Options for treatment-resistant depression

Why electroconvulsive therapy may be the best alternative to medication.

Although medications and psychotherapy are usually the first treatments offered to patients with major depression, they don’t work for everyone. As we reported in August 2008, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study found that about one-third of patients were unable to achieve full relief of symptoms (remission) even after trying four different strategies.

But the STAR*D data on relapse rates suggest that treatment-resistant depression may be even more common than remission rates might indicate. Relapse was a significant problem at each treatment level. By the end of the study, 50% of the patients who were able to achieve remission after trying a fourth treatment ended up relapsing within an average of 2.5 months.

By taking both relapse and remission rates into account for the entire study, Dr. J. Craig Nelson, an expert in treatment-resistant depression at the University of California, San Francisco, estimated that only 43% of patients enrolled in STAR*D were able to sustain their recovery. Other commentators have estimated that recovery rates may be even lower.

Thus, for treatment-resistant depression, clinicians remain interested in nonpharmacological ways to change brain function. Two FDA-approved options now exist: electroconvulsive therapy (ECT) and vagus nerve stimulation (VNS). In October 2008 the FDA also approved transcranial magnetic stimulation (TMS) for patients with depression who have not benefited from one antidepressant, but not for those who haven’t responded to multiple drugs.

Insurers have balked at paying for VNS because it has not proven any more effective than ECT—and they may also refuse to pay for TMS. Therefore, ECT remains the most practical alternative because it is effective, covered by health insurance, and readily available.

ECT at a glance

Although ECT is often regarded as a treatment of last resort, it is probably the most powerful tool available to treat depression. Misconceptions and stigma about ECT may explain why it is not used more often. Here’s a brief review of current ECT practice and several remaining challenges.

Who might benefit.

ECT is an option for any patient whose depression has not been relieved after trying three or more distinct drugs; for patients at risk for suicide (ECT works faster and more reliably than drugs); for women who are pregnant or have just given birth who don’t want to take antidepressants; and for elderly patients who either don’t respond to drugs as well as they used to, or who, with age, have become more sensitive to side effects.

Although ECT has been used in children and adolescents, the technique has not been well studied in this population. The American Academy of Child and Adolescent Psychiatry has produced guidelines for ECT treatment of adolescents, recommending that it be considered after a patient does not respond to two or more medications, or when symptoms are so severe that fast treatment is necessary.

How it works.

Before each treatment, the patient receives a short-acting anesthetic to prevent awareness of the procedure and to reduce discomfort. Other drugs are given to relax the muscles. While the patient is sleeping, the psychiatrist uses a special device to deliver an electrical impulse that stimulates the brain and causes a seizure.

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There are no outward signs of this seizure, but the doctor can watch it on a monitor (similar to an electroencephalogram) that measures electrical activity of the brain.

The mechanism of ECT action is not understood, but the seizure seems to restore the brain’s ability to regulate mood. It may enhance the transmission of chemical signals or improve blood flow to the brain; animal studies suggest it may stimulate the creation of new brain cells. It is the seizure (not the electrical stimulus) that generates improvement.

**Duration.** Therapy usually consists of three ECT sessions a week, for a total of six to 12 treatments.

**Side effects.** The most bothersome side effects are memory problems and difficulty concentrating, although certain ECT techniques may help reduce risk. Other side effects—partly from the anesthetic—include headache and nausea.

**Challenges in remission and relapse**

The Consortium for Research in ECT (CORE) and the Columbia University Consortium (CUC) concluded that ECT produced remission rates of 86% and 55%, respectively—higher than those achieved with medication in the STAR*D trial. (The CUC study had stringent remission criteria.) An analysis of 18 studies also found that ECT was more effective than drug therapy—although some studies may not have used optimal drug doses. Remission usually occurs relatively quickly with ECT, in an average of one to three weeks, compared with four to 12 weeks or longer with drug treatment.

In some medical centers, however, remission rates may not be as high as those achieved in university-based research studies, where the selection criteria for participation are carefully applied. A study of seven community hospitals, for example, reported that only 30% to 47% of patients achieve remission after ECT.

A persistent challenge is relapse after successful ECT treatment. Several options help reduce this risk. First, ECT can be tapered gradually once remission is achieved, by decreasing sessions from three times a week to once or twice a week, and then to once a month, rather than stopping abruptly. Other options include maintenance ECT therapy, maintenance drug treatment, or some combination of the two.

