-7 and 8 for the HADS [22].

2.3.2 Adherence measures

Participants reported their use of the tools either in a follow-up self-completed questionnaire (cohort 4, cancer survivors), or in an interview by a research assistant who was blind to the type of intervention provided (chronic condition cohorts 1-3; see Appendix 1 for details of the questions). All studies asked questions about tool use: which tools participants had used, looked at, tried or listened to (for audio tools). For cohorts 1-3, adherence data were collected both at 2 months (cohort 1) or 3 months (cohorts 2-3) and again at 6 months, allowing us to examine early vs. late adherence. For cohort 4, adherence data were collected at 6 months only. Follow-up questions among those reporting that they used a tool varied between cohorts (see Table 1). Cohorts 1 and 4 were asked whether they wrote in the Depression Workbook and/or the MMT, and whether they planned to continue to use the tools. The number of coach calls and their duration for each participant were extracted from coaching logs for cohorts 1, 2, and 4.

2.3.3 Depression outcome measures

For all cohorts, the Patient Health Questionnaire-9 (PHQ-9) was used to screen participants for eligibility [23]. However, the cut-off scores defining eligibility differed: a score of 5 or more was required for chronic condition cohorts 1-3; a score between 8 and 19 was required for cohort 4 (cancer survivors) because these cut-points are suggested for cancer patients [24], and because of concerns that cancer survivors with more severe depression

symptoms (PHQ-9 of 20 or more) are often not in a primary care setting in which their doctor could be notified, making referrals problematic. Depression outcomes were assessed at 6 months, using the PHQ-9 for chronic conditions cohorts 1-3 and the CES-D (Centre for Epidemiologic Studies Depression Scale) for cohort 4 (cancer survivors), because of its superior performance among cancer patients [25,26]. Because the primary outcome measure differed across the studies, we used psychometrically equivalent thresholds (less than 8 for the PHQ-9, less than 16 for the CES-D) [22] to define 6-month depression remission (either attainment of remission or maintenance for those meeting criteria for remission at study entry). Depression reduction was defined as a 50% reduction in depression symptom score from study entry to 6 months.

2.3.4 Satisfaction

Satisfaction with the intervention was measured in all studies with the Client Satisfaction Questionnaire (CSQ) [27,28]. High satisfaction was defined as a score of 9 or more out of 12 for the CSQ-3 or a score of 24 or more out of 32 for the CSQ-8.

2.4 Statistical methods

2.4.1 Objective 1: Differences across cohorts in depression outcomes

We tested the associations between patient characteristics and study cohort (1-5) with the Pearson Chi-square test, and one-way ANOVA [29,30]. The associations between 6-month binary outcomes and the study cohorts were tested using a logistic regression model [31], which included adjustment for patient characteristics; all pairwise comparisons [32] were examined using the Bonferroni correction [30], i.e. the level of significance after the correction was 0.005 (0.05/10 patient characteristics).

2.4.2 Objective 2: Differences in self-care tool use and coach calls across cohorts

Potential associations of adherence to individual self-care tools, combinations of tools (see Objective 4) and coach calls among cohorts 1-4, were tested using the Pearson Chi-square test and one-way ANOVA [29,30]. Study cohort 5 (usual care) was excluded from these analyses because no tools were given (adherence not relevant). The four self-care tools were: Depression Workbook, MMT, Relaxation, and Anxiety Workbook (cancer survivor cohort 4 only). For the first two tools, 3 binary variables were also included: Early vs late use, Wrote in tool (Y/N), and Plan to continue (Y/N). The two coach call measures were: the number of coach contacts, and the mean length of coach calls per patient.

2.4.3 Objective 3: Associations between adherence (self-care tool use and coach calls) with depression outcomes

We assessed the effect of each measure of adherence listed in Table 1 on two binary outcomes (depression remission and reduction). First, for each cohort 1-4 and each adherence measure, we fitted a logistic regression model [31] of outcome. We included covariates that differed among the 4 cohorts (Table 2): education, baseline PHQ-9 and SF12-PCS (MCS did not differ significantly across these 4 cohorts). Next, we repeated these analyses by pooling the data from cohorts 1-4 that used the same adherence and coaching measure, adding study cohort as a fixed effect. Finally, to examine whether the effects of adherence on the two depression outcomes were similar across study cohorts, we added an interaction term between the measure of adherence and the study cohort to each model in the pooled analysis. If the interaction effect was significant at the alpha level of 0.1, we removed the study cohort with the largest interaction effect and proceeded until the interaction test was no longer significant.

2.3.4 Objective 4: Adhering to multiple tools and outcomes

To explore whether joint use of 2 tools was associated with the depression outcomes, we created 2 composite binary variables: 1) Depression Workbook and MMT and 2) One Workbook and MMT (with Anxiety Workbook substituted for Depression Workbook in cohort 4).

2.3.5 Objective 5: Potential modifiers of associations between adherence, coaching and depression outcomes

Three potential modifiers were tested for each individual measure of adherence and for the two composite measures in Objective #4: 1) Target population [(limited to the 3 coached cohorts 1, 2, and 4) to avoid the confounding effect of coaching]; 2) Satisfaction with the intervention (Y/N); and 3) Clinically significant anxiety (Y/N). For each binary depression outcome, a logistic regression model was developed, with covariates: 1) measure of adherence), 2) modifier of interest, and 3) interaction term; stratified analyses were performed when the interaction term was significant at alpha 0.1.

2.3.6 Sensitivity analysis

Our primary analysis used data from all participants regardless of initial PHQ-9 score. In sensitivity analyses, we included only chronic condition cohort participants with initial PHQ-9 scores of 8-19, to make them more comparable to the cancer survivor cohorts.

All analyses were conducted with SAS University Edition and Stata 15.0.

