<<st2>>ORIGINAL ARTICLE

<<rrh>>iCBT for Depression in Older Adults With OA

<<lrh>>O'Moore et al

<<title>>Internet Cognitive Behavior Therapy for Depression in Older Adults With Knee Osteoarthritis: A Randomized Controlled Trial

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Objective. To determine the efficacy of an internet-based cognitive behavioral therapy (iCBT) program for depression in older adults with osteoarthritis (OA) of the knee and comorbid major depressive disorder (MDD).

Methods. We conducted a randomized controlled trial in 69 adults (ages ≥50 years) meeting criteria for MDD and OA of the knee with 1-week postintervention (week 11) and 3-month followup (week 24) end points. Patients were allocated to either a 10-week iCBT program for depression added to treatment as usual (TAU) or to a TAU control group. Primary outcomes were depression symptoms (9-Item Patient Health Questionnaire [PHQ-9]) and psychological distress (Kessler-10 [K-10]). Secondary outcomes included arthritis self-efficacy (Arthritis Self-Efficacy Scale [ASES]), OA pain, stiffness, physical function (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC]), and physical and mental health (Short Form 12-Item health survey physical component and mental component summaries). Depression status was assessed by blinded diagnostic interview (the Mini-International Neuropsychiatric Interview) at intake and followup.

Results. Intent-to-treat analyses indicated between-group superiority of iCBT over TAU on the primary outcomes (PHQ-9: Hedges g = 1.01, 95% confidence interval [95% CI] 0.47, 1.54; K-10: Hedges g = 0.75, 95% CI 0.23, 1.28), at postintervention and 3-month followup (PHQ-9: Hedges g = 0.90, 95% CI 0.36, 1.44; K-10: Hedges g = 0.94, 95% CI 0.41, 1.48), and on secondary OA-specific measures (ASES: Hedges g = –0.81, 95% CI –0.29, –1.33; WOMAC: Hedges g = 0.56–0.65, 95% CI 0.04, 1.18) at the 3-month followup. The majority of iCBT participants (84%) no longer met diagnostic criteria at 3-month followup.

Conclusion. Results support the efficacy of an iCBT program (requiring no face-to-face contact) for depression in individuals with comorbid depression and OA of the knee. Importantly, the benefits of the program extended beyond reduced depressive symptoms and distress to include increased self-efficacy and improved pain, stiffness, and physical function at followup.

<<hd1>>**INTRODUCTION**

Osteoarthritis (OA) is the most common form of arthritis and the leading cause of chronic disability in older adults (1,2). Approximately 1 in 5 adults with OA experience depressed mood (3–6). Due to increases in life expectancy, obesity, sedentary lifestyle, and an aging population, OA is the fastest growing major health condition worldwide (7–9). In addition, depression is predicted to account for the highest level of disability accorded to any physical or mental disorder worldwide by 2030 (10). In patients with OA, concomitant depression leads to increased use of pain medication (11), reduced adherence to treatment recommendations (12,13), reduced treatment benefits when regimens are followed (14), higher health care utilization, and increased burden regardless of age, disease duration, educational level, or body mass index (15,16). <<significance&innovations>>

SIGNIFICANCE & INNOVATIONS

- Approximately 1 in 5 adults with osteoarthritis (OA) experience depressed mood. Comorbid depression is associated with increased use of pain medication, reduced treatment benefits, higher health care utilization, and increased burden in OA patients.
- Significant barriers prevent access to evidence-based mental health care.
- This trial indicates that remotely accessible (internet-delivered) cognitive behavioral therapy is acceptable and efficacious for older patients with depression and OA.
- The benefits extend beyond reduced depressive symptoms, distress, and mental well-being to include improved arthritis-related self-efficacy, pain, stiffness, and physical function.

Despite the high prevalence of depression in OA patients, few access mental health treatment. Among older adults with both OA and depressed mood, only one-third report accessing treatment for mental illness in the previous year (4). Cognitive behavior therapy (CBT) is recommended as a first-line treatment for depressed patients with physical health conditions (17). Meta-analyses of psychological treatments for arthritis indicate the benefits of CBT in targeting depressive symptoms, pain coping, and physical disability (18,19). However, approximately 75% of depressed primary care patients report barriers that make it extremely difficult to

attend regular psychotherapy sessions (20). Internet-based CBT (iCBT) programs afford many benefits over the traditional face-to-face modality, such as high fidelity, reduced cost, greater accessibility, and convenience (21). Meta-analyses of iCBT for depression in the general population have demonstrated moderate to large effect sizes that provide evidence that iCBT is comparable to face-to-face CBT (23–25). Furthermore, specific benefits of iCBT for pain-related conditions have been reported (26,27). These factors suggest that iCBT may be particularly well-suited to older OA patients, particularly those with diminished mobility, and this form of intervention is aligned with the greater call for more accessible and flexible care pathways for arthritis (22).

