Sampling Biases in Studies of Gender and Schizophrenia: A Reply

by Jill M. Goldstein

Abstract

Some of the findings on gender differences in schizophrenia have been inconsistent, particularly, those regarding brain abnormalities. The inconsistency in findings most likely can be explained by sampling differences across studies. Walker and Lewine argue that the sampling differences can be explained, in large part, by gender differences in help-seeking behavior and commitment status. This article argues that commitment status does not explain sampling discrepancies in studies on gender differences in schizophrenia.

The main argument of Drs. Walker and Lewine (1993, this issue) is that inconsistencies in the literature on gender differences in schizophrenia can be explained by sampling differences across studies. Further, they argue that the sampling biases can in large part be attributed to gender differences in voluntary versus involuntary commitment status. They contend that schizophrenic males are more likely to be involuntarily committed because of their increased risk of socially deviant behavior. In contrast, schizophrenic females will be more likely to acknowledge their distress and seek voluntary treatment. Thus, samples of schizophrenic subjects with more involuntary patients will include males with less severe symptoms, because the threshold for involuntarily committing them is low. These samples will also include more severe females, because they are less likely to be involuntarily committed. On the other hand, samples of voluntary patients will include less severe females, because females are more likely to seek help regardless of severity, and more severe males because it would take a severe illness for a man to commit himself.

I would argue, as do Walker and Lewine, that inconsistencies in the literature on gender differences in schizophrenia are most likely due to differences in sampling across studies. However, I would also argue that involuntary versus voluntary commitment status is not a basis for making this argument. Rather, as I have mentioned previously, there is a gender difference in the proportion or prevalence of expressing particular forms of schizophrenia (Goldstein et al. 1990), and men may be at higher risk for greater severity. Thus, studies that use clinical samples of convenience may or may not sample those men and women who differ. For example, in a study that includes a clinical sample of chronically disabled schizophrenic patients, gender differences may be attenuated. This may occur because schizophrenic women have been found to have better prognoses than men (Angermeyer et al. 1989), and schizophrenic women who have either recovered or have little disability would not be found in a chronic sample. In a previous publication, we showed that, among patients with multiple hospitalizations, gender differences were attenuated compared to studies of first-admission patients (Angermeyer et al. 1989). I would argue that studies of gender differences in brain abnormalities that use chronically disabled schizophrenic patients may also produce attenuated gender effects. Chron-
ically disabled female schizophrenic subjects are also more likely to have earlier ages of onset, and thus, studies using these samples may have excluded women with better prognoses who have later onsets, for example, in their middle to late thirties or forties, a phenomenon that is more characteristic of females than males (Angermeyer and Kühn 1988). The women with better prognoses may also have fewer structural and functional brain abnormalities.

How does the above argument differ from Walker and Lewine's? We might make the same argument regarding severity of illness. That is, sampling chronic cases with early ages of onset would attenuate gender differences, because more severely ill women would be included and women with later ages of onset and less severe forms of the illness would be excluded. However, Walker and Lewine would extend their position by saying that controlling for gender differences in involuntary versus voluntary commitment status would, in large part, account for gender differences in severity and thus would explain discrepancies in studies on gender differences in schizophrenia. I would argue that using commitment status to account for gender differences is unnecessary, and in fact, there is some evidence against this position.

What does the help-seeking literature tell us about whether involuntary versus voluntary commitment status for schizophrenia differs by gender? Walker and Lewine argue that the help-seeking literature supports the argument that there are gender differences in involuntary versus voluntary commitment status for schizophrenia. They argue that gender differences in help-seeking behavior among schizophrenic patients leads, in part, to gender differences in commitment status, which in turn contributes to explaining gender differences in hospitalization patterns. That is, male and female schizophrenic patients are selectively hospitalized based on traditional perceptions of sex roles. However, almost all the studies quoted by Walker and Lewine regarding help-seeking behavior fail to focus specifically on schizophrenia as it is currently diagnosed using DSM-III and DSM-III-R (American Psychiatric Association 1980, 1987) schizophrenia (e.g., Kastrup 1987; Chu et al. 1989; Weyerer and Dilling 1991). Why would this be different than studying the influence of selection factors for DSM–II (American Psychiatric Association 1968)–diagnosed cases (e.g., Chu et al. 1989), psychotic patients in general (e.g., Kastrup 1987), or other diagnoses (Weyerer and Dilling 1991)?