Although maintenance ECT is usually delivered on a fixed calendar basis (such as once or twice a month), researchers are now trying to find ways to better tailor the treatment schedule to each patient’s symptoms.

**Memory and thinking problems**

ECT can cause three types of memory and thinking problems: retrograde amnesia (problems recalling events in the past), anterograde amnesia (reduced ability to retain new information), and postictal delirium (confusion following ECT). Studies have consistently found such deficits tend to be temporary, and many patients either don’t find them bothersome or find ways to cope. But others find them wrenching. Indeed, ECT-related memory problems are the main reason that patients refuse to consider ECT or decide to end treatment early. Several strategies may help reduce risk of ECT-related memory problems.

**Electrode placement.** During an ECT session, electrodes can be placed on one side of the skull (unilateral placement) or on each temple (bilateral placement). Studies have found that unilateral ECT is less likely to cause cognitive problems than bilateral ECT, yet may be just as effective. For this reason, patients usually initially undergo unilateral ECT, and then progress to bilateral ECT only if they don’t receive sufficient benefit from the unilateral treatments.

But unilateral treatments may not be appropriate for all patients. In order to work, ECT must overcome a patient’s “seizure threshold,” an individualized set point that determines what amount of electrical stimulation is necessary to induce a seizure. Unilateral ECT requires a stronger electrical stimulus to overcome a patient’s seizure threshold than bilateral.
ECT does. The ECT devices approved for use in the United States may not produce the energy levels necessary for unilateral placement of electrodes, especially in older patients, because seizure threshold increases with age.

Patients may also need to undergo more sessions of unilateral than bilateral ECT to achieve remission. In the CUC study, patients received an average of seven unilateral treatments followed by an average of three bilateral treatments—or a total of 10 treatments on average—to achieve remission. In contrast, the CORE study, which involved only bilateral treatment, found that patients required an average of seven sessions to achieve remission. For this reason, some clinicians advise starting with bilateral treatments.

**Pulse width.** Electricity is produced in waves. In ECT, the longer the pulse width (the space between peaks in the wave), the greater the chance of cognitive side effects. In the past, ECT devices used relatively long “sine wave” pulses. Today, most devices use shorter pulse widths that may also help prevent memory loss and other cognitive problems.

**Under investigation.** Researchers are investigating whether particular drugs or dietary supplements might help protect memory during ECT treatments. Researchers at Massachusetts General Hospital and McLean Hospital, for example, have conducted pilot studies with galantamine (Razadyne, Reminyl), a medication that modestly improves cognitive deficits in patients with Alzheimer’s disease. But the research is still in the early stages.

Although ECT is not a perfect treatment (and none is, after all), it remains the best alternative for patients who continue to struggle with disabling symptoms of depression even after taking several different medications. It works relatively quickly, it’s effective for most patients, and for some it may be life-saving.

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### ECT remission and relapse rates

<table>
<thead>
<tr>
<th>Study arm</th>
<th>Patients achieving remission with ECT</th>
<th>Relapse rates at 6 months, with various maintenance therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consortium for Research in ECT (CORE)</td>
<td>86%</td>
<td>Nortriptyline (Aventyl, Pamelor) and lithium 32%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ECT 37%</td>
</tr>
<tr>
<td>Columbia University Consortium (CUC)</td>
<td>55%</td>
<td>Placebo 84%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nortriptyline 60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nortriptyline and lithium 39%</td>
</tr>
</tbody>
</table>


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### Remission, relapse, and recovery

STAR*D investigators collected data about both remission rates (those listed below are based upon self-report after 14 weeks of treatment) and relapses that occurred at some point during follow-up. If patients did not adequately respond at one level, they progressed to the next.

