

A Non-Neuroleptic Treatment for Schizophrenia: Analysis of the Two-Year Postdischarge Risk of Relapse*

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Abstract

The efficacy of antipsychotic drug maintenance in reducing the risk of relapse among previously hospitalized schizophrenic patients has been well documented. However, data from an ongoing study comparing two cohorts of young first admission schizophrenics—one receiving neuroleptic-oriented treatment on the wards of a community mental health center (CMHC), the other an intensive interpersonal approach in a small homelike facility in the community (Soteria House)—raise questions about the routine use of neuroleptics with this population. Our questioning of this practice is based on data analyzed from these two cohorts by means of the life table, a statistical technique appropriate for longitudinal studies. Data are presented in two ways: (1) The overall effectiveness of the two independent treatment programs (Soteria, $N = 32$, vs. CMHC, $N = 36$) is compared in terms of the probabilities of not being readmitted over the 2-year postdischarge interval. (2) Analyses that look at the influence of the original treatment setting and postdischarge antipsychotic drug status on readmission rates are presented. Program comparisons reveal Soteria patients to have a consistently higher survival rate than CMHC patients throughout 2 years postdischarge. At 12 months postdischarge, the cumulative probability of remaining well (no readmissions) significantly favors the Soteria patients ($p < .05$,

Mantel^{x2}). The overall results of the Soteria program were achieved despite the fact that all CMHC patients received neuroleptics during their original inpatient stays and about 50 percent were maintained on neuroleptics up to the point of readmission or study termination, whereas only 10 percent of Soteria subjects were treated with or maintained on neuroleptics. The survival rates by postdischarge drug status and program affiliation show the Soteria no-drug group to have the highest proportion of survivors at almost every interval throughout 24 months, the CMHC drug-maintained group to have the lowest survival rate, and the CMHC unmaintained group to be surviving at a rate generally comparable to the Soteria no-drug group.

Studies examining the efficacy of antipsychotic drug maintenance in reducing the risk of relapse among previously hospitalized psychiatric patients have flourished during the past decade. The general findings are that neuroleptics provide the potential for truly preventive psychiatry. In a review of 24 controlled studies comparing relapse rates for schizophrenics on placebo and maintenance neuroleptics, Davis (1975) consistently found placebo patients to relapse more often than drug-treated patients. Hogarty and Ulrich (1977) found that although the risk of relapse declines with the passage of time, it is almost twice as high for placebo-treated patients (80 percent) as for drug-maintained patients (48 percent) after 2 years of treatment. Overall, relapse rates for schizophrenia, regardless of drug status, are 30-40 percent at 6 months, 35-50 percent at 1 year, and 65-75 percent at 3-5 years (Anthony, Cohen, and Vitalo 1978). Anthony, Cohen,

*The opinions expressed in this article are those of the authors and do not necessarily represent any official position of the National Institute of Mental Health.

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and Vitalo (1978, p. 367) point out in their recent review of followup studies, "Despite the variety in populations, institutions, and geographical regions, the recidivism data continue to show remarkable consistency." Thus, although undeniably helpful, neuroleptics have not proved curative. Fewer schizophrenic patients are now chronically institutionalized, but multiple readmissions—about 50 percent in the 2 years postdischarge—are a serious public health problem. Furthermore, it has been estimated that only 15 to 20 percent of schizophrenics living in the community achieve an average level of adjustment (i.e., being self-supporting or successfully functioning as a housewife) (Mosher and Winsilver 1971).

Despite the demonstrated ameliorative effects of neuroleptic drugs, there are compelling reasons to search for alternative forms of treatment. It is clear that the use of neuroleptic drugs entails increased risk, sometimes irreversible toxicities (Crane 1973), and the Food and Drug Administration has recently requested drug manufacturers to include a statement in the package insert noting that neuroleptics may possibly encourage the growth of breast tumors in women. There are suggestions in the literature that recovery in at least some schizophrenics may be impaired by treatment with neuroleptics (Crane 1973; Stein 1970; Rappaport et al. 1970). In addition, recent studies have shown relapse rates for depot oral fluphenazine to be nearly 50 percent in the first year postdischarge, indicating that drug non-compliance does not adequately explain early relapse (Hogarty et al., in press; Hooley et al. 1979). These findings would seem to run counter to the overwhelming evidence in the

literature that drug compliance is a crucial factor in reducing relapse.