Given the growing burden of OA and depression, the lack of people accessing depression treatment, and the interference of depression with OA treatment outcomes in this population, we investigated the effects of a validated iCBT program for depression (the Sadness Program [28]) in older adults with OA and comorbid depression. To our knowledge, no randomized trial has assessed the effects of an iCBT program for depression in this target population. We chose to examine the effects of this program in knee OA as it is the most frequent cause of mobility dependency and diminished quality of life (29) and can limit engagement in activities that could have mood reparative effects (i.e., behavioral activation). We hypothesized that relative to treatment as usual (TAU), the iCBT program would lead to 1) significantly greater reductions in depressive symptoms and psychological distress, and 2) improved overall mental health, self-efficacy, OA-related pain, and physical function.

<<hd1>>PATIENTS AND METHODS

<<hd3>>Study design. Based on our previous results (30), we calculated that a sample size of 25 per group would be needed to detect a between-group difference of 0.8 at posttreatment on the primary outcomes. Participants were recruited from February to October 2014 from 4 Australian health care organizations. The trial was approved by St. Vincent's Hospital Human Research Ethics Committee (Sydney, Australia), and participants provided electronic informed consent. Participants were included if they were ages ≥50 years, had a self-reported diagnosis of symptomatic knee OA based on radiographic criteria and knee pain on most days (in line with

American College of Rheumatology knee OA classification criteria [31]), met criteria for major depressive disorder (MDD) based on the clinician-administered Mini-International Neuropsychiatric Interview (MINI), were fluent in English, and had access to a computer with the internet. Participants were excluded if they met criteria for bipolar, psychotic, or substance dependence disorders, were taking antipsychotics or benzodiazepines, were not on a stable dose of antidepressant medication for at least 2 months, were currently suicidal based on both self-report and diagnostic interview, or were currently receiving CBT for depression.

<<hd3>>**Procedures.** Applicants completed online screening questionnaires via the research web site of the Clinic Research Unit for Anxiety and Depression (www.virtualclinic.org.au). Eligible participants were telephoned to determine whether they met diagnostic criteria for MDD, and if criteria were met, participants were randomly allocated to 1 of 2 groups: OA treatment as usual + iCBT for MDD (iCBT group), or the OA TAU control group who received the standard treatment they would receive for OA if they were not participating in the trial. Participants were allocated by simple randomization (1:1 allocation ratio) without any restrictions placed on the sequence (no stratification or blocking was used). Randomization was completed by an independent researcher not involved in the study, and group allocation was concealed in sequentially numbered opaque sealed envelopes. All participants were offered 1 entry into a gift-card draw following completion of the study.

<<hd3>>**Interventions.** The iCBT Sadness Program consists of 6 online lessons representing best practice CBT, as well as regular homework assignments and access to supplementary resources. The Sadness Program has been validated in a number of clinical efficacy and effectiveness trials (28,32–35). Each lesson comprises a cartoon narrative in which a character gains mastery over MDD symptoms by learning and implementing CBT skills. Patient queries throughout the program were primarily addressed by e-mail contact. If patients' Kessler-10 (K-10) and/or 9-Item Patient Health Questionnaire (PHQ-9) scores deteriorated significantly, telephone contact was made by a clinical psychologist.

<<hd3>>**Outcome measurements.** Primary outcomes included self-reported

depression severity according to the PHQ-9 (36) and general psychological distress according to the K-10 (37). Secondary outcomes included functional health and well-being measured by the physical (PCS) and mental (MCS) health component summary scores of the 12-Item Short Form health survey (SF-12) (38), self-efficacy measured by the Arthritis Self-Efficacy Scale (ASES) (39), and OA-specific pain, stiffness, and physical function according to the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (40). MDD diagnostic status was assessed according to the MINI, version 5.0 (41).

