

Gender and the Course of Schizophrenia: Differences in Treated Outcomes

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Abstract

A survey of the literature suggests that women tend to exhibit a more favorable course of schizophrenia than men. This seems to be true for a range of outcome measures, such as hospital treatment, psychopathology, and social adaptation. Due to methodological limitations, however, the empirical evidence for gender differences in outcome is not wholly consistent. In 1983, a study of first-admitted patients with *DSM-III* diagnoses of schizophrenia or schizophreniform disorder ($n = 278$) from the Greater Hannover area in the Federal Republic of Germany followed patients for an average of 3 years. The present study has followed these patients for an average of 8 years. When confounding factors (e.g., age and marital status) were controlled for, schizophrenic women showed a better course of hospital treatment, experienced a shorter length of hospital stay, and survived longer in the community after their first hospital admission. Only the number of hospitalizations did not differ significantly between the sexes in the present study in contrast to the original study.

During the last decade, there has been a growing recognition of gender differences in schizophrenia. One of the most consistent findings of psychiatric epidemiology is that the onset of the disorder is on average earlier in men than in women and that schizophrenic men are hospitalized earlier than women (Angermeyer and Kühn 1988). In addition, in a number of studies, differences have been shown in symptomatology (Lewine 1981; Goldstein and Link 1988), family history (Bellodi et al. 1986; Gold-

stein et al., in press), biological indices (Seeman 1985; Nasrallah et al. 1986), and treatment response (Seeman 1983; Lewine and Meltzer 1985). This article focuses on gender differences in the course of the illness. In the first part, an extensive overview of the literature on gender and the course of schizophrenia is presented. There is some controversy about whether gender differences in the course are present over a short-term observation period and then dissipate over time. The present study has extended a previous study (Angermeyer et al. 1989) from a 3- to an 8-year observation period. Results focus on one dimension of outcome, the course of hospital treatment.

A search was conducted for all publications up to the present time, regardless of language, on gender differences in schizophrenia. It was possible to locate 102 studies reporting on gender and course of the illness. Only studies using specified outcome measures (i.e., course of hospital treatment, psychopathology, or social adaptation) were included. As in our previous work, a meta-analysis (Smith et al. 1980) was not possible, since the information in these articles was not only heterogeneous but often incomplete. Therefore, a box-score method was used to investigate the number of times significant gender differences were demonstrated, although this does not account for the size of the differences. The method tends to produce Type II errors: thus, the size of gender differences will be underestimated.

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Regardless of the outcome measure examined, the pattern was essentially the same. Approximately one-half of the studies found that the course of schizophrenia was better in women than in men, and the other half demonstrated no significant gender differences. This was true for all three indicators of hospital treatment: rate of rehospitalization (27 studies; see table 1), length of hospital stay (28 studies; see table 2), and number of hospital admissions (10 studies; see table 3). The same was true for relapse rate and psychopathological status at followup (23 studies; see table 4) and for clinical course (19 studies; see table 5). Finally, out of 37 studies dealing with social adaptation, again, one-half showed a better outcome in women, and the other half did not yield significant gender differences. The same was true for studies concerned with global social adaptation (16 studies; see table 6), occupational status (28 studies; see table 7), and social integration (11 studies; see table 8). Only six studies found that the illness had a more favorable course in men than in women. Two of them concerned the rate of rehospitalization (Israel and Johnson 1956; Lehrman 1960), another two dealt with clinical course (Bleuler 1972; Guggenheim and Babigian 1974), and two dealt with occupational status (Hall et al. 1966; Schooler et al. 1967).

The literature thus suggests that if gender differences in the course of schizophrenia really do exist, they may favor female patients. The findings should be interpreted with caution, however, since there are methodological limitations to many of the studies reviewed. For example, in a number of studies the diagnostic criteria were not specified. This is important since it

has been shown that the use of more conservative diagnostic criteria may increase the gender effect (Lewine et al. 1984; Westermeyer and Harrow 1984). In addition, few studies used representative patient samples drawn from defined catchment areas. The fact that most studies included patients with multiple hospitalizations may have attenuated the effect of gender on outcomes, since the samples differentially excluded patients who were hospitalized once and recovered. If schizophrenic women do exhibit a better course of illness than schizophrenic men, the excluded patients will more likely be women (Goldstein 1988). Finally, there were few studies that controlled for confounding factors, such as age, age of onset, or marital status.