<table>
<thead>
<tr>
<th>Study arm</th>
<th>Treatment options</th>
<th>Achieved remission</th>
<th>Relapsed after remission</th>
<th>Average time to relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1 (initial treatment)</td>
<td>Citalopram (Celexa)</td>
<td>37%</td>
<td>34%</td>
<td>4.4 months</td>
</tr>
<tr>
<td>Level 2: Patients could choose to switch or augment, but were then randomized to a new option</td>
<td>Switch to bupropion (Wellbutrin), sertraline (Zoloft), venlafaxine (Effexor), or cognitive therapy</td>
<td>Augment citalopram with bupropion, buspirone (BuSpar), or cognitive therapy</td>
<td>31%</td>
<td>47%</td>
</tr>
<tr>
<td>Level 3: Patients could choose to switch or augment, but were then randomized to a new option</td>
<td>Stop current therapy and switch to mirtazapine (Remeron) or nortriptyline (Pamelor)</td>
<td>Augment current therapy with lithium or T3 thyroid hormone (Cytomel)</td>
<td>14%</td>
<td>43%</td>
</tr>
<tr>
<td>Level 4: Patients were randomized to one of the two treatments</td>
<td>Stop current therapy and receive tranylcypromine (Parnate) or mirtazapine plus venlafaxine</td>
<td></td>
<td>13%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Benefiting from mental health parity

Determining coverage, understanding the limits, appealing decisions.

Two significant changes in health insurance coverage of mental health and substance abuse disorders, enacted into law in 2008, will begin taking effect in 2010. The laws are part of a nationwide push for mental health parity, which aims to provide coverage for psychiatric disorders on a par with other medical disorders. Until recently, it was perfectly legal for many insurers to limit care for mental health and substance abuse services and require patients to pay more out-of-pocket costs for such services than they would pay for care for diabetes, heart disease, or other medical conditions.


An ongoing challenge for patients and clinicians, however, is to navigate the patchwork of parity provisions at the state and national levels. Further complicating matters is the larger health care environment. Although the Congressional Budget Office estimates that adding mental health parity will increase health insurance premiums by less than 0.4% a year, health care costs overall have been increasing dramatically. The Kaiser Family Foundation reported that average employer-sponsored premiums for family coverage increased 119% between 1999 and 2008.

It is therefore likely that employers and health insurers will continue to take steps to contain health insurance costs in the years ahead. Thus while parity may exist in the law, managed care constraints may limit the mental health care benefits patients can receive and services providers can offer.

**The Wellstone-Domenici Act**
The Wellstone-Domenici Act applies to any organization with 50 or more employees that offers group health insurance with mental health or substance abuse coverage. The law applies to self-funded plans, which is significant, because more than half of employer-sponsored plans are self-funded and therefore have not been subject to state mental health parity laws. The Wellstone-Domenici Act also goes well beyond the scope of an earlier 1996 federal parity law, which prohibited annual or lifetime financial limits on mental health coverage, but allowed other restrictions to continue, such as limits on outpatient visits or inpatient days.

*Conditions covered.* The Wellstone-Domenici Act allows health insurers to determine which mental health and substance abuse disorders they will or won’t cover—as all do now for medical conditions. In practical terms, insurers tend to limit coverage to treatments and services deemed “medically necessary.”

*Medical necessity.* Medically necessary care can be defined as generally accepted treatments that meet usual community standards of care. The definition generally excludes anything deemed experimental or not yet proven.

In practice, insurers have established their own definitions for medical necessity but have not made those definitions public. The Wellstone-Domenici Act now requires that an insurer provide, upon request, its criteria for determining medical necessity. When appealing a decision, the person making the claim needs to argue that a particular service was necessary, using the same criteria.

**Excluded services.** Health plans rarely list what services they cover. Sometimes the fastest way for patients to understand what mental health or substance abuse services are not covered is to look at the list of excluded conditions, which is usually contained in the back of a policy or in an appendix.

**Managed care controls.** Most group health plans now incorporate some form of managed care. Only 3% of employer-sponsored plans offer “conventional” fee-for-service coverage (which hardly makes it conventional any more). Well-known methods for managing both care and cost include requirements that patients receive prior authorizations for certain services, receive care only for certain periods of time (designated by utilization reviews), and receive care only from those clinicians who are part of “preferred provider networks” or other pre-approved lists.

**Carve-outs.** In addition, many managed care companies choose to “carve out” or subcontract the management of mental health and substance abuse coverage to an independent behavioral health care company. Insurers say the goal is to provide specialty services or negotiate discounts, but in practical terms it may mean that patients may have to deal with two sets of administrators—one for mental health and substance abuse services, and another for other medical services.

**Impact on state law.** Most states now have their own parity bills—some of which are more restrictive than the Wellstone-Domenici Act and some more expansive. Although the way that federal and state laws interact in health insurance is complex—and is still being determined by court cases—in general, the weaker state laws will remain intact. For instance, the state mental health parity law enacted in Vermont, considered one of
the most comprehensive in the country, will trump the new federal law.