3. RESULTS

3.1 Differences across cohorts in depression outcomes (objective 1)

Table 2 shows characteristics of the cohorts at baseline and 6 months. The age and sex distributions were similar among the cohorts, with mean age between 56.0 to 60.7, and the majority female (70.6% to 82.8%). However, a higher proportion of cancer survivors in cohorts 4 and 5 had university education. Participants with a chronic condition in cohorts 2 and 3 reported higher (better) MCS and lower (poorer) PCS than other cohorts. Note that MCS was no longer associated with cohort when cohort 5 was excluded in the subsequent analyses of adherence and outcomes.

After adjustment for PHQ-9, education, MCS, and PCS, there were significant differences across the cohorts in 6-month depression remission and reduction rates (Table 2). Depression outcomes were best for the 3 cohorts with coaching (1, 2, 4) and worst for the cohort that received usual care (5). Cohort 3 (self-guided) had outcomes that were intermediate between the coached and usual care cohorts. Pairwise comparisons indicated better symptom remission and reduction for cohorts 1, 2, and 4 (intervention with coaching) than cohort 5 (usual care). Among the coached cohorts, depression outcomes were better for the participants with chronic conditions (cohort 1 and 2) than for cancer survivors (cohort 4). For depression reduction only, there was also a significant difference between cohorts 1 (coached) and 3 (self-guided).

3.2 Differences in self-care tool use and coach calls across cohorts (objective 2)

There were significant differences across the 4 intervention cohorts in most of the measures of self-reported use of the self-care tools and number and duration of coach calls recorded in coach logs (Table 3). Cohort 3 (chronic condition self-guided) reported the lowest rates of use of all the tools. Cohort 4 (cancer survivors) members were more likely to report that they wrote in the Depression Workbook than the other cohorts. Compared to the coached chronic condition cohorts 1 and 2, the coached cancer survivor cohort 4 chose to receive fewer coach calls but these were longer in duration (mean of 14.6 minutes versus 12.1 and 10.9, respectively).

3.3. Associations between adherence (self-care tool use and coach calls) with depression outcomes (objective 3)

Tables 4 and 5 show the associations between the adherence measures and depression remission and reduction, respectively. As regards individual self-care tool use, none of the interaction p-values were less than 0.1, allowing pooled ORs across all cohorts to be computed. None of the pooled ORs for individual tools had 95% CIs that excluded the null value of one (i.e., not statistically significant). In examining results for individual cohorts, we note that use of the Depression Workbook and the MMT were significantly associated with remission and reduction only in cohort 1. Among users, early use, writing in these tools, and plans to continue

were not associated with remission (Table 4). However, in cohort 2 (chronic condition coached) early vs. late use of MMT was associated with a lower depression reduction rate (Table 5). Use of a relaxation tool or the Anxiety Workbook was not significantly associated with outcomes.

Among the coaching measures, neither number nor mean duration of coach calls were associated with either depression remission or reduction in pooled data (Tables 4 and 5). In some individual cohorts, longer mean call length was associated with lower rates of remission (cohort 4) or reduction (cohort 2).

3.4 Adhering to multiple tools and outcomes (objective 4)

As shown in Table 3, combined use of 2 tools, ranged from 36.2% to 76.5%, with lower combined use in the self-guided cohort 3. Results for combinations of tools and remission are shown in Table 4. For use of the Depression Workbook in conjunction with the MMT, there was a significant interaction with cohort; only data from the coached chronic condition cohorts 1 and 2 could be pooled, yielding a pooled OR for use of both core tools versus 0-1 tool of 4.21 (95% CI 1.73,10.28). For use of the Anxiety Workbook in cohort 4 (cancer survivors coached) rather than the Depression Workbook in conjunction with the MMT, the data from the 4 cohorts could be combined, resulting in an OR of 1.91 (95% CI 1.11, 3.28). Similar results were obtained for the reduction models (Table 5), except there was no interaction with cohort.

3.5. Potential modifiers of associations between adherence, coaching and depression outcomes (objective 5)

There were significant interactions ($p<0.1$) with target population in the coached cohorts 1 and 2 (chronic conditions) vs 4 (cancer survivors), for both depression outcomes (Table 6). Use of the MMT individually and of joint use of 2 CBT tools were associated with both outcomes in the chronic condition cohorts 1 and 2, but not the cancer survivor cohort 4. In contrast, there were no statistically significant interactions with either patient satisfaction or anxiety (Appendix 2).

3.6 Sensitivity analysis

Overall, the results of the sensitivity analysis were similar to those of the main analysis, although confidence intervals were wider because of the smaller sample size in the chronic condition cohorts (122 versus 179). The results of the sensitivity analysis for some of our key results are shown in Appendix 3.

4. DISCUSSION AND CONCLUSION

4.1 Discussion

Using pooled data, we have shown that an innovative guided self-care model using trained lay coaches achieves better depression outcomes than usual care, making it an attractive option for meeting the shortfall of psychological services. We also found that self-reports of the use of self-care tools based on CBT were associated with better outcomes. The use of pooled data offered potential gains in statistical power and the opportunity to examine the effects of adherence across different study populations. Heterogeneity in the effects observed appeared primarily due to the target population, with chronic condition patients showing stronger effects than cancer survivors.

Despite the evidence of effectiveness of the intervention among cancer survivors [10], the lack of associations between adherence and outcomes in the cancer survivor cohort is perplexing. It may be that precipitating and perpetuating factors for depression among cancer survivors are unique [33]. The MMT may have appeared less relevant to this population, who may have been preoccupied with fears about recurrence and survival [34,35]. These fears may also have led to longer average call length, even after adjustment for education and other covariates. Because of our desire to provide a more relevant workbook to the cancer cohort, we offered an alternative CBT tool, the Anxiety Workbook. Use of the Anxiety Workbook was (non-significantly) associated with remission; its inclusion in the analysis of joint use of 2 CBT tools reduced heterogeneity across the cohorts. CBT and self-management strategies are the recommended evidence-based treatments for depression in cancer survivors [36]. In future, tools that address fears of recurrence and survival should be considered for inclusion in CBT-based self-care interventions in cancer survivors.

