Treatment of Depression: Men and Women Are Different?

Using data from more than 1,000 twins from the vast birth-certificate-based Virginia Twin Registry of individuals born between 1940 and 1974, and assessing them with personal interviews at least 1 year apart, Kendler and Gardner (1) have produced insights into psychosocial risk factors for women and men with major depression. The risk factors that had the greatest impact on liability to major depression in women were neuroticism, divorce, and absence of parental warmth, social supports, and marital satisfaction. For men, they were childhood sexual abuse, conduct disorder, drug abuse, prior history of major depression, and financial, occupational, and legal stressful life events. Matching between twin brothers and sisters on genetic and familial environmental background (the nature of the twin design), the authors conclude that women's depressions are defined by deficiencies in caring relationships and interpersonal loss and men's by failure to achieve expected instrumental goals and lowered self-worth.

At first glance, the results seem to fulfill sexist stereotypes. Maybe the results are due to where the study was carried out (in Virginia, a state with large rural areas), or to the older age range of the sample (39 to 73 years), or to the lack of racial diversity in the all-Caucasian sample. There are few possibilities for replicating these findings in samples of different composition. If the findings generalize to younger birth cohorts and diverse samples, these differences might make a difference in treatment. Understanding of gender differences in psychosocial risk could contribute to the search for personalized treatment.

What Do We Know About Treatment of Men and Women?

Studies of depressed patients often yield smaller numbers of men than women (2). The established reasons for this include differences in help-seeking patterns and in prevalence rates. It is well known that women, at least in the United States, are more likely than men to seek treatment for nearly all disorders (excluding those specifically male related) (3, 4). This may be in part because women, more frequently than men, enter the health care system as soon as they become sexually active, for birth control or for pregnancy. However, if men are more likely to attribute their depression to failure in finances, occupation, and achievements, the health care system may not be a likely place for them to seek help. Prevalence rates of depression, too, are consistently higher in women than men across diverse cultures (see reference 5 for a discussion). With these caveats, there are still sufficient studies, especially when pooled in meta-analyses, to draw some conclusions.

Are different risk factors for men and women reflected in their treatment response? If women's depression is related to problems in caring relationships and men's to failure in achievement, you might expect psychotherapy to be more helpful for women. The Sequenced Treatment Alternatives to Relieve Depression Study (STAR*D) did not find a gender preference for cognitive-behavioral therapy

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(CBT) or any gender differences in response to CBT compared with medication (6). A 2008 meta-analysis (7) including 83 controlled clinical trials of psychotherapy for depression in which a psychological treatment was compared with a control condition found no association between effect size and gender, with one exception: women with postpartum depression had higher (better) effect sizes than other women. Sixty-seven of the 83 studies examined CBT. In virtually all individual studies, the authors noted that the large majority of participants were women, and some studies included only women. This raises again the problem of recruiting men to treatment or research and the issue of statistical power when looking at moderators of treatment effect in single studies. While individual studies may not have the power to show how gender affects treatment response, the pooling of studies in a meta-analysis can yield sufficient power.

The Cuijpers group, who brought us comprehensive meta-analysis of the depression psychotherapy literature (7), also shared their latest, as yet unpublished, findings about Internet psychotherapy. Men's reluctance to come to treatment might be less apparent in these studies. Primary data were reviewed from 18 randomized controlled trials comparing the effects of Internet-based guided self-help treatments for depression with no treatment control groups, including data from 747 male and 1,605 female depressed participants. In all but one study, the psychotherapy was CBT. Overall, the effects of treatment were significant and large (Cohen's d=0.74; 95% CI=0.60–0.87). Multilevel analyses of several sociodemographic and clinical predictors of outcome, including gender, were examined. No indication was found that gender was a significant predictor of outcome. The only significant predictor identified was baseline severity of depression, with more severe cases benefiting more from treatment than less severe cases, compared with the control group. CBT, the most widely used evidenced-based psychotherapy, is overrepresented in these reviews.

Understanding of gender differences in psychosocial risk could contribute to the search for personalized treatment.

What about gender differences in response to medication? STAR*D, with over 4,000 patients, found that lower remission rates on citalopram in the first stage of treatment were associated with having a lower income, being non-Caucasian, being less educated, and being male (8). Gender did not influence early attrition (9), and gender differences were not mentioned in Rush's (10) final summary of STAR*D. The overall results did not seem to vary by gender.

A study of 139 depressed male and 246 depressed female outpatients (11) receiving a range of antidepressant medication (selective serotonin reuptake inhibitors [SSRIs], tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, and reversible inhibitors of monoamine oxidase A) found no gender differences in course of treatment or treatment response. The authors noted differences in symptoms and comorbid psychopathology between men and women, which may be related to help-seeking selection bias, but these differences did not translate into differential outcomes.

Finally, a study of 235 depressed men and 400 depressed women (12) found that women had a more favorable response to sertraline than to imipramine. The reverse was true for men. The female response was primarily in premenopausal women, suggesting that female sex hormones may enhance response to SSRIs or inhibit response to tricyclics. This may be an interesting lead.

Despite this absence of evidence, if gender differences in treatment are raised among psychiatric clinicians, numerous clinical examples of the different psychotherapy content of men and women are described. Our rating assessments may not be subtle enough to detect gender differences, or perhaps gender is becoming more equalitarian, as worrying about work is not uncommon among women and struggles with relationships are the psychotherapy concern of at least some depressed men. No data on gender differences on the content of psychotherapy could be found.

Turning now to the family, do the different gender depression risk factors translate into a family impact? Currier et al. (13), in presenting findings from a large family history study, provided a comprehensive review of existing family studies. While they found higher rates of transmission of depression in the families of female as compared with male patients, which may reflect reporting bias, they note that studies with direct interviews of family members do not show the difference.

Studies of offspring (i.e., children at high risk for depression) are a variant of family studies. The serious impact of a depressed mother on her children has been shown in numerous studies (14). The effects of a depressed father are less known, again because the samples of fathers are too small (2, 15). A community sample of over 22,000 children found that depressed fathers as compared with mothers had about half the negative impact on their offspring's emotional behavioral health (16).

The corollary to the observation that parental depression has a negative impact on offspring may be seen in studies showing the positive effects of parental remission. At least three studies have shown that children's symptoms improve if their mothers' depression remits (17–19). This effect was seen whether the mother's remission was achieved with medication (in STAR*D) or with psychotherapy. This effect was also seen in studies of children who received treatment for depression, where it was observed that the children did not remit if the mother remained depressed (20). These studies included only mothers or had too few fathers for any conclusions to be drawn on paternal effects.

Conclusions

The implication of different risk factors for men and women remain elusive, as do the depressed men recruited for many of these studies. For all patients, and especially those with young children, the urgency of a prompt, rapid, and sustained remission, whether by medication or psychotherapy or both, to benefit the patients and their children is obvious. Recent efforts to develop targeted personalized treatment should help eventually to speed remission. Biomarkers, not psychosocial risk factors, may have more of a chance of personalizing treatment to achieve remission. Until that happens—and even if it does—patient-centered treatment using medication and/or psychotherapy that explores the psychosocial context of depression is likely to give the best chance of patient compliance and satisfaction, regardless of gender. Kendler and Gardner's findings remind us that women and men may become depressed in different contexts. These different risks offer a road map for clinicians in their formulation of the psychological issues important to the patients they treat.

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