

Effect of Telephone-Administered vs Face-to-face Cognitive Behavioral Therapy on Adherence to Therapy and Depression Outcomes Among Primary Care Patients A Randomized Trial

David	C.	Mohr,	PhD

Joyce Ho, PhD

Jenna Duffecy, PhD Douglas Reifler, MD

Leslie Sokol, PhD

Michelle Nicole Burns, PhD

Ling Jin, MS

Juned Siddique, DrPH

EPRESSION IS COMMON, WITH the 1-year prevalence rate of major depressive disorder estimated at between 6.6% and 10.3% in the general population 1,2 and roughly 25% of all primary care visits involving patients with clinically significant levels of depression.3 Psychotherapy is effective at treating depression,⁴ and most primary care patients prefer psychotherapy to antidepressant medication.5 When referred for psychotherapy, however, only a small percentage of patients follow through.6 Attrition from psychotherapy in randomized controlled trials is often 30% or greater7 and can exceed 50% in clinical practice.8

The discrepancy between patients' preference for psychotherapy and the low rates of initiation and adherence is likely due to access barriers. Approximately 75% of depressed primary care patients report barriers that make it extremely difficult or impossible to attend regular psychotherapy sessions.^{9,10} These barriers are largely

Author Video Interview available at www.jama.com.

2278 JAMA, June 6, 2012—Vol 307, No. 21

Context Primary care is the most common site for the treatment of depression. Most depressed patients prefer psychotherapy over antidepressant medications, but access barriers are believed to prevent engagement in and completion of treatment. The telephone has been investigated as a treatment delivery medium to overcome access barriers, but little is known about its efficacy compared with face-to-face treatment delivery.

Objective To examine whether telephone-administered cognitive behavioral therapy (T-CBT) reduces attrition and is not inferior to face-to-face CBT in treating depression among primary care patients.

Design, Setting, and Participants A randomized controlled trial of 325 Chicagoarea primary care patients with major depressive disorder, recruited from November 2007 to December 2010.

Interventions Eighteen sessions of T-CBT or face-to-face CBT.

Main Outcome Measures The primary outcome was attrition (completion vs noncompletion) at posttreatment (week 18). Secondary outcomes included masked interviewer-rated depression with the Hamilton Depression Rating Scale (Ham-D) and self-reported depression with the Patient Health Questionnaire–9 (PHQ-9).

Results Significantly fewer participants discontinued T-CBT (n=34; 20.9%) compared with face-to-face CBT (n=53; 32.7%; P=.02). Patients showed significant improvement in depression across both treatments (P<.001). There were no significant treatment differences at posttreatment between T-CBT and face-to-face CBT on the Ham-D (P=.22) or the PHQ-9 (P=.89). The intention-to-treat posttreatment effect size on the Ham-D was d=0.14 (90% CI, -0.05 to 0.33), and for the PHQ-9 it was d=-0.02 (90% CI, -0.20 to 0.17). Both results were within the inferiority margin of d=0.41, indicating that T-CBT was not inferior to face-to-face CBT. Although participants remained significantly less depressed at 6-month follow-up relative to baseline (P<.001), participants receiving face-to-face CBT were significantly less depressed than those receiving T-CBT on the Ham-D (difference, 2.91; 95% CI, 1.20-4.63; P<.001) and the PHQ-9 (difference, 2.12; 95% CI, 0.68-3.56; P=.004).

Conclusions Among primary care patients with depression, providing CBT over the telephone compared with face-to-face resulted in lower attrition and close to equivalent improvement in depression at posttreatment. At 6-month follow-up, patients remained less depressed relative to baseline; however, those receiving face-to-face CBT were less depressed than those receiving T-CBT. These results indicate that T-CBT improves adherence compared with face-to-face delivery, but at the cost of some increased risk of poorer maintenance of gains after treatment cessation.

Trial Registration clinicaltrials.gov Identifier: NCT00498706

JAMA. 2012;307(21):2278-2285

www.jama.com

structural and include time constraints, lack of available and accessible services, transportation problems, and cost.

Author Affiliations are listed at the end of this article. Corresponding Author: David C. Mohr, PhD, Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, 680 N Lakeshore Dr, Ste 1400, Chicago, IL 60611 (d-mohr@northwestern.edu).

A meta-analysis of trials of telephoneadministered psychotherapy found a mean attrition rate of 7.6%, suggesting that telephone delivery may reduce attrition.⁷ Telephone care has also been incorporated into aspects of collaborative care models that integrate mental health specialists into primary care settings.11 Although telephoneadministered psychotherapy for depression has been tested as a tool to deliver care and overcome access barriers within primary care, the underlying assumptions that it is as effective as faceto-face care and that it reduces attrition have not been examined.

We describe a randomized trial comparing standard face-to-face cognitive behavioral therapy (CBT) vs a telephone-administered cognitive behavioral therapy (T-CBT) for the treatment of depression in primary care. It was hypothesized that T-CBT would produce lower levels of attrition and secondarily that it would not be inferior in efficacy to face-to-face CBT.