Potential advantages and limitations
Dr. Richard G. Frank, a professor of health economics at Harvard Medical School, thinks the most important accomplishment of the 2008 Wellstone-Domenici Act is that it offers new financial protections to the most severely ill patients, who need intensive mental health treatment and inpatient care. Until now, for example, adults with bipolar disorder or schizophrenia might incur $15,000 to $20,000 in medical bills a year for inpatient stays and other intensive treatment—much of which has not been covered by insurance. With the new law, most of those costs will be covered.

The new law also eliminates arbitrary limits on outpatient visits, which will translate into fewer out-of-pocket expenses for patients who see therapists or addiction counselors on a continuing basis.

But Dr. Frank points out that the Wellstone-Domenici Act does not cover the types of services that many patients with the most severe mental illnesses need to support their recovery—but aren’t typically included in health insurance policies. These include services such as psychosocial rehabilitation and supportive employment services.

Many of the fears about mental health parity laws—namely, that they would dramatically increase costs for employers and drive up premiums for patients, or result in claims for frivolous services—have not been realized, even with broad parity laws. A dramatic example is the Federal Employees Health Benefits Program (FEHB), which started requiring parity for mental health coverage in 2001, following a directive by President Bill Clinton. An analysis of FEHB claims data found that most reimbursed services were for the treatment of anxiety, attention deficit hyperactivity disorder, depression, bipolar disorder, and schizophrenia.

Medicare mental health parity
Although it received less media attention than the Wellstone-Domenici Act, a law authorizing mental health parity for Medicare beneficiaries will be phased in over several years. Medicare enrolls patients who are 65 and older, as well as younger people who are permanently disabled.

Currently Medicare recipients must pay half of the cost for outpatient psychotherapy and other mental health services. Starting in 2010, the copay will be reduced gradually until it reaches 20% in 2014—equivalent to the current Medicare copay for other outpatient health services. The new law also provides expanded coverage for prescription antidepressants, antipsychotics, and anticonvulsants.

Be prepared; find help
Insurance counselors recommend that purchasers of insurance do the following on an annual basis.

Read the policy. Plans are renewed each year, and provisions may change. Take the time to know which services are covered, and which excluded.

Understand the rules. Identify which services require pre-authorizations or referrals, and which providers are included in a particular network. These rules are a major source of confusion.

Learn how to appeal. Every plan provides information on how to appeal decisions, whether for administrative reasons (such as whether a proper authorization was obtained) or for medical reasons (whether a service meets the criteria for medical necessity). Knowing this information in advance may make the appeals process easier.


For more references, please see www.health.harvard.edu/mentalextra.

The Paul Wellstone and Pete Domenici Mental Health Parity and Addiction Equity Act of 2008

<table>
<thead>
<tr>
<th>Provisions</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective date</td>
<td>On or after Jan. 1, 2010, depending on plan renewal date.</td>
</tr>
<tr>
<td>Plans affected</td>
<td>Large private group health insurance plans that offer mental health or substance abuse coverage in addition to medical and surgical coverage.</td>
</tr>
<tr>
<td>Scope of coverage</td>
<td>“Financial requirements” such as deductibles, copayments, coinsurance, out-of-pocket expenses, and annual and lifetime limits.</td>
</tr>
<tr>
<td></td>
<td>“Treatment limitations” such as limits on frequency of treatment, number of visits, days of coverage, and duration of treatment.</td>
</tr>
<tr>
<td>Conditions covered</td>
<td>Health insurers may determine which mental health and substance abuse conditions they will cover.</td>
</tr>
<tr>
<td>Denials</td>
<td>If a health insurer denies a claim, it must provide its criteria for “medical necessity” and explain why the service was not covered.</td>
</tr>
<tr>
<td>Out-of-network providers</td>
<td>If a health plan offers out-of-network coverage for medical and surgical services, it must also provide equivalent out-of-network coverage for mental health and substance abuse services.</td>
</tr>
<tr>
<td>Cost exemptions</td>
<td>A group health plan can qualify for exemption from the law if it finds that providing mental health and substance abuse coverage increases its costs by 2% or more in the first year, or 1% or more in subsequent years.</td>
</tr>
</tbody>
</table>

Alcohol abstinence vs. moderation
Degree of dependence predicts which strategy works best.

