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CBT Formats: Comparative Efficacy in Depression

Most formats of cognitive-behavioral therapy have similar efficacy in treating depression and may be considered alternatives on a par with individual CBT, according to the results of a network meta-analysis.[1]

Methods: Randomized clinical trials comparing acute individual, group, telephone, guided self-help, and unguided self-help CBT with another active treatment or with a control condition (i.e., wait list, care as usual, pill placebo) were identified. Only studies conducted in adult outpatients without comorbid anxiety or substance use disorders were included. Depression severity (measured with a validated instrument) and treatment acceptability (defined as the dropout rate for any reason) were the primary outcomes of interest.

Results: The analysis included 155 studies with >15,000 participants. Active treatments were individual CBT in 57 studies, group CBT in 45, guided self-help in 46, telephone CBT in 10, and unguided self-help in 21. In half of the studies participants met diagnostic criteria for depressive disorder, and in the rest they scored above a cutoff on a self-administered questionnaire. Most of the comparisons were well-examined, although there were few comparisons involving telephone CBT or pill placebo.

In a pairwise meta-analysis, individual, group, telephone, and guided self-help CBT were all more effective than wait-list (standardized mean differences* [SMD], 0.69–1.08) and care as usual (SMD, 0.52–0.83). Individual therapy was more effective than group therapy (SMD, 0.32) and pill placebo (SMD, 0.40). No other pairwise comparisons were statistically significant, possibly due to low statistical power.

In the network meta-analysis, no treatment emerged as clearly more effective than others. Differences among individual, group, guided self-help, and telephone CBT were small and generally not statistically significant. All of these treatments were significantly more effective than unguided self-help and the control conditions. Rankings for effectiveness and acceptability, ranging from 0 to 100% with higher values indicating greater likelihood that the therapy ranks among the most effective or most acceptable, are presented in the table (see next page).

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CBT delivery formats and control conditions, ranked by effectiveness		
Treatment format	**Effectiveness**	**Acceptability**
Group CBT	90.5%	51.8%
Individual CBT	77.6%	62.5%
Telephone-administered CBT	76.8%	67.7%
Guided self-help	55.8%	1.6%
Unguided self-help	30.9%	24.3%
Care as usual	19.5%	54.6%
Waiting list	0%	87.5%

Discussion: These results seem to support the wider use of alternative forms of CBT, which could make the therapy easier to deliver across different settings and populations. However, an accompanying editorial points out that while there appears to be little difference in efficacy between most formats, the quality of the evidence is limited by the small number studies involving some of the options.[2] Of note, while individual, group, and telephone CBT seem to have comparable acceptability, guided and unguided self-help, which have limited or no human interaction, are much less acceptable to patients.

Study Rating*—16 (89%): This study met most criteria for a systematic review/meta-analysis; however, the funding source was not included in the report.

[1]Cuijpers P, Noma H, Karyotaki E, Cipriani A, et al: Effectiveness and acceptability of cognitive behavioral therapy delivery formats in adults with depression: a network meta-analysis. *JAMA Psychiatry* 2019; doi 10.1001/jamapsychiatry.2019.0268. From Vrije Universiteit, the Netherlands; and other institutions. **Source of funding not stated. Three of 5 study authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.**

[2]Swartz H, Fournier J: Can network meta-analysis substitute for direct comparisons in psychotherapy trials [editorial]? *JAMA Psychiatry* 2019; doi 10.1001/jamapsychiatry.2019.0243. From the University of Pittsburgh School of Medicine, PA. **Both authors disclosed potentially relevant financial relationships.**

***See Reference Guide.**

Enhanced Contact Following Attempted Suicide

In a naturalistic observational study, enhanced contact following discharge after a suicide attempt was associated with fewer repeat attempts during the subsequent year than a single priority appointment with a psychiatrist.[1] A program of individual problem-solving psychotherapy was not significantly more effective than enhanced contact.

Methods: The study compared interventions offered by 3 Spanish community-based hospitals under a regional program that prioritizes psychiatric attention to suicide attempters. In this program, all patients receive a scheduled meeting with an outpatient psychiatrist within 7 days of their suicide attempt. This intervention, considered treatment as usual (TAU) for the study, has been shown to reduce repeat suicide attempts by 25%.[2] The present study included all suicide attempters who were discharged into each hospital's suicide prevention program over a 4-year period. In 1 hospital, the intervention was limited to the priority appointment. In another, participants received additional psychotherapy, consisting of 2 months of weekly, 30-minute individual, non-suicide-specific therapy focusing on problem-solving, stress reduction, and cognitive reformulation. The third hospital offered enhanced contact beginning with an appointment 3 days after discharge and continuing for 6–12 months. This program included outpatient visits with a psychiatrist trained in suicide prevention and 3 supportive telephone calls from the hospital, at months 1, 6, and 12. The primary study outcome was a recurrent suicide attempt, treated at the same hospital, within the year following discharge.

