as though patients with ≥3 baseline manic symptoms actually had lower 3-month Young Mania Rating Scale scores if they were given antidepressants, leading to the appearance that for these more severely mania-ridden patients, antidepressants actually had antimanic effects! Additionally, in that same figure, it appeared that the entirety of the supposed deleterious effect of antidepressants on 3-month Young Mania Rating Scale scores was accounted for by patients with only 1 baseline manic symptom. Patients with 0 or 2 baseline symptoms did not have differential 3-month Young Mania Rating Scale scores based on antidepressant treatment status. This rather odd set of findings seems to cast doubt on the confidence of the authors' conclusions about antidepressants and manic symptom outcomes.

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Dr. Rasmussen reports no competing interests.

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Dr. Goldberg Replies

TO THE EDITOR: We appreciate the comments by Dr. Rasmussen regarding our recent study of adjunctive antidepressants plus mood stabilizers for bipolar depression with concomitant mania symptoms. However, a few clarifications appear in order.

First, we did not assess discrete switches to frank mania or hypomania because our main goal was to determine whether adjunctive antidepressants were effective for bipolar patients when accompanied by any degree of mania. The observation that such usage worsened mania was a secondary result. We reported those results as worsening Young Mania Rating Scale scores because such dimensional outcomes are more sensitive measures of change than categorical outcomes. Many clinicians feel that mood destabilization only involves discrete "switching" from one affective pole to another, but such a categorical distinction is less meaningful when patients already manifest signs of both poles. In fact, if the "switch" phenomenon were categorical rather than dimensional, then antidepressant-induced "switching" from mixed to pure mania would, by definition, involve merely the retention of mania symptoms alongside reduction of depressive symptoms. This was not seen in our study.

Second, in Table 2, among subjects with no DSM-IV-defined mania symptoms, baseline Young Mania Rating Scale scores were higher in those who were antidepressant-free than antidepressant-treated. One must remember that the Young Mania Rating Scale was designed to assess change in inpatients rather than diagnose mania. It includes many nonspecific symptoms related to agitation and aggression and assigns lower-range scores on individual items for behaviors that are not necessarily pathological (whereas DSM-IV criteria are defined as falling outside the norm). Thus, our results may simply suggest that clinicians avoided antidepressants in those with nonspecific agitation/aggression despite the absence of DSM-IV mania criteria.

Third, as noted in the editorial accompanying our article, the observed significant interaction effect between baseline mania symptoms and antidepressant use that we depicted using a box plot (Figure 3) is complex: the slopes of the lines are different within each subgroup of patients with differing numbers of mania symptoms. Because of these changing relationships, it would have been a misinterpretation of the interaction effect to assume a simple linear relationship between the number of baseline mania symptoms and Young Mania Rating Scale severity score at follow-up. Rather, the interaction effect means that in the presence of any mania symptoms at baseline, Young Mania Rating Scale scores were higher after 3 months when antidepressants were added to mood stabilizers. Furthermore, in Figure 3, it would have been an overinterpretation (in a post hoc stratification within a subgroup analysis) to assert that there was any notable antidepressant-related improvement in mania in those with more than 3 baseline manic symptoms. The changes were not meaningfully different in magnitude between the two groups; their confidence intervals greatly overlapped.

We reiterate that the main finding of our study was the lack of efficacy of antidepressants for the treatment of bipolar depression, in this case when accompanied by mania symptoms. Consistent with findings reported previously from the STEP-BD randomized comparison of mood stabilizers with or without antidepressants for pure bipolar depression, our results contradict assumptions that antidepressants effectively treat bipolar depressive symptoms.

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Dr. Goldberg's disclosures accompany the original article.