There are also potential methodological explanations for the differences between the target populations. We collected adherence data from the cancer survivors (cohort 4) in a self-completed questionnaire at 6 months; these data were collected from the chronic condition cohorts through structured interviews at both at 2/3 and 6 months. This more frequent data collection may have improved the accuracy of recall of early tool use, reducing misclassification. The outcome measure also differed: PHQ-9 was used in the chronic condition cohorts and CES-D in the cancer cohort. However, we used psychometrically equivalent cut-points to define remission [22].

We included two “control” cohorts in our analysis: one cohort with chronic conditions that received the self-care tools without coaching (cohort 3) and one cohort (5) of cancer survivors that received usual care. All cohorts that received coaching had significantly better outcomes than the usual care cohort 5. Cohort 3 (chronic conditions self-guided) had outcomes

that were intermediate between those of the coached and usual care cohorts, consistent with evidence that self-guided self-care has lower effects than guided self-care [4], especially for outcomes like depression [5,11]. This more modest effectiveness might be explained by lower rates of tool use and perhaps sub-optimal use without the guidance provided by coaches. [37]. It may be that the coaching was the key effective component in cancer survivor cohort 4, providing attention and validation of distress beyond active cancer treatment. Such attentional effects are thought to account for the relatively strong placebo effects in depression research [38], which were also observed in the cancer survivor control cohort 5 in which one third was in remission at 6 months and 10% had 50% reduction of symptom severity (Table 2).

Several study limitations should be considered. First, although self-care tools and adherence measures were generally similar across studies, they were not identical. Second, our measures of tool use did not explore details of how specifically the tools were used, apart from when they were first used and whether the exercises were completed in writing. Third, despite the larger sample sizes resulting from data pooling, our study still lacked power to detect clinically significant heterogeneity or effects. Fourth, the exclusion of patients receiving psychological counseling reduces generalizability. However, the intervention was designed to be used as the first step in a stepped care intervention.; further it was not effective among those also receiving counseling [9].

4.2 Conclusions

An innovative self-care intervention for depression using coaching by trained lay coaches and CBT-based tools achieved superior outcomes compared to usual care. Among patients with chronic conditions, but not among cancer survivors, the guidance by a trained lay coach in the use of a CBT-based Depression Workbook in conjunction with an MMT was associated with improved depression outcomes.

4.3 Practice implications

Our results provide support for a model of guided depression self-care, using trained lay coaches. The evidence base for this coaching model continues to grow, extending it to be used alongside self-guided web-based stress management interventions [39], and in conjunction with a web-based intervention for post-partum depression and/or anxiety [40], in both examples with high satisfaction and preliminary evidence of efficacy .

This care model can mitigate the lack of access to mental health professionals. It is important to note that the coaches in our model play a different role than professional, certified

"health coaches"; they provide guidance and encouragement on use of the self-guided materials, but do not provide expert advice or use therapy (e.g., CBT).

The intervention is suitable for use as the first step of a stepped care depression treatment program [41]. CBT-based self-care tools (workbooks and MMT) should be the core tools provided. Further research is warranted on the key effective components of a depression self-care intervention in cancer survivors, although facilitation by coaches is clearly optimal in both cancer survivors and other chronic conditions. Approaches based on trans-diagnostic CBT should be considered in view of the frequent comorbidity of depression and anxiety [42].

The authors have no financial or any other kind of personal conflicts with this paper.

TABLE 1: Depression self-care intervention adherence cohorts

Variables	Cohort 1: DIRECTsc pilot (study 1) n=51	Cohort 2: DIRECTsc RCT coached arm (study 2) n=70	Cohort 3: DIRECTsc RCT self-guided arm (study 3) n=58	Cohort 4: CanDIRECT RCT intervention arm (study 4) n=96	Cohort 5: CanDIRECT RCT usual care arm (study 5) n=118
Inclusion criteria					
Population	Arthritis, Hypertension, Diabetes, COPD, Heart disease, Asthma	Any chronic physical conditions or chronic pain	Any chronic physical conditions or chronic pain	Active cancer treatments completed within past 10 years	Active cancer treatments completed within past 10 years
Age	Age 40+	Age 40+	Age 40+	Age 18+	Age 18+
PHQ-9 score	≥ 5	≥ 5	≥ 5	≥ 8 ≤19	≥ 8 ≤19
Intervention					
Toolkit	Yes	Yes	Yes	Yes	No
Coaching	Yes	Yes	No	Yes	No
Mean call length	12 minutes	11 minutes	-	15 minutes	-
Adherence measures					
Depression workbook					
Use	Yes	Yes	Yes	Yes	-
Early vs late use	Yes	Yes	Yes	No	-
Wrote in tool	No	Yes	Yes	Yes	-
Plan to continue	Yes	No	No	Yes	-
Mood monitoring					
Use	Yes	Yes	Yes	Yes	-
Early vs late use	Yes	Yes	Yes	No	-
Wrote in tool	No	Yes	Yes	Yes	-
Plan to continue	Yes	No	No	Yes	-
Anxiety workbook					
Use	No	No	No	Yes	-
Relaxation					
Use	No	Yes	Yes	Yes	-
Outcome measures (all measured 6 months after baseline)					
Primary (depression)	PHQ-9	PHQ-9	PHQ-9	CES-D	CES-D
Satisfaction	CSQ-8	CSQ-3	CSQ-3	CSQ-3	CSQ-3

PHQ-9: Patient Health Questionnaire, 9 item
CES-D: Center for Epidemiologic Studies Depression Scale
CSQ : Client Satisfaction Questionnaire, 3 and 8 item versions

TABLE 2: Baseline and outcome variables by cohort (n=393)

