Do No Harm: A Critical Risk/Benefit Analysis of Child Psychotropic Medication

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ABSTRACT. Prescriptions for psychiatric drugs to children and adolescents skyrocketed in the past ten years. Meanwhile, concerns of suicidality and industry bias in research have prompted regulatory investigation to assess claims that selective serotonin reuptake inhibitors (SSRIs) are safe and effective for children. Family clinicians may be unaware of the controversy or do not have the time or expertise to evaluate drug research. A five flaws analysis of clinical trial research, notably SSRI and stimulant studies, offers an efficient strategy for examining scientific claims. The authors recommend that therapists critically evaluate the scientific basis for medicating youths. Guidelines are provided to assist clinicians helping young people and their families make informed decisions.

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Within the last decade, prescriptions for psychiatric drugs to children and adolescents skyrocketed (Martin & Leslie, 2003; Olfson, Marcus, Weissman, & Jensen, 2002; Zito et al., 2003, Zito & Safer, 2005). Evaluating the records of almost a million youth, one of the most comprehensive studies to date concluded that child and adolescent psychotropic utilization rates nearly tripled from pre-nineties levels (Zito et al., 2003). According to the U.S. Food and Drug Administration (FDA), 11 million prescriptions for antidepressants were written for children under 18 in 2002 (Rigoni, 2004), an overall prevalence increase of 49% from 1998 (Delate, Gelenberg, Simmons, & Motheral, 2004). Between 2000 and 2003, spending for Attention-Deficit Hyperactivity Disorder (ADHD) drugs increased by 183% for children overall (Medco Health Solutions, Inc., 2004). A review of prescription data for 300,000 children ages 19 and younger concluded that, for the first time in history, spending for medications for childhood behavior problems eclipsed expenditure on any other child drug category, including antibiotics (Medco Health Solutions, Inc., 2004). This review found a 369% increase in spending on attention-deficit drugs for children under 5. Similarly, Zito et al. (2000) found a 580% rise in antidepressant use in the under-6 population.

Other trends are noteworthy. Children in foster care are 16 times more likely to receive a prescription than their non-foster care counterparts (Zito et al., 2003); children in child welfare settings receive psychotropic medications at 2 and 3 times the rate of children not involved with this system (Raghavan, Zima, Andersen, Leibowitz et al., 2005). Poly-pharmacy, prescribing two or more medications simultaneously, is becoming standard practice (Martin, Van Hoof, Stubbe, Sherwin, & Scahill, 2003, dosReis et al., 2005). Over 40% of youths treated by psychiatrists were prescribed two or more psychotropic medications (Duffy et al., 2005), and youths are increasingly prescribed combinations of atypical antipsychotics and anti-convulsants for non-psychotic problems (Zito & Safer, 2005). A study of more than 1.7 million privately insured youths from 1997–2000 found *reductions* in inpatient and outpatient mental health services with concomitant *increases* in the proportion of youths receiving medication (Martin & Leslie, 2003). Increasingly, "treatment" means medication. Nearly 9% of American children are taking one or more medications to

treat behavioral problems (Medco Health Solutions, Inc., 2004). Out of these diverse surveys a consistent picture emerges: Children and teenagers do not live, play, and work in "drug-free zones."

In this prescription era, parents face a daunting decision in how to resolve a child or adolescent's difficulties, now further complicated by the recent FDA revelations about the increased risk of suicide with selective serotonin reuptake inhibitors (SSRIs). Family clinicians may wonder about their role in assisting families as they weigh the pros and cons of medication. The FDA warning notwithstanding, many continue to assert that the "risk/benefit ratio" remains favorable. Without the tools to assess the scientific validity of these claims, however, clinicians are left to rely on others—the media and medication proponents—to translate safety and efficacy data. This article critically examines the science that justifies medical intervention for childhood emotional and behavioral distress. An empirical analysis of key antidepressant and stimulant trial research uncovers five major flaws that undercut study findings and final assertions. At the same time, this analysis teaches clinicians an efficient method for conducting a risk/benefit evaluation and influencing professional discourse in ways that expand the range of choices for children, adolescents, and their families.[1]

