# EnhanceMed™ Quarterly Clinical Update

*Highlighting Current Research and Market Updates Affecting Behavioral Health Medical Practitioners*

MAGELLAN HEALTH SERVICES

FALL 2012—VOL. 3, NO. 1

## Mental Health Medication Use on the Rise

One in five Americans is now taking at least one psychotropic medication, an alarming statistic to some mental health professionals. People are given psychotropic medication prescriptions by their family practitioners without an evaluation by a mental health professional. Also, there is mounting evidence from a number of studies that antidepressants provide little more effect than placebo in the treatment of depression. In fact, practice algorithms from several organizations suggest cognitive behavioral therapy or another psychosocial intervention might be equally as effective as any medications. The author believes more people would select a type of psychotherapy versus medication if they only knew how dangerous medications can be and what side effects they bring with them – and he suggests that patients should be provided evidence for informed choices.

Antipsychotics have been aggressively marketed to primary care prescribers and the public (via direct-to-the-consumer advertising) since this class of medications began to be accepted with the introduction of Prozac® in 1987. Another concern is that the medications have been promoted off-label. In the past few years, AstraZeneca, Forest, Glaxo, and Novartis have settled with the Food and Drug Administration (FDA) and the Justice Department. In addition to paying multi-million dollar fines, they have also signed a Corporate Integrity Agreement with the Department of Health and Human Services.

The sales of second-generation antipsychotics almost tripled from 1995 to 2008, and a published physician survey noted that more than half the prescriptions were for unapproved uses. Of particular interest is the use of neuroleptic agents in elderly nursing home residents and foster care children. The elderly are of concern because an FDA black box warning on all antipsychotic agents declares the increased risk of mortality in those patients with dementia-related psychosis. Several years ago, an increased use of antipsychotic and other psychotropic agents was noted in the foster care population in five states. Since then, there has been much discussion around the topic to include the development of federal best practice guidelines for this group.

Smith B. Inappropriate Prescribing. Monitor on Psychology. June 2012;43(6):36-40.

## Switching From Antipsychotic Polypharmacy to Monotherapy

Estimates of antipsychotic polypharmacy among patients with schizophrenia usually range from 10 percent to 30 percent. This rate appears to be increasing over time. So far, the only randomized controlled trials focusing on antipsychotic polypharmacy examined combinations with clozapine. Due to the risks and costs of antipsychotic polypharmacy, some organizations have started programs to reduce its prevalence. Antipsychotic polypharmacy is a common practice that continues despite a lack of supporting evidence and treatment guidelines that discourage it. This is the first report of a randomized trial examining the effectiveness of switching patients with schizophrenia from antipsychotic polypharmacy to monotherapy. The time to all-cause treatment discontinuation (defined as time to change in antipsychotic medication for any reason) was shorter for participants assigned to switch from polypharmacy to monotherapy than for patients assigned to stay on polypharmacy. Switching from polypharmacy to monotherapy resulted in treatment discontinuation much more often than did continuation of polypharmacy. The results supported trials of antipsychotic monotherapy for patients receiving multiple antipsychotics, with the plan that patients should be allowed to return to the polypharmacy combination if an adequate trial of antipsychotic monotherapy was not successful. The study demonstrated that switching to monotherapy can be accomplished for the majority of patients. Sixty-nine percent of those who switched to monotherapy remained on monotherapy for the six-month study period. On average, switching to monotherapy resulted in loss of body mass with no worsening of symptom control and no increase in hospitalization. This study did not examine whether starting polypharmacy is a good idea, but it does make it clear that patients on two antipsychotics may benefit from discontinuing one of the medications.

Susan M. Essock, et al. Effectiveness of Switching From Antipsychotic Polypharmacy to Monotherapy. *Am J Psychiatry.* 2011 Jul;168(7):702-8.

### DSM-5: Psychotic Disorders

A recent article published through the Psychosis Disorder Work Group, provides an update to the discussions occurring with the DSM-5 committee members. The author reports that there are modest changes planned to the diagnoses of psychosis disorders and most are to increase validity, to more clearly define disorders, and to improve treatment. Presently proposed with the update is an attempt to more clearly define the criteria for the diagnosis of schizoaffective disorder. The change will be to Criterion C, separating schizoaffective disorder from schizophrenia with prominent mood symptoms, and recognizing the diagnosis as longitudinal, or "lifetime." A way to measure the severity of the symptoms of schizophrenia will be added with the hope that this ranking measure will provide more information for research on the disease and for a better impact of treatment. Also planned is the introduction of Attenuated Psychosis Syndrome (APS) that is being discussed so that early psychotic symptoms can be identified and treated before extensive brain damage occurs. Recommendations of the Psychosis Disorder Work Group can be found at the DSM-5 website www.dsm5.org and will be reviewed by two expert committees appointed by the American Psychiatric Association. DSM-5 will probably be finalized in early 2013, with release in May 2013.

Tandon, R. Getting ready for DSM-5: Psychotic Disorders. *Current Psychiatry*. April 2012:11(4):E1-E4.

### More on APS

The authors of this article suggest that this new diagnosis has not been totally thought through. In their study, they noted a variety of false positives and false negatives that they feel could stigmatize many patients receiving it.