In the present report, we will focus on the 2-year postdischarge risk of relapse in two relatively small groups of newly diagnosed, young, first admission schizophrenics: one initially treated with neuroleptics on the wards of a community mental health center (comparison group); the other without neuroleptic drugs in a small, homelike facility in the community, Soteria House (experimental group). Half of the comparison group patients were maintained on neuroleptics postdischarge (a clinical decision), whereas less than 10 percent of patients in the experimental group received maintenance drug therapy. Our study is not a controlled clinical drug trial, but rather a presentation of data for two groups representing contrasting treatment approaches to schizophrenia. We will attempt to identify predictors of relapse for our sample both by program affiliation and the combined influence of treatment program and postdischarge drug status.

Program Descriptions

Soteria. Soteria House is a 1915-vintage, 12-room residence located on a busy street in a "transitional" neighborhood of a San Francisco Bay Area city. Due primarily to licensing laws, the house can accommodate only six patients at a time. One or two patients are admitted each month. The staff consists of six paid nonprofessional therapists, a project director, and a quarter-time project psychiatrist. In general, two regular staff members, a man and a woman, are on duty at any given time. The guiding philosophy at Soteria is that the schizophrenic reaction is an altered state of consciousness in an individual who is experiencing a crisis in

living. The disruptive psychotic experience is believed to have potential for reintegration and reconstitution, resulting in a more stable sense of self if the process is not prematurely aborted by neuroleptic drug use. By design, no neuroleptics are given during the subjects' first 6 weeks in the program. If there is no change in psychopathology by that time, drugs may then be prescribed. However, in the experimental samples reported here, only 3 percent received neuroleptics during their initial episodes of treatment. We have more completely described the research design (Mosher 1972), staff (Mosher, Reifman, and Menn 1973), milieu characteristics (Wendt et al., in press), and 1-year (Mosher, Menn, and Matthews 1975) and 2-year (Mosher and Menn 1978) followup results elsewhere.

Community Mental Health Center. The inpatient service of the community mental health center (CMHC) consists of one open and one locked ward of 30 beds each. About 250 patients are admitted each month. It is a well-staffed (1.5:1 staff-patient ratio) active treatment facility, which is oriented toward crisis intervention. High doses of neuroleptics are used, and rapid placement of patients in other parts of this relatively well-endowed county's treatment network is an immediate goal. Clinical decisions about neuroleptic drug use both during inpatient care and postdischarge are made by the individual psychiatrists responsible for the patient's care. The Soteria research team has no role in these decisions.

Research Methods

Sample Selection. All subjects are obtained from a screening facility, which is part of the CMHC complex containing our control wards. Ap-

proximately 600 new patients are seen there per month, of whom about 250 are hospitalized. Anyone meeting the following basic criteria is a potential study candidate:

- Clearly schizophrenic
- Deemed in need of hospitalization
- No more than one previous hospitalization for 2 weeks or less with a diagnosis of schizophrenia
- Age 16-30 (either sex)
- Unmarried, separated, widowed or divorced.

The selection criteria are designed to provide us with a relatively homogeneous sample of individuals diagnosed schizophrenic, but a group at risk for prolonged hospitalization or chronic disability. Early onset and being unmarried both predispose to chronic care (Strauss et al. 1977).

Treatment Assignment. Subjects meeting study selection criteria are identified without knowledge of the group to which they will ultimately be assigned. Study requirements are explained, and informed consent is obtained from the patient and his family, or significant other, if available. As only six residents can be accommodated in the experimental setting, intake is limited by bed availability. Therefore, consenting subjects are admitted to the experimental program if a bed is available. If no experimental bed is available, eligible consenting subjects are admitted to the comparison treatment group. Basically, this procedure results in treatment group assignment on a consecutively admitted, space-available basis. It should be emphasized that our samples are remarkably similar on demographic and baseline psychiatric symptomatology variables.