METHODS

Participants

Participants were recruited from November 2007 to December 2010 from general internal medicine clinics in the Northwestern Medical Faculty Foundation and Northwestern Memorial Physician's Group and from 4 primary care clinic members of Northwestern's Practice-Based Research Network in the Chicago area.

Participants were included if they met criteria for major depressive disorder, had a Hamilton Depression Rating Scale (Ham-D) score greater than or equal to 16, were aged 18 years or older, could speak and read English, and were able to participate in face-to-face or telephone therapy. Participants were excluded if they had visual or hearing impairments that would prevent participation; met diagnostic criteria for a severe psychiatric disorder (eg, bipolar disorder, psychotic disorders) or depression of organic etiology (eg, hypothyroidism) for which psychotherapy would be inappropriate; reported alcohol or substance abuse severe enough that 2 psychologists (D.C.M. and J.H.)

agreed psychotherapy would be inappropriate; met criteria for dementia by scoring less than 25 on the Telephone Interview for Cognitive Status¹²; exhibited severe suicidality, including a plan and intent or a suicide attempt in the past 5 years; were receiving or planning to receive individual psychotherapy; or had initiated antidepressant pharmacotherapy in the previous 10 days. Race and ethnicity were measured by self-report to characterize the sample.

This trial was approved by the Northwestern University institutional review board and was monitored by an independent data and safety monitoring board. In accordance with the Northwestern IRB-approved protocol, participants were sent a consent form, which was reviewed over the telephone with research staff prior to the eligibility interview. Patients signed and returned the consent form prior to randomization.

Randomization and Masking

An independent statistician used computer-generated randomization with a 1:1 ratio, stratified by antidepressant status and therapist, with block size of 4 within each stratum. To prevent allocation bias, randomization was conducted after entry criteria were confirmed. Clinical evaluators, who were masked to treatment assignment, enrolled and evaluated participants; if they became unmasked, participants were reassigned to another masked evaluator.

Treatments

Face-to-face CBT and T-CBT used the same CBT protocol,¹³ with treatment delivery medium being the only factor that varied between conditions. This treatment model has been adapted and validated for telephone administration.^{14,15} Participants received 18 45-minute sessions: 2 sessions weekly for the first 2 weeks, followed by 12 weekly sessions, with 2 final booster sessions during 4 weeks. All participants received a patient workbook that included 8 chapters covering CBT concepts, including behavioral activation, cognitive restructuring, and social support, along with 5 optional modules that covered common comorbidities and treatment content, including anxiety and worry, relaxation training, communication and assertiveness training, anger management, and insomnia.^{14,15}

T-CBT telephone calls were initiated by the therapist. Nine therapists, all PhD-level psychologists, provided both face-to-face CBT and T-CBT to eliminate therapist effects. Face-toface CBT was provided in the Preventive Medicine clinic at Northwestern University, located in the same medical center as the primary recruitment clinics. T-CBT was provided entirely over the telephone. Specific rules to ensure privacy and safety were discussed in the first session, such as being in a private place during telephone calls and not engaging in therapy while driving. Protocols were in place to ensure safety, which could include calling local emergency personnel to conduct a health and safety check in the event of severe suicidality.

All therapists received 2 days of initial training, followed by weekly supervised training from the Beck Institute Director of Education (L.S.) until the therapists reached the competence criterion defined as consistent scores of greater than or equal to 40 on the Cognitive Therapy Scale,16 at which point they began treating study participants. Once trained, therapists received weekly supervision by the Beck Education Director or a Beck-certified psychologist for at least 6 months, which could then be reduced to once every 2 to 3 weeks, as determined by the supervisor. All sessions were audiorecorded and 8% were rated on the Cognitive Therapy Scale for fidelity. Fidelity ratings were used in the supervision of the therapists.

This trial is focused on the treatment delivery medium. To prevent confounding through differences in the management of nonadherent patients across treatment arms, the therapist protocol included specific instructions for handling missed sessions and cancellations. A session was considered missed

if less than 24 hours' notice was given. If patients missed a session, they received 2 therapist telephone calls followed by a letter, after which, if still nonresponsive, the patients were determined to have discontinued treatment. Participants did not pay for treatment.

Outcome Assessment

The primary outcome was adherence to treatment, defined as attending therapy sessions. Participants were permitted to reschedule sessions if they notified their therapist 24 hours before a cancellation. The primary outcome was dichotomized as completion vs noncompletion of 18 sessions. Secondarily, we examined failure to engage in treatment (completion of ≤ 4 sessions), failure to complete (>4 sessions) but <18 sessions), and number of sessions completed.

