Controversies about Antidepressants and the Promotion of Evidence-Based Treatment Alternatives for Depression

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Emerging data suggest that antidepressant medications may not be as efficacious as once hoped and also may be associated with an increased risk of suicidal behavior in some patients. The media have begun to widely publicize these controversial findings, but often have failed to provide proper context and balance in the coverage. Public fears inadvertently provoked by scientific debates about antidepressants may lead more people to explore alternative treatments for depression that do not possess adequate evidence of effectiveness or safety. In this paper, we review the evidence behind antidepressant efficacy and safety concerns, analyze media coverage of these issues, and discuss the need for additional research on and dissemination of evidence-based treatment alternatives for depression.

The selective serotonin reuptake inhibitors (SSRIs) are a class of antidepressant medications that emerged onto the psychiatric scene in the 1990s. Their arrival was heralded as a modern drug miracle due to their putative efficacy and safety relative to earlier medications. Initial unbridled enthusiasm and aggressive industry marketing have made SSRIs among the most widely prescribed medications today, psychiatric or otherwise (IMS, 2003). In fact, antidepressant prescribing in relation to a diagnosis of depression increased 147.5% in the United States from 1990 to 1998, an effect driven mainly by the SSRIs (Skaer, Sclar, Robison, & Galin, 2000). Over the past several years, the media increasingly have highlighted controversial data suggesting that SSRIs are not as efficacious as once hoped (Gaudiano & Herbert, 2003) and that they may carry their own potentially lethal side effects (Sharp & Chapman, 2004). Additionally, there has been a dramatic rise in public interest in and use of unconventional medical practices for depression since the 1990s (Bongiorno, 2005; Eisenberg et al., 1998). The current heightened media coverage about the dangers of SSRIs is potentially confusing to the public and leaves them vulnerable to nontraditional medicine and mental health practitioners who promote scientifically questionable and potentially harmful treatments. It is unfortunate that evidence-based treatment alternatives for depression, such as effective psychotherapies, frequently have been given short shrift in the debate. In this article, we review the research behind the antidepressant efficacy and safety concerns, analyze the media's coverage of these controversies, and discuss the implications for evidence-based treatment alternatives for depression.

Controversies Surrounding Antidepressant Efficacy

Increasing evidence suggests that the placebo response in clinical trials of antidepressant medications is substantial and has been growing over the past 2 decades (Walsh, Seidman, Sysko, & Gould, 2002). Such data have led to much debate within the psychiatric community regarding the development and implementation of improved methodologies to ascertain the specific efficacy of antidepressants (Gaudiano & Herbert, 2005; Klein et al., 2002; Moncrieff, 2001). In order to examine

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the complex issues involved in evaluating antidepressant effects, however, the placebo concept itself first must be clearly understood.

The Placebo and Its Effects

The term *placebo* comes from the Latin phrase meaning "I shall please" (Shapiro & Shapiro, 1997). Its use in medicine began in the 19th century, when placebo referred to practices offered merely to placate patients and not cure them. By the mid-20th century, the double-blind, randomized, controlled trial became the gold standard for evaluating the efficacy of investigational drugs. In this context, placebo became used to refer to the inert substances used to separate the active biochemical effects of medications from those produced by expectancy and other extraneous factors (Leber, 2000). Although various definitions of medical placebos have been offered over the years, Shapiro and Shapiro (1997) provide a useful description:

> A placebo is any therapy (or that component of any therapy) that is intentionally or knowingly used for its nonspecific, psychological, or psychophysiological, therapeutic effect, or that is used for a presumed specific therapeutic effect on a patient, symptom, or illness but is without specific activity for the condition being treated. (p. 41)

In other words, a placebo can refer to an intentionally or unintentionally inert treatment provided by a practitioner. A placebo treatment is differentiated from the *placebo effect*, which refers to the "nonspecific psychological or psychophysiological therapeutic effect produced by a placebo" (p. 41). Although the placebo effect can be conceptualized more broadly or narrowly, general factors thought to be related to improvement after administration of a placebo include patients' and physicians' expectancies for improvement, and the general benefits proffered by a supportive relationship and therapeutic setting (Frank & Frank, 1993; Shapiro & Shapiro, 1997).

In his classic paper "The Powerful Placebo," Beecher (1955) estimated that placebos benefit approximately 30 to 40% of patients. Although the subject of some recent debate (Hróbjartsson & Gøtzsche, 2001), a convergence of evidence suggests the benefits of placebo treatments for a wide range of medical conditions, including asthma, pain, postoperative wound recovery, headache, nausea, and even surgical procedures such as arthroscopic knee surgery (Benedetti, Maggi, & Lopiano, 2003; Kirsch & Scoboria, 2001; Moseley et al., 2002; Wampold, Minami, Tierney, Baskin, & Bhati, 2005). Furthermore, placebo response rates vary as a function of the expectancy produced by the treatment, with known brand names, administration via injection, larger pill sizes, and higher "doses" producing increased effects (for a review, see Kirsch, 2005).

Antidepressants versus Inert Pill Placebos

In recent years, perhaps nowhere has the placebo response attracted more scrutiny than in antidepressant trials. Some critics have questioned the assumption that antidepressants are specifically efficacious for the conditions they are being used to treat (Antonuccio, Danton, DeNelsky, Greenberg, & Gordon, 1999; Fava, Evins, Dorer, & Schoenfeld, 2003; Gaudiano & Herbert, 2005; Greenberg, Bornstein, Greenberg, & Fisher, 1992; Moncrieff, 2001). For example, Kirsch and Sapirstein (1998) conducted a meta-analysis of 19 antidepressant trials with adult patients and found that inert pill placebos reproduced 75% of the improvement associated with the active medication. Furthermore, the study found a high correlation between drug and placebo response rates, and a substantial therapeutic effect from active drugs that are not typically considered antidepressants. These results support the argument that expectancy plays a key role in improvement associated with antidepressant treatment.

Although heavily criticized on methodological and conceptual grounds (for a detailed critique, see Klein, 1998), Kirsch, Moore, Scoboria, and Nicholls (2002) later published a replication of earlier results using the Food and Drug Administration database of antidepressant trials that includes unpublished studies. Results of this meta-analysis showed an even less robust drug effect, with placebo accounting for approximately 82% of the improvement. More specifically, the drug effect represented only an approximately 2-point improvement on the commonly used Hamilton Rating Scale for Depression. Although a statistically significant difference, Kirsch et al. questioned its clinical relevance. Other meta-analyses examining different sets of studies have shown similar results (e.g., Greenberg, Bornstein, Zborowski, Fisher, & Greenberg, 1994). Although the exact placebo-antidepressant difference varies from study to study, most researchers today agree that the placebo effect is associated with a substantial proportion of the improvement observed in antidepressant trials, often making it exceedingly difficult to demonstrate the efficacy of antidepressants (Charney et al., 2002).