Research Assessment. The measures below are a partial list of those com-

pleted at baseline (admission to the study) and at followup (6, 12, 18, and 24 months postadmission). All assessments are conducted by an independent research team that has no direct treatment responsibilities in either setting.

1. Baseline.

- **Diagnosis**—As per *DSM-II* (American Psychiatric Association 1968). For a subject to be included in the study, three independent diagnoses of schizophrenia must be in agreement.
- **Diagnostic symptoms**—A checklist of seven symptoms. Four of seven symptoms are required for inclusion in the study (Cole, Klerman, and Goldberg 1964).
- **Certainty of diagnosis**—A 7-point scale (Mosher, Pollin, and Stabena 1971).
- **Mode of onset**—Assesses acute/insidious onset types (Vaillant 1964).
- **Paranoid/nonparanoid status**—A short scale for rating paranoid schizophrenia (Venables and O'Connor 1959).
- **Inpatient Multidimensional Psychiatric Scale**—A widely used symptom rating scale producing scores on 10 psychotic syndromes (Lorr, Klett, and McNair 1963).
- **Global severity**—An overall measure of psychopathology.
- **Brief social history form**—A detailed description of a patient's and family's psychiatric and social history (Boothe, Schooler, and Goldberg 1972).

2. Followup.

- **Patient progress report**—For each 6-monthly interval, information on the subject's medication history, use of other treatment, living arrangements (including any hospital

readmissions), work status, social contacts, global severity, and improvement is obtained.

Methods of Analysis

Life Table Method. Widely used to study survivorship in various medical conditions, the life table method was first used in the psychiatric literature in studies of affective disorders by Fleiss et al. (1976) and Klerman et al. (1974). It has since been applied to schizophrenia outpatient data by Hogarty and Ulrich (1977) and Hogarty et al. (in press). The life table provides a useful means of displaying longitudinal data for psychiatric patients. The subsequent application of various mathematical models allows the clinical questions related to change in the risk of relapse over *N* months, and the continuing advantages of program affiliation, to be approached directly. The life table bases its estimates of risk on data from the total number of subjects in a study, including subjects administratively withdrawn and clinically relapsed, and provides data on the number of subjects at risk for a given interval of study, the proportion relapsed within an interval of time, and the cumulative proportion surviving throughout the study. Not only can the probability of surviving on a given treatment at a given interval of time be calculated, but the probability of ultimately surviving through subsequent periods of time can be determined as well. The pattern of relapse suggested by the life table contains the data that permits the "risk of relapse" to be disentangled from similar, but potentially confounding, criteria such as "cumulative percent relapsed" or "months in the community." These issues are discussed in detail by Hogarty and Ulrich (1977). A complete description of the analytic

methods we used is available in Fleiss et al. (1976).

The life table method was used in this study to compare the probabilities of not being readmitted to residential care first between the two programs, Soteria and the CMHC, and then among three treatment subgroups from these programs, defined by *postdischarge* usage of major tranquilizers: subjects never-treated with neuroleptics (Soteria only); those withdrawn from neuroleptics (CMHC only); and subjects continuously maintained on neuroleptics (CMHC only). A patient's discharge from his original stay in the experimental/control facility is defined as the common starting point in the life table analyses. Although discharge varies considerably between the two programs in terms of length of time from patient's initial admission to the study, it is the most appropriate starting point as we are simply concerned with assessing the efficacy of two treatment programs, each incorporating its own treatment modality, including short or long lengths of stays, rapid tranquilization with neuroleptics or minimal drug use, and high patient/staff ratio. All patients were followed up from discharge until the occurrence of a failure (defined as a readmission), termination well (no readmissions through 24 months postdischarge), or dropping out (lost to followup) at which point the elapsed time was calculated.

For the overall program comparison, all cases were included in which at least one followup evaluation was available after discharge, regardless of drug status, yielding a total of 32 experimental and 36 control cases. For the program by drug status comparison, six of the 32 experimental subjects were excluded because of postdischarge neuroleptic use, leaving 26 cases available for the

"never drug treated" group. The CMHC group of 36 split into 18 cases each for the "withdrawn" and "continuous" drug groups.