Variables	Cohort 1: DIRECTsc pilot (study 1) (n=51)	Cohort 2: DIRECTsc RCT coached arm (study 2) (n=70)	Cohort 3: DIRECTsc RCT self-guided arm (study 2)	Cohort 4: CanDIRECT RCT intervention arm (study 3) (n=96)	Cohort 5: CanDIRECT RCT usual care arm (study 3) (n=118)	Test	Significant pairwise comparisons (cohort #)
Baseline:						**p-value[2]**	
Age, mean (SD)	60.7 (10.2)	56.0 (11.4)	57.5 (11.2)	58.9 (10.9)	57.1 (13.1)	0.191	
Female, %	70.6	81.4	82.8	74.0	81.4	0.332	
Education, %						<0.001	
High school or less	21.6	41.4	50.0	10.4	17.0		
Some education beyond	47.1	30.0	27.6	33.3	28.8		
University	31.4	28.6	22.4	56.3	54.2		
Anxiety[1]	NA	71.4	58.6	57.3	64.7	0.252	
SF12-MCS	38.9 (11.3)	39.1 (10.7)	40.7 (10.8)	36.4 (8.1)	34.6 (9.2)	<0.001	
SF12-PCS	41.7 (11.2)	38.0 (10.7)	36.4 (10.6)	41.6 (9.9)	40.7 (9.2)	0.007	
PAM	61.0 (13.3)	61.6 (13.1)	58.9 (13.1)	56.9 (13.2)	57.3 (13.7)	0.100	
PHQ-9	12.4 (5.3)	12.2 (5.2)	12.3 (4.9)	11.9 (2.8)	12.3 (3.4)	0.969	
CES-D	NA	NA	NA	22.8 (8.1)	24.9 (10.1)	0.102	
6-month:						**p-value[3]**	
Outcomes: % [95%CI]							
Symptom remission[3,5]	64.2 [49.2; 79.3]	61.6 [48.6; 74.5]	42.0 [26.7; 57.3]	56.4 [45.4; 67.3]	33.5 [24.1; 43.0]	0.001	[1-5],[2-5],[4-5]
Symptom reduction[3,6]	55.2 [41.0; 69.3]	46.9 [34.7; 59.0]	26.4 [14.5; 38.2]	34.0 [24.2; 43.8]	9.5 [4.1; 15.0]	<0.001	[1-3],[1-5],[2-5],[4-5]
High satisfaction[4], %	76.0	84.3	82.5	84.8	NA	0.582	
(missing)	(1)	(0)	(1)	(4)			

SF-12 PCS: Physical Component Summary; MCS: Mental Component Summary; PAM :Patient Activation Measure NA:Not Applicable

PHQ-9: Patient Health Questionnaire; CES-D: Center for Epidemiologic Studies Depression Scale

[1]Cohort 2-3: GAD-7 (cut-off of 5.9 or more), Cohort 4-5: HADS-7 (cut-off of 8 or more) (GAD-7: Generalized Anxiety Disorder; HADS: Hospital Anxiety and Depression Scale)

[2]Pearson Chi-square for categorical variables and One way ANOVA for continuous variables; at alpha 0.05 the findings were the same for the comparison of cohort #1 to #4, except for SF12-MCS p-value=0.071

[3]Adjusted rates computed from the estimates obtained from logistic regression model; each model account for baseline PHQ-9, education, SF-12 MCS and PCS

[4]Cohort 1: CSQ-8: 24 or more, Cohort 2 to 5: CSQ-3: 9 or more (CSQ: Client Satisfaction questionnaire)

[5]Remission: For cohort 1 to 3, PHQ-9 score<8 and for cohort 4 and 5, CES-D score<16

[6]Reduction: 50% reduction in depression score at follow-up (compared to baseline)

*All pairwise comparisons (10) were tested; Bonferroni correction was applied, pairwise comparisons were significant at alpha = 0.005

TABLE 3: Use of tools and number of coach calls over the 6 month study period, by cohort (n=275)

	Cohort 1: DIRECTsc pilot (study 1) (n=51)	Cohort 2: DIRECTsc RCT coached arm (study 2) (n=70)	Cohort 3: DIRECTsc RCT self-guided arm (study 2) (n=58)	Cohort 4: CanDIRECT RCT intervention arm (study 3) (n=96)	p-value
Individual tools:	%	%	%	%	
Depression workbook					
User (any)	88.2	90.0	75.9	91.7	0.030
Among users (any)	*(n=45)*	*(n=63)*	*(n=44)*	*(n=88)*	
Early user (ref: late user)	66.7	93.7	88.6	NA	<0.001
Wrote in tool (ref: no writing)	NA	54.0	40.9	75.0	<0.001
Plan to continue[1] (ref: no plan)	73.3	NA	NA	77.3	0.661
Mood monitoring					
User (any)	82.4	45.7	37.9	75.0	<0.001
Among users (any)	*(n=42)*	*(n=32)*	*(n=22)*	*(n=72)*	
Early user (ref: late user)	81.0	81.3	86.4	NA	0.850
Wrote in tool (ref: no writing)	NA	78.1	77.3	66.7	0.392
Plan to continue[1] (ref: no plan)	61.8	NA	NA	58.3	0.737
				Tools	
Relaxation user (any)	NA	50.0	36.2	72.9	<0.001
Anxiety workbook user (any)	NA	NA	NA	75.0	
Combinations of tools:					
Depression Workbook plus Mood Monitoring (ref 0-1 tool)	76.5	45.7	36.2	71.9	<0.001
One Workbook plus Mood Monitoring (ref 0-1 tool)*	76.5	45.7	36.2	62.5	<0.001
Coaching:					
Number of coach contacts:					
1st quartile	9.0	8.0	NA	6.0	
Median	11.0	11.0	NA	9.0	
3rd quartile	14.0	15.0	NA	10.0	
Continuous (0 to 16), mean (SD)	10.7 (4.0)	10.6 (4.4)	NA	7.9 (3.5)	<0.001
(among the one with at least one coach contact)	(n=49)	(n=69)		(n=90)	
1st quartile	10.0	9.1	NA	11.4	
Median	11.8	10.3	NA	13.6	
3rd quartile	13.3	12.4	NA	17.5	
Continuous, mean (SD)	12.1 (4.5)	10.9 (3.0)	NA	14.6 (4.5)	<0.001