Findings have been even less sanguine in antidepressant trials with depressed children and adolescents. Early trials of tricyclic antidepressants with this population showed poor response rates coupled with potentially lethal health risks (Gadow, 1992). In their preliminary report, the American College of Neuropsychopharmacology (ACNP, 2004) reviewed both published and unpublished data from 15 randomized controlled trials of SSRIs in the treatment of childhood depression and concluded that fluoxetine, sertraline, paraoxetine, citalopram, and nefazodone are efficacious for children under age 18. However, these conclusions were based on the finding that the aforementioned medications had at least one positive clinical trial, regardless of whether or not other trials failed to replicate the effects. It is sometimes argued by antidepressant proponents that trials failing to replicate drug-placebo differences contain "assay sensitivity" problems, such that methodological weaknesses produce an inability to demonstrate superiority over placebo (Klein, 2000). However, such arguments have been criticized as representing a fundamental derailment of the scientific process, as it is assumed that there is a drug-placebo difference prior to the study even being conducted (Gaudiano & Herbert, 2005; Otto & Nierenberg, 2002). Other independent reviews of SSRI trials using child samples have reached conclusions different from those of the initial ACNP report (e.g., Whittington et al., 2004). In general, meta-analyses have suggested weak and inconsistent benefits for SSRIs over placebo for children and adolescents, with only fluoxetine showing reasonable support of efficacy at this time (for a review, see Kendall, Pilling, & Whittington, 2005). The recent complete ACNP report now agrees with the conclusions of these independent reviews (Mann et al., 2005).

One explanation for the superiority of antidepressants over inert placebos shown in some clinical trials is that these drugs are specifically efficacious in treating depression due to their unique biochemical properties. However, some critics assert that even when a reliable antidepressant-placebo difference is found, factors other than the drugs' chemical constituents are likely to be playing a substantial, if not complete, role in the results (Kirsch & Sapirstein, 1998; Moncrieff & Kirsch, 2005). The amount of improvement shown in patients treated with antidepressants is influenced by a number of methodological and statistical factors, including attrition rate, type of statistical analysis employed (e.g., intent to treat versus completer analyses), choice of outcome measure (e.g., categorical versus continuous), and sample size (Fava et al., 2003; Gaudiano & Herbert, 2005; Klein et al., 2002; Moncrieff, 2001). Additionally, problems with financial conflicts of interest have lead some to suspect the influence of "allegiance effects," referring to the observation that results of clinical trials often conform to the preexisting beliefs of the investigators (Luborsky et al., 1999). For example, research has demonstrated that industry funding and competing financial interests predict favorable study results independent of methodological quality (Kjaergard & Als-Nielsen, 2002), with effects demonstrated specifically in antidepressant research (Baker, Johnsrud, Crismon, Rosenheck, & Woods, 2003). Also, it is an underappreciated fact that antidepressant trials often fail to demonstrate the superiority of the investigational agent, even for FDA-approved medications (Khan, Khan, & Brown, 2002). The commonly found null results in these clinical trials contribute to the "file drawer problem," or the tendency for nonsignificant findings to be left unpublished and therefore hidden from public knowledge (Rosenthal, 1979). This phenomenon can result in an incomplete knowledge database for evaluating medication efficacy in systematic reviews (Melander, Ahlqvist-Rastad, Meijer, & Beermann, 2003). Thus, any meta-analytic review of antidepressant trials is likely to be an *overestimate* of efficacy if it does not include methodologically sound but unpublished data as well.

Antidepressant Side Effects, Unblinding in Clinical Trials, and "Active" Placebos

Another potentially confounding factor in antidepressant trials is related to the underlying theoretical assumptions of such investigations. The logic of the placebo-controlled trial is one of an additive model, at least in theory (Kirsch, 2000; Wampold et al., 2005) (see Figure 1). Although natural recovery may account for some improvement, no-treatment conditions in clinical trials are inadequate controls, because they do not eliminate factors associated with a placebo response (e.g., expectancy). Therefore, clinical trials require that the active medication be shown to produce an additive effect above and beyond the improvement produced by the administration of an intentional placebo treatment. In other words, the medication's effect is calculated by subtracting it from the placebo treatment's effect. This additive model relies on an important assumption—that the double blind is never broken and, therefore, that neither the patient nor the physician can distinguish between the treatment conditions. The experimental manipulation in antidepressant trials is assumed to be the specific chemical constituents of the investigational agent. However, if

the double blind in antidepressant trials is broken, the effects may no longer conceptually be additive, as the placebo condition will cease to control for all nonbiochemical factors related to improvement. Knowledge of treatment assignment could result in the medication and placebo treatments producing their effects through different mechanisms of action, as attributions for improvement would likely be dissimilar.

Antidepressants such as the tricyclics are associated with anticholinergic side effects, including dry mouth, constipation, blurred vision, urinary retention, and even delirium. Several authors have argued that unblinding is a major concern in antidepressant trials because of the telltale side effects produced by all antidepressants (Greenberg et al., 1992; Kirsch et al., 2002; Moncrieff, 2001). A variety of evidence supports the notion that detectable side effects represent a genuine methodological concern in antidepressant trials. Research has found that patients and clinicians often can guess the randomized condition above chance accuracy (Bystritsky & Waikar, 1994; White, Kando, Park, Waternaux, & Brown, 1992). Furthermore, detectable side effects have been shown to be an issue not only with older classes of antidepressants, but with the newer SSRIs as well (Piasecki, Antonuccio, Steinagel, Kohlenberg, & Kapadar, 2002). Although some have questioned whether correct guessing of treatment condition is in actuality an artifact of clinical improvement rather than side effects, research has shown that unblinding is at least partially independent of therapeutic effect (Basoglu, Marks, Livanou, & Swinson, 1997). Unfortunately, most antidepressant trials do not report the integrity of the blind or even assess it in the first place (Petkova, Quitkin, McGrath, Stewart, & Klein, 2000).

A further piece of evidence suggesting problems with unblinding comes from early research done using active placebos. An active placebo is a therapeutically inert substance that contains active agents that mimic the side effects of antidepressants. For example, the drug atropine, a muscarinic antagonist, has been used as an active placebo due to its ability to produce the anticholinergic side effects found with tricyclics (Moncrieff, 2001). As part of a Cochrane Review report, Moncrieff, Wessely, and Hardy (2001) conducted a meta-analysis of 9 early active placebo–controlled antidepressant trials. They found that only 2 out of 9 of the trials reported superiority of the antidepressant. Further, the pooled effect size difference between active placebo and antidepressant was small and not significantly different from zero. As these early antidepressant trials often possessed methodological limitations (e.g., small sample sizes), Moncrieff et al. also examined the association between the effect size difference and the quality of the study. Interestingly, study quality was inversely correlated with outcome, such that methodologically superior trials tended to show the smallest differences between active placebo and drug. These data suggest that less of an antidepressant effect is shown in studies using active versus inert placebos, further supporting the notion that unblinding may result in differing placebo response rates due to expectancy effects. However, as the quality and number of such studies is limited, only new data from well-designed active placebo trials will be able to clarify these issues. Unfortunately, we are not aware that any such studies are being conducted or planned.