At baseline, participants reported on demographic details, medication use, and OA history. All participants completed the PHQ-9 and K-10 at baseline, week 5, week 11 (1 week following iCBT, postintervention end point), and 3-month followup (week 24). The ASES, WOMAC, and SF-12 were administered at baseline, week 11, and at 3-month followup. iCBT participants additionally provided a rating about how logical the therapy seemed (where 1 = not at all and 9 = very logical), and how useful they thought the treatment would be in reducing their symptoms of depression (where 1 = not at all and 9 = very useful). Scores on these items were summed to derive a baseline "expectancy of benefit" rating. iCBT group participants completed the K-10 prior to each lesson, and adherence to the lessons was measured. iCBT group participants were asked 1) how satisfied they were that the program taught them the skills to manage depression, and 2) their confidence level in recommending the program to a friend with similar problems (where 1 = not at all, 5 = somewhat, and 9 = very). To assess diagnostic status at 3-month followup, a clinical psychologist blinded to treatment group administered the MINI (41). Additional measures (not reported here) included the Generalized Anxiety Disorder 7, Pain Detect Questionnaire, and Pain Catastrophizing Scale.

<<hd3>>Statistical analyses. Groups were compared at baseline using *t*-tests and chi-square analyses where the data consisted of categorical data. Intent-to-treat linear mixed models (accounting for missing data) were conducted for each of the dependent variables, with time, treatment group, and the time by group interaction entered as fixed factors in the model. Planned contrasts compared changes within and between groups from baseline to posttreatment (week 11) and 3-month followup (week 24). Between-group effect sizes using the pooled SD and adjusted for sample size (Hedges *g*) were calculated to compare between groups at posttreatment and 3-

month followup. Within-group effect sizes (Cohen's *d*) were calculated between pre- and posttreatment and between pre- and 3-month followup for each group. Reliable change index values, using test–retest reliability values of 0.84 (36), were calculated for the PHQ-9 scores to determine the proportion of each group who evidenced reliable improvements (or deterioration) between baseline and followup (42). To calculate SE of measurement values, SDs were derived from the current sample (PHQ-9 pretreatment pooled SD: 4.79).

<<hd1>>RESULTS

<<hd3>>Baseline characteristics. The mean ± SD age of participants (see Table 1 for sample characteristics) was 62 ± 7.07 years (range 50–81 years), and the majority were female (n = 55, 80%). <<T1>> Participants reported moderate levels of depression on the PHQ-9 at baseline, with 40% indicating antidepressant medications use (n = 28, 59%). Participants' mean ± SD age of onset of depression was 31.24 ± 17.89 years (range 5–75 years), and the majority had a recurrent history with 57 (82.6%) reporting 3 or more previous episodes.

<<hd3>>Expectancy of benefit and baseline between-group comparisons. Scores on the "expectancy to benefit" measure in the iCBT group were positive (mean ± SD 11.57 ± 3.79 years, range 4–18 years). There were no significant differences between the groups on pretreatment PHQ-9 or K-10 scores. Chi-square analyses indicated no between-group differences in any demographic characteristics (sex, marital status, educational status, employment status, or mean age of onset of depression; $P > 0.05$), with the exception of age. Participants in the iCBT group were older (mean ± SD age 63.16 ± 7.38 years) than the TAU group (mean ± SD age 59.68 ± 6.01 years; $t(67) = 2.01$, $P = 0.049$).

<<hd3>>Adherence. Of the 44 participants in the iCBT group, 37 participants completed all 6 lessons (84% adherence). Of the 44 participants, 42 completed posttreatment and 3-month assessments. Of the 25 participants in the TAU group who were eligible for analysis, 23 provided complete posttreatment data, and 24 provided followup data (see Figure 1 for participant flow). <<F1>> There was no evidence of group or baseline severity as predictors of dropout in logistic regressions

conducted at either time point (posttreatment or 3-month followup). We also carried out Little's Missing Completely At Random (MCAR) test, which was not statistically significant, suggesting that the data were missing at random (Little's MCAR: χ^2 = 0.57, 2 df; *P* = 0.75).