CHILDREN AND ANTIDEPRESSANTS: A FIVE FLAWS ANALYSIS

The failure of tricyclics (TCAs) to effectively treat children is well documented (see Birmaher, Ryan, Williamson, et al., 1996; Fisher & Fisher, 1997). During the 1990s, there was great hope for the "newer" antidepressants, the SSRIs. However, before 1997, a comprehensive 10-year review revealed a dearth of evidence that either TCAs *or* SSRIs were effective for children and adolescents (Birmaher et al., 1996). In spite of this, reviewers concluded "psychosocial and pharmacological treatments [for children] are vital" (p. 1581). The failure of researchers to prove that SSRIs worked for children contrasted with burgeoning child SSRI prescription rates. The Emslie et al. study (see Emslie, Rush, Weinberg et al., 1997), an 8-week, randomized, placebo-controlled, double-blind trial comparing the efficacy of fluoxetine (Prozac) and placebo, was the first attempt at a credible defense for SSRIs for children. Emslie et al. concluded that fluoxetine was effective for treating major depressive disorder in children and adolescents. The importance of the Emslie et al. study as a justification for prescribing SSRIs to youths cannot be underestimated.

It provided the basis for continued antidepressant prescription (albeit off-label) and represented the first of two randomized, controlled trials needed to accomplish FDA approval for the investigative drug for this age group. As a result of the 1997 Emslie et al. study and its 2002 follow-up (Emslie, Heiligenstein, Wagner, Hoog, Ernest et al., 2002), Prozac remains the sole SSRI approved for child and adolescent depression. Because of their status, the Emslie studies provide useful templates for analyzing five major flaws of drug research.[2]

Compromised Blind: Flaw # 1

Greenberg and Fisher (1997) assert that the validity of controlled studies, in which a placebo is compared to an active medication, depends upon the "blindness" of participants who rate the outcomes. To prevent bias, drug trial clients and researchers must not know or be able to guess who is getting the actual drug and who is getting the placebo. Greenberg and Fisher note that the use of inert sugar pills as the placebo in the vast majority of clinical trials actually makes it possible for most participants and clinicians to tell who is getting the investigative medication. Inert sugar pills, or inactive placebos, do not produce the standard side effect profile of actual drugs–dry mouth, weight loss or gain, dizziness, headache, nausea, insomnia and so on. Since study participants must be informed of the possibility and nature of side effects in giving consent, they are necessarily alert for these types of events (Antonnucio, Danton, & McClanahan, 2003). In addition, most studies track side effects as part of their research, and interviews about adverse effects are generally a component of the trial. Ongoing interviews that listen for or actively elicit information on side effects can easily reveal active versus inactive pill takers, effectively un-blinding the study and skewing results. In support of this theory, a meta-analysis of fluoxetine in the treatment of depression found a significant correlation between reports of side effects and outcome (Greenberg, Bornstein, Zborowski, et al., 1994).

Research participants have other ways of determining research group status. One review of blindness in antidepressant trials notes that participants are far from passive–they actively read subtle cues or attempt to discover their treatment status and do so with remarkable accuracy (Evan, Siobud-Dorocant, & Dardennes, 2000). In addition, many drug trial clients in placebo groups have previously been on drug regimens, even some just prior to entering the trial, and are therefore familiar with the effects of active medications. With so many ways to distinguish group identities in

studies using inactive placebos, any conclusions drawn by those rating outcomes are most likely compromised. Not surprisingly, trials using inert placebos (representing the bulk of published clinical trials) frequently find in favor of the investigative drug. However, a recent meta-analytic review of studies using active placebos found negligible if any differences between medication and placebo groups (Moncrieff, Wessely, & Hardy, 2004).

The Emslie et al. (1997) study used an inactive, sugar pill placebo, drawing into question the integrity of the study's double blind. In a later retrospective assessment, Emslie and colleagues determined that the blind "was clearly maintained" (Hughes et al., 2000, p. 593). When both the Prozac and placebo groups were considered together, without regard to client response, there was no trend in the prediction beyond what would be expected by chance. However, when clients' responses to treatment were considered, clinicians accurately predicted medication for responders (27 out of 31) and placebo for non-responders (26 out of 35). These represent approximate 87 and 74% rates of accuracy respectively, far from chance predictions. Of note, the FDA cited Lilly's own review of primary source records where "it was not uncommon to see notations defining the patient's blinded treatment, or in some cases to find fluoxetine plasma concentration results" (U.S Food and Drug Administration, 2001, June 25, p. 19).

