PSYCHIATRY ALERTS NOS

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Important Reminder . . . Delivery of *Psychiatry Alerts NOS* is now 100% electronic.

TMS Approved for OCD

The Brainsway Deep Transcranial Magnetic Stimulation System has received FDA approval for the treatment of obsessive-compulsive disorder not adequately responsive to medication, psychotherapy, or their combination. The Brainsway device is contraindicated in patients with metal objects or implanted stimulator devices in or near the head. These may include cochlear implants, deep brain stimulators, vagus nerve stimulators, aneurysm clips or coils, stents, and bullet fragments. During treatment with the device, patients are required to wear earplugs to reduce exposure to the loud sounds produced by the device, and jewelry and hair barrettes must be removed. Patients with a history of seizures should discuss this with their health care provider before receiving the treatment.

FDA New Release: FDA permits marketing of transcranial magnetic stimulation for treatment of obsessive compulsive disorder. Available at https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm617244.htm.

Combined Therapies for OCD

In a randomized trial, exposure and response prevention (ERP) combined with cognitive therapy (CT) was superior to a similar-intensity program of ERP alone in adult patients with obsessive-compulsive disorder.

Background: Comparative studies have shown ERP and CT to be similarly effective when used alone. However, ERP has been the most thoroughly investigated and is considered first-line treatment in international guidelines. The present study was conducted to determine whether adding elements of CT could improve the established efficacy of ERP.

Methods: Patients, recruited from a large community-based OCD clinic, met DSM-IV-TR criteria for OCD and had a score of >16 on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Both treatment groups received individual, manualized ERP in 16 hour-long weekly sessions. ERP-only therapists avoided formal cognitive restructuring techniques, while the combined ERP–CT program used the exposure task to activate specific cognitive methods and targeted obsessive beliefs. Adherence to the separate treatment protocols and treatment

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integrity were monitored by blinded raters using audiotapes of sessions. The primary study outcome was change from baseline in Y-BOCS score.

Results: A total of 127 patients were randomized, and 94 completed treatment—42 in the ERP group and 52 in the ERP–CT group. Most study discontinuations were not attributed to study treatments. In an intent-to-treat analysis,* both treatments were associated with large improvements (effect sizes,* 1.27 for ERP and 1.89 for ERP–CT). The combined treatment was significantly more effective than ERP alone (between-group effect size, 0.61; $p<0.005$). Both the obsessive and compulsive Y-BOCS subscales showed a larger improvement with ERP–CT than ERP alone (effect sizes, 0.53 and 0.63, respectively, for between-group difference; $p<0.005$ for both subscales). Among patients who completed the study, 46% of the ERP group and 65% of the ERP–CT group were classified as responders, with a ≥30% improvement in Clinical Global Impression (CGI) score ($p=0.052$). Some 23% of the ERP group and 44% of the ERP–CT group reached mild-illness status, with a ≥50% improvement on the CGI ($p<0.01$). When patients were classified by their predominant symptom subtype (i.e., contamination/washing, doubting-harming/checking, symmetry/ordering, or pure obsessions/"bad thoughts"), no subtype responded preferentially to either treatment. The 2 therapies had equivalent effects on anxiety and depression. Among the 75% of treatment completers who were followed 6 months after treatment, the between-group difference was maintained.

Rector N, Richter M, Katz D, Leybman M: Does the addition of cognitive therapy to exposure and response prevention for obsessive compulsive disorder enhance clinical efficacy? A randomized controlled trial in a community setting. *British Journal of Clinical Psychology* 2018; doi 10.1111/bjc.12188. From Sunnybrook Health Sciences Centre, Toronto, Canada; and other institutions. **Funded by the Canadian Institutes of Health Research. The authors did not include disclosure of potential conflicts of interest.**

***See Reference Guide.**

Image-Focused Therapy in Bipolar Disorder

In a preliminary study, an imagery-focused intervention reduced both anxiety symptoms and the duration of depressive episodes in patients with bipolar disorder.

Background: The study intervention—imagery-focused cognitive therapy (ImCT)—is based on the hypothesis that mental imagery might act as an "emotional amplifier", driving both mood instability and anxiety in bipolar disorder, as well as the frequent comorbidity of anxiety disorders with bipolar disorder and the role of imagery as a key cognitive mechanism for anxiety.