<<hd3>>Primary outcome measures and effect sizes. Age was entered as a covariate in all analyses because there was a significant difference between the groups at baseline (*P* = 0.049). Results and effect sizes are reported in Table 2. <<T2>> There were significant group by time interactions for the primary outcome measures (PHQ-9: F[3,191.03] = 9.82, *P* < 0.001 and K-10: F[3,190.06] = 6.37, *P* < 0.001). Posttreatment scores were significantly lower in the iCBT group relative to TAU on the primary outcomes, with a large between-group effect size for PHQ-9 scores (Hedges *g* = 1.01, 95% confidence interval [95% CI] 0.47, 1.54) and a medium effect size for the K-10 (Hedges *g* = 0.75, 95% CI 0.23, 1.28). Between-group comparisons revealed that 3-month followup scores were significantly lower in the iCBT group relative to TAU, with large between-group effect sizes for both the PHQ-9 (Hedges *g* = 0.90, 95% CI 0.36, 1.44) and K-10 (Hedges *g* = 0.94, 95% CI 0.41, 1.48).

Within-group contrasts in the iCBT group demonstrated large effect size reductions in depression and distress from pretreatment to posttreatment, and from pretreatment to 3-month followup (Table 2). The reductions in the TAU group were small and not significant, with the exception of a moderate reduction in K-10 scores from pretreatment to followup (*d* = 0.67, 95% CI 0.09, 1.26).

<<hd3>>Secondary outcome measures and effect sizes. With the exception of SF-12 PCS scores (F[2,110.66] = 0.17, *P* > 0.05), there were significant group by time interactions for all remaining secondary outcome measures (ASES: F[2,125.18] = 4.54, *P* > 0.05; WOMAC pain: F[2,125.78] = 5.99, *P* > 0.01; WOMAC stiffness: F[2,123.66 = 6.64, *P* < 0.01; WOMAC physical function: F[2,124.50] = 5.95, *P* > 0.01; and SF-12 MCS: F[2,112.93] = 11.41, *P* > 0.001).

Posttreatment scores on the SF-12 MCS were significantly higher (reflecting better mental health) in the iCBT group relative to TAU (Hedges *g* = 0.70, 95% CI 0.20, 1.21). There were no significant differences between groups at posttreatment on the WOMAC, ASES, or SF-12 PCS scores (Table 2).

Between-group comparisons of 3-month followup scores revealed that, relative to the TAU group, the iCBT group had significantly improved scores on all of the measures except for SF-12 PCS scores, which were small and not significant (Hedges g = 0.10, 95% CI −0.40, 0.61). Large between-group effect sizes were found for ASES (Hedges g = −0.81, 95% CI −0.29, −1.33) and SF-12 MCS scores (Hedges g = 0.87, 95% CI 0.34, 1.40), and moderate between-groups effect sizes were found for the remaining variables (Hedges g = 0.56–0.65, 95% CI 0.04, 1.18) (Table 2).

Within-group contrasts demonstrated a large improvement in mental health scores in the iCBT group from pretreatment to posttreatment (SF-12 MCS: d = −1.50, 95% CI −1.98, −1.02) and moderate to large effect size improvements for all measures from pretreatment to followup (d = 0.69–1.68, 95% CI 0.25, 2.17), with the exception of physical health scores (SF-12 PCS: d < 0.05*).* See Table 2 for additional nonsignificant results in the TAU group.

<<hd3>>Diagnostic status at followup and clinical significance at 3-month followup. In the iCBT group, 33 participants (84.6%) no longer met criteria for MDD versus 11 participants (50%) at followup in the TAU group. The proportion of recovered patients in the iCBT group was significantly higher than TAU (χ^2[1,61] = 8.38, P < 0.01). Of the iCBT group, 21 (47.7%) reliably improved compared to 3 (12.0%) in the TAU group. Of the iCBT group, only 1 (2.3%) evidenced deterioration on the PHQ-9, and 2 participants in the TAU group (8.0%) evidenced reliable deterioration. Regarding patient satisfaction, the majority of participants reported feeling somewhat to very satisfied with the program (n = 40, 95%) and somewhat to very confident in recommending the program to a friend (n = 39, 93%).

<<hd1>>DISCUSSION

To our knowledge, this is the first randomized controlled trial examining the effects of an iCBT program for depression in older adults with OA of the knee. Intervention participants who received iCBT reported fewer depressive symptoms, less distress, and improved overall mental health at program completion and 3 months following the program, compared with participants receiving usual care (who received the standard treatment they would receive for OA if they were not participating in the

trial). Results for depression were comparable to effects found in noncomorbid patients (30). Importantly, intervention participants also reported improved OA-related self-efficacy, pain, stiffness, and physical function 3 months after completing the program, compared with participants receiving usual care. These results indicate not only that treatment gains were maintained, but also that benefits extended beyond mental well-being to include improved self-reported OA functional and physical status. Given that the intervention did not include routine treatment of OA, the results support previous meta-analytic findings that psychological interventions can improve physical functioning for adults with arthritis (18,19).