Reliance on Clinician Ratings: Flaw # 2

Greenberg and Fisher (1997) demonstrate that clinicians and clients frequently differ substantially in their reading of how much improvement has actually occurred in a clinical trial. An extensive meta-analysis of 22 antidepressant studies involving 2,230 persons found that both "old" (e.g., Elavil) and "new" (e.g., Prozac) antidepressants showed an approximate 20% advantage over the placebo on clinician-rated measures, but *none* on client-rated measures (Greenberg, Bornstein, Greenberg, & Fisher, 1992). In short, when clients rate their *own* responses, they often experience no improvement on antidepressants beyond what can be attributed to hope and expectation. In the Emslie et al. (1997) study, 2 out of 4 clinician-rated measures indicated a difference between the placebo and SSRI groups. Two client-rated measures found *no difference*.

Time of Measurement: Flaw # 3

Antidepressants are almost never prescribed for short periods of time. This suggests that clinical trial findings are not measuring how well the

drugs do in actual life settings, since a typical trial time frame is 12 weeks. Additionally, differences between medication and placebo groups tend to dissolve by 16 weeks (Greenberg & Fisher, 1997). Without longer term follow-ups, conclusions about effectiveness in real life cannot be determined. Authors of many short-term clinical trials fail to adequately discuss time frame limitations or to modify accordingly claims made in conclusions. For example, Emslie et al. (1997) concluded that "fluoxetine in 20 mg/d is safe and effective in children and adolescents," (p. 1036) without mention of time.

Conflicts of Interest: Flaw # 4

In May of 2000, the editor of the *New England Journal of Medicine* called attention to the problem of "ubiquitous and manifold . . . financial associations" authors of drug trials had to the companies whose drugs were being studied (Angell, 2000, p. 1516). Since this time, there has been increasing pressure for medical journals to publicize funding sources and author ties to those sources to alert readers to potential conflicts of interest. The 1997 Emslie et al. study, published prior to disclosure requirements, did not identify author affiliations. Emslie et al.'s second fluoxetine trial for child and adolescent depression (Emslie et al., 2002) lists author affiliations on the first page. Here, readers learn that Emslie and Wagner are paid consultants for Eli Lilly, who funded the research and whose product was being investigated. The remaining six authors are listed as employees of Eli Lilly and "may own stock in that company" (p. 1205).

Minimization of Risks: Flaw # 5

A recent systematic evaluation of 82 medical charts of children and adolescents treated with SSRIs found that 22% experienced some type of psychiatric adverse event (PAE), typically a disturbance in mood (Wilens et al., 2003). Estimates of PAEs in child and adolescent studies is complicated by inconsistent methods of collecting side effect data (Greenhill et al., 2003) and benign, or misleading, assessments of data actually reported. For example, in the Emslie et al., 1997 study, 6% of participants taking Prozac dropped out due to manic reactions compared with 2% in the placebo group. If extrapolated to the general population, for every 100,000 children on Prozac, as many as 6,000 might be expected to experience this serious adverse effect. In addition, according to FDA documents, at least 2 participants receiving Prozac in this study actually attempted

suicide (U.S. Food and Drug Administration, 2001, June 25). However, the published study never mentions this fact; instead, it claims: "Side effects, as a reason for discontinuation, were minimal, affecting only 4 patients who were receiving fluoxetine" (Emslie et al., 1997, p. 1033).

Although Emslie's 2002 study purports to present both efficacy *and* safety data, it includes no tables (out of 4) detailing adverse events. Instead, adverse events are presented in narrative form, making it difficult to discern actual safety findings, particularly in relation to study discontinuers. For example, the study reports a 0.9% (n = 1) manic reaction for fluoxetine-treated participants compared with no manic reactions for those treated with placebo, a nonsignificant difference. However, of the 5 discontinued participants in the fluoxetine group, 3 reported manic-type responses including agitation and hyperkinesia, reactions the study deemed "nonserious." Of placebo discontinuers, 2 quit due to aggressive or self-mutilatory behavior, information the authors placed in the serious adverse event paragraph. If study completers are considered with those who discontinued, the comparison now is 4 (3.6%) manic-type adverse events for fluoxetine and 2 (1.8%) for placebo. However, given that the adverse event data was not presented in tabulated form, most readers will undoubtedly miss this important comparison.