The secondary outcome, depression severity, was measured with the interviewer-rated 17-item Ham-D¹⁷ and the self-reported Patient Health Questionnaire-9 (PHQ-9).18 Psychiatric diagnoses, including major depressive disorder, were evaluated with the Mini International Neuropsychiatric Interview.19 Remission used the Ham-D abbreviated 7-item scale criterion, whereas response was a 50% decrease in Ham-D symptoms.²⁰ To eliminate potential loss to follow-up because of access barriers, all interview assessments were conducted by telephone, and self-reports were administered online or by mail. Antidepressant use was assessed by interview. Before randomization, participants reported their treatment preference (face-to-face, telephone, or no preference). To identify any potential effects of systematic therapist expectation bias that might occur as a result of crossing therapist by treatment arm, therapists rated their expectations for patient outcome on a 7-point Likert scale after the second session.

Clinical evaluators, who had at least a bachelor's degree, received no fewer than 16 hours of training on the Mini International Neuropsychiatric Interview and Ham-D, including receiving didactic instruction, role playing, and performing ratings on a library of existing taped interviews. All study interviews were audiotaped and were supervised by a psychologist until reliable proficiency was established. Supervision continued thereafter every 1 to 2 weeks. One audiotape was randomly selected every 1 to 2 weeks for calibration ratings to ensure interrater reliability. The mean interclass correlations were 0.96. All training and supervision were performed by a licensed PhDlevel psychologist (J.H.).

Statistical Analysis

The study was designed to enroll 322 participants, resulting in 90% power for a 2-sided test at $\alpha = .05$ to detect a difference in nonadherence rates of 15% vs 30%.²¹ Although a meta-analysis found an attrition rate of 7.4% in telephone psychotherapy, 15% was used because heterogeneity was high and many trials were small.7 Attrition of 30% and greater is commonly observed in trials of face-to-face psychotherapy.⁷ Differences in baseline characteristics by treatment group, nonadherence rates, treatment preference, and posttreatment major depressive disorder were analyzed with t tests for continuous variables and χ^2 tests for categorical variables.

Although the rate of missing depression outcomes was low at each postbaseline point, ranging from 9% to 22%, we multiply imputed missing depression scores and generated 20 imputations for each missing value, using the R package MICE,²² in which incomplete variables are imputed one at a time according to a set of conditional densities.²³ Imputations were conducted separately by treatment group, and every imputation model was conditioned on a large number of relevant variables, including depression scores, demographics, and total number of CBT sessions attended. Using an imputation model that includes many auxiliary variables preserves relationships among variables and provides more precise and accurate imputations.24 In particular, by including the number of CBT sessions attended, we were able to preserve the relationship between amount

of treatment received and depression symptoms among patients with missing depression scores.

Longitudinal depression scores were modeled with repeated-measures linear regression models as implemented in the SAS procedure PROC MIXED (version 9.02). Time was treated as a categorical variable to account for nonlinear effects of time, and an unstructured covariance matrix was assumed. Differences by treatment group in major depressive disorder and remission at 3- and 6-month follow-up were assessed with logistic regression, as was treatment response. These analyses were performed on each of the 20 imputed data sets and results were combined by using the rules of Rubin.²⁵

During the trial, the data and safety monitoring board recommended changes in the planned analyses to replace the originally proposed analyses with a noninferiority analysis for depression outcomes. The noninferiority margin was not determined before the initiation of the trial, but it was determined before any analyses of outcome data and with the full knowledge and approval of oversight bodies. Noninferiority is established by showing that the true difference between 2 treatment arms is likely to be smaller than a prespecified noninferiority margin that separates clinically important from clinically negligible (acceptable) differences.^{26,27}

The clinical community has generally accepted 30% to 50% of the difference between treatment and control conditions as an acceptable definition for the noninferiority margin,^{27,28} and noninferiority trials of pharmacologic treatments have used the 50% criterion.²⁹⁻³¹ A recent meta-analysis of CBT found an overall effect size of d = 0.82.³² Accordingly, we used d=0.41 as the noninferiority criterion. A 1-sided test at $\alpha = .05$ of whether the difference in treatment groups is less than the noninferiority margin is equivalent to testing whether a 2-sided 90% CI around the treatment difference falls within the noninferiority margin. Accordingly, we calculated 90% CIs and rejected the null hypothesis of inferiority (in favor of

noninferiority) if the upper bound of the CI was less than d=0.41.

To assess variable antidepressant use across treatment arms, a repeatedmeasures analysis of the binary antidepressant use outcomes over time³³ was performed. To evaluate whether antidepressant use had differential effects by treatment group, antidepressant use and its interaction with treatment was included in our repeatedmeasures regression models for Ham-D and PHO-9.

RESULTS

The flow of patients through the study is depicted in the FIGURE. TABLE 1 summarizes the baseline demographics and psychiatric characteristics of the participants. There were no significant differences in these baseline variables across treatment arms. There was no significant difference in therapist expectations of participant outcomes across treatments (P=.83).