CONTROVERSIES SURROUNDING ANTIDEPRESSANT SAFETY

Questions surrounding the efficacy of antidepressants are not necessarily new, but neither are concerns over their safety. As is the case with any medication, antidepressants are associated with potentially lethal side effects, requiring their use to be closely supervised by a medical professional. Although systematic reviews have not suggested that SSRIs are more efficacious than their historical counterparts (Geddes, Freemantle, Mason, Eccles, & Boynton, 2000), one oft promoted advantage of SSRIs is their safety relative to earlier medications (Kasper, Fuger, & Moller, 1992). However, over the years there have been many reports of underappreciated side effects that have raised concerns about the safety of SSRIs, some of which are well supported (e.g., discontinuation syndrome, Lejoyeux & Ades, 1997) and others debatable (e.g., safety in pregnancy/breastfeeding, Gentile, 2005). A concern about a possible suicidality side effect of antidepressants has become one of the most hotly contested issues recently.

Antidepressant-Suicidality Link in Adults

Fears of a suicide effect emerged in 1990, when Teicher and colleagues (1990) reported that 6 patients without a prior history of suicidality developed intense suicidal preoccupation after beginning treatment with fluoxetine. The authors suggested that akathisia (an agitation syndrome that is sometimes produced by SSRIs) was related to the emergence of suicidal ideation in these patients. Other case reports later emerged describing a similar phenomenon.

However, antidepressant proponents largely dismissed these early published reports due to their small

sample sizes and the uncontrolled nature of the data. In addition, they argued that epidemiological studies failed to show an association between increased antidepressant use and a rise in suicide rates (Healy, 2003). Earlier meta-analyses of antidepressant trials did not provide much cause for concern either. For example, Khan and colleagues (2000) conducted a meta-analysis of the FDA database of adult antidepressant trials to investigate rates of suicide risk relative to placebo. Results failed to show a statistically significant difference between placebo, antidepressant, and active comparator conditions.

Healy has been one of the most controversial and outspoken critics of antidepressants. Using somewhat different methodology than Khan et al. (2000) by separating suicidal acts occurring during placebo treatment from those during the placebo wash out phase, Healy (2003) reported that the rates of suicide attempt or completion were significantly higher with SSRIs compared to placebo. Odds ratios suggested that suicidal behavior was over twice as likely to occur in those receiving antidepressants. More recently, Fergusson and colleagues (2005) conducted a meta-analysis of antidepressant trials for depression, anxiety, and neurosis from the Medline and Cochrane Collaboration registries. Results, which were based on analyses of more than 87,000 patients, showed a twofold greater risk of attempted suicide in the antidepressant group, which the authors concluded poses a significant public health concern even though the absolute risk remained relatively low. A recent publication-based study showed a nearly fivefold greater risk of suicide in elderly patients prescribed antidepressants (Juurlink, Mamdani, Kopp, & Redelmeier, 2006). Still, conclusions in adult samples remain tentative at this point as other meta-analyses using different datasets have found equivocal or contradictory findings (e.g., Gunnell, Saperia, & Ashby, 2005). The FDA recently has undertaken a systematic study of this topic and will issue a full report after their investigation is completed.

Antidepressant-Suicidality Link in Children and Adolescents

Although conclusions regarding an antidepressant-suicidality effect in adult clinical trials remain debatable, this effect has been much more widely acknowledged in child and adolescent studies since the emergence of compelling data. In December of 2003, the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA) issued a report warning that the SSRIs citalopram, escitalopram, paroxetine, and sertraline, and the related drug venlafaxine, were contraindicated in the treatment of depression in children under the age of 18 due to unfavorable risk-benefit ratios (Duff, 2003). Fluoxetine was excluded from this warning, although some have criticized this decision (see Kendall et al., 2005). The MHRA's conclusions were based on a systematic review of randomized controlled trials (RCTs) of these antidepressants in child and adolescent samples. Results of the MHRA's internal regulatory review showed that SSRIs generally were not efficacious for this population, and further were associated with an increased risk of suicidal thinking and behavior in the studies.

In the United States, the FDA undertook a similar study to investigate the efficacy and safety of SSRIs and atypical antidepressants in individuals under 18 (FDA, 2004b). Although the FDA also concluded that there was little support for the efficacy of the antidepressants studied, their conclusions were more tentative than those of the MHRA's report, citing insufficient data. After conducting a blinded reclassification of suicidal events in the RCTs, results showed a 71% increased risk of suicidality (i.e., ideation/self-harm) and a 134% increased risk of hostility and agitation relative to placebo in these trials. Other independent systematic reviews have reached similar conclusions (Jureidini et al., 2004; Whittington et al., 2004). These findings led the FDA to issue "black box" warnings for SSRIs that now describe the possibility of increased suicidality in juveniles (FDA, 2004a).

One question arises from the findings of serious adverse events in antidepressant trials: Why are such data only now coming to light? Several factors may have contributed to this problem. First, RCTs typically are designed to detect drug-placebo differences, and they are known to underestimate the likelihood of serious adverse events (Lasser et al., 2002). It is important to consider that absolute rates of completed suicide and self-harm in antidepressants trials are quite low, requiring the examination of datasets that include large numbers of patients in order for sufficient statistical power to be available to detect differences between conditions. Similar problems have been widely publicized recently regarding newly discovered adverse events associated with hormone replacement therapy for postmenopausal women and certain anti-inflammatory drugs for arthritis.

A second factor contributing to a delay in identifying increased suicidality with antidepressants relative to placebo is that the specific mechanism of action has been unclear. As discussed, many have suggested that the SSRIs produce agitation in some patients that has been linked to suicidality (Healy, 2003). However, as antidepressant trials were not designed to examine a suicidal-

ity effect, further data are needed to rule out other potential moderators or mediators, such as methodological flaws in the studies themselves, incomplete recording of adverse events, unknown patient characteristics, early symptomatic improvement, differential expectancy, or some combination of these variables that could contribute to the adverse events observed.

Finally, a further cause for the delayed warning of a suicidality concern may be industry bias and financial disincentives. Based on their meta-analysis of antidepressant trials for childhood depression, Jureidini et al (2004) asserted that "[i]n discussing their own data, the authors of all of the four larger [antidepressant] studies have exaggerated the benefits, downplayed the harms, or both" (p. 881). These critics point out that the authors of several of the large childhood antidepressant trials have been inconsistent in reporting their results, sometimes changing the primary outcome measure after failing to find an effect as originally hypothesized. Increasing recognition of how industry bias is affecting the validity of data has led to recent changes in the reporting and publishing of clinical trials, such as the policy requiring that only preregistered clinical trials will be published by certain medical journals (Fontanarosa, Flanagin, & DeAngelis, 2005).

Summary of Findings

To briefly review the evidence presented thus far, pooled data from numerous clinical trials suggest that there is a small but detectable difference between antidepressants and inert pill placebos. The exact magnitude of this effect varies from study to study due to methodological differences. Furthermore, evidence from trials using "active" placebos suggests that at least a proportion of this drug-placebo difference may be explained by discrepancies in patient expectancy, possibly due to unblinding in relation to side effects. In addition to questions of efficacy, antidepressants have been shown to be associated with increased suicidality relative to placebo in clinical trials. At this time, a suicidality effect has only conclusively been demonstrated in studies involving children and adolescents. Although many postulate that a drug-produced agitation syndrome is to blame, there currently is no clear explanation. However, observed effects on suicidal behavior are relatively small, and therefore were not fully appreciated until data from numerous trials were combined. Nevertheless, such findings suggest that regulatory agencies must consider the potential negative influence of industry bias in drug trials and develop tougher scrutiny and tighter control.