The FDA's analysis of Eli Lilly's integrated safety data pooled from 3 pediatric fluoxetine trials (Emslie's 2 trials plus an additional trial for children diagnosed with obsessive compulsive disorder) confirms a lack of transparency regarding critical safety data in published reports (U.S. Food and Drug Administration, 2001, June 25). This analysis indicates that 22 participants discontinued due to adverse events in all Prozac-treated groups compared with 5 in placebo groups. The comparison of suicide attempts between groups was 3 for fluoxetine and 1 for placebo, with at least one additional fluoxetine participant hospitalized due to suicidality. In the pooled analysis, 6 (2.6%) Prozac takers compared to none on placebo experienced manic reactions (a significant difference).

Mania and suicidality are not the only underplayed adverse effects in pediatric drug trials. The FDA, in approving Prozac for pediatric depression in 2003, required Eli Lilly to conduct Phase 4 trials to address the fact that after 19 weeks of treatment with fluoxetine, youths in one clinical trial gained an average of 1.1 cm less in height and about one kilogram less in weight compared to youths taking placebo (U.S. Food and Drug Administration, 2003, January 3). The 2002 Emslie study found significant cardiac effects on ECG readings between those on and those off fluoxetine (U.S. Food and Drug Administration, 2001, June 25). These effects were

not highlighted in original reports, nor do they appear in most information and marketing pertaining to pediatric use of Prozac.

Other Methodological and Rhetorical Strategies

The five flaws are not exhaustive of the strategies employed by researchers to gain the best possible result for their funding source (e.g., see Antonuccio, Danton, & McClanahan, 2003; Jureidini, Doecke, Mansfield, et al., 2004). Many studies, including Emslie et al. (1997), use a placebo run-in (also called placebo washout). In this procedure, placebos are given to all participants for one or two weeks prior to randomization. This is a single-blind process, meaning researchers but not participants know that the pill being taken is placebo. Those who respond are then excluded from the study. Presumably, a study is more objective by eliminating from the outset all those who are high placebo-responders. However, this strategy obviously compromises the supposed head-to-head comparison; placebo responders have already been "weeded out."

In studies where placebo run-ins are not used, other means can achieve a similar beginning bias. For example, Emslie's 2002 study of Prozac excluded those who had previously failed to respond to adequate antidepressant treatment. Exclusionary criteria, like placebo washouts and screening out nonresponders, increase the chances that the active medication group will significantly differentiate from the control group on outcome.

Strategies that use "last observation carried forward" and "intention to treat" approaches estimate data from assumed endpoints for dropouts based on observation before discontinuation. Unlike sound intention to treat studies, most childhood trials do not follow dropouts to determine their actual status. Additionally, the translation of continuous measures into categories, a common practice in childhood antidepressant trials, inflates differences between medication and control groups (Jureidini et al., 2004). Jureidini et al. report that the first Emslie trial changed its primary outcome measure between the trial's beginning and final study publication to show superiority of the investigative drug. Although Emslie et al. in 2002 failed to find a statistical difference between fluoxetine and placebo on their single, preselected primary outcome measure, the authors never clearly state this important fact. Instead, the authors highlight secondary measures throughout (e.g., remission, mean improvement). In spite of the fact that both Emslie studies failed to find in favor of Prozac on original primary measures of efficacy, they gained FDA approval for

"efficacy, tolerability, and safety" for fluoxetine in pediatric populations (see U.S. Food and Drug Administration, 2003, January 3).

STIMULANTS AND CHILDREN: A FIVE FLAWS ANALYSIS

Although stimulants, primarily Ritalin, have established their efficacy over placebo in small, short-term randomized clinical trials on narrowly defined Attention Deficit Hyperactivity Disorder (ADHD) symptoms (without consideration of design flaws), these successes have not extended to a wider range of outcome measures in real settings over a longer period of time. To address this criticism, the Multimodal Treatment Study of Children with ADHD (MTA) compared four treatments for ADHD: behavioral treatment (BT); medication management (MM); combined BT and MM; and a community comparison treatment control group (MTA Cooperative Group, 1999). The MTA is widely touted as proving that stimulants are more effective than behavioral intervention–it is the infrastructure of the stimulant prescription phenomenon in much the same way the Emslie et al. studies sustain antidepressant prescription. And similarly, it too can be evaluated using a five flaws critique.