In tables 1-8, the studies are arranged according to the length of the observation period: < 5 years, 5-10 years, and \geq 10 years. Inspection of the tables does not reveal a clear relationship between length of observation period and gender differences. However, two studies that had different followup periods suggest that gender differences may be attenuated over time (Biehl et al. 1986; Goldstein 1988).

This study tests whether gender differences in the course of hospital treatment observed in a group of schizophrenic patients followed, on an average, for 3 years, persist over an average of an 8-year observation period. The study attempts to replicate the findings that schizophrenic women experience fewer rehospitalizations, have shorter lengths of stay, and survive longer in the community than schizophrenic men.

Methods

The study was carried out in Hannover, the capital of Lower Saxony,

in the Federal Republic of Germany. Hannover (population 537,000) is the commercial and cultural center of the State of Lower Saxony, which extends from the mountainous highland of central Germany to the North Sea. Study methods have been presented in detail in a previous publication (Angermeyer et al. 1989). In brief, all four psychiatric hospitals serving the Greater Hannover area were included in the study (Psychiatrische Klinik der Medizinischen Hochschule Hannover, Städtische Nervenlinik Langenhagen, Niedersächsisches Landeskrankenhaus Wunstorf, and Wahrensdorfsche Anstalten Ilten). Four fourth-year medical students were trained to collect data systematically from the medical records of all first admission patients with a hospital diagnosis of schizophrenia (World Health Organization 1975) during the period between January 1, 1978, and December 31, 1982. Records for other clinical diagnoses that may have suggested the presence of schizophrenia were also checked (e.g., endogenous or functional psychosis and paranoid psychosis). Data were systematically checked by the first author for quality control. Only patients of German nationality who lived in the catchment area of the hospitals were included in the study to control for the effects of migration and transient residency.

Patients were followed from the day of their first admission until December 31, 1988. The observation period was therefore on an average of 8 years (range 6-11 years). Rehospitalizations and lengths of hospital stays were obtained from hospital records and clinic charts. The risk of underestimating the course of hospitalizations for our sample was negligible, given a study by Siede (1973) who demonstrated

Table 1. Studies on gender differences in risk of rehospitalization

Duration of followup	Risk of rehospitalization significantly lower		No significant gender difference
	Females	Males	
< 5 years	Watt & Szulecka (1979) Pietzcker et al. (1982) Angermeyer et al. (1982) Holding et al. (1983) Westermeyer & Harrow (1984) ¹ Angermeyer et al. (1989)		Orlinsky & D'Elia (1964) Schooler et al. (1967) Mandelbrote & Trick (1970) Westermeyer & Harrow (1984) ² MacMillan et al. (1986) Klusmann & Angermeyer (1986) Lopes (1987)
5–10 years	Achté & Apo (1967) ³ Nystrup (1976) ⁵ Körmendy & Schäfer (1983) Schäfer (1983)	Lehrman (1960)	Rennie (1939) Shepherd (1957) Achté & Apo (1967) ⁴ Nystrup (1976) ⁶ Watt et al. (1983) MacMillan et al. (1986)
≥ 10 years	Rennie (1939)	Israel & Johnson (1956) ⁷	Harris & Lubin (1954) Israel & Johnson (1956) ⁸ Hinterhuber (1973)
Unspecified	Cropley & Gazan (1969) ⁹ Jordá-Moscardo & Munk-Jørgensen (1986) Strömberg (1987)		Cropley & Gazan (1969) ¹⁰ Müller (1971)

¹DSM-II.²DSM-III.³Index admission 1950–52.⁴Index admission 1957–59.⁵Index discharge 1953.⁶Index discharge 1962.⁷Index admission 1913–22.⁸Index admission 1923–32 or 1933–42.⁹Living in foster home.¹⁰Living in family or living alone.

that <10% of psychiatric patients living in Hannover were admitted to hospitals outside of the four in the Hannover area.

The Sample. Six hundred three patients were rediagnosed using DSM-III-R criteria (American Psychiatric Association 1987) by two

research psychiatrists, one of whom was unaware of the study hypotheses. Rediagnoses were made from the medical records of the first hospital admission, which provided excellent information about patients' current state and development of psychopathology. Rediagnoses were reliably made as reflected in an overall κ of 0.93. A detailed

description of the reliability study and the final sample of patients is provided in our previous publication (Angermeyer et al. 1989). Schizophreniform disorder was included with schizophrenia, given that all of the patients were first admissions. A rationale for this is provided in Angermeyer et al. (1989).