Methods: The present report is based on the first 11 patients to receive treatment with ImCT at the Oxford (U.K.) Mood Action Psychology Programme (OxMAPP). Patients with a diagnosis of bipolar disorder I, II, or NOS who were not currently experiencing mania were referred to the program by their psychiatrists, with whom they maintained contact for risk management and clinical care. All ImCT sessions were delivered by 2 co-therapists, to enhance a non-hierarchical, collaborative relationship with the patient. During a 4-session structured assessment, patients identified a primary imagery target that was distressing, amenable to treatment, and plausibly linked to their mood instability. The patient was then taught to use imagery rescripting, positive imagery, competing tasks, and meta-cognitive techniques. Treatment consisted of 3–8 hourly sessions as needed, followed by a flexible number of spaced follow-up sessions. Patients received a mean of about 6 treatment sessions and 5 follow-up sessions. Patients' mood was assessed weekly, online or via text message, using the Quick Inventory of Depressive Symptomatology, Self-Report (QIDS-SR) and the Altman Self-Rating Scale for Mania (ASRM). Data were available for the 6 months preceding OxMAPP enrollment (baseline) to 6 months after the end of treatment.

Results: All 11 patients enrolled in the program completed treatment and follow-up. Nine of the 11 patients had a comorbid anxiety disorder, 5 were currently experiencing depression, and

10 were receiving pharmacotherapy. One patient provided no baseline data on mood. The remaining 10 patients had a small-to-medium reduction in depressive symptoms on the QIDS-SR from baseline to follow-up (effect size,* 0.38) and no change in ASRM mania symptoms. Duration of depressive episodes was significantly reduced from a mean of 4.6 weeks in the pre-treatment period to 0.85 weeks in the 6 months post-treatment (p=0.02). The number of depressive episodes was also reduced, but the difference did not reach statistical significance. Specifically, of the 7 patients who experienced a depressive episode during the baseline period, only 2 experienced a depressive relapse during follow-up and the duration was shorter. There were no changes in the number and duration of manic episodes. Patients experienced a large reduction (effect size, 2.82) in anxiety, evaluated with the Beck Anxiety Inventory, from baseline to 1 month after treatment completion.

Hales S, Di Simplicio M, Iyadurai L, Blackwell S, et al: Imagery-focused cognitive therapy (ImCT) for mood instability and anxiety in a small sample of patients with bipolar disorder: a pilot clinical audit. *Behavioral and Cognitive Psychotherapy* 2018; doi 10.1017/S1352465818000334. From the Oxford Institute of Clinical Psychology Training, U.K.; and other institutions. **Funded by the Wellcome Trust; the National Institute for Health Research; and other sources. Eight of 9 study authors disclosed potentially relevant financial relationships; the remaining author declared no competing interests.**

***See Reference Guide.**

Peer Mentors in Serious Mental Illness

In a randomized trial, patients with serious mental illness who were assigned a peer mentor had a reduced rate of rehospitalization compared with those receiving standard care. Peer mentoring may be an effective, highly specific way to help difficult-to-engage patients.

Methods: For this study, recovery mentors (RMs) who self-identified as being in recovery from serious mental illness were hired from the community and trained to provide support to persons discharged from a psychiatric hospital. RMs were trained in recovery philosophy and promotion; local resources; personal boundary considerations/safety; and cultural competence, with a core emphasis on identifying patients' strengths and providing individualized support. RMs functioned independently of the mental health system and were encouraged to provide support based on their own experience. Study participants with a psychotic or mood disorder were discharged from an urban academic medical center, after multiple prior hospitalizations in the previous 18 months. At discharge, patients were randomly assigned to the RM program or to usual care. Participants could request an RM with a preferred demographic profile, illness, or personal history. RMs were introduced to patients within 1 week of study entry and offered services for up to 9 months after discharge, with weekly contact encouraged. Because this was an exploratory study, a number of outcomes were analyzed, with none considered primary and no correction for multiple comparisons.

Results: Of well over 4000 patients admitted to the hospital over 2 years, only 307 met the study's strict eligibility criteria. Of the 93 patients who consented to randomization, 15 withdrew from the study, and only 22 of the 48 patients assigned an RM ever met with their mentor. These 22 participants met with their RM an average of 13 times, for a mean of 25 hours in total.

Within the first discharge month, 15% of the RM group and 38% of the standard care group were readmitted. Individuals who met with their RM had a mean of 270 days to rehospitalization, compared with 135 days for the standard-care group (p=0.03). Readmission rates at 9-month follow up were 48% and 66% in the RM and standard groups, respectively. Patients who interacted with their RM also had less severe drug problems during follow-up and greater improvements in physical health, self-care, and social functioning. There were no treatment effects on other outcomes such as functional health, hope, service satisfaction, or sense of community.

Discussion: These findings suggest peer mentoring may be worthy of further study. However, these results may not be widely generalizable because of low enrollment. Furthermore, the patients who did not participate may be a unique subgroup that require a more assertive, specialized engagement effort. These results provided no information about whether the program's effectiveness was due merely to the attention of an interested person, or to spending time with a mentor with recovery experience.