Statistical comparisons of the various groups in the life table analyses were made at all points in time simultaneously by means of a chi-square procedure developed by Mantel (1966). We will specifically focus our comparisons of cumulative probabilities of remaining continuously well at 6, 12, 18, and 24 months.

Characteristics Associated With Relapse. A traditional approach to predicting number of months to relapse, defined here as actual readmission to residential care, is to select the best possible subset of variables from a large pool of baseline psychopathological variables as well as social history and demographic variables, and relate this subset to time to relapse in a linear regression model. The problem that arises with this approach is that the dependent variable, number of months to relapse in this case, in linear regression should be normally distributed in order to obtain accurate results from the regression technique.

Because our data were bimodally distributed (i.e., into early relapsers and survivors), a different method, as suggested by Schooler et al. (1978), and described below, was used to investigate possible relationships between time to relapse and the group of baseline variables specified before. Our data were divided into three groupings of relapsers, omitting all administrative dropouts ($N = 4$): (1) those who relapsed within the first 3 months after discharge ($N = 20$); (2) those who relapsed between 4 months and 16 months after discharge ($N = 16$); and (3) those who survived in the community for 17 months or more ($N = 28$). Sixteen months was chosen be-

cause there was a 7-month gap after 16 months before another patient relapsed, and the number of cases lost due to administrative reasons was minimized.

For continuous baseline variables, we ran analyses of variance (ANOVAs), in the form of a 3×2 factorial model, i.e., three groupings of relapsers by two treatment groups, with the baseline variables as the dependent variable. We defined the treatment groups to be (1) the Soteria cases ($N = 32$) regardless of drug usage postdischarge and CMHC cases ($N = 36$) and (2) the Soteria cases minus the patients who used drugs postdischarge ($N = 26$) and CMHC cases ($N = 36$). The first definition we will refer to as the program comparison and the second as the program by drug status comparison. The CMHC group in the program by drug status comparison could not be further broken down into the "withdrawn" and "continuous" groups as we did in the life table analyses because of the small number of cases in each cell. These analyses allow us to determine if there are differences among the three groupings by relapse in general, or differentially by treatment group, for each of the continuous variables in our pool of baseline variables.

For the categorical baseline variables, contingency tables were computed and significant relationships determined by chi-square or exact probabilities. For example, using the variable sex, a 3×2 table (relapse groupings by treatment groups) was computed for males, and then another for females.

Results

Data will be reported in two ways: (1) by program comparisons without regard to what specific postdischarge treatment modality individual clients

received (drugs or not); (2) by program by drug status, which includes only Soteria subjects who received no drugs postdischarge and CMHC subjects who were either withdrawn (i.e., not on drugs continuously postdischarge) or maintained continuously on drugs postdischarge.

Baseline Program Comparisons. As shown in table 1, subjects in the two programs are remarkably similar on most demographic and admission psychiatric variables. However, the CMHC sample is significantly older by about 2 years ($p \leq .05$) than the Soteria sample; and the CMHC sample stayed a significantly shorter duration of time in the hospital ($p \leq .0001$) during their original stay (a difference expected because of the treatment orientation in each facility).

Baseline Program by Drug Status Comparisons. The Soteria nondrug, CMHC "withdrawn," and CMHC "continuous" drug groups are quite comparable on all demographic and admission psychiatric variables as shown in table 2. The expected Soteria/CMHC length of stay difference is found, but, in addition, the CMHC withdrawn subjects stayed significantly longer on the CMHC wards than did continuous drug subjects.