Attrition

Significantly fewer participants discontinued T-CBT (n=34; 20.9%)before session 18 compared with faceto-face CBT (n=53; 32.7%; P=.02). Attrition before week 5 was significantly lower in T-CBT (n=7; 4.3%) than in face-to-face CBT (n=21); 13.0%; P=.006), but there was no significant difference in attrition between sessions 5 and 18 (P=.31). T-CBT patients attended significantly more sessions (mean, 15.5; median, 17; SD, 4.4; interquartile range, 16-18) than those receiving face-to-face CBT (mean [SD], 13.7 [6.1]; median [IQR],17 [11-18]; *P*=.003).

Depression Outcomes

TABLE 2 shows the intention-to-treat depression outcomes on the Ham-D and the PHQ-9 according to multiply imputed values. In terms of changes from baseline, patients demonstrated significant improvements at posttreatment in both face-to-face (Ham-D Δ =-10.32; PHQ-9 $\Delta = -10.03$; P < .001) and T-CBT (Ham-D $\Delta = -9.25$; PHQ-9

 $\Delta = -10.12$; *P* < .001). At 6-month follow-up, changes from baseline remained significant in face-to-face CBT (Ham-D Δ =-10.69; PHQ-9 Δ =-10.46; P < .001) and T-CBT (Ham-D $\Delta = -7.78$; PHQ-9 Δ =-8.35; P<.001). There were no significant posttreatment differences between T-CBT and face-to-face CBT on the Ham-D (difference = 1.07; P=.22) or PHQ-9 (difference=-0.09; P=.89), although this difference was significant at 6-month follow-up on both the Ham-D (difference=2.91; P < .001) and PHQ-9 (difference = 2.12; P = .004).

Among T-CBT patients, 23% met criteria for major depressive disorder at

Figure. Flow of Participants Through the Trial

posttreatment compared with 25% in face-to-face CBT (P=.69). At 6-month follow-up, major depressive disorder rates were 29% and 26% in the T-CBT and face-to-face CBT groups, respectively (P=.57). At posttreatment, 27% of both T-CBT and face-to-face CBT participants met the Ham-D abbreviated 7-item scale criterion for full remission (P=.95). By 6-month followup, 19% of T-CBT vs 32% of face-toface CBT participants were fully remitted (P=.009). At posttreatment, 44% of T-CBT and 49% of face-to-face CBT participants met the response to treatment criterion of a 50% decrease on the HAM-D (P = .40).



Patient Health Questionnaire-9: MINI, Mini International Neuropsychiatric Interview.

Table 1. Baseline Demographics and Psychiatric Characteristics						
	No. (%)					
Characteristic	Face-to-face CBT (n = 162)	T-CBT (n = 163)	P Value			
Age, mean (SD), y	47.5 (13.5)	47.8 (12.6)	.87			
Female	127 (78.4)	125 (76.7)	.71			
Ethnicity ^a Hispanic or Latino	21 (13.0)	23 (14.1)	.76			
Race ^b African American	36 (24.0)	36 (24.3)				
White	98 (65.3)	89 (60.1)	.63			
>1 Race	12 (8.0)	18 (12.2)				
Other ^c	4 (2.7)	5 (3.4)				
Married/cohabitating	51 (31.7)	56 (34.4)	.61			
Education High school	14 (8.6)	20 (12.3)				
Some college	41 (25.3)	40 (24.5)	57			
Bachelor's degree	64 (39.5)	55 (33.7)	.01			
Advanced degree	43 (26.5)	48 (29.4)				
PHQ-9, mean (SD) ^d	16.4 (4.8)	17.2 (4.7)	.12			
Ham-D, mean (SD) ^e	22.8 (4.6)	22.9 (4.6)	.77			
Receiving active dose of antidepressant medication	56 (34.6)	54 (33.1)	.78			

Abbreviations: CBT, cognitive behavioral therapy; Ham-D, Hamilton Depression Rating Scale; PHQ-9, Patient Health Questionnaire–9; T-CBT, telephone cognitive behavioral therapy. ^aTwo missing values because of patients who elected not to answer. ^bTwelve missing values in the face-to-face CBT and 15 missing values in the T-CBT. ^cOther includes American Indian or Alaska Native, Asian, and Native Hawaiian or Pacific Islander.

^dThree patients in each group did not complete the PHQ-9 at baseline. The PHQ-9 scale range is 0-27 and higher scores indicate more severe depression. ^eThe Ham-D range is 0 to 52 and higher scores indicate more severe depression.

The posttreatment effect size was d=0.14 (90% CI -0.05 to 0.33) on the Ham-D and -0.02 (90% CI -0.20 to 0.17) on the PHQ-9. Both of these values were within the inferiority margin of d=0.41, indicating that T-CBT was not inferior to face-to-face CBT at the end of treatment. The 6-month follow-up effect size was d=0.37 (90% CI 0.19-0.55) on the Ham-D and 0.33 (90% CI, 0.14-0.52) on the PHQ-9. Both of these CIs were outside the inferiority margin, indicating that T-CBT was inferior to face-to-face CBT at 6-month follow-up.

