

# CMT Newsletter

April 20, 2009

## Inside This Issue

- 1 Introduction
- 2 Appropriate Prescribing of Antipsychotic Medications
- 3 Low-Dose Antipsychotic Prescribing
- 4 Contact Info



---

Despite these facts, antipsychotic medications are persistently prescribed at doses far too low to have an actual antipsychotic effect. The medical equivalent would be something like giving a patient with pneumococcal pneumonia a dose of penicillin only sufficient to inhibit 25% of bacterial activity. Very few infectious disease experts would countenance such a practice, and yet it is the rule when prescribing antipsychotic drugs.

---

## Introduction

Greetings,

Thousands of articles about behavioral health disorder treatment are published every month in the medical and scientific literature, making it impossible for the vast majority of primary care physicians and health care leaders and administrators to keep up. Even psychiatrists complain that the pace of new data acquisition far exceeds their ability to adjust clinical practice to keep it evidence-based and maximally cost-effective. The default position for many clinicians is to rely on information from pharmaceutical company representatives and from industry-sponsored CME programs. While such information is valuable, it of course does not pretend to give equal emphasis to generic and competitors' products or to non-pharmacological treatments (including psychotherapy and even no therapy).

The result of these problems is, sadly, that a great deal of behavioral health care is not consistent with cutting-edge science. Care Management Technologies (CMT) LLC is dedicated to helping health care plans and clinicians master and use the most recent and high-quality evidence in making treatment decisions, unencumbered by pharmaceutical company or any other proprietary influence.

Many of you have asked us to give you regular updates on some of the developments, trends and new findings that we use in creating and updating our products. Hence, we are pleased to present you with our first CMT Newsletter, a new bimonthly service that will highlight a single topic, summarize relevant new literature, and explain how CMT incorporates the information into its several programs.

This month, we address issues in "Appropriate Prescribing of Antipsychotic Medications" and in the next issue we will discuss prescribing opiates for chronic pain. As in everything we do at CMT, we welcome your feedback and suggestions for future work.

## Appropriate Prescribing of Antipsychotic Medications

*Reducing Polypharmacy: Can It Be Done?:* While there is no question that antipsychotic medication is the foundation of treatment for patients with schizophrenia and schizoaffective disorder, only recently has attention been placed firmly on the many ways in which antipsychotic drugs are used for which there is virtually no scientific basis. This month we summarize recent articles that highlight two such problematic areas: polypharmacy of antipsychotic medication and use of low-dose antipsychotic medication for non-indicated diagnoses.

Although there is almost no evidence to support the notion that a patient who does not respond to one antipsychotic medication will do any better when given two drugs at the same time, polypharmacy remains a widespread practice. When confronted with the lack of scientific support, clinicians sometimes insist that any attempt to wean patients off their antipsychotic medications in an effort to approximate monotherapy will surely result in catastrophic worsening of symptoms and deterioration in functioning. Some clinicians say that polypharmacy allows them to prescribe lower—and presumably better tolerated—doses of each individual drug, but in fact, as investigators from the University of British Columbia reported at this year's International Congress of Schizophrenia Research, polypharmacy is more likely to be associated with excessive doses.

---

*“Reducing Polypharmacy:  
Can it be done?”*

---



Mistler, Mellman and Drake recently put these dire predictions to a rigorous test (“A pilot study testing a medication algorithm to reduce polypharmacy,” *Qual. Saf. Health Care* 2009;18:55-58). These investigators developed a novel medication-reduction algorithm and compared its effects on 12 adult non-geriatric patients admitted to New Hampshire Hospital, a state-operated facility for patients with psychiatric illness. These patients were on three or more psychotropic agents and/or two medications within the same therapeutic class at the time of admission and agreed to participate in the algorithm-driven medication reduction attempt. Half of the patients had schizophrenia/schizoaffective disorder and the rest had bipolar disorder, depression or “other” diagnoses. A comparison group of 12 age-, number of medication-, and diagnosis-matched newly admitted patients who did not participate in the medication reduction attempt was retrospectively created.