NA: Not Applicable

[1] Cohort 1 at 2 months and Cohort 4 at 6 months

*Depression Workbook in cohorts 1-3, Anxiety Workbook in cohort 4

Table 4: ORs and 95% CIs for adherence measures and remission, by cohort and pooled

Tools	Cohort 1: DIRECTsc pilot (study 1) (n=51)	Cohort 2: DIRECTsc RCT coached arm (study 2) (n=70)	Cohort 3: DIRECTsc RCT self-guided arm (study 2) (n=58)	Cohort 4: CanDIRECT RCT intervention arm (study 3) (n=96)	Test Pooling OR	Pooled	Notes
	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	p-value	OR [95% CI]	
Individual tools:							
Depression workbook							
User (any)	**13.82 [1.35; 141.19]**	1.45 [0.27; 7.65]	1.28 [0.30; 5.49]	0.47 [0.09; 2.50]	0.148	1.40 [0.65; 3.01]	n=275
Among users (any)	*(n=45)*	*(n=63)*	*(n=44)*	*(n=88)*			
Early user (ref: late user)	4.12 [0.88; 19.25]	1.46 [0.14; 14.97]	0.37 [0.04; 3.76]	NA	0.174	1.86 [0.64; 5.38]	n=152
Wrote in tool (ref: no writing)	NA	1.93 [0.59; 6.34]	0.52 [0.11; 2.42]	1.04 [0.38; 2.85]	0.519	1.07 [0.56; 2.05]	n=195
Plan to continue[1] (ref: no plan)	0.37 [0.03; 4.98]	NA	NA	1.33 [0.47; 3.77]	0.351	1.03 [0.41; 2.62]	n=118
Mood monitoring							
User (any)	**9.64 [1.52; 61.08]**	**3.33 [1.08; 10.26]**	1.31 [0.32; 5.43]	0.90 [0.34; 2.39]	0.104	1.76 [0.99; 3.11]	n=275
Among users (any)	*(n=42)*	*(n=32)*	*(n=22)*	*(n=72)*			
Early user (ref: late user)	NA	0.37 [0.01; 2.33]	1.79 [0.19; 4.99]	NA	0.997	0.73 [0.19; 2.84]	n=96
Wrote in tool (ref: no writing)		0.82 [0.04; 15.23]	0.63 [0.02; 18.74]	1.04 [0.37; 2.88]	0.621	0.97 [0.41; 2.29]	n=126
Plan to continue[1] (ref: no plan)	0.26 [0.02; 4.06]	NA	NA	0.88 [0.33; 2.37]	0.417	0.71 [0.29; 1.74]	n=106
Relaxation user (any)	NA	0.89 [0.30; 2.62]	1.92 [0.47; 7.82]	0.85 [0.32; 2.22]	0.721	1.05 [0.57; 1.92]	n=224
Anxiety workbook user (any)	NA	NA	NA	1.78 [0.66; 4.75]	NA		
Combinations of tools:							
Depression Workbook plus Mood Monitoring (ref 0-1 tc	**7.09 [1.53; 32.89]**	**3.33 [1.08; 10.26]**	1.11 [0.26; 4.80]	0.89 [0.35; 2.27]	**0.055**	**4.21 [1.73; 10.28]**	n=121 (cohort 3 & 4
One Workbook plus Mood Monitoring (ref 0-1 tool)*	**7.09 [1.53; 32.89]**	**3.33 [1.08; 10.26]**	1.11 [0.26; 4.80]	1.26 [0.53; 3.01]	0.103	**1.91 [1.11; 3.28]**	n=275
Coaching:							
Number of coach calls:							
Moderate: >1st & <3rd quartile (ref: ≤1st quartile)	0.53 [0.11; 2.66]	1.51 [0.44; 5.21]	NA	0.66 [0.23; 1.91]	0.662	0.84 [0.42; 1.67]	n=217
High: ≥3rd quartile (ref: ≤1st quartile)	0.65 [0.11; 3.89]	1.54 [0.36; 6.59]	NA	1.18 [0.43; 3.25]		1.16 [0.55; 2.41]	
Continuous (0 to 16)	0.99 [0.84; 1.16]	1.06 [0.94; 1.19]	NA	1.03 [0.92; 1.16]	0.727	1.03 [0.96; 1.11]	n=217
Mean duration of coach contacts: *Patient with no contact were excluded (n=9)*							
Moderate: >1st & <3rd quartile (ref: ≤1st quartile)	0.49 [0.08; 2.93]	0.99 [0.25; 3.86]	NA	0.30 [0.10; 0.94]	0.235	0.52 [0.25; 1.10]	n=208
High: ≥3rd quartile (ref: ≤1st quartile)	0.76 [0.08; 7.58]	0.22 [0.04; 1.12]	NA	0.45 [0.13; 1.62]		0.44 [0.19; 1.03]	

OR [95%CI]: Odds Ratio and 95% Confidence Interval NA: Not Applicable

All the ORs were adjusted for education, PHQ-9 and SF-12 PCS; for the pooled ORs the same covariates were used, including the cohort as a fixed effect

Significant ORs are in bold font; Significant interactions (Test Pooling) at 0.1 are in bold font

[1]Cohort 1 at 2 month and Cohort 4 at 6 month *Depression Workbook in cohorts 1-3, Anxiety Workbook in cohort 4

TABLE 5: ORs and 95% CIs for adherence measures and reduction by cohort and pooled