Table 2. Studies on gender differences in length of hospital stay

Duration of followup	Length of hospital stay significantly shorter in		No significant gender difference
	Females	Males	
< 5 years	Angermeyer et al. (1982) Lopes (1987) Angermeyer et al. (1989)		Gittelman-Klein & Klein (1969) Watt & Szulecka (1979) Giel et al. (1984) Biehl et al. (1986) Kay & Lindenmayer (1987)
5–10 years	Auch (1962) ¹ Lassenius et al. (1973) ³ Möller et al. (1982) Salokangas (1983) ⁵ Goldstein (1988) Munk-Jørgensen (1986)		Farina et al. (1963) Auch (1962) ² Helgason (1964) Achté (1967) Lassenius et al. (1973) ⁴ Salokangas (1983) ⁶ Nyman & Jonsson (1983) Biehl et al. (1986)
≥ 10 years	Ciampi & Müller (1976) Goldstein (1988)		Harris & Lubin (1954) Hinterhuber (1973)
Unspecified	Raskin & Golob (1966) Cropley & Gazan (1969) ⁷ Stern (1970) Bland (1977) Strömberg (1987)		Harrow et al. (1969) Cropley & Gazan (1969) ⁸ McCabe (1975)

¹Index admission 1958–60.²Index admission 1946–51.³Index admission 1959–60.⁴Index admission 1944–46.⁵Index admission 1969.⁶Index admission 1965–67.⁷Living in foster home.⁸Living in family or living alone.

In brief, the sample consisted almost equally of men ($n = 137$ or 49%) and women ($n = 141$ or 51%). They were young, with over half being under 30 years of age. The majority (57%) had never been married, although almost one-third (29%) were currently married. One-third had completed college or university level, while another third had completed only elementary school. Thirty-five and one-half percent were unemployed or not in

training. Finally, they came equally from urban and rural areas around Hannover. Schizophrenic men were significantly younger at their first admission, more often never married, and more likely to be employed (Angermeyer et al. 1989).

Variables of Interest. The outcomes for this study included number of hospitalizations, duration of hospitalizations, and survivorship in the community after discharge from

the first psychiatric admission. The number of hospitalizations was divided by the duration of observation (in years), thus indicating person-years of followup. Duration of hospitalization was defined as the total number of days spent in inpatient treatment, divided by duration of observation in years. Outcome variables were transformed to their natural logarithm in the multivariate analyses. A rationale for this is provided in Angermeyer et al. (1989).

Table 3. Studies on gender differences in number of hospitalizations

Duration of followup	Number of hospitalizations significantly lower in		No significant gender difference
	Females	Males	
< 5 years	Angermeyer et al. (1982, 1989)		Gittelman-Klein & Klein (1969)
5-10 years	Fallik & Liron (1976) Gam (1980) Goldstein (1988)		Achté (1967) Salokangas (1983)
≥ 10 years	Goldstein (1988)		Affleck et al. (1976)
Unspecified	Cropley & Gazan (1969) ¹		Cropley & Gazan (1969) ²

¹Living in foster home.²Living in family or living alone.**Table 4. Studies on gender differences in psychopathological status at followup or relapse rate**

Duration of followup	Psychopathological status better/ relapse rate lower in		No significant gender difference
	Females	Males	
< 5 years	Brown et al. (1972) Glick et al. (1976) Vaughn & Leff (1976) Müller (1982) Vaughn et al. (1984)		Hogarty et al. (1974) Astrachan et al. (1974) Westermeyer & Harrow (1984) Giel et al. (1984) Kay & Lindenmayer (1987)
5-10 years	Nyman (1978) Salokangas (1983) Nyman & Jonsson (1983) Johnstone et al. (1984) Prudo & Blum (1987)		Achté (1967) Müller et al. (1982)
≥ 10 years	Lo & Lo (1977) Müller et al. (1986)		Huber et al. (1979) Rzewuska & Angst (1982) Ogawa et al. (1987) Steinmeyer et al. (1989)

Covariates used to explain gender differences in treatment outcomes were limited, given that this was a record study. Variables that have been found to be significantly and differentially related to gender among schizophrenic patients were

included, such as age at first hospitalization and premorbid functioning (Gittelman-Klein and Klein 1969; Nyman and Jonsson 1983; Angermeyer and Kühn 1988).