Compromised Blind/Reliance on Clinician Ratings: Flaws # 1 and # 2

With 144 subjects in each group, the MTA was superior to previous studies in numbers alone. It also surpassed its predecessors because it evaluated treatment for 14 months instead of the customary 12–16 weeks. Finally, rather than the simple clinician-rated outcome measures that characterize most studies, the MTA selected a total of 19 measures from multiple sources (parents, teachers, child, peers, and objective tests and observations) in multiple domains of functioning (ADHD symptoms, peer and parent-child relationships, classroom behavior, and academic achievement). At the 14-month endpoint, Pelham (1999), one of the principal investigators, summarized the following results:

1. All 4 groups showed dramatic improvement;
2. Medication management (MM) was superior to behavioral treatment (BT) on parent and teacher ratings of inattention and teacher ratings of hyperactivity, *but not on any of the other 16 measures;*

3. Combined treatment and MM did not differ on any dependent measure; combined treatment was better than BT on parent and teacher ratings of inattention and parent ratings of hyperactivity and oppositional behavior, and reading achievement (p. 982).

The MTA not only lacked a pill placebo control group, it also relied only on evaluations made by teachers and parents who were not blinded to the treatment conditions. At the same time, the only double-blind measure (blinded classroom raters) found no difference among any of the treatment groups. In fact, the subjects themselves (the 7–9 year old children) rated themselves as no more improved when using medication than when using behavioral or community alternatives. Interestingly, peer ratings concurred with this assessment. The negative findings from the blinded classroom observers, the children themselves, and their peers suggests that stimulant drugs offer no advantages over nonmedication alternatives.

Time of Measurement: Flaw # 3

In the MTA, assessment occurred at the 14-month endpoint while subjects were actively medicated. However, when this assessment was done, therapy had ended. In fact, endpoint measures were taken 4–6 months after the last, face-to-face, therapeutic contact. Thus, the endpoint MTA treatment comparison was between active MM treatment and *withdrawn* BT. Pelham (1999) claims that the study's design favored the drug from the outset, making the actual results even more surprising. The lack of difference on 16 of 19 measures (when MM was compared with BT) and on 19 of 19 measures (when community treatment of mostly medicated children was compared with BT) are significant indicators of medication nonsuperiority, especially given that these findings reflect comparisons between medication versus withdrawn therapy. Additionally, 75% of the children in the BT condition were maintained without medication for 14 months, including one-half of those who were medicated at study entry (Pelham, 1999).

A recently published 24-month follow-up of the MTA shows that the group differences are even smaller; the MM and combined groups lost much of their effect (up to 50%) while the BT and community groups retained their gains (MTA Cooperative Group, 2004a). At 24 months, the majority of parents in the BT group thought their children were doing well enough that they did not medicate them even after the study had

ended (Pelham, personal communication, April 21, 2003). The fact that the 14-month comparison was made between active MM and withdrawn BT, combined with the diminished differences between the groups at 24 month follow-up, casts significant doubt on any claims of stimulant superiority.

Conflicts of Interest: Flaw # 4

The reputation of the National Institute of Health (NIH), umbrella organization of the National Institute of Mental Health (NIMH), the MTA's sponsor, has come under fire following an investigation by the *LATimes* into widespread, hidden associations between NIH scientists and the biomedical industry (Willman, 2003). In a follow-up, Willman (2005) found that, despite congressional hearings and widespread publicity, the agency's ethical problems continue to be serious and widespread. The MTA was conducted before the Willman article and subsequent congressional investigations when nondisclosure was standard practice, and therefore no industry affiliations for any authors are listed. However, an online database published by a nonprofit health advocacy group, reveals that the MTA lead investigator, Peter Jensen, and at least five other MTA authors have significant ties to pharmaceutical firms (see Integrity in Science, http://www.cspinet.org/integrity/). Specifically, Jensen is listed as a consultant to Novartis, the makers of Ritalin, the drug under investigation in the MTA.

Minimization of Risks: Flaw # 5

In the MTA, 64% of the children were reported to have some adverse drug reactions; 11% were rated as moderate, and 3% as severe. Perhaps these adverse drug reactions accompanying stimulants explain the finding of the MTA study that parents significantly preferred the behavioral and combined treatments over medication alone. Even when medication is preferred, most parents do not desire to medicate their children for the long term and discontinue stimulants during late childhood or adolescence (Pelham, 1999). The 24-month follow-up report (MTA Cooperative Group, 2004b) validates parents' reluctance for long-term use–children taking stimulant medication showed a 1 cm per year reduction in growth compared to those children not taking stimulants, for a total loss of 4 cm since the study began. The FDA has recently reviewed adverse event reports for stimulants and is attaching warning labels to alert consumers of the risks of hallucinations suicidal ideation, and psychotic, aggressive

or violent behavior, as well as cardiovascular events (www.fda.gov/ohrms/dockets/ac/05/slides/2005-4152s2_07_Murphy.ppt–07-07-2005). Another category of ADHD drugs that include Adderall, was ordered off the market in Canada after reports of 20 sudden deaths in patients, including 12 strokes (Dooran, July 1, 2005).