The high level of adherence and robust effect sizes support previous findings that iCBT for depression is effective for older adults (43); these findings are extended to support the effectiveness of iCBT for older adults with depression and OA of the knee. These findings are significant given iCBT programs can overcome barriers to receiving face-to-face psychological and/or pharmacologic treatment in this population, such as cost, lack of accessibility, and pharmacologic side effects and interaction.

A number of limitations and caveats exist in interpreting these data. First, it was not possible to mask participants to treatment arm; however, diagnostic assessments were conducted by blinded clinicians at followup. Second, the intervention was not tailored for management of OA of the knee in older adults. The relationship between depression and pain is bi-directional; depression is known to exacerbate pain, pain can lead to depression, and both have strong negative impacts on treatment response (44,45). Future studies should examine whether a program that targets both depression and OA-related pain and functioning in older adults could lead to increased satisfaction and adherence. Although attrition was minimal, the results also must be interpreted in light of missing data from baseline to followup.

The mechanism by which iCBT has a positive impact on OA outcomes is still unclear, and future studies should examine whether iCBT reduces pain-related catastrophic cognitions (46,47) or sensitivity to pain (48,49), improves a person's estimations of ability (50), improves patient-practitioner relationship (51), adherence to effective pain management (12,13), and/or treatment benefits when regimens are followed (14). The outcomes of these studies may provide insight into why there were no significant changes in global physical functioning, and no between-group differences for arthritis-related self-efficacy, pain, stiffness, and physical function,

directly following the program; yet differences emerged 3 months later. It is likely that any notable changes in OA-specific variables such as pain or self-efficacy require time to interact with cognitive change mechanisms initiated through iCBT. It is possible that reduced depressive symptoms result in flow-on effects to OA variables over time, and perhaps programs that specifically target OA management may show more immediate effects.

From a health care perspective, primary care settings provide the initial points of service for both patients with OA and patients with depression, especially as individuals who seek care from physicians for OA are significantly more depressed than persons with OA who do not seek care (52). Unfortunately, disability and depression are often underestimated, unassessed, and untreated in patients with OA (4,53). A biopsychosocial approach is consistent with the recent emphasis on the holistic assessment of a person with OA (17). This approach could include routine depression screening in assessment of older patients with OA, especially those with risk factors, including being under the care of a general practitioner (52), low education status (52), perceiving or experiencing greater pain and fatigue, being female, and experiencing stressful life events (4,14,15). Medical management of OA of the knee could be supplemented with integrated evidence-based depression treatment, including iCBT, to maximize functional status and mental health well-being.

Internet delivered CBT appears to be an acceptable and efficacious intervention for older patients with depression and OA of the knee. The benefits extend beyond reduced depressive symptoms, distress, and mental well-being to include improved arthritis-related self-efficacy, pain, stiffness, and physical function. Future research is needed to assess whether the beneficial effects can generalize to individuals with other forms of osteoarthritis.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Williams had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. O'Moore, Newby, Andrews, Hunter, Bennell, Smith, Williams.

Acquisition of data. O'Moore, Newby, Hunter, Smith, Williams.

Analysis and interpretation of data. O'Moore, Newby, Smith, Williams.

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Figure 1. Flow of participants through the trial. PHQ-9 = 9-Item Patient Health Questionnaire; MDD = major depressive disorder; f2f = face-to-face.

Figure 2. Estimated marginal means and SEs for depression severity (according to the 9-Item Patient Health Questionnaire [PHQ-9]) and generalized distress (according to the Kessler-10 scale [K10]) at pretreatment, posttreatment, and 3-months' posttreatment, for the internet cognitive behavioral therapy group (**solid line, circles**) and the treatment as usual control group (**broken line, squares**). 3mFU = 3-month followup.

Figure 3. Estimated marginal means and SEs for The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores for the internet-based cognitive behavioral therapy group (**solid line, circles**) and the treatment as usual control group (**broken line, squares**). 3mFU = 3-month followup.