MEDIA COVERAGE: HELPING OR HYPING?

It is clear from the above discussion that the controversies involving antidepressants are complex and nuanced, often requiring sophisticated knowledge of psychopharmacology, clinical trial methodology, inferential statistics, psychopathology, and the placebo effect, to name just a few areas. As questions concerning antidepressant efficacy and safety are quite provocative and of high public health significance, it should come as no surprise that these issues have garnered their fair share of mass media coverage (i.e., print, television, radio, Internet) over the past few years. Unfortunately, the quality of this media coverage has been quite variable. Poor quality media coverage of the antidepressant controversies poses significant challenges for efforts aimed at informing the public of concerns, while simultaneously acknowledging the tentative nature of the conclusions.

Media Coverage of the Antidepressant Controversies

The media can act as an incredibly useful and powerful source of information for consumers, and many medical journalists provide reports that are a public service. Nevertheless, medical reporting frequently has been plagued by inaccuracies and sensationalism. For example, research suggests that the media exaggerate the benefits and downplay the potential harms of medications (Moynihan et al., 2000), fail to adequately report conflicts of interest and bias (Zuckerman, 2003), sensationalize health risks (Rowe, Frewer, & Sjoberg, 2000), overemphasize preliminary and pilot data (Schwartz, Woloshin, & Baczek, 2002), possess inadequate training in science and research issues (Entwistle, 1995), and fail to adequately publicize retracted or invalid findings previously reported (Rada, 2005). Frequently cited obstacles to accurate journalism include lack of time to properly investigate the topic, space to explain the issues involved, and knowledge of science and medicine (Larsson, Oxman, Carling, & Herrin, 2003).

Over the past few years, the media have been widely publicizing controversies about antidepressant medications. Sharp and Chapman (2004) reported that a Lexis-Nexis search of major news sources showed a 252% increase in stories discussing antidepressants and suicide between 2002 and 2003, with a similarly large increase

during the beginning of 2004 (when the review was conducted). We conducted an expanded Lexis-Nexis search for articles in major newspapers and magazines that contained the words "suicide" and "antidepressants" from 1995 through August 2005. Results are presented in Figure 2 and show a 458% increase in news coverage from 2003 to 2004, the approximate time that the MRHA and FDA issued their SSRI-suicidality warnings.

Sharp and Chapman (2004) also conducted a qualitative review of a randomly selected sample of 48% (n = 10) of the major news articles identified between January and March of 2004. They evaluated several criteria to assess the quality of the reporting. Most articles showed evidence of bias and sensationalism when reporting the potential antidepressant-suicide link. Although half of the articles acknowledged the tentative nature of the conclusions and discussed contradictory viewpoints, the information absent from the articles was perhaps more important. Only one article provided specific information about monitoring for warning signs in those taking antidepressants. Furthermore, none of the articles reviewed provided a discussion of evidence-based nonpharmacologic treatments for depression. These findings suggest that media coverage has largely focused on safety concerns, but then has failed to provide adequate information about safe and effective treatment alternatives.

Media Influence and the Potential for a Nocebo Effect?

One important question is whether this heightened media coverage of antidepressant concerns is likely to affect the public's perceptions and behaviors. In general, research suggests that the media can have a substantial influence on health behaviors. For example, a Cochrane Review of 5 relevant studies by Grilli, Ramsay, and Minozzi (2002) showed that mass media campaigns have a significant influence on health care utilization, clinical practice, and research interest in the direction of the position taken (favorable or unfavorable). In what Zuckerman (2003) calls "checkbook science," drug industry claims about antidepressant efficacy historically have been accepted at face value without a proper examination of the quality of the data supplied to support their claims. For years, early media presentations of antidepressants have touted their "wonder drug" status and ability to improve everything from one's personality to emotional problems in a pet (Montagne, 2001). However, media coverage is a type of double-edged sword, and it can easily influence public perception negatively as well as positively. For example, Einarson, Schachtschneider, Halil, Bollano, and Koren (2005) conducted interviews of callers at a women's information center following public health advisories warning of potential adverse events related to antidepressant use during pregnancy. They found that the media messages caused high levels of anxiety in the women. In addition, misunderstandings about the recommendations from the advisories resulted in some women discontinuing their medications inappropriately.

Most recent coverage of the antidepressants has been characterized by decidedly negative and overly alarmist copy. In fact, a sea change can be witnessed in media representations of antidepressants relative to the early stories touting antidepressants' benefits. Examples of recent provocative headlines concerning antidepressant-suicidality links in major newspapers include "Student, 19, in Trial of New Antidepressant Commits Suicide," "A Suicide Effect? What Parents Aren't Being Told about Their Kids' Antidepressants," "Seroxat and Prozac 'Can Make People Homicidal,'" and "Antidepressant Makers Withhold Data on Children." The current barrage of media coverage on antidepressants has probably played a role in the current sharp downtrend in antidepressant prescribing for children (Vendantam, 2005).

In addition, media descriptions of placebo response rates with antidepressant frequently convey an inaccurate impression to the public suggesting that placebos and the drugs are equivalent in efficacy (Gaudiano & Herbert, 2003). In a *Washington Post* article, Vedantam (2002) writes: "After thousands of studies, hundreds of millions of prescriptions and tens of billions of dollars in sales, two things are certain about pills that treat depression: Antidepressants like Prozac, Paxil and Zoloft work. And so do sugar pills" (p. A01). As noted earlier, although the effects are smaller than many might expect, pooled data show that antidepressants are often more effective than inert pill placebos. Furthermore, it is unlikely that the placebo effect would be as strong if not for the power of expectancies produced in these trials.

It is well known that positive expectancies can produce improvements in the absence of an efficacious treatment, but less attention has been given to when treatments produce iatrogenic or harmful effects. The *nocebo* (Latin meaning "I will harm") *effect* occurs when an inert substance or procedure produces a negative outcome (Barsky, Saintfort, Rogers, & Borus, 2002). On average, 20% of patients receiving a medical placebo report adverse side effects (Rosenzweig, Brohier, & Zipfel, 1993). The mass media have been

implicated as an important source of erroneous public beliefs about medications that foster negative expectancies (Barsky et al., 2002). Such phenomena raise the disquieting possibility that a nocebo response could result from media coverage overhyping antidepressants as ineffective or unsafe (Gaudiano & Herbert, 2003). An interesting example of a nocebo response due to changing treatment expectancies can be found in a recent antidepressant trial investigating brain changes related to improvement (Leuchter, Cook, Witte, Morgan, & Abrams, 2002). The lead investigator reported that the majority of placebo responders in the trial relapsed almost immediately after being unblinded upon study completion (Reid, 2002; Vendantam, 2002). Physicians must consider that media coverage sensationalizing the problems with antidepressants may provoke negative reactions in some patients currently being treated successfully with medications for their depression.

WHERE HAVE ALL THE EMPIRICALLY-SUPPORTED TREATMENTS FOR DEPRESSION GONE?