Tools	Cohort 1: DIRECTsc pilot (study 1) (n=51) OR [95% CI]	Cohort 2: DIRECTsc RCT coached arm (study 2) (n=70) OR [95% CI]	Cohort 3: DIRECTsc RCT self-guided arm (study 2) (n=58) OR [95% CI]	Cohort 4: CanDIRECT RCT intervention arm (study 3) (n=96) OR [95% CI]	Test Pooling OR p-value	Pooled OR [95% CI]	Notes
Individual tools:							
Depression workbook							
User (any)	**10.46 [1.01; 108.39]**	1.16 [0.23; 5.85]	0.89 [0.22; 3.71]	1.66 [0.30; 9.02]	0.384	1.68 [0.75; 3.76]	n=275
Among users (any)	*(n=45)*	*(n=63)*	*(n=44)*	*(n=88)*			
Early user (ref: late user)	1.70 [0.45; 6.37]	1.25 [0.15; 10.50]	0.57 [0.07; 4.49]	NA	0.624	1.25 [0.47; 3.34]	n=152
Wrote in tool (ref: no writing)	NA	1.30 [0.43; 3.94]	1.00 [0.23; 4.39]	1.17 [0.41; 3.33]	0.973	1.16 [0.61; 2.20]	n=195
Plan to continue[1] (ref: no plan)	0.20 [0.02; 2.20]	NA	NA	1.24 [0.41; 3.72]	0.190	0.82 [0.33; 2.05]	n=118
Mood monitoring							
User (any)	**7.39 [1.24; 43.99]**	2.34 [0.86; 6.39]	1.82 [0.49; 6.79]	0.74 [0.28; 2.00]	0.206	1.64 [0.94; 2.86]	n=275
Among users (any)	*(n=42)*	*(n=32)*	*(n=22)*	*(n=72)*			
Early user (ref: late user)	1.33 [0.22; 8.20]	**0.15 [0.01; 0.87]**	0.27 [0.01; 12.48]	NA	0.985	0.39 [0.11; 1.35]	n=96
Wrote in tool (ref: no writing)	NA	0.54 [0.07; 3.90]	0.87 [0.05; 16.47]	1.23 [0.42; 3.64]	0.566	1.12 [0.48 ;2.60]	n=126
Plan to continue[1] (ref: no plan)	0.14 [0.02; 1.17]	NA	NA	1.30 [0.46; 3.69]	**0.080**	1.30 [0.46; 3.69]	n=72 (cohort 1 removed)
Relaxation user (any)	NA	1.21 [0.45; 3.25]	1.60 [0.45; 5.63]	1.59 [0.57; 4.46]	0.895	1.38 [0.77; 2.49]	n=224
Anxiety workbook user (any)	NA	NA	NA	1.26 [0.45; 3.56]	NA		
Combinations of tools:							
Depression Workbook plus Mood Monitoring (ref 0-1 t	**6.30 [1.41; 28.18]**	2.34 [0.86; 6.39]	2.18 [0.56; 8.49]	0.98 [0.37; 2.56]	0.258	**1.87 [1.08; 3.22]**	n=275
One Workbook plus Mood Monitoring (ref 0-1 tool)*	**6.30 [1.41; 28.18]**	2.34 [0.86; 6.39]	2.18 [0.56; 8.49]	0.99 [0.40; 2.44]	0.249	**1.83 [1.08; 3.10]**	n=275
Coaching:							
Number of coach calls:							
Moderate: >1st & <3rd quartile (ref: ≤1st quartile)	0.60 [0.15; 2.44]	1.09 [0.35; 3.45]	NA	0.60 [0.20; 1.81]	0.634	0.72 [0.36; 1.41]	n=217
High: ≥3rd quartile (ref: ≤1st quartile)	1.18 [0.24; 5.88]	1.97 [0.52; 7.43]	NA	0.76 [0.28; 2.12]		1.08 [0.53; 2.18]	
Continuous (0 to 16)	1.01 [0.87; 1.17]	1.07 [0.95; 1.20]	NA	0.99 [0.88; 1.12]	0.681	1.03 [0.96; 1.10]	n=217
Mean duration of coach contacts:							
Patient with no contact were excluded (n=9)							
Moderate: >1st & <3rd quartile (ref: ≤1st quartile)	0.70 [0.16; 2.98]	0.57 [0.17; 1.95]	NA	0.49 [0.16; 1.49]	**0.092**	0.57 [0.24; 1.36]	n=139 (cohort 2 removed)
High: ≥3rd quartile (ref: ≤1st quartile)	1.67 [0.26; 10.83]	0.05 [0.01; 0.34]	NA	0.52 [0.15; 1.84]		0.81 [0.30; 2.18]	

OR [95%CI]: Odds Ratio and 95% Confidence Interval NA: Not Applicable

All the ORs were adjusted for education, PHQ-9 and SF-12 PCS; for the pooled ORs the same covariates were used, including the cohort as a fixed effect

Significant ORs are in bold font; Significant interactions (Test Pooling) at 0.1 are in bold font

[1]Cohort 1 at 2 month and Cohort 4 at 6 month *Depression Workbook in cohorts 1-3, Anxiety Workbook in cohort 4

TABLE 6: Target population as modifier of associations between adherence and depression outcomes (n=217)

