The following is an extract of:
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**Bottom Line:**
- In outpatient psychiatric visits, there was a significant increase nationwide in polypharmacy involving antidepressants and antipsychotics from 1996-2006.
- Prescriptions for ≥2 psychotropics increased from 42.6% in 1996-7 to 59.8% in 2005-6 (p<.001)
- Prescriptions for ≥3 psychotropics increased from 16.9% in 1996-7 to 33.2% in 2005-2006 (p<.001)
- The three most likely medication combinations remained relatively stable over the study years and were: antidepressants with sedative-hypnotics (23.1%), with antipsychotics (12.9%); and with other antidepressants (12.6%).
- Prescription of mood stabilizer polypharmacy remained stable.

This is the first study to examine trends in psychotropic polypharmacy in a nationally representative sample of office-based psychiatrists. The authors looked at trends in within- and between-class psychotropic polypharmacy from the years 1996-1997 and 2005-2006. Examined variables included: the most common within-and between-class combinations of psychotropic medications, sociodemographic and clinical characteristics.

**Study Background**
In clinical practice psychotropic polypharmacy has become increasingly common, especially among those with schizophrenia and mood disorders. While certain types of psychotropic polypharmacy can be necessary and effective, especially for bipolar and major depressive disorders, there remains inconclusive supporting evidence for this practice in treating schizophrenia and other psychiatric disorders. Quality improvement and physician education efforts have been aimed at limiting psychotropic polypharmacy to clinically necessary situations. However, gaps exist in the current knowledge surrounding patterns of psychotropic polypharmacy in routine clinical practice.

**Study Details**
This study analyzed data from 1996-2006 in the National Ambulatory Medical Care Survey (NAMCS), a national survey of office-based physicians, for whom visits were randomly sampled during a 1-week period (n=284,638). The main outcome measures were the number of medications and specific psychotropic combinations prescribed at each visit. The study sample was limited to visits to psychiatrists (n=13,079) made by adults >18 years in which the consumer given a psychiatric diagnosis. The study focused on four major drug classes: antidepressants, antipsychotics, mood stabilizers, and sedative-hypnotics. Other psychotropic medications were also assessed in calculating the total number of prescribed medications. Up to six psychotropic medications and three psychiatric diagnoses were recorded per visit. The primary source of payment was classified as private, Medicaid, Medicare, self
pay, or “other”. The authors also looked at age, sex, race/ethnicity, office setting, visit order (established vs. new visit), and geographical region.

Results and Limitations

Between 1996 and 2006, office visits involving ≥2 psychotropics increased from 42.6% to 59.8%, while those involving ≥3 psychotropics increased from 16.9% to 33.2% (OR 2.60, 99% CI 1.61-4.22, p<.001). Offices visits involving ≥2 psychotropics were more likely among those aged 45-64 years; those with diagnoses of major depression, bipolar disorder, anxiety disorders, or schizophrenia; those with comorbid disorders; and those with public or “other” insurance.

Antidepressants (61.7%) were the most frequently prescribed class, followed by sedative-hypnotics (31.5%), antipsychotics (22.4%) and mood stabilizers (12.4%). The most frequently prescribed combinations were antidepressants/sedative-hypnotics (23.1%), followed by antidepressants/antipsychotics (12.9%), and then antidepressants/antidepressant (12.6%). There was a significant increase over time of visits involving antidepressant/antipsychotic combinations, as well as those for ≥2 antipsychotics or ≥2 antidepressants. Over this time period prescription of mood stabilizer combinations remained stable.

The authors also found that significant time trends were mainly limited to co-prescription of ≥2 antidepressants or ≥2 antipsychotics, as well as combinations of these two classes. Time trends remained significant even after adjusting for psychiatric diagnosis and comorbidity. The authors also report on several important findings without discussion. These include: 1) there was decreased psychotropic polypharmacy in the elderly (≥65 yrs) relative to middle aged consumers; 2) no regional or racial differences were detected; 3) prescription of ≥2 psychotropics also increased by nonpsychiatric physicians at an even higher rate over these years (from 1.9% in 1996-1997 to 5% in 2005-2006); and 4) there was no change in the rate of patients referred from primary care to psychiatry.

The authors note several limitations, including: 1) the observational and cross-sectional nature of the study design which does not allow for looking at previous response to monotherapy or for looking at trends in psychotropic polypharmacy on clinical outcomes; and 2) the inability to look at medications prescribed by physicians other than the ones surveyed; and 3) the fact that patient duplication may have occurred since NAMCS only looks at visits, not at individual patients.

Clinical Implications

Between the years 1996-2006, there was an increasing nationwide trend in outpatient psychiatric visits for the prescription of psychotropic polypharmacy, especially for combinations involving antidepressants and antipsychotics and for the co-prescription of ≥3 psychotropics. The authors reason that a change in style in psychiatric practice may contribute to the increase in antidepressant/antipsychotic polypharmacy, and a growth in the off-label use of atypical antipsychotics as sedatives. The authors note that the recent increase in the rate of antipsychotic and antidepressant polypharmacy is consistent with results of other regional studies showing a recent increase in the use of these medications. Psychotropic polypharmacy has become more prevalent despite increased scientific investigation into this practice and attempts to delineate criteria for rational psychotropic polypharmacy. The authors emphasize the need for renewed efforts to limit the use of these combinations to clearly justifiable circumstances.

Drs. Mojtabai and Olfson report receiving research report and honoraria from various pharmaceutical companies.