At the time of admission, the intervention patients were on a mean of 3.7 medications and the comparison group patients were on 3.6. Compared to the comparison group, the algorithm-driven medication reduction group had a significant decrease in the number of medications taken with an equal drop in psychopathology as measured by the Brief Psychiatric Rating Scale (BPRS). These results are similar to those reported by Glick and colleagues in a 2006 *Journal of Clinical Psychiatry* paper. Mistler and colleagues concluded “Our results suggest that it is possible to counter the trend toward polypharmacy in a state hospital setting by explicitly focusing on reducing the number of psychotropic medications in the same class using a collaborative, evidence-based algorithm for patients who are already receiving co-prescriptions.”

The Mistler et al study is obviously small and involves hospitalized patients, so it should not be over-interpreted to mean that reducing polypharmacy will always work for every patient. Nevertheless, this is an important step in demonstrating that a concerted effort to reduce polypharmacy can be successful and that it need not entail clinical deterioration.

CMT's Behavioral Pharmacy Management (BPM) program has long included multiple Quality Indicators™ that alert the prescriber to potentially unnecessary polypharmacy. We remind the clinician that there is almost no evidence supporting polypharmacy, that it increases the risks for adverse events and drug-drug interactions, and that it is a costly undertaking with rare clinical payback. Our data show that clinicians respond to our audit and feedback efforts in this area by reducing the total mean number of medications their patients take without sacrificing clinical outcome. Thus, CMT is able to help clinicians and health plans improve care and reduce costs at the same time.

## Low-Dose Antipsychotic Prescribing

*What Is Going On With All the Low-Dose Antipsychotic Prescribing?* Given the complexity of psychiatric illness and the central nervous system, neuroscientists are understandably reluctant to make definitive statements about the brain biology underlying psychiatric symptoms. Research, however, is now sufficiently secure to allow us to assert with a fair degree of certainty that positive psychotic symptoms like hallucinations, delusions, and thought disorders are the direct result of excessive dopaminergic stimulation of the mesolimbic D2-dopamine receptors. The effectiveness of antipsychotic medications for reversing positive symptoms is closely related to the extent that they block dopamine binding to these receptors. Indeed, all marketed antipsychotic drugs have in common the property of D2 receptor antagonism, including the partial agonist aripiprazole.

Of course, this does not mean that an abnormality in any aspect of the dopamine neurotransmission system is the *cause* of schizophrenia. What it means is that as far as we now know, in order to stop a patient's hallucinations and delusions, an effective antipsychotic medication must occupy a sufficient number of mesolimbic D2 receptors and block dopamine from binding to them. How much drug is needed at the receptor depends on the drug's affinity for the receptor, sometimes designated as its Kd value in the pharmacokinetic literature. The higher the affinity an antipsychotic drug has for the D2 receptor the lower the dose of the drug needed to have a dopamine blocking effect. Haloperidol, with its extraordinarily high affinity for the D2 receptor, blocks more than 80% of mesolimbic dopamine receptors at doses around 5 mg per day. Quetiapine, on the other hand, with its very low affinity, requires at least a twice-daily dose of 300 mg to achieve similar D2 blockage.

Despite these facts, antipsychotic medications are persistently prescribed at doses far too low to have an actual antipsychotic effect. The medical equivalent would be something like giving a patient with pneumococcal pneumonia a dose of penicillin only sufficient to inhibit 25% of bacterial activity. Very few infectious disease experts would countenance such a practice, and yet it is the rule when prescribing antipsychotic drugs.