Tools	Outcome: Remission	Outcome: Reduction
	Results	**Results**
Depression workbook user (ref: non-user)		
Test of interaction with target population, p-value	**0.062**	0.623
Stratified by population, OR [95%CI]		
Cohort 1 to 2 (n=121)	3.14 [0.88; 11.15]	2.71 [0.77; 9.54]
Cohort 4 (n=96)	0.47 [0.09; 2.50]	1.66 [0.30; 9.02]
Mood monitoring user (ref: non-user)		
Test of interaction with target population, p-value	**0.040**	**0.046**
Stratified by population, OR [95%CI]		
Cohort 1 to 2 (n=121)	**4.33 [1.70; 11.06]**	**2.92 [1.27; 6.69]**
Cohort 4 (n=96)	0.90 [0.34; 2.39]	0.74 [0.28; 2.00]
Depression Workbook plus Mood Monitoring (ref 0-1 tool)		
Test of interaction with target population, p-value	**0.024**	**0.083**
Stratified by population, OR [95%CI]		
Cohort 1 to 2 (n=121)	**4.21 [1.73; 10.28]**	**3.10 [1.38; 6.96]**
Cohort 4 (n=96)	0.89 [0.35;2.27]	0.98 [0.37; 2.56]
One Workbook plus Mood Monitoring (ref 0-1 tool)*		
Test of interaction with target population, p-value	**0.086**	**0.077**
Stratified by population, OR [95%CI]		
Cohort 1 to 2 (n=121)	**4.21 [1.73; 10.28]**	**3.10 [1.38; 6.96]**
Cohort 4 (n=96)	1.26 [0.53; 3.01]	0.99 [0.40; 2.44]

OR [95%CI]:Odds Ratio and 95% Confidence Interval

All ORs were adjusted for cohort, education, PHQ-9 and SF-12 PCS and including the cohort as a fixed effect (for cohort 1 to 2 analyses); Significant ORs are in bold font; Significant interactions at 0.1 are in bold font

*Depression Workbook in cohorts 1-2, Anxiety Workbook in cohort 4

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APPENDIX 1 : Questions used to assess adherence

Cohort	DIRECTsc pilot (Cohort 1)	DIRECTsc intervention and control (Cohorts 2 and 3)	CanDIRECT (Cohort 4)
Mode:	Telephone interview	Telephone interview	Self-complete
Time point:	2 months and 6 months	3 months and 6 months	6 months only
Depression workbook:			
Use *Question wording:*	**At 2 months:** Of the self-care tools that we offered, which ones have you tried? *Allow the patient to answer first. Probe for the others not mentioned by the patient: did you try anything else? Use specific probes provided for each tool.* **At 6 months:** Did you use the Antidepressant Skills Workbook? o Yes o No	**At 3 months:** Another one of the materials you were given was the Antidepressant Skills Workbook. Did you read any of the sections of the Workbook? o Yes o No Did you listen to the CD that came with the workbook? o Yes o No **At 6 months:** Did you look at or use any of the materials in the binder during the last 3/6 months? Do you remember what you looked at or used? *Check all that apply and probe "Anything else?"*	Did you look at/listen to the Antidepressant Skills Workbook? oNo oI read some of/ all of the paper version oI listened to some of/ all of the audio version oI tried both the paper and audio versions
Coding:	Users defined as those for whom the Depression workbook was checked off at 2 months (early users) or 6 months (late users checked off at 6 months but not at 2 months)	Users defined as those who said yes to either paper or audio versions at 3 months (early users) or those for whom the Depression workbook was checked off at 6 months (late users checked off at 6 months but not at 3 months)	Users defined as those who selected any of the bottom three answer options listed above
Wrote in tool *Question wording:*	N/A	**At 3 months:** There were sections in the workbook where you could write things. Did you write anything in those sections? o Yes o No Did you do any of the writing exercises suggested in the CD? o Yes o No **At 6 months:** Some people like to make notes when using the tools in the binder. During the last 3/6 months, did you make notes in your binder, or in another place? Do you remember which sections you wrote in? Some of the sections included worksheets or places to take notes. We will not be collecting anything you have written, but are interested in finding out if people made notes for themselves. *Check all that apply and probe "Anything else?"*	Did you use the worksheets or complete any of the writing exercises described? oYes oNo

APPENDIX 2 : Modifiers of adherence measures Remission and Reduction outcomes

Tools	Outcome: Remission	Outcome: Reduction	Notes
	Results	Results	
Depression workbook user (ref: non-user)			
Test of interaction with Anxiety, p-value	0.277	0.762	3 studies (cohort 2 to 4), n=224
Stratified by Anxiety[1], OR [95%CI]			
Anxiety (n=139)	1.53 [0.46; 5.07]	1.26 [0.38; 4.16]	
No anxiety (n=85)	0.62 [0.16; 2.49]	1.17 [0.31; 4.41]	
Test of interaction with Satisfaction, p-value	0.447	0.465	4 studies (cohort 1 to 4), n=269
Stratified by satisfaction[2], OR [95%CI]			
Satisfied (n=222)	0.86 [0.30; 2.52]	1.71 [0.59; 4.99]	
Not satisfied (n=47)	2.54 [0.50; 12.93]	0.55 [0.08; 3.92]	
Mood monitoring user (ref: non-user)			
Test of interaction with Anxiety, p-value	0.137	0.485	3 studies (cohort 2 to 4), n=224
Stratified by Anxiety[1], OR [95%CI]			
Anxiety (n=139)	1.00 [0.45; 2.25]	1.15 [0.52; 2.52]	
No anxiety (n=85)	**2.89 [1.03; 8.12]**	1.88 [0.70; 5.00]	
Test of interaction with Satisfaction, p-value	0.678	0.627	4 studies (cohort 1 to 4), n=269
Stratified by satisfaction[2], OR [95%CI]			
Satisfied (n=222)	1.53 [0.79; 2.99]	1.51 [0.80; 2.83]	
Not satisfied (n=47)	1.27 [0.28; 5.76]	0.96 [0.13; 7.21]	
Depression Workbook plus Mood Monitoring (ref 0-1 tool)			
Test of interaction with Anxiety, p-value	0.239	0.456	3 studies (cohort 2 to 4), n=224
Stratified by Anxiety[1], OR [95%CI]			
Anxiety (n=139)	1.01 [0.46; 2.22]	1.26 [0.58; 2.74]	
No anxiety (n=85)	2.40 [0.86; 6.66]	2.22 [0.82; 5.97]	
Test of interaction with Satisfaction, p-value	0.823	0.950	4 studies (cohort 1 to 4), n=269
Stratified by satisfaction[2], OR [95%CI]			
Satisfied (n=222)	1.30 [0.67; 2.52]	1.60 [0.86; 2.99]	
Not satisfied (n=47)	1.83 [0.45; 7.50]	1.61 [0.26; 10.08]	
One Workbook plus Mood Monitoring (ref 0-1 tool)*			
Test of interaction with Anxiety, p-value	0.409	0.485	3 studies (cohort 2 to 4), n=224
Stratified by Anxiety[1], OR [95%CI]			
Anxiety (n=139)	1.32 [0.62; 2.79]	1.29 [0.62; 2.69]	
No anxiety (n=85)	2.44 [0.88; 6.81]	2.14 [0.81; 5.66]	
Test of interaction with Satisfaction, p-value	0.995	0.934	4 studies (cohort 1 to 4), n=269
Stratified by satisfaction[2], OR [95%CI]			
Satisfied (n=222)	1.60 [0.85; 3.02]	1.55 [0.85; 2.82]	
Not satisfied (n=47)	2.05 [0.49; 8.61]	2.17 [0.33; 14.37]	