O'Connell M, Sledge W, Staeheli M, Sells D, et al: Outcomes of a peer mentor intervention for persons with recurrent hospitalization. *Psychiatric Services* 2018;69 (July):760–767. From Yale University School of Medicine, New Haven, CT; and the VA Pittsburgh Healthcare System, PA. **Funded by Eli Lilly and Company; and other sources. The authors declared no competing interests.**

Predicting Conversion to Psychosis

A newly-developed model based on information obtained in an initial clinical interview has the potential to predict conversion to psychosis in clinical high-risk (CHR) individuals with nearly 75% accuracy.

Background: CHR is characterized by attenuated positive symptoms, and about one-third of CHR individuals convert to a psychotic disorder, usually within 2 years. In North America, CHR is identified mainly by the Structured Interview for Psychosis Risk-Syndromes (SIPS). The model described in the present study is based on clinical information and the SIPS questionnaire, including items suspected to be particularly informative but traditionally not scored by other research groups: violent ideation, violent behavior, and auditory and visual perceptual abnormalities.

Methods: Study participants were help-seeking individuals, aged 13–30 years, who were participating in an early detection and intervention program and met SIPS and DSM-5 criteria for CHR. All data used in developing the model were extracted from the baseline SIPS and the accompanying clinical interview. Over the next 2 years, participants were evaluated with the SIPS for conversion every 3 months or when conversion was suspected. The predictive model was developed and cross-validated within the same population.

Results: Of the 199 study participants (mean age, 20 years; 27% women), 64 (32%) converted to psychosis within the 2 years. Of 40 baseline variables evaluated, the model identified 17 factors that had predictive value for conversion to psychosis. After multiple cross-validation tests, 8 factors were most consistently associated with conversion. (See table.) Several other factors were also significant in the model: global assessment of functioning; perplexity and delusional mood; motor disturbance; suicidal ideation; history of sexual trauma; ideational richness; trouble with focus and attention; social functioning; and suicidal behavior. The risk score with the optimal combination of sensitivity and specificity* correctly identified 73% of converters and non-converters.

Model parameters predictive of conversion to psychosis

Most consistent predictors	Standardized coefficient estimate (odds ratio)*
Visual perceptual abnormalities†	-0.43 (0.65)
Dysphoric mood†	-0.29 (0.74)
Unusual thought content	0.28 (1.32)
Disorganization	0.26 (1.30)
Violent ideation	0.26 (1.30)
Race (nonwhite)	0.24 (1.27)
Social anhedonia	0.23 (1.26)
Violent behavior	0.20 (1.22)

†Negative coefficients indicate an inverse association.

Discussion: The model had a moderately strong ability to discriminate between converters and non-converters, performing comparably with or better than the commonly used North American Prodrome Longitudinal Study (NAPLS) model. The primary advantage of this proposed model is that all of the

information can be obtained in a single, 1–2-hour interview. The model will be made available online as a "risk calculator" after it has been validated in other populations.

Ciarleglio A, Brucato G, Masucci M, Altschuler R, et al: A predictive model for conversion to psychosis in clinical high-risk patients. *Psychological Medicine* 2018; doi 10.1017/S003329171800171X. From Columbia University, New York, NY; and other institutions. **Funded by the NIH; and other sources. Three of 15 study authors disclosed potentially relevant financial relationships; the remaining authors declared no competing interests.**

***See Reference Guide.**

Treating Binge Eating Disorder

According to a systematic review and meta-analysis, there is moderate support for the efficacy of cognitive behavioral therapy (CBT) and guided self-help in binge eating disorder. Evidence that is modest at best supports a few other psychological treatments or medications. There is no evidence on the long-term effects of any treatment.

Methods: A literature search identified randomized controlled trials of any psychotherapy, pharmacotherapy, or combination in patients with DSM-IV or DSM-5 binge eating disorder, regardless of age or weight status. Studies with high risk of bias were excluded from the meta-analysis. Outcomes of interest included remission, eating disorder symptoms or behaviors, weight loss, quality of life, and adverse effects.

Results: Of 99 publications that met inclusion criteria, 45 were excluded because of high risk of bias—usually because of unclear randomization procedure, non-blinded raters, or high dropout rates. The remaining 45 studies included 17 placebo-controlled medication trials, 23 studies of a psychological therapy versus wait-list or another control condition, and 5 comparisons of a drug–psychotherapy combination versus placebo. All studies were conducted in adult patients, and most patients were women with concurrent overweight or obesity.

Studies were pooled for meta-analysis if they had similar treatment and control conditions. Results were reported as the risk ratio (RR)* or the standardized mean difference (SMD)*. CBT was supported with moderate evidence: 4 studies, mostly in women with a mean body mass index (BMI) of 37 and was effective for most of the outcomes evaluated. (See table.) None of the studies reported adverse effects.