Although there are examples of credible reporting, health information presented in the mass media is often deficient. Critics have argued that media representations of antidepressant controversies frequently raise concerns but then fail to provide adequate guidance as to what individuals suffering from depression can or should do (Gaudiano & Herbert, 2003; Sharp & Chapman, 2004). We would argue that biased and sensationalistic media coverage of antidepressant controversies has the potential to create a treatment vacuum by fostering public confusion and ignorance. What will fill the void? Will practitioners and the public gravitate toward empirically informed treatment alternatives for depression in the wake of the antidepressant controversies, or will the ineffective and potentially harmful interventions being aggressively promoted by some be the true beneficiaries?

The Landscape of Medicine and Public Interest in Nontraditional Treatments

Prior to describing the alternatives to antidepressant medications and the most recommended options, it is important to consider the social context in which treatments for depression have been developed and used in medicine. For centuries, the manner in which medical care is provided has been a topic of much debate. In the modern era, beginning in the middle of the 19th century, the American Medical Association (AMA) has lobbied for empirically based treatments and strict guidelines to delineate the requirements for medical education and the parameters within which clinicians should practice. In the early 1900s the AMA supported Abraham Flexner in his production of the "Flexner Report" (Flexner, 1910), a detailed document of all U.S. medical schools in existence at that time. Flexner's report examined the entrance requirements and resources, including endowment, faculty, and facilities, at each medical school and made specific recommendations regarding the continuation of only those medical schools meeting the highest standards. By the 1930s this report was generally supported by governmental agencies and major medical institutions, encouraging the development of science-based medical training programs. Of course, the report also negatively affected some individuals in medical disciplines. For example, programs in rural areas and medical schools dedicated primarily to the training of African American physicians suffered and were forced to close. Additionally, the AMA's lobbying and the widespread acceptance of the Flexner Report had deleterious effects on "nonscientific" training programs in homeopathy and botanical medicine (Beck, 2004). Nonetheless, the momentum toward increased rigor in medical training and practice led to an increasingly evidence-based and scientific practice of contemporary medicine.

The same social forces that promoted modern medicine may also have contributed to some of its shortcomings, with psychiatry's overreliance on antidepressant medication being one example. An explanation of some factors driving modern psychiatric treatments may be found in medical anthropology, which has spent more than 40 years working to elucidate the effects of social forces on the practice of medicine. In a recent review, Hemmings (2005) identifies several shortcomings of modern medical practices, some of which are directly relevant to contemporary debate about the treatment of depression. For instance, "scientific medicine emphasizes technological fixes rather than psychosocial interventions" (p. 92), suggesting a bias toward the use of medication despite established efficacious nonpharmacological treatments. Further, Hemmings suggests that "medicine has lost focus on the person and their experience of illness . . . [and medicine] responds inadequately to patients' need to find meaning" (p. 92).

It is becoming increasingly apparent that treatments for depression be aimed at bolstering patients' sense of meaning and purpose, decreasing hopelessness, and improving the relationship between patients, families, and clinicians (Schulz & Patterson, 2004 **[AU: You**

asked me to add Miller & Reynolds, 2002 to refs list here; should that reference be cited here?]). Efforts toward these goals in contemporary medicine, including psychiatry, may be less than adequate. There are multiple barriers to effective depression treatment, including public stigma about mental illness, the failure of the primary care medical system to recognize and to provide effective treatment for depressed patients, and the lack of financial incentives to provide services other than medication in the current reimbursement climate (Pincus, Hough, Houtsinger, Rollman, & Frank, 2003). Although the evidence base for specific psychotherapies and some health behaviors continues to grow, primary care clinicians and contemporary psychiatrists do not receive education and information about nonpharmacological treatments for depression on par with antidepressant medications (Luhrmann, 2000; Pincus & McQueen, 1996). Emphasis on teaching psychotherapy to psychiatrists has been increasing, but it is unrealistic to expect trainees to develop competency in the practice of diverse psychotherapies (Yager & Bienenfeld, 2003). Furthermore, physicians in general practice, who treat the majority of noncomplicated cases of depression, receive limited training, if any, in psychotherapy. It is clear that physicians must be competent to diagnose, prescribe medication, and develop a comprehensive treatment plan that incorporates evidence-based interventions. However, treatment providers often fall short of this mark. Based on the results of a large-scale study examining physician-patient communication and treatment outcome in recurrent depression, the authors concluded: "Our main findings are that these patients were not being treated to full remission, complete wellness, and full function" (Schwenk, Evans, Laden, & Lewis, 2004, p. 1899).

Dissatisfaction with the routine treatment for depression that a patient might receive in a primary care physician's or psychiatrist's office may be one explanation for the increasing public interest in "nontraditional" or complementary and alternative medicine (CAM) interventions for depression (Gordon, 1990). In a prominent series of reports, the use of CAM for any medical condition increased between 1990 and 1997 and then remained notably high between 1997 to 2002, during which time approximately one in three survey respondents reported use of one or more CAM therapies, representing approximately 72 million American adults (Tindle, Davis, Phillips, & Eisenberg, 2005). Although some question the overly broad classification of what is considered CAM in this epidemiological research (Gorski, 1999), public and professional interest in CAM has prompted much discussion regarding the training of physicians (Wetzel, Kaptchuk, Haramati, & Eisenberg, 2003), the credentialing of CAM practitioners (Cohen, Hrbek, et al., 2005), and policies regarding the use of CAM in academic medical centers (Cohen, Sandler, Hrbek, Davis, & Eisenberg, 2005). Regarding the use of CAM for depression, Kessler and colleagues (2001) reported rates of 53.6% over a 12-month period in the United States. In a survey of nearly 9,000 consecutive visits to CAM practitioners in four states, it was noted that 7% to 11% of visits to acupuncturists, massage therapists, and naturopathic physicians were for mental health complaints (Simon et al., 2004). Also, up to 50% of the patients in this study had previously sought treatment from a conventional practitioner, and only a small minority (1–5%) of patients was referred to conventional practitioners. This suggests that some patients with major depression may be receiving CAM treatments for depression prior to exhausting options that are known from clinical trials to be efficacious.

Depression is a complex and heterogeneous phenomenon. It has taken considerable effort to transform public opinion away from the idea that mood symptoms are "all in one's head." However, the substituted contemporary catch phrase "chemical imbalance" also does not adequately convey the complexity of depressive illnesses. Modern conceptualizations of depression recognize it as a biopsychosocial syndrome requiring continued translational research. This research must seek to bridge understandings of genetics, environmental influence on gene expression, the relationship between neurophysiology and specific neuropsychiatric symptoms, and the social and cultural context in which depression occurs (Blazer, 2003; Nemeroff & Vale, 2005). Depression clearly has genetic underpinnings as evidenced by increased concordance in monozygotic (identical) versus dizygotic (fraternal) twins. Candidate genes that may contribute to the heritability of depression include those that code for the structure of the serotonin transporter, although this process may operate indirectly via the serotonergic modulation of more general "stress" reactions (Hamet & Tremblay, 2005). Contemporary investigations of how environment may impact depression have focused on exposure to stress, particularly in early life (Wurtman, 2005). Although these investigations will clearly help to elucidate how environment and genes may interact to produce depressive syndromes, they do little to speak to a patient's day-to-day experience of depression. This task has been left to psychological interventions, and the few remaining psychoanalytic psychiatrists (Gabbard, 2000). In addi-

tion, some alternative therapies, particularly those with roots in Eastern traditions, may have appeal to some patients' first-person experiences of depression for at least two reasons. First, some CAM treatments may produce pronounced positive expectancy and hopefulness by proposing interventions for those who have negative opinions about medication and psychotherapy. Second, CAM practitioners may be felt by patients to be more attentive to promoting wellness behavior rather than treating "illness" (Bongiorno, 2005; Gordon, 1996).