Results: A total of 1492 patients (mean age, 41 years; 70% female) were included in the analysis. More than half received only the priority appointment, 35% received psychotherapy, and 12% received enhanced contact. Because the 3 groups differed in several ways at study entry (e.g., those receiving psychotherapy had the lowest level of several clinical covariates suggesting decreased severity of illness), the outcome analysis was adjusted for patients' age, gender, previous suicide attempts, alcohol or drug abuse, and presence of mood and personality disorders.

During the year after discharge, 133 individuals (8.9%) made a repeat suicide attempt: 90 who received TAU (11.4%); 29 who received psychotherapy (5.5%); and 14 who received enhanced treatment (7.7%). Compared with the group receiving TAU, risk was reduced in the enhanced contact group (adjusted hazard ratio,* 0.56) and in the psychotherapy group (adjusted hazard ratio, 0.62). The number needed to treat* to prevent 1 additional suicide attempt was 5.3 for enhanced contact and 6.7 for psychotherapy.

Discussion: Risk of repeat suicide attempt is particularly high in the period following discharge. These results, which are likely to be widely generalizable to clinical settings such as general hospital emergency rooms where suicidal patients often receive care, suggest that extending follow-up with either psychotherapy or enhanced care can reduce repeated suicidal behavior.

[1]Martinez-Ales G, Angora R, Barrigon M, Roman-Mazuecos E, et al: A real-world effectiveness study comparing a priority appointment, an enhanced contact intervention, and a psychotherapeutic program following attempted suicide. *Journal of Clinical Psychiatry* 2019;80 (March/April):doi 10.4088/JCP.18m12416. From La Paz University Hospital, Madrid, Spain; and other institutions. **Funded by the University Carlos III, Madrid, Spain; and other sources. The authors declared no competing interests.**

[2]Martinez-Ales G, et al: An emergency department-initiated intervention to lower relapse after attempted suicide. *Suicide and Life-Threatening Behavior*. In Press.

***See Reference Guide.**

Tic Disorders: Practice Guideline

The American Academy of Neurology has released a new guideline for the treatment of tics in Tourette syndrome (TS) and other tic disorders. The primary aims are to help clinicians decide when to initiate treatment for tics and, if required, how to choose among evidence-based treatments and determine the best sequence or combination of these options. Practice recommendations are included for both the assessment and management of tics.

Clinicians must inform patients and their caregivers about the natural history of tic disorders and evaluate functional impairment related to the tics. In addition, they should provide information on psychoeducation for teachers and peers.

Because comorbidity with ADHD and OCD is common in TS, patients should be evaluated for these conditions. If present, the burden of symptoms should be assessed and appropriate treatment provided. Patients should also be evaluated for comorbid anxiety, mood, and disruptive behavior disorders, as well as suicidality. All comorbidities should be adequately addressed.

Patients and caregivers should be informed that watchful waiting is an acceptable approach for patients who do not experience functional impairment from their tics and that treatment rarely results in complete tic cessation. Physicians may prescribe the Comprehensive Behavioral Intervention for Tics (CBIT) as an initial treatment option for motivated patients. This can be provided via teleconference, internet, or face-to-face.

If medication is required, α-2 agonists may benefit both tics and comorbid ADHD; patients should be warned about possible sedation, and heart rate and blood pressure should be monitored. Antipsychotics may also be prescribed if the benefits are determined to outweigh

the risks. The lowest effective dose should be used, and patients should be monitored for movement disorders and hormonal and metabolic adverse effects. Electrocardiography and measurement of the QT interval should be conducted before starting treatment with pimozide or ziprasidone and if antipsychotics are coadministered with other agents that affect the QT interval. Botulinum toxin injections may be used to control bothersome, localized, simple motor tics and severly disabling vocal tics, but effects are temporary and injection can result in weakness and hypophonia. Topiramate can be prescribed if patients are informed of common adverse effects including cognitive and language problems, weight loss, somnolence, and increased risk of kidney stones.