Three variables were used as estimates of premorbid competence,

since the variable itself was not available in the medical records. Education, marital status, and employment status were used as indicators of functional development. Although this was far from ideal, both education and marital status

Table 5. Studies on gender differences in clinical course

Duration of followup	Clinical course more favorable		No significant gender difference
	Females	Males	
< 5 years	World Health Organization (1979)		Biehl et al. (1986)
5–10 years	Guggenheim & Babigian (1974) ¹ Nyman (1978) Watt et al. (1983) Fähndrich & Richter (1986)	Guggenheim & Babigian (1974) ²	Langfeldt (1937) Körmendy & Schäfer (1983) Biehl et al. (1986)
≥ 10 years	Huber et al. (1979) Müller et al. (1986)	Bleuler (1972)	Ciampi & Müller (1976) Khramelashvili & Liberman (1976) Sternberg (1981)
Unspecified	Liberman (1974) Shmaonova & Liberman (1979)		Angst et al. (1973) Buzanova (1981) Shmaonova & Liberman (1979) Iursinova (1982)

¹Only catatonic type, duration of psychotic episodes.²Only catatonic type, frequency of psychotic episodes.**Table 6. Studies on gender differences in global social adaptation**

Duration of followup	Global social adaptation better in		No significant gender difference
	Females	Males	
< 5 years	Holding et al. (1983) Schubart et al. (1986)		Schooler et al. (1967) World Health Organization (1979) Giel et al. (1984) Kay & Lindenmayer (1987)
5–10 years	Soskis et al. (1969) Salokangas (1983) Johnstone et al. (1984) Wattie & Kedward (1985) ¹ Prudo & Blum (1987)		Nyman et al. (1978) Biehl et al. (1986)
≥ 10 years	Bland & Orn (1978)		Bland et al. (1976) Ogawa et al. (1987)

¹Duration of followup 18 months–10 years.

Table 7. Studies on gender differences in occupational status

Duration of followup	Occupational status better in		No significant gender difference
	Females	Males	
< 5 years	Raskin & Dyson (1968) Pietzcker et al. (1982) Westermeyer & Harrow (1984) ¹	Hall et al. (1966) Schooler et al. (1967)	Gittelman-Klein & Klein (1969) Vogel & Vliegen (1975) Mantonakis et al. (1982) Westermeyer & Harrow (1984) ² Giel et al. (1984) Kay & Lindenmayer (1987)
5–10 years	Gam (1980) Körmendy & Schäfer (1983) Salokangas (1983) Nyman & Jonsson (1983) Wattie & Kedward (1985) ³		Lassenius et al. (1973) Nyman (1978) Möller et al. (1982)
≥ 10 years	Affleck et al. (1976) Huber et al. (1979) Steinmeyer et al. (1989)		Masterson (1956) Bleuler (1972) Bland et al. (1976) Ciompi & Müller (1976) Bland & Orn (1978) Müller et al. (1986)

¹DSM-II.²DSM-III.³Followup 18 months–10 years.**Table 8. Studies on gender differences in social integration**

Duration of followup	Social integration better in		No significant gender difference
	Females	Males	
< 5 years	Raskin & Dyson (1968)		Gittelman-Klein & Klein (1969) Westermeyer & Harrow (1984) Giel et al. (1984) Kay & Lindenmayer (1987)
5–10 years	Nyman (1978) Körmendy & Schäfer (1983) Salokangas (1983)		Nyman & Jonsson (1983)
≥ 10 years			Ciompi & Müller (1976)

have been found to be highly correlated with overall premorbid social competence scores (Zigler and Levine 1981).

Analytic Methods. Student's *t* tests were used to examine the relationship between gender and number of hospitalizations and length of hospital stays. Three analytic procedures were then used to examine gender differences in outcomes. Survival analysis was used to test for gender differences in community survival time (Lee 1980; Thompson and Weissman 1981). Survival analysis, using the Kaplan-Meier method, provides estimates that represent the probability that rehospitalization will occur at a particular time over the observation period. This method is advantageous because it controls for confounding due to mortality and makes full use of longitudinal data when there are varying observation periods. A multivariate survival analysis using Cox's regression model was used to explain gender differences in community survival (Cox 1972; Lee 1980). Ordinary least-squares regression was used to explain gender differences in length of hospital stays.

Results

Table 9 shows that the average number of hospitalizations did not differ significantly for men and women, although schizophrenic women were hospitalized less often than schizophrenic men. Schizophrenic women also spent significantly fewer days in the hospital than schizophrenic men over the 8-year observation period.