Antidepressant Effects

At baseline, 52 (32%) face-to-face CBT patients and 54 (33%) T-CBT patients were receiving antidepressants. During the course of the study, antidepressant use did not change significantly (P=.41), was not different across treatment arms (P=.70), and was not associated with depression outcomes in

either the face-to-face CBT (P=.92) or T-CBT (P=.83) patients. Baseline antidepressant use was also not associated with discontinuation of treatment in either face-to-face CBT (P=.29) or T-CBT (P=.91).

Patient Preferences

Before randomization, 117 (36.6%) participants indicated they would prefer face-to-face CBT, 89 (27.8%) preferred T-CBT, 114 (35.6%) indicated no preference, and 5 did not answer (P=.60). Receiving or not receiving one's preferred treatment was not statistically associated with adherence (P=.39) or depression outcomes (P=.76)for Ham-D; P = .18 for PHQ-9).

Demographic Predictors of Clinical Outcomes and Attrition

There were no significant 2-way (demographic × treatment) or 3-way (demographic × treatment × time) effects for age, sex, race, education, or

marital status on depression. Age, sex, race, marital status, and antidepressant status at baseline were unrelated to attrition. Education was significantly related to attrition (P=.02); participants with advanced degrees were more likely to complete treatment than those with some college education (P < .05), but there were no other significant differences across education groups.

Safety

There were no adverse events (eg, suicide, suicide attempt, psychiatric hospitalization) for either treatment condition.

COMMENT

This study confirmed that T-CBT produces significantly lower attrition rates compared with face-to-face CBT among depressed primary care patients, suggesting that telephone delivery can overcome barriers to adhering to faceto-face treatment. The effect of telephone administration on adherence appears to occur during the initial engagement period. These effects may be due to the capacity of telephone delivery to overcome barriers and patient ambivalence toward treatment. Access barriers likely exert their effects early in treatment, and thus the effect of the telephone on overcoming those barriers is most prominent in the first sessions. Patients who continue in faceto-face treatment for 5 or more sessions likely have fewer access barriers or are more motivated, and thus use of the telephone likely reduces attrition less during that period.

This trial found that T-CBT was as effective in reducing depressive symptoms as traditional face-to-face CBT at posttreatment, supporting our hypothesis. However, face-to-face treatment was significantly superior to T-CBT during the 6-month follow-up period. The size of these differences in group analyses did not reach the PHQ-9 criterion of 5 or more points for clinical significance³⁵ but was close to the Ham-D criterion of 3 points.34 However, it is likely that these effects are driven by subgroups who show greater risk of failure to maintain

2282 JAMA, June 6, 2012-Vol 307, No. 21

therapeutic gains. This effect may be an artifact of T-CBT's capacity to differentially retain patients with characteristics that leave them at greater risk for posttreatment deterioration.

If the finding that face-to-face treatment produces better maintenance of gains after treatment cessation is not an artifact, it suggests that longer-term follow-up is critical in research examining the effects of tele-mental health interventions, and telemedicine more broadly. There are at least 2 possible reasons that some patients may have poorer posttreatment outcomes in T-CBT. One is that the requirement that patients in faceto-face therapy physically attend sessions may serve as a form of behavioral activation. That is, that act of physically attending treatment may be therapeutic in a manner that promotes maintenance of gains in some patients. The other possibility is that the physical presence of the therapist, although not having an effect during treatment, contributes to the maintenance of gains, which suggests that human contact may have

unique qualities that exert their effects and contribute to resilience after contact has ceased.

The patient-clinician interaction can be conceptualized as a variety of cues and information transmitted through different verbal and nonverbal channels, each of which carries some unique information. Various telemedicine media (eg, telephone, videoconference, e-mail) limit the effectiveness of specific cues,³⁶ which may have both disadvantages and benefits. For example, in the context of a positive relationship, individuals are likely to make positive attributions in the absence of cues (for example in the absence of visual cues, patients would likely imagine a provider as being more like themselves and more sympathetic than the provider actually is).37 However, if difficulties or suspicions arise, attributions regarding missing cues can become overly negative (eg, imagining the clinician to be more uncaring than a complete set of cues would suggest), which may reduce the patient's commitment to treatment. Thus, future research should not only examine overall effects of the use of treatment delivery media on patient-clinician relationships and clinical outcomes but also identify the circumstances and patients for which specific media are most advantageous.