***EnhanceMed Quarterly Update Produced by Magellan Health Services***

## One of the Greatest Prescribing Challenges – Polypharmacy

Payne and Avery remind us that polypharmacy has the potential to increase adverse drug reactions and medication interactions as well as to decrease adherence to a medication regimen. (As a reminder, polypharmacy in the EnhanceMed program is the prescribing of any three or more medications to an individual.) In this age of evidence-based treatment, practitioners strive to follow recommended guidelines and algorithms, but they are usually developed around one disease state. With additional or more complex clinical problems, medications that might be used for the treatment of several diagnoses are often over-looked as one more pill is added to the array.

A study conducted by Moran in New York found a dramatic drop in antipsychotic polypharmacy once they required clinicians to obtain prior approval to prescribe more than two antipsychotics at once. After the program's discontinuation, the rate of polypharmacy rose again but was still well below baseline.

To decrease the use of polypharmacy, regularly review your patients' medications to assess their therapeutic benefit and the ongoing clinical need to continue them. Ask yourself if the potential benefits are outweighed by risks and side effects, and whether or not the patient is deriving a positive effect from the medications in combination.

Payne R, et al. Polypharmacy: one of the greatest prescribing challenges in general practice. *Br J Gen Pract*. 2011 Feb;61(583):83-4.
Moran M. State Based Program Reduces Polypharmacy. *Psychiatric News*. Nov 18, 2011;46(22):7A-7A

## Polypharmacy and Mortality in Schizophrenia

Finland's national databases have access to documentation of patient care and cause of death. A recent study including 2,588 hospitalized patients with a diagnosis of schizophrenia were followed from the point of enrollment in January 1, 2000, through December 31, 2007. The patients' medical records were linked to their drug prescriptions and mortality in the national registries. Measures for outcomes were computed in Hazard Ratios for all-cause mortality during the use of the co-administration of the medications, adjusting for demographics and clinical variables. The effect of antidepressant use was not studied, but it was observed that antipsychotic polypharmacy did not contribute to excess mortality from natural causes, while benzodiazepine use was associated with increased risk for all-cause mortality and suicide deaths. The results reveal that benzodiazepine use is associated with substantially increased risk of mortality among this population.

Tiihonen J et al. Polypharmacy with antipsychotics, antidepressants, or benzodiazepines and mortality in schizophrenia. Arch Gen Psychiatry 2012;69:476–83.

## Atypical Antipsychotic Augmentation in Major Depressive Disorder (MDD)

In the United States, we are seeing more psychotropic agents being advertised on television through direct-to-consumer (DTC) advertising. This includes a large amount of advertising for Abilify for the treatment of major depressive disorder.

In this article, Inappropriate Prescribing (see the first article), Mr. Smith makes two statements of interest:

- Patients who requested advertised drugs were nearly 17 times more likely to receive one or more new prescriptions than patients who did not request any drugs, and
- According to the Canadian Medical Association Journal (2003), American patients were twice as likely to request advertised drugs as patients in Canada, where most DTC advertising is prohibited.

Both Abilify and Seroquel XR are approved for adjunctive treatment of MDD:

- The key to their use is that they must be used together with an antidepressant, and the studies that were completed generally included only those members who failed one or more other antidepressant.
- The risk and benefits of these medications must be evaluated for every patient because many of the side effects of these medications are independent of dose and may place patients at risk.
- Many clinicians recommend prescription of these medications only after a patient has failed multiple antidepressants with adequate doses and durations.
- Clinicians are also encouraged to ask about adherence before changing or increasing the dose of medication.

### APS (continued)

This was a study of 1,218 treatment-seeking psychiatric outpatients (mean age 37.2 years of age) at a single center, who were screened using the Psychiatric Diagnostic Screening Questionnaire and who endorsed at least one psychotic experience from it (one of the co-authors receives royalties on the use of this test).
Dr. Gaudiano explains to us that the criteria for diagnosing psychotic disorder has been "loosened" and catches a lot of people in its "very wide net." He states that most of the patients diagnosed with APS will never develop a psychotic disorder, but many may well end up being treated with unnecessary neuroleptic agents, which have no proven record for the treatment of this prodromal stage. Also noted is that researchers did not identify a single individual for whom a diagnosis of APS alone could have been made.

Gaudiano B. Prevalence of attenuated psychotic symptoms (APS) and their relationship with DSM-IV diagnoses in a general psychiatric outpatient clinic. *J Clin Psychiatry.* Online ahead of print: October 2, 2012 (doi:10.4088/JCP.12m07788)

### Product Discontinuation: Suboxone® Sublingual (SL) tablets

Reckitt Benckiser Pharmaceuticals announced that it will voluntarily cease production of buprenorphine and naloxone (Suboxone) SL tablets, an opioid-dependency treatment. The individually sealed SL film formulation will remain available and replace the tablet form. The discontinuation decision was based on a recent analysis of accidental pediatric exposures based on data from the US Poison Control Centers that revealed that children were 7.8 to 8.5 times more likely to accidentally take Suboxone SL tablets than the Suboxone SL film depending on the study period. The distribution of Suboxone SL tablets is expected to be discontinued within the next six months or sooner.
http://www.rb.com/site/RKBR/Templates/MediaInvestorsGeneral2.aspx?pageid=1328&cc=GB

**For questions, contact Mike McDonald, PharmD, at 517-243-4132 or email PharmacyConsultation@magellanhealth.com**