Figure 1 depicts the results of the survival analysis with gender

predicting survivorship in the community. The difference between the genders was most marked at the beginning of the observation period and was attenuated toward the end of the observation period (Breslow $\chi^2 = 4.21$, $df = 1$, $p = 0.04$) (Breslow 1974). By 1-year postdischarge, 45 percent of the schizophrenic men had been rehospitalized as compared with 26 percent of the schizophrenic women. By the end of the second year after discharge from the first inpatient treatment, the rates of rehospitalization were 52 percent and 37 percent, respectively. However, 3 years later (i.e., 5 years postdischarge), almost as many men as women had been rehospitalized (69% vs. 63%).

The next set of analyses tested whether the effect of gender on length of hospital stay and survivorship in the community could be explained or was mediated by factors found in past research to be related to both gender and length of hospital treatment. Therefore, length of hospital stay was regressed on age at first hospitalization, education, marital status, and employment status. These covariates were also used in the Cox regression model, in which rehospitalization after a first inpatient admission defined the hazard (Cox 1972). The results of the multiple regression showed that the effects of the covariates did not wholly account for the effect of gender on length of hospital stay. Gender still had a significant effect after covariates were partialled out (see table 10).

In addition, to explain gender differences in community survival, the same covariates were used in Cox's regression model. Results showed that there remained an overall trend for men to be at higher risk for rehospitalization, even after these

covariates were controlled ($\chi^2 = 10.52$, $df = 5$, $p = 0.06$).

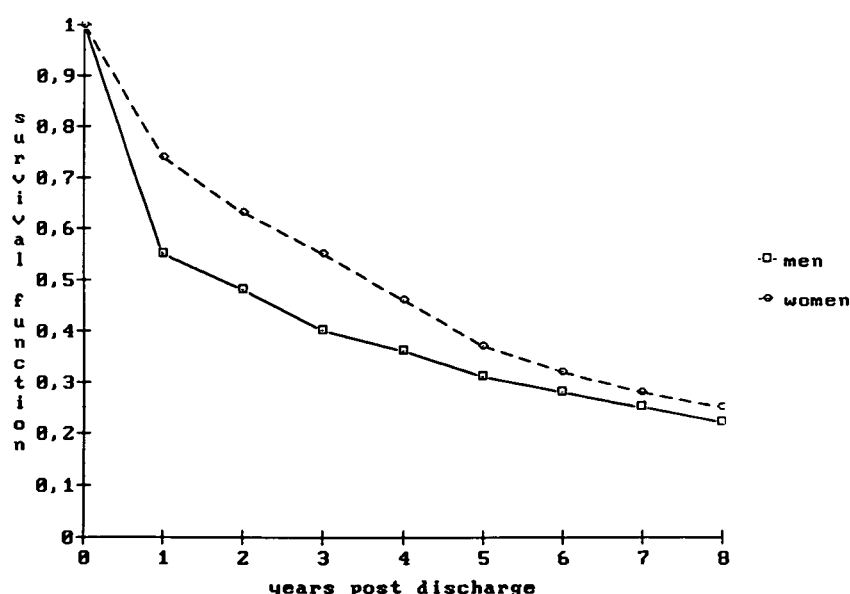
Finally, analyses were conducted controlling for duration of symptoms before the first hospitalization to examine possible differences between patients with schizophrenia versus schizophreniform disorder. One hundred ninety-nine cases out of the 278 (or 72%) had sufficient information to code this variable. Results again showed that when duration of symptoms before the first hospitalization was controlled, schizophrenic men spent significantly more time in the hospital ($b = -0.103$, $\beta = 0.173$, $p = 0.01$) and tended to be at higher risk for rehospitalization ($\chi^2 = 12.35$, $df = 6$, $p = 0.05$).

Discussion

Our findings demonstrate that over an observation period of, on average, 8 years, there remain significant gender differences in the course of treatment. This is an extension of our previous work showing that gender had an impact after a 3-year observation period. Schizophrenic men spent significantly more time in the hospital and were at significantly higher risk for rehospitalization than schizophrenic women. These findings were not wholly explained by social background characteristics such as age, marital status, education, or employment status. In addition, gender differences in outcomes were not an artifact of the inclusion of schizophreniform disorder in the sample, since findings remained when controlling for duration of symptoms before first hospital admission. Schizophrenic men also experienced fewer hospitalizations than schizophrenic women, but the differences were not significant. The

Table 9. Gender differences in number of hospitalizations and length of hospital stay (*t* test, 2-tailed)

	Men (<i>n</i> = 137)		Women (<i>n</i> = 141)		<i>t</i>	<i>p</i>
	Mean	SD	Mean	SD		
Number of hospitalizations (per year)	0.39	0.35	0.34	0.29	1.27	0.204
Length of hospital stay (per year)	34.9	34.4	24.0	16.6	3.35	0.001

Figure 1. Survivorship outside hospital after discharge from first inpatient treatment by gender

failure to find a significant difference is in contrast to our previous study demonstrating significant gender differences in the number of hospitalizations over a 3-year period.

