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From the editor

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Off-label prescribing
Cutting-edge psychopharmacology

"Off-label" may evoke an uncomfortable sense of therapeutic mischief, yet the term describes a vital evolution of scientific discovery in pharmacotherapy. Because no FDA-approved drugs are available for many psychiatric disorders, patients would suffer needlessly if psychotropics were not used off-label.

The Agency for Healthcare Research and Quality recently reported on the "Efficacy and comparative effectiveness of off-label use of atypical antipsychotics."[1] Its findings confirm other published studies of the widespread off-label uses of second-generation antipsychotics (SGAs). In Georgia's Medicaid system, for example, a large proportion of antipsychotics, antidepressants, and mood stabilizers are prescribed off-label.[2]

Clinicians, in fact, use psychotropics off-label for many legitimate reasons, including:

No other options. In a recent study,[3] we found that only 12% of DSM-IV-TR categories have an approved drug, leaving 88% of psychiatric disorders with no "official" pharmacologic treatment. Obviously, compassionate practitioners use whatever is available to alleviate the suffering of the many psychiatric patients for whom no drug has been approved.

Through trial and error over time, clinicians have found multiple uses for SGAs and other psychotropics in many symptoms or diagnoses. Clinicians have engaged in this necessary innovative process for years—even decades—before some diagnostic categories eventually obtained an FDA-approved drug.

88% of DSM-IV-TR diagnostic categories have no FDA-approved drug treatments

In my opinion, this process is vital to the scientific "discovery" process that precedes controlled clinical trials that ultimately confirm what clinicians have collectively observed. It also is a vital scientific partnership between clinicians who generate hypotheses about additional drug efficacies and researchers who test these hypotheses to produce evidence-based findings.

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'Real-world' clinical issues. On-label psychotropic use is supported by short-term studies of very "clean" samples of patients, who often are not representative of community-based practice. When the drug is launched in the "real world," however, it is used in much more complicated patients who may be treatment-resistant and have comorbid medical or psychiatric disorders or substance abuse.

We go off-label when we maintain patients on drugs approved only for acute use

Clinicians often find that a higher (off-label) dose can be more effective for real-world patients than the lower doses that worked in FDA-required pre-approval trials. Thus, off-label use of a high-dose SGA may have better efficacy in some patients than the narrow range of approved dosages.

Maintenance therapy dilemmas. Years may pass before we see maintenance studies for an antipsychotic that has been approved for acute treatment of schizophrenia or mania. But clinicians are highly unlikely to discontinue that drug after a patient successfully responds within a few weeks. Thus, we essentially practice off-label psychopharmacology whenever we maintain a patient on a drug approved only for acute uses.

Combination therapies. No antipsychotic combinations are approved for schizophrenia, yet more than one-third of chronic schizophrenia patients in the United States are concurrently receiving 2 or more concurrent SGAs.[4] Combining antipsychotics is often regarded as dubious off-label polypharmacy, yet clinicians stand by their observations that patients who do not improve with 1 drug may respond when another is added.

Although combination pharmacotherapy is not supported by credible evidence—controlled trials of 2 SGAs vs 1 combined with a placebo—clinicians again might be discovering options for treatment-resistant or refractory patients before FDA trials are conducted.

Simpler dosing for better adherence. A drug may be approved for twice-daily (bid) administration, yet clinicians might soon discover that prescribing it once daily (qd) is equally or even more effective because of improved patient adherence. Off-label dosing may be rational and even better than the official dose schedule, yet a drug company might never go through the costly process of repeating its clinical trial to demonstrate that bid and qd dosing are equivalent. Thus, practitioners will continue to use the drug off-label based on clinical experience, not on research data.

Scientific implications. Aside from advancing psychopharmacologic practices and discovering new treatments, off-label data also could shed light on a potential shared neurobiology among psychiatric disorders. Off-label prescribing ultimately might help us reconceptualize the overlapping neural pathways of several axis I and axis II disorders, all of which appear to be improved by the same pharmacologic agent such as an atypical antipsychotic. It might even prompt us to coin a new name for antipsychotics, such as "neurostabilizers."

Write and tell me what term you would coin for a class of drugs with multiple psychiatric uses.

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