Patient preference for treatment is another important consideration in depression treatment, especially given the fact that several different types of treatment have been shown to be about equally effective. The majority of studies show that most patients clearly prefer psychotherapy over antidepressant treatment, but they are much more likely to receive antidepressants in certain settings (e.g., primary care) (van Schaik et al., 2004). Patients' preferences can effect treatment compliance, and there is some evidence that preferences affect treatment outcome. If credible treatment alternatives for depression exist, then patients should be provided with options, especially as several treatments have been shown to be cost-effective and justifiable in comparison to antidepressant treatment. However, patients' preferences must ultimately be weighted against the evidential warrant supporting the use of the particular treatment.

Evidence-Based Treatment Options for Depression

Treatment guidelines. There are legitimate arguments against reliance on a narrow medical model that views depression largely or exclusively as a medical illness (e.g., diabetes) that (a) is related directly to a neurotransmitter dysregulation and (b) requires pharmacological treatment. Further, consumers appear to be quite interested in and motivated to explore nonpharmacologic approaches. However, we would argue that the answer is not in "alternative" medicine, per se, but in evidence-based treatment alternatives. Nonpharmacologic treatments should not be dismissed out of hand simply because they fail to superficially resemble conventional medical treatment. To the contrary, there is a need for expanded research on non-antidepressant treatments for depression, which may require a very different approach to treating the syndrome (e.g., deep brain stimulation). However, the assessment of the validity of such treatment alternatives should always rely on firm scientific data.

Evidence-based medicine (EBM) is defined as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients" (Sackett, Rosenberg, Gray, Haynes, & Richardson, 1996, p. 71). In addition to the emphasis of EBM in psychiatry, there is an emerging movement within psychology to specify practice guidelines for treating psychological problems (Herbert & Gaudiano, 2005). EBM relies on hierarchical levels of evidential warrant. Evidence of efficacy and safety from methodologically sound RCTs are considered the best scientific evidence and therefore given the most weight in the decision-making process. However, in addition, EBM provides specific recommendations for choosing treatments based on the quality and amount of the evidence, as well as an analysis of risk-benefit ratios. One advantage of EBM is that clear direction is provided based on state-of-the-art scientific data meant to provide optimal treatment selection. We believe that this general framework should be utilized when evaluating evidence-based treatment options for depression.

Certain scientific groups have provided specific guidelines for the treatment of depression, including the UK's National Institute for Clinical Excellence (NICE). After a systematic review of available data on treatments for depression and based on consensus from an expert panel, NICE guidelines (2004) recommend a stepped care model based on depression severity (summarized in Table 1). In addition to medication, psychological interventions play a key role as evidence-based treatments for depression. They form the primary intervention for more mild forms of depression, and are legitimate treatment alternatives to antidepressants for moderately to severe depression, depending on patient preferences and risk-benefit assessments. Further, for more severe depression, psychological treatments are particularly useful when combined with medication for certain patients. Although the use of psychological treatments during all strategies of depression treatment is consistently recommended in evidence-based guidelines, such treatments are often unavailable or, when available, still underutilized (Williams et al., 1999). The lack of evidence-based practice guidelines in psychology is probably a contributing factor to the underutilization of evidence-based psychotherapy, as psychiatric guidelines are often biased toward medication treatments (Herbert & Gaudiano, 2005).

Evidence-based psychotherapies. Several types of psychotherapy represent credible alternatives to antidepressant medication when it is contraindicated (e.g., children, elderly, pregnancy, noncompliance, comorbid medical conditions, suicidality risk). Cognitive behavior

therapy (CBT) is one of the best-known efficacious treatments for depression. CBT approaches are typically skills-based and focus on efforts to modify the negative cognitions and maladaptive behaviors characteristic of depression. Common examples of CBT approaches include cognitive therapy (Beck, Rush, Shaw, & Emery, 1979), behavioral activation (Martell, Addis, & Jacobson, 2001), problem solving therapy (Nezu, Nezu, & Perri, 1989), and couples-focused approaches (Beach & Jones, 2002). A strong body of research has demonstrated that CBT is as effective as antidepressants in clinical trials, even for those with more severe forms of depression (DeRubeis et al., 2005). Furthermore, CBT has been shown to be superior to antidepressants at preventing relapse, cost-effective, and easily adaptable to various formats and settings (for a review, see Hollon, Haman, & Brown, 2002). For example, research has supported the use of guided self-help versions of CBT for mildly depressed primary care patients (Richards et al., 2003). There also is emerging evidence that CBT is safe and effective for juvenile depression, and should be recommended as the frontline treatment (Bostic, Rubin, Prince, & Schlozman, 2005). At this point, cognitive-behavioral interventions are the most empirically supported psychological treatments for depression.

Another credible psychotherapy option for depression is *interpersonal psychotherapy* (IPT), which focuses more on psychosocial and relationship problems, including grief, role disputes, role transitions, and interpersonal deficits. Numerous clinical trials have documented its efficacy for the treatment of depression (for a review, see Weissman & Markowitz, 2002). For example, a large multisite National Institute of Mental Health Treatment of Depression Collaborative Research Program study found that IPT showed efficacy similar to CBT and antidepressant medication and superiority over pill placebo (Elkin et al., 1989). However, current availability of IPT providers in the community is more limited than CBT.

Additionally, there is emerging evidence to suggest that *combined treatment with pharmacotherapy plus psychotherapy* may be more efficacious for some patients than either treatment alone. Recent meta-analyses show that combined treatments (typically including CBT) tend to show modest effect size gains over monotherapies, particularly for more severely depressed patients (Friedman et al., 2004). Similar findings are beginning to emerge in studies of childhood depression. For example, a recent large clinical trial comparing fluoxetine, CBT, or a combination of the two relative to placebo found that patients improved most in the combined treatment condition (March et al., 2004). However, it is important to emphasize that patients in this condition were not blinded as to antidepressant treatment, rendering conclusions tentative. One potential advantage of combined treatment is that patients can be monitored more regularly for medication side effects and emergent suicidality, and be provided with psychotherapy that better addresses symptom-related distress, quality of life, and social support needs. Perhaps most importantly in the current discussion, research is beginning to suggest that combined treatments may ameliorate the antidepressant-suicidality risk found in patients taking antidepressants alone (Kendall et al., 2005).