The findings of this study suggest that telephone-delivered care has both advantages and disadvantages. The acceptability of delivering care over the telephone is growing, increasing the potential for individuals to continue with treatment. A survey of primary care patients found that nearly 19% of patients who desired behavioral and psychological care wanted telephone treatment, and an additional 44% would consider it.38 The data from this trial suggest that preferences for delivery medium do not affect adherence or outcome. The telephone offers the opportunity to extend care to populations that are difficult to reach, such as rural populations, patients with chronic illnesses and disabilities, and individu-

Fable 2. Intention-to-Treat Depression Outcomes							
	Fa	Face-to-face CBT		T-CBT			
Instrument	No. Observed	Model-Based Mean (95% Cl) ^a	No. Observed	Model-Based Mean (95% Cl) ^a	Between-Group Difference (95% CI)	<i>P</i> Value	
Ham-D ^b							
Baseline	162	22.83 (22.34 to 23.33)	163	22.83 (22.34 to 23.33)			
Week 4	149	17.86 (16.96 to 18.77)	155	18.07 (17.16 to 18.98)			
Week 9	147	16.45 (15.40 to 17.51)	154	15.62 (14.60 to 16.65)			
Week 14	143	14.18 (12.97 to 15.39)	151	14.94 (13.77 to 16.12)			
End of treatment (week 18)	141	12.51 (11.22 to 13.81)	152	13.58 (12.42 to 14.74)	1.07 (-0.63 to 2.76)	.22	
Δ Baseline to week 18		-10.32 (-11.62 to -9.02)		-9.25 (-10.42 to -8.09)			
3-mo follow-up	136	12.33 (11.01 to 13.64)	146	14.58 (13.45 to 15.71)	2.25 (0.52 to 3.99)	.01	
6-mo follow-up	133	12.14 (10.84 to 13.45)	134	15.06 (13.84 to 16.27)	2.91 (1.20 to 4.63)	<.001	
Δ Baseline to 6 mo		-10.69 (-11.99 to -9.39)		-7.78 (-8.98 to -6.57)			
PHQ-9 ^c							
Baseline	159	16.76 (16.24 to 17.29)	160	16.76 (16.24 to 17.29)			
Week 4	142	10.09 (9.21 to 10.97)	152	10.78 (9.92 to 11.64)			
Week 9	144	8.62 (7.64 to 9.59)	151	9.05 (8.13 to 9.96)			
Week 14	138	7.77 (6.73 to 8.82)	144	8.55 (7.53 to 9.56)			
End of treatment (week 18)	136	6.74 (5.74 to 7.73)	150	6.65 (5.72 to 7.58)	-0.09 (-1.35 to 1.17)	.89	
Δ Baseline to week 18		-10.03 (-11.05 to -9.00)		-10.12 (11.08 to -9.15)			
3-mo follow-up	134	6.60 (5.56 to 7.64)	144	7.59 (6.60 to 8.58)	0.99 (-0.40 to 2.38)	.16	
6-mo follow-up	126	6.30 (5.24 to 7.37)	128	8.42 (7.38 to 9.46)	2.12 (0.68 to 3.56)	.004	
Δ Baseline to 6-mo follow-up		-10.46 (-11.53 to -9.39)		-8.35 (-9.40 to -7.29)			

Abbreviations: CBT, cognitive behavioral therapy; Ham-D, Hamilton Depression Rating Scale; PHQ-9, Patient Health Questionnaire–9; T-CBT, telephone cognitive behavioral therapy. ^aThese are values based on parameter estimates from the mixed-effects models and use multiply imputed data from all time points to predict means at each point. ^bThe Ham-D range is 0 to 52. A difference of 3 points on the Hamilton scale has been identified as clinically significant.³⁴

°The PHQ-9 range is 0-27. A difference of 5 or more points on the PHQ-9 is considered a clinically meaningful response to treatment.³⁴

©2012 American Medical Association. All rights reserved.

JAMA, June 6, 2012—Vol 307, No. 21 2283

als who otherwise have barriers to treatment.^{14,39} Telephone psychotherapy would also meet at least 1 of the key attributes of the advanced medical home, namely, to "provide enhanced and convenient access to care not only through face-to-face visits but also via telephone, e-mail, and other modes of communication."⁴⁰ However, the increased risk of posttreatment deterioration in telephone-delivered treatment relative to face-to-face treatment underscores the importance of continued monitoring of depressive symptoms even after successful treatment.

Several limitations and caveats exist in interpreting these data. First, this efficacy trial used CBT for depression. Although we are unaware of reasons why these results cannot be generalized to other forms of psychotherapy and other common mental health problems such as anxiety disorders, we cannot rule out the possibility that these findings are treatment or disorder specific. Second, this sample was fairly well educated, potentially limiting generalizability to lower socioeconomic groups. Third, it was not possible to mask patients to treatment arm.

Our findings demonstrate that T-CBT can reduce attrition and is as effective as face-to-face CBT at posttreatment for depression among primary care patients. However, the increased adherence associated with T-CBT may come at the cost of some increased risk of poorer outcomes after treatment cessation.

Author Affiliations: Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois (Drs Mohr, Ho, Duffecy, Burns, and Siddique and Ms Jin); Department of Medicine Division of General Internal Medicine, Northwestern University (Dr Reifler); and Beck Institute for Cognitive Therapy, Bala Cynwyd, Pennsylvania (Dr Sokol). Dr Reifler is now with Rosalind Franklin University of Medicine and Science, North Chicago, Illinois.