In a recent analysis of claims' data for 830 patients in Oregon recently started on an atypical (second generation) antipsychotic medication, Hartung and colleagues (J Clin Psychiatry 2008;69:1540-1547) found that only 15% turned out to actually have a diagnosis of schizophrenia. Another 27% had bipolar disorder. Most of the patients had diagnoses of either depression or anxiety, neither of which are currently approved indications for any antipsychotic drug (aripiprazole is approved by the FDA for treatment refractory depression and quetiapine is approved for bipolar depression). Many patients, including more than 80% of those on quetiapine, were taking subtherapeutic doses. Thus, most patients receiving antipsychotic medications in the study were getting them at doses that have little or no antipsychotic effect for reasons that have nothing to do with psychosis or mania.

At doses of less than 100 mg quetiapine has very little effect on dopamine activity but it is a strong antagonist of the histamine-1 (H1) receptor. Thus, giving a patient 25 or 50 mg of quetiapine has about the same effect as giving the patient an OTC antihistamine, like diphenhydramine (Benadryl). Low dose quetiapine undoubtedly will help the patient sleep better in much the same way as do any of a number of non-prescription sleep aids available on your local drug store shelves (like Tylenol PM, Sominez, NyQuil, etc). It will also contribute to weight gain and health care expense; Hartung and colleagues state in their paper that Oregon Medicaid spends about \$2.5 million annually on subtherapeutic doses of quetiapine. If a prescription medication for insomnia is needed, generic zolpidem would provide the same benefit at much lower cost and without the metabolic consequences.

Antipsychotic medications are invaluable tools in treating psychotic illnesses and because of them patients with schizophrenia who were once consigned to live their lives in dismal institutions are now able to achieve new levels of independence and quality of life. But they, like all powerful and effective medicines, have serious adverse consequences and are not intended as cure-alls. Hartung et al have provided a valuable service by pointing out the widespread use of inappropriate doses of antipsychotic drugs for inappropriate reasons. A CMT Quality Indicator™ alerts clinicians and health plans to low-dose antipsychotic medication prescriptions and advises re-evaluation of the clinical situation and consideration of safer, less costly alternatives for treating anxiety, depression, and insomnia. This alert will be strengthened in coming months by offering more explicit dose guidelines and new supporting references.



---

*"What Is Going On With All the Low-Dose Antipsychotic Prescribing?"*

---

## Contact us

Jack Gorman, MD	Chief Scientific Officer & Sr. VP, CNS	<a href="mailto:jgorman@cnsnet.com">jgorman@cnsnet.com</a>	914-997-4007
Carol Clayton, PhD	VP, Operations	<a href="mailto:cclayton@cnsnet.com">cclayton@cnsnet.com</a>	919-674-2547
Harold Carmel, MD	VP, Clinical Services	<a href="mailto:hcarmel@cnsnet.com">hcarmel@cnsnet.com</a>	919-674-0270
Susan Clifton	Director, CMT Account Management	<a href="mailto:sclifton@cnsnet.com">sclifton@cnsnet.com</a>	919-674-2527
Janie Shivar	CMT Account Manager	<a href="mailto:jshivar@cnsnet.com">jshivar@cnsnet.com</a>	919-674-0285
Lynn Hamilton	CMT Account Manager	<a href="mailto:lhamilton@cnsnet.com">lhamilton@cnsnet.com</a>	214-601-5816
Al Thompson	Director, Account Implementation	<a href="mailto:athompson@cnsnet.com">athompson@cnsnet.com</a>	919-674-2522
Chris Slocum	Director, Business Operations	<a href="mailto:cslocum@cnsnet.com">cslocum@cnsnet.com</a>	214-766-1169
Sandra Ballentine	Director, Clinical Field Operations	<a href="mailto:sballentine@cnsnet.com">sballentine@cnsnet.com</a>	214-563-2589
Paul Stuve	CMT Account Manager	<a href="mailto:pstuve@cnsnet.com">pstuve@cnsnet.com</a>	573-645-2023
Leigh Steiner	CMT National Account Executive	<a href="mailto:lsteiner@cnsnet.com">lsteiner@cnsnet.com</a>	217-891-1439

## COMING UP

In the next issue of our newsletter we will discuss the latest scientific evidence on *Prescribing Opiates for Chronic Pain*.