Considering these troubling finding and parents' preference for short term stimulant use, the importance of family therapists' role in helping families takes on even greater weight. In summary, the MTA fails to provide convincing evidence that stimulant medication should be privileged over any other option; a risk/benefit analysis does not support stimulant medication as a first line of defense.

CRITICAL ANALYSIS IN ACTION

In June, 2004, on the front page of *The New York Times*, "Antidepressant Seen as Effective in Treatment of Adolescents" described unpublished results from a "landmark" NIMH financed study, The Treatment of Adolescent Depression Study (TADS), comparing the efficacy of Prozac, cognitive-behavioral therapy (CBT), CBT plus Prozac, and placebo (Harris, 2004). According to the story, Prozac helps teenagers overcome depression far better than talk therapy. Within days, other media celebrated the news. "The take-home message is that medication works, that suicide risk is minimal and that the positive effects of the medicine outweigh the risk" (McKenzie, 2004).

Several months after the TADS' press releases, the full study appeared in print (see TADS Team, 2004). An inspection of this study readily reveals the five flaws. First, out of 4 separate treatment conditions, blinding was attempted in only the fluoxetine and placebo groups. The placebos were inactive, calling into question the blind between these conditions. Second, the study's two primary measures were clinician-rated. Results from the two primary endpoint scales mirrored earlier Prozac trials: the categorical measure indicated superiority for Prozac, the continuous measure showed no difference, and the adolescent self-report measure indicated no difference between placebo and Prozac. While other endpoint comparisons in TADS favored the combined medication/CBT arm, these cannot indicate superiority of this condition over others since both participants and investigators were aware that they were receiving an active medication and the full range of CBT intervention. Only the combined group received all components from both medication and CBT alone

groups, including an additional pharmacotherapist who monitored dosage and "offered general encouragement about the effectiveness of pharmacotherapy for MDD" (TADS Team, 2004, p. 809). Even the TADS investigators acknowledge that, because of inequities in conditions and lack of blinding, the "'active ingredient' in improvement cannot be specified" (p. 818).

Third, the TADS trial was 12 weeks in duration; after 12weeks, participants were unblinded. Fourth, lead investigator, John March, has received funding from Eli Lilly, Prozac's manufacturer, and has extensive ties with the pharmaceutical industry (see www.integrityinscience.org). Five others of the 11 researcher, Emslie included, have financially benefited from Eli Lilly funding (Lenzer, 2004), and the funding source, National Institute of Mental Health (NIMH) is part of the National Institute of Health, which has come under scrutiny for its lax standards regarding researchers' industry connections (Willman, 2003, 2005). What is now known about endemic conflicts of interest within the NIH casts a long shadow over the first Emslie study in 1997, funded by the NIMH, where investigator affiliations were not revealed.

Finally, the TADS recorded 6 suicide attempts by Prozac takers compared to 1 by non-Prozac takers, with more than double the incidence of harmful behavior in the Prozac compared to placebo groups. Nevertheless, the authors recommended that "medical management of MDD with fluoxetine, including careful monitoring for adverse events, should be made widely available, not discouraged" (TADS Team, 2004, p. 819). TADS' findings regarding increased incidence of harmful and suicidal behavior, in conjunction with compromised methodology, continues to suggest an unfavorable risk/benefit profile for Prozac for adolescents.

RISK/BENEFIT ANALYSIS AND ETHICS

The FDA, following recommendations of the joint panels established to examine the risk of suicidality for youths taking antidepressants, directed manufacturers to revise their labels to include a "black box warning" (U.S. Food and Drug Administration, October 15, 2004). The warning alerts providers and consumers that antidepressants increase the risk of suicidal thinking and behavior (suicidality) in depressed children and adolescents and can contribute to clinical worsening or unusual changes in behavior. (http://www.fda.gov/cder/drug/antidepressants/SSRIlabelChange.htm). Despite this warning, and despite known significant adverse events for antidepressants

and other psychotropic drugs for youths, Zito & Safer's (2005) study confirms continued increases in prescriptions for teens and children.