A debate that started in the 1960s remains an important one in the addiction field: is it possible to control problem drinking, or must the drinker give up alcohol completely?

Clinicians often find that patients who enter alcohol treatment for the first time say they would like to find ways to cut back on their drinking rather than abstaining. And many people who have not yet developed symptoms of alcohol dependence, as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), such as high tolerance or withdrawal symptoms, are nevertheless in danger of crossing the line into dependence.

Yet it may be difficult to encourage people at any stage of a drinking problem to seek help, owing to a combination of denial, stigma, and other barriers to care. Offering counseling on moderation may help convince some problem drinkers to seek help before they suffer painful consequences.

Dr. Thomas W. Irwin, program director of the McLean Center at Fernside, a residential drug and alcohol program affiliated with McLean Hospital, recently described a standard clinical approach for working with patients to determine whether moderation or abstinence makes the most sense when trying to address an alcohol problem.

Severity predicts relapse
Research into moderate or “controlled” drinking has shown that this strategy can be successful for patients who have not yet developed a pervasive pattern of alcohol abuse, or who have experienced few negative consequences from drinking. It also helps to be young, female, employed, in a stable social situation, and confident about moderating intake. The goal is to help patients set goals and drinking limits before they cross the line into dependence.

But the research shows clearly that moderation is unlikely to be successful for patients who already meet criteria for dependence, whether defined by the DSM-IV or by a variety of assessment tools.

One study, for example, followed the outcomes of drinkers for three to eight years after they participated in behavioral self-control training, a therapy designed to instill moderate drinking behavior. The researchers found that as severity of dependence increases, likelihood of patients’ being able to reduce their drinking to moderate levels, and keep it there, goes down dramatically (see table). For the most dependent drinkers, abstinence may be the only option.

Moderation as motivation
Moderation can be used, however, to motivate patients to change.

Many patients are ambivalent about giving up alcohol, even though they recognize that dependence is straining their marriages or jeopardizing their jobs. The sad reality is that alcohol has become so integral to their existence that they can’t imagine what life would be like without it. A patient who expresses a desire to start drinking in a more controlled way is indicating a desire to change a behavior. Motivational interviewing can help patients progress toward change. With this technique, clients set the agenda, and the therapist acts as a partner in dialogue rather than an authority (see Harvard Mental Health Letter, January 2006).

Demanding abstinence too soon may just end up driving away a patient who is at the brink of dealing with addiction more directly. When a patient expresses a desire to moderate drinking, it can alert the clinician to a teachable moment. Patients who try to limit drinking for a while and find they are unable to do so may then realize that they have already developed dependence. This may be enough to motivate them to try to abstain.


For more references, please see www.health.harvard.edu/mentalextra.
In brief

MRI scans reveal altered brain response to criticism in patients with social phobia

Generalized social phobia is the most common type of anxiety disorder. Patients with this disorder avoid social situations and are at higher risk for depression, alcohol abuse, and drug abuse. Many imaging studies have suggested that the disorder may involve abnormal activation of certain parts of the brain in response to other people’s facial expressions.

A study published in October 2008 extended these findings by examining the brain’s response to criticisms. The study enrolled 17 patients with generalized social phobia and 17 healthy controls.

When patients with generalized social phobia read negative statements about themselves, functional MRI scans revealed increased blood flow to the prefrontal cortex and amygdala—an indicator of increased activity in areas of the brain responsible for emotion. Healthy controls did not show similar patterns of activation while reading negative comments about themselves. There were no significant differences in brain activity between the two groups while reading negative comments about someone else, or while reading positive comments.

The leading psychological theories implicate several aberrant mental processes in patients with social phobia, including the tendency to ruminate about what went wrong at past social events or how they failed to perform at particular tasks. The study, while small, helps researchers better understand what is going on in the brains of patients with social phobia when they view themselves so negatively.


Screening patients with heart disease for depression

In September 2008, the American Heart Association (AHA) recommended that clinicians routinely screen patients with heart disease for depression. Among other reasons, the experts noted that in a large recent survey, about 9% of patients with coronary artery disease suffered from major depression in a 12-month period, compared with about 5% of people who do not have a chronic medical illness. The American Psychiatric Association has endorsed the recommendations.

The AHA recommends that clinicians ask two questions when they see patients with heart disease:

- In the past two weeks, have you felt little interest or pleasure in doing things?
- In the past two weeks, have you felt down, depressed, or hopeless?