Author Contributions: Dr Mohr 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 concept and design: Mohr, Duffecy, Sokol.

Acquisition of data: Mohr, Ho, Duffecy, Reifler, Burns. Analysis and interpretation of data: Mohr, Ho, Duffecy, Jin, Siddique.

Drafting of the manuscript: Mohr, Ho, Duffecy, Jin, Siddique.

Critical revision of the manuscript for important intellectual content: Mohr, Ho, Duffecy, Reifler, Sokol, Burns, Siddique.

2284 JAMA, June 6, 2012—Vol 307, No. 21

Statistical analysis: Ho, Jin, Siddique. *Obtained funding:* Mohr.

Administrative, technical, or material support: Mohr, Ho, Duffecy, Reifler, Burns.

Study supervision: Mohr, Ho, Duffecy, Reifler, Sokol. Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Funding/Support: This study was funded by research grant NIMH R01-MH059708 to Dr Mohr.

Role of the Sponsor: The funding agency had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Online-Only Content: The Author Video Interview is available at http://www.jama.com.

Additional Contributions: We thank Greg Simon, MD, Group Health Research Institute; Amber Bauer-Gambla, private practice; Kelly Glazer-Baron, PhD, Northwestern University; Sarah Kinsinger, PhD, Northwestern University; Kenneth Lehman, PhD, Northwestern University (now at Birmingham, Alabama Veterans Administration Medical Center); Katherine Schaefer-Berg, PhD, Depression and Anxiety Specialty Clinic of Chicago; Vicky Singh, PhD, Northwestern University; and Paula Young, PhD, The Family Institute at Northwestern University. All therapists were compensated by the study for treatment provided. Dr Simon was also compensated for his role as chair of the data and safety monitoring board.

REFERENCES

1. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of *DSM-III-R* psychiatric disorders in the United States: results from the National Comorbidity Survey. *Arch Gen Psychiatry*. 1994; 51(1):8-19.

 Kessler RC, Berglund P, Demler O, et al; National Comorbidity Survey Replication. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003; 289(23):3095-3105.

3. Herrman H, Patrick DL, Diehr P, et al. Longitudinal investigation of depression outcomes in primary care in six countries: the LIDO study: functional status, health service use and treatment of people with depressive symptoms. *Psychol Med*. 2002;32(5): 889-902.

4. Cuijpers P, van Straten A, Bohlmeijer E, Hollon SD, Andersson G. The effects of psychotherapy for adult depression are overestimated: a meta-analysis of study quality and effect size. *Psychol Med*. 2010;40(2): 211-223.

5. Dwight-Johnson M, Sherbourne CD, Liao D, Wells KB. Treatment preferences among depressed primary care patients. *J Gen Intern Med*. 2000;15 (8):527-534.

6. Jaycox LH, Miranda J, Meredith LS, Duan N, Benjamin B, Wells K. Impact of a primary care quality improvement intervention on use of psychotherapy for depression. *Ment Health Serv Res.* 2003;5(2):109-120.

 Mohr DC, Vella L, Hart S, Heckman T, Simon G. The effect of telephone-administered psychotherapy on symptoms of depression and attrition: a meta-analysis. *Clin Psychol (New York)*. 2008; 15(3):243-253.

8. Wierzbicki M, Pekarik G. A meta-analysis of psychotherapy dropout. *Prof Psychol Res Pr.* 1993; 24:190-195.

9. Mohr DC, Ho J, Duffecy J, et al. Perceived barriers to psychological treatments and their relationship to depression. *J Clin Psychol*. 2010;66(4):394-409.

10. Mohr DC, Hart SL, Howard I, et al. Barriers to psychotherapy among depressed and nondepressed primary care patients. Ann Behav Med. 2006;32(3): 254-258.

11. Gilbody S, Bower P, Fletcher J, Richards D, Sutton AJ. Collaborative care for depression: a cumulative meta-analysis and review of longer-term outcomes. *Arch Intern Med.* 2006;166(21):2314-2321.

12. Desmond DW, Tatemichi TK, Hanzawa L. The Telephone Interview for Cognitive Status (TICS): reliability and validity in a stroke sample. *Int J Geriatr Psychiatry*. 1994;9:803-807.

13. Beck JS. *Cognitive Therapy: Basics and Beyond.* New York, NY: Guilford Press; 1995.

14. Mohr DC, Hart SL, Julian L, et al. Telephoneadministered psychotherapy for depression. *Arch Gen Psychiatry*. 2005;62(9):1007-1014.

15. Mohr DC, Likosky W, Bertagnolli A, et al. Telephone-administered cognitive-behavioral therapy for the treatment of depressive symptoms in multiple sclerosis. *J Consult Clin Psychol*. 2000;68(2):356-361.

16. Vallis TM, Shaw BF, Dobson KS. The Cognitive Therapy Scale: psychometric properties. *J Consult Clin Psychol*. **1986**;54(3):381-385.

17. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23:56-62.