It is important to note that although psychological treatments such as CBT have a substantial base of outcome research to support their use, the mechanisms of action producing their effects remain elusive, similar to the situation with antidepressants. For example, some research suggests that CBT, IPT, and antidepressants are generally equivalent in efficacy (Elkin et al., 1989). Further, dismantling studies have failed to convincingly demonstrate that multicomponent CBT interventions are any more efficacious than stripped-down interventions that focus on basic behavioral strategies (Jacobson et al., 1996). The question arises as to whether it is necessary to establish that the improvements from psychotherapy are beyond those produced by a placebo effect, as is the case with drug research. Attempts have been made to study specific psychological treatments for depression compared with experimentally designed "placebo" psychotherapies, but conceptual and practical issues make such efforts virtually impossible (Herbert & Gaudiano, 2005). As Kirsch (2005) notes, attempting to categorize the effects produced by psychological treatments as "real" versus "placebo" demonstrates a fundamental misunderstanding of the concept. He argues: "A placebo is something that is sham, fake, false, inert, and empty. [Effective] psychotherapy is none of these. In this sense, it is different from medical placebos, and it does not deserve the pejorative connotations associated with the term" (p. 7). Although some have attempted to rely on the distinction between "specific" and "nonspecific" factors in defining placebo psychotherapy, such classifications are necessarily arbitrary and contingent upon the particular theoretical orientation of the discussant. For example, the therapeutic alliance is conceptualized as a nonspecific factor in CBT, but as a specific factor in many psychodynamic treatments (Herbert & Gaudiano, 2005).

Psychotherapy is by definition a psychological treatment, meaning that it operates mainly as a verbal or experiential process in the absence of direct physical (or

chemical) manipulation. Therefore, it is conceptually misguided to attempt to prove psychotherapy efficacy beyond placebo effects. Such is not the case in drug research, where it is meaningful to separate the effects produced by the biochemical properties of the agents themselves from all extraneous factors, including any and all psychological effects such as expectancy. If a specific drug effect is not demonstrated, then the evidence suggests that the mechanisms of action include important psychological factors such as expectancies, the specific domain of psychotherapies. In psychotherapy research, the proper focus of attention should be on defining the precise psychological mechanisms associated with effective treatments for depression (including antidepressants) that may be responsible for the majority of improvement witnessed (e.g., expectancies, behavioral activation). This is not to say that the quality of research on psychotherapies should be any less rigorous than drug research, only that the interpretations and aims of such research necessarily differ. This goal can be achieved using RCT methodologies adapted for psychotherapy research, including dismantling studies, comparison trials, and process research (Herbert & Gaudiano, 2005).

Other alternatives to antidepressant treatment. There are treatment options other than antidepressants and psychotherapy for depression that may be considered by patients based upon the severity of their depressive symptoms and patient preferences. For those patients with severe depression who have not adequately responded to medication and psychotherapy, practice guidelines typically recommend the use of electroconvulsive therapy (ECT), based on a long history of efficacy and increasing understanding of the mechanisms of action (Greenberg & Kellner, 2005). Other novel neurostimulatory treatments for resistant severe depression under investigation have shown some promise, including vagus nerve stimulation (VNS), repetitive transcranial magnetic stimulation, magnetic seizure therapy, electroencephalogram biofeedback, and deep brain stimulation (George et al., 2002; Trivedi, 2003). However, more research on the safety and efficacy of these procedures is needed before promoting their widespread use.

For those with depression that is not severe and treatment resistant, there are alternatives to medication and psychotherapy that may be seen as compatible with both "traditional" and CAM approaches. Although there are fewer controlled studies to support its use at this time, the prescription of *mild exercise* has been found to be a useful intervention for treating less severe forms of depression (Lawlor & Hopker, 2001), and is recommended in the NICE guidelines (NICE, 2004). In addition, based on results from several placebo-controlled studies, *light therapy* is an interesting environmental intervention that may be effective for depressive syndromes with or without a seasonal pattern (Tuunainen, Kripke, & Endo, 2004).

Furthermore, there are a variety of nutritional supplements or medicinal herbs that may have antidepressant effects, of which the most investigated and the most commonly known in the United States is *Hypericum perforatum* or St. John's wort (Linde, Mulrow, Berner, & Egger, 2005; Walsh et al., 2002). Use of this herb may produce a beneficial effect for people with mild or moderate depression; however, as with any medicinal, its use requires careful assessment of the associated risks and benefits. Nevertheless, many trials have failed to show its superiority to placebos, as is the case with traditional antidepressant medications. Other popularly promoted agents include gingko biloba, Lavendula angustifolium, chromium, melatonin, fish oil (containing omega-3 fatty acids), folic acid, s-adenyosyl-l-methionine (SAMe), l-tryptophan, vitamin E, and zinc (Bongiorno, 2005; Walsh et al., 2002). However, there is little support for the efficacy of these agents, and this fact, combined with potential contraindications and side effects, may make them poor alternatives for some patients.

Finally, it is important to note that concerns over antidepressant safety raise intriguing questions about the adequacy of our knowledge about other treatments for depression. First, known severe side effects are associated with nutritional or herbal treatments of depression. Of particular concern is the potential risk of serotonin syndrome when St. John's wort is used in combination with another serotonergic antidepressant (Zhou, Chan, Pan, Huang, & Lee, 2004). Also, Kava, a medicinal herb considered for use as an anxiolytic, has been associated with acute toxicity and liver failure (Perez & Holmes, 2005). Further, controversy has surrounded the recent FDA approval of VNS for treatment resistant depression, as some have questioned its efficacy and safety (Rosack, 2004). There are even warnings that light therapy should be used cautiously due to concerns that it may provoke hypomanic states in some patients (Tuunainen et al., 2004).

Although currently there is little information to suggest an increase in suicidality in efficacious psychotherapies, the possibility cannot be completely ruled out. It is only because of the systematic collection of adverse events required in drug trials with thousands of patients accumulated over many decades with antidepressants that has allowed us to identify a possible suicidality

effect in some patients. In fact, studies of psychotherapies rarely report isolated adverse events, and there is no database established to systematically collect such data. The potential problems emerging with antidepressants suggest the need for closer scrutiny of the safety of nonpharmacological treatments for depression as well. Ultimately, treatment decisions for depression must be based on assessments of risk-benefit ratios for particular patient groups (e.g., children and adolescents), as well as patient preferences based on the best available data.

Conclusion

Much confusion can be witnessed today among researchers, practitioners, and the public alike related to concerns surrounding antidepressant efficacy and safety. Proposals being offered in light of the antidepressant controversies tend to emphasize the need for more costly and time-consuming research to be conducted to further investigate pharmacologic treatments. However, we hope that the current spotlight being placed on antidepressants will not leave nonpharmacologic treatments for depression in the dark. In addition to better research on antidepressants, current concerns about pharmacologic treatments for depression should underscore the need for the development and testing of evidence-based treatment alternatives. Fortunately, psychotherapies such as CBT have enough support to promote their use today. Nevertheless, the newly appreciated problems with antidepressants should highlight the need for improvements in our conceptualization of depression, including the biological underpinnings, relevant psychological constructs, and psychosocial context in which it occurs. Further, much more research is needed into the safety of these nonpharmacologic treatments for depression, including psychotherapy.

