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SAFETY FIRST

Thank you for the interview, "Protect yourself against patient assault," and the accompanying reprint of Dr. John Battaglia's article "Is this patient dangerous?" (CURRENT PSYCHIATRY, November 2006, p. 15-24, 25-32). Both give sound clinical guidelines for psychiatrist safety without being insensitive or "blaming the victim" in the case of Dr. Wayne Fenton's tragic death allegedly at the hands of a patient. Although implicit, however, the need to develop and maintain appropriate boundaries needs to be more explicit and discussed.

From what we know, Dr. Fenton saw the patient in his office on a weekend with no one else present other than the patient's father, who waited outside. One eulogy said that Dr. Fenton helped install a carpet in a different patient's residence after the patient was released from the hospital. Both examples surely are instances of going "the extra mile" to help troubled patients, and Dr. Fenton was known as a master clinician who received some of the most difficult cases.

On the other hand, customary boundaries regarding how and where to see patients were not taken. Perhaps Dr. Fenton thought the rewards of breaking these boundaries outweighed the risks. Nevertheless, development and maintenance of boundaries should be undertaken as one way to ensure safety. When making exceptions, extra precaution should be taken.

H. Steven Moffic, MD
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Dr. Battaglia responds

I wholeheartedly agree with Dr. Moffic's points about the need to take extra precautions when going outside customary boundaries. However, our discipline treads in muddy waters on the issue of what is appropriate when working outside such boundaries.

The extremes of sexual or financial exploitation are clear, but otherwise the entire spectrum of interaction between patient and clinician can be appropriate under certain circumstances. For example, in my work with the Madison (WI) Program of Assertive Community Treatment, I often see patients in their homes, help them with grocery shopping, or assist them with other daily tasks. Although these behaviors do not fit an office model, they are not uncommon in community work and do not necessarily break boundaries.

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CONTINUED CONCERNS ABOUT SGAS

Although the article "Avoiding EPS is key to realizing 'atypical' benefits,'" by Drs. Rajiv Tandon and Robert J. Constantine (CURRENT PSYCHIATRY, November 2006 p. 35-45), is more balanced than some reviews of the CATIE findings, it emphasized avoiding extrapyramidal symptoms (EPS) while ignoring two other features that are important when choosing an antipsychotic.

The first is the propensity for causing weight gain, hyperglycemia, and hyperlipidemia. The CATIE phase 1 investigation showed that second-generation antipsychotics (SGA)—especially olanzapine—are much more likely to cause these health-threatening complications compared with the first-generation antipsychotic (FGA) perphenazine.

The second consideration is cost. I am aware of economic arguments in favor of SGAs, especially if they prevent hospitalizations. However, in light of CATIE and the British CUtLASS 1 studies, it is unconscionable to not consider the huge difference

in cost between SGAs and FGAs. Recent reports indicate that SGAs continue to outpace almost all other medications in price increases. This adds to society's health-cost burden and creates a cruel inequity for those without prescription coverage.

It is an oversimplification of our clinical duty to refer to avoiding EPS as the "key" to antipsychotic treatment. We can only wish it were that simple.

Dennis Helmuth, MD, PhD
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Table

Study populations of SGA-FGA comparison trials

	Age	Age at onset	Duration of illness
CATIE (Lieberman et al, 2005)	40	24	16
Olanzapine (Beasley et al, 1998)	38.6	23.9	14.7
Risperidone (Csernansky et al, 2002)	40.3	24.4	15.9
Amisulpride (Rein and L'Heritier, 1999)	36	na	na
Ziprasidone (Arato et al, 2002)	50	na	na
Risperidone (Marder et al, 1994)	37.4	21.7	15.7
Risperidone (Marder, 2003)	43.5	na	na
Aripiprazole (Kane et al, 2002)	38.6	22.3	16.3

STUDY SAMPLES KEY TO ASSESSING RISK

We agree with Drs. Tandon's and Constantine's explanation of the difference between the results of the CATIE trial[1] and previous studies—specifically that CATIE showed no differences between 4 SGAs and an intermediate potency FGA on EPS and tardive dyskinesia (TD). As the authors suggest, these results are best explained by the use of high-dose, high-potency haloperidol as the comparator in pre-CATIE studies, which magnified differences between FGAs and SGAs. A recent study has further suggested that in most of these trials the doses of haloperidol were above FDA-approved levels,[2] and few, if any, used prophylactic anticholinergics, further biasing the comparisons.

Drs. Tandon and Constantine further assert that the CATIE sample was at less risk of EPS or TD than previous samples because it excluded first-episode patients and those with TD and addressed a population that had used medications for 14 years without a history of adverse effects. CATIE—like any other ethical human investigation—excluded patients if they had well-documented, drug-related, adverse reactions to any of the proposed treatments.

Many, if not most, FDA registration trials (the source of most data on EPS with SGAs) excluded all patients with previous exposure to the new SGA drugs they tested but did not apply this criterion to patients exposed to older drugs. Thus the trials were more likely to include patients who would have responded poorly to FGAs than those who would have responded poorly to SGAs. Others have recognized that this reduces the validity of such FGA-SGA comparisons.[3]

In the table (*above*), we present data comparing population characteristics from CATIE, from a meta-analysis that identified all 4 published controlled trials that have examined TD outcomes in FGA and SGAs,[4] and from several other well-known comparable trials. The CATIE sample was similar to patients who participated in the other trials in average age, age of onset, and duration of illness.