A great deal of the literature on help-seeking behavior has involved nonpsychotic disorders (Greenley and Mullen 1990), not schizophrenia. It is not clear that selection factors significantly affect hospitalization patterns for schizophrenia or other psychotic disorders. Given that earlier criteria for schizophrenia, such as in DSM–II, included significantly more women than men with affective disorders (Lewine et al. 1984), it is unclear in studies using DSM–II–diagnosed schizophrenic patients (e.g., Chu et al. 1989) whether the effect of gender can be attributed to schizophrenic women or to women with affective disorders. For example, people with affective disorders are treated and perceived differently by clinicians than those with schizophrenia, especially regarding prognosis or treatment success (McDonald-Scott et al. 1992). Relatives may also view these disorders, or symptoms associated with them, differently in their kin (McDonald-Scott et al. 1992). This may in turn affect their commitment behavior toward the patient. Thus, for example, if DSM–II–diagnosed schizophrenic women are more likely to be rediagnosed as having affective disorders by current criteria, then perhaps findings on gender differences in commitment behavior in studies using these diagnostic criteria are not a function of gender differences in schizophrenia.

Some evidence supporting this argument comes from an earlier study of ours that investigated the impact of gender on help-seeking behavior and rehospitalization patterns among schizophrenic patients (Goldstein and Kreisman 1988). We studied the impact on rehospitalization and length of stay of mothers’ and fathers’ tolerance of symptomatic deviance expressed by their schizophrenic sons versus daughters, and their parents’ feelings of responsibility for their care. We were specifically interested in whether social role expectations of sons versus daughters would influence the parents’ perceptions of symptoms. The study was controlled for severity of symptoms. We examined affective and psychotic symptoms. (Deficit symptoms were not well measured in this study.) Further, we tested whether the parents’ tolerance of symptomatic deviance and feelings of responsibility for care, in turn, had an effect on hospitalization patterns.

Most studies of family attitudes about schizophrenia combine all relatives’ attitudes. If investigators are interested in gender, they ex-
amine the relatives' attitudes toward male versus female ill relatives. We assumed that mothers and fathers would have different responses to sons and daughters than siblings or spouses would have to each other. Further, we hypothesized that the parents' responses would depend on the type of symptoms expressed by their offspring. Given that there is evidence that schizophrenia is expressed differently in males and females (Lewine 1981; Goldstein and Link 1988), it was essential to control for type and severity of symptoms in order to test directly for the effect of sex-specific social role expectations. (This has not been done by other studies of family attitudes, most likely because it was assumed that the illness was the same in men and women.) Findings showed that the tolerance of symptoms, in part, depended on the sex of the offspring, but that tolerance differed for mothers and fathers. However, when severe psychosis was expressed by either proband, both parents expressed a low tolerance of symptoms in sons and daughters, and felt less responsibility for their care. This would argue against Walker and Lewine's hypothesis that there are significant differences in the commitment behaviors of families toward actively psychotic schizophrenic sons and daughters.

Further, tolerance of deviance and family responsibility for care explained small proportions of the variance in rehospitalization patterns over a 10-year period (Goldstein and Kreisman 1988). Thus, although social norms and expectations associated with sex had some effect on hospitalization patterns, it was not a primary factor in understanding gender differences in inpatient service use for schizophrenia.

What does the commitment status literature tell us about whether there are gender differences among schizophrenic patients? There are only a few studies in the literature, of which I am aware, that have specifically examined gender differences in commitment status for schizophrenia. One found that schizophrenic male patients were more likely to be involuntarily committed than schizophrenic female patients (Linsky 1970). However, this study was conducted in 1970, and therefore current diagnostic criteria were not used. Given Lewine's work mentioned above (Lewine et al. 1984), it is unclear from Linsky's (1970) study whether schizophrenic women were more often voluntarily admitted, or whether those women who were voluntarily admitted were more likely to be affective disorder patients.