Table 1. Baseline demographics and sample characteristics for the iCBT and TAU groups*

	iCBT group (n = 44)	TAU group (n = 25)
Age, mean ± SD years†	63.16 ± 7.38	59.68 ± 6.01
Sex		
Male	6 (13.6)	8 (32.0)
Female	38 (86.4)	17 (68.0)
Marital status		
Single/never married	1 (2.3)	0 (0)
Married/de facto	31 (70.4)	18 (72)
Separated/divorced/widowed	12 (27.3)	7 (28)
Educational status		
Less than high school	9 (20.5)	6 (24.0)
High school	2 (4.5)	2 (8.0)
Tertiary (diploma)	5 (11.4)	6 (24.0)
Tertiary (university degree)	10 (22.7)	6 (24.0)
Other certificate	12 (27.3)	3 (12.0)
Trade certificate	6 (13.6)	2 (8.0)
Employment status‡		
Full-time paid work	8 (18.2)	9 (36.0)
Part-time paid work	8 (18.2)	7 (28.0)
Unemployed	4 (9.1)	0 (0.0)
Student	1 (2.3)	1 (4.0)
Retired	19 (43.2)	5 (20.0)
Disability support	4 (9.1)	3 (12.0)
Current antidepressant medication use	20 (45.5)	8 (32.0)
Current medication (class)		
SSRI	6 (30.0)	5 (62.5)
SNRI	9 (45.0)	3 (37.5)
Other	5 (20.0)	0 (0.0)
Current OA medication use type		
Analgesia (acetaminophen combinations)	40 (90.9)	23 (92.0)

Nonsteroidal antiinflammatory drugs	16 (36.0)	9 (36.0)
COX-2 inhibitors	8 (18.0)	4 (16.0)
Topical antiinflammatory/liniments	22 (50.0)	14 (56.0)
Oral opioids	4 (9.0)	1 (4.0)
Oral corticosteroids	1 (2.2)	0 (0.0)
Glucosamine/chondroitin products	10 (22.7)	9 (36.0)
Age of onset, mean ± SD years†	29.23 ± 18.31	34.83 ± 16.86
Number of past depressive episodes		
0	1 (2.3)	1 (4.0)
1–2	6 (13.6)	4 (16.0)
3–5	17 (38.6)	7 (28.0)
6–9	5 (11.4)	4 (16.0)
≥10	15 (34.1)	9 (36.0)

* Values are the number (percentage) unless indicated otherwise. iCBT = internet-based cognitive behavior therapy; TAU = treatment as usual; SSRI = selective serotonin reuptake inhibitor; SNRI = selective norepinephrine reuptake inhibitor; OA = osteoarthritis; COX-2 = cyclooxygenase 2.

† Significant between-groups difference at $P < 0.05$.

‡ Highest level of education achieved.

Table 2. Estimated marginal means ± SDs for primary and secondary outcome measures, within-group effect sizes (ES), and between-group ES*