All the ORs were adjusted for cohort, education, PHQ-9 and SF-12 PCS and including the cohort as a fixed effect; Significant ORs are in bold font; Significant interaction at 0.1 are in bold font; *Depression Workbook in cohorts 1-3, Anxiety Workbook in cohort 4

[1]Cohort 2-3: GAD-7 (cut-off of 5.9 or more), Cohort 4-5: HADS-7 (cut-off of 8 or more)

(GAD-7: Generalized Anxiety Disorder; HADS: Hospital Anxiety and Depression Scale)

[2]Cohort 1: CSQ-8: 24 or more, Cohort 2 to 5: CSQ-3: 9 or more (CSQ: Client Satisfaction questionnaire)

OR [95%CI]:Odds Ratio and 95% Confidence Interval

APPENDIX 3 :Sensitivity analyses among patients with PHQ-9: 8 to 19 [Table 2 and 6]

Table 2-sensitivity: Baseline and outcome variables by cohort (n=336)

Variables	Cohort 1: DIRECTsc pilot (study 1) (n=51)	Cohort 2: DIRECTsc RCT coached arm (study 2) (n=70)	Cohort 3: DIRECTsc RCT self-guided arm (study 2) (n=58)	Cohort 4: CanDIRECT RCT intervention arm (study 3) (n=96)	Cohort 5: CanDIRECT RCT usual care arm (study 3) (n=118)	Test	Significant pairwise comparisons (cohort #)
PHQ-9: 8 to 19	**n=36**	**n=45**	**n=41**	**n=96**	**n=118**		
6-month:						**p-value[1]**	
Outcomes: % [95%CI]							
Symptom remission[1,2]	57.0 [39.2; 74.8]	61.1 [45.7; 76.4]	40.4 [22.7; 58.1]	55.0 [44.1 65.9]	32.2 [23.0; 41.5]	0.004	[2-5],[4-5]
Symptom reduction[1,3]	48.7 [32.0; 65.5]	49.6 [34.3; 64.9]	33.5 [17.8; 49.3]	32.6 [22.9; 42.3]	9.2 [3.9; 14.4]	<0.001	[1-5],[3-5],[2-5],[4-5]

PHQ-9: Patient Health Questionnaire; CES-D: Center for Epidemiologic Studies Depression Scale

[1]Adjusted rates computed from the estimates obtained from logistic regression model; each model account for baseline PHQ-9, education, SF-12 MCS and PCS;

[2]Remission: For cohort 1 to 3, PHQ-9 score<8 and for cohort 4 and 5, CES-D score<16

[3]Reduction: 50% reduction in depression score at follow-up (compared to baseline)

*All pairwise comparisons (10) were tested; Bonferroni correction was applied, pairwise comparisons were significant at alpha = 0.005

Table 6-sensitivity: Target population as modifier of associations between adherence and depression outcomes; Sensitivity analysis, PHQ-9: 8 to 19 (n=177)

Tools	Outcome: Remission Results	Outcome: Reduction Results
Depression workbook user (ref: non-user)		
Test of interaction with target population, p-value	**0.066**	0.566
Stratified by population, OR [95%CI]		
Cohort 1 to 2 (n=81)	3.71 [0.65; 21.30]	3.12 [0.54; 17.89]
Cohort 4 (n=96)	0.47 [0.09; 2.50]	1.66 [0.30; 9.02]
Mood monitoring user (ref: non-user)		
Test of interaction with target population, p-value	0.173	**0.092**
Stratified by population, OR [95%CI]		
Cohort 1 to 2 (n=81)	**3.52 [1.19; 10.42]**	**3.35 [1.19; 9.40]**
Cohort 4 (n=96)	0.90 [0.34; 2.39]	0.74 [0.28; 2.00]
Depression Workbook plus Mood Monitoring (ref 0-1 tool)		
Test of interaction with target population, p-value	0.130	0.193
Stratified by population, OR [95%CI]		
Cohort 1 to 2 (n=81)	**3.13 [1.11; 8.81]**	**2.89 [1.08; 7.71]**
Cohort 4 (n=96)	0.89 [0.35;2.27]	0.98 [0.37; 2.56]
One Workbook plus Mood Monitoring (ref 0-1 tool)*		
Test of interaction with target population, p-value	0.336	0.199
Stratified by population, OR [95%CI]		
Cohort 1 to 2 (n=81)	**3.13 [1.11; 8.81]**	**2.89 [1.08; 7.71]**
Cohort 4 (n=96)	1.26 [0.53; 3.01]	0.99 [0.40; 2.44]

OR [95%CI]:Odds Ratio and 95% Confidence Interval

All ORs were adjusted for cohort, education, PHQ-9 and SF-12 PCS and including the cohort as a fixed effect (for cohort 1 to 2 analyses); Significant ORs are in bold font; Significant interactions at 0.1 are in bold font

*Depression Workbook in cohorts 1-2, Anxiety Workbook in cohort 4