The guideline also calls for rigorous evaluation of several medications that are in development or are currently prescribed off-label for tics, including the first-generation antipsychotic fluphenazine, the investigational selective D1 antagonist ecopipam, and the vesicular monoamine transporter type 2 (VMAT2) blockers tetrabenazine, deutetrabenazine, and valbenazine.

Where regional legislation allows, physicians may prescribe cannabis-based treatment for adults with treatment-resistant tics and for those already self-medicating with cannabis. Patients must be reminded that cannabis impairs driving ability.

Deep brain stimulation (DBS) may be an option for patients with severe tics that are resistant to behavioral therapy and medication. However, multidisciplinary evaluation, which includes the psychiatrist, a neurologist, and a neurosurgeon, should be competed to confirm that TS is the primary diagnosis and to determine if the benefits of DBS outweigh its risks. DBS should only be undertaken after behavioral therapy and multiple medication trials have failed or if they are contraindicated.

Pringsheim T, Okun M, Müller-Vahl K, Martino D, et al: Practice guideline recommendation summary: treatment of tics in people with Tourette syndrome and chronic tic disorders. *Neurology* 2019;92:896-906. doi 10.1212/WNL.0000000000007466. From the University of Calgary, Alberta, and other institutions. **Funded by the American Academy of Neurology. Eleven of 13 authors disclosed potentially relevant financial or nonfinancial relationships; the remaining 2 authors declared no competing interests.**

Common Drug Trade Names*: deutetrabenazine—*Austedo*; tetrabenazine—*Xenazine*; topiramate—*Topamax*; valbenazine—*Ingrezza*; ziprasidone—*Geodon

Medication Effects on rTMS

According to an exploratory observational study of broad categories of medication, concomitant use of stimulants or benzodiazepines, but not other psychotropic classes, influences the clinical outcome of repetitive transcranial magnetic stimulation (rTMS) for depression.

Methods: Charts were retrospectively reviewed for consecutive patients who underwent rTMS at a single center over an 8-year period. The analysis was limited to patients who had baseline medication data available, were evaluated with the 30-item Inventory of Depressive Symptomatology Self-Report (IDS-SR30), and received ≥10 rTMS sessions for nonpsychotic major depressive disorder. Concomitant medications were classified in 13 different categories. All patients were scheduled for 30 rTMS sessions, initially to the left dorsolateral prefrontal cortex. After the first 2 weeks, rTMS could be intensified or altered to bilateral or right-sided, based on clinical response and judgment. The primary outcome of the analysis was change in IDS-SR30 score from baseline to 2 weeks, when uniform rTMS protocols diverged, and at weeks 4 and 6. Response was defined as a ≥50% decrease in IDS-SR30 score.

Results: The sample included 181 individuals, 92% of whom were taking ≥1 psychotropic medication. (See table, next page.) Of patients receiving only left-sided rTMS, 47% responded by week 6, as did 19% of those who had right-side rTMS added.

At 2 weeks, 2 types of medication were associated with outcome: stimulants with larger symptom reductions than average (p=0.05) and benzodiazepines with less improvement (p=0.02). These effects remained significant in models adjusted for age, baseline anxiety, and total number of medications. In the analysis of outcomes throughout the 6-week treatment period, psychostimulant use remained significantly associated with improvement (p=0.03). The response rate at 6 weeks was lower in benzodiazepine users than nonusers (16.4% vs 35.5%; p=0.008) and higher in stimulant users than nonusers (39.2 vs 22%; p=0.02).

Drug classes used by>20% of patients undergoing rTMS for depression	
Atypical antidepressant	40.3%
Benzodiazepine	39.8%
SSRI	34.3%
Antiepileptic	32.0%
Atypical antipsychotic	30.9%
Psychostimulant	30.9%
SNRI	23.2%

Discussion: Although initial clinical trials of rTMS evaluated monotherapy, in practice it is usually added to medication. Current clinical guidelines address concomitant medications only from a safety perspective. There are plausible mechanisms to explain the effects of these medication classes on outcome. rTMS increases cortical GABA signaling, which is impaired in depression, and benzodiazepines could interfere with this effect. Stimulants may increase neuroplasticity via adrenergic pathways. The study authors note that information on comorbid diagnoses and/or in treatment resistance could not be factored into the analysis and the findings were not corrected for multiple comparisons. Thus, the results must be viewed as preliminary and require replication.