Life Table: Program Comparisons. As shown in figure 1, consistently more Soteria-treated patients survived over 24 months postdischarge. Although fluctuating somewhat, Soteria patients had about a 20 percent better chance than CMHC patients of having never been rehospitalized at each point in time. At 12 months postdischarge, the cumulative probability of having not been rehospitalized significantly favors ($p \leq .05$)

Table 1. Comparison of demographic and baseline psychiatric variables: Program comparisons

	Soteria (N = 32)	CMHC (N = 36)
Demographic data		
Age: Mean \pm SD	20.9 \pm 3.3	22.9 \pm 4.3 ¹
Sex: Male	16 (50%)	21 (58%)
Female	16 (50%)	15 (42%)
Marital status:		
Never married	26 (81%)	28 (83%)
Widowed, divorced, separated	6 (19%)	6 (17%)
Education:		
Postgraduate	—	2 (6%)
Completed college	1 (3%)	2 (6%)
Some college	17 (53%)	17 (53%)
Completed high school	5 (16%)	6 (19%)
Some high school	9 (28%)	5 (16%)
Father's social class:		
Mean \pm SD	3.0 \pm 1.1	3.0 \pm 1.1
Number of days in original stay:		
Mean \pm SD	159.4 \pm 139	24.4 \pm 30.0 ²
Median	120	15
Admission psychiatric data		
Diagnosis	All schizophrenic All schizophrenic	
Number of symptoms:		
Mean \pm SD	5.4 \pm 1.0	5.3 \pm .8
Acute/insidious score:		
Mean \pm SD	2.4 \pm 1.2	2.7 \pm .9
Acute	15 (50%)	17 (59%)
Insidious	15 (50%)	17 (59%)
Paranoid score:		
Mean \pm SD	12.7 \pm 5.1	12.1 \pm 5.5
Paranoid	15 (47%)	10 (36%)
Nonparanoid	17 (53%)	18 (64%)
Global severity:		
Mean \pm SD	5.3 \pm 1.2	5.3 \pm .8
Global improvement (prediction of outcome):		
Mean \pm SD	2.6 \pm .9	2.9 \pm 1.0

¹ $p < .04$.

² $p < .00001$.

Table 2. Comparison of demographic and baseline psychiatric variables: Program by drug status comparisons

	Soteria nondrug (N = 26)	CMHC unmaintained (N = 18)	CMHC continuous (N = 18)
Demographic data			
Age: Mean ± SD	21.3 ± 3.4	22.6 ± 3.6	23.1 ± 5.0
Sex: Male	13 (50%)	8 (44%)	13 (72%)
Female	13 (50%)	10 (56%)	5 (28%)
Marital status:			
Never married	21 (81%)	15 (83%)	15 (83%)
Widowed, divorced, separated	5 (19%)	3 (17%)	3 (17%)
Education:			
Postgraduate	—	2 (12%)	—
Completed college	1 (4%)	1 (6%)	1 (6%)
Some college	16 (62%)	9 (53%)	8 (53%)
Completed high school	4 (15%)	4 (24%)	2 (13%)
Some high school	5 (19%)	1 (6%)	4 (27%)
Father's social class:			
Mean ± SD	3.0 ± 1.1	2.7 ± 1.1	3.4 ± 1.1
Number of days in original stay:			
Mean ± SD	142.8 ± 100 ¹	33.2 ± 40 ²	15.7 ± 10 ³
Median	115	18	10
Admission psychiatric data			
Diagnosis	Schizophrenic	Schizophrenic	Schizophrenic
Number of symptoms:			
Mean ± SD	5.3 ± 1.1	5.5 ± .8	5.1 ± .8
Acute/insidious score:			
Mean ± SD	2.3 ± 1.2	2.7 ± 1.1	2.6 ± .6
Acute	11 (46%)	10 (67%)	7 (50%)
Insidious	13 (54%)	5 (33%)	7 (50%)
Paranoid score:			
Mean ± SD	12.7 ± 5.4	12.6 ± 4.9	11.7 ± 6.1
Paranoid	13 (50%)	5 (36%)	5 (36%)
Nonparanoid	13 (50%)	9 (64%)	9 (64%)
Global severity:			
Mean ± SD	5.3 ± 1.2	5.3 ± .5	5.4 ± 1.1
Global improvement: (prediction of outcome)			
Mean ± SD	2.6 ± 1.0	3.0 ± 1.2	2.8 ± .8

¹ Significant intergroup difference between Soteria nondrug and CMHC continuous group ($p < .0001$).

² Significant intergroup difference between Soteria nondrug and CMHC unmaintained group ($p < .001$).

³ Significant intergroup difference between CMHC unmaintained and CMHC continuous groups ($p < .0001$).

