disorder, the adoption of persistent dissociation within this diagnosis allows improved clinical utility and, therefore, strengthens the relevance of this diagnosis.


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## Monotherapy Versus Polypharmacy for Hospitalized Psychiatric Patients

TO THE EDITOR: Franca Centorrino, M.D., et al. (1) observed that patients who received antipsychotic polypharmacy received a median total final antipsychotic dose that was 78% higher than in patients who received antipsychotic monotherapy, with no appreciable gain in clinical benefit. This was based on a relatively small number of patients (N=140) who were admitted to the hospital in 1998 for relatively brief lengths of stay (usually less than 1 month).

The dosing data is consistent with what we have observed within the 17 hospitals operated by the New York State Office of Mental Health, a system that serves seriously and persistently mentally ill patients for lengths of stay that can extend for many months. Prescribing and demographic information for all inpatients is available to us in a research database, and we have previously published reports of the co-prescribing of antipsychotics (2–4). An analysis of data for one calendar day (Nov. 15, 2003) revealed that the proportion of patients with schizophrenia or schizoaffective disorder receiving combinations of antipsychotics was 1,611 of 3,134 (51.4%), with 1,396 (44.5%) receiving two antipsychotics and 215 (6.9%) receiving three or more. The mean dose prescribed for monotherapy was 5.2 mg/day of risperidone, 23.7 mg/day of olanzapine, or 690.7 mg/day of quetiapine. When it was used in combination with other antipsychotics, the dose of 5.0 mg/day of risperidone, 22.8 mg/day of olanzapine, and 630.8 mg/day of quetiapine did not differ meaningfully from the monotherapy dose. Major dose reductions in either or both antipsychotic medications were not seen. A limitation to our 1-day snapshot—and also applicable to Dr. Centorrino's 3-day minimum observation period—was the lack of information on the extent to which antipsychotic co-prescribing is influenced by a cross-titration process that occurs during the switching of antipsychotics rather than a deliberate long-term plan.

At present, whether antipsychotic co-prescribing is clinically more efficacious or not remains unknown. A major confound that will need to be addressed, especially among the seriously and persistently ill in our state institutions, is that the purported association between polypharmacy and poor outcome does not necessarily mean that polypharmacy leads to poor outcome but that poor outcome may lead to aggressive prescribing that includes high doses and polypharmacy. This is the same type of confound that has plagued dose-response studies with flexible rather than fixed-dose designs. Although Dr. Centorrino argued that there is probably no benefit, it remains to be tested using an appropriately designed (randomized, double-blind, fixed-dose) clinical trial.


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TO THE EDITOR: Dr. Centorrino et al. are to be commended for addressing an important issue that is becoming more and more a focus of clinical concern, given the growing use of multiple antipsychotic medications administered simultaneously (1). This has increasingly become the case, given the favorable side effect profile of atypical antipsychotic medications, which allow combination strategies to be considered more readily as an option. However, while the authors imply that short-term combination treatment strategies are associated with "major increases in drug exposure, adverse events, and time in the hospital but with no apparent gain in clinical benefit" (p. 700), the authors failed to consider seriously the option that this patient subpopulation receives only antipsychotic combinations because it does not respond to single antipsychotic medications after a period of time and may therefore be considered treatment resistant. Thus, they may fall into a subclass of schizophrenia patients who exhibit a biological subtype of the illness that is treatment resistant and more prone to side effects (in addition to higher doses and a