Another study conducted in the early 1980s found no significant gender differences in commitment status for schizophrenia. Rosenfield (1982) investigated whether psychiatrists had a differential bias in hospitalizing schizophrenic men versus women, controlled for clinical history, in an emergency room setting (Rosenfield 1982). The third study was one that we conducted on a representative population of first-admission schizophrenic patients in Hanover, Germany (Angermeyer et al. 1989). We found that there was no significant gender difference in involuntary versus voluntary commitment status for schizophrenic patients diagnosed by DSM-III criteria (with no limitation of age at onset to 45). Further, we found that commitment status did not significantly predict risk for rehospitalization or number of rehospitalizations over a 3-year period and did not explain the effect of gender on rehospitalization. Involuntary commitment status significantly contributed to length of hospital stay, but accounted for only a small proportion (7%) of the effect of gender on length of stay. Further, this study could not control for symptom severity, and therefore it is unclear whether even the small effect of gender on length of stay accounted for by commitment status would hold if gender differences in symptom severity were controlled.

This study also tested for the effects of other help-seeking behavior on hospitalization patterns. Compared to schizophrenic men, women in this sample were significantly more likely to have sought outpatient treatment before their first hospitalization, even though there were no significant gender differences in duration of symptoms (Angermeyer et al. 1989). This would seem to support Walker and Lewine's position. However, help-seeking behavior did not have a significant effect on rehospitalization patterns, nor did it explain the effect of gender on rehospitalization. This study was controlled for the effects of marital and employment status.

The results of these three studies (Rosenfield 1982; Goldstein and Kreisman 1988; Angermeyer et al. 1989) suggest that once a person diagnosed with schizophrenia is disabled enough to become hospitalized, illness factors are more likely to explain gender differences in selection into treatment. In fact, the general medical literature on help-seeking behavior has also shown that the
more severe the illness, the less likely that gender will have a significant effect on help-seeking behavior (Marshall et al. 1982).

What does other literature on gender differences in schizophrenia tell us about the effect of commitment status on discrepancies in studies of gender differences? Walker and Lewine (1992) “assume that samples drawn from State hospital inpatient facilities, … will contain a higher proportion of involuntary patients than will samples drawn from outpatient or private inpatient facilities” (p. 4).

Thus, according to their argument regarding gender differences in commitment status, studies using inpatient State hospital patients rather than outpatient or private hospital samples would include more severely ill females. Gender differences would therefore be attenuated. The difficulty with this argument is that commitment status is confounded with severity of illness. Although I would agree that gender differences would be attenuated in samples of chronically disabled schizophrenic patients, I would argue that this would not be accounted for by controlling for commitment status. Rather, I would argue that identifying gender differences in schizophrenia may in part depend on where along the continuum of chronicity the sample was drawn.

One test of the difference between Walker and Lewine’s argument and my emphasis would be to examine gender differences in an outpatient sample (i.e., voluntary status) of chronically disabled schizophrenic patients. This kind of sample would eliminate confounding of commitment status with chronicity or severity. We have recently completed a pilot study of gender differences in brain dysfunction in schizophrenia using a sample of chronically disabled outpatients compared to normal controls (Goldstein et al. 1992, submitted for publication b). Preliminary results suggest that gender differences in neuropsychological dysfunction are attenuated in this kind of sample compared to the few other published studies in the literature examining these issues (e.g., Haas et al. 1989; Hoff et al. 1992).