Many family clinicians are on the "front lines" in schools and community settings. Yet, many often do not have the time or expertise to sift through drug studies and to engage in informed critical analysis. For example, they may not know that, in the Emslie studies, Prozac outperformed placebo on only two clinician-rated measures. They may not know that all other major drug trials of SSRIs for those under 18 suffer from similar design problems, including inactive placebos and inadequate lengths of time, and have indicated negligible or no benefit over placebo; or that in the MTA, the endpoint measures were taken long after behavior therapy had ended. They may also be unaware of the true extent of industry influence on research and the dissemination of research as advertisement into the general public. Antonuccio et al. (2003) detail the vast reach of the pharmaceutical industry–from Internet, print, and broadcast media, direct-to-consumer advertising, "grassroots" consumer-advocacy organizations, and professional guilds to medical schools, prescribing physicians, and research–even into the board rooms of FDA. They conclude, "It is difficult to think of any arena involving information about medications that does not have significant industry financial or marketing influences" (p. 1030).

Saturation of popular and professional media accompanied by the inability to make informed evaluations of research reinforces medical discourse. In the process, the credibility of nonmedical options, particularly stand-alone (not combined with medication) psychotherapy and behavioral approaches to affect desired results recedes into the background. Despite its lack of backing by multibillion dollar corporate entities, psychotherapy for children and adolescents has a strong tradition of proven efficacy (e.g., see Birmaher et al., 2000; Kazdin, 2003; Michael & Crowley, 2002; Nock, 2003). These options, however, may go unnoticed and underutilized.

The following offers family clinicians guidelines for assisting families deciding on medication for their youngest members:

1. Conduct a thorough and systematic assessment of the child or adolescent's problem, combining information from the youth, parents, school, and other significantly involved persons.
2. Develop a conjoint framework for understanding the problem based on the youth, family, and significant others that includes developmental, environmental, and interactional explanations.

3. Develop a conjoint plan that follows the assessment and framework of understanding. If medication is part of the plan, make sure all involved, including the youth, are aware of potential risks, particularly known adverse events, the meaning of off-label prescription, and the lack of studies supporting combining psychotropic medications. Suggest resources for obtaining additional information about risks and benefits, including physicians and unbiased sources.
4. Work collaboratively with the youth, family, and significant others to implement the plan, modifying as needed based on systematic feedback on progress. If medication is part of the plan, assist the youth and significant others to view positive change as resulting from the efforts of all, in particular the youth, in overcoming the problem, and include discussion of a time frame for discontinuation of medication.

Lack of critical awareness takes on greater weight where children are concerned; children trust adults to know and to make good decisions in their interests. An ethical approach requires that clinicians in the field and those most involved in helping families with medication decisions become aware of the relationship between a profit-driven industry and science, and what that science actually reveals. Becoming informed through critical analysis enables clinicians to assist clients to look beyond the ads and brochures in making decisions about their child's course of treatment. Of course, family therapists encourage clients to seek information from a variety of sources, including physicians or other helpers within the family network. Only then can an accurate risk/benefit analysis be undertaken. Without a reasonable skepticism and active critique, clinicians, even with the best intentions, are complicit in a for-profit enterprise where client interests take a back seat.

When concerned parents approach us, family therapists can be knowledgeable about pediatric psychopharmacology *and* ready with a range of non-medical strategies to match client preferences. This may mean becoming fluent in a psychopharmacology critique. In this way, children, adolescents, and caregivers, via an informed therapist, have access to information that can assist them in choosing a path that best suits their own preferred means of dealing with difficulty. The profession can then say it truly respects the rights of clients to make decisions, and helps clients understand the consequences of those decisions; it can then say that it does no harm, especially to our youngest and most vulnerable clients.

NOTES

1. It is not the authors' aim to discredit individual preferences for or experiences with medication, or to claim that medications may not be helpful for certain individuals at certain times in their lives. Instead, the authors hope to provide a counterpoint to medical discourse, thereby making space for other points of view and other options.

2. The Emslie studies are used to illustrate the authors' critical framework because these studies are the sole basis for government sanction for the prescription of any antidepressant to those under 18. The authors could not have chosen other articles, as none others rise to the level of methodological standard required for FDA approval, despite widespread belief that multiple studies support the practice of antidepressant prescription for adolescents.

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