Hunter A, Minzenberg M, Cook I, Krantz D, et al: Concomitant medication use and clinical outcome of repetitive transcranial magnetic stimulation (rTMS) treatment of major depressive disorder. *Brain and Behavior* 2019; doi 10.1002/brb3.1275. From the University of California, Los Angeles. **Source of funding not stated. Four of 8 study authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.**

Privacy Concerns with Mental Health Smartphone Apps

Popular smartphone apps for depression or smoking cessation frequently transmit users' personal data to third parties, usually Google or Facebook, which use the information to target advertising. Many of the apps do not disclose sharing in their privacy policies, thereby denying users the opportunity to decide whether this sharing is acceptable.

Methods: A search of the Android and iOS marketplaces identified 36 of the most popular free depression or smoking cessation apps available in the U.S. and Australia. The group included 15 Android-only apps, 14 iOS-only apps, and 7 available on both platforms, a sample comprising about 8% of all available depression apps and 6% of smoking cessation apps. Each app's privacy policy, if one was available, was reviewed using a previously developed schema of quality criteria. The intended use of data sharing with third parties—either for advertising and marketing or for analytics, which is done to inform product improvement—was evaluated when this information was stated in the privacy policy. Each of the apps was installed on test devices and the destination of shared data from a simulated user was tracked.

Results: Of the 36 apps, nearly one-third did not have a privacy policy that was disclosed at user enrollment or available on the app website. Of those with a privacy policy, 88% described primary use of collected user data (e.g., administering accounts, contacting users, providing and improving services), and 64% described secondary uses, such as conducting investigations. About half of the apps provided users with information about how to opt out of data sharing or how to delete data. Nearly two-thirds of the apps indicated in their privacy policies that data

would be shared with advertisers and >50% stated that data would be shared with both advertisers and analytics providers. The privacy policy for only 6 apps (24%) stated that strong identifiers, such as name, email address, and date of birth, would not be shared with advertisers, and only 1 app stated that it would not share any user data with third parties.

When actual data transmission was tracked, 33 of the 36 apps (92%) were found to transmit data to a third party. Among the apps found to transmit data, 9 apps (25%) lacked a privacy policy, 5 apps (14%) had a privacy policy that failed to disclose the transmission, and 3 apps (9%) explicitly stated that transmission would not occur. A large majority of the apps (81%) transmitted data to Google or Facebook, but only about 60% disclosed this transmission in their privacy policy. A total of 9 apps (27%) sent a strong identifier to the third party—either a fixed device identifier or in 1 case a user name. Most apps sent an advertising identifier, a numerical key that can be used to track user behavior. Two apps transmitted user-reported health information, including substance use. Social logins—usernames and passwords shared between different platforms for convenience—were present for Google in 3 apps and for Facebook in 7.

Discussion: Most health care apps survive by selling subscriptions to users or selling users' personal data to third parties. These apps often describe themselves as "wellness apps" to avoid regulations that protect patient data. Although the present study did not identify transmission of information that would directly identify an individual or how the information was used, the transmission could enable advertisers to generate linkable information about mental health status. Google explicitly limits this type of use, but Facebook advertises its availability to app developers, raising the possibility of advertising targeting mental illness.

Huckvale K, Torous J, Larsen M: Assessment of the data sharing and privacy practices of smartphone apps for depression and smoking cessation. *JAMA Network Open* 2019; doi 10.1001/jamanetworkopen.2019.2542. From the University of New South Wales Sydney, Randwick, Australia; and Beth Israel Deaconess Medical Center, Boston, MA. **Source of funding not stated. The authors declared no relevant financial relationships with commercial sources.**

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Hazard Ratio: A measure of the risk of an event relative to exposure, or the probability of an event occurring in an exposed group versus a non-exposed group. A hazard ratio of 0.5 indicates that 1 group has half the risk of the other group.

Number Needed to Treat (NNT): Indicates how many patients need to be treated for 1 to benefit. The ideal NNT is 1, where everyone improves with treatment. The higher the NNT value, the less effective the treatment.

Standardized Mean Difference: The difference between two normalized means. Used for comparison of data obtained using different scales, a value of 0–0.2 is considered a negligible effect, 0.2–0.5 a small effect, 0.5–0.8 a medium effect, and >0.8 a large effect.

Study Rating: A measure of how well a study conforms to quality standards. The study rating uses a checklist system based on the comprehensive Strength of Evidence Report from the Evidence-based Practice Center Program of the Agency for Healthcare Research and Quality (AHRQ). The rating checklists are posted at www.alertpubs.com.

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