If a patient with heart disease answers “yes” to either question, then the AHA recommends further evaluation or a referral to a mental health professional.

As we reported in January 2008, the link between heart disease and mood works both ways. Depression can exacerbate heart disease, and heart problems can make depression worse. So it makes sense to attend to mind as well as heart.


Post-discharge counseling helps hospitalized smokers quit

A review of hospital-based stop-smoking programs in nine countries concluded that only the programs that continued after inpatient treatment ended enable patients to remain smoke-free.

Dr. Nancy Rigotti, director of the Tobacco Research and Treatment Center at Massachusetts General Hospital, collaborated with two colleagues to analyze 33 clinical trials of interventions conducted between 1999 and 2007. Programs were divided into four categories, ranging from a single brief contact in the hospital to a program involving counseling that extended beyond the inpatient stay.

The researchers found that only the programs that involved stop-smoking counseling during an inpatient stay, followed by one month or more of counseling and support after discharge, increased the chances of smokers being able to quit. These long-lasting programs increased the chances of smoking cessation by 65%. The three less-intensive categories of intervention had no impact on quit rates. There was some evidence that nicotine replacement therapy might help further boost quit rates, but this was hard to determine since it was typically offered in conjunction with counseling.


WEBextra For more information about electroconvulsive therapy and mental health parity, or to view a video about seasonal affective disorder, visit www.health.harvard.edu/mentalextra.
Parents who are trying to choose the right treatment for a child diagnosed with an anxiety disorder are apprehensive (with justification) about the effects of psychotropic medication on the developing brain. Yet when they seek psychotherapy for their children, they often learn that a good therapist is hard to find and that the costs in time and money can be difficult for families to bear.

An article published in the Oct. 30, 2008, issue of *The New England Journal of Medicine* should help clarify the relative value of various treatment options for anxiety disorders in children, especially separation anxiety, generalized anxiety disorder, and social phobia. The authors reported on a 12-week, randomized, controlled trial comparing cognitive behavioral therapy (CBT), the antidepressant sertraline (Zoloft), the combination of the two, and a placebo drug. Almost 500 children with these disorders, ranging in age from 7 to 17, participated in the research. More than 80% of children receiving combined therapy experienced significant improvement, compared with 60% of children receiving only CBT and 55% of those receiving only sertraline. The difference between CBT and sertraline response was not statistically significant, but both solo treatments were more than twice as effective as the placebo.

This study, funded by the National Institute of Mental Health and conducted at several sites around the United States, was well crafted. Subjects were ethnically and racially diverse. Psychotherapy was administered by experienced therapists employing a standardized treatment under careful supervision. The children receiving sertraline were evaluated in eight sessions of 30 to 60 minutes each. This design enabled investigators to compare the efficacy of one treatment against the other and against placebo. Researchers also could measure how well sertraline was tolerated compared to placebo, and assess what risks the sertraline group bore compared with groups not receiving medication.

Children receiving the antidepressant did describe a higher number of mild adverse effects, such as sedation, sleeplessness, and fidgeting, when compared with non-medicated children. Reassuringly, given highly publicized concerns about suicide risk, no child attempted suicide. And children taking sertraline did not report suicidal or homicidal ideas more frequently than did children taking placebo.

This study is encouraging because it provides solid evidence that anxiety treatments work. It underscores the efficacy of CBT. Apprehensions about medication side effects make CBT a good first option for many children. And for those children who do receive antidepressant treatment, the study provides more reassurance that, with careful monitoring, the medication option is relatively safe. The big jump in efficacy seen with combined treatment is a boon for the almost half of children who do not get relief from either treatment alone.

The authors hint that the same great results may be hard to achieve in the real world. Despite efforts to recruit socioeconomically disadvantaged children into the study, that population of youngsters was underrepresented. Even children who are less disadvantaged commonly do not have access to the kind of care provided in the study. Also, the mechanisms behind treatment efficacy are not known. Subjects may have seen a better outcome because of a combination of two distinct therapeutic mechanisms (simply put, the talk therapy plus the medication). Or they may have felt better because they got to spend more overall time with clinicians.

Either way, the study celebrates the value of high-quality treatment for anxiety in children. It provides reassurance to those who worry about adverse effects. And—for those who design health policy—it offers encouragement to improve access to high-quality care for those children who need it.

Michael Craig Miller, M.D.
Editor in Chief