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Prevalence and Recovery From Anorexia Nervosa

TO THE EDITOR: In the August 2007 issue of the *Journal*, Anna Keski-Rahkonen, M.D., Ph.D., et al. (1) reported substantially higher lifetime prevalence and recovery rates from anorexia nervosa than rates reported in previous studies. To reach these conclusions, the authors diagnosed their subjects retrospectively after interviewing them by telephone. The diagnosis and assessment of recovery relied on the estimation of body mass index. The authors reported values of body mass index 5.9 to 10.2 years earlier, with a precision of 0.1 kg/m^2 (Table 1, Table 2), and a rate of recovery that was almost the same at 5 out of 6 points in time (six, eight, seven, seven, seven, and two patients [Figure 1]). Thus, in six subjects who recovered at least 4.5 years before the telephone interview, body mass index increased from approximately 16 to normal in 6 months. Assuming that their height was 1.6 m and their

normal body mass index was 20, these patients gained 10 kg (1.6×1.6×4) in 6 months. An anorexia patient with a body mass index of 16 needs to eat approximately 2500 kcal per day in order to increase her weight at this rate, provided that her level of activity is low. While this marked increase in body mass index is possible, it is not consistent with other clinical reports or observations in clinical practice. For example, one of the authors previously reported that there was no significant increase in body mass index in 20 weeks in anorexia patients with an average body mass index of 17.3 (2).

Retrospective estimates of body mass index reported by Dr. Keski-Rahkonen et al. suggest a level of precision that may not be entirely plausible. The authors referred to two studies supporting the possibility that telephone interviews can provide reliable retrospective information (3, 4). However, one of these studies examined a group comprised of mostly normal weight individuals (3), and in both studies the time interval between the telephone interview and the determination of body weight was shorter than the corresponding interval in the study conducted by Dr. Keski-Rahkonen et al.

Dr. Keski-Rahkonen et al. should have made an estimate of the error associated with recalling body weight many years later and an estimate of the differences between a population of individuals with anorexia and a population of normal-weight individuals in order to address this limitation of their conclusions.

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Disorders of Sex Development: Improving Care for Affected Persons and Their Families

TO THE EDITOR: In their clinical case conference, published in the October 2007 issue of the *Journal*, J. Michael Bostwick, M.D., and Kari A. Martin, M.D., (1) correctly pointed out that clinical management of intersex conditions is highly controversial. They failed to note, however, two recent and important developments aimed at improving care in this area.

One recent development is the Consensus Statement on Management of Intersex Disorders (2). This document, which grew out of a conference of 50 international experts in diverse medical specialties, marked the first time researchers and clinicians thoroughly revisited the medical standard of care for diagnoses of intersex conditions since John Money and his associates first proposed treatment standards in the 1950s. Participants agreed to recommend several important changes to care that demonstrate a significant shift in thinking for the treatment of intersexuality.

Owing to the recognition that patients and parents (and even clinicians) find the terminology and labels surrounding intersex conditions confusing and stigmatizing, participants adopted a new nomenclature in which *intersex* was replaced by the more general descriptor "disorders of sex development," which refers to congenital conditions in which chromosomal, gonadal, or anatomical sex development is atypical. Terms such as hermaphroditism and gender-based diagnostic labels are to be replaced with clinically descriptive terms (e.g., androgen insensitivity syndrome).

Acknowledging that there are minimal systematic outcome data pertaining to genital surgery, that orgasmic capability may be harmed by such surgery, and that there is little documentation to support the widely held belief that early surgery relieves parental distress about atypical genitals, the Consensus Statement on Management of Intersex Disorders states that surgery should only be considered for young girls with "severe" genital virilization. Participants also noted that psychological care should be integral to medical care, that homosexuality should not be construed as an indication of incorrect gender assignment, and that the potential for fertility—originally emphasized for female gender assignment only—should be an important consideration for male gender assignment as well.

The second development is the publication of the *Clinical Guidelines for the Management of Disorders of Sex Development in Childhood* and *the Handbook for Parents* (3, 4). Outlining a patient-centered model of care, these guidelines were developed in consultation with clinical specialists, affected individuals and their families, and patient support groups.

Much remains to be done to improve care for persons and families affected by disorders of sex development. However, these two developments are important steps in that direction.

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