The lack of a significant gender difference for number of hospitalizations is somewhat surprising given that other previous work has

demonstrated such differences over observation periods longer than 8 years (Goldstein 1988). However, the Goldstein study also showed that gender differences were attenuated at 10 years as compared to 1- to 5-year observation periods (Goldstein 1988). That may in part be due to the finding that schizophrenic women respond

better and to lower doses of neuroleptics (Seeman 1983). Reflecting the fact that differences in neuroleptic response are most likely due to the effects of estrogens, these differences are found primarily for women at premenopausal ages (see Seeman and Lang 1990, this issue). Thus, as women age and reach menopause, gender differences in the course of treatment are attenuated or may disappear over time (Seeman and Lang 1990, this issue). Since a number of the women in our study were in their forties and older at 8 years after admission, they may have already experienced menopause.

The study reported here was a record study, and therefore information was not under the control of the authors. As mentioned previously, however, less than 10 percent of patients in the Greater Hannover area are not hospitalized at the study hospitals, and therefore it is unlikely that the attenuation of gender differences in number of hospitalizations was due to loss of information.

Findings in this study also showed that gender differences in treatment were not wholly accounted for by age at first hospitalization or premorbid indicators such as education, marital status, and employment status. Future studies must examine other factors found to be differentially related to gender among schizophrenic patients to illuminate gender differences in the course of treatment. These include a wide variety of factors ranging from genetic history (Bellodi et al. 1986; Goldstein et al., in press), structural and functional brain differences (Nasrallah et al. 1986; Gur and Gur 1990, this issue; Lewine et al. 1990, this issue), and response to neuroleptics (Young and Meltzer

Table 10. Regression coefficients for prediction of total length of hospital stay for gender, controlling for age and indicators of premorbid social competence

	<i>b</i>	β	<i>t</i>	<i>p</i>
Age	0.002	0.084	1.16	0.25
Marital status ¹	-0.046	-0.076	-0.97	0.33
Education ²	-0.006	-0.008	-0.13	0.89
Occupational status ³	0.058	0.087	1.42	0.16
Gender ⁴	-0.107	-0.179	-2.63	<0.01

Note.— $R^2 = 0.04$; R^2 adjusted for number of variables and sample size = 0.025; $F = 2.39$; $df = 5, 272$; $p = 0.038$.

¹Never married = 0; ever married = 1.

²9 years of school or less = 0; over 9 years of school = 1.

³Employed (paid work) = 0; unemployed = 1.

⁴Men = 0; women = 1.

1980; Nedopil et al. 1983; Seeman 1983), to illness and family behavior and the social consequences of illness (Niskanen and Pikhanen 1972; Kessler et al. 1979; Clausen et al. 1982; Prüss et al. 1984; Gibbons et al. 1984; Hogarty 1985; Goldstein and Kreisman 1988; Haas et al. 1988; Linden et al. 1988).

Further, an understanding of gender differences in treatment may in part be related to gender differences in other dimensions of outcome. Our review of the literature suggests that schizophrenic women tend to show a better course of illness than schizophrenic men, regardless of the outcome. Thus, gender differences in constitution, early premorbid history, and adult social role expectations may provide advantages for women that generalize across domains of outcome. An understanding of these differences and their relationship to the course of illness and treatment may provide clues to the nature of schizophrenia and thus are important to consider in future research endeavors.

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Videotape on Schizophrenia Available

The Video Center of the George Warren Brown School of Social Work, Washington University, in collaboration with the St. Louis Chapter of the Alliance for the Mentally Ill and the Department of Mental Health of the State of Missouri, has produced a videotape entitled **Living with Schizophrenia: A Video Manual for Families Caring for Mentally Ill Relatives**.

The videotape was designed to provide an inexpensive channel for furnishing a basic level of psychoeducation to families who may otherwise not receive any information.

Specifically targeted for the family that lives with a mentally ill relative, the videotape uses the experiences of actual families to present practical information about coping with problems common to families living with a mentally ill person.

For more information about the rental or purchase of this videotape, please contact:

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