Selected outcomes of meta-analysis of treatments for binge eating disorder

Outcome	CBT vs wait list (RR or SMD)	CBT self-help vs wait list (RR or SMD)
Remission	RR, 0.40	RR, 0.25
Binge eating frequency	SMD, 0.83	SMD, 0.51
Eating disorder psychopathology	SMD, 0.50	SMD, 0.58
BMI	No difference	No difference
Depression	SMD, 0.42	SMD, 0.31

Other treatments had modest support, but only for limited outcomes. Interpersonal therapy, SSRIs, and lisdexamfetamine (*Vyvanse*) had modest effects on remission or reducing the frequency of binge eating. Lisdexamfetamine was the only treatment that reduced weight, and the effects were modest, with low-quality evidence.

None of the studies presented results separately for patients with and without obesity. The majority of studies did not report long-term follow-up. Few studies evaluated treatment effects on quality of life, an important concern in binge eating disorder.

Ghaderi A, Odeberg J, Gustafsson S, Rastam M, et al: Psychological, pharmacological, and combined treatments for binge eating disorder: a systematic review and meta-analysis. *PeerJ* 2018; doi 7717/peerj.5113. From the Karolinska Institute, Stockholm, Sweden; and other institutions. **Funded by the Swedish Agency for Health Technology Assessment, and Assessment of Social Services. The authors declared no competing interests.**

***See Reference Guide.**

Ketogenic Diet for Mood Disorders

According to a literature review, despite a lack of clinical studies, the ketogenic diet appears to be a promising intervention meriting research in mood disorders, particularly in treatment-resistant presentations. The diet has potentially metabolic, neurotrophic, neuroprotective, and antiinflammatory effects that may improve the course of mood disorders, and it is well tolerated, although adherence can be challenging.

The ketogenic diet is a high-fat, adequate-protein, low-carbohydrate diet that forces the body to use fats rather than carbohydrates as its main energy source. Fats are converted by the liver into ketones, which replace glucose as the main source of energy in the brain. The use of ketone bodies as fuel in the brain involves multiple enzymatic cascades with far-reaching effects, and ketone bodies are thought to be a more efficient source of energy than glucose. The diet also affects different monoamines including dopamine, noradrenaline, and serotonin. Effects on GABA and glutamate transmission may be important mechanisms underlying the anticonvulsant effects of this diet.

According to observational studies, the ketogenic diet has been effective in patients with epilepsy, and there have been reports of positive effects in schizophrenia and mood disorders. In animal models of depression, the ketogenic diet has had similar effects to antidepressant drugs. The potential for the ketogenic diet in treatment-resistant mood disorders rests in part on its metabolic effects. The diet reduces body weight and can help control obesity, insulin resistance, and metabolic syndrome, which are strongly correlated with treatment resistance in mood disorders. The diet also influences some of the mediators of treatment resistance: deprivation of brain-derived neurotrophic factor (BDNF), oxidative imbalances, and persistent, low-grade systemic inflammation. The diet increases BDNF in animals and has also been shown to have antioxidant and antiinflammatory effects.

Brietzke E, Mansur R, Subramaniapillai M, Martinez V, et al: Ketogenic diet as a metabolic therapy for mood disorders: evidence and developments. *Neuroscience and Behavioral Reviews* 2018; doi 10.1016/j.neubiorev.2018.07.020. From the University of Toronto, Canada; and other institutions. **Source of funding not stated. The authors did not include disclosure of potential conflicts of interest.**

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Effect Size: The effect size represents the amount of change in outcome that can be attributed to treatment, where 0.2 indicates a small effect, 0.5 a medium effect, and 0.8 a large effect. It is relatively independent of clinical significance, and large effect sizes do not ensure treatment efficacy.

Intent-to-Treat Analysis (ITT): An analysis based on initial treatment intent, not on the treatment actually administered or completed. In an ITT analysis, everyone who begins treatment is included regardless of treatment completion.

Odds Ratio: A comparison of the probability of an event in 2 groups. An odds ratio of 1 implies that the event is equally likely in both groups. An odds ratio greater than 1 indicates that the event is more likely to occur in that group than in the comparison group.

Risk Ratio: The risk of an event (or of developing a disease) relative to exposure. Relative risk is a ratio of the probability of the event occurring in the exposed group versus the control (non-exposed) group.

Sensitivity and Specificity: Statistical measures of the performance of binary classification tests. Sensitivity measures the proportion of actual positives that are correctly identified (i.e., the percentage of sick people who are correctly identified as having the condition). Specificity measures the proportion of negatives that are correctly identified (i.e., the percentage of healthy people who are correctly identified as not having the condition). A perfect predictor would have 100% sensitivity and specificity.

Standardized Mean Difference: The difference between 2 normalized means—i.e. the mean values divided by an estimate of the within-group standard deviation. The standardized mean difference is used for comparison of data obtained using different scales, a value of 0 to 0.2 is considered a negligible effect, 0.2 to 0.5 a small effect, 0.5 to 0.8 a medium effect, and >0.8 a large effect.