Beasley et al[5] similarly presented an analysis that excluded patients without TD at baseline, which we believe is the optimal population to use

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when evaluating medication-related risk for TD. CATIE is the only study that conducted a sound randomization comparing FGAs and SGAs in patients without current TD who are at risk for it, and—more than other studies—used an unbiased and thus more informative comparator.

Unfortunately there have been numerous factual errors in published critiques of CATIE. In one, CATIE was deemed disappointing[6] because it had "a large percentage of discontinuations for all causes," but the data presented for comparison were from a 28-week study[7]—less than half as long as the 72-week CATIE trial. CATIE, in fact, had better overall follow-up rates than the cited study at 28 weeks and also had better long-term follow-up rates than either the paper by Beasley et al[5] or by Csernansky et al[8]—the most often cited "long-term" studies comparing FGAs and SGAs on TD.

Another commentary, like that of Drs. Tandon and Constantine, described CATIE patients as having more chronic illness that those in other trials, with "24 years since first treatment,"[9] a misreading of the average age of first onset (which was 24) as if it was the average duration of illness (which was 16 years).

Many commentators have further asserted that because patients with TD at baseline "were not randomly assigned to conventional drugs" the comparison of either outcomes or TD risk was invalid.[6,9] As noted above, comparison of side effect risk is properly tested by trials involving patients without that risk at onset.

CATIE represented a major investment of public dollars to learn more about antipsychotic medications. Erroneous critiques needlessly mislead the professional community about what can be learned from this initiative.

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Drs. Tandon and Constantine reply

We thank Dr. Helmuth and the principal investigators of CATIE for their interest in our article and the opportunity to further clarify a key learning point from CATIE.

Dr. Helmuth acknowledges our balanced review but suggests that cost and metabolic side effects should be considered along with lower EPS liability in selecting antipsychotic therapy. We agree. Avoiding EPS while obtaining a good antipsychotic effect is one key consideration in providing optimal antipsychotic therapy. Other adverse effects, patient preference, cost, and other factors are all important considerations in this complex process of individually optimizing antipsychotic treatment.

The CATIE investigators agree with our interpretation of the study's principal findings. They

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take exception, however, to our suggestion that CATIE's finding of no FGA-SGA difference in EPS and TD may be related to its relatively low assay sensitivity to detect such differences because the sample studied was at low risk for EPS and TD.

While accepting our description of the study sample as accurate, they disagree that it was at low risk for EPS and TD. Patients who have been ill for 16 years and received antipsychotic treatment for an average of 14 years without developing TD or severe EPS (as in CATIE) are by definition at low risk for EPS and TD.

We agree that patients without current TD and who are at risk for developing it comprise the best study population to investigate differential risk for TD; however, patients who have not developed it, despite 14 years of antipsychotic therapy, are at very low risk for developing it at all. First-episode patients without prior antipsychotic exposure would be an optimal study population, but such patients were excluded from CATIE.

Drs. Rosenheck and colleagues do not disagree with any of the other assertions in our article; they are, however, critical of "numerous factual errors in other published critiques of CATIE." We cannot address such supposed inaccuracies, which are best taken up with authors of those commentaries.

To extract maximum value from this important initiative, we must better understand CATIE's findings in the context of its study design and the results of other relevant studies. Neither mischaracterization nor overinterpretation of CATIE's findings helps clinicians, patients, and policy-makers.

The essence of our article was that avoiding motor, cognitive, and affective EPS due to unmodulated dopamine blockade is the key to realizing the "atypical benefits" of a broader spectrum of efficacy and lower risk of TD during antipsychotic therapy. Neither Dr. Helmuth nor Drs. Rosenheck and colleagues appear to disagree with this assertion. Avoiding broadly defined EPS appears to be critical to improving cognition, dysphoria, and negative symptoms with SGAs and FGAs. The lower risk of TD observed with SGAs also appears to be related to the greater ease with which they can provide an equivalent antipsychotic effect without EPS.

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LOOKING AT THE BIG PICTURE

Thank you for Dr. Henry Nasrallah's editorial, "Our mission: To meet your needs," which questions mental health professionals' role and suggests new ways of looking at our clients (CURRENT PSYCHIATRY, September 2006, p. 11-2). Finally, someone is questioning the DSM-IV-TR, the woeful lack of breakthroughs in many disorders, the interface between medicine and psychiatry, and the disparity of payment for mental health treatment.

Psychiatry could be leading thinking on a wider basis. With proper focus, emotional health could be a primary factor in physical medicine rather than the other way around. People who are mentally healthy are less likely to be physically ill, but there is no research to prove this.

Consider taking the focus off the individual patient and looking at larger systems such as the family, church, and community. Psychotherapy will not be able to heal and help people to have successful and productive lives if it stays mired in the individual. Looking at systems allows psychiatry to lead rather than follow and engage in wellness activities such as consulting for schools, families, and political systems. But the profession must look at itself first.

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