Other evidence to support this position includes research on gender differences in a “representative” population of schizophrenic patients, regardless of the type of facility from which the sample was drawn. In a representative sample, selection bias is not a problem. Thus, if significant gender differences are found in representative samples of schizophrenic patients, one is more likely to argue that a lack of significant gender effects in clinical samples of convenience may be due to sampling biases. Goldstein and colleagues, who reported a number of gender differences in schizophrenia, analyzed data from a State hospital facility (Goldstein et al. 1989). The sample was representative of the population of treated schizophrenic patients for a large catchment area because it was the only State psychiatric facility available in Iowa that admitted acute patients (82% of the schizophrenic sample were first admissions). Beiser and Iacono, who conducted a community study of schizophrenia, found a number of significant gender differences in schizophrenia (Beiser 1992; Iacono and Beiser 1992). They sampled from inpatient and outpatient facilities and found that only about 10 to 13 percent of schizophrenic patients were never hospitalized, and there was no gender difference in unhospitalized patients (Beiser, personal communication 1989). Castle and colleagues, who also studied a representative sample of treated schizophrenic subjects, reported a number of significant gender differences in schizophrenia (Castle et al. 1992). These studies suggest that discrepancies in clinical studies of gender differences in schizophrenia, for example, those involving gender differences in brain abnormalities, may have more to do with sampling biases, since representative samples of schizophrenic patients have demonstrated significant gender differences on a number of measures.

Other sampling biases raised by Walker and Lewine. It is unclear how other sampling issues raised by Walker and Lewine (e.g., differential refusal rates or mortality) would influence gender differences in schizophrenia. For example, Brotman and coworkers (1992) found a higher rate of refusals among females than males, even though, as Walker and Lewine argue, the compliance literature suggests that males would be more likely to refuse participation than females. Further, regarding differential mortality among males and females, a recent study of ours demonstrated that, compared to female normal controls, suicide among young female schizophrenic patients was as high as among young male schizophrenic subjects (Goldstein et al., submitted for publication a).

Thus, it is unclear how these other sampling biases might, in general, influence the gender composition of a particular sample. Rather, one must address whether these issues may be confounding factors on a study-by-study basis.

In conclusion, although Walker,
Lewine, and I agree that discrepancies in studies on gender differences in schizophrenia are most likely due to sampling differences, we disagree over what would explain these differences. I have argued that commitment status will not account for discrepancies in studies on gender differences. Commitment status is an indicator of severity of illness and selection into treatment. As an indicator of severity, it may provide insights into discrepancies across studies. However, as an indicator of selection into treatment, the evidence cited above suggests that it would account for very little variance in gender differences in schizophrenia. A more fruitful approach to understanding discrepancies in studies of gender differences may be to fully characterize the disorder within males and females as well as between the sexes in order to compare samples across studies. In fact, in numerous studies, even the distribution of the sample by sex is unreported.

Perhaps our disagreement in approach stems from our difference in professional fields. I am arguing from an epidemiologic point of view, and asking, what does the distribution of schizophrenia look like, where do males and females fall on that distribution, and who would be included or excluded in certain clinical samples? Walker and Lewine may be framing their hypothesis from a clinical researcher’s point of view. That is, what is the influence of gender on the perceptions of clinicians and family members toward this disorder, and how do these perceptions affect treatment patterns? Neither approach excludes the other. In fact, one of the nice things about Walker and Lewine’s argument is that it is testable. Replication of negative study findings on the relationship between gender, commitment status, and hospitalization (Rosenfield 1982; Angermeyer et al. 1989) is testable. Further, I cannot agree more with Walker and Lewine that investigators must identify the characteristics of their sample within and between the sexes and the population from which they are drawn in order to evaluate the context in which we can understand the study findings. In doing so, we will better understand the growing body of literature on gender differences in schizophrenia and its contribution to understanding the etiology and course of schizophrenia.

References


Goldstein, J.M.; Seidman, L.J.; Turner, W.M.; and Tsuang, M.T. “The Effects of Gender and Neurodevelopmental Deficits on Adult Neuropsychological Dysfunc-


Acknowledgments

This manuscript was partially prepared while Dr. Goldstein was a Fellow in the NIMH Clinical Research Training Program (MH-16259) at Massachusetts Mental Health Center. The author is grateful to Susan Santangelo and Bruce G. Link, Ph.D., for helpful comments on an earlier draft and Deborah L. Catt for manuscript preparation.

The Author

Jill M. Goldstein, Ph.D., is Assistant Professor of Psychiatry, Harvard Medical School, Division of Psychiatric Epidemiology and Genetics, Brockton/West Roxbury Veterans Affairs Medical Center; and Research Fellow, Laboratory of Neuropsychology, Massachusetts Mental Health Center, Brockton, MA.