Efforts to develop and test nonpharmacologic treatments such as psychotherapy face an uphill battle in the current economic climate. It is clear that no "psychotherapy industry" exists to fund research on psychological treatments for depression as exists for drugs. Psychotherapy researchers currently must rely almost entirely on federal funding, which increasingly is limited. This has created an urgent need for additional funding to test nonpharmacologic treatments for depression, to train practitioners in their use, and to disseminate this information to the media and public. It is unlikely that such changes will occur overnight, but increased public awareness and promotion of evidence-based treatments for depression, including but not limited to antidepressants, is essential. Unfortunately, contemporary medicine is not well versed in health and wellness promotion, and there may be economic disincentives toward providing health education during physician visits (e.g., these are more time consuming and less easily billed as services). Therefore, the media may be a useful resource in these endeavors, as they represent a powerful vehicle for increasing public awareness of legitimate treatment options and the urgent need for additional research in these areas.

A common complaint among journalists is that it is difficult to find credible researchers willing to be interviewed (Larsson et al., 2003). However, researchers should view such interviews as part of their public health duty. Media interviews can be used to provide information on credible alternatives to antidepressants, to warn against the use of unvalidated treatments, and to emphasize the need for increased governmental funding in these areas. Researchers and treatment providers who speak to the media should spend more time educating journalists as to the full complexity of the issues surrounding antidepressant concerns, so as not to inadvertently foster nocebo expectations. Any discussion should include clear recommendations about how patients should handle concerns about taking antidepressants. Additionally, knowledgeable researchers should make themselves readily available to the media to discuss not only antidepressant controversies, but also to provide information concerning other valid treatment options. Finally, the use of formal workshops provided to inform journalists about controversial medical findings has been used successfully in the past (Arnold, 2003), and should be explored in the case of the antidepressant controversies.

A positive example of media coverage of the antidepressant-suicidality controversy can be found in a recent article in the *Washington Post* (McMillen, 2004). The piece discusses the emerging evidence for using CBT or IPT for juvenile depression based on preliminary studies. Further, the article emphasizes the need for increased research efforts to assure that these psychotherapies are truly safe and efficacious. Unfortunately, such coverage tends to be the exception rather than the rule. Perhaps Steven Sharfstein (2005), the recent American Psychiatric Association president, puts it best:

> As we address these Big Pharma issues, we must examine the fact that as a profession, we have allowed the biopsychosocial model to become the bio-bio-bio model. In a time of economic constraint, a "pill and an appointment" has dominated treatment.

> We must work hard to end this situation and get involved in advocacy to reform our health care system from the bottom up. (p. 3)

Ultimately, it will take a concerted effort among researchers, practitioners, the media, and consumers to promote evidence-based treatments for depression in light of the current antidepressant controversies.

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Table 1: National Institute for Clinical Excellence's (NICE) Guidelines for the Treatment of Depression in Primary and Secondary Care

Treatment Provider		Target of Intervention	Evidence-Based Treatment Recommendations
Step 1	General practitioner	Recognition	Assessment
Step 2	Primary care team, primary care mental health worker	Mild depression	Monitoring, guided self-help (e.g., CBT), exercise, brief psychological treatments (e.g., PST)
Step 3	Primary care team, primary care mental health worker	Moderate to severe depression	Medication, psychological treatments (e.g., CBT, IPT)
Step 4	Mental health specialists	Treatment-resistant, recurrent, atypical, psychotic depression, and those at significant risk	Medication, complex psychological treatments, combined treatments
Step 5	Inpatient teams	Safety risk, severe neglect	Medication, combined treatments, ECT

CBT = cognitive behavior therapy; IPT = interpersonal psychotherapy; PST = problem-solving therapy; ECT = electroconvulsive therapy
Adapted from National Institute for Clinical Excellence (NICE). (2004). *Depression: Management of depression in primary and secondary care (National Clinical Practice Guideline Number 23).* London: Author. Retrieved July 17, 2006 from http://www.nice.org.uk/page.aspx?o=cg023#documents.

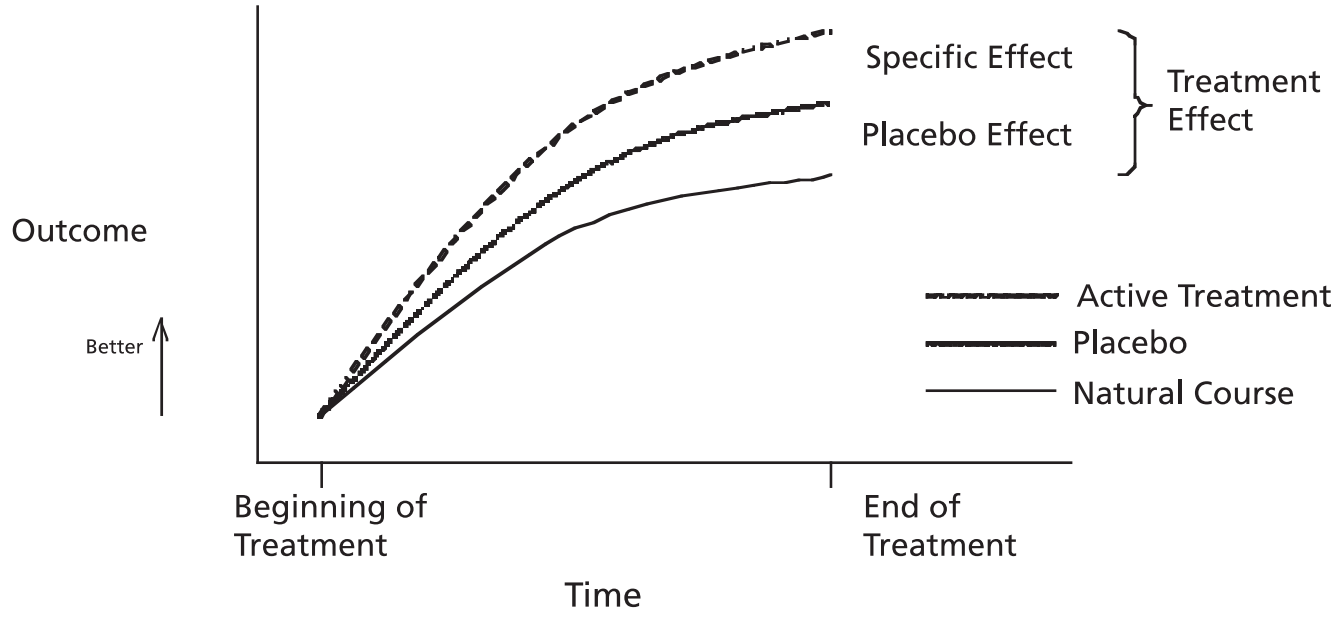

Figure 1. The Additive Model of Treatment Effects in Clinical Trials

Reproduced from Wampold, B.E., Minami, T., Tierney, S.C., Baskin, T.W., & Bhati, K.S (2005). The placebo is powerful: Estimating placebo effects in medicine and psychotherapy from randomized clinical trials. Journal of Clinical Psychology, *61*, 835–854.

Figure 2. Lexis-Nexis search results for articles containing the words "suicide" and "antidepressant" in major newspapers and magazines.