18. Kroenke K, Śpitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16(9):606-613.

19. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for *DSM-IV* and *ICD-10. J Clin Psychiatry*. 1998;59(suppl 20):22-33, quiz 34-57.

20. Frank E, Prien RF, Jarrett RB, et al. Conceptualization and rationale for consensus definitions of terms in major depressive disorder: remission, recovery, relapse, and recurrence. Arch Gen Psychiatry. 1991; 48(9):851-855.

21. Dupont WD, Plummer WD Jr. Power and sample size calculations: a review and computer program. *Control Clin Trials*. 1990;11(2):116-128.

22. R Foundation for Statistical Computing, R: A Language and Environment for Statistical Computing [computer program]. Vienna, Austria; R Foundation for Statistical Computing; 2009.

23. Van Buuren S, Groothuis-Oudshoorn K. MICE: multivariate imputation by chained equations in R. *J Stat Softw.* 2011;45:1-67.

24. Collins LM, Schafer JL, Kam CM. A comparison of inclusive and restrictive strategies in modern missing data procedures. *Psychol Methods*. 2001;6 (4):330-351.

25. Rubin DB. *Multiple Imputation for Nonresponse in Surveys.* New York, NY: Wiley; 1987.

26. D'Agostino RB Sr, Massaro JM, Sullivan LM. Noninferiority trials: design concepts and issues: the encounters of academic consultants in statistics. *Stat Med*. 2003;22(2):169-186.

27. Nutt D, Allgulander C, Lecrubier Y, Peters T, Wittchen U. Establishing non-inferiority in treatment trials in psychiatry: guidelines from an expert consensus meeting. *J Psychopharmacol*. 2008;22(4):409-416.

28. Jones B, Jarvis P, Lewis JA, Ebbutt AF. Trials to assess equivalence: the importance of rigorous methods. *BMJ*. 1996;313(7048):36-39.

29. Perahia DG, Kajdasz DK, Royer MG, Walker DJ, Raskin J. Duloxetine in the treatment of major depressive disorder: an assessment of the relationship between outcomes and episode characteristics. *Int Clin Psychopharmacol.* 2006;21(5):285-295.

30. Lee P, Shu L, Xu X, et al. Once-daily duloxetine 60 mg in the treatment of major depressive disorder: multicenter, double-blind, randomized, paroxetinecontrolled, non-inferiority trial in China, Korea, Taiwan and Brazil. *Psychiatry Clin Neurosci.* 2007; 61(3):295-307.

Downloaded From: http://jama.jamanetwork.com/ on 06/20/2012

31. Szegedi A, Kohnen R, Dienel A, Kieser M. Acute treatment of moderate to severe depression with hypericum extract WS 5570 (St John's wort): randomised controlled double blind non-inferiority trial versus paroxetine [published correction appears in *BMJ*. 2005;330(7494):759]. *BMJ*. 2005;330(7490): 503.

32. Cuijpers P, Smit F, Bohlmeijer E, Hollon SD, Andersson G. Efficacy of cognitive-behavioural therapy and other psychological treatments for adult depression: metaanalytic study of publication bias. *Br J Psychiatry*. 2010; 196(3):173-178.

Hardin JW, Hilbe JM. *Generalized Estimating Equations*. New York, NY: Chapman and Hall; 2003.
National Institute for Clinical Excellence. *Depres-*

sion: Management of Depression in Primary and Secondary Care. London, England: National Institute for Clinical Excellence; 2004.

35. MacArthur Foundation's Initiative on Depression and Primary Care. *The MacArthur Initiative on Depression and Primary Care at Dartmouth and Duke: Depression Management Toolkit.* Hanover, NH: Dartmouth; 2004.

36. Mohr DC, Cuijpers P, Lehman K. Supportive accountability: a model for providing human support to enhance adherence to eHealth interventions. *J Med Internet Res.* 2011;13(1):e30.

37. Walther JB, Parks MR. Cues filtered out, cues filtered in: computer-mediated communication and relationships. In: Knapp ML, Daly JA, eds. *Handbook*

of Interpersonal Communication. 3rd ed. Thousand Oaks, CA: Sage Publications; 2002:529-563.

Mohr DC, Siddique J, Ho J, Duffecy J, Jin L, Fokuo JK. Interest in behavioral and psychological treatments delivered face-to-face, by telephone, and by Internet. Ann Behav Med. 2010;40(1):89-98.
Himelhoch S, Mohr D, Maxfield J, et al. Feasibil-

39. Himeinocn S, Monr D, Maxielo J, et al. Feasibility of telephone-based cognitive behavioral therapy targeting major depression among urban dwelling African-American people with co-occurring HIV. *Psychol Health Med*. 2011;16(2):156-165.

40. The Advanced Medical Home: A Patient-Centered, Physician-Guided Model of Health Care. Philadelphia, PA: American College of Physicians; 2006:4.

If you would hit the mark, you must aim a little above it.

-Henry Wadsworth Longfellow (1807-1882)