	Baseline (T1), mean ± SD	Posttreatment (T2), mean ± SD	3-month followup (T3), mean ± SD	Within, *t*(df), T1, T2	Within, ES (95% CI), T1, T2	Within, *t*(df), T1, T3	Within, ES (95% CI), T1, T3	Between, ES (95% CI), T2	Between, *F*(df), T3	Between, ES (95% CI), T3
PHQ-9 iCBT	13.95 ± 4.78	7.65 ± 4.73	6.19 ± 4.68	8.53(191.44)	1.48 (1.00, 1.95)†	10.21(192.45)	1.68 (1.19, 2.17)†	1.01 (0.47, 1.54)†	11.98 (1, 155.85)	0.90 (0.36, 1.44)‡
PHQ-9 TAU	12.75 ± 4.80	12.46 ± 4.70	10.48 ± 4.75	0.29(191.21)	0.05 (–0.51, 0.62)§	2.32(190.09)	0.52 (–0.06, 1.09)§	–	–	–
K-10 iCBT	28.17 ± 7.10	19.65 ± 7.00	18.10 ± 6.87	8.95(190.53)	1.30 (0.83, 1.76)†	10.38(191.22)	1.63 (0.09, 1.26)†	0.75 (0.23, –1.28)‡	13.13 (1, 126.71)	0.94 (0.41, 1.48)†
K-10 TAU	28.32 ± 7.10	24.96 ± 6.95	24.71 ± 7.01	2.63(190.16)	0.49 (–0.08, 1.07)§	3.61(189.33)	0.67 (0.09, 1.26)¶	–	–	–
ASES iCBT	114.66 ± 37.61	127.74 ± 37.20	146.02 ± 36.85	–2.57(125.34)	–0.35 (–0.78, 0.07)§	–5.95(126.62)	–1.00 (–1.45, –0.55)	–0.40 (–0.91, 0.11)§	10.26 (1, 115.91)	–0.81 (-0.29, –1.33)¶
ASES TAU	108.99 ± 37.65	112.77 ± 36.78	114.83 ± 37.33	–0.55(124.86)	–0.09 (–0.65, 0.48)§	–0.87(124.25)	–0.15 (–0.72, 0.41)§	–	–	–
SF-12 MCS iCBT	33.49 ± 9.75	43.67 ± 10.02	45.98 ± 11.14	–6.87(110.80)	–1.50 (–1.98, –1.02)†	–7.58(115.02)	1.07 (0.61, 1.52)	0.70 (0.20, 1.21)§	11.41 (2, 112.93)	0.87 (0.34, 1.40)¶
SF-12 MCS TAU	35.66 ± 9.80	36.53 ± 10.05	36.62 ± 10.95	–0.44(110.53)	–0.13 (–0.70, 0.44)§	–0.45(114.10)	0.06 (–0.52, 0.61)	–	–	–
SF-12 PCS iCBT	32.67 ± 8.36	32.36 ± 8.17	33.88 ± 8.99	0.24(108.48)	0.05 (–0.37, 0.48)§	–0.85(112.79)	0.11 (–0.31, 0.53)	0.03 (–0.54, 0.47)§	0.17 (2, 110.66)	0.10 (–0.40, 0.61)§
SF-12 PCS TAU	31.97 ± 8.40	32.64 ± 8.06	32.88 ± 9.21	–0.40(108.20)	–0.12 (–0.61, 0.52)§	–0.49(111.85)	0.10 (–0.47, 0.66)	–	–	–
WOMAC pain iCBT	9.93 ± 3.71	8.77 ± 3.63	7.42 ± 3.62	2.31(1, 125.94)	0.33 (–0.10, 0.76)§	4.80(127.24	0.69 (0.25, 1.12)†	0.28 (–0.22, 0.79)§	5.96 (1, 117.73)	0.63 (0.11, 1.15)¶
WOMAC pain TAU	9.35 ± 3.70	9.81 ± 3.64	9.76 ± 3.67	–0.68(125.46)	–0.12 (–0.69, 0.44)§	–0.62(124.84)	–0.07 (–0.64, 0.49)§	–	–	–

WOMAC stiffness iCBT	4.54 ± 1.72	3.74 ± 1.68	3.30 ± 1.69	3.35(1,123.76)	–0.38 (–0.05, 0.81)§	5.04(124.78)	0.84 (0.40, 1.28)†	0.35 (–0.15, 0.86)§	6.42 (1, 118.42)	0.65 (0.14, 1.18)¶
WOMAC stiffness TAU	4.24 ± 1.72	4.34 ± 1.68	4.43 ± 1.71	–0.31(123.61)	–0.04 (–0.61, 0.52)§	–0.61(122.34)	–0.12 (–0.69, 0.44)§	–	–	–
WOMAC function iCBT	32.31 ± 11.21	28.7 ± 11.08	24.07 ± 10.99	2.44(1, 124.25)	0.29 (–0.14, 0.71)§	5.39(125.45)	0.78 (0.34, 1.22)†	0.12 (–0.38, 0.63)§	4.66 (1, 112.62)	0.56 (0.04, 1.08)¶
WOMAC function TAU	30.00 ± 11.35	30.12 ± 10.98	30.34 ± 11.12	–0.06(125.38)	–0.01 (–0.58, 0.55)§	–0.17(122.68)	–0.03 (–0.60, 0.53)§	–	–	–

* Within-group ES = Hedges *g*; between-group ES = Hedges *g* with Hedges *g* pooled SD. Sample sizes for T1: n = 44 for internet-based cognitive behavior therapy (iCBT), n = 25 for treatment as usual (TAU); T2: n = 42 for iCBT, n = 23 for TAU; T3: n = 42 for iCBT, n = 24 for TAU. 95% CI = 95% confidence interval; PHQ-9 = 9-Item Patient Health Questionnaire; K-10 = Kessler 10-Item Psychological Distress Scale; ASES = Arthritis Self-Efficacy Scale; SF-12 = Short Form 12-Item health survey; MCS = mental component summary; PCS = physical component summary; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

† $P < 0.001$.

‡ $P < 0.01$.

§ Not significant.

¶ $P < 0.05$.